Abstracts and Case Studies From the College of American Pathologists 2019 Annual Meeting (CAP19)

Abstract and case study poster sessions will be conducted during the 2019 College of American Pathologists Annual Meeting (CAP19), which is scheduled for September 21 to 25, 2019. The meeting will take place at the Gaylord Palms Resort & Convention Center, Kissimmee, Florida. The poster sessions will occur in the CAP19 Exhibit Hall. Specific dates and times for each poster session are listed below; “poster focus” times are dedicated poster-viewing periods. Also shown before each poster session are the subject areas that will be presented.

POSTER SESSION 100: SUNDAY, SEPTEMBER 22, 2019
Noon–3:30 PM; Poster Focus, Noon–1 PM
Gastrointestinal and Liver Pathology; Cytopathology; Pathology Education; Administrative and Regulatory Affairs

Comparison of New and Traditional Gastrointestinal Markers for Differentiating Upper Versus Lower Site of Origin
(Poster No. 1)

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Context: Traditional markers for differentiating upper from lower gastrointestinal (GI) tumors (CK7, CK20, and CDX2) frequently show overlapping phenotypes. Recent studies have shown consistent expression of special AT-rich sequence-binding protein 2 (SATB2) and death decoy receptor 3 (DcR3) in colorectal neoplasms (CRCs).

Design: Immunostains for SATB2, DCR3, CDX2, CK7, and CK20 were applied to 40 CRCs, including appendiceal, right- and left-sided tumors; 40 gastric adenocarcinomas (GACs); and 40 esophageal adenocarcinomas (EACs). Intensity of expression was graded as 0 = negative, 1 = weak, 2 = moderate, and 3 = strong, relative to control cells in each preparation. Area of expression was graded as 0 = negative, 1 = 1%–5%, 2 = 6%–50%, 3 = >50%. Immunostains were analyzed as dichotomous (+/-) variables with the χ2 or Fisher exact tests and as continuous variables by calculating a staining score (SS = area score + intensity score) with the Student t test to detect differences in expression.

Results: Most significant differences in expression were found for SATB2 and CK7 (p < .001). By contrast, CK20 (CRC, 100%; GAC, 82.5%; EAC, 69.2%), DCR3 (CRC, 90%; GAC, 50%; EAC, 65.4%), and CDX2 (CRC, 98%; GAC, 75%; EAC, 92%) were frequently expressed by upper and lower GI tumors. Marker combinations with the highest discriminative power were (1) CK7/CX20: CRC, 80%; GAC, 22.5%; EAC, 0%; (2) CK7/SATB2: CRC, 68%; GAC, 8%; EAC, 0%; and (3) CK7/SATB2: CRC, 3%; GAC, 60%; EAC, 58%.

Conclusions: SATB2 and CK7 provide high discriminative power for differentiating upper from lower GI tumors; CK7/SATB2 is characteristic of CRC; and CK7/SATB2 is characteristic of GAC and EAC. CK20, DCR3, and CDX2 are frequently expressed in upper and lower GI neoplasms.

Clinical and Pathologic Findings in 2 Young Siblings With Lysosomal Acid Lipase Deficiency
(Poster No. 2)

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Lysosomal acid lipase deficiency (LAL-D) is a rare autosomal recessive lysosomal storage disease caused by mutations in the LIPA gene, which produces cholesteryl ester and triglyceride accumulation predominantly in hepatocytes, adrenal glands, and gastrointestinal tract. The first pediatric patient with LAL-D in Colombia was recently reported in the literature. We describe 2 additional cases of this rare pathology occurring in 2 siblings, aged 5 and 7 years, who presented with hepatomegaly, dyslipidemia, and abnormal liver function. A liver biopsy was done in both siblings, and this revealed portal infiltration by foamy macrophages and a prominent microvesicular steatosis in hepatocytes (Figure 1, A), but only the older sibling had evidence of advanced liver fibrosis. Immunostaining for lysosomal markers, including cathepsin D and LAMP-1 (Figure 1, B), reflected the lysosomal nature of the lipid vacuoles. After enzymatic confirmation, both siblings started enzyme replacement therapy with sebelipase α. Follow-up transaminase levels and lipid profile showed a notorious decrease in AST and ALT, and a slight increase in HDL cholesterol. Genetic sequence analysis of the LIPA gene was performed, and this showed the c.[894G>A];[386A>G] mutation. It is important to increase awareness of this rare disease among pathologists. The expression of

An Immunohistochemical and Cytogenetic Analysis of Mesothelial Proliferative Lesions of Unknown Malignant Potential

(Poster No. 3)

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Context: Benign multicystic peritoneal mesothelioma (BMPM) and well-differentiated papillary mesothelioma (WDPM) of the abdominal cavity are uncommon entities, with few cases found in the literature. It is imperative to provide additional information regarding the nature of these lesions to better guide management in these patients.

Design: All surgical pathology files were examined, and all diagnoses of BMPM and WDPM at our institution were selected from 1995 to 2017. The clinical and pathologic data were reviewed in detail. Immunohistochemical stains and cytogenetic studies were then performed in all cases.

Results: Five cases of BMPM and 1 case of WDPM were identified. The average age was 47 years. Five patients (83%) were female and 1 patient (17%) was male. The WDPM case was positive for deletion of p16 (CDKN2A) by FISH, and all cases of BMPM were negative. p53 stain was strongly positive in one BMPM case (Figure 2) and moderately positive in 2 cases. MB-1 stain showed focal positivity on 3 BMPM cases. One case showed ER and PR staining. No cases showed BAP1 loss.

Conclusions: Three cases of BMPM showed at least moderate expression of p53 and the case of WDPM was positive for deletion of p16 by FISH, suggesting that some of these lesions may harbor true malignant potential. Additionally, the patient with WDPM was found to have MEN1 syndrome. The possibility of shared genetic pathways for these lesions should be considered. Testing these lesions for molecular aberrations and exploring the possibility of shared genetic pathways for these lesions to better guide management in these patients.

Intrahepatic Cholangiocarcinoma Collision With Primary Hepatic MALT Lymphoma: A Case Report and Literature Review

(Poster No. 5)

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A collision tumor is an extremely rare phenomenon that consists of 2 histologically distinct neoplasms occurring within the same organ with no significant overlap. Each tumor displays a different histogenesis and tumorigenesis pathway. The occurrence of synchronous adenocarcinoma and lymphoma has been reported within a lymph node and a variety of extranodal sites, such as the gastrointestinal tract, lung, and bone marrow; however, the hepatobiliary system is seldom involved. Primary hepatic lymphoma is in itself a rare entity, with most cases displaying diffuse large B-cell lymphoma. Primary hepatic mucosa-associated lymphoid tissue (MAL) lymphoma is an even rarer event, and its collision with intrahepatic cholangiocarcinoma makes a novel finding, which, to our knowledge, has not been described in the literature. We present a case of a 78-year-old woman who underwent a partial hepatectomy for a biopsy-proven intrahepatic cholangiocarcinoma (Figure 4, A). Detailed microscopic examination identified atypical monotonous lymphoid cells intermingled with the glands and...
Expression of Prostate-Specific Membrane Antigen in Peritumoral Vessels Differentiates Primary Cholangiocarcinoma From Metastatic Pancreatic Adenocarcinoma

(Poster No. 6)

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Context: Distinguishing primary cholangiocarcinoma (CC) from metastatic pancreatic ductal adenocarcinoma (PDAC) is challenging as there are no reliable markers available. Recent studies show that prostate-specific membrane antigen (PSMA) is expressed in the endothelium of neovascularization of solid malignancies and can be detected by PSMA-targeted imaging technology. Here we studied PSMA expression pattern in primary CC and metastatic adenocarcinomas.

Design: Forty-nine cases of liver mass resections were collected. Immunohistochemical stains for PSMA and CD34 were performed. The expressions of PSMA in tumor cells and neovascular endothelium were analyzed separately. The presence of vascular structures was highlighted by CD34 expression.

Results: Twenty-two cases (22 of 49; 44.9%) showed PSMA expression on the peritumoral vascular structures, 5 cases (10.2%) showed expression on tumor cells, and the rest lacked expression of either. All of the 7 cases of primary CC showed PSMA vascular expression (Figure 5, A and B) compared with none of the 8 cases of metastatic PDAC ($P < .01$) (Figure 5, C and D). In addition to the PDACs, none of the other metastatic adenocarcinomas were positive for PSMA. Metastatic prostate carcinoma showed PSMA expression in tumor cells (5 of 8; 62.5%), 2 of which also showed peritumoral vascular positivity. Fifty-nine percent (13 of 22) of hepatocellular carcinomas showed expression on tumor cells, and the rest lacked expression of PSMA. Peritumoral PSMA expression was found in 5 of 7 cases of primary CC (71.4%).

Conclusions: Primary CCs have universal peritumoral neovascular PSMA expression, whereas most metastatic adenocarcinomas, including PDAC, do not have a similar PSMA expression pattern. Our findings suggest that evaluating PSMA expression in the peritumoral vessels may help distinguish primary CC from metastatic adenocarcinomas, especially in morphologically challenging PDACs.

A Rare Case Report of Spontaneous Rupture of Hepatic Angiomyolipoma With Literature Review

(Poster No. 8)

Kotaro Takeda, MD (takedak18@ecu.edu); Ding Dai, MD; Wen Zhong, MD; Swati Prashant Satturwar, MD; Ann Sutton, MD. Department of Pathology and Laboratory Medicine, East Carolina University and Vidant Medical Center, Greenville, North Carolina.

Angiomyolipoma (AML) is a rare benign mesenchymal tumor composed of vessels, smooth muscle, and adipose tissue. AML frequently occurs in the kidney, but it can occur in other organs such as the liver. AML is usually asymptomatic and incidentally identified because of its indolent growth. We report a case of spontaneous rupture...
A 52-year-old man was admitted because of sudden onset of severe abdominal pain, hypotension, and anemia. Abdominal CT revealed a 9-cm hemorrhagic heterogeneous mass in the left lobe of the liver and a significant amount of acute hemoperitoneum. Emergency embolization for the hepatic artery feeding the mass was performed. Forty-seven days later a left hepatectomy was performed. The left lobe contained a 7.5-cm ruptured cystic mass with marked necrosis and hemorrhage. Microscopically, the tumor consisted of sheets of atypical pleomorphic epithelioid and short spindle cells with pale eosinophilic and vacuolated cytoplasm, focal mature adipose tissue, and numerous thickened wall blood vessels (Figure 6, A and B). Tumor cells were positive for human melanin black (HMB) 45, smooth muscle actin, Melan-A, and caldesmon, and negative for HepPar-1 and cytokeratin 7 (Figure 6, C and D). Pathologic diagnosis was hepatic AML. Hepatic AML could cause, albeit rarely, spontaneous rupture, as in this case. Literature review shows that ruptured hepatic AML is large (average diameter 8 cm) without sex or age preference, and accurate diagnosis before surgery is challenging. This case provides important information for differential diagnosis of ruptured hepatic mass.

A Unique Case Report of Rectal Prolapse as an Initial Manifestation of Malignant Peritoneal Epithelioid Mesothelioma

(Ding Dai, MD, PhD (daid14@ecu.edu); Kotaro Takeda, MD; Ann Sutton, MD. Department of Pathology and Laboratory Medicine, East Carolina University, Greenville, North Carolina.

Malignant peritoneal mesothelioma is a rare aggressive tumor with typical growth pattern of a locally expansive mass. The most frequently reported initial symptoms are abdominal pain, abdominal swelling, anorexia, marked weight loss, ascites, and paraneoplastic syndromes (ie, hypoglycemia, venous thrombosis, and thrombocytosis). Rectal prolapse as an initial clinical manifestation of peritoneal epithelioid mesothelioma has never been reported. We report an unusual case of a 90-year-old woman with severe rectal prolapse for 1 month who underwent full-thickness rectal repair. During the surgery, upon approaching the peritoneal reflection, it was noted to be bulging with ascites and had significant nodularity on the external surface. The peritoneum was opened and ascites fluid was evacuated. Perirectal peritoneum was embedded with carcinomatosis implants. The histology of the mass revealed infiltrative nests and sheets of uniform and sharply defined epithelioid mesothelial cells with prominent nuclei, which is consistent with malignant peritoneal epithelioid mesothelioma. The tumor cells were positive for calretinin, cytokeratin 5/6 (CK5/6), and Wilms tumor 1 (WT1) but negative for B72.3, MOC31, p53, carcinoembryonic antigen (CEA), estrogen receptor (ER), and CD15. The diagnosis was further confirmed by electron microscopy that showed focal areas with numerous elongated microvilli and enlarged desmosomes. Given the rarity of malignant peritoneal mesothelioma, this case may provide added information for clinicians regarding their natural history and optimal management (Figure 7, A through D).

A Rare Case of Severe Chronic Bowel Obstruction Associated With Brown Bowel Syndrome/Intestinal Lipofuscinosis

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A 61-year-old alcoholic man with history of cholecystectomy presented with a 20-year history of recurrent bowel obstruction and 30-pound weight loss. After numerous attempts at conservative management, exploratory laparotomy was performed that showed no mechanical cause. However, the obstruction persisted and intensified. A CT scan confirmed small bowel obstruction and megacolon. A total abdominal colectomy was performed, with ileostomy. Grossly, there was intestinal dilation up to 15 cm with prominent brown discoloration of bowel wall. No strictures or other fixed obstruction were identified. Microscopic examination revealed prominent lipofuscin-like pigment deposition involving the muscularis propria, muscularis mucosae, and the vascular smooth muscle. Histochemical staining was positive for PAS, and negative for iron and calcium, consistent with lipofuscin. The gross and histologic findings fit with brown bowel syndrome (BBS). BBS is a very rare condition characterized by lipofuscin deposits predominantly within the smooth muscle of the muscularis mucosae and/or muscularis propria that imparts a brown color to the bowel. It is generally thought to be a smooth muscle mitochondrial myopathy due to chronic vitamin E deficiency secondary to fat malabsorption syndromes, resulting in free radicals causing peroxidation of unsaturated membrane lipids with accumulation of lipofuscin. BBS may be seen in patients with alcohol abuse, malnutrition, chronic bowel inflammation, and intestinal lymphangiectasia. Our patient’s severe chronic intestinal pseudo-obstruction, low levels of certain fat-soluble vitamins (A, D, and E), significant weight loss, and history of cholecystectomy with alcohol abuse correlates with BBS clinically.

Malignant Gastrointestinal Neuroectodermal Tumor of 49-Year-Old Patient With Remote History of Lymphoma

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Malignant gastrointestinal neuroectodermal tumor (GNET) is a rare entity that exclusively occurs in or near the gastrointestinal tract. It is predominantly found in young adults with frequent local recurrence and metastasis. Here, we report a case of a 49-year-old man who presented with abdominal pain and weight loss. Abdominal CT scan revealed an ileal tumor with mesenteric lymphadenopathy. Lymphoma was highly suspected clinically because of his remote history of thymic B-cell lymphoma. A core needle biopsy of mesenteric node was...
inconclusive because of limited tumor for further study. A right hemicolectomy was performed. Grossly, an ulcerated tumor involving full thickness of ileum with multiple tumor-replaced lymph nodes was identified. Histologically, the tumor grew in diffuse sheets and nests with focal pseudovascular and pseudopapillary patterns. The tumor cells were large, epithelioid, and polygonal with eosinophilic or clear cytoplasm and vesicular chromatin. Abundant multinucleated osteosarcoma-like giant cells were present. The tumor cells showed diffuse strong positivity for S100 and Sox10 but were negative for melanocytic markers. EWSR1-ATF1 gene fusion was identified by FISH analysis. Histologically, GNET can mimic many epithelial and nonepithelial gastrointestinal tumors. It is extremely challenging to make a diagnosis from previous core biopsy, especially with a past medical history of lymphoma. Awareness and recognizing this entity and its diagnostic criteria are necessary for pathologists to avoid misdiagnosis.

**Metastatic Malignant Pleural Mesothelioma: A Rare Cause of Jejunum Intussusception**

(Poster No. 12)

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Intussusception is the telescoping of a proximal segment of the gastrointestinal tract into an adjacent distal segment. It is a rare cause of obstruction in adults. Malignant pleural mesothelioma is an uncommon neoplasm of mesothelial origin that can be difficult to diagnose. Here, we report an unusual case of small bowel intussusception in an adult due to metastatic pleural mesothelioma. A 62-year-old woman presented with abdominal pain, constipation, and emesis. Computerized tomography revealed jejunal obstruction secondary to intussusception. She underwent segmental resection, which revealed a 2.7-cm, well-circumscribed mass involving the muscularis propria and abutting the serosa. Microscopically, the tumor was composed of sheets of large epithelioid and spindle cells with prominent nucleoli, areas of necrosis, frequent mitosis, and lymphovascular invasion. The patient was previously diagnosed with pleural mesothelioma 15 months prior. She had metastasis to an aortocaval lymph node and was receiving chemotherapy. Pleural biopsy showed mesothelioma with epithelioid cells diffusely positive for WT-1, calretinin, D2-40, and CK5/6. However, the jejunal tumor cells were positive for WT-1 but faintly positive for calretinin. (Figure 8), D2-40, and CK5/6. Stains were negative for CK20, villin, and CDX-2. These findings were consistent with metastatic pleural mesothelioma. Small bowel high-grade malignancies with minimal mucosal involvement and extensive lymphovascular invasion are more commonly metastasis than primary. If the history of prior malignancy is remote or unknown, it is important to include mesothelioma in differential diagnoses with carcinoma, sarcoma, lymphoma, and melanoma. Moreover, performing multiple mesothelial markers can be beneficial, as patchy and faint staining makes the diagnosis challenging.

**Manual Count of Mitosis May Provide More Accurate Grading of Neuroendocrine Tumors of the Gastrointestinal Tract and Pancreas as It Correlates With Prognostic Data as Compared With Using Phospho-Histone H3 Antibody–Detected Mitosis**

(Poster No. 13)

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**Context:** Phospho-histone H3 is associated with mitotic chromatin condensation in late G2 and M phase of the cell cycle. This study aims to confirm the reliability of a manual count of phospho-histone H3–positive cells on immunohistochemically stained slides (MC-PHH3) in neuroendocrine tumors of gastrointestinal tract and pancreas compared with manual mitotic counting on H&E–stained slides (MMC-HE) and manual count of the Ki-67 proliferation index (MC-Ki67).

**Design:** The study included 134 patients with neuroendocrine tumors of the gastrointestinal tract and the pancreas from our institution from 2011 to 2017. MC-Ki67 and MMC-HE were retrieved from the pathology report. MC-PHH3 was assessed by a board-certified pathologist as counts/5 mm².

**Results:** Manual counting showed 108 cases of G1, 21 of G2, and 5 of G3 tumors according to World Health Organization grading criteria. There was good spearman correlation between MC-PHH3 and MC-Ki67 (correlation coefficient 0.64, P < .001) and moderate correlation between MMC-HE and MC-PHH3 (correlation coefficient 0.43, P < .001). The moderate correlation may be due to overestimation of the MC-PHH3 count secondary to fixation, background lymphocytes, and edge artifact staining.

**Conclusions:** Given the significance of neuroendocrine tumors and neuroendocrine carcinoma grading based on mitotic count, we propose that although phospho-histone H3 may not be a sufficient replacement for MMC-HE, it may serve as a confirmatory marker when MMC-HE and MC-Ki67 are discrepant.

**Focal Nodular Hyperplasia With Steatohepatitis-like Changes: An Unusual Occurrence**

(Poster No. 14)

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Focal nodular hyperplasia (FNH) is the second most common benign hepatocellular lesion with an incidence of 0.6% to 3%. Classic histologic features include nodular architecture divided by thick fibrous septa, dystrophic vessels, and bile ductular reaction. There is a paucity of literature regarding FNH with fatty change/steatohepatitis-like change, which can be confused with steatohepatitis variant of hepatocellular carcinoma. We report an unusual case of FNH with steatohepatitis-like changes. A 44-year-old woman presented with a few days’ history of right abdominal pain. Computed tomography showed a 3.0-cm solitary mass on liver segment 5, for which hepatic segmentectomy was performed. The resection specimen showed a 3.0-cm pale-yellowish nodule (Figure 9, A). Microscopy showed nodules of hepatocytes separated by thick fibrous septa with thick-walled vessels (Figure 9, B).
Lesional hepatocytes showed moderate steatohepatitic changes (ballooned hepatocytes, and lobular inflammation) with moderate macrovesicular steatosis (about 40%) (Figure 9, C). There was focal mild pericellular fibrosis. Thick hepatocellular plates/cords >3 cells wide were focally present. Interface showed ductular reaction (highlighted by CK 7) (Figure 9, D). Thin rim of background liver was histologically unremarkable, without significant steatosis or steatohepatitis. We present this case of FNH to highlight the unusual occurrence of steatohepatitis-like changes within the lesional hepatocytes, which should not be confused with steatohepatitic variant of hepatocellular carcinoma. Common classical features of FNH including thick-walled vessels within the fibrous septa, ductular reaction, and thick fibrous bands are helpful in differentiating FNH from hepatocellular carcinoma.

Transmural Herniating Fibrous Obliteration of the Appendix: A Unique Case Mimicking Stage T4 Carcinoma Prompting Surgical Excision
(Poster No. 15)

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Fibrous obliteration of the appendix is common and found in ~10% of appendices. It is usually an incidental finding in appendices removed for other reasons (such as acute appendicitis) and is not by itself an indication for surgery. We present a case of a 50-year-old woman who underwent an elective hysterectomy and salpingo-oophorectomies for chronic pelvic pain. Intraoperatively, serosal nodules of the appendix raised concern for carcinoma, prompting appendectomy. Grossly, 8 firm, tan nodules studded the appendiceal serosa. The nodules ranged from 2 to 10 mm maximally and appeared to randomly involve the entire length of the appendix. Cross-sectioning showed mushroom-shaped lesions comprising transmural growths (“stems”) herniating through the wall to form serosal surface implants (“caps”). Microscopy confirmed transmural extrusion of intra-appendiceal fibro-oblitative tissue causing serosal nodule formation. Additionally, the tip of the appendix contained a 3-mm well-differentiated neuroendocrine tumor and 1 microscopic focus of intramural endometriosis; both were distant from the foci of herniating fibro-oblitative tissue. Immunohistochemical staining showed the protrusions of fibro-obliterative tissue contained the typical mix of cells seen in fibrous obliteration of the appendix including neural cells, myofibroblasts, fibroblasts, endothelium, and smooth muscle cells. Features of diverticulosis, appendicitis, neuroma, and fibrous adhesions were absent. In summary, we present a novel, previously unreported variant of fibrous obliteration remarkable for transmural and serosal nodular involvement of the appendix. The condition mimicked invasive carcinoma intraoperatively prompting appendectomy (Figure 10).

Aggressive Esophageal Carcinoma With Multilineage Differentiation by Immunohistochemistry
(Poster No. 16)

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Adenocarcinoma is the most common type of esophageal cancer in the United States. We present a report of an esophageal cancer with adenocarcinoma, neuroendocrine, and squamous cell differentiation. The patient was a 58-year-old man with a remote history of orthotopic heart transplantation for ischemic cardiomyopathy who presented with intractable nausea, vomiting, abdominal pain, and watery diarrhea. A computed tomography scan revealed a solitary lung nodule and multiple hypoattenuated liver lesions. On endoscopy, a large ulcerated gastroesophageal junction mass was identified with submucosal extension into the gastric cardia. Biopsies of the liver and gastroesophageal lesions revealed a poorly differentiated neoplasm with patchy myxoid stroma and dyskeratosis (Figure 11, A). The background esophageal epithelium demonstrated focal goblet cell metaplasia. By immunohistochemistry, the neoplastic cells were variably positive for MOC-31 (Figure 11, B) and p63 (Figure 11, C) and strongly positive for synaptophysin (Figure 11, D), consistent with multidirectional differentiation. Clinical laboratory tests found elevated chromogranin A levels. The patient’s condition deteriorated rapidly within 2 weeks of the diagnosis with progressive somnolence and confusion. Here we present an exceptionally rare case of an aggressive esophageal carcinoma with multilineage differentiation.

Primary Neuroendocrine Carcinoma Arising as a Polypoid Lesion in the Common Bile Duct With Cervical Spine Metastases
(Poster No. 17)

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Primary biliary tract neuroendocrine tumors are extremely rare and account for 0.2%–2% of all gastrointestinal neuroendocrine tumors. Paucity of enterochromaffin cells in the biliary tract is the reason for paucity of these tumors at this location. Chronic inflammation of bile duct epithelium is responsible for metaplasia of enterochromaffin cells and formation of neuroendocrine tumors. We report a case of an 83-year-old woman who presented with epigastric pain, nausea, heartburn, fatigue, and weight loss and later developed jaundice. Results of her liver function tests were elevated. She had a remote history of malignant melanoma of skin. Computed tomographic scan and endoscopic ultrasound showed biliary distension with a 2.6 × 2.1 × 2.0-cm mass in the distal common bile duct. She underwent a pancreateoduodenectomy, cholecystectomy, and retroperitoneal lymphadenectomy. Distal common bile duct revealed a 4.5 × 2.2 × 1.5-cm sessile 3-cm wide mass morphologically consistent with neuroendocrine tumor (Figure 12). Her chest radiograph showed 3 lesions with surrounding soft tissue masses and central lucencies (Figure 12). The patient had evidence of lung metastases. The patient underwent a wedge resection of a lung lesion which was consistent with neuroendocrine tumor (Figure 12). The patient was lost to follow-up. In conclusion, primary neuroendocrine tumors of the biliary tract are extremely rare. The clinical history of a melanoma patient with non-specific symptoms is important.
Histopathologic Findings in Biopsies From Endoscopically Normal Adult Duodenums: Is Routine Biopsy Necessary?

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Context: During upper endoscopy, routine biopsies are often taken from endoscopically normal duodenums. To our knowledge, there has not been a recent assessment of the diagnostic yield or influence on management of routine biopsy of endoscopically normal duodenums.

Design: The laboratory information system was searched for patients who had duodenal biopsies between January and June 2018. The upper-endoscopy reports were reviewed and only biopsies from 500 endoscopically normal duodenums were included. The pathologic findings in the duodenal biopsies and the patient indications for upper endoscopy were recorded. Cost saving analysis was performed.

Results: Twenty-seven of 500 patients (5.4%) with endoscopically normal duodenums had abnormal histopathology. The most common histopathologic findings were peptic duodenitis (51.9%), increased intraepithelial lymphocytes (25.5%), and gastric heterotopia (11.1%). One patient with increased intraepithelial lymphocytes had subsequent positive celiac serology, 1 patient had subsequent negative celiac serology, and the remaining 5 patients had no celiac serology. The most common clinical presentation in these patients was epigastric pain, nausea, vomiting, and heartburn. The most common clinical presentation in patients with peptic duodenitis was dysphagia and heartburn. The patient charge for 1 duodenal biopsy was $601. The laboratory cost to process 1 duodenal biopsy was $55.

Conclusions: CL-HCC is a cryptic variant of HCC and often evades pretransplant detection. The etiology of CL-HCC remains diverse. Further research is necessary to determine the carcinogenesis and to improve methods of detection.

Amyloidosis—An Act of Deception

(Poster No. 20)

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Amyloidosis is improper deposition of insoluble protein in tissue that impairs its function and architecture. The liver is commonly affected and manifests with hepatomegaly and abnormal function tests. We report a
A 59-year-old African American woman. She was epihepatocholangiocystic with stable vitals: bilirubin, 24.3; INR, 2; creatinine, 4.2; and MELD score of 40 with rapidly declining renal function. Results of magnetic resonance cholangiopancreatography were negative. Her workup was unrevealing, and she was deemed to have decompensated cryptogenic cirrhosis. She received simultaneous liver and kidney transplant. Explanted liver revealed extensive amyloidosis, AL amyloid κ type. Bone marrow biopsy and flow cytometry were negative without plasma cell dyscrasia. Further workup suggested no systemic involvement. AL amyloidosis is a rare disease. Liver involvement occurs in 62%–90% of cases but is usually limited to hepatomegaly with elevated alkaline phosphatase and occurs in the setting of systemic amyloidosis. Stigmata of chronic liver disease are rare: hyperbilirubinemia is seen in 6% of patients and suggests poor prognosis. Our patient’s explanted liver revealed extensive amyloid deposition within portal, periportal, and focally in septa (Figure 14, A). Congo red was positive (Figure 14, B and C). Trichrome confirmed cirrhosis (Figure 14, D). Her hepatic amyloidosis was unique in the severity of symptoms and level of organ involvement that led to ACLF and ultimately transplantation. Hepatic amyloidosis is usually limited to hepatomegaly and abnormal laboratory values but can present as hepatic failure and should be considered in patients with otherwise unclear etiology of liver disease.

Synchronous Gastric Multifocal Gastrointestinal Stromal Tumor and Gastric Adenocarcinoma

(Poster No. 21)

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An 88-year-old man presented for gastrectomy for gastric adenocarcinoma after receiving neoadjuvant chemotherapy. Gross examination revealed multiple firm serosal nodules (Figure 15, A) ranging from 0.1 to 0.5 cm overlying a palpable 5.5-cm luminal mass (Figure 15, C). They were presumed to be extension or metastatic spread of the gastric adenocarcinoma. Microscopically, the luminal mass was confirmed to be gastric adenocarcinoma (Figure 15, D; intestinal type, [y] pT1bpN0). The serosal nodules were composed of spindled cells in a hyalinized and partially calcified stroma and were CD117+ (Ventana Medical Systems, Tucson, Arizona) and DOG1 (Figure 15, B; Cell Marque, Rockland, California) immunoreactive consistent with multifocal gastrointestinal stromal tumor (GIST) ([m] pT1pN0). Small GISTS are often asymptomatic and not infrequently incidentally identified during operation or pathologic examination for another pathologic process—neoplastic or otherwise. This case is unusual as the GISTS were multifocal in a patient without a known GIST-associated syndrome. However, his past medical history was notable for a neurofibroma, congenital hypertrophy of the retinal epithelium, and a sister who died from a nonspecified gastric cancer in her early 50s. Although the occurrence of multifocal GISTS outside the setting of a syndrome is more common than previously thought, the combined diagnosis of a multifocal GIST and gastric adenocarcinoma is rare. This patient’s concurrent neoplasms and medical history hint at an underlying genetic cause, which may provide further evidence for a shared neoplastic driving mechanism.

Isolated Ischemic Necrosis of the Cecum Mimicking Malignancy in a Patient With Chronic Heart Disease

(Poster No. 22)

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Isolated ischemic necrosis of the cecum (ISNC) is a rare condition that occurs in patients with low-flow state. Right lower abdominal pain is the most common symptom and clinically resembles acute appendicitis. We report herein a case of ISNC presenting as a distinct mass-forming lesion mimicking malignancy in an 87-year-old man with hypertension and chronic heart disease who presented to the emergency room with right abdominal pain. CT imaging showed focal wall thickening and contour bulge along the medial aspect of the ascending colon suspicious for colonic neoplasm. Laparoscopic right hemicolectomy was performed and a mass lesion in the cecum was identified intraoperatively. Gross examination revealed a 5.0 × 3.7-cm tan-brown, well-demarcated mass with scalloped border and necrotic surface. Histologic examination demonstrated acute ischemic necrosis with transmural hemorrhage and abscess consistent with perforation. At the periphery of the lesion, there were relatively normal-appearing arteries juxtaposed by abnormal ones exhibiting intimal thickening consisting of finely granular amphophilic material morphologically resembling amyloid. Yet Congo red stain was negative, whereas elastin stain was positive, confirming segmental vascular elastosis likely causing ischemia. There was no evidence of epithelial dysplasia or carcinoma. The patient survived surgery and recovered well clinically. Cecal ischemia has been described in association with a variety of clinical entities; however, this is the first...
case report where it presents as a mass-forming lesion mimicking malignancy. In patients with long-standing history of hypertension and heart disease, ISNC should be considered in the differential diagnosis of right lower quadrant pain (Figure 16).

**PD-L1 Expression in Colorectal Carcinoma: Clinicopathologic, Microsatellite Instability, and BRAF Correlates**

*(Poster No. 23)*

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**Context:** There is growing evidence of the role of immune therapy in colorectal cancers. We have investigated the expression of PD-L1 in colorectal carcinoma and in its microenvironment and correlated expression with clinicopathologic parameters, microsatellite instability, and BRAF mutation status.

### Correlation of Tumor Characteristics With PD-L1 Expression in Tumor and Tumor Infiltrating Lymphocytes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PD-L1 Positive Expression in Tumor, No. (%)</th>
<th>PD-L1 Positive Expression in Tumor-Infiltrating Lymphocytes, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor</td>
<td>No. (%)</td>
<td>P Value</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td>.07</td>
</tr>
<tr>
<td>Up to 50 (64)</td>
<td>21 (47.7)</td>
<td>19 (38)</td>
</tr>
<tr>
<td>&gt;50 (46)</td>
<td>23 (52.3)</td>
<td>31 (62)</td>
</tr>
<tr>
<td>Laterality</td>
<td></td>
<td>.12</td>
</tr>
<tr>
<td>Right (60)</td>
<td>28 (63.6)</td>
<td>35 (70)</td>
</tr>
<tr>
<td>Left (50)</td>
<td>16 (36.4)</td>
<td>15 (30)</td>
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<tr>
<td>Differentiation</td>
<td>.30</td>
<td>.1</td>
</tr>
<tr>
<td>Well (46)</td>
<td>15 (34.1)</td>
<td>15 (30)</td>
</tr>
<tr>
<td>Moderate (45)</td>
<td>19 (43.2)</td>
<td>21 (42)</td>
</tr>
<tr>
<td>Poor (19)</td>
<td>10 (22.7)</td>
<td>14 (28)</td>
</tr>
<tr>
<td>pT</td>
<td></td>
<td>.57</td>
</tr>
<tr>
<td>T1/T2 (15)</td>
<td>7 (16)</td>
<td>8 (16)</td>
</tr>
<tr>
<td>T3/T4 (95)</td>
<td>37 (84)</td>
<td>42 (84)</td>
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<tr>
<td>pN</td>
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<td>N0 (56)</td>
<td>22 (50)</td>
<td>28 (56)</td>
</tr>
<tr>
<td>N1 (28)</td>
<td>10 (22.7)</td>
<td>12 (24)</td>
</tr>
<tr>
<td>N2 (26)</td>
<td>12 (27.3)</td>
<td>10 (20)</td>
</tr>
<tr>
<td>Distant metastasis</td>
<td>.03</td>
<td>.12</td>
</tr>
<tr>
<td>Present (8)</td>
<td>6 (13.6)</td>
<td>6 (12)</td>
</tr>
<tr>
<td>Absent (102)</td>
<td>38 (86.4)</td>
<td>44 (88)</td>
</tr>
<tr>
<td>BRAF expression</td>
<td>.009</td>
<td>.14</td>
</tr>
<tr>
<td>Positive (12)</td>
<td>9 (20.5)</td>
<td>8 (16)</td>
</tr>
<tr>
<td>Negative (98)</td>
<td>35 (79.5)</td>
<td>42 (84)</td>
</tr>
<tr>
<td>MLH1/PM2 loss</td>
<td>.007</td>
<td>.97</td>
</tr>
<tr>
<td>Present (10)</td>
<td>8 (18.2)</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Absent (100)</td>
<td>36 (81.8)</td>
<td>45 (90)</td>
</tr>
</tbody>
</table>

**Results:** PD-L1 in tumor cells was seen in 40% of cases, in tumor-infiltrating lymphocytes in 45.5%, BRAF 600VE in 11%, MLH1/PM2 loss in 9%, and MLH2/MSH6 loss in 12.7%. PD-L1 was expressed in >5% of cells in 17.3% of cases, 5%–50% in 15.5%, and >50% in 7.2%. Correlates of PD-L1 expression are shown in the Table. Further PD-L1 expression was analyzed in synchronous primary and metastatic lymph node (n = 37). Concordant expression was evident in 65% of cases, whereas 35% of cases showed discordance.

**Conclusions:** PD-L1 was expressed in a fair number of colorectal cancers. BRAF was significantly coexpressed with PD-L1.

**Pancreatic Adenosquamous Carcinoma Presenting as Duodenal Diverticulum**

*(Poster No. 25)*

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Primary pancreatic adenosquamous carcinoma (PASC) is an extremely rare clinical entity with an incidence of approximately 4% in all pancreatic malignancies. We report a case of PASC presenting as duodenal diverticulum. A 79-year-old white man was referred to the hospital. Computed tomography revealed a large duodenal diverticulum at the third portion of the duodenum associated with a 4.3-cm mass at the pancreatic head. No additional mass was identified. Serum carcinoembryonic antigen (CEA 0.8 ng/mL) and CA19-9 (19 U/mL) were within normal limits. Peritoneal amylose level was significantly high (6298 U/L). Fine-needle aspiration and EUS-guided biopsy confirmed malignant cell present. Subsequently pancreaticoduodenectomy was performed. Gross examination revealed a large well-defined, pale tan-yellow, firm mass (5.1 x 3.5 x 3.1 cm) with a central cavity and necrosis. The cavity opened to the duodenal mucosal surface. Microscopically, the mass showed large nests of tumor cells with marked central necrosis. The tumor predominantly exhibited squamous differentiation with focally vague glandular features. No neuroendocrine differentiation was noted. The tumor cells showed enlarged, irregular nuclei with vacuolated chromatin. An increased mitotic figure (16/10 per high-power field) and Ki-67 (85%) was identified. Immunohistochemical studies revealed tumor cells were strongly positive for p63, p40, and CK8/18 and negative for synaptophysin, chromogranin, CK19, CK20, and CDX2. A literature review was...
performed. The PASC presented as a large mass with central necrosis, which may be a pathologic feature for PASC. Pancreatectoduodenectomy is the common treatment of choice. Close follow-up should be applied to detect possible early recurrence and distal metastasis (Figure 17).

Congenital Epidermoid Cysts of the Liver
(Poster No. 26)

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1Department of Pathology, Beth Israel Deaconess Medical Center, Boston, Massachusetts; 2Department of Medical Education, Tsinghua University, Beijing, China; 3Department of Pathology, Boston Children's Hospital, Boston, Massachusetts.

Congenital epidermoid cysts of the liver are an uncommon finding, with only 14 previously reported cases. Their pathogenesis is poorly understood. Aside from a recent report documenting pancytokeratin staining, no other descriptions of this entity have included immunohistochemical findings. We report 2 rare cases of hepatic epidermoid cysts, the first evaluated with a broad panel of immunohistochemistry with the aim of elucidating histogenesis. Both cases were detected on second-trimester antenatal ultrasound in otherwise developmentally unremarkable females. The cysts enlarged slowly after birth and were resected at ages 2 and 6 months, both for the indication of avoiding potentially more difficult surgery in the future. Grossly, the cysts were unilocular (4.8 cm) and multilocular (7.0 cm). Microscopically, both were lined by stratified nonkeratinizing squamous to focally transitional-like epithelium and surrounded by a paucicellular fibrous stroma (Figure 18, A). In the multilocular cyst, hepatocytes as well as fibrous stroma populated the septa (Figure 18, B). Epithelial cells were positive for HBME-1 (Figure 18, C), p63, CK19, CEA, Cam5.2, and CK7 in the luminal 1–2 layers only (Figure 18, D) and EMA. D2-40, WT-1, calretinin, and Ca19-9 were negative. Interestingly, similar immunohistochemical staining is seen in splenic epidermoid cysts. Similar to our cases, these entities stain with p63 as well as CEA, CK7 (luminal 1–2 layers only), and HBME-1; they are negative for calretinin and WT-1. Immunohistochemical overlap with splenic epidermoid cysts suggests a shared pathogenesis and immunoreactivity for HBME-1 and p63 detracts from the hypothesis that hepatic epidermoid cysts derive from underlying hepatobiliary elements.

Primary Esophageal Adenocarcinoma Metastasis Distantly to Thigh Soft Tissue: A Case Report and Molecular Studies
(Poster No. 27)

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Adenocarcinoma of the esophagus is the most common tumor in the distal esophagus. Distant metastasis to skeletal muscle is extremely rare. Here we report a case of esophageal adenocarcinoma metastasizing to the thigh skeletal muscle and presenting as a mass. The patient is a 60-year-old man with no significant past medical history who was experiencing dysphagia with 30-pound weight loss during 3 months. Endoscopy showed a mass at the gastroesophageal junction. A biopsy demonstrated crowded glands with pleomorphism and luminal necrosis, infiltrating into the lamina propria mixed with scattered single cells. The epithelial cells are hyperchromatic with angulated nuclei, vesicular chromatin, and a high nuclear to cytoplasm ratio. A final pathologic diagnosis of at least intramucosal adenocarcinoma was made (Figure 19, A and B). PET images showed a nonspecific hypermetabolic nodule between muscles of the right distal lateral thigh. An ultrasound-guided fine-needle aspiration of the nodule was performed. Cytology smears showed a hypercellular specimen composed of cohesive, crowded groups, mixed with single malignant cells demonstrating nuclear hyperchromasia and pleomorphism, occasional prominent nucleoli, and fine, vaculated cytoplasm (Figure 19, C). Immunohistochemical staining for AE1/AE3 is diffusely strong, supporting the diagnosis of metastatic adenocarcinoma from the patient’s known esophageal primary (Figure 19, D). PD-L1 immunostaining was negative. Molecular studies revealed no reportable alteration with companion diagnostic including microsatellite status, FGFR3 amplification, TP53 R273C, and TP53 R282W. A literature search shows our study is the first case report of an esophageal adenocarcinoma with distant metastasis to the thigh.

Unusual Presentation of Fibroelastosis in Gallbladder
(Poster No. 28)

Roula Katerji, MD (Roula_katerji@urmc.rochester.edu); Jennifer J. Findeis-Hosey, MD. Department of Pathology, University of Rochester, New York.
Fibroelastosis is characterized by proliferation of fibroelastic tissue. Although elastosis is commonly seen in sun-exposed areas such as the skin, fibroelastosis of visceral organs is rarely reported. Here we present an unusual case of fibroelastosis of the gallbladder with masslike features. A 62-year-old man with a past medical history of intermittent abdominal pain underwent laparoscopic cholecystectomy for cholelithiasis and recurrent cholecystitis at time of concurrent sleeve gastrectomy. Grossly the gallbladder lumen was filled with green sludge and 4 green-yellow choleliths. There was a 1.4 x 1.0-cm area of firm white-gray mural thickening (up to 0.6 cm in thickness) of the fundus, with associated serosal puckering. Histologically the gallbladder was characterized by chronic cholecystitis. The area of mural thickening demonstrated nodular aggregates of homogenous amorphous eosinophilic refractile nonpolarizable material in the submucosa and surrounding the blood vessels (Figure 20, A and B). Within the eosinophilic material, thick and haphazardly oriented fibers were identified. Congo red staining was negative for amyloid (Figure 20, C). Verhoeff–van Giessen stain highlighted the elastin fibers within the nodular areas (Figure 20, D). There was no dysplasia or malignancy. Fibroelastosis of the gallbladder is an underrecognized entity, with only rare reported cases. It has been postulated to be the result of bile leakage into the interstitium with local tissue response to cytokines. As seen in this case, fibroelastosis of the gallbladder bears close resemblance to amyloidosis and mass-forming lesions; the diagnosis can be aided by histochemical studies and pathologists should be aware of this interesting diagnosis to avoid misinterpretation.

Utility of Dual-Color, Double Immunohistochemical Staining to Evaluate Biopsy Specimen for Autoimmune Gastritis

Kemin Xu, MD (kemin.xu@wmchealth.org); Qiqi Ye, MD; Christopher Gault, MD; Humayun K. Islam, MD; Minghao Zhong, MD. Department of Pathology, Westchester Medical Center at New York Medical College, Valhalla.

Context: The histologic diagnosis of autoimmune gastritis (AIG) depends on separate antral and body biopsy specimens. However, in actual practice, pathologists often receive few biopsy samples from undesignated locations. In addition, determining site of origin is further complicated by the characteristic antralization of oxyntic mucosa or intestinal metaplasia seen in AIG. Given the distinct distribution of gastrin-producing neuroendocrine cells (G cells) in the stomach, we hypothesize that dual-color, double immunohistochemical (IHC) staining of gastrin and synaptophysin is a simple, quick, and reliable method to evaluate biopsy specimen for AIG in a single slide.

Design: We included 30 cases of AIG and 80 cases of normal control, Helicobacter-associated gastritis (HPG), reactive gastritis (RG), and chronic gastritis without defined cause (CG) collected between 2010 and 2018. The specimens were subjected to sequential IHC staining of gastrin and synaptophysin.

Results: Thirty cases showed oxyntic antralization mucosa with marked chronic inflammation/intestinal metaplasia and some separate fragments of unremarkable antral mucosa in random gastric biopsy. Double IHC staining demonstrated enterochromaffin-like cell (ELC) hyperplasia (highlighted by synaptophysin with brown chromogen) and sparing gastrin staining (negative for red chromogen) in the same fragment of tissue. This IHC pattern was not present in all other non-AIG cases, including normal, HPG, RG, and CG.

Conclusions: Our results demonstrated that this double IHC stain is sensitive and specific for AIG. Compared with traditional single, separate IHC staining, this dual-color, double IHC staining is much easier to interpret. This technique will be especially useful for specific cases where minimal tissue is available.

Intra-abdominal Desmoid Tumor as the Initial Presentation of Familial Adenomatous Polyposis

Tracy R. Shachner, DO (tshachner@utmck.edu); Alan D. Grindstaff, MD. Department of Pathology, University of Tennessee Medical Center, Knoxville.

Intra-abdominal desmoid tumors are slow-growing, locally aggressive spindle cell neoplasms. They exhibit a slight female predominance and can be either sporadic or associated with familial adenosis polyposis (FAP). FAP is caused by mutations in the APC gene, a tumor suppressor gene. Patients with FAP have an increased risk of developing colorectal carcinoma, gastric and small bowel adenomatous polyps, bone osteomas, intra-abdominal desmoid tumors, and other neoplasms. The lifetime risk of colorectal cancer is essentially 100%, usually in the third decade of life. A 24-year-old woman presented to the trauma bay in extremis and was emergently taken to the operating room. Exploratory laparotomy revealed a greater than 20-cm abdominal tumor adherent to multiple organs and perforating the stomach. She underwent tumor resection, subtotal gastrectomy, splenectomy, distal pancreatectomy, adrenalectomy, and partial transverse colectomy. Gross examination of the en bloc resection revealed a large, firm, white mass invading and adherent to the colon, pancreas (Figure 21, A), stomach, and spleen. The stomach was completely carpeted with small polyps (Figure 21, B), and additional polyps were noted in the transverse colon. Microscopic examination of the tumor revealed a bland spindle cell neoplasm with myxoid stroma (Figure 21, C). The tumor demonstrated nuclear reactivity with β-catenin, consistent with intra-abdominal desmoid tumor. The stomach (Figure 21, D) and colon polyps represented tubular adenomas. Genetic testing revealed a pathologic mutation (c.5803delC) in the APC gene, consistent with classic FAP. This case highlights the importance of awareness of the association between desmoid tumors and FAP to ensure appropriate genetic counseling and clinical follow-up is obtained.

Abstracts
A Case of Fatal Disseminated Histoplasmosis Presenting as Liver Failure in a Patient Receiving Methotrexate Therapy
(Poster No. 31)
Behtash Nezami, MD (behtash.nezami@uhhospitals.org); Wendy Liu, MD, PhD. Department of Pathology, University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, Ohio.

Tumor necrosis factor inhibitors are used for a range of nonmalignant diseases and are associated with a variety of opportunistic infections. We present a diagnostically challenging case of disseminated histoplasmosis presenting with liver failure as a complication of immunosuppression from methotrexate therapy for psoriasis. A 47-year-old man was admitted with fever, joint pain, right upper quadrant discomfort, and jaundice, and was diagnosed with acute hepatitis. Eight months earlier, he was diagnosed with psoriatic arthritis and was started on adalimumab and methotrexate. Viral and fungal etiologies were ruled out on blood samples, and he was discharged after psoriatic arthritis medications were discontinued. Two days later he returned with nonbilious emesis and high bilirubin and liver enzymes. Broad spectrum antibiotics and antitubal agents were initiated. He subsequently developed respiratory failure, fever, tachycardia, and altered mental status, requiring intubation. Liver biopsy revealed portal chronic inflammation, Kupffer cell hyperplasia, and poorly formed granulomas. GMS fungal stains were negative. Within 2 days he became acidotic, anuric, and hypotensive. He expired 18 days after the initial presentation. Autopsy revealed bilateral pneumonia, severe congestion, and hepatomegaly with extensive necrosis. GMS stain demonstrated yeast forms consistent with histoplasma. Results from urinary histoplasma antigen test were reported positive (after his death). This case illustrates the risk of missing opportunistic fungal infections in patients receiving methotrexate therapy for nonmalignant diseases. The diagnosis of histoplasmosis was only made at postmortem examination. Autopsy revealed bilateral pneumonia, severe congestion, and hepatomegaly with extensive necrosis. GMS stain demonstrated yeast forms consistent with histoplasma.

Conclusions: Incidental findings on sleeve gastrectomy specimens can have important clinical implications. Proper treatment for H pylori gastritis may prevent complications such as peptic ulcer disease, gastric cancer, and gastric lymphoma. Histologic evaluation has a high sensitivity and specificity for detecting H pylori when combined with special or immunostains. Atypical patterns of inflammation should prompt the pathologist to pursue further workup such that proper treatment may be initiated.

<table>
<thead>
<tr>
<th>Prevalence of Helicobacter pylori Gastritis in Sleeve Gastrectomy Specimens</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. (%) of Cases</strong></td>
</tr>
<tr>
<td><strong>Total No. of cases (5 y)</strong></td>
</tr>
<tr>
<td><strong>Ancillary studies performed</strong></td>
</tr>
<tr>
<td><strong>H pylori gastritis</strong></td>
</tr>
<tr>
<td><strong>Diagnosed based on H&amp;E</strong></td>
</tr>
<tr>
<td><strong>Diagnosed based on ancillary studies</strong></td>
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Clinicopathologic Features of Signet Ring Cell Carcinoma on Gastric Biopsy
(Poster No. 33)
Qingzhao Zhang, MD, PhD1 (qzhang@pennstatehealth.psu.edu); Huili Li, MD, PhD;2 Zhaohai Yang, MD, PhD2 1Department of Pathology, Penn State Health Medical Center, Hershey, Pennsylvania; 2Department of Pathology and Laboratory Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia.

Context: Biopsy diagnosis of gastric signet ring cell carcinoma can be challenging because of poorly cohesive cancer cells dispersing in benign tissue. This study aimed to identify clinicopathologic features to help avoid misdiagnosis.

Design: Twenty-five signet ring cell carcinomas diagnosed on gastric biopsy were identified in our database (2004–2018). The slides were reviewed for pathologic features. The clinical presentations and endoscopic features were evaluated.

Results: Clinical presentations were pain (33%), nausea/vomiting (17%), dysphagia (15%), stenosis/obstruction (9%), metastasis including ascites or Krukenberg tumor (8%), bleeding (8%), incidental finding (4%), diarrhea (4%), and anorexia (4%). Endoscopic features included mass (35%), thickened gastric wall (27%), ulceration/hemorrhage (23%), stenosis (8%), and friable mucosa (7%). The pathologic findings in nonneoplastic tissue were as follows: chronic inflammation (92%), lamina propria expansion (84%), glandular withering (76%), acute inflammation (48%), intestinal metaplasia (40%), and foveolar hyperplasia (36%). Three patients (10%) underwent more than 1 biopsy before a definitive diagnosis. Clinical presentations were small bowel obstruction, ascites, and dysphagia. Endoscopy in all 3 patients revealed thickened gastric wall without mass. The initial biopsy from the 3 patients showed chronic inflammation, glandular withering, intestinal metaplasia, lamina propria expansion, and foveolar hyperplasia; only 1 case had a few atypical cells.

Conclusions: Firm diagnoses were not reached on initial biopsy in 12% of patients with signet ring cell carcinoma. Main endoscopic findings were mass, thickened gastric wall, and ulceration. In cases with few tumor cells, pathologic features including chronic inflammation, lamina propria expansion, and glandular withering may provide clues to malignancies.

Prevalence of Helicobacter pylori in Sleeve Gastrectomy Specimens and a Case Report of Large Ectopic Pancreas Polyp
(Poster No. 34)
Subhashree Mallika Krishnan, DO (subhashree.mallikakrishnan@beaumont.org); Ping Zhang, MD, PhD; Zhenhong Qu, MD, PhD.

Helicobacter pylori Gastritis in Sleeve Gastrectomy Specimens
(Poster No. 32)
Joyce Y. Ren, MD (joyce.ren@stonybrookmedicine.edu); Jingguan Liu, MD, PhD. Department of Pathology, Stony Brook University Hospital, Stony Brook, New York.

Context: Helicobacter pylori gastritis has been reported to be associated with obesity. We aimed to study the prevalence of H pylori gastritis in sleeve gastrectomy specimens.

Design: We retrospectively reviewed sleeve gastrectomy specimens from our institution during the past 5 years. The rate of diagnosis of H pylori gastritis was assessed.

Results: A total of 284 sleeve gastrectomy specimens were evaluated during the past 5 years. Ancillary studies were performed in 61 cases (21.5%). Nineteen cases (6.7%) were diagnosed with H pylori gastritis, all of which were first-time diagnoses. Of these, H pylori gastritis was diagnosed based on H&E sections in 7 cases; an immunostain or special stain was performed in 12 cases (see Table). Histologic features that prompted ancillary studies include active chronic gastritis (9 cases), inactive chronic gastritis (7 cases), and prominent lymphoid follicles (4 cases). Treatment was initiated promptly in 14 cases. Additionally, hematopathology consultations were obtained for 3 cases because of the presence of prominent lymphoid aggregates in the absence of H pylori. Further workup revealed incidental monoclonal B-cell lymphoproliferative process in 2 of the cases, confirmed by B-cell receptor gene rearrangement by polymerase chain reaction.

Conclusions: Incidental findings on sleeve gastrectomy specimens can have important clinical implications. Proper treatment for H pylori gastritis may prevent complications such as peptic ulcer disease, gastric cancer, and gastric lymphoma. Histologic evaluation has a high sensitivity and specificity for detecting H pylori when combined with special or immunostains. Atypical patterns of inflammation should prompt the pathologist to pursue further workup such that proper treatment may be initiated.
Design: A retrospective analysis was performed on SG cases signed out by 4 pathologists from 2017 to 2018. We calculated the percentage of *H pylori* positive cases out of the total number of SG cases.

**Results:** A total of 223 cases were reviewed, of which 7.62% (n = 17) were confirmed to be positive for *H pylori* infection based on immunohistochemical staining (detecting rate from 0% to 15% among 4 pathologists).

**Conclusions:** Our data show a total of 7.62% positive cases for *H pylori* infection with a wide range of detecting rate among pathologists, indicating that SG specimens should be submitted for histopathologic evaluation, similar to other investigations. The acute inflammation most likely resulted from irritation of the large ectopic pancreatic polyp rather than *H pylori* infection in this case report.

**A Rare Case Report of Metastatic Colorectal Cancer to Sphenoid Wing**

(Poster No. 35)

Subhashree Mallika Krishnan, DO (subhashree.mallikakrishnan@beaumont.org); Wei Li, MD, PhD. Department of Anatomic Pathology, Beaumont Health, Royal Oak, Michigan.

Metastatic colorectal cancer to the orbit and paranasal sinuses is rare. There have only been 5 previously published reports describing the involvement of sinonasal tract secondary to metastatic colorectal cancer. We report a case of a 54-year-old woman who was diagnosed with rectal adenocarcinoma in 2017, status post chemoradiation therapy (2017) and surgical resection (2018), with pathologic staging of ypT3N0R2b with acute onset of facial pain and numbness. Patient initially developed numbness of right face (approximately 2 months postsurgery), at which time computed tomography (CT) scan of head was unremarkable. She was reportedly symptom free until approximately 8 months postsurgery when she had pain of right face and jaw. CT scan of sinuses showed soft tissue infiltration (2.25 cm in greatest dimension; Figure 24, A, with arrow) surrounding right pterygoid bone with extension into pterygopalatine fossa, sphenopalatine foramen, and Vidian canal with surrounding demineralization of the sphenoid bone. She underwent right endoscopic sphenoidotomy with biopsy of the mass that was microscopically consistent with moderately differentiated adenocarcinoma with mucin production, with immunohistochemistry consistent with colorectal origin. She underwent radiation therapy to the right skull base without any further reported complications or any other metastatic lesions thus far. The 5 previously published reports present cases with varying signs and symptoms including isolated vision loss, exophthalmos, and as incidental findings with metastatic colon cancer to other organs. To our knowledge this is the first case presentation with symptoms of unilateral facial numbness and pain secondary to metastatic colon cancer to the sphenoid wing.

**Muir-Torre Syndrome: A Classical Presentation With Unexpected Findings**

(Poster No. 36)

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Muir-Torre syndrome (MTS), a variant of autosomal dominant Lynch syndrome, is characterized by at least 1 visceral malignancy and 1 cutaneous neoplasm of sebaceous differentiation, with or without keratoacanthomas. The gene mutated in MTS is 90% MSH-2 and 10% MLH-1. A 48-year-old African American woman was diagnosed with sebaceous adenoma of the scalp. The patient provided a family history of scalp lesions and colon cancer at age 45 in her mother and colon cancer in 4 maternal relatives before the age of 50. This patient’s sebaceous neoplasm showed loss of expression of MSH-2 and MSH-6 by immunohistochemistry, raising suspicion for MTS. Two years later, the patient underwent colonoscopy for hematochezia, constipation, and weight loss, which discovered a circumferential fungating sigmoid colon mass. Biopsies were consistent with adenocarcinoma with patchy loss of MSH-2 and MSH-6 by immunohistochemistry. Given the patient’s history of sebaceous neoplasm and colon cancer with a pathogenic mutation in MSH-2 c.2047G>A (p.Gly683Arg), the diagnosis of MTS was confirmed. Sigmoidectomy revealed invasive colorectal adenocarcinoma with mucinous features. Additionally, prophylactic total hysterectomy and bilateral salpingo-oophorectomy was performed, and endometrial endometrioid adenocarcinoma FIGO grade 2 was diagnosed. Current guidelines recommend patients diagnosed with colon cancer or endometrial cancer undergo mismatch repair testing to screen for Lynch syndrome. For MTS, sebaceous neoplasms, especially in patients less than 60 years old, should be tested for microsatellite instability, and if testing is positive the patient should undergo screening for visceral malignancies.

**Withdrew**

(Poster No. 37)
Adenosquamous Carcinoma of the Pancreas: A Rare Case Report
(Poster No. 38)

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Pancreatic adenosquamous carcinoma is rare and accounts for only 1%–2% of exocrine pancreatic malignancies. This variant shows squamous and glandular differentiation, and the former should represent at least 30% of the entire tumor for diagnosis. This tumor is associated with poorer prognosis than the conventional pure ductal adenocarcinomas. We present a case of this rare entity in a 53-year-old woman who presented with severe abdominal pain. Computed tomography scan of the abdomen showed a hypodense lesion in the neck/proximal body of the pancreas. Fine-needle aspiration cytology of the lesion showed few atypical cells suspicious for carcinoma. The patient underwent a distal pancreatectomy. Grossly, a poorly circumscribed yellow-white firm mass (5.0 × 5.0 × 4.2 cm) was identified within the pancreas. Microscopically, the tumor showed a poorly differentiated carcinoma composed of areas showing squamous differentiation admixed with conventional ductal adenocarcinoma (Figure 25, A). Immunostains and special stains confirmed the squamous component by positivity of p63 and CK5/6 (Figure 25, B) and the adenocarcinoma component by positivity of CDX2 (Figure 25, C) and mucicarmine (Figure 25, D). The tumor was negative for chromogranin and synaptophysin. Multiple regional lymph nodes were negative for tumor (0/16). The patient received adjuvant chemotherapy and was alive at 3-month follow-up. In summary, we present this rare case of pancreatic adenosquamous carcinoma. It is important to recognize and distinguish it from conventional pancreatic adenocarcinoma, as the metastatic lesions may show only squamous or glandular component, and treatment may include additional modalities directed at the squamous component.

Syphilitic Proctitis Presenting as Masslike Lesion Mimicking Lymphoma
(Poster No. 39)

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There was a 4-fold increase in prevalence of syphilis between 2002 and 2015. In 2017 alone, there were 30,644 cases of primary and secondary syphilis reported in the United States. Here, we report a case of syphilitic proctitis in a 34-year-old man with an unusual presentation. He presented with left lower quadrant pain that was unrelieved by lactulose. A palpable rectal mass was found during digital rectal examination. A CT scan of the abdomen and pelvis revealed multiple enlarged pelvic lymph nodes and thickening of the rectal wall. Colonoscopic examination revealed a nonobstructing, ulcerated, 1.5-cm submucosal mass in the rectum. Clinically, the differential diagnosis included a mass-forming rectal lymphoma or adenocarcinoma. Microscopically, colonic mucosa showed marked expansion of lamina propria with a mixed inflammatory infiltrate of lymphocytes, histiocytes, and occasional plasma cells. Frequent nonnecrotizing granulomas were identified in the lamina propria and submucosa. There was focal mild active colitis with cryptitis and rare crypt abscesses. Crypt architectural distortion was not present. PAS, GMS, and AFB stains did not highlight any microorganisms. A molecular and immunohistochemical workup was negative for lymphoma. Treponema pallidum immunohistochemistry demonstrated abundant spirochetes consistent with syphilitic proctitis. Syphilis continues to present a clinical and pathologic diagnostic challenge. The pathologist is often the first to suspect the diagnosis of syphilis proctitis on the basis of histomorphology. The presence of numerous granulomas and the relative paucity of plasma cells in the inflammatory infiltrate were unusual findings in this case.

Pancreatic Neuroendocrine Microadenoma: Clinicopathologic Study of 10 Cases
(Poster No. 40)

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Context: Pancreatic neuroendocrine microadenoma (<0.5 cm in diameter) is a precursor lesion for pancreatic neuroendocrine tumor (PNET) in MEN syndromic patients or sporadic cases. It has been rarely reported in literature as an incidental finding in pancreatectomy specimens resected for other conditions such as cystic pancreatic disease. We herein report 10 cases of incidentally identified microadenomas to characterize the clinicopathologic features.

Design: A retrospective search for “pancreas” and “microadenoma” was performed in our institution’s pathology database for years 2003–2019. Relevant clinical information, including survival data, was collected from electronic medical records.

Results: Ten cases were identified, consisting of 7 women and 3 men, with an average age of 68 years (range, 36–75 years). Among them, 5 patients (50%) were diagnosed with diabetes mellitus, 3 (30%) with morbid obesity, and 1 (10%) with MEN syndrome. Microadenoma(s) occurred more frequently in the tail of pancreas (n = 6; 60%). The majority were single focus of tumor (n = 6; 60%). The associated pancreatic pathologic findings included intraductal papillary mucinous neoplasm (n = 5), PNET (n = 2, 1 MEN patient), solid pseudopapillary neoplasm (n = 1), mucinous cystic neoplasm (n = 1), pancreatic ductal adenocarcinoma status post neoadjuvant therapy (n = 1), chronic pancreatitis (n = 1), and gunshot wound debridement (n = 1). Immunostains revealed negative insulin, positive glucagon, and low Ki-67 labeling index (<1%) in all tumors. All patients survived after an average of 20 months on follow-up.

Conclusions: This case series, the largest reported so far, establishes pancreatic neuroendocrine microadenoma, a biologically benign tumor, as an incidental finding associated with a variety of benign and malignant conditions.

A Rare Case of Intraductal Papillary-Tubular Neoplasm
(Poster No. 41)

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A 76-year-old woman presented to the emergency room with chief complaint of abdominal pain. Laboratory workup confirmed the diagnosis of gallstone pancreatitis. Computerized tomography scan showed masslike intraluminal filling defect within the gallbladder and patient subsequently underwent cholecystectomy procedure. On gross examination, the gallbladder showed an exophytic mass near the fundus that measured 2.5 cm. Microscopic sections revealed a tubulopapillary lesion with multiple lineages of neoplastic epithelium including biliary (Figure 26, A) (40%) with eosinophilic cytoplasm, vesicular nuclei, prominent nucleoli, and positive staining with MUC1 (Figure 26, B); gastric foveolar (40%) with apical mucus and basally located nuclei; intestinal (Figure 26, C) (20%) with goblet cells; and positive staining with MUC2 (Figure 26, D) and CDX2. Focal high-grade dysplasia was also identified without invasive carcinoma. Intracholecystic papillary-tubular neoplasm (ICPN) is a rare lesion with a reported incidence of <0.5% in cholecystectomies. ICPN has a predilection for females (female to male ratio of 2:1), and the mean age of presentation is 64 years. This lesion was previously classified as adenomas (both intestinal and pyloric types), papillary carcinoma in situ, and papillomatosis. ICPN is a unique neoplasm that can show variable cellular lineages, a spectrum of dysplasia, and a combination of papillary and tubular growth patterns. It is important to recognize this tumor because ICPN is a relatively indolent neoplasm and should be distinguished from a more aggressive pancreatobiliary-type gallbladder carcinoma, which has a less favorable prognosis.

**Unique Histopathologic Presentation of Hepatitis E Viral Infection in a Liver Biopsy**

(Poster No. 42)

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Hepatitis E virus (HEV) is now increasingly recognized as an emerging infection in developed countries. The histopathologic features of acute HEV infection are variable but have overlapping features with other acute viral hepatitides, including lobular disarray, lobular and portal inflammation, prominent Kupffer cells, and hepatocyte necrosis and regeneration. We report a case of HEV infection with unique histopathologic features. A 70-year-old man with a history of hypertension and skin cancer presented from an outside hospital with a 2-week history of progressive malaise, anorexia, dark urine, and jaundice after eating a buffalo burger while on vacation in South Dakota. His liver enzymes were elevated (AST 4796 U/L, ALT 6358 U/L, ALK-P 300 U/L, total bilirubin 8.6 mg/dL). Hepatitis A, B, and C and EBV and CMV serologies were nonreactive. A liver biopsy showed a dense sinusoidal lymphohistiocytic infiltrate (CD68+, CD163+) with focal hepatocyte necrosis (Figure 27). The lymphocytes were composed of mainly T cells with a mixture of CD4 and CD8 cells. Occasional B cells were seen but no large B cells were identified. Plasma cells, eosinophils, and neutrophils were present but not prominent. AFB, GMS, CMV, adenovirus, treponemal stains, and EBER in situ hybridization did not highlight any pathogenic organisms. The overall histopathologic features led to the broad etiologic consideration of infectious agents, hematologic process, and medication-associated injury. Hepatitis E serology testing later revealed increased immunoglobulin M (IgM) and IgG antibodies. This case highlights the importance of considering HEV infection in the differential diagnosis of acute liver injury pattern with prominent lymphohistiocytosis.

**Ixabepilone Effect on the Gastrointestinal Tract: Innocent Bystander or Potential Toxin?**

(Poster No. 43)

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Ixabepilone is a chemotherapeutic agent approved by the food and drug administration in 2007 for use in metastatic and locally advanced breast cancer. Its main indication is when anthracycline and taxane are no longer effective because of progressive disease or resistance, or when they are contraindicated because of toxicity. Ixabepilone is a semisynthetic analogue of the epothilone B class that stabilizes microtubules, resulting in mitotic arrest and apoptosis. To the best of our knowledge, this is the first report describing the histologic effect of ixabepilone on the gastrointestinal tract mucosa. An 80-year-old woman with a history of metastatic ductal breast carcinoma presented 6 months after the initiation of ixabepilone with worsening dysphagia and regurgitation. An upper endoscopy was performed, which showed mild mucosal erythema involving the gastroesophageal junction and the stomach. Histologically, numerous apoptotic bodies and ring mitoses were identified in the gastroesophageal junction and stomach epithelium, highly suggestive of mitotic arrest and medication-induced injury. The histologic changes with ixabepilone are reminiscent of taxane and colchicine effects on the gastrointestinal tract mucosa and have been associated with colchicine, but not taxane, toxicity. Although these 3 medications belong to different drug classes and have different binding sites, they are all microtubule-stabilizing agents, blocking mitosis and resulting in cell death. Whether these histologic findings represent clinical toxicity from ixabepilone is not entirely clear; however, the symptoms along with the endoscopic and histologic findings suggest mucosal injury. Awareness of this possible medication-induced injury is essential to avoid missing potential toxicity.

**A Rare Case of Primary Leiomyoma of Liver**

(Poster No. 44)

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Leiomyomas are benign smooth muscle neoplasms commonly originating in the uterus. Primary hepatic leiomyoma is very rare. It is an isolated pathology occurring in the liver without any coexisting leiomyomas. It has been reported to occur in immunocompromised individuals or those with Epstein-Barr virus, but may also occur in healthy individuals. However, sometimes leiomyomas occur in unusual locations, making the diagnosis clinically and radiologically very challenging. We report a case of a 54-year-old healthy woman with abdominal pain and discomfort for a year. On CT scan there was a 2-cm lesion in the liver, and MRI done a year later confirmed the findings with an increase in the size of the lesion. Biopsy of the lesion demonstrated low-grade spindle cell proliferation with low-grade cytologic features. No atypia, mitotic activity, or necrosis was identified. Immunohistochemical stains showed positivity for actin, calponin, and caldesmon (focally) and were negative for desmin, keratin, p63, estrogen receptor, progesterone receptor, WT-1, CD117, Dog1, HMB45, and S-100. Vascular markers CD31 and CD34 were only expressed in vessels and were negative in lesional cells. The overall morphologic features were not of GIST, solitary fibrous tumor, neurotibroma, PEComa, vascular, adipocytic, or epithelial neoplasms. The lesion was most compatible with a low-grade, myxoid, spindle cell lesion with muscle differentiation consistent with leiomyoma. Hepatic leiomyoma is assumed to arise from smooth muscle cells that line the biliary tree or blood vessels of the liver parenchyma. Our patient underwent a partial hepatectomy along with microwave ablation of a liver tumor (Figure 28).

Primary Hepatic Adenosquamous Carcinoma in a White Woman Masquerading as Hepatic Abscess
(Poster No. 45)

Smitha Mruthyunjayappa, MD (smruthyunjayappa@uabmc.edu); Chirag Patel, MD; Leona Council, MD; Sameer Al Difilah, MD. Department of Pathology, UAB, Birmingham, Alabama.

Primary hepatic adenosquamous carcinoma is a rare variant of hepatic carcinoma with aggressive clinical behavior. To our knowledge, 75 cases have been reported in the English literature. Herein we report a case of 63-year-old white woman who presented with dull abdominal pain. CT scan revealed a “liver abscess.” She was treated with antibiotics for 5 weeks without significant clinical improvement. Both MRI and repeated CT scan were consistent with an abscess that had increased in size. Laboratory results showed leukocyte count of 7100 /μL and alkaline phosphatase of 149 U/L, whereas tumor markers (CA 19-9 and AFP) were within normal range. The patient underwent partial hepatectomy. An intraoperative examination revealed a 7.5-cm ill-defined mass (Figure 29, A). Frozen section analysis was consistent with carcinoma. Final pathologic diagnosis was adenosquamous carcinoma of the liver. Microscopically, the tumor showed abundant central necrosis with a rim of squamous cell carcinoma constituting 95% of the tumor (Figure 29, B) intermixed with adenocarcinoma and focal intrahepatic high-grade biliary intraepithelial neoplasia (Figure 29, C). A transitional zone between the 2 histologic patterns was identified (Figure 29, D). The squamous component was strongly positive for p63 and the glandular component showed strong positivity for CK19. Postoperative course was uneventful. The patient underwent 5 cycles of 5-fluorouracil and oxaliplatin. In the following 8 months, the patient developed hepatic-colocutaneous fistula and small bowel obstruction. Because of the rarity of this cancer, no therapeutic strategies have been established. Hence it becomes important to report all individual experience-based information.

Identification of a New Hepatocellular Neoplasm in Transplanted Liver
(Poster No. 46)

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Hepatocellular carcinoma (HCC) is the second most common cause of cancer-associated death. Liver transplant is one treatment modality for patients with HCC who are amenable to surgical resection. However, the recurrence rate of HCC after liver transplant is up to 11% at 3 years. The newly developed HCC/hepatic neoplasms in the transplanted liver could be de novo or recurrence from original liver. Knowing the origin of the new tumor in transplanted liver is important for the understanding of the pathogenesis and clinical management of hepatic neoplasms in liver transplant patients. A new hepatocellular neoplasm was identified in a 74-year-old man 4.7 years posttransplant. Histochemical studies (H&E, trichrome, reticulin stains) and immunohistochemistry studies (CK7, CD34, etc) were used to compare the morphology and molecular changes of the original HCC and the newly developed neoplasm in the transplant. Also, tissue blocks of explanted liver and the recent liver mass biopsies were sent to Mayo Clinic Laboratories for specimen source identification. A panel of 12 DNA markers that recognize highly variable regions of human DNA were used in a polymerase chain reaction-based assay to compare the DNA isolated from the 2 tissue resources. The morphology, histology, and immunohistochemistry studies showed that the newly developed neoplasm was different from the original HCC. Genetic results indicated that the newly identified neoplasm was derived from donor tissue, rather than being a recurrence of his prior HCC. Thus, a de novo hepatocellular neoplasm was identified in transplanted liver.

PAX8 Expression in Carcinomas of the Biliary Tract: A Potential Diagnostic Pitfall
(Poster No. 47)

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Context: Paired box protein 8 (PAX8) is a transcription factor expressed in benign and malignant tissues of thyroid, kidney, and the Mullerian system. Expression of PAX8 is regarded as uncommon in biliary tract carcinomas but has not been well studied.

Design: Forty-two primary cholangiocarcinomas with both a clinical and pathologic diagnosis were identified from 2002 to 2017. PAX8 immunohistochemistry with a polyclonal antibody (1:1000; 10336-1-AP, Proteintech) was performed and the results were interpreted by 2 pathologists using the 4-tier system: strong diffuse (>75% of the tumor

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Conclusion: Variable PAX8 expression is detected in one-third of primary cholangiocarcinomas, with strong staining seen in about 5%--15%. Therefore, PAX8 staining in hepatobiliary tumors is not invariably indicative of metastatic disease. High PAX8 expression in biliary tract carcinoma is associated with worse overall survival, may indicate a more aggressive tumor phenotype, and may be a useful prognostic biomarker for cholangiocarcinoma.

WATS Adversely Affects Subsequent Biopsy Evaluation

Poster No. 48

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Context: Barrett esophagus (BE) is a premalignant condition characterized by replacement of normal esophageal squamous mucosa with columnar epithelium. BE is traditionally monitored via endoscopy and forceps biopsies for the presence of dysplasia; however, the sensitivity of this method is limited because of sampling error. Recently, adjunctive sampling via wide-area transepithelial sampling with 3D analysis (WATS), an abrasive brushing technique that renders fullthickness sampling of the epithelium with analysis aided by computer imaging systems, has been shown to increase detection of BE and dysplasia. The order of WATS to traditional targeted and random biopsies has not been reported. Design: Cases having undergone WATS with subsequent biopsy and cases without WATS using forceps biopsy alone were provided by a participating gastroenterologist. Following internal review board approval, the slides were deidentified, randomized, and evaluated by 2 pathologists for quality, as graded by overall intactness of the surface epithelium. Cases were assigned a score from 1 to 3, with score 1 being none/minimal intact surface epithelium and 3 being near-complete intactness.

Results: The average quality score for cases having undergone WATS was 2.24 compared with cases without prior WATS having an average score of 2.54 (P = .049). Conclusions: WATS significantly adversely impacts the quality of subsequent biopsies by disrupting the surface epithelium. Although this may not affect the interpretability of the biopsies overall, we recommend the collection of biopsies prior to brushing.

Grading of Total Mesorectal Excision Specimens: An Interobserver Variability and Quality Assurance Study

Poster No. 49

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Context: Total mesorectal excision (TME) is the standard of care for patients with rectal cancer. The assessment of TME adequacy is a quality assurance measure as it predicts local recurrence risk. There are 3 grades of TME: complete (3), nearly complete (2), and incomplete (1). We sought to compare the assessment of TME grade among surgeons (Ss), pathologists (Ps), and pathologists’ assistants (PAs).

Design: Prospective, blinded grading of TME specimens was performed between November 1, 2017 and February 1, 2019, by the S performing the procedure (CC, FF, LT, JS), at least one pathologist (CWM, ARH), and at least one PA (EAS, LAK). Grades were submitted to one PA who maintained the data. Weighted k (WK) values were used so that a difference between grades 1 and 3 would be weighted as a greater disagreement than between grades 2 and 3.

Results: Thirty-one specimens were examined by each S, at least one P, and one PA. Interobserver variability for all specimens was moderate agreement (WK = 0.525) between PAs, moderate agreement (WK = 0.489) between Ps, slight agreement (WK = 0.199) between Ss and Ps (WK = 0.199), moderate agreement (WK = 0.545) between Ps and PAs, and fair agreement (WK = 0.369) between Ss and Ps (summarized in Table). Conclusions: There are only a few prior studies comparing interobserver variability of grading TME specimens. Most recently, a Canadian group demonstrated interrater reliability between 0.85 and 0.92 among Ps, PAs, pathology residents, and Ss. The worst agreement occurred between Ss and Ps, similar to our study. In the future, the best approach to TME grading may be multidisciplinary consensus.

Pancreatic Neuroendocrine Tumor With Ossification in a Case of Multiple Endocrine Neoplasia Type 1

Poster No. 50

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Multiple endocrine neoplasia (MEN), type I, is a hereditary condition associated with tumors of the parathyroid, pituitary, and pancreatic islet cells. Pancreatic neuroendocrine tumor is a common presentation. A few cases of neuroendocrine tumors with ossification have been reported in lung and stomach; however, to our knowledge, there are no known cases of pancreatic neuroendocrine tumors with ossification reported in literature so far. We report a case of a 34-year-old woman with a medical history of multiple endocrine neoplasia type 1 who presented with a 1.8-cm pancreatic mass that was discovered during screening MRI. Distal pancreatectomy was performed. The specimen was thoroughly and meticulously sectioned. Grossly, a well-circumscribed mass (size 1.3 cm) with tan-yellow homogenous cut surface was identified in pancreatic tail and body. Histologically, the tumor showed desmoplastic stroma with characteristic endocrine cells. Pancreatic neuroendocrine tumor is a common presentation. A few cases of pancreatic neuroendocrine tumors with ossification have been reported in lung and stomach; however, to our knowledge, there are no known cases of pancreatic neuroendocrine tumors with ossification reported in literature so far. We report a case of a 34-year-old woman with a medical history of multiple endocrine neoplasia type 1 who presented with a 1.8-cm pancreatic mass that was discovered during screening MRI. Distal pancreatectomy was performed. The specimen was thoroughly and meticulously sectioned. Grossly, a well-circumscribed mass (size 1.3 cm) with tan-yellow homogenous cut surface was identified in pancreatic tail and body. Histologically, the tumor showed desmoplastic stroma with characteristic endocrine cells.
An Incidental Finding of Helicobacter pylori–Negative Gastric MALT Lymphoma in a Sleeve Gastrectomy Specimen: An Emphasis on Grossing and Sampling Techniques

(Poster No. 51)

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A 54-year-old man underwent a laparoscopic sleeve gastrectomy for morbid obesity. Preoperative physical examination, review of systems, and peripheral blood work did not hint at any evidence of a hematolymphoid malignancy. On gross examination of his gastrectomy specimen, the serosa had a focal area of hemorrhage but there were no masses, ulcers, or other abnormalities (Figure 32, A). Representative sections were taken of the hemorrhagic region, along with several routine random areas of normal mucosa. Other than the focal area of hemorrhage, there was little evidence to indicate an underlying pathologic process or malignancy, as small hemorrhagic areas are common findings in surgical specimens. On histologic examination, sections taken from the hemorrhagic areas showed a diffuse atypical lymphoid infiltrate extending into the lamina propria and submucosa, with nodular pattern and focal germinal centers (Figure 32, B). In addition, there was an associated architectural distortion with gastric glandular atrophy. The lymphoid cells were positive for CD43, BCL-2, and CD20 (Figure 32, C), with β2-microglobulin (Figure 32, D). They were negative for CD5, CD23, CD138, BCL-6, and cyclin D1. The proliferation index by Ki-67 was low (1–5%). Helicobacter pylori stain on 3 of the blocks was negative. With these histologic findings, the patient was diagnosed with an incidental mucosal-associated lymphoid tissue (MALT) lymphoma. In conclusion, our case emphasizes the importance of examining surgical specimens both macroscopically and microscopically for the identification of incidental malignant findings in asymptomatic patients. In addition, it is imperative to perform representative sampling on these specimens.

A 54-year-old man underwent a laparoscopic sleeve gastrectomy for morbid obesity. Preoperative physical examination, review of systems, and peripheral blood work did not hint at any evidence of a hematolymphoid malignancy. On gross examination of his gastrectomy specimen, the serosa had a focal area of hemorrhage but there were no masses, ulcers, or other abnormalities (Figure 32, A). Representative sections were taken of the hemorrhagic region, along with several routine random areas of normal mucosa. Other than the focal area of hemorrhage, there was little evidence to indicate an underlying pathologic process or malignancy, as small hemorrhagic areas are common findings in surgical specimens. On histologic examination, sections taken from the hemorrhagic areas showed a diffuse atypical lymphoid infiltrate extending into the lamina propria and submucosa, with nodular pattern and focal germinal centers (Figure 32, B). In addition, there was an associated architectural distortion with gastric glandular atrophy. The lymphoid cells were positive for CD43, BCL-2, and CD20 (Figure 32, C), with β2-microglobulin (Figure 32, D). They were negative for CD5, CD23, CD138, BCL-6, and cyclin D1. The proliferation index by Ki-67 was low (1–5%). Helicobacter pylori stain on 3 of the blocks was negative. With these histologic findings, the patient was diagnosed with an incidental mucosal-associated lymphoid tissue (MALT) lymphoma. In conclusion, our case emphasizes the importance of examining surgical specimens both macroscopically and microscopically for the identification of incidental malignant findings in asymptomatic patients. In addition, it is imperative to perform representative sampling on these specimens.
Context: Less than 3% of pancreatic ductal adenocarcinoma (PDA) patients are ≤45 years old (very-early-onset pancreatic cancer [VEOPC]) and rarely carry germline mutations. Limited data exist on the underlying molecular pathways and its potential impact in management and survival. This study aims to characterize clinicopathologic features and molecular alterations in VEOPC.

Design: Cases were identified through retrospective pathology database search. Patients <45 years old (VEOPC) with available clinical data, H&E-stained slides, and paraffin blocks were included. A matched population of PDA in older patients (>45 years) was selected. Molecular profiles were available in a subset of cases; additional molecular characterization of the remaining cases is being completed.

Results: Summarized findings are shown in the Table. There were no definitive associations between known risk factors, histopathologic features, and VEOPC, except poor differentiation of the tumors. VEOPC showed a greater diversity of molecular alterations in all 4 cases tested in comparison with the known TTP3 and KRAS mutations in the matched control. VEOPC was associated with a reduced number of living patients and had a worse overall survival.

Conclusions: Known risk factors and histopathologic parameters were not different among the cases studied and matched controls with the exception of histologic tumor grade. VEOPC cases revealed greater diversity of molecular alterations and shorter survival. The study suggests that perhaps the greater complexity of the underlying molecular alterations in VEOPC may explain worse tumor differentiation and may have an impact on overall survival.

Elimination of Upfront Helicobacter pylori Immunohistochemistry Leads to Decreased Detection Rates

(Poster No. 53)

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Context: Helicobacter pylori (HP) is a class I carcinogen responsible for gastrointestinal ulcers and malignancies. Although many American laboratories performed upfront staining for detection, we have ceased this practice secondary to CMS reimbursement changes and practice recommendations put forth by the Rodger C. Hagitt Gastrointestinal Pathology Society. We studied the effect of this change on our HP detection rate.

Design: We retrospectively analyzed the rate of HP detection before and after the practice change (2011–2013 and 2016–2018, respectively). The first 500 patients from each time frame were analyzed to assure significant differences in M:F ratio or race ($p = 1$, $P = .6$). The HP detection rate dropped by 53.8% during the study period (10.4% to 4.6%). Available histology demonstrated postimplementation cases to more frequently have moderate to marked neutrophils and atrophy, intestinal metaplasia, and plasma cell–predominant inflammation. The study supported the Rodger C. Hagitt recommendations put forth by the Rodger C. Hagitt Gastrointestinal Pathology Society.

Conclusions: Reimbursement and practice changes negatively affected our practice. The HP detection rate decreased by more than half postimplementation, suggesting an increased risk of undetected infection. Postimplementation cases demonstrate more typical histology patterns, including more plasmacytic and neutrophilic inflammation and intestinal metaplasia, whereas other patterns (lymphocyte predominant) are likely underrecognized.

Ciliated Foregut Cyst of the Pancreas: A Differential Diagnosis to Consider in the Diagnosis of Pancreatic Cystic Lesions

(Poster No. 55)

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Foregut cysts are benign congenital malformations that originate from the primitive foregut. They are commonly seen in the mediastinum and can occur anywhere along the gastrointestinal tract. However, pancreatic foregut cysts are very rare, with only a few cases reported in the literature. We report a case of a 44-year-old woman who presented with intermittent abdominal pain for 2 weeks. Abdominal CT scans revealed a fluid attenuation focus in the pancreas measuring 7.1 cm and demonstrating septations with calcifications (Figure 33, A). The mass was resected along with a splenectomy (Figure 33, B). Histopathologic examination of the mass showed a multicystic lesion with surrounding atrophic pancreatic tissue and calcifications (Figure 33, C). The cysts had a ciliated epithelial lining that was cuboidal to columnar with areas associated with immunity modulation that potentially can affect various organs/functions, especially the gastrointestinal tract, with manifestations ranging from self-limited diarrhea to colitis. Steroids are the first-line remedy for immunotherapy-related adverse events. However, steroids are associated with reactivation of opportunistic pathogens and complicated clinical courses. A 65-year-old man was managed with nivolumab for stage 4 small cell carcinoma of the lung and developed immunotherapy-induced diarrhea. Subsequently steroids were administered with partial symptom resolution. However, 3 weeks later the patient returned with worsening diarrhea and abdominal cramping refractory to medical management. Imaging, endoscopy, and pathology investigations were conducted. Radiology and colonic endoscopy findings were unremarkable; random colon biopsies were performed. The differential diagnosis was vast given the worsening gastrointestinal symptoms and preceding immunotherapy-related diarrhea. Though difficult, it is crucial to distinguish the etiologies as the management differs. Microscopic examination revealed architecturally intact colonic mucosa with peculiar apical basophilic epithelial fringes, the so-called false brush border, highlighted by Warthin–Starry stain, with minimal inflammation identified. These findings were highly consistent with enterocolonic spirochetosis. Metronidazole was administered, followed by quick resolution of the patient’s symptoms. This case highlights the novel presentation of symptomatic spirochetosis, manifested by spirochete-colonizing gastrointestinal epithelium, and the importance of a timely diagnosis in minimizing patient morbidity/mortality. Steroid administration–associated spirochetosis and immunotherapy-related gastrointestinal adverse events share similar clinical pictures, yet the involved mechanisms are different. Therefore, the implicated diagnostic workup, therapeutic strategies, and corresponding clinical courses are distinct.

Clinically Unsuspected Enterocolonic Spirochetosis Following Steroid Management of Immuno-therapy-Induced Diarrhea in a Lung Cancer Patient

(Poster No. 54)

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Immunotherapy targeting programmed cell death-1 has expanded rapidly for managing advanced malignancies. Of note, immunotherapy is associated with immunity modulation that potentially can affect various organs/functions, especially the gastrointestinal tract, with manifestations ranging from self-limited diarrhea to colitis. Steroids are the first-line remedy for immunotherapy-related adverse events. However, steroids are associated with reactivation of opportunistic pathogens and complicated clinical courses. A 65-year-old man was managed with nivolumab for stage 4 small cell carcinoma of the lung and developed immunotherapy-induced diarrhea. Subsequently steroids were administered with partial symptom resolution. However, 3 weeks later the patient returned with worsening diarrhea and abdominal cramping refractory to medical management. Imaging, endoscopy, and pathology investigations were conducted. Radiology and colonic endoscopy findings were unremarkable; random colon biopsies were performed. The differential diagnosis was vast given the worsening gastrointestinal symptoms and preceding immunotherapy-related diarrhea. Though difficult, it is crucial to distinguish the etiologies as the management differs. Microscopic examination revealed architecturally intact colonic mucosa with peculiar apical basophilic epithelial fringes, the so-called false brush border, highlighted by Warthin–Starry stain, with minimal inflammation identified. These findings were highly consistent with enterocolonic spirochetosis. Metronidazole was administered, followed by quick resolution of the patient’s symptoms. This case highlights the novel presentation of symptomatic spirochetosis, manifested by spirochete-colonizing gastrointestinal epithelium, and the importance of a timely diagnosis in minimizing patient morbidity/mortality. Steroid administration–associated spirochetosis and immunotherapy-related gastrointestinal adverse events share similar clinical pictures, yet the involved mechanisms are different. Therefore, the implicated diagnostic workup, therapeutic strategies, and corresponding clinical courses are distinct.
showing stratification, and the cyst walls consisted of spindled smooth muscle (Figure 33, D). These findings were consistent with a foregut cyst. Pancreatic foregut cysts have nonspecific clinical presentations, mimicking true cysts of the pancreas, pancreatic pseudocysts, or even pancreatic cystic neoplasms. Distinguishing them from other cystic lesions can be difficult because they have very similar clinical and radiologic features. Fine-needle aspiration demonstrating ciliated epithelium is said to be sufficient for preoperative diagnosis. However, definitive diagnosis is usually made based on histopathologic examination after resection. This case highlights the importance of considering ciliated foregut cysts in the differential diagnosis of cystic lesions occurring in the pancreas.

**Follicular Pancreatitis, a Recently Described Variant of Chronic Pancreatitis Masquerading as Mucinous Cystic Neoplasm**

(Poster No. 56)

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Follicular pancreatitis is a rare entity of the pancreas, which is characterized histologically by prominent lymphoid follicles with reactive germinal centers. Herein we report a case of follicular pancreatitis presenting in a 69-year-old woman who had been followed since 2016 for a slowly enlarging cystic mass of the pancreatic tail without communication to the main pancreatic duct. CT scan showed a 29 × 21-mm single-compartment lesion without septa and a thin outer wall. Endoscopic ultrasound was performed in January 2019. At that time CEA and amylase levels of the cyst were drawn, which were 517 and 29, respectively. Because of this, a diagnosis of mucinous cystic neoplasm was made, and the patient had a distal pancreatectomy and IPN, respectively. Because of this, a diagnosis of mucinous cystic neoplasm was made, and the patient had a distal pancreatectomy and IPN, respectively. Because of this, a diagnosis of mucinous cystic neoplasm was made, and the patient had a distal pancreatectomy and IPN, respectively.

ROR1 Expression by Immunohistochemistry in Biliary Tract Carcinomas

(Poster No. 57)

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**Context:** Biliary tract carcinomas, including gallbladder carcinoma and cholangiocarcinoma, are aggressive malignancies needing more effective treatment. Receptor tyrosine kinase–like orphan receptor 1 (ROR1) is highly expressed in various malignancies with minimal expression in normal adult tissues, making it an attractive immunotherapy target. In this study, we analyzed expression of ROR1 by immunohistochemistry in this subset of tumors and compared it with various clinicopathologic features.

**Design:** A total of 110 cases of biliary tract carcinomas resected between 2000 and 2014 were identified at our institution. Tissue microarrays were constructed using 1-mm duplicate cores, immunostained for ROR1 (dilution 1:7; cat# 564464, BD Biosciences), and scored for staining intensity (0–3) and percentage tumor cell staining. H-scores were calculated (intensity × percentage: low 0–1; moderate >1–2; high >2–3) and compared with clinicopathologic features available for 73 cases. Statistical analysis was performed using Fisher exact test and Student t test.

**Results:** Moderate to high expression was seen in 94.5% (69 of 73) of cases. All well-differentiated carcinomas (4 of 4) showed moderate to high expression. Seventy-five percent of cases with low expression (3 of 4) were poorly differentiated carcinomas. There were no significant differences between moderate- and high-staining groups with regard to origin, tumor size, age, gender, grade, or prevalence of lymphovascular invasion, perineural invasion, or nodal metastasis at the time of resection (P = .07 to >.99).

**Conclusions:** Moderate to strong ROR1 expression by immunohistochemistry was present in most biliary tract carcinomas, suggesting ROR1 could be a potential target for therapy in these malignancies. There was no significant correlation between ROR1 expression and other clinicopathologic data analyzed.

**Primary Pancreatic Gastrointestinal Stromal Tumor: A Rare Case Report and Review of the Literature**

(Poster No. 58)

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Primary pancreatic gastrointestinal stromal tumor (GIST) is exceedingly rare. A 52-year-old woman presented with abdominal pain and a 7-cm mass was seen in the pancreatic head (Figure 35, A). Subsequent endoscopic ultrasound-guided fine-needle aspiration biopsy showed a spindle cell neoplasm (Figure 35, B) diffusely positive for CD117, consistent with GIST. Tumor size remained the same despite treatment with imatinib, and a pancreaticoduodenectomy was performed. The
scores were seen in 73% of LVI percent had high H scores, with 71% of these showing LVI. Low H (18 versus 33 mm, were associated with smaller tumor size compared with low H scores. No differences in marker expression were seen in GBCs versus CCs.

e22 associated with poorly differentiated tumors (73%;

to distinguish GBCs from CCs.

to moderate SRC expression appeared to be an adverse factor, whereas

Differentiated tumors whereas high CDH17 expression was associated

differentiated tumors. High CDH17 expression was associated with smaller tumor size, suggesting utility as a prognostic marker. Low

data. Design: A total of 110 resections were identified at our institution (2000–2014). Tissue microarrays were constructed; immunostained for

Correlation with clinicopathologic data.

Our study is the first to evaluate the expression of SRC, CDH17, and c-MYC in gallbladder carcinomas and cholangiocarcinomas by immunohistochemistry.

Expression of SRC, CDH17, and c-MYC in Gallbladder Carcinomas and Cholangiocarcinomas by Immunohistochemistry

Poster No. 59

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Context: We previously identified mutations of SRC in gallbladder carcinomas (GBCs) and cholangiocarcinomas (CCs). We sought to characterize expression of SRC in these tumors by immunohistochemistry, in addition to CDH17 and c-MYC, and correlate with clinicopathologic data.

Design: A total of 110 resections were identified at our institution (2000–2014). Tissue microarrays were constructed; immunostained for SRC (1:600; Abcam), CDH17 (1:450; Novus Biologicals), and c-MYC (1:100; Cell Marque); graded by H score (staining intensity × percentage tumor staining); and correlated with data available for 73 cases. Statistical analysis was performed using Fisher exact test and Student t test.

Results: For SRC, 77% had moderate to high H scores; 91% of poorly differentiated tumors had low to moderate H-scores. Low to moderate H scores were associated with poorly prognostic factors: 83% lymphovascular invasion (LVI+), 80% perineural invasion (PNI+); 81% lymph node metastases (LN+). For CDH17, low H scores were associated with poorly differentiated tumors (73%; P = .02) and poor prognostic factors (79% LVI+, 72% PNI+, 73% LN+). High H scores were associated with smaller tumor size compared with low H scores (18 versus 33 mm, P = .02). For c-MYC, 68% had low H scores. Ten percent had high H scores, with 71% of these showing LVI. Low H scores were associated with perineural invasion (PNI+), lymph node metastases (LN+), and 73% of LN+ cases. No differences in marker expression were seen in GBCs versus CCs.

Conclusions: Low CDH17 expression was associated with poorly differentiated tumors whereas high CDH17 expression was associated with smaller tumor size, suggesting utility as a prognostic marker. Low H scores were associated with high-risk tumors. SRC expression appeared to be an adverse factor, whereas overexpression of c-MYC was not significant. No markers were useful to distinguish GBCs from CCs.

Solid Pseudopapillary Neoplasm of the Pancreas With Pleomorphic Degenerative Changes in a Male Patient

Poster No. 60

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Solid pseudopapillary neoplasm (SPN) of the pancreas is a rare entity with low-grade malignant potential and accounts for less than 3% of all pancreatic exocrine tumors. Most cases occur in young females and as a rare entity. A 46-year-old man presented with left abdominal pain for a year. Computed tomography scan revealed a 5.7-cm solid and cystic pancreatic mass. Endoscopic ultrasound-guided fine-needle aspiration revealed clusters of uniform small cells in a hemorrhagic background. These cells had little pleomorphism, fine chromatin, and pale cytoplasm. Cell block displayed loosely cohesive, round to oval uniform cells with inconspicuous nuclei, surrounding rare thin delicate vascular cores (Figure 36, A). The neoplastic cells were positive for β-catenin, vimentin, CD56, and CD10, and negative for CK7, CK20, progesterone receptor, S-100, trypsin, and chymotrypsin.

Microscopic examination of the subsequent distal pancreatectomy showed solid and pseudopapillary growth patterns (Figure 36, B). Degenerative changes with extensive necrosis and hemorrhage were seen, along with areas of pleomorphic and atypical multinucleated giant cells (Figure 36, C). β-catenin showed aberrant nuclear immunoreactivity (Figure 36, D). The presence of atypical or multinucleated giant cells appears to have no prognostic significance and is considered a degenerative change. Our case highlights the importance of including SPN in the differential diagnosis in a male patient with complex pancreatic lesion and incorporating immune studies to achieve an accurate diagnosis. It was previously suggested that SPN in males can behave more aggressively. It is worthwhile to have interval follow-up on this patient population because ~15% of SPNs have the potential for malignant transformation.

Gastric Mixed Adenoneuroendocrine Carcinoma: A Rare Yet Aggressive Entity That Is Frequently Underdiagnosed

Poster No. 61

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Context: Gastric mixed adenoneuroendocrine carcinoma (MANEC) is a rare entity associated with aggressive clinical course and ominous patient outcome. Histomorphologically, MANEC tumors mimic “simple” carcinomas frequently, posing significant diagnostic challenges. A missed MANEC diagnosis is detrimental to patient management and prognosis.

Design: Until now only limited gastric MANEC cases were reported, with a spectrum of histopathologic heterogeneity. To determine the main diagnostic challenges, the histomorphologic and immunophenotypic profiles of gastric MANECs in our institute during a 5-year span were reviewed.

Results: A total of 8 gastric MANECs were retrieved, including 2 originally misclassified. The first missed MANEC was diagnosed adenocarcinoma without essential immunohistochemical investigation; this tumor was composed of small or intermediate-sized cells with scant cytoplasm and fusiform nuclei with granular chromatin and inconspicuous nucleoli. The second missed MANEC was called poorly differentiated neuroendocrine carcinoma, however, the glandular structures and mucin component were overlooked. Immunostains showed positive synaptophysin (7 of 8), chromogranin (4 of 6), and CD56 (7 of 7) in neuroendocrine components, whereas the adenocarcinoma portions were positive for CEA (3 of 5), pan-cytokeratin (5 of 5), and CK7 (5 of 5) but negative for neuroendocrine markers.

Conclusions: MANECs are defined as containing at least 30% of both neuroendocrine and adenocarcinoma components. The proportions and behavior of both components influence the management and patient outcome, and deserve close attention, as MANECs are aggressive tumors with rapid progression. It is pivotal to carefully
An Unusual Gastric Poorly Differentiated Adenocarcinoma Mimicking Lymphoepithelioma-like Carcinoma in a 21-Year-Old Woman

(Poster No. 63)

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Poorly differentiated gastric adenocarcinomas (PDGACs) possess clinicopathologic diversity. Here we describe an unusual case of PDGAC associated with an intense and accentuated lymphocytic infiltrate, features characteristically seen in lymphoepithelioma-like gastric carcinoma (LLGC), in a young woman. A 21-year-old woman presented to our hospital for second opinion because of worsening epigastric pain and anemia, with an original outside diagnosis of erosive hemorrhagic gastritis. Limitis plastica with malignant ascites and nodal metastasis was suspected upon endoscopy- and ultrasonography-guided rebiopsy. Microscopically, the rebiopsy showed sheets of round to polygonal neoplastic cells with poorly defined cell borders, large nucleoli, and prominent eosinophilic cytoplasm, intersecting with a dense lymphocytic population. Immuno-histochemistry labeled these cells with pankeratin, CD20, and intact CD79a, with a strongly positive reaction for EBV-encoded small RNA-1 (EBER) and CD20. These findings in this PDGAC case mimic features typically seen in LLGC. Our patient was not a surgical candidate because of advanced disease stage; modified chemotherapy was initiated following next-generation sequencing. In contrast to LLGC, PDGAC is associated with an ominous clinical course and survival rate; a misclassification of these 2 could bring detrimental consequences to patients. Indeed, a definitive diagnosis of LLGC was not established in this biopsy based on these intriguing histology and aggressive disease progression. An accurate diagnosis should rest on systematic histomorphology and ancillary testing, combined with clinical and laboratory evidence. The mismatch repair proteins status and molecular profile of the tumor essentially play key roles in clinical decision making.

Assessment of Perineural Invasion in Low-Grade Stage IIA Colon Cancer Using AE1/3/S100 Dual Immunohistochemical Staining

(Poster No. 64)

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Context: Perineural invasion (PNI) is an independent adverse prognostic factor in colon cancer and may be an indication for chemotherapy. This study investigated the utility of AE1/3/S100 dual immunohistochemical (IHC) staining in the assessment of PNI in low-grade stage IIA colon adenocarcinoma.

Design: The pathology database (2001–2016) was queried for low-grade stage IIA colon carcinoma. A total of 134 cases were identified with a mean age of 69.8 years (33–88), 43 from the left and 91 from the right colon. Dual AE1/3/S100 IHC was performed. H&E and IHC slides were independently reviewed by 3 pathologists to assess PNI and interobserver variability.

Results: In the original pathology reports, PNI was identified in 9 cases (6.7%), indeterminate in 2 (1.5%), negative in 106 (79%), and not
Assessment of Lymphovascular Invasion in Low-Grade Stage IIA Colon Cancer Using CDX2/CD31 Dual Immunohistochemical Staining

(Qingzhao Zhang, MD, PhD1; Guang Chen, MD, PhD2; Zhaohai Yang, MD, PhD3; Guoli Chen, MD, PhD1; Richard Judelson, MD, PhD4; Richard Judelson, MD; Xiaoqin Zhu, MD; Xiaofei Wang, MD, PhD5; Richard Judelson, MD; Xioqin Zhu, MD; Xiaofei Wang, MD, PhD5; Richard Judelson, MD; Xiaoqin Zhu, MD; Xiaofei Wang, MD, PhD5)

Context: Lymphovascular invasion (LVI) in stage IIA colon cancer is associated with a worse prognosis and is an indication for chemother-apy. This study investigated the utility of CDX2/CD31 dual immuno- histochemical staining (IHC) in LVI assessment in low-grade stage IIA colon adenocarcinoma.

Design: The pathology database (2001–2016) was queried for low-grade stage IIA colon carcinoma. A total of 115 cases were identified with a mean age of 69.5 years (33–88); 43 were from the left and 72 from the right colon. CDX2/CD31 IHC was performed. H&E and IHC slides were independently reviewed by 3 pathologists to assess LVI and interobserver variability.

Results: In the original report, LVI was identified in 21 (18.3%), indeterminate in 12 (10.4%), negative in 80 (69.6%), and not mentioned in 2 cases. Upon independent review of H&E slides, complete agreement among 3 pathologists was reached in 79 cases (68.7%): 4 (3.5%) positive and 75 (65.2%) negative for LVI. At least one observer called indeterminate and positive in 21 (18.3%) and 22 (19.1%), respectively. By CDX2/CD31 dual IHC, the 3 pathologists had complete agreement in 105 cases (91.3%): 5 (4.3%) positive and 100 (87%) negative. At least one observer called indeterminate and positive for LVI in 7 (6.1%) and 10 cases (8.7%), respectively. The Fleiss k for interobserver agreement on IHC was moderate (k = 0.59) (Figure 39).

Conclusions: Compared with H&E, CDX2/CD31 IHC reduced the number of cases considered indeterminate or positive for LVI. The IHC showed improved interobserver reproducibility, with only 4.3% cases being considered positive for LVI.

Pancreatic Neuroendocrine Tumor With Main Pancreatic Duct Invasion

(Sepideh Madahian, MD; Richard Judelson, MD; Xiaoqin Zhu, MD; Xiaofei Wang, MD, PhD)

Intraductal extension of pancreatic neuroendocrine tumors (PNETs) is a rare growth pattern. Only 9 PNETs with this growth pattern have been reported. We recently identified 2 cases of PNETs invading into the main pancreatic duct (MPD). Two cases were obtained with imaging finding of distal pancreatic lesions. Fine-needle aspiration confirmed diagnosis of PNETs, which led to distal pancreatectomies. Case 1 involves a 78-year-old man who presented with abdominal pain and elevated lipase (>600 U/L). Endoscopic ultrasound showed a hypoechoic mass in the distal pancreatic body and hyperechoic walls in the MPD. Grossly, the pancreatic mass (6.3 cm) filled and obstructed the MPD. Microscopically, the tumor showed invasion into the MPD, and intrapancreatic and extrapancreatic large veins. Case 2 involves a 51-year-old woman who presented with abdominal pain. Endoscopic ultrasound showed a hypoechoic mass in the tail of the pancreas. Grossly, the pancreatic mass (4.1 cm) extended into the MPD. Microscopically, both cases were confirmed by Ki-67, synapto-physin, and chromogranin immunostains to be well-differentiated PNETs, grade 2, showing invasion into the MPD (Figure 40, A and B). Both tumors were negative for glucagon, gastrin, and somatostatin. There is no evidence of recurrence and metastatic disease after 3–month postsurgical follow-up in either case. It is noted that well-differentiated PNETs can have MPD and large vein invasion. However, the clinical outcome of patients with this presentation is yet to be determined.

Primary retroperitoneal mucinous cystic neoplasm (PRMCN) is extremely rare, and its etiology, pathogenesis, and prognosis remain unclear, with histology being similar to that of ovarian or pancreatic counterparts. We herein report an unusual case of PRMCN with malignant transformation leading to multifocal invasive adenocarcinoma from our institution. The patient was a 23-year-old overweight woman presenting with fever, nausea, vomiting, and abdominal pain who on imaging was found to have a 17-cm cystic lesion in the right midabdomen exerting mass effect on the liver and right ureter. She underwent right hemicolectomy and en bloc resection of a retroperitoneal mass with a subsequent pathologic diagnosis of multifocal invasive moderately to poorly differentiated adenocarcinoma arising in a primary mucinous cystic neoplasm with low- and high-grade dysplasia of retroperitoneum. The adenocarcinoma was invading through the mucinous cyst wall with fistula tract formation and intestinal serosa and into muscularis propria of small and large intestine. Immunohistochemically tumor cells were positive for CK7, pankeratin, and MOC-31 with high Ki-67 proliferative index, and
negative for CK20, CDX-2, PAX-8, TTF-1, calretinin, and WT1. Subsequent thorough oncologic, radiologic, and tumor-marker workup failed to identify any primary tumors in our patient with 12 months' surveillance after surgery being recurrence free. There are no pathognomonic clinical or radiologic findings for primary retroperitoneal mucinous cystic neoplasm, making the preoperative diagnosis challenging. Delay in diagnosis and treatment may lead to complications such as rupture, infection, and malignant transformation, as in our case. Surgical resection and pathology report are crucial to facilitate accurate diagnosis and treatment.

An International Effort to Diagnose a Rare Entity—Neuroendocrine Tumor in the Liver in a Young Ethiopian Woman

(Poster No. 68)

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Primary well-differentiated neuroendocrine tumors (WD-NET) of the liver are exceedingly rare, and liver metastasis in a young patient is also rarely reported. We present a case of probable metastatic WD-NET, World Health Organization grade II, in the liver of an otherwise healthy 26-year-old Ethiopian woman. The patient complained of vague right upper quadrant abdominal pain and was found to have a 20 × 16 × 9-cm, well-delineated, partially cystic and solid mass in the right lobe of the liver by CT scan. The lesion was an assumed hepatic adenoma given her history of taking oral contraceptives. The mass was resected and the tissue was histologically examined by hematoxylin and eosin staining. Morphologically, the tumor appeared as sheets of crowded cells with areas of pseudopapillary configuration with occasional pseudosarotie formation and areas of necrosis. The cells appeared to have ample pink cytoplasm without definitive cell borders and low-grade nuclei with a vesiculated and “salt-and-pepper” chromatin pattern (Figure 41, A and B). Immunohistochemistry revealed the tumor was strongly positive for chromogranin (Figure 41, C) and synaptophysin. CDX-2 showed weak positivity (Figure 41, D) and Ki-67 was approximately 5%. Because of the limited ancillary testing methods available at the Ethiopian laboratory, 2 US-based pathology institutions worked with the laboratory to make a diagnosis. Because of this multi-institutional and international collaboration, the patient will receive further workup to determine if this lesion represents a primary or metastatic tumor.

Intracholecystic papillary-tubular neoplasm (ICPN) is a rare neoplasm of the gallbladder. The association of ICPN and primary sclerosing cholangitis (PSC) is extremely rare. Herein, we report such a case of a patient with long-standing PSC and ICPN, pyloric gland subtype with various metastatic features. A 48-year-old man with history of ulcerative colitis and PSC cirrhosis was incidentally found to have a 0.5-cm polyp in the gallbladder during routine endoscopic retrograde cholangiopancreatography that remained stable for 6 years until a recent MRI showed a new indeterminate 1.5-cm gallbladder lesion. Follow-up ultrasound revealed a hypoechoic, multilobulated vascular lesion with infoldings. A cholecystectomy was performed. On gross examination, a 0.8-cm polyp on the gallbladder fundus along with multiple detached friable fragments in the lumen was identified. Histologically, the lesion showed a papillary-tubular architecture with a fibrovascular core, findings consistent with ICPN. No invasive carcinoma was identified. The background showed chronic cholecystitis with pyloric gland metaplasia demonstrating mixed classic, inverted nuclei and Paneth cell types (Figure 42, A through D). Immunohistochemistry showed the ICPN and background pyloric gland metaplastic epithelium to be strongly positive for MUC-6, whereas MUC5AC was weakly positive and MUC-1 and MUC-2 were negative, ruling out biliary and intestinal subtypes. Among the different ICPN phenotypes, the pyloric gland type has the lowest risk for malignant transformation. This unique case of an ICPN arising in a patient with UC and PSC cirrhosis confirms the importance of close clinical follow-up with imaging followed by surgery when needed and appropriate immuno-histochemical studies to guide patient management.

Clinicopathologic Features of Metastatic Small Cell Carcinoma of the Prostate to the Liver: A Series of 4 Cases

(Poster No. 70)

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Context: Small cell carcinoma of the prostate makes up approximately 0.5% to 2% of all prostate carcinomas. It is an aggressive subtype with a poor prognosis and overall decreased survival. Neuroendocrine differentiation within prostatic adenocarcinoma has been demonstrated to be hormone independent; thus, most small cell carcinomas occur in patients with conventional prostate adenocarcinoma following androgen deprivation therapy.
Design: Four patients with prostate adenocarcinoma treated with androgen deprivation therapy, which evolved to small cell carcinoma with liver metastasis, were identified from departmental archives for 2018. Slides were reviewed and clinicopathologic variables were analyzed.

Results: The average age at liver metastasis was 73 years (range, 68–76 years). Two patients developed liver metastasis more than a decade following initial diagnosis, whereas 2 presented with advanced prostate cancer shortly prior to liver metastasis. Histologically, all liver lesions were composed of nests of cells with high nuclear to cytoplasmic ratios, granular chromatin, and frequent mitoses. All cases were synaptophysin, chromogranin, and AE1/AE3 positive and had a Ki-67 labeling index of ≥70% of neoplastic cells. NKX3.1 was negative in all but one case, which demonstrated only weak positivity. Prostate-specific antigen (PSA) levels were normal to near normal in all patients. Three of 4 patients died after the diagnosis of liver metastasis.

Conclusions: Our case series highlights the importance of considering a prostate primary, even in the setting of normal PSA levels and loss of prostate immunohistochemical markers, when diagnosing a metastatic neuroendocrine lesion in the liver. Additionally, when small cell carcinoma of the prostate metastasizes to the liver, it portends a particularly dismal prognosis.

Positive Antimitochondrial Antibodies in Patients With No Histologic Evidence of Primary Biliary Cholangitis on Liver Biopsy: A Rare Scenario Observed in a Series of 5 Patients

(Poster No. 71)

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<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age, y/Sex</th>
<th>Abnormal Laboratory Results</th>
<th>Comorbidities</th>
<th>Liver Biopsy Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>19/M</td>
<td>AMA (30.3 units) ALT (78 IU/L)</td>
<td>DM, obesity (BMI = 45)</td>
<td>SH (grade 1, stage 1)</td>
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<tr>
<td>2</td>
<td>42/M</td>
<td>AMA (33.2 units) ALT (138 IU/L)</td>
<td>DM, obesity (BMI = 37)</td>
<td>SH (grade 2, stage 3)</td>
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<td>57/F</td>
<td>AMA (44.9 units) ALT (89 IU/L) AST (86 IU/L)</td>
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<td>SH (grade 2–3, stage 3)</td>
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<tr>
<td>4</td>
<td>68/M</td>
<td>AMA (30.2 units) ALP (339 IU/L)</td>
<td>Pancreatic adenocarcinoma</td>
<td>Macrolucent steatosis, stage 2–3 fibrosis</td>
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<tr>
<td>5</td>
<td>79/M</td>
<td>AMA (45.5 units) ALP (190 IU/L) AST (42 IU/L)</td>
<td>Bile duct stone</td>
<td>Macrolucent steatosis, stage 2–3 fibrosis</td>
</tr>
</tbody>
</table>

Summary of results

n = 5  Mean age = 53 y (range, 19–79 y); male 4/5, female 1/5

Characteristics of Patients With Positive AMA Serology and No Histologic Evidence of PBC

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; BMI, body mass index; DM, diabetes mellitus; SH, steatohapatitis. a Normal values: AMA, <25 units; ALT, <55 IU/L; AST, <34 IU/L; ALP, <150 IU/L; BMI, <25. b 2 of 3 criteria (ALP, AMA, histologic evidence of PBC) must be present for diagnosis of PBC. c Denotes required criterion for diagnosis of PBC.

Context: Primary biliary cholangitis (PBC) is a chronic autoimmune liver disease characterized by the destruction of interlobular bile ducts leading to the development of cholestasis and progressive liver damage. Elevated alkaline phosphatase, positive antimitochondrial antibodies (AMA), and histologic evidence of PBC are diagnostic features of PBC seen in patients without extrahepatic biliary obstruction or comorbidities affecting the liver. This series aims to describe clinicopathologic features of rare patients who present with positive AMA but without histologic features of PBC.

Design: Five liver biopsies obtained from patients with positive AMA that showed no histologic evidence of PBC were reviewed (August 2017–February 2019) and clinicopathologic characteristics were analyzed.

Results: All patients underwent liver biopsy to exclude the presence of PBC due to positive AMA serology (Table). All 5 had comorbidities that affect the liver, none known to cause positive AMA. A male-predominant patient series (4:1) ranged in age from 19 to 79 years. Histologic features of PBC, such as nonsuppurative destructive cholangitis, florid-duct lesion, or destruction of interlobular bile ducts/ductopenia, were not seen. Biopsies from all patients displayed nonalcoholic fatty liver disease (steatosis/steatohepatitis) accompanied with varying degrees of fibrosis.

Conclusions: Although highly suspicious for PBC, positive AMA serology may be seen in patients who show no histologic evidence of PBC, as seen in our patient series. Exclusion of false-positive results and rare conditions that may cause positive AMA serology other than PBC is necessary. Because sole AMA positivity reportedly may indicate significant risk of developing active PBC in succeeding years, clinical follow-up of these rare patients is warranted.

Renal Cell Carcinoma With Gastric Metastasis: A Rare Cause of Gastrointestinal Bleeding

(POSTER No. 72)

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Gastrointestinal bleeding is a clinical manifestation that often requires intervention with biopsy and histologic examination because of the possibility of an underlying malignancy. However, metastasis to the stomach is uncommon, with an occurrence of up to 0.7% in various neoplasms. We present a case of a 91-year-old man who presented with gastrointestinal bleeding and underwent esophagogastroduodenoscopy that revealed a 0.9 × 0.6 × 0.5-cm gastric polyp. It consisted of malignant tumor cells with nested growth patterns of clear cells with areas of hemorrhage (Figure 43, A and B). Typical morphology for a gastric neoplasm was not seen. Tumor cells within tissue were positive for vimentin, PAX-8 (nuclear) (Figure 43, C), and AE1/3. Tumor cells were negative for CK7 (D), CK20, CD10, and CD68. The morphology and immunohistochemical findings supported the diagnosis of meta-
A Case of Dubin-Johnson Syndrome Presenting as Neonatal Cholestasis With Paucity of Interlobular Bile Ducts

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Dubin-Johnson syndrome is an autosomal-recessive disorder that typically presents as jaundice in young adulthood. Mutations in the ABCC2 gene, which encodes the MRPs2 transporter, lead to impaired hepatic biliary excretion, conjugated hyperbilirubinemia, and black discoloration of the liver. We report an unusual case presenting as neonatal cholestasis with paucity of interlobular bile ducts. Following an uncomplicated pregnancy and delivery, a newborn female was noted to have conjugated hyperbilirubinemia since birth. On the seventh day of life, total bilirubin was 17.26 mg/dL (reference range, 0.1-1.3 mg/dL) with a direct bilirubin of 6.38 mg/dL (reference range, 0.0-0.3 mg/dL); γ-glutamyltransferase was 1333 U/L (reference range, 2-151 U/L), and serum aminotransferase levels were within normal limits. At 6 weeks of age, a liver biopsy was performed and revealed cholestasis with ductular proliferation and a paucity of interlobular bile ducts. Endoscopic retrograde cholangiopancreatography demonstrated an intact intrahepatic and extrahepatic biliary tree, ruling out biliary atresia. Molecular genetic testing was negative for Alagille syndrome but showed heterozygous mutations in the ABCC2 gene: c.2302 C>T, a pathogenic variant reported in patients with Dubin-Johnson syndrome, and c.1386 G>A, a variant of unknown significance. Immunohistochemistry for MRPs2 showed absent canalicular staining, supporting the diagnosis of Dubin-Johnson syndrome. Paucity of interlobular bile ducts is seen in Alagille syndrome, biliary atresia, and certain infections, metabolic diseases, and chromosomal disorders, but is not typically seen in Dubin-Johnson syndrome. This case illustrates an unusual presentation of Dubin-Johnson syndrome occurring in a neonate with the unexpected histologic finding of paucity of interlobular bile ducts.

Colonic Epithelioid Leiomyoma With ERG Expression: A Potential Diagnostic Pitfall and the First Reported Case

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Colonic leiomyomas (LM) are relatively common lesions discovered incidentally during colonoscopy, particularly in the distal sigmoid colon and rectum. Patients are diagnosed at an average age of 62 years and there is a slight male predominance (2.5:1). Histologically, LMs are well-circumscribed lesions that arise from the muscularis mucosae and occupy the submucosa. They are composed of well-differentiated smooth muscle cells characterized by cigar-shaped nuclei and abundant eosinophilic cytoplasm. LMs stain positively for desmin and actin and are negative for CD34, CD117, S-100, and cytokeratin. Here, we present a case of a 53-year-old woman with a past medical history significant for irritable bowel syndrome and gastroesophageal reflux disease who presented for screening colonoscopy. Colonoscopy revealed a 3-mm polyp in the ascending colon. Histopathologic analysis revealed normal colonic mucosa overlying a well-circumscribed, submucosal-based nodule (Figure 44). The nodule was composed of epithelioid cells, some with intracytoplasmic vacuoles, in a matrix reminiscent of chondroid. The epithelioid cells stained positively for ERG, and the stroma stained positively for smooth muscle actin. Additional immunohistochemical stains, including desmin, DOG1, c-KIT, CD31, cytokeratin AE1/AE3, CD34, and S-100, were negative. Given the morphologic and immunophenotypic findings, in addition to reported ERG expression in tumors with cartilaginous differentiation, this mesenchymal polyp was most compatible with a benign epithelioid leiomyoma with chondroid-type matrix, and to our knowledge, this is the first description of this type of colon polyp. Lastly, we demonstrate the importance of recognizing ERG positivity in cartilaginous lesions so as to not render a misdiagnosis of epithelioid hemangioendothelioma.

Expression of DNA Mismatch Repair Proteins, PD-1, and PD-L1 in Barrett Neoplasia

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**Context:** Microsatellite instability (MSI) is prognostic for survival in many cancers and has been reported inconsistently in esophageal adenocarcinoma (EAC) and rarely reported in Barrett esophagus (BE) with low- and high-grade dysplasia.

**Design:** Immunohistochemical stains for PMS2, MSH6, PD-1, and PD-L1 were performed on 50 cases of BE, 48 cases of BE with low-grade dysplasia (LGD), 50 cases of BE with high-grade dysplasia (HGD), and 50 cases of EAC.

**Results:** All cases of BE (50), LGD (48), and HGD (50) had intact nuclear expression of PMS2. One case of BE out of 50 (2%) had a loss of nuclear expression of PMS2. All cases of BE (50), LGD (48), HGD (50), and EAC (50) had an intact nuclear expression of MSH6. All cases of BE (50) and LGD (48) were negative for PD-1. One case of HGD (2%) and 2 cases of EAC (4%) were PD-1 positive. Similarly, all cases of BE (50), LGD (48), and HGD (50) had a PD-L1 CPS score <1 except 1 case of EAC (2%) that had a CPS score >1.

**Conclusions:** In our study we found 2% of EACs to be MSI-H, which was lower than in other studies. MSI tumors usually have an increased mutational burden with increased PD-L1 expression due to increased tumor-infiltrating lymphocytes. However, the MSI-H EAC in this study has low PD-L1 expression (CPS score <1). We conclude that MSI pathway is not very common in esophageal adenocarcinoma (EAC) and its precursors. PD-1 and PD-L1 are similarly seldom expressed in these tumors.

**A Child With Severe Anemia and Unusual Duodenal Pathologic Findings**

**Poster No. 77**

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Schistosomiasis is the second most prevalent parasitic disease globally. The worms causing schistosomiasis are not found in North America, but the disease should be suspected in patients emigrating from endemic areas. The intestinal involvement in schistosomiasis is relatively common, with the 2 major species, Schistosoma japonicum, primarily involving the small intestine, and Schistosoma mansoni, principally involving the large intestine. We report an unusual case of S mansoni present in the duodenum, as well as the large bowel. An 11-year-old boy presented with fatigue, dizziness, and abdominal pain. Results of laboratory tests showed severe microcytic hypochromic anemia. He recently emigrated from Tanzania with a positive serology test for Schistosoma spp. at the time of immigration. He was prescribed praziquantel but compliance was poor. No improvement was seen despite adequate doses of iron prescribed, and no source of blood loss was identified. The upper and lower gastrointestinal scopes were unremarkable, and biopsies were obtained to rule out eosinophilic/ collagenous gastritis, duodenitis, or colitis. Histopathologic examination of the duodenal biopsies revealed multiple granulomata in sub/mucosa, with viable and calcified parasitic eggs (125 by 50 μm). The eggs showed a thin transparent shell and a typical lateral spine, consistent with S mansoni (Figure 45). There was also diffuse involvement of the colon, supporting a diagnosis of chronic recurrent/residual diffuse intestinal schistosomiasis. The microscopic examination of excreta remains the gold standard for diagnosis of schistosomiasis. Serologic tests are indicated for travelers or immigrants from endemic areas. Pathology remains a powerful tool for elucidating long-standing residual/recurrent cases manifested with severe or untreatable symptoms.

**Metastatic Hepatobiliary Cystadenocarcinoma Mimicking a Gynecologic Malignancy**

**Poster No. 78**

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Hepatobiliary cystadenocarcinoma is a rare malignancy associated with ovarian-like stroma and overtly malignant glands that has a favorable prognosis if completely resected, analogous to minimally invasive adenocarcinoma arising in mucinous cystic neoplasms of the pancreas. Ovarian mucinous neoplasms may have a similar histologic appearance and are known to occasionally contain mural nodules of anaplastic carcinoma. We report a case of hepatobiliary cystadenocarcinoma that subsequently presented as metastatic disease mimicking a primary gynecologic malignancy. The 30-year-old patient had a history of completely resected hepatobiliary cystadenocarcinoma 2 years prior to presentation without adjuvant therapy. She presented to her gynecologist with pelvic pain and vaginal bleeding. Physical examination revealed diffuse nodularity along the anterior vaginal wall and imaging showed a 5.8 × 4.1-cm pelvic mass with diffuse metastatic disease. Biopsies of the vaginal wall and an inguinal lymph node showed nests of pleomorphic cells with squamoid and glandular features concerning for metastatic ovarian carcinoma (Figure 46, A); however, immunohistochemistry was negative for PAX8 and ER but positive for CDX2. Subsequent review of the patient’s prior resection revealed a cystic mucinous neoplasm with mural nodules of adenosquamous and anaplastic carcinoma (Figure 46, B through D), the latter previously reported only rarely in hepatobiliary cystadenocarcinoma. This case highlights the histologic overlap between hepatobiliary and ovarian neoplasms, which may present a diagnostic challenge, particularly in the setting of incomplete history. Additionally, the unusual presence of an anaplastic component in the patient’s original tumor portends a worse prognosis; therefore, additional therapy should be considered in these patients.
Follicular dendritic cell sarcoma (FDCS) is a rare neoplasm occurring in both lymph nodes and extranodal sites. We report an unusual case of FDCS involving ileocecal valve. A 34-year-old man was admitted with blood in his stool for 1 month. MRI showed a 4.1-cm mass in cecum close to the ileocecal valve (Figure 47, A). He underwent right hemicolectomy with a preoperative diagnosis of gastrointestinal stromal tumor (GIST). Grossly, there was a tan ulcerated polypoid mass at the ileocecal valve measuring 4.5 × 3.7 × 2.8-cm (Figure 47, B). Microscopy revealed a multilobulated mass centered in the muscularis propria with extension into subserosa and focally extending into colonic mucosa, consisting of ovoid to spindle cells arranged in fascicles, storiform, and whorled architecture in a background of prominent lymphocytic infiltrates (Figure 47, C). The neoplastic cells had eosinophilic fibrillary cytoplasm, ovoid to spindled nuclei, vesicular chromatin, and small nucleoli. There was mild cytologic atypia without necrosis. Mitotic rate was up to 10/10 per high-power field. Immunostaining showed tumor cells were positive for CD21 (Figure 47, D), CD23, and CD35, and negative for C-kit, DOG1, SMA, AE1/3, S100, SOX10, CD34, ALK, and EBER. A diagnosis of extranodal FDCS, French Federation of Cancer Centers Sarcoma Group grade 1, was entertained. No postoperative chemoradiation was administered, in expectation of a favorable clinical outcome. We present this unusual case to highlight the importance of having a wide differential diagnosis for spindle cell tumors of the GI tract. Attention to morphologic details and judicious use of immunostains can help arrive at the correct diagnosis.

Budd-Chiari Syndrome: Presentation of Pathologic Findings in 2 Cases
(Poster No. 81)
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Budd-Chiari syndrome (BCS) refers to the broad clinical spectrum associated with hepatic venous outflow obstruction, regardless of the etiology and level of obstruction. Liver specimens with BCS are uncommonly seen by pathologists given the rarity of the disease and the sensitivity and specificity of radiologic studies. We present 2 cases of a 36-year-old African American woman and a 50-year-old white man who presented to our institution with symptoms of fever, abdominal pain, nausea, vomiting, and jaundice. Imaging studies revealed thrombosis within the inferior vena cava and hepatic veins in the former and within the intrahepatic portion of portal vein in the latter. Both patients underwent orthotopic liver transplantation. Gross examination showed swollen, congested explanted livers with reddish purple, “nutmeg-appearing” cut surfaces and multiple venous thrombi causing near-complete luminal occlusion (Figure 48, A). Histologic sections revealed sinusoidal dilatation and congestion with extensive portal and hepatic hemorrhage necrosis (Figure 48, B). Hypervascular veins within numerous occlusive thrombi (Figure 48, C) and marked intimal thickening and luminal narrowing. Diffuse nodular regenerative hyperplasia was also seen (Figure 48, D). BCS should be differentiated from hepatic sinusoidal obstruction syndrome and cardiac congestive hepatopathy. Both conditions can present with similar clinical and radiologic findings as BCS; however, clinical history and radiologic findings can help make the distinction. Surgery is almost always mandatory in BCS, and prognosis generally depends upon the underlying cause and the severity of outflow obstruction. Our first patient died 3 months following her liver transplantation, whereas our patient died 3 months following her liver transplantation, whereas our.
second patient continues follow-up and is recovering well 10 months following surgery.

Nivolumab Monotherapy Induces Upper and Lower Gastrointestinal Crohn-like Features: A Novel Case Report

(Poster No. 82)

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Immunotherapy agents such as cytotoxic T-lymphocyte antigen 4 and programmed cell death protein-1 inhibitors show significant efficacy in treating advanced malignancies but are associated with numerous immune-related adverse events. These can manifest as severe gastroenteritis and colitis mimicking inflammatory bowel disease. This case represents a potentially rare presentation of a patient on nivolumab therapy who developed new-onset inflammation of the upper and lower gastrointestinal tract. Although colitis and gastritis are less common with nivolumab monotherapy, concurrent involvement of the upper and lower GI tract has not previously been reported. A 78-year-old man was diagnosed with metastatic lung adenocarcinoma in 2015 and treated with nivolumab immunotherapy. In 2016, he developed increased bloating, diarrhea, and loss of appetite. Upper and lower endoscopy showed Barrett esophagitis, gastritis, grade II intestinal hemorrhage, multiple clean based ulcers in the terminal ileum, and colon polyps. Esophageal biopsy revealed extensive squamous repair reaction and keratin pearl formation, which was considered suspicious for squamous cell carcinoma, microabscesses, and squamous metaplasia. Stomach biopsy showed marked intraepithelial chronic active inflammation with cryptitis and intestinal metaplasia with negative Helicobacter pylori immunostaining and gastric dysplasia in some areas. Colon biopsy revealed areas of normal colonic mucosa with areas of cryptitis and crypt abscesses and transmural inflammation. Although these histologic findings are consistent with inflammatory bowel disease, this patient had no evidence of bowel inflammation on colonoscopy in 2014 and no known history of GERD or gastritis. Nivolumab was withheld temporarily and prednisone was given to the patient, which improved his symptoms.

Atrophic Gastritis: A Confusing Terminology Needing Revision

(Poster No. 83)

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Context: Atrophic gastritis (AG) has 2 defined etiologies: autoimmune atrophic gastritis (AAG), and chronic Helicobacter pylori infection. AG is defined as destruction of gastric glands followed by fibrosis and/or metaplasia and is thus nonspecific. The aim of our study was to identify cases with parietal cell atrophy (PCA) of oxyntic mucosa specifically, and to define its associations.

Design: A retrospective data search from January 2014 through November 2018 retrieved 111 biopsies with the diagnosis of AG. The pertinent clinical data and follow-up biopsies were reviewed.

Results: AG was diagnosed in 2.2% (111 of 4947) of total stomach biopsies, comprising 86 patients (male to female ratio of 1:3.4) with mean age of 56 years (range, 29–77 years). All cases showed PCA in oxyntic mucosa. H pylori was positive on histology in 8%. Serologically, in tested patients, 59% had positive antiparietal antibody and 80% had positive intrinsic factor. Gastrin was elevated in 83% of tested patients. Histologically, intestinal metaplasia was identified in 84%. In those in which synaptophysin was done, ECL-cell hyperplasia was identified in 87%. Concurrent neuroendocrine tumors were identified in 12%.

Conclusions: In our study, PCA showed a higher association with AAG than H pylori. Histologic AG is a nonspecific diagnosis and may not prompt adequate autoimmune workup by the gastroenterologist, leading to potential delays in diagnosis and treatment. This fact, and the recognition that AG is a challenging diagnosis in random gastric sampling, led us to develop an algorithmic approach (Figure 49) for the workup and diagnosis of parietal cell atrophy, with the goal of providing early and accurate diagnosis.

A Rare Entity of Anal Ductal Carcinoma

(Poster No. 84)

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Anal ductal carcinoma is a rare entity. Here we report an interesting case of a 57-year-old woman who presented with hematochezia 18 months prior to presentation. Her initial anorectal examination showed mass at the left aspect of the anal verge that was mobile and quite firm. Biopsy of the mass showed adenocarcinoma originating from the rectum. A subsequent colonoscopy was done that showed the mass originating above the perianal skin with no other lesions elsewhere in the colon. No metastatic lesions were found on CT scan and a bulky lesion involving the perianal skin was found on MRI. During this presentation the patient finally underwent an abdominoperineal resection. The specimen revealed a moderately differentiated tumor, characterized by scattered solitary glands, undermining the squamous mucosa of the anal canal and perianal skin (Figure 50, A) and extending into the sphincter muscle. Focal glands showed mucinous patterns. Immunohistochemical staining showed the adenocarcinoma to be strongly immunoreactive for CK7 (Figure 50, C), with only scattered focal immunoreactivity for CK20 (Figure 50, B). The adenocarcinoma...
was nonimmunoreactive for CDX2, and many of the tumor cells were strongly reactive for p16 (nuclear and cytoplasmic; Figure 50, D). This immunoprofile is consistent with anal gland ductal adenocarcinoma, and with the positive p16 suggests a relationship with HPV-related dysplasia, as the patient had a history of condyloma acuminatum.

**Analysis of MicroRNA Signature in Liver Neoplasms**

*(Poster No. 85)*

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**Context:** MicroRNAs (miRNAs) are globally dysregulated in many tumors and play an integral role in tumorigenesis. In liver, miRNAs are abundant, modulate many cellular functions, and play an important role in pathogenesis of liver diseases. Growing evidence suggests that miRNAs can be used as potential diagnostic and therapeutic markers in various tumors including liver neoplasms. We aimed to identify differentially expressed miRNAs in liver neoplasms and use the findings as novel diagnostic tools to differentiate them.

**Design:** We profiled 17 candidate miRNAs on 41 samples; 9 hepatic adenomas (HAs), 4 well-differentiated hepatocellular carcinomas (HCCs), 6 moderately differentiated HCCs, 5 poorly differentiated HCCs, 10 focal nodular hyperplasias, and 7 normal liver samples. Total RNA was isolated from formalin-fixed, paraffin-embedded tissue. Complementary DNA and real-time polymerase chain reaction were performed using ABI TaqMan microRNA kits and Roche LightCycler480. Moderated test was used to identify differentially expressed miRNAs.

**Results:** Our analysis showed that 8 miRNAs (miR221, miR222, miR223, miR200, miR375, miR126, miR301, and miR422) were significantly down-regulated in HA compared with WD-HCC. We further explored these 8 miRNAs with Ingenuity’s IPA pathway analysis to gain functional interpretation of them and their predicted mRNA targets (showing 867 targets). These miRNAs are associated with hepatocellular carcinoma based on the IPA knowledge base. In addition, causal network analysis revealed top master regulators (network corrected P value < .001) were 3 miRNAs (miR221, miR200, and miR301/130) from the signature that act on these mRNA targets.

**Conclusions:** The targets of these miRNAs are attractive potential diagnostic and therapeutic markers. We are currently analyzing miRNA signatures in a larger cohort of patients to isolate specific genes dysregulated in liver neoplasms.

**A Paraganglioma Involving the Gallbladder Wall and Cystic Vessels**

*(Poster No. 86)*

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Paragangliomas are extra-adrenal neuroendocrine tumors derived from embryonic neural crest cells that arise from many sites, including the head and neck, mediastinum, retroperitoneum, and multiple organs. They may be sporadic or occur in various hereditary tumor syndromes. It is extremely rare for paragangliomas to arise from biliary tumors, even in the absence of signs and symptoms of catecholamine excess and syndromic disease.

**Prolapse of the Right Colon Through a Colostomy Due to Ogilvie Syndrome**

*(Poster No. 87)*

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Bowel pseudo-obstruction, also known as Ogilvie syndrome, is an abnormality of intestinal motility severe enough to produce the clinical features of intestinal obstruction. It is characterized by a functional obstruction of the colon in which the mechanism is poorly understood. Normal intestinal motility relies on the interaction between nerves and hormones that causes rhythmic contraction of smooth muscle subunits. The most common cause of acute pseudo-obstruction are drugs that decrease intestinal motility. Potassium chloride tablets may cause gastrointestinal ulceration, bleeding, and obstruction. A 66-year-old man presented with abdominal pain and distention. He was on aripiprazole, potassium chloride, Prolixin, and insulin. He was found to have intestinal pseudo-obstruction complicated by intestinal perforation. He underwent exploratory laparotomy and transverse loop colostomy. The resection specimen consisted of a 17-cm right hemicolectomy with attached terminal ileum and appendix, which had prolapsed through the colostomy site. No fibrous adhesions were identified on the serosal surface. The diagnosis was Ogilvie syndrome. Ileus is a common side effect related to treatment. Potassium chloride and aripiprazole and Prolixin can cause ileus with potentially fatal consequences. The new guidelines for patients with multiple comorbidities treated with medications should include recommendations about monitoring and interventions to avoid ileus among them.

**Malignant Transformation of Hepatocyte Nuclear Factor 1z (HNF1z)–Mutated Hepatocellular Adenoma**

*(Poster No. 88)*

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Hepatocellular adenoma (HCA) is a heterogeneous entity. Four subtypes can be discerned with the application of immunohistochemistry: HNF1z-mutated subtype, inflammatory subtype, β-catenin–activated subtype, and a subset of adenomas that are unclassified with currently available tools in anatomic pathology. Although malignant transformation of HCA is more frequent in β-catenin–activated adenomas, extremely rare cases of malignant transformation of HNF1z-mutated HCA have been reported in patients with MODY3 and liver adenomatosis. Here we present a case of an 80-year-old woman without a history of MODY3 or liver adenomatosis who presented with abdominal discomfort. An abdominal CT with contrast
revealed a heterogeneously enhancing mass replacing the left hepatic lobe. Left trisegmentectomy revealed a 13.5 × 12.2 × 6.5-cm yellow to tan, well-circumscribed, multilobulated tumor with a fleshy, hemorrhagic area. On microscopic examination, the fleshy and hemorrhagic area of the tumor had markedly thickened cell plates, aberrant architecture, and nuclear atypia, consistent with hepatocellular carcinoma. The remainder of the tumor was composed of a hepatocellular proliferation without portal structures and with prominent unpaired arterioles; the cells showed diffuse steatosis without significant cytologic atypia, consistent with the diagnosis of HCA. Immunohistochemical stains showed that fatty acid–binding protein was lost in both the adenoma and the carcinoma components and β-catenin staining demonstrated retained membranous staining. Our case describes malignant transformation of HNF1a-mutated HCA in a patient without MODY3 and adenomatosis, and provides a detailed immunohistochemical characterization of an otherwise rarely described entity (Figure 52).

Intraductal Polypoid Undifferentiated Carcinoma With Minimal Invasion: A Rare Presentation

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Undifferentiated carcinomas of the pancreas are rare neoplasms and have a much poorer prognosis than the typical ductal adenocarcinomas. We herein report a case of an incidental intraductal polypoid undifferentiated carcinoma with pleomorphic giant cells (sarcomatoid carcinoma) in a 92-year-old man diagnosed during evaluation of worsening chronic constipation. Upper endoscopic ultrasound revealed a well-defined mass in the periampullary region that extended within the pancreatic duct, with upstream duct dilation. Fine-needle aspiration of the lesion was consistent with an adenocarcinoma. Subsequently, the patient underwent Whipple procedure and a 4.5 × 1.5 × 1.2-cm tan-pink, polypoid mass (Figure 53, A, B) was identified within the pancreatic duct. The pathologic examination showed an undifferentiated carcinoma composed of spindle cells with marked pleomorphism and giant cells and a focal area of conventional ductal carcinoma (Figure 53, C). The tumor showed minimal invasion into the pancreatic parenchyma (Figure 53, D) and 22 lymph nodes were negative for metastasis. Immunostains showed the spindle cells to be positive for vimentin and focally positive for EMA and AE1/3. Most of the undifferentiated carcinomas presented as large cystic tumors involving the pancreatic parenchyma. Only a few cases have been reported in the literature to show predominantly intraductal growth and those were subcentimeter in size. In spite of the known aggressive nature of these tumors, in our case the tumor was large and confined to a polyp with minimal invasion into the underlying pancreatic parenchyma. This is suggestive of early-stage tumor with favorable clinical outcome and postsurgical chemotherapy is probably not warranted.
recurrence of the prior ampullary lesion in the distal pancreas, most likely secondary to ampullectomy. Intraductal tumor seeding secondary to ampullectomy has been rarely reported, and this is important to distinguish from a new primary tumor in the remnant pancreas because of its potential effect on treatment modality.

**Unusual Autoimmune and Viral Hepatitis–like Features in Progressive Familial Intrahepatic Cholestasis Liver Biopsies Confounding Diagnosis and Management**

(Poster No. 91)

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Progressive familial intrahepatic cholestasis (PFIC) is a group of autosomal recessive cholestatic disorders of mainly pediatric population resulting in types 1, 2, and 3. Liver biopsy in type 1 shows cholestasis, whereas type 2 is associated with giant cell hepatitis and type 3 with mainly ductular proliferation. We report 2 patients, aged 12 and 2 years, who harbored mutations consistent with PFIC1/2 and PFIC3, respectively, and presented for orthotopic liver transplant. Liver biopsies revealed an autoimmune/viral hepatitis–like picture, the significance of which has not been well characterized in PFIC patients. The first patient reported a 14-kg weight loss with pruritus, hepatosplenomegaly, and jaundice. Liver biopsy in type 1 showed cholestasis, and type 3 showed bridging fibrosis, raising a differential diagnosis of acute liver injury. The patient was treated with prednisone with complete clinical response. The second patient presented with elevated liver transaminases and jaundice. Liver biopsy revealed marked active hepatitis with occasional plasma cells and bridging fibrosis, raising a differential diagnosis of autoimmune hepatitis (Figure 15, left). The patient was treated with prednisone for 20 mg/dL, and IgM 253 mg/dL. No specific serologic autoimmune features were found. Liver biopsy showed moderate activity of active hepatitis with occasional plasma cells and bridging fibrosis, raising a consideration of autoimmune hepatitis (Figure 55, left). The patient received immunosuppressive treatment with prednisone with complete clinical response. The second patient presented with elevated liver function test results. Liver biopsy showed significant active hepatitis with interface and lobular activity, cholestasis, and bile duct proliferation (Figure 55, right), raising a differential diagnosis of viral hepatitis. Hepatitis–like features are generally absent in PFIC type 1 whereas giant cell hepatitis can be seen in PFIC type 2. Autoimmune hepatitis and primary sclerosing cholangitis have been rarely reported in PFIC patients. These features may be within the spectrum of PFIC–related changes or represent a concomitant etiology, warranting awareness and further investigations given the therapeutic implications.

**Fulminant Clostridium difficile Colitis in a Young Patient After Only 3 Days of Antibiotic Therapy**

(Poster No. 92)

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In the United States, Clostridium difficile infection (CDI) affects up to 3 million patients per year. Up to 8% of hospitalized patients can develop CDI. Twenty-five percent of patients with CDI may develop CD-associated diarrhea; 1%–3% may progress to fulminant CD colitis (FCDC), which has a high mortality rate (35%–80%) and requires prompt operative intervention. A 23-year-old man, a nursing home resident with a history of anoxic brain injury secondary to ventricular fibrillation arrest, was hospitalized for evaluation of fever associated with cough productive of greenish sputum. He had developed abdominal distention with diarrhea and vomiting immediately prior to admission. He had a 3-day history of antibiotic (linezolid and piperacillin and tazobactam) use. CT scan of the abdomen showed severe thickening in the wall of the ascending colon and he underwent total colectomy. The colon was grossly dilated with maximum 11-cm dilation in the cecum and ascending colon. The mucosa was edematous with maximum bowel thickness of 1.2 cm in the ascending colon. Yellow pseudomembranes were observed throughout the colon but primarily clustered in the cecum and ascending colon. The histologic changes were consistent with type I lesion, characterized by superficial mucosal necrosis with erupting spray of fibrinopurulent exudate. Clostridium difficile toxin B gene was detected in the stool sample by qualitative polymerase chain reaction. Fulminant colitis in a young patient is most often associated with inflammatory bowel disease. However, the differential diagnosis should include FCDC even though length of antibiotic therapy may be short (3 days in our case).

**Sessile Serrated Adenoma of the Appendix With High-Grade Dysplasia and Rupture**

(Poster No. 93)

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Sessile serrated adenomas (SSA) of the appendix have been associated with acute appendicitis. One report in the literature shows that when entirely submitted, SSA can be found in up to 20% of appendices sent for acute appendicitis in patients 30 years or older. However, most cases of SSAs of the appendix appear to be small, appearing in 3 or fewer cross sections when the entire appendix is submitted. We report a case of an SSA entirely replacing the appendix with resulting rupture. A 68-year-old man presented with a 1-week history of shortness of breath, fatigue, and generalized weakness. Shortly after admission he reported increasing shortness of breath and abdominal pain. A CT of the abdomen at that time was consistent with acute appendicitis complicated by rupture. Because of a rapid decline in status, definitive surgery was delayed until a month later. The specimen consisted of a distorted appendix with a fungating, polypoid mass near the tip of the appendix. The entire appendix was submitted, with every section showing SSA. A small area from the tip of appendix showed high-grade dysplasia. No invasive carcinoma or dissecting mucin was identified. We hypothesize the rupture was secondary to mass effect of the SSA. This case highlights a rare example of extensive SSA replacement of the appendix. Although there is little literature about peritoneal seeding in SSAs, because of the long interval between perforation and surgery as well as the high-grade dysplasia, close follow-up with the patient is necessary.

**Appendiceal Spirochetosis: A Fuzzy Presentation**

(Poster No. 94)

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Human intestinal spirochetosis (IS) is a colonization of the intestines by spirochetes, most commonly *Bachyspiria* spp. Histologically, IS presents as thickened intestinal brush border. Although this finding is usually incidental, spirochetal invasion beyond surface epithelium with associated gastrointestinal symptoms has been reported. IS is thought to be associated with oral-anal contact and is most common among immunocompromised homosexual men and populations in subsistence conditions. Here we discuss a rare case of appendiceal spirochetosis presenting as vague appendicitis in a previously healthy young woman. A 21-year-old, sexually active, afebrile, HIV-negative woman presented to the emergency department complaining of nausea, vomiting, and acute abdominal pain that migrated to the right lower quadrant within 48 hours. She also complained of nausea, vomiting, and acute abdominal pain that migrated to the right lower quadrant within 48 hours. She also complained of nausea, vomiting, and acute abdominal pain that migrated to the right lower quadrant within 48 hours. She also had a history of shortness of breath, fatigue, and generalized weakness. Shortly after admission he reported increasing shortness of breath and abdominal pain. A CT of the abdomen at that time was consistent with acute appendicitis complicated by rupture. Because of a rapid decline in status, definitive surgery was delayed until a month later. The specimen consisted of a distorted appendix with a fungating, polypoid mass near the tip of the appendix. The entire appendix was submitted, with every section showing SSA. A small area from the tip of appendix showed high-grade dysplasia. No invasive carcinoma or dissecting mucin was identified. We hypothesize the rupture was secondary to mass effect of the SSA. This case highlights a rare example of extensive SSA replacement of the appendix. Although there is little literature about peritoneal seeding in SSAs, because of the long interval between perforation and surgery as well as the high-grade dysplasia, close follow-up with the patient is necessary.
HNF1-α Inactivated Hepatocellular Adenoma With β-Catenin Activation  
(Poster No. 95)

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Hepatocellular adenomas (HCAs) constitute a heterogeneous group of benign liver tumors with variable risk of malignant transformation. HCAs are classified into 4 major subtypes: HNF1-α inactivated (HNF1A-I), β-catenin activated, inflammatory, and unclassified. β-Catenin is part of the Wnt signaling pathway. HNF1A inactivation and β-catenin Wnt signaling activation are usually mutually exclusive in HCA, possibly because of distinct tumorigenesis pathways. We report the case of a 63-year-old woman with an incidental 18-mm enhancing liver nodule found during workup for shortness of breath. She had a 10-year history of hormone replacement therapy. The liver nodule was biopsied, and microscopic examination revealed a well-differentiated hepatocellular proliferation displaying marked steatosis and mild sinusoidal dilatation without bile ducts, inflammation, or reticulin disruption. Immunohistochemically, the neoplastic cells showed positive membranous staining for β-catenin without nuclear staining and were diffusely positive for glutamine synthetase (GS) and negative for CRP, serum amyloid A (SSA), and glypican 3, with loss of hepatocellular nuclear staining. B-CAT-ACT. Diffuse GS expression is thought to be reflective of Wnt signaling pathway deregulation and is considered a surrogate feature of B-CAT-ACT in HCAs, even in the absence of immunohistochemical β-catenin nuclear staining. B-CAT-ACT is found in ~1% of HNF1A-I HCA. Overall, HNF1A-I HCA has a relatively low risk of progression. However, any HCA with B-CAT-ACT should be followed up closely because of increased risk for malignant transformation.

Isolated Collagenous Disease of Gastroesophageal Junction  
(Poster No. 96)

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A 46-year-old man with long-standing symptoms of gastroesophageal reflux disease and diarrhea was admitted to the endoscopy clinic. He had been followed for his irritable bowel syndrome for 4 years prior to this. The upper endoscopy showed an irregular Z line of the gastroesophageal junction, features of a short segment Barrett esophagus, and hiatus hernia. Mucosal biopsy of the gastroesophageal junction showed an increased thickness of the subepithelial collagen layer, up to 100 μm, confirmed by trichrome staining (Figure 1). The collagen fibers focally extended into the lamina propria and surrounded glands/crypts and superficial vessels. The squamous epithelium showed basal hyperplasia and spongiosis. Focal sloughing of squamous and columnar epithelial cells was present. There was mild chronic inflammation in the lamina propria. No mucosal eosinophilia, intestinal metaplasia, dysplasia, or yeast/fungus was present. There was no histomorphologic finding suggestive of scleroderma. Stomach biopsies (corpus and antrum) showed mild chronic inflammation and proton pump inhibitor effects. There was no evidence of acute inflammation or Helicobacter pylori. No increased thickness of the subepithelial collagen layer or intraepithelial lymphocytosis was found in the stomach, duodenum, terminal ileum, or colon biopsies.

Common Variable Immunodeficiency Mimicking Celiac Sprue: An Unusual Presentation in an Older Adult  
(Poster No. 97)

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Common variable immunodeficiency (CVID) is a heterogenous clinical disease secondary to impaired B-cell differentiation and defective immunoglobulin production. CVIDs are commonly diagnosed at young age because of recurrent infections. Gastrointestinal symptoms are usually malabsorption or diarrhea. The histopathology of CVID in the gastrointestinal system can demonstrate various morphologic abnormalities, including lymphocytic colitis, collagenous enterocolitis, and celiac sprue. We present a case of CVID in a 75-year-old woman with gastrointestinal involvement as celiac sprue. The patient had a history of recurrent ear infections and pneumonia and presented with weight loss and several months of severe persistent diarrhea. Her celiac serology was negative, whereas immunoglobulin levels of immunoglobulin G (IgG) and IgA were 50% lower than normal levels.
Combined hepatocellular cholangiocarcinoma (cHCC-CC) is a rare malignant tumor of the liver, more aggressive than hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (CC). Patients often present with locally advanced and/or metastatic disease. Little is known about the molecular alterations of this tumor. Here we report a case of cHCC-CC with molecular analysis by next-generation sequencing (NGS). A 57-year-old woman with no history of viral hepatitis or cirrhosis presented with masses in the liver, spleen, and lung; lytic bone lesions; and enlarged hilar lymph nodes. Ultrasound-guided core biopsy was performed on the liver mass. Numerous single and groups of pleomorphic cells with irregular, hyperchromatic nuclei and prominent nucleoli were seen on the imprints (Figure 60, A). Biopsies showed a tumor with trabecular and glandular patterns composed of malignant cells with eosinophilic cytoplasm, round to oval nuclei, and prominent nucleoli. Mucin was noted in the neoplastic glands. Focal necrosis was identified (Figure 60, B). The tumor was diffusely positive for HSA, CK7, CK19, and CEA-p, indicating combined features of HCC and CC (Figure 60, C and D). CK20, CDX2, TTF-1, napsin-A, arginase, glypican 3, CA19.9, GATA-3, and PAX-8 immunostains were negative. A diagnosis of chCC-CC was rendered. KRAS pGly12Asp mutation was detected. PD-L1 was negative. Previously KRAS alterations in chCC-CC have been reported only in Japanese cases. KRAS mutations are common in CC and seem to be associated with worse prognosis. They are infrequent in HCC and implications of KRAS alterations in chCC-CC are not known. Additional molecular studies are warranted, which may improve the treatment and prognosis of this tumor by targeted therapies.
PMS2 expression was completely lost in tumor cells, benign crypt epithelium, stromal cells, and inflammatory cells, consistent with biallelic homozygous germline mutation (Figure 61, C). MLH1 (Figure 61, D), MSH2, and MSH6 mismatch repair proteins were retained in tumor cells as well as nontumor cells. Pathologists and clinicians should be aware of this condition in young patients developing multiple malignancies to warrant an early referral to a genetic counselor and adequate cancer surveillance.

Actinomycosis Mimicking Colonic Carcinoma in a Woman With an Intrauterine Device

(Poster No. 101)

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Actinomycosis is a rare infection with variable presentation that is difficult to diagnose preoperatively. It is commonly locally infiltrative and has been reported to mimic carcinoma radiologically and clinically because of chronicity and associated inflammation. We present the case of a 42-year-old woman with bowel obstruction and outside diagnosis of colonic adenocarcinoma. CT of abdomen (Figure 62, A) showed a 5.0 × 4.7 × 3.5-cm midtransverse colon mass, a 4.0 × 3.9 × 1.9-cm peritoneal mass, and multiple implants. The patient had an intrauterine device for 16 years prior to presentation. The patient underwent an extended right hemicolectomy and en bloc small bowel resection. Gross examination did not identify tumor but revealed a segment of colon and small bowel with focal loss of mucosal folds and thickened wall up to 1.8 cm with dilated proximal bowel. Histologically, the thickened bowel wall showed extensive acute and chronic inflammation with granulation tissue and necrosis. Rare sulfur granules were identified on hematoxylin and eosin staining. Gram-positive filamentous rods were highlighted by Gram stain and were also PAS-D and GMS positive (Figure 62, B through D). ABF stain was negative. Surgically, there was no connection between the uterus and colon. The intrauterine device was removed in case of indolent infection. The patient was discharged on 6–12 months of antibiotics. In conclusion, actinomycosis is a rare infection sometimes associated with intrauterine devices and can mimic malignancies within the pelvis and abdomen. Intraabdominal actinomycosis can be extremely difficult to diagnose preoperatively because of the wide range of presentations.

The Ability of Transient Elastography to Predict Hepatic Fibrosis in Nonalcoholic Fatty Liver Disease Patients

(Poster No. 102)

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Context: Assessment of fibrosis in nonalcoholic fatty liver disease (NAFLD) is important in predicting disease progression. Transient elastography (TE) is a noninvasive estimation of hepatic fibrosis and when combined with controlled attenuation parameter can assess the degree of hepatic steatosis. In this study, we compare the results of fibrosis obtained from transient elastography with those obtained from liver biopsy.

Design: We reviewed 16 NAFLD patients who underwent transient elastography followed by liver biopsy. The following parameters were recorded: steatohepatitis, steatosis in liver biopsy (mild, ≤33%; moderate–severe, >33%), fibrosis in liver biopsy (Brunt score 0–1, no or sinusoidal fibrosis; 2–3, sinusoidal fibrosis with portal fibrosis or bridging fibrosis; 4, cirrhosis), TE steatosis score (S score; S1, 11%–33%; S2–3, >33%) and TE fibrosis result (F 0–1, no or mild scarring; F 2–3, moderate–severe scarring; F 4, cirrhosis).

Results: Sixteen patients were identified, and steatohepatitis was present in 88% of these patients (Table). The degree of steatosis was concordant between TE and liver biopsy in most F 0–1 and F 4 patients, but it was not concordant in more than half of the F 2–3 patients. The degree of fibrosis was concordant with liver biopsy in 55% of F 0–1 patients, 25% of F 2–3 patients, and none of the F 4 patients.

Conclusions: Discrepancy in fibrosis was noted in 62% of the patients when compared with liver biopsy. TE results are more reliable in cases with low TE fibrosis (F 0–1), whereas TE fibrosis of 4 needs to be confirmed by liver biopsy.

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<th>Results</th>
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A Hospital-Based Prospective Study of 2 FIT Assays for Detecting Premalignant and Malignant Colorectal Lesions

(Poster No. 103)

Yipeng Geng, MD, PhD (ygeng@mednet.ucla.edu); Opal Reddy, MD; Omai Garner, PhD; Hauling Zhao, MS; Weibo Yu, MD; Jianyu Rao, MD. Department of Pathology, University of California, Los Angeles.
Context: Fecal blood–based screening has been shown to be an effective strategy in reducing colorectal cancer mortality. The goal of this project was to compare the efficacy of 2 commercial FIT tests, Polymedco (P-FIT) and Hemosure (H-FIT), in detecting premalignant and malignant colorectal lesions.

Design: This is a hospital-based prospective study. Consecutive nonselective stool samples were collected during a 3-month study period at UCLA and analyzed by P-FIT and then H-FIT tests. Follow-up data including colonoscopy for up to 3 years were obtained by reviewing the hospital electronic record.

Results: A total of 808 stool samples from individual patients were tested. P-FIT was positive in 307 samples (38%) and negative in 511 (62%). H-FIT was positive in 367 samples (45%) and negative in 451 (56%). The overall concordance of the 2 tests was 90%, and the 2 tests showed overall similar performance characteristics in detecting tubular adenoma and more advanced lesions. However, there were 8 samples that tested positive by P-FIT and negative by H-FIT, whereas 68 samples tested positive for H-FIT but negative for P-FIT. Among these 68 patients with only H-FIT positivity, 26 underwent colonoscopy, with 10 (38%) showing precancerous adenomatous lesions or malignancy. Meanwhile, among the 8 patients with only P-FIT positivity, 5 underwent colonoscopy, with 1 patient (20%) showing tubular adenoma (p² = 2.9; P < .1).

Conclusions: Two FIT tests (P-FIT and H-FIT) showed similar test performance characteristics in detecting tubular adenomatous and above lesions. The H-FIT showed a slightly higher sensitivity than P-HIT in detecting tubular adenoma and more advanced lesions.

Novel Trilineage Differentiation in a Poorly Differentiated Pancreatic Carcinoma

(Poster No. 104)

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Among pancreatic carcinomas, the World Health Organization recognizes a category with mixed differentiation, including mixed acinar-neuroendocrine carcinoma, mixed acinar-ductal, and mixed acinar-neuroendocrine-ductal carcinoma. Adenosquamous carcinoma is considered a distinct entity with bilineage differentiation whose diagnosis requires at least 30% of both components. The histopathologic identification of each component could be challenging in poorly differentiated tumors, especially with preceded neoadjuvant treatment; a third lineage/component in a pancreatic adenosquamous carcinoma has not been reported. A 73-year-old man presented for second opinion regarding his recently resected pancreatic tumor following neoadjuvant chemotherapy and newly identified metastatic disease involving liver. The outside diagnosis stated poorly differentiated adenocarcinoma (ypT2N0). His case was requested and reviewed. Review of the outside Whipple case identified a 2.5-cm tumor with unequivocal adenosquamous histomorphology, confirmed by positive CK5/6 and CDX2 immunostains performed at our institute. Remarkably, synaptophysin, chromogranin, and CD56 immunostains also highlighted most tumor cells. The histomorphology and immunophenotypes were most consistent with trilineage differentiation (Figure 63). Subsequent mutational analysis detected loss of CDKN2A and CDKN2B and mutation of SMAD4, ARID1A, and CTNNB1 genes, and stable microsatellites. Patient was originally managed with Gemzar and FOLFIRINOX. Based on these newly acquired findings and liver metastasis, Abraxane treatment was initiated and clinical trials were offered. To our knowledge, this is the first pancreatic carcinoma identified with simultaneous trilineage adenosquamous and neuroendocrine differentiation. We believe that astute histomorphologic evaluation and systemic immunohistochemistry are essential in reaching an accurate diagnosis. The impact of this subclassification on the clinical management and patient outcome awaits further investigation.

Rare Case Report: Granular Cell Tumor of Cecum

(Poster No. 105)

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Granular cell tumor (GCT) was considered a neoplasm of Schwann cell origin. GCT of gastrointestinal tract, especially of the colon, is very rare. We report a case of a patient with GCT of cecum and discuss the histopathologic and immunohistochemical features. The patient is a 32-year-old woman who was found to have a 1.5-cm subepithelial lesion distal to appendiceal orifice during screening colonoscopy because of her history of Crohn disease. The initial biopsy of cecum mucosa overlying the mass demonstrated focal active colitis, consistent with her Crohn disease. The patient subsequently underwent laparoscopic right hemicolectomy. Macroscopically, a firm, well-circumscribed mass was covered by cecal mucosa measuring 1.5 × 2 cm. Histologically, this submucosal tumor was composed of plump histiocyte-like cells with abundant granular eosinophilic cytoplasm and centrally located nuclei. The tumor cells were diffusely positive for S-100, CD 56, and inhibin by immunohistochemistry (IHC) and negative for synaptophysin and neurofilament. During a 3-year follow-up, she has been well without tumor recurrence. GCT in the cecum is rare, generally found incidentally, and follows a benign course. However, malignant GCTs have been described but are extremely uncommon. We must be aware of the possibility of GCT when we deal with submucosal tumors in the colon. Histologic examination and IHC stains can help guide our diagnosis.

A Case of Syphilitic Proctocolitis Mimicking Inflammatory Bowel Disease

(Poster No. 106)

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A 62-year-old man presented with acute generalized abdominal pain and absence of bowel movements for 4 days. He denied anal pain, bloody stool, and discharge. He stated being in a long-term relationship with his male partner. Results of HIV screen were negative and no sexually transmitted disease was reported. CT of the abdomen and pelvis revealed circumferential rectal thickening with perirectal and pelvic lymphadenopathy concerning for malignancy. Coloscopy showed multiple polyps in the sigmoid colon and rectum with inflamed distal rectal mucosa. Biopsies revealed tubular adenomas with occasional lymphocytes, plasma cells, and histiocytes within the lamina propria. Random rectal biopsies demonstrated expansion of the lamina propria and submucosa by chronic lymphoplasmacytic infiltrates, prominent lymphoid aggregates, and poorly formed granulomas (Figure 64, A and B). Acid-fast bacteria stain, Gomori methenamine silver, and Steiner modified silver did not reveal infectious microorganisms. Because of high level of suspicion, Treponema pallidum immunostaining was performed, showing spirochetes within the lamina propria of the rectal polyps (Figure 64, C), compatible with syphilitic proctosigmoiditis. Subsequent serology revealed positive RPR and reactive confirmatory T pallidum particle agglutination test. Furthermore, rectal C. trachomatis nucleic acid amplification testing was also positive. We report a case of...
syphilitic proctocolitis and concurrent C. trachomatis infection with unusual presentation. Tissue biopsy helped make the diagnosis, initiating prompt treatment and preventing onward transmission. Because of increases in the incidence of sexually transmitted diseases, including isolated infectious proctocolitis, caused by T. pallidum and C. trachomatis, a high index of suspicion is warranted for timely recognition and treatment.

**An Unusual Mixed Endocrine-Exocrine Tumor of Pancreas**  
(Poster No. 107)  
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Intraductal papillary mucinous neoplasm is a cystic mucin producing exocrine neoplasm of the pancreatic duct. This neoplasm can be concurrently associated with pancreatic neuroendocrine tumor (PanNET). We report an uncommon case of mixed intraductal papillary mucinous neoplasm (IPMN) and PanNET. Only 8 such cases have been previously reported in the literature. A 63-year-old man was found to have an incidental 2.8-cm multiseptated cyst in the tail of the pancreas. Endoscopic ultrasound with fine-needle aspiration revealed a PanNET. Distal pancreatectomy and splenectomy were performed and revealed a well-circumscribed, cystic mass filled with mucin measuring 3 × 3 cm. Microscopic examination showed the cyst wall lined by tall columnar mucinous epithelium, gastric phenotype, intermixed with subepithelial sheets of well-differentiated mildly anisomorphic cells expressing synaptophysin and chromogranin. The proliferation index was 2%. Low-grade dysplasia was noted in the IPMN. No high-grade dysplasia or carcinoma was seen. The background pancreas showed an additional focus (0.5 cm) of well-differentiated neuroendocrine tumor in a background of chronic pancreatitis. Association of pancreatic ductal lesions and PanNET is uncommon and can present in 2 patterns. The most common pattern is intraductal papillary mucinous neoplasm with PanNET occurring as concurrent yet 2 discrete lesions. The second is mixed pattern, which is very uncommon, shows intermingling of both components, and requires the presence of endocrine differentiation in at least one-third of tumor volume. This includes the rare intraductal PanNET, mixed intraductal papillary mucinous neoplasm and PanNET (our case), and mixed adenocarcinoma and neuroendocrine carcinoma.

**Idiopathic Myointimal Hyperplasia of the Mesenteric Veins**  
(Poster No. 108)  
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Idiopathic myointimal hyperplasia of mesenteric veins (IMHMV) is a rare disease of unknown etiology that classically affects the rectosigmoid colon and mimics inflammatory bowel disease. We present a case of a 62-year-old man with a past medical history of hypertension, hyperlipidemia, and chronic colitis of unknown etiology. A previous biopsy performed from the rectosigmoid colon showed patchy ischemic colitis associated with vascular ectasia and intravascular fibrin thrombi with no chronicity or granuloma seen. Hence, the patient’s colitis was refractory to medical management, surgical intervention with total colectomy, and end ileostomy was opted. Gross findings revealed inflammation and wall thickening affecting mainly the distal colon. On histologic examination, the distal and sigmoid colon showed ischemic colitis. The mesenteric veins, confirmed by EVG stain, were significantly thickened and tortuous and the lumens narrowed or obliterated with medial-intimal hyperplasia and fragmentation of elastic lamina (Figure 65, A and B). Focal organizing thrombi with recanalization were identified, and no vasculitis was seen. The veins in the proximal portion of the mesentery were generally uninvolved. The findings rendered a diagnosis of idiopathic myointimal hyperplasia of the mesenteric veins. This entity has mainly been diagnosed after pathologic review of colectomy specimen, as the biopsy findings are usually suggestive of an ischemic etiology and nonspecific. Awareness of this disease will assist in understanding the etiology and permit adequate management for these patients who are many times misdiagnosed with inflammatory bowel disease.

**Adenosquamous Carcinoma of the Pancreas: A Challenging Case**  
(Poster No. 109)  
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A 66-year-old woman presented with fatigue, abdominal pain, and anemia. On imaging, a 9.5-cm mass involving the pancreatic tail with direct extension into (or possibly from) the stomach was identified. Concurrent nodules in the liver, lung, spleen, adrenal glands, colon, and
omentum were discovered. Endoscopic evaluation of the stomach demonstrated irregular friable mucosa in the cardia. Histologic sections of the irregular gastric mucosa revealed a biphasic malignant neoplasm composed of glandlike spaces lined by cells with abundant cytoplasmic mucin, framed by a multilayered squamous-transitional epithelium (Figure 66, A). No intestinal metaplasia or dysplasia were identified. Both mucinous and squamous components were positive for CK7 (Figure 66, B), whereas only the squamous component expressed CK5/6 (Figure 66, C) and only the glandular component expressed monoclonal CEA (Figure 66, D). Taken all together, the findings were diagnostic of adenosquamous carcinoma. Adenosquamous carcinoma is a rare tumor with extremely poor prognosis. Although it can be found in several locations, it represents only 3% of pancreatic exocrine malignancies and less than 0.5% of gastric malignancies, respectively. In both pancreas and stomach, the tumor typically presents at late stage. In this case, concurrent involvement of both organs raised concern regarding the site of origin. As immunohistochemistry is insufficient for distinguishing between tumors from these 2 sites, the combination of imaging features (major lesion in the pancreas), endoscopic observation (absence of significant mass lesion on the gastric mucosa), and microscopic findings (absence of in situ neoplasia in the stomach) supported pancreas as the primary site.

Pancreatic Adenocarcinoma Involving Entire Pancreas With Extensive Pancreatic Intraepithelial Neoplasia Without Mass Lesion: A Rare Finding

(Poster No. 110)

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Pancreatic adenocarcinoma is the most common type of pancreatic neoplasm. It is one of the most lethal human cancers. Most tumors form a mass lesion with or without obstruction of duct. Diffuse involvement of the pancreas is extremely uncommon. Here we describe a case of pancreatic adenocarcinoma with extensive pancreatic intraepithelial neoplasia involving the entire pancreas without forming a mass on radiology and gross. A 63-year-old man presented with abdominal discomfort and nausea for a few months. Computer tomography revealed diffuse irregular dilatation throughout the main pancreatic duct in the body and tail without mass (Figure 67, A). A resection of distal pancreas and spleen was performed. Grossly, no definite mass lesion was identified. Histopathology revealed invasive, moderately differentiated adenocarcinoma on a background of chronic atrophic pancreatitis. Also noted was extensive pancreatic intraepithelial neoplasia involving both branch and main pancreatic duct. Two months postsurgery the patient underwent fine-needle aspiration of pancreas, which showed malignant cells in papillary-tubular architecture favoring well-differentiated adenocarcinoma versus adenocarcinoma arising in an intraductal tubular-papillary neoplasm. A Whipple procedure was performed. Grossly, no mass was seen. Sections revealed similar histopathology as the previous resection (Figure 67, B through D). At 2 months postsurgery follow-up visit, the patient was doing well clinically and scheduled for future adjuvant chemotherapy. The current case highlights an unusual feature of pancreatic adenocarcinoma in the form of no mass lesion, associated with extensive pancreatic intraepithelial neoplasia involving the entire pancreas. The exact prognostic significance of this rare finding needs further exploration.

Mesothelioma With Clear Cell Features: Possibly a Distinct Variant With Unique Genetic Signature and Indolent Clinical Course

(Poster No. 111)

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Malignant mesotheliomas are rare neoplasms of mesothelial cell origin. They can be classified based on morphology into epithelial, sarcomatoid, or mixed types. Peritoneal epithelioid mesothelioma with clear cell features is very rare and mimics various malignancies, posing a diagnostic challenge. Here we report a rare case of primary peritoneal mesothelioma with predominantly clear cell features and a unique molecular signature. A 68-year-old man who had multiple liver nodules on imaging was admitted for worsening abdominal pain. He complained of intermittent abdominal pain for more than 10 years. Longitudinal follow-up of the patient’s abdominal images during 10 years showed slowly progressive liver lesions. Microscopic examination of resected tumors revealed pleomorphic epithelioid neoplasm with clear cytoplasm, distinct cell borders, optically clear chromatin, and prominent nuclei embedded in a vascular stroma. Immunohistochemistry showed that the tumors were positive for AE1/3, vimentin, carbonic anhydrase IX, TFE1/33, and GATA3 and negative for PAX-8, arginase-1, hepatocyte-specific antigen, inhibin, S100, DOG1, CD117, CD31, TTF-1, p63, smooth muscle actin, and HMB45. CancerType ID testing favored the diagnosis of mesothelioma with 90% probability, a diagnosis that was further confirmed by calretinin and WT1 positivity. Foundation genomic testing showed VHL Y98fs*24 mutation, a unique genetic mutation that to our knowledge was never previously described in mesothelioma. In summary, this is a rare case of primary peritoneal mesothelioma with clear cell features presenting as liver masses. The tumor had a unique genetic mutation and behaved in an indolent manner, in contrast to what is commonly seen in mesotheliomas.

Neonatal Giant Cell Hepatitis: Are There Histopathologic Predictors of Clinical Outcome?

(Poster No. 112)

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Context: Neonatal giant cell hepatitis (NGCH) is a histologic pattern of liver injury seen in a subset of infants with persistent neonatal jaundice. Although some infants recover with medical management, others develop progressive liver injury. Data on clinical follow-up are limited on prior NGCH studies. NGCH cases at our institution were retrospectively reviewed to identify histologic attributes that may predict adverse clinical outcome.

Design: Institutional archives were queried (January 1990 to April 2018) for liver biopsy reports in infants (age <1 year) with key words “giant cell" and “hepatitis." Slides were evaluated for histologic features by 3 hepatobiliary pathologists blinded to identifying information. Clinical diagnoses and outcomes were recorded. Correlations were assessed by χ² test.

Results: Follow-up data (range, 4 weeks through 20 years) were available in 18 of 22 infants with NGCH aged 3 to 26 weeks (mean = 12 weeks) at the time of diagnosis. Eight infants (44%) developed progressive liver disease, of whom 3 were successfully transplanted but 5 (28%) died of disease. Ten patients (56%) had improving liver function at last follow-up. Etiology of NGCH was idiopathic in 8 (44%), bile duct atresia in 3 (16%), portal parenteral nutrition in 2 (22%), biliary atresia in 1, perinatal asphyxia in 1, and sepsis in 1. There was a strong association of fibrosis stage ≥2 (P = .002), ductular cholestasis (P = .03), as well as patchy or confluent necrosis (P = .03), with progressive liver disease.
**Conclusions:** Fibrosis (stage ≥2), ductular cholestasis, and necrosis appear to predict progressive liver disease in NCH.

**Mixed Carcinosarcoma and High-Grade Neuroendocrine Neoplasm: Unusual Triphasic Tumor of the Gallbladder**

(Poster No. 113)

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Gallbladder carcinosarcoma is one of the rarest subsets of gallbladder malignancies. To date, 108 cases have been reported worldwide. To our knowledge, this case represents only the second reported patient with a primary gallbladder cancer displaying both carcinosarcoma and neuroendocrine components. Herein we report a 71-year-old man with a gallbladder mass discovered on CT scan (Figure 68, A). The patient underwent a radical cholecystectomy with regional lymphadenectomy and en bloc resection of liver segments IV and V. Macroscopically, a 3.5-cm polypoid mass near the gallbladder fundus was examined. Grossly, the lesion showed necrosis and cystic changes filled with mucin. Microscopically, the tumor demonstrated moderately differentiated adenocarcinoma with focal chondroid differentiation (Figure 68, B and C) and high-grade neuroendocrine tumor component (Figure 68, D) arising in a cystic papillary neoplasm. The neuroendocrine neoplasm was positive for chromogranin and synaptophysin. Ki-67 proliferation index was ~50%. The patient did not receive adjuvant chemotherapy in the setting of complete surgical resection. Surveillance CT scan taken 47 months after initial diagnosis (done at 6-month intervals) demonstrated extensive metastasis. The patient is currently receiving chemotherapy. Because of the low incidence and poor prognosis of this tumor, it is essential to gather all individual experience-based information.

**Pancreatic Undifferentiated Carcinoma With Osteoclast-like Giant Cells: A Case Report and Review of Literature**

(Poster No. 114)

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Undifferentiated carcinomas of the pancreas are extremely rare nonendocrine pancreatic neoplasms accounting for 5% of all pancreatic malignant tumors. Undifferentiated carcinoma with osteoclast-like giant cells (UC-OGC) is a rare subtype. It is mainly composed of 2 cellular components including osteoclast-like giant cells (OGCs) and ovoid to spindle-shaped highly pleomorphic mononuclear tumor cells. UC-OGC is currently considered a distinct variant of pancreatic ductal adenocarcinoma (PDAC). Prognosis is poor and most patients survive less than a year. Patients with a pure UC-OGC have better prognosis than those with an UC-OGC with an associated conventional PDAC component. We report a 66-year-old man who presented with weight loss and constipation. Abdominal CT showed a pancreatic head mass with pancreatic ductal dilatation. Fine-needle aspirate of the mass was suggestive of adenocarcinoma and occasional multinucleated giant cells were also detected. The patient underwent pancreatoduodenectomy following 11 cycles of chemotherapy. On gross examination there was a 2.3 × 2.2 × 1.8-cm, well-defined, pale tan, firm mass in the pancreatic head (Figure 69, A). Microscopic examination revealed round to spindle-shaped cells, highly pleomorphic mononuclear cells, and multinucleated OGCs (Figure 69, C) adjacent to the pancreatic duct (Figure 69, B) with areas of necrosis and hemorrhage. No epithelial glandular malignant elements were recognizable. Immunohistochemical studies showed the malignant spindled and pleomorphic cells were positive for vimentin and caldesmon and negative for keratins AE1/AE3 and CAM5.2. The multinucleated giant cells were positive for CD68. These findings were consistent with undifferentiated carcinoma with OGCs. In conclusion, we report a rare case of undifferentiated carcinoma with OGCs. Fewer than 100 cases have been reported in literature.

**Esophageal Small and Large Cell Neuroendocrine Carcinoma: Predictors of Survival Compared With Adenocarcinoma**

(Poster No. 115)

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**Context:** Neuroendocrine carcinoma (NEC) of the esophagus is extremely rare. The objective of this study was to compare the tumor characteristics and overall survival (OS) between esophageal small and large cell NEC, and with adenocarcinoma (EAC).

**Design:** Esophageal NECs were selected from the National Cancer Database (2004–2013). Multivariable analysis and Kaplan-Meier method were performed. The prognostic factors for EAC were derived from the literature.

**Results:** Of 483 selected patients with esophageal NEC, 11.8% were large and 88.2% small cell. The median age was 66. NEC more commonly presented in males (68%). Most of the NECs were >4 cm (80% in large versus 68% in small cell). The rate of esophagectomy was 21% in large versus 5.9% in small cell (P < .001); 88% of NECs had chemotherapy. Multivariable analysis showed that tumor >4 cm (hazard ratio [HR], 1.53; P = .03) and stage IV (HR, 4.16; P < .001) were associated with significantly worse OS, whereas small cell type (HR, 0.51; P = .02), esophagectomy (HR, 0.18; P = .01), and chemotherapy (HR, 0.38; P < .001) were predictors of better OS in
A Rare Papillocystic Variant of Acinar Cell Carcinoma in the Pancreas

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Acinar cell carcinoma (ACC) with papillocystic growth of the pancreas is a rare variant that can mimic intraductal neoplasms. We present a case of a 75-year-old man who initially presented with 2 months of epigastric pain, nausea, and vomiting, and was found to have an epigastric cystic mass arising from the pancreatic neck. The patient underwent a complex surgery to remove a 25-cm cystic mass that was adherent to the pancreas, stomach, duodenum, and gallbladder with metastasis to the diaphragm and liver. Grossly, the mass was 40% cystic and 60% solid. The solid component contained small, cystic loculations with prominent papillary excrescences and was filled with milky fluid and grumous material (Figure 71, A). Histologic features included both cystic and papillary architecture lined by cuboidal cells with granular, eosinophilic cytoplasm and conspicuous nucleoli (Figure 71, B through D). Immunohistochemical stains demonstrated that the neoplastic cells were trypsin, BCL-10, and chymotrypsin positive, consistent with acinar cell differentiation. Papillocystic variant of ACC is a diagnostic challenge because of its rarity and morbidologic overlap with the more common intraductal papillary mucinous neoplasm, which carries a more indolent course. There are only a handful of reported cases of papillocystic ACC. Previous reports suggest that this variant is less aggressive than conventional ACC. Here we present a rare, large, and relatively aggressive case. Our understanding of how this growth pattern impacts survival and management is limited. Recognizing this rare entity is essential for appropriate treatment and further study of its clinical behavior.

A Rare Papillocystic Variant of Acinar Cell Carcinoma in the Liver

(Poster No. 116)

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Rhabdomyosarcoma (RMS) is a common soft tissue sarcoma in children that can infrequently present in adulthood. Rarely RMS arises in solid organs. Although embryonal and alveolar RMS are the most common (>80% of all) histologic subtypes encountered, rare variants can occur. We report on a case of spindle cell/sclerosing variant of RMS in the liver of a 57-year-old woman. To the best of our knowledge, this is the first report of spindle cell/sclerosing variant of RMS in adult liver. The patient presented with shortness of breath, epigastric discomfort, and fatigue in May 2018. Magnetic resonance imaging revealed an 18.5-cm left hepatic lobe mass impinging on the heart and multiple nodules in the omentum. The patient underwent partial hepatectomy and left hemidiaphragm resection later in May 2018. Gross examination revealed an 18.5-cm liver mass abutting but not grossly invading the diaphragm (Figure 70, A). Histology revealed spindle cells arranged in a storiform pattern with pale eosinophilic cytoplasm, elongated nuclei, rare mitoses (up to 5/10 per high-power field), and foci of necrosis. Frequent rhabdomyoblasts with cross-striations and areas of stromal hyalinization with pseudovascular arrangement of tumor cells were noted (Figure 70, B and C). Immunohistochemically, neoplastic cells showed expression of desmin (strong and diffuse) and myogenin (patchy; Figure 70, D) but no expression of cytokeratins, HMB-45, or Melan-A. Fluorescent in situ hybridization was negative for FOXO1 gene rearrangement. Cytogenetics demonstrated hypodiploidy. The morphology, immunoprofile, and molecular features are consistent with a spindle cell/sclerosing variant of RMS. The patient is disease free 9 months post adjuvant chemotherapy.

Is “Adenomyomatous Hyperplasia” Truly Myomatous?: A Comparative Analysis of Myofibroblastic Proliferation in Adenomyomatous Hyperplasia, Chronic Cholecystitis, and Gall Bladder Carcinoma by Immunohistochemistry

(Poster No. 118)

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Adenomyomatous hyperplasia (AH) of the gallbladder, reported in 1%-8.7% of cholecystectomies, is hypothesized to be an exaggerated form of chronic cholecystitis, but the exact pathogenesis of this entity is still unknown. AH consists of cystically dilated sinuses/glads with a surrounding spindle cell proliferation that is thought to be composed predominately of smooth muscle cells. Myofibroblasts are contractile and secrete a variety of biochemical modulators, influencing the microenvironment by the “field effect.” Myofibroblasts can be immunohistochemically distinguished from smooth muscle cells by their desmin negativity. The primary objective of this study is to quantify and compare the myofibroblastic proliferation in AH, chronic cholecystitis, and gallbladder carcinoma.

Context: Adenomyomatous hyperplasia (AH) of the gallbladder, reported in 1%-8.7% of cholecystectomies, is hypothesized to be an exaggerated form of chronic cholecystitis, but the exact pathogenesis of this entity is still unknown. AH consists of cystically dilated sinuses/glads with a surrounding spindle cell proliferation that is thought to be composed predominately of smooth muscle cells. Myofibroblasts are contractile and secrete a variety of biochemical modulators, influencing the microenvironment by the “field effect.” Myofibroblasts can be immunohistochemically distinguished from smooth muscle cells by their desmin negativity. The primary objective of this study is to quantify and compare the myofibroblastic proliferation in AH, chronic cholecystitis, and gallbladder carcinoma.

Design: Eighteen cases of AH and 5 cases each of chronic follicular cholecystitis, chronic cholecystitis, and gallbladder carcinoma were stained with actin and desmin. The percentage of myofibroblasts was estimated by the difference between actin and desmin staining.

Results: The percentage of actin staining was significantly higher in AH and gallbladder carcinoma as compared with chronic follicular and...
chronic cholecystitis ($P = .04$). The percentage of desmin staining did not show any significant difference between the 4 groups. The estimated myofibroblastic population was significantly higher in AH and gallbladder carcinoma as compared with chronic follicular and chronic cholecystitis ($P = .005$).

**Conclusions:** The spindle cell proliferation around cystically dilated glands in AH is composed predominantly of myofibroblasts and not smooth muscle cells as previously described. This finding suggests that a derangement in epithelial-stromal interactions is the underlying pathophysiology in AH. This in turn raises the suspicion of a possible neoplastic nature of the glandular component in this entity.

**An Extremely Rare Case of Extrahepatic Mucinous Cholangiocarcinoma With Signet Ring Cell Features**

(Poster No. 119)

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An 80-year-old man presented with weight loss and obstructive jaundice symptoms. CT scan of abdomen showed moderate intrahepatic biliary duct dilatation with mass and soft tissue thickening in the region of proximal common hepatic duct that was highly suspicious for hilar cholangiocarcinoma (ie, Klatskin tumor). He underwent percutaneous transhepatic cholangiography (PTC), which was nondiagnostic and was complicated by acute kidney injury and acute ascending cholangitis. After treatment with fluids and antibiotics, he underwent extended right hepatectomy and Roux-en-Y hepaticojejunostomy. Grossly, diffuse thickening of the hepatic hilar area, hepatic ducts, cystic duct, and common bile duct with a mucoid appearance was identified. Microscopically, the tumor was composed entirely of well-defined pools of mucin with detached clusters of malignant cells and many signet ring cells (Figure 72). Hepatic ducts showed areas of high-grade biliary intraepithelial neoplasia (bILIN III). Cystic duct demonstrated a range of precursor lesions including bILIN-3, predominantly intestinal type, and a small tubular adenoma (intestinal type). There was overt mucinous carcinoma in situ in the cystic duct, and based on these findings, invasive carcinoma likely arising from the cystic duct was favored. Pure mucinous cholangiocarcinoma is an exceedingly uncommon entity, and it is usually large and advanced at the time of diagnosis with more aggressive behavior than ordinary carcinomas. Fewer than 20 cases of pure mucinous cholangiocarcinoma have been reported in the literature, and signet ring cell carcinoma of the extrahepatic bile ducts is extremely rare, with only 5 reported cases with very poor outcomes.

**Transition of This Rare Form of Dysplasia to Carcinoma on Gastric Biopsy**

(Poster No. 120)

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Gastric tubule neck dysplasia (TND) represents a rare precursor lesion of some diffuse-type gastric carcinoma (DTGC). It is believed to originate from the neck region of the oxyntic glands. This is a rare and problematic diagnosis, especially on small gastric biopsies, because it develops deep in nonmetaplastic epithelium of the neck region and the mucosal surface is commonly spared. We present our experience with 2 such cases, highlighting the histopathologic features suggestive of TND and the utility of IMP3 in identifying the transition to DTGC. A 43-year-old man and 66-year-old woman with a friable gastric mass in the body of the stomach underwent a small gastric biopsy that was negative for malignancy. A repeat “jumbo” biopsy demonstrated gastric oxyntic mucosa with normal surface and foveolar epithelium and an abnormally elongated gastric neck region in which cords of enlarged, atypical, cuboidal cells had large vesicular nuclei, prominent nucleoli, and pale acidophilic cytoplasm suggestive of TND (Figure 73, A). An abrupt transition from TND to invasive DTGC was clearly identified and confirmed by positive immunostain for IMP3 (Figure 73, B). On gastric resection, a DTGC with positive lymph nodes was identified. The tumor was metastatic to the omentum and stage IV in the 43-year-old whereas it was restricted to the stomach and stage III in the 66-year-old. Although TND is IMP3 negative, the areas of abrupt transition to DTGC become IMP3 positive. In summary, in a small biopsy, the presence of IMP3-positive cells at the advancing front of TND is predictive of DTGC. Additional cases are needed to support our conclusion.

**Sarcina ventriculi: A New Case Series on an Old Bug**

(Poster No. 121)

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*Sarcina ventriculi* is an anaerobic gram-positive coccus found in acidic environments that has been increasingly reported in the upper gastrointestinal tract. Infection by *S ventriculi* has been associated with delayed gastric emptying and, in the setting of gastric ulcers, emphysematous gastritis and gastric perforation. We present 2 cases of *S ventriculi* infection. The first case is of a 58-year-old man with a history of esophageal adenocarcinoma who had undergone esophagectomy. Follow-up esophagogastroduodenoscopy 8 months later showed an area of erythema in his neo-esophagus and retained food material at the anastomosis. Biopsies taken from the neo-esophagus showed acute esophagitis and *Sarcina* organisms (Figure 74, A and B). He received no antibiotic treatment and remained asymptomatic. The second case is of a 9-year-old boy with a history of esophagitis and pyloric stenosis who presented with persistent emesis. Esophagogastroduodenoscopy demonstrated purulence with sloughing...
of the mucosa in his esophagus and an ulceration immediately distal to the
gastric antrum. Biopsies of the midesophagus showed ulceration and S ventriculi (Figure 74, C) and the proximal esophagus showed
eosinophilic esophagitis. Biopsies of the gastric body also showed rare Sarcina organisms in a background of mild chronic inflammation (Figure 74, D). He was placed on ciprofloxacin and metronidazole with repeat biopsy 2 months later showing no S ventriculi. To our knowledge, we report the first case of S ventriculi infection associated with eosinophilic esophagitis. Although the pathogenesis of S ventriculi is unclear, awareness of the bacteria is important as treatment in symptomatic patients may prevent complications such as gastric perforation.

We are presenting a case of an 88-year-old woman with mildly elevated liver enzymes. CT demonstrated numerous hypervascular liver lesions ranging from 1 to 3 cm (Figure 75, A). Ultrasound-guided liver fine-needle aspiration was performed, which consisted of rare benign hepatocytes and blood elements in the smear. Concurrent percutaneous liver biopsy revealed a bland spindle cell proliferation in a “patternless pattern” (Figure 75, B) with multiple small vessels (Figure 75, C). Tumor cells had low mitotic activity. Immunohistochemical studies were performed and tumor cells were positive for STAT-6 (Figure 75, D), CD34, and Bel-2 and negative for C-kit, pancytokeratin, S100, SMA, desmin, arginase, and synaptophysin. The histomorphology and immunohistochemical profile were characteristic for SFT. SFT in the liver is a very rare mesenchymal tumor. As this is a mesenchymal lesion, fine-needle aspiration may not always yield a sufficiently cellular smear for definitive diagnosis. The definitive diagnosis is established by the histologic examination and immunohistochemical studies, especially STAT-6. The outcome of SFT mostly depends upon the resectability of the tumor. The patient passed away within a month after the diagnosis secondary to cardiac comorbidities.

Rare Hepatic Adenocarcinoma Expressing Synaptophysin and Inhibin
(Poster No. 123)
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We present a case of a 28-year-old woman with no significant medical liver history who presented with a large hepatic mass. Gross examination revealed a 15-cm well-demarcated and unencapsulated mass. Cut sections of the tumor were fleshy white with variably sized smooth-lined cysts. There was focal hemorrhage and myxoid change and no significant necrosis. H&E sections showed tumor cells arranged in glands, microcystic, and cystic patterns with focal nesting and solid growth. There was mild cytologic atypia, no necrosis, and rare mitotic figures. Focal calcifications and small vessel lymphovascular invasion were present. Immunohistochemical stains showed tumor cells positive for cytokeratin AE1/AE3, cytokeratin 7, MOC-31, inhibin, and synaptophysin (weak). FOXL2 was focally positive. A Ki-67 proliferation index was 10% overall. Tumor cells were negative for cytokeratin 20, HepPar-1, arginase, glypican-3, PAX-8, TTF-1, GATA-3, ER, PR, chromogranin, CD68, PLAP, SF1, Melan-A, calretinin, WT-1, D2-40, and EMA. Results of a next-generation sequencing assay analyzing mutations in 50 cancer-related genes were negative. To our knowledge, this is the fifth reported case of a hepatic adenocarcinoma expressing inhibin A in a young woman. The term “cholangioblastoid variant of intrahepatic cholangiocarcinoma” has been suggested, although the histogenesis is unclear. The distinctive morphology and immunoreactivity for inhibin and neuroendocrine markers are similar to our case. The natural history of this tumor is unclear because of its rarity, although aggressive features have been described. Our patient is alive after 1 year; however, more studies are needed to understand the biology and behavior of this unique tumor.

A Rare Case of Gastroesophageal Junction Sarcina ventriculi Infection in a 71-Year-Old White Man
(Poster No. 124)
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Sarcina ventriculi is a gram-positive anaerobic organism that can rarely infect human beings. Sarcina is not generally present in the normal healthy human stomach; however, it has been reported in the setting of pyloric ulceration and/or stenosis. To our knowledge, only 19 cases of human infections by this microorganism have been described in literature to date. We present a case of S ventriculi infection in a 71-year-old white man who presented with dysphagia to solid foods. The patient had a past medical history of Helicobacter pylori–positive chronic active gastritis status post therapy eradication. Endoscopic examination revealed congested, edematous-appearing mucosa at the GE junction without frank ulcerations or erosions. Thick yellow material was noted throughout the esophageal mucosa that was difficult to clear with water spray. Gastric and duodenal mucosae were unremarkable. Multiple tissue biopsies showed structures occurring in tetrads with molding and flattening of the cell borders, suggestive of S ventriculi. An interesting
highlight of our case was the prior history of *H* *pylori*–positive chronic active gastritis, for which he was treated with triple therapy resulting in the eradication of *H* *pylori*. This association between *S* *ventriculi* and *H* *pylori* has only been previously mentioned in 2 cases. The patient in our case was treated with 2 weeks of antibiotics with improvement of his dysphagia symptom. Follow-up repeated esophagogastroduodenoscopy examination revealed the eradication of the microorganism. It is important for pathologists to recognize this rare microorganism and recommend proper clinical management to the clinician (Figure 76).

Comparing Independent Pathologist Evaluation Reporting Grading and Staging Results Based on Histology Activity Index and Batts-Ludwig Scoring Systems

(Poster No. 125)

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Context: Liver biopsy is the gold standard method used in confirming the diagnosis and evaluating the severity of chronic viral hepatitis. Interobserver variability is an important factor in systems used for evaluating liver biopsies. In this study, we evaluated interobserver variability in the Batts-Ludwig and Histology Activity Index systems, 2 of the most commonly used systems in the management of chronic viral hepatitis patients.

Design: In this cross-sectional study, 254 patients with chronic viral hepatitis who referred to Alzahra Hospital, Isfahan, Iran from 2012 to 2017 were recruited consecutively. Liver biopsy samples that were stained with H&E and reticulin were included in the study. Three pathologists, expert in assessing liver biopsies, evaluated the samples based on the Histology Activity Index and Batts-Ludwig systems separately and reported grading and staging scores for each sample. Data were analyzed using SPSS software using the Kendall correlation test. P values <.05 were considered statistically significant. Satisfactory agreement among observers was defined as a correlation of above 0.7.

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Abbreviation: HAI, Histology Activity Index.

Results: Among a total of 254 patients with a mean age of 45.6 ± 12.5 years, Kendall correlation showed a reasonable correlation between pathologist results in both scoring systems (Table); however, in one occasion the correlation between the first and second pathologists reporting grading of chronic hepatitis based on the Batts-Ludwig system showed a low score of below 0.7 (r = 0.65, P < .001).

Conclusions: Both systems are valuable in terms of grading and staging chronic viral hepatitis, but the Histology Activity Index system showed a higher performance in evaluating liver biopsy samples.

Noninvasive Blood Tests for Detection of Significant Fibrosis and Nonalcoholic Steatohepatitis in Morbid Obesity

(Poster No. 127)

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Context: Studies have found that some noninvasive blood tests (NIBTs) can predict significant fibrosis (SF) on liver biopsy in patients with obesity and nonalcoholic fatty liver disease; however, the subpopulation of morbid obesity (MO) patients has not been well studied. This study was designed to determine the ability of NIBTs to predict nonalcoholic steatohepatitis (NASH) and SF specifically in MO patients.

Design: We reviewed the clinical and laboratory data (6 months before surgery) of MO patients who underwent gastric bypass surgery

Hepatic Angiomyolipoma With Sarcomatous Transformation and Metastasis

(Poster No. 126)

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Angiomyolipomas are rare mesenchymal neoplasms that belong to the perivascular epithelioid cell tumors group (PEComa). They frequently develop in the kidney but very rarely are detected in the liver. Angiomyolipoma is benign in nature and malignant sarcomatous transformation is an extremely rare event. We report a case of hepatic angiomyolipoma with sarcomatous transformation and distant metastasis. A 57-year-old woman was found to have a microscopic hematuria on a routine checkup. This led to imaging that failed to find the cause of the hematuria but incidentally detected a 7.5-cm liver mass. Hepatocellular carcinoma was entertained in the radiologic differential diagnosis and she underwent a liver lobectomy. Histologic sections of the tumor demonstrated a biphasic neoplasm composed of a sarcomatoid component with extensive central necrosis and numerous atypical mitoses, distinct from the more epithelioid component. By immunohistochemistry, the tumor cells were positive for Melan-A, focally positive for smooth muscle actin, and also patchy positive for HMB-45, mainly in the epithelioid component. Immunostains for pancytokeratin, HepPar1, and glypican 3 were negative. The morphology and immunophenotype were consistent with an angiomyolipoma with sarcomatous transformation. A year later the patient developed a lung nodule that showed a similar morphology and immunoprofile to her liver tumor; hence, this lesion was diagnosed as metastasis to the lung. Hepatic angiomyolipoma is very rare and often misdiagnosed as hepatocellular carcinoma on imaging studies. Histopathology with immunohistochemistry is the gold standard of the diagnosis for hepatic angiomyolipoma with malignant transformation and distinguishing it from hepatocellular carcinoma and other tumors in the liver (Figure 77).

Noninvasive Blood Tests for Detection of Significant Fibrosis and Nonalcoholic Steatohepatitis in Morbid Obesity

(Poster No. 127)

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Context: Studies have found that some noninvasive blood tests (NIBTs) can predict significant fibrosis (SF) on liver biopsy in patients with obesity and nonalcoholic fatty liver disease; however, the subpopulation of morbid obesity (MO) patients has not been well studied. This study was designed to determine the ability of NIBTs to predict nonalcoholic steatohepatitis (NASH) and SF specifically in MO patients.

Design: We reviewed the clinical and laboratory data (6 months before surgery) of MO patients who underwent gastric bypass surgery
with wedge liver biopsy during 3 years at George Washington University. Inclusion criteria were MO (BMI ≥40 kg/m² or >35 kg/m² with diabetes or hypertension) and data for sex, age, BMI, platelets, AST, ALT, and albumin; exclusion criteria were other potential causes of liver pathology, including alcohol. NIBT scoring systems included NAFLD fibrosis, BARD, APRI, and FIB4 scores and cutoffs to estimate SF on biopsy calculated using the GIHEP online calculator and compared with biopsy determinations of SF and evidence of NASH.

**Results:** A total of 105 patients with MO included 7 with SF and 11 with NASH; age 45 ± 10 years, BMI 47.2 ± 9.1 kg/m², and 85.7% female. Diabetes was more prevalent in patients with SF versus NSF (85.7% versus 43.9%) and those with NASH (63.6%). ALT was elevated (>40 IU/L) in 25.7% of cases (85.7% of cases with SF and 72.7% with NASH).

**Conclusions:** A simple ALT test had the best combination of sensitivity and specificity for detecting SF on liver biopsy in MO in comparison with other NIBTs.

### Extremely Rare Entity: Primary Biliary Cholangitis, Primary Sclerosing Cholangitis Overlap

(***Poster No. 128***)

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Primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC) are 2 distinct, well-studied entities. Overlap of PBC-PSC is a very rare condition with only 10 cases reported, which shows simultaneous features of PBC and PSC. We herein report a case with clinical, pathologic, and radiologic findings that are consistent with an overlap syndrome of PBC and PSC. A 45-year-old woman with a 10-year history of Crohn disease and PBC controlled with ursodeoxycholic acid was treated with obeticholic acid and colestipol for 4 months. A reduction of ductal/portal tract ratio (0.5; normal <0.9) was observed in an IBD patient. PBC-PSC overlap, although rare, is very important to highlight classic histologic features of both entities, which are supported by both clinical and radiologic means.

### Immunohistochemical Analysis Using a MUM1 (Clone MRQ-43) Antibody Highlights Parietal Cells and Assists the Evaluation of Parietal Cell Pathology

(***Poster No. 130***)

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**Context:** Parietal cells are impaired in conditions including atrophic and autoimmune gastritis. They can be difficult to identify in small crushed and inflamed biopsies. We used immunohistochemistry (IHC) with the MUM1 (MRQ-43) antibody to demonstrate parietal cells in normal gastric mucosa and in inflammatory conditions.

**Design:** Thirteen biopsies with diagnosis of atrophic gastritis were analyzed (n = 13) and compared with controls (normal stomach n = 2, fundic gland polyph n = 1). Immunohistochemistry (IHC) performed with the MUM1 (MRQ-43) antibody to demonstrate parietal cells in normal gastric mucosa and in inflammatory conditions.
stained by IHC using the antibody to MUM1 (clone: MRQ-43, Roche Ventana). The cases were also stained by a different MUM1 clone (EAU32). Morphologic evaluation and comparison of parietal cells in H&E and in MUM1-stained IHC slides was performed.

Results: MUM1 clone MRQ-43 stained both nucleus and cytoplasm of parietal cells in normal gastric mucosa and nonneoplastic gastric body. Also, expected MUM1 clone MRQ-43 staining was seen in the nucleus of intramucosal plasma cells and lymphocytes (Figure 79, A and B). Parietal cells were not demonstrated by other clones on MUM1 antibody (EAU32). In 13 cases of atrophic gastritis variable MUM1 MRQ-43 staining was seen. This facilitated demonstration of parietal cells and grading of atrophy.

**Conclusions:** IHC staining for MUM1 clone MRQ-43 highlights parietal cells in gastric body mucosa and assists the evaluation of parietal cell pathology. It can aid interpretation of small/crushed biopsies where morphology is not well preserved.

**Cronkite-Canada Syndrome**

*(Poster No. 131)*

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Cronkite-Canada syndrome is an extremely rare nonhereditary polyposis syndrome of unknown etiology with fewer than 500 reported cases since its first description in 1955. It is most prominent in the Japanese population and is one of the few polyposis syndromes that presents in middle-aged adults. It is a syndrome of polyposis as well as distinct ectodermal abnormalities including skin hyperpigmentation, alopecia, and onychodystrophy. Patients usually present with a combination of abdominal pain, diarrhea, weight loss, and malabsorption. The polyps are hamartomatous, closely resemble juvenile polyps, and occur throughout the gastrointestinal tract while sparing the esophagus. Although malignant transformation of these polyps is controversial, this syndrome has a mortality rate as high as 60%, with death resulting from malnutrition, gastrointestinal bleeding, or infection. We report a case of Cronkite-Canada syndrome in a 60-year-old Asian man with no significant medical or family history who first presented to an outside hospital with a partial bowel obstruction. Esophagogastroduodenoscopy and colonoscopy showed extensive polyposis of the stomach, the duodenum, and the entire colon (Figure 80, A and B). The patient underwent treatment with antibiotics and bowel rest at that time. In July 2018, he was referred to our institution for evaluation of worsening epigastric/midabdominal pain, loss of appetite, unintentional weight loss, and protein-losing enteropathy (albumin 2.1 g/dL). Gastric, duodenal, and colorectal biopsies obtained on repeat esophagogastroduodenoscopy showed reactive hyperplastic changes with no granulomatous inflammation or adenomatous lesions, in a background of hypoplastic mucosa with marked architectural disruption, confirming a diagnosis of Cronkite-Canada syndrome (Figure 80, C and D).

**Impact of Liver Biopsy Size on Histopathologic Evaluation of Liver Allograft Rejection**

*(Poster No. 132)*

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**Context:** Optimal biopsy length has been studied in chronic viral hepatitis but not in the transplant setting. The aim of this study was to determine influence of biopsy length on diagnostic accuracy in transplant rejection.

**Design:** We retrospectively reviewed liver core biopsies in patients with graft dysfunction. One investigator bracketed segments at intervals of 1, 1.5, 2, and 3 cm, and a second investigator evaluated the slides. An assessment according to Banff criteria was performed. A RAI score of 1–5 was considered mild rejection, 6–7 moderate rejection, and 8–9 severe rejection.

**Results:** Sixty-eight patients were included in the study. The length of biopsy strongly correlated with the number of portal tracts (P < .001). Smaller biopsies tended to both underestimate and overestimate ductopenia. Rejection rates increased from 73.53% to 79.41% with increase in length from 1 to 2 cm and moderate rejection increased from 11.76% to 33.82%. At 1.0 and 1.5 cm no cases of severe rejection were detected; at 2.0 cm there was 1 case; and at 3.0 cm 2 cases were detected.

**Conclusions:** An increased likelihood of rejection diagnosis was associated with increase in length from 1 to 2 cm. The increased length has greater influence on severity of rejection with moderate rejection increasing from 11.76% to 38.23% from 1 to 2 cm. Small biopsies can cause overdiagnosis and underdiagnosis of ductopenic rejection. There is not a consensus regarding the optimal length of core biopsy, but this study suggests that a minimum length of 2 cm should be obtained for confident exclusion (detection) of severe rejection.

**Mixed Adenocarcinoma–Large Cell Neuroendocrine Carcinoma: A Potential Diagnostic Pitfall**

*(Poster No. 133)*

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Mixed adenocarcinoma–neuroendocrine carcinoma, also called mixed adeno-neuroendocrine carcinoma, is a rare, high-grade malignant neoplasm. Its true prevalence is not precisely defined because of its rare occurrence. A 91-year-old man presented with anemia and hemoccult-positive stool. Colonoscopy revealed a polypoid and ulcerated mass in the ascending colon. A biopsy of the mass was diagnosed as invasive moderately to poorly differentiated adenocarcinoma. The diagnosis of the resection specimen was mixed adenocarcinoma–large cell neuroendocrine carcinoma. Seven of 17 lymph nodes were positive for metastatic carcinoma. The diagnosis of the resection specimen was mixed adenocarcinoma–large cell neuroendocrine carcinoma. The patient had...
a remote history of appendectomy; therefore, this neoplasm could represent a primary neoplasm of colon or recurrence of an appendiceal goblet cell carcinoid neoplasm. The former is favored with occurrence of a single isolated mass in this presentation. Mixed adenoendocrine–large cell neuroendocrine carcinoma has a poor prognosis with its aggressive nature and high recurrence rate. The correct categorization of the tumor has clinical value with substantially different clinical behavior and management compared with conventional adenocarcinoma.

Submucosal Lipoma of the Cecum: A Rare Case of Adult Ileocolic Intussusception

(Mohamed Alshal, MBBCCh (Mohamed.alshal@downstate.edu); Mouney Alawad, MD; Charles Shan, MD. Department of Pathology, SUNY Downstate Medical Center, Brooklyn, New York; Department of Pathology, Kings County Hospital Center, Brooklyn, New York.

Ileocolic intussusception is a rare cause of acute abdomen in adults. In most cases it is secondary to a malignant neoplasm in the colon. This case is of a 66-year-old woman who presented to the emergency department with right lower quadrant pain for the previous 2–3 months that became worse the previous night. She also reported intermittent diarrhea for the past 3 weeks and 2 episodes of bloody bowel movements. She also mentioned 15–20-pound weight loss during the last few months. She denied any fever, chills, dysuria, rectal pain, or hematemesis. CT of abdomen and pelvis was done and showed evidence of CMV and HHV8 were negative. The patient underwent a right hemicolectomy for histopathology, which showed granulation tissue with acute inflammation and inflammatory exudate. Immunohistochemical stains for CMV and HHV8 were negative. The patient underwent a right hemicolectomy with primary anastomosis, which showed a 6 × 5 × 3-cm pink, lobulated, well-circumscribed, firm, 1-cm nodule in the right lower quadrant. On-site ultrasound evaluation demonstrated an almost isoechoic 1.0-cm mass with relatively smooth margins. Smears from the ultrasound-guided FNA demonstrated lymphoid tissue with dermal filler material and associated multinucleated giant cell inflammatory reaction. Foreign body granulomas present a new diagnostic challenge for cytopathologists because of the increasing popularity of injectable facial dermal fillers. The cytologic smears usually demonstrate variably sized foreign body microspheres with associated variable inflammatory reaction (Figure 82).

Effect of the Paris System for Reporting Urinary Cytology With Histologic Follow-up

(Prih Rohra, MD (prih.rohra@rush.edu); Fernando A. Ocampo Gonzalez, MD; Lei Yan, MD; Ji-Weon Park, MD. Department of Pathology, Rush Medical Center, Chicago, Illinois.

Context: The Paris System for Reporting Urinary Cytology provided a standardized reporting system whose main focus was the diagnosis of high-grade urothelial carcinoma (HGUC). We conducted a study to see the impact of the Paris System on our cytologic diagnoses with associated histology.

Design: We reviewed our pathology database regarding urinary specimens in the year before implementation of the Paris System and the year after. We gathered the data regarding cytologic diagnosis and concurrent/subsequent histology, focusing on the atypical and negative for high-grade cannot rule out low-grade (NHL) diagnostic categories.

Results: From 2016 to 2017, 486 specimens were identified before implementation of the Paris System and diagnosed as follows: 81% negative for HGUC, 10% atypical, 2% suspicious, 5% NHL, <1% low grade or unsatisfactory. From 2017 to 2018, 602 specimens used the Paris System and diagnosed as follows: 83% benign/negative, 10% atypical, 2% suspicious, 5% HGUC, <1% low grade or unsatisfactory. From 2017 to 2018, 602 specimens used the Paris System and were diagnosed as follows: 81% negative for HGUC, 6% atypical, 3% suspicious, 4% HGUC, 4% NHL, <1% low grade. Focusing on the atypical category before the Paris System, histology was available for 13 of 49 cases (31%). Of these, 40% had HGUC. Regarding the atypical category after Paris, histology was found in 21 of 36 cases (58%). Of these, 52% were HGUC. Regarding NHL, concurrent histology was found in 13 of 26 cases (50%). Of these, 77% were low grade.
Conclusions: Our study showed that the Paris System lowered the rate of atypical from 10% to 6%. After the Paris System, atypical corresponded to a higher rate of high-grade urothelial carcinoma. Also, the NHL category had a high positive predictive value for diagnosing low-grade urothelial carcinoma.

A Rare Case of Disseminated Cryptococcal Infection in a 27-Year-Old Pregnant Woman

(Poster No. 137)
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Cryptococcus is a potentially life-threatening opportunistic pathogen in immunocompromised (Cryptococcus neoformans) or immunocompetent (Cryptococcus gattii) patients. We report a rare case of mediastinal cryptococcosis with superimposed meningitis in a 27-year-old woman (gravida 4, para 1, 0-2-1) at 26 weeks’ gestation. The patient presented for 2 to 3 weeks of dyspnea and chest pain. She denied recent travel and exposure to pigeons or caves. She had a past history of asthma and rheumatoid arthritis. CT revealed a lobulated anterior mediastinal mass with right hilar adenopathy (Figure 83, A) clinically and radiographically suspicious for lymphoma. Fine-needle aspiration (Figure 83, B) showed multinucleated giant cells engulfing yeast forms. Core biopsy (Figure 83, D), morphologically consistent with Cryptococcus species. During her hospitalization, she developed meningeal symptoms; cerebrospinal fluid (CSF) fungal culture showed 1 colony of C. neoformans. Cryptococcal antigen titer was 1:5 in CSF and 1:320 in blood. She initiated treatment with amphotericin with a good clinical response. She has continued to receive outpatient amphotericin, which will continue until delivery, then be switched to fluconazole. At the time of this submission, the pregnancy was in the third trimester without complication. To our knowledge, this is the first reported case of mediastinal cryptococcal lymphadenitis with meningitis during pregnancy in the United States. Because of the unusual presentation, Cryptococcus was not considered initially on the differential diagnosis. The pathologist’s awareness and ability to recognize cytologic features of Cryptococcus was important for rapidly providing the accurate diagnosis.

Cytologic Appearance of Pancreatic Cystosis on Fine-Needle Aspiration

(Poster No. 138)
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A 22-year-old white man with cystic fibrosis presented with newly discovered cystic lesions in the pancreas as a result of a magnetic resonance imaging performed after he developed insulin-dependent diabetes mellitus. Endoscopic ultrasound evaluation revealed multiple macrocystic and microcystic components without mural nodules. One of the cysts in the body of the pancreas was in clear direct communication with the nondilated main pancreatic duct. Fine-needle aspiration of 2 cysts was performed and showed foamy macrophages and rare ductal as well as acinar cells (Figure 84, A). Cell blocks showed nonpolarizable pink crystalloid material and small nonlamellated concretions consistent with inspissated secretions (Figure 84, B). Special stains for chymotrypsin and trypsin highlighted the acinar cells (Figure 84, C). Periodic acid–Schiff, with and without diastase, was negative. Biopsy of the cyst wall showed ductal epithelial cells with underlying fibrotic stroma (Figure 84, D). This is the first description of the fine-needle aspiration appearance of pancreatic cystosis. We discuss the cytologic differential diagnosis of cystic lesions of the pancreas and the biochemical as well as imaging findings used to arrive at the diagnosis.
the utility of molecular studies in differentiating CCS from the diagnostic pitfall of melanoma. CCS is an especially diagnostically challenging entity when it presents in uncommon locations such as the head and neck region.

The Importance of Being “On Site” in Rapid Evaluations of Pediatric Thyroid Fine-Needle Aspiration: A Retrospective Review

(Poster No. 140)

Michael Quinton, MD; Zhongxin Yu, MD; Jason Wagner, MD; Evan Fowle, DO; JoElle Peterson, MD; Rachel Conrad, MD. Departments of Pathology and Radiology, University of Oklahoma, Oklahoma City.

Context: Nondiagnostic pediatric thyroid fine-needle aspirations can delay patient care and increase costs because of subsequent repeat biopsies and additional operating room and anesthesia time.

Design: We retrospectively reviewed consecutive pediatric thyroid aspirations, comparing nondiagnostic rates on cases with rapid cytologic evaluation “off site” (300 feet from the operating room with results called to clinicians) versus cases with on-site rapid cytologic examination and face-to-face communication with clinicians in the operating room.

Results: Fifty-one patients (12 males, 39 females; age range, 5–20 years) underwent 66 aspirates. These were examined for nondiagnostic rates, number of smears and passes per case, and time from starting procedure to reporting results (Table). There was good correlation between final cytologic diagnoses and subsequent surgical resection findings.

Conclusions: Our nondiagnostic pediatric thyroid aspirations appear to decrease when an on-site interpreter provides rapid evaluation. This corresponds with a trend in fewer passes/smears and shortened procedure time. We had observed that by the time rapid nondiagnostic results were called from off site, clinicians had often wrapped up the procedure so that little subsequent action was taken, resulting in a higher nondiagnostic rate. In contrast, with on-site evaluations, there was almost immediate feedback on each needle pass so that additional passes could be readily implemented as needed. As a result, the final nondiagnostic rate was reduced. Our findings may also help decrease nondiagnostic results in other settings that use rapid cytologic evaluations. Limitations of this study include small sample size, incomplete documentation of procedure times, and variability in operators/interpreters.

Comparison of Off-Site Versus On-Site Delivery of Rapid Cytologic Evaluation Results

<table>
<thead>
<tr>
<th></th>
<th>Rapid Evaluation Performed Off Site</th>
<th>Rapid Evaluation Performed On Site</th>
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<tbody>
<tr>
<td>Final nondiagnostic results, No./Total (%)</td>
<td>4/25 (16)</td>
<td>2/41 (5)</td>
</tr>
<tr>
<td>No. of smears per case, mean ± SD</td>
<td>9.6 ± 3.9</td>
<td>7.5 ± 3.0</td>
</tr>
<tr>
<td>No. of passes per case, mean ± SD</td>
<td>4.9 ± 2.0</td>
<td>4.0 ± 1.7</td>
</tr>
<tr>
<td>Time from start of ultrasound to rapid result, mean ± SD, min</td>
<td>52.9 ± 19.2a</td>
<td>40.1 ± 21.5b</td>
</tr>
<tr>
<td>Time from start of anesthesia to rapid result, mean ± SD, min</td>
<td>44.0 ± 15.8a</td>
<td>32.4 ± 11.3c</td>
</tr>
<tr>
<td>Time from start of surgical procedure/biopsy to rapid result, mean ± SD, min</td>
<td>28.4 ± 13.7a</td>
<td>18.8 ± 12.1c</td>
</tr>
</tbody>
</table>

a Total 18 cases.
b Total 34 cases.
c Total 23 cases.

The Risk of Malignancy Excluding NIFTP for the Bethesda System for Reporting Thyroid Cytopathology: A Single-Institutional Study With 5224 Thyroid Aspirates

(Poster No. 141)

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Context: Reclassification of encapsulated noninvasive follicular variant of papillary carcinoma as noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) may have affected the implied risk of malignancy (ROM) for the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC).

Histologic Correlation of Cytologic Diagnosis Categorized by TBSRTC

<table>
<thead>
<tr>
<th></th>
<th>BNN</th>
<th>FA</th>
<th>NIFTP</th>
<th>M</th>
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<tbody>
<tr>
<td>ND (57)</td>
<td>34</td>
<td>5</td>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>B (551)</td>
<td>432</td>
<td>43</td>
<td>10</td>
<td>66</td>
</tr>
<tr>
<td>FLUS (245)</td>
<td>90</td>
<td>60</td>
<td>23</td>
<td>72</td>
</tr>
<tr>
<td>FN (141)</td>
<td>21</td>
<td>63</td>
<td>6</td>
<td>51</td>
</tr>
<tr>
<td>SM (61)</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>54</td>
</tr>
<tr>
<td>M (251)</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>250</td>
</tr>
<tr>
<td>Total (1306)</td>
<td>581</td>
<td>174</td>
<td>41</td>
<td>510</td>
</tr>
</tbody>
</table>

Design: The cases included nondiagnostic (ND) (3.8%), benign (B) (74%), follicular lesion of undetermined significance (FLUS) (9.3%), follicular neoplasm (FN) (4.3%), suspicious for malignancy (SM) (1.5%), and malignant (M) (7.1%). Of 5224 aspirates, 1306 (25%) had corresponding surgical resections. Follow-up histologic diagnoses were designated benign nonneoplastic (BNN), follicular adenoma (FA), NIFTP, papillary microcarcinoma 1 (PMC 1, size ≤0.5 cm), PMC-2 (size 0.6–1 cm), and malignant (size >1 cm).
**RESULTS:** Results of histologic follow-up were tabulated (Table). Forty-one cases of NIFTP accounted for 3.1% of all follow-up resection specimens. The most common corresponding preoperative cytologic diagnosis was FLUS (56%), followed by benign (24.3%), FN (14.6%), ND (2.4%), and SM (2.4%). No NIFTP cases had a malignant preoperative fine-needle aspiration diagnosis. The ROM including PMC for each category was ND 29.8%, B 12%, FLUS 29.4%, FN 39%, SM 88.5%, and M 99.6%. The ROM excluding PMC was 12.3% for ND, 1.5% for B, 15.1 for FLUS, and 22.7 for FN. Most PMC-1 cases were incidental findings, as the most common correlating cytologic diagnosis was benign.

**Conclusions:** NIFTP constituted a small proportion of follow-up cases (3.1%), and no corresponding preoperative cytologic diagnoses were malignant. The ROM excluding PMC and NIFTP for each category was consistent with the TBSRTC.

### Quantitative Profiling of Cancer Cell Morphology With Serous Effusion Samples by Machine Learning

(Paper No. 142)

**Ding Dai, MD, PhD** (daid14@ecu.edu); Heng Hong, MD, PhD; Safaa A Al-Qaysi, PhD; Xin-Hua Hu, PhD. Departments of 1Pathology and Laboratory Medicine and 2Physics, East Carolina University; Greenville, North Carolina; 3Department of Pathology, Wake Forest Baptist Medical Center at Wake Forest University, Winston-Salem, North Carolina.

**Context:** Cytologic diagnosis of cancer cells in serous effusion specimens is very challenging. To develop new methods of improved efficacy, it is of significant interest to obtain their quantitative morphometric features for cell profiling.

**Design:** Effusion specimens from 6 patients with ovarian or lung cancers were collected and cytology slides were prepared with Papanicolaou stain. A total of 242 malignant cells and 318 benign cells were randomly selected by cytopathologists based on cytologic criteria. The images of the cells were processed with ImageJ to calculate the cell area ($A_c$) and nuclear area ($A_n$). All of the 560 cells were clustered by Gaussian mixer model (GMM) based on the 2D morphology parameters ($A_c$, and $A_n$) of each cell by the choice of GMM algorithm.

**Results:** We found that when the cells were divided into 3 clusters, about 64% of the cells can be well characterized by the GMM algorithm: 96.8% of the cells in the large cell cluster were malignant cells, and 97.3% of the cells in the small cell cluster were benign cells (Table). The medium cell cluster contains a mixture of benign and malignant cells.

**Conclusions:** Application of quantitative morphology analysis allows clustering of effusion cells objectively with a machine-learning tool requiring no training. Although our current result can identify malignant cells with high specificity, the sensitivity is still not high enough for practical clinical use. This study is an encouraging beginning for future research to rapidly profile perfusion cells by morphometric features for the identification of malignant cells in clinical samples.

<table>
<thead>
<tr>
<th>Distribution of Malignant and Benign Cells in Different Clusters</th>
</tr>
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<tbody>
<tr>
<td>Cluster Groups</td>
</tr>
<tr>
<td>Malignant cells, No. (%)</td>
</tr>
<tr>
<td>Benign cells, No. (%)</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

$A_c = 189.7 \pm 292 \mu m^2$; $A_n = 153.4 \pm 176 \mu m^2$.

$A_c = 106.1 \pm 45.8 \mu m^2$; $A_n = 42.2 \pm 19.8 \mu m^2$.

$A_c = 31.0 \pm 5.8 \mu m^2$; $A_n = 16.98 \pm 5.0 \mu m^2$.

### Cerebrospinal Fluid Cytology, Imaging, and Laboratory Findings in Patients With Neoplastic Meningitis

(Paper No. 143)

**Wen Zhong, MD** (zhongw16@ecu.edu); Philip J. Boyer, MD, PhD; Deepak Donthi, MD; Karyn Prenshaw, MD. Department of Pathology and Laboratory Medicine, East Carolina University and Vidant Medical Center, Greenville, North Carolina.

**Context:** Neoplastic meningitis (NM), representing dissemination of malignant cells within the meninges and cerebrospinal fluid (CSF), is a late and often fatal central nervous system complication of advanced neoplasms. Diagnosis is based on clinical manifestations, radiographic findings, and CSF analysis.

**Design:** In this retrospective study, 141 abnormal CSF cytology specimens from 71 patients were identified during a 10-year period at our institution. Cytology glass slides were reevaluated by a board-certified cytopathologist. Clinical, radiologic, and CSF laboratory data were reviewed.

**Results:** A large majority of patients (95.8%) had nonprimary malignancies with brain, spinal cord, and/or leptomeningeal involvement, including 37 with nonhematopoietic solid tumors and 31 with hematopoietic malignancies. A clinical diagnosis of NM was made in 65 patients based on cytologic, flow cytometric, and/or radiographic data. Magnetic resonance imaging revealed contrast enhancement suggestive of leptomeningeal spread in 71.8% of patients with solid malignancies; it was less predictive of and sensitive for hematopoietic malignancies (35.7%). Flow cytometry, performed on more than half of hematopoietic cases, demonstrated 100% positivity. Elevated CSF white cell counts and protein concentrations were noted in 62.2% and 46.4% of cases, respectively. Glucose concentrations, unlike previous studies, were not strongly associated with NM. The prognosis of patients with NM was devastating, with a median survival of 1.5 months (3 days–27 months).

**Conclusions:** Cytologic evaluation of CSF is an important tool in the definitive diagnosis of NM, with or without imaging abnormality. Negative cytologic and radiographic findings do not exclude NM, particularly if the clinical presentation and laboratory data are strongly suggestive of the diagnosis.

**Improvised “Flip Out” Method for Rapid Cytologic Assessment of Echinococcus**

(Paper No. 144)

**Aaron P. Rupp, MD** (arupp@salud.unm.edu); Samuel J. Reynolds, MD. Department of Pathology, University of New Mexico, Albuquerque.

Echinococcal infection is exceedingly rare in the United States and may escape consideration in the differential diagnosis of lung masses. Cytologic findings including hooklets may elude identification if malignancy is highly suspected. Confirmation of cyst wall may require special stain. Prompt identification on routine cytology may be critical for treatment and prognosis. Of note, rapid on-site evaluation is often used for assessment and triage in lung masses of unknown etiology. Rapid identification of *Echinococcus* may be critical if inadvertently detected at rapid on-site evaluation, as risk of anaphylaxis or spread may occur with sampling. We report a 60-year-old man presenting with subacute hemoptysis. Imaging demonstrated a 6.5-cm right middle lobe lung mass with multiple locules of air with radiologic differential of malignancy versus chronic infection. Bronchoscopy demonstrated an endobronchial mass that extravasated fluid upon biopsy. Cytology demonstrated fragments of acellular strips consistent with lamellated cyst wall. A rare potential hooklet was noted on screening. A rapid, improvised adjustment of the condenser (termed “flip out”) resulted in
markedly improved visualization of hooklets (Figure 86, A through D), which allowed a presumptive diagnosis to be rendered. By paired-sample t tests, improvement in identification of hooklets (P < .001) and reduced screening duration (P < .05) was demonstrated in pathologists (n = 7) at our institution using the flip-out method. This rare case illustrates cytologic assessment of *Echinococcus* can be statistically bolstered by using the flip-out method. Suspicion of *Echinococcus* carries potentially critical procedure implications, especially if noted during rapid on-site evaluation, as well as important treatment and prognostic implications.

**Frequency of First-Time Diagnoses of Malignancy in Pleural Fluids and Identification of Common Primary Sites of Malignancy**

*(Poster No. 145)*

Caitlin M. Darrell, MD (cddarell@bidmc.harvard.edu); Liza M. Quintana, MD. Department of Pathology, Beth Israel Deaconess Medical Center, Boston, Massachusetts.

**Context:** Pleural fluids are a common cytology specimen and cytologic analysis allows for the diagnosis of malignancy metastatic to pleural fluid. Patients with malignant effusions often have known cancer diagnoses, but in some cases the specimen represents the first presentation of malignancy. Evaluation of the fluid and correct categorization of the malignancy provides the opportunity for minimally invasive identification of a primary carcinoma.

**Design:** Cytology reports were retrieved from the digital archive for all malignant pleural fluid specimens from January 1, 2016, through December 31, 2018, at our institution. For each case, a prior diagnosis of malignancy was noted if identified.

**Results:** A total of 2,374 pleural fluid specimens were identified; 470 (19.8%) were positive for malignancy. A total of 203 cases (42.2%) represented first-time positive pleural fluids in patients with known cancer diagnoses, with some representing first-time diagnoses of metastasis. Ninety-two specimens (19.6%) represented initial presentation and diagnosis of a previously unknown malignancy. Workup by immunohistochemistry revealed that in both groups the most common primary site was lung (Table).

<table>
<thead>
<tr>
<th>Primary Source</th>
<th>First-Time Diagnosis</th>
<th>First Positive Pleural Fluid (Known Malignancy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>55</td>
<td>52</td>
</tr>
<tr>
<td>Gynecologic</td>
<td>14</td>
<td>26</td>
</tr>
<tr>
<td>Pancreatobiliary</td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>Breast</td>
<td>0</td>
<td>41</td>
</tr>
<tr>
<td>Hematologic</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Gastroesophageal</td>
<td>1</td>
<td>18</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Colorectal</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Small cell</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>Nonspecific</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total cases</strong></td>
<td>92</td>
<td>203</td>
</tr>
</tbody>
</table>

**Conclusions:** In patients with no prior cancer history or diagnosis of metastases, a pleural fluid specimen represents a significant opportunity to identify the malignancy without need for additional invasive tests, allowing for targeted testing, including molecular assays, and treatment. Knowledge of the most frequent primary sites for malignant pleural effusion allows the pathologist to better predict the source and tailor the immunohistochemical workup accordingly. In our cohort, carcinomas of unknown primary represent a significant proportion of malignant pleural effusions. Overall, the most frequent unknown primary site for malignant pleural fluids is pulmonary followed by gynecologic origin.

**Cytologic Evaluation of Metastatic Sarcoma in a Patient With Uterine Carcinosarcoma**

*(Poster No. 146)*

Roger A. Fecher, MD, PhD (rfecher@montefiore.org); Siba El Hussein, MD; Antonio Cajigas, MD; Samer Khader, MD. Department of Pathology, Montefiore Medical Center, Bronx, New York.

Studies of the pathobiology of carcinosarcoma have provided mounting evidence consistently supporting the existence of a cancer stem cell giving rise to 2 distinct populations either through “divergent differentiation” or subsequent “dedifferentiation.” Elucidation of the directionality of this transition would benefit our understanding of clinical progression and guide therapy. Here we present a case of a uterine carcinosarcoma with metastasis of the sarcomatous component to a pelvic lymph node. A 74-year-old woman with history of uterine carcinosarcoma was found to have a 6.1-cm pelvic lymph node on imaging; CT-guided fine-needle aspiration revealed spindle cells arranged in whorls and sheets. Morphologically, these cells (Figure 87, A) resembled focal low-grade areas of the sarcomatous component in the prior surgical specimen (Figure 87, B). Because the carcinomatous component classically metastasizes, the presence of only the sarcomatous component within the metastasis may provide insight into the directionality of carcinosarcoma development. In the setting of “dedifferentiation,” only the cell population with increased metastatic potential is expected to metastasize. In the setting of “dedifferentiation,” metastasis of the most metastatic population and subsequent dedifferentiation could lead to both cell populations (or either individually) within the metastasis. We hypothesize that in our case the carcinomatous component metastasized to the lymph node with subsequent dedifferentiation of the epithelial component into a pure low-grade sarcoma. The absence of rhabdomyosarcoma differentiation (which constituted the majority of the sarcomatous component in the carcinosarcoma) in the metastatic sarcoma supports this theory.

This unique presentation provides further insights into the pathogenesis of carcinosarcoma.

**Unique Cytomorphology of Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma**

*(Poster No. 147)*

Jessica Petrone, MD (jpetrone@path.wustl.edu); Rebecca Chernock, MD; Zhongren Zhou, MD. Department of Pathology and Immunology, Washington University School of Medicine, St Louis, Missouri.

**Context:** Diffuse sclerosing variant of papillary thyroid carcinoma (DSV-PTC) is a rare, aggressive variant. The histologic features include diffuse thyroid involvement, lymphocytic infiltration, and squamous metaplasia. Here we compare the histologic and cytomorphologic features of DSV-PTC.

**Design:** A search was performed for DSV-PTC in surgical specimens with corresponding cytology specimens from 1995 to present at a single academic institution. All slides were evaluated for preset criteria by 2 pathologists with head and neck pathology or cytopathology specialization.

**Results:** Six cytology specimens and 5 surgical specimens among 4 patients were found. All primary tumors displayed extrathyroidal extension, neck lymph node metastasis, and classic PTC nuclear features; however, intranuclear cytoplasmic inclusions were rare. All primary tumors displayed histologic features characteristic of DSV-PTC. A majority showed areas with micropapillary architecture and hobnail cells. All the cytology cases showed moderate or high cellularity and classic nuclear features of PTC. Lymphocytes were present in all cases. Other features including psammoma bodies, squamous metaplasia, and hobnail cells were present in 67%–83% of cases. Micropapillary architecture was absent in the cytology specimens (Table).

**Conclusions:** Cytology specimens of DSV-PTC are often moderately to highly cellular and display classic features of PTC. Unique cytologic features include hobnail cells, background lymphocytes, and squamous metaplasia, and when present in conjunction with classic PTC features...
may suggest DSV-PTC variant. The DSV-PTC surgical specimens often display areas with micropapillary architecture and hobnail cells, features often associated with the aggressive hobnail variant of PTC; thus, DSV-PTC should be excluded before diagnosing the hobnail variant.

<table>
<thead>
<tr>
<th>Histologic and Cytomorphologic Features of DSV-PTC</th>
<th>Surgical Excision Primary Tumor</th>
<th>Cytology Specimen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 4)</td>
<td>(n = 6)</td>
</tr>
<tr>
<td>Nuclei, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enlargement</td>
<td>4 (100)</td>
<td>6 (100)</td>
</tr>
<tr>
<td>Clearing</td>
<td>4 (100)</td>
<td>6 (100)</td>
</tr>
<tr>
<td>Grooves</td>
<td>4 (100)</td>
<td>5 (83)</td>
</tr>
<tr>
<td>Intranuclear cytoplasmic inclusions</td>
<td>4 (100)</td>
<td>4 (67)</td>
</tr>
<tr>
<td>Psammoma bodies, No. (%)</td>
<td>4 (100)</td>
<td>5 (83)</td>
</tr>
<tr>
<td>Lymphocytic infiltration/ background lymphocytes, No. (%)</td>
<td>4 (100)</td>
<td>6 (100)</td>
</tr>
<tr>
<td>Squamous metaplasia, No. (%)</td>
<td>4 (100)</td>
<td>5 (83)</td>
</tr>
<tr>
<td>Micropapillary pattern, No. (%)</td>
<td>3 (75)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Hobnail cells, No. (%)</td>
<td>3 (75)</td>
<td>4 (67)</td>
</tr>
</tbody>
</table>

Abbreviation: DSV-PTC, diffuse sclerosing variant of papillary thyroid carcinoma.

The Core Needle Biopsy Wash: Assessing Cellular Adequacy for Ancillary Studies

Weiguo Liu, MD, PhD1; Xiaobing Jin, MD, PhD1; Katherine Cwiklinski, BS2; Wilfrido Mojica, MD.1 Departments of 1Pathology and 2Medicine, University at Buffalo, New York.

Context: The use of the core needle biopsy (CNB) to obtain diagnostic tissue has gained in popularity. The increasing demand for molecular testing has created a new problem in tissue management—the loss of adequate amounts of material from an already limited specimen. Herein we introduce a novel approach in the processing of the CNB and assess whether this method will quantitatively suit the needs for molecular testing.

Design: Twenty-nine CNBs were performed on ex vivo tumor resection specimens. Processing of the core was modified by introducing the tissue and needle into a buffer solution. After incubation, the tissue core was sent for traditional FFPE processing. A cell count was performed on the remaining supernatant and then processed by thin-layer cytology technology to document the recovery of targeted cells.

Results: The number of cells counted in the supernatant varied, with 3 specimens having <1,000 cells, 5 between 1,000 and 10,000, 16 between 10,000 and 100,000; and 5 having >100,000 cells. The cytologic appearance of the cells were in keeping with the biopsied source, as confirmed by comparison with the originating FFPE CNB tissue.

Conclusions: Cells dislodged from the CNB procedure are normally lost, leading to the loss of a valuable resource. Some molecular platforms can work with input material requiring only 300 cells, making this approach, which is not normally practiced in today’s laboratory, a consideration in the processing of CNB specimens.

Pelvic Inflammatory Pseudotumor With Sodium Polystyrene Sulfonate Crystals Diagnosed by Endoscopic Ultrasound-Guided Fine-Needle Aspiration Cytology

Twisha H. Oza, MD2; Amir Baniahshemi, MD1; Arnold H. Szporn, MD; Christopher J. DiMaio, MD.1

A 55-year-old man developed a presumed bowel perforation following treatment with the cation-exchange resin sodium polystyrene sulfonate (Sodium polystyrene sulfonate (SPS) (Kayexalate, Concordia Pharmaceutical Inc, Barbados) in 2005. He presented to another facility in October 2016 with a pelvic mass. Endoscopic ultrasound-guided fine-needle aspiration performed at that time was reported to be benign. Follow-up magnetic resonance imaging in May 2017 showed a 6.7 × 6.1 × 5.3-cm mass between the bladder and rectum with heterogeneity, areas of peripheral enhancement, and central necrosis with some calcifications. The patient was referred to our institution for further evaluation and endoscopic ultrasound-guided fine-needle aspiration was performed in December 2017. Scattered nonnecrotic polygonal cells with peripheral notching, blue in air-dried Diff-Quik-stained direct smears and magenta in Papanicolaou-stained smears (Figure 88) were seen in a background of marked acute inflammation. In a hematoxylin and eosin–stained cell block section (Figure 88), these structures were lavender with a fish-scale (FS) appearance, consistent with SPS crystals. Surgical pathologists are relatively familiar with SPS–associated gastrointestinal tract injury. In surgical specimens, SPS typically presents with FS. To the best of our knowledge, the cytologic morphology of SPS has not been previously described and there have been no previous reports of its diagnosis by FNA. In our direct smears, SPS lacks the FS appearance so typically seen in paraffin-embedded tissue sections, as well as in our cell block section, but rather demonstrates peripheral notching, a feature that may potentially be considered diagnostic.

Dr DiMaio serves as a consultant with Boston Scientific and Medtronic.

Cytologic Diagnosis of Ectopic Intrathoracic Thymic Tissue in a Young Child

Lopa Modi, MBBS, MD1; Osvaldo Hernandez, MD1; Brenda Kohn, MD, PhD; Yin Shi, MD, PhD; Aylin Simsr, MD; Chrystia Slywotzky, MD; Wei Sun, MD; Xiao-Jun Wei, MD.1 Departments of 1Pathology, 2Pediatrics, and 3Radiology, NYU Langone Medical Center, New York City, New York.

Ectopic intrathoracic thymic tissue is due to an aberrant migration during embryogenesis and it is an uncommon finding in thyroid nodules in children. Because the prevalence of thyroid malignancy and its stages are much higher in children than in an adult population, cytologic and histologic diagnostic procedures are likely pursued for definitive diagnosis. We report such a case in a 6-year-old girl diagnosed by ultrasound-guided fine-needle aspiration biopsy. Our patient was found to have an incidental 0.9 × 0.3 × 0.6-cm oval, hypoechoic nodule with multiple linear and punctate echogenic foci in pararenal space, as well as in left kidney (Figure 89, A) on sonogram during a workup for a mild increase of thyroid peroxides antibodies. Differential diagnosis included colloid cyst, malignancy, and intrathyroid thymic tissue. She underwent ultrasound-guided aspiration biopsy under sedation. The smears showed abundant small lymphocytes mixed with scattered epithelioid cells and aggregates, and a few well-formed whirled, keratinizing epithelial pearls consistent with Hassall corpuscles (Figure 89, B). Occasional tingible body macrophages and multinucleated giant cells were also noted. No thyroid elements were seen in these samples. These morphologic features, in conjunction with the sonographic appearance, are compatible with intrathyroidal ectopic thymus tissue. It is important to recognize characteristic sonographic appearance and the pathognomonic features in cytology. Metically searching for Hassall corpuscles is the key to achieve an accurate diagnosis. Flow cytometry.
and immunohistochemistry can be helpful in reaching a diagnosis. However, they require more samples and higher cost. Diagnosis is important to prevent unnecessary surgery on a child.

**Rhabdomyoma Presenting as a Thyroid Nodule in a Patient With Birt-Hogg-Dubé Syndrome**

(Poster No. 152)

Margaret Black, MD1 (margaret.black@nyumc.org); Xiao-Jun Wei, MD2; Yei Sun, MD2; Anthony Simms, MD2; Raquel Negron, CLT2; Mari Hagiwara, MD2; Aaron K. Chidakel, MD2; Steven Hodak, MD2; Mark S. Persky, MD4; Yan Shi, MD, PhD1. Departments of Pathology, Radiology, Endocrine, and Otolaryngology, New York University, New York City, New York.

Extracardiac rhabdomyoma is an uncommon benign skeletal muscle tumor with a predilection for the head and neck region. However, it is extremely rare to present as a thyroid nodule. We report a case of rhabdomyoma diagnosed by thyroid fine-needle aspiration (FNA) in a patient with Birt-Hogg-Dubé (BHD) syndrome. A 60-year-old man with BHD syndrome presented for recurrent pneumothorax. Chest CT incidentally identified a thyroid nodule. Subsequent sonography found a 4.44 × 2.28 × 2.82-cm solid, hypoechocic nodule in the right upper pole with smooth margins and no calcification. Ultrasound-guided FNA revealed scattered clusters and isolated large polygonal cells with abundant granular cytoplasm and small peripherally located nuclei. Vague striations suggestive of skeletal myocytes were identified (Figure 90, A through D). No atypia, mitosis, or necrosis was seen. No thyroid follicular cells or colloid were identified. Immunocytochemistry demonstrated diffuse positivity for desmin, supporting the diagnosis of rhabdomyoma. Subsequent imaging studies suggested that the mass may be extrathyroidal and compressing the right thyroid lobe; surgery is planned. The diagnosis of rhabdomyoma on FNA is challenging because of its cytologic similarity to normal skeleton muscle. Differential diagnosis includes Hurthle cell neoplasm, granular cell tumor, and colloid nodule, especially with a scant sample. Adequate radiologic data and use of ultrasound guidance for FNA are critical for an accurate diagnosis. BHD syndrome is a rare autosomal dominant disease due to germline mutations in the FLCN gene that is associated with skin lesions, lung cysts, and kidney tumors. Its association with rhabdomyoma has been suggested in the literature.

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**Roadblocks to Cell Blocks: Predictive Modeling of Preanalytic Variables Associated With Cell Block Production**

(Poster No. 151)

Troy Hutchens, MD, PhD (troy.hutchens@uphs.upenn.edu); Rose-ann L. Wu, MD, MPH, Department of Pathology and Laboratory Medicine, Hospital of the University of Pennsylvania, Philadelphia.

**Context:** The preparation of cell blocks from fine-needle aspiration specimens enables further microscopic, immunohistochemical, and molecular evaluation essential for providing complete diagnostic and prognostic details. The process of producing a cell block is labor intensive and only sometimes successful. This study aims to identify features that associate with and predict cell block production.

**Design:** Cytopathology reports for select fine-needle aspiration specimens performed at the Hospital of the University of Pennsylvania in 2017 were collected. A data set (N = 3486) was created by extracting preanalytic features (technique, tissue type, gross color, gross turbidity, number of passes) and an outcome measure of cell block production. Logistic regression was performed to identify feature variables that independently associate with cell block production. A model of cell block production was created by comparing multiple supervised machine-learning algorithms with 10-fold cross-validation. Data analysis was performed in R/RStudio.

**Results:** Multiple variables were significantly associated with cell block production (P < .05; Table). In validation studies, a random forest-generated model was able to predict cell block production with an accuracy of 93% (sensitivity 96%, specificity 79%). Retrospective application of the model identified 561 specimens in which cell block production would fail.

**Conclusions:** Logistic regression can identify variables that are independently associated with outcomes in complex data sets with multiple strong confounders. Machine learning–generated predictive models are powerful tools that can be integrated into laboratory procedures for process improvement, such as reducing wasted effort on cell block production.
Management Implications of Preoperative Fine-Needle Aspiration Diagnoses of Warthin Tumors Reclassified According to the Milan System for Reporting Salivary Gland Cytopathology (TMS)

(Poster No. 154)

Sulaiman Farooqui, DO (sulaiman.farooqui@lumc.edu); Reza Eshraghi, MD; Stefan Pambuccian, MD; Swati Mehrotra, MD. Department of Pathology, Loyola University Medical Center, Maywood, Illinois.

Context: The Milan System (TMS) for Reporting Salivary Gland Cytopathology categorizes Warthin tumor (WT) in the “benign neoplasm” category, associated with a risk of malignancy of <5%. However, this diagnosis cannot always be made, as the cytologic diagnosis can be challenging in the setting of extensive cystic changes, infarction, or squamous and mucinous metaplasia. The aim of this study was to determine the management implications of preoperative TMS cytologic diagnoses of surgically resected WTs.

Design: We performed a 20-year (1999–2019) retrospective review of all surgically resected WTs with preoperative cytologic diagnoses were reclassified according to TMS.

Results: Sixty-eight of 216 surgically resected WTs had preoperative fine-needle aspiration (FNA) cytologic diagnoses (FNA; Table). Of the 9 cases (13.2%) diagnosed as category III, IVB, or V, 5 had a histologic diagnosis of infarcted WT and 1 had extensive mucinous metaplasia. Five of 9 patients received appropriate clinical management based on intraoperative frozen section diagnosis. However, 2 cases, 1 “SUMP” and 1 “suspicious,” received limited nodal dissection or total parotidectomy with neurorraphy.

Conclusions: Most WTs are accurately diagnosed on FNA and are managed appropriately. In cases with SUMP or suspicious diagnoses, frozen section diagnosis can be used to guide surgical management.

### TMS Cytologic Diagnoses of 68 Cases With Preoperative FNA

<table>
<thead>
<tr>
<th>TMS Category</th>
<th>No. of Cases</th>
<th>% of Cases</th>
<th>Histologic Follow-up, No./Total Cases (%)</th>
<th>Risk of Malignancy, No./Total Cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Nondiagnostic</td>
<td>0</td>
<td>0.00</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>II. Nonneoplastic</td>
<td>16</td>
<td>23.53</td>
<td>4/16 (25)</td>
<td>2/16 (12.5)</td>
</tr>
<tr>
<td>III. AUS</td>
<td>3</td>
<td>4.41</td>
<td>0/3</td>
<td>0/3</td>
</tr>
<tr>
<td>IV. Neoplasm</td>
<td>43</td>
<td>63.24</td>
<td>6/43 (14)</td>
<td>6/43 (14)</td>
</tr>
<tr>
<td>A. Benign</td>
<td>148</td>
<td>47.60</td>
<td>46/148 (31)</td>
<td>46/148 (31)</td>
</tr>
<tr>
<td>B. Salivary gland neoplasm of uncertain malignant potential</td>
<td>24</td>
<td>7.70</td>
<td>10/24 (42)</td>
<td>10/24 (42)</td>
</tr>
<tr>
<td>V. Suspicious</td>
<td>7</td>
<td>2.30</td>
<td>3/7 (43)</td>
<td>3/7 (43)</td>
</tr>
<tr>
<td>VI. Malignant</td>
<td>32</td>
<td>10.30</td>
<td>24/32 (75)</td>
<td>24/32 (75)</td>
</tr>
</tbody>
</table>

Classical Hodgkin Lymphoma: Cytopathologic and Histologic Correlation

(Poster No. 155)

Maria del Mar Rivera Rolon, MD (mariariv@utmb.edu); Evgeniya Angelova, MD, PhD; Adam L. Booth, MD; Cecilia Clement, MD. Department of Pathology, University of Texas Medical Branch, Galveston.

Context: Classical Hodgkin lymphoma (CHL) is a lymphoid neoplasm characterized by large mononuclear and multinucleated cells in a mixed inflammatory background (Figure 91). Neoplastic cells typically constitute 0.1%–10% of the cellular infiltrate producing a diagnostic challenge on fine-needle aspiration (FNA) because of limited tissue, sampling variability, and decreased utility of flow cytometry. The aim of this study is to evaluate the accuracy of FNA in CHL.

Design: We performed an electronic search at our institution from 2015 to 2018 for biopsy proven diagnoses of CHL that had preceding or concurrent FNA from the same site. FNA site, patient age, sex, and histologic diagnosis were evaluated.

Results: We identified 16 cases (10 men, 6 women) with a median age of 31.5 years (range, 21–82 years). Cervical lymph nodes (n = 5) were the most common site of involvement, followed by supravacular lymph nodes (n = 3). Two patients (12.5%) had a prior diagnosis of CHL. Thirteen cases (81%) showed concordance with cytologic diagnosis. Sixty-nine percent (n = 11) of cases demonstrated eosinophils in the background. Three cases (19%) had discrepant results by FNA. Discrepancies were attributed to extensive fibrosis, abundant necrosis, and absence of diagnostic cells. Flow cytometry immunophenotyping was performed on 93.7% of cases (n = 15) with no B- or T-cell abnormalities.

Conclusions: FNA is a rapid, reliable method to establish an early diagnosis of CHL. However, in some cases an excisional biopsy is needed to give an accurate diagnosis. Factors such as extensive fibrosis and necrosis could render a false negative diagnosis in FNA samples.
Endoscopic Ultrasound-Guided Fine-Needle Aspiration of 2 Undifferentiated Carcinomas With Osteoclast-like Giant Cells of the Pancreas With Literature Review

(Poster No. 156)

Seunghyug Kwon, MD, MPH; Kayla M. Hoerschgen, BS; Poonam Sharma, MD. Department of Pathology, Creighton, Omaha, Nebraska.

Undifferentiated carcinoma of the pancreas with osteoclast-like giant cells (UCPOGC) is an extremely rare and aggressive neoplasm. Histologically the tumor mimics giant cell tumors of the bone, and although many studies suggest the histogenesis to be epithelial in origin, this remains controversial. We recently encountered 2 such cases from different patients, both of which were biopsied by EUS-guided fine-needle aspiration biopsy within the same week. In case 1, abundant multinucleated osteoclast-like giant cells and many uniform mononuclear cells were present, suggesting the possibility for repeat FNA, which may have led to more conclusive diagnoses. The potential change in clinical management also supports use of the new Milan classification system.

Fine-Needle Aspiration Biopsy in the Diagnosis and Classification of Malignant Liver Tumors: Six Hundred Twenty-Four Cases From a 9-Year Retrospective, Single-Institutional Study

(Poster No. 158)

Lin Zhang, MD, PhD; Zhenjian Cai, MD, PhD; Ji-Weon Park, MD; Lin (Lin.Zhang.1@uth.tmc.edu); Zhenjian Cai, MD, PhD; Ji-Weon Park, MD. Department of Pathology and Laboratory Medicine, McGovern Medical School, The University of Texas Health Science Center at Houston.

Context: Liver is one of the most commonly involved organs by metastatic disease and virtually any malignancy can spread to the liver. In addition, a number of primary tumors can arise in the liver. Fine-needle aspiration biopsy is the most commonly used method to evaluate liver masses. Given the tremendous variety of neoplasms that occur in the liver, diagnosis can be challenging.

Design: We retrospectively reviewed malignant lesions in the liver diagnosed by imaging-guided fine-needle aspiration biopsy in our institution between 2010 and 2018. Patients’ medical records and selected slides were reviewed.

Impact of the Milan System for Reporting Salivary Gland Cytopathology With Clinical and Histologic Correlation

(Poster No. 157)

Josean Ramos, MD (josean_ramos@rush.edu); Ji-Weon Park, MD; Lei Yan, MD. Department of Pathology, Rush University Medical Center, Chicago, Illinois.

Context: With the recent proposed changes in diagnostic categories outlined by the Milan System for Reporting Salivary Gland Cytopathology, it is important to examine the impact on cytopathologic diagnoses and patient management.

Design: All salivary gland fine-needle aspiration (FNA) specimens at our institution from 2016 through 2018 were classified based on general diagnostic category and management. The cases were then reclassified according to the Milan System and the results were compared.

Results: Eighty-five cases were identified with original cytopathologic diagnostic categories, including nondiagnostic (5%), benign/negative (39%), salivary gland neoplasm (40%), atypical (9%), and malignant (7%). Using the Milan system, they were reclassified as nondiagnostic (22%), nonneoplastic (14%), atypia of undetermined significance (5%), neoplasm: benign (38%), neoplasm: salivary gland neoplasm of uncertain malignant potential (SUMP; 13%), suspicious for malignancy (1%), and malignant (7%). Thirty-seven cases had follow-up surgical excision; of these, 11 were histologically malignant and 26 were histologically benign. In regard to clinical management, with the Milan recommendations, 15% would have had a potential change in how they would have been followed. Of the malignant surgical excisions, 3 cases called negative/benign before would have shifted to nondiagnostic using the Milan System.

Conclusions: Using the Milan System, there was an increase in nonneoplastic, neoplasm: benign, and neoplasm: SUMP, thus providing further information regarding risk of malignancy and proper follow-up. There was also a substantial increase in the number of nondiagnostic cases, suggesting the possibility for repeat FNA, which may have led to more conclusive diagnoses. The potential change in clinical management also supports use of the new Milan classification system.

Frequency of Various Cytologic Diagnoses in 624 Liver Fine-Needle Aspiration Biopsies

<table>
<thead>
<tr>
<th>Cytologic Diagnosis</th>
<th>No. (%) of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastatic adenocarcinoma</td>
<td>317 (50.8)</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>96 (15.4)</td>
</tr>
<tr>
<td>Cholangiocarcinoma</td>
<td>72 (11.5)</td>
</tr>
<tr>
<td>Neuroendocrine tumor/carcinoma</td>
<td>56 (9.0)</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>22 (3.5)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>17 (2.7)</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>11 (1.7)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>4 (0.6)</td>
</tr>
<tr>
<td>Mixed hepatocellular and cholangiocarcinoma</td>
<td>3 (0.5)</td>
</tr>
<tr>
<td>Thymic carcinoma</td>
<td>2 (0.3)</td>
</tr>
<tr>
<td>Hepatoblastoma</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Parangangioma</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Carcinoma, not otherwise specified</td>
<td>21 (3.4)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>624 (100)</strong></td>
</tr>
</tbody>
</table>

Results: A total of 624 cases were identified (Table). Metastatic adenocarcinoma is the most common malignancy involving liver (317 cases; 50.8%), followed by hepatocellular carcinoma (96 cases; 15.4%), cholangiocarcinoma (72 cases; 11.5%), neuroendocrine tumor/carcinoma (56 cases; 9.0%), squamous cell carcinoma (22 cases; 3.5%), and lymphoma (17 cases; 2.7%). Rare malignant tumors in liver included sarcoma (11 cases; 1.7%); including Epstein-Barr Virus–positive leiomyosarcoma, leiomyosarcoma, gastrointestinal stromal tumor, undifferentiated pleomorphic sarcoma, myxoid liposarcoma, and embryonal sarcoma), metastatic melanoma (4 cases; 0.6%), mixed hepatocellular and cholangiocarcinoma (3 cases; 0.5%), thymic carcinoma (2 cases; 0.3%), parangangioma (1 case; 0.2%), mesothelioma (1 case; 0.2%), and hepatoblastoma (1 case; 0.2%). Twenty-one cases (3.4%) were diagnosed as carcinoma, not otherwise specified, because of lack of specific protein expression or limited biopsy tissue.

Conclusions: A tremendous variety of neoplasms can occur in liver. Accurate diagnosis is vital for proper patient management. Familiarization with morphologic features and judicious use of accessory studies are essential for accurate diagnosis.
Pelvic Washing Cytology From Patients With FIGO Grade I and II Endometrial Adenocarcinoma Following Hysterectomy

(Disclaimer No. 159)

Marriam Aalai, MD (marriam.aalai@nyulangone.org); Duc Vo, MD; Mala Gupta, MD; Behnam Rafiee, MD. Department of Pathology, NYU Winthrop Hospital, Mineola, New York.

Context: In 2009, the FIGO staging system for uterine endometrial carcinoma (EC) eliminated pelvic washing cytology (PWC). Nevertheless, PWC is still performed during hysterectomies for the positive results with EC FIGO grade III are associated with adenomal and lymph node involvement. However, there are a small percentage of low-grade (FIGO I and II) EC cases with positive PWC, leading to the assumption that hysterectomies may be associated with tumor dissemination into the peritoneal cavity. In this retrospective study, we aimed to identify factors that may correlate with PWC results of low-grade EC.

Design: PWC reports in 2016 to 2018 were compiled through PowerPath. The PWC results were categorized into positive, suspicious, inconclusive, and negative. The corresponding surgical reports focused on low-grade EC, highlighting 4 factors: operative procedure (laparoscopic hysterectomy/abdominal hysterectomy), lymph node status (positive/negative), and lymphovascular invasion (positive/negative). P values were calculated for each.

Results: A total of 183 EC cases were reviewed, 131 laparo-scopic hysterectomies were performed, and 43 total abdominal hysterectomies. Lymphovascular invasion was identified in 178 cases; 27 were positive and 151 were negative. Lymph node dissections were performed in 167 cases; 9 were positive and 138 were negative. The P values between the procedures showed no statistical significance with the PWC results. There was statistical significance between positive lymphovascular invasion and lymph node metastasis with PWC results ($P = .002$ and $P < .001$, respectively).

Conclusions: This study demonstrated that the procedure performed in low-grade EC was not correlated with PWC results. However, the presence of lymphovascular invasion and lymph node metastasis increased the risk of positive PWC.

Intranodal Palisaded Myofibroblastoma of Paraesophageal Lymph Node: A Case Report and Cytology Findings

(Disclaimer No. 160)

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Intranodal palisaded myofibroblastoma (IPM) is a rare benign mesenchymal tumor of lymph nodes, usually located in inguinal nodes, originating from smooth muscle cells and myofibroblasts. We report a peculiar case of IPM in a paraesophageal lymph node, an uncommon site. A 70-year-old woman, during workup for an atrial myxoma, was incidentally found to have a right paraesophageal enlarged nodule. Positron-emission tomography showed moderate focal uptake. A fine-needle aspiration of the lesion exhibited an aspising showing clusters of spindle cells within a collagenous stromal background. Immunohistochemistry revealed moderate staining for CD117, weak smooth muscle antigen (SMA), and negative desmin, desmin, and pan-cytokeratin, which favored a low-grade spindle cell neoplasm suggestive of gastrointestinal stromal tumor. The lesion was excised and showed a 5.0×3.1×2.0-cm well-circumscribed mass with a tan-pink to red-purple, rubbery cut surface. Histology revealed spindle cells with areas of nuclear palisading, replacing the architecture of the lymph node. There was focal hemorrhage and stellate areas of collagenous deposit with calcifications, consistent with amianthoid fibers. No necrosis or mitosis was identified. Immunostaining was positive for SMA, BCL-1/cyclin D1, and TLE, and negative for pan-cytokeratin, CD117, DOG-1, S100, SOX-10, desmin, EKG, CD34, H3K27m3, and BCL2. SS18 gene rearrangement was positive. Diagnosis of IPM is often difficult because of the confusion with other primary or metastatic spindle cell neoplasms in the lymph node, including schwannoma, melanoma, and leiomyoma, among others. Recognition and proper diagnosis of this lesion helps with optimal clinical management of the patient because of its indolent clinical course.

Trichomonas Vaginalis Infection and Its Association With Risk of Cervical Cancer and Human Papillomavirus Status

(Disclaimer No. 161)

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Context: Low trichomonas vaginalis (TV) infection prevalence in developed countries may be due to its incidental diagnosis and treatment during routine screening. Many countries are adopting a new model of testing based on high-risk (HR) human papillomavirus (HPV), known to be associated with squamous intraepithelial lesions (SILs). There is limited and conflicting literature on the relationship between TV and SIL. The aim of this study is to determine the TV prevalence in different age groups and evaluate its association with SIL, bacterial vaginosis (BV), and HPV.

Design: Retrospective study for cytologic histologic correlation was performed on 10 546 cases from 2017. HPV results were available in 7081 cases.

Results: Mean age was 49 years; range was between 15 and 84 years. A total of 249 patients (2.3%) were TV positive. The prevalence was highest in age group 21–29 (3.2%). A total of 4386 of 7081 cases were HPV positive (61.9%). The association between TV and HPV was not significant ($P < .07$). The association between TV and BV was significant ($P < .001$). A total of 4649 of 10 546 cases (44%) showed squamous abnormalities. SIL was demonstrable in 52.6% of TV-positive and 43.9% of TV-negative patients. HG-SIL was greater in TV-positive vs TV-negative patients (P = .007). HPV-positive patients with TV showed more SILs than those without TV ($P < .04$). ASCH patients with TV showed higher grade SIL on follow-up than those without TV ($P < .005$).

Conclusions: TV is more common with BV and HPV coinfections. HPV and ASCH patients with TV showed significant SIL. Although TV can be detected incidentally through cytology-based cervical screening, a transition to HPV testing is likely to result in its increased prevalence.

An Unusual Case of Pulmonary Adenocarcinoma With Signet Ring Cell Differentiation Diagnosed by Cytologic Assessment of Pleural Fluid

(Disclaimer No. 162)

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Signet ring cell (SRC) adenocarcinoma is a subtype of mucin-producing adenocarcinoma that originates in various organs, particularly the stomach. Because primary adenocarcinomas of the lung show signet ring cell components in only 0.14%–1.9% of cases, a thorough workup should be conducted to be certain that a pulmonary lesion does not represent metastasis from a separate primary site. We report a case of a 46-year-old man with adenocarcinoma of the lung with signet ring cell differentiation diagnosed by cytologic examination of pleural fluid. Imaging studies had showed left upper lobe consolidation and pleural effusion and a 6-mm subpleural nodule. Pleural fluid cytology showed a predominating population of relatively bland round cells with single prominent cytoplasmic vacuoles and eccentric crescent-shaped nuclei predominantly as well as a second rare population of markedly pleomorphic larger cells. A mucicarmine stain performed on the pleural fluid cell block highlighted numerous mucin-filled vacuoles in the signet-ring-like cells. Immunostains in the cell block showed that the neoplastic cells were positive for cytokeratin AE1/AE3 and cytokeratin 7, and nuclear positivity for TTF-1, and were negative for cytokeratin 20, calretinin, and CDX-2. A diagnosis of metastatic adenocarcinoma with signet ring cell differentiation was made, compatible with pulmonary primary. The presence of signet ring cell differentiation in primary pulmonary adenocarcinoma is very uncommon and appropriate immunohistochemical staining workup is important for accurate diagnosis. Cytologic evaluation of the pleural fluid may be the initial step in assessment and management of these patients.

The Application of the Paris System for Reporting Urine Cytology in Atypical Urine Samples

(Disclaimer No. 163)

Carla R. Caruso, MD (carlitacaruso@gmail.com); Fan Lin, MD; Haiyan Liu, MD. Department of Pathology, Geisinger Medical Center, Danville, Pennsylvania.
**Context:** The lack of a standardized system for evaluation of urine samples has resulted in inconsistent diagnoses. The Paris System for Reporting Urinary Cytology (TPS) aims to detect high-grade urothelial carcinoma (HGUC) by standardized criteria applied to nonsuperficial and nondegenerated urothelial cells. We attempted to validate classification of atypical urine samples by TPS.

**Design:** Retrospective and blinded analysis of urine specimens diagnosed as atypical from 2016 to 2017 and reclassification by TPS atypical urothelial cells (AUC) criteria: major (nuclear to cytoplasmic ratio >0.5) and minor (hyperchromasia, irregular nuclear membrane and clumped chromatin). Cohort patients were selected from AUC cases with cytology (69), biopsy (27), or both (40) follow-ups. Original AUCs were subgrouped into benign, atypical, low-grade urothelial carcinoma, and HGUC groups according to subsequent follow-up findings.

**Results:** AUC cases of 136 patients (102 men, 71 ± 13 years) were reviewed. Fifty belonged to the benign group, 23 atypical, 16 low-grade urothelial carcinoma, and 47 HGUC. After TPS, 14 of 50 cases (28%) in the AUC-benign group were downgraded to negative for HGUC and 18 of 47 (39%) in the AUC-HGUC group were reclassified as suspicious for HGUC (13 of 47) and HGUC (5 of 47). Necrosis was identified in 9 of 13 cases of the suspicious group. Combined specificity for suspicious HGUC and HGUC was 78%, and negative predictive value for negative HGUC was 64% (Table).

**Conclusions:** TPS is objective and practical, classifying cases into negative, suspicious, and HGUC. Downgrading AUC to negative will decrease unnecessary follow-ups whereas upgrading to malignant will benefit patients with prompt management. As TPS applies to viable urothelial cells, tumor necrosis hampers HGUC diagnosis.

<table>
<thead>
<tr>
<th>Atypical Urothelial Cell Follow-up Subgroups Reclassified by The Paris System</th>
<th>The Paris System for Reporting Urinary Cytology Categories</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Benign</td>
</tr>
<tr>
<td>Negative for high-grade urothelial carcinoma</td>
<td>14</td>
</tr>
<tr>
<td>Atypical urothelial cells</td>
<td>34</td>
</tr>
<tr>
<td>Suspicious for high-grade urothelial carcinoma</td>
<td>2</td>
</tr>
<tr>
<td>High-grade urothelial carcinoma</td>
<td>0</td>
</tr>
<tr>
<td>Low-grade urothelial neoplasia</td>
<td>0</td>
</tr>
</tbody>
</table>

**Outcome of Interpace Diagnostics Molecular Testing in Unsatisfactory Thyroid Nodules**

(Poster No. 164)

**Estelle Oertling, MD** (eertlin@tulane.edu); Yousif Al Rubaye, MBChB; Wendi O‘Connor, MD; Zahraa Ghandour, MD; Clarissa Richard, CT (ASCP); Emad Kandil, MD; Krzysztof Moroz, MD. Departments of Pathology and Surgery, Tulane University, New Orleans, Louisiana.

**Context:** Fine-needle aspiration (FNA) of thyroid nodules is an accurate test in malignancy risk assessment. An unsatisfactory thyroid FNA has a 5%–10% risk of malignancy. Recommended management for unsatisfactory results is to repeat the aspiration with ultrasound guidance. Intercpace Diagnostics (IP) offers a molecular test (ThyGeNEXT mutation panel and ThyraMIR microRNA analysis) for unsatisfactory and indeterminate thyroid aspirations. The goal of this study was to retrospectively review the IP test results for unsatisfactory aspirations and compare with subsequent surgical resection outcomes.

**Design:** A total of 324 patients with 443 nodules were aspirated between February 2018 and February 2019. Thirty-two of the aspirations (7%) were cytologically unsatisfactory and were referred for IP testing.

**Results:** Of the 32 cytologically unsatisfactory aspirations, 24 (75%) were diagnostic by IP. Four of those cases (12.5%) revealed IP abnormalities: 3 cases with NRAS mutations and negative ThyraMIR, and 1 case with no mutations but positive ThyraMIR. Surgical resections were performed in 3 of the cases with IP abnormalities. One of the cases (positive for NRAS Q61K) demonstrated follicular variant of papillary thyroid carcinoma, 2 cases were benign, and the fourth case is without surgical follow-up.

**Conclusions:** Cytologically unsatisfactory FNA specimens can demonstrate IP molecular abnormalities and have an increased risk of malignancy. IP molecular testing may be a valid alternative to repeated ultrasound-guided FNAs in unsatisfactory thyroid aspirations.

<table>
<thead>
<tr>
<th>Unsatisfactory Thyroid FNAs With IP Abnormalities and Surgical Resection Diagnoses</th>
<th>Case</th>
<th>ThyGeNEXT</th>
<th>ThyraMIR</th>
<th>Surgery Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No mutations</td>
<td>Positive</td>
<td>Nodular hyperplasia</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>NRAS Q61K</td>
<td>Negative</td>
<td>Papillary thyroid carcinoma, follicular variant</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>NRAS Q61K</td>
<td>Negative</td>
<td>No surgery</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>NRAS G13R</td>
<td>Negative</td>
<td>Dominant Hürthle cell adenomatoid nodule</td>
<td></td>
</tr>
</tbody>
</table>

**The Prevalence and Surgical Outcome of Thyroid Fine-Needle Aspiration With Hürthle Cell Morphology**

(Poster No. 165)

**Saman Seyed Ahmadian, MD** (saman.seyedahmadian@jhsmiami.org); Gala M. Godoy Brewer, MD; Julio Diaz Perez, MD, PhD; Carmen Gomez Fernandez, MD. Department of Pathology, University of Miami, Florida.

**Context:** There is a paucity of literature on the frequency and risk of malignancy for the predominance of Hürthle cells on cytology aspirates. We sought to evaluate the prevalence and outcome of aspirates with a predominance of Hürthle cells categorized as III or IV based on the Thyroid Bethesda System (TBS).

**Design:** TBS III and IV cases diagnosed in a 24-month period were retrieved from our database and correlated with available molecular and surgery results.

**Results:** Of 627 TBS III and IV thyroid aspirates, 44 (7%) had Hürthle cell predominance. Most (32; 72%) were categorized as “atypia of undetermined significance, Hürthle cell type” (AUS-H); 12 cases (28%) were “follicular neoplasm, Hürthle cell type” (FN-H). Nineteen aspirates were sent for Afirma molecular testing. Of these, 11 were “suspicious” and 4 had surgery with 1 patient diagnosed as malignant (papillary thyroid carcinoma follicular variant [PTC-FV] with Hürthle cells). Twenty cases were sent for ThyroSeq molecular testing; 6 returned with molecular alterations and 13 had surgery, from which 2 cases were diagnosed as malignant: (1) follicular thyroid carcinoma with p53 mutation and (2) PTC-FV with NRAS mutation. No patient with benign molecular testing developed cancer after 1–2 years of follow-up.

**Conclusions:** Hürthle cell rich aspirates are rare and most cases are benign. The risk of malignancy is low (6%). The most common molecular alteration with ThyroSeq testing is RAS and the most common malignancy is PTC-FV with Hürthle cell changes.

**Diagnostic Challenge of Large B-Cell Lymphoma of Pancreas on Cytology as a Primary Presentation**

(Poster No. 166)

**Samantha Mattoo, DO** (smattoo@augusta.edu); Asad Ullah, MD; Alex Clavijo, MD; Luis Velasquez Zarate, MD; Intisar Ghilelib, MD; Diana Metry, MBCHB; Natasha Savage, MD; Nikhil Patel, MD. Department of Pathology, Medical College of Georgia, Augusta.

Primary pancreatic lymphoma represents <2% of all lymphomas and ~0.5% of all pancreatic neoplasms. Although secondary pancreatic involvement from systemic disease can occur, cytoligic diagnosis is rarely performed considering the typical multinorgan dissemination. Pancreatic involvement may be misdiagnosed as pancreatic carcinoma if there is no previous history of lymphoma, leading to incorrect therapeutic management. It is clear that tissue sampling is crucial for a correct diagnosis. Endoscopic ultrasound has emerged as the most cost-effective and safe procedure, and it is now recognized as the first-line procedure in the management of solid and cystic pancreatic masses. However, the diagnosis of pancreatic lymphoma with endoscopic ultrasound and fine-needle aspiration remains challenging for both clinicians and pathologists. We present a case of a 54-year-old man...
who initially presented with recent weight loss, vague abdominal pain, and supraduvalicular lymphadenopathy with elevated lipase. CT scan showed a 6.2 × 5 × 5-cm pancreatic mass encasing the splenic vein. EUS-FNA of the pancreatic mass was performed and revealed singly dispersed cells with irregular membranes and multiple nuclei in the background of lymphoglandular bodies. Immunohistochemical stains were positive for CD20 and CD45, but negative for pan-keratin and pan-melanoma. The diagnosis of large B-cell lymphoma was made, which is the most common subtype of lymphoma to involve the pancreas. Accurate diagnosis of this entity is critical, as the 5-year survival for pancreatic adenocarcinoma is 8.5% and 62.5% for pancreatic diffuse large B-cell lymphoma. Moreover, the therapy is vastly different.

The Objective Structured Pathology Experience: Objective Structured Pathology Examination

(Banner No. 167)

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Context: Pathology resident assessment concerning quality and patient safety focuses on standardized examinations. Clinical specialties use the well-studied Objective Structured Clinical Examination to evaluate residents. We adapted a pathology-focused version, termed the Objective Structured Pathology Experience (OSPE).

Design: The OSPE evaluated first- and second-year residents during 2 years. Twenty-one residents participated, 8 in both years. The OSPE consisted of 3 parts. The first simulated a surgical pathology sign-out session, with an emphasis on cancer diagnosis and reporting standards. The second was a frozen section with a surprise malignancy, and included the surgeon questioning the diagnosis. The third consisted of case-based challenges that focused on quality assurance. Each consisted of slides showing discrepancies with the history or gross description; residents were not told the cases contained preanalytic issues. Interactions were scored using the Pathology Milestones guidelines provided by the Accreditation Council for Graduate Medical Education; 13 milestones were tested.

Results: Average milestone score was 1.42/5 for first- and 2.25/5 for second-year residents. A debrief was held with all participants that explored quality assurance, pathology standards, and professionalism.

Conclusions: This OSPE shows that using a simulated environment is a useful and standardized method to evaluate pathology residents. The OSPE also identified deficiencies early in resident training. The scores of trainees may be used as a metric to follow development over time and also provide documentation of trainee evaluation. Further development will allow the OSPE to be used to evaluate residents in other areas of pathology, from cancer staging to laboratory management.

(POSTER NO. 168)
Withdrawn.

Establishing a Resident-Driven Clinical Elective and Diagnostic Consultative Service in a Low-Resource Setting of Quetzaltenango, Guatemala

(Poster No. 169)

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Context: Pathology services in low-resource global health settings are often not prioritized, suffering because of inadequate access to vital resources essential for accurate diagnoses and appropriate patient care. This project sought to improve diagnostics in the resource-limited setting of rural Guatemala by establishing an interinstitutional clinical elective including quality improvement and a consultative service.

Design: Two resident pathologists traveled to a large regional hospital in Quetzaltenango, Guatemala, following 35 hours of Spanish language education, to complete a 4-week clinical rotation. This hospital’s laboratory processes approximately 8000 general surgical and cytologic specimens annually, primarily by hematoxylin and eosin staining, without access to immunohistochemical stains or other ancillary tests. The primary goals were to establish a mutually beneficial collaboration with the local pathologist, provide bidirectional educational experiences, and strengthen a diagnostic consultative service with the residents’ home institution.

Results: The residents assisted the pathologist in evaluating a wide variety of general surgical and cytology cases (approximately 220), including frozen sections and autopsy. The case evaluation often required in-person discussions with Spanish-speaking clinicians, providing opportunities for educational exchange. Improvements to the routine staining procedure were assessed. Approximately 10 cases were selected in concert with the local pathologist for consultative review at the home institution.

Conclusions: This is the second iteration of the clinical rotation in Guatemala, which is intended to continue on a semiannual basis with financial support from the home institution. This resident-driven initiative seeks to strengthen the collaboration with Guatemalan pathologists in a low-resource area by promoting institutional education and an invaluable, growing consultative service.

Concordance Between Clinical and Pathologic Staging for Head and Neck Tumors

(Poster No. 170)

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Context: In head and neck cancer, clinical and radiographic findings designate pretreatment clinical staging and determine management. Prior studies demonstrated significant discrepancies between clinical and pathologic staging in head and neck cancer patients. Here, we reviewed cases from a tertiary hospital to assess if this was true in our institution.

Design: We retrospectively reviewed a combination of databases to identify patients with head and neck tumors (2014–2018). From a total of 413 patients, we selected 77 who underwent surgical excision. For inclusion, complete preoperative clinical staging with lymph node status, pathohistologic information on involved lymph nodes, and survival data were required.

Results: Discrepancies at the level of overall tumor stage were noticed in 42.9% of all cases. More specifically, 18.2% were up-staged
after surgical excision and histopathologic examination and 24.7% were down-staged. Changes in staging occurred in 70% of cases in terms of primary tumor extent (T stage), and in 30% because of change in the lymph node status. In 65% of the cases the pT stage was overestimated clinically, with discrepancies observed across all 4 pT stages.

**Conclusions:** Our results are consistent with the presented literature and indicate that there is significant discrepancy of clinical versus pathologic staging. An intergroup ECOG study showed such discrepancy in 50% of patients, with pathologic stage being a superior outcome predictor. Another study found discrepancies in lymph node involvement in about one-third of patients. This was also reproduced here. It would be interesting to speculate whether changing technology or altered radiologic criteria might alter this poor concordance.

**Teaching Pathology to Medical Students in Front of the Microscope: Does This Type of Small-Group Learning Increase Interest in Pathology?**

*(Poster No. 171)*

Clarissa E. Jordan, BS (clarissa.jordan@bcm.edu); Derek J. Danner, MD; Stephanie Holdener, MD; Christine G. Roth, MD. Department of Pathology and Immunology, Baylor College of Medicine, Houston, Texas.

**Context:** Pathology in medical school is traditionally taught in the form of classroom-based lectures, which may limit students’ perception of what pathologists do and how they make diagnoses. The medical student pathology interest group has partnered with pathology residents at our institution to host interactive microscopy small-group sessions covering clinically relevant pathology at a multiheaded microscope. These were designed to align with concurrent topics in the medical school’s organ system-based curriculum for second-year medical students. The goal of this study was to determine if this intervention increased medical student awareness and interest in the field of pathology.

**Design:** All second-year medical students were invited to participate in 5 resident-led small-group sessions via social media announcements. An electronic survey was distributed to medical students immediately after their participation.

**Results:** Twenty-six students participated in the microscopy sessions, and 88% (23 of 26) responded to the postsession survey. Eighteen of 23 respondents (78%) agreed/strongly agreed that they learned something new about pathology as a medical specialty, and 9 of 23 (39%) agreed/strongly agreed that they are now more interested in pathology than they were prior to the session.

**Conclusions:** The “near peer” teaching of medical students by pathology residents in this small-group, interactive format increases student awareness of the specialty of pathology and may increase student interest in the field. Future efforts will expand the number of these microscopy sessions and assess the eventual specialty choice of the participants.

**Hidden Landmines in RCM: Understanding Trends That Impact Financial Performance of Laboratories and Pathology Practices**

*(Poster No. 172)*

Diana Richard, BA1 (drichard@xifin.com); Stephanie Denham, BBA.2 Departments of 1Anatomic Pathology Program Development and 2New Customer Accounts, XIFIN, Inc, San Diego, California.

**Context:** With layers of complexity in revenue cycle management, it is pertinent that laboratories and pathology practices understand the challenges that may unknowingly be impacting revenue. This includes the financial and operational impact of recent payer and regulatory trends, including but not limited to (1) The Devil in the Details: Denials, Timely Filing, and Successful Appeals Processes, including appealing medical necessity, timely filing, catching payer errors through intelligent processing and fighting for corrective action, and reducing patient bad debt through effective engagement; and (2) Performance Benchmarking and Financial Strategy, including understanding current performance and exploring diversification.

**Design:** A number of trends in payer behaviors and reimbursement go unnoticed because of outdated RCM management practices. Even known areas of reimbursement deficiency can be neglected because of a lack of resources or knowledge of an effective resolution. Trends in the laboratory and pathology industry, the root of the obstacles, and how practices can better manage each of those challenges are discussed.

**Results:** Five benefits can be obtained: (1) A better understanding of current denial patterns; (2) learning how to appeal common denials and better manage contractual allowables; (3) tips and tricks for patient engagement; (4) benchmarking the current performance of RCM; and (5) discussing the process of incremental cost and assessing cost per test.

**Conclusions:** The goal is to provide valuable insight on new ways to manage the most common denials proactively, ensure payers are reimbursing at their contracted rate, improve and increase patient’s propensity to pay, manage overall performance, and understand cost to drive financial health and future ROI.
Infiltrate, which was consistent with low-grade follicular lymphoma and metastatic breast carcinoma. It was admixed with an atypical lymphoid infiltrate composed of large cells with reniform nuclei and amphophilic cytoplasm; the cells stained positive for CD1a and S100. The lesion was characterized by an atypical, large, discohesive cells with abundant eosinophilic cytoplasm, high nuclear to cytoplasmic ratio, fine nuclear chromatin, and inconspicuous nucleoli. Flow cytometry revealed an abnormal blast population positive for CD45, CD34, HLA-Dr (partial), CD15 (dim), CD2, CD5, CD3, CD7, CD8, CD38 (bright), CD56 (dim), and terminal deoxynucleotidyl transferase (TdT). The patient was diagnosed with T-cell acute lymphoblastic leukemia (T-ALL); she was admitted to the hospital, and chemotherapy was initiated. A posttreatment bone marrow biopsy revealed a hypocellular marrow with no abnormal T-cell population. Eight months after the diagnosis of T-ALL, the patient’s parents noted multiple lesions on her face and trunk. A punch biopsy (Figure 1, B) was performed, revealing a superficial dermal infiltrate composed of large cells with reniform nuclei and amphophilic cytoplasm; the cells stained positive for CD1a and S100. The lesion was consistent with Langerhans cell histiocytosis. A positron emission tomography–computed tomography scan did not reveal any pathologic abnormality, and the patient was prescribed topical corticosteroids in addition to her chemotherapy for T-ALL.

Metastatic Breast Carcinoma and Follicular Lymphoma Involving the Duodenum as a Collision Tumor

Asha C. Sigei, MD1, Elena Gertsen, MD, PhD2
1Department of Pathology, East Tennessee State University, Johnson City, Tennessee; 2Department of Pathology, Watauga Pathology Associates, Johnson City Medical Center, Johnson City, Tennessee.

Collision tumors, defined as a coexistence of 2 morphologically distinct independent tumors in the same organ, are extremely rare. Few gastrointestinal cases have been previously reported. Involvement of duodenum is extremely rare with fewer than a dozen cases reported. We describe a duodenal collision tumor composed of follicular lymphoma and metastatic breast carcinoma. A 77-year-old woman presented with several months of progressive slurred speech. Imaging showed a 4.0-cm well-circumscribed mass near the right cerebellar vermis that was not present earlier that year. Microscopically, the tumor was composed of a diffuse proliferation of atypical, large, discohesive cells with abundant eosinophilic cytoplasm, sharp cell borders, and pleomorphic vesicular nuclei with prominent nucleoli and minimal background inflammation (Figure 3). By immunohistochemistry, the malignant cells were positive for CD68, CD163, CD4, and vimentin and were negative for an extensive immunohistochemical panel. The cells demonstrated multiple gene mutations, including therapeutically targetable BRAF N581T. In
histiocytic sarcomas outside of the central nervous system. BRAF V600E mutations are common. However, as demonstrated by this case, it may be prudent to evaluate central nervous system histiocytic sarcomas for additional BRAF mutations because they may be targetable. Unfortunately, this patient was unable to complete radiation and temozolomide therapy because of side effects and died within weeks.

**Cytogenetic and Molecular Landscape of Hispanic Myelodysplastic Syndrome Patients From Puerto Rico**

(Poster No. 4)

Ruifang Zheng, MD (zhengru@njms.rutgers.edu); Zhiwei Yin, MD; Nawar Matti, MD; Jie-Gen Jiang, MD. Department of Pathology, Rutgers New Jersey Medical School, Newark.

**Context:** Patients with myelodysplastic syndrome (MDS) have a high rate of cytogenetic abnormalities and molecular mutations. The detailed cytogenetic and molecular features in Hispanic patients with MDS have not been reported. The aim of this study was to investigate the cytogenetic and molecular landscapes in the above patient population.

**Design:** The results of cytogenetic and 40-gene myeloid molecular profile of 290 Hispanic patients with MDS from Puerto Rico between 2009 and 2018 were analyzed retrospectively.

**Results:** There were 168 men and 122 women in this study with an age range of 33 to 99 years and a median age of 74 years. A total of 284 patients (93.4%) had karyotypes available. Of those 39% had abnormal karyotypes (111 of 284), including complex karyotype(s) (10.6%), 5q (12.1%), 7 or 7q (6.7%), -8 (6.0%), 20q (5.3%), and -Y (5.3%). The rate of complex karyotypes was similar to that reported in white patients with MDS but significantly lower than that in African-American patients with MDS. The overall mutation rate in the 290 patients was 93.4% (271 of 290). The commonly mutated genes were SF3B1 (26.6%), TET2 (26.2%), ASXL1 (17.6%), DNMT3A (13.8%), TP53 (12.1%), RUNX1 (10.3%), U2AF1 (8.3%), SRSF2 (7.9%), and EZH2 (5.2%). The mutation rates of the following genes are statistically different from that reported in white patients: SF3B1, TET2, DNMT3A, TP53, JAK2, BCR, STAG2, and NF1, among which TP53 mutation is supporting a B12 deficiency and subacute combined degeneration. The patient was given a daily oral cobalamin supplement and her symptoms gradually improved. The elevated B12 result led to unnecessary and expensive tests. Vitamin B12 is stored in the liver and may be released upon hepatic insult such as acetaminophen overdose. If the hemogram and smear morphology suggest a B12 deficiency, then further confirmatory testing must be pursued in spite of a normal or elevated B12 result.

**Conclusions:** Our study demonstrated distinct cytogenetic and molecular landscapes in Hispanic patients with MDS, and these distinctions may potentially affect the clinical outcome of the patients.

**Diffuse Large B-Cell Lymphoma With Abrerrant Expression of Multiple T-Cell Markers: Report of a Challenging Case**

(Poster No. 5)

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Abrerrant expression of multiple T-cell markers on mature B-cell non-Hodgkin lymphoma is rare. Most reported cases are diffuse large B-cell lymphomas (DLBCL) with expression of a few (up to a maximum of 4) T-cell markers, with CD3 expression being very rare. We present an interesting case of DLBCL with aberrant expression of multiple T-cell markers in a 56-year-old woman presenting with cervical and axillary lymphadenopathies. Lymph node biopsy revealed effacement of the architecture with sheets of large atypical cells with abundant eosinophilic cytoplasm, marked nuclear irregularities, small prominent nucleoli and high mitotic rate with foci of tumor necrosis. Immunophenotyping by flow cytometry could not be performed because fresh tissue was not available. An extensive panel of immunoperoxidase stains revealed the atypical cells to be strongly positive for CD45, CD20, CD79a, Pax5, Mum1, Bcl2, Bcl6, CD3, CD4, CD5, CD7, CD30, and CD43 but negative for CD8, CD10, CD15, ALK-1, CK7, GATA3, SOX10, Cam 5.2, and LMP1 (EBV) with high Ki-67 (80%). This pattern of expression of all B- and T-cell markers was highly unusual. Molecular studies revealed clonal rearrangement of immunoglobulin heavy chain gene without evidence of clonal T-cell receptor gene rearrangement. This case is similar to the case reported by Dumlao et al., in which large atypical cells were diagnosed as DLBCL, non-Hodgkin centroblastic type, with aberrant T-cell marker expression. Cyto genetic studies demonstrated BCL6 rearrangement and trisomy 12, supporting our diagnosis. To our knowledge, this is the only case of DLBCL with aberrant expression of as many as 6 T-cell markers, which makes this case unique and worth reporting.

**ALK-Negative Anaplastic Large Cell Lymphoma: A Rare Leukemic Presentation**

(Poster No. 7)

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Anaplastic large cell lymphoma (ALCL) is a CD30þ T-cell neoplasm that involves both the lymph nodes and extranodal sites, including bone, skin, and soft tissue. Classically, the lymphoma cells are large with abundant cytoplasm and pleomorphic horseshoe-shaped nuclei, but there are other histologic variants, including lymphohistiocytic and small cell. Lymphoma cells can either have coexpression of the ALK protein (ALKþ) or not (ALK−) depending on whether a chromosomal translocation involving the ALK gene is present. A variety of B- and T-
cell non-Hodgkin lymphomas can present with leukemic phase, but there are only 20 reported cases of ALCL with leukemic phase, with most of these cases being ALK+ small cell variant. We present a case of ALCL, ALK- with leukemic transformation in a 58-year-old man at disease relapse after an autologous stem cell transplant. He presented with a marked leukocytosis (370 10^9/L), with a predominance of atypical lymphocytes (Figure 5, A). A bone marrow biopsy was performed which showed a hypercellular marrow (>90%) with a diffuse, sheetlike infiltrate of atypical lymphoid cells that had moderate agranular blue cytoplasm and nuclei with deep folds and condensed chromatin (Figure 5, B and C). Immunohistochemical analysis demonstrated the neoplastic cells to be positive for CD30 (Figure 5, D) and CD3 without ALK1. Flow cytometry of the peripheral blood revealed an atypical population (95%) that expressed only CD2, HLA-DR, and dim ALK1. Flow cytometry of the peripheral blood showed an atypical population (95%) that expressed only CD2, HLA-DR, and dim ALK1. Immunohistochemical analysis demonstrated the neoplastic cells to be positive for CD30 (Figure 5, D) and CD3 without ALK1. Flow cytometry of the peripheral blood revealed an atypical population (95%) that expressed only CD2, HLA-DR, and dim cytoplasmic CD3. This case serves as a rare presentation of a leukemic transformation of ALCL ALK-, which has only been described once in the literature.

**Image 37x406 to 280x562**

**Use of LEF1 Immunohistochemistry as Evidence of an Etiologic Relationship Between CLL and CHL in Patients With the Hodgkin Variant of Richter Syndrome**  
(Poster No. 8)

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**Context:** A small subset (<1%) of patients with chronic lymphocytic leukemia (CLL) develops classic Hodgkin lymphoma (CHL) (Richter syndrome), but the clonal relationship between these 2 remains unclear.

**Design:** We searched our database for patients with CLL seen between 2006 and 2019 who subsequently developed CHL. LEF1 expression was assessed using fixed, paraffin-embedded tissue and rabbit monoclonal anti-LEF1 antibodies (clone EPR2029Y from Abcam, Cambridge, Massachusetts). As a control we used 10 cases of de novo nodular sclerosis Hodgkin lymphoma, which were all negative for LEF1.

**Results:** All samples showed an appropriate internal control staining in small T lymphocytes (Figure 5, A). A bone marrow biopsy was performed which showed a hypercellular marrow (>90%) with a diffuse, sheetlike infiltrate of atypical lymphoid cells that had moderate agranular blue cytoplasm and nuclei with deep folds and condensed chromatin (Figure 5, B and C). Immunohistochemical analysis demonstrated the neoplastic cells to be positive for CD30 (Figure 5, D) and CD3 without ALK1. Flow cytometry of the peripheral blood revealed an atypical population (95%) that expressed only CD2, HLA-DR, and dim cytoplasmic CD3. This case serves as a rare presentation of a leukemic transformation of ALCL ALK-, which has only been described one other time in the literature.

**Image 297x157 to 540x400**

**Diagnostic Challenge of Acute Myeloid Leukemia Resolved by Cuplike Nuclei**  
(Poster No. 9)

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Nucleophosmin (NPM1) gene mutations are common genetic aberrations reported in de novo acute myeloid leukemia (AML), which have characteristic cuplike nuclei. Here we report on a 68-year-old woman who presented with abdominal pain, leukocytosis, and coagulopathy. Numerous blasts with a medium-sized subset with cuplike nuclei, few cytoplasmic, azurophilic granules and no Auer rods were identified on peripheral blood smear (Figure 6, A and B). Bone marrow aspirate and core biopsy demonstrated a hypercellular marrow almost completely replaced by blasts (Figure 6, C). Flow cytometry of the bone marrow aspirate showed 92% blasts, most of which were CD34+ and HLA-DR+ and CD117+ and CD33+ (Figure 6, D). Based on the clinical presentation and the immunophenotype we had a high suspicion for a microgranular variant of acute promyelocytic leukemia and all-transretinoic acid therapy was started. Fluorescence in situ hybridization studies did not detect t(15;17) or RARA rearrangement and raised a diagnostic challenge. Blasts with cuplike nuclei prompted gene-mutation analysis, which revealed an NPM1 mutation, confirming our suspicion of this characteristic AML entity; however, a TET2 mutation was also detected. Cytogenetic analysis showed a normal female karyotype 46,XX[20]. In the absence of FLT3-ITD mutations, an NPM1 mutation in cytogenetically normal AML is associated with a favorable prognosis. Only a few cases with both NPM1 and TET2 mutations have been reported in the literature, and the prognosis of an NPM1 mutation associated with a TET2 mutation is not well understood. Our patient failed the first induction therapy and achieved complete molecular remission after the second induction, and is awaiting a stem cell transplant.

**A Case of Classic Hodgkin Lymphoma Involving the Uterine Cervix and Presenting as Vaginal Spotting**  
(Poster No. 10)

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Classic Hodgkin lymphoma (CHL) is a clonal lymphoid neoplasm derived from B cells. It usually involves the lymph nodes. Although cases with extranodal involvement by CHL have been reported, involvement of the uterine cervix by CHL is an extremely uncommon phenomenon. Herein, we report an unusual case of a 51-year-old woman with nodular sclerosis CHL, diagnosed via right inguinal lymph node biopsy. After 2 cycles of chemotherapy, she presented with vaginal spotting and, upon computed tomography, was demonstrated a uterine cervical lesion with hypermetabolic activity. Tissue biopsy sections of uterine cervix showed cellular infiltrate consisting of large atypical cells including many lacunar cells and occasional Reed-Sternberg cells in a background of mixed reactive cells including small- to medium-sized lymphocytes, histiocytes, plasma cells, eosinophils, and neutrophils. Immunohistochemical stains show that the large atypical cells were positive for CD30, CD15, and MUM1 and were weakly positive for PAX5. In situ hybridization for Epstein-Barr virus-encoded RNA was negative. The morphologic and immunohistochemical findings were consistent with involvement by nodular sclerosis CHL. This case demonstrates a rare presentation of CHL because it may pose a diagnostic problem if its existence is not considered in the differential diagnosis. Furthermore, we reviewed the literature and found only one previous publication describing uterine cervix involvement by CHL. Although it is very rare, CHL involvement should be included in the differential diagnosis, and an appropriate workup should be performed to establish the diagnosis. Furthermore, we reviewed the literature and found only one previous publication describing uterine cervix involvement by CHL. Although it is very rare, CHL involvement should be included in the differential diagnosis, and an appropriate workup should be performed to establish the diagnosis.

Nasopharyngeal B Cell Lymphoma With Both IGH/CCND1 Rearrangement and MALT1 Gene Amplification

(Poster No. 11)

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Mantle cell lymphoma (MCL) is characterized by the t(11;14)(q13;q32)/CCND1. MALT1 gene overexpression is the most common genetic event in MALT lymphoma. Identification of CCND1 and MALT1 gene overexpression has a key role in the diagnosis of MCL and MALT lymphoma. Several unusual variants of mantle cell lymphoma have been described, with variable morphologic, immunophenotypic, and genetic characteristics. Here, we report an unusual nasopharyngeal B cell lymphoma with both CCND1 rearrangement and MALT1 amplification. The patient was a 60-year-old man with a recent clinical history of “cutaneous MALT lymphoma.” A positron emission tomography oncology study revealed intense fluorodeoxyglucose avidity in the nasopharyngeal region, highly suspicious for malignancy. A biopsy of the nasopharyngeal lesion was performed. Histologic examination showed focal expansion of the mantle zone surrounding residual germinal centers. Flow cytometry demonstrated monoclonal B cells, CD23+ with variable CD5 expression. Lymphocytes in the mantle zone were positive for CD20, BCL1, and weakly positive for CD5 by immunohistochemistry. Interestingly, fluorescence in situ hybridization studies were positive for standard and variant IGH/CCND1 rearrangement (85%) and MALT1 gene amplification (60%). Further staging evaluations showed minimal bone marrow lymphoma involvement and increased fluorodeoxyglucose avidity in bilateral tonsillar regions and regional nodes of the neck, indicative of systemic disease. The overall findings were consistent with nasopharyngeal mantle cell lymphoma with both CCND1 and MALT1 gene overexpression. To our knowledge, this is the first such case reported in the literature. Recent studies have shown that the MALT1 gene may be involved in the MYC pathway regulation in MCL, which represents a promising target for future therapies in patients with MCL.

Genomic Profile of Hispanic Acute Myeloid Leukemia Patients From Puerto Rico

(Poster No. 12)

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Context: Ethnic and racial disparities have been demonstrated in the outcome of some cancers, including acute myeloid leukemia (AML), which has been attributed to a combination of biologic and nonbiologic factors. Previous studies revealed the presence of mutations of adverse prognostic significance at higher frequencies in Hispanic than white patients with AML. Here, we report the genomic landscapes in Hispanic patients with AML from Puerto Rico (PR) in the largest study to date.

Design: Genomic data of Hispanic patients with AML from PR harbor greater frequencies of mutations associated with adverse prognosis, consistent with the previously reported studies. However, more genes with mutations were reported here in the largest study to date.

Unusual Presentation of Hairy Cell Leukemia in the Lymph Nodes and Pancreas

(Poster No. 13)

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Hairy cell leukemia (HCL) is an uncommon, indolent B-cell neoplasm with unique clinical, morphologic, immunophenotypic, and molecular features. The patients typically present with splenomegaly, pancytopenia, and monocytopenia. The lymphoma primarily involves spleen, bone marrow, and peripheral blood. Lymph node and other extramedullary organ involvement by HCL is rare and usually secondary. Herein, we present an unusual case of HCL involving lymph nodes and pancreas. A 70-year-old man underwent a Whipple procedure for intraductal papillary mucinous neoplasm. Histologic sections of peripancreatic lymph nodes demonstrated effacement of the lymphoid architecture by a proliferation of abnormal small lymphocytes with condensed chromatin, increased eosinophilic cytoplasm, and distinguished cellular borders (Figure 7, A). Foci of similar lymphoid infiltrates were identified in pancreatic parenchyma (Figure 7, B). Immunohistochemical workup showed these cells to be positive for standard and variant IGH/CCND1 rearrangement, BCL2, CBLN D1, and BRAF and were negative for CD3, CD5, CD23, SOX11, and BCL6. A fluorescence in situ hybridization study was negative for CCND1/IGH fusion. The BRAF V600E mutation was detected by polymerase chain reaction. A diagnosis of HCL was rendered. Primary presentation of HCL in the lymph nodes is extremely rare. In the current case, there was no splenomegaly on magnetic resonance cholangiopancreatography. No “hairy” cells were identified in the peripheral blood smear. Although a bone marrow evaluation was not performed, the patient had an unremarkable complete blood cell count, without monocytopenia. Additionally, these lymphoma cells were positive for CD10, uncommon for HCL. This case demonstrates
the variability in clinical and immunophenotypic presentation of HCL, which may pose a diagnostic challenge.

**Myeloid Neoplasm With JAK2 V617 Mutation and Monocytosis**  
(Poster No. 14)

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An 83-year-old woman presented with an abnormal complete blood cell count showing marked leukocytosis (32.3 × 10^9/L) with neutrophilia and monocytosis (4.2 × 10^9/L) and mild normocytic anemia (hemoglobin, 10.9 g/dL). Physical examination showed no splenomegaly. A peripheral blood smear demonstrated increased monocyte numbers with atypical morphology and no blasts were seen. She underwent bone marrow examination, which revealed hypercellular (~80%) marrow with myeloid hyperplasia, increased small hypolobated or monolobated megakaryocytes and mild myelofibrosis (MF-1). Flow cytometry analysis showed monocytosis with CD56 expression and no increase in CD54+ blasts. BCR-ABL1 rearrangement was not detected by polymerase chain reaction (PCR) analysis. JAK2 V617F mutation was detected by qualitative PCR. Given that the JAK2 mutation was detected in a proliferative marrow, a diagnosis of Ph-negative myeloproliferative neoplasm with monocytosis was favored. However, further quantitative PCR showed the mutation frequency of JAK2 V617F was 17%. Next-generation sequencing analysis was performed on the concurrent bone marrow aspirate specimen. Somatic mutations were detected in several genes including ASXL1 (c.3077delG; variant allele frequency [VAF], 35%), JAK2 (c.1849G>T; VAF, 10%), NRAS (c.179G>A; VAF, 11%), SRSF2 (c.283C>A; VAF, 54%), and CBL (c.1146A>C; VAF, 49%) (Table). The variants detected are highly associated with chronic myelomonocytic leukemia (CMM) based on the morphology and molecule mutation profile. A final diagnosis of CMML was rendered. Overall, this case demonstrates the considerable challenge in distinguishing between CMML and a Ph-negative myeloproliferative neoplasm with monocytosis when the JAK2 V617F mutation is present and illustrates the importance of combining molecular studies with myeloid mutations to understand the clinical and prognostic significance of these findings.

### CD123 Expression Varies in Adult B-Lymphoblastic Leukemia/Lymphoma

(Poster No. 16)

Kirill Lyapichev, MD; Brian Wong, MD; Zhihong Hu, MD; Mariana Kersh, MS; Marina Konopleva, MD, PhD; Nitin Jain, MD; Elias J. Jabbour, MD; Jeff Jorgensen, MD, PhD; Joseph D. Khoury, MD; Sa Wang, MD; Sergei Konoplev, MD, PhD. Departments of 1-Hematology and 2-Pathology, University of Texas MD Anderson Cancer Center, Houston.

**Context:** Anti–CD123 therapies are being investigated in patients with hematologic malignancies. We investigated the expression of CD123 in newly diagnosed adult patients with different subtypes of B-lymphoblastic leukemia/lymphoma (B-ALL).

**Design:** We retrospectively analyzed CD123 expression in adult patients with untreated B-ALL seen at our institution between 2015 and 2017. CD123 expression was assessed by multiparameter flow cytometry (MFC) with allotypy-specific (APC)–conjugated anti–CD123 antibody (clone 7G3, BD Pharmingen Bioscience, San Jose, California) for the percentage of neoplastic cells expressing CD123, median fluorescence intensity (MFI), and MFI ratio over the control. CD123 expression was considered positive if detected on >20% of blasts.

**Results:** The study included 95 patients with a median age of 45 years (range, 18–82 years) (51 [34%] Ph+; 42 [28%] not otherwise specified [NOS], 25 [17%] Ph-like CRLF2; 11 [7%] hypodiploid; 8 [5%] MLL; 7 [5%] hyperdiploid; 4 [3%] Ph-like non-CRLF2; and 2 [1%] E2A-PBX1). CD123 was expressed in all cases, except for 6 patients (4% [3 NOS, 2 hypodiploid, and 1 Ph-like CRLF2]). CD123 expression showed marked variations in all groups. CD123 expression was significantly lower in patients with hypodiploid and E2A-PBX1+ (P < .01). When we divided patients into CD34+ and CD34− groups, CD123 percentage (P < .001), CD123 MFI (P < .001), and CD123 MFI ratio (P = .04) were significantly higher in CD34− group. CD123 expression was highest in patients with Ph-like non-CRLF2+ disease, but the difference did not reach statistical significance.

**Conclusions:** CD123 is expressed in most adult patients with B-ALL, but it shows significant variations in intensity. This observation makes the use of anti–CD123 targeted therapy promising in adult patients with B-ALL but warrants preclinical testing.

### Novel Presentation of Aggressive B-Cell Lymphoma With CD5/CD10 Dual Expression and MYD88 L265P Mutation

(Poster No. 15)

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A 66-year-old man with no previous history of lymphoma presented with severe acrocyanosis, neurologic dysfunction, fever, and cytopenias. Positron emission tomography/computed tomography showed splenomegaly and numerous hypermetabolic, unenlarged lymph nodes. Positron emission tomography/computed tomography (PET/CT) showed splenomegaly with severe acrocyanosis, neurologic dysfunction, fever, and cytopenias. PET/CT was positive for lymphoplasmaacytic lymphoma but is also associated with poor prognosis in large B-cell lymphoma. Although isolated CD5 or CD10 expression is not unusual in large B-cell lymphoma or lymphoplasmaacytic lymphoma, concurrent expression of both markers is very rare in either entity, and has not been previously reported in conjunction with the MYD88 L265P mutation. Long-term follow-up is necessary to understand the clinical and prognostic significance of these findings.

### CD123 Expression Varies in Adult B-Lymphoblastic Leukemia/Lymphoma

(Poster No. 16)

Kirill Lyapichev, MD; Brian Wong, MD; Zhihong Hu, MD; Mariana Kersh, MS; Marina Konopleva, MD, PhD; Nitin Jain, MD; Elias J. Jabbour, MD; Jeff Jorgensen, MD, PhD; Joseph D. Khoury, MD; Sa Wang, MD; Sergei Konoplev, MD, PhD. Departments of 1-Hematology and 2-Pathology, University of Texas MD Anderson Cancer Center, Houston.

**Context:** Anti–CD123 therapies are being investigated in patients with hematologic malignancies. We investigated the expression of CD123 in newly diagnosed adult patients with different subtypes of B-lymphoblastic leukemia/lymphoma (B-ALL).

**Design:** We retrospectively analyzed CD123 expression in adult patients with untreated B-ALL seen at our institution between 2015 and 2017. CD123 expression was assessed by multiparameter flow cytometry (MFC) with allotypy-specific (APC)–conjugated anti–CD123 antibody (clone 7G3, BD Pharmingen Bioscience, San Jose, California) for the percentage of neoplastic cells expressing CD123, median fluorescence intensity (MFI), and MFI ratio over the control. CD123 expression was considered positive if detected on >20% of blasts.

**Results:** The study included 95 patients with a median age of 45 years (range, 18–82 years) (51 [34%] Ph+; 42 [28%] not otherwise specified [NOS], 25 [17%] Ph-like CRLF2; 11 [7%] hypodiploid; 8 [5%] MLL; 7 [5%] hyperdiploid; 4 [3%] Ph-like non-CRLF2; and 2 [1%] E2A-PBX1). CD123 was expressed in all cases, except for 6 patients (4% [3 NOS, 2 hypodiploid, and 1 Ph-like CRLF2]). CD123 expression showed marked variations in all groups. CD123 expression was significantly lower in patients with hypodiploid and E2A-PBX1+ (P < .01). When we divided patients into CD34+ and CD34− groups, CD123 percentage (P < .001), CD123 MFI (P < .001), and CD123 MFI ratio (P = .04) were significantly higher in CD34− group. CD123 expression was highest in patients with Ph-like non-CRLF2+ disease, but the difference did not reach statistical significance.

**Conclusions:** CD123 is expressed in most adult patients with B-ALL, but it shows significant variations in intensity. This observation makes the use of anti–CD123 targeted therapy promising in adult patients with B-ALL but warrants preclinical testing.

### A Rare Case of Plasmablastic Lymphoma in Urinary Bladder

(Poster No. 17)

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A 78-year-old man with a history of lymphoma presented with hematuria and a 3-cm bladder tumor. Histology revealed noninvasive high-grade papillary urothelial carcinoma on the epithelial surface as well as large atypical tumor cells involving the muscularis propria of bladder. Immunohistochemical stains were highlighted as follows: positive for vimentin, CD138, CD168, MUM1, EMA, and CD68 and negative for all other immunostains including AE1/AE3, CAM 5.2, CKS 5–6, CK18, S100, MART-1, PSA, PLAP, OCT3/4, PSAP, CD45, CD3, CD20, PAX5, CD30, GATA3, TTF-1, CD31, CK20, desmin, myogenin, CD117, synaptophysin, chromogranin, PAX8, myoD1, HHV8, NKX3.1, and SOX10. IIni did not show loss of expression. In addition, in situ hybridization studies for Epstein-Barr virus (EBV) were positive. Based on this immunohistochemical staining pattern, a diagnosis of plasmablastic lymphoma (PBL) was made. The patient expired 3 months after the diagnosis. This is the first case in which PBL was observed in...
bladder synchronized with urothelial carcinoma. PBL is a very rare B-cell lymphoproliferative disorder with an aggressive clinical behavior. PBL is significantly associated with conditions of immunodeficiency, particularly HIV and EBV infection. Although PBL is most commonly observed in the oral cavity of HIV^+ patients, it can also be observed at extraoral sites in HIV^± patients. MYC translocation has been identified in more than 50% of PBL cases on genetic studies. MYC translocation is present more frequently in EBV^+ tumors (74%) than in EBV^− tumors (43%). Because of its rarity, optimal treatment has not been established. The clinical outlook is very aggressive. The median overall survival is 19 months (Figure 8).

**Myeloid Sarcoma With Megakaryoblastic Differentiation Presenting as an Obstructive Small Bowel Mass**  
(Poster No. 18)

**Rong Xia, MD, PhD** (rongshya@gmail.com); Ning N. Chen, MD, PhD. Department of Pathology, State University of New York, Downstate Medical Center, Brooklyn.

Myeloid sarcoma is a rare extramedullary tumor consisting of myeloid blasts, with or without maturation. Myeloid sarcoma may occur in any part of the body, most frequently affecting the skin and lymph nodes, and it may occur de novo or in association with acute myeloid leukemia or myeloproliferative neoplasms. This neoplasm most commonly displays a myelomonocytic or pure monoblastic morphology. Tumors with megakaryoblastic differentiation are extremely uncommon and may occur in association with transformation of a myeloproliferative disorder. Myeloid sarcoma presenting as an obstructive small-bowel mass is very rare and diagnostically challenging. We report a case of a 33-year-old previously healthy man. The patient presented in the emergency department with a 2-week history of intermittent abdominal pain worsening during the previous 24 hours. Computed tomography imaging showed a small-bowel obstruction with an 8-cm mass. Histopathology examination showed diffuse infiltrative small blastoid cells forming sheets that effaced the normal small-intestinal epithelium, with many scattered multilobulated giant cells and numerous mitoses (Figure 9, A). On immunohistochemistry, the neoplastic cells were strongly positive for CD61, CD43, CD34 (Figure 9, B through D), and CD117, scatter positive for MPO, and negative for CD33, TdT, CD163 and lysozyme, confirming the diagnosis of myeloid sarcoma with megakaryoblastic differentiation. Bone marrow biopsy revealed normal hematopoiesis. Molecular study revealed mutations of KRAS Q22K and WT1 T377fs*68. To our knowledge, this is the first report of myeloid sarcoma with megakaryoblastic morphology presenting as an obstructive mass in the small bowel, and the first report of KRAS and WT1 mutations associated with myeloid sarcoma.

**Hunting Down the Blasts: A Chronic Myeloid Leukemia Case With Unusual Blast Phase Transformation With Phenotypic Switching at Pleura**  
(Poster No. 19)

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Chronic myeloid leukemia (CML), BCR-ABL^+ , is a granulocytic-predominant myeloproliferative neoplasm arising from hematopoietic stem cells with translocation t(9,22)(q34.1;q11.2). CML presents initially with a chronic phase followed by accelerated and/or blast-phase transformation. An 85-year-old man presented with 3-years history of BCR/ABL1 (p210) positive CML, chronic phase, on imatinib. Initial marrow biopsy showed no increase in blasts. However, complex cytogenetics abnormalities with the so-called major route karyotypic abnormalities, including deletion 7, +8, and +21 were detected. The patient developed pleural effusion and underwent thoracentesis and decortication. Flow cytometry of the pleural fluid showed no increase in blasts. Sections from the pleura showed fibrotic tissue with sheets of blasts that had irregular nuclei contour, open chromatin, distinct nucleoli, and moderate amount of cytoplasm (Figure 10, A). Immunoperoxidase studies highlighted 2 populations of blasts: the first population was positive for E-cadherin (Figure 10, B), A1-spectrin, glycophorin, and CD117, compatible with erythroid blasts, whereas the second population was positive for CD33 (Figure 10, C), MPX, CD68 (Figure 10, D), and CD45 (dim), compatible with myeloid blasts. With no increased blasts on bone marrow biopsy, the complex cytogenetics abnormalities indicated CML accelerated/blast phase transformation. Our case shows an unusual bone marrow–sparing blast-phase transformation in the pleura with myeloid and erythroid differentiation. The poor-prognostic phenotypic changing of the blast-phase transformation has been reported in CML after tyrosine kinase inhibitor
Hepatosplenic T-Cell Lymphoma With Blastoid Morphology, Mimicking Lymphoblastic Leukemia

(Poster No. 20)

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A 44-year-old man presented with progressive dyspnea, abdominal pain, fatigue, fever, weight loss, and night sweats. During hospital admission, he was found to have massive hepatosplenomegaly and abnormal liver function tests. A bone marrow evaluation was performed. Peripheral blood smear revealed pancytopenia with rare circulating enlarged lymphocytes with deep-blue cytoplasm. Aspirate smears revealed many cells of medium size, increased nuclear-to-cytoplasmic ratio, and open chromatin, imparting a blastoid appearance with many lymphoglandular bodies. The bone marrow biopsy revealed infiltration with blastoid cells in a serpiginous pattern involving the marrow without expression of TCR-ß, further confirming this diagnosis. This represents an extremely rare initial presentation of SLL in a case with a unique clinical presentation.

First Manifestation of Small Lymphocytic Lymphoma in a Myelolipoma: Case Report and Literature Review

(Poster No. 21)

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Myelolipomas are benign lesions composed of variable amounts of hematopoietic elements and mature adipose, accounting for 3% of all adrenal masses. Literature review revealed only a few cases of hematologic malignancy involving myelolipoma in isolation. We report a case of small lymphocytic lymphoma (SLL) involving an adrenal myelolipoma as the first and only manifestation of the disease. Our case is that of a 52-year-old man who was incidentally found to have a left adrenal mass discovered during computed tomography for nephrolithiasis 5 years before the current presentation. He had a complete blood cell count within reference range and no lymphadenopathy. An elective adrenalectomy was eventually performed because of increasing size on surveillance imaging. Gross examination revealed a brown-tan, well-circumscribed and nonencapsulated mass measuring 3.1 cm. Histologic sections revealed classic findings diagnostic of myelolipoma with scattered lymphoid aggregates comprising predominantly CD20+ B cells with aberrant CD5 expression (negative for cyclin D1) consistent with SLL. In patients with established chronic lymphocytic leukemia (CLL)/SLL, involvement by lymphoma in multiple organs is a common finding; however, initial presentation of SLL within an adrenal myelolipoma in a patient with a complete blood cell count within reference range is novel and has not been reported in the literature. Interestingly, the 2 reported cases of SLL were in extraadrenal myelolipomas with a concurrent CLL component (Figure 12). The pathogenesis of myelolipoma itself is obscure and the evolution of a lymphoid malignancy within it is further elusive. This case represents an extremely rare, initial presentation of SLL in a case with a unique clinical presentation.

A Case of Chronic Lymphocytic Leukemia With t(14;19)(q32;q13.3), Trisomy 12, and Central Nervous System Involvement

(Poster No. 22)

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Chronic lymphocytic leukemia (CLL) is the most common leukemia in elderly adults and typically characterized by marked lymphocytosis and indolent clinical behavior but rarely involving the central nervous system (CNS). Here, we present a case of CLL with unusual cytogenetic findings and CNS involvement. A 54-year-old man with asthma and a history of disseminated zoster presented with a 7-month history of diffuse lymphadenopathy. He presented with headache, nausea, vomiting, and white blood cell count of 118K/l, with 71% lymphocytes and 2% prolymphocytes. Flow cytometry performed on blood detected many abnormal B cells with expression of CD5, CD11c, CD19, CD20, CD22, CD23 (partial), CD38 (partial), and HLA-DR with k light chain restriction. Microscopic examination of cerebrospinal fluid showed atypical small lymphocytes and rare slightly enlarged forms consistent with involvement by leukemia that was verified by flow cytometric analysis. Bone marrow chromosomal and fluorescent in situ hybridization analysis identified an abnormal cell population showing t(14;19)(q32;q13.3) and included subclones showing trisomy 12 and trisomy 21. The t(14;19)(q32;q13) translocation has been
described in rare cases of CLL with trisomy 12. To our knowledge, this translocation has never been associated with CNS involvement. Although CLL is the most common leukemia in elderly adults, CNS involvement is rare. The clinical manifestations of CLL involvement of the CNS include headache, cranial nerve palsies, cerebellar signs, and sensory motor deficits. Patients with CNS involvement by CLL are thought to have a poor prognosis. Detection of t(14;19)(q32;q13) represents another unusual finding and may have an association with CNS involvement.

**Aggressive EBV-Negative NK/T-Cell Posttransplant Lymphoproliferative Disorder Arising in a Patient With a Chronic NK-Cell Lymphoproliferative Disorder and Primary Myelofibrosis**

(Poster No. 23)

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We present the case of a 43-year-old man with refractory primary myelofibrosis treated with an allogeneic stem cell transplant. Over 2 years since his original diagnosis and treatment, his peripheral blood smear showed a white blood cell count within reference range, with atypical appearing lymphocytes with enlarged nuclei, vacuoles, and fine granules. Flow cytometry demonstrated 62% NK cells with abnormal KIR marker expression and an otherwise normal immunophenotype. T cells were unremarkable. The patient abruptly developed massive splenomegaly, B symptoms, and pancytopenia. After splenic embolization, the white blood cell count rose from within reference range to >200 × 10^9/L over the course of 2 days. Peripheral blood flow cytometry showed a neoplastic population accounting for 85% of events, which expressed CD2, partial CD3, CD7, partial CD16, CD56, and CD45. This population was negative for CD5, CD4, CD8, CD10, CD34, CD57, and TDT. EBER in situ hybridization was negative. Cytogenetic analysis demonstrated a complex karyotype with 2 separate clones present. Clonal T-cell gene rearrangements were present, further supporting T-cell differentiation. The patient rapidly deteriorated and died within 2 months. This case is an unusual example of a highly aggressive Epstein-Barr virus–negative posttransplant lymphoproliferative disorder with an NK/T-cell immunophenotype arising in the setting of a chronic NK-cell lymphoproliferative disorder.

**Xanthogranuloma/Histiocyte-Rich Pseudotumor in a Patient Posttreatment for Aggressive Diffuse Large B-Cell Lymphoma**

(Poster No. 24)

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Postradiation/chemotherapy pseudotumors have rarely been described. In this report, we present a case of posttreatment xanthogranuloma of the neck. The patient was a 34-year-old, nonsmoker, white man with cutaneous diffuse large B-cell lymphoma (DLBCL) of the scalp, who was treated with external radiation therapy in 2011. In 2015, he developed cervical lymphadenopathy, which was negative for malignancy. In 2017, the mass increased in size and the biopsy revealed DLBCL. A staging positron emission tomography (PET) scan showed splenic involvement. The patient received cyclophosphamide, doxorubicin, vincristine, and prednisone, plus rituximab (R-CHOP) for 4 months. After-treatment PET imaging revealed residual activity in right neck node and he underwent consolidative radiation therapy in March 2018. He presented 6 months after treatment with refractory right cervical lymphadenopathy seen on PET–computed tomography (CT) with increasing standardized uptake value from 3 to 5.4 in 6 months and 18F-fluorodeoxyglucose (FDG) avidity (Figure 13, A). He had no weight loss, fevers, night sweats, dysphagia, odynophagia, otalgia, pain/tenderness, hoarseness, bleeding, hemoptysis, or cranial neuropathies. The patient underwent complete resection of the neck mass. Histologic sections revealed histiocytic infiltrate with giant cells, cholesterol clefting, hyalinizing necrosis, dystrophic calcification and scattered small lymphocytes, morphologically consistent with xanthogranuloma. CD68 marked the diffuse histiocytic infiltrate (Figure 13, B through D). Posttherapy pseudotumors were florid in response to chemotherapy-induced tumor necrosis. Although a PET-CT scan is helpful in differentiating nonviable tissue, the numerous histiocytes in pseudotumors may appear metabolically active and mimic relapse of disease. An excisional biopsy can be helpful for determining relapse and need for further treatment.

**An Incidental Finding of Triple-Hit High-Grade B-Cell Lymphoma After Cholecystectomy**

(Poster No. 25)

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A previously healthy 43-year-old woman presented with abdominal pain. She was diagnosed with acute cholecystitis and underwent cholecystectomy. During the operation, the surgeons noted abnormally increased amounts of peritoneal fluid that was collected for analysis. Cytologic examination of peritoneal fluid showed numerous neoplastic cells with irregular nuclei, fine chromatia, prominent nucleoli, scant agranular cytoplasm, and cytoplasmic vacuoles (Figure 14, A). The gallbladder showed no evidence of involvement, but retrospective examination of a periductal lymph node from the cholecystectomy specimen showed sheets of blastoid cells (Figure 14, B). Flow cytometry of the peritoneal fluid demonstrated aberrant B cells with CD10 expression (Figure 14, C) and I. restriction (Figure 14, D). By immunohistochemistry, the cells were positive for CD10, CD20, BCL2, BCL6, and PAX5 and were negative for CD3 and TDT. Epstein-Barr virus is situ hybridization was negative. Ki-67 showed a proliferation index greater than 90%. Fluorescence in situ hybridization...
showed MYC, BCL2, and BCL6 gene rearrangements. A diagnosis of de novo, high-grade B-cell lymphoma with triple-hit rearrangements was rendered. Bone marrow staging revealed involvement by lymphoma with similar blastoid morphology. Cytogenetic analysis revealed a complex karyotype: 44,X,-X,t(3;14)(q27;q32);34,del(3)(q12q29),+dic(3;9)(p13;p24),4,der(4)add(4)p12[4]add(4)q31,der(8)t(8;14)[q24;q32];7,9,add(9)q21,add(10;q22),del(11)q21,t(14;18)(q32;q21), del(17)(p11.2),+t[13]/46.XY[7]. The patient received aggressive treatment but had an unsatisfactory clinical course before she was transferred to hospice. This is an unusual presentation of high-grade B-cell lymphoma.

Typically, patients with high-grade B-cell lymphoma often present with severe clinical symptoms and widespread disease. However, this patient demonstrated an aggressive clinical course and poor prognosis despite a negative medical history, no previous diagnosis of lymphoma, and no symptoms.

A Rare Case of Lymphoblastic Transformation of Follicular Lymphoma With BCL6 and MYC Rearrangements

(Poster No. 26)

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A 44-year-old HIV+ man presented with cervical lymphadenopathy. Histologic sections of his cervical lymph node excisional biopsy showed complete effacement by focal back-to-back neoplastic follicles composed of sheets of large neoplastic cells, consistent with a grade 3B follicular lymphoma (Figure 15, A). Fluorescence in situ hybridization showed BCL6 rearrangement without MYC or BCL2 rearrangement. The patient’s cerebrospinal fluid and bone marrow were negative for involvement by lymphoma. One year later, the patient presented with headaches and third-nerve palsy. Cytology examination of his cerebrospinal fluid showed malignant cells with fine chromatin and prominent nucleoli (Figure 15, B). Flow cytometry analysis of cerebrospinal fluid revealed neoplastic cells that expressed CD19, CD20, and terminal deoxynucleotidyl transferase (TDT; Figure 15, D). Fluorescence in situ hybridization analysis showed fluorescence in situ hybridization of BCL6/3q in 89.0% of nuclei, a rearrangement of MYC/8q in 93.0% of nuclei, and a gain of BCL2/18q in 71% of nuclei. Bone marrow biopsy had 80% to 90% cellularity with abnormal blasts (Figure 15, C) that stained positive for CD79a, PAX5, MUM1, BCL6, and TDT. Conventional cytogenetics showed a complex karyotype: 54.XY,del(X)q(22q23),-1,add(1)(p12),-der(2)t(3;10)(p10;q10),-5,add(3)(p12),t(3;22)(q27;q11.2),-6,add(6)(q13),+7,add(7)(q32),+10,add(10)(q25),+12, add(12)(q24.3),t(14;17)(q32;q25)[7]/46.XY[13]. A diagnosis of transformation of follicular lymphoma to a B-cell lymphoblastic leukemia was rendered. The patient was placed on salvage chemotherapy with rituximab, dexamethasone, cytarabine, cisplatin, and intrathecal methotrexate. A literature review showed follicular lymphoma with lymphoblastic transformation often demonstrates BCL2 and MYC rearrangements. MYC and BCL6 rearrangements, as seen in this patient, are exceedingly rare. The clinical significance of these findings remains unclear; more studies can be performed for the optimal therapeutic approach.

Comparison of MYC Break-Apart and IGH/MYC Dual-Fusion Probe Sensitivity for Detection of MYC Rearrangements in Large B-Cell Lymphomas

(Poster No. 27)

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Context: Large B-cell lymphomas (LBCL) are a heterogeneous group of B-cell malignancies. Rearrangements in the C-MYC (MYC) gene along with additional rearrangements in BCL2 and/or BCL6 have been recognized as a diagnostic criterion for “double/triple-hit” high-grade B-cell lymphoma and represent an important prognostic indicator. Routinely, MYC break-apart (LSI-MYC) and IGH/MYC fusion (IGH/MYC) probes are used to assess the MYC status. Because MYC can frequently be partnered with non-IGH genes, LSI-MYC demonstrates greater sensitivity than IGH-MYC does. Recently, it has been indicated that concurrent evaluation for both LSI-MYC and IGH/MYC may decrease false-negative rates because occasional (~4%) LSI-MYC-negative cases are IGH/MYC-positive. In this study, we retrospectively evaluated the concordance of these 2 methods of MYC rearrangement detection.

Design: Cases of LBCL with concurrent LSI-MYC (Vysis, Abbott Molecular, Des Plaines, Illinois) and IGH/MYC (IGH/MYC/CEP8 triple color probe, Vysis, Abbott Molecular) fluorescence in situ hybridization results were retrospectively selected from the ARUP laboratories database (October 2013–January 2019). The results were analyzed for concordance.

Results: Of 151 patients, 16.6% demonstrated abnormal MYC results. IGH/MYC and LSI-MYC were congruent in 93.4% of cases. LSI-MYC-negative and IGH/MYC-positive cases represented 6.6% of total cases and 40% of MYC-rearranged cases. No LSI-MYC-negative cases demonstrated IGH/MYC rearrangement.

Conclusions: MYC rearrangement in LBCL is important for diagnosis, treatment, and prognosis. Recent publications suggest ordering both LSI-MYC and IGH/MYC to decrease LSI-MYC false-negative rates. In our cohort, all 25 patients with MYC-rearranged LBCL did not benefit from additional IGH/MYC testing. In a reference laboratory setting, up-front ordering of both tests is perhaps convenient but not cost-effective. Other approaches, including cascade testing may be beneficial.

Therapy-Related Acute Myeloid Leukemia With Aberrant PAX5 Expression

(Poster No. 28)

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The expression of PAX5, a B-cell-specific transcription factor in acute myeloid leukemia (AML) is very rare. We present a case of aberrant PAX5 expression in a therapy-related AML. The patient was an 11-year-old boy with a history of T-lymphoblastic leukemia after chemotherapy who subsequently developed therapy-related AML. He received a stem cell transplant and was in remission. Six months later, he presented with neutropenic fever and a right clavicular mass. A biopsy of the mass revealed sheets of mononuclear cells with round-to-irregular nuclei and pleomorphic cytoplasm (Figure 16, A). Initial immunohistochemical stain showed these mononuclear cells were positive for PAX5 (Figure 16, B). A concern for B-cell neoplasm was raised. Additional stains showed tumor cells were positive for CD33 (Figure 16, C) and lysozyme (Figure 16, D) and were negative for CD20, CD27, OCT2, BOB1, CD3, and MPO. A diagnosis of myelodysplastic syndrome with therapy-related AML was rendered. Subsequent flow cytometry analysis of bone marrow showed a blast population positive for CD33, HLA-DR, CD38, CD64, and CD11B. Cytogenetics study showed a complex karyotype: 47,XY,der(1)t(1;11)(q42;q13),t(1;2)[p22;q22],add(5)(p11),+8,+9,der(10;17)(q10;q10),+11,der(19)(11;19),add(20)(p13),del(20)(p12),+mar1L+mar2[2]. PAX5 is regarded as a B-cell lineage marker. Its expression in AML may present diagnostic challenges, particularly in an extramedullary site as seen in our case. Previous publications indicated aberrant PAX5 expression in AML was com-
monly associated with t(8; 21) karyotype. However, our case is a therapy-related AML with a complex karyotype. The current case broadens our knowledge of PAX5+ AML, which may help us to avoid potential diagnostic errors in the practice.

Hemophagocytic lymphohistiocytosis (HLH) is an aggressive disease that results from excessive immune activation. It commonly affects infants younger than 18 months. Primary HLH follows autosomal-recessive inheritance whereas secondary HLH occurs after a triggering agent (immunodeficiency, systemic viral infections, lymphoma, etc.). Diagnostic criteria rely on either molecular criteria and/or clinicopathological criteria. We describe a 16-year-old boy who presented with fever, maculopapular rash, splenomegaly, anemia, thrombocytopenia, elevated liver enzymes, and hyperbilirubinemia. Serologic testing results for Epstein-Barr virus (EBV) viral capsid antigen (VCA) and EBV nuclear antigen (EBNA) were positive. The patient was diagnosed with EBV hepatitis; however, suspicion for concomitant HLH was raised. Additional workup showed serum levels of the following: triglycerides, 216 mg/dL (reference range, <150 mg/dL); ferritin, 1342 ng/mL (reference range, 12–150 ng/mL); fibrinogen, 124 mg/dL (reference range, 150–400 mg/mL); sIL-2, 3333 U/mL (reference range, 45–110 U/mL); CD107a, 13% (reference range, 11%–35%); and interleukin 18 (IL-18), 64 197 pg/mL (reference range, 89–540 pg/mL). Bone marrow examination revealed rare hemophagocytic. His genetic HLH panel testing showed XIAP variant of uncertain clinical significance. The patient was treated with dexamethasone and cyclophosphamide. His symptoms improved with complete blood cell count and liver function study within reference range at 6-month follow-up. The patient fulfills 7 of 8 criteria required for the diagnosis of HLH. The association between HLH and EBV infection has been reported in the literature. It has been suggested that EBV-associated HLH carries a higher mortality rate unless diagnosed early. We conclude that diagnosis of HLH in a patient with EBV infection requires a high degree of suspicion. Prompt diagnosis is necessary to attain a better chance of survival.

Discordance Between Morphologic Findings and Ancillary Testing in Acute Myeloid Leukemia

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**Context:** Acute myeloid leukemia (AML) typically presents with uniform and widespread marrow involvement in the biopsy, aspirate, and ancillary tests. However, rare cases of AML show discordant morphologic biopsy, aspirate cytometry, and/or cytogenetic studies. These included 2 cases of de novo AML with mononcotic differentiation, 2 cases of AML with myelodysplasia-related changes, and 1 case of chronic myelomonocytic leukemia that transformed to AML. In all cases, the discrepancy was due to patchy marrow involvement by AML. The patchy nature of the disease involvement was evident both on biopsy and aspirate. One case showed variable blast percentages among different aspirate preparations, and the other showed focal disease that was more apparent on the aspirate, with extensive abnormalities in the karyotype.

**Conclusions:** De novo AMLs with monocytic differentiation and AMLs arising in myelodysplastic syndrome or chronic myelomonocytic leukemia rarely show heterogeneous marrow involvement. Evaluation of a generous biopsy is recommended, and cases with discordant findings require close evaluation of the biopsy, aspirates, and ancillary tests.

A Rare Case of Composite Mantle Cell Lymphoma and Classic Hodgkin Lymphoma

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After extensive literature review, we found only 8 reported cases of composite mantle cell lymphoma and Hodgkin lymphoma. Here, we present a case of a 92-year-old woman with indolent mantle cell lymphoma with concurrent Hodgkin lymphoma. The patient presented to the clinic because of multiple enlarged lymph nodes in the right neck. Imaging studies and excisional biopsy were performed. The lymph nodes revealed effacement of the nodal architecture by a predominantly
monotonous proliferation of small mature lymphocytes, extensive granulomatous reaction, and clusters of epithelioid histiocytes (Figure 17, A). Focal areas showed scattered Hodgkin/Reed-Sternberg cells (Figure 17, B). The monotonous lymphoid proliferation was positive for CD20, CD23, cyclin D1 (Figure 17, C), CD5 (dim), BCL2, and CD23 and was negative for CD10, SOX11, and CD3. The Hodgkin/Reed-Sternberg cells were positive for CD30, CD15, PAX5 (dim), and EBER by in situ hybridization and were negative for CD20 and CD3. Flow cytometric analysis showed a monoclonal B-cell population that was positive for CD19, CD20, CD23, and FMC7 and negative for CD5, CD10, and CD200, with a x-surface immunoglobulin (lg) light chain restriction (Figure 17, D). Molecular testing was positive for monoclonal IgH1 gene rearrangement in frameworks 1 and 2. Fluorescence in situ hybridization and were negative for CD10, SOX11, and CD3. The Hodgkin/Reed-Sternberg was negative for CD10, SOX11, and CD3. Flow cytometric analysis showed a monoclonal B-cell population that was positive for CD19, CD20, CD23, and FMC7 and negative for CD5, CD10, and CD200, with a x-surface immunoglobulin (lg) light chain restriction (Figure 17, D). Molecular testing was positive for monoclonal IgH1 gene rearrangement in frameworks 1 and 2.

A Unique Case of Adult T-Cell Leukemia/Lymphoma With Potential Pitfalls in Diagnosis

(Poster No. 34)

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Adult T-cell leukemia/lymphoma (ATLL) is an aggressive T-cell neoplasm that develops in individuals infected with human T-cell lymphotropic virus (HTLV-1). The immunophenotype is most frequently of a CD25+ regulatory T cell. We report a unique case of ATLL in a 61-year-old man originally from Jamaica who was found to have extensive lymphadenopathy with no initial lymphocytosis or the classic abnormal “flower” lymphocytes on peripheral blood smear. Lymph node biopsy showed complete effacement by a diffuse infiltrate of atypical medium-sized lymphocytes that were strongly positive for B-cell marker CD20, T-cell markers CD2, CD3, CD4, and CD5, and also expressed PD1. The lymphocytes were negative for CD25 and additional B-cell markers. Because of the patient’s nationality, HTLV-1 serologic testing was performed and was found to be positive. Thus, the diagnosis of ATLL was rendered. PD1 expression is a known follicular T-cell marker and along with a negative CD25, may lead to a misdiagnosis of angioimmunoblastic T-cell lymphoma. Additionally, only a handful of reported ATLL cases have been found to be CD20+; some of which were initially misdiagnosed as diffuse large B-cell lymphoma. In this case, although the lymphoma showed an unusual staining pattern, the combination of patient epidemiologic factors, clinical suspicion, and positive HTLV-1 serology supported the diagnosis of ATLL. Overall, a negative CD25 does not rule out ATLL. HTLV-1 serology as well as extensive B-cell and T-cell markers must be tested in such patients to avoid misdiagnosis, which could lead to incorrect therapies.

The Pathogenesis Between 21-Antitrypsin Deficiency and JAK2V616F Mutation

(Poster No. 35)

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21-Antitrypsin deficiency is a rare disorder associated with the SERPIN1 gene, which results in an inherited disease affecting the lungs and the liver. We present a case report of a patient with liver cirrhosis and emphysema secondary to 21-antitrypsin deficiency. After orthotopic liver transplant, examination of his native liver revealed cirrhotic nodules highlighted by reticulin stain (Figure 18, A) and first time an unusual pattern of fragmented staining confined to germinal centers in a recently treated infection. Our review suggests that this pattern should not be ignored and may indicate dramatic response to treatment.
periodic acid–Schiff–diastase-positive eosinophilic inclusions (Figure 18, B). Eight years after liver transplantation, the patient presented to the emergency department twice in 1 year for hemothysis and shortness of breath. An unprovoked pulmonary embolism was diagnosed on both occasions, and evaluation with a complete blood cell count, prothrombin time, D-dimer, factor V Leiden, factor II mutation, and lupus anticoagulant had negative results. Nine months after his second pulmonary embolism, the patient had persistently elevated hemoglobin and hematocrit levels, with the highest hemoglobin at 20.9 g/dL and hematocrit at 65.3%. Further investigation revealed positivity for JAK2V617F mutation. The patient’s bone marrow biopsy revealed a hypercellular marrow (30%–60%; Figure 18, C) with increased erythropoiesis and megalakaryocytopoiesis, consistent with polycythemia vera. The erythrocytes had megaloblastic changes, nuclear dysmaturation, and nuclear budding. The megalakaryocytes had dysplastic features, including naked, hypolobated, and hyperlobated forms with focal clustering (Figure 18, D). The patient was managed with rivaroxaban and hydroxyurea, and occasional phlebotomy. To our knowledge, this is the first case of coexisting SERPINA1 gene mutation and JAK2V617F mutation. We describe several hypotheses for the potential pathogenesis for the association between the 2 disease entities.

Involvement of Small Intestine and Kidney by Lymphoproliferative Disorder in Post Renal Transplantation: A Case Report and Review of Literature

(Poster No. 36)

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Posttransplant lymphoproliferative disorder (PTLD), manifested by irregular proliferation of B- or T-cells in the lymphoid tissue, is a challenging entity to diagnose and treat. It presents with wide spectrum of clinical and histologic findings. We present a case of 52-year-old woman with a history of multiple allograft kidney transplants for lupus nephritis. She was found to have hypermetabolic lesions in transplant kidney on imaging, suspicious for malignancy, 10 years after her last kidney transplant. Renal biopsy revealed atypical large lymphoid proliferation with abundant necrosis (Figure 19, A and B). Ancillary studies were positive for CD20 (Figure 19, C), CD30, EBV, MUM1, and BCL2 and were negative for CD3, CD5 CD10, BCL6, cyclin D1, and CD138. Ki-67 (Figure 19, D) was about 90%. Diagnosis of monomorphic B-cell PTLD (large B-cell lymphoma) was concluded. She underwent treatment with rituximab. A month later, she developed acute onset of abdominal pain and was admitted to the hospital with bowel perforation. She underwent emergency surgery with a partial small-intestinal resection. Microscopy revealed lymphoma at the site of the perforation, consistent with previous known history of B-cell lymphoproliferative disorder. Clinical-pathologic correlation was of utmost importance in this case. The number of renal transplant recipients who developed PTLD within the small intestine is limited in the literature, with only a few cases reported with histologically proven PTLD. The literature suggests that patients with renal transplants who develop PTLD within their intestine are associated with a better prognosis when compared with those with other locations.

Identification of BCR-JAK2 Fusion in Mantle Cell Lymphoma

(Poster No. 38)

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JAK2 is a member of the Janus family of cytoplasmic nonreceptor tyrosine kinases located on chromosome band 9q22. JAK2 contributes to the pathogenesis of myeloproliferative neoplasms (MPN) and has been reported in acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS). Conversely, JAK2 rearrangements are very rare and are associated with an aggressive course and poor outcome. We describe the first reported case of t(9;22)(p24;q11.2) with BCR-JAK2 fusion in mantle cell lymphoma (MCL). A 65-year-old woman presented with cough, shortness of breath, and increasing fatigue. Complete blood cell count showed anemia and white blood cells of 32.6 x 10^9/L with a predominant population of lymphoid cells with blastic morphology. Immunophenotype by flow cytometry revealed B

Solid Extracavitary Primary Effusion Lymphoma Presenting as a Perihematomalignancy

(Poster No. 37)

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Primary effusion lymphoma (PEL) is an HHV-8–associated B-cell neoplasm, most often occurring in the setting of immunodeficiency, primarily HIV. It is characterized by an effusion involving the pleural, pericardial, and peritoneal spaces. PELs are B-cell malignancies, which do not express pan-B-cell markers. They have a postgermin center derivation and, accordingly express CD138 and lack T-cell and NK-cell expression. In rare cases, lymphomas with the same immunophenotype can occur as solid masses not associated with an effusion. These are termed extracavitary PEL. There have been 55 cases described involving various anatomic sites. We report a case of extracavitary PEL occurring as a large perihematic mass. Our patient is a 31-year-old HIV+ man who presented with fever, abdominal pain, and constipation. Computed tomography scan revealed a 9.0-cm soft tissue mass adjacent and extending into the liver. A biopsy of the perihematic mass showed a diffuse infiltrate composed of large atypical cells with plasmablastic features (Figure 20, A). The tumor cells were positive for CD45, CD138 (Figure 20, C), MUM1, CD30, and C-MYC and lacked expression of CD20, PAX5, CD79a, CD3, ALK, and CD5. The Ki-67 was very high (Figure 20, D). The HHV-8 (Figure 20, B) stain was strongly and diffusely positive ascertaining a diagnosis of extracavitary PEL. Our patient was given high-dose steroids but expired while awaiting transfer to an outside institution, highlighting the aggressive course of these malignancies. According to the absence of the typical effusion, detection of PEL can present a challenge. In this report, we aim to increase awareness of this rare and aggressive entity.
cells with moderate to bright CD19, bright CD20, dim CD123, dim CD11c, and bright monotypic kappa-surface light chain were negative for CD5 and CD10. A pleural effusion showed similar neoplastic cells that marked as B cells with CD5 positivity by flow cytometry. Bone marrow biopsy showed a B-cell neoplasm with nodular and interstitial pattern of infiltration and positive CD5, cyclin D1, and SOX11 by immunohistochemical staining. Co-occurrence with systemic manifestations of the disease revealed a complex karyotype, including the characteristic cytogenetic alteration t(11;14)(q13.232) associated with MCL and t(9;22) (p24;q11.2). Fluorescence in situ hybridization studies subsequently confirmed IGH-CCND1 and BCR-JAK2 fusions. BCR-JAK2 fusion has been described in 11 cases, including MPN, AML, B-lymphoblastic leukemia/lymphoma, and Burkitt lymphoma but not in MCL. Given the prognostic and therapeutic implications, it is crucial to recognize the presence of rearrangement of the JAK2 gene in association with different hematologic malignancies.

**An Unusual Presentation of Extranodal Rosai-Dorfman Disease Involving the Appendix**

(Poster No. 39)

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Rosai-Dorfman disease (RDD) is a rare condition that primarily involves the lymph nodes and presents as painless cervical lymphadenopathy. However, with systemic manifestations of the disease, it is characterized by histiocytic cell proliferation. In approximately 43% of cases, it may involve extranodal organs, but the gastrointestinal tract is an extremely rare site for this condition. We present an unusual case of appendiceal RDD. A 79-year-old man with history of diabetes mellitus and left colon resection for invasive adenocarcinoma presented with severe right-sided back pain for 3 days, not associated with fever or other symptoms. Abdominal computed tomography scan showed a 3 × 3 × 2.5-cm rounded, complex, cystic, or possibly solid nodule at the distal aspect of the appendix. Appendectomy was performed. The specimen was a well-differentiated pericapsular solid mass abutting the appendix and extending to adjacent soft tissues. Histologic sections showed histiocytic proliferation (Si100) and CD163 with distinctive emperipolesis and mixed inflammatory background. Immunoglobulin (Ig) G highlighted a few plasma cells with polytypic kappa and lambda expression. IgG4 (<40% of kappa-positive plasma cells), IgM, and IgA were also positive in few plasma cells. Epstein-Barr virus–encoded RNA in situ hybridization and fluorescence in situ hybridization for ALK gene rearrangement were negative. All of these findings are consistent with RDD. Although commonly self-limiting, RDD may have an aggressive clinical course and might be fatal. It is important to differentiate this entity from other close mimics such as tuberculosis, lymphoma, and sarcoidosis, and reactive histiocytosis, each requiring a different approach to management.

**Expansion of a Hairy Cell Leukemia Clone Following Remission of Acute Promyelocytic Leukemia**

(Poster No. 40)

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Hairy cell leukemia (HCL) is an uncommon mature B-cell leukemia characterized by pancytopenia. Concomitant HCL and acute myeloid leukemia is rarely reported. We present a case of a 71-year-old woman who initially presented with pancytopenia when she went for cardiac catheterization for 2-vasel disease. She was diagnosed with acute promyelocytic leukemia (APL) with PML/RARA translocation and a small clone of hairy cell leukemia (7% of total leukocytes). The patient was treated with a modified version of ATRA/arsoenic trioxide. Two months later, the patient achieved hematologic recovery and no morphologic, immunologic, or cytogenetic evidence of residual APL. However, an expanding clone of HCL was also detected on bone marrow morphology (40% total leukocytes), confirmed by bone marrow morphotopography and flow cytometry. To our knowledge, this case of secondary expansion of HCL after treatment and complete remission of APL has not been previously described. Reporting of this uncommon case is to highlight the possibility of such finding after remission of APL.

**Diagnostic Significance of Immunophenotypic Aberrancy of Monocytes in Myeloid Neoplasms**

(Poster No. 41)

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**Context:** Abnormal differentiation and maturation asynchrony in monocyte populations are common in myeloid neoplasms. This study sought to determine which immunophenotypic features of monocytes can differentiate myeloid neoplasms from reactive conditions.

**Design:** Seventy-one flow cytometry cases from Oregon Health and Science University were retrospectively reviewed. All cases were performed with Beckman Coulter Navios (Indianapolis, Indiana) color flow cytometry with the following antibody panel: CD9, CD11b, CD13, CD14, CD15, CD16, CD33, CD45, CD56, CD64, and HLA-DR.

**Results:** The age of patients ranged from 1 to 89 years (26 females and 45 males). Samples included 44 bone marrow aspirates and 27 peripheral blood specimens. Clinical diagnoses included 23 acute myeloid leukemia (AML) cases, one chronic myelomonocytic leukemia (CMML) case, 16 myelodysplastic syndrome (MDS) or myelodysplastic syndrome/myeloproliferative neoplasm (MDS/MPN) cases, and 8 myeloproliferative neoplasm (MPN) cases. Seventeen cases had normal/nonhematopoietic diagnoses, and 6 patients were healthy after stem cell transplant. Monocyte immunophenotypic aberrancy is defined as expression of CD15 or CD16, or the absence of CD4, CD13, or HLA-DR; 17 of 23 AML (74%), 8 of 16 MDS (50%), 0 of 8 MPN (0%), and 1 of 1 CML (100%) cases had one or more aberrant surface marker expressions. In comparison, only 1 of 23 healthy cases (4%) showed immunophenotypic aberrancy (partial CD15). AML/MDS cases most commonly showed low of CD9 expression (11 cases), followed by loss of HLA-DR and expression of CD15 (6 and 5 cases, respectively).

**Conclusions:** Monocytes often show aberrant antigen in AML, MDS, and MPN/MPN (54%; 26 of 48), with only rare aberrancy noted in MPN and normal/reactive conditions (4%; 1 of 23). Identification of abnormal antigen expression by flow cytometry is an additional tool to differentiate myeloid neoplasms from reactive disorders.

**A Case of High-Grade B-Cell Lymphoma With MYC and BCL2 Translocation With an Excellent Response to Chemotherapy**

(Poster No. 42)

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“High-grade B-cell lymphoma with MYC and BCL2 rearrangements” is a new entity under the new category of high-grade large B-cell lymphoma in the 2016 revision of the World Health Organization classification. These lymphomas are characterized by poor response to standard therapy and an aggressive clinical course with extremely poor prognosis, overall survival in the range of 4.5 to 6 months and a 1-year survival of <30%. We present a case of a 44-year-old man who initially presented to the hospital with left leg pain. He was found to have a pathologic left femur lytic lesion and fracture on radiologic studies. Left femur bone biopsy showed a neoplastic lymphoid proliferation associated with necrosis and an immunophenotype of positivity for CD20, CD79a, CD10, BCL2, BCL6, and kappa restriction and negative for CD5, CD30, PAX5, TdT, EBV, BCL1, MUM1, and c-MYC and a high proliferative index (Ki-67 = 70%–80%). MYC and BCL2-IGH [14,18] rearrangements were detected by fluorescence in situ hybridization. Bone marrow biopsy showed no involvement of B-cell lymphoma. Positron emission tomography (PET)-computed tomography scan was performed and showed hypermetabolic fluorodeoxyglucose (FDG) foci in left upper-lobe pulmonary nodules, multiple left cervical lymph nodes and left paraspinal soft tissue mass, suspicious for metastatic disease. Clinical staging of the patient was NCCN-IPI stage IV (high moderate risk). The patient received 6 cycles of EPOCH therapy (rituximab, etoposide phosphate, prednisone, vincristine sulfate [Oncovin], cyclophosphamide, and doxorubicin hydrochloride [hydroxydaunorubicin]) with intrathecal methotrexate and showed no abnormal FDG uptake on most recent PET scan (6...
months after initial diagnosis). The patient is now in complete remission for 10 months after initial diagnosis.

**A Unique Case of an Epstein-Barr Virus–Positive Marginal Zone Lymphoma in an Immunocompetent Patient**

(Poster No. 43)

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Epstein-Barr Virus (EBV)–positive marginal zone lymphoma (EBV⁺ MZL) is a very rare entity that has only been described in the immunocompromised setting. Currently, the World Health Organization recognizes EBV⁺ MZL as a posttransplant lymphoproliferative disorder. Our case suggests EBV⁺ MZL can also be found outside of the immunocompromised setting and may be significantly underreported. A 59-year-old man with no previous medical history of disease presented to the emergency room with right lower-quadrant abdominal pain. Computed tomography scans showed an enlarged, dilated appendix as well as diffuse lymphadenopathy. Excision of the appendix and a regional lymph node showed interfollicular involvement by a monotonous population of small to occasionally intermediate-sized lymphocytes with many plasmacytic forms. Immunohistochemical studies demonstrated extensive EBV-encoded RNA in situ hybridization studies demonstrated extensive positivit, especially within the plasmacytic cells. These findings are most compatible with an EBV⁺ MZL. Ten cases of EBV⁺ MZL have been reported outside of the posttransplant setting. All of those cases were described to be in patients with immunodeficiencies. This patient had no immunodeficient disorders and was significantly younger than other reported cases. A number of morphologic similarities can be seen between this case and the other reported cases, including the plasmacytic differentiation and the EBV positivity predominating in the plasmacytic cells. As EBV studies are currently not routinely performed on low-grade lymphomas, this case suggests that EBV⁺ MZL may be significantly underreported especially in cases with plasmacytic differentiation.

**Atypical γδ T-Cell Reaction in a Case of Listeria Meningitis**

(Poster No. 44)

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γδ T cells are commonly found in response to Listeria monocytogenes infection in mice; however, human models have not yet been reported. Moreover, γδ T-cell response in cerebral spinal fluid samples in conjunction with Listeria meningitis has not been described. A 64-year-old man with a medical history of hepatitis C, cirrhosis, and end-stage renal disease presented with altered mental status, fever, and neck stiffness. A lumbar puncture revealed opening pressure within reference range, but elevated glucose, protein, lactate dehydrogenase, and white blood cell count. Cytology revealed a markedly hypercellular sample with a lymphocytic pleocytosis, including some enlarged forms with irregular nuclear contours. Rare cells contained intracytoplasmic bacteria (Figure 21, A). Flow cytometric immunophenotyping revealed a prominent CD4/CD8–negative T-cell population with decreased CD5 expression (Figure 21, B and C). A suspicion of malignancy was considered, but imaging was without mass lesion, lymphocytes had a plasmacytoid, reactive appearance, and Gram stain (Figure 21, D) cultures recovered Listeria monocytogenes. A literature search revealed that γδ T cells are activated by the protein components of Listeria, and the level of activation of these T cells appears to be tissue specific and dose dependent. Studies performed on the liver, spleen, and intestines of mice revealed variable response times but an overall significant increase in γδ T cells. It appears that Listeria monocytogenes has a tendency to trigger an unusually strong response in γδ T-cell activation as seen in this patient. This phenomenon has not been described in the cerebral spinal fluid, let alone within human samples. Unfortunately, the patient rapidly succumbed to disease.

**Comparing Common Diagnostic Procedures for Lymphoma: Our Institutional Experience**

(Poster No. 45)

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Context: Lymphoma is commonly diagnosed by fine-needle aspiration (FNA), core needle biopsy (CNB) or excision, with many studies describing advantages of one technique over another. FNAs and CNBs are being increasingly used although many believe these techniques procure tissue that is inadequate or nondiagnostic or results with nonspecific diagnoses. The lack of a definitive diagnosis can result in additional procedures, exposing patients to increased risk, and using additional resources and clinician time.

Design: A retrospective study was performed to evaluate our institutional techniques in diagnosing lymphoma. All primary diagnoses of lymphoma from sites amenable to FNA and CNB in 2012 to 2016 were reviewed, with selected specimens categorized by method(s) of procurement, date of procedure(s), and final diagnoses.

Results: Identified patients (n = 115) were categorized by FNA/CNB, excision, or FNA/CNB with excision, Twenty-four (21%) were diagnosed by FNA/CNB and treated, with 17 of the 24 (71%) receiving a World Health Organization (WHO) diagnosis. Sixty-three (55%) were diagnosed by excision and treated, 61 of the 63 (97%) receiving a WHO diagnosis. Twenty-eight (24%) underwent an FNA/CNB followed by excision, with 2 of the 28 (7%) receiving a WHO diagnosis from FNA/CNB and 26 (93%) receiving a WHO diagnosis from excision. Median time from FNA/CNB to excision was 19.5 days (range, 3–77 days). The use of FNA/CNB required an excision 63% of the time (33 of 52) to establish a WHO diagnosis and 50% of the time to initiate therapy (26 of 52).

Conclusions: In patients with lymphadenopathy because of lymphoma, the use of FNA/CNB increased the likelihood of additional procedures and lengthened the time to diagnosis and/or treatment when compared with excision.

**Distinguishing Classic Hodgkin Lymphoma Posttransplant Lymphoproliferative Disorder From Other Types of Posttransplant Lymphoproliferative Disorders**

(Poster No. 46)

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Posttransplant lymphoproliferative disorder (PTLD) is a lymphoplasmacytic proliferative disorder in the setting of hematopoietic stem cell or solid organ transplant. Subclassification of PTLD is divided into nondestructive, polymorphic, monomorphic, and rarely, classic Hodgkin lymphoma (CHL) type. Most monomorphic PTLD cases are B-cell type, with <15% of cases being T- or NK-cell type. Most cases of PTLDs are Epstein-Barr virus (EBV) related. The incidence of PTLD is <1% in patients with kidney transplants, lowest of all transplant
Dilemma Between Nodular Lymphocyte-Predominant Hodgkin Lymphoma With Diffuse Growth Pattern and T-Cell/Histiocyte-Rich Large B-Cell Lymphoma

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Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) accounts for approximately 5% of Hodgkin lymphoma with indolent behavior and increased tendency for local recurrence or progression. Histopathologic variants of NLPHL, especially with diffuse pattern, are difficult to distinguish from a closely linked entity, T-cell/histiocyte-rich large B-cell lymphoma (THRLBCL). Distinction is critical for optimal management. A 36-year-old man presented with lymphadenopathy. Cervical lymph node biopsy revealed nodular architecture effacement by diffuse infiltration of small lymphocytes and histiocytes with admixed scattered large atypical cells showing pleomorphic irregular and multinucleated nuclei contours, vesicular chromatin, prominent nucleoli, and moderate cytoplasm, resembling popcornlike cells (Figure 23, A). The large atypical cells were positive for CD20 (Figure 23, B), PAX5, BCL2, BCL6, CD79A, CD45, OCT2, MYC, P53, and Ki67 and were negative for CD3 (Figure 23, C), CD10, CD15, CD30, IgD, LMP1, and MUM1. CD3 and PGMI highlighted prominent background small T cells and histiocytes. CD21 (Figure 23, D) showed the absence of follicular dendritic-cell meshwork. Additional extensive sections revealed a nodular growth pattern of focal large atypical cells. The morphologic and immunophenotypic features suggested NLPHL, with a diffuse growth pattern (pattern E). Although the predominant diffuse growth pattern put THRLBCL on the top of differential diagnosis, the identification of focal nodular neoplastic areas were compatible with a variant of NLPHL. The unusual growth pattern might indicate THRLBCL-like transformation of NLPHL, which is often associated with a higher risk of progression and needs aggressive management, including R-CHOP (rituximab, cyclophosphamide, doxorubicin hydrochloride [hydroxydaunorubicin], vincristine sulfate [ Oncovin], and prednisone) or similar regimen. The findings raise awareness of the extensive sampling of specimen for microscopic examination for an accurate classification in these types of cases for appropriate clinical treatments.

Importance of Distinguishing Small Cell Variant of T-Cell Prolymphocytic Leukemia From Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

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T-cell prolymphocytic leukemia (T-PLL) is an aggressive postthymic T-cell leukemia, typically occurring in adults older than 30 years. Because it is rare with a poor response to conventional chemotherapy and short survival, familiarity with T-PLL, particularly the small cell variant, is important because it is unlikely to be suspected at initial morphologic review. A 65-year-old Haitian man, with a medical history of aortic valve replacement, hypertension, and gout, presented with progressive dyspnea, fatigue, and sweating but no fevers. He had marked leukocytosis (white blood cell count, 288 × 10^9/L). Peripheral blood smear showed increased small mature-appearing lymphocytes with inconspicuous nuclei and smudge cells, mimicking chronic lymphocytic leukemia (Figure 24, A and B). However, flow cytometry revealed an aberrant T-cell population positive for CD2, cCD3, CD5, CD4, CD7, and CD52 and negative for TdT, CD56, CD57, CD25, and B-cell markers. Leukapheresis was performed for tumor lysis syndrome. Hypercellular bone marrow biopsy displayed a diffuse predominantly small, atypical lymphoid infiltrate (Figure 24, C and D). T-cell leukemia/lymphoma protein immunostain appeared positive (dim). Based on lymphocytosis (>100 × 10^9/L), generalized lymphadenopathy, hepatosplenomegaly and negative human T-cell leukemia/lymphoma-virus serology, the findings were consistent with T-PLL, small cell variant. Karyotypic analysis could not be performed. The patient became hemodynamically unstable and passed away on day 3 of hospital admission. Immunophenotypic analysis is essential in differentiating small cell variant of T-PLL from chronic lymphocytic leukemia. Performing additional markers by flow cytometry, such as CD52 for anti-CD52 monoclonal antibody alemtuzumab therapy and T-cell leukemia/lymphoma protein for detecting residual T-PLL after therapy is helpful.
Megakaryocytic Differentiation in Relapsed Acute Myeloid Leukemia With t(6;9)(p23;q34.1); DEK-NUP214

(Poster No. 49)

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The World Health Organization recognizes 2 acute myeloid leukemias (AMLs) with maturation of the megakaryocytic lineage: AML with t(1;22)(p13.3;q13/1);RBM15-MKL1 and acute megakaryoblastic leukemia. We now describe a case of megakaryocytic differentiation in AML with t(6;9)(p23;q34.1); DEK-NUP214. A 22-year-old man presented with cough, dysphagia, and appetite loss for 6 weeks. Complete blood cell count showed pancytopenia and bone marrow contained 50.8% blasts and 2.6% basophils. Factor VIII immunohistochemistry highlighted a normal number of megakaryocytes with atypical features but no increased megakaryoblasts. Flow cytometry showed bright CD34, CD13, and CD36, moderate CD33, moderate CD117, heterogeneous MPO and CD45, and dim CD64 and CD 61. Blasts were negative for CD11b, CD15, HLA-DR, CD16, CD14, CD22, CD3, TDT, CD41, CD42, and related B-cell and T-cell antigens. Molecular studies showed t(6;9)(p23;q34.1); DEK-NUP214 fusion, with CEBPA and WT1 mutations. Therapy included induction with cytarabine/daunorubicin and consolidation with intermediate dose cytarabine. Days 14 and 69 bone marrow results showed treatment effect and no acute leukemia. Ten months later the patient presented with diffuse pain, fever, chills, and cough for 1 week. Bone marrow showed recurrent AML with 63.2% blasts and 3.0% basophils. Molecular studies were identical to initial diagnosis with an additional FLT3-ITD mutation. Flow cytometry showed 50.8% blasts with a subpopulation of blasts (22%) expressing CD42, CD41, CD61, and CD45. Immunohistochemistry for factor VIII, CD42b, and CD61 highlighted 20% megakaryoblasts and marked increased atypical megakaryocytes. To our knowledge, this is the first case to describe AMO with secondary hemophagocytosis. The patient was started on the SMILE chemotherapy regimen (dexamethasone, methotrexate, ifosfamide, L-asparaginase, etoposide) and is awaiting bone marrow transplant. This case contributes to the few cases of aggressive NK-cell leukemias with hemophagocytic syndrome in white individuals.

Hemophagocytic Lymphohistiocytosis-like Presentation of Aggressive Natural Killer-Cell Leukemia in a White Man

(Poster No. 50)

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A rare neoplasm, aggressive natural killer (NK)-cell leukemia is characterized by a systemic proliferation of NK cells and is commonly seen in the Asian population. This neoplasm has been demonstrated to be associated with Epstein-Barr virus but is uncommonly associated with hemophagocytosis. A 21-year-old white man presented with fever, back pain, and severe fatigue. Further assessment revealed pancytopenia, elevated serum lactate dehydrogenase, elevated ferritin, hepatosplenomegaly, and serology studies consistent with infectious mononucleosis. Based on the clinical suspicion of hemophagocytic lymphohistiocytosis, he underwent bone marrow biopsy remarkable for hypercellularity, areas of necrosis, an increased population of highly atypical blastlike mononuclear cells (Figure 25, A), and histiocytic hyperplasia with increased phagocytic activity (Figure 25, B). By flow cytometry, 40% lymphoid cells were identified, with 58% T cells and a CD4 ratio of 0.8:1, 5% B cells, and 35% NK cells. The NK population was positive for CD7, CD56, CD2, CD16 (partial), and CD8 (minimal) and was negative for surface CD3 and CD57. On biopsy, there were 40% to 50% CD56+ blastlike cells (Figure 25, C) positive for CD3, CD7, granzyme B, and Epstein-Barr virus-encoded RNA (EBER; Figure 25, D). Molecular studies were negative for clonality in the T-cell lymphoid population and the hemophagocytic lymphohistiocytosis next-generation sequencing panel was also negative for mutations. Overall, these findings were consistent with an EBER-positive aggressive NK-cell leukemia with secondary hemophagocytosis. The patient was started on the SMILE chemotherapy regimen (dexamethasone, methotrexate, ifosfamide, 1-asparaginase, etoposide) and is awaiting bone marrow transplant. This case contributes to the few cases of aggressive NK-cell leukemias with hemophagocytic syndrome in white individuals.

An Unusual Case of Primary Diffuse Large B-Cell Lymphoma of the Urinary Bladder

(Poster No. 51)

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An 84-year-old woman presented with lethargy, weight loss, and lower urinary tract symptoms. Computed tomography urogram demonstrated diffuse bladder-wall thickening. Cystoscopy revealed a necrotic lesion affecting >80% of the mucosal surface of the bladder. Urine cytology revealed rare degenerated atypical cells with high nuclear-cytoplasmic ratio. Bladder biopsy showed sheets of large basloid neoplastic cells with vesicular chromatin and prominent nucleoli (Figure 26, A, B). Although mostly discohesive, there was focal molding of tumor cells. The differential of high-grade carcinoma (including neuroendocrine carcinoma) and lymphoma was considered. The tumor cells were negative for BCL1, BCL6, CD10, CD30, Epstein-Barr virus–encoded RNA (EBER) (Figure 26, C), synaptophysin, chromogranin, and CD56 immunostains and were positive for CD45, CD20 (Figure 26, D), PAX5, and MUM1. Ki-67 was positive for CD7, CD56, CD2, CD16 (partial), and CD8 (minimal) and was negative for surface CD3 and CD57. On biopsy, there were 40% to 50% CD56+ blastlike cells (Figure 25, C) positive for CD3, CD7, granzyme B, and Epstein-Barr virus-encoded RNA (EBER; Figure 25, D). Molecular studies were negative for clonality in the T-cell lymphoid population and the hemophagocytic lymphohistiocytosis next-generation sequencing panel was also negative for mutations. Overall, these findings were consistent with an EBER-positive aggressive NK-cell leukemia with secondary hemophagocytosis. The patient was started on the SMILE chemotherapy regimen (dexamethasone, methotrexate, ifosfamide, 1-asparaginase, etoposide) and is awaiting bone marrow transplant. This case contributes to the few cases of aggressive NK-cell leukemias with hemophagocytic syndrome in white individuals.
Plasmablastic Lymphoma With Both Leukemic and Tumor Phase, and Epstein-Barr Virus–Infected Marrow Megakaryocytes

(Poster No. 52)
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Plasmablastic lymphoma (PBL) is proliferation of large neoplastic cells, most of which resemble B immunoblasts or plasmablasts that have plasmacytic phenotype. PBL most frequently presents as a mass in extranodal regions of the head and neck, in particular the oral cavity, with >1% of cases including the skin, bone, etc. Although PBL is mainly an extranodal lesion with rare cases showing nodal involvement however no leukemic phase of PBL has been reported. A 33-year-old HIV+ man was diagnosed with hemophagocytic histiocytes after chemotherapy. Peripheral blood slide review showed plasmacytoid large cells, and subsequent flow cytometry was performed. However, the patient died and an autopsy was performed. Bone marrow biopsy showed significant hemophagocytic histiocytes with pleomorphic large plasma cells which were polyclonal by k/λ, in situ hybridization. The circulating plasmablastic cells showed the morphologic and immunophenotype of surface and cytoplasmic k/λ, CD19+, CD20+, CD38+, CD30+, and EBV+ and CD30+. PBL lymph node and spleen showed similar features (k/λ light-chain+, CD19+, CD20+, CD38+, CD30+, EBV+, and CD30+). PBL is very difficult to diagnose because it does not express common B-cell–associated antigens and is frequently confused with plasma cell myeloma or HHV8+ large cell lymphoma. This case was extremely challenging because PBL initially presented in the leukemic phase and subsequent positron emission tomography and computed tomography scans did not show any lymphadenopathy or extranodal lesion to establish a tissue diagnosis. However, during the autopsy lymph nodes and spleen showed diffuse involvement by PBL. Initial bone marrow showed large pleomorphic polyclonal plasma cells with Epstein-Barr virus–infected marrow megakaryocytes.

Epstein-Barr Virus–Negative and Epstein-Barr Virus–Positive Aggressive Natural Killer Cell Leukemia: Clinopathologic Study of 2 Cases

(Poster No. 53)
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Aggressive natural killer cell leukemia (ANKL) is a rare fulminating malignant disorder of mature natural killer (NK) cells, closely associated with Epstein-Barr virus (EBV), and which preferentially affects Asians. We report 2 cases of ANKL in non-Asians, which were diagnosed in our institution during the course of 2 years. A 67-year-old, African-American woman, with a history of hepatitis C, presented with ascites. Her computed tomography scan displayed ill-defined small granular lymphocytes (CD19+, CD30+, CD56+, CD8+, and EBV+) in peripheral blood smear. A bone marrow aspirate and biopsy was performed and revealed ANKL with CD56+ NK cells. The patient refused further treatment and died. Limited cases of EBV–ANKL with more indolent behavior have been reported. However, our case appeared clinicopathologically similar to EBV–ANKL, with a rapidly fatal course. Thus, in addition to a timely diagnosis of ANKL, further research is essential for a better understanding of its etiopathogenesis, prognostic factors, and potential therapeutic targets.

Myelodysplastic/Myeloproliferative Unclassifiable Neoplasm Presenting as Extramedullary Hematopoiesis in Lymph Nodes

(Poster No. 54)
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Extramedullary hematopoiesis (EMH) is defined as the development and growth of hematopoietic tissue outside of the bone marrow. Typically, it occurs during fetal development but can also occur in adults as a compensatory mechanism for abnormal hematopoiesis because of various deficiency disorders and pluripotent stem cell disorders. It may occur in a variety of sites with liver and spleen being the most common, and others including lymph nodes, pleura, retroperitoneum, breast, etc. A 64-year-old Hispanic man, presented with a fever of unknown origin. Clinical and laboratory examination showed splenomegaly, leukopenia, and abnormal liver function tests. Bone marrow biopsy displayed an atypical large lymphoid interstitial infiltrate, dilated sinusoids with increased macrophages, and hemophagocytosis. The immunophenotyping findings showed true NK cell lineage and EBV positivity. Overall, the findings were consistent with a diagnosis of ANKL. The patient's condition deteriorated despite treatment and he died. Limited cases of EBV–ANKL with more indolent behavior have been reported. However, our case appeared clinicopathologically similar to EBV–ANKL, with a rapidly fatal course. Thus, in addition to a timely diagnosis of ANKL, further research is essential for a better understanding of its etiopathogenesis, prognostic factors, and potential therapeutic targets.

Biphenotypic Plasma Cell Myeloma: A Rare Entity

(Poster No. 55)
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Plasma cell myeloma is a clonal proliferation of neoplastic plasma cells and usually expresses a monoclonal heavy and/or light chain

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immunoglobulin. Only 2% cases of plasma cell myeloma with dual expression of κ and λ light chains have been described in the literature. A 54-year-old man with a history of prostate carcinoma after brachytherapy presented with constant and worsening lower thoracic back pain for 5 months. The magnetic resonance imaging revealed a compression fracture of the thoracic 8, 9, and 10 vertebrae. Differential diagnosis included osteoporosis, trauma, and metastatic disease. Bone scan ruled out the possibility of the metastatic disease. Fine-needle aspiration cytology and biopsy of the involved vertebrae showed numerous atypical plasma cell infiltrates that were positive for CD138, MUM1, and CD56 with a mixed pattern staining for κ and λ light chains. Serum protein electrophoresis and immunoblot showed no monoclonal band. The urine immunofixation was positive for Bence Jones protein. The bone marrow biopsy revealed abnormal cell infiltrate, consistent with a high-risk disease. In addition, we strongly believe that this unusual rare entity should be considered for the proper characterization of myeloma. This entity often has a high frequency of complex cytogenetic and fluorescence in situ hybridization abnormalities, associated with a high-risk disease. In addition, we strongly believe that this unusual rare entity should be reported and followed up to clearly define its pathogenesis and prognostic implications.

**A Study of 84 Cases of Bone Marrow Amyloidosis: Caution Advised as Deposits Are Frequently Extramedullary**

(Poster No. 56)

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**Context:** Bone marrow (BM) biopsy is a minimally invasive but commonly used procedure to follow up and diagnose patients with most hematologic disorders. Detection of amyloid in BM specimen can be the first evidence of amyloidosis. We reviewed our Congo red-positive BM cases and subcategorized the location of the amyloid deposits and its relation to type of amyloidosis and its associated conditions.

**Design:** We reviewed 800 BM biopsies cases (1999-2018) from within our institution and found 84 patients with positive Congo red staining and a diagnosis of amyloidosis.

**Results:** The male to female ratio was 1.3:1 with an average age of 65 years (range, 26–94 years). Plasma cell (PC) percentage ranged from 1% to 80% with a mean of 13.46% and median of 8%. Twenty-nine of 84 patients (35%) had their first diagnosis of amyloidosis on BM. Thirty-three of 84 patients (39%) had ≥10% PCs; of which, 25 (76%) met the criteria for multiple myeloma. Forty-five of 84 patients (54%) had typed the amyloid as light chain (AL, n = 41), inflammation (AA, n = 2), and old age (ATTR, n = 2). The location of the amyloid deposits was subcategorized as marrow stroma (n = 19), vessel walls (VWs) without stromal deposits (n = 26), periosteal soft tissue (POST, n = 19), and location not specified (n = 19). Studying the type of amyloid deposits in relation to the location of the amyloid revealed that all cases of stromal deposits were AL amyloidosis, but AA and ATTR deposits were found in vessel walls and/or periosteal soft tissue (Figure 27).

**Conclusions:** There is significant heterogeneity of amyloid distribution in patients with AL-amyloidosis with extramedullary/periosseous amyloid deposits being more frequent than medullary. Although AL amyloid is the most common type of amyloid in the BM, the pathologist should have high index of suspicion for non-AL amyloidosis especially if the deposits are present in the VWs or POST.

**Histiocytic Sarcoma: Molecular Evidence of Transdifferentiation From B-Cell Lymphoma**

(Poster No. 57)

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Histiocytic sarcoma (HS) is a rare, aggressive tumor defined as a malignant proliferation of cells with morphologic and immunophenotypic features of mature histiocytes. HS may arise in 3 scenarios: sporadic/de novo, associated with mediastinal germ cell tumor, or associated with lymphoid malignancy. The patient was a 74-year-old man who presented with a 40-pound weight loss, jaundice, hepatosplenomegaly, and palpable lymph nodes. Bone marrow biopsy and lymph node excision were performed. The bone marrow was cellular and extensively replaced by large B lymphocytes, consistent with large B-cell lymphoma (Figure 28, B). Histologic sections of the lymph node demonstrated architectural obliteration by malignant-appearing histiocytes, consistent with HS, and morphologically and immunophenotypically distinct from the lymphoma (Figure 28, D). B-cell lymphomas have been reported to transdifferentiate into various histiocytic neoplasms, most commonly HS. Transdifferentiated HS more often expresses B-cell transcription factor OCT2, compared with sporadic cases, although it may be patchy. Transdifferentiated HS has a greater frequency of monoclonal immunoglobulin gene rearrangements or *IGH-BCL2* fusion. Fluorescence in situ hybridization studies done on our case showed both tumors having *BCL6* rearrangements and *IGH-BCL2* fusion. In both neoplasms, analysis by next-generation sequencing of immunoglobulin heavy chain for all 3 frameworks did not amplify the immunoglobulin κ gene demonstrated a monoclonal population in both tumors using identical V-J rearrangement patterns with 100% sequence homology (Figure 28, A [bone marrow] and C [lymph node]). This study lends immunophenotypic and molecular support to the theory of transdifferentiation because the HS showed evidence of clonal derivation from the B-cell neoplasm.
An Unusual Presentation of Adult T-Cell Lymphoma as Primary Lymphoma of the Patella

(Poster No. 60)

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A 58-year-old woman from Grenada with no past traumatic event presented with ambulation problems resulting from pain and limited range of motion of the left knee. Physical exam showed no skin lesions, lymphadenopathy, or hepatosplenomegaly. An expansile lytic lesion of the left patella was noted on x-ray and magnetic resonance imaging of the left knee. Core needle biopsy of the mass showed spindle cell proliferation in a fibrotic and scattered small lymphocytic background. The neoplastic cells were pleomorphic and hyperchromatic with rare atypical mitotic figures. Immunohistochemistry revealed that neoplastic cells were CD4+, CD8+ (variable), CD25+, and FoxP3- (minor subset T cells with a loss of CD7 and a high proliferation index (Ki-67, 60%-70%), consistent with the immunophenotype of adult T-cell leukemia/lymphoma (ATLL). No peripheral blood and bone marrow involvement of T-cell lymphoma was identified on morphologic evaluation and flow cytometry. Other laboratory workup showed hypercalcemia, elevated lactate dehydrogenase (LDH; 243 U/L), and HTLV-1 antibodies identified by Western blot. In addition, positron emission tomography scan revealed hypermetabolic uptake within the patella and a single node within the left popliteal fossa, likely a regional nodal involvement. Overall, these findings support the diagnosis of primary ATLL of the patella. ATLL most commonly presents within the skin, lymph nodes or viscer, and/or peripheral blood, and it is rare being a primary bone lymphoma. Primary ATLL of the patella has not been previously reported.

Notch Inhibition Suppresses Acute Promyelocytic Leukemia Proliferation via Cell Cycle Arrest and Apoptosis

(Poster No. 61)

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Context: Notch signaling contributes to the tumorigenesis and disease progression of acute promyelocytic leukemia (APL). Here we used the APL cell line HL-60 to characterize the molecular pathways of Notch inhibition and North activation during leukemia cell proliferation.

Design: Cultured HL-60 cells were treated for 48 hours with Notch activator Jagged-1 and inhibitor DAPT and LY-411575. After harvesting the cells, RNA was extracted for real-time polymerase chain reaction analyses of Notch downstream Hes1 and Hey1, cell cycle proliferation regulator CCND1, and cell cycle arrest regulator p21 and p53 gene expression levels. Leukemia cell apoptosis was examined by mitochondrial JC-1 membrane potential, MitoTracke Red CMXRos, and annexin V FITC apoptosis detection kit.

Results: DAPT significantly decreased Hes1 and Hey1 mRNA levels in HL-60 cells. Jagged-1 increased Hes1, Hey1, and cyclin D1 gene expressions. DAPT increased gene expression of p21 and p53. JC-1 assay revealed an 11-fold increase in the percentages of apoptotic cells by Notch inhibitor LY-411575. Annexin V FITC apoptosis assay demonstrated similar findings. MitoTracker Red CMXROS (Thermo Fisher, Ann Arbor, Michigan) and MitoTracker (Life Technologies, Waltham, Massachusetts) assays showed no significant differences in final live and dead cells in different treatments.

Conclusions: p21 is activated by p53 and is associated by cell cycle arrest. We found that Notch inhibitors suppress APL cell proliferation by upregulating p53 and p21, which induce cell cycle arrest and apoptosis, and down-regulating Hes1 and Hey1. Notch activator upregulates cell cycle proliferation regulator cyclin D1. Further studies are being pursued to elucidate the interactions of cell cycle regulators and Notch pathway target genes in APL.

Rare Presentation of Hodgkin Lymphoma Involving Bone Marrow as Posttransplant Lymphoproliferative Disorder

(Poster No. 62)

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Posttransplant lymphoproliferative disorder (PTLD) is a group of neoplastic disorders of lymphoid or plasmacytic proliferation that develop as a complication of immunosuppression in recipients of solid organ or allogeneic hematopoietic stem cell transplantation. Recipients of lung and heart transplants have among the highest incidence rates of PTLD, with heart transplant patients potentially having late-onset PTLD. Moreover, Hodgkin lymphoma may rarely manifest as PTLD, and bone marrow involvement by PTLD is uncommon and portends poor prognosis. Here, we discuss a case of Hodgkin lymphoma as an unusual and rare presentation of PTLD arising in a 9-year-old boy after heart transplantation because of hypoplastic left heart syndrome. He developed fevers, fatigue, decreased activity, increased stool output, weight loss, and abdominal masses over 4 weeks. On admission, Epstein–Barr virus (EBV) viremia was detected. A positron emission tomography scan showed diffuse adenopathy. Lymph node biopsy would have been challenging; thus, a bilateral bone marrow biopsy was performed. Scattered, large, atypical cells with multiple nuclei and prominent nucleoli were identified. The atypical cells were positive for PAX5 (weak nuclear) and CD30 by PAX5/CD30 multiplex stains and prominent nucleoli were identified. The atypical cells were positive for PAX5 (weak nuclear) and CD30 by PAX5/CD30 multiplex stains and were negative for CD15. CD45 was mainly negative and CD20 was variably positive in a subset of the large atypical cells. Epstein–Barr–encoding RNA in situ hybridization was positive in a subset of large atypical cells. These observations were diagnostic for Hodgkin lymphoma, EBV+ and CD15−, as a posttransplant lymphoproliferative disorder. Classic Hodgkin lymphoma PTLD, the least-common major form of PTLD, is almost always EBV+ and fulfills the diagnostic criteria for classic Hodgkin lymphoma.

Concurrence of γ Heavy Chain Disease, T-Cell Large Granular Lymphocytic Leukemia, and Monoclonal B-Cell Lymphocytosis

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γ heavy chain disease (gHCD) is a rare indolent disease, characterized by production of truncated immunoglobulin heavy chain without associated light chain. Very few cases in association with other lymphoid neoplasms have been reported. We present a case of a 69-year-old woman with concurrent gHCD, T-cell large granular lymphocytic leukemia (T-LGL), and monoclonal B-cell lymphocytosis.

She was diagnosed with T-LGL 15 years before this presentation, when flow cytometry revealed increased CD57/CD3/CD8-positive T cells with decreased CD4:CD8 ratio and partial loss of CD55. T-cell polymerase chain reaction confirmed clonality and cytogenetics revealed monosomy 17. Six years later, presence of clonal B cells with plasmacytic differentiation expressing CD19, CD20, CD22, FMC7, and CD11c and lacking immunoglobulin light chain expression, CD5, CD23, or CD10 was found in the blood. MYD88 mutation analysis was negative and a diagnosis of monoclonal B cell lymphocytosis, marginal zone phenotype was favored. Three months before this presentation, she developed macrocytic anemia and absolute neutropenia. Peripheral blood and bone marrow showed persistence of B-cell and T-cell lymphoproliferative processes. In addition, bone marrow flow cytometry demonstrated 2.2% abnormal plasma cells overlapping with B cells by CD45/SSC, and expressing CD38/CD138/CD20/CD19/CD45 with the absence of both CD56 and cytoplasmic light chain. Immunostains showed cytoplasmic immunoglobulin G heavy chain–only in lymphoplastic-cytic cells (Figure 30, A and B), supporting the diagnosis of gHCD. Throughout the entire course, she has been monitored without treatment. This may represent an unusual case of evolving marginal zone leukemia/lymphoma with γ heavy chain–only expression and concurrent T-LGL leukemia.

Myeloid Sarcoma Presenting as Cholecystitis in a Patient With Treatment-Related Acute Myeloid Leukemia

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Myeloid sarcoma (MS), also known as chloroma, is a rare, malignant neoplasm, occurring in 2% to 8% of patients with acute myeloid leukemia (AML). It consists of extramedullary myeloid blasts and is associated with a poor prognosis. Here we report a case of MS in the gallbladder of a patient with AML presenting with cholecystitis. A 44-year-old woman developed treatment-related AML after chemotherapy for the management of breast ductal carcinoma. Her AML had complex cytogenetics, including t(6;16)(p21;q24) and chromosome 16 inversion, which was then lost. The patient had multiple relapses despite chemotherapy after each one. She also had a recent history of recurrent liver abscesses and chronic cholecystitis, for which she underwent cholecystectomy (surgery deferred because of pancytopenia). Four months later, imaging showed significant gallbladder-wall thickening with 2 new hypodense areas within the gallbladder wall. Subsequently, she underwent cholecystectomy. Gross examination showed a 9-cm gallbladder with a 1-cm thick wall. Histopathologic examination showed diffuse infiltration of the lamina propria, with focal involvement of fibromuscular layer, by sheets of immature cells, along with marked acute and chronic inflammation. Considering the patient’s history of AML, MS was suspected. Immunohistochemical stains were performed, and tumor cells were positive for CD45 (dim), MPO, CD117, and CD34, confirming the diagnosis of MS. Our case is unique because gallbladder MS is very rare. Timely diagnosis is key because of the high associated mortality. MS associated with treatment-related AML with complex cytogenetics after breast cancer treatment has not been previously reported in literature (Figure 31).

Amyloidoma of the Stomach in a Patient With a History of Refractory Marginal Zone Lymphoma of the Mucosa-Associated Lymphoid Tissue Type

(Profiler No. 65)

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Systemic amyloidosis can occur in many nonneoplastic and neoplastic conditions. The latter includes plasma cell neoplasms and non–Hodgkin lymphomas, especially marginal zone lymphoma of the mucosa-associated lymphoid tissue type (MALT lymphoma). Localized nodular amyloidosis or amyloidomas are very rare. We present the case of a 64-year-old woman with chronic anemia who was found to have a large gastric mass diagnosed as MALT lymphoma with plasmacytic
patients with autoimmune disease, including psoriasis. Early recognition of this disease is crucial because it may precede a clinical diagnosis of autoimmune disease, and it may help initiate immunosuppressive therapy for symptom relief (Figure 33).

Composite Mantle Cell and Diffuse Large B-Cell Lymphoma and the Utility of Molecular Studies

(Poster No. 67)

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Composite lymphomas are defined by the presence of 2 different lymphomas within a single organ and account for approximately 1% to 4.7% of all lymphomas. Here we present a case of a 56-year-old man who was found to have an enlarged cervical lymph node. Histologic features included diffuse large cells with vesicular chromatin that effaced the nodal architecture (Figure 34, A). Within the sinuses was a population of small lymphocytes with angulated nuclei and dense chromatin. The large cells were positive for CD45, CD20, CD79a, CD5 (weak), CD10 (subset), and BCL6; they were negative for cyclin D1, BCL2, MUM1, SOX11, CD19, and CD23. The small cells were positive for cyclin D1, CD20, CD5 (strong), BCL2, and SOX11 (subset); they were negative for CD19, CD10, CD3, CD23, and BCL6. These findings were consistent with composite mantle cell and diffuse large B-cell lymphoma. Microdissection guided by cyclin D1 stains (Figure 34, C and D) and subsequent IGH gene rearrangement analysis by polymerase chain reaction revealed 2 distinct clones (Figure 34, B). There are 3 reported cases of composite mantle cell and diffuse large B-cell lymphoma. In this case, the mantle cell component was subtle because the tumor cells resided in the sinuses, prompting a bone marrow biopsy that uncovered mantle cell lymphoma. Currently, management is directed toward the more-aggressive lymphoma; thus, in this case, identification of the second lymphoma changed the therapeutic approach. This case demonstrates the diagnostic challenge in identifying composite lymphomas and the utility of molecular diagnostics with microdissection in supporting the diagnosis.

IgG4 Disease as a Mimicker of Reactive Follicular Hyperplasia in a Patient With Psoriasis

(Poster No. 66)

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A 26-year-old woman with a history of psoriasis presented to the emergency department with abdominal pain and flu-like symptoms. Incidentally, she was found to have an enlarged right axillary node measuring 3.6 cm on computed tomography scan. No other adenopathy was noted. An excisional biopsy was performed which showed follicular hyperplasia with follicular expansion of interfollicular zones. Germinal centers and interfollicular zones showed a dense lymphoplasmacytic infiltrate rich in immunoglobulin G4+ (IgG4+) plasma cells (IgG4+/IgG+ plasma cell ratio >40%, with IgG4+ cells >100/high-power field). A diagnosis of type II IgG4-related lymphadenopathy was rendered. Lymphadenopathy is observed frequently in patients with immunoglobulin G4-related disease (IgG4-RD) and often is the first manifestation of the disease. IgG4-RD is a morphologic mimic of various lymphadenopathies, such as Castleman disease, reactive follicular hyperplasia, T-cell lymphoma, inflammatory myofibroblastic tumor, and others. Autoimmune diseases, including rheumatoid arthritis, pancreatitis, and sclerosing cholangitis, can be associated with IgG4-RD. There is paucity of literature describing IgG4-RD in the setting of psoriasis, which may also be associated with IgG4-RD. Our case illustrates the importance of recognizing this relatively new entity, particularly in the context of
High-Grade B-Cell Lymphoma, Not Otherwise Specified: A Diagnostically Challenging Case
(Poster No. 68)
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High-grade B-cell lymphoma, not otherwise specified (HGBCL-NOS), is a heterogeneous category of aggressive mature B-cell lymphomas that lack MYC and BCL2 and/or BCL6 rearrangements and do not fall into the category of diffuse large B-cell lymphoma (DLBCL) or Burkitt lymphoma (BL). However, it does share many morphologic, immunophenotypic, and genetic features. The diagnosis of HGBCL-NOS should be reserved for cases in which classification as DLBCL or BL is not possible. We report on a 71-year-old woman with a previous B-cell lymphoma treated with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine hydrochloride [hydroxydaunorubicin], vincristine sulfate [Oncovin], and prednisone). The peripheral blood (PB) and bone marrow (BM) aspirate smears had numerous atypical lymphoid cells with Burkitt-like morphology including medium size, slightly irregular nuclei, one or more nucleoli, and deep-blue vacuolated cytoplasm. In the BM biopsy, the atypical lymphocytes had a lymphoblast-like morphology. Flow cytometry was positive for CD45, CD10, CD19, CD38, and HLA-DR and was negative for CD20 and surface light chains. Immunohistochemical stains were positive for CD45, CD10, CD19, CD38, and HLA-DR and was negative for CD20 and CD99. Fluorescence in situ hybridization showed ALK rearrangement, loss of MYC, and gain of 13q. MYC rearrangement was not detected. Based on these findings, the diagnosis of HGBCL-NOS was made. Little information is available for HGBCL-NOS because these lymphomas and the double-hit lymphomas with a similar morphology were described together before the WHO 2017 classification. This was a diagnostically challenging case in which the morphology mimicked BL on smears yet looked like lymphoblasts on biopsy sections. The overall findings were inconsistent with neither BL and nor B-lymphoblastic leukemia/lymphoma and definitive diagnosis was based on cytogenetics.

Anaplastic Lymphoma Kinase–Positive Large B-Cell Lymphoma: A High-Grade CD45-Positive Malignancy Which Is Mostly Negative for Lineage Specific Markers
(Poster No. 69)
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We report an unusual case of anaplastic lymphoma kinase (ALK)-positive large B-cell lymphoma (LBCL) in a previously healthy 17-year-old boy who presented with extensive cervical lymphadenopathy. Excisional lymph node biopsy revealed complete nodal effacement by nests of malignant cells with amphiphilic cytoplasm, open chromatin, and a distinct large nucleolus (Figure 35, A). Initial immunohistochemical (IHC) studies showed malignant cells were weakly positive for CD45 (Figure 35, B) but negative for CD20, CD3, and CD43 as well as a broad panel of markers of carcinoma, sarcoma, and melanoma. Further studies revealed the malignant cells were positive for CD4 and MUM1 (Figure 35, C) and variably positive for CD138 and EMA. The cells were negative for further T cell (CD2), B cell (CD79a), myeloid (MPO, CD68, CD117), and stem cell markers (CD34). Follow-up IHC studies revealed the malignant cells were positive for ALK (Figure 35, D), OCT2, and BOB1. Fluorescence in situ hybridization (FISH) studies showed an ALK rearrangement in 2p23, confirming the diagnosis of ALK+ LBCL. ALK+ LBCL is a very rare variant of diffuse LBCL, accounting for <1% of all diffuse LBCLs. The lack of expression of standard B-cell lineage markers can make the diagnosis challenging unless the pathologist is thinking of this unusual entity. All cases contain an ALK arrangement detectable by FISH. This case illustrates the importance of considering ALK+ LBCL in the workup of a high-grade CD45− malignancy, which is mostly negative for lineage-specific markers. The patient is undergoing treatment with a novel CHOP (cyclophosphamide, doxorubicin hydrochloride [hydroxydaunorubicin], vincristine sulfate [Oncovin], and prednisone) + crizotinib therapy, based on the ALK rearrangement.

A Decade of Recurrent, Transient Pancytopenia in a Multiple Sclerosis Patient With Superimposed Parvovirus B19 Infection
(Poster No. 70)
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Parvovirus B19 (PVB19) causes a spectrum of diseases in humans. In bone marrow, it affects erythroid precursors, causing red blood cell lysis, reticulocytopenia, and eventually anemia. We present a case of a 57-year-old woman with a history of multiple sclerosis treated intermittently with glatiramer acetate, an immunomodulator drug. For the previous 10 years, the patient presented with recurrent transient pancytopenia every time she received treatment, with no definite etiology or hematologic diagnosis. Recently, a bone marrow aspirate and core biopsy were performed revealing dramatically decreased erythropoiesis with markedly enlarged erythroblasts. Microscopic examination revealed multiple giant pronormoblasts with pseudopods and viral inclusions. This was further confirmed by a positive PVB19 immunostain on the bone marrow biopsy and elevated PVB19 immunoglobulin (Ig) M and IgG antibodies titers from the patient’s serum (11.89 IV and 3.39 IV, respectively). The patient’s pancytopenia resolved immediately after intravenous immunoglobulin therapy. Studies have demonstrated that long-term glatiramer acetate treatment has not been associated with any hematologic dysfunction. We suspect the patient had a persistent parvovirus infection, which can occur in patients with underlying chronic disease affecting the bone marrow, such as a combined T-cell and B-cell defects, acute lymphoblastic leukemia, Hodgkin disease, and AIDS. Although studies demonstrate patients with multiple sclerosis can be infected by PVB19, no significant homology between PVB19 and myelin proteins has been found. For a diagnosis of recurrent transient pancytopenia in any immunosuppressed patients, PVB19 infection should be considered; furthermore, the pathogenesis also needs to be investigated to provide targeted therapy.

Rare Prolymphocytic Progression of Chronic Lymphocytic Leukemia With 2 Novel Cytogenetic Aberrations
(Poster No. 71)
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B-cell prolymphocytic leukemia is a rare but aggressive lymphoid malignancy which can occur de novo or be seen as a result of progression from chronic lymphocytic leukemia. We report a rare case of chronic lymphocytic leukemia with history of chronic lymphocytic leukemia that showed novel complex karyotypes and cytogenetic abnormalities. Our patient was diagnosed with chronic lymphocytic leukemia in 2010 and had relapsed multiple times even with multiple rounds of chemotherapy. Cytogenetic studies in 2010 showed normal...
male karyotype; however, comprehensive cytogenetic and molecular analysis was not performed. In late 2018, the patient presented with worsening lymphocytosis, anemia, and thrombocytopenia. The peripheral blood smear revealed around 60% prolymphocytes and a diagnosis of B-cell prolymphocytic leukemia was established. Conventional chromosomal analysis revealed complex karyotypes including inv(9)(p24q11), t(10;22)(q22;q13), del(11)(q13q23);ATM gene deletion, and der(22)t(1;22)(q10;p10). Chromosomal microarray analysis (array comparative genomic hybridization) and fluorescence in situ hybridization confirmed a deletion of 11q14.1–q23.3 including ATM gene, and additionally showed a gain at 1q21.1–q44 and a cryptic deletion of 22q11.22 (516 Kb loss) involving the immunoglobulin λ gene. These results suggested a progression of chronic lymphocytic leukemia to B-cell prolymphocytic leukemia. In summary, we report a novel finding of gain at 1q21.1–q44, which has only been reported once in B-cell prolymphocytic leukemia, and a second novel finding of t(10;22)(q22;q13), which, to our knowledge, has not been described in progressed B-cell prolymphocytic leukemia.

An Unusual Collision: Composite Lymphoma in a Patient With Invasive Ductal Carcinoma

(POSTER NO. 72)

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Collision tumors are a rare, but known phenomenon in which 2 histologically distinct neoplasms intersect with one another at a single anatomic location. Importantly, collision tumors are considered a coincidental occurrence of 2 tumors with unique pathogeneses. In contrast, composite lymphomas are defined as the presence of 2 morphologic and immunophenotypically distinct lymphoid neoplasms, which are thought to arise from a common progenitor cell. We present the case of a 78-year-old woman with a known history of follicular lymphoma and grade 1 invasive ductal carcinoma who presented for definitive surgical management of her breast cancer. A lumpectomy with sentinel lymph node biopsy was performed demonstrating a 0.9-cm focus of invasive ductal carcinoma. In addition, atypical, perilobular lymphoid infiltrates in the breast tissue and a dense lymphoid proliferation in the sentinel lymph nodes were identified, warranting immunohistochemical evaluation (Figure 36, A and B). CD20 was positive in multiple nodules which coexpressed CD10 and BCL2 and in the interfollicular areas which did not coexpress CD10 (Figure 36, C and D). In addition, the presence of central CD10 and BCL2 negativity within the nodules raised the likelihood of follicular lymphoma with follicular colonization by marginal zone lymphoma. After evaluation of fluorescence in situ hybridization and B-cell clonality studies, the tumor was classified as a composite lymphoma composed of follicular lymphoma grade 1 to 2 and marginal zone B-cell lymphoma in the presence of an invasive ductal carcinoma. This case illustrates the importance of evaluating atypical lymphoid infiltrates in the breast for the presence of a lymphoproliferative disorder.

Polycythemia Vera in a Pediatric Patient: A Rare Cause of Unexplained Neutropenia

(POSTER NO. 73)

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Polycythemia vera (PV) is a chronic myeloproliferative neoplasm more commonly seen in adults. PV in pediatric patients is rare, and a high index of suspicion is necessary to reach the diagnosis. The presence of unexplained neutropenia at diagnosis is uncommon. We report on a 7-year-old girl with a 3-year history of chronic headaches, abdominal pain, mild thrombocytopenia, and unexplained neutropenia. Hemoglobin and hematocrit had remained mostly within reference range. Upon referral to our hematology clinic, she was found to have erythrocytosis (Hgb, 17.2 g/dL), thrombocytopenia (platelets 826k/μL), and neutropenia (960k/μL). Further laboratory work revealed a markedly decreased erythropoietin level (1.1 mIU/mL) and a secondary cause for polycythemia was essentially ruled out. A myeloproliferative neoplasm was suspected. Bone marrow biopsy showed pancytopenia with a proliferation of pleomorphic megakaryocytes and focal increase in reticulin fibrils. Testing for JAK2 p.V617F mutation was positive. The patient met all major and minor World Health Organization diagnostic criteria for PV. Our case demonstrates the importance of considering a myeloid neoplasm in pediatric patients presenting with unexplained neutropenia. PV can progress to myelodysplastic syndrome or acute myeloid leukemia (up to 20% lifetime risk) and carries an increased risk of thrombotic events. Neutrophilic leukocytosis at disease outset is associated with an increased risk of recurrent thrombosis. It is therefore important that the diagnosis be made as early as possible in the course of the disease. A high index of suspicion is required to diagnose these rare but important cases.

Green Neutrophilic Inclusions: A Variant of Ceroid Histiocytosis?

(POSTER NO. 74)

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Context: There have been 71 cases of green granule neutrophilic inclusions reported in the literature, with most of these publications being in the past decade. These granules have been associated with acute liver injury and a mortality rate ranging from 30% to 70% thus earning a nickname of ‘granules of death.’

Design: In our institution, green granules have been being reported during an 18-month screening period in 9 patients. All patients with green neutrophilic inclusions were critically ill, 6 of 9 (67%) with elevated liver enzymes, and they presented with sepsis or some form of shock, which correlates with the previous data. The mortality rate was 67%, 6 patients died within 19 days of hospital stay and 3 patients survived. Recently studies investigating the composition of these granules have shown them to be lipid-rich via electron microscopy and Sudan black and stained positively for periodic acid–Schiff.

Results: We propose a hypothesis that these green granule inclusions in neutrophils are analogous to those found in ceroid (sea blue) histiocytosis, which are a result of accumulation of lipofuscin or ceroid in the cytoplasm of macrophages. Lipofuscin or ceroid accumulation is reported in cases of increased cell turnover and is seen in chronic myeloid leukemia and some cases of hepatic diseases or infections. Neutrophils have phagocytic capabilities and may accumulate lipid-rich granules in their cytoplasm during these times of systemic infection.

Conclusions: The above data support the multifactorial pathogenesis of these granules; however, further studies are warranted for better understanding their clinical significance.

Genetic Alterations of Non-CML Myeloproliferative Neoplasms in 1384 Hispanic Patients From Puerto Rico

(POSTER NO. 75)

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Abstracts
Context: The chronic myeloproliferative neoplasms (MPNs) are clonal proliferation disorders of myeloid lineage including chronic myeloid leukemia (CML), polycythemia vera, essential thrombocythemia, and primary myelofibrosis. Despite an insidious clinical onset, all of the MPNs have a potential to progress and terminate as bone marrow failure because of marrow fibrosis, myelodysplastic syndrome, or blast transformation. With the advance in developing novel target therapies, the evaluation of molecular profiles of MPNs becomes critical. Although the genetic alterations of MPNs are extensively studied in general populations, very limited data are available for Hispanics. We investigated the mutational frequencies of a set of genes associated with MPNs in Puerto Rican Hispanics.

Design: A retrospective study of non-CML MPN cases in Puerto Rican Hispanics was performed by collecting and analyzing polymerase chain reaction/next-generation sequencing results of Jak2, MPL, and CALR.

Results: The frequencies of jak2 and MPL mutations in non-CML MPN of Puerto Rican Hispanics were 68.9% (742 of 1085) and 5.9% (26 of 437), respectively (Figure 37). The average age of patients with the jak2 mutation was 67.8 years. The average age of patients with the MPL mutation was 66.3 years. Additionally, the frequency of CALR mutation was also evaluated in a few patients and was 45% (9 of 20) in jak2 MPNs. The average age of patients with the CALR mutation was 61.3 years. Overall, the male to female ratio was 0.9 (370 of 407) for all patients with non-CML MPN. Interestingly, we also found that 2 cases that harbored both jak2 and MPL mutations.

Conclusions: Non-CML MPNs of Puerto Rican Hispanics demonstrate a distinct molecular landscape from those of other ethnic/racial populations, which might affect their clinical treatment and outcome.

Trisomy 12-Positive Chronic Lymphocytic Leukemia and Associated Long-Standing Light Chain Amyloidosis
(Poster No. 76)

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Immunoglobulin (Ig) light chain (AL) amyloid deposition is rarely associated with lymphoplasmyastic neoplasms. A 79-year-old man was incidentally diagnosed with colonic amyloidosis, which led to a diagnosis of chronic lymphocytic leukemia (CLL) with t(11;14) and trisomy 12. Lesional cells had an atypical morphology (Figure 38, A) and an immunophenotype indicating acute promyelocytic leukemia (APL). Bone marrow involvement by CLL, in time, reached 80%; however, amyloid deposition was not detected. The patient underwent chemotherapy with various agents: chlorambucil, rituximab, bendamustine, and ibritinib. IgG-κ was detected in his serum, progressively increasing to 3.13 g/dL. He developed bilateral, orbital soft tissue mass formation. On biopsy, dense fibrous tissue with amyloid deposition (Figure 38, B) and rare small aggregates of lymphocytes and plasma cells were noted. The lymphoid aggregates consisted of larger subsets of CD20+ (Figure 38, C) and CD5+ B-lymphoid cells than CD3+ T cells (Figure 38, D). Also present was a small subset of scattered κ-restricted plasma cells. Comparative molecular studies identified, in the orbital tissue, Ig heavy chain gene rearrangements with similar-sized bands to those detected in a previous patient’s biopsies with CLL involvement. Mass spectrometry analysis detected κ AL amyloid deposition. His bone marrow had <20% lymphocytes and 6% plasma cells, and fluorescence in situ hybridization was positive for trisomy 12 but had no AL amyloid deposition. Although only few cases report an association between CLL and AL amyloidosis, to our knowledge, trisomy 12-positive CLL and slow progression of AL amyloidosis (>20 years) has not been previously reported.

Acute Prepromyelocytic Leukemia With NPM1 Mutation Associated With TET2, DNMT3A, and FLT3 Mutations: An Acute Myeloid Leukemia Mimicking Acute Promyelocytic Leukemia
(Poster No. 77)

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We present the case of a 73-year-old man with a white blood cell count of 240.7K/μL, hemoglobin of 11.6 g/dL, platelet count of 27K/μL, and 98% peripheral blood (PB) and bone marrow (BM) blasts with only a few single Auer rods (no “faggot” cells), many myeloperoxidase-positive granules and a CD34+ /HLA-DR+ /CD13+/CD33+/CD45- immunophenotype indicating acute promyelocytic leukemia (APL). Fluorescence in situ hybridization (FISH) for acute myeloid leukemia (AML) including APL and karyotyping results were normal. He was treated with standard AML therapy, which put his disease in remission. Next-generation sequencing of marrow aspirate showed CEBPA, DNMT3A, NPM1, and TET2 mutations. Nine months later, AML relapsed with 85% BM and 70% PB blasts with all the features of the original AML. Real-time polymerase chain reaction and mate-pair sequencing did not detect PML/RARA fusion or any other RARA abnormality. FLT3-ITD mutation was detected. He died a few days after the relapse. Our case shows morphologic, cytochemical, immunophenotypic, FISH, chromosomal, and molecular features that have been described in “myeloid AML-NPM1,” a type of AML that shows neoplastic cells arrested at a promyelocytic stage. We think it should be called an acute prepromyelocytic leukemia (APPL) associated with NPM1 mutation (“APPL-NPM1”) because this designation emphasizes its morphologic and immunophenotypic resemblance to APL. Myeloid AML-NPM1 usually harbors TET2, IDH1/2, DNMT3A, and FLT3 mutations. Our case showed TET2, DNMT3A, and FLT3 mutations. The combination of NPM1, FLT3, and DNMT3A mutations portends a grave prognosis. Our patient relapsed and died 9 months after the diagnosis. He received 7 + 3 AML therapy, but the APL treatment should be tried.
CD10-Negative Follicular Lymphoma With Numerous Lacunar Cells and Reed-Sternberg Cells Mimicking Classic Hodgkin Lymphoma

(Paper No. 78)

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Follicular lymphoma is often a straightforward diagnosis, but occasionally unusual diagnostic features might be encountered resulting in diagnostic conundrums and even a misdiagnosis. We report a unique case of a 66-year-old woman who presented with an enlarged occipital lymph node effaced by a multinodular infiltrate within a fibrotic background. The nodules consisted of centrocytes, centroblasts (>15/ high-power field) and frequent Hodgkin-like cells, including lacunar and Reed-Sternberg cells. The lymphoma cells, which included the Hodgkin-like cells were positive for CD45 and B-cell markers CD20, OCT2, and BOB1 and were negative for CD10. Additionally, the Hodgkin-like cells expressed CD30. Cytogenetics did not demonstrate the BCL2/IGH translocation that is typically associated with follicular lymphoma. Despite the lack of CD10 expression, the nodular growth pattern along with the coexpression of BCL6 and BCL2 and the lack of a mixed inflammatory background ultimately supported a diagnosis of follicular lymphoma with grade 3A and 3B components. A lymphoma presenting despite the lack of CD10 expression raises suspicion for classic Hodgkin lymphoma, nodular sclerosis type; however, similar to our case, these features have been infrequently encountered in follicular lymphoma. Further adding to the challenge, our case lacked the classical immunophenotypic and cytogenetic features typically seen in follicular lymphoma, which increased the potential for misdiagnosis. This case highlights key diagnostic morphologic and immunophenotypic features essential to reaching the correct diagnosis.

Bone Marrow Biopsies With Extensive Necrosis Are Frequently Associated With Hematolymphoid Neoplasms

(Paper No. 79)

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Context: Bone marrow biopsies with extensive necrosis pose diagnostic challenges, particularly when viable material is limited.

Design: The Pathology Database System at Johns Hopkins was searched for bone marrow biopsies with patchy or extensive necrosis between July 2007 and July 2018.

Results: Forty-three cases were identified in 36 patients. Twelve patients had acute myeloid leukemia; 7 at diagnosis, 2 at relapse, and 3 after chemotherapy. Diagnosis was accomplished by morphologic evaluation of the aspirate (n = 1) via flow cytometry of the marrow (n = 4) or from peripheral blood (n = 2). Four patients had B-lymphoblastic lymphoma at diagnosis (n = 1), after relapse (n = 2), and after chemotherapy (n = 1). Flow cytometry results were positive in 3 of 3 cases. Eight lymphoma cases displayed necrosis including large B-cell lymphoma (n = 5), Burkitt lymphoma (n = 1), and peripheral T-cell lymphoma (n = 2). CD20 immunostains were positive in the necrotic tissue in 3 of 3 large B-cell lymphoma cases. Two patients with classic Hodgkin lymphoma exhibited patchy necrosis after treatment, although no definitive lymphoma involvement was seen. Five patients with other hematolymphoid conditions were identified. Solid tumors with extensive necrosis included prostate cancer (n = 1), neuroblastoma (n = 1), and Ewing sarcoma (n = 1). Necrotic cases included one patient with multisystem organ failure and multiple biopsies from one patient with myelodysplastic syndrome who showed infection-related necrosis only.

Conclusions: Most cases demonstrating significant marrow necrosis are associated with neoplastic infiltrates (94%, 34 of 36), specifically hematolymphoid neoplasms (91%, 31 of 36). Even in extensively necrotic marrows, flow cytometric evaluation of the blood or marrow may be diagnostic in acute leukemia, and a CD20 immunostain may be helpful in detecting mature B-cell lymphoma.

A Case of Vitamin B12-Induced Megaloblastic Anemia Masquerading as Pure Erythroid Leukemia

(Paper No. 80)

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Megaloblastic anemia can mimic pure erythroid leukemia morphologically and immunologically and pose a diagnostic challenge. We present the case of a 57-year-old man with a history of hypothyroidism presenting with shortness of breath and fatigue. Complete blood cell count revealed severe pancytopenia with normocytic anemia (hemoglobin, 4.5 g/dL; mean corpuscular volume, 89 fl; white blood cell count, 1,860/μL; and platelet count 28k/μL). Additional testing revealed markedly elevated lactate dehydrogenase and decreased haptoglobin. No parietal cell antibodies were detected. Peripheral blood smear showed no increase in blasts. Bone marrow biopsy showed hypercellular bone marrow (90%) with > 80% erythroid precursors and 35% erythroblasts (Figure 39, A). The erythroid elements were immunoreactive for E-cadherin (60%); Figure 39, C). CD117 (20%); Figure 39, D), CD71, and glycophorin A (subset) and were negative for CD34. The aspirate smear (Figure 39, B) showed predominantly immature erythroid element with cytologic atypia (nuclear budding, irregular nuclear contours). Occasional giant metamyelocytes and giant bands were noted. Iron stain revealed ringed sideroblasts, accounting for 5% to 9% of erythroid cells. Flow cytometry, karyotype analysis, and fluorescence in situ hybridization panel for myelodysplastic syndromes were unremarkable. The overall morphologic and immunohistochemical findings could be compatible with pure erythroid leukemia. However, the patient had a remote history of vitamin B12 deficiency, and a CD20 immunostain may be diagnostic in acute leukemia, and a CD20 immunostain may be helpful in detecting mature B-cell lymphoma.

Bing Neel Syndrome: A Case With Myd88 (L265p) Gene Mutation Successfully Treated With Ibrutinib

(Paper No. 81)

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Bing Neel syndrome (BNS) is a rare manifestation of Waldenström macroglobulinemia (WM) that results from infiltration of the central nervous system by malignant lymphoplasmacytic cells. There are approximately 100 cases of BNS reported in literature with fewer than 10 cases treated successfully with ibrutinib. We report a case of 64-year-old woman who presented with worsening headaches, hoarding deficit and recurrent sinusitis for 3 months. The patient had profound fatigue, night sweats, and 100-pound-weight-loss over 2 years. A brain magnetic resonance imaging scan revealed peripherally enhancing lesions and subdural empyema with a midline shift. A biopsy of the right frontal lobe showed abscesses as well as infiltration by B-cell non-Hodgkin lymphoma (CD20+, PAX5+, CD5-, CD10-). Computed tomography scan revealed enlarged lymph nodes above and below the diaphragm. Inguinal lymph node biopsy revealed lymphoplasmacytic lymphoma with similar immunohistochemical profile. Polymerase
chain reaction–based DNA sequencing demonstrated the presence of an MYD88 mutation (Figure 40). Serum protein electrophoresis and immunofixation revealed an immunoglobulin M (IgM) monoclonal spike (IgM protein, 1.4 g/dL; k/λ ratio, 37.9). The patient was treated with ibrutinib and responded clinically with resolution of headaches and hearing deficit within 2 weeks. WM is a rare B-cell lymphoproliferative disorder characterized by the presence of serum IgM paraprotein with bone marrow infiltration by lymphoplasmacytic lymphoma. WM is primarily localized in bone marrow; 15% to 20% of patients have extramedullary disease. BNS is a rare complication of WM resulting from the central nervous system being infiltrated by lymphoplasmacytic cells. Estimated 3-year survival rate is 60%. Treatment of WM before BNS diagnosis as well as being older than 65 years and having a platelet count less than 100 were associated with worse outcome.

Epstein-Barr Virus Positivity May Not Preclude the Diagnosis of ALK-Negative Anaplastic Large Cell Lymphoma

(Poster No. 82)

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Context: ALK-negative (ALK-) anaplastic large cell lymphoma (ALCL) is defined as a CD30+ T-cell neoplasm that is not reproducibly distinguishable on morphologic grounds from ALK+ ALCL. The 2017 World Health Organization classification states that ALK- ALCLs are consistently negative for Epstein-Barr virus (EBV)–encoded small RNA (EBER) and LMP1. However, several authors have reported evidence of EBV positivity in some ALK- ALCL cases.

Design: We describe 3 cases of ALK- ALCL, one of them showing neoplastic cells with strong in situ hybridization EBV positivity.

Results: Patients presented with advanced disease and peripheral, thoracic, and/or abdominal lymphadenopathy; patient 1 was also found to have gastrointestinal tract involvement. Microscopic examination of the small-bowel resection (patient 1) and lymph node biopsy (patients 2 and 3) specimens revealed sheets or clusters of large, pleomorphic neoplastic cells; “kidney-shaped” hallmark cell morphology was identified in a cell subset in patient 2. Immunohistochemical studies demonstrated that neoplastic large cells were, in all cases, strongly positive for CD30 and MUM1 and negative for B-cell markers, ALK protein was undetectable, and Ki-67 proliferation index was increased (range, 60%–90%). Tumor cells were positive for CD4 and CD43 in 2 cases (patients 2 and 3), whereas a null immunophenotype was possible in the other patient. Clonal T-cell receptor (TCR) gene rearrangements were detected in 2 cases (patients 1 and 2). Neoplastic cells were strongly positive for EBER-1 only in patient 1.

Conclusions: These results provide evidence that EBV involvement may not preclude the diagnosis of ALK- ALCL. The EBV role in the pathogenesis of EBV+ ALK+ ALCL cases requires further investigation.

A Case of γ Heavy Chain Disease (Franklin Disease) Diagnosed on a Liver Biopsy

(Poster No. 83)

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Heavy chain disease is a form of paraproteinemias characterized by excessive production of short and truncated heavy chains because of a deletion in the amino-terminal portion, causing the heavy chains to lose the ability to form disulfide bonds with the light chains. Here we present a case of a 90-year-old man who presented with abdominal pain and weight loss. Magnetic resonance imaging showed hepatosplenomegaly and dilated common bile duct. Laboratory results were significant for elevated liver enzymes along with elevation of antinuclear antibodies. A subsequent liver biopsy was performed, and hematoxylin-eosin sections revealed liver parenchyma infiltrated by a polymorphic population of cells comprised of lymphocytes, histiocytes, and eosinophils, with rare plasma cells. Occasional ill-defined granulomas were also seen. Rare plasmacytoid lymphocytes showed Dutcher bodies. Immunohistochemical staining revealed the lymphocytes were highlighted by CD79A, CD20, and PAX5. These cells were positive for immunoglobulin (Ig) G and negative for k, λ, IgA, IgD, IgM, and IgG4. Immunofixation of serum protein revealed the presence of monoclonal γ heavy chain, confirmatory for γ heavy chain disease. γ-Heavy chain disease (Franklin disease) is a exceedingly rare B-cell lymphoplasma cell-proliferative disorder that may be associated with autoimmune diseases. Patients typically succumb to a rapidly declining clinical course and die of infection if left untreated or misdiagnosed.

Splenogonadal Fusion: A Very Rare Congenital Anomaly in the Differential Diagnosis of a Testicular Mass During Intraoperative Frozen Analysis

(Poster No. 84)

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Splenogonadal fusion is a rare congenital anomaly characterized by fusion of the spleen and the gonad. It is classified either as continuous, in which there is a direct anatomic connection between the spleen and the gonad, or discontinuous, in which there is no direct connection.

Clinical diagnosis of splenogonadal fusion is challenging because it may be misdiagnosed as a malignant gonadal tumor leading to an unnecessary orchiectomy. Roughly one-half of these cases are diagnosed in patients younger than 10 years. The incidence is 15 times greater in males and it occurs almost invariably in the left gonad (97%). The main differential diagnoses include lymphoma or a germ cell tumor. We report a case of an 11-year-old boy presenting with recurrent left testicular pain. Ultrasound revealed a hypervascular lesion (0.7 × 0.7 × 0.6 cm) in the upper pole of the left testis, consistent with possible “torsion of the appendix testis.” An incisional biopsy with intraoperative consultation revealed splenic tissue with normal white and red pulp separated from the seminiferous tubules by a fibrous capsule (Figure 41, A). The correct microscopic identification of heterotopic splenic tissue at the time of frozen section analysis allowed for preservation of the patient’s gonad and fertility. Positive CD8 immunohistochemical staining confirmed the diagnosis (Figure 41, B). Splenogonadal fusion remains a diagnostic challenge that should be a
consideration in the differential diagnosis in young males presenting with a history of a stable left-sided testicular mass.

Metastatic Carcinoma to Testis: Report of 2 Cases

(Poster No. 85)

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Metastases to the testis are uncommon, with incidence varying from 0.06% to 3.6%. When they occur, they are likely to be clinically occult and incidentally found on resection. Here, we report 2 cases, one from a prostate adenocarcinoma primary and the second from an appendiceal mucinous adenocarcinoma. Final pathology reports from orchietomy specimens were reviewed from 2008 to 2018 using the laboratory information system at our hospital, which yielded 2 potential cases. After reviewing the full history, these cases were selected for the study. The first case was of a 70-year-old man with prostate cancer admitted for surgical castration. On admission, the patient was asymptomatic, lacking testicular discomfort. Grossly, the orchietomy specimen revealed normal testes; however, on microscopy atypical glandular proliferation was seen. Immunohistochemistry (IHC) analysis revealed positivity with AMACR, NKK 3.1, and P50Is and negativity with OCT 3/4, inhibin, and basal markers. This immunoprofile confirmed the diagnosis of metastatic prostatic carcinoma. The second case is of a 46-year-old man, who underwent appendectomy with right hemicolecotomy for an incidentally found mucinous adenocarcinoma of the appendix. He reported intermittent right-sided scrotal pain, so a radical orchietomy was performed. Grossly, the orchietomy specimen revealed an aggregate of thick, yellow, mucinous material within the spermatic cord. Microscopically, metastatic low-grade mucinous adenocarcinoma was found. IHC analysis revealed the malignancy to be positive for CDX2 and CK20, consistent with an intestinal primary (Figure 42). Because of low incidence, metastatic tumors in the testes are often overlooked, especially when metastases are small and asymptomatic, which may present as a diagnostic challenge. When an abnormal intratesticular component is identified microscopically, a detailed history and comprehensive microscopic review with IHC panel should be used for accurate diagnosis and for determination of the primary site of origin of the tumor.

Evaluation of Copy-Number Variation in Clear Cell Papillary Renal Cell Carcinoma by Targeted Next-Generation Sequencing

(Poster No. 86)

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Context: Clear cell papillary renal cell carcinoma (CCPRCC) is a recently recognized entity that is a subtype of renal cell carcinoma (RCC). Little is known about the copy-number variation (CNV) and/or chromosomal changes in CCPRCC. Here, we investigated whether any particular recurrent CNV/chromosomal change could be associated with CCPRCC.

Design: Targeted next-generation sequencing, the AmpliSeq for Illumina focus panel (San Diego, California), was used in this study. The study samples included 16 normal DNA specimens from human blood cells, 10 formalin-fixed paraffin-embedded samples of CCPRCC, and 150 formalin-fixed paraffin-embedded samples of solid tumors. CNV of all amplicons was first normalized (normalization for library size, GC content, and amplicon length) by read coverage with 16 normal blood samples and then assigned statistical significance to putative CNV resulting from the segmentation of normalized profiles and gene-aware correction of the predicted CNV.

Results: The healthy individual’s peripheral blood cells showed no chromosomal changes and/or CNVs. Only one case showed a chromosome 4 deletion, which may not be a recurrent change associated with CCPRCC.

Conclusions: Our data demonstrate that CCPRCC does not show chromosomal changes and/or CNVs. Only one case showed a chromosome 4 deletion, which may not be a recurrent change associated with CCPRCC.

Utility of Whole Slide Imaging for the Interpretation of Frozen Section Renal Transplant Donor Biopsies

(Poster No. 87)

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Context: Microscopic evaluation of donor kidney biopsies (DKBs) is required to determine donor suitability for transplant in selected cases. Two hematoxylin-eosin–stained frozen sections of wedge biopsies are evaluated preimplantation and a final interpretation is performed on the formalin-fixed frozen remnant. We evaluated whole slide imaging (WSI) as an appropriate alternative to on-site microscopic evaluation by comparing the interobserver and intraobserver variability of pathologists from 2 institutions using WSI to interpret DKBs.

Design: Frozen section slides of 60 deidentified DKBs were retrospectively scanned and reviewed using the Motic EASYSCANT PRO 6 system (Motic INC, Hong Kong, China). Four blinded pathologists reported 6 histopathologic features using WSI. The respective frozen and permanent slides were also reviewed by microscopy. k Statistics and intraclass correlation were used to assess intraobserver and interobserver variability between digital and microscopic interpretations of frozen and permanent slides with an acceptable k ≥ 0.6.

Results: Interobserver agreement among all pathologists using WSI varied by criteria, with k ranging between 0.0778 and 0.8341. However, there was substantial intraobserver agreement for all evaluated criteria among the pathologists interpreting frozen DKBs by WSI and microscopy, with k ranging between 0.6601 and 0.9170. Intraobserver agreement for pathologists interpreting frozen DKBs by WSI and
respective permanents was variable, with \( \kappa \) ranging between 0.1878 and 0.8101 (Table).

**Conclusions:** From the overall low interobserver and intraobserver variability, we believe WSI is an acceptable alternative to microscopic evaluation of frozen DKBs for transplant suitability.

### Comparison of Criteria by WSI Versus Frozen Glass Slides and Permanents in DKBs

<table>
<thead>
<tr>
<th>Histopathologic Features</th>
<th>WSI Versus Glass Slide</th>
<th>WSI Versus Permanent</th>
</tr>
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<tbody>
<tr>
<td>Intraglomerular fibrin thrombi (presence/absence)</td>
<td>( \kappa = 0.8662, P &lt; .001 )</td>
<td>( \kappa = 0.8101, P &lt; .001 )</td>
</tr>
<tr>
<td>Acute tubular necrosis (presence/absence)</td>
<td>( \kappa = 0.7141, P &lt; .001 )</td>
<td>( \kappa = 0.1878, P &lt; .001 )</td>
</tr>
<tr>
<td>Interstitial fibrosis (&lt;10%, 10%–30%, 31%–60%, &gt;60%)</td>
<td>( \kappa = 0.7825, P &lt; .001 )</td>
<td>( \kappa = 0.5772, P &lt; .001 )</td>
</tr>
<tr>
<td>Degree of interstitial inflammation (none, focal, multifocal)</td>
<td>( \kappa = 0.9170, P &lt; .001 )</td>
<td>( \kappa = 0.3927, P &lt; .001 )</td>
</tr>
<tr>
<td>Degree of arteriolar nephrosclerosis (none, mild, moderate, marked)</td>
<td>( \kappa = 0.8593, P &lt; .001 )</td>
<td>( \kappa = 0.4918, P &lt; .001 )</td>
</tr>
<tr>
<td>Intravascular fibrin thrombi (presence/absence)</td>
<td>( \kappa = 0.6601, P &lt; .001 )</td>
<td>( \kappa = 0.4978, P &lt; .001 )</td>
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**Texas-Red–Filtered Fluorescent Microscopy Enhances the Specificity of Congo Red Satin for Amyloidosis**

*(Poster No. 88)*

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**Context:** The tissue diagnosis of amyloidosis is traditionally made by hematoxylin-eosin stain and confirmed by Congo red stain, both examined by routine light microscopy (LM). Examination of Congo red–stained tissue by Texas-red–filtered fluorescent microscopy (TRFM) is known to enhance the Congo red–positive amyloid, thus increasing the diagnostic sensitivity. However, false-positive congophilia is well documented. This study aimed to determine whether TRFM can mitigate that false-positivity and thus improve the specificity of the Congo red stain.

**Design:** Seventy-one tissue samples were categorized into 2 groups. Group 1 included 11 samples with amyloidosis. Group 2 consisted of 60 cases in which amorphous eosinophilic structures reminiscent of amyloid were seen on hematoxylin-eosin–stained tissue sections. Congophilic areas in each case were identified by LM. The same areas were then examined by TRFM.

**Results:** Of group 2 cases, 83% showed congophilia and “apple-green” birefringence with variable intensity by LM examination. Under TRFM, 18% of those cases showed a positive signal, whereas no enhancement was noted in the rest. Structures such as fibroelastic tissue, uromodulin renal casts, thyroid colloid, and bone spicules showed congophilia on LM, but no positive signal on TRFM. Among the 11 cases in group 1, the diagnosis was missed in 2 cases (heart and liver biopsies) when initially examined by LM because amyloid deposits were scant whereas TRFM definitively confirmed the diagnosis in these cases.

**Conclusions:** TRFM reduces the false-positive rate and increases the specificity of the Congo red stain for amyloid compared with LM alone.

**Utility of α-Methylacyl Coenzyme A Racemase in the Diagnosis of Urothelial Carcinoma In Situ: Expression in Difficult Cases**

*(Poster No. 89)*

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**Context:** Urothelial carcinoma in situ (CIS) in the bladder can be difficult to diagnose because of factors including procedural artifact, minimal tissue sampled, therapy-related changes, and various CIS growth patterns. There is minimal knowledge regarding the expression of α-methylacyl coenzyme A racemase (AMACR) in urothelial CIS and no information on its utility in routine clinical practice. The aim of this investigation was to assess the expression of AMACR in bladder cases in which testing was performed in routine clinical practice.

**Results:** Sensitivity of AMACR in CIS diagnosed without IHC was 100%. Sensitivity was 73% and specificity was 97% in cases of CIS with AMACR performed during routine practice with inconsistent intensity, compared with 95% sensitivity and 80% specificity of CK20, which had consistent, strong intensity.

**Conclusions:** AMACR results were usually positive in urothelial CIS and negative in nonneoplastic urothelium and thus may be a useful ancillary diagnostic test. However, it is important to note that AMACR was less sensitive in cases that were equivocal on IHC than those that were not and that, in cases of CIS with IHC performed during routine practice, CK20 was more sensitive with more-consistent, strong staining than AMACR.

**Metastatic Clear Cell Renal Cell Carcinoma Masquerading as a Hemorrhoid**

*(Poster No. 90)*

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Metastatic renal cell carcinoma involving the anal canal is extremely rare. To date only 2 cases have been reported in literature. We present a case of an 88-year-old woman with a history of stage IV renal cell carcinoma diagnosed after left radical nephrectomy. She presented with rectal bleeding and a polypoid anal mass of 1-month duration. The mass was initially thought to be a large thrombosed external hemorrhoid. She developed anemia from bleeding, for which she received multiple blood transfusions. Postnephrectomy, the patient was placed on immunotherapy and pazopanib. Grossly, a 4.5-cm variegated hemorrhagic polypoid mass with a stalk was received. Histologically, the anal lesion revealed clear cell renal cell carcinoma, identical to the previously resected left renal mass, consistent with metastasis. The anal tumor was positive for RCC and PAX8 and was negative for CK 20 and CDX2 (Figure 44). To our knowledge, this is the third report of renal cell carcinoma metastatic to this site. Clinicians should be aware that although rare, rectal bleeding with a “hemorrhoidal” mass in a patient with a remote history of renal cell carcinoma may represent delayed metastasis to the site.

**Sclerosing PEComa of the Kidney: Radiographic and Pathologic Findings**

*(Poster No. 91)*

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Perivascular epithelial tumors (PEComas) are a group of neoplasms that include renal angiomylipoma. These neoplasms arise in skin, soft tissue, and visceral organs and are characterized by the presence of perivascular epithelioid cells. Sclerosing PEComa is an uncommon variant characterized by extensive stromal hyalinization, predominantly reported in the retroperitoneum and pelvis. We report a case of sclerosing PEComa of the kidney. The patient was a 70-year-old woman who presented with vague abdominal pain and constipation. Computed tomography scan of the abdomen and pelvis revealed a 20 × 19 × 18-cm retroperitoneal lipomatous mass with variable density and calcification encasing and arising from the lower pole of the right kidney (Figure 45, A). Radical nephrectomy and resection of the mass revealed a yellow, lobulated surface and tan-white fibrous areas with calcification. Areas of cystic change contained hemorrhagic fluid. Microscopy showed adipose tissue, blood vessels, spindle cells in fascicles and nests, and large zones of dense collagen with calcification and variably sized irregular spaces (Figure 45, B and C). Some spaces were filled with altered blood and associated with hemosiderin-laden macrophages. Rare adipocytes showed binucleation and mild atypia. Spindle cells were HMB45þ (Figure 45, D) and actinþ. Adipocytes were MDMP2 and CDK4þ. Sclerosing PEComa is very uncommon, and we present only the fourth reported case in the literature arising in the kidney. The size of this tumor and the large areas of sclerosis and calcification resulted in the clinicoradiographic concern for sarcoma. Correct pathologic diagnosis is necessary for appropriate therapy.

Among men with pathogenic germline ATM mutations, 74% (17 of 23) had ATM loss by IHC. Of those, 76% (13 of 17) had homogeneous ATM protein loss in all tumor cells within a dominant tumor nodule, suggesting that ATM loss was an early clonal event. On thermomechanical analysis, ATM loss was seen in 3.3% (31 of 944) of tumors evaluable for ATM status by IHC and was significantly more common in tumors with Gleason scores of 9 and 10 (20 of 198; 10.1%) than in all other Gleason grades (11 of 746; 1.5%; P < .001).

**Conclusions:** Validated ATM IHC is a sensitive assay for detecting underlying genomic ATM alterations. ATM protein loss appears to be an early event and is significantly enriched in high-grade prostate cancers.

Adult Granulosa Cell Tumor of the Testis

(Poster No. 93)

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Granulosa cell tumors of the testis are exceedingly rare, approximating less than 0.5% of all sex cord–stromal tumors. We describe the case of a 40-year-old man with no significant medical history who noted increased low-back pain and left scrotal discomfort with a palpable testicular mass. An ultrasound was performed revealing a 1.21 × 0.97-cm mildly heterogenous predominantly hypoechoic mass with vascularity located in the superolateral aspect of the left testis. A computed tomography scan of the abdomen was unremarkable. AFP and HCG tumor markers were within reference range. A radical orchiectomy was performed and gross examination revealed a 1.2 × 0.7 × 0.7-cm tan-white mass that extended to and possibly involved the tunica albuginea without extension into the overlying epididymis or tunica vaginalis. Microscopic examination revealed a nested and trabecular hypercellular lesion (Figure 46, A) composed of spindled cells with eosinophilic cytoplasm and elongated vacuolated nuclei with rare grooves and scattered nuclei (Figure 46, B). Rare mitoses were identified. The tumor invaded the rete testes. A panel of immunohistochemical stains including inhibin, pankeratin, SMA, and CD56 was used to aid in characterization of the neoplasm. The neoplastic cells were positive for inhibin (Figure 46, C) and CD56 (Figure 46, D). The cells were negative for SMA and pankeratin. A reticulin special stain highlighted the nested architecture of the tumor.

Ovarian-Type Clear Cell Adenocarcinoma of the Testis: An Extremely Rare Occurrence With Unique Clinical Presentation

(Poster No. 94)

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Ovarian-type clear cell adenocarcinomas are rare among men, with the highest frequency found in patients with Li-Fraumeni syndrome. Germline mutations in the Li-Fraumeni syndrome tumor suppressor gene, TP53, are responsible for Li-Fraumeni syndrome and result in high penetrance of breast, sarcoma, brain, and soft tissue cancers. Mutations in the Li-Fraumeni syndrome tumor suppressor gene, TP53, are responsible for Li-Fraumeni syndrome and result in high penetrance of breast, sarcoma, brain, and soft tissue cancers. Mutations in the TP53 gene result in loss of function, and, in turn, the TP53 protein is not able to prevent cell cycle progression and cell death in response to DNA damage. With the development of TP53 mutations, tumors develop that are reliant on ATM loss for continued proliferation. ATM loss is associated with the development of TP53 mutant neuroendocrine prostate cancers, in which ATM loss along with TP53 loss defines a large population of tumors that are dependent on ATM loss for continued proliferation. These tumors are enriched for TP53 mutant prostate cancers and are clonally enriched for ATM loss.

**Materials and Methods:** To test the hypothesis that ATM loss is a frequent event in TP53 mutant prostate cancers, we evaluated the frequency of ATM loss among 23 tumors with pathogenic germline ATM mutations, as well as more than 1000 additional primary prostate carcinomas using tissue microarrays.

**Results:** ATM loss by IHC was found in 14% (7 of 49) of primary Gleason pattern 5 tumors. Four cases had adequate sequencing results and all had underlying pathogenic ATM mutations. Of the remaining 42 cases (86%) without ATM protein loss, none had ATM alterations.
Ovarian-type tumors may rarely occur in the testis. We report a case of clear cell carcinoma of the testis presenting as a hydrocele, an exceedingly rare entity with a unique clinical presentation, which heretofore has not been reported in the literature. A 71-year-old man presented with a 1-month history of right-sided hydrocele, previously diagnosed as epididymo-orchitis. Scrotal ultrasound showed a large, complex, right hydrocele; no evidence of an intratesticular mass was seen. A hydrocelectomy was performed; gross examination showed a fibromembranous saccular structure, with a 2.4 × 1.8-cm nodular mass located on the surface. Microscopic exam showed a layer of fibromuscular tissue, compatible with hydrocele sac, with an exophytic neoplastic proliferation composed of papillary structures lined by cells with eosinophilic to clear cytoplasm (Figure 47, A and B). The mitotic rate was low (2 of 10 high-power fields), and no significant pleomorphism or necrosis was observed. Immunohistochemical studies showed positivity for EMA, CAM 5.2, CK7 (focal), PAX8 (Figure 47, C), AR, CA19-9 (focal), and WT-1 (focal); stains for CK20, ER, and PR were negative. Ki-67 showed staining of 40% of the tumor cells (Figure 47, D). The overall findings were consistent with mullerian-type clear cell adenocarcinoma, a rare and clinically aggressive entity with only 2 cases reported in the literature to date, both of which initially presented with diffuse metastatic disease. Our case demonstrates a deceptively innocuous presentation of this malignancy and highlights the importance of careful histopathologic examination and ancillary studies, with appropriate differential considerations, in arriving at the correct diagnosis.

Radiation-Induced Osteosarcoma of the Urinary Bladder
(Poster No. 95)

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Radiation therapy is a commonly used treatment for many types of malignancies. Although it is effective in treating primary malignancies, it also puts patients at increased risk for developing secondary malignancies in the radiation field, including sarcomas. The risk of developing radiation-induced sarcoma ranges from 0.09% to 0.11%. Osteosarcoma, defined as the production of malignant bone/osteoid by neoplastic cells, is the most common radiation-induced sarcoma. Although it is the most common overall, osteosarcoma of the urinary bladder is extremely rare and must be differentiated from more-common entities such as carcinosarcoma and sarcomatoid carcinoma. Many subtypes exist, including osteoblastic and chondroblastic. Additional histologic variants include telangiectatic and, rarely, small cell osteosarcoma. We report a case of bladder osteosarcoma in a patient with a history of prostate cancer treated with radiation therapy 10 years prior. An 86-year-old man presented with gross hematuria. He underwent cystoscopy and transurethral resection of a bladder tumor. Microscopic examination of the tumor revealed a heterogeneous malignant neoplasm, demonstrating areas of osteoblastic differentiation (Figure 48, A) with small, uniform, hyperchromatic neoplastic cells producing eosinophilic, dense malignant osteoid, and areas of chondroblastic differentiation (Figure 48, B) forming immature cartilage. The tumor was strongly reactive with vimentin (Figure 48, C) and nonreactive with pancytokeratin (Figure 48, D), prostate-specific antigen, prostate-specific acid phosphatase, and synaptophysin immunohistochemical stains. No evidence of urothelial or prostatic adenocarcinoma were identified in the biopsy specimen. Therefore, a diagnosis of high-grade osteosarcoma, small cell variant, was rendered. This case report emphasizes the importance of identifying patients at risk for developing radiation-induced sarcoma and providing them with proper clinical follow-up.

Receiver Operating Characteristic Curves Reveal Kidney Injury Molecule-1 Being Sensitive for Identifying Acute Tubular Injury
(Poster No. 96)

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Context: Kidney injury molecule-1 (KIM-1) staining has been shown to be useful in identifying acute proximal tubular injury, but its sensitivity and specificity in correlation with serum creatinine (sCr) have not been well established in renal biopsies.
Design: We randomly selected 184 renal biopsies (children younger than 20 years and adults) with acute renal diseases. Patients' sCr levels were obtained, and the renal biopsies were immunostained for KIM-1. Spearman correlation between sCr and KIM-1 scores was computed, and receiver operating characteristic (ROC) curves were used to examine the sensitivity and specificity of using sCr to predict KIM-1 scores.

Results: KIM-1 staining scores were significantly correlated with sCr levels ($P < .05$) in all age groups. The ROC curve showed the area under the curve (AUC) in pediatric cases was 0.74, which demonstrated KIM-1 as a fair index in correlating with sCr (median sensitivity, 82%; specificity, 43%). In adults, the AUC was 0.87 (median sensitivity, 83%; specificity, 53%), indicating that KIM-1 was an even better index in the adults (Figure 49).

Conclusions: We found that positive KIM-1 was significantly correlated with elevated sCr levels, and this correlation was categorized as "good" when plotted on a ROC curve in adults. Therefore, KIM-1 staining is a sensitive marker in identifying acute tubular injury.

RARE PRESENTATION OF PENILE SQUAMOUS CELL CARCINOMA EMERGING AT INJECTION SITE OF OIL-BASED SUBSTANCE

(Poster No. 97)

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Squamous cell carcinoma (SCC) of the penile shaft is extremely rare and it occurs more in developing countries. At present, there are few described risk factors known to trigger the development of penile SCC. We present a case of a middle age man who had a history of a mass emerging at an injection site of oil-based material (Vaseline, Unilever, Hospital, Washington, DC). The subcutaneous tissue shows numerous lipid vacuoles embedded in sclerotic stroma and infiltrate of foamy histiocytes and scattered multinucleated giant cells consistent with lipogranuloma (Figure 50, C and D). To our knowledge, the association between squamous cell carcinoma and lipogranuloma at an injection site of an oil-based substances has been reported once in the literature. Along with our case, this raises the question of possible correlation between both entities. Further studies are needed to clarify the pathophysiology of developing the SCC in presence of oil-based substances.

OSSOGENIC METAPLASIA IN THE LAMINA PROPIA OF THE URINARY BLADDER UNDERLYING A PAPILLARY UROTHELIAL CARCINOMA WITH FOCAL MICROINVASION

(Poster No. 98)

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Stromal ossosseous metaplasia rarely occurs in association with urothelial carcinoma of the urinary bladder. In the few cases reported in the literature, stromal osseous metaplasia was typically seen within, or associated with, large deeply invasive primary, or even less commonly, metastatic urothelial carcinoma. Those tumors often had concomitant hemorrhage and necrosis. In the context of a large invasive tumor, the metastatic bone often raised a differential that includes sarcomatoid carcinoma with heterologous osseous elements. We report a case of osseous metaplasia of bladder lamina propria associated with a minimally invasive urothelial carcinoma. A 68-year-old man, former heavy smoker, presented with gross hematuria. A computed tomography scan showed a 1.2-cm bladder lesion adjacent to the right ureterovesicular junction. No opacities were identified on the computed tomography scan. Transurethral resection was performed. Histopathologic examination revealed a papillary urothelial carcinoma, high-grade, with focal microinvasion of the lamina propria. There was extensive mature bone formation in the underlying lamina propria. A few bone fragments were in contact with the foci of microinvasion, but many other fragments appeared to float below the noninvasive portions of the papillary urothelial carcinoma without being in contact with it. Osseous metaplasia extended well beyond the foci of microinvasion. This case illustrates that some urothelial carcinomas promote osseous metaplasia even when minimally invasive or noninvasive, and that this phenomenon is not limited to large invasive tumors, or specifically associated with the presence of hemorrhage and necrosis within the tumor.

EOSINOPHILIC SOLID AND CYSTIC RENAL CELL CARCINOMA: A CASE REPORT OF A RECENTLY DESCRIBED ENTITY

(Poster No. 99)

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Eosinophilic solid and cystic renal cell carcinoma is a recently described rare kidney tumor that is not yet included in the World Health Organization classification of renal neoplasia. There is newly emerged evidence to determine the nature of the tumor; however, it is generally a low-grade neoplasm with rarely reported metastatic potential.
We present a case of a 75-year-old woman with history of chronic kidney disease, who was found to have an enlarging left renal mass over a period of a few months. No history of hereditary disease was reported. An magnetic resonance imaging scan revealed a 4.3-cm, complex, nonenhancing cystic mass involving the upper pole of the right kidney with no evidence of metastasis. Partial nephrectomy was performed. The tumor exhibited solid and cystic architecture, voluminous eosinophilic cytoplasm with cytoplasmic stippling (Figure 51). The tumor cells expressed diffuse positivity for PAX8 and vimentin; patchy staining for CA9, AMACR, CD10, CK20, and cathepsin K; and were negative for HMGB-45, Melan-A, AE1/AE3, and CK7. No evidence of TFE3 and TFF1 gene rearrangement identified by fluorescence in situ hybridization. These finding supported the diagnosis of eosinophilic solid and cystic renal cell carcinoma. Future molecular and cytogenetic studies will help improve knowledge of the entity; in our case, awareness of morphologic as well as immunohistochemical features of this neoplasm helped establish an accurate diagnosis because it overlaps with other renal neoplasms with oncotypic features such as epithelioid angiomylipoma and translocation-associated carcinomas.

**Juxtaglomerular Cell Tumor With Renal Vein Invasion**  
*(Poster No. 100)*

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Juxtaglomerular cell tumor (JGCT) is a rare and mostly benign renal tumor arising from the juxtaglomerular apparatus and most commonly seen in young females. Only 4 cases of atypical JGCT (defined by vascular invasion, necrosis, high mitoses, large size (>8 cm), clinical recurrence, or metastasis) have been reported, of which one case presented with metastasis. Because of its rarity, the long-term behavior of JGCT even with the afore-defined atypical histology, is still unknown. We present a case of JGCT in a 42-year-old normotensive woman with a well-defined 2.3-cm right renal mass. Microscopically, the tumor was composed of relatively uniform and small-sized cells with eosinophilic fine granular cytoplasm and round nuclei with smooth chromatin and inconspicuous nucleoli in a background of abundant hemangiopericytic-like vasculatures (Figure 52, A). The focus of the invasion into the renal vein was easily notable (Figure 52, B). No small vessel invasions were identified. The tumor stained for CD34 (Figure 52, C) and SMA and was negative for PAX8 and HMB-45. Electron microscopy showed spheroid to polygonal nuclei with smooth chromatin and inconspicuous nucleoli. The second area showed immature monoclonal plasma cells which were positive for CD138 and λ light chain, consistent with plasmacytoma.

Plasmacytoma and Metastatic Prostate Adenocarcinoma, Synchronous Malignancy in Supraclavicular Lymph Node  
*(Poster No. 101)*

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Synchronous presentation of primary nodal plasmacytoma and prostate cancer is rare. We describe a case of 96-year-old man with a remote history of prostate cancer, presenting with complaints of abdominal and lower-back pain for 6 months and recent onset of bilateral hip pain. Imaging showed a small-bowel mass, multiple enlarged infrarenal, mesenteric, and retroperitoneal lymph nodes, and an enlarged left supraclavicular lymph node as well as numerous lytic bony lesions. Laboratory results at presentation were as follows: lactate dehydrogenase, 0.9 U/L; white blood cell count, 3.6 hemoglobin, 8 g/dL; platelets, 197 k/µL. Urinalysis showed proteinuria, and creatinine was 1.76 mg/dL. Prostate-specific antigen was elevated at 47 ng/mL at presentation. Serum protein electrophoresis showed monoclonal immunoglobulin (Ig) A light chain, and urine protein electrophoresis showed overflow λ light chain with an abnormal κ to λ free light chain ratio of 0.02 (reference range, 0.26–1.65). Immunofixation electrophoresis demonstrated the presence of IgA λ monoclonal gammopathy. Supraclavicular lymph node biopsy was performed. Morphologically, 2 types of neoplastic cells were identified (Figure 53). One area showed immature monoclonal plasma cells which were positive for CD138 and λ light chain, consistent with plasmacytoma. The second area showed fused glands with prominent nuclei, forming cribriform patterns without intervening stroma. These neoplastic cells were positive for prostate-specific antigen and prostatic acid phosphatase and negative for CK7 and CK20. Based on morphology and immunohistochemistry, a diagnosis of plasmacytoma and metastatic adenocarcinoma of the prostate in one lymph node was made. The patient received palliative therapy, and he died 1 month after biopsy.
progression with cord compression at T4 to T6 for which he underwent laminectomy. A biopsy taken during the laminectomy showed prostate adenocarcinoma with glandular areas, clear cell areas, foci of squamous differentiation, and rare foci of pilomatrix differentiation. The latter included grey-blue cornification and intracytoplasmic red trichohyalin granules. Immunohistochemical studies showed positivity of the lesional cells for pancytokeratin and EMA. The foci with squamous differentiation expressed p40 and the glandular component was positive for NKX3.1 and Pax8. The patient continued to physically decline, and he was transferred to comfort care. The clinical presentation and history of metastatic adenocarcinoma in this case were helpful in interpreting the rare morphology of squamous differentiation of prostate adenocarcinoma. To our knowledge, pilomatrix differentiation in metastatic prostate adenocarcinoma has not been previously described (Figure 54).

Multifocal Renal Carcinoid Tumor Arising in a Horseshoe Kidney

(Poster No. 103)

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Neuroendocrine tumors of the kidney are extremely rare, accounting for less than 1% of reported renal malignancies. This is because neuroendocrine cells are not found in normal renal parenchyma. Rarer still are primary renal carcinoid tumors arising in horseshoe kidneys. Of the few case reports detailing renal carcinoid tumors arising in horseshoe kidneys, all but one confirms unifocal malignancy. Although unifocal carcinoid tumors may be associated with a less-aggressive clinical course compared with tumors arising in anatomically normal kidneys, there is one report of a multifocal tumor with distant metastasis to the thyroid at the time of diagnosis. We report the case of a 43-year-old woman with 3 renal masses measuring 2.8, 4.5, and 8.3 cm, within the right upper pole of a horseshoe kidney who underwent partial nephrectomy in December 2018. Histologic findings were identical within all 3 masses, showing proliferations of monomorphic cells with neuroendocrine cytology and a trabecular growth pattern (Figure 55, A). Immunohistochemical stains were positive for synaptophysin (Figure 55, B) and neuron-specific enolase (Figure 55, C). The Ki-67 proliferation index was less than 3% (Figure 55, D). There was no radiographic evidence of metastatic disease at the time of resection and she remains without evidence of disease recurrence 3 months after resection. Our case highlights the importance of awareness of the occurrence of neuroendocrine tumors within the kidney, especially in the horseshoe kidney. In combination with judicious tumor sampling and immunohistochemistry, these tumors can be distinguished from more-common renal parenchymal and urothelial neoplasms.

Patient With Urinary Bladder Collagenous Vasculopathy Presenting With Recurrent Gross Hematuria

(Poster No. 104)

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Collagenous vasculopathy is an extremely rare localized vascular disease with unknown etiology. To date, it has only been described in skin. Here, we report a patient with urinary bladder collagenous vasculopathy who presented with recurrent episodes of painless gross hematuria during a 10-year period in an 82-year-old man. Cystoscopic examination revealed bladder mucosa with vascular engorgement and bleeding at the bladder neck with blood clot. No mass or tumorlike lesion was visualized. The patient’s significant medical history included cold agglutinin hemoglobinuria. Under microscopy, the friable tissue excised from the hemorrhagic site showed patchy small- to medium-sized vessels with prominent medial and adventitial fibrocollagenous hyalinization. The intimal was relatively preserved with occasional lymphocytic infiltrates (Figure 56, A and B). The perivascular hyalinizing material was highlighted by PAS and trichome staining (Figure 56, C and D). The stains for amyloid P, Congo red, IgM, and κ and λ light chains were all negative. This staining pattern was consistent with fibrocollagenous tissue without IgM, light chain or amyloid deposits. No attributable causes of these changes were notable in this case. The presence of occasional intimal inflammatory cell infiltrates seems to be in line with the plausible etiology of repeated endothelial cell injury. In summary, this is the first case of collagenous vasculopathy reported in a visceral organ (specifically, urinary bladder) as the cause of recurrent
Kidney Injury Molecule-1 Is a Useful Marker to Detect Renal Cell Carcinoma

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Context: We have previously reported that kidney injury molecule-1 (KIM-1) stains positively in clear cell renal cell carcinoma (RCC) and papillary RCC. Additionally, we have shown RCC patient’s urine levels of KIM-1 are elevated before surgery and reduced after nephrectomy. High serum KIM-1 in patients with RCC is reported to predict patients’ development of RCC within 5 years.

Design: We reviewed the serum levels of KIM-1 in 10 patients with localized RCC that stained positively for KIM-1 and demonstrated increased urine KIM-1. We compared these results with the serum and urine KIM-1 results of 3 patients with benign renal lesions after nephrectomy. Lastly, we stained 8 cases with metastatic RCC for KIM-1 and Pax8.

Results: We found that 7 of 10 patients (70%) with localized RCC had increased serum KIM-1, up to 100-fold higher than reference range serum level. After nephrectomy, 5 available RCC cases had reduced serum KIM-1. By contrast, only 1 of 3 controls was found to have reduced serum KIM-1 after nephrectomy. In cases with metastatic RCC, KIM-1 stained positively in 7 of 8 cases (88%), whereas PAX8 was positive in 5 of 8 cases (62%).

Conclusions: KIM-1 staining may be a valuable marker in identifying metastatic RCC, in combination with PAX8. In addition, our serum data for KIM-1 were consistent with findings of high serum KIM-1 levels in patients with RCC from the recent Center for Cancer Research (National Cancer Institute, Bethesda, Maryland) study, implying its usefulness in detecting recurrent or metastatic RCC.

Association of Karyomegalic Interstitial Nephritis With Focal Segmental Glomerulosclerosis

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Karyomegalic interstitial nephritis (KIN), first described in 1974, is an uncommon form of chronic tubulointerstitial nephritis. KIN is defined by the presence of markedly enlarged, hyperchromatic nuclei with prominent nucleoli mainly involving tubular epithelial cells of the kidney accompanied by marked interstitial fibrosis. The disease presents as asymptomatic proteinuria, progressing to chronic kidney disease, and eventually leading to end-stage renal disease by 30 to 40 years. Very little is known about the etiology of this disease; however, genetic risk factors and possible association with human leukocyte antigen (B27/35) is suspected. It has also been linked to FAN1 (FANCD2/FANC1-associated nucleosome mutation). We present 2 rare cases of KIN with associated focal segmental glomerulosclerosis. Both patients presented with nephrotic range proteinuria and the biopsies of both cases demonstrated marked enlargement of tubular nuclei in some tubules, meeting the KIN diagnosis criteria (nuclei were 3 to 5 times larger than the uninvolved tubular nuclei suggested by some authors in previous studies). Interestingly, in the first biopsy of one case, the patient was diagnosed with minimal change disease; however, his hematoxylin-eosin sections showed patchy tubular attenuation with readily recognizable tubular cell mitotic figures, indicating concurrent acute tubular injury. Under electron microscope, all biopsies exhibited diffuse foot-process effacement with microvillus transformation and podocyte hypertrophy with cytoplasmic vacuoles, suggesting podocyte injury. Similar cytoplasmic vacuolization was also observed in the tubular epithelial cells. In both cases, the injury factor targeted both podocytes and some tubular cells.

Round Cell Variant of Prostatic Stromal Tumor of Uncertain Malignant Potential: Report of a Rare Case

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Prostatic stromal tumors of uncertain malignant potential (STUMP) are rare stromal tumors, which until recently had 4 recognized histologic variants. Recently, 7 cases of a new “round cell variant of STUMP” were described in a single case series. We report the eighth case of this variant in a 63-year-old man with benign prostatic hypertrophy, elevated prostate-specific antigen, and compressive symptoms secondary to a large pelvic cystic mass without communication to the urinary bladder. The pelvic cyst and a portion of the prostate were removed in several unoriented portions. The excised tissue was composed of numerous well-circumscribed tan-yellow nodules intermingled with multiple smooth-lined cysts. A separate portion of the cyst wall exhibited multiple tan-brown plaques and variably-sized tan-white to tan-yellow nodules without hemorrhage or calcification. Microscopy revealed a hypercellular stroma with a monotonous population of rounded nuclei. Focal degenerative atypia and phyllodes growth pattern were observed. Prominent basal cell layers were present, along with focal conspicuous nucleoli, consistent with high-grade prostatic intraepithelial neoplasia. There was apparent extraprostatic extension of cystic benign prostatic hypertrophy, which is unusual for STUMP. It is unclear whether a subset or all “prostatic cystadenomas” are extraprostatic STUMP’s or whether this was unique. The clinical course of prostatic STUMP’s cannot be determined based on histologic features, and the round cell variant may be difficult to differentiate from benign prostatic hypertrophy.

Arch Pathol Lab Med
Dystrophic Calcification of Urinary Bladder Wall: A Rare Complication of Local Therapy for Bladder Tumors

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Dystrophic calcifications of the bladder are rare, and single case reports have attributed them to intravesical mitomycin-C, Bacillus Calmette-Guerin (BCG) therapy, or simply transurethral resection of bladder tumor (TURBT). We report 3 cases of bladder wall calcifications that we encountered during routine practice. Patient 1 is a 65-year-old man with recurrent high-grade papillary urothelial carcinoma of the right bladder wall, treated with BCG. Cystoscopy 16 months later showed an erythematous area at the site. Biopsy revealed dystrophic calcification with reactive urothelium. Patient 2 is a 69-year-old man with high-grade papillary carcinoma who underwent TURBT. One month later, cystoscopic biopsy of the same site showed inflammation, giant cells, necrosis, and dystrophic calcifications. Patient 3 is a 71-year-old man with recurrent low-grade urothelial carcinoma treated with local mitomycin-C therapy. Seven months later, computed tomography scan of the pelvis showed an area of superficial lake-type calcification adherent to the previous tumor site. Biopsy revealed chronic cystitis with extensive dystrophic calcifications. All 3 patients had urine pH within reference range and negative findings in urine cultures, ruling out alkaline-encrusted cystitis and confirming the calcifications as dystrophic. In all 3 cases, dystrophic calcifications occurred at the site of the resected tumor suggesting that the TURBT injury is the cause. Mitomycin-C and BCG affect the whole bladder, thus diffuse or multifocal calcifications would be expected if either was the cause. It is possible that those therapies influence dystrophic calcification deposition at the TURBT site by promoting tumor necrosis. Because of some overlap in histologic findings, encrusted cystitis should be excluded before making a diagnosis of dystrophic calcification.

A Case of Prostate Carcinoma With Squamous Differentiation Secondary to Treatment With Docetaxel and Leuprolide

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Squamous cell carcinoma is a rare entity in the prostate, representing less than 1% of all prostatic carcinomas. Up to 60% of cases occur in the setting of a prior diagnosis of prostate adenocarcinoma. Prognosis is poor, with an average survival of 24 months. We report the case of a 49-year-old man with a 2-year history of T4N1M1b prostate carcinoma (Gleason 5 + 4 = 9), after treatment with docetaxel and leuprolide, who presented with hematochezia. Imaging studies revealed a 7.5-cm mass completely replacing the prostate with extension into the rectum and no evidence of bladder or anus involvement. Focal erosion of the rectal mucosa was identified by colonoscopy, and ultrasound-guided fine-needle aspiration of the underlying mass was performed. Histologic examination of the cell block showed multiple groups of cohesive cells with enlarged, pleomorphic nuclei and amorphous eosinophilic cytoplasm (Figure 57, A). Immunohistochemical stains for CK5/6 (Figure 57, B) and p63 (Figure 57, C) were diffusely positive, whereas p16 and GATA3 were negative. NKK3.1 (Figure 57, D) and prostate-specific antigen showed rare faint staining. Given the patient’s clinical, imaging, and cytologic findings, prostate carcinoma with squamous differentiation was favored. Previous case reports of this entity have documented patient histories of prior radiation or hormonal therapy. In this case, the patient had received docetaxel, a chemotherapeutic agent, which may have been a contributing factor to the development of prostate carcinoma with squamous differentiation. Our case therefore supports the potential association between a history of chemo-hormonal therapy and the subsequent development of squamous differentiation of prostate carcinoma.

Lymphoid Proliferations in Renal Parenchyma: Lymphoma Versus Pseudolymphoma

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Lymphoid proliferations forming masses within the kidney have not been well described in the literature. Our review identified only a case series of 14 renal lymphomas that were initially suspected to be primary renal carcinomas. Additionally, there have been case reports of “pseudolymphomas” of the kidney—lymphoid proliferations that appear concerning but are benign. We present 2 interesting cases seen at our institution. The first case was of a 6-cm mass in the hilum of the kidney. By histology, the mass was composed of a well-circumscribed plasmacytoid/lymphoid proliferation. An immunohistochemical panel was consistent with a reactive follicular hyperplasia, but B-cell clonality studies revealed a clonal population. The diagnosis was “extranodal marginal zone lymphoma with extreme plasma cell differentiation.” The patient elected not to follow-up with oncology, but returned to the clinic 2 years later, with systemic marginal zone lymphoma. The second case was of a partial nephrectomy for a 2.7-cm, well-circumscribed renal mass, suspected to be a primary renal cell carcinoma. By histology, the mass was composed of a lymphoid proliferation without any immunohistochemical abnormalities. Unlike the prior case, B-cell clonality studies were negative for a monoclonal population. The diagnosis of “intraparenchymal reactive follicular hyperplasia” was discussed with the clinician with the caveat that this may be an evolving atypical lymphoma. The patient declined the follow-up with oncology. At a 6-month urology visit, there was no evidence of lymphoma. We present these cases as a demonstration of the subtle distinctions between lymphomas and pseudolymphomas.

The Impact of Routine Frozen Section Analysis During Partial Cystectomy on Surgical Margin Status and Long-Term Oncologic Outcomes

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Context: The role of intraoperative frozen section analysis (FSA) during partial cystectomy (PC) in the surgical margin (SM) status relating to patient outcomes remains uncertain. We aimed to investigate the utility of routine FSA of the SMs in patients undergoing PC.
Design: A retrospective review identified 74 consecutive patients who underwent PC for bladder carcinoma at our institution from 2004 to 2018. FSA was correlated with the diagnosis of the frozen section control, the status of final SM, and the prognosis.

Results: There were no significant differences in tumor size, histology, or tumor grade/stage between the FSA (n = 66) and non-FSA (n = 38) groups. Five cases were FSA-positive (n = 7; 11%), atypical (n = 10; 15%; revised to benign [n = 4], atypical [n = 4], and carcinoma [n = 2] on the frozen section controls), and negative (n = 49; 74%). Ten (77%) of 13 initial FSA+ (6 of 7, atypical, 4 of 6; excluding benign diagnoses on the controls) cases achieved negative conversion by excision of additional tissue. Final SM was positive in 6 FSA+ (9%; 1 FSA-positive, 5 FSA-atypical, and 2 FSA-negative) cases versus 2 (25%) of non-FSA cases (P = 0.20). Kaplan-Meier analysis further revealed that FSA did not significantly contribute to preventing intravesical recurrence (P = 0.89), progression (P = 0.28), or cancer-specific mortality (P = 0.52). Nonetheless, initial positive/atypical FSA was strongly associated with reduced progression-free (P = 0.002) and cancer-specific (P = 0.004) survival rates, compared with initial negative FSAs.

Conclusions: Performing FSA during PC does not appear to have any significant effect on final SM status or long-term oncologic outcomes. However, as seen in a subset of initial FSA-positive/atypical cases, select patients may benefit from the routine FSA. Meanwhile, positive/atypical FSA was associated with significantly poorer prognosis.

Loss of DNA Mismatch Repair Proteins in Prostate Cancer

(Poster No. 113)
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Context: Recent studies have suggested an increased risk of prostate cancer (PC) in men with Lynch syndrome driven by germline mutations in mismatch repair (MMR) genes. However, the incidence and clinical implication of MMR deficiency in sporadic PCs remain poorly understood.

Design: We immunohistochemically stained for MLH1/MLH2/MSH2/MSH6/PMS2 in a set of tissue microarrays consisting of 220 radical prostatectomy specimens and evaluated the relationship between loss of their expression and available clinicopathologic features.

Results: In 50 cases, 6 (2.7%), 37 (16.8%), and 27 (12.3%) PCs, respectively. Loss of at least one MMR protein was identified in 50 cases (22.7%). There were no statistically significant associations between MMR deficiency and pathologic grade, Gleason score, or pT/pN stage. Nonetheless, the levels of preoperative prostate-specific antigen (PSA) were significantly (P = 0.02) elevated in patients with MMR deficiency (mean, 9.12 [9.01] ng/mL), compared with those without normal PSA (5.76 [3.17] ng/mL). There were five cases (6.8%) showing loss of at least two MMR proteins, which was not significantly associated with PSA level or tumor grade/stage. Additionally, 5 cases (2%) and 2 cases (0.9%) showed losses of at least 3 MMR proteins and all 4 proteins, respectively. Kaplan-Meier analysis revealed no significant associations between loss of MLH1 (P = 0.37), MSH2 (P = 0.35), MSH6 (P = 0.96), or PMS2 (P = 0.67) or at least one (P = 0.46), 2 (P = 0.49), or 3 (P = 0.35) MMR proteins and biochemical recurrence.

Conclusions: MMR protein loss was seen in a subset of PCs. Interestingly, it was associated with significantly higher levels of PSA. However, immunohistochemical detection of MMR proteins in our PC tissue microarray was found to be not very helpful in predicting tumor recurrence following radical prostatectomy.

Expression of Estrogen Receptor-B, Glucocorticoid Receptor, and FOXO1 in Nonmuscle-Invasive Bladder Tumors and Its Prognostic Significance

(Poster No. 114)
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Context: Recent evidence suggests that steroid hormone receptor signals, including estrogen receptor β (ERβ) and glucocorticoid receptor (GR), are implicated in the outgrowth of urothelial cancer. This study aimed to determine the role of ERβ/GR expression in nonmuscle-invasive bladder tumors in predicting patient outcomes.

Design: We immunohistochemically stained for ERβ and GR, as well as a transcriptional factor/potential tumor suppressor FOXO1, known to physically interact with ERβ/GR, in a set of tissue microarray consisting of 75 nonmuscle-invasive bladder tumors. We then evaluated the relationship between their expression and the prognosis.

Results: ERβ and GR were positive in 18 (24.0%; all weak [1+] and 72 (96.0%; 18 [24.0%] 1, 32 [42.7%] moderate [2+], and 22 [29.3%] strong [3+] tumors, respectively, whereas FOXO1 was positive in 14 (18.7%); all 1+ tumors. Kaplan-Meier analysis and log-rank test revealed that patients with ERβ/GR (2+/3+) tumors had significantly higher rates of recurrence-free survival, compared with those with ERβ/GR (2+/3+) tumors (P = 0.03). However, there was no significant difference in recurrence-free survival between ERβ/GR (0/1) versus ERβ/GR (0/1) tumors (P = 0.66). Similarly, a significant difference in recurrence-free survival was detected between ERβ/GR (2+/3+) versus FOXO1+ versus ERβ/GR (2+/3+) versus FOXO1+ tumors (P = 0.046), but not between ERβ/GR (2+/3+) versus ERβ/GR (2+/3+) versus FOXO1+ tumors (P = 0.23). Meanwhile, no significant associations between ERβ/GR/FOXO1 expression and disease progression defined as the development of muscle-invasive tumor or metastasis, were found.

Conclusions: These findings suggest that inhibition of ERβ signals may prevent urothelial tumorigenesis and/or disease recurrence, especially in patients with nonmuscle-invasive bladder tumors showing strong GR expression. Moreover, FOXO1 may contribute to the interplay between ERβ and GR signals in urothelial cells.

Immunohistochemistry of Latrophilin-3 as a Prognosticator in Bladder Cancer

(Poster No. 115)
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Context: Others and we have indicated that androgen-mediated androgen receptor (AR) signaling has a critical role in urothelial tumorigenesis and cancer progression. Meanwhile, our DNA microarray data suggest that latrophilin-3 (LPHN3) represents a downstream effector of AR in bladder cancer cells. LPHN3 is a G-protein–coupled receptor in which a spider venom latrotoxin binds, and whose genetic alterations have been linked to attention-deficit hyperactivity disorder that is diagnosed approximately 3 times more often in boys than in girls.

Design: We immunohistochemically stained for LPHN3 in 145 bladder tumors and paired nonneoplastic bladder tissues. We then evaluated the relationship between its expression and clinicopathologic features of our patient cohort.

Results: LPHN3 was positive in 52% (47%, 1+; 5%, 2+) of tumors, which was significantly (P = 0.049) higher than in nonneoplastic urothelial tissues (37%, all 1+). However, there were no significant associations between LPHN3 expression and tumor grade or pT/pN stage. As expected, there was a trend to correlate between AR and LPHN3 expression in tumors (P = 0.06). In addition, Kaplan–Meier analysis and a log-rank test revealed strong associations of LPHN3 positivity with the recurrence of nonmuscle-invasive tumors (P = 0.08) as well as disease progression (P = 0.009) or cancer-specific mortality (P = 0.008) in patients with muscle-invasive tumors. Multivariate analysis further identified LPHN3 immunoreactivity as an independent prognosticator in muscle-invasive tumors [hazard ratio, 2.485 (P = 0.02] for progression; hazard ratio, 2.869 [P = 0.03] for mortality.

Conclusions: LPHN3 expression is upregulated in bladder tumors and is correlated with AR expression. Moreover, immunohistochemical detection of LPHN3 is found to be useful for predicting the recurrence and progression of bladder cancer.

TFB-Mutated Melanotic Renal Cell Carcinoma

(Poster No. 116)
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MiT family translocation tumors are a group of neoplasms characterized by nested epithelioid cells, melanin pigmentation, staining for melanocytic markers, and a young age. To date, only a few cases have been reported. Herein, we report a case of melanotic renal cell carcinoma presenting in an older patient. The patient is a 59-
year-old man who presented with severe inguinal hidradenitis and was incidentally found to have a renal mass. On imaging, the mass was enhancing with a mixed cystic/solid appearance. Grossly, a 4-cm, yellow to tan-gray, heterogeneous mass centered within the renal pelvis was present. Microscopically, it was predominantly solid with occasional cystic areas and was formed of cells with abundant eosinophilic cytoplasm and scattered cytoplasmic clearing. Occasional dark-brown granular pigments along with scattered multinucleated giant cells were present. Numerous calcifications were noted. Immunohistochemically, the tumor was positive for Melan-A, cathepsin K, cytokeratin AE1/AE3, CK7, and EMA and was negative for CK20, desmin, caldesmon, and TFE3. Fluorescence in situ hybridization analysis for TFE3 translocation was negative; however, TFE3 immunostain was positive. Fontana-Masson stain and bleach preparation confirmed the presence of melanin pigment. No lymph node metastasis was present. On follow-up, the patient is still alive and free of disease at 11 months after nephrectomy. In summary, this case illustrates an unusual age of presentation and highlights the importance of confirming the diagnosis.

**Postinfectious Glomerulonephritis and Membranoproliferative Glomerulonephritis With Exclusive or Dominant C3 Versus True C3-Glomerulopathy (C3G)? A Diagnostic Dilemma**

*(Poster No. 117)*

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**Context:** C3G is a recently introduced entity resulting from dysregulation in the alternative pathway of the complement-activating system. Diagnostic criteria of C3G, based on the 2013 consensus report, includes C3 immunofluorescence stain that is 2 orders of magnitude greater than any other immune reactants on a scale of 0 to 3. Our study presents a diagnostic conundrum encountered in clinical practice of accurately classifying heterogeneous groups of immune-mediated glomerulonephritis that mimic C3G based on immunofluorescence stain pattern.

<table>
<thead>
<tr>
<th>Comparison of Morphologic Findings Between Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Membranoproliferative Glomerulonephritis</strong></td>
</tr>
<tr>
<td><strong>(17 Cases), No. (%)</strong></td>
</tr>
<tr>
<td>C3 Group (n = 7)</td>
</tr>
<tr>
<td>Non-C3 Group (n = 10)</td>
</tr>
<tr>
<td>Neutrophils</td>
</tr>
<tr>
<td>2 (29)</td>
</tr>
<tr>
<td>P = .94</td>
</tr>
<tr>
<td>Crescents</td>
</tr>
<tr>
<td>0 (0)</td>
</tr>
<tr>
<td>P = .05</td>
</tr>
<tr>
<td>Subendothelial deposits</td>
</tr>
<tr>
<td>3 (20)</td>
</tr>
<tr>
<td>P = .20</td>
</tr>
<tr>
<td>Mesangial deposits</td>
</tr>
<tr>
<td>7 (78)</td>
</tr>
<tr>
<td>P = .92</td>
</tr>
<tr>
<td>Subepithelial deposits</td>
</tr>
<tr>
<td>7 (70)</td>
</tr>
<tr>
<td>P = .99</td>
</tr>
<tr>
<td>Tubuloreticular structures</td>
</tr>
<tr>
<td>1 (11)</td>
</tr>
<tr>
<td>P = .44</td>
</tr>
<tr>
<td>&quot;Humplike&quot; deposits</td>
</tr>
<tr>
<td>0 (0)</td>
</tr>
<tr>
<td>P = .99</td>
</tr>
</tbody>
</table>

Note: There was no significant difference in all measurements (χ² test, α = .05).

**Design:** A retrospective review of kidney biopsy reports from 2005 to 2018 identified 62 immune-mediated glomerulonephritides; 18 cases (29%) met the diagnostic criteria of C3G, designated as the C3 group. Statistical analysis between the different groups was performed using the χ² test (P<.05).

**Results:** Of the 62 immune-mediated glomerulonephritides, 14 (23%) were postinfectious glomerulonephritis (PIGN), and 17 (27%) were membranoproliferative glomerulonephritis (MPGN). Nine of 14 PIGN (64%) and 7 of 17 MPGN (41%) qualified for classification as C3G based on immunofluorescence stain criteria. Histologic and electron microscopic findings of C3 and non-C3 groups of PIGN and MPGN were compared, and there were no morphologic features differentiating these 2 groups (Table).

**Conclusions:** Exclusive/predominant C3 deposits in isolation can be seen in significant numbers of PIGN and MPGN cases, although these may not necessarily indicate defective alternative pathway-mediated disorders. Given the absence of morphologic differences and lack of readily available/cost-effective methods to detect alternative pathway deregulation, differentiating true C3G from other PIGN/MPGN can be challenging, particularly in light of differing prognostic and therapeutic implications, warranting comprehensive/total complement serum analysis in these patients.

Collision Tumor of Urothelial Carcinoma With Clear Cell Papillary Renal Cell Carcinoma

*(Poster No. 118)*

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Collision tumors are composed of independent but concurrent tumors with distinct cell lineage that grow into one another. The presence of concurrent urothelial carcinoma (UCa) with clear cell (conventional) renal cell carcinoma (RCC) has been previously described. However, to our knowledge, the association of UCa with clear cell papillary RCC has not yet been reported. The case involves a 78-year-old man with a history of heavy smoking and complex urologic conditions including a right renal mass, bilateral stents for hydronephrosis and a filling defect in the right proximal ureter. The patient underwent diagnostic ureteroscopy and biopsy of the right ureteral mass, which demonstrated a high-grade UCa with squamous differentiation. He subsequently underwent a nephroureterectomy. Gross examination showed an 8.0-cm tan-white, ill-defined mass in the renal pelvis and an adjacent 1.5-cm, tan-pink, well-circumscribed mass in the lower pole. The renal pelvic mass was a high-grade UCa with extensive squamous differentiation. The lower-pole mass exhibited features of a clear cell papillary RCC characterized by tubular and papillary architectures lined by low-grade clear cells with linearly arranged nuclei (Figure 58). The tumor was diffusely positive for CK7 and was negative for AMACR and CD10 by immunohistochemistry, indicating a clear cell papillary RCC. Herein, we report the first case of a renal collision tumor composed of UCa with extensive squamous differentiation and clear cell papillary RCC.
A Case Report of a Primary Mucinous Adenocarcinoma of the Prostatic Urethra: An Exceedingly Rare Diagnosis

(Poster No. 119)

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Mucinous adenocarcinoma of the prostatic urethra is exceedingly rare. The distinction from a conventional prostatic mucinous adenocarcinoma and secondary infiltration from a colonic or bladder adenocarcinoma can be diagnostically challenging. We present a case of a 78-year-old African-American man who presented with urinary retention, hematuria, and mucosuria. Computed tomography scan showed an enlarged prostate with a localized abnormal 3-cm area in the right lobe and a prostate-specific antigen of 1.77 ng/mL. An initial diagnosis of prostatic duct adenocarcinoma and mucinous adenocarcinoma was made on transurethral resection of bladder tumor. Subsequent investigations did not reveal any tumor in the urinary bladder or colon. The patient then underwent cystoprostatectomy with bilateral pelvic lymph node dissection. Gross examination revealed a markedly dilated prostatic urethra with an ill-defined mass with a mucoid cut surface centered around the prostatic urethra (Figure 59, A and B). Microscopic examination revealed a mucinous adenocarcinoma with dissecting mucin and signet-ring cells in a background of extensive glandular and papillary intestinal metaplasia with dysplasia of the prostatic urethra (Figure 59, C and D). The tumor was positive for CK7, CK20, and CDX2 and negative for NKX3.1 and GATA-3. No prostatic acinar or ductal adenocarcinoma was identified. The patient remained cancer free at 3 months at surgery. In contrast to mucinous adenocarcinoma of the prostate, mucinous adenocarcinoma of the prostatic urethra is characterized by extracellular dissecting mucin, signet cells, and lack of expression for NKX3.1. The distinction has therapeutic implications because hormonal therapy is not recommended for mucinous adenocarcinoma of the prostatic urethra in contrast to conventional prostatic adenocarcinoma with mucinous features.

Clear Cell Papillary Renal Cell Carcinoma in a Case of Transplanted Kidney

(Poster No. 120)

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Clear cell papillary renal cell carcinoma (CCPRCC) is a recently recognized entity. Rare cases of CCPRCC have been recognized in allograft kidney, accounting for 3% of renal cell carcinoma (RCC) in transplanted kidneys according to limited literature. Because of overlapping morphology, it may be misdiagnosed as other subtypes of RCC with clear cell changes or papillary architecture. Here we report on a 63-year-old woman with a history of Fabry disease with cardiomyopathy, end-stage renal disease after deceased donor kidney transplantation 19 years earlier with chronic rejection, who presented for evaluation and management of 2 large masses in the transplanted right kidney. She underwent intervention radiology embolization of the transplanted kidney with simultaneous permcath placement for hemodialysis, followed by right nephrectomy of transplanted kidney. Histology showed small tubules and papillae composed of neoplastic cells with clear cytoplasm and characteristic linear arrangement of apically displaced low-grade nuclei. By immunohistochemistry, the neoplastic cells were positive for CD10 (diffuse and strong), EMA (diffuse and strong), vimentin, E-cadherin, and PAX8 (focal) and were negative for CD10, racemase, and CD117. The morphology and immunohistology profile were most consistent with CCPRCC (2 foci, 6 cm and 11.2 cm). No sarcomatoid areas were identified despite the presence of extensive necrosis, which is likely due to ischemia caused by the combination of the large tumor size and the chronic rejection. CCPRCC is an indolent renal epithelial neoplasm. Therefore, it is of crucial importance to differentiate CCPRCC from other subtypes of RCC to ensure appropriate treatment plan.

Crescentic Glomerulonephritis: A Confounding Initial Presentation of a Female Infant With Denys Drash Syndrome

(Poster No. 121)

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Denys-Drash syndrome (DDS) is a rare cause of steroid-resistant nephrotic syndrome typically associated with a de novo mutation in the WT1 gene. DDS is characterized by a triad of male pseudohermaphroditism, steroid-resistant nephrotic syndrome because of diffuse mesangial sclerosis, and risk of Wilms tumor. Females (karyotype XX) with this syndrome have normal female genitalia leading to under-recognition. An 8-month-old girl was transferred to our facility with acute oligoanuric renal failure, respiratory failure, hypoalbuminemia, and severe metabolic acidosis. Renal biopsy revealed crescentic glomerulonephritis with tubulointerstitial nephritis (Figure 60, A).

Immunofluorescence demonstrated C3 deposition (Figure 60, B) raising the possibility of C3 glomerulonephritis. With clinical diagnosis of acute renal failure, steroid therapy was initiated followed by dialysis. As urine output improved, nephrotic-range proteinuria was established. DNA sequencing for genes implicated in infantile nephrotic syndrome demonstrated a heterozygous missense mutation in the WT1 gene. DDS is characterized by a triad of male pseudohermaphroditism, steroid-resistant nephrotic syndrome because of diffuse mesangial sclerosis, and risk of Wilms tumor. Females (karyotype XX) with this syndrome have normal female genitalia leading to under-recognition. An 8-month-old girl was transferred to our facility with acute oligoanuric renal failure, respiratory failure, hypoalbuminemia, and severe metabolic acidosis. Renal biopsy revealed crescentic glomerulonephritis with tubulointerstitial nephritis (Figure 60, A).
Adenocarcinoma In Situ of the Rete Testis  
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(dr.khaile.alobaidy@gmail.com); Yu Yang, MD; Thomas M. Ulbright, MD. Department of Pathology, Indiana University, Indianapolis.

Adenocarcinoma of the rete testis is a rare testicular malignancy that was first described in 1945. It mostly occurs in middle-aged to older patients. Herein, we describe the first case of adenocarcinoma in situ of the rete testis. This noninvasive tumor occurred in a 73-year-old man who presented with testicular pain and was noted to have a mass within the right testis on preoperative imaging. Grossly, a 2.5-cm, well-encapsulated mass was noted. The mass was found to be a solid nodule that was fixed to the testicular hilium. Microscopically, the tumor was confined to the rete testis and showed focal transition from benign to malignant rete epithelium. It had papillary and solid architecture and formed columnar and epithelioid cells with abundant clear cytoplasm. The nuclei were round to oval, with moderate atypia, prominent nucleoli, and occasional mitotic figures. Psammomatous calcifications and necrotic foci, mostly round to oval, with moderate atypia, prominent nucleoli, and occasional mitotic figures. Psammomatous calcifications and necrotic foci, mostly round to oval, with moderate atypia, prominent nucleoli, and occasional mitotic figures. Psammomatous calcifications and necrotic foci, mostly round to oval, with moderate atypia, prominent nucleoli, and occasional mitotic figures. Psammomatous calcifications and necrotic foci, mostly round to oval, with moderate atypia, prominent nucleoli, and occasional mitotic figures. Psammomatous calcifications and necrotic foci, mostly round to oval, with moderate atypia, prominent nucleoli, and occasional mitotic figures.

Immunohistochemically, the tumor cells stained strongly for WT1 (nuclear), PAX8 (nuclear), and Ber-EP4 and focally for ER; they were negative for inhibin, napsin A, protein, p63, and SALL4. The nonneoplastic epithelium of the rete testis showed an identical immunostaining pattern. In summary, the immunomorphologic features supported the diagnosis of a primary intrarete papillary adenocarcinoma. Unlike the other published cases, this tumor was completely confined to the rete testis without evidence of stromal invasion. This case, in essence, therefore represents the first reported example of an “in situ” adenocarcinoma of the rete testis.

Renal Cell Carcinoma With Sarcomatoid Differentiation: Does the Underlying Primary Affection Prognosis?  
(Poster No. 123)

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Context: Renal cell carcinoma (RCC) is known to undergo epithelial-mesenchymal transformation, exhibiting a sarcomatoid differentiation (SD). Studies indicate that the presence of SD in RCC portends a poor prognosis. It is unclear whether the underlying primary histology affects prognosis. Here we assessed the association between SD and RCC subtypes.

Design: We extracted data from the Surveillance, Epidemiology and End Result (SEER) database (2010–2015) comprising 3 RCC subtypes with SD: clear cell, papillary, and chromophobe. Only records with microscopically confirmed diagnosis and active follow-up were considered. The Cox proportional hazard model was used to determine the relative importance of the prognostic parameters: age, stage, and histologic type.
Renal Cell Carcinoma With Extensive Rhabdoid Features: An Uncommon Case

(Poster No. 126)

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Adult renal cell carcinoma (RCC) with rhabdoid features is uncommon. RCC with rhabdoid differentiation exhibits aggressive behavior and poor prognosis. We report here the histologic and immunohistochemical findings of an RCC case with at least 90% of rhabdoid component. The patient was a 57-year-old woman who presented with hematuria, flank pain, and severe anemia. Computed tomography showed a 12.8 \times 11.8 \times 11.7-cm, left renal mass with inferior vena cava thrombus. The patient underwent a left radical nephrectomy with inferior vena cava thrombectomy. Gross examination of the specimen revealed a large superior-pole mass with multiple perinephric tumor deposits beyond Gerota fascia. Histologic studies showed the tumor arranged in sheets or nests with fine vascularity. The tumor was infiltrated with rhabdoid morphology comprised at least 90% of the tumor. Abundant necrosis and extensive vascular invasion were noted. Immunohistochemistry revealed the tumor was positive for PAX8 and CD10. The intensity of PAX8 and CD10 staining was positive for PAX8 and CD10. The intensity of PAX8 and CD10 staining was weak or moderate in rhabdoid tumor cells with marked nuclear pleomorphism and clear cytoplasm. The tumor was negative for CD117 and CK7. A diagnosis of clear cell RCC with extensive rhabdoid features was rendered. The awareness of decreased intensity of PAX8 and CD10 immunostaining in pleomorphic rhabdoid cells is important to identifying metastasis of RCC with rhabdoid features. This finding of different staining intensities of PAX8 and CD10 is first described here to our knowledge.


(Poster No. 127)

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Context: Multiparametric magnetic resonance imaging (mpMRI) enables targeted biopsy (TBx) of suspicious prostate lesions. mpMRI is interpreted using the Prostate Imaging Reporting and Data System (PIRADS), a 5-point scale rated from most probably benign (1) to most probably malignant (5). Ideally, mpMRI TBx should result in higher diagnostic yield of prostate cancer compared with conventional systematic biopsy. However, false-negative mpMRI have occurred in TBx of lesions scored PIRADS 4 or 5 resulting in benign pathology. The objective of our study was to elucidate the causes of the discrepancy in these cases.

Design: This single-institution, retrospective study included 171 prostate TBx from PIRADS 4/5 lesions that were microscopically negative for prostate cancer from 125 patients from July 2015 through October 2017. The percentage of these pathologic diagnoses was analyzed.

Results: The most-common diagnosis was normal prostatic glands and stroma (62%) with other benign findings comprising 38% of the total TBx (Z-score, 3.082; P = .001). Of these findings, inflammation (chronic or acute) was the most common (51%) followed by high-grade prostatic intraepithelial neoplasia (26%). Few TBx (2% of total) consisted of only benign stroma with no glands (Table).

Conclusions: At our institution, the most-common diagnosis for false-negative mpMRI PIRADS scores 4 or 5 was normal prostatic glands and stroma, which was statistically more common than all other benign findings combined (P = .001). The second most-common finding was inflammation (acute or chronic). Radiologically, false-negative TBx may be due to interpreter’s experience, mpMRI technical quality, or overcalling suspicious lesions. False-negative due to sampling error may be because of clinicians missing a radiologic lesion or the prostatic tissue entirely.

<table>
<thead>
<tr>
<th>Diagnostic Finding of Prostatic Gland Multiparametric MRIs</th>
<th>TBx Involved, No.</th>
<th>Total TBx, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign prostatic glands and stroma</td>
<td>106</td>
<td>62</td>
</tr>
<tr>
<td>Inflammation (chronic or acute)</td>
<td>33</td>
<td>19</td>
</tr>
<tr>
<td>High-grade prostatic intraepithelial neoplasia</td>
<td>17</td>
<td>10</td>
</tr>
<tr>
<td>Atrophy</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Benign prostatic stroma</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Atypical small acinar proliferation</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

PD-L1 Positivity Associated With Presence of Tertiary Lymphoid Structures and High-Stage Disease in Upper Tract Urothelial Carcinoma

(Poster No. 128)

Maria E. Smith, BS; Sarah J. Farahani, MD, MPH; Timothy Chao, PhD; Matthew B. Palmer, MD, PhD; Aileen G. Arriola, MD; Priti Lal, MD. Department of Pathology and Laboratory Medicine, Hospital of the University of Pennsylvania, Philadelphia; Department of Pathology and Laboratory Medicine, Temple University Hospital, Philadelphia.

Context: Persistent antigen exposure leads to accumulation of lymphocytes and subsequent lymphoid neogenesis or tertiary lymphoid structures (TLSs). TLSs have gained attention because of their association with progression in malignancy. We investigated the relationship of tumor microenvironment with respect to PD-L1, PD-1, cytotoxic T cells, and TLS in upper tract urothelial carcinoma (UTUC) only cases and compared them to UTUC associated with urothelial bladder carcinoma (UTUC + UBC).

Design: We retrospectively identified 72 patients with UTUC. Representative slides were reviewed, and TLSs were counted. Immunohistochemical stains for CD8 (clone C8/144B, Dako, Carpinteria, California), PD-L1 (E1J2J, Cell Signaling Technology, Danvers, Massachusetts), and PD-L1 (E1J2J, Cell Signaling Technology, Danvers, Massachusetts) were performed. CD8+ and PD-L1+ cells were counted, and an H score for PD-L1+ membranous staining was determined. Statistical analysis was performed with Stata 12 (StataCorp, College Station, Texas).

Tumor Characteristics and Key Statistical Findings Related to PD-L1 and PD-1

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Results, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UTUC only, n = 72</td>
<td>41 (56.9)</td>
</tr>
<tr>
<td>UTUC + UBC diagnosed in any order, n = 72</td>
<td>31 (43.1)</td>
</tr>
<tr>
<td>TLS present, n = 69</td>
<td>23 (33.3)</td>
</tr>
<tr>
<td>PD-L1 positivity in any compartment, n = 69</td>
<td>38 (55.1)</td>
</tr>
<tr>
<td>PD-L1 positivity in any compartment and presence of TLS OR 3.8; 95% CI</td>
<td>1.2–10.8; P = .02</td>
</tr>
<tr>
<td>PD-1+ cell counts and presence of TLS Difference of means, to –7.1; P = .01</td>
<td></td>
</tr>
<tr>
<td>PD-1+ cell counts and presence of PD-L1 in any compartment Difference of means, to 40.6; 95% CI –61.3 to 19.8; P &lt;.001</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: OR, odds ratio; TLS, tertiary lymphoid structure; UBC, urothelial bladder carcinoma; UTUC, upper tract urothelial carcinoma.
UTUC + UBC. TLSs were also associated with a greater number of infiltrating PD-1+ cells ($P = .01$; Table).

**Conclusions:** This is one of the first comparative studies of the tumor microenvironment in UTUC and in UTUC + UBC. We report the presence of TLSs in UTUC and provide insight into their association with PD-L1 expression. Future investigations are warranted to confirm that the presence of TLSs has an important role in immune modulation in UTUC.

**Renal Ectopic Lymphoid Mass in a Systemic Lupus Erythematosus Patient Mimicking Renal Cell Carcinoma**

*(Poster No. 129)*

Arash Lahouti, MD (alahoutha@northwell.edu); Alyssa Yurovitsky, MD; Michael A. Feuerstein, MD; Pamela D. Unger, MD. Department of Pathology, Lenox Hill Hospital, New York, New York.

Ectopic lymphoid tissues can develop in autoimmune diseases and are usually a microscopic finding. We report a case of a 48-year-old woman with a history of systemic lupus erythematosus (SLE) who was found to have a left lower-pole renal mass on computed tomography scan. Subsequent magnetic-resonance contrast studies showed a 3.3-cm mass adjacent to the renal vein demonstrating T2 heterogeneous after-contrast enhancement. The radiographic impression was a renal cell carcinoma, and she underwent radical nephrectomy. Gross examination revealed a 3.7-cm well-circumscribed white-pink fleshy mass located in the hilum (Figure 62, A). Microscopic examination of the mass revealed a lymphoid infiltrate involving the medulla and hilar adipose tissue consisting of B cells, T cells, plasma cells, and follicles with germinal center formation (Figure 62, B and C). Plasma cells showed polyclonal expression of $\kappa$ and $\lambda$ light chains. Remaining kidney showed patchy reactive lymphoid aggregates and occasional sclerosed glomeruli. Focal small-vessel vasculitis with fibrioid necrosis was seen surrounding the mass (Figure 62, D). Flow cytometry studies showed no evidence of a T-cell lymphoproliferative disorder. Although a small subset of B cells lacked light chain expression, a reactive process was favored. Epstein-Barr virus−encoding region studies by in situ hybridization were negative. Polymerase chain reaction studies did not show evidence of clonal B-cell gene rearrangement. The final diagnosis was reactive lymphoid mass. To our knowledge, this is the first case of renal ectopic lymphoid tissue producing a “tumor mass” in a patient with SLE mimicking renal cell carcinoma.

**Urothelial Carcinoma With Unusual Histologic Presentation: Combined Squamous and Rhabdoid Variants**

*(Poster No. 130)*

Dalia Ibrahim, MD, MSc (dalia.ibrahim@utoledo.edu); Abdelaof Al Agha, MPH, MBA, PA; Rana Shadid, MD; Nicole Dominiak, MD. Department of Pathology, University of Toledo Medical Center, Toledo, Ohio.

Invasive urothelial carcinoma illustrates broad cytoarchitectural variations. Urothelial carcinoma of urinary bladder with squamous differentiation or with rhabdoid differentiation is an aggressive variant that is associated with poor prognosis and poor response to therapy. Only a few cases of bladder urothelial carcinoma with squamous differentiation have been reported and only 2 cases with rhabdoid differentiation. However, review of the recent literature illustrates that there were no cases reported of bladder urothelial carcinoma with combined squamous and rhabdoid differentiation. We report a case of a 71-year-old woman who presented with acute renal insufficiency and bilateral hydronephrosis. Ultrasound and computed tomography scan were concerning for a bladder mass. Cystoscopy revealed an exophytic tumor in the bladder. Histologic examination showed invasive, high-grade urothelial carcinoma with squamous (Figure 63, A and B) and rhabdoid features (Figure 63, C and D). A positron emission tomography scan was performed for full staging, which showed increased radiotracer uptake in the left supraclavicular and retroperitoneal, periaortic, and mediastinal lymphadenopathy. Computed tomography scan showed bilateral pulmonary metastasis and pleural effusion. The clinicopathologic features of this case support the aggressive clinical behavior of urothelial carcinoma with squamous or rhabdoid differentiation and demonstrated a very rare case of combined squamous and rhabdoid features. Recognition of rare variants of urothelial carcinoma is imperative and not only has important prognostic and therapeutic implications but also presents diagnostic challenges in pathology practice.
However, Congo red demonstrated delicate deposits displaying green-looking glomeruli on hematoxylin-eosin and periodic acid–Schiff stains. Nephrotic range proteinuria. Renal biopsy showed essentially normal-treatment. We report on a 26-year-old man who presented with younger patients causing a challenge in diagnosis and delay in prevalent in older patients (older than 50 years) but is very rare in by deposition of monoclonal immunoglobulin light chain. It is most fourth cause of nephrotic range proteinuria and Congo red should be examined proactively because the amount of amyloid in the biopsies can be minimal despite extensive systemic disease. This case illustrates the dramatic and rapidly progressive AL amyloidosis in a young patient and emphasizes the role of a pathologist in early diagnosis (Figure 65).

Immunoglobulin light chain amyloidosis (AL) amyloidosis is caused by deposition of monoclonal immunoglobulin light chain. It is most prevalent in older patients (older than 50 years) but is very rare in younger patients causing a challenge in diagnosis and delay in treatment. We report on a 26-year-old man who presented with nephrotic range proteinuria. Renal biopsy showed essentially normal-looking glomeruli on hematoxylin-eosin and periodic acid–Schiff stains. However, Congo red demonstrated delicate deposits displaying green birefringence under polarized light. Electron microscopy showed fibrillary deposits of amyloid in the mesangial areas and rare segments of glomerular basement membrane forming subepithelial spikes. By immunofluorescence the deposits were λ restricted, and the diagnosis of AL-λ amyloidosis was made. Bone marrow biopsy revealed 20% λ-restricted plasma cells and deposits of amyloid in the bone marrow stroma. The patient’s clinical course rapidly deteriorated with development of marked malabsorption, weight loss, and elevated troponins.

Cardiac magnetic resonance imaging suggested cardiac amyloidosis and a gastrointestinal biopsy proved presence of extensive amyloid deposits in the lamina propria, submucosa, and vessel walls in several sites. Despite initial improvement with chemotherapy, the patient developed sepsis with multiorgan failure and died 5 months after his initial presentation with proteinuria. In nondiabetic adults, amyloidosis is the fourth cause of nephrotic range proteinuria and Congo red should be examined proactively because the amount of amyloid in the biopsies can be minimal despite extensive systemic disease. This case illustrates the dramatic and rapidly progressive AL amyloidosis in a young patient and emphasizes the role of a pathologist in early diagnosis (Figure 65).

A Strikingly Quick and Deadly Progression of Immunoglobulin Light Chain Amyloidosis in a Young Individual

(Poster No. 132)

Sulaiman Farooqui, DO, Sara Javidiparsijani, MD, Jamie Chin-Theodorou, MD, Maria Picken, MD, PhD. Departments of Pathology and Internal Medicine, Loyola University Medical Center, Maywood, Illinois.

Immunoglobulin light chain amyloidosis (AL) amyloidosis is caused by deposition of monoclonal immunoglobulin light chain. It is most prevalent in older patients (older than 50 years) but is very rare in younger patients causing a challenge in diagnosis and delay in treatment. We report on a 26-year-old man who presented with nephrotic range proteinuria. Renal biopsy showed essentially normal-looking glomeruli on hematoxylin-eosin and periodic acid–Schiff stains. However, Congo red demonstrated delicate deposits displaying green birefringence under polarized light. Electron microscopy showed fibrillary deposits of amyloid in the mesangial areas and rare segments of glomerular basement membrane forming subepithelial spikes. By immunofluorescence the deposits were λ restricted, and the diagnosis of AL-λ amyloidosis was made. Bone marrow biopsy revealed 20% λ-restricted plasma cells and deposits of amyloid in the bone marrow stroma. The patient’s clinical course rapidly deteriorated with development of marked malabsorption, weight loss, and elevated troponins. Cardiac magnetic resonance imaging suggested cardiac amyloidosis and a gastrointestinal biopsy proved presence of extensive amyloid deposits in the lamina propria, submucosa, and vessel walls in several sites. Despite initial improvement with chemotherapy, the patient developed sepsis with multiorgan failure and died 5 months after his initial presentation with proteinuria. In nondiabetic adults, amyloidosis is the fourth cause of nephrotic range proteinuria and Congo red should be examined proactively because the amount of amyloid in the biopsies can be minimal despite extensive systemic disease. This case illustrates the dramatic and rapidly progressive AL amyloidosis in a young patient and emphasizes the role of a pathologist in early diagnosis (Figure 65).

### Unusually Large, Cystic Synovial Sarcoma of Kidney

(Poster No. 133)

Isma Noaman, FCPS (isma.noaman@sihs.org.pk); Sania Shuja, MD, PhD; Muhammad I. Nazir, MD. Department of Pathology, Shalamar Institute of Health Sciences, Lahore, Pakistan.

Primary synovial sarcoma of the kidney is an extremely rare tumor with a reported mean size of approximately 7 cm. Here we present a case of an unusually large-sized (32 cm) synovial sarcoma of the kidney, which, to our knowledge, has not been previously reported in the English literature. A 33-year-old man presented with massive abdominal distension for the previous 6 months. High-resolution computerized tomography (HRCT) showed a large cystic mass in the abdomen measuring 32 × 28 × 20 cm, which appeared to arise from the right kidney, displacing the inferior vena cava and aorta. The patient underwent right nephrectomy, and a multicystic tumor was removed in multiple pieces. Pathologic examination showed a biphasic, malignant neoplasm with cystic and mesenchymal components. The cystic component was lined by hobnail epithelial cells and the mesenchymal component was composed of overtly malignant spindle cells with numerous mitoses including atypical mitoses. The neoplastic cells revealed positive staining for PAX8, TLE1, CK, and EMA and negative staining for CD99, WT1, and CD34. Fluorescence in situ hybridization to detect the t(X; 18), although the diagnostic gold standard, was not performed because of nonavailability in our setup.

### Metastatic Clear Cell Adenocarcinoma of the Prostate: A Diagnostic Quandary

(Poster No. 134)

Linh Ho, MD (Linh.Ho@ucdenver.edu); Julene Moore, MD; Lian Zhang, MD; Ann Thor, MD; Francisco G. La Rosa, MD. Department of Pathology, School of Medicine, University of Colorado Anschutz Medical Campus, Aurora.

Clear cell prostatic adenocarcinoma is extremely rare and has only been described in a few case reports. Hence, metastatic lesions pose diagnostic challenges because of their rarity and because they show similar histopathology to clear cell carcinomas from other tissue origins. We present the case of a 73-year-old man with right hip pain who was found to have L3 to L4 vertebral lesions by magnetic resonance. Cytopathology evaluation of a computed tomography–guided fine-needle aspiration of that lesion revealed epithelioid cells with enlarged nuclei and prominent nucleoli (Figure 66, A; Papanicolaou smear), and hematoxylin-eosin paraffin sections showed clusters or sheets of a clear cell tumor (Figure 66, B), which stained positive for CD10, leading to the initial diagnosis of metastatic clear cell renal cell carcinoma. However, imaging studies showed no renal lesions, and further laboratory analysis detected a markedly elevated prostate-specific antigen of 68 ng/mL. Follow-up prostate biopsies revealed bilateral widespread prostatic adenocarcinoma, Gleason grade 5 + 4 (score = 9; grade-group 5) with multifocal perineural invasion and extraprostatic extension. This cancer showed focal areas of clear cell morphology, involving approximately 20% of the tumor (Figure 66, C). A retrospective staining for prostate-specific antigen of the bone
metastasis was strongly positive (Figure 66, D), as well as for prostate-specific alkaline phosphatase and racemase; tumor cells were negative for pax6, confirming that the metastatic lesion was of prostatic origin. Pathologists need to be aware that metastatic clear cell tumors may originate from different genitourinary tract tissues, requiring different treatment options. Thus, a diligent review of clinical history, as well as radiographic and laboratory correlations are required for correct interpretation.

**Is Pyelitis Glandularis of Intestinal Type a Precancerous Lesion? A Rare Case of Adenocarcinoma of the Renal Pelvis in a Patient With Long-standing Chronic Pyelonephritis**  
(Poster No. 135)

Behtash Nezami, MD1 (behtash.nezami@uhhospitals.org); Gregory MacLennan, MD,2 1Department of Pathology, University Hospitals Cleveland Medical Center/Case Western Reserve University, Beachwood, Ohio; 2Department of Pathology, University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, Ohio.

Urothelium in any part of the urinary collecting system may undergo glandular metaplasia. When the metaplastic change includes the presence of goblet cells, it is termed intestinal metaplasia. The condition may be described as cystitis glandularis, ureteritis glandularis or pylitis glandularis, depending upon its location. There has been debate regarding the premalignant potential of cystitis glandularis of intestinal type (CGIT), stimulated by intermittent reports that implicate CGIT as a precursor of adenocarcinoma. We report an exceptionally rare case of adenocarcinoma of the renal pelvis that arose in a setting of pylitis glandularis and adenocarcinoma in situ of the renal pelvis. A 47-year-old man with a history of spina bifida and neurogenic bladder since birth, requiring cystectomy with ileal conduit in childhood, presented with fevers, chills, and purulent drainage from a cutaneous fistula in the right flank, with associated cellulitis. Abdominal computed tomography scan disclosed a multiloculated cystic and solid renal mass. Biopsies of the mass revealed adenocarcinoma that expressed CDX2 and CK20. A right nephrectomy was performed. The kidney contained a 9.0-cm poorly circumscribed tan-white irregular mass arising within the upper collecting system of the kidney, extensively obliterating the renal parenchyma and extending into the perirenal adipose tissue. The adenocarcinoma appeared to have arisen in a background of extensive pyelitis glandularis of the intestinal type, in some areas merging with adenocarcinoma in situ. The kidney showed extensive xanthogranulomatous pyelonephritis. This case is another example of adenocarcinoma that appears to have arisen in association with very long-standing inflammation, complicated by development of urothelial intestinal metaplasia (Figure 67).

**Smooth Muscle Hyperplasia of the Testicular Adnexa: A Clinicopathologic Study of 12 Cases**  
(Poster No. 137)

Fatimah Alruwaii, MBBS (falruwai@iupui.edu); David Grignon, MD. Department of Pathology, Indiana University School of Medicine, Indianapolis.

**Context:** Smooth muscle hyperplasia of the testicular adnexa (SMH-TA) is a rare mass-forming intrascrotal lesion. Herein, we discuss our experience over a period of 13 years.

**Design:** Twelve SMH-TA cases were found. The morphologic features were reviewed, and clinical information was obtained.

**Results:** The mean age was 51 years (range, 24–82 years). Five cases were right sided, six were left sided and the laterality was unknown for one. Six patients presented with orchialgia as the sole symptom. Two had a concurrent incarcerated inguinal hernia and one had a recent trauma. The remainder of the patients presented with mass (n = 6) with or without pain. Six patients have undergone ultrasound imaging, which showed a mass (n = 4), hematoxylin (n = 1), or no abnormalities (n = 1). Six patients had previous surgeries in the inguinal region (varicocelectomy, spermatocelectomy, orchiopexy, vasectomy, and hernia repair). Other potential contributing factors included histories of epididymitis (n = 2), concurrent inguinal hernias (n = 2), organizing hematomas (n = 2), epididymal cysts (n = 2), undescended tests (n = 1), ischemic scar (n = 1), and granulomatous vasculitis (n = 1). Grossly, the mean size was 1.7 cm. The lesions had ill-defined, focally cystic, pink-tan nodular surfaces. Microscopically, the lesions were composed of vaguely nodular and ill-
A Case Report of an Incidental Synchronous Renal Neoplasm: A Collision Tumor of Clear Cell Renal Cell Carcinoma, Papillary Renal Cell Carcinoma, and Oncocytoma

(Poster No. 138)

Michelle M. McDonald, DO (Michelle.M.McDonald@uth.tmc.edu); Brenda Mai, MD, MBA; Gustavo E. Ayala, MD. Department of Pathology and Laboratory Medicine, University of Texas Health Science Center, Houston.

Synchronous neoplasms arising in the kidney are rare. To our knowledge, we present the first case report of 2 malignant renal cell carcinomas in collision with a renal oncocytoma in an ipsilateral kidney. A 61-year-old man presented to the emergency department with abdominal pain several days after undergoing a Nissen fundoplication. Further evaluation revealed a bowel perforation with an intra-abdominal abscess. On imaging, an incidental heterogeneous enhancing mass measuring 6.0 x 4.0 x 3.9 cm within the superior pole of the right kidney was identified, concerning for renal cell carcinoma (RCC). Subsequently, the patient underwent a partial nephrectomy and sectioning of the specimen revealed a 5.5 x 3.7 x 3.4-cm variegated yellow hemorrhagic cystic multiloculated mass with necrosis (Figure 69, A). The tumor extended grossly into the perirenal adipose tissue and into major vessels. Histologic examination of the specimen revealed a collision tumor comprising a clear cell RCC (Figure 69, B), oncocytoma (Figure 69, C), and papillary RCC (Figure 69, D). There was positive staining for PAX8 in all 3 masses. RCC antigen and AMACR were positive in the clear cell RCC only whereas CK7 was positive only in the oncocytoma and AMACR was positive in the papillary RCCs; it was deemed that there was aberrant staining of AMACR in the clear cell RCC. CAIX was positive in the clear cell RCC only whereas CK7 was positive only in the papillary RCC. Identification and classification of synchronous tumors is important for radiologic interpretation, preoperative biopsies, and fine-needle aspirations, gross examinations and sampling techniques, and prognostic determination.

Histopathologic Features of Prostate Cancer Not Detected on Magnetic Resonance Imaging: Radical Prostatectomy Findings on 33 Cases

(Poster No. 140)

Kanika Taneja, MD1 (ktaneja1@hfhs.org); Mustafa M. Deeabajah, MD2; Mohamed Alhmar, MD; Shaheen Alaneed, MD2; Sean R. Williamson, MD3; Nilesh S. Gupta, MD.1 Departments of 1Pathology and Laboratory Medicine and 2Urology, Henry Ford Health System, Detroit, Michigan.

Context: The association between regions of interest (ROI) identified through magnetic resonance imaging (MRI) of the prostate and radical prostatectomy (RP) findings has been extensively studied. However, the pathology of prostate cancer (PCA) that does not produce visible changes on magnetic resonance imaging (MRI) is not well characterized.

Invasive Stratified Mucin-Producing Carcinoma of the Penis: An Unusual Entity in a Rare Location

(Poster No. 139)

Maira Gaffar, MD1 (mgaffar@ufl.edu); Jennifer Reppucci, DO2; Ashwini Eknakula, MD3; Sara Falzarano, MD1; Padraic O’Malley, MD2; Michael Feely, DO1. Departments of 1Pathology and 2Urology, University of Florida, Gainesville.

Invasive stratified mucin-producing carcinoma (ISMC) and its in situ counterpart stratified mucin-producing intraepithelial lesion (SMILE) are uncommon entities of the uterine cervix. Although currently classified as a variant of adenocarcinoma by the World Health Organization, the precise histogenesis is largely unknown. Although these lesions are infrequently appreciated in the gynecologic tract, only 2 reported cases have been recognized within the penis. To increase awareness of this entity, we report the case of an ISMC arising in the penis of a 76-year-old man. After presenting with a foreskin lesion, the patient underwent circumcision at an outside facility with initial reporting of his pathology as invasive squamous cell carcinoma. Upon internal review, foci of glandular differentiation were noted. The patient went on to develop a recurrence of that mass involving his glans penis and distal shaft. A radical penectomy was performed with the resulting tumor demonstrating infiltrating sheets, nodules, and trabeculae of polygonal tumor cells with vesicular chromatin and prominent nucleoli. Scattered tumor cells exhibited intracytoplasmic mucin vacuoles (Figure 70, A and B), highlighted with a mucicarmine stain (Figure 70, C and D). Immunohistochemical studies revealed expression of both P63 and MOC31 with no reactivity for P16. In situ hybridization studies were negative for human papilloma virus (HPV) serotypes 16, 18, 31, 33, and 51 as well as HPV E6/E7 or MAML2 rearrangements. Given these features, a diagnosis of ISMC of the penis was rendered. This case demonstrates that ISMC may be unrelated to HPV in the penis and that these lesions can show divergent differentiation exemplified by expression of both P63 and MOC31.
**Design:** We performed a retrospective study of MRls performed for clinical suspicion of PCA between 2015 and 2018 to identify patients who had PCA on ultrasound-guided prostate biopsy but did not have any ROI identified on an MRI of the prostate. We then retrieved the pathology slides on these prostatectomies to characterize their morphology.

**Results:** During our study period, preoperative MRI was performed on 120 patients with RP, and 33 patients (21%) with PCA did not have an ROI identified in patients with myeloma and is the most common cause of acute renal failure for those patients. Herein, we present the case of a 60-year-old woman with Crohn disease and hypertension who presented with an acute rise in serum creatinine of unknown etiology, from a baseline of 0.97 mg/dL to 4.2 mg/dL, over a 6-week period. The most common pattern was infiltrative growth with cancer glands intermingling between benign glands. Ten of 33 patients (30%) had extraprostatic disease (9 of 33, PT3a; 1 of 33 PT3b).

**Conclusions:** Our study outlines the limitations of MRI because some clinically significant PCAs may not be detected. Clinicians should be aware of this limitation and pay attention to other preoperative variables in their decision making and management of patients with PCA.

## A Case of Light Chain Myeloma Cast Nephropathy Associated With Congo Red–Positive, Nonamyloid Lamellated Casts in a Patient With Multiple Myeloma

**Poster No. 141**

Marc A. Rodriguez, MD; Dereen Mohammed Saeed, MD (dmoham9@uic.edu); Frederick Behn, MD; Suman Sethy, MD, PhD. Department of Pathology, University of Illinois, Chicago.

The most common incidence of cancer globally for men is prostate cancer (PCa)—1.4 million cases annually. The incidence of PCa has been growing in Asian countries, partially because of comprehensive implementation of early detection systems. Interestingly, a large prospective cohort study showed that the Westernized dietary pattern was associated with a greater risk of total PCa among Japanese men. In this study, we compare the clinicopathologic features of PCa between patients in the United States and in China.

## Comparison of Clinicopathologic Features of Prostate Cancer Between Patients in the United States and in China

**Poster No. 143**

Rong Xia, MD, PhD (rongshya@gmail.com); Xiaoyan Liu, MD; Fei Chen, MD; Jia Bao, PhD; Yongzhou Shao, PhD; Dongwen Wang, MD; Xin Wang, MD; Xian Lu, MD; May T. Tun, MD; Jonathan Melamed, MD; Hebert Lepor, MD; Peng Lee, MD, PhD; Fang-Ming Deng, MD, PhD; Guoqing Ren, MD, MD. Department of Pathology, State University of New York Downstate Medical Center, Brooklyn; Department of Pathology, The First Hospital of Zhejiang University, Zhejiang, China; Departments of Pathology, Biostatistics, and Urology, New York University School of Medicine, New York; Department of Urology, The First Hospital of Shanshi Medical University, Shanshi, China.

**Context:** The most common incidence of cancer globally for men is prostate cancer (PCa)—1.4 million cases annually. The incidence of PCa has been growing in Asian countries, partially because of comprehensive implementation of early detection systems. Interestingly, a large prospective cohort study showed that the Westernized dietary pattern was associated with a greater risk of total PCa among Japanese men. In this study, we compare the clinicopathologic features of PCa between patients in the United States and in China.

### Comparison of Clinicopathologic Features of Prostate Cancer Between Patients in the United States and in China

<table>
<thead>
<tr>
<th></th>
<th>United States (n = 299)</th>
<th>China (n = 414)</th>
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<tbody>
<tr>
<td><strong>Mean</strong></td>
<td><strong>SD</strong></td>
<td><strong>Mean</strong></td>
</tr>
<tr>
<td>Age</td>
<td>63.53</td>
<td>7.10</td>
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<tr>
<td>Prostate-specific antigen</td>
<td>6.30 (4.90, 9.20)</td>
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### Prostate-specific antigen

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</tr>
<tr>
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<td>15</td>
<td>5.03</td>
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<tr>
<td>5</td>
<td>36</td>
<td>12.08</td>
<td>51</td>
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### Extraprostatic extension

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<th>%</th>
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<tr>
<td>1</td>
<td>120</td>
<td>40.13</td>
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</tr>
<tr>
<td>2</td>
<td>52</td>
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### Positive surgical margin

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<th>No.</th>
<th>%</th>
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<tr>
<td>1</td>
<td>18</td>
<td>6.04</td>
<td>68</td>
<td>16.43</td>
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<td>5</td>
<td>36</td>
<td>12.08</td>
<td>51</td>
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### Stage

<table>
<thead>
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<th>T3 (3, 3a, 3b)</th>
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<th>Lymph node metastasis</th>
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<td>126</td>
<td>1</td>
<td>26</td>
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<td>260</td>
<td>148</td>
<td>5</td>
<td>24</td>
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<td>4</td>
<td>62.80</td>
<td>35.75</td>
<td>1.21</td>
<td>5.80</td>
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### Design

Case cohorts included 713 PCa prostatectomy cases sequentially treated since 2016, including 299 cases from the United States, and 414 cases from 2 different teaching hospitals in China. The parameters including patient’s age, preoperative prostate-specific immunohistochemical stains were supportive of the diagnosis of SDH RCC. The mass was negative for CK7 and CAIX and positive for EMA and racemase, as well as staining a patchy positive for CD117 and CD10, and importantly, immunohistochemical stains of multiple sections of the mass showed a lack of SDHB staining. This case is unusual because of the large size of the tumor at diagnosis, compared with the average size of 5.1 cm reported in current literature. A careful histologic examination and awareness of such a rare tumor particularly in young patients are instrumental for the correct diagnosis, prompt genetic evaluation, and proper management.
antigen (PSA) level, Gleason score, grade group, stage and focality were analyzed and compared using 2-sample t tests, the Wilcoxon rank sum test, the Pearson $\chi^2$ test, and the Fisher exact test.

**Results:** Significant difference were demonstrated in the mean age of patients, the preoperative PSA, the extracapsule extension, the Gleason scores, and the grade groups (Table). Patients with PCs in the Chinese group were older than patients in US group ($P < .05$). The preoperative PSA levels in the Chinese group were higher than those of the US group ($P < .05$). Gleason score group 2 was more common in the US group than it was in the Chinese group, whereas the US group has higher rates of lymph node metastasis than did the Chinese patients ($P < .05$).

**Conclusions:** All these data suggest that characteristics of PCs are different, influencing treatment strategies (including surgical case selection criteria) between the US and Chinese groups.

**Segmental Renal Dysplasia in an Adult Masquerading as Suspected Carcinoma**

(Poster No. 144)

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Renal dysplasia is defined as abnormal metanephric differentiation resulting in disorganized development of the kidney parenchyma, which can be diffuse, segmental, or focal. Coexisting abnormalities of the collecting system are often seen, resulting in symptoms of obstruction. The degree of dysplasia and associated anomalies are responsible for the variable presenting symptoms in these patients. Renal dysplasia is most commonly diagnosed on fetal ultrasound, around the time of birth or during childhood and rarely presents in adults. We report an unusual case of segmental renal dysplasia in a 44-year-old woman presenting with a history of recurrent urinary tract infections and left flank pain. A magnetic resonance imaging scan showed multiple small cystic lesions within the left kidney and a 2.5×4.2×2.2-cm hyperintense cystic lesion in the left upper pole that was suspicious for carcinoma. Left partial nephrectomy was performed. Gross evaluation showed a 4-cm partial nephrectomy specimen with a 0.9-cm cystic structure filled with a dark-red to brown friable blood clot and thinned renal parenchyma (0.5 cm in maximum thickness). Microscopically, sections of the kidney showed disorganized parenchyma distorted by cysts of different sizes lined by cuboidal epithelium with calcifications (Figure 71, A). Sections also showed primitive immature ducts lined by undifferentiated cuboidal epithelium and fibromuscular collar composed of spindle cells arranged around the primitive ducts (Figure 71, B and C). Scattered islands of metaplastic cartilage were also present (Figure 71, D). The patient was diagnosed with segmental renal dysplasia secondary to an upper pole moiety and duplicated left renal collecting system.

**Testicular Juvenile Granulosa Cell Tumor in an Undescended Testis**

(Poster No. 145)

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Testicular juvenile granulosa cell tumor is a rare tumor arising from specialized gonadal stroma of the testicle; very few cases have been reported in the English literature. It was first reported in 1985 because of its histologic similarity to the ovarian granulosa cell tumor. Despite its rarity, this tumor is the most frequent congenital testicular neoplasm and most common testicular tumor in the first 6 months of life. A 17-day-old male infant delivered via cesarean section secondary to preeclampsia revealed an undescended pelvic right testicle with a predominantly cystic lesion on ultrasound. α-Fetoprotein and inhibin-A levels were elevated, whereas lactate dehydrogenase and human chorionic gonadotropin levels were within reference range. Orchietomy was performed and gross examination showed a well-circumscribed cystic mass, measuring 1.2 cm in greatest dimension. Histology showed numerous cysts lined by single or multiple layers of granulosa cells and separated by a fibrous stroma (Figure 72, A). Tumor cells had a moderate amount of eosinophilic cytoplasm and had round to oval nuclei with inconspicuous nucleoli (Figure 72, B). Immunohistochemistry showed the tumor cells to be positive for CAM 5.2 (Figure 72, C), inhibin (Figure 72, D) and calretinin. Differential diagnoses included teratoma, cystic dysplasia of the testicle, Sertoli cell tumor, and yolk sac tumor. Follow-up after 12 months showed no evidence of disease recurrence in our case. Testicular juvenile granulosa cell tumor is considered a benign entity because local recurrence and metastasis have never been reported. After surgical removal of the involved testicle is performed, no further management is required.

**BRAF-PID1 Fusion Brain Stem Glioma: A Unique Fusion Molecule**

(Poster No. 146)

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A 55-year-old man presented with subacute progressive right-sided hemiparesis, hemisensory loss, and hemidysmetria. A magnetic resonance imaging scan showed a 2.7×2.9-cm round enhancing cystic lesion in the dorsal left pons with mass effect on the fourth ventricle. Magnetic resonance spectroscopy demonstrated an increased choline to creatine ratio and decreased N-acetylaspartate suggestive of neoplasm. Histology showed a glial tissue neoplasm with low cellularity and focal atypia. The lesion was negative for mitosis, necrosis, microvascular proliferation, and Rosenthal fibers. Immunostains were positive for GFAP, ATRX, EGF receptor, and p53 (>80%). Ki-67 proliferation labeling index was low (3%–5%). IDH1-R132H antibody showed negative staining in tumor cells. Findings were consistent with...
a grade 2 astrocytoma. Next-generation sequencing showed BRAF-V600 fusion, which is not the normal fusion seen in pilocytic astrocytoma or ganglioglioma. To our knowledge, this tumor represents a previously unreported genetic variant, whose clinical significance is unclear. If this fusion results in a novel protein product, such a product could offer a new target for drug therapy. Importantly for clinicians, BRAF inhibitor therapy, which is undergoing clinical trials for BRAF V600-mutant pediatric primary brain tumors, targets BRAF mutations, rare fusion proteins, and so is not relevant to this type of genetic variant.

**Atrial Myxoma Presenting With Hemorrhage and Multifocal Infarcts in Brain of a 59-Year-Old Man: Uncommon Outcome for the Most Common Primary Heart Neoplasm**

(Poster No. 147)

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Atrial myxomas are the most common primary neoplasm of the heart. In addition to effects on the heart and mitral valve, adverse effects on the brain include embolization of either fragments of the neoplasm or thrombus formed in the atrium in the setting of stasis. We report a case of a patient presenting with neurologic symptoms from multifocal bled lesion with subsequent identification of a large atrial myxoma. A 59-year-old man presented with progressive headaches, visual changes, and anomic aphasia. Brain imaging revealed a 2.3 × 2.1 × 2.0-cm enhancing mass in the left occipital lobe along with multiple, smaller lesions in the cerebral hemispheres and the cerebellum. Computerized tomography scan of his chest revealed a 3.5 × 2.5-cm lobular lesion within the left atrium and ventricular, spanning the mitral valve. Histologic evaluation of the resected heart lesion revealed an atrial myxoma with complex papillary excrescences. Resection of the left occipital lobe lesion identified embolic myxoma in vessels and free in the brain with associated subacute and chronic hemorrhage. Symptomatic atrial myxomas have been reported in patients ranging from childhood to the eighth decade variably coming to clinical attention because of cardiac or embolization-related symptoms. When brain emboli are identified, ischemic infarcts are much more common than hemorrhages. This case is remarkable for its late presentation, the size of the cardiac lesion, the multifocal nature of cerebral hemisphere and cerebellar lesions, and the comparison of histologic and immunohistochemical features of both the heart and brain lesions.

**Neurosarcoïd of Petrocivius**

(Poster No. 148)

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Sarcoidosis is an idiopathic granulomatous disease affecting about 0.01% to 0.03% of the population in the United States. Neurosarcoidosis is even rarer, occurring in approximately 5% to 13% of sarcoidosis, either in isolation or in systemic sarcoidosis with a predilection for cranial nerves. However, other nervous system tissues can be involved, including meninges, brain parenchyma (especially hypothalamus), spinal cord, and peripheral nerves. We report on a case of a 50-year-old woman with a medical history of sarcoidosis. She presented with chronic migrainous headaches, nausea, vomiting, and photophobia. A magnetic resonance imaging scan of the brain showed abnormal, narrow-enhancing signal within the clauoid, left petroclival region, and the petrus apex and epidural solid enhancement extending into the Meckel cave and left lateral cavernous sinus (Figure 73, A). Endoscopic biopsy of a clival lesion showed several small noncaseating granulomas with multinucleated histiocyte giant cells highlighted by immunostains for CD68 (Figure 73, B through D, arrows). Special stains were negative for acid-fast bacilli, bacteria, or fungal infection. In view of the clinical background, the biopsy findings were consistent with neurosarcoid granulomatous inflammation. Neurosarcoidosis is among the least sites affected by the disease and the diagnosis may be challenging when it occurs in isolation; however, it is a diagnostic consideration in patients with known systemic sarcoidosis who develop neurologic complaints. Cerebrospinal fluid examination with pleocyto- sis, ACE and protein-level elevation are suspicious but not conclusive for the diagnosis and biopsy is essential for diagnosis. Even in the setting of known systemic disease, the diagnosis is made after exclusion of other causes of noncaseating granulomas by laboratory, special stains, and correlation with imaging studies and compatible clinical setting.

**Widespread Pelvic Metastases From Primitive Neuroectodermal-Tumor Component of Cranial Glioblastoma: Complication From a Rare Variant of Glioblastoma and Its Therapeutic Impact**

(Poster No. 149)

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Glioblastoma, the most aggressive malignant primary brain tumor, has a poor prognosis despite advances in multimodality treatment. Glioblastoma with primitive neuroectodermal-like tumor component (PNET-like) is a rare, recently recognized variant in the World Health Organization classification, with postulated origin from divergent primitive cells differentiated along glial-neuronal cell types. The prognostic/therapeutic implications of PNET-like component in glioblastoma are not well characterized because of the rarity of this variant. Some studies showed lower recurrence rate (36%) and longer survival (15–44 months), compared with classic glioblastoma; however, these tumors have increased risk of cerebrospinal fluid dissemination and extracranial metastases. We present an example from a 55-year-old man with a history of left frontal low-grade astrocytoma 16-years prior, which was treated with surgery and chemoradiation. A recent magnetic resonance imaging (MRI) scan revealed a rapidly increasing swelling and vasogenic edema with heterogenous enhancement around the previous resection cavity (Figure 74, A). Histology of the resection showed glioblastoma with a prominent PNET-like component and focal gemistocytic astrocytoma (Figure 74, B). He received chemo- radiation, but the tumor recurred after 15 months and reexcision showed only low-grade astrocytic tumor component. An MRI of the pelvis (8 months later) showed extensive osseous metastases throughout the L3 to L5 vertebra, pelvis, sacrum, proximal femora, and left pyriformis muscle emanating from the left S3 neural foramen (Figure 74, C). Biopsy showed metastatic PNET-like component of glioblastoma (Figure 74, D). He is currently completing a palliative course of radiotherapy to the tumor metastases. In summary, PNET-like component in glioblastoma is very rare and arises in secondary type of glioblastoma. The capacity of this variant to seed through cerebrospinal fluid and extracranial metastases warrants craniospinal
radiation and scanning for metastases and may respond to additional platinum-based chemotherapy.

**Isocitrate Dehydrogenase Mutations Are Associated With Different Expression and DNA Methylation Patterns of OLIG2**

(Poster No. 150)

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**Context:** The mutation status of isocitrate dehydrogenase (IDH) genes (ie, IDH1 and IDH2) has become an integral part of the classification of both lower-grade gliomas (LGGs) and glioblastomas (GBMs). OLIG2 is expressed in all grades of diffuse gliomas. Deletion of OLIG2 in glioma models results in a decelerated growth and a shift of gene expression patterns (PMID: 27165742). In this study, we used data from The Cancer Genome Atlas (TCGA) to explore the relationship between IDH mutation status and OLIG2 patterns.

**Design:** The publicly available data of clinical and phenotypic information, somatic mutation, gene expression, and DNA methylation of LGG and GBM cohorts from TCGA were obtained from the University of California, Santa Cruz Xena browser.

**Results:** Our repeat analyses confirmed that patients with IDH-mutated (MT) gliomas have significantly better prognoses than those with IDH-wild type (WT) tumors in both cohorts (Figure 75, A). OLIG2 expression is significantly greater in IDH MT tumors in both LGG (mean, 1.78; range, 1.41–2.14 folds; n = 505; P < .001) and GBM cohorts (mean, 1.21; range, 0.79–1.64 folds; n = 241; Figure 75, B). IDH MT tumors have a significant DNA-hypermethylation region (eg, cg08412398, up to 0.47 in difference of median β value; Figure 75, C, red arrow) and a significant hypomethylation region (eg, cg07601542, up to −0.56 in difference; Figure 75, C, green arrow), in both LGG and GBM cohorts.

**Conclusions:** OLIG2 expression is greater in IDH MT glioma than it is in WT ones. The upstream DNA sequence of OLIG2 also shows differentially methylated regions. These findings suggest that the roles of OLIG2 may differ between IDH MT and WT gliomas.

**Isolated Central Nervous System Relapse of Acute Myeloid Leukemia in a Patient With Worsening Chronic Graft-Versus-Host Disease**

(Poster No. 151)

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Central nervous system (CNS) involvement by acute myeloid leukemia (AML) is rare, particularly in posttransplant patients with graft-versus-host disease (GVHD). We report an unusual case of leukemic relapse isolated to the CNS in a 38-year-old woman with a history of AML with t(8;21) diagnosed 6 years prior and currently after a second hematopoietic stem cell transplant and chronic GVHD treated with tacrolimus and prednisone. The patient recently presented with new-onset seizure activity and superior sagittal sinus (SSS) thrombosis, which prompted discontinuation of rivanoxaban and initiation of enoxaparin. During that time, she was also started on ibrutinib, followed by rituximab, and extracorporeal photopheresis because of worsening chronic GVHD. No significant changes were seen on follow-up complete blood cell count, and persistent complete donor chimera was demonstrated by quantitative polymerase chain reaction (qPCR). Furthermore, peripheral blood RUNX1-RUNX1T1 fusion transcripts, although detectable, were below the limit of quantitation for the reverse transcription-qPCR assay. Two months after her presentation with SSS thrombosis, a follow-up magnetic resonance imaging scan showed a heterogeneously enhancing lesion centered at the SSS measuring 4.4 x 2.2 x 1.5 cm. The patient underwent craniotomy for biopsy and debulking. Flow cytometric and morphologic findings were consistent with recurrent AML. We, therefore, describe a case of recurrent AML in a patient on anti-B- and T-cell immunosuppressive therapy for worsening chronic GVHD and emphasize the importance of considering the possibility of relapsed disease confined to the CNS. Furthermore, we highlight the limitations of even the current high-sensitivity assays when used in isolation in similar clinical contexts.

**Multiple and Aggressive Vertebral Body Hemangiomas Presenting as Metastatic Disease: Case Report and Diagnostic Radiopathologic Correlation**

(Poster No. 152)

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A 63-year-old woman with a history of papillary thyroid carcinoma presented with lower-back pain radiating to her lower limbs. Whole spine imaging showed multiple vertebral lesions. The lesion at T7 demonstrated an epidural extension, which caused severe canal stenosis (Figure 76, A). Image-guided core needle biopsy showed fragments of bone and fibrous tissue with no tumor cells identified. Cytopathologic evaluation of aspirated fluid revealed blood elements only. Given the “malignant” radiologic appearance of the lesions, the patient underwent T7 laminectomy and posterior T5 to T9 surgical fusion. The resection specimen showed multiple vertebral body hemangiomas (VBHs; Figure 76, B and C). VBHs are the most common tumors of the VBHs; Figure 76, B and C). VBHs are the most common tumors of the
spinal axis. They are usually asymptomatic and found incidentally; however, they can be aggressive if they display extraordinary extensions causing cord compression and neurologic symptoms. Most VBHs are diagnosed radiologically via their characteristic imaging findings; however, the diagnosis can be challenging in cases of atypical or aggressive hemangiomas, particularly if multiple. Core biopsies are usually nondiagnostic because of the fragility of the thin-walled blood vessels and aspirated fluid cytology generally only shows blood elements, making definitive diagnosis difficult. However, the pathologist should consider VBHs as a differential diagnosis. This might in turn guide the clinical/radiology team to use more specialized imaging modalities (eg, magnetic resonance angiography) for better visualization of those lesions, which might avoid the need for unnecessary surgical treatments.

Cytokeratin 19 Expression in Different Brain Cyst Subtypes
(Poster No. 153)

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Context: Intracranial brain cysts may have ectodermal origin or congenital origin. The exact origin of some of these cysts is still obscure. Cytokeratin 19 is a 40-kDa protein that is specifically expressed in the periderm, the transiently superficial layer that envelopes the developing epidermis.

Design: Cytokeratin 19 staining was performed on all cystic brain lesions diagnosed in our laboratory; 17 epidermoid cyst (tumor), 12 colloid cyst, 6 arachnoid cysts, 6 Rathke cleft cysts, 2 neuroglial cysts, and 3 craniopharyngiomas.

Results: Cytokeratin 19 was expressed in 15 of 17 epidermoid cysts (Figure 77, A), 12 of 12 colloid cysts (Figure 77, B), 5 of 6 arachnoid cysts, 6 of 6 Rathke cleft cysts, 2 of 2 neuroglial cysts (Figure 77, C), and 34 of 34 craniopharyngiomas (Figure 77, D).

Conclusions: Cytokeratin 19 is expressed in all brain cyst subtypes examined; however, it does not differentiate one brain cyst type from another. This expression is probably because cytokeratin 19 is expressed in embryologic cells of the epidermis, which may be the origin of most of brain cysts.

Choroid Plexus Papilloma: Atypical Presentation as Pure Hemorrhage Without Imaging Evidence of a Tumor
(Poster No. 154)

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Choroid plexus papilloma (CPP) is a rare, slow-growing, benign (World Health Organization [WHO]) grade 1 neoplasm, arising from the choroid epithelium. CPP represents 0.4% to 0.6% of all primary intracranial tumors and accounts for 1.5% to 4% of pediatric brain tumors. CPPs generally arise in the fourth ventricle in adults and the atrium of lateral ventricles in children. Clinically, CPPs usually present with raised intracranial pressure and radiographically, present as homogeneous or heterogeneous, cauliflower-like masses. Surgical removal is the treatment of choice. We report on a case of a 67-year-old woman who presented with sudden onset of left-sided weakness and headache. Computed tomography (CT) scan revealed a large, right parietal hemorrhage with minimal subarachnoid and intraventricular hemorrhage. Findings from a CT angiogram were negative. The patient underwent urgent partial evacuation of the parietal hematoma. Histopathology revealed an intraventricular hypercellular choroid plexus with unorganized blood products. The epithelium was crowded, vacuolated with focal atypia and stromal microlcalfication, and showed acute necrotic changes in some stromal stalks. The choroid epithelium was positive for synaptophysin, S100, and CAM 5.2 focally and was negative for EMA and GFAP. Mitotic activity was very low (<2 mitosis/high power field). Neither hematoxylin-eosin nor trichrome/VVG provided support for concomitant vascular malformation. A diagnosis of choroid plexus papilloma (WHO grade 1) was made. Patient’s condition slowly improved, despite severe neurologic deficits, without recurrence. The presentation of this case as a pure hemorrhage without imaging evidence of a tumor is virtually unprecedented, to our knowledge. Only approximately 3 cases have been reported to present with hemorrhage, but imaging suggested the presence of a tumor.

Distinct Progesterone Receptor and Ki-67 Expression Profiles in Different WHO Grade Meningiomas
(Poster No. 155)

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Context: Although progesterone receptor (PR) and proliferation marker (Ki-67) expression are not required for current World Health Organization (WHO) classifications of meningioma, their expression profiles are closely related to grade. This study aimed to investigate the association between PR and Ki-67 expression in different WHO grade meningiomas.

Design: Thirty cases of WHO grade 1, 38 cases of WHO grade 2, and 6 cases of WHO grade 3 between 2011 and 2018 were immunohistochemical stained for PR and Ki-67.

Results: For WHO grade 1 tumors, 4 of 30 cases (13.3%) showed high expression for Ki-67 (>10%), and 21 of 30 (70%) cases showed strong PR expression (>80%). For WHO grade 2 tumors, 2 of 18 cases (11.1%) showed high expression for Ki-67, and 15 of 18 cases (83.3%) showed strong PR expression in tumors with brain invasion. Sixteen of 20 cases (80%) showed high Ki-67 expression, and 5 cases showed strong PR expression in WHO grade 2 tumors with atypical, chordoid or clear cell morphology. For WHO grade 3 tumors, all 6 cases (100%) showed high expression for Ki-67 and variable or no expression for PR.

Conclusions: An inverse relationship was observed between Ki-67 and PR expression and tumor grade, with higher Ki-67 expression and lower PR expression with increasing tumor grade. However, expression profiles for Ki-67 and PR in WHO grade 2 tumors with brain invasion was similar to that of WHO grade 1. Pathologists should consider ancillary testing for Ki-67 and PR expression when diagnosing meningioma.
High-Grade Posterior Fossa Neuroepithelial Tumor With Mixed Histologic Features and a Novel Molecular Signature in a Child: Case Report and Review of the Literature

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A 3-year-old boy presented to the emergency department with a 2-week history of emesis. Magnetic resonance imaging of the brain showed a posterior fossa mass lesion with solid and cystic components measuring 4.3 × 3.2 × 3.8 cm. The patient underwent a gross total resection. After multiple pathologic reviews, diagnosis of high-grade neuroepithelial tumor with features of ependymoma and primitive neuroectodermal tumor (PNET) was made. Whole exome sequencing revealed a novel mastermind-like domain 1 (MAML1)-BEND2 domain containing 2 (BEND2) fusion. The patient underwent proton beam radiotherapy. Three months after treatment, magnetic resonance imaging showed relapsed disease in the posterior fossa with nodular and leptomeningeal enhancement. He is currently receiving chemotherapy for relapsed disease. BEND2 fusions with meningioma 1 (MNN1) have been identified previously in PNET with astroblastoma histology and in most histologic astroblastomas. Astroblastomas are characterized by perivascular pseudorosettes composed of tumor cells with prominent processes extending to a central blood vessel, perivascular hyalinization and frequent necrosis. MAML1 fusions with yes-associated protein (YAP1) have been reported in supratentorial ependymomas. Microscopically, ependymomas have hallmark ependymal perivascular pseudorosettes and true rosettes. True rosettes, composed of columnar cells around a central lumen, are diagnostic of ependymoma but are not always present. Our patient's tumor contained histologic features of both ependymoma and PNET, which are not always present. Our patient's tumor showed histologic features of both ependymoma and PNET, which correlate with the gene partners found in the novel MAML1-BEND2 fusion. This is the first report, to our knowledge, of a brain tumor of this histologic and molecular character and we suggest that it represents a novel entity with aggressive clinical behavior.

Urinary Bladder Involvement in Neurofibromatosis Type 1

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Plexiform neurofibromas (PNs) are specific for the diagnosis of neurofibromatosis type 1 (NF1), and are most commonly located in the spine and nerve plexuses. PN complications may include dysfunction of the innervated tissue and rare malignant transformation. PNs affecting the lower spinal cord may cause urinary bladder symptoms but very rarely dysfunction because of primary urinary bladder involvement. We searched our database for cases of lesions associated with NF1. From more than 200 surgical and autopsy cases with prior diagnosis of NF1, we found only 2 patients presenting with urinary bladder involvement. Clinical symptoms were not specific and included obstructive uropathy and acute urinary tract infections; a thickened bladder wall was also seen on imaging. Both patients required surgical management; a 22-year-old man with outlet obstruction requiring transurethral resection of a bladder neck tumor, and a 26-year-old woman with several large bladder tumors (Figure 78, A) requiring radical cystectomy with ileal conduit. Histopathology in both cases showed multiple PNs with proliferation of peripheral nerves, large nerve bundles with nodular appearance, and prominent myxoid matrix (Figure 78, B; the cystectomy patient demonstrated a ganglioneurofibromatous compo- nent (Figure 78, C) highlighted with immunohistochemistry for neurofilament (Figure 78, D), $\text{S100}$, $\text{CD56}$, and NSE. Both NF1 patients are doing well with no significant complications. It is important to consider the presence of bladder wall PN lesions in patients with NF1 complaining of urinary dysfunction and/or showing abnormal bladder imaging. However, because of its rarity of presentation, specific therapy has not been established, and a conservative approach is preferred unless complications ensue.

Neuropathologic Applications of Microscopy With Ultraviolet Surface Excitation: A Concordance Study of Human Primary and Metastatic Brain Tumors

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Context: As the advancement of molecular profiling in brain tumor diagnostics increases, the expenditure of tissue on conventional histology has left either inadequate material to pursue molecular studies or has subjected patients to repeated risky procedures to harvest additional brain tissue. In response, microscopy using ultraviolet surface excitation (MUSE) has been developed as a novel, and importantly, tissue-sparing, method of obtaining morphologic imaging. Here, we intended to establish the reliability and diagnostic accuracy of MUSE image analysis versus standard processing in the diagnosis of benign and malignant human central nervous system tumors.

Design: MUSE images were generated alongside traditional formalin-fixed, paraffin-embedded microtome sections. Hematoxylin–eosin–stained slides of the same brain tissue biopsy were compared in a blind analysis by a panel of anatomic pathologists. Discrepancies in diagnosis were assigned grades of (0) equivalent, (1) minor difference probably not clinically significant, (2) intermediate difference (eg, differences in size measurements or grade), or (3) major difference (eg falsely positive/negative).

Results: In surgical resections of 24 adult patients (mean age, 54 years) with newly diagnosed brain and spinal cord tumors, 7 of 24 were diagnosed by conventional methodology with diffuse astrocytic/oligodendrogial tumors, 8 of 24 with meningiomas, 3 of 24 with ependymal/chordoid plexus tumors, 3 of 24 with tumors of cranial/paraspinal nerves, and 3 of 24 with metastatic tumors. Concordance reached 97% between MUSE versus light microscopy diagnostics, with 94% within the pathologist panel.

Conclusions: Diagnostic-quality histologic images of central nervous system tumors are reliably generated by MUSE imaging on a rapid, tissue-sparing basis. Further, evaluation of more diagnostically challenging cases by board-certified neuropathologists is warranted to assess potential in routine neuropathology practice.

Pontocerebellar Hypoplasia: A Case Report With Phenotype-Genotype Mismatch

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Pontocerebellar hypoplasia (PCH) is a group of autosomal recessive neurodegenerative disorders with 11 subtypes based upon clinical, radiologic, biochemical features, and gene defects. The common characteristics are cerebellar hypoplasia with variable level of atrophy of the cerebellum and the ventral pons. Reported cases for PCH 3-11 are rare, therefore the clinical spectrum of these disorders has not been completely revealed yet. We report the clinical and autopsy findings of a patient with PCH having a genetic mutation pattern typical for PCH4 but with additional phenotypic features observed in PCH7 and PCH9. The patient was an 11-day-old girl born at 33 weeks of gestation. During pregnancy, the mother had polyhydramnios and experienced sporadic abnormal fetal clonic movements. At birth, the girl had myoclonic jerks, jitteriness, respiratory difficulty, and swallowing impairment. Magnetic resonance imaging showed microcephaly with brainstem and cerebellar hypoplasia, lack of myelination of the posterior limb of the internal capsule bilaterally, absence of pontine projection fibers, optic atrophy and diffuse coro callosal thinning with possible callosal dysplasia. At autopsy, brain findings included microcephaly severe olivopontocerebellar hypoplasia, dilated lateral ventricles, and an unroofed fourth ventricle. Histologically, there was extensive neuronal dropout in the brainstem and cerebellum, with simplified inferior olivary nucleus and fragmentation of cerebellar dentate nuclei. The patient had compound pathogenic A307S (missense) and A360GdelX81 (frameshift) mutations in the TSEN54 typical for PCH4. Although most of these findings are consistent with PCH4, corpus callosum dysplasia is associated with other PCH types such as PCH7 and PCH9, whereas TSEN54 mutation is not associated with these PCH subtypes.

Glioblastoma With Ependymal Features

(Poster No. 160)

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Glioblastoma (GB) may present with various morphologic patterns: giant cell GB, GB with PNET component, GB with oligodendrogial component, gliosarcoma, adenoid GB, small cell GB, and granular cell GB. It is important to identify the variants of GB because some have worse prognosis than others do. We report on a 54-year-old man who presented with progressive, expressive aphasia and 2 radiographically high-grade neoplasms in the left temporal lobe on magnetic resonance imaging. Histologically, one of the biopsies looked like classic GB, whereas the second one had ependymal features, such as extensive perivascular pseudorosettes (Figure 79, A) and minimal nuclear pleomorphism. The possibility of 2 different types of brain tumors (GB and high-grade ependymoma) was initially entertained. Both lesions were in the temporal lobe. Both had abundant mitoses, necrosis, focal endothelial hyperplasia, strong glial fibrillary acidic protein expression, dotlike cytoplasmic epithelial membrane antigen (EMA) positivity (in many of the atypical cells; Figure 79, B), and a Ki-67 proliferation index was 20% to 25% in both tumors. Although the dotlike EMA positivity is most often encountered in ependymomas, it may also be seen in GB. Based on the similarity of the above findings, we believe that the 2 lesions are most likely GB with varying morphologic features, rather than 2 distinct types of brain tumor. The lesions were found to be IDH1 wild type and were negative for methylation of the MGMT gene. Even within the same patient, GB can have varying morphologic features and exhibit dotlike cytoplasmic EMA positivity.

Histologic and Immunohistochemical Assessment of Cerebral Endovascular (Mechanical) Thrombectomy

Specimens: Clinicopathologic Correlations for New Acute Ischemic Stroke Treatment

(Poster No. 161)

Aisha Kousar, MD (kousara18@ecu.edu); Robin L. Harrison, BS; Richard T. Dalyai, MD; Hilal A. Kaanan, MD; Wen Zhong, MD; Philip J. Boyer, MD, PhD. 1Department of Pathology, East Carolina University, Greenville, North Carolina; 2Department of Pathology, Brody School of Medicine, Greenville; 3Department of Neurosurgery, Vidant Neurosurgery, East Carolina University, Greenville.

Context: Treatment of ischemic stroke has most commonly relied on therapeutic administration of tissue plasminogen activator with the goal of preserving salvageable, ischemically compromised brain parenchyma. Endovascular thrombectomy provides an additional tool in the therapeutic armamentarium for treatment of ischemic stroke. Limited studies have evaluated histologic findings in thrombectomy specimens.

Design: Thrombectomy specimens from 20 patients were evaluated macroscopically, histologically, and immunohistochemically (CD68 and CD34). Features relevant to the age of the thrombus were assessed, including evidence of white blood cell changes (neutrophil nuclear loss, macrophage activation, and hemophagocytosis) and evidence of organization (endothelial cell lining or invading thrombus) with reviewers blinded to clinical history. Chart review and clinicopathologic correlation was conducted.

Results: Thrombectomy specimens were evaluated from 8 men and 12 women, ages 20 to 91 years. Evidence of organization was noted focally in all specimens, comprising from less than 5% to 50% of the thrombus. Clinical correlates included arterial fibribulation in 10, ventricular thrombus on echocardiogram in 9, carotid dissection in 1, and atherosclerotic plaque in aorta or and carotid in 7. The specimens with the most advanced organization were seen in a patient with a previous mycotic infect and a left ventricle thrombus by echocardiogram being treated with warfarin and a patient with arterial fibribulation subarachnoid on warfarin with a left atrial thrombus by echocardiogram.

Conclusions: Histologic evaluation of thrombectomy specimens supplements clinical data with the goal of identifying the source of the thrombus and preventing future emboli. This evaluation also provides an important quality-control tool for the thrombectomy procedure.

Inflammatory Cerebral Amyloid Angiopathy With Spontaneous Subarachnoid Hemorrhage: A Rare Presentation Discovered at Autopsy

(Poster No. 162)

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Cerebral amyloid angiopathy (CAA) is characterized by the deposition of amyloid-β in medium and small artery walls and can be associated with cerebral hemorrhage and infarcts. CAA-related inflammation is an unusual variant of CAA characterized by a prominent angiitic and often granulomatous reaction that can lead to enhanced vessel fragility. We report on the case of a 76-year-old man who presented with the sudden onset of severe headaches and altered gait, who was found to have frontal subarachnoid hemorrhages. The patient eventually developed seizure like activity and altered mental status, requiring intubation and intensive care unit-level care. He was eventually extubated, but remained persistently encephalopathic and obtunded for several weeks, eventually expiring after being transitioned to comfort measures. The encephalopathy was attributed cerebral infarction because of vasospasm in the setting of subarachnoid hemorrhage. A complete autopsy was performed, which demonstrated resolving subarachnoid hemorrhages over the cerebral convexities and bilateral infarcts in multiple vascular territories. Microscopic examination showed widespread thickening of the intracortical and leptomeningeal vessels associated with granulomatous inflammation and focal destruction of vascular walls. These vessels stained positively for amyloid-β and Congo red and demonstrated intracytoplasmic amyloid-β in giant cells (Figure 80). This case highlights an unusual presentation of this rare entity because CAA-related inflammation generally manifests with subacute cognitive decline, seizures, or as a mimic of transient ischemic attacks and is rarely seen in association with subarachnoid hemorrhage.
Intracranial Fibromatosis Mimicking Meningioma: A Case Report and Review of Literature
(Poster No. 163)

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Intracranial fibromatosis is exceptionally rare. Most reported cases are in the base of the skull and in children. We report an unusual case of an intracranial fibromatosis over the cranial convexity mimicking meningioma. A 65-year-old man with a prior history of right tentorial meningioma (grade 1), following resection 3 years prior presented with progressive swelling over the left occipital region. Magnetic resonance imaging revealed a dura-based lesion of the left occiput, invading the overlying bone. The clinical and radiologic impression was that of a recurrent meningioma. Although intracranial fibromatosis has been previously reported, the tumor eventually extended into the sinuses and upper nasal cavity. Histologically, all resections were essentially identical in all resections and showed strongly reactivity for fibrillary acidic protein nonreactivity, but 1 of the 2 was S100 reactive and the other showed CAM 5.2 and TTF-1 reactivity with glial fibrillary acidic protein nonreactivity, but 1 of the 2 was S100 reactive with glial fibrillary acidic protein nonreactivity, but 1 of the 2 was S100 reactive. The spindle cells were immunoreactive to SMA and desmin. A pathogenic mutation (c.133T→C) was found in the exon 3 of the FLCN gene. No clinically significant gene fusions were identified. Although intracranial fibromatosis has been previously reported, this case is unusual in that it arises as a predominantly dura-based mass, mimicking a convexity meningioma. Although rare, intracranial fibromatosis should be considered in the differential diagnosis of meningioma, particularly in a patient with a history of prior cranial surgery.

Central Nervous System Involvement of Autoimmune Lymphoproliferative Syndrome With CTLA-4 Haploinsufficiency Presenting With Pediatric-Onset Evans Syndrome
(Poster No. 164)

Nupur Sharma, MD1 (sharmanu18@ecu.edu); Cathleen M. Cook, MD, MD7; Koneti V. Rao, MD8; Stefania Pittaluga, MD, PhD9; Raven V. Delgiudice, MD10; Lauren MD, PhD11; Bethany W. Villee, MD12; Lenwood P. Smith, MD13. Departments of 1Pathology, 2Pediatric Hematology/Oncology, and 3Brody School of Medicine, East Carolina University, Greenville, North Carolina; Departments of 4Hematology and 5Hematopathology, National Institutes of Health, Bethesda, Maryland; 6Department of Neurosurgery, Vidant Medical Center, Greenville, North Carolina.

Evans syndrome is defined by a combination of autoimmune hemolytic anemia and immune thrombocytopenia. Clinical presentation includes manifestations of immune dysregulation, found in primary immune deficiencies; autoimmune lymphoproliferative syndrome (ALPS), including a variant with cytotoxic T lymphocyte antigen-4 (CTLA-4) mutation; and other settings. ALPS-CTLA-4 is a rare disease process with an increased risk for progression to lymphoma. We present a case of ALPS with a novel frameshift mutation, c.160 deletion in allele 1 of the CTLA-4 gene, presenting with Evans syndrome. A 6-year-old girl presented with cervical lymphadenopathy, direct antiglobulin test–positive anemia, thrombocytopenia, and leukopenia. The differential diagnosis included etiologies related to bone marrow infiltration, bone marrow failure, primary immune deficiencies, and autoimmune disorders. Evaluation including bone marrow biopsy, flow cytometry, cytogenetics, and molecular studies revealed findings diagnostic of ALPS with a CTLA-4 gene mutation. When being treated with sirolimus and corticosteroids, the patient developed a progressive rash and left eye blurriness. Magnetic resonance imaging revealed a contrast-enhancing corpus callosum lesion raising concern for progression of her lymphoproliferative disease to lymphoma. Brain biopsy was negative for malignancy but notable for atypical perivascular lymphocytic infiltrates. Pediatric-onset Evans syndrome presentation should prompt physicians to perform extensive screening for mutations in the growing pool of genes involved in primary lymphoproliferative and immune deficiency diseases with autoimmunity, including CTLA-4 mutation (haploinsufficiency). This is the first report of histologic findings in brain involvement in ALPS because of CTLA-4 haploinsufficiency. Findings mirror those previously reported from biopsy of lung and gastrointestinal system lesions of patients with this disease process.

A Case of Papillary Oncocytic Pituitary Tumor: Unusual Morphologic and Immunohistochemical Features
(Poster No. 165)

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We present a case of a papillary oncocytic pituitary tumor in a 67-year-old woman, with features similar to 2 prior reported cases. Our patient presented with a bitemporal hemianoptic field defect and was found to have a sellar tumor. Despite multiple resections (n = 4) during a 12-year period and radiotherapy, the tumor eventually extended into the sinuses and upper nasal cavity. Histologically, all resections were similar and showed a papillary tumor (Figure 82, A) composed of bland epithelioid cells with abundant eosinophilic cytoplasm (Figure 82, B), round eccentric nuclei with occasional nuclear grooves and infrequent mitoses (2 per 50 high-power fields). Immunohistochemical stains were essentially identical in all resections and showed strongly reactivity for CK7, CAM 5.2, AE1/3, EMA, and vimentin but nonreactivity for thyroglobulin, S100, CEA, napsin, transthyretin, CD68, SOX10, Bcl2, ER, PR, synaptophysin or chromogranin. Tumor cell nuclei were reactive for TTF-1. TP53 and Ki-67 labeling indices were 15% to 20% and 25% to 30% respectively, somewhat elevated from the prior resection. Molecular studies revealed EGFR and EZH2 mutations. The 2 prior reported cases showed CAM 5.2 and TTF-1 reactivity with glial fibrillary acidic protein nonreactivity, but 1 of the 2 was S100 reactive with a FLCN mutation. Spindle cell oncocytoma of the adenohypophysis is reactive for S100 and nonreactive for CAM 5.2/cytokeratin. Granular cell tumors of the neurohypophysis and pituitary tumors are...
reactive for S100 and nonreactive for CAM 5.2. Therefore, this is the third reported case of a papillary oncocytic tumor of the pituitary, “POPT,” which should be considered with any oncocytic sellar tumor and requires close follow-up despite its bland appearance.

We present the case of a 28-year-old man with a medical history, 10 years prior, of multiple low-grade astrocytoma, which had been stable following resections. He presented asymptptomatically for a routine screening magnetic resonance imaging scan that showed a left frontal lesion with ring enhancement (Figure 83, A). At resection, the tumor measured 5.4 × 5.4 × 4.1 cm. Pathologic analysis showed an infiltrating astrocytoma with brisk mitotic activity, microvascular proliferation, and necrosis (Figure 83, B). There were focal nodules of round blue cells with remarkable proliferation rate suggestive of a primitive neuronal component. Furthermore, the tumor had an unusually loose cystic-appearing focus (Figure 83, C) and an area that demonstrated perivascular rosettes (Figure 83, D). Staining displayed strong p53 expression, ATRX loss, and a high Ki-67 index. Glial fibrillary acidic protein labeled a subset of cells but was negative in primitive areas. ATRX expression was lost. The Ki-67 labeling index was high (>90%). Neurofibromatosis showed a loss of staining. EGF showed strong positive staining. Neu-N and EMA results were negative. The PHH3 marker for mitotic activity showed >10 mitosis/10 high-power fields. The findings were negative for MGMT methylation or BRAF mutation. Fluorescence in situ hybridization showed abnormal 1p36 and monosomy for 19 chromosome. Histologic features coupled with this set of genetic abnormalities represents a tumor not previously documented, to our knowledge, in the literature.

Spectrum of Proliferative Hematopoietic Lesions Seen in the Central Nervous System at a Single Medical Center: Diffuse Large B-Cell Lymphomas and More

(Necker No. 166)

Nupur Sharma, MD1 (sharmanu18@ecu.edu); Raven V. Delgado, BS2; Bryan J. Dangott, MD3; Bethany D. Vallangeon, MD4; Philip J. Boyer, MD, PhD5; Darla K. Liles, MD6; Lenwood P. Smith, MD7; Regis G. Hoppennot, MD8; Jasmin Io, MD9; Keith A. Tucci, MD10; Richard T. Dalvai, MD11; Shawn M. Collins, MLT1; Renuka Malenie, MD1; Stuart K. Lee, MD11. 1Departments of 1Pathology, 2Brody School of Medicine, and 3Internal Medicine (Hematology/Oncology), East Carolina University, Greenville, North Carolina; 4Department of Neurosurgery, Vidant Medical Center, Greenville.

Context: A relatively restricted group of hematopoietic lesions is recognized in the central nervous system (CNS), comprising approximately 2% of all CNS tumors. Although diffuse large B-cell lymphoma, both primary and secondary, is most common, a range of other hematopoietic lesions can also occur in the CNS.

Design: This retrospective study summarizes CNS hematopoietic lesions diagnosed during the previous 10 years at a single medical center. Literature searches were conducted.

Results: A wide range of lesions was identified, mostly B-cell neoplasm variants. The most common neoplasm was diffuse large B-cell lymphoma, both primary (arising in the CNS) and secondary (arising first outside of the CNS) variants. In addition, cases of posttransplant lymphoproliferative disorder, extranodal marginal zone lymphoma, follicular lymphoma, intravascular large B-cell lymphoma, and autoimmune lymphoproliferative syndrome were identified. Optimal diagnosis usually required a biopsy; however, in some cases, the diagnosis was definitively made with cerebrospinal fluid evaluation, avoiding the need for a biopsy. In some cases in which lymphoma was strongly suspected clinically, including in a renal transplant patient, treatment with corticosteroids was undertaken prior to biopsy, and histopathologic and flow cytometric findings were nondiagnostic. One of these patients was subsequently revealed to have a diffuse large B-cell lymphoma on rebiopsy after discontinuation of corticosteroid therapy.

Conclusions: For optimal diagnosis and treatment, it is critical that clinicians and pathologists be aware of the range of hematopoietic lesions seen in the brain, the reduced sensitivity of biopsy with prebiopsy steroid therapy, and specimen limitations and requirements for optimal evaluation.

Transformation of Low-Grade Astrocytoma Into Glioblastoma With Pervascular Pseudo–Rosette-like Differentiation and Diffuse Cystic Areas: Unique Genomic Alterations Noted (CTNNB1 S37P, IDH1 R132C, ATRX F1780fs 31, MLH1 Duplication Exons 1–13, TP53 L194F)

(Po r No. 167)

Scott Wolfe, DO1 (swolfe@northwell.edu); Kristen Steslow, PhD2; Mark Mittler, MD3; Mansoor Nasim, MD, PhD3. 1Departments of 1Pathology and 2Neurosurgery, Northwell Health, Roslyn, New York.

Pituitary Hyperplasia Secondary to Occult Bronchial Carcinoid Mimicking Pituitary Adenoma in a Patient With Acromegaly: A Diagnostic Pitfall With Clinical Consequences

(Po r No. 168)

Garrett Fitzpatrick, MD (gfitzpatrick@ufl.edu); Jesse L. Kresak, MD. Department of Pathology, University of Florida, Gainesville.

Pituitary hyperplasia is rare and can present in a variety of clinical settings, making the diagnosis challenging. We report a unique case of somatotroph hyperplasia mimicking pituitary macroadenoma. A 30-year-old woman presented with enlarging feet and 1 year of amenorrhea. Physical exam revealed thick fingers and facial features suggestive of acromegaly. Magnetic resonance imaging revealed a 1.9 × 1.4-cm homogeneously enhancing lesion in the pituitary fossa abutting the optic chiasm and with suprasellar extension (Figure 84, A). The suspected pituitary macroadenoma was resected transphenoidally. Histologic analysis revealed predominantly eosinophilic cells, yet significant admixed basophils and chromophobes (Figure 84, B). The
Masson Tumors Developing Inside Spinal Neoplasms: A Radiologic Malignancy Mimic

(Poster No. 169)

Herleen Rai, MD (herleen.rai@uhhospitals.org); Marta Couce, MD, PhD; Mark Cohen, MD. Department of Pathology, University Hospitals Cleveland Medical Center, Cleveland, Ohio.

Masson tumor (intravascular papillary endothelial hyperplasia [IPEH]) is a benign entity of uncertain histogenesis, predominantly considered a reactive proliferation of endothelial cells within organizing intravascular thrombi. These lesions can occur everywhere; however, spinal cord involvement and existence within primary central nervous system neoplasms are extremely rare. We present 2 unusual cases of Masson tumors, developing inside a schwannoma in the cervical spine and within grade 2 thoracic ependymoma. A 38-year-old man presented with a right neck mass steadily increasing in size during a 4-month period. Imaging revealed a right parapharyngeal space mass adjacent to the great vessels, compatible with a lower cranial nerve schwannoma most likely arising from the vagus nerve. During surgical resection, it was discovered that the mass was arising from a cervical rootlet and not connected the vagus nerve. Histopathologic examination revealed a schwannoma with a focal area of IPEH, staining positive with CD31 and ERG in endothelial cells. In a second case, a 48-year-old man presented with a 2-month history of progressive back pain, worsening lower-extremity weakness, and gait instability. Magnetic resonance imaging showed a 3-cm left heterogeneously enhancing retro-orbital mass involving the frontal lobe. Immunostains demonstrated the tumor cells exhibited p16 and p63 staining in endothelial cells. In a second case, a 48-year-old man with a history of neurocysticercosis presented with recent onset of left eye pain. Magnetic resonance imaging showed a calcified, left lower-lobe mass, which was resected and diagnosed as a typical carcinoid. Insulin-like growth factor 1 levels drastically decreased after carcinoid resection, supporting the clinical significance of this rare but consequential diagnostic pitfall.

Retro-orbital NUT Carcinoma With Intracranial Involvement in a 62-Year-Old Man

(Poster No. 170)

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NUT carcinoma is an aggressive tumor defined by rearrangement of the NUTM1 gene on chromosome 15, usually a reciprocal t(15;19) translocation of NUTM1/BRD4. It typically presents in teens and young adults with midline location in midline upper-airway locations but has been described in other locations and at all ages. Resistance to conventional therapies and rapid clinical course are characteristic. Histologically, the tumor is composed of sheets of fairly uniform cells with round to oval nuclei and eosinophilic cytoplasm. Focal abrupt squamous differentiation is common, as is tumor necrosis and brisk mitotic activity. A 62-year-old man with a history of neurocysticercosis presented with recent onset of left eye pain. Magnetic resonance imaging showed a 3-cm left heterogeneously enhancing retro-orbital mass involving the frontal lobe. Immunostains demonstrated the tumor cells exhibited p16 and p63 expression (Figure 85, D), weak keratin AE1/AE3 and CK 8/18, while CK7, EMA, CK20, SMA, TTF-1, S100, synaptophysin, and GATA3. Flow cytometry and lymphoid markers were negative. INI1 was retained; NUT immunohistochemistry and fluorescence in situ hybridization for BRD4/NUT fusion were positive, establishing the diagnosis. The patient is undergoing radiation and chemotherapy. We conclude that the former designation as NUT “midline” carcinoma should not preclude considering it in the differential diagnosis of poorly differentiated small blue cell tumors of the orbit.

Unusual Orbit Involvement by Primary Carcinoid Tumor

(Poster No. 171)

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Carcinoid tumors are low-grade, malignant tumors derived from enterochromaffin cells. As a result, carcinoid tumors most commonly involve the gastrointestinal tract, lung, ovary, and breast. Only 3 cases of primary carcinoid tumor of the orbit have been described so far. Here, we report on a 36-year-old woman with a low- to intermediate-grade neuroendocrine tumor with medial rectus muscle involvement of the left eye diagnosed in 2017. The patient last became symptomatic 7 months prior, with new onset pain and redness in her left eye. The anterior debulking biopsy was diagnosed as a low-grade neuroendocrine tumor. The neoplastic cells were positive for pan-keratin, CAM 5.2, EMA, Ber-EP4, chromogranin, and synaptophysin and were
negative for CEA, estrogen and progesterone receptors, GATA3, vimentin, S100, SMA, MSÁ, CD3, and CD34. A systemic workup failed to find any primary tumor outside of the orbit. Further imaging revealed a 1.8 × 1.5 × 2.1-cm homogeneously enhancing lesion in the orbit. She underwent orbital exenteration. The mass was well circumscribed and composed of typical carcinoid tumor with a low mitotic index. The tumor cells were negative for TTF-1, weakly positive for CDX-2, and the Ki-67 was approximately 10%. Since the patient's initial diagnosis 2 years ago, no additional tumors have been found. Although very rare primary carcinoid tumors of the orbit have been previously described; this is the first reported case of medial rectus muscle involvement with negative systemic workup, with interesting implications for the putative histogenesis of these tumors in the orbit.

A Case Report Study of Signet Ring Cell Histiocytoid Carcinoma of the Eyelid

(Poster No. 172)

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A 66-year-old man presented with a 1-year history of left upper eyelid ptosis. Magnetic resonance imaging of the orbit showed an ill-defined mass involving both upper and lower left eyelid with orbital extension involving intraconal and extraconal spaces with subtotal encasement of the globe without intracranial or nodal spread. A biopsy of the lesion was performed and diagnosed as an infiltrative carcinoma, histiocytoid type. The patient then went on to have exenteration of the left eye with wide surgical resection and postoperative radiation. The lesion was consistent with histiocytoid carcinoma, which extensively involved the eyelid, conjunctiva, orbit, muscles of the eyelid, extraocular muscles, periorbital adipose tissue and lacrimal gland. On light microscopic examination, the lesion consisted of monomorphic histiocytoid cells with indistinct cell borders arranged between collagen fibers, occasionally forming short files with mild atypia. The tumor diffusely infiltrated the dermis without epidermal involvement. The nuclei were round/oval with finely granular chromatin with occasional nucleoli. Mild to moderate pleomorphism was observed focally. Very rare signet-ring cells and mitoses were observed. Perineural invasion was present with positive skin and soft tissue margins. The lesion showed positive immunohistochemical staining for CAM 5.2, CK AE1/AE3, CK 7, GCDFP, E-cadherin, and BER-EP4. The lesion was negative for ER/PR, CK 5, CK6, CK 20, CD68, and S100. Signet-ring cell histiocytoid carcinoma of the eyelid has been published in 30 cases in English literature to date. Furthermore, through thorough immunohistochemical studies it is imperative to rule out metastatic signet-ring cell histiocytoid carcinomas from other sites.
A Fatal Case of Staphylococcus pettenkoferi Bacteremia in a Skilled Nursing Facility Patient

(Poster No. 2)

Hansen Lam, MD (hansen.lam@mountsinai.org); Matthew Shapiro, MD; Morgan Blakely, MD; Bruce Petersen, MD. Department of Pathology, Molecular and Cell-Based Medicine, Icahn School of Medicine at Mount Sinai, New York, New York.

Coagulase-negative staphylococci have been increasingly implicated in bacteremia, specifically in patients with indwelling devices and those who are immunocompromised. Staphylococcus pettenkoferi is a relatively newly characterized and rarely identified species of coagulase-negative staphylococci, first described in 2002 and reported in only 10 cases since then. We present a case of S. pettenkoferi bacteremia, likely precipitating fatal arrhythmia in a patient with multiple indwelling devices and medical comorbidities. The patient was a man older than 90 years who was residing in a skilled nursing facility who had a medical history significant for congestive heart failure, diabetes mellitus type 2, remote cerebral vascular accident requiring gastric tube placement, and end-stage renal disease requiring catheter hemodialysis. He presented to the emergency department after new-onset seizure-like activity and abnormal EKG results. He underwent workup for possible causes of seizure, with suspected etiology being secondary to encephalomalacia from prior right-sided cerebral infarct and occult bacteremia. Staphylococcus pettenkoferi was isolated in 2 of 2 blood cultures using matrix-assisted laser desorption ionization time-of-flight mass spectrometry. Two days subsequent to admission, he experienced sudden hypothermia and atrial fibrillation, and, despite appropriate medical therapy, developed bradycardia and pulseless electrical activity with intermittent ventricular fibrillation. To the authors’ knowledge, this is the first case report of human S. pettenkoferi infection and associated death in the United States and adds to the growing body of evidence regarding the pathogenicity of S. pettenkoferi in patients with indwelling devices and those at risk for nosocomial infections.

Results: A total of 9 of 33 patients died of pure cardiovascular complications (including ischemic heart disease, congestive heart failure with arrhythmia, ruptured aortic aneurysm, sudden cardiac death, and hypertensive cardiomyopathy), 7 of 33 patients died of pneumonia alone, 4 of 33 died of combined cardiovascular and respiratory pathologies (including ischemic heart disease, cardiomegaly, congestive heart failure, and chronic obstructive pulmonary diseases), 3 of 33 died of cerebrovascular accidents, 3 of 33 died of pulmonary embolism, 3 of 33 died of sepsis, 2 of 33 died of cancer, 1 of 33 died of complications of advanced AD, and 1 of 33 died of anoxic brain injury (Figure 2).

Conclusions: Cardiovascular and pulmonary complications are the leading causes of death in patients with AD in our series.

Pulmonary Lymphangioleiomyomatosis: An Autopsy Case Report and Review of Literature

(Poster No. 4)

Christian Salib, MD (christian.salib@wmchealth.org); George Kleinman, MD. Department of Pathology, Westchester Medical Center, Valhalla, New York.

A Fatal Case of Staphylococcus pettenkoferi Bacteremia in a Skilled Nursing Facility Patient

(Poster No. 2)

Hansen Lam, MD; Matthew Shapiro, MD; Morgan Blakely, MD; Bruce Petersen, MD. Department of Pathology, Molecular and Cell-Based Medicine, Icahn School of Medicine at Mount Sinai, New York, New York.

Coagulase-negative staphylococci have been increasingly implicated in bacteremia, specifically in patients with indwelling devices and those who are immunocompromised. Staphylococcus pettenkoferi is a relatively newly characterized and rarely identified species of coagulase-negative staphylococci, first described in 2002 and reported in only 10 cases since then. We present a case of S. pettenkoferi bacteremia, likely precipitating fatal arrhythmia in a patient with multiple indwelling devices and medical comorbidities. The patient was a man older than 90 years who was residing in a skilled nursing facility who had a medical history significant for congestive heart failure, diabetes mellitus type 2, remote cerebral vascular accident requiring gastric tube placement, and end-stage renal disease requiring catheter hemodialysis. He presented to the emergency department after new-onset seizure-like activity and abnormal EKG results. He underwent workup for possible causes of seizure, with suspected etiology being secondary to encephalomalacia from prior right-sided cerebral infarct and occult bacteremia. Staphylococcus pettenkoferi was isolated in 2 of 2 blood cultures using matrix-assisted laser desorption ionization time-of-flight mass spectrometry. Two days subsequent to admission, he experienced sudden hypothermia and atrial fibrillation, and, despite appropriate medical therapy, developed bradycardia and pulseless electrical activity with intermittent ventricular fibrillation. To the authors’ knowledge, this is the first case report of human S. pettenkoferi infection and associated death in the United States and adds to the growing body of evidence regarding the pathogenicity of S. pettenkoferi in patients with indwelling devices and those at risk for nosocomial infections.

Results: A total of 9 of 33 patients died of pure cardiovascular complications (including ischemic heart disease, congestive heart failure with arrhythmia, ruptured aortic aneurysm, sudden cardiac death, and hypertensive cardiomyopathy), 7 of 33 patients died of pneumonia alone, 4 of 33 died of combined cardiovascular and respiratory pathologies (including ischemic heart disease, cardiomegaly, congestive heart failure, and chronic obstructive pulmonary diseases), 3 of 33 died of cerebrovascular accidents, 3 of 33 died of pulmonary embolism, 3 of 33 died of sepsis, 2 of 33 died of cancer, 1 of 33 died of complications of advanced AD, and 1 of 33 died of anoxic brain injury (Figure 2).

Conclusions: Cardiovascular and pulmonary complications are the leading causes of death in patients with AD in our series.
Autopsy Findings in a Rare Case of Twin Reversed Arterial Perfusion Sequence
(Poster No. 5)

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Twin reversed arterial perfusion (TRAP) sequence is a rare complication of monochorionic twin gestations affecting 1 in 35,000 births. TRAP sequence occurs when a normal “pump” twin perfuses a malformed recipient twin via artery-artery anastomosis. Increased arterial pressure in the “pump” twin causes reversal of blood flow in the recipient twin. As a result, the recipient twin receives only deoxygenated blood, and severe malformations occur. We report a rare autopsy case of TRAP sequence fetus at 26 weeks’ gestation. At autopsy, the fetus was incompletely formed, with fetal hydrops. The head was poorly developed, with incomplete skull and absent mature midline facial structures. The upper extremities were absent, as was the distal right lower extremity. Internal examination revealed an incomplete complement of internal organs. No cardiac tissue was found grossly or microscopically. Several solid organs, including a single kidney, adrenal gland, pancreas, and ovarian tissues, were identified. Gross and microscopic examination of the brain revealed hydranencephaly, with an immature, 4-layered cerebellum (Figure 4, A through D). An immature hindbrain/mesencephalon was present, with complete absence of the telencephalon. An anomalous smooth muscle-lined tubular structure was present continuous with the renal collecting duct system that was segmentally lined by urothelial, intestinal, and keratinizing squamous epithelium. A chromosomal microarray was performed, revealing normal female karyotype. The fetus was classified as acardiac aneuploidy, which represents a minority of TRAP sequence cases. Although fetal TRAP sequence usually incurs a high mortality in the “pump” twin, the sibling survived delivery and is alive and thriving 8 months after delivery.

Epidemiology of Suicide in an Iowa Cohort
(Poster No. 6)

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Context: Suicide is an ongoing public health problem in the United States. Epidemiologic evaluation of suicide is important to characterize and identify at-risk populations.

<table>
<thead>
<tr>
<th>Cohort Characteristics, Total and by Sex</th>
<th>Total, No. (N = 657)</th>
<th>Male, No. (n = 509)</th>
<th>Female, No. (n = 146)</th>
<th>P Value (Missing = 2)</th>
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Design: This is a descriptive analysis of 657 suicide decedents autopsied by the University of Iowa Hospitals and Clinics between July 1, 2003, and June 30, 2018. Data were obtained via autopsy report abstraction. Statistical analyses were conducted using SAS 9.3.
**Results:** Decedents were primarily white (88.2%) and male (75.7%; Table). Average age was 43 years. Suicides were more likely to occur at a residence (69.3%), earlier in the week, and in the late night to early morning hours. Suicides were most likely to occur in spring and least likely in winter. The most common method was a firearm (44.6%), most often a handgun (61.3% of firearm suicides). Nearly one-half (42.8%) of decedents left a note or similar communication. Approximately one-quarter (22.1%) of suicides were without a known identified life stressor or known inciting event, a phenomenon that was markedly more common among men. Women were more likely to have a known mental health condition, prior contact with mental health care, or prior suicidal behavior.

**Conclusions:** We found that, statistically speaking, the typical profile of a suicide is a white male who used a firearm in his place of residence. More than half of decedents left no communication of intent to commit suicide, and one-quarter—more commonly men—had no known life stressor or other specifically identified motivating factor. Future studies should seek to further elucidate factors leading to suicide in this at-risk population.

**Autopsy Findings in a Case of Bordetella holmesii Endocarditis in a Child With Asplenia, Congenital Heart Disease, and Heterotaxy Syndrome**

(Poster No. 7)

Geetika Goyal, MD (drgeetika.goyal@outlook.com); Cyril D’Cruz, MD. Department of Pathology, Saint Barnabas Medical Center, Livingston, New Jersey.

Bordetella holmesii, a strictly aerobic Gram-negative coccobacillus, is a rare cause of septicemia and endocarditis in young immunocompromised patients with asplenia. Bordetella holmesii was first isolated in 1983, and further classification and characterization were described in 1995. There have been a few case reports of B holmesii endocarditis in literature, with previous cases reported in living patients. The mortality from infection is not high. We report autopsy findings in a case of endocarditis caused by B holmesii resulting in the death of a child, with endocarditis being the primary cause of death. The deceased was a 9-year-old African American boy with asplenia, complex congenital heart disease with dextrocardia, hypoplastic left heart syndrome, right ventricle–dominant atrial ventricular canal, and double-outlet right ventricle with severe valvular pulmonary stenosis. There was abdominal heterotaxy and pulmonary hypertension. The child presented with difficulty in breathing and not feeling well. Despite support measures, the child died. Ultrasound examination of the heart revealed a single atrioventricular valve with large vegetations and thrombi. These vegetations on microscopic examination showed the presence of Gram-negative bacteria with coccobacillary morphology. Initial blood cultures grew Bordetella species, alerting the public health officials to the possibility of pertussis, but the organism was identified as B holmesii. The same organism was cultured from the heart at autopsy (Figure 5).

**Cultural Competency in Forensic Pathology: A Case Report of Suicide by Oleander Poisoning**

(Poster No. 9)

Eshaan J. Daas, BS (edasa@email.arizona.edu); Andrea L. Wiens, DO,1 2 Department of Medicine, University of Arizona College of Medicine, Phoenix; 2Department of Pathology, Maricopa County Office of the Medical Examiner, Phoenix, Arizona.

Thevetia peruviana (yellow oleander), a member of the dogbane family of plants, has historically been used for medicinal benefits in arrhythmias, asthma, and indigestion despite limited research supporting its efficacy. In countries such as Sri Lanka and India, it has also been used as a method for self-harm with strong cultural ties following its discovery as a cardiotoxic agent with potent sugar and steroid moieties.
sessions capable of inhibiting the sodium-potassium pump found in cardiac myocytes. Cases of suspected oleander poisoning require investigative measures beyond the standard autopsy protocol and require an appropriate index of suspicion. We present a case of a 30-year-old woman from India with a medical history significant for depression who collapsed suddenly. She arrived in the emergency department with vomiting, junctional bradycardia, tachypnea, and incomplete right bundle branch block. Urine drug screen was negative. Death ensued despite appropriate medical intervention and life-saving efforts. At autopsy, the decedent was a well-developed, well-nourished adult woman with mildly congested conjunctivae. Internal examination was grossly unremarkable. Postmortem toxicology testing for standard drugs of abuse was negative. Thorough scene investigation uncovered receipts and packaging for yellow oleander seeds with additional evidence of a toxic oral preparation. A suicide note found at the death scene indicated the decedent intentionally consumed the oleander seeds the morning of her death. Targeted toxicity testing confirmed a high oleandrin concentration in postmortem blood. This case highlights the importance of cultural competency and informed death scene investigation to complement postmortem examination in order to reach accurate clinical conclusions.

**Formalin Pigment Removal With Alcoholic Ammonium Hydroxide Significantly Increases the Quality of Autopsy Tissue Slides**

*(Poster No. 10)*

Kyriakos Chatzopoulos, MD (Chatzopoulos.Kyriakos@mayo.edu); Benjamin J. Van Treeck, MD; Elise R. Venable, MBBS; Vishnu V. Serla, MBBS; Trenton J. Wirth, HTL(ASCP); Fazi Amirahmadi, PhD; Alissa A. Peterson, HTL(ASCP); Peter T. Lin, MD. Department of Anatomic Pathology, Mayo Clinic, Rochester, Minnesota.

**Context:** High-quality hematoxylin-eosin slides are essential for accurate diagnosis in anatomic pathology. Formalin pigment is a common artifact in autopsy histology, reducing the quality of hematoxylin-eosin slides and potentially leading to misinterpretation.

**Design:** Archival histologic material from 31 autopsy cases was scored by 4 evaluators for the presence of formalin pigment, and clinicopathologic data were obtained through chart review. Formalin pigment was removed from selected slides with 2 different methods (alkyphenol ethoxylate and alcoholic ammonium hydroxide), stained with hematoxylin-eosin, and assessed for percentage of reduction in pigment. Impact on routine implementation of the procedure was assessed by stakeholders.

**Results:** Duration from time of death to autopsy was correlated with the average amount of pigment accumulation (Spearman $p = 0.01$). Tissues of decomposed decedents accumulated significantly more formalin pigment than the rest of the cohort (Kruskal-Wallis test; $P < 0.01$). The most affected organs were liver, spleen, pancreas, heart, brain, kidney, and lungs. Alcoholic ammonium hydroxide reduced the pigment by 99%. Interobserver agreement for pigment assessment was excellent for pretreated slides and slides treated with alcoholic ammonium hydroxide (Crombach $\alpha = 0.96$ and 0.99). Within our histology laboratory, routine implementation of pigment removal in decomposed cases is estimated to increase workload by 0.07%, with negligible impact on expenses and no need for additional full-time equivalents.

**Conclusions:** Routine removal of formalin pigment with alcoholic ammonium hydroxide significantly increases the quality of histology-eosin slides of autopsy tissues, especially of decomposed decedents, with negligible impact on laboratory logistics and expenses.

**Aortoesophageal Fistula: A Case of Fatal Upper Gastrointestinal Bleeding of Unknown Origin**

*(Poster No. 11)*

Carlo De la Sancha, MD (cdelasan@iu.edu); Joseph Curran, MD; Rong Fan, MD. Department of Pathology, Indiana University School of Medicine, Indianapolis.

Aortoesophageal fistula constitutes a rare, usually fatal event. In most reported cases, an aortoesophageal fistula results from an ateriosmual formation of an aberrant right subclavian artery in elderly patients or from nasogastric tube intubation in young patients with an aberrant right subclavian artery. We report a case of an 8-week-old female patient with diagnosed vascular ring composed of patent ductus arteriosus, aberrant left subclavian, and right-sided aortic arch (Figure 7, A). After being intubated to overcome obstruction, she developed massive upper gastrointestinal hemorrhage that led to her death. Previous urgent thoracotomy revealed no clear evidence of erosion and no clear source of bleeding. Autopsy examination revealed an aortoesophageal fistula at the level of the vascular ring, with the esophageal opening 4 cm below the hyoid bone. Probing of the lumen led to the ascending aorta (Figure 7, B and C). When intubated, the mechanism underlying the development of a fistula usually involves the induction of limited necrosis of the digestive and arterial walls by pulsatile compression of the esophageal wall between the arterial wall and rigid intubation catheter. This leads to thrombosis of the vasa vasorum as well as to ischemia of the digestive wall. With time, ulceration and ultimately arteriogenic fistula appear. Clinical diagnosis of this complication is difficult because of its extreme rarity. In the absence of any evidence suggesting the possibility of an anomaly of the aortic arch system, there are no specific manifestations.
We report a stillborn baby with tetra-phocomelia (Figure 9) born to a diagnostic feature, and only a few cases have been reported to date. Tetra-phocomelia, a rarest of rare defect, is a key clinical deficiency of postmortem examination in selected cases without definite clinical diagnosis.

Pseudo-Roberts Syndrome: An Entity or Not?
(Poster No. 14)
Behzad Salari, MD (bsalari@wustl.edu); Louis P. Dehner, MD. Department of Pathology and Immunology, Washington University in St Louis, Missouri.

Roberts syndrome is a rare genetic disorder characterized by growth deficiencies, including hypomelia or phocomelia of 4 limbs, oligodactyly, micrognathia, microcephaly or encephalocele, and other anomalies. Tetra-phocomelia, a rarest of rare defect, is a key clinical diagnostic feature, and only a few cases have been reported to date. We report a stillborn baby with tetra-phocomelia (Figure 9) born to a 32-year-old G2 P1 T0A0L1 mother who presented at 30 weeks of gestation. Prenatal and postnatal imaging and autopsy findings included schizencephaly, phocomelia of 4 limbs, micrognathia, hypoplastic ears, oligodactyly, cardiopulmonary malformations (double-outlet right ventricle, ventricular septal defect, pulmonary artery atresia, and bicuspid aortic valve with aortic valve regurgitation), severe hypospadias with diminutive rudimentary penis and labial scrotum, retrodisplaced anus, and other anomalies. Microcephaly was found on prenatal imaging, but autopsy examination did not document it. Given the various skeletal anomalies found on autopsy and imaging evaluations, at least phenotypically, it fit into the Roberts syndrome spectrum. According to molecular testing (karyotype, prenatal chromosome microarray, and gene testing for ESCO2 gene), however, the infant did not have the mutation that has been associated with this disorder. In a sense, this infant could possibly be labeled as the first report of pseudo-Roberts syndrome because many of the phenotypic anomalies in this infant are characteristic of Roberts syndrome but in the absence of a mutation in the ESCO2 gene.

Unusual Case of Progressive Multifocal Leukoencephalopathy in a Patient With Sjögren Syndrome Clinically Presenting as Transverse Myelitis
(Poster No. 13)
Ifeoma Onwubiko, MD, MPH (ionwubi1@hfhs.org); Kanika Tanega, MD; Nilesh Gupta, MD; Abir Mukherjee, MD. Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, Michigan.

Progressive multifocal leukoencephalopathy (PML) is a rare demyelinating disease caused by reactivation of JC virus and affecting typically subcortical and periventricular white matter of immunocompromised hosts (HIV infection, hematologic malignancies). We present an unusual case of PML predominantly affecting cervical spinal cord and brainstem in an immunocompetent host. A 65-year-old woman presented with vertigo, hemiparesis, and right-sided weakness. Magnetic resonance imaging (MRI) of the brain without contrast showed T2 signal abnormality involving the medulla extending into the upper cervical cord to the C2 to C3 level. Further workup showed positive ANA, elevated SS-A/Ro, and SS-B/La antibodies consistent with Sjögren syndrome. The patient deteriorated rapidly, dying 8 days after the onset of acute respiratory failure. Autopsy showed multifocal white matter lesions with perivascular lymphocytic cuffing, microglial nodules, influx of activated microglial, and numerous oligodendroglial nuclei with ground-glass inclusions in the spinal cord, brainstem, cerebellum, and cerebral hemisphere. The inclusions were immunoreactive with Simian virus-40, P53, and MIB-1 immunostains. The distribution of the lesions was predominantly in the medulla and upper cervical cord, correlating with premortem MRI. A rare subset of PML cases can occur in association with connective tissue disorders (Sjögren in this case), with SLE being the most common. Predominantly spinal involvement by PML is also rare. PML should be considered in the differential diagnosis of spinal cord/brainstem lesions, particularly in patients with connective tissue disorders. This highlights the importance of postmortem examination in selected cases without definite clinical diagnosis.

Lymphoma at Autopsy: A Case of Double-Hit Diffuse Large B-Cell Lymphoma With Neurolymphomatosis and Hematogenous Spread
(Poster No. 15)
Benjamin Graham, MD1 (Benjax1023@gmail.com); Matthew Roesch, DO2; Ady Kendler, MD, PhD2; Kristina Brannock, MD.1 1Department of Pathology, University of Cincinnati Medical Center, Cincinnati, Ohio; 2Department of Pediatrics, Dayton Children’s Hospital, Dayton, Ohio.

Diffuse large B-cell lymphoma (DLBCL) with central nervous system (CNS) involvement is very rare and is termed neurolymphomatosis. We report a case of a 57-year-old man with DLBCL with double-hit status (MYC and BCL2 rearranged), refractory to treatment with hyper-central venous access devices, initially presenting with bowel obstruction. Despite treatment, the patient presented months later with left-sided Bell palsy, pancytopenia, and epistaxis. Imaging studies demonstrated multifocal involvement of lymphoma within the leptomeninges, cauda equina, cranial nerves, intercostal nerves, brachial plexus, and left sciatic nerve. A peripheral blood smear with flow cytometry demonstrated circulating DLBCL (Figure 10, A). The patient demonstrated pneumonia on imaging, and chemotherapy was temporarily stopped. The patient was subsequently found unrespon-
sive in bed and was pronounced dead. At autopsy, disseminated lymphoma was seen in the cerebral cortex, cerebellum, brain stem, leptomeninges, the cranial nerves, and a sympathetic ganglion. Histologically, lymphoma cells were seen surrounding vessels in the CNS, including Virchow-Robins spaces of the cerebellum (Figure 10, B), and diffusely involving the oculomotor nerve (Figure 10, C). DLBCL was additionally found within the lungs (Figure 10, D), pericardium, gastrointestinal system, and vasculature adventitia, as well as having possible liver and spleen involvement. The findings in this case likely underestimate CNS involvement because the patient also had dysphagia and acute respiratory arrest (oxygen saturation of 43% just before death). These findings suggested possible vital brain center and phrenic nerve involvement. This case represents, to the authors’ knowledge, the first reported autopsy case of a chemotherapy-refractory, double-hit DLBCL with hematogenous spread and neurolymphomatosis.

**Difficult to Breathe: An Autopsy Case of Type III Tracheal Agenesis**  
(Poster No. 16)

Stephanie L. Holdener, MD (stephanie.holdener@bcm.edu); Mohammed Ahmed, MD; Ya Xu, MD. Department of Pathology, Baylor College of Medicine, Houston, Texas.

According to Floyd classification, there are 3 anatomic types of tracheal agenesis. Type I is characterized by a short segment of trachea failing to form, resulting in a distal tracheoesophageal fistula. Type II, the most common, is characterized by a common bronchus connecting the right and left bronchi to the esophagus distally. Type III is characterized by the right and left main pulmonary bronchi arising independently from the esophagus, as described in our case of a male newborn with 29 4/7 weeks’ gestation who was born via spontaneous vaginal delivery to a 26-year-old woman. The pregnancy was significant by an initial abnormal quad screen with negative subsequent screen. The newborn failed to cry and had bradycardia. Multiple intubation attempts with positive pressure ventilation resulted in minimal improvement. Grossly, there was tracheal agenesis, with bilateral main pulmonary bronchi arising independently from the mid-esophagus. Duodenal atresia was present, and the anus was imperforate. Histologic examination confirmed the transition of esophageal squamous mucosa to bronchial respiratory epithelium with cartilaginous rings present within the bronchial submucosa and distal esophageal submucosa. There was a proximal blind-ending tracheal pouch anterodistal to the larynx, and fusion of the thyroid and cricoid cartilage. Tracheal agenesis results from abnormal development of the tracheoepulmonary complex during the first 8 weeks of gestation. We hope this case presentation will expand the literature on associated findings and provide awareness for early diagnosis and potential surgical treatment (Figure 11).

**Thrombotic Thrombocytopenic Purpura With Graves Disease: A Rare and Tragic Case With Loss of Fetus and Mother**  
(Poster No. 17)

Junlin Zhang, MD1 (junlin.zhang@bswhealth.org); Laura L. Baugh, DO1; Joseph M. Guileyardo, MD2; William C. Roberts, MD. Departments of 1Pathology and 2Baylor Heart and Vascular Institute, Baylor University Medical Center, Dallas, Texas.

Thrombotic thrombocytopenic purpura (TTP) may be seen with other autoimmune disorders, such as immune hemolytic anemia and systemic lupus erythematosus, but it is rarely associated with Graves disease (GD). The relationship of one autoimmune disease with the increased risk of a second autoimmune disease needs further investigation. We report a rare case of TTP with GD and describe some implications of this phenomenon. A 39-year-old woman developed TTP while pregnant. She initially responded to plasma exchange but quickly relapsed, eventually requiring therapeutic abortion for control. Unfortunately, her TTP recurred again and remained refractory to additional plasma exchanges. Terminally, she developed gastrointestinal hemorrhage and a cardiac arrest. Autopsy findings included fibrin microthrombi throughout the heart with foci of hemorrhage and necrosis. Intravascular microthrombi in the lungs were associated with acute cor pulmonale and right ventricular dilatation, and microthrombi involving the gastrointestinal mucosa produced petechial hemorrhage. An unexpected finding included diffuse enlargement of the thyroid gland (weighing 95 g) with histologic features of partially treated GD (diffusely abnormal gland with colloid follicles and intervening areas of hyperplasia). The dramatic response of both GD and TTP to plasma exchange encourages further exploration of immune modulator therapy in treating these disorders. Plasma exchange for TTP also had partially treated this patient’s GD. Although TTP with GD is uncommon, patients with thyrotoxicosis and thrombocytopenia should be screened for TTP because of the high mortality associated with delayed treatment of TTP.
Fatal Urinary Bladder Hemorrhage Following Foley Catheterization in a Patient With Bladder Outlet Obstruction and Waldenström Macroglobulinemia

(Poster No. 18)

Annie N. Samraj, MBBS (asamraj@uw.edu); Miles McDonough, MD; Dennis D. Reichenbach, MD; Florencia G. Jalikis, MD; Desiree A. Marshall, MD. Department of Pathology, University of Washington, Seattle.

An 83-year-old man with Waldenström macroglobulinemia presented with urinary retention, necessitating catheterization. Imaging demonstrated a bladder mass with hydronephrosis, “consistent with primary bladder malignancy.” Approximately 1950 mL was emptied following catheterization. He returned to the emergency department the next day with hematuria; hematocrit had precipitously dropped to 16% (28% previous day). He was admitted for hemorrhage control and postobstructive renal failure due to “bladder malignancy.” Hemorrhage was refractory to aggressive blood transfusions and bladder irrigation, and he transitioned to comfort care. At autopsy, there was bilateral hydronephrosis with a remarkably enlarged bladder containing ~1000 mL of blood with clots. The wall was trabeculated consistent with chronic bladder outlet obstruction; microscopy demonstrated smooth muscle hypertrophy interspersed with collagen deposition and abundant hemorrhage (Figure 12). Benign prostatic hyperplasia was present.

No tumor was identified grossly or microscopically. Flow cytometry demonstrated the known B-cell lymphoma with plasmacytic differentiation. Usually, hematuria following bladder decompression is transient and minimal. In bladder outlet obstruction, the high pressure necessary to void results in structural changes creating a weak, friable bladder. Historically, it was hypothesized that catheterization with sudden decompression and large volume emptying can cause epithelial sloughing leading to disastrous bleeding ("decompression or ex-vacuo hematuria"). In this patient, multiple factors—bladder outlet obstruction, bleeding diathesis due to Waldenström macroglobulinemia, and antiplatelet therapy—led to unrestrained bleeding. The authors could not identify any other case report of fatal bladder hemorrhage initiated by catheterization in the literature, making this case remarkably unique. Clinicians should be vigilant when confronted with prolonged bleeding following catheterization.

Use of Autopsy to Dissolve Diagnostic Ambiguity: Colorectal Adenocarcinoma With Clostridium septicum Sepsis

(Poster No. 19)

Kara L. Roncin, MD (Kara.Roncin@UHHospitals.org); Claire W. Michael, MD. Department of Pathology, University Hospitals Cleveland Medical Center, Cleveland, Ohio.

We report a case of a 55-year-old man who presented with nonspecific symptoms and a wide differential that was rectified via autopsy. The patient had a recent diagnosis of hypertension and hyperlipidemia. Following a 6-hour flight, he presented with cramping pain in the left buttocks and left-hand paresis with no history of musculoskeletal injury. He reported vomiting and constipation that resolved prior to presentation. At home, the patient experienced dyspnea, nausea, and chest pain that required advanced cardiac life support. Crepitation was noted in the anterior chest and left thigh. The patient was unresponsive to all resuscitative efforts. At autopsy, there was violaceous mottling of the left anterior thigh, buttocks, and bilateral flanks, with numerous bullae and skin sloughing. The peritoneal cavity contained 1500 mL of serosanguinous fluid. Multiple organs had marked autolysis, congestion, and crepitis. A 3.7-cm ulcerated cecal mass was identified. Microscopic examination revealed invasive, moderately differentiated adenocarcinoma with mucinous differentiation (pT2NMX). There was diffuse infection with Clostridium septicum, a Gram-positive bacilli of the normal gut flora and an aggressive cause of sepsis. Bacterial gas-production expansion of preexisting atherosclerotic plaques was the most likely cause of reported chest pain, in combination with bacterial lung infection leading to dyspnea. Perineural bacteria may have contributed to extremity paresthesia. This case raises the awareness of including C septicum sepsis in the differential diagnosis, as well as the significance of timely screening. It also underscores the value of autopsy to resolve diagnostic ambiguities, which provided closure and personalized screening recommendations for family members.

Neonatal Thrombocytopenia With Chromosome (11,18) Translocation in Fetal Autopsy

(Poster No. 20)

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Severe neonatal thrombocytopenia is uncommon in the newborn population. The causes of thrombocytopenia in neonates are diverse and include immune, inherited, and acquired disorders. Congenital thrombocytopenias usually present in the first 72 hours of life and do not respond to regular therapies. We report a case of neonatal thrombocytopenia with chromosomal translocation in a neonatal autopsy (gestational age 30 weeks). A 35-year-old mother who is heterozygous factor V Leiden, homozygous MTHFR gave birth to a
Neonatal Severe Combined Immunodeficiency With Rare Chromosome 19 Microdeletion and Hypoplasia of the Reticuloendothelial System

(Preceptor No. 21)

Autumn V. Hammonds, DO (asvano2@uky.edu); Al Smith, MD; Rebekah Waikel, PhD; William O’Connor, MD; Anna Castiglione-Richmond, MD. Department of Pathology and Laboratory Medicine, University of Kentucky, Lexington.

An 1892-g female was delivered vaginally at 31.5 weeks’ gestation to a 29-year-old G2, P2 mother. Pregnancy was complicated by polyhydramnios, and the congenital thrombo-cytopenia. The latter finding makes it worthy to investigate the relationship of chromosome 18 aberrations and single/double-vessel umbilical cord. The microarray analysis showed a gain of short arm of chromosome 11 and a loss of the long arm of chromosome 18, consistent with unbalanced translocation. The cause of death of the infant was massive intracranial hemorrhage (Figure 13, C) as well as hyaline membrane disease. Cytogenetic examination revealed a normal female diploid karyotype (46,XX), which excludes trisomy 18 as a cause for dysmorphic features and 2-vessel umbilical cord. The microarray analysis showed a gain of short arm of chromosome 11 and a loss of the long arm of chromosome 18, consistent with unbalanced translocation. The latter finding makes it worthy to investigate the relationship of chromosome 18 aberrations and single/double-vessel umbilical cord, IUGR, polyhydramnios, and the congenital thrombo-cytopenia.

Pathologic Findings in the Spleen in Adult Autopsies: A Ten-Year Community Teaching Hospital Experience

(Preceptor No. 22)

Gagandeep Kaur, MD (Gagandeep.Kaur@vchn.org); Kaitlyn Williams, BS; Ramapiya Vidhun, MD; Jessica Dodge, MD. Department of Pathology and Laboratory Medicine, Danbury Hospital, Danbury, Connecticut.

Context: Splenic pathology other than splenomegaly is relatively uncommon in adult autopsies. There is not much recently published literature about splenic pathology in adult autopsies. We report our 10-year autopsy experience in a community teaching hospital. We also report how many of the splenic abnormalities had been diagnosed prior to death.

Design: The laboratory information system was searched for autopsies performed between January 1, 2008, and December 31, 2018. Patients age <18 years and partial autopsies that did not examine the abdomen were excluded. The autopsy reports were reviewed, and splenic pathologic findings were recorded. The electronic medical records of patients who had splenic pathology were reviewed to determine if the splenic abnormalities had been diagnosed prior to death.

Results: Of 378 autopsy reports reviewed, 123 patients (32.5%) had splenic pathology. Splenomegaly, capsular fibrosis, accessory spleens, infarcts, hematopoietic neoplasms, nonhematopoietic neoplasms, infection, and granulomas were the most common abnormalities (Table). A total of 31 of 123 patients (25.2%) had multiple splenic abnormalities. Twenty-two patients (17.9%) had received diagnosis prior to death. None of the patients died of splenic pathology.

Conclusions: Although splenic pathology was seen in approximately one-third of our adult autopsies and one-quarter of abnormal spleens showed multiple abnormalities, premortem diagnosis was infrequent. The spleen is an unsung hero. It filters blood to remove senescent and damaged red blood cells, removes pathogens, and assists in immunity while seldom becoming involved by neoplasms or causing death.

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Fatal Primary Dedifferentiated Adamantinoma of the Rib With Lung Metastasis

(Preceptor No. 23)

Ghulam Ilyas, MBBS1 (ghulam.ilyas@downstate.edu); Mouyed Alawad, MD2; Agha Wajdan Baqir, MBBS2; Jonathan D. Somma, MD.2 1Department of Pathology, SUNY Downstate Medical Center, Brooklyn, New York; 2Department of Pathology, LSU Health Sciences Center, New Orleans, Louisiana.

Adamantinoma is an extremely rare, slow-growing primary bone tumor comprising <1% of all bone tumors. Male patients in their second to third decade are more commonly affected, and >90% of tumors are located at the fibula, tibia, femur, ulna, or radius. We present an autopsy case of primary dedifferentiated adamantinoma of the rib with lung metastasis. The deceased, a 51-year-old man, had several comorbidities in addition to a posterior chest wall mass. Chest x-ray and computed tomography film revealed osteolytic mass of the right second and third ribs and lung nodules. Autopsy findings were significant for a right posterior upper chest wall tumor (7 cm) involving ribs 2 and 3, adjacent soft tissues, and vertebral column (Figure 14), as well as multiple bilateral necrotic tumor nodules within lung parenchyma (0.5–2 cm). Histologically, the tumor at all sites was similar, showing a range of morphology from sarcomatoid to rhabdoid to undifferentiated cells in a fibrous stroma. However, some sections, particularly those from the second rib, demonstrated an infiltrating glandular histology. This peculiar variant of rib adamantinoma showed that in addition to mesenchymal-to-epithelial transformation in the early stage of development, progression to an aggressive subtype may be associated with epithelial-to-mesenchymal transition (“sarcomatoid dedifferentiation”). Because of its rarity and various clinicoradiologic and histologic patterns, adamantinoma may resemble numerous conditions. This case shows that adamantinoma should be included in the differential diagnosis because its distinction has important implications for treatment and prognosis.
Acute Respiratory Distress Syndrome Secondary to AIDS-Related Kaposi Sarcoma: An Autopsy Correlation

(Poster No. 24)

Neeraja Yerrapotu, MD (neeraja.yr@gmail.com); Evi Abada, MD, MS; Tapan Bhavsar, MD, PhD; Sudeshna Bandyopadhyay, MD. Department of Pathology, Wayne State University, Detroit, Michigan.

AIDS-related Kaposi sarcoma (KS) is one of the 4 epidemiologic forms of KS and commonly presents with localized/disseminated mucocutaneous and visceral involvement. HIV-positive patients at risk include those with low CD4 counts and/or high viral loads. Pulmonary involvement in AIDS-related KS has been associated with pleural effusions, as well as endobronchial and parenchymal tumors. However, acute respiratory distress syndrome has been a rare presentation. Here, we present the case of a 28-year-old man with multiple high-risk factors and unknown HIV status who presented to the emergency department with abdominal pain, oral lesions, unintentional weight loss, breathlessness, and hemoptysis. A diagnosis of AIDS was made based on a rapid HIV test and CD4 count of 14/μL. Imaging studies revealed multiple hepatic lesions and diffuse lymphadenopathy. A diagnosis of KS was made on inguinal lymph node biopsy (Figure 15, A; HHV8 stain). He developed acute respiratory distress syndrome, rapidly deteriorated, and died shortly thereafter. Extensive workup for viral, fungal, and bacterial etiologies was negative. Gross examination at autopsy revealed diffuse visceral (Figure 15, B), abdominal lymphadenopathy (Figure 15, C), and focal gingival purple-red lesions. Microscopic examination of the lung, liver, and lymph nodes revealed spindle cells and vascular proliferations focally positive for HHV8 and CD31 consistent with the involvement of KS. Interestingly, in addition, the alveolar spaces in the lungs showed a spectrum of changes, including hyaline membranes and intraluminal proliferation of organizing fibroblasts consistent with the clinical diagnosis of acute respiratory distress syndrome, which has not been described in the literature thus far (Figure 15, D).

Expeditied Autopsy of a Lethal Bladder/Prostate Pediatric Embryonal Rhabdomyosarcoma

(Poster No. 25)

Margaux M. Canevari, DO (margaux328@gmail.com); Constance DiAngelo, MD; Carly R. Varela, MD; Clayton Brittingham, DO; Christopher Rossi, MD. Departments of 1Pathology and 2Radiology, Walter Reed National Military Medical Center, Bethesda, Maryland; 3Department of Pathology, Children’s National Medical Center, Washington, DC; 4Department of Pediatrics, Division of Hematology and Oncology, Children’s National Health System and Inova Fairfax Hospital, Falls Church, Virginia.

We present the autopsy case of a 2-year-old boy who initially presented at 16 months with a several-week history of irritability and change in bowel habits. He was non–syndromic-appearing, with a palpable pelvic mass. Magnetic resonance imaging demonstrated a heterogeneously enhancing pelvic mass (Figure 16, A) displacing and compressing the bladder with outlet obstruction and hydronephrosis. Biopsy showed an embryonal rhabdomyosarcoma (Figure 16, B) with FOXO1 gains and hyperdiploid karyotype. Staging evaluation revealed localized disease. Imaging indicated partial response as the patient was undergoing chemotherapy and proton beam radiation. However, toward the end of therapy, follow-up imaging showed localized tumor progression. Subsequent biopsy revealed viable tumor with no treatment effect. The relapse tumor was found to have mutations in the following genes: NFI, TSC2, FGFR4, and TP53. Because of his disease progression and no curative treatment options, he was transitioned to hospice care and died. The family requested tumor debulking for research purposes. An expedited autopsy, defined as less than or equal to 6 hours from time of death, was performed as per research protocol. The tumor encased the pelvis (Figure 16, C), with complete obstruction of his bowel and bladder, with 9 cm of fungating mass protruding from his rectum (Figure 16, D). Multiple liver metastases were newly identified. This case highlights clinicopathologic information from a lethal embryonal rhabdomyosarcoma case and the role of expedited autopsy for research to help support family wishes.

Congenital Mesoblastic Nephroma: An Unusual Presentation of a Typically Uncomplicated Congenital Malignancy

(Poster No. 26)

Brett Kurpiel, BA; Evi Abada, MD; Elsieha Shanes, MD; Robin LeGallo, MD. Department of Pathology, University of Virginia, Charlottesville.

Congenital mesoblastic nephroma (CMN) is a relatively rare neonatal renal tumor with distinct forms, including classical, cellular, and mixed. Gestational symptoms include polyhydramnios and hydrops fetalis, and the tumor may be identified on routine prenatal ultrasound. These tumors are small, averaging 5 cm, and are surgically excised. Survival rates approach 95% to 100%. Here we describe an unusual case of CMN presenting at delivery. The pregnancy had been uncomplicated, and a 30-week ultrasound was performed without identification of a mass. The infant was born by vacuum-assisted vaginal delivery at 37 weeks and 4 days. At birth the infant had abdominal distension and apnea requiring immediate resuscitation. Abdominal ultrasound found significant hemoperitoneum, and the infant was taken to the operating room for surgical exploration, which showed a large, hemorrhagic retroperitoneal mass. A biopsy was done. The infant died on the second day of life after withdrawal of care because of ongoing seizures and complications of hypoxic injury. Autopsy revealed a 13.6-cm hemorrhagic mass originating in the right kidney (Figure 17, A and B). Histologically, the mass consisted of a monomorphous population of spindle cells with plump, ovoid nuclei and focal apoptotic cells (Figure 17, C). Break-apart fluorescent in situ hybridization studies showed a disruption of ETV6, consistent with a diagnosis of cellular CMN (Figure 17, D). Although outcomes are typically good in cases of CMN, the large tumor size and traumatic birth with resulting hemoperitoneum
make this case unusual. This case highlights the need for better understanding of the growth and clinical presentation of CMN to advance prenatal diagnostic techniques.

Disseminated Tuberculosis Masquerading as Metastatic Testicular Cancer: Another Case Report Proving Why Autopsies Must “Stay Alive”

(Poster No. 27)

Michael Pagacz, MD1 (michael@pagacz.ca); Pukhray Basra, MD2; Christopher Antonio Febres-Aldana, MD3; Vicky Loescher, MD2; Robert Poppiti, MD4; Cristina Vincentelli, MD1 Departments of 1Pathology and 3Radiology, Mount Sinai Medical Center, Miami Beach, Florida.

Historically, the benefits of performing autopsies are widely documented. Despite the declining rates of hospital autopsies worldwide, it is important to recall that the clinicopathologic correlation provided by autopsies is critical in the education of physicians as well as in serving as a tool to ensure high quality of medical diagnostics and patient care. We report the case of a 43-year-old Haitian man with altered mental status, ataxia, and urinary incontinence. A computed tomography scan of the head revealed ventriculomegaly, multiple cerebral and cerebellar nodules, and meningeal enhancement. Additional imaging showed a right testicular mass, diffuse retroperitoneal lymphadenopathy, and a left adrenal gland nodule. The preliminary diagnosis was a metastatic testicular malignancy. The patient died without a definitive diagnosis, and an autopsy was requested. Postmortem findings were those of disseminated tuberculosis showing a miliary pattern in the lungs, as well as extensive involvement of the leptomeninges, brain, right epididymis, and testicle. Meningeal findings included obliterative endarteritis with thrombosis, which significantly contributed to the patient’s death. Postmortem cultures grew Mycobacterium tuberculosis. This is another case that demonstrates the value of the autopsy. Autopsies, once performed on 50% of all hospital deaths in the United States, have now dropped to approximately 4.3%. Internists and pathologists alike agree on the educational value and benefits of autopsies; therefore, measures should be put in place to facilitate the process of autopsy request and consent in all hospitals.

Communication between pathologists and clinicians must be encouraged to ensure that the value of the autopsy is not forgotten.

Reform of the Autopsy Consenting Process to Reflect Adequate Informed Consent: One Teaching Institution’s Experience

(Poster No. 28)

Erica R. Vormittag-Nocito, MD (evormi2@uic.edu); Tracy Wads-worth, MD; John V. Groth, MD. Department of Pathology, University of Illinois at Chicago, Illinois.

Context: As the number of autopsies performed declines, it is important to assess whether the practice of consenting for autopsy remains at required standards. Limited US practice data suggest autopsy consent forms lack helpful information for clinical providers who have deficiencies in their understanding of the autopsy procedure. Additionally, controversy over organ retention in other countries has led to large-scale reform for autopsy consenting practices. Therefore, our aim is to evaluate current autopsy consenting practices in our institution.

<table>
<thead>
<tr>
<th>Survey Questions</th>
<th>% Responding Yes (N = 30)</th>
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<tr>
<td>Have you ever witnessed an autopsy being performed?</td>
<td>20 (6)</td>
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<tr>
<td>Do you feel comfortable identifying next of kin who is legally eligible to sign consent for autopsy?</td>
<td>80 (24)</td>
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<tr>
<td>Do you feel that you provide adequate informed consent for autopsy?</td>
<td>17 (5)</td>
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<tr>
<td>Do you feel you have a full understanding of what occurs during a full and partial/limited autopsy?</td>
<td>7 (2)</td>
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<td>During the consenting process do you discuss who is eligible to consent?</td>
<td>33 (10)</td>
</tr>
<tr>
<td>During the consenting process do you discuss the timeframe of when the autopsy will be performed and by whom?</td>
<td>17 (5)</td>
</tr>
<tr>
<td>During the consenting process do you discuss when the body will be available for transportation (disposition)?</td>
<td>3 (1)</td>
</tr>
<tr>
<td>During the consenting process do you discuss when the family can expect a preliminary report, a final report, and a CNS report from Pathology?</td>
<td>10 (3)</td>
</tr>
<tr>
<td>During the consenting process do you present the options of a full autopsy and a partial/limited/restricted autopsy?</td>
<td>13 (4)</td>
</tr>
<tr>
<td>During the consenting process do you discuss the details of what a full/partial/restricted autopsy entail?</td>
<td>3 (1)</td>
</tr>
<tr>
<td>During the consenting process do you discuss what organs are not returned to the body for burial?</td>
<td>0 (0)</td>
</tr>
<tr>
<td>During the consenting process do you explain that part of the procedure is to take a portion of each organ for evaluation under a microscope and these tissues are not returned to the body?</td>
<td>17 (5)</td>
</tr>
<tr>
<td>During the consenting process do you notify the family that photographs of the external body and internal organs may be taken as the pathologist deems appropriate?</td>
<td>0 (0)</td>
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<tr>
<td>During the consenting process do you notify the family of any questions the clinical team wants to have answered by performing the autopsy?</td>
<td>37 (11)</td>
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<tr>
<td>During the consenting process do you discuss any questions the family members want answered by having the autopsy performed?</td>
<td>33 (10)</td>
</tr>
<tr>
<td>During the consenting process do you discuss with the family whether the autopsy process will be able to answer their questions?</td>
<td>47 (14)</td>
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Design: A cross-sectional survey of 17 questions regarding autopsy consenting practices was created using Google Forms. Internal medicine residents were notified of the survey during a residents’ meeting, which was distributed 24 hours later electronically via email to all internal medicine residents from the internal medicine residency director. Results were collected 6 days after distribution.

Results: The Table highlights the survey questions and the percentages of yes responses for each question. This survey had 46 responders. Of the responders, 30 had consented for an autopsy. Eighty percent of responders are comfortable with identifying next of kin to...
sign consent for an autopsy, although for the remainder of the questions the response rate for yes varied from 0 to 47%.

Conclusions: Internal medicine residents at our institution reported deficiencies regarding their understanding of autopsy practices at our institution. This identifies the need to provide additional resources and training regarding autopsy practices to those providing consent for autopsies and/or involve pathologists in the consenting process, in order to ensure that proper consent is obtained.

A Case Report of Neck Splenosis
(Poster No. 29)

Zijian Wang, MD (zwang1@metrohealth.org); Joseph Tomaszefski, MD; Devereaux Sellers, MD; Rania Rayes-Danan, MD; Salman Ayub, MD. Department of Pathology, MetroHealth Medical Center, Cleveland, Ohio.

Splenosis, the autotransplantation and implantation of splenic tissue after splenic trauma or splenectomy, often occurs in the mesentery, omentum, peritoneum, and liver. Splenosis in the neck is seldom reported. Here we report a case of neck splenosis identified during autopsy. A 52-year-old man, status-post remote hysterectomy and left nephrectomy for trauma, was transported to the emergency department for cardiac arrest after experiencing “flu-like” symptoms for 5 days. The patient died shortly after arrival at the hospital. At autopsy, multiple red-brown nodules were found in the omentum, and single nodules were found in the liver and neck. The neck nodule, located in the area of the thyroid gland, weighed 25 g, and was irregularly shaped, spongy, and hemorrhagic. Microscopic examination of the neck nodule indicated a varied cellular milieu, including small lymphocytes (some in aggregates) and mononuclear cells in the background of a hemorrhagic and vaguely sinusoidal architecture. Attached to a peripherally hyalinized capsule were internal perpendicular fibrous trabeculae. Hyalinized blood vessels were present within this nodule. Other nodules in omentum and liver had similar histologic features. Immunohistochemistry studies of a representative omental nodule indicated scattered CD3+ T cells, CD8+ cells lining the sinusoids, multiple aggregates of CD20+ B cells, and diffuse CD68 expression in the nodules. These findings supported the histologic diagnosis of splenosis. Splenosis may occur after injury to spleen and subsequent surgical treatment. Compared with intraabdominal and thoracic splenosis, neck splenosis is rarely reported. Juxtathyroidal splenosis may be mistakenly diagnosed as accessory thyroid tissue or thyroid lesions clinically.

Fatal Multifocal Cerebral Infarction Due to Paradoxical Thromboembolism in a Patient With Uterine Leiomyomatosis
(Poster No. 30)

Luisa A. Lerma, MD (alerma@uw.edu); Daniel F. Gallego, MD; Desiree A. Marshall, MD; Florencia G. Jalikis, MD. Department of Pathology, University of Washington, Seattle.

A 57-year-old woman had a long history of recurrent deep venous thrombosis (DVT), for which she was placed on rivarixoban. Because of menorrhagia and anemia she would intermittently discontinue anticoagulation. She was also known to have severe pulmonary hypertension. Echocardiogram to confirm the presence of a patent foramen ovale. Because of the extent of cerebral infarction, she received thrombolytic therapy. While in the recovery area, the patient developed left hemiparesis. An emergency brain computed tomography scan demonstrated the presence of multifocal arterial occlusions, for which she received thrombolytic therapy. Because of the extent of cerebral infarction, she was placed on comfort care and died. At autopsy, multiple leiomyomas (Figure 18, A). The enlarged uterus was causing mechanical obstruction of the inferior vena cava, with stasis and subsequent DVT (Figure 18, B). DVT was associated with recurrent pulmonary embolism which led to pulmonary hypertension. Paradoxical thromboembolism through a 0.8-cm patent foramen ovale (Figure 18, C) led to massive multifocal cerebral ischemia (Figure 18, D). Here we described a very rare case of a massively enlarged uterus due to leiomyomatosis, with mechanical compression of the inferior vena cava leading to recurrent deep venous, pulmonary, and paradoxical thromboembolism. A fatal outcome in this case may have been avoided by prophylactic hysterectomy and adherence to prophylactic anticoagulation.

When Autopsy Is the Only Answer: Challenging Cases in Pediatric Autopsy Pathology
(Poster No. 31)

Nicolas Millan, MD (Nicolas.millan@jhmi.org); Sadhna Ahuja, MD; Alicia Hirzel, MD, MPH. Department of Pathology, University of Miami Miller School of Medicine/Jackson Health System, Miami, Florida.

The technologic age has seen a decline in autopsy requests. However, anatomic pathologists are still required to learn the techniques that are instrumental in providing answers to family and clinicians. Even with all the advances in medicine, sometimes the autopsy is the only answer.
Importance of C5b-9 Immunohistochemical Staining in Gestational Alloimmune Liver Disease

(Poster No. 32)
Lauren Kroll-Wheeler, MD (krollwhl@med.umich.edu); Allecia Wilson, MD. Department of Pathology, Michigan Medicine, Ann Arbor.

Gestational alloimmune liver disease (GALD) has recently been recognized as the most common cause of neonatal hemochromatosis. The diagnosis of GALD has both maternal and neonatal importance, because proper treatment can not only increase survival and prevent the need for liver transplantation in the neonate but can also entirely prevent fetal damage in subsequent pregnancies. Neonatal hemochromatosis is often diagnosed through magnetic resonance imaging or biopsy detection of iron within extrahepatic organs. Not all cases of GALD present with neonatal hemochromatosis, however, and negative immunohistochemical staining of hepatic tissue for C5b-9 is necessary for exclusion of the disease. We present a case of a 42-day-old male infant born at 38 weeks gestation with acute liver failure and coagulopathy. Magnetic resonance imaging performed at age 5 days showed liver iron to be within normal limits, and GALD was ruled out as a cause of his symptoms. On autopsy, the liver was dark, nodular, and small, weighing 105 g (expected 133 g based on age; Figure 20, A). Histologic sections showed extensive hepatocyte injury with giant cell changes, ductal proliferation, and prominent fibrosis with cirrhosis (Figure 20, B). C5b-9 immunohistochemistry staining was performed and showed extensive expression within the liver parenchyma (Figure 20, C). Iron deposition was found within the pancreas (Figure 20, D), myocardium, and thyroid. The final diagnosis and cause of death was GALD. This case highlights the importance of histologic examination and immunohistochemical staining to definitively rule out GALD as a cause of acute liver failure in newborns.

Disseminated Fungal Infection by Rhizopus pusillus in a Patient With Drug-Induced Stevens-Johnson Syndrome

(Poster No. 34)
Rebecca Yoda, MD (byoda@uw.edu); Daniel F. Gallego, MD; Desiree A. Marshall, MD; Florencia G. Jalikis, MD. Department of Pathology, University of Washington, Seattle.

We report an unusual case of unsuspected disseminated infection by Rhizopus pusillus with meningoencephalitis leading to death. A 76-year-old woman with a history of lung adenocarcinoma treated with prophylactic corticosteroids and chemoradiation developed weakness and altered mental status 5 days after completing therapy. She was given a diagnosis of neutropenic sepsis due to Klebsiella pneumoniae and was treated with broad-spectrum antibiotics. Her hospital course was complicated by drug-induced Stevens-Johnson syndrome. On hospital day 9 she developed shock with hematocrit drop and cardiac arrest. Resuscitative efforts were unsuccessful, and the patient died. Autopsy confirmed skin and mucosal (oral cavity, pharynx, esophagus, and stomach) involvement by Stevens-Johnson syndrome. The stomach was erythematous and determined the likely source of hemorrhage. Unexpectedly, extensive angioinvasive fungal pneumonia (Figure 22, A and B) and meningoencephalitis were identified (Figure 22, C and D). Polymerase chain reaction performed on paraffin-embedded tissue yielded R. pusillus. Death was attributed to mixed shock, septic, and hypovolemic in the setting of disseminated fungal infection and upper gastrointestinal bleeding due to mucosal involvement by Stevens-Johnson syndrome. Rhizopus pusillus is a saprophytic fungus not associated with human disease, highlighting the need for diagnostic advances in the setting of unexpected opportunistic infection.

Multifocal Postsurgical Heterotopic Ossification: A Rare Finding Incidentally Discovered at Autopsy

(Poster No. 33)
Steven D. Gilday, MD, PhD (gildays@ucmail.uc.edu); Yuan Huang, MD, PhD; Benjamin E. Criss, DO; Kristina R. Brannock, MD. Department of Pathology and Laboratory Medicine, University of Cincinnati, Ohio.

Heterotopic ossification (HO) is the pathologic formation of bone within soft tissues, which can occur in the context of surgery, trauma, neurologic injury, and genetic disorders. Although HO is a well-known complication of orthopedic procedures, it is a rare sequela following nonorthopedic surgery. Here, we present an autopsy case of HO simultaneously involving the patient’s abdominal wall and tracheostomy site. The patient was a 36-year-old man with cerebral palsy, refractory seizures secondary to Lennox-Gastaut syndrome, chronic ileus, and ventilator-dependent respiratory failure who ultimately died due to aspiration pneumonia. Postmortem examination revealed an incidental 10 × 4 × 3 cm calcified abdominal wall mass adjacent to the insertion of the gastrostomy tube (Figure 21, A, representative cross section). Histology showed a thick rim of fibrous tissue surrounding trabecular bone with predominantly fatty and highly vascularized marrow (Figure 21, B and C). Similar foci of ectopic bone displaying prominent endochondral ossification were found at the tracheostomy site (Figure 21, D). These asymptomatic lesions were not detected clinically despite multiple imaging studies. This case of HO is particularly unique because of the multifocal presentation and because ectopic bone formation is rarely reported in the abdomen or the neck. The etiology of HO is not fully understood but is likely multifactorial. Interestingly, the patient’s history of severe neurologic injury is an independent risk factor for HO; thus, the combination of prior surgery, neurologic compromise, and other unknown genetic factors together may have led to the development of multifocal HO in this case.
Autopsies Are Indispensable in the Advancement of Patient Care: Report of an Unusual Presentation and Fatal Outcome of an Autopsy-Diagnosed Case of Advanced Idiopathic Interstitial Pneumonia

(Poster No. 35)

Evi Abada, MD, MS (evi.abada@wayne.edu); Kunil Raval, MD, PhD; Sudeshna Bandopadhyay, MD. Department of Pathology, Wayne State University School of Medicine, Detroit, Michigan.

Despite scientific and technologic advances in medicine, the correlation of clinical diagnoses with findings at autopsy continues to expand medical knowledge, thus proving indispensable in the care and management of patients. This is particularly essential in rare diseases with protean presentations. Here, we report the case of a 53-year-old man who presented with major complaints of severe worsening abdominal pain and weight loss of approximately 100 pounds of 3 months’ duration. He had no prior history of respiratory disease; however, symptoms of mild dyspnea and a productive cough were obtained during additional history taking. Blood tests revealed an elevated lipase of 220 U/L, and he was admitted and treated for pancreatitis. Computed tomography scans of the abdomen and chest were done and were suggestive of pneumonia. He was placed on multiple antibiotics but developed worsening respiration that necessitated hyperbaric oxygen. He developed acute respiratory distress syndrome and died after 10 days of admission. Histopathologic examination of autopsy lung specimens revealed severe lung damage (Figure 23, A through D) secondary to diffuse alveolar damage, superimposed on extensive interstitial fibrosis, with features of honeycomb. These findings were consistent with advanced interstitial/end-stage lung disease in a patient without prior significant respiratory disease. In summary, although he did not present with the classic symptoms of breathlessness and cough in interstitial lung diseases, this case highlights an unusual presentation that was only confirmed at autopsy, thus emphasizing the unique role of clinicopathologic correlations in the advancement of patient care and creating opportunities for further research studies.

AA Amyloidosis Complicating Gout: An Unusual Presentation

(Poster No. 36)

Rebecca Graziano, MA (rag185@rwjms.rutgers.edu); James Van Gurp, MD; Gina Prochilo, DO; Billie Fyle-Kirschner, MD. Department of Pathology, Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey.

AA amyloidosis as a complication of long-standing gout is uncommon, with fewer than 30 cases reported in the literature. The present case describes a 60-year-old woman with AA amyloidosis arising in association with chronic tophaceous gout, leading to systemic complications, including ischemic bowel disease with massive gastrointestinal hemorrhage, diagnosed at postmortem examination. Complete autopsy confirmed the presence of amyloid protein deposition in multiple organs as well as chronic active tophaceous gout (polarized microscopy of tophi content performed); amyloid-containing tissue was submitted to a reference laboratory for mass spectrometric protein characterization. Autopsy revealed amyloidosis in the heart, spleen, liver, gastrointestinal (GI) tract, and kidney. Massive GI hemorrhage due to amyloid angiopathy affecting the intestine was the cause of death. Changes related to chronic gout were noted in the joints (active draining tophi involving lower extremities) and kidneys (uric acid nephropathy). This case demonstrates multiple unusual findings, including massive GI hemorrhage related to amyloid angiopathy affecting GI vasculature, as well as AA amyloidosis that is most likely related to gout. Little is known about the pathogenesis of AA amyloidosis complicating gout. Although chronic gout has an inflammatory component, it is unlike that of traditional chronic inflammatory disease, which may be among the reasons amyloidosis does not occur in gout with the same frequency it does in other diseases. Lack of clinical suspicion, both premortem and postmortem, may also be contributing to underdiagnosis. This case highlights the need for clinicians and pathologists to be aware of this unusual but potentially life-threatening association of AA amyloidosis with gout.

Brain Autopsy Consultations From the Medical Examiner’s Office: A 5-Year Single-Institution Experience

(Poster No. 37)

Yanel De Los Santos, MD (ydelo002@ufl.edu); Kaitlin Weaver, DO; James Breeden, BS; Catherine Weldon, MBA; Wendy Stroh, DO; William Hamilton, MD; Anthony Yachnis, MD; Jesse Kresak, MD. Department of Pathology, University of Florida, Gainesville.

Context: Neuropathologists play a critical role in forensic medicine, serving as consultants for regional medical examiner offices (MEOs). This retrospective study aims to establish decedent demographics and categorize the incidence of autopsy findings in consult brains received serving as consultants for regional medical examiner offices (MEOs).

Design: A retrospective study of a single MEO from the 8th District Office: A 5-Year Single-Institution Experience

Results: A total of 376 neuropathology consultations were performed during the 5-year period. There was an increase from 50 to 94 annually. Criteria for consultation included history of neurologic disease or head trauma, sudden death, or age <2 years. The average age was 24 years (range, 1 day to 101 years; males, 72%). Ethnic distribution varied from regional population, with 70% white (regional 80%), 25% black...
(15%), 2% Asian (2%), and 2% Hispanic (6%). Inmates accounted for 28% of cases. The incidence of each manner of death was 39% accident, 35% natural, 13% undetermined, 7% homicide, and 4% suicide. Neuropathologies were categorized, resulting in the following: 45% cerebrovascular, 32% trauma, 22% hypoxic-ischemic injury, 14% neurodegenerative, 9% normal, 7% tumor, 5% hyperacute injury, 3% reactive/inflammatory, and 2% developmental. A significant association was observed between manner and age, sex, ethnicity, and inmate status (P < .001 each). Neuropathology corroborated the cause of death in 66% of cases (Table).

Conclusions: Neuropathologic evaluation provided diagnostic information in >90% of cases. Ethnic distribution varies from the regional population. This analysis shows that neuropathology consultation provides insight into cause and manner of death and helps forensic pathologists more accurately evaluate and report medicolegal deaths in our district.

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<tr>
<th>Neuropathology Consultations: Summary of Findings</th>
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<tr>
<td><strong>Accident</strong>, %</td>
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<tr>
<td>Male</td>
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<tr>
<td>White</td>
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Abstracts

Unveiling a Masquerade: An Autopsy Case Report of an Adult With Hemophagocytic Lymphohistiocytosis Mimicking Sepsis

(Poster No. 38)

Oluwadamilare Ajayi, MBChB (ajayioe@ucmail.uc.edu); Kristina Brannock, MD, Department of Pathology and Laboratory Medicine, University of Cincinnati Medical Center, Cincinnati, Ohio.

A 47-year-old African American man presented with fever, nausea, and vomiting. The patient's history was significant for 3 previous systemic inflammatory response syndrome (SIRS)/sepsis–like episodes, and he was given a diagnosis of an immunodeficiency syndrome with natural killer cell dysfunction. Although he was evaluated for familial hemophagocytic lymphohistiocytosis (HLH), a specific disease-associated mutation was not identified. During admission he was noted to have liver failure, acute kidney injury, elevated ferritin, anemia, and thrombocytopenia. The patient received blood transfusions for symptomatic lower gastrointestinal tract bleeding and was managed for hepatorenal syndrome. He subsequently developed respiratory distress and a SIRS/sepsis–like presentation. He became hypotensive after continued rectal bleeding and showed hematemesis during intubation. The patient died after going into cardiac arrest. An autopsy revealed incomplete cirrhosis, ulcerative esophagitis, and extensive hemophagocytic infiltrates of multiple organs, especially bone marrow (Figure 24, A), spleen (Figure 24, B), and lymph nodes (Figure 24, C). Esophagus (Figure 24, D), stomach, intestines, lungs, myocardium, and urinary bladder were also involved. The immediate cause of death was attributed to circulatory shock, due to underlying hemophagocytic syndrome, due to the primary immunodeficiency syndrome and possibly secondary to infection (although not definitively proven). Retrospectively, the patient met at least 5 of the 8 criteria required for the diagnosis of HLH (fever, splenomegaly, bicytopenia, elevated ferritin, and hemophagocytosis). This case demonstrated that the initial presentation of HLH can be vague and can masquerade as a common infection. A high index of suspicion is therefore required to make a diagnosis of HLH, in order to establish care early.

Cardiac Outflow Anomaly With Large 5q31.3q32 Microdeletion Involving PURA and POU4F3

(Poster No. 39)

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Purine-rich element binding protein A (POURA) encodes transcriptional activator protein Pur-a and plays a significant role in neuronal development. 5q31.3 microdeletion syndrome, encompassing all or part of PURA, has been reported in few individuals, with overlapping 5q31.2q31.3 microdeletion varying in size from 360 kb to 2.6 Mb. Here, we report on a young individual with the largest (12.3-Mb) deletion extending from 5q31.3 to 5q32, involving both PURA and POU4F3 genes. POU4F3 gene, expressed in the sensory cells of the inner ear, is associated with progressive hearing impairment. A 1-day-old male infant, born at 27 weeks’ estimated gestational age to a 19-year-old mother, was identified to have a 5q31.3q32 microdeletion. The patient was prenatally diagnosed with congenital heart disease and was further found to have tetralogy of Fallot. The patient exhibited severe craniofacial abnormalities consistent with 5q microdeletion syndrome, including broad forehead, dolichocephaly, hypertelorism, long philtrum, and a tanded upper vermillion. Further cranial abnormalities included absence of nasal bone, thickened nuchal fold, and venricular system dilatation with a lateral ventricle hematoma. The cardiac abnormality led to the patient’s early death after 1 day. This patient is the youngest individual reported with a 5q31.3 microdeletion syndrome, involving a large deletion (12.3 Mb) extending from 5q31.3 to 5q32. This case represents an early picture of a patient with 5q31.3 microdeletion syndrome involving both PURA and POU4F3 genes and highlights the significance of investigating patients with early craniofacial abnormalities. Accompanying POU4F3 mutation was not previously reported in patients with 5q31.3 microdeletion syndrome.

“Empty Sella” Syndrome: More Than Just an Incidental Radiographic Finding

(Poster No. 40)

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Empty sella syndrome is often an incidental finding of little clinical implication. However, cases of significant endocrine abnormalities, although relatively rare, have been reported in patients with empty sella syndrome. A 63-year-old woman with a history of a left parietal stroke,
global aphasia, seizures, schizophrenia, and diabetes reported malaise during the previous week. On the morning of admission, she was found to be hypotensive, bradycardic, and hypothermic (84°F). A seizure was observed during transport. In the emergency department, the patient developed cardiac arrest and underwent 3 rounds of attempted resuscitation before a return of spontaneous cardiac activity was achieved. Low cortisol levels and also noted in the medical record. Despite supportive and therapeutic measures after admission, she did not recover and was transitioned to comfort care. When the patient was admitted, magnetic resonance imaging was performed to assess for stroke. Postmortem radiology review revealed an absent pituitary gland. A grossly shrunken and compressed pituitary gland was observed during autopsy. Additionally, the adrenal glands had markedly atrophic cortical regions. Microscopic evaluation of the pituitary revealed small, compressed bands of adenohypophysis; small, dilated cystic structures involving the pars intermedia; and intense vascular congestion. Additional microscopic evaluation of the adrenal gland showed marked cortical thinning, consistent with atrophy. In our opinion, the patient died of global hypoxia-ischemia following a cardiac arrest, which likely occurred on a complex and multifactorial basis. The patient’s condition may have been associated with clinically significant adrenal cortical atrophy and hypofunction, secondary to empty sella syndrome (Figure 25).

SNP-Microarray Molecular Analysis of Hepatoblastoma Discovered on Autopsy of Infant With Trisomy 18
(Poster No. 41)
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Embryonal cancers are an often-overlooked complication of trisomy 18, with more than 70 cases of documented malignancies in patients with trisomy 18, of which hepatoblastoma is the most common. We present the case of an infant who died at age 8 months and arrived for autopsy with a past medical history significant for trisomy 18, ventricular septal defects, and bronchopulmonary dysplasia. On autopsy, multiple features of trisomy 18 were evident, including clenched fists with overlapping second and fifth digits, micrognathia, webbing of second and third toes, and ventricular septal defect. Of note, the cut surface of the liver showed a tan pink mass in the left lobe of the liver measuring 0.7 × 0.5 cm. Histologically, the mass was well demarcated (Figure 26, A) and unencapsulated, with cells in a trabecular growth pattern and enlarged nuclei with course granular chromatin (Figure 26, B). Special stains were positive for Hep Par-1, consistent with hepatoblastoma. Hepatoblastoma of trisomy 18 has not been previously characterized by single-nucleotide polymorphism (SNP)-microarray analysis, and array analysis showed no secondary mutation (Figure 26, C), demonstrating that trisomy 18 is sufficient for disease development. An extensive review of the potential oncogenic driver mutations led to SETBP1 (18q12.3) as a putative link between embryonal cancers and trisomy 18, because aberrations of SETBP1 have been observed in 16 reported cases of non–trisomy 18-related hepatoblastoma.

Programmed Death Ligand-1 (PD-L1) Expression in Pediatric Tufted Angioma/Kaposiform Hemangioendothelioma
(Poster No. 42)
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Context: Kaposiform hemangioendothelioma (KHE) and tufted angioma (TA) are classified as vascular tumors with locally aggressive and benign growth potential. Interestingly, both TA and KHE share a unique feature of increased risk of Kasabach-Merritt phenomenon (KMP). Despite recent advances in therapeutic strategies, management of KHE/TA remains challenging, and this is particularly true for those tumors occurring in critical regions, such as the base of the skull or head and neck. Programmed death receptor-1 (PD1) and its receptor, programmed death ligand-1 (PD-L1), are key regulatory physiologic immune checkpoints that play pivotal roles in regulating host immune responses. This project aims at evaluating the expression of PD-L1 by immunohistochemistry in a series of KHE/TA.
Design: Children with KHE/TA are included in this study. A representative paraffin-embedded tissue block from the tumor was immunostained with PD-L1 (Dako). We scored the PD-L1 expression on the percentage of the viable tumor cells exhibiting complete circumferential or partial linear plasma membrane staining at any intensity.
Results: Five children with KHE/TA were studied. The location of the tumor included right eye/base of the skull, mesentery, right parotid area, mediastinum, and right upper thigh/inguinal region. PD-L1 immunostaining showed diffuse and strong membranous positivity in 100% of tumor cells in 2 cases, in 80% of tumor cells in 1 case, and in 50% of tumor cells in 2 cases.
Conclusions: We describe, for the first time, 5 cases of KHE/TA with diffuse and strong positivity for PD-L1. We believe this finding represents a major milestone in the management of this type of vascular tumors.
Extragastrointestinal Malignant Gastrointestinal Neuroectodermal Tumor in a 35-Year-Old Woman
(Poster No. 43)
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Malignant gastrointestinal neuroectodermal tumor (GNET) is a rare, recently recognized distinct clinicopathologic entity. It was originally labeled “clear cell sarcoma-like tumor of the GI tract” because it shares the histologic features of clear cell sarcoma but was subsequently found to have neuroendocrine differentiation as well. With fewer than 50
cases reported in literature, there is limited knowledge about its clinical behavior and prognosis. Because GNET is not a well-known entity, the tumor may be misdiagnosed as several other lesions. Here, we report a case of an extragastrointestinal (extra-GI) GNET. To our knowledge, this likely represents the first reported extra-GI GNET case in the English-language literature. A 35-year-old Hispanic woman presented with unrelenting, burning abdominal pain for 3 weeks. Computed tomography scan showed a cystic mass situated between the liver, right kidney, and pancreatic head. Histologically, the 10.6 × 9 × 4.8 cm well-circumscribed, solid cystic mass revealed pseudopapillary, microcystic, and sheetlike growth with primitive blue cell appearance and rare mitotic activity. Tumor cells were polygonal, with variable amounts of eosinophilic cytoplasm and vesicular chromatin. Immunohistochi- mically, the cells expressed vimentin, variable CD68, and synaptophysin. EWSR1 (22q12) rearrangement was detected by fluorescent in situ hybridization. After surgical resection, the patient is currently undergoing imaging surveillance and will begin radiation therapy if there is any sign of cancer recurrence. Careful attention to the histomorphology in combination with the unique immunohistochem- ical profile and cytogenetics help to distinguish this tumor from its mimickers. Finally, our case demonstrates these tumors may rarely occur outside the gastrointestinal tract.

Mycetoma of the Foot: A Diagnostic Challenge

(Poster No. 44)

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Mycetoma is a mutilating, chronic, granulomatous infection of subcutaneous tissues that can be caused by bacteria (actinomyetoma) or fungi (eumycetoma). It usually affects the feet and legs (subcutaneous tissues that can be caused by bacteria (actinomyetoma)) or fungi (eumycetoma). It usually affects the feet and legs (or fungi). Various cultures of the right foot, with recurrent fistula formation and purulent drainage, showed prominent degenerative bone changes in the second metatarsal and biopsy specimens were taken during surgical debridements, but the results are currently not known.

Phosphaturic Mesenchymal Tumor: A Rare Case With Atypical Histology

(Poster No. 45)

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Phosphaturic mesenchymal tumors (PMTs) are extremely rare tumors frequently associated with osteomalacia. Even with the association, diagnosis is often delayed because of nonspecific symptoms (muscle/bone pain), lack of clinical suspicion, and furthermore, misdiagnosis due to rarity and histologic overlap with other mesen- chymal tumors. Oncogenic osteomalacia is reversible after removal of the tumor; thus, an accurate diagnosis of PMT remains critical. Classical histology of PMT includes bland spindled cells embedded in a hylalinated to partially calcified matrix with prominent vasculature. PMT often has a benign clinical course with a low recurrence rate. Criteria for malignancy are not well defined, with fewer than 5 cases reported with metastasis, 2 cases of which showed atypical histology. We present a case of PMT with an emphasis on histologic findings. Our patient is a 30-year-old woman with a history of bilateral hip fractures one year ago who presented with weakness and multiple falls. She was hypophosphotemic, with low 1a,25-dihydroxyvitamin D3, normal calcium and parathyroid hormone, and an elevated FGF23 plasma level. Ultimately, octreotide scintigraphy confirmed a 2.3-cm ovoid enhancing mass in the left foot (dorsal first interdigital space), which was excised. Histologically, most areas showed classic features; however, there were areas with fibrosarcoma-like fascicular architecture and increased mitotic figures. FGF23 mRNA by chromogenic in situ hybridization was positive. Diagnosis of PMT was rendered, with the recommenda- tion of close follow-up because of low malignant potential. On follow-up, the patient is currently undergoing imaging surveillance and will begin radiation therapy if there is any sign of cancer recurrence.

Pleomorphic Liposarcoma in Mandible: Rare Sarcoma and Rare Location

(Poster No. 46)

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Mandibular liposarcoma is rare, and most reported cases are low grade. Pleomorphic liposarcoma (PLS), the most aggressive and rare variant of liposarcoma, is exceedingly rare, and to our knowledge only 1 or 2 cases are reported in mandible. We present a case of an 83-year-old woman with a recurrent ulcerative lesion in the right retromolar trigone. The lesion was biopsied/partially excised 3 times (at outside facilities) with different diagnoses: (1) mixed epithelial and spindle cell neoplasm; (2) myxoid liposarcoma; and (3) poorly differentiated liposarcoma but negative for MDM2 amplification by fluorescent in situ hybridization. Right segmental mandibulectomy showed relatively well-demarcated tumor (3.5 × 3.3 × 2.9 cm) with a variagated cut surface of grey myxoid and solid areas with focal hemorrhage, 20% necrosis, and invasion of mandibular bone (Figure 28, A). Tumor histology showed PLS with variable-size lipoblasts (S100+ up to giant pleomorphic lipoblasts and brisk mitoses (25 per 10 high-power fields) with abnormal figures. Myxoid microcystic and solid areas of round epithelioid, clear, and finely vacuolated tumor cells were prominent in the tumor (Figure 28, B through D). Resection margins were negative for tumor, and adjuvant chemoradiotherapy was recommended. Liposarcoma predominantly occurs in the extremities, retroperitoneum, or trunk and is extremely rare in oromaxillofacial region. PLS behaves aggressively, with a poor prognosis, high rate of recurrences (40%), metastases (40%), and 5-year mortality rate of 35%. PLS may display a heterogenous histologic spectrum. Lipoblastic differentiation (particularly pleomorphic malignant lipoblasts) is the clue for diagnosis of PLS. The heterogenous histologic spectrum in PLS may pose diagnostic challenges in limited biopsy sampling, like this case. 

Abstracts
Analysis of 356 Tumors Tested for EWSR1 Gene Rearrangement by Fluorescence In Situ Hybridization (FISH) Technique: Experience at a Tertiary Cancer Referral Center in India

(Poster No. 47)

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Context: Ewing sarcoma (ES) is characterized by EWSR1 gene rearrangement in up to 95% of cases. Incidentally, various other tumors also display EWSR1 rearrangement. Few studies have shown modification in the diagnosis of ESs after molecular testing.

Design: A total of 356 cases, mostly soft tissue tumors and tested for EWSR1 gene rearrangement by fluorescence in situ hybridization technique during the years 2011 to 2018 at our institution, were analyzed.

Results: EWSR1 result was interpretable in 305 tumors (85.6%), including EWSR1+ tumors (179; 58.6%) and EWSR1- tumors (126; 41.3%). Among 179 EWSR1+ tumors, there were 157 cases (87.7%) of ES, and 22 (12.2%) were other tumors, most frequently gastrointestinal neuroectodermal tumors (n = 6), followed by extraskeletal myxoid chondrosarcomas (n = 5) and desmoplastic small round cell tumors (n = 4). Based on only clinicopathologic and immunohistochemical features, diagnosis of ES was rendered in 107 of 157 cases (66.8%), whereas diagnosis of ES as a differential diagnosis was offered in 33 of 157 cases (21%). In 18 of 157 cases (11.4%), diagnosis of ES was not offered with clinicopathologic and immunohistochemical results. Among 163 cases finally diagnosed as ES, 6 (3.6%) lacked EWSR1 rearrangement. EWSR1 rearrangement test was useful in validating 157 of 163 cases (96.3%) of ES.

Conclusions: This constitutes one of the first studies on EWSR1 gene rearrangement testing from our subcontinent and reinforces the need and value of this test in confirming Ewing sarcomas, at least in cases with equivocal histopathologic diagnosis, even in limited resource settings. It is also useful in reinforcing diagnoses of various other tumors characterized by EWSR1 rearrangement.

Spindle Cell Variant of Ameloblastic Carcinoma: A Rare Odontogenic Neoplasm Mimicking Sarcoma

(Poster No. 48)

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Ameloblastic carcinoma is a malignant epithelial odontogenic neoplasm. We present a rare case of the spindle cell variant of ameloblastic carcinoma. A 20-year-old woman presented with an incidental cystic lesion in the left maxilla identified by a computed tomography scan. Scan showed an expansile solid and cystic mass displacing the left third maxillary molar tooth into the outflow tract of the left maxillary sinus. The resection specimen revealed a 3.9-cm solitary lobulated tan-white mass protruding into the maxillary sinus arising from the deep portion of the left upper alveolar ridge. Microscopically (Figure 29, A and C), the tumor consisted of small foci of atypical epithelium intermixed with an abrupt transition to sarcomatoid areas of densely cellular bland spindle cells. The spindle cells demonstrated fascicular architecture with mild to moderate atypia and rare mitoses. Immunohistochemical staining demonstrated that both epithelial and spindle cell components were positive for AE1/AE3 (Figure 29, B, CK8/18, D2-40 (Figure 29, D), and TLE, whereas they were negative for SMA, desmin, EMA, ERG, CD34, S100, MUC4, and calretinin. Ki-67 proliferation index was up to 10%. Florescence in situ hybridization for SYT was negative. In addition to that, the findings of distinct minimal nuclear atypia and unique architecture were more concerning for common spindle cell neoplasm, like synovial sarcoma and biphenotypic sinonasal sarcoma. Hence, diagnosis of ameloblastic carcinoma becomes more challenging for pathologists because of the high likelihood of other potential sarcomatous mimics. Only 12 cases of this variant have been reported in the literature to date.

Nora Lesion: Bizarre Parosteal Osteochondromatous Proliferation of the Tibia

(Poster No. 49)

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Bizarre parosteal osteochondromatous proliferation, also known as Nora lesion, is an uncommon, benign but locally aggressive lesion defined as an osteochondromatous exostosis involving the surface of small tubular bones. Its occurrence in the tibia is exceedingly rare. Nora lesion usually grows rapidly and often recurs. Also, its bizarre histologic features and relatively unusual clinical behavior can mimic malignancy, leading to subsequent unnecessary management. We present a distinctive persistent case of Nora lesion in a 35-year-old woman who presented with a few weeks’ history of a mass in the proximal right tibia. The mass was increasing in size and associated with pain and pressure sensation while kneeling. Imaging showed a 1.0 × 0.8 cm peripherally enhanced lesion located on the anterior medial margin of the tibial tuberosity (Figure 30, A and B). Complete excision was attempted twice, with recurrence and persistent enlarging lesion that now measured 1.8 × 1.7 cm and involved approximately 50% of the patellar tendon. Sections of the lesion showed irregular spindled cartilaginous and osseous differentiation, with occasional enlarged hypercellular chondrocytes, calcified chondroid, and osseous foci with deeply purplish blue mineralization but no significant cytologic atypia or mitoses (Figure 30, C and D). The plan is to achieve a complete third excision, with a fairly aggressive approach, before the extensor tendons are compromised. Although benign but recurrent and locally aggressive, a unique management plan with frequent follow-up is required for
its unpredictable clinical course, as seen in this case report of Nora lesion in an unusual location.

**Synovial Sarcoma of Plantar Foot: Clinical Similarity and Distinction From Plantar Fibromatosis**

(Poster No. 50)

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Soft tissue sarcomas of the foot are rare; of these, synovial sarcoma (SS) is the most common. SSs tend to be small, with deceptively slow growth, delaying diagnosis (2–20 years) and clinically mimicking benign processes, particularly plantar fibromatosis or calcifying aponeurotic fibroma. We report a case of a left foot mass in a 47-year-old woman presenting for 2 to 3 years with recent increase in growth and pain. Magnetic resonance imaging revealed a 5.5 cm x 3.2 cm plantar mass interdigitating between the third and fourth metatarsal spaces (Figure 31, A), with bone erosion and spotty calcification. Excisional biopsy revealed SS (grade III) with biphasic spindle (Figure 31, B) and epithelial (Figure 31, C) cells positive for pancytokeratin (AE1/AE3), EMA, CD99, BCL-2, calponin, and TLE-1 (Figure 31, D). Body scan was negative for metastases. High transmetatarsal amputation was performed. Gross and microscopic examination revealed a soft lobulated tumor as described in imaging, with negative resection margin (pT2bNxMx). About 13% of SSs occur in the foot with no specific radiographic features except for spotty/fine calcifications (15%–20% cases). Classic tumor histology is biphasic pattern of malignant spindle cell fascicles and epithelial components with the immunohistochemical profile described in our case. Monophasic SS (purely spindle/rarely epithelial) can be a diagnostic challenge, particularly if poorly differentiated. TLE1 immunostaining and translocation t(x;18) (p11; q11) are excellent discriminators of SS from other sarcomas. Wide surgical excision or amputation is the mainstay of treatment. Adjunct chemotherapy and radiotherapy are considered for tumors >8 cm, and chemotherapy for metastases. In view of the aggressive treatment, underdiagnosis or overdiagnosis of SS should be avoided.

**Intratumoral Extramedullary Hematopoiesis in Solitary Fibrous Tumor of the Breast**

(Poster No. 52)

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Extramedullary hematopoiesis (EMH), defined as hematopoiesis occurring in organs outside of the bone marrow, in solitary fibrous tumor (SFT) is exceedingly rare, with only 2 cases reported to date in the English-language literature. EMH is typically associated with hematologic disorders; the exact pathogenic mechanism underlying EMH in solid tumors, such as SFT, is largely unknown. We report a case of EMH in SFT of the breast in a 57-year-old woman. The patient presented with an incidentally found right axillary mass on routine screening mammography. Initial core biopsy revealed histologic and immunophenotypic findings consistent with SFT. Subsequent excisional biopsy grossly showed a well-circumscribed, nonencapsulated nodule measuring 3.2 x 3.0 x 1.7 cm, with a white, firm, bulging, and focally whorled cut surface without hemorrhage or necrosis (Figure 32, A). Histologically, the tumor displayed a patternless architecture with hypocellular and hypercellular areas comprising bland oval-to-spindle cells in a variably collagenous and myxoid stroma, along with prominent perivascular hyalinization and branching staghorn vessels (Figure 32, B). No brisk mitotic activity, cytologic atypia, necrosis, or infiltrative pattern was seen. However, a few foci with various trilineage hematopoietic elements, including erythroid and myeloid precursors and megakaryocytes (Figure 32, C and D), consistent with EMH, were also noted. Immunohistochemically, the tumor cells expressed CD34 and STAT6 but lacked desmin, SMA, S100, SOX-10, and EMA expression, supporting the diagnosis of SFT. Subsequent clinical follow-up revealed no underlying hematologic disorders. To the best of our knowledge, this is the first reported case of intratumoral EMH associated with SFT of the breast.
Tumorlike Subcutaneous Granuloma in a TNF-Alpha Inhibitor–Treated Patient
(Poster No. 53)

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Tumor necrosis factor (TNF) has been found to play a role in the pathogenesis of granulomatous disease. We report a rare case of tumorlike subcutaneous granulomatous disease in a patient with psoriatic arthritis during TNF-alpha inhibitor therapy. A 52-year-old man presented with an enlarging left buttock soft tissue mass for about 2 months. Patient denied injury or trauma to the region. Magnetic resonance imaging revealed an ill-defined soft tissue mass within the medial/inner subcutaneous fat of the left buttock with an infiltrative appearance, measuring 4.8 × 3.3 × 4.8 cm. Differential diagnosis included complex pilonidal lipoma, dermoid tumor, and sarcoma. The mass lesion was widely excised, which grossly appeared as a firm, homogeneous nodular lesion. Results of AFB and fungal cultures were negative. Permanent sections showed extensive small granulomas and homogeneous nodular lesion. The lesion extended to the inked superior, inferior, and posterior margins. The granulomas were tightly arranged and predominantly confined to the subcutis, leaving epidermis of the skin unremarkable. The patient's medical history included psoriatic arthritis, for which he was on a TNF-alpha inhibitor (etanercept) 25 mg subcutaneously twice weekly. This is a rare case of tumorlike subcutaneous granulomatous disease in a patient treated with TNF-alpha inhibitor. The lesion clinically and radiologically mimics malignancy and was treated with wide excision. We present the case to promote the recognition of TNF-alpha inhibitor–induced granulomatous condition and the interest for further investigation.
FOXO1 at 13q14, confirming the diagnosis of ERMS. To our knowledge, FLI-1 immunohistochemical reactivity has not been described in cases of ERMS. FLI-1 is positive in Ewing sarcoma/PNETs because they harbor the chromosomal translocation t(11;22); it has been proposed as a useful marker in the differential diagnosis of SRBCTs. However, using a limited immunohistochemistry panel might potentially lead to an incorrect diagnosis. This case emphasizes the importance of interpreting FLI-1 in the context of other immunohistochemical markers when approaching a case of SRBCT.

Malignant Transformation of Lipomatosis: Well-Differentiated/Dedifferentiated Liposarcoma Developing in a Patient With Lipomatosis

(Poster No. 56)

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Lipomatosis is a rare benign condition that is characterized by the presence of multiple abnormal fat depositions in the body. Malignant transformation of lipoma to liposarcoma in patients with lipomatosis is exceptional, with only 2 published case reports in the literature. The malignant tumor was well differentiated and myxoid liposarcoma in those reports. We herein report on an 88-year-old man with prior history of multiple surgeries for lipoma from different parts of his body, including abdominal wall and left forearm. In 2013, he presented with a recurrent left forearm mass that was diagnosed as well-differentiated liposarcoma at an outside institution for the first time. Since then, he has had multiple surgeries and multiple recurrences of his left forearm tumor. In 2018, he was referred to our institution for his recurrent left forearm tumor, which measured approximately 25 cm. Histologic examination of the resected left forearm tumor revealed a wide spectrum of neoplastic proliferation. Most of the tumor consisted of undifferentiated atypical spindle cells that was consistent with dedifferentiated liposarcoma (Figure 36, C and D). Areas of well-differentiated liposarcoma were also identified (Figure 36, A and B). The spindle cells were positive for desmin and negative for EMA, SMA, pankeratin, and S100. Ki-67 showed a proliferative rate of 30%. Fluorescence in situ hybridization analysis for MDM2 gene amplification confirmed the diagnosis of well-differentiated/dedifferentiated liposarcoma. Here, we report on the first case of dedifferentiated liposarcoma in a patient with lipomatosis as also being overall the third case of malignant transformation of lipomatosis.

Dysplastic Lipoma in Tacoma: An Emerging Entity

(Poster No. 57)

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Dysplastic lipoma is a unique mature lipomatous neoplasm with characteristic adipocyte morphology, a rare association with pediatric retinoblastoma, overexpression of p53 by immunohistochemistry, and absence of MDM2 gene amplification by fluorescent in situ hybridization. Other names for this tumor have included “subcutaneous minimally atypical lipomatous tumor” and “anisometric cell lipoma.” Dysplastic lipoma is associated with a male predominance, multifocality, and a predilection for the posterior neck, shoulders, and upper back. We report on a 34-year-old woman with a history of retinoblastoma and a family history of pleomorphic spindle cell sarcoma who presented with a 2.5-cm subcutaneous posterior neck mass. Histologic features included size variation of adipocytes, fat necrosis, and focal mild adipocytic nuclear atypia (Figure 37, A, B, and C). No spindled stromal cells were identified. Immunohistochemistry staining for p53 highlighted rare atypical adipocytes (Figure 37, D). Fluorescence in situ hybridization testing was negative for MDM2 gene amplification. This case is unique because the patient had the rare association with retinoblastoma, is female, and had a family history of pleomorphic spindle cell sarcoma. A dysplastic lipoma must be distinguished from a conventional lipoma, because dysplastic lipomas have an increased tendency to recur. Dysplastic lipoma is benign and treated with local excision only; therefore, distinguishing this entity from a lipoma-like atypical lipomatous tumor is necessary to avoid overtreatment.
Primary Pulmonary Extraosseous Ewing Sarcoma: A Case Report and Review of the Literature

(Poster No. 58)

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Ewing sarcoma family of tumors (ESFT) is a group of small round blue cell tumors that collectively have common histologic morphology, immunohistochemical staining pattern, and the characteristic translocation involving the EWSR1 gene. One of the members of the ESFT is extraskelatal Ewing sarcoma (EES). EES commonly arises from soft tissue and is documented to arise with a decreasing frequency from the chest wall, pelvis, paraspinal region, and retroperitoneum. Rarely, EES can arise from visceral organs. We present a rare case of EES arising from the lung. Our patient is a 49-year-old woman who was found to have a mass in her right lung on a screening imaging study for a BRAF mutation. Whole-body imaging showed a single enlarging, hypermetabolic pulmonary mass. A lobectomy was performed, and grossly the specimen showed a soft, yellow-white, and vaguely circumscribed mass. Microscopically, small round cells with high nucleus to cytoplasm ratio were present (Figure 38, A). Tumor cells were diffusely positive for CD99, FLI-1, and PAS/D (Figure 38, B, C, and D, respectively). Finally, fluorescence in situ hybridization came back positive for rearrangement of the EWSR1 gene, confirming the diagnosis of EES. Review of the literature shows limited documented cases of primary pulmonary ESFT. Our patient has completed 5 rounds of chemotherapy, and follow-up computed tomography has not shown any signs of recurrence at 6 months after surgery. We present this rare case of primary pulmonary EES in a patient with BRAF mutation in order to heighten the awareness of this entity as a primary pulmonary neoplasm.

Low-Grade Malignant Neoplasm of Uncertain Type Mimicking Epithelioid Schwannoma

(Poster No. 59)

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Although morphology, immunohistochemistry, and molecular testing help with the diagnosis of soft tissue tumors (STTs), some cases remain unclassified, posing diagnostic challenges. A 33-year-old woman presented in 2014 with a 1.9-cm soft tissue nodule on her left foot dorsum. Excision of the nodule revealed a well-circumscribed, diffusely S100+ and SOX10+ bland epithelioid neoplasm with collagen IV retention around cell nests and IN1 retention. The findings were considered typical for the diagnosis of epithelioid schwannoma. In 2016, the patient presented with a 4.0-cm rapidly growing mass at the previous surgical site, for which she underwent wide excision with negative margins. The tumor consisted of multinodular, infiltrative epithelioid cell proliferation without nuclear atypia, mitoses, or necrosis. Immunohistochemically, tumor cells were weakly positive for S100 and negative for SOX10, SMA, desmin, EMA, HMW-keratin, p63, GFAP, CD117, collagen IV, and synaptophysin. Fluorescence in situ hybridization did not demonstrate EWSR1 gene rearrangement. Genetic testing identified ACTB-GLI1 rearrangement (reported in a variety of STTs, including solitary fibrous tumors, myofibroma, monophasic synovial sarcoma, mesenchymal chondrosarcoma, and metastatic endometrial stromal sarcoma). The findings were interpreted as low-grade malignant neoplasm of uncertain type. Slides from the first resection were reviewed, and they were interpreted as low-grade malignant peripheral nerve sheath tumor. Two months later, the patient had another local recurrence with left inguinal lymphadenopathy, both of which were excised to reveal involvement by the same neoplasm. Despite the current progress in the molecular era, some STTs remain unclassifiable, with unpredictable behavior, and may act aggressively despite a bland appearance that mimics benign entities.

Case Report of Superficial CD34+ Fibroblastic Tumor in a Pediatric Patient

(Poster No. 60)

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Superficial CD34+ fibroblastic tumor (SCPFT) is a newly recognized entity, with features of superficial location, marked pleomorphism, very low mitotic rate, diffuse CD34 immunoreactivity, and intermediate malignant potential with very low risk of recurrence. All reported cases are in adults. A healthy 14-year-old girl presented with a 3.0 × 3.0 × 2.6 cm subcutaneous mobile mass on her upper back that was diagnosed as an undifferentiated pleomorphic sarcoma on biopsy at an outside institution. Gross examination revealed an unencapsulated, tan-pink, lobulated, glistening soft tissue mass. Microscopically, a well-circumscribed and densely cellular tumor involved the superficial and deep dermis, not involving the overlying epidermis. The margin was mostly sharp. Tumor was predominantly epithelioid in a solid growth pattern with some spindled cells forming fascicles. There was abundant eosinophilic cytoplasm, marked anisocytosis, and anisonucleosis with pleomorphic nuclei, coarse chromatin, and prominent nucleoli. Abundant inflammation was seen in the background, composed of lymphocytes, histiocytes, and plasma cells. There was no necrosis, hemorrhage, cystic change, or myxoid areas with hyalinizing blood vessels. Mitoses were infrequent (<1 per 50 high-power fields). Immunohistochemistry was performed. Tumor cells showed diffuse strong reactivity for CD34 and partially nuclear reactivity for P53. Tumor cells were negative for CD68, ALK, ROS1, NTRK3, MDM2, S100, SMA, CD117, CD10, and CD68. Expression of INI-1 was retained; margins were negative. No additional therapy was offered, and the patient is free of disease. This is the first case of a superficial CD34+ fibroblastic tumor in a child.

Prenatal Retroperitoneal Teratoma: An Unusual Entity

(Poster No. 61)

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Retroperitoneal teratomas are extremely unusual in infancy. We report on a 3-month-old asymptomatic male with a retroperitoneal mass found initially during his mother’s prenatal visit by sonogram at 38 weeks’ gestation. Subsequent sonographic examination on his fourth day of life revealed a 4.1 × 4.1 × 3.4 cm left retroperitoneal mass with calcification; his urine vanillylmandelic acid was not elevated. A diagnosis of neuroblastoma was favored. Because localized infant neuroblastoma often shows spontaneous regression, observation with follow-up was justified in this patient. Follow-up examination showed increased mass size to 7.7 × 6.6 × 5.5 cm. Meta-iodobenzylguanidine scan showed positive uptake. The patient underwent mass resection with left adrenalectomy. Resection specimen showed a 6.5 × 6.5 × 5.3 cm well-circumscribed mass attached to uninvolved adrenal gland (Figure 39, A). Sectioning revealed a variegated solid and cystic mass. Microscopic examination showed teratoma composed predominantly of neural tissue (Figure 39, D), skin (Figure 39, C), gastrointestinal (Figure 39, B), and respiratory tissue, bone, and cartilage (Figure 39, B); pigmented retinal tissue, and adipose and muscular tissue. No immature neuroectodermal elements were identified. The entire adrenal gland was free of tumor. Most reported neonatal suprarenal masses are due to adrenal hemorrhages, followed by neuroblastoma, and rarely teratoma. Retroperitoneal teratomas are

Image 37x261 to 280x443
A 51-Year-Old Woman With Breast Cancer and Primary Epithelioid Hemangioendothelioma Mimicking Carcinoma Metastasis

(Poster No. 62)

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Epithelioid hemangioendothelioma (EHE) is a rare, malignant tumor with unpredictable clinical course, ranging from an indolent to a highly aggressive disease that mimics other epithelioid neoplasms. We present an interesting case of a 51-year-old woman with a chief complaint of intermittent chest pain. Her past medical history was significant for left breast cancer in 2009, diagnosed at the age of 39 years, and right breast cancer diagnosed in 2013, treated with bilateral mastectomy and breast reconstruction. Computed tomography scan performed for her recent intermittent chest pain revealed 3 nodules measuring 6 mm in greatest dimension in the left lung, a 2.9-cm mass in the right upper extremity, and a vertebral osseous lesion with characteristic radiographic features and a constellation of multiple bone metastases (unlike soft tissue liposarcoma). In summary, we describe an intraosseous pleomorphic liposarcoma, epithelioid subtype, in a patient with retinoblastoma. This rare subtype has not been previously described in association with retinoblastoma. Pathologists should consider this rare entity when a pleomorphic or epithelioid intraosseous tumor is encountered in a retronblasta patient.

Liposclerosing Myxofibrous Tumor of the Skull

(Poster No. 64)

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Liposclerosing myxofibrous tumor (LSMFT) is a rare benign fibro-osseous lesion with characteristic radiographic features and a constellation of aggressive disease that mimics other epithelioid neoplasms. We present a case of a second primary malignancy in a boy with bilateral retinoblastoma.

Pleomorphic Liposarcoma as Second Primary Malignancy in a Child With Bilateral Retinoblastoma

(Poster No. 63)

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Retinoblastoma results from inactivation of the RB1 gene, and retinoblastoma patients with germ-line mutations also have a risk of developing second malignant neoplasms, most commonly osteosarcoma, fibrosarcoma, chondrosarcoma, epithelial tumors, Ewing sarcoma, leukemia/lymphoma, melanoma, and central nervous system tumors. We report a case of a second malignant neoplasm in a boy with bilateral retinoblastoma in infancy, treated with chemotherapy and brachytherapy. Following the initial diagnosis, genetic workup revealed a heterozygous frameshift mutation in exon 11 of RB1 and also a heterozygous novel missense mutation in exon 25. At age 9 years he presented with worsening right leg pain. Magnetic resonance imaging showed an aggressive-appearing lesion of the distal femur concerning for osteosarcoma. Positron emission tomography scan showed dominant right femur avidity and widespread skeletal involvement of a malignant process (Figure 41, A). Core biopsy of the femoral lesion showed a high-grade neoplasm featuring nests and trabeculae of monomorphic epithelioid cells (Figure 41, B) with vacuolated cytoplasm and pleomorphic lipoblasts (Figure 41, C). Immunostains were negative for pankeratin, desmin, S100, Hep Par-1, SATB2, ERG, calretinin, inhibin, and IDH1. p53 was not expressed, indicating a “null” mutation (Figure 41, D). Although multiple metastases of an epithelioid cell tumor suggest a carcinoma, primary bone liposarcoma often demonstrates multiple bone metastases (unlike soft tissue liposarcoma). In summary, we describe an intraosseous pleomorphic liposarcoma, epithelioid subtype, in a patient with retinoblastoma. This rare subtype has not been previously described in association with retinoblastoma. Pathologists should consider this rare entity when a pleomorphic or epithelioid intraosseous tumor is encountered in a retinoblastoma patient.
Undiagnosed Gout Mimicking Osteomyelitis Leading to Amputation

Behnam Rafiee, MD

We present 5 patients who underwent amputation for presumed diagnosis of acute osteomyelitis with failure to respond to appropriate antibiotic therapy. However, pathologic examination of the amputated specimens revealed gout tophi that were confirmed by polarized light microscopy. None of the patients had previous history of gout. The patients’ age range was 52 to 86 years. The sites of involvement included distal ulna, left second toe (2 cases), right fifth toe, and left fourth metatarsal bone. Gout is an inflammatory arthritis that mostly involves the metatarsophalangeal joint that is also a common site for nonhealing foot ulcer and cellulitis/osteomyelitis. Acute gouty arthritis may be clinically difficult to distinguish from acute osteomyelitis, because both conditions may present with joint pain, swelling, tenderness, leukocytosis, and elevated erythrocyte sedimentation rate. Acute gouty arthritis when associated with cortical destruction can mimic osteomyelitis on radiographs and magnetic resonance imaging. Similarly, ulcerated gout can mimic a nonhealing foot ulcer, such as that seen in diabetes, peripheral vascular disease, and osteomyelitis. It is essential to consider gout as an uncommon but important differential diagnosis for osteomyelitis and nonhealing foot ulcer. Appropriate diagnosis of gout, confirmed biochemically, results in different and definitive treatment choices, and spares the patient from further unnecessary antibiotic therapy or surgery. So, it is imperative for clinicians to be mindful of the clinical and radiologic presentations of acute gout that can resemble infection. This case series emphasizes the importance of considering gout as a differential diagnosis of nonhealing ulcer before surgical intervention.

Metastatic Colonic Glomus Tumor: A Case Report With Comprehensive Molecular Profiling

Ana I. Hernandez, MD

We report the case of a 58-year-old man found to have hepatic metastatic disease from a primary colonic malignant glomus tumor (GT) diagnosed 4 years earlier. To the best of our knowledge, this is the first report of metastatic colonic GT in the English-language medical literature. GTs represent a poorly understood, rare mesenchymal neoplasm arising from a neuro-myo-arterial structure. interrogation of 324 genes on paraffin-embedded tissue revealed a microsatellite-stable tumor with a low mutation burden (5 Muts/Mb). NOTCH2 rearrangement, and ATRX exon duplication. NOTCH2 rearrangements have been previously described in the literature in malignant GTs. This is the first reported case of an ATRX gene mutation in a GT. ATRX gene has been reported previously in angiosarcomas and other tumors pathways because it is implicated in the alternative lengthening of telomeres. NOTCH2 and ATRX represent potential targets for therapy and decreased roles for radiation therapy and immune checkpoint inhibitors. We are intrigued by the growing evidence demonstrating benefits of combination PARP inhibitors and VEGF blockade. The underlying pathogenesis of GT is broad and complex. After review of the literature, we propose a pathway where alternative telomeric lengthening and NOTCH signaling play a central role in malignant GT transformation. This is a single case that requires further investigation into this molecular progression. As our knowledge of this tumor class advances, a more complete picture can be elucidated, as can additional lines of precision therapy.

Osteosarcomatous Divergence in Dedifferentiated Liposarcoma Presenting as a Colonic Mass

Jeenal Gordhandas, MD

We present a 72-year-old man with constipation who underwent colonoscopy revealing a right colon mass compressing on the lumen extrinsically. Computed tomography imaging showed a 7.0-cm mass with exophytic growth and foci of calcifications. Gross examination of the right hemicolectomy specimen demonstrated a calcified intramural mass extending into the mesocolic fat, without involvement of the mucosa. Histologically, most of the tumor was composed of bony trabeculae and osteoid matrix with intervening highly atypical cells, resembling an extraskeletal osteosarcoma. A thin rim of atypical spindled and pleomorphic cells was identified in the periphery of the mass. In addition, foci of mature-appearing adipose tissue containing rare atypical hyperchromatic stromal cells, consistent with a well-differentiated liposarcoma (WDL), were detected around the periphery of the mass and the retroperitoneal resection margin (Figure 43). The findings suggested that WDL may have arisen in the retroperitoneum and secondarily involved the colon with a DDL component and heterologous osseous differentiation. Immunohistochemical studies showed diffuse positivity for SATB2 in the atypical cells between bony trabeculae, and negative staining for CD117, DOG-1, desmin, SMA, S100, and pancytokeratin. Immunohistochemistry in situ hybridization demonstrated level amplification of MDM2 gene, supporting the diagnosis of WDL and DDL with heterologous osteosarcomatous differentiation. This case illustrates an unusual initial presentation of a DDL as a colonic mass causing compression of the colon and constipation.
Giant Bilateral Xanthomas of Achilles Tendons With Extensive Extracellular Cholesterol Crystal Deposition but Normolipidemic State—A Rare Presentation

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Tendinous xanthoma is characterized by accumulations of lipid-laden macrophages and usually is associated with hyperlipidemia. We report a case of giant bilateral Achilles tendinous xanthomas with extensive cholesterol crystals but normal lipid profile, which is rarely seen. A 48-year-old woman presented with masses and pain on the posterior aspect of her bilateral lower legs for 2 years, as well as recent growth. She denied any traumatic onset. Physical examination revealed bilateral lower extremity enlargement extending to Achilles tendon body without skin lesions and varicosities. Her lipid panel results were all normal. Magnetic resonance imaging scans showed masslike enlargement of the Achilles tendons with a heterogeneous appearance. The core biopsy showed densely collagenous fibrous tissue, abundant extracellular cholesterol crystal deposition and surrounding multinucleated giant cells, and scattered lymphocytes, leading to the diagnosis of soft tissue with crystalloid-like material and foreign body giant cell reaction (Figure 44, A). The patient subsequently underwent resection of the bilateral masses. Both masses were intratendinous and well circumscribed (16.0 cm in greatest dimension; Figure 44, B). The histologic features, in addition to the findings on core biopsy, included a proliferation of predominantly foamy histiocytes (Figure 44, C and D). The final diagnosis was rendered as giant tendinous xanthoma of Achilles tendon. This case has raised the awareness that core biopsy may not represent lesions as a whole, which may result in misdiagnoses; when biopsies of giant tendinous masses do not show the most characteristic feature of xanthoma (foamy macrophages) and lipid profile is normal, xanthoma should still be considered as a differential diagnosis.

Primary Synovial Diffuse Large B-Cell Lymphoma

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Non-Hodgkin lymphoma (NHL) represents a diverse group of lymphomas that vary in cell type and cell size. Musculoskeletal involvement only occurs in about 25% of NHL cases. In these cases, skeletal involvement is usually secondary and is rarely the primary site of the neoplasm. In those rare instances of a primary skeletal NHL, synovial involvement is even less common and is usually caused by adjacent bone disease. We present an unusual case in which an 88-year-old man with longstanding osteoarthritis and chronic pain underwent a total knee arthroplasty for degenerative changes. Prior to the procedure he had no indications or symptoms associated with malignancy, nor did he have a history of autoimmune or rheumatic disease. Intraoperative assessment demonstrated copious fleshy synovial tissue (Figure 45, A). Subsequent morphologic and immunohistochemical findings were consistent with diffuse large B-cell lymphoma (DLBCL) of post–germinal center phenotype (CD20, Figure 45, B; BCL-6, Figure 45, C) with anaplastic morphology and high proliferative index (Ki-67, Figure 45, D). Staging procedures, including a total-body positron emission tomography/computed tomography scan and bone marrow biopsy, demonstrated no evidence of metastatic disease or bone marrow involvement. These findings support the assertion that the synovium was the primary site of the lymphoma. Rare cases of primary synovial NHL have been reported in literature. As an aggressive malignancy with an unusual presentation, this case demonstrates the importance of recognition and early diagnosis of primary synovial DLBCL.

Primary Myxofibrosarcoma of Bone Presenting With Bone-Only Metastases

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Primary myxofibrosarcoma (MFS) of bone is exceedingly rare. We present a low-grade MFS of the bone presenting with bone-only metastases. A 33-year-old man presented with dull aching pain over the left medial clavicle for several months. Computed tomography
revealed a 4-cm lytic mass involving the left clavicular head (Figure 46, A) and other lytic osseous lesions involving the right second rib, left humerus, spine, and pelvic bones (Figure 46, B). Computed tomography-guided bone biopsy of the right iliac bone lesion showed a spindle cell proliferation, not further classified. Subsequent open biopsies of the left clavicular mass and iliac mass showed characteristic findings of a low-grade myxofibrosarcoma, including proliferation of spindled to occasionally pleomorphic cells in a myxoid stroma with scattered curvilinear blood vessels (Figure 46, C and D). The patient underwent wide resection of the left proximal clavicle and curettage, cementation and fixation of the left proximal humerus, and adjuvant chemotherapy with cisplatin, doxorubicin, and methotrexate. The disease progressed with additional metastases to left femur and lung, and the patient died 2 years after initial diagnosis. In summary we describe the first case of low-grade primary MFS of bone presenting with bone-only metastases and pursuing an aggressive course. Deep-seated low-grade MFSs occurring in the bone appear to pursue a more aggressive course than their more frequent soft tissue counterparts.

Heterologous Osteosarcomatous Differentiation in Sarcomas Other Than Osteosarcoma: Frequency and Histotype Associations

(Poster No. 72)

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Context: Heterologous osteosarcomatous differentiation is an uncommon phenomenon observed in a variety of sarcomas and epithelial tumors. Divergent osteosarcomatous differentiation in sarcomas may cause diagnostic confusion with extraskeletal osteosarcoma. Herein, we study heterologous osteosarcomatous differentiation in various sarcomas to assess the frequency of the phenomenon, as well as the specific histotypes with which it is associated.

Design: A retrospective search of an institutional pathologic database from 2010 to 2019 was performed to identify sarcomas that were described as displaying osteosarcomatous differentiation. Pure osteosarcomas were excluded.

Results: From 449 soft tissue sarcomas that were diagnosed during this period, 8 (1.8%) showed heterologous osteosarcomatous differentiation. The patients ranged in age from 46 to 72 years (mean, 56; 4 women and 4 men). The cases included 3 of 44 de differentiated liposarcomas arising in the retroperitoneum (6.8%), 4 of 28 cases of intermediate to high-grade pulmonary artery intimal sarcomas (14.2%), and 1 of 38 malignant peripheral nerve sheath tumors (2.6%). All tumors were of intermediate to high FNCLCC grade. Immunohistochemical studies for SATB2 were performed in the 3 most recent cases, all of which showed strong nuclear immunoreactivity, supporting an osteoblastic differentiation in these tumors.

Conclusions: Heterologous osteosarcomatous differentiation is rare. Our data indicate that heterologous osteosarcomatous differentiation is most commonly associated with high-grade sarcomas, and the histotypes that most commonly display this change are intimal sarcomas and dedifferentiated liposarcomas. Sarcomas with heterologous osteosarcomatous differentiation should be distinguished from extraskeletal osteosarcoma, given the potentially different implications for prognosis and therapy.

Loss of H3K27me3 Expression in Chordoma

(Poster No. 73)

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Context: Chordomas are a rare and aggressive bone tumor of notochord origin affecting axial skeletal bones. Aside from alterations involving brachyury, these tumors have relatively quiescent genomes, suggesting that epigenetic mechanisms may be involved. One that has been explored in sarcomas is loss of H3K27 trimethylation, which is an important mechanism for tumor growth/survival in malignant peripheral nerve sheath tumors (MPNSTs). These tumors harbor mutations in genes involved in the polycomb receptor complex 2, which regulates histone methylation. Recently, other studies have reported occasional loss in other spindle cell soft tissue tumors. The role of H3K27me3 expression has not been extensively studied in bone tumors like chordomas.

Design: Tissue microarrays from 111 formalin-fixed, paraffin-embedded decalcified chordoma specimens were prepared from 93 patients (including 78 primary, 27 recurrent, and 8 metastatic tumors). Anti-H3K27me3 (1:200; clone C36H11; Cell Signaling Technology) immunohistochemistry was performed. Both extent and intensity of labeling were recorded. Loss of expression was defined as <10% of
A Rare Case of Round Cell Sarcoma With CIC-DUX4 Mutation Mimicking a Phlegmon: Analysis and Review of Literature

(Poster No. 74)

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Undifferentiated round cell sarcomas with CIC-DUX4 translocation are emerging as a distinct group of tumors because of the variation in the morphologic and clinical outcome for the patient. The World Health Organization currently classifies this entity under undifferentiated sarcomas with round cell phenotype. It is debated to be a variant of Ewing sarcoma or a stand-alone entity. We discuss our experience with this entity presenting as a phlegmon clinically. A 31-year-old African American man presented with a right upper quadrant abdominal mass. An incision and drainage were performed at an outside hospital suspecting an intra-abdominal abscess following streptococcal pharyngitis. He returned with pain and prolonged bleeding from the incision site. A computed tomography scan showed a 7.8-cm solid cystic mass concerning for neoplasm versus phlegmon. Microscopic examination of the excised mass showed a cellular, multinodular malignant neoplasm (Figure 48, A through D). Immunohistochemistry showed focal positivity for CD99 (much less than one would expect in Ewing sarcoma) and diffuse nuclear positivity for both WT-1 and ETV4, rendering a final diagnosis of round cell sarcoma with CIC gene rearrangement. This case provides important information regarding distinct clinical presentation of round cell sarcoma. The patient is doing well on chemotherapy, without radiologic evidence of metastatic disease or local recurrence 1 year postoperatively.

Histologic Change Spectrum in Treated Rhabdomyosarcoma: Diagnostic Dilemma and Potential Intraoperative Evaluation Pitfalls

(Poster No. 75)

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Rhabdomyosarcoma is a primitive skeletal muscle sarcoma. It is the most common pediatric soft tissue tumor that occurs during the first decade of life. It responds well to chemotherapy, with an overall survival rate of 65%. Therapy-related changes may vary, and evaluating a postchemotherapy case may cause a diagnostic dilemma. Different degrees of cytodifferentiation are documented in treated rhabdomyosarcoma. Because of this chemotherapy-induced cytodifferentiation, tumor may become hypocellular, with less rhabdoid differentiation and with prominent myxoid changes. Such myxoid changes may represent a potential diagnostic pitfall, particularly in a small biopsy or during intraoperative evaluation. We present a case of a 15-year-old male patient who presented in October 2015 with acute airway obstruction, and computed tomography confirmed pharyngeal mass. A diagnosis of embryonal rhabdomyosarcoma (FOXO1) was made. He underwent tumor debulking and received chemotherapy for intermediate risk disease. His tumor showed minimal response to therapy; therefore, he later received a salvage chemotherapy in October 2018, followed by tumor resection. Morphologically, the tumor demonstrated prominent hypocellular myxoid area, scattered atypical spindle cells with hyperchromasia alternating with foci of hypercellular area with rhabdomyoblasts (Figure 49, A). The tumor cells, including the hypocellular myxoid area, were positive for desmin (Figure 49, B) and had few cells staining for myogenin. His pretreatment biopsy was reviewed and showed hypercellular tumor proliferation with similar patchy myogenin expression (Figure 49, C and D); no myxoid changes were seen. To prevent a possible diagnostic dilemma, it is essential for practicing pathologists to be aware of such therapy-related changes and reevaluate the initial pretreatment surgical specimens when evaluating treated rhabdomyosarcomas.
pleomorphism and 4 mitoses in 50 HPFs (Figure 50, A and B). Immunostains showed diffuse and strong staining for smooth muscle actin (Figure 50, D), caldesmon, and HMB-45 (Figure 50, C), and focally for Melan-A, with a Ki-67 of 5% to 10%, and were negative for DOG1, CD117, S100, desmin, BCL2, ALK, myogenin, and CD34. Because of its size, mitotic activity, and metastasis, the diagnosis of malignant PEComa was made. Malignant pediatric PEComas are extremely unusual, with approximately 16 cases reported in the literature; only 3 have been documented in children younger than 5 years. This entity constitutes a diagnostic challenge for pathologists, requiring a careful histologic examination and appropriate immunohistochemistry for correct diagnosis.

**Atypical Osteomyelitis and Bone Infarction Due to Mucormycosis in the Postoperative Period After Anterior Cruciate Ligament Reconstruction**

(Poster No. 77)

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Acute osteomyelitis in postoperative anterior cruciate ligament reconstruction (ACLR) is exceptional; only 28 cases have been reported in the literature with osteomyelitis of several causes. The etiology is usually due to bacterial causes; there are few fungal reports (mycosis). Two cases of patients with osteomyelitis due to mucormycosis in postoperative ACLR are described. The first case involves a 37-year-old man with pain, joint effusion, and edema in a surgical wound in the second postoperative week. The second case involves a 17-year-old male with discharge of seropurulent fluid from a surgical wound 10 days after a surgical procedure. In both patients, magnetic resonance imaging showed metaphyseal centromedullary bone infarction around the femur tunnel, with the tibia surrounded or encapsulated, with a sign of peripheral halo with double signal (Figure 51, A and B). Due to the aggressive behavior, both underwent surgical debridement with a graft removal and fixation system. The cultures were negative, and the histopathologic study in both cases showed the presence of nonseptate hyphae with bifurcation at right angles corresponding to zygomycetes (Figure 51, C and D). The identification and late management of this pathology can be associated with greater bone destruction, loss of joint support, and greater functional sequelae for the patient. For this reason, early detection implies a reduction of the damage caused, being important the suspicion of a mycotic etiology as a cause of cases of osteomyelitis in which a causal agent is not clear by conventional cultures.

**Well-Differentiated Inflammatory Liposarcoma: A Case Report of an Uncommon Variant of a Common Sarcoma**

(Poster No. 78)

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Well-differentiated liposarcoma or atypical lipomatous tumor may exhibit a dense, chronic inflammatory infiltrate obscuring the adipocytic origin of this neoplasm, resulting in a diagnostic challenge. Herein, we present a case of a 75-year-old woman with a palpable right thigh mass that measured 6.5 cm in greatest dimension without hemorrhage or necrosis. Microscopically, the tumor was composed uniformly of mature adipocytes with focal areas of myxoid stromal change; no thickened fibrous septae containing atypical stromal cells and lipoblasts were seen. There was dense chronic lymphoplasmacytic infiltration with lymphoid follicle formation throughout the tumor, raising the differential diagnosis of lymphoma, inflammatory pseudotumor, or lipogenic tumor with prominent inflammation (Figure 52). Immunohistochemical stains for different lineage markers, including STAT6, pancytokeratin cocktail, S100, SOX10, smooth muscle actin, desmin, muscle-specific actin, CD34, and ALK-1, were all negative. Immunohistochemical stains for hematolymphoid markers, including CD3, CD20, CD5, CD10, CD23, and CD43, demonstrated a polymorphous population of T and B lymphocytes. In situ hybridization for κ and λ showed polyclonal populations of plasma cells. These results ruled out a lymphoproliferative disorder. Fluorescence in situ hybridization testing showed MDM2 amplification in the adipocytic areas, establishing a diagnosis of well-differentiated inflammatory liposarcoma. Without ancillary testing, this case would have otherwise been misdiagnosed as another entity in the differential diagnosis. To avoid overlooking this uncommon variant of liposarcoma, it is important to sample extensively.
to detect diagnostic areas and submit material for ancillary molecular testing that is a crucial aid in making the correct diagnosis.

**A Rare Case of Epithelioid Hemangioendothelioma Arising From the Coronary Sinus and Presenting With Pulmonary Tumor Embolism**  
(Poster No. 79)

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Epithelioid hemangioendothelioma (EHE) is a rare low- to intermediate-grade malignant angiocentric vascular neoplasm representing less than 1% of all vascular tumors. EHE is composed of cords of epithelioid endothelial cells in a characteristic myxohyaline stroma. Most tumors harbor a WWTR1-CAMTA1 fusion. Most common locations of EHE are the liver, lungs, bones, and soft tissue. Herein, the authors present a rare case of EHE arising from the coronary sinus. A 39-year-old man with a history of chest pain and dyspnea and a diagnosis of recurrent pulmonary embolism was transferred from an outside hospital with acute chronic thromboembolic pulmonary hypertension and cardiogenic shock. The patient proceeded to undergo a pulmonary thromboendarterectomy and resection of right atrial clot for presumed chronic thromboembolic pulmonary hypertension. Intraoperatively, it was discovered that the patient’s symptoms were caused by a tumor arising from the coronary sinus and involving the right atrium with pulmonary tumor embolism. Microscopic examination of the excised mass and tumor emboli demonstrated cords of epithelioid cells with cytoplasmic vacuolation (Figure 53, A), representing primitive angiogenesis, embedded in a myxohyaline stroma (Figure 53, B). The tumor cells were diffusely positive for vascular markers ERG (Figure 53, C), CD31 (Figure 53, D), and CD34, and they were focally positive for keratins. The histology and immunoprofile were diagnostic of EHE. Despite maximal surgical resection of the tumor, the patient died of his disease after the procedure. In summary, we present a rare case of EHE arising from the coronary sinus with pulmonary tumor embolism and clinical symptoms mimicking chronic thromboembolic pulmonary hypertension.

![Image 53](image_url)

**Epithelioid Myxofibrosarcoma: A Rare Morphologic Variant**  
(Poster No. 81)

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Epithelioid myxofibrosarcoma (epithelioid MFS) is a rare variant of myxofibrosarcoma (MFS), with only few cases reported in the English-language literature. Herein, we present a case of this uncommon entity. The patient is a 62-year-old man who presented with a rapidly growing mass in his left shoulder. Magnetic resonance imaging showed a 29-cm-deep mass on the lateral aspect of the left shoulder, extending to the acromioclavicular joint region and nearly to the dermis. Gross examination showed a 21-cm lobulated mass with a yellow-tan to red-brown heterogenous cut surface with focal areas of hemorrhage. Microscopically, the tumor showed alternating hypocellular and hypercellular areas. The hypocellular areas were composed of atypical spindle cells in a myxoid background, with prominent curvilinear thin-walled blood vessels. The hypercellular areas consisted of large epithelioid cells with a moderate amount of eosinophilic cytoplasm and rounded nuclei. No lipoblasts were identified. Immunostains for pankeratin, S100 protein, CD34, and desmin were negative. The case was signed out as epithelioid MFS, high grade. When compared with conventional MFS, the epithelioid variant seems to show a higher risk of local recurrence (approximately 70%) and a notably increased risk of distant metastases within a relatively short time frame (50%), mainly to lungs and retroperitoneum. It is important for the general pathologist to be familiar with the morphologic and immunohistochemical characteristics of epithelioid MFS because it carries a worse prognosis compared with usual MFS.

**Rhabdomyosarcoma of Adrenal Gland: A Rare Case Report**  
(Poster No. 80)

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Rhabdomyosarcoma (RMS), a malignant soft tissue sarcoma, is thought to arise from totipotent embryonic connective tissue. RMS is a highly aggressive tumor with a propensity for advanced and disseminate-grade malignant angiocentric vascular neoplasm also involving the adrenal gland in adults, and only 2 cases have been previously reported. Here, we report on a 65-year-old woman without significant past medical history who presented with abdominal pain for 2 weeks. Abdominal computed tomography (CT) showed a 15-cm adrenal mass with central necrosis. The patient underwent CT-guided left adrenal biopsy. Microscopic examination revealed a malignant pleomorphic neoplasm characterized by proliferation of atypical spindle cells with abundant eosinophilic cytoplasm. brisk mitotic activity and extensive necrosis were present. Scattered rhabdoid cells with eccentric nuclei and dense perinuclear cytoplasmic eosinophilic globules were appreciated (Figure 54, A and B). Immunohistochemistry revealed diffuse positive staining for MyoD1 (Figure 54, C), desmin and vimentin, focal positive staining for myogenin (Figure 54, D), and negative staining for pancytokeratin, Cam5.2, CD45, CD34, S100, and Mart-1, confirming the diagnosis of rhabdomyosarcoma. In conclusion, we present this unusual case of pleomorphic RMS in the left adrenal gland to raise awareness of this entity when considering the differential diagnosis of an adrenal mass.

![Image 54](image_url)
Comprehensive Analysis DNA and RNA of Bone and Soft Tissue Lesions Using a 170-Gene Panel on a Next-Generation Sequencing Analysis (NGS Platform)

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Context: Currently, next-generation screening techniques are being widely used as a tool in routine oncology diagnostic workflows. Identification of single-nucleotide variants, indels, copy number variations, splice variations, and gene fusions in bone and soft tissue lesions (BSLs) can provide substantial tumor-specific information for diagnosis and targeted treatment. Even though fluorescence in situ hybridization and polymerase chain reaction techniques are the current gold standard in fusion detection, they are limited in the number of genes and variants they can detect in parallel plus the necessity to know the specific target partners. The major advantage of using RNA sequencing technology is its ability to accurately identify fusions of all genes in the panel in a single sequencing assay, even without prior knowledge of fusion partners or breakpoints.

Design: DNA and RNA from 158 samples (mixture of known patient specimens with BSL, known College of American Pathology proficiency specimens, and synthetic reference standards [Acrometrix-Hotspot panel and Seracare-Fusion-V2 panel]) were used. Libraries were prepared using the Illumina-TruSight-Tumor-170 kit and sequenced on NextSeq-550. Sequencing analysis and variant calling were performed using the Basespace-TST170-App.

Results: Overall we were able to validate manufacturer analytic claims for all the variant groups in our validation; for small variants, >98% sensitivity and 100% specificity at 5% allele frequency at positions with coverage ≥250X was obtained.

Conclusions: We anticipate that this approach of obtaining high-resolution data from formalin-fixed, paraffin-embedded samples in the assessment of single-nucleotide variants, indels, copy number variations, splice variations, and gene fusions in 1 assay using DNA and RNA creates efficiencies in sample use, time, and cost that will facilitate testing in BSL that was not previously possible.

Small Bowel Obstruction With Incidental Heterotopic Mesenteric Ossification

(Dongpo M. Salas, MD (dongpo.salas@gmail.com); Nail Alouch, MD. Department of Pathology, Creighton University, Omaha, Nebraska)

A 76-year-old man presented to the emergency department with severe lower abdominal pain. Physical examination and initial workup were consistent with small bowel obstruction. Given the patient’s history of exploratory laparotomy, it was thought to be related to adhesions. The patient underwent open laparotomy for lysis of adhesions and segmental small bowel resection. On gross examination, the mesentery contained a 7.5-cm, ill-defined, fibrotic, and locally calcified mass. Histologic sections showed spindle cell proliferation with areas of increased cellularity and varying degrees of atypia. Some areas showed increased mitotic activity, up to 4 mitoses per 10 high-power fields (Figure 56, A, B, and C). Zones of lamellar mature bone were also seen. Cells were positive for smooth muscle actin immunostain and negative for CD34, β-catenin, S100, and DOG-1. Ki-67 index was up to 20% (Figure 56, D). The initial differential diagnosis was broad and it included benign reactive processes as well as sarcomas. The case was sent for expert opinion, and the diagnosis of heterotopic mesenteric ossification was rendered. Heterotopic mesenteric ossification is an extremely rare reactive pseudosarcomatous spindle cell proliferation with associated bone formation. The increased cellularity, presence of atypical cellular features, and increased mitotic activity may lead to misinterpretation as sarcomatous neoplasm. Most reported cases in the literature were thought to be related to prior abdominal surgery or trauma, as in our case. The significance of this lesion, besides resembling malignancies, is its association with a high recurrence rate. We believe that it is critical to recognize the clinical and histologic features of heterotopic mesenteric ossification.
A Rare Case of Extranodal Histiocytic Sarcoma Presenting With Primary Bone Tumor

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Histiocytic sarcoma (HS), a rare hematopoietic neoplasm (<0.5% of non-Hodgkin lymphomas) with aggressive characteristics and poor outcomes, can present as localized disease confined to the skin, lymph nodes, and intestinal tract, or as disseminated disease. Usually the age is 30 years or younger. It is very aggressive; 50% of patients die of disease, and usually it is associated with B symptoms (fever, night sweats, 10% or more weight loss), lymphadenopathy, hepatosplenomegaly, and peripheral blood cytopenia. We report on a 25-year-old man who presented with right knee pain and denied headache, blurry vision, chest pain, fever, chills, change in appetite, or bowel and urinary symptoms. Medical examination was unremarkable. Magnetic resonance imaging findings were significant for a long (4.8-cm) segment right distal femur destructive lesion in the supracondylar region medially. There was complete cortical destruction medially, with a large soft tissue extension measuring 9 cm in superior to inferior extent (Figure 57, A). Histopathology examination showed hypercellular tumor composed of sheets of highly pleomorphic cells with abundant granular to foamy eosinophilic cytoplasm and frequent nuclear inclusion (Figure 57, B). Special stains showed tumor cells were negative for eosinophilic crystalloid material in the cytoplasm by PAS and PASD, which did not support the diagnosis of alveolar soft part sarcoma. Additional immunostains showed tumor cells were positive for p16, CD68 (Figure 57, C), and CD163 (Figure 57, D), and negative for MDM2, CD99, and SATB2. The findings suggested histiocytic origin of tumor cells and ruled out dedifferentiated liposarcoma or osteogenic sarcoma.

Solitary Fibrous Tumor of the Spine: A STAT Diagnosis

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Malignant solitary fibrous tumor (SFT) is a rare entity that is thought to account for less than 2% of soft tissue tumors. Of the SFT group, about 10% arise in deep tissues, and when involving the central nervous system the tumor is typically intracranial and arising from the dura. Our case is a rare presentation of this entity in the spine. The patient is a 47-year-old man without any past medical history who presented with back pain radiating to the left leg for 2 weeks. Magnetic resonance imaging of the lumbar spine showed a vividly enhancing 1.3 x 2.6 cm intradural extramedullary mass extending from the inferior margin of T11 to the mid portion of T12. The mass was displacing and compressing the cauda equina. After resection, microscopic exam revealed a classic, “patternless architecture” of highly cellular atypical spindle cells with active mitotic count, up to 22 per 10 high-power fields (Figure 58, A). Immunohistochemical staining demonstrated positivity for CD34 (Figure 58, B) as well as nuclear staining for STAT6 (Figure 58, C). Although CD34 is a sensitive marker for SFT, STAT6 is a highly sensitive and highly specific marker to diagnose this tumor. The patient was treated with localized excision. Although SFT of the spine is rare, it is important to consider SFT as a diagnosis in cases of spindle cell neoplasm.
cytologically bland chondromyxoid stroma that suggested chondromyxoid fibroma and chondrosarcoma as diagnostic considerations. Resection of the tumor showed a 3.5-cm tan tumor in the mandible, and predominantly chondromyxoid pattern of proliferation of mainly bland spindle cells with foci of mild to moderate atypia. There was no prominent mitotic activity or necrosis seen. There were chondroid areas present and clear areas of invasion into surrounding bone with osteoid deposition around moderate atypical hyperchromatic nuclei. These features were consistent with an unusual variant of gnathic osteosarcoma and histologically best designated as “chondromyxoid fibroma like osteosarcoma.” Interpretation of this rare entity is challenging, especially on biopsy samples, and differential diagnosis considerations include fibro-osseous lesions, chondrosarcoma, and chondromyxoid fibroma. We have presented a most unusual case of CMF-like osteosarcoma and found that the diagnosis rested on the invasive pattern seen on the resection specimen.

Extraintestinal Malignant Gastrointestinal Neuroectodermal Tumor of the Urinary Bladder (Poster No. 89)

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Malignant gastrointestinal neuroectodermal tumor (GNET) is a highly aggressive malignant neoplasm of neuroectodermal origin arising in the gastrointestinal tract. It is characterized by clear cell sarcoma-like features, including overlapping morphologic appearances, expression of S100 and SOX10, and similar genetic rearrangements, namely EWSR1/ATF1 t(12;22)(q13;q12) and EWSR1/CREB1 t(12;22)(q34;q12). Importantly, however, whereas clear cell sarcoma displays true markers of melanocytic differentiation, GNET exhibits features of neural/neuroendocrine differentiation and lacks expression of true melanocytic markers. We present an extremely unusual case of an extragastrointestinal GNET occurring in the urinary bladder of a 36-year-old man who presented for evaluation of a bladder tumor. No other sites of involvement, including the gastrointestinal tract, were present. The cytoprostaticetomy specimen revealed nests of large polygonal cells containing eosinophilic to clear cytoplasm and round nuclei with prominent nucleoli, infiltrating the bladder wall (Figure 59, A and B, hematoxylin-eosin, original magnification ×40 and ×200). Mitotic figures were readily apparent. The differential diagnosis initially included paraganglioma, melanoma, and neuroendocrine carcinoma. Tumor cells expressed synaptophysin, CD56, NSE, SOX10, and S100, and were negative for Melan-A, MITF, and HMB-45. Next-generation sequencing disclosed an EWSR1/ATF1 gene fusion, confirming a diagnosis of extragastrointestinal GNET. To our knowledge, this represents the first case described of GNET arising outside of the gastrointestinal tract. Diagnostic pitfalls for this entity include melanoma, clear cell sarcoma, and neuroendocrine carcinoma. The bladder location also raised the possibility of paraganglioma. These findings also indicate that this highly aggressive malignant neoplasm may arise from neural crest-derived cells from other visceral locations outside of the gastrointestinal tract.

FUS Gene Rearrangement in 2 Cases of Myoepithelial Tumor of Soft Tissue: Case Report and Literature Review (Poster No. 90)

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Myoepithelial tumor of soft tissue is a relatively recently described entity with a spectrum of histologic findings. These tumors occur more commonly in ages <50 years with a propensity for affecting the extremities and limb girdles. Myoepithelial tumors commonly express pancytokeratin, EMA, S100, and GFAP. Most myoepithelial tumors harbor a EWSR1 gene rearrangement with a variety of fusion partners; however, recent case reports also describe FUS rearrangements with similar fusion partners. We report 2 cases of EWSR1 myoepithelial tumors of soft tissue, for which fluorescence in situ hybridization analysis confirmed FUS rearrangement. The first case involves a 29-year-old pregnant woman who presented with a right retroperitoneal mass extending to the right thigh. Complete resection revealed a 3-cm partially cystic and hemorrhagic mass. The second case involves a 15-year-old female presenting with a painless left lower extremity mass for which she underwent surgical excision. Microscopic examination in both cases showed plump epithelioid cells with a background chondromyxoid matrix. Cytologic features in the first case were atypical enough to warrant designation as myoepithelioma carcinoma, whereas the second case was classified as myoepithelioma. Both cases showed diffuse expression of pancytokeratin, EMA, S100, and SOX10, and were negative for GFAP and myogenic markers. Both cases also retained nuclear INI1 expression. These 2 cases support the addition of FUS gene analysis to EWSR1 tumors where the pathologic findings are suggestive of myoepithelial tumor, and they underscore emerging awareness that rearrangements of the FUS gene can substitute for EWSR1 rearrangements.

Epithelioid Hemangioma Involving Acetabulum (Poster No. 91)

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A 30-year-old man presented with a history of right hip pain for 9 months. Computed tomography showed an extensive lytic lesion involving the anterior right acetabulum and pubic root with associated pathologic fracture. A CT-guided core biopsy showed an infiltrative, well-differentiated vasoformative neoplasm composed of small capillary-sized vessels lined by plump epithelioid endothelial cells with myxoid stroma. Portions of the tumor had well-formed vessels with intercellular lumina, whereas other more cellular and solid portions had only intra cellular lumina. The tumor was diffusely CD31 positive. Pankeratin stained a subset of epithelioid cells. Differential diagnosis included epithelioid hemangioendothelioma and epithelioid hemangioma. This distinction is critical given the propensity for multifocality, metastasis, and aggressive treatment approach for epithelioid hemangioendothelioma. Although the tumor was quite cellular in portions, in expert consultation by a soft tissue/bone pathologist, the tumor cells were larger than observed in epithelioid hemangioendothelioma and were diagnostic of epithelioid hemangioma. This interpretation was further supported by a lack of expression of fusion RNA or mutations involving tested genes, including CAMTA1 or FUS. Immunohistochemistry showed diffuse diffuse S100 and SOX10, and similar genetic rearrangements, namely EWSR1/CAMTA1 t(2;22)(q34;q12). Importantly, however, whereas clear cell sarcoma displays true markers of melanocytic differentiation, GNET exhibits features of neural/neuroendocrine differentiation and lacks expression of true melanocytic markers. We present an extremely unusual case of an extragastrointestinal GNET occurring in the urinary bladder of a 36-year-old man who presented for evaluation of a bladder tumor. No other sites of involvement, including the gastrointestinal tract, were present. The cytoprostaticetomy specimen revealed nests of large polygonal cells containing eosinophilic to clear cytoplasm and round nuclei with prominent nucleoli, infiltrating the bladder wall (Figure 59, A and B, hematoxylin-eosin, original magnification ×40 and ×200). Mitotic figures were readily apparent. The differential diagnosis initially included paraganglioma, melanoma, and neuroendocrine carcinoma. Tumor cells expressed synaptophysin, CD56, NSE, SOX10, and S100, and were negative for Melan-A, MITF, and HMB-45. Next-generation sequencing disclosed an EWSR1/ATF1 gene fusion, confirming a diagnosis of extragastrointestinal GNET. To our knowledge, this represents the first case described of GNET arising outside of the gastrointestinal tract. Diagnostic pitfalls for this entity include melanoma, clear cell sarcoma, and neuroendocrine carcinoma. The bladder location also raised the possibility of paraganglioma. These findings also indicate that this highly aggressive malignant neoplasm may arise from neural crest-derived cells from other visceral locations outside of the gastrointestinal tract.

Cellular Angiofibroma in a Patient With Multiple Spindle Cell Lipomas (Poster No. 92)

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Cellular angiofibroma is a rare, benign mesenchymal tumor that resembles spindle cell lipoma (SCL) and mammary-type myofibroblastoma. It has been shown that these tumors share monoallelic deletion of 13q14, which includes the RB1 locus, further suggesting linkage between these tumors. Here we describe a patient who...
presented with a cellular angiofibroma with a history of numerous resections for SCLs. A 65-year-old man presented with an 18-cm pelvic mass. His past medical history was significant for removal of more than 20 SCLs (Figure 60, A). The patient additionally reported that a paternal uncle had a similarly sized soft tissue lesion of the abdomen. The patient’s tumor was removed with a portion of adhered prostate gland. The specimen consisted of a 1.28-kg mass with a smooth external surface. Sections showed a lesion entirely composed of bland spindled cells arranged in short bundles and fascicles with numerous thick-walled vessels and stromal hyalinization (Figure 60, B). Tumor cells were immunoreactive with antibodies to CD34 and desmin and were nonreactive with antibodies to S100 and MDM2. Retinoblastoma protein expression was lost. The tumor was diagnosed as cellular angiofibroma. It has been reported that some patients develop multiple SCLs in a familial pattern. We present a man with numerous SCLs who developed a cellular angiofibroma with a possible family history of similar lesions. We believe this case further substantiates the close relationship of these tumors and suggests that cellular angiofibroma can sometimes occur syndromically with SCLs.

Impact of 2018 Updated HER2 Testing Guidelines in Breast Cancer: The Experience From a Single Institution

(Supplementary Table 1, Table 2)

**Materials and Methods**

Cases of breast cancer from our institution (2015–2018), 312 cases had HER2 IHC and were included in our study. We analyzed the impact of the 2018 guideline and defined the frequency, immunohistochemical, and pathologic correlations. All cases with HER2 IHC results of ≥0 were subjected to HER2 FISH.

**Results**

Overall, 69 of 312 cases were HER2 IHC 3+, and 85 of 312 were FISH amplified. Patient ages were 24 to 92 years. Histologic grades were 11%, 42%, and 36% for grades 1, 2, and 3, respectively; 78% were ER positive; 62% were PR positive. In 32 cases in group 4 (equivocal), only 1 was HER2 by the 2018 guideline with 3+ IHC, and 31 cases (97%) were reclassified as HER2 2+. Two cases were in group 2 (ratio >2; HER2 copy number <4); both were HER2 by 2018 guidelines. Only 1 case was in group 3: Her2 ratio = 1.7, HER2 copy = 6.5, IHC 2+. This case was considered positive under both 2013 and 2018 guidelines. Among the 33 reclassified HER2 cases (31 from group 4 and 2 from group 2), their clinical and pathologic features were similar to group 5 (HER2- group). Most of them involved older patients, low grade, and ER/PR-positive tumors.

**Conclusions**

Our current study has validated the 2018 HER2 guideline, which ensures a significant portion of patients do not have to receive unnecessarily costly and potentially very toxic anti-HER2 therapy.
age at diagnosis was 63.9 years (range, 50–75 years). The diagnosis of OBC was made during the workup for cytopenia and bone pain. Immunohistochemistry stains were consistent with breast primary (Table). In the vast majority of patients, the tumor cells were positive for ER and PR, and were negative for HER2. For treatment, 8 patients received aromatase inhibitor treatments, 2 received chemotherapies, and 1 received radiation. Of 6 patients with follow-up information available, all died within 24 months, with a median survival of 13.8 months.

Conclusions: OBC presenting as bone marrow metastasis without primary breast lesion or axillary nodal involvement is very rare. The frequent presenting symptoms and signs include bone pain and cytopenia. In spite of adequate therapy, the prognosis of these patients is poor, with a median survival of only 2 years.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Cancer Imaging</th>
<th>Positive IHC</th>
<th>Negative IHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mammogram + random biopsy:</td>
<td>Pancytokeratin, CK7, GATA-3, ER, PR</td>
<td>TFF-1, HER2</td>
</tr>
<tr>
<td>2</td>
<td>Mammogram + MRI:</td>
<td>Pancytokeratin, CK7, GATA-3, ER, GCDFP-15</td>
<td>CDX2, TFF-1, PR, HER2</td>
</tr>
<tr>
<td>3</td>
<td>Mammogram + ultrasound + MRI:</td>
<td>ER, PR, CK7, GCDFP-15, MOC-31</td>
<td>CK20, TFF-1</td>
</tr>
<tr>
<td>4</td>
<td>Mammogram + negative</td>
<td>CK7, CK20 (partial), ER, GCDFP-15</td>
<td>P16, mammaglobin, TFF-1, synaptophysin, chromogranin, PR</td>
</tr>
<tr>
<td>5</td>
<td>Mammogram + ultrasound + MRI:</td>
<td>ER, PR, AE1/AE3, CK7</td>
<td>HER2, chromogranin, CK20, TFF-1</td>
</tr>
<tr>
<td>6</td>
<td>Mammogram + MRI:</td>
<td>CK7, CD138, GCDFP-15</td>
<td>CD3, CD20, CD34, CK20, ER, PR, HER2, synaptophysin, chromogranin, TFF-1</td>
</tr>
<tr>
<td>7</td>
<td>Mammogram + negative</td>
<td>ER, PR, EMA, CK7, GCDFP-15, CEA</td>
<td>CK20, CD45, S100, CEA, TFF-1, NSE, HER2</td>
</tr>
<tr>
<td>8</td>
<td>Mammogram + ultrasound + CAT scan:</td>
<td>CK7, CK22, ER, PR</td>
<td>CK20, CD45, S100, CEA, TFF-1, NSE, HER2</td>
</tr>
<tr>
<td>9</td>
<td>Mammogram:</td>
<td>CK7</td>
<td>TFF-1, PAX-8, CDX2, PAX-8</td>
</tr>
<tr>
<td>10</td>
<td>Mammogram + negative</td>
<td>AE1/AE3, ER, CK7</td>
<td>CK20, k and λ light chains, HER2</td>
</tr>
</tbody>
</table>

Abbreviation: MRI, magnetic resonance imaging.

Hormone Receptors and HER2/neu Overexpression in Breast Carcinomas in Patients of West African Origin Seen at Lagos State University Teaching Hospital, Nigeria

(Poster No. 96)

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Context: Breast carcinoma is a disease of utmost concern to the individual, family, and society at large. The current trend in the management of breast carcinoma involves hormonal therapy. Consequently, the hormone expression of the tumor in the individual involved must be known if he or she is to benefit from such therapy.

Design: This is a prospective study of estrogen and progesterone receptors as well as HER2/neu overexpression of all breast carcinomas seen at the Lagos State University Teaching Hospital, Ile-Ife, Nigeria, during a period between April 1, 2016, and September 30, 2018, evaluated by automated immunohistochemistry.

Results: The total number of cases analyzed during the period under study was 107, comprising 105 women and 2 men with an age range of 26 to 88 years and a mean age of 52 ± 13 years. The tumors fell into histologic grade II (71.0%) and grade III (29.0%). They expressed ER, PR, and HER2/neu positivity in 42.1%, 33.6%, and 30.8% of cases, respectively. Triple-negative breast cancer was 35.5%. Male breast cancers presented as invasive ductal carcinoma and exhibited staining pattern similar to that of the female breast cancer.

Conclusions: This study shows that breast carcinomas occurred predominantly in females of younger age and presented with tumors, most of which were of high grade and exhibited triple negativity. This observation is relevant to any therapeutic decisions and management of these patients. Improvement in breast carcinoma screening programs so that the disease can be detected early is also advocated.

Breast Carcinoma Pitfall: Rosai-Dorfman Disease

(Poster No. 97)

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Rosai-Dorfman disease (RDD) is an uncommon benign histiocytic proliferation that can be present in multiple organs. It rarely occurs in the breast. Overall, RDD is a painless, firm, and poorly defined lesion that can radiologically mimic a breast cancer. The diagnosis of breast RDD is challenging, especially on a small biopsy specimen. We report a unique case of breast RDD with a literature review including common presentation, differential diagnosis, and recommended management. A 42-year-old asymptomatic woman underwent a routine screening mammogram that revealed a dense mass lesion with irregular borders in the left breast. A core-needle biopsy was performed, with a diagnosis of RDD. Subsequently, a lumpectomy was performed. Gross examination of the lumpectomy specimen showed a 1.5 × 1.2 × 1.0 cm white, firm, and ill-defined mass. Histologic examination of the mass revealed a histiocyte proliferation in a sheetlike and nodular pattern admixed with dense hyalinized collagen bands. Large polygonal histiocytes formed syncytia, which displayed abundant pale and foamy cytoplasm with indistinct cell borders. Intermediate to large round vesicular nuclei were present, usually eccentrically located and with small, conspicuous nucleoli. Scattered histiocytes with enpulled intact lymphocytes were identified, suggestive of emperipolesis. Immunohistochemical study showed lesional histiocytes that displayed diffuse strong positivity for both S100 and CD68, and were negative for CD1a. The final pathologic diagnosis was RDD. Given the rarity of breast RDD, this case may provide additional information for the correct diagnosis, thereby avoiding unnecessary diagnostic tests and treatment (Figure 62).

PD-L1, P53, and Mismatch Repair Protein (MMR) Expression Patterns in Invasive Ductal Carcinoma With Neuroendocrine Features

(Poster No. 98)

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Context: Invasive ductal carcinoma with neuroendocrine features (IDCN) of breast is uncommon. Programmed death ligand-1 (PD-L1) is expressed in breast cancer. MSI status can be used as a predictive marker for response to PD-1 blockade in stage IV cancer patients. Expression of p53 is commonly seen in triple-negative breast cancer (TNBC) patients who have worse prognosis. We wanted to identify expression patterns of PD-L1, p53, and MMR on IDCNs.

Design: PD-L1 expression in tumor cells (TCs) and immune cells (ICs) were assessed as percentages of positive tumor cells. The percentage of PD-L1+ TCs or ICs was categorized as: 0 (<1%), 1 (1%–10%), and 2/3 (>10%). Mismatch repair protein expression was characterized as positive when ≥10% of tumor cell nuclei stained positively.

Results: Thirty-one IDCN cases were identified. A total of 7 tumors (22.5%) had tumor cell PD-L1 expression at TC1, and the other 24 cases were TC0 (77%). A total of 11 tumors (35%) showed PD-L1 expression on immune cells at level IC2/3, and 2 tumors (42%) showed IC1. Of these, 5 were grade 3, 4 were grade 2, and 2 were grade 1, and 3 were p53+ and 2 tumors (both grade 3: 1 PD-L1+, 1 PD-L1-) showed MLH1/ PMS2 instability (6%).

Conclusions: In our population, PD-L1+IC2/3 IDCNs were higher grade and more likely to be p53+ positive than PD-L1- tumors. Patients with high-grade IDCN tumors may benefit from PD-L1 antibody treatment despite the poor prognosis associated with p53 expression. Additionally, the MSI tumors were high grade, which demonstrates MSI status can also be a predictive marker.

Metastatic Well-Differentiated Neuroendocrine Tumors in the Breast

(Poster No. 99)

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Metastatic well-differentiated neuroendocrine tumors in the breast are rare. Because of their overlapping clinical, histologic, or radiologic features, they can be mistaken for invasive breast carcinoma. Correct diagnosis is vital to the appropriate treatment. We report a case of a 49-year-old woman who presented for evaluation of a breast mass. Screening mammogram demonstrated a well-circumscribed oval isodense mass in the upper inner quadrant of the left breast. Her past medical history was significant for an ileal well-differentiated neuroendocrine tumor with liver metastasis diagnosed 9 years previously, followed by a resection of terminal ileum and right colon, and she has been on lanreotide injections. Histology of her breast needle core biopsy showed nests of small uniform tumor cells with regularly dispersed chromatin separated by dense connective tissue bands. The tumor cells are diffusely and strongly positive for synaptophysin, chromogranin, and CDX2, weakly positive for ER; and negative for CK7 and GATA3. The immunophenotype, in conjunction with the clinical history and cellular morphology, supports the diagnosis of metastatic well-differentiated neuroendocrine tumor with ileal origin. Considering the patient is asymptomatic from a breast standpoint, her liver metastasis is indolent and well controlled with lanreotide; there is no evidence for resection because it would not change her prognosis. However, close imaging follow-up and elective lumpectomy were offered to the patient because she had significant anxiety over the new diagnosis. This report clearly shows the importance of the combined clinical history, and histologic and immunohistochemical analyses for correct diagnosis of a metastatic well-differentiated neuroendocrine tumor in the breast.

An Unusual Presentation of Mammary Paget Disease in a Male

(Poster No. 100)

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Mammary Paget disease (MPD) in a male is extremely rare and comprises only 1.5% of all male breast cancers. The typical presentation of MPD is a scaling crust on the nipple and areola. MPD is characterized by epidermal invasion by neoplastic cells that originate from ductal carcinoma in situ (DCIS) and migrate from the nipple ducts to the epidermis and spread radially as single and clustered cells. Pagetoid spread is not unique to MPD and can be seen in other processes, such as melanoma, mycosis fungoides, and invasive carcinoma. A 78-year-old man presented with scaly skin lesion associated with itching on the right breast. A punch biopsy of the skin lesion was diagnosed as Bowen disease. The patient underwent a wide excision with removal of the nipple-areolar complex and underlying breast tissue. Gross examination revealed a 65 × 63 mm raised, scaly skin lesion with areas of hyperpigmentation and hypopigmentation involving the entire areola and adjacent periareolar skin. Histopathology of the nipple lesion showed high-grade DCIS with involvement of the nipple ducts. A panel of immunostains was performed to establish the diagnosis of MPD because the estrogen receptor status of DCIS did not match with Paget cells. There have been 57 total cases of MPD reported in males thus far. In reporting this case, we highlight some of the unusual findings: MPD can mimic Bowen disease and MPD may not always represent epidermotropism from underlying DCIS.

Auxiliary Lymphadenopathy Unrelated to Breast Carcinoma in Female Patients: A Retrospective Analysis

(Poster No. 101)

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Context: Axillary lymphadenopathy in females can be the first manifestation of an occult or clinically evident breast carcinoma. However, systemic neoplastic and nonneoplastic processes may involve the axillary lymph nodes, clinically mimicking a metastatic breast carcinoma. Literature on axillary lymphadenopathy unrelated to breast carcinoma in female patients is lacking or limited to single case reports. We undertook a retrospective study to assess the pathologic findings in female patients presenting with axillary lymphadenopathy unrelated to breast carcinoma.

Design: Departmental archives from 1993 to 2018 were searched for axillary lymph node specimens in females. A review of medical charts was performed and axillary nodal biopsies for evaluation of lymphadenopathy were further reviewed. Patients with a history of breast carcinoma and biopsies performed for cancer staging purposes were excluded from the study.

Results: Ninety-eight cases were reviewed. Twenty cases were excluded after review of medical records revealed history of breast carcinoma or performance of axillary biopsy for cancer staging. Of the 78 remaining cases, the mean patient age was 58.6 years (median, 57 years; range, 19–91 years). Histologic diagnoses included hematologic neoplasms (n = 28; 35.9%), reactive/inflammatory (n = 27; 34.6%), metastatic carcinoma (n = 11; 14.1%), metastatic melanoma (n = 10; 12.8%), and sarcoma (n = 2; 2.6%). Of the 51 malignant cases, 15 (29.4%) represented the initial tissue diagnosis.

Conclusions: Axillary lymphadenopathy in females can involve many neoplastic and nonneoplastic processes other than breast carcinoma and can be the initial presentation of metastatic disease. A total of 18 of the 78 cases represented (65.4%) different metastatic processes, suggesting that histologic evaluation should be considered for any female with unexplained lymphadenopathy.

Genetic Alterations and Their Association With Clinicopathologic Characteristics in Breast Carcinoma: A Single Academic Institution Experience

(Poster No. 102)

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Context: Breast carcinomas (BCs) are heterogeneous and associated with numerous genomic alterations. We sought to investigate these alterations and their association with clinicopathologic characteristics. Design: The cohort included 223 BCs with FoundationOne next-generation sequencing results. Clinicopathologic characteristics and their association with genetic alterations were analyzed using Fisher exact test with adjusted P values calculated (Bonferroni correction).

Results: A total of 150 different mutations were identified (total = 1088). The most prevalent (>5%) included the following: TP53 (53.8%), MYC (22%), CCND1 (19.7%), FGFR3 (17%), FGFR4 (16.6%), FGFR3 (16.1%), ZNF703 (14.8%), ERBB2 (13.9%), FGFR1 (13.5%), P TEN (10.8%), CDH1 (9.4%), GATA3 (9.4%), ZNF217 (8.5%), RB1 (8.1%), BRCA2 (7.2%), ERBB2 (6.7%), AURKA (6.3%), EMSY (6.3%), CDKN2A/B (5.8%), MAFK31 (5.4%), and NOTCH2 (5.4%). All cases were...
categorized into 3 biomarker groups: hormone receptor positive (HR+: n = 129), HER2 positive (HER2+: n = 16), and triple-negative (TN; n = 78). As expected, ERBB2 alteration was most common in HER2+ BCs. GATA3 and ESR1 mutations were only identified in HER2+ or HER2- BCs. The following mutations were enriched in TN BCs: TP53, PTEN, RB1, and CDKN2A/B. In HR+ BCs, the following mutations were enriched: FGFR1, FGFR4, FGF19, FGF21, and CDH1. As expected, CDH1 mutation was predominantly found in lobular carcinomas. The following mutations were enriched in metastatic carcinomas: p53, PTEN, MCL1, CDKN2A/B, and NOTCH2. DNA damage repair (DDR) gene mutation(s) may be associated with increased tumor mutation burden, tumor neoantigens, and immune reaction. We found an overall DDR gene mutation rate of 19.7% but no significant difference among BC groups (Table).

Conclusions: We have summarized genetic alterations and their association with clinicopathologic characteristics in 223 BCs. Our data lay the groundwork for targeted therapy in BCs, including immunotherapy in patients with DDR-mutated BCs.

| DDR Gene Mutations in 223 Breast Carcinomas With FoundationOne Test Results |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Mutated Genes | HER2+ BC | HER+ BC | TNBC | Total |
| Mutations | No. (%) | No. (%) | No. (%) | No. (%) |
| BRCA2 | 1 (6.3) | 13 (10.1) | 2 (2.6) | 16 (7.2) |
| BRCA1 | 0 (0.0) | 2 (1.6) | 6 (7.7) | 8 (3.6) |
| ATM | 1 (6.3) | 4 (3.1) | 1 (1.3) | 6 (2.7) |
| FANCA | 0 (0.0) | 2 (1.6) | 1 (1.3) | 3 (1.3) |
| CHEK2 | 1 (6.3) | 2 (1.6) | 0 (0.0) | 3 (1.3) |
| BRIP1 | 0 (0.0) | 2 (1.6) | 0 (0.0) | 2 (0.9) |
| ATR | 0 (0.0) | 0 (0.0) | 1 (1.3) | 2 (0.9) |
| BLM | 0 (0.0) | 0 (0.0) | 1 (1.3) | 1 (0.4) |
| FANCC | 1 (6.3) | 0 (0.0) | 0 (0.0) | 1 (0.4) |
| RAD51 | 0 (0.0) | 0 (0.0) | 1 (1.3) | 1 (0.4) |
| RAD50 | 0 (0.0) | 0 (0.0) | 1 (1.3) | 1 (0.4) |
| Total | 4 (25.0) | 26 (20.2) | 14 (17.9) | 44 (19.7) |

Assessing Breast Terminal Duct Lobular Unit Involution: A Computational Pathology Approach (Poster No. 103)

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Context: The nonreceptor tyrosine kinase ACK1 (also known as TNK2) is highly activated in breast cancer, with expression of phosphorylated ACK1 (pACK1-Tyr284) correlating with proliferation and invasion. We have identified a potent ACK1-specific small molecule inhibitor, (R)-9bMS, that significantly compromises breast cancer tumorigenesis. However, the immunohistochemical expression of ACK1 and its activated form pACK1-Tyr284 in breast cancer have not been well characterized.

Design: Sections from formalin-fixed, paraffin-embedded tissue microarrays composed of breast cancer cores were stained separately with hematoxylin-eosin, ACK1-specific, and pACK1-Tyr284–specific antibodies (n = 399). Staining intensity was scored semi-quantitatively by blinded readers. Statistical analysis was performed by χ2 test.

Results: Both ACK1 and pACK1-Tyr284 immunostaining did not differ with respect to ER/PR/HER2 status (ACK1: χ2 = 4.23, P = .12; pACK1-Tyr284: χ2 = 5.71, P = .06; Figure 63). When grouped together, breast cancers stained more frequently for pACK1-Tyr284 than ACK1 (87% versus 33%; χ2 = 66.7, P < .001).

Conclusions: Breast carcinomas have high rates of ACK1 and pACK1-Tyr284 immunoreactivity, irrespective of hormonal status. This is in contrast to normal breast tissue, which possesses minimal ACK1 and pACK1-Tyr284 expression. Interestingly, we found more pACK1-Tyr284 than ACK1 staining in these tumor samples, which could be due to aberrant activation of ACK1 by other receptor tyrosine kinases in the setting of carcinogenesis. Additional studies are needed to determine if these immunostains are predictive of response to ACK1 inhibition by (R)-9bMS. If so, ACK1 and pACK1-Tyr284 immunostaining may have potential as a predictive biomarker to direct ACK1-targeted therapies, not only in triple-negative breast cancer but in all molecular subtypes.
Prognostic Significance of Magee Equations (Poster No. 105)

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Context: Magee equations (MEs) are multivariable models that were developed to estimate the oncotype DX recurrence score on invasive breast carcinomas (PMID: 23503643). ME3 has been shown to have chemopredictive value in the neoadjuvant setting (PMID: 28548119).

Design: To further evaluate the prognostic value of MEs, we used a data set of 130 well-characterized ER+/HER2− invasive breast carcinomas with relatively long-term follow-up (average follow-up of 95 months). MEs were calculated and divided into low (18–30), intermediate (18–30), and high (31 or higher) scores. Kaplan-Meier survival curves of disease-free survival (DFS) and overall survival (OS) were analyzed with respect to MEs. P values were obtained using the log rank test.

Results: All MEs are prognostic for DFS (P values of .001, .001, and .001). ME1 and ME3 are prognostic for OS (P values of .007 and .03; Figure 64). When the cohort was divided into lymph node−negative and lymph node−positive subgroups, all MEs remained prognostic for DFS (P values of .02, .03, .006) but not for OS in the lymph node−negative subgroup. Within the lymph node−positive subgroup, ME1 and ME3 remained prognostic for DFS (P values of .004 and .02).

Conclusions: In addition to the predictive nature of Magee equations (published earlier), Magee equations provide prognostic information in ER+/HER2− tumors. The inclusion of Ki-67 labeling index in ME1 and ME3 suggests tumor cell proliferation is an important determinant of DFS in such tumors.

A Rare Case of High-Grade Adenosquamous Carcinoma of the Breast: Case Report and Review of Literature (Poster No. 106)

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Metaplastic breast carcinoma (MBC) is a rare primary breast malignancy that comprises a heterogeneous group of carcinomas. MBCs are broadly categorized into 3 categories: carcinomas with squamous/spindle cells, matrix-producing carcinomas, and carcinomas with true mesenchymal component. Most adenosquamous carcinomas are low-grade metaplastic carcinomas, and the high-grade adenosquamous carcinoma is very rare, with limited literature. We present a case of 44-year-old woman with a biopsy-proven invasive ductal carcinoma of right breast who had been receiving neoadjuvant chemotherapy. She underwent simple mastectomy with sentinel lymph node biopsy in our facility. Grossly the lesion was multifocal with skin ulcerations. Histologic examination of the lesion revealed a significant component of squamous cell carcinoma with areas of mixed glandular and squamous component, with some pure low-grade invasive ductal carcinoma. The squamous and adenosquamous carcinoma showed numerous mitoses with high-grade nuclear features. Immunohistoch- emistry was performed which showed squamous component positive for p40, p63, and CK5/6, whereas glandular components were positive for CK7, thus confirming the adenosquamous differentiation. The tumor showed focal positivity for ER in both squamous and glandular components. Sentinel lymph nodes were negative for carcinoma. High-grade adenosquamous carcinoma may have weakly positive ER/P, not like the most common low-grade adenosquamous carcinoma with triple-negative phenotype, and high-grade adenosquamous carcinoma is a true metaplastic carcinoma with aggressive clinical behavior. Further recognition of this rare breast cancer is required for studying its clinical behavior, prognosis, and effective therapy.

Absence of Insulin-like Growth Factor II Messenger Ribonucleic Acid Binding Protein-3 (IMP3) Immunostain Is Characteristic of Mammary Carcinomas (Poster No. 107)

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Context: IMP3 is a member of the human insulin-like growth factor II mRNA binding protein (IMP) family. Although its expression is readily detected by immunohistochemistry (IHC) in a wide variety of malignant neoplasms, we discovered by serendipity that IMP3 is not detectable in mammary carcinomas. We confirmed this observation by examining IMP3 expression in additional cases.

Design: Routinely processed tissues with breast epithelial carcinoma (Table) were examined for IMP3 expression by routine IHC. Sections of paraffin-embedded tissue blocks cut at 4 μm and processed routinely were stained for IMP3 with a mouse monoclonal antibody to IMP3 (Dako Corp) at 1:200 dilution following the vendor’s protocol. The immunostain intensity was graded by both extent and intensity (Table). Viable immature chorionic villi were used as a positive control. Positive stain was defined as >5% tumor cells stained weakly intense (grade 1 of 3). GATA3, a well-established IHC marker of breast epithelium, was also stained for confirmation.

Summary of IMP3 Detection Results in Breast Carcinomas

<table>
<thead>
<tr>
<th>Pathologic Diagnosis</th>
<th>Specimen</th>
<th>No. of Cases</th>
<th>Bloom-Richardson-Elston Grading System Grade</th>
<th>IMP3/GATA3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive ductal carcinoma</td>
<td>Breast</td>
<td>8</td>
<td>1–2</td>
<td>Negative/3+</td>
</tr>
<tr>
<td>Invasive ductal carcinoma</td>
<td>Breast</td>
<td>1</td>
<td>3</td>
<td>3+/3+ positive</td>
</tr>
<tr>
<td>Invasive ductal carcinoma</td>
<td>Breast</td>
<td>3</td>
<td>3</td>
<td>Negative/3+ positive</td>
</tr>
<tr>
<td>Invasive lobular carcinoma</td>
<td>Breast</td>
<td>3</td>
<td>1–2</td>
<td>Negative/3+</td>
</tr>
<tr>
<td>Metastatic ductal carcinoma node</td>
<td>Lymph node</td>
<td>8</td>
<td>1–2</td>
<td>Negative/3+</td>
</tr>
<tr>
<td>Metastatic ductal carcinoma bone</td>
<td>Bone</td>
<td>3</td>
<td>1–2</td>
<td>Negative/3+</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>26</td>
<td>26</td>
<td>IMP3 = 25 of 26; GATA3 = 26 of 26</td>
</tr>
</tbody>
</table>

Results: Positive immunostain for IMP3 was absent in >95% of invasive ductal and lobular carcinomas, and it was only detected in 1 poorly differentiated tumor examined (Table). All tumors examined stained strongly for GATA3 and were confirmed as being of breast origin by clinical history/follow-up and other IHC studies.
**Risk Stratification of Women With Early-Onset Breast Cancer: Comparing Patient Groups <35 Years of Age With Patients Ages 36–45 Years**

(Poster No. 108)

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**Context:** According to the Surveillance, Epidemiology, and End Results (SEER) data, approximately 11% of women with a diagnosis of breast cancer are younger than 45 years. Having a family history (FH) of breast cancer among first-degree relatives has long been considered a prerequisite for starting breast cancer surveillance before the age of 50 years. Here, we sought to study the physical attributes and FH of cancer in women by focusing separately on age groups <35 years and 36 to 45 years.

**Design:** The electronic database was searched from 2016 to 2018 for women ages 45 years and younger with new diagnoses of breast cancer. Patient demographics, mammographic findings, and FH of cancers were collected.

**Results:** During the 3-year period, 20 patients age <35 years and 61 patients between 36 and 45 years of age received a diagnosis of breast cancer. Both groups of women were overweight, with mean body mass indices of 28.4 and 30.6, respectively (Table). Women ages <35 years had significantly denser breasts and consisted of fewer smokers than the older group. In both groups, FH of breast and/or gynecologic (ovarian/uterine) cancers was more prevalent among second- and third-degree relatives. In each group with an FH of cancer, about 60% had family members with other types of cancers (which included gastrointestinal, prostate, and thyroid cancers, melanoma, and hematologic malignancies, but excluded other skin cancers, and lung and head/neck cancers).

**Conclusions:** Our limited study indicates that gathering family histories of all cancer types and among all degrees of relatives is critical when risk stratifying women for early-onset breast cancer.

| Characteristics and FH of Cancers in Women With Early-Onset Breast Cancer |
|-----------------------------|-----------------------------|
| Age ≤35 Years  | Age 36–45 Years |
| No.           | 20              | 61               |
| Mean age, y   | 31.6            | 42.1             |
| Race, white:black:other | 15:5:0           | 39:21:1          |
| Mean body mass index | 28.4            | 30.6             |
| Smokers, %    | 15              | 43               |
| Dense breasts present, % | 84              | 54               |
| FH of cancer present, % | 65             | 80.3             |

Patients with an FH of breast/gynecologic cancers in

- 1° relatives only: 0/3
- 2° only: 8/28
- 1° + 2°: 0/10
- 3° only: 2/5
- 2° + 3°: 0/1

Patients with an FH of other cancers in

- 1° relatives only: 1/14
- 2° only: 6/10
- 1° + 2°: 0/3
- 3° only: 0/1
- 2° + 3°: 0/2

**Loss of Smooth Muscle Myosin Heavy-Chain Expression in Breast Lobules Secondary to Surgery-Related Reparative Changes: Hitherto Unreported Finding With Diagnostic Implications**

(Poster No. 109)

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**Context:** Myoepithelial cell (MEC) layer loss in an atypical mammary epithelial proliferation indicates invasive disease. MECs may show variable expression of immunohistochemistry (IHC) markers, especially in a setting of in situ carcinoma and sclerosing lesions. We describe a previously unreported variation in the MEC IHC pattern, which, along with morphologic features, mimics invasive carcinoma.

**Design:** A series of consecutive re-excision specimen (July 2016–July 2017) were reviewed. Tissue sections with terminal duct lobular units (TDLUs) and surgery-related reparative changes were identified. IHC was performed for smooth muscle myosin heavy chain (SMMS-1; Dako), p63 (4A4, Biocare Medical), calponin (CALP; Dako), keratin 5/6 (D5/16 B4, Dako), and S4BE12 (34B E12, Dako) on a Dako autostainer. The IHC pattern was compared between TDLUs with and without surgery-related reparative changes.

**Results:** Seventeen tissue blocks, from 15 re-excisions, were selected for IHC. Seven foci were identified where TDLUs were entraped in the reparative changes and showed obliteration of the acinar lumina. With repair-related cytologic atypia and stromal reactive changes overall morphologic features were suspicious for an invasive process (Figure 65, A). In these TDLUs smooth muscle myosin heavy chain expression was completely absent (Figure 65, B). Conversely, p63 (Figure 65, C) and calponin expression was intact. Keratin 5/6 and S4BE12 were strongly positive in entire TDLU cells.

**Conclusions:** Discordant MEC immunophenotype in TDLUs secondary to surgery-related reparative changes with selective loss of smooth muscle myosin heavy chain is a novel finding. Pathologists should be aware of this IHC pitfall to avoid overdiagnosing a benign reparative process as invasive disease.

**Rare In Situ Carcinoma Associated With Adenoid Cystic Carcinoma of the Breast**

(Poster No. 110)

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Adenoid cystic carcinoma (ACC) of the breast is histologically similar to its counterpart in the salivary glands and is very rare. In situ lesions are rarely observed associated with ACC. Herein we describe the case of a 53-year-old woman who presented with a 1.7-cm upper outer quadrant, well-circumscribed nodule on screening mammogram. Core needle biopsy of the nodule revealed solid nests of basaloid neoplastic cells with focal areas of pseudolumina formation. The neoplastic cells had an intermediate nuclear grade and were positive for CD117 and focally positive for CK5/6 and NSE. Immunohistochemical stains with p63, synaptophysin, and chromogranin were negative. The lesion was also negative for estrogen receptor, progesterone receptor, and HER2/neu oncogene. A diagnosis of ACC was rendered. Upon conservative surgical excision of the lesion, a firm, grey-white, irregular 2.0-cm mass was identified. It had histologic and immunophenotypic features similar to malignancy.
Pleomorphic Adenoma of the Breast: A Potential Morphologic and Molecular Pitfall

(Poster No. 111)

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Pleomorphic adenoma of the breast (PAB) represents a diagnostic challenge given its rarity and resemblance to other entities in samples of limited size. We present the case of a 54-year-old woman with an incidental 1.1-cm positron emission tomography–avid periareolar mass. Core needle biopsy revealed a low-grade glandular proliferation that was interpreted as invasive ductal carcinoma, grade 1 (Figure 66, A). The lesion was ER+, PR+, and HER2 1+. Immunohistochemistry (IHC). Oncotype Dx testing reported a “high-risk” lesion (risk score of 26, recurrence risk of 16% at 9 years, and an absolute benefit of chemotherapy of >15%). The patient underwent lumpectomy with sentinel node excision, with a plan for postlumpectomy chemotherapy. Final histologic examination revealed a well-circumscribed mass comprising low-grade glands embedded in myxoid stroma (Figure 66, B and C). The p63 IHC highlighted a prominent myoepithelial component (Figure 66, D), and the lesion was classified as a PAB. Because of the diagnostic discrepancy between the biopsy and resection, p63 was retrospectively performed on the prior core, revealing a previously unappreciated component of myoepithelial cells. Given this revised diagnosis, we advised the clinical team to disregard the Oncotype Dx score, because this test is not validated for salivary- or breast-type tumors and PABs have favorable outcomes with surgical management. This case well illustrates the difficulty of diagnosing PABs in small samples. Additionally, this is the first report of Oncotype Dx profiling performed on a PAB and underscores the risk of unnecessary genomic testing on limited samples and the potential for unwarranted chemotherapy in patients with a spurious high-risk score.

Extensive Mucin Pool With a Single Cluster of Definitive Residual Invasive Ductal Carcinoma After Neoadjuvant Chemotherapy

(Poster No. 112)

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The presence of residual mucin pools after neoadjuvant chemotherapy (NACT) within resection specimens from the rectum is well described. In treated breast cancer, this phenomenon is described less frequently. Here, we present a case from a 74-year-old woman treated with NACT for invasive ductal carcinoma with mucinous features whose resection specimen demonstrated large, residual mucin pools with only a single small cluster of viable tumor cells. Prior to treatment, the patient presented with a 4.1-cm breast mass and a 5.3-cm axillary mass on magnetic resonance imaging, both of which demonstrated Nottingham grade 2 invasive ductal carcinoma with mucinous features (Figure 67, A). The tumor was positive for estrogen receptor (ER), negative for progesterone receptor (PR), and positive for HER2. The patient then received combination NACT (trastuzumab, pertuzumab, carboplatin, and docetaxel). Following NACT, lumpectomy and axillary lymph node dissection were performed. The entire gross tumor bed seen within the lumpectomy was submitted for microscopic examination. Microscopic examination revealed an extensive mucin pool measuring 3.6 cm. Only a single cluster of residual tumor cells were observed (Figure 67, B). In addition, the 5.5-cm left axillary lymph node demonstrated replacement by abundant mucin with scattered foamy histiocytes (Figure 67, C). However, viable tumor cells were not identified within the lymph node, and cytokeratin stains were negative. This case highlights an uncommon example of how invasive ductal carcinoma with mucinous features responded to NACT.
had at least one <2 mm margin. A total of 12 RFID cases (18%) underwent re-excision, of which 2 cases yielded positive margins. In the WL group, 3 cases (5%) had positive margins, 11 (20%) had at least one <1 mm margin, and 16 (29%) had at least one <2 mm margin. A total of 5 WL cases (9%) had follow-up re-excisions, with 1 case remaining with a positive margin. There was no statistically significant difference between margin positivity (11% versus 5%; P = 0.2, Fisher exact test) and re-excision rates (18% versus 9%; P = 0.1, χ² test) between RFID and WL groups.

**Conclusions:** Margin status, including margin positivity, close margins, and re-excision rate in RFID tag localization, is similar to WL procedures.

### Cystic Neutrophilic Granulomatous Mastitis: Association With Corynebacterium Species and Role of 16s rRNA Gene Sequencing in Identification

(Poster No. 114)

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**Context:** Cystic neutrophilic granulomatous mastitis (CNGM) is a distinctive form of granulomatous mastitis (GM) that may be associated with *Corynebacterium*. In this study we reviewed the pathology from all patients with a diagnosis of GM to determine: (1) how many have classic features of CNGM and (2) if 16s rRNA gene sequencing can help identify bacteria.

**Design:** The database was searched for all breast specimens with “granulomatous” in the diagnosis (January 2013–August 2018). Patients with ipsilateral prior excisions and/or implants were excluded. Pertinent clinical information was collected. All available slides were reviewed for granulomas with neutrophil-lined cystic vacuoles. The 16s rRNA gene sequencing was performed on a subset of cases.

**Results:** A total of 31 patients met inclusion criteria. After review, 18 were classified as CNGM. Almost all were symptomatic or had a palpable mass. CNGM patients were younger than those with GM. Cultures were sent on 13 CNGM/5 GM (2%); 42% had received antibiotics. *Corynebacterium* grew in 3 patients, 2 with CNGM. The 16s rRNA gene sequencing was performed on 4 CNGM and 2 GM using primers for V1 to V3 region, followed by sequencing a shorter fragment of the V3 region; no *Corynebacterium* was identified.

**Conclusions:** CNGM is an underrecognized histologically distinct form of mastitis that tends to occur in women age ≤40 years and has a suggested association with *Corynebacterium*. In our study, only 15% of CNGMs were culture positive; *Corynebacterium* was also isolated from 1 GM. Additional testing, such as 16s rRNA gene sequencing, is currently of limited value; *Corynebacterium*-specific polymerase chain reaction may be of value.

### Minimizing HER2/neu Status Misclassification in Breast Cancer by a Dual Testing Strategy

(Poster No. 115)

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**Context:** The American Society of Clinical Oncology and the College of American Pathologists (ASCO/CAP) recommend determining human epidermal growth factor 2 (HER2/neu) status for all invasive breast cancers. Patients with “positive” results are eligible for HER2/neu-targeted therapies. The commonly used testing modalities to determine HER2/neu status are immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH). Studies have demonstrated that although the concordance rate between these modalities is high, there is a small discordance rate. Misclassification of HER2/neu status may have significant clinical consequences. Most institutions use a “reflex-testing strategy” for determining HER2/neu status (ie, cancers screened with IHC, and FISH performed in equivocal cases). However, some institutions perform both FISH and IHC (dual testing strategy) on all cancers to maximize diagnostic accuracy. The cost-effectiveness of dual testing and reflex testing strategies are comparatively assessed herein.

**Design:** We compared the dual and reflex testing strategies using a decision analysis model. Probabilities were obtained from our institutional invasive breast cancer cohort. Quality-adjusted life-years (QALYs) and costs were extracted from the literature. Costs were converted to 2018 US dollar values. One-way, two-way, and probabilistic sensitivity analyses with acceptability curves were performed.

**Results:** The cost-effectiveness analysis showed that the reflex testing strategy had lower cost ($44,470.99) and less effectiveness (10.28 QALYs). The dual testing strategy cost was $45,908.86 and its effectiveness was 10.30 QALYs. The incremental cost-effectiveness ratio was $70,051.55/QALYs. The dual-testing strategy is cost-effective 80% of the time at a $100,000 willingness-to-pay threshold (Figure 68).

**Conclusions:** A dual testing strategy is more cost-effective than a reflex-testing strategy for the determination of HER2/neu status in invasive breast cancers.

### FISH and IHC Results

<table>
<thead>
<tr>
<th>IHC/FISH Status</th>
<th>Amplified FISH, n (%)</th>
<th>Unamplified FISH, n (%)</th>
<th>Total</th>
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<tbody>
<tr>
<td>IHC Score 0/1+ (negative)</td>
<td>16 (10)</td>
<td>793 (73)</td>
<td>809</td>
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<tr>
<td>IHC Score 2+ (equivocal)</td>
<td>36 (22)</td>
<td>283 (26)</td>
<td>319</td>
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<tr>
<td>IHC Score 3+ (positive)</td>
<td>113 (68)</td>
<td>6 (&lt;1)</td>
<td>119</td>
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<tr>
<td>Total</td>
<td>165</td>
<td>1082</td>
<td>1247</td>
</tr>
</tbody>
</table>

* Percentages calculated from the total number of FISH results.

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**The Cost-Effectiveness of a Dual HER2/neu Testing Strategy on Invasive Breast Cancers**

(Poster No. 116)

**Nosaibah Hariri, MBBS** (nosaibahh@yahoo.com); Somaye Zare, MD; James Murphy, MD, MS; Oluwole Fadare, MD. Departments of **Radiation Medicine and Applied Sciences, University of California, San Diego.**

**Context:** The guidelines for determining human epidermal growth factor receptor2 (HER2/neu) status in breast cancers recommend using immunohistochemistry (IHC) and/or fluorescence in situ hybridization (FISH). Although many institutions use a reflex testing strategy (wherein tumors are screened with IHC, and FISH is performed if IHC results are equivocal), others adopt a dual testing strategy (in which IHC and FISH are performed on all cancers) to minimize misclassification. We report herein an institutional experience using the dual-testing strategy. The cost-effectiveness analysis showed that the reflex testing strategy had lower cost ($44,470.99) and less effectiveness (10.28 QALYs). The dual testing strategy cost was $45,908.86 and its effectiveness was 10.30 QALYs. The incremental cost-effectiveness ratio was $70,051.55/QALYs. The dual-testing strategy is cost-effective 80% of the time at a $100,000 willingness-to-pay threshold (Figure 68). **Conclusions:** A dual testing strategy is more cost-effective than a reflex-testing strategy for the determination of HER2/neu status in invasive breast cancers.
Dermatofibrosarcoma Protuberans of the Breast: A Rare Presentation of a Rare Entity

Debbie R. Walley, MD1 (darigney@unc.edu); Mary C. Bailey, BS2; Israh Akhtar, MD.1 1Department of Pathology and 2School of Medicine, University of North Carolina Medical Center, Jackson, North Carolina.

Dermatofibrosarcoma protuberans (DFSP) is a rare and locally aggressive tumor of the dermis and subcutis. It usually occurs in adults in the second to fourth decades and has a slight male predominance. DFSP typically occurs on the trunk and extremities and less frequently in the head and neck. DFSP rarely presents in the breast. Here, we present a case of a 20-year-old woman with a palpable mass in the lower inner quadrant of the left breast that had been present for 3 months. The nodular mass was discovered incidentally on chest imaging following trauma. An ultrasound was performed that demonstrated an 8 × 6 × 8 mm irregular hyperechoic mass at the 7 o’clock position of the left breast 9 cm from the nipple, BI-RADS category 4. The patient underwent an ultrasound-guided biopsy. Microscopic examination of the biopsy showed a spindle cell proliferation with infiltration into the adipose tissue. Myofibroblastoma was the first differential diagnosis; however, the infiltrative pattern of the tumor mandated additional tests, including fluorescence in situ hybridization to rule out a DFSP. Immunohistochemical staining showed positive staining for CD34, which can be positive in DFSP typically occurs on the trunk and extremities and less frequently in the head and neck. DFSP rarely presents in the breast. Here, we present a case of a 20-year-old woman with a palpable mass in the lower inner quadrant of the left breast that had been present for 3 months. The nodular mass was discovered incidentally on chest imaging following trauma. An ultrasound was performed that demonstrated an 8 × 6 × 8 mm irregular hyperechoic mass at the 7 o’clock position of the left breast 9 cm from the nipple, BI-RADS category 4. The patient underwent an ultrasound-guided biopsy. Microscopic examination of the biopsy showed a spindle cell proliferation with infiltration into the adipose tissue. Myofibroblastoma was the first differential diagnosis; however, the infiltrative pattern of the tumor mandated additional tests, including fluorescence in situ hybridization to rule out a DFSP. Immunohistochemical staining showed positive staining for CD34, which can be positive in DFSP. A diagnosis of DFSP was confirmed, and the patient was referred to a breast surgeon for wide local excision of the lesion. Conventional DFSP does not metastasize, but is prone to recurrence, making wide margins imperative for definitive treatment.

S100 and SOX10 Expression by Triple-Negative Breast Cancer: A Potential Pitfall

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It is well established that S100 immunoreactivity has been seen in a significant subset of breast cancers. However, less commonly known is that these malignancies frequently express SOX10 as well. In the setting of metastatic disease or cutaneous extension of breast malignancy, this presents a potential diagnostic pitfall. Here we review a case of a 63-year-old woman who presented with a well-circumscribed 15-mm breast lesion located 5 mm from the epidermis, but without evidence of overlying skin involvement. The tumor demonstrated pleomorphic nuclei, prominent nucleoli, abundant eosinophilic cytoplasm, and occasional binucleation (Figure 69, A). Immunohistochemistry for estrogen receptor and progesterone receptor were negative, as was HER2 in situ hybridization. Given the morphologic suggestion of a-apocrine differentiation, androgen receptor staining was also performed and was entirely negative. Because the tumor was in close proximity to the epidermis and lacked the typical basalloid appearance of most triple-negative, androgen receptor-negative breast carcinomas, the differential diagnosis was widened to include malignant melanoma. Immunohistochemistry for S100 (Figure 69, B) and SOX10 (Figure 69, C) was therefore performed and revealed strong diffuse positivity, further suggesting a melanoma diagnosis. Furthermore, additional breast markers (GATA3, mammaglobin) were entirely negative. Broad-spectrum cytokeratin staining, however, was strongly and diffusely positive (Figure 69, D), supporting the final diagnosis of high-grade breast carcinoma. Review of the literature confirmed common S100 and SOX10 expression among high-grade breast carcinomas and underscores the importance of including cytokeratin immunohistochemistry before diagnosing malignant melanoma in this context.

Cystic Neutrophilic Granulomatous Mastitis Masquerading as Carcinoma

Jordan M. Steinberg, MD1 (jsteinberg3@northwell.edu); Iskender Genco, MD2; Panagiotis A. Manolas, MD2; Rachel Webman, MD2; Sabina Hajiyeva, MD.1 Departments of 1Pathology and Laboratory Medicine and 2Surgery, Lenox Hill Hospital, New York, New York.

Historically, granulomatous mastopathies are characterized by lobulocentric granulomas in the setting of a tender breast mass with suppuration. In 2003, Taylor et al described a series of cases involving granulomatous mastitis with similar histologic features and a strong association with Corynebacterium. Among the Corynebacterium species, the lipophilic C. kroppenstedtii has been described as the most prevalent. Accordingly, the presence of cysts or vacuoles is commonly seen on histologic examination. Because imaging is typically nonspecific or can have worrisome features, these lesions are usually biopsied to rule out malignancy. We present a case of this rare but important entity. A 29-year-old woman presented with a painful mass in the right breast at the 9 o’clock position accompanied by nipple discharge. There was no history of trauma. The ultrasound showed an irregular hypoechoic lesion corresponding to the site of the palpable abnormality, suspicious for carcinoma. The patient underwent an ultrasound-guided core biopsy that showed marked acute and chronic inflammation with foci of distorted benign epithelium with perilobular granulomas (Figure 70, A through C). A Gram stain (Figure 70, D) demonstrated club-shaped Gram-positive bacilli within the cleared central portion of the neutrophil-lined microcystic spaces. This supported the diagnosis of cystic neutrophilic granulomatous mastitis. Because the infectious agent may be lipophilic, cultures tend to be negative. Proper culturing would require a lipid-enriched medium or more advanced detection techniques. Given the morbidity and potential for disfigurement that accompany granulomatous mastopathies, antimicrobial treatment should be timely and accurate. We aim to increase awareness of this poorly recognized entity.
Axillary Silicone Lymphadenopathy: Report of a Rare Case
(Poster No. 120)
Alicia G. Dessain, MD (alicia.dessain@gmail.com); Natalie Ciomek, MD. Department of Pathology, Tufts Medical Center, Boston, Massachusetts.

A 69-year-old woman with a history of right breast ductal carcinoma in situ treated with bilateral mastectomy and silicone breast implant reconstruction presented 18 years later with ipsilateral axillary lymph node enlargement. Computed tomography scan demonstrated bulky right retropectoral and axillary lymph nodes, measuring up to 2.5 cm, and a suggestion of intracapsular rupture of the right implant. A diagnostic excisional biopsy was performed. Grossly, a 2.9-cm lymph node was received. Microscopically, the lymph node was nearly completely replaced by a mixture of multinucleated giant cells, some with asteroid bodies, and macrophages associated with refractile material consistent with silicone (Figure 71, A and B). No metastatic carcinoma was present by pankeratin immunohistochemistry. Because of the patient’s personal request to definitively exclude lymphoma, an extensive lymphoma workup was performed. Residual lymphoid tissue demonstrated follicular and interfollicular PAX5+/CD3+/CD5+/CD7+/CD4+/CD8+ T lymphocytes by immunohistochemistry. No aberrant population was detected by flow cytometry. Results of T-cell rearrangement studies were negative. Silicone lymphadenopathy is a known but rare complication following cytometry. Results of T-cell rearrangement studies were negative. Silicone lymphadenopathy can be a diagnostic consideration in these clinical settings after the exclusion of neoplastic processes.

Identification of Triple-Negative Pure Apocrine Carcinoma of the Breast: Correlation of Apocrine Histology and Androgen Receptor Immunohistochemistry With Molecular Subtype
(Poster No. 122)
Alexander Strait, MD (alexander.m.strait@hitchcock.org); Natasha Mariano, BS; Evelien Schaafsma, MS; Chao Cheng, PhD; Todd Miller, PhD; Armijna Kettenbach, PhD; Jonathan Marotti, MD. 1Department of Pathology and Laboratory Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire; Departments of Biochemistry and Cell Biology, 2Biomedical Data Science, and 3Molecular and Systems Biology, Geisel School of Medicine at Dartmouth, Hanover, New Hampshire.

Context: Histologic identification of true apocrine differentiation in breast cancers can be difficult, and many nonapocrine breast carcinomas express androgen receptor (AR). We attempted to identify triple-negative (TN) pure apocrine carcinomas based on histology and AR immunohistochemistry, and correlated the pathologic review with subsequent molecular analysis.

Design: A total of 119 primary TN breast cancers were screened for apocrine cytology; a subset (51) had AR immunohistochemistry. Using formalin-fixed, paraffin-embedded tissue, genome-wide RNA sequencing was performed on 50 cases, and TN subtype was assigned according to the Lehmann et al classification. Quantitative comprehensive proteomic analysis was performed on 42 cases.

Results: A total of 7 tumors (7 of 119; 6%) displayed prominent apocrine features, including abundant eosinophilic cytoplasm and prominent nucleoli, of which 6 demonstrated diffuse, strong AR immunostaining (Allred score 8; Figure 73, A and B). Forty-eight percent of tumors without prominent apocrine features were AR+ (Allred score 2–7). A total of 5 of 5 cases with apocrine cytology, high AR immunostaining, and available RNA sequencing data were classified as luminal androgen receptor (LAR) subtype. Two tumors with nonapocrine cytologic features were classified as LAR subtype. Quantitative proteomic analysis identified a significant increase in protein expression of apocrine markers, such as HMGR-2, PIP, and GGT1, in TN tumors of the LAR subtype compared with other subtypes.
Conclusions: The combination of diffuse, prominent apocrine cytology and AR immunostaining (Allred score 8) was predictive of the LAR molecular subtype; however, in our cohort, rare tumors without these features were also classified as LAR. Further investigation of proteomic data is underway to identify additional markers of TN apocrine breast carcinoma.

Lobular Neoplasia Diagnosed on Core Needle Biopsy: A Twelve-Year Single-Institution Review With Radiology-Pathology Correlation

(Poster No. 123)

Yailleen D. Guzman-Arocho, MD (yguzman@bidmc.harvard.edu); Zahra Karimi, MD; Tejas S. Mehta, MD; Jordana Phillips, MD; Gabrielle Baker, MD. Department of Pathology, Beth Israel Deaconess Medical Center, Boston, Massachusetts.

Context: Lobular neoplasia (LN) encompasses atypical lobular hyperplasia and classic lobular carcinoma in situ. Management of LN diagnosed on core needle biopsy remains controversial. The purpose of this study was to review biopsies in which LN represented the highest-risk lesion for radiology-pathology correlation, associated histologic findings, and upgrade rates.

Design: Biopsies with LN (2003–2015) were identified. Cases with higher-risk lesions were excluded. Hematoxylin-eosin–stained slides and radiologic images were reviewed to assess whether LN represented the target, represented part of the target, or was incidental.

Results: Of 171 LN cases, imaging was performed for screening, breast symptoms, follow-up, and other/unknown. Biopsy indications were calcifications, nonmass enhancement, and mass/ asymmetry. LN was a component of the target in 22 cases (13%) and was incidental in 149 cases (87%). A total of 15 of 22 in the target group had excision, with 1 upgrade to atypical ductal hyperplasia. A total of 92 of 149 in the incidental group underwent excision, with 14 upgrades (atypical ductal hyperplasia, n = 9; ducal carcinoma in situ, n = 2; invasive carcinoma, n = 3). Two cases with incidental LN were deemed discordant on review and were excised. None of the 64 cases without excision developed invasive carcinoma after follow-up.

Conclusions: Although typically an incidental finding, LN may represent the target or a component of the target lesion. Given the upgrade rate in this series, correlation with imaging is critical to assess which cases with LN warrant excision.

Mammary Rosai-Dorfman Disease With and Without Associated Axillary Lymphadenopathy: Insights for Practitioners of Breast Surgical Pathology

(Poster No. 124)

Sindhu Shetty, MD1 (shettyss2@ccf.org); Nidhi Sharma, MD2; Christine N. Booth, MD; Olaronke Oshila, MD1; Erin P. Downs-Kelly, DO; Jesse K. McKenney, MD; Charles D. Sturgis, MD.1 1RJ. Tomsich Pathology and Laboratory Medicine Institute and 1Department of Radiology, Cleveland Clinic, Cleveland, Ohio.

Context: Rosai-Dorfman disease (RDD) is an uncommon non-Langerhans cell histiocytosis causing painless enlargement of lymph nodes, with marked sinusoidal dilatation and accumulation of activated histiocytes (S100+, CD68+, and CD1a+) with emperipolesis. Extranasal RDD (ERDD) is rare, being most often reported in the skin, paranasal sinuses, orbit, and bone. ERDD is uncommon in the breast and can mimic carcinoma. We report our experience with ERDD of the breast and RDD of the axillary lymph nodes from the perspective of breast surgical pathologists.

Design: Natural language search queries (CoPathPlus, Tucson, Arizona) retrieved all “Rosai-Dorfman” reports from the interval 1995 to 2018. Cases involving the breast and axillary lymph nodes were included. Clinical data were collected (Epic, Verona, Wisconsin). All hematoxylin-eosin and immunohistochemistry sections were reexamined (SS/CDS).

Results: Six cases were identified. All patients were female, with a mean age of 58 years. Four patients had breast involvement, with most presenting as masses. Lymphoma was suspected in both patients with lymphadenopathy. Carcinoma was suspected in 3 patients with breast ERDD. Mammary ERDD showed sheets of histiocytes (Figure 74, A) with less lymphophagocytosis (Figure 74, B) and more fibrosis than nodal disease and with accompanying background lymphoplasmacellular infiltrates (Figure 74, C) that may cuff vessels (Figure 74, D).

Conclusions: ERDD of the breast is rare in clinical practice and may be confused with granulomatous processes, immunoglobulin G4 (IgG4) lesions, neoplastic histiocytes, lymphomas, carcinomas, and others. Although breast recurrences were documented in our series, none of the patients had systemic RDD. Practitioners of breast pathology should be cognizant of this uncommon entity.

A Rare Presentation of a Breast Mass: Pilar Cyst (Trichilemmal Cyst)

(Poster No. 125)

Lacey Durham, BS1; Paloma del C. Monroig-Bosque, MD, PhD1 (pmmonroig-bosque@houstonmethodist.org); Mary Schwartz, MD,2 1Round Rock Regional Campus, Texas A&M University College of Medicine, Round Rock; 2Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Texas.

Pilar cysts, also known as trichilemmal cysts, arise from the external root sheath of the hair follicle. They occur mainly in older women, are usually asymptomatic, and usually present with a dermal/subcutaneous nodule. More than 90% are present on scalp, and approximately 10% are on the back. They are uncommonly found elsewhere, with very rare cases described in the breast. We report a case of a pilar cyst in the breast to increase recognition of this unusual lesion, helpful in guiding clinical management. A 33-year-old woman had a past medical history of a right breast mass. Because of a lack of medical insurance, a mammogram and ultrasound were performed 2 years after the initial presentation. A vacuum-assisted right breast core biopsy yielded acellular keratin, raising consideration of an epidermal inclusion cyst. For 3 years the mass continued to grow and cause discomfort. A follow-up mammogram showed a 3.7-cm lesion with skin adherence, concerning for malignancy. Resection of the mass demonstrated a unilocular cyst with smooth lining and variable wall thickness (0.1–0.5 cm), filled with yellow-white, pasty material. The histologic findings were of a circumscribed cyst lined by bland squamous epithelium with absent granular layer, filled with compact eosinophilic keratin. The overall features were those of a pilar cyst. Pilar cysts are mostly benign and rarely occur in the breast.
However, they can present as a mass-forming lesion concerning for malignancy. The differential diagnosis includes epidermoid inclusion cysts, squamous metaplasia of lactiferous ducts, and cystic well-differentiated squamous cell carcinoma of the breast (Figure 75).

Clear Cell Hidradenoma of the Breast  
(Poster No. 126)  
Raima A. Memon, MD (rmemon@uabmc.edu); Shi Wei, MD, PhD. Department of Pathology, University of Alabama, Birmingham.

Clear cell hidradenoma (CCH) is an uncommon adnexal tumor usually arising from eccrine glands and commonly seen on the face and the upper extremities. CCH arising from the breast is extremely rare, and only a few cases have been reported. Here we report a CCH of breast with a papillary architecture closely mimicking an intraductal papilloma. A 20-year-old woman presented with a left breast mass and tenderness not related to her monthly cycles and no nipple drainage. Ultrasound showed a complex, cystic, and solid mass. A biopsy revealed a benign papillary lesion suggestive of intraductal papilloma. The subsequent excisional specimen demonstrated an intracytic tumor with a prominent papillary configuration with a subset of cells exhibiting clear cell morphology. Rare mucinous cells were also seen. The lesional cells showed minimal cytologic atypia and rare mitotic figures. The tumor was diffusely positive for CK7, AE1, CK5/6, and p63, but it was negative for smooth muscle myosin heavy chain, calponin, and ER. The collective histologic and immunophenotypic features were mostly consistent with a CCH. Fluorescence in situ hybridization analysis showed MAML2 gene rearrangement, further confirming the diagnosis. The patient was found to have 2 new lesions at 6-month follow-up, biopsies of which demonstrated CCHs. CCH may rarely occur in the breast and can be multifocal. Moreover, the presence of a prominent papillary architecture may lead to misdiagnosis of intraductal papilloma. Some of the useful diagnostic clues include coexpression of low- and high-molecular keratins and p63 but negativity for other myoepithelial markers.

Invasive Lobular Carcinoma: Classical and Pleomorphic Types of the Male Breast  
(Poster No. 127)  
Kavitha Juvale, MBBS (kavitajj@gmail.com); Aditi Ranade, MD. Department of Pathology, UHS, Vestal, New York.

Carcinoma of the male breast is rare, representing only 1% of all breast cancers, with infiltrating ductal carcinoma comprising most cases (74%–95%). Lobular breast carcinoma (LBC) is exceptionally rare, making up less than 1% of all male breast malignancies. We report an interesting case of mixed invasive ductal and lobular (showing both classical lobular, 90% and 10% pleomorphic components, Nottingham grade 2) carcinoma and carcinoma in situ (lobular and ductal types) in a 76-year-old man. Chest/breast ultrasound showed an irregular hypoechoic lesion and right axillary lymphadenopathy. Mammogram showed a spiculated mass in the corresponding location of the breast. Histopathology images of excised tumor are shown. Positron emission tomography computed tomography showed multiple bone lesions. The tumor cells were E-cadherin– in focus of ductal carcinoma and E-cadherin+ in the lobular carcinoma; ER/PR+, HER2/neu FISH+, and Ki 68%. The patient did receive 10 cycles of radiation as well as chemotherapy (gemcitabin and cisplatin) and is currently on tamoxifen, palbociclib, and denosumab. Our patient had no obvious risk factors for breast cancer; there was no family history of breast cancer, and no known exposure to estrogens or estrogenic agents. Although the rate of breast cancer is increasing in males, which might be due to better diagnostic modalities or higher suspicion, there is no guideline as to how we should screen high-risk males for breast cancer. The only guidelines for breast cancer screening in males are for patients testing positive for BRCA and those having gynecomastia. Such male patients should have annual mammograms.

A Tale of Two Tumors: Collision of a Primary Breast Low-Grade Follicular Lymphoma and Recurrent Breast Carcinoma  
(Poster No. 128)  
Hani Katerji, MD (hani_katerji@urmc.rochester.edu); Roula Katerji, MD; Rana Ajabnoor, MD; Ioana Moisini, MD, PhD. Department of Pathology, University of Rochester, Rochester, New York.

Primary breast lymphoma is an uncommon entity that accounts for less than 0.5% of primary breast tumors, with follicular lymphoma being exceedingly rare. The occurrence of synchronous primary breast lymphoma and breast carcinoma is extremely unusual, and, to the best of our knowledge, has been reported only once in the literature. Here, we report a case of recurrent breast carcinoma with a concurrent primary follicular lymphoma in an elderly woman. An 87-year-old woman with a history of bilateral invasive ductal carcinoma treated with lpectomy and radiation 20 years prior presented for evaluation of a newly discovered lump in the left breast. Imaging showed 4 irregular masses. A core needle biopsy of one of the nodules was performed and showed high-grade invasive ductal carcinoma. Total left mastectomy ensued. Histologically, 3 of the 4 foci showed features consistent with high-grade invasive ductal carcinoma not otherwise specified with associated ductal carcinoma in situ (Figure 76, A and B). The fourth focus showed a vaguely nodular architecture, comprising small and medium-sized cleaved cells without nucleoli (Figure 76, C), negative for pancytokeratin. This unexpected finding prompted a more comprehensive use of immunohistochemical stains; CD20 (Figure 76, D), BCL-2, and BCL-6 were positive in the cells of interest, consistent with low-grade follicular lymphoma. This particular focus was not admixed or associated with the ductal carcinoma identified in the remaining 3 foci. Expert opinion from the hematopathology division was sought and the diagnosis of collision tumor was issued. The importance of precisely diagnosing and classifying such cases is tantamount because management is often complicated and an interdisciplinary approach is imperative.

Invasive Cribriform Carcinoma of the Male Breast  
(Poster No. 129)  
Iskender Genc, MD (isgenco@northwell.edu); Jordan M. Steinberg, MD; Sabina Hajiyeva, MD. Department of Pathology and Laboratory Medicine, Lenox Hill Hospital, New York, New York.

Invasive cribriform carcinoma (ICC) was first described in 1983 by Page et al as invasive carcinoma with a predominant cribriform growth...
pattern. It is relatively rare, making up 0.8% to 3.5% of breast carcinomas, and in the male breast there have been fewer than 10 cases reported in the literature. We report an additional case of ICC in the male breast. A 65-year-old man presented with a palpable right breast mass that was biopsied under ultrasound guidance. The biopsy showed neoplastic ductal proliferation with cribriform architecture and was signed out as ductal carcinoma in situ with intermediate nuclear grade and cribriform pattern. The excision specimen showed the same histologic features comprising neoplastic ductal proliferation with cribriform architecture; however, the neoplastic ducts showed infiltrative borders (Figures 77, A and B). Immunohistochemical stains for p63 (Figure 77, C) and SMMH (Figure 77, D) to highlight the myoepithelial cells were negative around the ducts, which was consistent with invasive cribriform carcinoma. The same immunohistochemical stains were performed on the biopsy retrospectively, which showed the same staining pattern, confirming the diagnosis of invasive cribriform carcinoma instead of ductal carcinoma in situ with cribriform pattern. We herein describe a rare type of invasive carcinoma of the male breast, drawing special attention to the potential for misinterpretation of the biopsy specimen due to overlapping architectural features between the in situ and invasive forms.

Apocrine-Type Encapsulated Papillary Carcinoma of the Breast
(Poster No. 130)

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A 68-year-old woman presented with an abnormal mammogram showing 1.5-cm, oval, well-circumscribed high-density mass with coarse calcifications in the 6 o’clock position of the left breast. A biopsy was performed at an outside institution, and the diagnosis of severe ductal apocrine atypia was rendered. Lumpectomy was performed, and it showed well-circumscribed papillary lesion surrounded by thick, fibrous capsule (Figure 78, A). The papillae were lined by apocrine cells with moderate-severe atypia (Figure 78, B). Immunostains confirmed the lack of myoepithelial layer within the fibrovascular cores as well as the periphery of the lesion. Tumor cells were positive for androgen receptor (Figure 78, C), Her2/neu (score 3+; Figure 78, D), GATA3, and a breast cocktail (mammoglobin and GCDFP-15), although they were negative for ER, PR, and Pax-8. Ki-67 proliferation index was 10%. No invasion was identified. Findings were consistent with encapsulated papillary carcinoma, apocrine type. The pathologic stage was pTis. An encapsulated papillary tumor composed of entirely apocrine epithelial cells is very rare. To date, there are 11 cases reported in the literature. Most cases were negative for Her2 testing, and they had excellent prognosis without recurrence (3–41 months of follow-up). Although our case did not perform a definite invasive component, the cytologic atypia and strong HER2 staining may indicate a more aggressive behavior. The limited number of reported cases and the short follow-up periods for some warrant a closer follow-up. It is important to recognize the atypia in the apocrine cells and correlate with the imaging studies in order not to classify such lesions as benign apocrine papilloma.

Patterns of Expression of EZH2 in Human Breast Proliferative Lesions
(Poster No. 131)

Sarah Sutherland, BS§ (sarahsutherland24@gmail.com); Louis A. Gaboury, MD, PhD, FRCPath. Departments of ‘Microbiology and Immunology, and ‘Pathology and Cell Biology, University of Montreal, Montreal, Québec, Canada.

Context: Epigenetic changes are currently being recognized as important factors in breast cancer development, one of the most common cancers in American women. EZH2 is an essential protein whose main function is to bring about DNA methylation and induce transcriptional silencing. A growing body of evidence suggests that it may also respond to microenvironmental cues to alter signaling pathways. We hypothesize that altered pattern of EZH2 expression is linked to breast cancer development.

Design: Formalin-fixed, paraffin-embedded tissue samples from different types of breast proliferative lesions both benign and malignant were collected from surgical resection specimens. EZH2 (clone D2C9, 1:50) standard immunohistochemistry was performed on tissue microarray (n = 96). We sought to investigate the protein location within the cell (cytoplasmic or nuclear) and the level of expression (low = 0–33%; moderate = 34%–66%; high = 66%–100%) in each case.

Abstracts
Results: Our results indicate that EZH2 is present mainly in the cytoplasm of 75% to 100% of cells of benign breast lesions with varying intensities; levels of expression are also elevated in ductal carcinoma in situ (Figure 79, A). However, its expression was markedly reduced in both low-grade invasive ductal (Figure 79, B) and lobular (Figure 79, C) carcinomas. In sharp contrast, in high-grade cancers, such as triple-negative breast tumors, EZH2 expression was found into the nucleus of 40% to 100% of cells with intermediate to high intensity (Figure 79, D).

Conclusions: Patterns of EZH2 overexpression could potentially be used as a predictive biomarker of precancerous and cancerous lesions.

Low and High Pretreatment Ki-67 Expression May Predict Ki-67 Levels After Neoadjuvant Chemotherapy in Breast Cancer

(Poster No. 132)

Patricia Zot, MD (patricia.zot@vcuhealth.org); Lorraine Colon Cartagena, MD; Matthew Gayhart, MD; Raghavendra Pillappa, MD; Michael Idowu, MD; Valentina Robila, MD. Department of Pathology, Virginia Commonwealth University, Richmond.

Context: Patients who do not achieve complete pathologic response (pCR) to neoadjuvant chemotherapy (NAC) differ in terms of prognosis, and Ki-67 has been proposed as an additional predicting factor. The objective of the current study is to investigate the change in Ki-67 expression before and after NAC to determine whether differences may be predictive of response outcomes.

Design: A set of patients who did not achieve pCR after NAC were selected for evaluation of posttreatment Ki-67. The Ki-67 expression on needle core biopsies was recorded, and a 20% was used as the cutoff between percent low and high positive tumor cells. The changes in Ki67 profiles were then correlated with tumor hormonal status, response to NAC, and disease progression.

Results: Using a 20% cutoff, all cases with low Ki-67 on biopsy showed either no change or a further Ki-67 reduction (range, 0–95%). Of cases with high Ki-67 on biopsy (Table), 40% had a significant Ki-67 increase (range, 23%–112%), predominantly of triple-negative phenotype (62%). Three cases with Ki-67 increase (range, 25%–90%) presented with distant metastases less than 3 years after surgical excision. The remainder of the cases showed a reduction in Ki-67 after treatment, equally distributed among all 3 tumor hormonal phenotypes.

Conclusions: Cases with low Ki-67 on biopsy show a further reduction of Ki67 in residual carcinoma. In contrast, a significant proportion of cases with high Ki67 before treatment had a significant increase in Ki-67, predominantly in triple-negative carcinoma, and are, in our cohort, associated with early metastases.

Response to NAC and Distribution of Ki-67 Change in Cases With High Ki-67 on Biopsy

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<tr>
<th>Response to NAC</th>
<th>Increased Ki-67 Status After NAC, % (n = 13)</th>
<th>Decreased Ki-67 Status After NAC, % (n = 20)</th>
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<tbody>
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<td>Probable response</td>
<td>84.61</td>
<td>65</td>
</tr>
<tr>
<td>No definite response</td>
<td>15.39</td>
<td>35</td>
</tr>
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Nodular Hidradenoma of the Breast: A Rare Mimic of a Breast Papillary Neoplasm

(Poster No. 134)

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Nodular hidradenoma (NH), a benign primary cutaneous adnexal tumor, arises from the sweat gland apparatus at various anatomic sites. NH of the breast is rare and poses significant diagnostic difficulty given the broad spectrum of breast tumors. Herein, we describe a case of NH of the breast mimicking primary breast papillary neoplasm and low-grade papillary urothelial neoplasm. A 24-year-old woman presented with a left breast mass, increasing in size during a few months’ duration. A 3-cm violaceous mass was palpable in the lateral left breast. Sonography revealed a complicated cystic architecture at 3 o’clock, 15 cm from the nipple. Core biopsies demonstrated a low-grade papillary neoplasm that was dissimilar in appearance to conventional intraductal papilloma of the breast, with features reminiscent of low-grade papillary urothelial carcinoma. A localized excision revealed a circumscribed, deep dermal neoplasm with solid and cystic portions overlying breast parenchyma (Figure 80, A). The solid portion contained lobulated and papillary aggregates composed of monomorphic, cuboidal keratinocytes with eosinophilic cytoplasm and focal ducts (Figure 80, B). Necrosis and atypical mitoses were absent. The tumor cells were positive for CK5/6 (Figure 80, C) and p63 (Figure 80, D), focally positive for estrogen receptor, and negative for mammoglobin and uroplakin II. With clinicopathologic correlation, a diagnosis of NH of the breast was rendered. Our case of NH in the breast highlights that sweat gland tumors, although rarely situated within breast parenchyma, should be a diagnostic consideration for pathologists when evaluating superficial breast tumors to avoid misdiagnosis and overtreatment.

Angiolipoma of the Breast—A Rare Entity: Radiologic-Pathologic Correlation

(Poster No. 133)

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Context: Angiolipoma is a rare benign lesion of the breast; its distinction from other neoplastic lesions may pose a clinical dilemma. Radiologic evaluation of breast lesions in its different modalities is frequently used; its ability to correctly characterize angiolipoma is a characteristic pathologic pattern. Radiologic studies may aid in correctly identifying the benign nature of the lesion, however, the lack of specific radiologic features requires the excision of these lesions.

Results: A total of 11 patients were identified to include 8 women (age range, 28–70 years) and 3 men (age range, 39–67 years), with 6 lesions involving the left breast and 5 involving the right. Prior radiologic evaluation included both mammogram and ultrasound. Radiologically, 5 lesions were characterized as benign, 3 as suspicious, and in the remaining 3 no lesion was identified. All lesions except 1 core biopsy were excised to reveal a characteristic histopathologic admixture of dominant mature adipocytes with a recognizable vasculature component and rare microthrombi in small vessels.

Conclusions: Angiolipoma of the breast is a rare benign entity with a characteristic pathologic pattern. Radiologic studies may aid in correctly identifying the benign nature of the lesion; however, the lack of specific radiologic features requires the excision of these lesions.

Stiff Person Syndrome as a Presentation of Male Breast Cancer

(Poster No. 135)

Timothy I. Miller, MD (timmil@med.umich.edu); Kristine Konopka, MD. Department of Pathology, University of Michigan, Ann Arbor.
Stiff person syndrome is a rare neurologic disorder characterized by progressive muscle stiffness, rigidity, and spasms involving the axial skeletal muscles. Most patients demonstrate autoantibodies directed against glutamic acid decarboxylase or amphiphysin. In rare cases, patients with an underlying malignancy, such as breast cancer, present with a paraneoplastic form of the syndrome. Here, we discuss a 55-year-old man with no significant past medical history who presented with neurologic complaints, including stiffness, exaggerated startle, and gait disorder. He underwent extensive workup, including serologic testing, which was helpful in demonstrating anti-amphiphysin antibodies. He received a diagnosis of stiff person syndrome and was treated with baclofen, cyclophosphamide, intravenous immunoglobulin, and therapeutic plasmapheresis; however, the patient experienced minimal symptomatic improvement. Given the association of stiff person syndrome with malignancy, an oncologic workup was initiated. A computed tomography scan of his chest revealed a 9-mm retroareolar nodule that, upon biopsy, showed invasive ductal carcinoma. Following modified radical mastectomy, the patient’s stiff person syndrome was significantly improved. To our knowledge, this is the first reported case of paraneoplastic stiff person syndrome as the presenting feature in a man with breast cancer. This case highlights that breast cancer should be considered in cases of stiff person syndrome, regardless of the patient’s sex.

**Flat Epithelial Atypia: Is Surgical Excision Indicated?**

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**Context:** Flat epithelial atypia (FEA) is a proliferative breast lesion, and there is no consensus on proper management. The risk for carcinoma in FEA is lower than other lesions with atypia; however, the precise risk stratification and the need for surgical intervention have been debated. Therefore, we studied the rate at which FEA lesions were upgraded after excision.

**Design:** Pathology records were queried for FEA diagnosed on core needle biopsy from 2008 to 2018, and analysis was based on original sign-out diagnosis. We excluded cases with no record of excision, prior history of breast carcinoma, or biopsies that contained synchronous invasive carcinoma, DCIS, LCIS, ADH, papilloma, or radial scar.

**Results:** A total of 207 cases were identified, with 170 of these being excluded: 40 for lack of surgical excision, 5 for prior cancer history, and 125 for synchronous lesions. Of the remaining 37 cases, 1 (3%) was upgraded to invasive carcinoma, 1 (3%) to DCIS, 7 (19%) to LCIS, 3 (8%) to ADH, 5 (14%) to papilloma, and 1 (3%) to radial scar, and 19 (51%) cases were not upgraded (Figure 81).

**Conclusions:** A total of 49% of FEA cases were associated with other significant breast pathology not present in the initial core biopsies. This strongly supports the practice of excision of FEA lesions. A limitation of the study design is the selection bias that is introduced when cases are excluded for lack of surgical excision, because these cases likely represent the cases of lower clinical concern. This challenge is inherent in all upgrade-upon-excision studies and is impossible to avoid.

**From a Benign Core Biopsy to Malignancy in 12 Months: A Case of Rapidly Evolving Metaplastic Carcinoma**

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Metaplastic carcinomas account for less than 1% of all invasive mammary carcinomas. They represent a morphologically heterogeneous group of breast cancers in which the glandular epithelial cells undergo transformation into an alternate cell type, either non glandular epithelial (squamous cell) or non epithelial cell types (spindle cell, chondroid, or myoid). A 71-year-old woman underwent a left breast core biopsy in early 2018 with a diagnosis of sclerosed intraductal papilloma. She then developed a postprocedure hematoma that resolved. One year later, a hemorrhagic cystic lesion grew at the biopsy site, which required excision and drainage. On follow-up 1 month later, the lesion recurred with serosanguineous drainage. Magnetic resonance imaging revealed an 8-cm irregular mass with heterogeneous internal signal intensity and rim enhancement. A total mastectomy was performed. Gross examination revealed an 11-cm hemorrhagic necrotic mass with an exophytic component protruding through the skin (Figure 82, A). There were areas of squamous differentiation with atypical spindle cells positive for p63 (Figure 82, B and C). The carcinoma cells showed acantholytic features and loss of E-cadherin expression with formation of pseudovascular spaces containing blood acid and neutral mucin (Figure 82, D). ER, PR, and HER2 were negative. These findings supported the diagnosis of metaplastic carcinoma. Squamous metaplasia has been reported in intraductal papillomas and reparative epithelium of ducts and lobules at healing biopsy sites. We propose that the squamous metaplasia was the probable precursor for the metaplastic carcinoma.
Heterogeneous PD-L1 Expression in Non–Small Cell Lung Carcinoma

(Poster No. 139)

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**Context:** Programmed cell death protein 1 (PD-1) is a cell surface protein that modulates immune response. Cancer microenvironments alter the programmed death ligand-1 (PD-L1)/PD-1 pathway, promoting tumor progression and metastasis. PD-L1 immunotherapy is currently a US Food and Drug Administration (FDA)–approved treatment modality for several aggressive malignancies, including non–small cell lung carcinoma (NSCLC), and is regarded as a predictive biomarker. However, the heterogeneity of PD-L1 expression has not been previously studied. Expression heterogeneity includes paired primary and metastatic tumors, and within a single tumor (intra-tumoral). This study will guide pathologists when selecting appropriate block(s) for PD-L1 IHC evaluation.

**Design:** A total of 150 cases (2000–2018) were included in this study: 46/23 paired cases of primary and metastasis (intertumor-mets) and 104 cases of single tumor (intratumoral). PD-L1 immunohistochemistry and hematoxylin-eosin–stained slides were reviewed. Positive staining was the percentage of viable tumor cells with partial or complete membrane staining.

**Results:** PD-L1 expression ranged from 0 to 100% among cases, with higher PD-L1 expression seen in higher tumor grades. PD-L1 expression showed minimal heterogeneity among intertumor-mets and intratumor cases, in cases of similar tumor morphology; however, heterogeneity was observed among intertumor-mets and intratumor cases, in cases of different tumor morphology (Figure 84). No difference was observed between paired primary and metastatic tumors. Women had higher PD-L1 expression compared with men, with differences of 10.1% and 19.4% between primary and metastatic lung adenocarcinomas, respectively.

**Conclusions:** Pathologists should comment on tumor morphologic differences when interpreting PD-L1. PD-L1 positivity should be assessed on different tumor morphology in heterogeneous NSCLC tumors, and reported separately on each distinct component.
May be common to obstructive lung diseases and warrants further study. Although not statistically significant, parenchymal representing obstructive lung disease without systemic corticosteroid use in severe asthma, we included COPD cases, markedly reduced in severe asthma. To account for systemic correction.

**Design:** Video-assisted thoracoscopic surgery biopsies from non–asthmatic, never-smoker controls (n = 7), chronic obstructive pulmonary disease (COPD) patients (n = 4), and patients meeting European Respiratory Society/American Thoracic Society severe asthma criteria (n = 9) were subjected to α-SMA immunostaining (clone-1A4, Roche). Slides were digitized and analyzed on Aperio ImageScope (Leica Biosystems, Nussloch, Germany). At ×2 magnification, 5 selections, each the area of a ×10 field, were chosen for analysis per slide, excluding bronchovascular bundles. Each ×10 field was then evaluated, and small airways and vessels were manually excluded. The positive pixel count algorithm was used to quantitate α-SMA expression (Figure 85, A), reported as % positivity (% positive pixels / total pixels). P values were calculated by 1-way analysis of variance with Holm-Sidak correction.

**Results:** Severe asthmatics (Figure 85, B) displayed significantly lower α-SMA positivity than controls (12.2% versus 25.2%; P = .005; Figure 85, C). COPD patients (Figure 85, D) showed a trending decrease in α-SMA positivity compared with controls (16.6% versus 25.2%, P = .11).

**Conclusions:** We show alveolated parenchymal α-SMA expression is markedly reduced in severe asthma. To account for systemic corticosteroid use in severe asthma, we included COPD cases, representing obstructive lung disease without systemic corticosteroid treatment. Although not statistically significant, parenchymal α-SMA was also reduced in COPD. This suggests parenchymal α-SMA loss may be common to obstructive lung diseases and warrants further study into possible mechanisms and consequences of this phenomenon.

**Lymphoepithelioma-like Carcinoma of the Lung**

(Xiaofeng Zhao, MD (xiaofeng.zhao@tuhs.temple.edu); Ioannis Ioannidis, MD, PhD. Department of Pathology, Temple University Hospital, Philadelphia, Pa.)

Lymphoepithelioma-like carcinoma of the lung is a rare subtype of non–small cell carcinoma with a strong predilection for young nonsmoking Asians. We report a case of lymphoepithelioma-like carcinoma in a 77-year-old African American woman. The patient who had osteopenia presented to the emergency department with chest pain after a fall. Computed tomography without contrast showed multiple fractures in the posterior left 10th and 11th ribs and an incidental 1.2-cm nodule in the upper lobe of the right lung. The patient underwent bisegmentectomy, and a challenging frozen section revealed dense lymphoid infiltrate with only rare scattered cohesive clusters of atypical epithelioid cells, raising the possibility of a lymphoproliferative process. Permanent sections demonstrated additional syncytial clusters of large, monomorphic polygonal epithelioid cells with prominent nuclei admixed with florid lymphoplasmacytic inflammatory infiltrate (Figure 86, A and B). The possibility of metastatic nasopharyngeal carcinoma was considered but was excluded clinically. Immunohistochemical stains showed that the epithelioid cells were positive for AE1/AE3 (Figure 86, C) and CK7, and that the lymphocytic infiltrate was nonneoplastic, consisting predominantly of CD3+ T cells. The tumor was negative for Napsin-A, p63, p40, neuroendocrine markers, and Epstein-Barr encoding region in situ hybridization (Figure 86, D). Even though latent Epstein-Barr virus infection has been shown to play a carcinogenic role in Asians, it does not seem to be part of the pathogenesis of lymphoepithelioma-like carcinoma in Western populations. Our case confirms that lymphoepithelioma-like carcinoma can be encountered in non-Asian patients and should be included in the differential diagnosis of lymphocyte-rich malignant neoplasms of the lung.

**Thyroid Transcription Factor 1 (TTF1)–Positive Adenocarcinoma in a Solitary Lung Mass: Not Always a Primary Lesion**

(Poster No. 143)

Muhammad Masood Hassan, MD (mhassanaimec@gmail.com); Tammey Naab, MD; Ali Afsari, MD; Mohd Elmughtaba Ibrahim, MD. Department of Pathology, Howard University Hospital, Washington, DC.

TTF1 is a nuclear protein expressed by lung type II pneumocytes, thyroid follicular cells, and parafollicular C cells. In the spectrum of lung neoplasms, TTF1 expression is used to differentiate primary lung adenocarcinoma (TTF1+) from primary squamous cell carcinoma (usually TTF1–) and metastatic carcinoma (usually TTF1–). However, up to 25% of primary gastric adenocarcinomas can be TTF1+. A 64-year-old man was found to have a solitary 1.3-cm left lower lobe spiculated lung mass on chest computed tomography (CT). Biopsy revealed glands lined by pseudostratified nuclei demonstrating patchy strong TTF1 expression. Two years previously, the patient had presented with weight loss, reflux, and a gastroesophageal junction mass, which was biopsy proven to be CDX2+ invasive moderately differentiated adenocarcinoma. At that time, chest CT scan had revealed no lung mass. One year later, after chemoradiation, an esophagectomy revealed ypT2pN1 residual adenocarcinoma with origin in the cardia. The primary gastric and metastatic adenocarcinoma in one lymph node demonstrated patchy strong TTF1 expression, confirming that the lung adenocarcinoma represented a metastasis from the gastric primary. Our case proved the point that not every solitary lung mass composed of TTF1 positive glands is a primary lung adenocarcinoma. TTF1 expression is not always lineage specific. Careful review of the patient's

**Primary Lesion**

(Poster No. 143)

Muhammad Masood Hassan, MD (mhassanaimec@gmail.com); Tammey Naab, MD; Ali Afsari, MD; Mohd Elmughtaba Ibrahim, MD. Department of Pathology, Howard University Hospital, Washington, DC.

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past medical history, comparison of histologic features, and immunohistochemical correlation should be performed in order to arrive at the correct diagnosis, which significantly impacts patient management. Expensive molecular profiling of primary lung adenocarcinoma was avoided in this case.

**Strongyloides stercoralis** Hyperinfection Simulating Acute Exacerbation of Chronic Obstructive Pulmonary Disease

(Poster No. 144)

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*Strongyloides stercoralis* is a nematode with a complex life cycle involving skin, lungs, and gastrointestinal (GI) tract of the host. We report 2 cases of *Strongyloides* infection in patients immunocompromised by steroid therapy for their chronic obstructive pulmonary disease (COPD). Both the patients presented with malena, worsening dyspnea, productive cough, and eosinophilia. Results of blood and stool cultures were negative. In case 1, chest x-ray showed severe emphysema. Endoscopy showed reactive gastropathy with multiple antral erosions. Histology showed helminths within crypts that were morphologically consistent with *Strongyloides*. Patient was treated with ivermectin and symptoms improved. In case 2, chest x-ray showed prominent bilateral interstitial edema. Sputum examination showed rare Gram-positive cocci and Gram-negative rods, the cultures did not grow. Endoscopy showed gastritis and biopsies showed *Strongyloides* in gastric crypts, but there was no significant histologic reaction. This patient received ivermectin but died 20 days later due to septic shock and presumed Gram-negative meningitis. These cases were both notable for the recent onset of GI symptoms superimposed on the chronic pulmonary problems, which appeared to be unrelated. Treatment of the pulmonary symptoms as acute exacerbations of COPD was a reasonable approach given the high frequency of COPD and GI diseases in the elderly. Histologic evaluation of the nonspecific endoscopic findings, which could have been assumed to be steroid- and stress-related gastropathy, provided a critical diagnostic pointer to the unified diagnosis. A high index of suspicion is needed when immunocompromised steroid use can lead to unusual parasitic syndromes, such as *Strongyloides* hyperinfection.

**Pulmonary Tuberculosis With Exuberant Simultaneous Squamous Metaplasia Mimicking Malignancy in a Patient With Systemic Lupus Erythematosus**

(Poster No. 145)

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Patients with systemic lupus erythematosus (SLE) are known to be susceptible to tuberculosis (TB), especially in endemic areas. Squamous metaplasia (SM) involving bronchial mucosa is a preneoplastic change observed in certain TB patients. Histomorphologically, SM, when severe, can pose a diagnostic challenge by mimicking a malignant process. This mandates a systemic and conservative approach to avoid false-calling and overaggressive management. A 17-year-old non-smoking male patient with several years of SLE and recently diagnosed pulmonary TB presented to our institution for a second opinion and further management. Computed tomography scan revealed multiple parenchymal nodules and bronchial stenosis mainly involving the right upper lobe. Bronchial biopsy was performed. Histologically, extensive metaplastic and thickened stratified squamous epithelium was seen, with focal papillomatous enlargement, and it was underlined by dense fibrous stroma. The architectural and cytologic atypia prompted ancillary testing, including Ki-67 and p53 immunostains to monitor its neoplastic potential. Variable p53 and Ki-67 labeling was observed, predominantly within the middle and lower thirds of the squamous epithelium. These findings illustrated no malignancy and indicated no necessity for aggressive surgical resection. Bronchial SM due to coexisting SLE and TB represents an important diagnostic pitfall for practicing pathologists. When papillomatous features are encountered in a squamous "lesion" sampled from patients with compromised immunity, one should add SM into the differential diagnosis, especially when dealing with young patients. Awareness of this entity and its potential to mimic an aggressive squamous neoplasm is essential for reaching an accurate diagnosis and avoiding overtreatment.

**Rapidly Enlarging Lung Nodule: An Unusual Presentation of Endometriosis**

(Poster No. 146)

Bing Han, MD, PhD; Veronica Merelo Alcocer, MD (veroniamerce@pennstatehealth.psu.edu); Wei Huang, MD, PhD. Department of Pathology, Penn State Hershey Medical Center, Hershey, Pennsylvania.

Thoracic endometriosis is an exceedingly rare condition and is a commonly misdiagnosed entity. Four clinical presentations are recognized, the most common being pneumothorax, reported in approximately 72% of cases, hemoptysis in 14%, hemorthorax in 12%, and lung nodule in 2%. The presentation of endometriosis as an asymptomatic lung nodule is extremely rare; the only cases found in the literature so far were associated with hemoptysis or hemorthorax. Our patient is a 49-year-old woman with surgical history of hysterectomy due to leiomyomas and an incidental finding of endometriosis in the uterosacral ligament at the time of the surgery. During computed tomography (CT) scan, multiple incidental small lung nodules were noted, and these were followed by a pulmonologist. One year later a new CT scan demonstrated a suspicious 1.1-cm lung nodule in the right upper lobe. The nodule progressed in size compared with the first CT (Figure 87, A). CT-guided fine-needle aspiration biopsy of the lesion showed benign-looking glands surrounded by fibrous stroma (Figure 87, B). Immunostaining for CD10 was positive in the stroma (Figure 87, C), and p63 was strongly positive in the glands (Figure 87, D), supporting the diagnosis of endometriosis. The presentation of thoracic endometriosis as asymptomatic lung nodule with no other associated symptoms is very rare, but it should be considered in the differential diagnosis of rapidly growing lung nodules, especially in female patients with a past medical history of pelvic endometriosis.

**Bronchogenic Cyst of the Diaphragm: Report of a Rare Case**

(Poster No. 147)

Hansini Laharwani, MD (laharwanihansini724@gmail.com); Anu Abraham, MD; Israh Akhtar, MD. Department of Pathology, University of Mississippi Medical Center, Jackson.

Embryologic development of bronchogenic cyst is unclear. They commonly arise from the tracheobronchial tree during the developmental process as a result of late or abnormal budding of the ventral lung bud leading to a blind pouch filled with fluid. They are congenital lesions arising most commonly in the mediastinum and very rarely within the diaphragm. They comprise 10% to 15% of all primary mediastinal masses and are classified as either mediastinal or intrapulmonary. Our patient is a 55-year-old female nonsmoker with a history of chronic obstructive pulmonary disease (COPD) having a complex 9-cm partially calcified diaphragmatic mass identified by computed tomography scan with multiloculated cavity with mixed density, centered between the left hemidiaphragm and left lower lobe pleura. A core needle biopsy done 3 years prior revealed fibrous tissue with no evidence of malignancy. The mass was followed up by imaging, with no increase in size. An excision...
was done, and histologically the cyst wall was composed of respiratory-type epithelium and cartilage, mucous gland, and fibrous tissue compatible with intradiaphragmatic bronchogenic cyst with focus of chronic inflammation, necrosis, and dystrophic calcification in the cyst wall. The differential diagnosis included lesions arising as a result of an embryologic error associated with other congenital pulmonary malformation, including congenital lobar emphysema and lymphangiomia, even though they are extremely rare. If the mass is abutting the mediastinum, pericardial cyst, and if the cyst has air, then abscess or infected bullae should be considered as well (Figure 88).

Pulmonary Hyalinizing Granuloma: A Challenging Diagnosis of Exclusion in a Patient Presenting With Superior Vena Cava Syndrome

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Pulmonary hyalinizing granuloma (PHG) is a rare lung disease with fewer than 150 cases reported in the literature. A 39-year-old woman with unremarkable medical history presented with swelling of the face, neck, and upper extremities that remained refractory to steroid therapy, prompting a computed tomography (CT) scan that showed a mediastinal mass encasing the superior vena cava (SVC; Figure 89, A), 2 right pulmonary nodules, and a splenic lesion. CT-guided biopsy of the mediastinal mass, lung mass, and the subsequent lung wedge resection revealed a paucicellular hyalinizing spindle cell proliferation with focal necrosis, and admixed chronic inflammatory cells (Figure 89, C and D). The spindle cells were positive for SMA, factor XIIIa, vimentin, and β-catenin, and negative for CD34, S100, ALK-1, STAT-6, ERG, CD21, CD23, and MUC4. Cytogenetic studies for ALK, ROS1, and negative for CD34, S100, ALK-1, STAT-6, ERG, CD21, CD23, and MUC4. Cytogenetic studies for ALK, ROS1, and MAML2 gene rearrangement. A diagnosis of low-grade mucoepidermoid carcinoma was rendered, despite the lack of overt squamous differentiation and absence of p63 reactivity. The patient was managed conservatively considering the central location of the endobronchial mass.

NUT Midline Carcinoma—An Unusual Presentation: Case Report of a Patient Presenting With Pericardial Effusion

Sara Masood, MD (masood@etsu.edu); Emily R. Patterson, MD. Department of Pathology, ETSU, Johnson City, Tennessee.
NUT midline carcinoma (nuclear protein in testis) is a rare and unique entity that was reclassified as a separate entity by the World Health Organization in 2015. The cell line Ty-82 was initially discovered by Kubonishi et al. It is a poorly differentiated carcinoma typically seen in the upper aerodigestive tract. It has also been found in bone, bladder, abdominal retroperitoneum, pancreas, and salivary glands. We report a case of a 72-year-old woman with a pericardial effusion. On echocardiogram, an echogenic mass was identified in the pleural space with no evidence of cardiac tamponade. The patient underwent endoscopic evaluation of the left mainstem bronchus, diaphragm, and left upper lobe. Histologic features demonstrated a poorly differentiated carcinoma with neuroendocrine-like features. Immunohistochemistry was focally positive for CD56 and negative for epithelial, mesothelial, melanocytic, lymphoid, and myeloid markers, and negative for TTF1, Napsin-A, CD138, GATA3, MOC 3, Pax8, vimentin, desmin, and synaptophysin. NUT stain revealed stippled nuclear positivity, confirming the diagnosis. The patient died a few weeks after the diagnosis, reiterating the aggressive course of this disease. In two-thirds of the cases NUT is fused to BRD4 in a t(15;19) (q14, p13.1) translocation to form the BRD4-NUT gene. The remainder are fused with BRD3 and other uncharacterized genes known as NUT variant. There is no predilection for sex, with a median age at diagnosis of 16 years (range, 0.1–78 years) and an average life span of 6.7 months. Identification of this rare entity is essential for future targeted therapy of NUT midline carcinoma.

### Pediatric Hypersensitivity Pneumonitis: Clinicopathologic Characteristics of Two Cases With Fungal Triggers

(Paper No. 151)

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Hypersensitivity pneumonitis (HP) is a rare form of diffuse lung disease that rarely presents in childhood. Asthma or pneumonia-like clinical presentation may lead to diagnostic delay, especially in children. We present 2 cases of pediatric HP. Case 1 was a 6-year-old boy with a history consistent with uncontrolled asthma, and thought to have recurrent pneumonia. Case 2 was a 5-year-old girl with chronic cough. Both cases had a history of weight loss, clubbing, and negative infectious workup with patchy ground-glass lung opacities on chest computed tomography. On transbronchial lung biopsy, case 1 demonstrated classic histologic features of subacute HP, including lymphocytic interstitial pneumonitis, chronic bronchiolitis, and non-necrotizing interstitial and peribronchial granulomas. Case 2, however, showed subtle histologic findings on initial transbronchial biopsy, leading to other diagnostic considerations, such as pulmonary sarcoidosis. Characteristic histologic features of subacute HP were confirmed on a subsequent thoracic surgical lung biopsy. Serologic testing demonstrated elevated immunoglobulin G (IgG) levels toward multiple fungal agents, including *Thermoactinomycetes* and *Aspergillus* species in case 1 and *Aspergillus fumigatus* in case 2. Both patients underwent environmental changes with avoidance of the identified triggers and received 3 courses of methylprednisone pulse therapy and are asymptomatic >1 year after presentation. A diagnosis of HP may be considered on pediatric lung biopsies with granulomatous interstitial and peribronchial inflammation, if infectious etiologies are excluded. Integration of exposure history, radiology, and serology can facilitate a timely diagnosis. Although bird antigen triggers are common, HP due to fungal triggers is sparsely reported, with rare cases triggered by *Aspergillus fumigatus* alone.

### Programmed Death Ligand-1 Expression and Related Markers in Pleuropulmonary Blastoma

(Paper No. 152)

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**Context:** Pleuropulmonary blastoma (PPB) is a rare neoplasm of pleuropulmonary mesenchyme in children. PPB is linked to the DICER1 mutation and has 3 subtypes, I to III. This is the first study to investigate the expression of programmed death ligand-1 (PD-L1) and related markers in PPB.

**Design:** Cases were collected from departmental archives and the International PPB/DICER1 Registry. Immunohistochemistry for PD-L1, programmed death receptor-1 (PD-1), CD8, and DNA mismatch repair (MMR) genes was performed. The combined positive score (CPS) of PD-L1 tumor cells and the percentage of PD-1 and CD8, plus PD-1/CD8 ratio, were assessed.

**Results:** A total of 27 cases were collected, consisting of type I (n = 8), type II (n = 10), and type III (n = 9) PPB. The median age at diagnosis was 2.6 years (range, 3 weeks to 12 years). Follow-up data were available for 18 patients (type I, 5 of 5; type II, 5 of 6; and type III, 5 of 7 still alive). PD-L1 CPS of 80% was seen in 1 (1 of 27; 3.7%) child with type II PPB. PD-1/CD8 was 95%. The patient is alive on follow-up. The rest of the cases (26 of 27; 96.3%) showed absent PD-L1 membranous staining. A heterogeneity pattern of staining was observed for PD-1 and CD8 among and within tumors. In general, for cases with both tumor and tumor–normal tissue interface, the density of PD1 and CD8 in the interface area is approximately 10 times higher than the one density within tumor. The MMR proteins were retained in all cases.

**Conclusions:** We present preliminary data on DICER1 mutation interactions with immune cells and DNA mismatch repair gene products in PPB.

### An Unusual Presentation of Biphasic Pulmonary Blastoma: Extension Through Pulmonary Vein Into the Left Atrium

(Paper No. 153)

Maryam Noori Koloori, MD (maryam.noorikoloori@downstate.edu); Tahmineh Haidary, MD; Rong Xia, MD; Jianying Zeng, MD. Department of Pathology, SUNY Downstate Medical Center, Brooklyn, New York.

Biphasic pulmonary blastoma is a rare aggressive neoplasm comprising <0.1% of all resected malignant pulmonary neoplasms. It is one of the biphasic tumors of the lung in which epithelial and mesenchymal components have a primitive appearance resembling fetal lung at 11 to 18 weeks of gestational age. Here, we present a case of a 52-year-old woman who presented to the emergency department with severe dizziness. The patient also had a history of progressive dyspnea and cough for the previous 6 months and experienced a 30-pound unintentional weight loss. Computed tomography (CT) scan of thorax revealed a 7- to 8-cm right upper lobe mass extending via pulmonary vein into the left atrium (Figure 91, A). Brain CT scan revealed multiple enhancing masses in the right posterior cerebrum and cerebellar hemispheres, suggestive of metastatic disease. Histologic examination of CT-guided biopsy of the mass showed a biphasic neoplasm with epithelial and mesenchymal elements. The epithelial component consisted of branching glands lined with pseudostratified uniform columnar cells with relatively small nuclei, inconspicuous nucleoli, and

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supranuclear and subnuclear cytoplasmic vacuoles. The mesenchymal component consisted of packed primitive small homogeneous ovoid cells. The cells had single nuclei with inconspicuous nucleoli and high nuclear-to-cytoplasmic ratios (Figure 91, B). The epithelial neoplastic cells were positive for TTF1 (Figure 91, C), and β-catenin immunostaining showed cytoplasmic and nuclear positivity in both epithelial and mesenchymal elements (Figure 91, D), supporting the diagnosis of pulmonary blastoma. Our case demonstrates pulmonary blastoma behaves aggressively not only by tumor metastasis, but also by aggressively local growth, like here, where it extended to the heart.

Mesothelioma Recurrence in Multiple Lymph Nodes 8 Years After Pleurectomy and Chemotherapy

(Aster No. 154)

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A 78-year-old man presented with mediastinal lymphadenopathy. He had a past medical history of pleural mesothelioma, desmoplastic type, status postpleurectomy with lymph node dissection (pN0) and intraoperative chemotherapy (8 years prior) and prostatic adenocarcinoma (3 years prior) with recent bone metastasis treated with radiation and hormonal therapy. Computed tomography showed mediastinal lymphadenopathy, including enlarged perbronchial and interlobar lymph nodes. Endobronchial ultrasound-guided transbronchial fine-needle aspiration of these lymph nodes was performed. The smears of both lymph nodes were hypercellular, demonstrating cohesive clusters of large epithelioid tumor cells with abundant dense cytoplasm, hyperchromatic nuclei, and prominent nucleoli in a background of numerous polymorphous lymphoid cells (Figure 92, A and B). Immunohistochemical studies were performed on the cell block sections (Figure 92, C), which showed the tumor cells to be positive for calretinin, WT-1, and D2-40 (Figure 92, D), and negative for PSA, PLAP, and TTF-1 stains. A diagnosis of metastatic mesothelioma was rendered on both lymph nodes. Although the tumor was originally diagnosed as desmoplastic/sarcomatoid mesothelioma, both lymph node metastases lacked the sarcomatoid/spindled morphology and were of pure epithelioid type. Compared with the epithelioid mesotheliomas, the less common desmoplastic mesotheliomas have poorer prognosis. Lymph node metastasis is uncommon in epithelioid and biphasic mesotheliomas; it is rare in desmoplastic/sarcomatoid mesothelioma. The patient is well 9 months from the recurrence. The unusual aspects of this case are 2-fold: (1) there was a very long interval to recurrence (8 years), and (2) the originally diagnosed desmoplastic/sarcomatoid mesothelioma had a purely epithelioid phenotype in the metastasis.

Unusual Presentation of Müllerian Cyst in Posterior Mediastinum of an Adolescent Female

(Aster No. 155)

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Müllerian cysts are not uncommonly found in the pelvis and anterior mediastinum of adult women. However, they are rare in the posterior mediastinum, especially in adolescents and children. For this reason, the lesion is often clinically misdiagnosed in adults as bronchogenic cyst or esophageal duplication cyst. Posterior mediastinal Müllerian cysts have most often been described in adult women in the fourth to sixth decades. To our knowledge only 1 previous childhood case has been reported, in an 18-year-old woman. A 17-year-old previously healthy female presented with recent symptoms of headache and right-sided hand numbness. Magnetic resonance imaging of the spine revealed a type 1 Arnold Chiari malformation and a 1.5 × 1.0 × 1.5 cm nonenhancing cystic lesion in the posterior mediastinum adjacent to the T6 vertebro body without communication with the esophagus. Video-assisted thoracoscopic surgical resection was performed, revealing a cystic mass with clear fluid running the length of the sixth thoracic vertebral body. The cyst was collapsed intraoperatively and removed without complication. Microscopic examination revealed a thin-walled cyst lined by ciliated cuboidal cells consistent with Müllerian differentiation. The Müllerian origin of the cyst was confirmed by strong positive staining with PAX-8 and estrogen receptor. Although it is a rare lesion, Müllerian cyst should be considered in the differential diagnosis of posterior mediastinal cystic lesions (ie, bronchogenic and esophageal duplication cysts) both in children and adults.

Disseminated Cocccidioidomycosis in a Patient With Untreated HIV Infection/AIDS

(Aster No. 156)

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Coccidioidomycosis is an infection caused by the dimorphic fungus Coccidioides sp. Two genetically and epidemiologically different species are identified to cause disease in humans (Coccidioides immitis and Coccidioides posadassi). The fungus is endemic in and regions of the southwestern United States and Latin America. Inhalation of the fungus arthroconidia is usually the primary route of infection. We present a case of disseminated coccidioidomycosis occurring in a 39-year-old Hispanic man with a history of AIDS (CD4 count of 49 cells/µL) who presented with headache, fever, and weight loss. The patient reported working as a construction worker in Arizona 10 years prior. Lumbar puncture revealed a traumatic cerebrospinal fluid (CSF) with an elevated white blood cell count of 2105 cells/mm³ (normal range, 0-5 cells/µL) who presented with headache, fever, and weight loss. The patient reported working as a construction worker in Arizona 10 years prior. Lumbar puncture revealed a traumatic cerebrospinal fluid (CSF) with an elevated white blood cell count of 2105 cells/mm³ (normal range, 0-5 cells/µL) composed of 79% neutrophils. Multiplex polymerase chain reaction test on CSF (FilmArray ME, BioFire Diagnostics) was negative. Computed tomography of chest revealed multiple interstitial nodules initially
Evolution of a Modified Two-Tier Testing Algorithm for Lyme Disease Starting With the Immunetics C6 EIA and Followed by the VIDAS Lyme IgM II and IgG II EIA in an Endemic Region

(Roger No. 158)

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Context: The standard two-tiered testing (STTT) algorithm for Lyme disease (LD) consists of an enzyme immunoassay (EIA) followed by Western blotting (WB). This works well in the late stages of LD but has low sensitivity in the early stages. A C6 EIA has been used as a stand-alone test or an alternate second-tier test, in a modified two-tier test (MTTT). We evaluated the performance of an MTTT algorithm consisting of C6 EIA as a first tier and VIDAS (Biomérieux) dissociated IgM/IgG Lyme EIA as a second-tier test.

Design: A total of 120 serum samples of C6-equivocal/positive were tested for LD using WB (lgM/lgG) and VIDAS (lgM/lgGII). An additional 95 C6-negative serum samples were also tested with WB (lgM/lgG) and VIDAS (lgM/lgGII).

Results: Of the 120 cases, 16 were equivocal and 104 were positive for C6. Of the positive cases, 46.6% were positive for VIDAS-IgMII and 54.3% were positive for VIDAS-IGGII, whereas 51.4% were positive for WB-IgM, and 33.9% for WB-lgG. Overall 42.7% of C6-positive cases were not confirmed using either VIDAS or WB. At higher C6 indices, the correlation between C6, VIDAS, and WB was significantly better. Of the 95 C6-negative cases, 2.1% were positive for VIDAS-lgM and 2.1% were positive for VIDAS-lgGII. For both LD and Lyme IgM and IgG samples were negative with WB.

Conclusions: The STTT algorithm for LD has low sensitivity in the early stages. The C6-EIA has higher sensitivity but lower specificity than the STTT if used alone. Our data indicate that a MTTT consisting of the C6-EIA followed by the dissociated VIDAS results in greater specificity than the C6 alone, while providing greater sensitivity than the STTT.

Unusual Organism—Paracoccus yeei in the United States: A Case of Surgical Wound Infection and a Case of Fatal Sepsis

(Paper No. 159)

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Paracoccus yeei is a rare human pathogen. It is a Gram-negative, aerobic, nonfermenting, catalase- and oxidase-positive cocacobacillus. It is mainly isolated from soil, marine environments, and sewage. Only 12 human cases are reported in the literature, 3 cases of peritonitis, 2 eye infections, 2 skin infections, and 1 case each of myocarditis, otitis, bacteremia, cirrhosis, and arthritis. We present 2 additional cases, both identified in the United States—a case of fatal sepsis and a case of postoperative wound infection. The first patient was a 21-year-old previously healthy woman who presented 12 days after cesarean delivery with surgical wound discharge that grew 40% P yeei and 60% mixed skin flora. The patient responded to a 10-day course of trimethoprim-sulfamethoxazole. The second patient was a 73-year-old woman with a past medical history of chronic obstructive pulmonary disease and type 2 diabetes who presented with pneumonia. She was given vancomycin and piperacillin/tazobactam, but her condition worsened with acute hypoxic respiratory failure. An aerobic blood culture bottle collected prior to an antimicrobial administration was positive at 51.5 hours, and Gram stain showed Gram-negative diplococci. Matrix-assisted laser desorption ionization time-of-flight mass spectrometry identified P yeei with a Bruker value of 2.0 using the research use-only database. The patient died on day 10 of hospitalization, despite pan sensitivity of the organism to all tested antimicrobials. Matrix-assisted laser desorption ionization time-of-flight mass spectrometry readily identifies this unusual organism. Characteristic Gram stain morphology can readily confirm the identification.

Case of Cerebral Phaeohyphomycosis Due to Scolecobasidium Species

(Paper No. 160)

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Cerebral phaeohyphomycosis caused by *Scolecobasidium* species, a ubiquitous fungus that can be a contaminant, or an asymptomatic colonizer, has not been previously described. A 59-year-old immuno-suppressed patient with autosomal dominant polycystic kidney disease, status after renal transplantation, presented with confusion, neck pain, and difficulty ambulating. Magnetic resonance imaging revealed discitis-osteomyelitis with fluid collections in the cervical and thoracic spine, and multiple brain lesions involving the frontal, periventricular, and subcortical regions, consistent with extension of spinal infection. Because of the patient’s worsening clinical status on empiric antibiotics, infectious disease recommended biopsy for culture and targeted therapy; however, neurosurgery felt the patient could not withstand the procedure. Risks and benefits were discussed while clinical decline continued. Eight days after admission, computed tomography-guided aspiration of the paraspinal fluid collection was performed. Cultures were negative for bacteria, but after 3 days of incubation they grew a dark pigmented mold. The colonies grew well enough to perform lactophenol cotton blue tape preparation for speciation 21 days after aspiration, 10 days after the patient had died. When the preliminary culture showed mold, testing for (1,3)-β-D-glucan in serum showed a high level (>500 pg/mL). In absence of any other organisms isolated, *Scolecobasidium* species was considered a true pathogen. This case suggests of infection by angioinvasive fungus, was identified in the paraspinal fluid collection. Initial examination led to the identification of *Aspergillus niger*, characterized by radiate conidial heads. However, further microscopic evaluation demonstrated wide hyphae with sparse septae, and sporangiophores terminated in swollen vesicles with radial merosporangiae filled with spores, characteristic of *S racemosum* (Figure 95, C). The patient was too unstable for surgical debridement and was started on levofloxacin, isavuconazole, and amphotericin B, with improvement in respiratory function. His hospital course was complicated by graft-versus-host disease, and he remains on antifungals at 103 days after transplantation. To our knowledge, this is the second case of pulmonary infection caused by *S racemosum* reported in the literature.

Coinfection by *Pneumocystis jiroveci* and *Cryptococcus neoformans* as the First Presentation of HIV Infection

(Poster No. 162)

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Coinfection by *Pneumocystis jiroveci* and *Cryptococcus spp* is uncommon in HIV patients, especially as an early presentation of the disease. A 47-year-old woman presented with progressive shortness of breath, productive cough, and significant weight loss during a course of 3 weeks. Radiologic examination revealed bilateral ground-glass opacities suggestive of atypical pneumonia. Blood culture was negative, and bronchoscopy was performed. The bronchoalveolar lavage specimen was sent for culture and microscopy. Microscopic examination of the specimen using Giemsa stain revealed pink, foamy material along with pleomorphic, oval-shaped organisms with a thick peripheral halo (Figure 96). Gomori methenamine-silver nitrate staining highlighted crushed ping-pong ball–shaped fungal microorganisms consistent with *P jiroveci* as well as thick capsuled fungal microorganisms consistent with *Cryptococcus spp*. A mucicarmine stain highlighted the capsule of the Cryptococcus organisms. Culture of the bronchoalveolar lavage confirmed presence of *Cryptococcus neoformans*. HIV Ag/Ab combo testing with reflex to Western blot analysis was positive for HIV-1 with a viral load of 249 000 copies/mL. Our case emphasizes the need for close inspection of sputum and lavage specimens for possible concurrent infections in the setting of immunocompromised patients. Different treatment regimens are needed for the 2 organisms that further stress the significance of timely diagnosis and appropriate treatment for the patients.
central nervous system involvement has been reported. *Cladophialophora hantana* is the most common dematiaceous fungus associated with central nervous system phaeohyphomycosis, but rare cases of *Bipolaris* species have been reported. We report a case of a 60-year-old man with a past medical history of ulcerative colitis and primary sclerosing cholangitis who presented to the hospital 17 days after orthotopic liver transplantation with a 1-week history of constant headache, mental status changes, and aphasia. He was found to have a left temporal lobe mass on magnetic resonance imaging (MRI) concerning for an infectious process (Figure 97, A). He was placed on broad-spectrum antimicrobial therapy but had worsening aphasia and subsequent progression of the mass on MRI required emergent surgical debridement by left temporal craniotomy. Microscopic examination of the biopsy tissue obtained from the procedure showed pyogranulomatous inflammation with pigmented, sporelike structures present in multinucleated giant cells on hematoxylin-eosin stain (Figure 97, B). Grocott methenamine silver stain also highlighted short segments of septate hyphae (Figure 97, C). Cultures from the surgical debridement grew a pigmented mold that had thick-walled, oblong conidia with 3 to 5 septations. A germ tube test showed germ tubes originating from both ends of the conidia consistent with *Bipolaris* species (Figure 97, D). The patient’s mental status significantly improved following surgical debridement, 2 weeks of liposomal amphotericin B, as well as long-term treatment with voriconazole, which was later switched to posaconazole.

**Disseminated Microsporidiosis With Intestinal Cryptosporidium Coinfection in a Patient With Kaposi Sarcoma and Castleman Disease Presenting With Acute Kidney Injury**

(Poster No. 164)

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Microsporidia are obligate intracellular parasitic fungi that cause opportunistic infections in humans. This is a case report of a 35-year-old man with a 12-year history of HIV/AIDS, recently started on highly active antiretroviral therapy, who presented with intermittent fever for 2 months, cough with sputum, nausea, vomiting, and loose watery stools for 8 days. On admission serum creatinine was 4.5 mg/dL. His CD4 count was less than 40 per mm³, and he had an undetectable viral load. He also received a diagnosis of intestinal cryptosporidiosis, BK virus, HHV-8–associated Kaposi sarcoma, and HHV-8–associated multicentric Castleman disease. Sputum for culture was sent. Acute kidney injury was initially considered to be prerenal due to nausea/vomiting. Because of worsening renal functions a kidney biopsy was performed. Sputum Gram stain showed intracellular Gram-positive spores with a beltlike stripe in the center. Calcofluor white stain showed intracellular fluorescent spores. The kidney biopsy was notable for intratubular and interstitial histocyte aggregates. *Microsporida* was highlighted by Gram stain and Grocott methenamine silver in the kidney biopsy. Immunohistochemistry demonstrated presence of *Microsporida* in kidney biopsy, as did transmission electron micrography, showing 1 to 2 micron spores in the cytoplasm in different stages of development. This case report highlights the importance of *Microsporida* to be considered in the differential diagnosis of an immunosuppressed patient presenting with fever and acute renal failure, while illustrating the appearance of these microorganisms in multiple preparations.

**Mycobacterium Spindle Cell Pseudotumor Caused by Mycobacterium xenopi: Case Report and Literature Review**

(Poster No. 165)

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Mycobacterial spindle cell pseudotumor (MSP) is a rare benign lesion characterized by a proliferation of spindle-shaped histiocytes containing acid-fast mycobacteria. These lesions are most commonly reported to occur in the lymph nodes, skin, spleen, and brain of immunocompromised patients, with surprisingly few cases from the lung. This is the first case report of mycobacterial spindle cell pseudotumor in association with *Mycobacterium xenopi*. The patient is a 42-year-old woman status after kidney-pancreas transplantation. She presented for evaluation of a culture positive for mycobacterium infection. Computed tomography scan of the chest revealed dense masslike collapse consolidation of the left lower lobe of the lung. Histology revealed a proliferation of uniform spindle cells with mixed inflammatory infiltrate in the background. The cells were positive for CD68 and CD1 but were negative for CD99, CD30, CKA/E1/AE3, CK 8/18, CD34, desmin, ALK, and Von Kossa immunostains. FITES stain showed numerous acid-fast positive mycobacteria, identified as *M. xenopi* (Figure 98). The patient was treated with amikacin, linezolid, and dalfazamine, showing improvement. This is the first report of *M. xenopi* causing a spindle cell pseudotumor. *Mycobacterium xenopi* is a well-known contaminant of laboratory samples, thus causing health care–acquired disease. Boylan et al recently published the first series of cases of lung spindle cell pseudotumor. This is a challenging histopathologic diagnosis because of its rare incidence and its spindled tumorlike appearance. The differential diagnosis is broad and includes both benign and malignant entities. We highlight the importance of the clinical context in which these lesions typically present and the morphologic spectrum of features is seen.

**Evaluation, Validation, and Implementation of the Idylla System as a Rapid Molecular Testing for Precision Medicine**

(Poster No. 166)

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Context: The Idylla mutation test is an automated, polymerase chain reaction (PCR)-based mutation testing system. The advantages of this system can greatly impact the delivery of precision medicine.

Design: We performed evaluation, validation, and implementation of this system for routine testing of BRAF, EGFR, KRAS, and NRAS using formalin-fixed, paraffin-embedded cancer samples.

Results: All 4 Idylla test systems showed excellent concordance with reference methods. The analytic sensitivity ranged from 94.66% to 100% depending on the cartridge, and specificity was 100%. A few discordant results were noted and further investigated: KRAS Q61L misclassified as Q61H; KRAS Q61R not identified; false-negative EGFR double-mutation L861Q and G719A; and false-negative EGFR double-mutation T790M and exon 19 deletion. The level of detection was determined to be 1% or 5% for the variants with available reference material. The turnaround time was shortened by 7 days on average.

Conclusions: The Idylla molecular testing system is an accessible, rapid, robust, and reliable testing option for both routine and challenging formalin-fixed, paraffin-embedded specimens.

Molecular Profiling in Small Cell Transformation of EGFR-Mutated Non–Small Cell Lung Carcinoma

(Poster No. 167)

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Small cell carcinoma (SCC) transformation occurs in 3% to 10% of EGFR-mutated non–small cell lung carcinomas (NSCLCs) following anti-EGFR tyrosine kinase inhibitor (TKI) therapy. We reported here on a 67-year-old woman who initially presented with a lung mass, hilar lymphadenopathy, and multiple osseous lesions. Both lung cytology and biopsy showed Napsin-A and TTF-1 adenocarcinoma (Figure 99, A and B). A 50-gene hotspot next-generation sequencing (NGS) assay was positive for an EGFR exon 19 deletion with a likely subclonal PIK3CA E545K mutation. Patient was treated with the TKI therapy osimertinib and remained stable for 10 months. Subsequent fine-needle aspiration of an enlarging right supraclavicular lymph node showed typical small cell carcinoma morphology (Figure 99, C) with immuno-reactivity for chromogranin and synaptophysin (Figure 99, D). The identical exon 19 EGFR mutation along with the PIK3CA mutation was also detected by plasma-based NGS. The patient rapidly declined and died shortly after receiving chemotherapy. Among 38 EGFR-mutated cases tested by hotspot NGS at our hospital before and after treatment with TKIs, 13 (34%) gained EGFR T790M, 4 lost mutations seen at diagnosis, 2 gained mutations, and 2 had more complex mutation shifts, but the remainder 20 (53%) had stable mutation patterns with the commonly profiled genes in this panel. This case and the cumulative mutation data at our institution and elsewhere suggest that the mechanisms underlying NSCLC recurrence and SCC transformation following TKI therapy are likely multifactorial and require further study.

A Pediatric Acute Myeloid Leukemia With a Novel Three-Way Translocation, t(8;10;21)(q22,p12;q22.1) Involving 10p12

(Poster No. 168)

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The translocation t(8;21)(q22;p12), resulting in the fusion of RUNXI/RUNX1, is present in 1% to 5% of acute myeloid leukemia (AML) cases and is associated with a favorable prognosis. We report on the case of a 15-year-old previously healthy girl with a unique variant translocation of t(8;21). She presented with 6 days of fever, chills, myalgias, and light-headnedness. Peripheral blood smear showed pancytopenia with 5% large circulating blasts with round to slightly irregular nuclear contours, abundant cytoplasm, and occasional cytoplasmic granules (Figure 100, A). No Auer rods were visualized. Bone marrow aspiration demonstrated 80% blasts with similar features (Figure 100, B). By flow cytometry blasts expressed CD34, CD13, cytoplasmic myeloperoxidase, variable CD117, CD33, CD15, CD19, partial CD79a, terminal deoxynucleotidyl transferases, and dim Pax-5. Fluorescence in situ hybridization (FISH) detected 14% of interphase cells with single gene fusion signal, and metaphase FISH determined the RUNXI/RUNXI fusion was on the der(8), which is consistent with the pathogenic RUNXI/RUNXI fusion (Figure 100, C). Chromosome studies confirmed a 3-way translocation involving 8q22, 10p12, and 21q22, that is, t(8;10;21)(q22;p12;q22), resulting in a RUNXI/RUNXI fusion product on the abnormal der(8) (Figure 100, D). Her initial chemotherapy course was complicated by distributive shock following the first dose of etoposide. She tolerated the remainder of therapy well after supportive treatment and achieved molecular cytogenetic remission. She has been closely followed and has remained in remission to date. Although several variant translocations have been reported, the translocation t(8;10;21)(q22;p12;q22) discovered in our case has never been described, and its impact on prognosis remains to be determined.

Molecular Testing for Identification of Tissue Origin of Poorly Differentiated Tumors: Utility and Impact on Patient Management

(Poster No. 169)

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Context: We report on the impact of molecular studies on determination of tumor type/primary site, and subsequently the patient management and outcome.

Design: The pathology database was searched for cases of poorly differentiated tumors that were referred during the last 5 years for
molecular-type testing. Clinical and pathologic data were obtained from medical records and pathology reports, respectively.

**Results:** Twenty-two cases were referred for identification of primary tumor/tumor type by molecular analysis. A report was received in 18 cases; tissue was insufficient for analysis in 3 cases. Molecular analysis confirmed the immunohistochemistry (IHC) profile in 4 cases, suggested a primary site in 4 cases in which IHC was equivocal, and was indeterminate in 3 cases. In 4 cases, the results were unexpected by the morphology and IHC. In 2 cases, molecular testing established the tumors to be primary to the liver surface and bone. In most cases, the suggested primary site was not confirmed by a follow-up biopsy. A total of 3 patients received palliative care and 12 received chemotherapy. Clinical follow-up was available in 10 patients; of those, 4 were alive more than a year after diagnosis.

**Conclusions:** Molecular identification of poorly differentiated tumors is useful in confirming histologic diagnosis, or suggesting a primary site in cases that are equivocal on IHC. Because many patients were at a disease stage too advanced to withstand further investigations or undergo aggressive therapy, the clinical team did not confirm the suggested primary site. Thus, impact of molecular testing could not be discerned in most cases.

**Differential Expression Profile of MicroRNAs in Gastroenteropancreatic Neuroendocrine Tumors**

*(Poster No. 170)*

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**Context:** Neuroendocrine tumors (NETs) are a heterogeneous group of neoplasms arising from epithelial endocrine cells that can be challenging to evaluate histologically. The molecular basis of GEP-NETs involved cell signaling pathways, such as PI3K/AKT/mTOR, Notch1, and Wnt, which are activated constitutively in 80% of cases. Epigenetic factors, like microRNAs (miRNAs), could be involved in posttranscriptional regulation. We used a bioinformatic approach to select a group of miRNAs that might regulate the expression of genes involved in those pathways. Our objective was to determine the profile of differential expression of these miRNAs in GEP-NETs, in tumor tissue, and in adjacent normal tissue.

**Design:** We selected and processed 30 cases (tumor and adjacent nontumor tissue of each one) corresponding to patients with a diagnosis of GEP-NETs from small intestine and pancreas at the Fundación Santa Fe de Bogotá. Total RNA was isolated from paraffin-embedded tissues; quantification of the miRNA expression level was performed using TaqMan MicroRNA assays, and the differential expression was estimated by applying the comparative method ΔCt and ΔΔCt. Statistical significance of each miRNA expression was evaluated applying Student t-test with α = 0.05.

**Results:** We found downregulated miR-19a, whereas miR-96, miR-145, miR-182, and miR-200a were upregulated in small intestine tumor tissue (Table). Additionally, we observed overexpression of miR-182 and miR-145 in pancreatic tumor tissue.

**Conclusions:** We report a significant dysregulation of all 5 miRNA between tumor and non-tumor tissue of GEP-NETs and provide new perspective to understand this pathology and a potential biomarker for GEP-NETs.

### Results for Small Intestine and Pancreas

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**Oxidative Phosphorylation Correlates With Clinically Significant Molecular and Immune Features in Melanoma Brain Metastases**

*(Poster No. 171)*

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**Context:** Oxidative phosphorylation (OXPHOS) mediates resistance to BRAF and MEK inhibitors in melanoma. Recently, we showed that melanoma brain metastases (MBMs) have higher expression of OXPHOS genes than patient-matched extracranial metastases. Notably, our studies demonstrated that OXPHOS varies among MBMs. To improve our ability to treat high-OXPHOS MBMs, we report here the molecular and immune features that associate with OXPHOS in MBMs.

**Design:** We applied an OXPHOS gene signature to RNA sequencing data from surgically resected MBMs (n = 88). Clustering by these genes identified MBMs with significant enrichment (high-OXPHOS; n = 21) and depletion (low-OXPHOS; n = 25) of OXPHOS genes. The EdgeR/lma/voom pipeline was used to perform differential gene expression (DGE) analysis between high- and low-OXPHOS MBMs. Pathway analyses were performed via ensemble of gene set enrichment analyses (EGSEA). The ESTIMATE and MCP-Counter R packages were used to assess immune infiltrates from voom-transformed counts. Quantitative analysis of P-S6 and P-PRAS40 was performed by immunohistochemistry.

**Results:** RNA sequencing analysis identified that high-OXPHOS MBMs were characterized by significant enrichment of PGC1a and mTOR signaling and significant depletion of ImmuneScores, T cells, cytotoxic lymphocytes, B lineage cells, and NK cells versus low-OXPHOS MBMs. We observed significantly higher P-S6 staining in high-OXPHOS MBMs but did not observe differences in P-PRAS40 staining.

**Conclusions:** Significant differences in mTOR (enriched) and immune (depleted) signaling were identified in high-OXPHOS MBMs. Preclinical studies will evaluate if OXPHOS sensitizes MBMs to mTOR inhibitors and promotes resistance to immunotherapies. An improved understanding of the clinical, prognostic, and predictive values of OXPHOS status in MBMs could translate into improved outcomes for these patients.

Dr Tetzlaff has served on advisory committees for Novartis, Myriad Genetics, and Seattle Genetics. Dr Davies has served on advisory committees for Roche/Genentech, BMS, Novartis, GSK, and Sanofi-Aventis.

**Ecotropic Viral Integration Site 1 Gene Rearrangement in De Novo Acute Promyelocytic Leukemia**

*(Poster No. 172)*

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Ecotropic viral integration site 1 (EVI1) is a proto-oncogene whose overexpression is associated with aggressive disease in myeloid leukemia. It functions as transcription factor by encoding nuclear zinc finger protein. EVI1 is 1 product of the myelodysplasia syndrome.
associated protein 1 (MDS1) and EVI1 complex locus (MECOM). They can either encode separate proteins or be expressed as one protein. EVI1 is antagonist to MDS1/EVI1. We report a case of 68-year-old man who presented to the emergency department with aphasia. He was diagnosed with left temporal intraparenchymal hemorrhage on computed tomography scan. Complete blood count revealed pancytopenia, and blast cells with Auer rods were noted on peripheral blood analysis. Bone marrow aspirate was markedly hypercellular for the patient’s age. A 500-cell differential count demonstrated 88% abnormal promyelocytes; focal Auer rods were noted. On flow cytometry, the abnormal cells (91%) were found to display dim CD45 and moderate to increased side scatter. Expression for CD13, CD33, CD64, CD117, and MPO (bright) were found. Real-time polymerase chain reaction assay detected 127.81% PML-RARA L-form fusion transcripts to ABL. The findings were characteristic of acute promyelocytic leukemia (APL). Cyto genetic study identified t(15;17) by karyotype and fluorescence in situ hybridization (FISH). EVI1 gene rearrangement by FISH was also identified. The findings suggest a recently acquired abnormality related to disease progression. After receiving ATRA, the PML-RARA/ABL fusion transcript went down to 5.44% and FISH detected no EVI1 gene rearrangement. To our knowledge, no case of EVI1 in association with de novo APL has ever been reported (Figure 101).

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Establishing Diagnostics in Kenya: Fluorescence In Situ Hybridization for Burkitt Lymphoma

(Poster No. 174)

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Context: Burkitt lymphoma (BL) is a common pediatric cancer in sub-Saharan Africa. Despite advances in care, prognosis is poor. Delay of diagnosis of the disease results in delay of treatment. We hypothesized that improved diagnostics specific for the disorder would improve care and survival. We set out to establish fluorescence in situ hybridization (FISH) for BL to advance the accuracy and diagnosis of BL in the AMPATH Reference Laboratory at Moi Teaching and Referral Hospital (MTRH) in Eldoret, Kenya. Diagnostic testing for BL at Moi Teaching and Referral Hospital standardly includes only morphology of biopsy specimens by hematoxylin and eosin staining.

Design: FISH is a molecular cytogenetic tool for identifying recurring translocations in pediatric leukemia. In BL, t(8;14)(q24;q32) is the characteristic cytogenetic translocation involving the juxtaposition of IGH to MYC on chromosome 14 resulting in MYC dysregulation. Probes, which flank the IGH and MYC breakpoints, create a dual color, dual fusion signal pattern when applied to BL cells containing the translocation (Figure 102). We introduced a FISH BL diagnostic strategy including establishing a laboratory with equipment and reagents; training personnel; providing standard operating procedures specific to the new AMPATH FISH laboratory; and validation of the testing.

Results: Validation of specimens included cell lines, touch preps, bone marrow, and fine-needle aspiration.

Conclusions: We have successfully established FISH as a diagnostic test in Eldoret, Kenya. We present the validation results and correlation of the testing with existing diagnosis by histopathology and, in some cases, flow cytometry.
An inhibin-B level approximately 6 weeks post surgery was found to have a 14.0×13.0×11.0-cm solid, lobulated, heterogeneous pelvic mass. Serum tumor markers showed an elevated inhibin-B level of 315 pg/mL, raising clinical suspicion for a granulosa cell tumor. She underwent bilateral salpingo-oophorectomy and final histopathologic examination revealed a fibrothecoma with elevated inhibin serum level in a patient with Down syndrome. This rare presentation of a benign sex cord–stromal tumor with radiographic findings of a solid ovarian mass and increased serum inhibin level is an important clinical mimic of granulosa cell tumor.

Clinical Outcome of Ovarian Serous Borderline Tumors Might Be Affected Not Just by Pathologic Tumor Stage but Also by Tumor Molecular Characteristics in Further Guiding Clinical Management

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Context:Serous borderline tumors (SBTs) are known to have favorable behavior and better survival; however, long-term follow-up indicates SBT could represent a molecularly heterogeneous group with different potential for disease progression. Currently, molecular characteristics of SBT are not considered in guiding postoperative management. We correlate the pathologic stage of SBT with follow-up data to understand the driving biologic forces within this disease category.

Design:Retrospectively, 85 SBTs were identified between 2000–2013 at our institution; 42 patients lost to follow-up or who died of unrelated causes were excluded; 43 patients were analyzed. Unfavorable biologic behavior was determined as documented recurrence, progression to serous carcinoma, metastasis, or death from disease.

Results:Of 43 patients, 5 (11.6%) had SBT with unfavorable biologic behavior, including 1 at stage III, 1 stage IC, and 1 stage IA; 2 had incomplete staging. The remaining 38 patients with clinically favorable SBT were alive at follow-up, including 13 at stage IA/B, 14 stage IC-II, and 3 stage III; 8 had incomplete staging.

Conclusions:In this study, SBTs with unfavorable clinical outcome include not only higher-stage but also lower-stage tumors. On the other hand, SBTs with favorable clinical outcome included tumors at lower stages, as well as at higher stages. Tumor stage might not be the sole determining factor for clinical outcome, and other factors (such as molecular) might affect tumorigenesis in SBT. As shown recently, BRAF V600E mutation in SBT may imply a more favorable clinical outcome, thus mutational analysis may provide risk stratification to further guide and improve management.

First Case of an Inhibin-B–Producing Fibrothecoma in a Patient With Trisomy 21

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Elevated serum inhibin is associated with granulosa cell tumors. Other sex cord–stromal tumors often show positive immunohistochemical staining for inhibin, but without measurable concentrations in serum. Only a few other reports of inhibin-B–producing benign sex cord–stromal neoplasms have been published (2 fibromas, 1 thecoma, and 3 fibrothecomas), and none have been in patients with Down syndrome. We present the first case of an inhibin-B–producing fibrothecoma with elevated inhibin serum level in a patient with trisomy 21. A 52-year-old woman with Down syndrome and abdominal pain was found to have a 14.0×13.0×11.0-cm solid, lobulated, heterogeneous pelvic mass. Serum tumor markers showed an elevated inhibin-B of 315 pg/mL, raising clinical suspicion for a granulosa cell tumor. She underwent bilateral salpingo-oophorectomy and final histopathologic examination revealed a fibrothecoma. The tumor was positive for inhibin by immunohistochemistry and reticulin-invested individual cells (Figure 1). An inhibin-B level approximately 6 weeks post surgery was <10 pg/mL. Patients with Down syndrome have a greater risk of leukemias and a decreased risk of solid tumors as compared to the general population, although ovarian dysgerminomas have been reported. This is the first case report to our knowledge of an inhibin-B–producing fibrothecoma in a patient with Down syndrome. This rare presentation of a benign sex cord–stromal tumor with radiographic findings of a solid ovarian mass and increased serum inhibin level is an important clinical mimic of granulosa cell tumor.

Histopathologic Changes in Uterine Smooth Muscle Tumors Treated With the Selective Progesterone Receptor Modulator (Ulipristal Acetate, Fibristral)

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Context:Approximately 80% of women of reproductive age have uterine leiomyomas (LMs). Ulipristal acetate (UPA) is the only selective...
progestrone receptor modulator approved for the management of LMs in Canada. Specific endometrial changes induced by this type of medication are well described in the literature; however, the potential effects of this medication on smooth muscle neoplasms and myometrium have not yet been addressed. The goals of the study were to determine if the use of UPA is associated with any specific histologic changes in the myometrium/LMs and if there is an increase in the incidence of smooth muscle neoplasms.

Design: We performed a retrospective review of pathology records and slides, from 2012 to 2018 at The Ottawa Hospital, of women with LM who received preoperatively UPA and who underwent hysterectomy, myomectomies, submucosal resection of leiomyomas, and polypectomies. A total of 297 were retrieved, 13 cases were excluded. The data were analyzed by using descriptive statistics.

Results: Most patients had conventional LMs (78.5%), about 11.6% of patients had LMs of the special type. The incidence rate for stromal tumors of uncertain malignant potential was 1.34%, and for adenocarcinoma it was 0.45%, which is in keeping with general population incidence rates for these entities. No specific changes in myometrium and in LMs are seen in patients treated with UPA. (Figure 2, A, adenosarcoma; B, hypercellular LM; C, LM with bizarre nuclei; D, STUMP).

Conclusions: Preoperative use of UPA is not associated with an increased incidence of STUMP, leiomyosarcomas, and special subtypes of LMs.

Differential Expression of Vascular Endothelial Cadherin in Endometrial Cancers and Tumor-Associated Vasculature

(Poster No. 5)

Brustmann Hermann, MD, PhD (ddbrustmann@hotmail.com), Department of Pathology, Landesklinikum Baden-Moedling, Baden, Austria.

Context: Endometrial cancer (EC) can be assigned to endometrioid carcinomas (EECs, type 1) and nonendometrioid cancers with the most common type being serous endometrial carcinomas (SECs, type 2). Vascular endothelial cadherin (VE-CAD) may play an important role in endothelial biology through control of cohesion and organization of intercellular adherens junctions, which is thought to maintain newly formed vessels.

Design: VE-CAD immunoeexpression was evaluated in 94 ECs consisting of EEC (n = 78) and SEC (n = 16). They consisted of stages FIGO IA (n = 68) and IB to IV (n = 26), and grades 1/2 (n = 69) as well as 3 (n = 25). Eleven patients died of their cancers. Immunostaining in tumor epithelia was scored for quantity and quality. Endothelia of tumor-associated vasculature were scored as diffusely positive in a circumferential manner, or partially reactive/negative (0%–90% of endothelial cells).

Results: Positive, predominantly cytoplasmic and to some extent membranous VE-CAD immunoreactivity was a common finding in all EC cases investigated. High scores were related to endometrioid type 1 histology (P < .02). Diffuse endothelial staining was related to type 1 EEC (P < .001), grade 1/2 (P < .001), FIGO IA EC (P = .04), and tumor-free survival (P = .001).

Conclusions: Epithelial expression of VE-CAD is associated with low-grade and type 1 EEC. VE-CAD expression in tumor-associated endothelial cells was significantly reduced in high-grade EEC and SEC, respectively, as well as high-stage tumors, with impact on prognosis.

Aggressive tumor biology of EC may be associated with dysregulation of vascular permeability by downregulation of VE-CAD and thus, adherens junctions, facilitating intravascular tumor spread.

All Slides Matter: Incidental Adenoma Malignum of the Cervix Discovered in a Patient Following Hysterectomy for Uterine Leiomyoma

(Poster No. 6)

Evi Abada, MD, MS (evi.abada@wayne.edu); Sudeshna Bandypadhyay, MD; Nagla Salem, MD; Rouba Ali-Fehmi, MD, Department of Pathology, Wayne State University School of Medicine, Detroit, Michigan.

Adenoma malignum, also known as minimum deviation adenocarcinoma, is a rare HPV-negative variant of well-differentiated adenocarcinoma of the endocervix. It is difficult to diagnose in surgical pathology specimens owing to its deceptively benign appearance. This is a case of a 43-year-old woman with a history of menorrhagia and metrorrhagia and radiology interpretation of multiple degenerating uterine fibroids. Preoperative Pap testing and hysteroscopic dilatation and curettage were noncontributory. Total abdominal hysterectomy and bilateral salpingectomy were performed for leiomyoma. Gross examinations confirmed the presence of uterine leiomyomata, with no abnormality in the endometrium, cervix, and fallopian tubes. However, microscopically, the cervix revealed well-spaced, deeply invasive, variably sized glands with irregular outlines/haphazard arrangements, lined by cells showing mild to moderate cytologic atypia. Both lymphovascular and perineural invasion were seen. Further sampling of the entire cervix and endometrium confirmed that the abnormal glands (Figure 3, A and B) were only confined to the cervix with the involvement of all 4 quadrants. Immunohistochemical staining revealed positive p53 and CK7. Ki-67 showed a high proliferative index within the lesion. Monoclonal CEA, calretinin, CD10, and P16 were all negative. A diagnosis of adenoma malignum stage pT1b2 was made. This case was reviewed at the multidisciplinary tumor board and the patient is currently being managed with platinum-based chemotherapy and radiotherapy and is doing well. Cases such as this underscore the importance of adequately sampling surgical resection specimens, with careful attention to microscopic details regardless of presurgical diagnoses, as incidental pathologies may be unearthed, which could have significant implications on a patient’s clinical outcome.

Mismatch Repair Deficiency Rate in Uterine Carcinosarcoma: A 2-Institution Retrospective Review

(Poster No. 7)

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Context: Immunohistochemistry for mismatch repair (MMR) proteins is recommended in endometrial carcinomas as a screening test for
Lynch syndrome. MMR deficiency is reported in approximately 30% of endometrial carcinomas. Few studies have evaluated the rate of MMR loss in uterine carcinosarcomas.

**Design:** A 5-year retrospective database search of uterine carcinosarcomas was performed at 2 academic institutions. The histologic diagnoses and MMR immunohistochemistry interpretations were confirmed by a gynecologic pathologist.

**Results:** Sixty-two cases of uterine carcinosarcomas with available MMR immunohistochemistry results were identified. Sixty cases (97%) showed intact expression and 2 cases (3%) showed loss of MLH1/MSM2. Both cases of MMR deficiency were due to hypermethylation. Three additional cases initially diagnosed as carcinosarcoma also revealed MMR deficiencies; however, given the lack of clear mesenchymal differentiation, these cases were reclassified as dedifferentiated endometrial carcinoma and were subsequently excluded from the study.

**Conclusions:** The rate of MMR deficiency is lower in uterine carcinosarcoma than in endometrial carcinoma. No cases of Lynch syndrome were identified in our review, as both cases identified with MMR deficiencies were due to somatic hypermethylation. In the setting of MMR loss, the diagnosis of carcinosarcoma should be reevaluated owing to the significant interobserver variability seen among pathologists making this diagnosis and the low rate of MMR deficiency observed in uterine carcinosarcomas.

**Extraterine Low-Grade Endometrioid Stromal Sarcoma With Unusual Features: Case Report and Review of Literature**

**(Poster No. 8)**

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Low-grade endometrioid stromal sarcoma, the extraterine counterpart to low-grade endometrial stromal sarcoma, is uncommon; fewer than 100 cases have been reported. These tumors may be related to endometriosis and can be diagnostically challenging given their rarity, unusual location, and variable histologic features. A 61-year-old woman with history of hysterecomy 14 years prior, due to reportedly benign indications, presented with 3 weeks of worsening pelvic pain. Computed tomography imaging revealed a predominantly low-grade spindle cell proliferation with areas of fibroma-like stroma, sex cord-like elements (Figure 4, A), smooth muscle differentiation confirmed by positive desmin and h-caldesmon staining, epithelioid cells, and hyaline plaques (Figure 4, B). Only rare areas contained the classic histologic appearance of low-grade endometrial stromal sarcoma consisting of monomorphic cells with scant cytoplasm and oval nuclei surrounding spiral arteriole-like vessels (Figure 4, C). The tumor cells were diffusely positive for CD10 (Figure 4, D), WT-1, ER, and PR, and negative for inhibin, calretinin, and cytokeratins. Rare foci of endometriosis were identified in the ovaries. This case illustrates the variable histologic features of extraterine low-grade endometrioid stromal sarcoma that can make diagnosis difficult. Thorough sampling and immunohistochemistry help to reach the correct diagnosis.

**Placental Fibrinoid Deposit and Platelet Aggregation in Normal Pregnancy and Complications**

**(Poster No. 9)**

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**Context:** There are multiple types of fibrinoid deposits within the placentas and the nature of these fibrinoid deposits is poorly understood.

**Design:** The fibrinoid deposits within normal pregnancy and the pregnancy-related complications are studied by using the routine H&E stain and immunostaining for CD42b expression as a marker for platelet aggregates.

**Results:** The subchorionic fibrinoid (Langhans stria, Langhans fibrinoid layer) and the basal fibrinoid (Rohr stria) are associated with platelet aggregates positive for CD42b expression by immunostaining. Perivillous fibrinoid is also associated with platelet aggregates in placentas including accelerated villous maturation in preeclampsia, intervillous thrombosis, infarcts, and infectious villitis. The platelet aggregates with CD42b expression are present on the syncytiotrophoblasts, suggesting the initiation origin of coagulatory cascade, leading to thrombosis. Trophoblastic cyst content and fibrinoid medial necrosis of vasculopathy are not associated with CD42b expression. Persistent endovascular trophoblasts in vasculopathy (CD56-related vasculopathy) are not associated with platelet aggregates, although CD42b expression is present in decidual vascular thrombosis. Maternal floor infarction is not associated with platelet aggregates and CD42b expression, and the etiology of maternal floor infarction is not related to maternal coagulopathy (Figure 5).

**Conclusions:** The fibrinoid deposits are mostly from maternal circulation and these fibrinoid deposits are likely related to the change of the laminar flow at specific locations, leading to damage of the syncytiotrophoblasts and activation of extrinsic coagulatory cascade. The nature of fibrinoid medial necrosis in vasculopathy and maternal floor infarction is unknown. Further investigation of these fibrinoid deposits will help understand the mechanism of the fibrinoid formation.

**Chemotherapy-Induced Epithelial to Mesenchymal Transformation in Ovarian Serous Carcinomas**

**(Poster No. 10)**

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**Context:** The standard ovarian cancer therapy is surgery + neoadjuvant and platinum-based chemotherapy. Usually, the disease recurs and become resistant to chemotherapy. One hypothesis is epithelial to mesenchymal transformation (EMT). We investigated chemotherapy-induced EMT in ovarian carcinomas.

**Design:** Between 2009 and 2018, we found 12 pairs of prechemotherapy and postchemotherapy high-grade serous ovarian carcinomas.
We reviewed slides, clinical course, and follow-up. We performed IHC for E-cad, EMA, CD138, vimentin, and SOX9 and scored them by intensity (0, 1+, 2+, 3+) and percentage of staining (0%–100%). We calculated the combined score by multiplying the above (range, 0–300). We calculated the sum of the epithelial markers, $EP = (E-cad + EMA + CD138)$; and mesenchymal markers (Vimentin + SOX9) pre and post chemotherapy and compared the results. We scored the tumor morphology, discohesion, prominent nucleoli, and pleomorphism. Correlation studies were performed by Pearson method and the findings were statistically calculated with paired t test.

**Results:** Total prechemotherapy epithelial score in all cases is 5343 and decreased to 4035 post chemotherapy. Total of mesenchymal markers in prechemotherapy tumors was 1996 and increased to 2529 post chemotherapy. Comparison of prechemotherapy and postchemotherapy EP markers showed significant difference ($P = .02$). Comparison of prechemotherapy and postchemotherapy MES markers was not significant. Correlation studies show prechemotherapy CD138 is inversely correlated with postchemotherapy SOX9 values ($R = -0.667$, $P = .02$). Postchemotherapy E-cad was inversely correlated with tumor discohesion ($R = -0.54$, $P = .03$). Tumor morphology trends toward higher score in postchemotherapy specimens (Figure 6). These data were not statistically significant ($P > .05$).

**Conclusions:** We investigated chemotherapy-induced EMT in ovarian serous carcinomas. We showed there is a trend toward loosing epithelial markers and expressing mesenchymal markers along with morphologic changes. Larger studies are required to show the statistical significance of the results.

### Retiform Variant of Sertoli Cell Tumor of Ovary: A Case Report and Literature Review

**Poster No. 11**

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Sertoli-Leydig cell tumors are rare sex cord–stromal neoplasms that account for less than 0.5% of all primary ovarian tumors. The retiform variant is even rarer and may pose diagnostic challenge especially during intraoperative consultations. We report a case of a 46-year-old woman who presented with symptomatic anemia, and imaging revealed a 5.6-cm largely cystic left adnexal mass. She subsequently underwent surgery, and intraoperative frozen sections revealed a low-grade solid and cystic neoplasm (Figure 7, A). Permanent sections of the tumor demonstrate significant retiform growth pattern forming anastomosing, slithike, irregular spaces or multicystic, cistive, or papillary architecture (Figure 7, B). The rest of the tumor consists of open or compressed Sertoli cell tubules. The tumor cells are low columnar to cuboidal with oval to round nuclei and pale cytoplasm. There is no significant nuclear atypia or mitotic figures. No heterologous or Leydig cell components are identified. The tumor cells are positive for inhibin (Figure 7, C), calretinin, CD99, FOXL2 (Figure 7, D), with patchy positivity for CD56. The morphologic and immunophenotypic features are consistent with retiform variant of Sertoli cell tumor. Because of their variable morphologic patterns, retiform Sertoli-Leydig cell tumors often present a diagnostic challenge. It could be confused with serous papillary cystadenocarcinoma and yolk sac tumor. An immunohistochemistry panel is essential in evaluating these tumors. FOXL2 antibody shows superior staining quality over other commonly used sex cord–stromal tumor markers such as inhibin, Calretinin, and CD56.
In 2014, from molecular data, the World Health Organization (WHO) reclassified ovarian transitional cell carcinoma (TCC), a rare tumor (<1% of all ovarian tumors), as a variant of high-grade serous/ endometrioid carcinoma. However, the WHO classification still retains TCC as a separate entity among the tumors of fallopian tube (FT) and primary peritoneum. In addition, the College of American Pathologists (CAP) includes TCC as a diagnosis separate from serous carcinoma as part of its protocol for cancers of “ovary or fallopian tube or primary peritoneum.” We recognized this as yet irreconcilable classification of TCC in a case involving a 69-year-old woman with abdominal pain. Ultrasonography revealed a large left adnexal mass (Figure 8), and CA 125 level was 1966.2 (reference range, ≤35.0 U/mL). The 8-cm excised ovarian mass was well circumscribed, had a rubbery consistency, and contained areas of necrosis and hemorrhage. Tumor cells exhibited insular pattern resembling urothelial carcinoma without Brenner component and were positive for WT1, CK7, p53, and p16, and negative for CK20. These findings are consistent with the diagnosis of ovarian high-grade serous carcinoma with predominantly transitional cell growth pattern. We believe that failure to properly classify ovarian TCC per WHO classification in the CAP protocol may result in inappropriate management of the patient. A revision of the CAP protocol is warranted for clarity and consistency. Furthermore, WHO classification needs to address whether TCC of FT and peritoneum is still a distinct entity.

Collision Tumor of Uterus: A Report of 2 Rare Phenomena and Brief Review of Literature
(Poster No. 14)

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Collision tumor indicates 2 or more tumorigenic events within a single organ. We report 2 cases of uterine collision tumors. The first case was that of a 75-year-old woman who presented with postmenopausal bleeding and diagnosed endometrial adenocarcinoma on Pap test. A total hysterectomy was performed to reveal 2 discrete lesions in the uterine cavity. Morphologically and immunohistochemically the 2 lesions were distinct; mass No. 1 showed high-grade serous carcinoma arising from serous endometrial intraepithelial carcinoma (Figure 9, A), whereas mass No. 2 was confirmed as carcinosarcoma (Figure 9, B). The patient received additional pelvic radiation and vaginal vault boost. In the second case, a 66-year-old woman presented with a large amount of ascites. Fine-needle aspiration biopsy showed high-grade carcinoma of gynecologic origin. Following neoadjuvant chemotherapy, an exploratory laparotomy was performed. An enlarged uterus contained a polypoid mass and 3 leiomyomata measuring up to 11 cm. Microscopically, the polypoid mass showed endometrial serous carcinoma arising in conjunction with an atrophic polyp. In addition, undifferentiated uterine sarcoma was identified confined to the leiomyoma and showing necrosis, cytologic atypia, and increased mitosis (Figure 9, C) with CD10 positivity (Figure 9, D). Including our cases, 23 uterine collision tumor cases have been published. The collision of endometrioid carcinoma and stromal sarcoma was the most common. Carcinosarcoma, serous carcinoma, leiomyosarcoma, choriocarcinoma, small cell carcinoma, hepatoid carcinoma, squamous cell carcinoma, and lymphoma were also reported. The treatment and prognosis are determined by the more aggressive component. Careful and thorough gross examination, and histopathologic evaluation with the assistance of immunohistochemistry are crucial for diagnosis.

CD138 Variable Expression in Endometrium: A Potential Diagnostic Pitfall
(Poster No. 15)

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Context: Immunohistochemistry (IHC) is used in pathologic practice to identify lines of differentiation. However, IHC is vulnerable to preanalytic, analytic, and postanalytic factors, which affect reproducibility. Evaluation of IHC in the endometrium highlights these challenges owing to the variable expression of proteins during menstrual cycle. Syndecan-1 (CD138), an extracellular matrix receptor member of the transmembrane heparan sulfate proteoglycan family, is expressed on the surface of epithelial and stromal cells. The purpose of this study was to evaluate variable expression of CD138 in endometrial samples in different phases of menstrual cycle.

Design: Endometrial samples from 120 patients were analyzed. Endometrial dating was performed by using the Noyes criteria. Evaluation of CD138 was performed manually with assessment of both glands and stroma by 2 pathologists independently.

Results: Eighty-six samples were identified as secretory: 81 with strong diffuse and 5 with strong focal basolateral epithelial pattern of CD138 expression. Three of the secretory samples demonstrated strong
focal stromal expression and 1, strong diffuse stromal expression. Thirty-four samples were identified as proliferative: 24 with strong diffuse and 10 with strong focal basal epithelial CD138 expression. Seventeen of the proliferative samples demonstrated strong focal and 9 strong diffuse stromal CD138 expression (Figure 10).

Conclusions: CD138 IHC expression varies during the menstrual cycle. A strong diffuse basolateral epithelium pattern without stromal expression is indicative of secretory endometrium, a basal epithelium, and focal stromal pattern is indicative of proliferative endometrium. The pathologist should be aware of these patterns during antibody validation and clinical utilization.

A Comparative Analysis of Immunohistochemical Profile of Ovarian Serous Carcinoma Before and After Neoadjuvant Chemotherapy

(Qiqi Ye, MD, PhD1 (qiqi.ye@vwmhealth.org); Kemin Xu, MD, PhD1; Rugved Pattarkine, MD2; Tana Pradhan, DO2; Liying Han, MD, PhD2; Minghao Zhong, MD, PhD1. 1Departments of Pathology and Obstetrics and Gynecology, Westchester Medical Center, Valhalla, New York.

Context: The main strategies for management of advanced-stage ovarian serous carcinoma are either primary surgery followed by chemotherapy or cytoreductive interval surgery following chemotherapy. Our aim is to compare the expression of p53, p16, ER, PR, and PD-L1 in prechemotherapy and postchemotherapy specimens from patients with ovarian serous carcinoma who received surgery after chemotherapy.

Design: Retrospective review of all ovarian serous carcinoma cases (250 cases) identified 10 patients with paired prechemotherapy and postchemotherapy specimen. Immunohistochemistry staining (IHC) was carried out for p53, p16, ER, PR, and PD-L1 in prechemotherapy and postchemotherapy specimens from patients with ovarian serous carcinoma who received surgery after chemotherapy.

Results: All 10 patients had chemotherapy responses that included necrosis, calcification, and histiocytes accumulation with cholesterol cleft. Ten cases were positive for P16, and 9 cases showed abnormal p53 staining; all 10 cases were concordant for both markers in prechemotherapy and postchemotherapy specimen. On the other hand, ER was positive in 8 cases, and PR was positive in 6 cases; prechemotherapy and postchemotherapy IHC concordance for ER and PR was 90% and 80%, respectively. PD-L1 positivity ranged from 0% to 10% in 10 cases, and prechemotherapy and postchemotherapy IHC concordance was 70%. Interestingly, 2 discordant cases had increased PD-L1 expression with excellent chemotherapy response (Figure 11).

Conclusions: IHC expression of p53 and p16 on biopsy remains unchanged after chemotherapy, suggesting the reliability of p53 and p16 to confirm the origin of surgically resected carcinoma. On the other hand, ER and PR expression exhibits variable expression before and after chemotherapy, and the variability is likely associated with chemotherapy response. PD-L1 increased expression after chemotherapy may suggest excellent chemotherapy response.

Primary Synovial Sarcoma of the Uterine Cervix

(Elmira Vaziri Fard, MD, MPH (Elmira.VaziriFard@uth.tmc.edu); Songlin Zhang, MD, PhD; Michael Covinsky, MD. Department of Pathology and Lab Medicine, University of Texas Health Science Center at Houston.

Synovial sarcoma is a translocation-associated soft tissue malignancy frequently affecting young adults. The classic translocation is t(X;18)(p11.2;q11.2): SS18-SSX1/2 fusion. Synovial sarcoma tends to favor the distal extremities but can also arise in other locations. To date, no case of primary synovial sarcoma of the cervix has been reported. We report a case of a 42-year-old female with no prior history who presented to clinic with vaginal spotting for 3 months and was found to have a 5x6 necrotic mass in the uterine cervix. The mass was evacuated from the vagina and sent for pathologic diagnosis. Sections showed proliferation of monotonous epithelioid to spindled cells with scant eosinophilic cytoplasm, round to slightly irregular nuclei, variable nucleoli, and frequent mitosis in a background of delicate capillary and occasional thick-walled vessels (Figure 12, A). The only present normal tissue was cervical epithelium (Figure 12, B). On immunohistochemical workup, tumor cells were negative for pan cytokeratin, OSCAR, EMA, chromogranin, S100, SMA, desmin, myogenin, WT1, CD117, CD34, and BRG1. CD45 was positive in few inflammatory cells. Cyclin D1 showed partial weak to moderate nuclear reactivity. CD99 demonstrated strong diffuse membranous reactivity (Figure 12, C) and BCL-2 showed strong cytoplasmic and possible membranous staining (Figure 12, D). FISH results for EWSR1, BCOR, and CIC gene rearrangements were negative; however, FISH results for SS18 (SYT) (18q11) gene rearrangement were positive. Monophasic synovial sarcoma diagnosis was rendered. With this case reported, it is imperative to include synovial sarcoma in the differential diagnosis for spindle cell sarcoma with monotonous and primitive histology in the GYN tract.

Atypical Lipoleiomyoma of the Uterus

(Jessica A. Lawson, MD (thejalawson@gmail.com); Karen S. Strenge, MD1; Thomas P. Baker, MD. 1Department of Pathology, Madigan Army Medical Center, JBLM, Washington; 2Department of Pathology, the Joint Pathology Center, Silver Spring, Maryland.

A lipoleiomyoma is a rare variant of uterine fibroid. The overall incidence is reportedly between 0.03% and 0.2%. We present a case of an atypical uterine lipoleiomyoma with a lipoblastic component resembling a well-differentiated liposarcoma/atypical lipomatous tumor. A 46-year-old obese woman presented to the gynecology oncology clinic with a past medical history significant for heavy irregular menses requiring packed red blood cell transfusion and a recent biopsy suggestive of complex atypical hyperplasia. Magnetic resonance imaging of the pelvis demonstrated an enlarged fibroid uterus with a dominant 3.7 × 2.8 × 2.3-cm intramural mass in the fundus, most consistent with a necrotic fibroid. A hysterectomy with bilateral salpingectomy and right oophorectomy was performed. Gross examination revealed multiple fibroids and a well-circumscribed yellow-white soft nodule within the anterior uterus consistent with the dominant mass identified on MRI. Histologically, this nodule consisted of pleomorphic spindle cells admixed with mature adipocytes surrounded by a rim of smooth muscle cells (Figure 13, A). The adipocytic component showed variation in adipocyte size, cellular atypia, and lipoblasts (Figure 13, B). MDMP2 gene amplification showed...
Uterine Adenosarcoma: A Small Case Series

(Poster No. 19)

Mei Lin, MD (Mei.Lin@uth.tmc.edu); Nirmal Aakash, MD; Zhenjian Cai, MD, PhD; Songjin Zhang, MD, PhD; Saluja Kanan, MD; Hui Zhu, MD, PhD. Department of Pathology and Laboratory Medicine, University of Texas Health Science Center at Houston.

Context: Uterine adenosarcomas are uncommon malignancies composed of benign epithelial and malignant stromal components. They can have a wide spectrum of clinical and pathologic presentations. Some cases are indolent and can be treated with local excision with preservation of the uterus, while other cases demonstrate aggressive behavior and present as large infiltrative masses and distal metastases. Pathologically, low-grade adenosarcoma can mimic benign polyp, while high-grade cases may demonstrate severe nuclear pleomorphism, high mitotic activity, and show heterologous elements including chondrosarcoma, rhabdomyosarcoma, and liposarcoma components. Diagnosis can be challenging for both low- and high-grade cases. In this study, we retrospectively reviewed 7 cases of uterine adenosarcoma. We summarized clinical presentations, pathologic features, and molecular changes of uterine adenosarcoma.

Design: Seven cases that were originally diagnosed as uterine adenosarcoma during the last 5 years were retrieved from the routine surgical pathology files. Patients’ medical records and all slides, including hematoxylin-eosin and immunohistochemically stained slides, were retrieved and reviewed.

Results: The patients’ ages ranged from 23 to 89 years. Macroscopically, tumors ranged from 4.5 to 19 cm. Microscopically, 2 cases were low-grade adenosarcoma, and 5 cases had sarcomatous overgrowth with high-grade component. A heterologous component was seen in 2 cases. FISH for MDM2 amplification was performed in 5 of these cases, and 2 cases were positive.

Conclusions: Uterine adenosarcoma is an uncommon malignancy that affects patients with a wide age range. A wide spectrum of clinical and pathologic presentations can be seen. MDM2 amplification is present in a subset of uterine adenosarcomas.

Molecular Findings in a Rare Case of Malignant Brenner Tumor

(Poster No. 20)

Lucy Wang, DO (lucy.wang@nyulangone.org); Pratibha S. Shukla, MD. Department of Pathology, New York University Medical Center, New York.

Brenner tumor is an uncommon surface epithelial tumor of the ovary that makes up 1% to 2% of all ovarian neoplasms. It resembles urothelial neoplasms and is thought to arise from Walthard cell rests. Given that malignant Brenner tumors are extremely rare, results of next-generation sequencing on this entity have not been reported. We report a case of a 71-year-old woman who presented with right-sided abdominal pain and heavy vaginal bleeding. Computed tomography revealed a 15 × 10 × 13-cm complex, solid, and cystic mass in the right adnexa. Resection showed a mass that consisted of multilocular cysts with luminal papillary projections and an adjacent solid fibrous area. Microscopic examination showed adjacent benign, atypical proliferative and malignant Brenner tumor components (Figure 14, A). Areas of mucinous microcystic change were noted. The malignant component showed diffuse sheets of tumor cells with highly pleomorphic nuclei and brisk mitotic activity (Figure 14, B). All 3 components showed diffuse immunohistochemical staining for CK7 and GATA-3. Ki-67 stain showed <1% proliferation in the benign component, 5% to 10% in the atypical proliferative component, and >25% in the malignant component. Next-generation sequencing revealed amplification of MDM2 and CCND1 genes. Immunohistochemistry showed nuclear staining for MDM2 in malignant component (Figure 14, C) and nuclear staining for cyclin D1 in atypical proliferative and malignant components (Figure 14, D). Benign Brenner tumor component was negative for MDM2 and Cyclin D1. This case emphasizes new molecular findings in a malignant Brenner tumor that may help guide targeted drug therapy in this rare malignancy.
clinopathologic features and MMR-protein immunohistochemistry expression of AGCT.

**Design:** We retrospectively reviewed 80 AGCT cases of 72 patients, during an 11.5-year period. Age at diagnosis, presenting symptoms, obstetric history, and hormone treatment were assessed. Pathologic features evaluated included tumor size, mitotic index (among others). MMR IHC expression was concomitantly tested.

**Results:** There were 67 primary tumors and 13 recurrences. Mean age was 53.3 years; and median follow-up time, 18 months. Stage distribution was as follows: stage I, 74.6%; II, 3%; III, 14.9%; IIB, 4.5%; IIIA-C, 3%. No loss of MMR expression was seen by immunohistochemistry (50 cases). Nulliparity was associated with an earlier age of onset ($P = .004$) and with a relative risk of 2.4 (1.3–4.6; 95% CI) of developing AGCT before the age of 50 years ($P = .04$). Median tumor size and mitotic count were 7 cm and 3, respectively. Patients on hormonal therapy had a higher median number of mitoses than nontreated patients ($P = .01$); however, no differences in tumor size ($P = .13$) or disease stage ($P = .39$) were seen (Figure 15, A through D).

**Conclusions:** MMR testing might not be useful in patients with AGCT. Nulliparity might be associated with an earlier age of onset. Patients on hormone therapy can present with a high mitotic index, which might not necessarily be indicative of a more aggressive tumor.

**Highly Differentiated Follicular Carcinoma of Ovary: Use of Imprint Cytology at Intraoperative Consultation**

*(Poster No. 22)*

Alice Dobi, MD, PhD (alice.dobi@uphs.upenn.edu); Sun A. Kim, MD; Edward James, MD; Ming Zhang, MD, PhD; Lamzabi Ihab, MD. Department of Pathology, Pennsylvania Hospital, Philadelphia.

Highly differentiated follicular carcinoma of ovary is a rare entity that is known to arise in struma ovari. Clinical presentation and radiologic features mimic other cystic ovarian neoplasms. Morphologically, it does not show features of malignancy typically seen in the thyroid. Thus, intraoperative diagnosis of this entity can be challenging. We hereby report a case of a highly differentiated follicular carcinoma of ovary in a 52-year-old woman who presented with significant abdominal bloating for 3 months. Imaging showed a 12.5-cm left adnexal mixed cystic and solid mass, adhering to the bowel with associated pelvic ascites. The mass was examined intraoperatively and showed multilocular cysts filled with straw or red-brown gelatinous fluid. Microscopically, the tumor consisted of small and large follicles with proteinous material and bland-looking cuboidal cells, suggestive of struma ovari and granulosa tumor cell with extensive cystic changes, while imprint cytology slides showed fluid with focal cracking artifact favoring the former (Figure 16, A). The histology of the ovarian mass in the permanent section resembled goiterous thyroid tissue (Figure 16, B). However, invasion of endocervical stroma, uterine wall, and colonic serosa (Figure 16, C), and presence of tumor nodules in omentum (Figure 16, D), led to the diagnosis of highly differentiated follicular carcinoma of ovary. Notably, intraoperative imprint cytology revealing colloid with cracking artifact is helpful in differentiating struma ovari-associated neoplasm from other tumors of ovary. Owing to the striking resemblance of highly differentiated follicular carcinoma of ovary to benign thyroid goiter, searching for invasive and metastatic foci is crucial for correct diagnosis.

**Case Report of Placental Mesenchymal Dysplasia With Unique Features Related to Gestational Age, Immunohistochemistry Profile, and Cytogenetics**

*(Poster No. 24)*

Damodaran Narayanan, MBBS, PhD (dnarayanan@uwhealth.org); Michael Fritsch, MD, PhD. Department of Pathology and Laboratory Medicine, University of Wisconsin Hospital and Clinics, Madison.

Placental mesenchymal dysplasia (PMD) is a rare abnormality due to androgenetic/biparental mosaicism characterized by an enlarged cystic placenta, patchy cistern-like villi among normal-appearing villi, and abnormal fetal vessels. We present a case of PMD with unique features related to gestational age, p57 staining, and cytogenetics. A 20-week preg
female fetus was delivered stillborn to a 28-year old gravida 3, para 2 mother. At autopsy, the disrupted placenta was extremely large (850 g), with variably sized cysts, and the fetal surface contained abnormally large dilated vessels. Histologic sections revealed dilated, edematous, cellular villi intermixed with normal-appearing villi without trophoblast proliferation, and numerous abnormal fetal blood vessels (Figure 18, A and B). p57 immunostaining in PMD is biphasic where stromal cells of all villous cytotrophoblast cells and maternal decidua (Figure 18, C and D). This staining pattern is consistent with the entire placenta being involved by PMD. In usual cases of PMD, abnormal villi outgrow the more normal villi as gestation progresses, thereby often resulting in fetal demise late in gestation. In this case, the entire placenta was involved at an early gestational age of 20 weeks. Cytogenetic studies revealed heterozygous 17q12 deletion, a chromosomal abnormality not previously identified in PMD. The unique features of this case include p57 staining indicating involvement of the entire placenta by PMD at an early gestation of 20 weeks and associated novel cytogenetic results.

Chronic Histiocytic Intervillositis: A Rare Placental Entity Causing Poor Fetal Outcome
(Poster No. 25)
Erin Gorton, DO (erin.e.gorton.mil@mail.mil); Ashleigh Felpel, DO. Department of Pathology, Madigan Army Medical Center, Tacoma, Washington.

Chronic histiocytic intervillositis of the placenta is a rare and severe form of abnormal maternal immune response to the fetal placenta that can occur in any trimester of pregnancy. One study reports an overall prevalence of 9.6 per 1000 miscarriages and 0.6 per 1000 in second- and third-trimester placentas. It is described as an intervillous infiltrate of maternal mononuclear cells with or without villous and perivillous fibrin deposition. We report the case of a 30-year-old woman G8, P0,1-6-1, presenting at 29 weeks and 6 days with severe fetal growth restriction and abnormal umbilical artery Doppler readings on ultrasonography. Labor was induced and the infant female was born at a weight of 420 g. She was admitted to the NICU and passed away 23 days later. At gross examination, the placenta weighed 141.3 g and had a velamentous cord insertion. Upon sectioning, several placentals infarcts, both recent and remote, and white to pink fibrotic parenchyma were identified throughout the disc. Histologic examination revealed accelerated villous maturation, features of severe early onset placental insufficiency (small for gestational age, accelerated villous maturation, infarctions), perivillous fibrin, and the presence of mononuclear cell infiltrate consistent with chronic histiocytic intervillositis (Figure 19, A). The histiocites in the villous spaces stained positively for CD68 (Figure 19, B). We hypothesize that the patient’s repeated abortions are secondary to previously undiagnosed chronic histiocytic intervillositis in her prior pregnancies.
of crowding of villi appear to show more influence on birth weight than other parameters (Figure 20).

**Conclusions:** This study concludes that villous crowding, DVI, and chorangiosis show statistically significant increased prevalence in GDM placentae compared to normal cases. Birth weight of babies born to GDM mothers was found to be influenced by maximum diameter of placenta, placental volume, and villous crowding. Presence of DVI also influences birth weight to a lesser extent, but negatively.

**Universal Screening of Lynch Syndrome in Patients With Endometrial Carcinoma by Immunohistochemistry: Our Institutional Experience**

(POSTER NO. 28)

Neelima Valluru, MD (neelimavalluru@outlook.com); Xiuzhen Duan, MD. Department of Pathology, Loyola University Medical Center, Maywood, Illinois.

CONTEXT: Lynch syndrome (LS) is a hereditary cancer identified in about 5% of endometrial cancers. Our objective was to examine universal screening of LS in patients with endometrial carcinoma.

DESIGN: Our institution started screening all patients with endometrial cancer for LS from October 2014. We retrospectively reviewed our database for all hysterectomy resections for endometrial cancer from 2014 to 2017 and identified cases with loss of nuclear staining of MMR proteins by IHC. Tumors with dual loss of MLH1/PMS2 were subjected to methylation testing. All nonmethylated cases were subjected for germline mutation testing. All nonmethylated cases were subjected for germline mutation testing.

RESULTS: Among the 4 cases without DNA methylation, 2 patients had a germline mutation test and were confirmed having the test; and 1 patient refused testing. Eight of 10 diagnosed with LS (38-year-old and 69-year-old); the other one is considered having the test; and 1 patient refused testing. Eight of 10 diagnosed with LS (38-year-old and 69-year-old); the other one is considered having the test; and 1 patient refused testing.

**Conclusions:** IHC testing of MMR protein is an effective screening method for LS syndrome patients older than 50 years, based on our experience.

**Applying Amsterdam Criteria to Unsubmitted Term Placentas Identifies Significant Maternal Pathology**

(POSTER NO. 29)

Precious Ann Y. Fortes, MHS* (pfortes@mednet.ucla.edu); Carla Janzen, MD, PhD; Margarida Yun Yong Lei, BS; Teresa Chanlaw, MPH; Sarah H. Choi, BS; Sitram Vangala, MS; Peggy Sullivan, MD, Departments of 1Pathology and Laboratory Medicine, 2Obstetrics and Gynecology, 3Pediatrics, and 4Medicine Statistics Core, David Geffen School of Medicine at University of California Los Angeles.

CONTEXT: Studies that address the value of Amsterdam criteria for placental pathology examination do not exist, to date. The goal of this study was to assess the ability of Amsterdam criteria to identify significant maternal pathology in a cohort of largely discarded placentas.

DESIGN: This is a prospective case-controlled study at a single institution. Subjects were selected on the basis of 3 maternal clinical categories: normal, hypoxic (including ischemic placental disease), and inflammatory (BMI ≥ 30 and any type of diabetes). Amsterdam criteria were applied to all placentas for gross and microscopic review, blinded by clinical history. On the basis of Amsterdam criteria, a pathologic score was assigned to each placenta for both microscopic hypoxic findings and microscopic inflammatory findings. The pathologic scores were correlated with clinical categories, using concordance and logistic regression analyses.

RESULTS: Forty-three term pregnancies with favorable fetal outcomes were prospectively identified from 2017–2018. Of the 43 cases, only 1 placenta was submitted to pathology. Twenty of 43 cases (46.5%) showed agreement between clinical and pathologic categories (P = .06). The microscopic hypoxic score showed near significant positive association with clinical hypoxia (odds ratio = 1.66, P = .08, area under the curve = 0.71) as shown in the Table. The inflammatory score was not significant (P = .72).

**Conclusions:** The study demonstrates that the Amsterdam criteria showed near significant association with hypoxia/ischemic placental disease in a blinded review of discarded placentas. Wider use of Amsterdam criteria may help demonstrate the value of placental examination by pathologists for identifying significant maternal disease. This in turn may help promote greater adherence to CAP placental guidelines for submission to pathology.

**Microscopic Hypoxia Score (0-6)**

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<td>2 (13%)</td>
<td>13 (46%)</td>
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<tr>
<td>1</td>
<td>4 (27%)</td>
<td>8 (29%)</td>
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<tr>
<td>2</td>
<td>6 (40%)</td>
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**Prostatic and Transitional Cell Metaplasia of the Endocervix in a Female to Male Transgender Patient**

(POSTER NO. 30)

James O. Long, MD (james.o.long3.mil@mail.mil); John M. Childs, MD. Department of Pathology, Walter Reed National Military Medical Center, Bethesda, Maryland.

Transitional cell metaplasia is a common occurrence in female to male transgender patients on hormone therapy. We report on a significantly less established association of prostatic gland metaplasia of the endocervix. A 31-year-old female to male transgender patient underwent loop electrosurgical excision procedure for a high-grade squamous intraepithelial lesion diagnosed on routine Papimicroaure smear with inadequate sampling on colposcopy. Cytosmear for human papillomavirus was negative and he had been on testosterone therapy for 10 months before the procedure. A 1.2-cm portion of grossly unremarkable cervix was submitted for histologic examination. The...
metaplasia, as they are mimics of high-grade squamous dysplasia and prostate-specific markers on prostatic metaplasia of the cervix in a patient undergoing a female to male transition. With an estimated 1 million adult transgender patients in the United States, it is important to recognize the changes of atrophy, transitional cell, and prostatic metaplasia, as they are mimics of high-grade squamous dysplasia and glandular atypia.

First Case Report of Concurrent Hotspot P. D1709N and Splice Site Mutations in DICER1 Gene in a Patient With an Unclassified Sex Cord–Stromal Tumor

(Xiaoyan.Huang@downstate.edu; Yang Liu, MD; Raavi Gupta, MD; Ning Neil Chen, MD, PhD. Department of Pathology, SUNY Downstate Medical Center, Brooklyn, New York.)

Ovarian sex cord–stromal tumor, not otherwise specified (OSCST-NOS), presents a diagnostic challenge owing to its vast heterogeneity. It lacks both specific morphologic features and hallmark genetic aberrations. DICER1 hotspot p. D1709N mutation is commonly associated with Sertoli-Leydig cell tumor. We report an OSCST-NOS with a novel DICER1 splice site c. 2256+1G->A mutation in addition to the hotspot mutation. The patient was a 28-year-old woman diagnosed with OSCST-NOS 2 years prior. She received 6 cycles of chemotherapy and later presented with recurrent pelvic masses and subsequently underwent tumor resection. Strong morphologic similarity was observed between the primary and recurrent tumors. Tumor cells are round and monotonous with mainly solid growth pattern. The nuclei are round, and cytoplasm is eosinophilic or clear. Immunohistochemical staining shows that tumor cells are strongly positive for inhibin, WT1, and CD56; moderately positive for CD10 and cyclin D1; weakly positive for CAM 5.2 and AE1/3; and negative for Calretinin, Synaptophysin, Chromogranin, PLAP, Myogenin, MSA, and S100. Next-generation sequencing from CARIS reveals that DICER1 gene of the tumor cells shows p. D1709N and c. 2256+1G->A mutations. The mutation frequencies are 49% and 47%, respectively. To the best of our knowledge, this current case is the first reported OSCST-NOS that harbors the c. 2256+1G->A DICER1 mutation, which is affecting messenger RNA splicing (human splicing finder, version 3.1) and may have additive effect to tumorigenesis with the hotspot p. D1709N mutation. These 2 concurrent mutations may contribute to this tumor’s unique morphology.

Negative Cervical Biopsies in a Setting of a Concurrent Pap Smear Showing High-Grade Intraepithelial Lesions or Adenocarcinoma: Should We Be Doing More? A 2-Year Institutional Experience

(Jinhong Hu, MD, PhD (jih001@ucsd.edu); Mariah Leivo, MD; Andres Roma, MD; Oluwole Fadare, MD; Somaye Zare, MD; Farnaz Hasteh, MD. Department of Pathology, University of California, San Diego.)

Context: The diagnosis of high-grade intraepithelial lesions (HSILa) on Pap smears leads to diagnostic excisional procedures, and further intervention is determined by histopathologic diagnosis. The general recommendation for negative biopsy with concurrent HSIL on cytology is close follow-up with colposcopies with/without excisional procedures.

Design: A computer-based search of our archives identified 154 cases of cervical biopsies with concurrent cytology specimen showing HSIL or
adecarcinoma. The cervical biopsies with discordant results from the cytology specimen were reviewed by at least 2 pathologists and further analyzed with deeper-level sections and p16 immunostaining.

**Results:** Sixty-eight percent (104/154) of biopsies showed concordant cytologic results in which 86% (90/104) were CINI/III or squamous cell carcinoma and 14% (14/104) were adenoecarcinoma. However, 22% (32/154) showed discordant biopsy results, in which (1) 62% (31/50) were positive for both initial and deeper-level sections and p16 immunostaining; (2) 16% (8/50) showed inconclusive results, eg, mucous or endometrial tissue; and (3) 22% (11/50) showed benign cervical biopsies without further workup. These benign cases were reexamined (using deeper-level sections, p16 immunostaining, and consensus by at least 2 pathologists) and 27% (3/11) showed high-grade dysplasia. Overall, when deeper-level section and/or p16 immunostaining were used on supposedly benign biopsies, underlying dysplasia was revealed in 47% (28/59) of cases.

**Conclusions:** We propose that concurrent negative surgical specimens of Pap smears showing HSIL should be further evaluated with consensus review, deeper-level sections, and/or p16 immunostaining. Routine incorporation of these practices in the described clinical scenario may ultimately prevent underdiagnoses of HSIL on cervical biopsies.

**Sarcomatoid Differentiation of Adult Granulosa Cell Tumor of Ovary**

(Poster No. 34)  
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Adult granulosa cell tumors (AGCTs) are rare and constitute less than 5% of all ovarian neoplasms. Sarcomatoid differentiation in AGCT is a less common presentation and is frequently mistaken with other sarcomas in ovarian and extraterraneal sites. We report a case of a 51-year-old woman with a right adnexal mass who underwent total hysterectomy with bilateral salpingo-oophorectomy. The right ovary presented with AGCT component and single cells in the fibroma component.

**40% to 70%** in the GCT and AGCT component, 15%). The mitotic rate in the granulosa cell tumor component was high (30-50 mitotic figures per 10 high-power fields). Immunohistochemistry showed patchy positivity for inhibin and calretinin, stronger in the granulosa cell tumor component. Ki-67 was 40% to 70% in the GCT and <5% in the fibroma. Reticulin immunostain was positive in the fibers around nests of tumor cells in the AGCT component and single cells in the fibroma component. Desmin and smooth muscle actin (SMA) showed focal and patchy positivity, respectively. WT1 was negative. AGCT presenting with sarcomatoid variant can present as fusiform to spindled cells arranged in a haphazard way, mimicking sarcomas. Clues to distinguish this entity from sarcomas include presence of nuclear grooves, haphazard architecture, high mitotic rate, presence of admixed theca and luteinized cells, and minimal squamoid differentiation. Immunohistochemistry showed positivity for inhibin and calretinin, partial loss of reticulin staining around spindle cells.

**Mesonephric-like Adenocarcinoma of the Uterine Corpus: A Case Report With Molecular Analysis**

(Poster No. 35)  
Theresa Spivey, MD1 (Theresa.Spivey@UHospitals.org); Brian Richardson, BSc2; Xiaohua Yang, PhD3; Michael Cartwright, MSc2; Mark Cameron, PhD2; Christina Bagby, DO1; Raymond Redline, MD1; Steven Waggoner, MD2; Sanjita Ravishankar, MD2; Stefanie Avril, MD3. Departments of 1Pathology and 2Obstetrics & Gynecology, Case Western Reserve University School of Medicine and University Hospitals Cleveland Medical Center, Cleveland, Ohio; 3Department of Population and Quantitative Health Sciences, Case Western Reserve University School of Medicine and Case Comprehensive Cancer Center, Cleveland, Ohio.

Mesonephric adenocarcinoma is a rare gynecologic malignancy primarily arising in the uterine cervix. Mesonephric-like Mullerian adenocarcinoma represents a newly recognized subset of endometrial carcinoma that has morphologic, immunophenotypic, and molecular overlap with mesonephric adenocarcinoma, while also showing evidence of Mullerian origin. We present a case of a mesonephric-like uterine adenocarcinoma initially diagnosed as Federation of Gynecology and Obstetrics (FIGO) grade 1-2 endometrioid carcinoma on biopsy, along with immunohistochemical and molecular studies. A 65-year-old woman presented with postmenopausal bleeding and thickened endometrium. Biopsy and subsequent hysterectomy were performed. A 2.1 cm exophytic mass involving endometrial cavity and fundus was identified, showing inner half with myometrial invasion, and a combination of ductal and papillary growth patterns. Lymphovascular invasion was present without involvement of 8 pelvic sentinel lymph nodes. Immunohistochemistry showed intact mismatch-repair proteins, wild-type p53, absence of estrogen and progesterone receptor, diffuse GATA-3, patchy TTF-1, and negative WT-1, CD10, calretinin. Overall, findings were consistent with a FIGO-stage IA mesonephric-like Mullerian adenocarcinoma. From the limited literature on this entity, we sought to compare the molecular alterations of this carcinoma with a previously analyzed cohort of endometrial carcinomas (n = 51). Whole-transcriptome RNA sequencing demonstrated that our case shared transcriptomic features with a subcluster of endometrioid, serous, undifferentiated carcinomas, and carcinosarcomas, and with “copy-number-high” and “copy-number-low” molecular subtypes. DNA sequencing is ongoing. Our findings of overlapping transcriptomic features between mesonephric-like adenocarcinoma and various histologic and molecular subtypes of endometrial carcinoma further support the proposed Mullerian origin. Additional studies are warranted to define the prognosis of this newly recognized endometrial carcinoma histotype.

**Uterine Sarcoid-like Granulomatous Reaction in Association With Combination Ipilimumab and Nivolumab Therapy**

(Poster No. 36)  
Akriti Gupta, MBBS, MD1 (akge2@virginia.edu); Elisheva Shanes, MD2; Kathie L. Hullfish, MD3; Linda R. Duska, MD2; Helen P. Cathro, MBChB. Departments of 1Pathology and 2Obstetrics & Gynecology, University of Virginia, Charlottesville.

Immunotherapy targeting checkpoint inhibitors has become standard of care for an increasing number of tumors. Combination therapy with CTL-4 (Ipilimumab) and PD-1 (Nivolumab) checkpoint inhibitors is approved for patients with metastatic melanoma. A 52-year-old woman presented with postmenopausal bleeding having been on this regimen for 11 months to treat stage IV metastatic melanoma. Examination revealed a prolapsed uterus, and imaging showed a uterine mass suggestive of a leiomyoma with a normal endometrial stripe. The patient underwent vaginal hysterectomy and pelvic floor repair. Gross examination of the hysterectomy specimen was unremarkable except for a myometrial nodule, which on histologic examination proved to be a leiomyoma. Microscopic examination of the endomyometrium revealed extensive involvement of the myometrium by well-defined, nonnecrotizing granulomas with associated pale eosinophilic acellular debris. A presumptive diagnosis of a sarcoid-like granulomatous reaction was made, and an association with ongoing immunotherapy was suggested. This was supported by the patient’s recent history of biopsy-proven distal esophagitis, which is a reported upper gastrointestinal side effect of immunotherapy. Granulomatous inflammation is a rare but recognized immune-related adverse event associated with immune checkpoint inhibitor therapy. Systemic and localized granulomatous inflammation within the lung, skin, and spleen has been previously described. This is the first report of this finding in the uterus. It underscores one of the systemic side effects of these drugs and contributes to a more complete enumeration of potential reactions to cancer immunotherapy.

**Ki-67 Labelling Index in Exaggerated Placental Site: A Need for Careful Interpretation**

(Poster No. 37)  
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Exaggerated placental site (EPS) is a rare, benign gestational trophoblastic disease derived from exuberant infiltration of the myometrium by implantation-site intermediate trophoblast, or a failure of the regression of implantation over time. While EPS poses no increased risk of persistent gestational trophoblastic disease, its
malignant counterpart, placental site trophoblastic tumor, is often chemoresistant with reported cases of metastasis. As both lesions share a similar immunohistochemical profile, a critical differentiating criterion is the Ki-67 labelling index: Ki-67 is typically less than 1% in EPS and greater than 8% in placental site trophoblastic tumor. We report the case of a 30-year-old woman presenting with persistent vaginal bleeding, postmenopausal bleeding, and pain with intercourse for complete molar pregnancy. Serum β-human chorionic gonadotropin level was markedly elevated, and transvaginal ultrasonography showed findings consistent with gestational trophoblastic disease. Hysterectomy with bilateral salpingectomy revealed a 2.1-cm tan-red ill-defined endometrial lesion. Histologic examination revealed single markedly atypical cells permeating the myometrium, with accompanying inflammatory cells. These tumor-like cells were positive for HPL, B-HCG, and GATA3, and negative for p63 and PLAP. At low-power magnification, Ki-67 staining appeared to show an increased proliferative index, but examination at higher magnifications demonstrated predominant staining of inflammatory cells with tumor-like cells largely negative (<1%). These findings were overall consistent with a diagnosis of EPS. The patient required no further treatment and remained asymptomatic at follow-up 7 months later. This case highlights the critical need for careful interpretation of the Ki-67 labelling index, in addition to histologic and immunophenotypic features, when evaluating EPS.

Relapse of Primary Diffuse Large B-Cell Lymphoma of the Central Nervous System to the Gynecologic Tract

(Poster No. 38)

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Primary diffuse large B-cell lymphoma (DLBCL) of the central nervous system (CNS) is a distinct form of aggressive B-cell non-Hodgkin lymphoma, which infrequently disseminates outside of the CNS. We report an unusual case of primary DLBCL of the CNS, which disseminated to the gynecologic tract. Two years after treatment of her lymphoma with chemoradiation therapy followed by autologous stem-cell rescue, this 63-year-old postmenopausal woman presented with vaginal bleeding. Clinical evaluation revealed a 12-cm friable mass extending from the left wall of the vagina. A biopsy of the mass showed diffuse infiltration of squamous mucosa by abnormal mononuclear cells, associated with necrosis, hemorrhage, and focal ulceration. Cytologically, the infiltrate comprised medium-to-large cells with round nuclei, vesicular chromatin, prominent nucleoli, and scant cytoplasm. By immunohistochemistry, these cells were monoclonal (κ restricted), EBV-negative B cells with a high Ki-67 proliferation index and a non-germinal-center phenotype. FISH studies demonstrated no rearrangements of MYC, BCL2, or BCL6. Immunoglobulin heavy chain gene rearrangement studies were performed on the patient’s initial primary DLBCL of the CNS and her newly diagnosed lymphoma. In both specimens, a PCR product of 260 nucleotides was amplified, suggesting a clonal relationship. In addition, a novel PCR product of 325 nucleotides was amplified from the vaginal lymphoma, which was not present in her CNS lymphoma, raising the possibility of secondary genetic alterations acquired after her initial diagnosis with primary DLBCL of the CNS. This case should heighten awareness of the ability of primary DLBCL of the CNS to disseminate beyond the CNS.

Human Papilloma Virus Associated With Giant Genital Seborrheic Keratoses

(Poster No. 39)

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A 56-year-old woman was referred to our gynecology department for pelvic organ prolapse with multiple skin masses on the external genitalia and groin. Physical examination demonstrated 4 exophytic verrucous and partially pigmented masses on the mons pubis (5.0 × 3.0 cm), right labium major (4.5 × 3.0 cm), left labium major (2.5 × 1.0 cm), and left groin (4.5 × 3.5 cm) with no fistula or abscess formation. Papanicolaou smear result of a year ago was normal. All skin lesions were completely excised during transvaginal hysterectomy, anterior and posterior enterocoele repair, and vaginal vault suspension. The differential diagnoses included verrucous carcinoma/Buschke-Loewenstein tumor, invasive squamous cell carcinoma, condyloma lata, and condyloma acuminatum. Histopathology review of the skin masses demonstrated giant irritated seborrheic keratosis (SK) with papillomatosis/verruciform features. Focal viral cytopathic changes were present. Extensive histopathology evaluation did not detect high-grade squamous dysplasia or squamous cell carcinoma. Human papillomavirus (HPV) DNA testing on formalin-fixed, paraffin-embedded tissue by polymerase chain reaction detected low-risk HPV DNA (6/11). HPV has been detected in anogenital lesions with histologic features of SK that include horizontal orientation, horn pseudocysts without cytopathic koliocytic changes. HPV DNA has been reported to be present in about 40% of SK-like lesions from the genital area. In dermatology, per Dr Ackerman’s recommendation, SKs that contain HPV are considered a form of condyloma acuminate. Gynecologists, general surgeons, and surgical pathologists need to be aware of the association of HPV with SK in the genital area, which may be quite large and extensive.

Novel Driver Mutation of YWHAE Gene Amplification Identified in High-Grade Endometrial Stromal Sarcoma

(Poster No. 40)

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Endometrial stromal sarcoma (ESS) is a rare malignant uterine tumor that arises from endometrial stroma. The World Health Organization separates ESS into low-grade (LG-ESS), high-grade (HG-ESS), and undifferentiated uterine sarcoma (UUS). LG-ESS resembles proliferative phase endometrial stroma and tends to show intravascular growth and myometrial invasion with characteristic JAZF1/SUZ12/EPC1/PHF1 rearrangements. UUS is a tumor with marked cytologic atypia, nonspecific differentiation, and complex chromosomal abnormalities, and is a diagnosis of exclusion. HG-ESS presents with high-grade cytologic features and harbors a t(10;17) YWHAE-NUTM2 fusion rearrangement. Recently, a group of ESSs harboring BCOR aberrations has been described, either ZC3H7B-BCOR rearrangement or internal tandem duplications in the last exon. We present a case of a 66-year-old woman with an enlarged uterus, and computed tomography scan showing a heterogeneous solid and cystic lesion diffusely infiltrating the myometrium. Grossly, a yellow-white well-circumscribed whorled mass was present with focal areas of hemorrhage and necrosis, surrounded by tan-red gelatinous, slightly friable necrotic parenchyma (Figure 23, A). Histologically, the tumor showed tongueslike destructive myometrial invasion composed of haphazard fascicles with variably cellular areas. There was prominent pleomorphism and high mitotic activity (Figure 23, B and C). Immunohistochemistry showed a patchy subset of CD10 and in majority cyclin-D immunopositivity within the tumor (Figure 23, D). FISH studies were performed, evaluating the t(10;17) translocation characteristic of HG-ESS. Interestingly, YWHAE amplification was identified without rearrangement of the YWHAE locus. Nevertheless, we conclude that owing to morphologic and immunohistochemical findings, this amplification supports the diagnosis of high-grade endometrial stromal sarcoma. This represents an
Choriocarcinomatous Differentiation as a Mimic of High-Grade Serous Carcinoma: A Diagnostic and Immunohistochemical Pitfall

(Poster No. 41)

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Choriocarcinoma is a malignant neoplasm of syncytiotrophoblast, cytotrophoblast, and intermediate trophoblastic cells, most commonly presenting as a gestational-type tumor or in association with a germ cell tumor. There have been few reported cases of high-grade endometrial and serous carcinoma with choriocarcinomatous differentiation, since first described in 1972. Given the overlap in immunohistochemical staining, particularly with p53 and p16, choriocarcinomatous differentiation can be mistaken for high-grade serous carcinoma. We report a case of a 59-year-old woman with increased vaginal discharge and a 3.9-cm solid-appearing mass in the endometrial cavity. Both the endometrial biopsy and hysterectomy showed a high-grade endometrioid carcinoma. However, a separate, poorly differentiated, sheetlike population of cells with marked cytologic atypia, significant pleomorphism, and multinucleation was also identified (Figure 24, A). Immunohistochemical staining revealed diffuse nuclear overexpression of p53 and strong diffuse p16 staining in the poorly differentiated component, and wild-type expression of p53 (Figure 24, B) with patchy p16 expression in the endometrioid carcinoma. Given the immunoprofile and severe atypia, the tumor was initially interpreted as a mixed endometrioid and serous carcinoma. Additional review of the histomorphology with human chorionic gonadotropin immunohistochemical staining (Figure 24, C) classified the “serous” component as a choriocarcinomatous differentiation of the endometrioid tumor. Non-gestational choriocarcinoma is a highly aggressive trophoblastic tumor. Somatic choriocarcinomatous differentiation should be maintained in the differential diagnosis of high-grade carcinomas with marked cytologic atypia, multinucleation, and an immunoprofile suggestive of high-grade serous carcinoma, to expand therapeutic options with programmed death-ligand 1 (PD-L1) immunotherapy.

Malignant Transformation of Leiomyoma to Aggressive Leiomysarcoma After 20 Years and Genetic Comparison of Malignant Transformation by Single Nucleotide Polymorphism Microarrays and Targeted Mutational Analysis

(Poster No. 43)

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A 45-year-old woman underwent total transabdominal hysterectomy for symptomatic uterine fibroids. Histologic examination of the uterus with attached cervix was unremarkable, and the separate 13 × 8.8 × 6-cm fibroid revealed an atypical leiomyoma with an increased mitotic rate of 6 to 7 mitoses/10 high-power fields. The patient presented 20 years later with diffuse nodules ranging from 2 to 12 cm throughout the peritoneum, which was surgically removed and histologically classified as an aggressive leiomyosarcoma. Single nucleotide polymorphism microarray demonstrated complex genomic alterations that were shared between both samples, demonstrating the leiomyosarcoma developed from the atypical leiomyoma from 2 decades earlier. This malignant transformation can be attributed, at least in part, from the later genetic aberrations, including mosaic losses at 5q23q26.2, 8p23.3p11.23, 14q21.3q31.1, mosaic gains of 1q21.1q44 and 21p11.2q22.3, amplification of 8p11.23q24.3, and total loss of chr18. Interestingly, a review of the literature reveals another case of leiomyosarcoma malignant transformation to leiomyosarcoma that only shared del(14q), making this a

An Unusual Cervical Smooth Muscle Tumor With Rhabdoid Morphology and Perinucleolar Haloes

(Poster No. 42)

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Cervical smooth muscle tumors are rare, although leiomyosarcoma is the commonest malignant mesenchymal cervical tumor. Diagnostic criteria are lacking for cervical smooth muscle tumors of uncertain malignant potential (STUMP). Their morphology overlaps with unusual-appearing leiomyomas found in fumarate hydratase (FH)–deficient, hereditary leiomyomatosis and renal cell cancer (HLRCC) syndrome. This predisposes index cases and their families to an aggressive form of papillary RCC that includes intracytic papillary and tubulocystic areas, and orangophilic macronucleoli with perinuclear halos. A 37-year-old woman had a new Papanicolaou smear with atypical squamous cells of undetermined significance, despite negative high-risk HPV testing and 4 prior negative smears. At colposcopy, 2 distinct cervical tumors were grossly consistent with leiomyomas. Microscopically, the 2.8-cm tumor was a leiomyoma. The other 2.5-cm tumor demonstrated marked anisonucleosis, extremely large reddish nucleoli, chromatin clearing, focal rhabdoid features, and 3 mitotic features per 10 high-power fields (Figure 25). IHC stains demonstrated positive staining for desmin and MSA. INI-1 had intact nuclear staining. HMB-45, S100, Melan-A, myoglobin, cyclin D1, EMA, and Myo-D were negative. The differential diagnosis included an atypical epithelioid leiomyoma and a smooth muscle tumor suggestive of FH gene mutation; however, IHC for FH was diffusely positive. The tumor was therefore interpreted as an epitheloid STUMP. On follow-up cervical biopsy, no squamous lesion was found. It was important to exclude an FH-mutant leiomyoma because of the implications for both the patient and her family. Given the uncertain prognosis of the epithelioid STUMP at this location, the patient was referred for oncologic follow-up.
Gonadoblastoma Involving Bilateral Ovaries in a Patient With Swyer Syndrome

(Poster No. 44)

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Gonadoblastoma is an uncommon tumor occurring almost exclusively in patients with disorders of sex development, who have either molecular evidence of a Y chromosome. Phenotypically, 80% of patients with gonadoblastoma are females and 20% are males. Gonadoblastoma per se does not demonstrate invasive behavior; however, 50% of the specimens demonstrate evidence of local overgrowth by the germinal component, and approximately 10% of these germinomas have demonstrated metastases. Additionally, the rate of contralateral disease for all patients is substantial at 36%. We present a case of bilateral gonadoblastoma with a minor dysgerminoma component in a 17-year-old phenotypically female patient with primary amenorrhea. Significant clinical findings were mild clitoromegaly, nonpalpable ovaries, and ultrasonographic evidence of bilateral streaked gonads. FISH study demonstrated 46XY karyotype. Prophylactic bilateral salpingo-oophorectomy was performed. Histologic sections showed primitive germ cells and sex cord–stromal cells surrounded by ovarian-type stroma and nests of dysgerminoma-like germ cells and sex cord derivatives resembling immature Sertoli and granulosa cells with extensive calcification and hyalinization. Immunohistochemical stains in dysgerminoma demonstrated immunoreactivity for PLAP, CD117, and OCT3/4, while sex cord–stromal component demonstrated immunoreactivity for inhibin and calretinin. The pathologic diagnosis of gonadoblastoma can be challenging; it is often misdiagnosed as a nonepithelial germ cell tumor. Only a few cases of nonepithelial germ cell tumors have been reported in patients with gonadoblastoma. Given the significant association of a dysgerminoma component with gonado-blastoma, extensive bilateral sampling is imperative to evaluate and document the evidence or lack of a dysgerminoma component.

High-Grade Müllerian Adenosarcoma Without Sarcomatous Overgrowth: Report of 2 Cases

(Poster No. 45)

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Mullerian adenosarcoma (MAS) is an extremely rare neoplasm that typically arises in the endometrium as well as extrapelvic sites. Histologically, adenosarcoma is composed of benign epithelium and malignant stroma akin to phyllodes tumor of the breast. The cytology of the stromal component is typically low grade, resembling endometrial stroma. Sarcomatous overgrowth (SO) comprising pure sarcoma occupying at least 25% of the tumor may show a high-grade cytologic atypia. Myometrial invasion and SO are the only features associated with poor prognosis. Marked cytologic atypia (CA) in the stromal component without SO is rare and prognosis is unclear. We report 2 cases of MAS with high-grade nuclei without SO: (1) a 62-year-old woman, with a polypoid cervical mass and an abnormally thickened and complex endometrium on imaging, had a hysterectomy; and (2) a 48-year-old woman with a uterine serosal mass intraoperatively had a hysterectomy. The tumors in both patients had similar morphology with benign-appearing endometrial glands and malignant stroma, periglandular cuffing of stromal cells, and frequent mitoses, consistent with MAS. The malignant stromal component showed marked CA. SO was not seen in either patient. Neither patient had evidence of disease 6 and 52 months after diagnosis. Current recommendation in MAS without SO is to report the stromal component as “low-grade” or “high-grade,” based on CA, as anecdotial evidence suggests that even small focus of “high-grade” sarcoma may result in an adverse behavior. In our cases, high-grade CA does not seem to alter behavior (Figure 27).
Neurofibromas are uncommon within the oral cavity and rarely affect the tongue.

**Design:** Eleven cases of lingual neurofibroma were retrospectively reviewed from the files of Southern California Permanente Medical Group hospitals. Morphologic features, immunohistochemical characteristics, and outcome data were analyzed.

**Results:** The study group included 7 females and 4 males ranging in age from 30 to 84 years (mean, 61). Most lesions presented as a painless lingual mass or swelling localized to the posterior or base of the tongue. None of the patients had neurofibromatosis 1 (NF1). All tumors were solitary, unencapsulated, ill-defined nodules characterized microscopically by loosely arranged spindle cells with wavy nuclei in a collagenous to myxoid stroma. A pleomorphic pattern of growth was observed in 1 case. Mitotic activity was inconspicuous. Nuclear atypia and hypercellularity were absent. By immunohistochemistry, the lesional spindle cells were strongly immunoreactive for S100 protein in all tumors evaluated (10/10). Treatment consisted of local excision in all cases. There have been no recurrences during clinical follow-up (range, 17–79 months; mean, 38.7 months).

**Conclusions:** Neurofibromas of the tongue are exceptionally rare and should be distinguished from other neural and spindle cell neoplasms that can arise at this anatomic site. They seem to occur as sporadic, solitary lesions, unassociated with NF1. Lingual neurofibromas follow a benign clinical course without risk of recurrence.

**Schwannaoma of the Tongue: A Clinicopathologic Study of 16 Cases**

(Poster No. 49)

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**Context:** First described by Verocay, schwannoma is a benign, encapsulated peripheral nerve sheath tumor, typically composed of cellular Antoni A and loose myxoid Antoni B areas. While commonly encountered in the head and neck region, schwannoma involving the tongue is extremely rare. Here we present a series of 16 examples of lingual schwannomas.

**Design:** Sixteen cases of schwannomas affecting the tongue were retrospectively reviewed from the files of Southern California Permanente Medical Group hospitals. Clinical characteristics, morphologic features, immunohistochemical characteristics, and outcome data were analyzed.

**Results:** The study group included 10 males and 6 females ranging in age from 12 to 80 years (mean, 32.5). Most were painless or slowly growing lingual mass. Length of symptoms ranged from 5 to 63 months (mean, 14.4) with lesions ranging from 0.3 to 3.1 cm (mean, 1.1). Of the 16 cases, 10 were located on the anterior two-thirds, 5 involved the posterior or base of tongue, and 1 was unspecified as to location. The tumors were well circumscribed and characterized with typical histologic features for schwannoma. By immunohistochemistry, the lesional cells were strongly immunoreactive for S100 protein in all cases evaluated (11/11). Other various immunohistochemical markers tested negatively in few selected cases. There have been no known recurrences to date, with clinical follow-up information available for all patients (range, 1–96 months; mean, 32.8).

**Conclusions:** Lingual schwannomas are uncommon and should be differentiated from other spindle cell neoplasms occurring at this site. Schwannomas of the tongue are benign lesions without risk of recurrence.

**Spindle Cell Lipoma Arising From the Parapharyngeal Space: A Rare Location**

(Poster No. 50)

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Spindle cell lipoma is a relatively uncommon benign tumor that accounts for approximately 1.5% of adipocytic neoplasms, which usually arises from the posterior neck, shoulder, and back of adult males (90% of all cases) in their 40s to 60s. We present a case of a 27-year-old woman who consulted for an 8-month history of globus
sensation and subsequent development of dysphagia. A magnetic resonance imaging was performed, and this showed a 3.0 × 2.7 × 2.5-cm, well-circumscribed, right parapharyngeal mass with high signal intensity on T2-weighted imaging, which produced a mass effect on the oropharyngeal wall and narrowed considerably the airway lumen to about 8 mm (Figure 29, A). The patient underwent complete resection of the mass via a transoral approach without any complication. Histologic analysis revealed a neoplasm composed of bland spindle cells surrounded by a variably myxoid stroma and ropey collagen bundles, with mast cells and a limited component of mature adipocytes (Figure 29, B), focally involving a minor salivary gland (Figure 29, C). Immunohistochemical stains were diffusely positive for CD34 (Figure 29, D), but negative for myosin, SMA, cytokeratin AE1/AE3, CD56, claudin, MUC4, GLUT1, p53, p63, SOX10, EMA, and S100. Loss of Rb expression was also noted. These findings were consistent with a spindle cell lipoma focally compromising a minor salivary gland in the parapharyngeal space. It is relevant to note that the diagnosis of this tumor can be challenging, especially when it arises in atypical locations oropharyngeal wall and narrowed considerably the airway lumen to about 8 mm (Figure 29, A). The patient underwent complete resection of the mass via a transoral approach without any complication. Histologic analysis revealed a neoplasm composed of bland spindle cells surrounded by a variably myxoid stroma and ropey collagen bundles, with mast cells and a limited component of mature adipocytes (Figure 29, B), focally involving a minor salivary gland (Figure 29, C). Immunohistochemical stains were diffusely positive for CD34 (Figure 29, D), but negative for myosin, SMA, cytokeratin AE1/AE3, CD56, claudin, MUC4, GLUT1, p53, p63, SOX10, EMA, and S100. Loss of Rb expression was also noted. 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These findings were consistent with a spindle cell lipoma focally compromising a minor salivary gland in the parapharyngeal space. It is relevant to note that the diagnosis of this tumor can be challenging, especially when it arises in atypical locations.
Ameloblastic Carcinoma With Squamous Differentiation Arising From an Odontogenic Cyst

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Ameloblastic carcinoma accounts for approximately 2% of all odontogenic neoplasms. It can originate de novo or from a preexisting ameloblastoma. Only 2 cases of ameloblastic carcinoma originating from an odontogenic cyst have been reported in the English literature. We present a case of ameloblastic carcinoma with squamous differentiation arising from an odontogenic cyst. A portion of the cyst’s lining resembled the poorly differentiated component of this tumor, but focally showed a squamoid and bland odontogenic appearance. The diagnosis of ameloblastic carcinoma with squamous differentiation arising from an odontogenic cyst was rendered. Owing to the rarity of ameloblastic carcinoma, this report provides useful insight into the varied morphologic features of this entity, such as squamous differentiation. In addition, it supports the hypothesis that ameloblastic carcinoma can arise from a benign odontogenic cyst.

Salivary Duct Carcinoma of the Parotid Masquerading as Primary Cutaneous Neoplasm

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Problem in the recognition of salivary gland tumors is a reflection of the number, diversity, and morphologic complexity of this group of neoplasms. We present the case of a 76-year-old man with a history of cutaneous squamous cell carcinoma, and prostatic adenocarcinoma. The patient reported a nontender firm nodule at the left postauricular area that had been growing for several weeks. Clinically, the lesion was believed to be a calcified epidermal inclusion cyst, but a biopsy was performed to address the possibility of a metastasis from the prostate. Histology revealed a tumor composed of cords and ducts of malignant epithelial cells with eosinophilic cytoplasm, vesicular nuclei, and prominent nucleoli. The cells infiltrated the dermis but did not show connection to the overlying skin. The differential diagnosis included a primary cutaneous carcinoma, a metastasis from the prostate, and a primary parotid carcinoma with extension into the skin. Further workup located a small midline mass in the nasal turbinates. Microscopically, the primary tumor was hypercellular with sheets of primitive-appearing small round cells. Scattered foci of keratinization and glandular structures mingled with the small round cell component. Mitoses and necrotic cells were numerous. Mucicarmine was positive in scattered glands. At this point in the workup, the differential diagnosis included sarcomas such as synovial sarcoma, malignant peripheral nerve sheath tumor, and rhabdomyosarcoma, as well as metastatic adenocarcinoma. Immunohistochemical staining was performed to address the possibility of a metastasis from the prostate. Tumor cells lacked expression of NUT-1, desmin, Melan-A, S100, synaptophysin, SOX10, EBER, EWSR1, FLI1, calretinin, NKX2.2, and retained SMARC B1 and SMARCA4 expression. CancerTYPE ID testing results reported a 90% probability of synovial sarcoma. Foundation One testing revealed an SHH mutation and low mutation burden. He was treated with radiation, cisplatin, and pembrolizumab therapy with rapid marked reduction in tumor burden and symptoms. In summary, we present a rare case of a salivary duct carcinoma with molecular findings and short-term follow-up.
from the superficial lobe of the parotid with secondary extension into the overlying dermis. This case represents a pitfall in diagnosing salivary gland tumors as primary cutaneous neoplasm because of similar histogenesis and close proximity of those entities.

**HPV- Small Cell Carcinoma Arising in the Lingual Frenulum With Liver Metastases: Presentation of a Rare Case**

(Poster No. 57)

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Small cell neuroendocrine carcinomas (SNECs) of the head and neck are uncommon neoplasms typically found in the larynx, salivary glands, and sinonasal areas. Occurrence in the oral cavity is extremely rare with fewer than 15 cases in the world. We report a case of a 60-year-old woman, a tobacco user, who was discovered to have an incidental multilobular mass (2.0 cm) in the right lingual frenulum during a routine workup for pneumonia. The mass was biopsied, revealing a high-grade neoplasm growing in infiltrative nests and lobules consisting of small/medium-sized cells with high nuclear to cytoplasmic ratio, nuclear molding, hyperchromasia, inconspicuous nucleoli, and necrosis. Foci of “pagetoid” intraepithelial neoplastic cells in the overlying mucosa were observed. No squamous or glandular differentiation was identified. The immunohistochemical profile showed positive staining for AE1/AE3, TTF-1, chromogranin, synaptophysin, and CD56, with a proliferative index (Ki-67) of nearly 100%. Of note, confluent p16 staining was observed and subsequent testing for HPV E6/E7 RNA in situ hybridization was confirmatory. Immunostains were negative for CK-20, p40, and S100. Lymphovascular invasion and E6/E7 RNA in situ hybridization was confirmatory. Immunostains were used in selective cases to confirm the metastatic nature of the tumor and rule out a primary malignancy.

**Secondary Head and Neck Mucosal Sites From Various Primary Malignant Neoplasms**

(Poster No. 58)

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Context: Secondary head and neck mucosal tumors are rarely encountered in clinical practice and may be confused clinically, radiographically, or pathologically with a primary neoplastic process. We undertook a retrospective study to assess the clinical and pathologic characteristics of these neoplasms.

Design: Department of pathology archives from 1994 to 2018 were searched for a diagnosis of tumor metastasis to head and neck mucosal sites. A review of patient medical records and pathology data from our institution was performed.

Results: Thirty-seven cases of metastasis were identified (males, n = 20). Twenty-four of the 37 cases (65%) were epithelial carcinoma of parotid with the liver being the sole site of isolated metastasis to the liver bypassing lung is very unusual and thought to be by way of lymphovascular spread. A 73-year-old man presented to our institution with recurrent right facial nerve paralysis. A right parotid mass was discovered and fine-needle aspiration showed adenoid cystic carcinoma. Preoperative imaging workup for metastatic disease revealed a solitary liver lesion with central necrosis. No other suspicious metastatic foci were identified. A radical right parotectomy followed by a left hepatectomy were performed, demonstrating low-grade adenoid cystic carcinoma with extraglandular extension, perineural and lymphovascular invasion, 25 negative lymph nodes, and a metastatic focus in the liver consistent with pT4aN0M1 disease. Postoperative chemotherapy and radiation therapy were administered and the patient remains free of residual disease and tumor recurrence at the 1-month follow-up. We present a rare case of adenoid cystic carcinoma of parotid with the liver being the sole site of isolated metastatic disease.

**Amyloid-Producing MALT Lymphoma With Tonsillar and Cervical Lymph Node Involvement: A Clinical Mimicker of Oropharyngeal Squamous Cancer**

(Poster No. 60)

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Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) is a mature low-grade B-cell neoplasm usually with an indolent clinical course. MALT lymphomas can occur in numerous extranodal sites including the gastrointestinal tract, lung, salivary gland, skin, and oropharynx. We present a case of MALT lymphoma in a 73-year-old man, clinically mimicking an oropharyngeal squamous cell carcinoma. The patient presented with a base-of-tongue presentation of the primary disease, clinicians should include a metastatic lesion in their differential diagnosis.

### Patient Clinical Characteristics

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Mean (range)</th>
<th>57 (11–88)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presenting symptoms, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache or dizziness</td>
<td>15 (40)</td>
<td></td>
</tr>
<tr>
<td>Blurred vision, worsening vision, vision loss, diplopia</td>
<td>12 (32)</td>
<td></td>
</tr>
<tr>
<td>Eye pain, redness, swelling, epiphora</td>
<td>6 (16)</td>
<td></td>
</tr>
<tr>
<td>Nasal or sinus obstruction</td>
<td>5 (13)</td>
<td></td>
</tr>
<tr>
<td>Anatomic location involved, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sphenoid sinus</td>
<td>6 (16)</td>
<td></td>
</tr>
<tr>
<td>Sella turcica</td>
<td>5 (14)</td>
<td></td>
</tr>
<tr>
<td>Orbit</td>
<td>4 (11)</td>
<td></td>
</tr>
<tr>
<td>Intrasalural</td>
<td>2 (5)</td>
<td></td>
</tr>
<tr>
<td>Skull base</td>
<td>2 (5)</td>
<td></td>
</tr>
<tr>
<td>Frontal sinus</td>
<td>2 (5)</td>
<td></td>
</tr>
<tr>
<td>Nasopharyngeal</td>
<td>2 (5)</td>
<td></td>
</tr>
<tr>
<td>Clivus</td>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>Ethmoid sinus</td>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>Maxillary sinus</td>
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<td></td>
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<tr>
<td>Pyriform sinus</td>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>Temporal fossa</td>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>Pterygopalatine fossa</td>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>Oral maxilla</td>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>Multiple synchronous head mucosal sites</td>
<td>7 (19)</td>
<td></td>
</tr>
</tbody>
</table>
mass and an enlarged cervical lymph node. Not surprisingly, metastatic squamous cell carcinoma was at the top of the clinical differential diagnosis. Biopsy of the base-of-tongue revealed tonsillar parenchyma with unremarkable surface mucosa and effacement of the underlying follicular architecture by an atypical mononuclear lymphoid population (Figure 33, A). Focal amyloid deposition was also present. The lymphoid population demonstrated expression of CD20, BCL2, and weak CD10 in a subset of cells (Figure 33, B). The cells lacked expression of CD3, CD5, BCL6, CD23, CD43, and Cyclin-D1. κ and λ in situ hybridization demonstrated λ light-chain excess, and IGH gene rearrangement studies confirmed clonality. A subsequent cervical lymph node fine-needle aspiration (Figure 33, C) and core needle biopsy (Figure 33, D) showed giant cells, monocytoid lymphocytes, prominent amyloidosis, and a light-chain restriction of the lymphoid population. This case highlights several unusual findings and factors to consider when confronted with a potential MALT lymphoma diagnosis including (1) CD10 expression, (2) amyloid deposition, and (3) a clinical presentation suggestive of an oropharyngeal squamous cell carcinoma.

**Xanthogranulomatous Sialadenitis of the Parotid Gland: An Extremely Rare Mimic of Neoplasia**

*Maryna A. Vazimitsel, MD, PhD (vazimitselm@health.missouri.edu); Katsiaryna D. Laziuk, MD; Richard D. Hammer, MD. Department of Pathology and Anatomical Sciences, University of Missouri Columbia School of Medicine, Columbia.*

We present a case of a 65-year-old man with a prolonged history of left parotid gland swelling. Imaging studies revealed a mass consistent with pleomorphic adenoma. The patient underwent a superficial parotidectomy, showing a 3.0 × 1.7 × 1.5-cm ill-defined firm tan-yellow lesion in the salivary gland and extending into adjacent muscle. Frozen section diagnosis raised the possibility of a lymphoproliferative process. Histologic sections showed a highly cellular granulomatous inflammatory process with numerous foamy and fat-laden macrophages, multinucleated giant cells, spindle-shaped cells, and lymphoplasmacytic infiltrate. Rare crystals were noticed. Acid-fast and Gomori methenamine-silver nitrate special stains were negative for organisms. Immunoperoxidase studies with appropriate controls were performed with the following antibodies: CD1a, CD3, CD4, CD8, CD20, CD23, CD68, CD138, κ, λ, IgG, IgG4, S100, ALK, p53, Actin-SM, and D2-40 and showed no specific diagnosis. Flow cytometric analysis revealed no monocytic B-cell population, abnormal T-cell population, or blast cell population. After an extensive workup of the resection specimen, no specific underlying tumor, cyst, or hematolymphoid process was identified. The lesion was diagnosed as idiopathic xanthogranulomatous sialadenitis. Xanthogranulomatous sialadenitis is an extremely rare tumor-like inflammatory process that Agaimy et al proposed to divide into a primary (idiopathic) and secondary forms. Most reported cases are secondary and often preceded by FNA or a Warthin tumor. Idiopathic xanthogranulomatous sialadenitis is a diagnosis of exclusion, and careful investigation for an underlying lesion or systemic disease should always be attempted.

**Indoleamine 2,3-Dioxygenase Expression in High-Risk Human Papillomavirus-Positive and Negative Head and Neck Squamous Cell Carcinomas**

*Joseph D. Coppock, MD, PhD (jdc5xc@virginia.edu); Anne M. Mills, MD; Edward B. Stelow, MD. Department of Pathology, University of Virginia, Charlottesville.*

**Context:** Owing to the increasing incidence, the number of patients with high-risk (HR) human papillomavirus (HPV)–related head and neck squamous cell carcinomas (HNSCCs) with failed treatment, recurrent disease, late metastasis, and death are also increasing. An immune response is required for clearance of this antigenic cancer subtype. Indoleamine 2,3-dioxygenase (IDO) is an enzyme with available inhibitors demonstrated to be upregulated by cancer and dendritic cells, leading to tryptophan depletion within the tumor microenvironment, regulatory T-lymphocyte activation/expansion, and impaired cytotoxic T-cell response.
Design: A tissue microarray of primary and metastatic HNSCCs was constructed containing 17 primary HR-HPV–positive (HPV+), 36 primary HPV-negative (HPV−), 11 metastatic HPV−, and 14 metastatic HPV+ HNSCCs. HR-HPV status was determined by RNA in situ hybridization (ISH). IDO expression was compared by immunohistochemistry. At least 5% IDO tumor cell staining was considered positive.

Results: HR-HPV+ cases were more likely to be IDO-positive (IDO+) (43% [12/28]) than HPV− cases (16% [8/50], P = .01). No significant difference in IDO+ cases was identified between primary (32% [12/38]) and metastatic (32% [8/25]) cancers (P = 1.0). Seven of 17 primary HPV− cancers (41%) were IDO+ and 45% (5/11) of metastatic HPV− cancers were IDO+ (P = 1.0). Five of 36 primary HPV+ cancers (14%) were IDO+ and 21% (3/14) of metastatic HPV+ cancers were IDO+ (P = .67) (Table).

Conclusions: IDO positivity is observed in a subset of HNSCCs, suggesting a potential role for therapeutic inhibition, particularly in the setting of HPV infection. The consistent IDO expression rates observed between metastases and primaries argues against progressive IDO expression in metastasis.

<table>
<thead>
<tr>
<th>Primary and Metastatic HNSCC IDO and HPV Status</th>
<th>HPV RNA ISH + (28)</th>
<th>HPV RNA ISH − (50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary (53)</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>IDO+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IDO−</td>
<td>10</td>
<td>31</td>
</tr>
<tr>
<td>Metastasis (25)</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>IDO+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IDO−</td>
<td>6</td>
<td>11</td>
</tr>
</tbody>
</table>

Abbreviations: HNSCC, head and neck squamous cell carcinoma; HPV, human papillomavirus; IDO, indoleamine 2,3-dioxygenase; ISH, in situ hybridization.

Spindle Cell Rhabdomyosarcoma: A Diagnostic Challenge in an Immunocompromised Woman

(Schuharazad Abro, MBBS (schuharazad@gmail.com); Swati Mehrotra, MD; Vijayalakshmi Ananthanarayanan, MD. Department of Pathology, Loyola University Medical Center, Maywood, Illinois)

A 66-year-old woman with a past medical history of acute myeloid leukemia, status post stem cell transplant, later complicated by graft-versus-host disease, presented with dysphagia, voice change, and an oral lesion without constitutional symptoms. Physical examination showed a 3.0-cm exophytic mass in her left oropharynx. An excisional biopsy was performed and the histologic examination showed submucosal lesion composed of spindle cells arranged in fascicles with acute inflammatory cells and mononuclear cells. Furthermore, the spindle cells were monotonous, bland looking with centrally located elongated nuclei and small prominent nucleoli. Focal areas of loose myxoid stroma and necrosis with inconspicuous mitotic activity were also identified (Figure 35, A). The tumor cells were positive for desmin (Figure 35, B), SMA (Figure 35, C), and myogenin (Figure 35, D), while negative for EBV, EBER-ISH, epithelial, vascular, melanocytic, hematopoietic, and neuronal markers. This immunohistochemical profile was suggestive of spindle cell rhabdomyosarcoma (RMS). Spindle cell RMS is an uncommon variant of RMS. The mean age is 29 years with a predilection for males, involving mainly paratesticular and intra-abdominal regions. This case report was particularly interesting and challenging, as it does not fit the typical epidemiologic profile of this tumor, and its occurrence in a post bone marrow transplant setting has not been described to the best of our knowledge.

Clear Cell Sarcoma-like Tumor of the Gastrointestinal Tract: An Unusual Presentation in the Oral Cavity

(Allison Cooper, MD (allison.cooper@bswhealth.org); Wei Zhang, MD. Department of Pathology, Baylor University Medical Center, Dallas, Texas)

Clear cell sarcoma–like tumor of the gastrointestinal tract (CCSLGT), also called malignant gastrointestinal neuroectodermal tumor, is a rare tumor that expresses S100 and SOX10 and demonstrates EWSR1-CREB1 and EWSR1-ATF1 gene fusions. Unlike clear cell sarcoma, CCSLGt lacks melanocytic differentiation. CCSLGt most frequently arises in the small intestinal wall, but also occurs in the colon and stomach. Presentation within the oral cavity is rare, with fewer than 5 cases reported in the literature. We present the case of a 45-year-old woman with complaints of tongue swelling during the last year. Past medical history included nasopharyngeal carcinoma treated with radiation more than 15 years prior. Imaging demonstrated a 5.3-cm heterogeneous mass in the floor of mouth. Fine-needle aspiration demonstrated bland spindle cells and matrix. Upon resection, histologic sections showed spindled epitheloid nuclei with lightly eosinophilic cytoplasm and focal cytoplasmic clearing (Figure 36, A and B). Nucleoli were inconspicuous. Occasional nuclear pseudo-inclusions and large areas of necrosis were present. Immunohistochemical stains were positive for S100 and SOX10 (Figure 36, C). Malignant melanoma was considered; however, melanocytic markers including HMB-45 (Figure 36, D) and Melanoma cocktail were negative. MITF and tyrosinase were also negative. EBV, EBER-ISH, epithelial, vascular, melanocytic, hematopoietic, and neuronal markers were negative for EBV, EBER-ISH, epithelial, vascular, melanocytic, hematopoietic, and neuronal markers. This immunohistochemical profile was suggestive of spindle cell rhabdomyosarcoma (RMS). Spindle cell RMS is an uncommon variant of RMS. The mean age is 29 years with a predilection for males, involving mainly paratesticular and intra-abdominal regions. This case report was particularly interesting and challenging, as it does not fit the typical epidemiologic profile of this tumor, and its occurrence in a post bone marrow transplant setting has not been described to the best of our knowledge.

Basal Cell Carcinoma Arising in a Fasciocutaneous Free Flap Reconstruction for a Patient With Squamous Cell Carcinoma of the Tongue

(Anna Shestakova, MD (gshestak@uci.edu); Tjonson Tjoa, MD; William Armstrong, MD. Departments of
Treatement of an advanced invasive squamous cell carcinoma of the oral cavity often requires a complex surgery. Resection of a tumor leads to a deficit that is often reconstructed with a vascularized flap from another area of the body. We present a unique case of a de novo basal cell carcinoma arising in a fasciocutaneous flap in a patient with a primary squamous cell carcinoma of the tongue. A 52-year-old man presented with an invasive squamous cell carcinoma of the left tongue. Hemiglossectomy and left radial forearm free flap reconstruction of the resection defect was performed. On routine follow-up, a small lump was noticed at the reconstruction site. The patient’s intraoral tissue defect was reconstructed with a fasciocutaneous free flap from the left forearm, which was clear of lesions at the time of surgery. Histopathologic examination of the excisional biopsy demonstrated a second primary basal cell carcinoma arising in a skin flap. To our knowledge, this is the first report of a basal cell carcinoma arising in a skin flap in a patient with a squamous cell carcinoma of the tongue. Basal cell carcinoma is the most common skin cancer, and is known to be associated with sun exposure. Surgeons and pathologists need to be aware of a possibility of a primary basal cell carcinoma. Choosing a donor site for the cutaneous flap with the least prior sun exposure might decrease probability of developing a second primary skin cancer (Figure 37).

**Odontoma With Calcifying Epithelial Odontogenic Tumor-like Features**  
(Poster No. 67)

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1Department of Pathology and Laboratory Medicine, Cleveland Clinic Foundation, Cleveland, Ohio; Departments of 2Anatomic Pathology and 3Oral and Maxillofacial Surgery, Southeast Alabama Medical Center, Dothan.

Odontoma is the most common odontogenic tumor. Usually its diagnosis is straightforward when combining radiologic-histopathologic findings. The classic presentation is a young patient with an asymptomatic well-demarcated radiolucency containing a homogenous or multilobular radiopaque material, which on histologic examination contains disorganized tooth components. Calcifying epithelial odontogenic tumor is an uncommon neoplasm showing eosinophilic epithelial cells in nests or sheets with mild-moderate pleomorphism, amylod deposition, and calcifications, often as concentric Liesegang rings. We report a case of a 20-year-old man with an incidental radio-opaque lesion of the right mandible. Imaging showed a well-circumscribed radiolucency in the mandible, which contained multiple radio-opaque structures suggestive of microdontia (Figure 38, A). Histology showed a lesion composed of disorganized enamel, dentin, and bone with psammomatous calcifications (Figure 38, B). Islands of bland epithelium with abundant eosinophilic cytoplasm showing mild nuclear pleomorphism are present associated with Congo red–positive amorphous light-pink stromal material consistent with amyloid (Figure 38, C and D). The final diagnosis was odontoma with calcifying epithelial odontogenic tumor-like areas. Although features of calcifying epithelial odontogenic tumor have been described with other odontogenic lesions, mainly adenomatoid odontogenic tumors and ameloblastoma, such findings have not been reported before in association with odontomas, to the best of our knowledge. This unusual feature can lead to a misdiagnosis as a calcifying epithelial odontogenic tumor, especially when rendered without correlating with the radiologic findings, which in this case were classic. Correct identification is critical, as the treatment of calcifying epithelial odontogenic tumor requires conservative surgical resection, carrying a risk of recurrence that requires long-term follow-up.

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**HPV Genotyping in Cervical Swab, Compared to Cheek Mucosa Swab, in Sexually Active Women**  
(Poster No. 68)

Hussam Abu-Farsakh, MD (flab@yahoo.com); Altaf Ijmail, PhD. Department of Pathology, First Medical Lab, Amman, Jordan.

**Context:** HPV is a sexually transmitted disease. The mode of transmission is by direct skin to skin or skin to mucosa contact. The virus enters the nucleus of squamous cells. Its DNA integrates within the DNA of the squamous cell. Different types of HPV genotypes have different components of E6 and E7 oncogenes.

**Design:** Twenty-one women who were positive for HPV from cervical swabs, as performed by polymerase chain reaction (PCR), and who reported to have had oral sex, were selected to have extensive viral genotyping. Those same women also provided a cheek mucosa swab for HPV genotyping. The genotypes from cervical swab were compared to the genotypes from the cheek swab.

**Results:** There was concordance of 92% between the HPV genotypes from the cervical swab and the genotypes from the inner cheek mucosa.

**Conclusions:** Oral sex transmits HPV to the mucosa of the inner cheek with similar genotypes as those from the cervical swab. Inner cheek PCR testing for HPV can replace cervical swab HPV genotyping by PCR in sexually active women.

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**Reverse Somatic Mutations as Key Player in Malignant Transformation of an Odontogenic Myxoma**  
(Poster No. 69)

Lina X. Hu, MD1 (lina.hu@downstate.edu); Taobo Hu, PhD2; Hong Xue, MD, PhD3; 1Department of Pathology, SUNY Downstate, Brooklyn, New York; 2Department of Life Science, Hong Kong University of Science & Technology, Hong Kong, China.

Two types of single nucleotide variations, gain-of-heterozygosity (GOH) and loss-of-heterozygosity (LOH), occur in 3 patterns observed by in-depth genetic study in a longitudinal case of an odontogenic myxoma in the process from benign to malignant transformation. A series of tissue samples with the histologic observation of sarcomatous transformation of odontogenic myxoma from an 82-year-old man were studied by using the next-generation sequencing AluScan method to detect mutation patterns in both benign-appearing and malignant components with peripheral blood white blood cell DNA as germline control. A total of 47 non-synonymous single nucleotide variants in 41 genes were detected in the germline with 3 nonsense mutations occurring in 3 genes, namely, **LRRFIP1**, **CA11**, and **TUBA8**, and the remainder were missense mutations. Any base position in the tissue samples different from germline genotype was considered as a somatic mutation. Three
Human Papillomavirus–Positive Oropharyngeal Squamous Cell Carcinomas Show a Marked Increase in PD-L1 Expression Relative to Viral-Negative Tumors

Poster No. 70

Adel Mikhail, PhD; Tina McKeegan, MS; Jason Bice, MS; Vicky Amann, MS; Gerard J. Nuovo, MD

Design: Fifty-three squamous cell carcinomas of the oropharynx from the Discovery Life Sciences HPV head and neck tool kit were tested for HPV DNA by using a PCR-based method with individual type-specific probes for most high-risk HPV types. Immunohistochemistry was done for p16 and PD-L1 with the results read blinded to the HPV analyses.

Results: HPV DNA was detected in 38 of 53 tumors (72%). Analysis of the viral-negative tumors demonstrated that PD-L1 was detected in 2/15 (13%), whereas p16 was present in 1/15 (6%). In comparison, PD-L1 was strongly expressed (>10% of the tumor and/or inflammatory cells) in 14/38 HPV-positive tumors (37%) with p16 evident in 29/38 (76%) (each increased with P < .001).

Conclusions: HPV-positive oropharyngeal squamous cell carcinomas show a marked increase in PD-L1 expression, compared to their viral-negative counterparts. This strongly suggests that the viral-positive tumors should be much more susceptible to checkpoint inhibitor therapy than the viral-negative lesions.

NUT Carcinoma of the Sublingual Gland Simulating Primitive Neuroectodermal Tumor/Ewing Sarcoma in a 28-Year-Old Woman

Poster No. 71

Rumeal D. Whaley, MD (rdwhaley@iu.edu); Rachel E. Dougherty, MD; Shaoxiang Chen, MD, PhD. Department of Pathology and Laboratory Medicine, Indiana University School of Medicine, Indianapolis.

NUT carcinoma is a rare poorly differentiated carcinoma that is highly aggressive and resistant to multiple treatment modalities. The BRD4-NUT fusion gene is the most common molecular event of NUT carcinoma. To date, 10 cases have been described in the salivary glands, only 2 of which have been described in the sublingual gland. We present a case of NUT carcinoma immunophenotypically mimicking primitive neuroectodermal tumor/Ewing sarcoma in the sublingual gland of a 28-year-old woman. The patient had no significant past medical history and presented with left submandibular swelling for several weeks. Imaging revealed a large necrotic mass involving the sublingual gland. Subsequent fine-needle aspiration and core biopsy revealed a high-grade malignant neoplasm. Resection and lymph node dissection revealed a highly cellular, cytologically malignant neoplasm composed of poorly differentiated rounded or epithelioid cells with variable amounts of faintly eosinophilic cytoplasm and plump vesicular nuclei with variably prominent nucleoli. The mitotic rate was brisk and extensive necrosis was apparent. The neoplastic cells stained positively for CD99, FLI-1, and synaptophysin. There was focal positivity for chlamydia. Immunohistochemistry for AE1/AE3, CK7, CK20, smooth muscle actin, calponin, calcitonin, p63, napsin A, TTF1, S100, androgen receptor, and Melan-A was negative. EWSR1 gene rearrangement by fluorescence in situ hybridization confirmed NUTM1 gene rearrangement. This case highlights the importance of including this rare disease in the differential diagnosis of poorly differentiated salivary gland carcinomas even if the carcinoma markers are negative.

An Unusual Presentation of a Rare HPV-Related Disorder: Heck Disease

Poster No. 72

Fareed Rajack, MD (frajack@huhosp.org); Ali Afsari, MD; Esther L. Childers, DDS; Henry Paul, MD; Tammy J. Naab, MD. Department of Pathology, Howard University Hospital, Washington, District of Columbia.

Focal epithelial hyperplasia (FEH), also known as Heck disease, is a rare HPV-related disorder usually presenting with multiple verruciform, sessile, tan papules or nodules in the oral cavity, having a predilection for the lower lip, tongue, and labial and buccal mucosa. Ethnic groups, especially Native Americans, Eskimos, and Indians in Central and South America, are most often affected, and immunosuppression is postulated to be a confounding factor. Solitary lesions have been reported in individuals ranging in age from 2 to 85 years. In the literature, FEH is described as a benign condition that heals spontaneously and usually requires no treatment. A 57-year-old HIV-negative black man presented with a painless sessile, tan papule on his left lower lip. He has no significant past medical history. Histologic findings include acanthosis, broad elongated rete ridges with fusion, papillary surface, parakeratosis, superficial keratinocytes showing koliocytic change characteristic of HPF infection, and scattered mitotic cells in the mid and upper layers of the mucosa. Mitotic cells are mitotic-like figures, related to nuclear...
fragmentation due to HPV infection, and are pathognomonic for FEH. P16 was negative. HPV genotype analysis was negative for HPV 16, 18, 6, 11, 31, 33, 45, 51, 52, 56, 58, 59, and 68. FEH or Heck disease is a rare benign HPV-related disorder, most often associated with non–high-risk HPV subtypes 13 and 32. It should not be confused with dysplasia due to mitosoid cells, which mimic mitoses.

**Nonsyndromic Congenital Buccal Lipoma: A Rare Case Report**

(Poster No. 73)

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Solitary mature lipoma is the most common benign mesenchymal tumor. It occurs primarily in mid to late adulthood, is very uncommon in childhood, and is extremely rare at birth. Of the 15% to 20% of cases involving head and neck, only 1% to 4% are intraoral; these are frequently associated with syndromes. An extensive literature search uncovered no previous reports of syndromic or nonsyndromic congenital buccal lipoma. We report a rare case of a female infant who was delivered at term by repeated cesarean section without any prenatal and intranatal complications or trauma. The oral cavity was partially obstructed by a soft tissue mass that was attached to the right upper posterior ridge between the lateral wall of the tongue and the palate. On excision the mass was yellow and hemorrhagic. On serial sectioning, cut surfaces were uniformly smooth and soft. Microscopically, the lesion comprised a well-circumscribed tumor of mature adipocytes with delicate fibrocollagenous septae. No other tissue types (dermoid and epidermoid), myxoid changes, spindle cells, mitotic activity, atypia, malignant changes, or infiltrating margins were identified. No other malformations or syndromes were identified. The diagnosis was congenital buccal lipoma. The primary differential diagnoses include traumatic pseudolipoma, dermoid or epidermoid cysts, pleomorphic adenoma, myxoid lipoma, angiolipoma, hemangiomma, lymphangiomma, spindle cell lipoma, and infiltrating lipomatosis. All of these were excluded. Surgical excision of the tumor was successful; there have been no signs of recurrence after 2.5 years.

**Tyrosine Crystalloid Within a Myoepithelial Neoplasm**

(Poster No. 74)

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Several types of crystalloids, including collagenous, tyrosine-rich, and nontyrosine/amylase, are intimately associated with different salivary gland neoplasms, including mixed tumors (pleomorphic adenomas), myoepithelial tumors, and carcinoma ex pleomorphic adenoma. In particular, pure myoepitheliomas can further classify salivary gland lesions. We performed a literature review for crystalloid inclusions in salivary gland lesions and found the 3 dominant forms of crystalloids encountered (collagenous, tyrosine-rich, and nontyrosine/amylase) in salivary gland neoplasms (pleomorphic adenoma, myoepithelioma, oncocytoma, and carcinoma ex pleomorphic adenoma) in our literature review. We found 7 cases of myoepitheliomas and myoepithelial carcinomas diagnosed at our institution during the past 5 years. We report a case of myoepithelioma of salivary gland neoplasm containing abundant tyrosine crystalloids (Figure 40). Myoepithelial differentiation was confirmed by strong p63 and partial S100 and SMA positivity. We note the association of different types of crystalloid with salivary gland neoplasms, and that tyrosine is typically associated with pleomorphic adenomas, and that its association with a pure myoepithelioma is a rare entity, with only 1 other mention of this rare phenomenon in a case report. We found no other myoepithelial neoplasms diagnosed from the 7 cases at our institution with similar findings. Salivary gland neoplasms are heterogeneous entities, and crystalloid inclusions are uncommonly found. Our study demonstrates that tyrosine crystalloid can rarely be seen in myoepithelial neoplasms.

**Congenital Eulis Presenting as Multiple Obstructive Masses**

(Poster No. 75)

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Congenital eulis (Neumann tumor, granular cell tumor of the newborn) is a very rare hamartomatous lesion arising from the gingival mucosa of the alveolar ridge of a newborn. It typically presents in females (8:1) as a solitary central mass. Spontaneous regression has been reported but, more frequently, prompt simple surgical excision relieves mechanical obstruction with no recurrence or damage to future dentition. Histogenesis is controversial; whereas other granular cell tumors have neurogenic features, congenital eulis is a different entity. We present here the case of a newborn female with 2 distinct pedunculated masses, arising from the upper alveolar ridge. Histologically, under an intact squamous epithelium the mass of confluent polygonal cells with eosinophilic granular cytoplasm had no mitoses and infiltrated the surrounding connective tissue. Immunostains were strongly positive for PAS and vimentin, with weak positivity for CD68 and negativity for S100, CD34, and NSE. The diagnosis of congenital eulis was rendered. Owing to rare occurrence, histogenesis of congenital eulis remains enigmatic. Hypotheses of origin include odontogenic epithelium, pericytes, fibroblasts, histiocytes, nerve, smooth muscle, and primitive undifferentiated mesenchyma. In the present case, the negative S100 stain excludes a neurogenic etiology, whereas vimentin positivity suggests mesenchymal derivation. Our case highlights the need for further study of these rare cases to learn more precise etiopathogenesis and behavior of this entity. This case adds to the mounting evidence that congenital eulis derives from a mesenchymal origin, unlike other granular cell tumors. Awareness of this congenital lesion is important for timely prenatal diagnosis and management.

**Olfactory Neuroblastoma With Divergent Epithelial Differentiation: The Concept of Mixed Olfactory Neuroblastoma and Carcinoma**

(Poster No. 76)

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Olfactory neuroblastoma is an aggressive malignancy arising from neuroectoderm of the olfactory membrane. It has a bimodal peak of incidence in the second and sixth decades of life. Patients usually respond well to complete surgical resection followed by radiotherapy with a very good overall survival. Morphologically, it is characterized by a lobular growth pattern of round blue cells in a neurofibrillary background and rosette formation. Histologic grade varies from the well-formed lobular pattern to the sheets of pleomorphic cells with extensive necrosis. A few cases may show glandlike configuration, but true gland formation and
A Case Report of Mixed Follicular and Solid Variant of Papillary Thyroid Carcinoma

Zijian Wang, MD (zwang@metrohealth.org); Caroline Abramovich, MD; Omid Savyar, MD. Department of Pathology, MetroHealth Medical Center, Cleveland, Ohio.

Solid/trabecular variant of papillary thyroid carcinoma (PTC) is a poorly characterized variant, predominantly reported in children with a history of radiation exposure. We report a case of mixed follicular and solid variant PTC in a 13-year-old girl who had no prior history of irradiation and presented with an enlarging and painless right thyroid mass. Fine-needle aspiration biopsy revealed atypia of undetermined significance. Right thyroid lobectomy was performed. A 4.6 × 4.0 × 2.5 cm solid, soft, brown nodule was identified grossly. Microscopic examination demonstrated a well-circumscribed neoplasm with capsular and vascular invasion and a heterogeneous histology of mixed follicular (70%) and solid/trabecular (30%) architectural patterns. Papillary structures were not present. Nuclear features of papillary carcinoma were best seen in the solid areas and were intermixed within the follicular-patterned areas. The solid regions of the tumor showed marked atypia and increased mitotic activity, up to 11 mitoses per 10 high-power fields. Immunohistochemistry showed strong CK19 positivity in the solid pattern and focal positivity in the follicular pattern, high-power fields. Immunohistochemistry showed strong CK19 positivity (CAM 5.2 and AE1/AE3; Figure 41, A and B). Immunostaining was performed and revealed strong uniform keratin positivity (CAM 5.2 and AE1/AE3; Figure 41, C) and focal neuroendocrine positivity (Synaptophysin; Figure 41, D). Overall, the findings are compatible with an olfactory neuroblastoma with divergent glandular differentiation.

Sclerosing Polycystic Adenosis (SPA) of salivary gland is a rare, reactive disease that resembles sclerosing adenosis of the breast. We present a case of 40-year-old woman with a palpable mass in the right neck. Upon parotidectomy, a round, well-demarcated, fleshy-white mass was identified. Histologically, a well-circumscribed epithelial proliferation composed of a haphazardly admixed population of serous acini and ducts with surrounding myoepithelial cells with prominent intralesional sclerosis was noted. Apocrine differentiation with some of the acini containing markedly enlarged zymogen granules was noted. Some dilated duct spaces were seen without significant cystic component. The lesion was cytologically bland with no significant atypia, mitotic activity, or necrosis. Immunohistochemical studies demonstrated the acini were diffusely positive for Sox10, only weakly and focally positive with DOG-1, while some of the lesional myoepithelial cells were positive for SMA, p40, and S100. Mammaglobin was negative. SPA is composed of ductal and acinar components with different types of cells, including vacuolated, apocrine, mucous, clear/ballooned, foamy, columnar, oncocyte-like, and squamous cells. The presence of large acinar cells with abundant eosinophilic cytoplasmic granules is very characteristic for SPA. SPA is a benign lesion, with only occasional local recurrences following resection. There have been no reported metastasis or tumor-related death and no additional therapy is indicated. SPA should be considered in the differential diagnosis of lesions of the salivary glands with well-circumscribed epithelial proliferation, particularly an acinic cell carcinoma or adenocarcinoma, not otherwise specified.

A Rare Case of Epithelial-Myoepithelial Carcinoma of Sublingual Gland

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A 69-year-old woman presented with a left sublingual gland mass. Grossly the tumor (4.0 × 3.5 × 2.2 cm, 14 g) revealed a tan-white, homogeneous cut surface. Histologically, it showed a multinodular appearance with bands of fibrosis (Figure 42, A). The tumor cells were arranged in nests with dual cell layers (Figure 42, B) composed of inner epithelial cells positive for AE1/AE3 (Figure 42, C) and outer myoepithelial cells positive for p63 (Figure 42, D). The differential diagnosis includes epithelial- myoepithelial carcinoma (EMC), adenoid cystic carcinoma, and pleomorphic adenoma. Our case lacked the typical mesenchymal myxoid, mucoid, or chondroid material as noted in pleomorphic adenoma. Adenoid cystic carcinoma can have a similar morphology to EMC with hyalinized stroma surrounding and separating the tumor cells into thin strands. In contrast to EMC, the cells in adenoid cystic carcinoma are smaller with peg- or carrot-shaped hyperchromatic nuclei. Our case had a characteristic bilayered histology; therefore, a diagnosis of EMC was rendered. An accurate diagnosis relies on morphologic and immunohistochemical features. EMC is rare and represents approximately only 5% of all salivary gland malignancies. It
arises most commonly in the parotid gland (70%), followed by submandibular gland (12%), minor salivary glands, and palate (18%). EMC of sublingual gland origin, as in our case, is extremely rare and fewer than 5 cases have been reported in the literature.

**HPV-Related Multiphenotypic Sinonasal Carcinoma: Report of 2 Cases**

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Human papillomavirus (HPV)-related multiphenotypic sinonasal carcinoma (HRMSC) is a recently described entity, localized to sinonasal tract, associated with high-risk HPV. Very few cases have been described in literature. We report 2 cases of HRMSC occurring in a 54-year-old woman and 66-year-old man with similar clinical presentation of nasal bleed and obstruction. Computed tomography scan showed a polypoid lesion in the left nasal cavity (Figure 43, A), extending posteriorly into choana. Histopathology of the resected masses showed a tumor composed predominantly of solid sheets of basaloid cells with high mitotic activity (Figure 43, B) and focal areas of bizarre tumor giant cells (Figure 43, C). Perineural invasion is not frequent local recurrences and rare metastases, in spite of its high-grade misdiagnosis. HRMSC behaves in a relatively indolent manner with high-grade, basaloïd adenoid cystic-like morphology.

**Diagnostic Challenges of an Unusual Case of Subglottic Inflammatory Myofibroblastic Tumor Mimicking Xanthogranuloma**

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Inflammatory myofibroblastic tumor (IMT) is rare and has mostly been described as case reports in children and young adults. We present a case of a subglottic IMT with unique histologic features mimicking xanthogranuloma. The patient was a 43-year-old woman with no known airway history who presented with dyspnea on exertion and worsening stridor during a 6-month period. Tracheoscopy revealed a large subglottic mass and computed tomography showed a 1.6-cm subglottic soft tissue mass arising from the left true vocal cord, with approximately 73% airway narrowing. Initial biopsy demonstrated a submucosal tumor composed of prominent histiocytes (confirmed with CD68 and CD163 immunostains), abundant Touton-type giant cells, and admixed lymphoplasmacytic infiltrate (Figure 44, A). These histiocytes were negative for CD1a (Figure 44, C). Acid-fast bacilli and Gomori methenamine-silver stains were negative for acid-fast or fungal microorganisms, respectively. These findings raised the possibility of a xanthogranuloma family lesion. A subsequent biopsy revealed a bland spindle cell lesion with admixed inflammatory infiltrates without significant giant cells (Figure 44, B). An immunohistochemical stain for ALK was positive in most spindle cells (Figure 44, D). Multiplex fusion analysis by targeted next-generation sequencing detected a PRKARIA-ALK fusion transcript, supporting the diagnosis of IMT. IMT can present with various histologic patterns though giant cell-rich IMT has rarely been described. The presence of abundant giant cells may therefore lead to inappropriate dismissal of IMT as a diagnostic consideration and thus delay definitive diagnosis.
hybridization identified an IgH/BCL2 heavy chain (IgH expression. B-cell clonality studies revealed a clonal immunoglobulin (Figure 45). Immunohistochemistry showed CD20, CD10, and BCL-2 predominantly of small-cleaved lymphocytes with rare centroblasts. The microscopic examination of the cyst revealed the typical Warthin tumor architecture with a predominantly follicular pattern, composed of oncocytic epithelial cells overlying a lymphoid stroma, often with germinal centers. Secondary malignancies arising from the constituents of the tumor are uncommon, with lymphomas exceedingly rare with few reported cases. We present the case of a 72-year-old man with a 12-month history of a right parotid mass, with a 2 pack/day smoking history. Computed tomography revealed bilateral parotid masses with multiple right-sided cystic and solid parotid masses, the largest 3.5-cm. The patient underwent a right parotidectomy with facial nerve dissection. Gross examination revealed a 6.2-cm, 48-g gland with a 12-month history of a right parotid mass, which was a pack/day smoking. Warthin tumors have a papillary architecture with a double layer of oncocytic epithelial cells overlying a lymphoid stroma, often with germinal centers. Secondary malignancies arising from the constituents of the tumor are uncommon, with lymphomas exceedingly rare with few reported cases. We present the case of a 72-year-old man with a 12-month history of a right parotid mass, with a 2 pack/day smoking history. Computed tomography revealed bilateral parotid masses with multiple right-sided cystic and solid parotid masses, the largest 3.5-cm. The patient underwent a right parotidectomy with facial nerve dissection. Gross examination revealed a 6.2-cm, 48-g gland with a brown, gelatinous fluid-filled cyst and a fleshy, pale tan-pink area. Microscopic examination of the cyst revealed the typical Warthin tumor architecture and cell populations but with an atypical lymphoproliferative process with a predominantly follicular pattern, composed predominantly of small-cleaved lymphocytes with rare centroblasts (Figure 45). Immunohistochemistry showed CD20, CD10, and BCL-2 expression. B-cell clonality studies revealed a clonal immunoglobulin heavy chain (IgH) gene rearrangement and fluorescence in situ hybridization findings for MYB (6q23) and NUTM1 (15q14) were negative. High-risk HPV E6/E7 RNA in situ hybridization was positive. A diagnosis of carcinoma with squamous features and suggestion of myoepithelial differentiation was rendered. As many HPV-related entities in the oropharynx are already well described, we offer this case as a consideration for a HPV-related multiphenotypic carcinoma located in the oropharynx given the significant overlap in features between the entity described in the sinonasal tract.

Oncocytic Papillary Cystadenoma: An Unusual Variant Presenting as Laryngeal Ventricular Cyst

Samantha Mattox, DO (smattox@augusta.edu); Luis Velasquez Zarate, MD; Asad Ullah, MD; Rebecca Kunak, DO; Saleh Heneidi, MD; Paul Biddinger, MD; Sravan Kavuri, MD. Department of Pathology, Medical College of Georgia - Augusta University, Augusta.

Cystadenoma arising from the larynx is a rare benign minor salivary gland tumor that can show mucinous or papillary morphology. The epithelial lining of the salivary gland tumor can present with oncocytic features, which is attributed to an increased number of mitochondria.

Human Papillomavirus–Related Oropharyngeal Carcinoma With Myoepithelial Differentiation: A Case of HPV-Related Multiphenotypic Carcinoma in the Oropharynx?

Catherine Gonsalves, MD; Danielle Harrell, DO; Ruth Asirvatham, MD; Agnes Nall, MD; Marino Leon, MD. Department of Pathology, University of Florida, Gainesville; Ear Nose & Throat Associates of Manatee PA, Bradenton, Florida.

Human papillomavirus (HPV)-related multiphenotypic sinonasal carcinoma is a rare entity, previously described as HPV-related carcinoma of the sinonasal tract with adenoid cystic-like features. Fewer than 100 cases are described in the literature with all cases located in the sinonasal tract. It is currently placed under non-keratinizing squamous cell carcinoma and not yet recognized as a separate entity by the World Health Organization. We present a case of a 73-year-old man with an unremarkable past medical history who was found to have a palpable lymph node in his neck. Subsequent evaluation showed a right tonsillar mass, which was biopsied. Histologically, the tumor showed 2 distinct patterns: squamous cell carcinoma and a basaloid pattern arranged in sheets and nests. The tumor cells within the basaloid pattern were immunohistochemically reactive for AE1/AE3, CAM 5.2, p40, SOX10, and p16 with patchy reactivity for smooth muscle actin and focally with smooth muscle myosin heavy chain. Squamous cells were reactive for p40, p16, and AE1/AE3. INI-1 and NUT were nonreactive by immunohistochemistry, and fluorescence in situ hybridization findings for MYB (6q23) and NUTM1 (15q14) were negative. High-risk HPV E6/E7 RNA in situ hybridization was positive. A diagnosis of carcinoma with squamous features and suggestion of myoepithelial differentiation was rendered. As many HPV-related entities in the oropharynx are already well described, we offer this case as a consideration for a HPV-related multiphenotypic carcinoma located in the oropharynx given the significant overlap in features between the entity described in the sinonasal tract.

Human Papillomavirus–Related Oropharyngeal Carcinoma With Myoepithelial Differentiation: A Case of HPV-Related Multiphenotypic Carcinoma in the Oropharynx?

Catherine Gonsalves, MD; Danielle Harrell, DO; Ruth Asirvatham, MD; Agnes Nall, MD; Marino Leon, MD. Department of Pathology, University of Florida, Gainesville; Ear Nose & Throat Associates of Manatee PA, Bradenton, Florida.
We present a rare case of oncocytic papillary cystadenoma (OPC) of the larynx, which has a combination of these features. The World Health Organization defines OPC tumors as entities that closely resemble Warthin tumor but lack its classical lymphoid component. These lesions are more frequently seen in elderly women, and the immunohistochemical profile and molecular genetic features are largely unknown. We present a case of an 84-year-old woman, former smoker, who presented with progressive dysphonia, dysphagia, and shortness of breath. Laryngoscopy revealed a large, smooth mass originating from the ventricle of the right vocal fold. Subsequent biopsy demonstrated cyst wall fragments lined by a bilayer of large columnar to cuboidal oncocytic cells that had granular eosinophilic cytoplasm, round to oval nuclei with finely dispersed chromatin, and small but distinct nucleoli (Figure 46). The surrounding stroma was slightly fibrotic with scant lymphoid elements. No nuclear pleomorphism, increased mitoses, or necrosis was identified. In the larynx, benign salivary gland tumors are rare and less frequent than malignant varieties. Awareness of rare benign entities like OPC helps ensure proper management and avoidance of unnecessary therapy.

High-Grade Undifferentiated Sarcoma Arising out of a Recurrent Ameloblastic Fibroma: Report of a Second Case
(Poster No. 86)
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High-grade sarcomatous differentiation of benign odontogenic neoplasms, while rare, has been reported; however, transformation of an ameloblastic fibro-odontoma into a high-grade sarcoma has only been reported once. Herein, we describe a case of a 21-year-old man who presented with a large mass of his right mandible. The patient had a remote history of ameloblastic fibro-odontoma, curetted at this site 15 years prior. A computed tomography scan reveals a large mass centered in the region of the left lacrimal sac, medially expanding to the nasolacrimal duct with bony erosions of the adjacent nasal bone. The histologic features are those of a nonkeratinizing SCC composed of interconnecting squamous ribbons invading with broad pushing borders. The mitotic rate is brisk (Figure 48, A). The tumor is diffusely positive for the squamous marker p40 by immunohistochemistry (Figure 48, B). The tumor is also immunohistochemically positive for p16 and positive for high-risk HPV by chromogenic in situ hybridization, which demonstrates transcriptionally active high-risk HPV within the neoplasm (Figure 48, C and D). The findings are consistent with an HPV-related SCC. To the best of our knowledge, this is the first case reported in the lacrimal sac and the prognostic significance of HPV-related carcinomas that arise outside of the oropharynx is still unclear.

Variable Expression of S100 in Sinonasal Melanoma: A Potential Diagnostic Pitfall
(Poster No. 88)
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Context: Sinonasal melanoma (SNM) is a rare, aggressive malignancy. The diagnosis is often quite challenging owing to anatomic limitations, frequent lack of pigmentation, variable histologic appearances, and aberrant differentiation (eg, positivity for cytokeratin, desmin, and neuroendocrine markers). S100 is routinely used as a standard screening marker for SNM, but it may lack optimal sensitivity. Our objective was to study the immunohistochemical expression of S100 in SNM and determine its diagnostic value by comparing it to SOX10.

Design: Twenty-two cases of SNM were retrieved from the archival files. The patients’ ages ranged from 36 to 90 years, with a mean of 65.9 years. Sections from blocks of formalin-fixed, paraffin-embedded tissue were used for immunohistochemical analysis and stained for S100 and SOX10. The extent and intensity of immunostaining was recorded.
**Results:** S100 immunoreexpression was quite variable in the SNM cases. While 9 of 22 cases exhibited diffuse, strong staining as expected, 8 of 22 cases showed only focal expression and 5 of 22 cases demonstrated no staining at all. In comparison, all 22 SNM cases (100%) had diffuse, strong immunolabeling for SOX10.

**Conclusions:** Our study demonstrated that S100 immunoreexpression is extremely variable in SNM. As a result, S100 is insufficiently sensitive to be used as a screening marker for SNM. We believe that SOX10 should replace it for that purpose. Weak or even absent S100 staining should not dissuade pathologists from the possibility of SNM. Indeed, for a high-grade sinonasal tumor pathologists should have a low threshold for using additional markers to exclude the possibility of SNM.

**Adamantinoma-like Ewing Sarcoma of the Head and Neck**  
(Poster No. 89)

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Adamantinoma-like Ewing sarcoma is a rare variant of the Ewing sarcoma family of tumors that resembles classic adamantinoma of bone. The histologic features include basaloïd nests, squamous pearls, and intraepithelial growth; the immunoprofile shows diffuse cytokeratin and p40. Strikingly isomorphic nuclei are present, similar to other translocation-associated sarcomas. Ewing sarcoma in situ hybridization usually confirms the diagnosis. Patients presented at Baylor St Luke’s Hospital, Houston, Texas. Immunohistochemical stains were performed with a Leica Bond III Immunostainer according to manufacturer specifications. FISH studies for FUS and EWSR1 (22q12) were performed and interpreted at ProPath Services LLC (Dallas, Texas). Reverse transcription PCR for Ewing sarcoma was performed and interpreted at Mayo Clinic Laboratories in Rochester, Minnesota. A 25-year-old man presented with a left submandibular mass that had been present for several months and increasing in size. On imaging a 3.3-cm lobulated, well-circumscribed, mildly heterogeneously enhancing mass was observed on the left submandibular gland. Microscopic examination showed a nested architecture formed by epithelioid cells with basaloïd features. Immunohistochemical stains showed tumor cells positive for P40 (strong), P63 (diffuse), CD99, synaptophysin, AE1/AE3, CAM 5.2 (patchy), CK5/6, E-cadherin, P16 (patchy), NKX2.2, and INI1 but negative for Desmin, actin, and S100. FISH was positive for FUS rearrangement and negative for EWSR1 (22q12) gene rearrangement. EWSR1-FLI1 and EWSR1-ERG fusion transcripts were not detected on reverse transcription PCR. A high index of suspicion and a combination of morphologic features, immunohistochemical stains, and molecular studies are essential to make the correct diagnosis.

**Should We Perform Upfront Alcian Blue/Periodic Acid–Schiff Staining for Identification of Intestinal Metaplasia in Every Distal Esophagus Biopsy?**  
(Poster No. 90)

Sujal I. Shah, MD (shah2si@ucmail.uc.edu); Dani S. Zander, MD; Divya Sharma, MD. Department of Pathology and Laboratory Medicine, University of Cincinnati Medical Center, Cincinnati, Ohio.

**Context:** Barrett esophagus is a well-known risk factor for esophageal adenocarcinoma. Diagnosis relies on histologic identification of intestinal metaplasia (IM), readily identified by presence of goblet cells on routine hematoxylin-eosin (H&E). Alcian blue/periodic acid–Schiff (AB/PAS) stain is rarely needed to diagnose IM. A quality improvement project was performed to determine both the frequency of AB/PAS staining and the savings of $6500 annually if upfront staining was discontinued. Upfront AB/PAS is not performed by any of the 26 responding institutions.

**Conclusions:** There is no diagnostic value in performing upfront AB/PAS staining on distal esophageal biopsies. AB/PAS should only be performed in cases indeterminate on H&E. We propose an alternative option of cutting an unstained slide at initial sectioning, which can be used for AB/PAS in indeterminate cases, with minimal impact on turnaround time.

**A Quality Improvement Project for Autopsy Photography**  
(Poster No. 91)

Mario A. Rascon, MD (mrascon@epcounty.com). Office of the Medical Examiner, El Paso County, El Paso, Texas.

**Context:** The importance of high-quality photographic documentation during autopsy lies primarily in the potential role these photographs play not only as teaching tools, but also in the criminal justice system, as they commonly are presented to jurors, attorneys, and judges during proceedings, hearings, or trials. High-quality photography not only helps in providing fair and accurate depictions of autopsy findings, but also reflects on the perceived professionalism and competency of the institution. This project aimed to fairly and accurately depict autopsy findings, free of distractions and artifacts, while presented in the least graphic manner possible.

**Design:** Autopsy photographs for 20 consecutive cases were analyzed for undesirable features including (1) background distractions; (2) bloody specimen; (3) lack of focus; (4) mislabeled specimen; (5) inadequate lighting; and (6) poor or confusing orientation. After that, an intervention took place, consisting of the acquisition of a professional photography station and purchasing background boards. Twenty postintervention cases were then analyzed following the same guidelines to identify undesirable features.

**Results:** Undesirable features were reduced by 80% (427 pre intervention to 82 post intervention) (Figure 49).

![Figure 49](image_url)

**Conclusions:** Background and lighting issues were the top undesirable features both before and after the intervention, which requires a relative small monetary investment and minimal training to improve.

**Using Size Templates in the Grossing Laboratory to Minimize Cassette Stuffing and Tissue Reprocessing**  
(Poster No. 92)

Grant Williams, MD (gmwilliams728@gmail.com); Kevin Krauland, MD. Department of Pathology, San Antonio Uniformed Services Health Education Consortium, San Antonio, Texas.

**Context:** Before evaluation by a pathologist, tissue must be grossed, placed into a cassette, fixed in formalin, and embedded in paraffin. If too much tissue is placed in the cassette, the processing and histology will not be optimal and the tissue block may need reprocessing.

**Design:** At our institution, reprocessing of tissue blocks is most commonly due to cassette stuffing. One reason for this problem is that cassettes are wider than the wells where the tissue is fixed. The cassettes are 2.9 × 2.7 × 0.4 cm and the wells are 3.1 × 2.4 × 0.4 cm. We created size templates (2.7 × 2.2 × 0.3 cm) to have at the grossing bench that were the maximum size for optimal processing. We looked at rates of reprocessing for 45 days before and after placing the size templates at the grossing bench to see if available size templates were helpful in preventing cassette stuffing. In addition, we educated residents in their use each morning.

**Results:** During the 90 days where data were recorded there were 33 grossing days in each 45-day period. The number of surgical cases was similar between the periods. The interventions resulted in a decrease in number of days that tissue was reprocessed between periods (pre...
Utility of Flow Cytometry in Low Cellularity Specimens: Is There a Minimal Acceptable Cutoff to Perform Flow Cytometry?

Devin R. Broadwater, MD (broadwaterdevin@gmail.com); Lynn M. Messersmith, DO; Grant M. Williams, MD; David T. Lynch, MD. Department of Pathology, Brooke Army Medical Center, San Antonio, Texas.

Context: Flow cytometry is an important test in diagnosing hematopoietic diseases. Although the test is widely used when clinicians suspect the diagnosis of leukemia or lymphoma, the utility of testing low cellularity specimens has not been studied. Here, the usefulness of performing flow cytometry in minimally cellular specimens is explored.

Design: We retrospectively reviewed flow cytometry reports at Brooke Army Medical Center from January 1, 2016, to December 31, 2018. Peripheral blood and bone marrow specimens were excluded. Data regarding demographics, history, specimen type, cell count, viability, and diagnosis were recorded. Significant findings were defined by any abnormal hematoLogic population. Findings were statistically analyzed.

Results: A total of 872 reports were included. Mean study age was 48.5 years (range, 2–97). Male to female ratio was 1.5:1. Most specimens were lymph nodes (491). There were 219 reports (25%) with significant findings and 653 (75%) with no significant findings. History of hematologic malignancy did not predict a significant finding. There was a statistically significant difference between cell counts of flow reports with no significant finding versus those with significant findings (mean, 5.3 × 10^3/μL versus 9.5 × 10^3/μL, respectively; P = .005).

Cellularity below 0.1 × 10^3/μL yielded the lowest significant finding rate (1%). Samples with cellularity below 0.1 × 10^3/μL rarely provide a significant finding. These results question the utility of performing flow cytometry on low-cellularity specimens.

Gross Digital Images in Academic Medicine: Applications and Perceptions

Charles E. Middleton IV, MD (cemiddle10@gmail.com); Varsha Manucha, MD. Department of Pathology, University of Mississippi Medical Center, Jackson.

Context: Gross examination of a surgical specimen not only plays a crucial role in the final diagnosis but also aids in the accurate staging of cancer resection specimens. Consequently, photography of gross specimens has become an important part of the surgical pathology resident training curriculum. The objective of this study is to assess the applications of gross images in an academic institution as perceived by residents and pathologists.

Design: An anonymous survey was issued to the surgical pathologists (13), and to the residents (7, excluding interns) at our institution. The questions were designed to address the application of gross images in an academic setting. The implementation of gross pictures for teaching purposes, conferences, and a variety of other functions was addressed.

Survey Responses

<table>
<thead>
<tr>
<th>Survey Questions</th>
<th>Residents (PGY2–4)</th>
<th>Attendings (&lt;5 y)</th>
<th>Attendings (&gt;10 y)</th>
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<tr>
<td>3–5 specimens photographed (per day)</td>
<td>83%</td>
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</tr>
<tr>
<td>5–10 minutes spent imaging (per specimen)</td>
<td>50%</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Find imaging disruptive</td>
<td>83%</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Find imaging educational</td>
<td>67%</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Photograph frozen before dissection</td>
<td>0%</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>View photographs when available</td>
<td>67%</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Prefer to see specimen first hand</td>
<td>—</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Only review images if there is a question</td>
<td>—</td>
<td>75%</td>
<td>67%</td>
</tr>
<tr>
<td>Photograph frozen if assigned to someone else</td>
<td>—</td>
<td>50%</td>
<td>17%</td>
</tr>
</tbody>
</table>

Most important applications of imaging:

- Diagnosis — 100% 100%
- Tumor boards — 25% 83%
- Teaching — 75% 83%
- Publications — 50% 17%

Results: The survey was completed by 10 of 13 surgical pathologists and 6 of 7 residents. All attending physicians preferred to review complicated surgical specimens in real time, while 7 of 11 attending physicians reviewed digitized images only if they had additional questions. Residents averaged 5 to 10 minutes taking photographs and considered it useful, even though it was disruptive to their workflow.

Conclusions: Most surgical pathologists (regardless of experience) had a clear preference to review complicated surgical specimens first hand. For pathologists with <5 years of experience, publications were a priority, while those with >10 years of experience felt routine diagnosis was the most important application of gross digital photography. Most residents agreed that digitized gross images are beneficial to their educational experience even though it is disruptive to their workflow.
Is Flow Cytometry Immunophenotyping Necessary in the Initial Evaluation of Myelodysplastic Syndrome?

(Poster No. 95)

Grant Williams, MD (gwilliams728@gmail.com); David Lynch, MD. Department of Pathology, SAUSHEC, San Antonio, Texas.

Context: Flow cytometry immunophenotyping (FCI) is a diagnostic tool used in a wide array of hematolymphoid malignancies. The updated 2017 WHO diagnostic criteria for myelodysplastic syndromes (MDS) do not require FCI. Clinicians commonly request FCI to be used as part of initial diagnostic evaluation of MDS despite its unclear role in diagnosis. Herein, the utility of performing FCI in suspected MDS is explored.

Design: Bone marrow biopsies obtained for suspected new diagnosis of MDS in 2018 at a single institution were reviewed. Biopsies on patients with existing hematopoietic neoplasms and without concurrent FCI were excluded.

Results: A total of 64 bone marrow biopsies were included. Of the 64 biopsies, 16 (25%) were diagnosed as MDS, 41 (64%) were negative, and 4 cases (6%) were acute myeloid leukemia. FCI detected 2 cases (3%) with monoclonal B-cell populations and 1 case (2%) of a monoclonal plasma cell population. FCI detected increased blasts in 18 cases (28%), ranging from 2% to 45% (median, 5.4%). In all cases of MDS, FCI provided no additional information. Instead, final diagnosis was based on morphologic dysplasia and the blast percentage from the aspirate manual count.

Conclusions: FCI could potentially be deferred from the initial diagnostic evaluation of MDS. Pathologist screening of aspirate smears will identify the minor subset of cases requiring FCI, such as acute myeloid leukemia. Eliminating routine FCI from initial diagnostic evaluation of MDS could lead to significant cost savings and improved efficiency.

Microsatellite Stable Colon Adenocarcinoma With an Immunogenic Phenotype: Challenges in Diagnosis and Treatment

(Poster No. 97)

James J. Saller, MD (sallerjames@gmail.com); Dahui Qin, MD, PhD; Seth Felder, MD; Domenico Coppola, MD. Departments of Pathology and Gastrointestinal Surgery, Moffitt Cancer Center, Tampa, Florida.

Context: Patients with deficient microsatellite mismatch repair (dMMR) colorectal cancer (CRC) may respond to immune checkpoint inhibition in contrast to microsatellite stable CRCs. A proportion of microsatellite stable tumors, however, display histomorphologic features characteristic of dMMR, consistent with an increased immunogenic response, and representing a subset that may also derive benefit from immune checkpoint inhibition therapy. In this case series, we review tumors where the histologic features suggestive of dMMR were in disagreement with the microsatellite mismatch repair (MMR) results. We discuss possible causes of such disagreement.

Design: Three patients with CRC suggesting histomorphologic immunogenicity underwent evaluation by immunohistochemistry, next-generation sequencing, and/or polymerase chain reaction (Table).

Results: The collection of findings compatible with an immunogenic response was similarly observed in all patients. The first case highlights limiting factors inherent to laboratory testing of MMR status; a biopsy was initially interpreted as microsatellite stable, but upon review, was interpreted as dMMR. The second case examines the challenges in reconciling histologic characteristics traditionally associated with dMMR CRCs, but ultimately determined to be microsatellite stable. This case is an example of an immunogenic consensus molecular subtype-3 CRC, which have been reported in the literature. The third case emphasizes microsatellite instability of colonic mucinous CRC, resulting from MLH1-methylation and/or MSH6 mutation (Table).

Conclusions: Here we demonstrate the challenges encountered in establishing MMR status when confronted with conflicting results from histology, immunohistochemistry, polymerase chain reaction, and next-generation sequencing. Given that dMMR status has been shown to be a biomarker for immune checkpoint inhibition responsiveness, the importance of accurate identification is critical.

<table>
<thead>
<tr>
<th>Summary of Findings for Cases of Immunogenic Colon Adenocarcinoma*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Case</strong></td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
</tbody>
</table>

Abbreviations: IHC, immunohistochemistry; MSI-H, high-level microsatellite instability; MSS, microsatellite stable; NGS, next-generation sequencing; PCR, polymerase chain reaction; TILs, tumor-infiltrating lymphocytes; TMB, tumor mutational burden (mutations/megabase).

* The IHC antibodies (MLH1, MSH2, MSH6, and PMS2) were acquired by DAKO. The PCR-based assay by ARUP was based on 5 microsatellite loci (MONO-27, BAT25, BAT26, NR-21, and NR-24); NGS was performed by using the Moffitt STAR Solid Tumor Panel for cases 1 and 2, whereas for case 3, NGS was performed by using the TruSight Tumor 26 Gene Set.
Use of Whole Slide Imaging for Quality Control Review of Immunohistochemical Stain Controls at a Multisite Academic Institution Enhances Workflow

(Tara Saunders, MD (Tara.Saunders@ucsf.edu); Yuri Murphy, BS; Sarah Bowman, BA; Sarah Umetsu, MD, PhD; Yunn-Yi Chen, MD, PhD; Zoltan Laszik, MD, PhD Department of Pathology, University of California San Francisco.

Context: Our institution’s histology laboratory serves 3 distant sites and uses couriers to transport glass slides between sites. Immunohistochemical (IHC) stains are run in 3 to 4 separate batches per day. A subset of stains uses off-slide controls that are evaluated for quality control (QC) purposes by select pathologists residing at different sites. We evaluated how whole slide imaging can facilitate review of IHC controls.

Design: Starting in August 2018, off-slide IHC controls being evaluated by an off-site pathologist were scanned by Philips whole slide imaging system (Andover, Massachusetts) with direct integration of images into the laboratory information system. The time from scanning start to scanning completion was compared to the courier schedule to determine when glass slides would have arrived at their destination.

Results: A total of 207 batches of IHC controls had a complete record of scanning times available for review. Of these, 183 batches (88.4%) were available for review earlier (average 58.8 minutes earlier) than the glass slides, while 24 batches (11.6%) were available later (average 14.4 minutes later). Owing to limited courier runs, the late afternoon batch was often available for review much earlier (>90 minutes, which allowed QC to be completed the same day instead of the following.

Conclusions: Whole slide imaging is a valuable tool to facilitate review of histology materials and improve turnaround time at a multisite institution. Digital images simplify troubleshooting of problematic stains and make the IHC controls more accessible to other pathologists. Step-by-step integration of digital pathology into the histology laboratory workflow allows for gradual testing and troubleshooting of the platform and workflow.

The Role of Helicobacter pylori Ancillary Study on Chronic Gastritis

(Xiaojin Zhu, MD, PhD (xiaojin.zhu@gmail.com); Sepideh Madahian, MD; Yang Zong, MD, PhD; Karen Dresser, BS; Xiaofei Wang, MD. Department of Pathology, University of Massachusetts Memorial Medical Center, Worcester.

Context: Current recommendation for Helicobacter pylori ancillary study by the Gastrointestinal Pathology Society (GIPS) is when chronic inactive/active gastritis is encountered. Our previous quality analysis, presented at the 2014 CAP meeting, supported the GIPS recommendation that “up front” stains on all gastric biopsies are unnecessary. This is a follow-up retrospective study to analyze the efficacy of H pylori immunohistochemistry (IHC) since our institute adopted GIPS recommendations.

Design: The study included 106 cases of gastritis with ancillary H pylori IHC and 100 cases without significant gastritis and H pylori IHC. The chronic inflammation was subclassified into diffuse, superficial bandlike, clusters of plasma cells (>5 plasma cells/cluster; >2 clusters), focal lymphoid aggregates, and scattered/mild inflammation. Helicobacter pylori IHC was applied to 100 nongastritis cases.

Results: Positive H pylori IHC was observed in 21% of cases. The positive cases showed diffuse chronic inflammation (41%), superficial bandlike inflammation (50%), clusters of plasma cells (4.5%), or scattered/mild inflammation (4.5%). Negative group consisted of scattered/mild inflammation (65%), clusters of plasma cells (13%), lymphoid aggregates (17%), and diffuse and superficial bandlike inflammation (5%). Helicobacter pylori-positive group had a higher proportion of active inflammation than the H pylori-negative group (P < .001). One hundred cases with no indication for H pylori ancillary study were reevaluated and confirmed to be H pylori-negative by IHC.

Conclusions: Helicobacter pylori organisms were detected in one-fifth of gastritis cases. Mild scattered mononuclear inflammation was rarely associated with H pylori, and activity is likely related to H pylori infection, further validating GIPS recommendations.

Pathologic Evaluation of Appendectomy Specimens in Patients Older Than 40 Years: Is Submitting the Entire Appendix Indicated?

(Laleh Montaser Kouhsari, MD (lmontase@bidmc.harvard.edu); Chelsea Marcus, MD; Jonathan N. Glickman, MD. Department of Pathology, Beth Israel Medical Center, Boston, Massachusetts.

Context: Most appendectomies are performed for acute appendicitis and represent sections of the appendiceal tip and the proximal margin are submitted for histologic examination. The justification for this sampling is that this amount of tissue examination is usually sufficient to render the primary diagnosis, while still retaining sensitivity for incidental diagnoses such as unsuspected neoplasia. At Beth Israel Medical Center and many academic medical centers, appendectomy specimens from patients older than 40 years are submitted in entirety, to further exclude the possibility of neoplasia; however, the utility of this approach has not been examined.

Design: We retrospectively analyzed the demographic and histopathologic data of 189 consecutive patients (118 patients ≤40 years old and 71 patients >40 years old) at Beth Israel Medical Center who underwent appendectomy for a clinical diagnosis of appendicitis. Histopathologic findings of the appendectomy specimens were compared between the groups.

Results: Eighty-one percent of patients ≤40 years old had a pathologic diagnosis of acute appendicitis as compared to 59% of patients >40 years old (P = .002). The second most common diagnosis in patients ≤40 years old was unremarkable histology and in patients >40 years old it was interval resolution of appendicitis. One patient >40 years old had an incidental sessile serrated adenoma. Otherwise, there were no instances of neoplasia among the selected specimens.

Conclusions: Entirely submitting appendectomy specimens performed for appendicitis in patients >40 years old does not improve diagnostic yield. Oversubmission of tissue may result in overutilization of laboratory resources, without significantly improving quality of care.

Withdrawn.
Quality Validation Study Practices: Lessons Learned Through TLE1
(Poster No. 102)

Michael Occidental, BA (michaeloccidental@yahoo.com); Sara Shalin, MD, PhD. Department of Pathology, University of Arkansas for Medical Sciences, Little Rock.

Context: Well-designed antibody validations are an important part of a high-functioning, quality laboratory. To ensure that correct diagnoses are being rendered when a case is difficult enough to require immunohistochemical staining, it is important to design the validation study to test feasible and appropriate conditions. We report how varying conditions within a validation can affect outcome, using our experience validating a new clone of TLE1, a marker expressed in synovial sarcoma.

Design: Cases of synovial sarcoma and spindle cell mimickers were selected for our validation cohort for a new Ventana predilute TLE1 antibody (clone 1F5). Protocol optimization required adjustment of antigen retrieval time, antibody incubation time, and selection of additional “negative” controls following literature review.

Results: Initial staining protocols resulted in robust staining of synovial sarcomas (high sensitivity) but unacceptably high numbers of positively staining “negative” controls (low specificity). Adjusting antigen retrieval and antibody incubation time provided acceptable sensitivity and specificity. Ultimately, 12 of 13 positive controls stained positively, while 11 of 15 negative controls were negative with final staining protocol. Four negative cases showing moderate diffuse positivity were all schwannomas. Literature review reported TLE1 staining in neural neoplasms, a caveat conveyed to pathologists upon completion of validation.

Conclusions: Antibody validations may require titration of assay conditions to achieve acceptable sensitivity and specificity. In addition, tissue selected for negative controls should mimic conditions encountered in practice in which the antibody may be used. In this manner, antibody validations represent essential components of quality practice in anatomic pathology.

Building a Better Cell Block: Keeping It Simple With a Plan-Do-Study-Act Cycle
(Poster No. 103)

Ryan P. Austin, MD (ryan.p.austin10.mil@mail.mil); Brandon K. Peterson, MD. Department of Pathology, Naval Medical Center San Diego, California.

Context: Early detection screening tests and minimally invasive sampling techniques result in small biopsies of early lesions. Pathologists must render accurate diagnoses and reserve tissue for molecular-based testing. Optimization of cell block quality is therefore essential in practice in which the antibody may be used. In this manner, antibody validations represent essential components of quality practice in anatomic pathology.

Design: Our approach used a Plan-Do-Study-Act cycle approach. We developed a process map and performed a failure modes analysis in collaboration with our department’s histology and cytology technicians. We retrospectively reviewed cell blocks from 179 core biopsies and fine-needle aspirations and assessed adequacy by using a semiquantitative cell block scoring system based on the amount of diagnostic material present. Percentages of cases with “indeterminate” final diagnoses were also quantified. After optimization, data were recollected prospectively on 171 cell blocks during a 3-month period.

Results: A number of simple modifications were made to the cell block production process. After optimization, the cell block score improved from 1.11 to 1.46 (P < .001), and the rate of indeterminate diagnoses decreased from 15.1% to 6.4% (P = .009).

Conclusions: The use of structured process improvement strategies can effectively optimize existing processes in the anatomic pathology laboratory, resulting in a significant improvement in diagnostic quality, without the need to introduce and validate novel processes or procedures.

Balancing Care and Cost: A Quality Improvement Study on the Utilization of Immunohistochemistry to Detect Helicobacter pylori in Gastric Biopsies
(Poster No. 104)

Yuho Ono, MD (yono@bidmc.harvard.edu); Yigu Chen, MPH; Pamela Stravitz; Jonathan N. Glickman, MD, PhD. Department of Pathology, Beth Israel Deaconess Medical Center, Boston, Massachusetts.

Context: In patients with Helicobacter pylori gastritis, detection of organisms in gastric biopsies leads to appropriate treatment and prevention of disease progression. Although organisms are usually visualized on routine hematoxylin-eosin–stained slides, immunohistochemical stains (IHC) can be used to detect rare or morphologically atypical organisms. Overutilization of IHC is a potential drain on laboratory resources and a source of increased patient costs.

Comparison of Helicobacter pylori Detection and IHC Utilization Between the Study Intervals

<table>
<thead>
<tr>
<th></th>
<th>Before (n = 1434)</th>
<th>After (n = 1415)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cases with Hp infection</td>
<td>126 (8.8%)</td>
<td>96 (6.8%)</td>
<td>.05</td>
</tr>
<tr>
<td>Method of Hp detection</td>
<td>n = 126</td>
<td>n = 96</td>
<td>.004</td>
</tr>
<tr>
<td>H&amp;E only</td>
<td>106 (84.1%)</td>
<td>74 (77.1%)</td>
<td></td>
</tr>
<tr>
<td>IHC only</td>
<td>13 (10.3%)</td>
<td>22 (22.9%)</td>
<td></td>
</tr>
<tr>
<td>Both H&amp;E and IHC</td>
<td>7 (5.6%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Cases with suspected Hp infection</td>
<td>n = 410</td>
<td>n = 312</td>
<td></td>
</tr>
<tr>
<td>Total IHC ordered</td>
<td>304 (74.1%)</td>
<td>237 (76.0%)</td>
<td></td>
</tr>
<tr>
<td>IHC results</td>
<td>n = 304</td>
<td>n = 237</td>
<td>.24</td>
</tr>
<tr>
<td>Positive for Hp</td>
<td>20 (6.6%)</td>
<td>22 (9.3%)</td>
<td></td>
</tr>
<tr>
<td>Negative for Hp</td>
<td>284 (93.4%)</td>
<td>215 (90.7%)</td>
<td></td>
</tr>
<tr>
<td>IHC order by type of gastritis</td>
<td>n = 304</td>
<td>n = 237</td>
<td>.04</td>
</tr>
<tr>
<td>Active gastritis</td>
<td>78 (25.7%)</td>
<td>85 (35.9%)</td>
<td></td>
</tr>
<tr>
<td>Inactive gastritis</td>
<td>194 (63.8%)</td>
<td>129 (54.4%)</td>
<td></td>
</tr>
<tr>
<td>No gastritis</td>
<td>32 (10.5%)</td>
<td>23 (9.7%)</td>
<td></td>
</tr>
<tr>
<td>Cases with patient history of Hp infection</td>
<td>n = 102</td>
<td>n = 96</td>
<td>.51</td>
</tr>
<tr>
<td>IHC ordered</td>
<td>70 (68.6%)</td>
<td>70 (72.9%)</td>
<td></td>
</tr>
<tr>
<td>No IHC ordered</td>
<td>32 (31.4%)</td>
<td>26 (27.1%)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: H&E, hematoxylin-eosin stain; IHC, immunohistochemical stain.

Design: A single-institution retrospective review was performed on pathology reports for 2849 patients with gastric biopsies obtained within 3-month intervals before and after revisions were implemented to the Hp pylori IHC ordering criteria. For 722 patients with suspected Hp pylori infection, reports were reviewed for presence of Hp pylori organisms, performance of IHC, type of gastritis, and history of Hp pylori infection. Frequency of Hp pylori infection and IHC ordering practices were compared between the 2 intervals by using a χ² analysis, with significance set at P < .05.

Results: Overall frequency of Hp pylori infection was 7.8%. Helicobacter pylori organisms were more frequently detected by hematoxylin-eosin slides, and in patients with active gastritis and/or...
patients with history of *H pylori* infection. After IHC ordering criteria were reviewed and revised, a slightly increased diagnostic yield (r=2.7%, P = .24) and a decreased utilization for nonactive gastritis cases (~10.2%, P = .04) were observed (Table).

**Conclusions:** The diagnostic yield of *H pylori* IHC is low, especially when performed on patients with inactive gastritis and/or patients without a history of *H pylori* infection. In this single-institution experience, revisions to IHC ordering criteria led to higher diagnostic yield and reduced utilization in lower-yield cases, leading to a more cost-effective use of stains.

A Comparison of Test Pricing and Turnaround Time for Selected Laboratory Tests Between Pakistan and the United States

(Poster No. 105)

Sania Shuja, MD, PhD; Urfa Shafi, FCPS (urfa.shafi@sihs.org.pk); Muhammad Dilawar, MCPs, FCPS; Toqeer Butt. Department of Pathology, Shalamar Institute of Health Sciences, Lahore, Pakistan.

**Context:** The global market for health care is predominantly insurance based in the United States, and primarily a self-pay model in Pakistan. The price for anatomic pathology (AP) and clinical pathology (CP) services in Pakistan vary 2- to 3-fold among various private institutions. We compared test pricing and turn-around time (TAT) in a few major institutions in Pakistan and the United States.

**Design:** The TAT data were collected by making phone calls to selected private institutions to document time given to patients for test results after submission of sample. The combined test load of the above institutions was greater than 50,000 per day for AP and CP tests. For AP services we included CPT (current procedural terminology) codes 88305 through 88309, and for CP services, CPT 80076 for liver function tests (LFTs) and CPT 80069 for renal function tests (RFTs). Test pricing for the United States was obtained from a Web site (lni.wa.gov).

**Results:** Charges for AP services (small and large specimens) in Pakistan ranged from $12.00 to $56.00 (US price, $130.00–$766.00), and TAT was reported as 10 days compared to 2 to 6 days in the United States. For CP services, charges ranged for RFTs from $5.7 to $11.7 and for LFTs from $7.8 to $14.3 (US test prices: $15.12 and $14.23, respectively). In Pakistan the TAT for RFTs and LFTs was 6 to 8 hours (United States: 6 hours).

**Conclusions:** AP services are up to 10-fold more expensive in the United States, while CP services are almost similar in price to those in Pakistan. TAT for CP services is comparable, while TAT for AP services needs to be drastically improved in Pakistan.

The Impact of Beaker on College of American Pathologists Electronic Cancer Checklist Compliance

(Poster No. 106)

Michael P. Crawford, MD (mpc5u@virginia.edu); Anne M. Mills, MD. Department of Pathology, University of Virginia, Charlottesville.

**Context:** The College of American Pathologists (CAP) requires an audit of 300 (or 10% of all cancer resection cases) electronic cancer checklists (eCC) annually to ensure reporting compliance and completeness. The Beaker module of the Epic Phase II medical record system has integrated synoptic reporting that promises automatic updating of all eCC templates. Utilization of this system would therefore be expected to improve eCC reporting compliance.

**Design:** The surgical pathology division’s annual 300-case eCC audits were reviewed from 2016–2018. The rates of discrepancy were recorded, as were the nature of specific templating errors.

**Results:** See Table.

**Conclusions:** eCC reporting compliance does not differ significantly pre- and post-Beaker implementation. Under Beaker, eCC reporting errors were primarily attributable to the failure of the system to delete an out-of-date ovarian cancer eCC template. Furthermore, rare complete omissions of cancer templates still occur. These results underscore the fact that even an electronic system that promises automatic template updating is not infallible—nor are the pathologists inputting the templates—and regular, meticulous audits remain necessary to ensure CAP compliance.

<table>
<thead>
<tr>
<th>Year</th>
<th>Compliance</th>
<th>Discrepant Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016 (pre Beaker)</td>
<td>97.1% (301/310)</td>
<td>Small bowel carcinoma: no synoptic issued.</td>
</tr>
<tr>
<td>2017 (pre Beaker)</td>
<td>98.3% (300/304)</td>
<td>Endometrial carcinoma: lymph node staging not specified in template.</td>
</tr>
<tr>
<td>2018 (post Beaker)</td>
<td>97.3% (299/307)</td>
<td>Pancreatic endocrine tumor ( incidental): no synoptic issued.</td>
</tr>
</tbody>
</table>

Appropriateness of Ordering Practices for *Clostridium difficile* Testing: A Single Center Study

(Poster No. 107)

Shamima Sultana, MD1 (Shamima.Sultana@wmchealth.org); Faisal M. Ronny, MD, PhD2; Faisal Saquib3; Hank Wang, PhD.1 1Department of Pathology, Westchester Medical Center, Valhalla, New York; 2Department of Pathology, New York Medical Center, Valhalla; 3Department of Pathology, New York Medical College, Valhalla.

**Context:** A variety of diagnostic tests and algorithms with different diagnostic sensitivity and specificity are in use by different hospitals and laboratories for *Clostridium difficile* testing (CDT), but improper test requests are common for patients with no diarrhea, patients with diarrhea after use of laxatives within 48 hours, patients with diarrhea with an alternative cause, and repeated testing or test for cure. Our tertiary care hospital reported higher CDT than US national average since 2016. Therefore, a questionnaire that is a prerequisite for ordering CDT was implemented in May 2018 in the hospital to educate and enhance appropriateness of ordering practices for CDT. The aim of this study was to detect and compare the changes before and after that intervention for improving our facilities’ performance of reportable CDT metrics.

**Design:** We retrieved data for CDT test orders from January 2017 until December 2018 and compared before and after the implementation questionnaire, which is a prerequisite for ordering CDT, and evaluated for changes due to adherence to the inclusion/exclusion criteria mentioned in the preordering questionnaire.

**Results:** The results showed that the ordering number of CDT has been reduced (in 2017: total 2708; in 2018: total 2368). There has also
be an increased specimen rejection rate (in 2017: total 64; in 2018: total 96).

Conclusions: Continuing education of clinicians on clinical indication of CDT, reinforcing more stringent test ordering algorithms to block inappropriate ordering, and determining more objective criteria to determine the acceptability of stool samples help improve CDT ordering.

Correlation Between Tissue Processing Preanalytics and Hematoxylin-Eosin Stain Quality in Biopsy Specimens

((Poster No. 108)

Elizabeth A. Chilipala, BS; Robert Lott, BS; Elizabeth Sheppard, MBA; Mansoor Nasim, MD, PhD. 1Department of Histology, Premier Laboratory, Boulder, Colorado; 2Department of External Quality Assessment, Roche Tissue Diagnostics, Tucson, Arizona; 3Department of Global Market Access, Roche Tissue Diagnostics, Tucson, Arizona; 4Department of Pathology, Northwell Health Laboratories, Lake Success, New York.

Context: The Histology Quality Improvement Biopsy Program (Histo-QIP) is offered in the United States and abroad to assess the quality of the hematoxylin-eosin (H&E) stain in biopsy specimens, assessing slides from hundreds of institutions yearly. Data were compiled to determine if fixation and processing errors can lead to poor H&E stain quality.

Design: The Histo-QIP Program aids in improving preparation of histologic slides in anatomic pathology laboratories. The CAP/NSH Histology Biopsy Series consists of laboratories sending slides from the following biopsy samples: bladder, cervical, colon, endometrial, prostate, skin, and stomach. For each sample set submitted participants receive an evaluation. Comparison of the fixation and processing scores with the corresponding staining scores for the H&E stain in biopsy samples submitted from the past 6 years was reviewed to determine any correlation between those 2 parameters.

Results: Review of the summary data shows a direct correlation between samples that have fixation and processing errors also demonstrating the hematoxylin nuclear artifact of nuclear stain not crisp, slightly smudgy, with chromatin patterns inadequately defined. Crisp nuclear detail is vital for diagnosis. Summary of all data showed an R² value of 0.816 between the parameters evaluated (Figure 51). Upon review of several years of data, 29% of biopsy samples submitted demonstrated fixed and processing errors and 30% demonstrated the H&E staining error of nuclear stain not crisp.

Conclusions: Extensive H&E staining errors and poor stain quality are prevalent within the biopsy series of the Histo-QIP Program and can be directly correlated to fixation and processing errors.

Evaluation of the Correlation Between the Frozen Section Diagnosis and Final Diagnosis Reports

(Poster No. 109)

Mohammad H. Shokouh-Amiri, MD (mshoko2@uic.edu); Robert Post, MD; John Groth, MD; Elizabeth Wiley, MD. Department of Pathology, University of Illinois at Chicago.

Context: Accurate evaluation of a provided tissue sample by frozen section (FS) plays a significant role in any intraoperative consultation to provide the surgeons the best results to make the final decisions before any further interventions. Results of the FS diagnosis can be considered as the tip of an iceberg, with several invisible high-risk preanalytical, analytical, and postanalytical steps, such as proper tissue sampling, labeling, and communicating the results. To optimize the accuracy of the FS diagnosis and optimize patient care, the expertise of the pathologist(s) and experience of the frozen section team are required. Internal review of the FS slides by the surgical pathology faculty is expected in most pathology departments, including ours. Our goal was to assess the correlation.

Design: We retroactively reviewed 713 FS consults, from July 2017 to December 2018. In our department, we run an extra monthly FS-final diagnosis (FS-FD) correlation evaluation, performed by the surgical pathology fellow(s) or resident for quality control and quality assurance purposes for all FS cases. We collected cases of discrepancies, designated as major or minor, in which the fellows or resident identified a discrepancy.

Results: We found an overall discrepancy rate of 2.5%, with 8 major (1.1%) and 10 minor (1.4%) discrepancies, and 1 referral.

Conclusions: Our records of major and minor discrepancies are significantly lower than most published data, and those few major discrepancies were discovered only through the extra monthly reviews of the FS-FD Correlation Project, which we will elaborate in this report.

Methylenetetrahydrofolate Reductase Mutation Presenting as Palmoplantar Occlusive Vasculopathy

(Poster No. 110)

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Methylenetetrahydrofolate reductase (MTHFR) is an enzyme, encoded by the MTHFR gene, which is involved in numerous vital reactions in the body, including folate metabolism and the processing of amino acids. This rate-limiting enzyme converts homocysteine to methionine, an important DNA methylator and gene regulator. Although various genetic polymorphisms have been described in the literature, mutations in the MTHFR gene have been associated with hyperhomocysteinemia. This finding can manifest in a variety of manners including neural tube defects, malignancy such as colon cancer, congenital anomalies, cardiovascular disease, and neurological disorders including Alzheimer disease. Though presentation is commonly seen in childhood, adult cases of deficient folate metabolism have been reported with neurologic symptoms and thromboembolic events described. Herein, we present a case of MTHFR mutation as the vasculopathic etiology of painful, papular lesions on the palmoplantar surfaces of the bilateral hands and feet in a 69-year-old man. A punch biopsy of the hemorrhagic neoplasms revealed focal epidermal necrosis with associated occluded vessels, superficial perivascular and interstitial lymphohistiocytic inflammation, and red blood cell extravasation. Further workup of the occlusive vasculopathy with secondary epidermal necrosis revealed a serum electrophoresis monoclonal IgM peak and elevated homocysteine levels. Genetic testing was recommended and revealed a homozygous MTHR mutation with 2 copies of C677T. Palmoplantar occlusive vasculopathy is an unusual presentation of a rare genetic MTHFR mutation that follows an autosomal recessive inheritance pattern. We highlight this case to highlight the importance of genetic testing and a thorough histopathologic evaluation when investigating vasculopathic etiologies.

Characterization of the Inflammatory Infiltrate Associated With Basal Cell Carcinoma, Squamous Cell Carcinoma, and Melanoma in Biopsy and Excision Specimens

(Poster No. 111)

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Context: The current understanding of cancer biology has recognized the relationship of the immune system. We examined the inflammatory infiltrate around a skin cancer in a biopsy and its excision.
**Abstracts**

**Design:** Cases of basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma (MM) were examined for eosinophils, plasma cells, mast cells, and neutrophils. Also, the immunostains CD1a, CD3, CD4, CD8, CD56, and CD68 were applied. A cell count was performed in the areas of highest concentration.

**Results:** The inflammatory infiltrate between the biopsy and excision specimens did not appear significantly different (P > 0.1). Eosinophils and neutrophils appear more commonly to be associated with SCC than BCC or MM, although there was considerable variation between the specimens. Plasma cells appeared more commonly in specimens with BCC and SCC than MM. Langerhans cells (CD1a) were most commonly found in SCC followed by BCC, while MM. SCC had the highest number of T cells (CD3) as compared to BCC and MM. BCC and SCC had a predominance of T helper (CD4) over T suppressor (CD8) cells, while MM was equivocal. Also, macrophages (CD68) were more common in cases of BCC and SCC than MM. Natural killer cells (CD56) were more common in SCC, while SCC and MM rarely contained them. Mast cells were not increased in any of the cancer specimens.

**Conclusions:** The biopsy procedure does not appear to significantly alter the inflammatory pattern already associated with the skin cancer. However, each of the skin cancers appears to elicit a unique inflammatory pattern, but its significance is not well understood.

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**Incidental Squamous Cell Carcinoma in the Wall of an Epidermal Inclusion Cyst in a Patient on Immunosuppressive Therapy**

*Poster No. 112*

Ifeayinwa Asuzu, MBBS; Kingsley Ebare, MBBS; Youyuan Xu, MD. Department of Pathology, Staten Island University Hospital, Staten Island, New York.

Epidermal inclusion cysts are the most common benign cutaneous cysts, occurring anywhere on the body and most frequently on the face, scalp, neck, and trunk. Epidermal inclusion cysts have been postulated to arise most often along embryonic fusion lines from invagination of keratinized squamous epithelium. Epidermal cysts are usually asymptomatic but may rarely give rise to malignancy. In this case underlying risk factors such as ultraviolet light exposure, older age, fair skin (Fitzpatrick skin types I-III), and immunosuppression may be present. We present a case of incidental well-differentiated squamous cell carcinoma in the wall of a gluteal epidermal inclusion cyst in a middle-aged man who is a smoker and is on immunosuppressive therapy for rheumatoid arthritis. He has a medical history of rheumatoid arthritis and SCC had a predominance of T helper (CD4) over T suppressor (CD8) cells, while MM was equivocal. Also, macrophages (CD68) were more common in cases of BCC and SCC than MM. Natural killer cells (CD56) were more common in SCC, while SCC and MM rarely contained them. Mast cells were not increased in any of the cancer specimens.

**Conclusions:** The biopsy procedure does not appear to significantly alter the inflammatory pattern already associated with the skin cancer. However, each of the skin cancers appears to elicit a unique inflammatory pattern, but its significance is not well understood.

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**Predominance of Lymphatic Differentiation in Cutaneous Kaposi Sarcoma**

*Poster No. 113*

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Kaposi sarcoma (KS) is a vascular proliferative disease of both cutaneous and mucosal sites, and has been associated with immunosuppression but also in the setting of human herpesvirus 8 (HHV8) infection. The lesion is commonly characterized by a lymphomatoid pattern but can also show typical hemangioma-like lesions. HHV8/podoplanin and HHV8/CD31 double-immunostained slides were examined and scored by 2 observers. We examined 3 to 15 high-power fields, using 10× or 20× objective, depending on tissue specimen size. The extent of colocalization was evaluated by using the following scoring system: 0 (0%), 1 (1%–10%), 2 (11%–50%), 3 (51%–100%).

**Results:** All the cutaneous lesions had a consistently high ratio of HHV8 and podoplanin coexpression, whereas the ratio for HHV8 and CD31 was significantly lower. In the mucosal lesions both HHV8 and podoplanin and HHV8 and CD31 showed high ratios of coexpression.

**Conclusions:** Compared to blood vascular phenotype, there is a lymphatic dominance in cutaneous KS (Table). In contrast, in mucosal lesions, both phenotypes are equally expressed.

**Scores and P Values Calculated for Kaposi Sarcoma Lesions**

<table>
<thead>
<tr>
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**A Rare Case of Eccrine Carcinoma Negative for ER and PR Immunostains**

*Poster No. 114*

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Eccrine carcinoma is a rare malignancy of the skin. It is typically found in the lower extremities and equally affects men and women. We present a case of eccrine carcinoma of the skin originating from the upper extremities. The patient was a 63-year-old man who did not have any history of malignancy. He presented with a mass at the interspace between fourth and fifth digits of the right hand. The mass had been growing in size but did not cause pain at rest. Surgery was performed to excise the mass entirely. The morphology of tumor showed glandular differentiation with an infiltrating pattern, consistent with eccrine carcinoma of the skin (Figure 53, A). The tumor cells were positive for CK7 immunostain (Figure 53, B), but negative for CK20. Although the patient had no known history of malignancy, a series of immunohistochemical stains, including TTF-1, PSA, CDX2, GATA3, and PAX8, were performed to rule out any possible metastatic carcinoma. The results for the aforementioned immunostains were all negative, further indicating the diagnosis of eccrine carcinoma of the skin. Interestingly, whereas previous reports have displayed that eccrine carcinoma are positive for ER and/or PR immunostains, our results showed that ER (Figure 53, C) and PR (Figure 53, D) immunostains were both negative. The major purpose of this case report is to expand the literature of the rare eccrine carcinoma of the skin. We would also like to demonstrate the unique immunohistochemical pattern of negative ER and PR staining in our case.
A Histopathologic Study of Granulomatous Skin Lesions at a Tertiary Care Hospital in Nepal
(Poster No. 115)

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Context: Granulomatous skin lesion is a common lesion noted in biopsies for which various causes may be responsible. Our aim was to study different granulomatous skin lesions and to determine the etiology of the lesion by using histopathologic techniques and staining with hematoxylin-eosin, periodic acid–Schiff, Ziehl-Neelsen, Fite, and Giemsa stains.

Design: This observational study was carried out for a period of 1 year from August 2015 to July 2016 in the Department of Pathology at Bir Hospital and Civil Service Hospital on skin biopsies showing granulomatous lesions. These biopsies were stained with special stains and evaluated.

Results: Of a total of 734 skin biopsies, 42 cases had granulomatous reaction. Nonnecrotizing granuloma (64.3%) was the most common type of granuloma (Figure 54, A). The most common cause was leprosy (Figure 54, D) (35.6%) followed by tuberculosis (33.4%). Other etiologies include fungal infections (9.6%; Figure 54, B), granuloma annulare (7.2%), erythema nodosum (7.2%), epidermal cyst (4.8%), and granulomatous rosacea (2.2%). Caseous necrosis was present in 7.5% cases of tuberculosis, and acid-fast bacilli were noted in 66.6% of these cases (Figure 54, C). Use of special stains could show the etiologic agent in only 6 cases (2 cases each of leprosy, tuberculosis, and fungal infection).

Conclusions: The most common type of granuloma was non-necrotizing granuloma, and leprosy was the most common cause. Special stains were found to play a supporting role in finding the etiology of granulomatous lesion in a limited number of cases only, and hematoxylin-eosin evaluation was sufficient to diagnose most of the cases.

Syringocystadenoma Papilliferum in Conjunction With a Verrucous Carcinoma
(Poster No. 116)

Darren Brow, MD (darren.brow@jax.ufl.edu); Arun Gopinath, MD; Reeba Omman, MD. Department of Pathology, UF Health, Jacksonville, Florida.

Syringocystadenoma papilliferum (SP) is a benign solitary lesion derived from apocrine or eccrine glands. Most commonly located on the scalp, it is often associated with a nevus sebaceous of Jadassohn and trichoblastomas. It is rare to see SP in conjunction with a verrucous carcinoma (VC). We report the fourth known case of an SP in conjunction with a VC (Table). The patient is a 58-year-old man with a slow-growing skin lesion on the left posterior shoulder for 18 years. The lesion was exophytic with a central, firm, crusty, gray-tan, friable mass, and was excised with adequate margins. Microscopically, verrucous squamous proliferation with pushing borders, hyperkeratosis, and underlying lymphocytic inflammation with focal areas of papillae-containing plasma cells was present. The patient had no recurrence after 4 months. SP lesions are slow growing; found typically on scalp, face, and head and neck regions; may present as 3 different types: plaque (scalp), linear (face, head and neck), and solitary nodular (trunk, extremities); and have 3 distinct stages of growth: infantile, adolescent, and adult. It is during the adult stage that malignant transformation may occur. Verrucous carcinoma is slow growing, minimally invasive, and rarely metastasizes, but has a tendency to recur. The cutaneous lesions are typically found in the oral cavity, anogenital and plantar regions, but rarely on the extremities. The treatment of these lesions is complete surgical excision and the prognosis is good. In conclusion, this case represents a rare occurrence of SP with a VC or malignant component.

<table>
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Subcutaneous Splenosis Mimicking Metastases in Hemoglobin C Disease: An Unusual Case

(Poster No. 118)

Sandra A. Van Horn, MD; Jodi Speiser, MD; Kumaran Mudaliar, MD. Department of Pathology, Loyola University Medical Center, Maywood, Illinois.

Splenosis is believed to be the autotransplantation of splenic tissue nodules stemming from splenic trauma or splenectomy. Splenosis typically presents as multiple asymptomatic palpable nodules and is most often observed in abdominal surgical scars. Subcutaneous splenosis can be a concerning radiologic finding and can pose a histopathologic challenge. We present a case of a 38-year-old woman with a history of complicated hemoglobin C disease who was 7 years post splenectomy for splenomegaly and thrombocytopenia. Two subcutaneous nodules were incidentally discovered on physical and computed tomography examinations during an unrelated evaluation for chest pain. Further radiologic workup revealed multiple superficial ill-defined soft tissue lesions and yielded a broad differential diagnosis. The clinical differential diagnosis included cutaneous endometriosis, hemoma, metastases, or thrombosed perivascular lesions. Additional biopsies of the subcutaneous nodules were submitted for histopathologic evaluation, which revealed benign-appearing, lobulated vascular lesions with prominent endothelial vessels. The histologic differential diagnosis includes splenosis and vascular malformation/hemangioma. Immunohistochemically, the endothelium of some vessels was stained with CD31, and Bcl-2. After CD31 highlighted littoral cells lining some of the vascular spaces. The mitotic index was low. The histologic pattern was consistent with splenic red pulp. Thus, the lesions were determined to be subcutaneous splenosis. This case emphasizes the diagnostic challenge of subcutaneous splenosis, for which complete clinical history and accurate radiologic evaluation are essential for histopathologic diagnosis.

Eosinophilic Annular Erythema in an Adult Patient With Rheumatoid Arthritis

(Poster No. 119)

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Eosinophilic annular erythema (EAE) is a relatively recently described, rare dermatosis presenting as annular plaques that resolve without sequelae but with tendency to recur. There is controversy regarding the relationship of EAE to Wells syndrome, an inflammatory dermatitis presenting with erythematous plaques that resolve with hyperpigmentation and atrophy. We present a case of a 53-year-old woman with rheumatoid arthritis who presented with pruritic, annular, edematous, and erythematous plaques thought clinically to be granuloma annulare. Lesions were distributed on the scalp, lateral face, trunk, and extremities with sparing of palms and soles. Routine laboratory tests were significant for an absolute eosinophil count of 610 Kjul (0.6%). Histopathologic examination revealed a perivascular lymphohistiocytic infiltrate with many eosinophils in the interstitium. Flame figures were absent and direct immunofluorescence testing was negative. Of note, flame figures are the hallmark of Wells syndrome and can rarely be seen in EAE depending on the timing of the biopsy, with well-developed lesions having a higher likelihood of having them. A diagnosis of EAE was rendered. Treatment with prednisone led to resolution of the patient’s lesions and pruritus. An association between EAE and chronic conditions including autoimmune thyroid disease, Churg-Strauss syndrome, and autoimmune hepatitis has been previously suggested in literature. To our knowledge, this is the first case of EAE in an association with rheumatoid arthritis. Although the precise relationship of rheumatoid arthritis and EAE is unclear, our case supports the idea that EAE is a distinct clinical entity rather than a variant of Wells syndrome.

Extraocular Sebaceous Carcinoma on the Back

(Poster No. 120)

Shahad Abdulameer, MD (shahad.abdulameer@lumc.edu); Jodi Speiser, MD; Kumaran Mudaliar, MD. Department of Pathology, Loyola University Medical Center, Maywood, Illinois.

Sebaceous carcinomas (SCs) are traditionally segregated into 2 categories: periorcular and extraocular. While periorcular SCs are not uncommon, extraocular SCs are relatively rare. Extraocular SCs most often occur on the head and neck, but are very uncommon on other sites such as the back. Clinically, they can present as an erythematous nodule or papule with possible ulceration. Histologically, they are poorly circumscribed with an infiltrative growth pattern and show significant cytologic atypia, a high mitotic activity with atypical mitotic figures, and particular necrosis. Here, we present a case of a 74-year-old man with an left upper back skin nodule. The nodule initially started small and increased in size during a 6-month period. No other skin lesions were identified and a biopsy of the nodule was performed. Histologic sections showed a tumor with an irregular infiltrative lobular growth pattern. The tumor was composed of a disorderly admixture of basophilic germinative sebaceous cells and more mature cells with vacuolated cytoplasm with focal areas of keratinization. The cells were pleomorphic and had round to oval nuclei with prominent nucleoli (Figure 56, A and B). Immunohistochemical
Arch Pathol Lab Med

Abstracts

A Rare Case of Isolated Cutaneous Rosai-Dorfman Disease Clinically Mimicking Leukemia Cutis

(Hani Katerji, MD; Roula Katerji, MD; Jonathan Soh, MD; MaryGail Mercurio, MD; Glynnis A. Scott, MD. Department of Pathology, University of Rochester, New York.)

Rosai-Dorfman disease (RDD) is a distinctive idiopathic histioproliferative disorder with a diagnosis that might be challenging and difficult to make, especially when the primary presentation site is extranodal. Isolated cutaneous-RDD is an extremely rare entity that is not well documented. Herein, we report a case of isolated cutaneous-RDD with an unusual clinical presentation. A 73-year-old woman with history of breast ductal carcinoma in situ, status post mastectomy, presented with multiple red-brown monomorphic papules and macules on her face, arm, and legs (Figure 57, A). A biopsy was performed and showed atypical lymphoid infiltrate with abundant histiocytes. The atypical cells stained strongly positive for androgen receptor (Figure 56, C), CK7 (Figure 56, D), and EMA, and negative for Ber-EP4. These findings were consistent with extraocular SC. On excision, no residual carcinoma was present.

Bone Marrow Metastasis of Malignant Melanoma in a Child, Arising Within a Congenital Melanocytic Nevus

(Saadia Haleema, MD (shaleema@health.southalabama.edu); Shalla Akbar, MD; Sandhya Rani Dasaraju, MD; Elizabeth Manci, MD; Jacek Polski, MD; Department of Pathology, University of South Alabama, Mobile.)

Malignant melanoma (MM) is rare in children but the risk increases in giant congenital melanocytic nevi (GCMN). Families of children with GCMN are advised to carefully monitor skin for changes suggestive of MM; furthermore, bone marrow (BM) metastasis in MM is exceptional especially in childhood. We report a rare case of a 4-year-old girl with a GCMN that transformed to MM with rapid metastasis to the BM. She was closely followed up by her physician but did not follow up for a year at which time the nevus has rapidly enlarged in size. Microscopically, the lesion showed discohesive nests of pleomorphic melanocytes with hyperchromatic nuclei and prominent nucleioli in the dermis and epidermis. Characteristic features of congenital nevus were present. The malignant cells were positive for SOX-10, Pan-mel, and P21. P16 was positive in the nevus part and negative in the malignant lesion. The malignant cells had a wild-type BRAF gene. A few months later, PET scan showed metastasis to the vertebrae, sacrum, bilateral ilium, bilateral femurs, and tibia. Microscopically, the BM was involved by very large, pleomorphic, highly atypical cells with vacuolated cytoplasm as single cells as well as in clusters. The right side was extensively involved, resulting in almost dry aspirate. SOX-10 was intensely positive. This case shows that MM in childhood can arise within congenital melanocytic nevi and can metastatize to BM. The disease prognosis depends on the stage of the disease; therefore, close surveillance is indispensable in children with a predisposition to melanoma.

Cutaneous Rosai-Dorfman Disease With Long-Term Follow-up

(Sepideh Mehravaran, MD (sepidehmehrvaran@gmail.com); Bhuvaneswari Krishnan, MD; Hafeez Diwan, MD; Hamza Mugahed, MD. Department of Pathology, Baylor College of Medicine, Houston, Texas.)

Rosai-Dorfman disease (RDD) is a rare benign self-limiting disease of unknown etiology. It is primarily a disease that involves lymph nodes but occasionally can present as isolated extranodal manifestation. A purely cutaneous form is rare and is considered by some as a separate entity. We report a case of a 73-year-old man with more than a 9-year history of cutaneous RDD. The patient presented with a 3×3-cm multilobulated, violaceous, tan-brown, firm heterogeneous plaque with hypopigmented foci and previous biopsy scars. No lymphadenopathy or organomegaly was identified by further examination and positron emission tomography scan. Five biopsies were performed at different durations in the last 9 years and showed similar histologist findings consisting of a dense dermal lymphohistiocytic infiltrate admixed with numerous plasma cells and few neutrophils. The histiocytes were enlarged, some with foamy cytoplasm and some with intracytoplasmic lymphocytes (emperipolesis). Histocytes were positive for CD68 and S100, and negative for CD1a. This is the first case of cutaneous RDD with a 9-year follow-up showing no resolution of the disease. Purely cutaneous RDD is rare, comprising only 3% of RDD cases. In this patient, with follow-up of 9 years, there is no systemic involvement of the disease nor was additional cutaneous involvement identified. It is important to differentiate cutaneous RDD from other diseases with histiocytic proliferation, including Langerhans cell histiocytosis, Erdheim-Chester disease, and juvenile xanthogranuloma, since the clinical implications are different.

Melanoma: Our Experience With 100 Histologically Challenging Cases
(Poster No. 124)

Ravindra Kolhe, MD, PhD; Saleh Heneidi, MD (SHENEIDI@augusta.edu); Sravan Kavuri, MD; Vamsi Kota, MD; Ashis Mondal, PhD. Department of Pathology, Augusta University, Augusta, Georgia.

Context: Most melanomas can be accurately diagnosed on an adequate biopsy. However, for specific subsets of melanocytic proliferations, there exist conflicting and/or ambiguous features that preclude a definitive consensus diagnosis on a histologic ground. The goal of the current study is to investigate the utility of single nucleotide polymorphism microarray (SNPM) in melanoma diagnosis.

Design: The whole genome SNPM was performed on the DNA isolated from formalin-fixed paraffin-embedded specimens following the manufacturer's protocol (OncoScan assay, Affymetrix Inc, Santa Clara, California). The raw data were analyzed in Chromosome Analysis Suite 3.0 software and were matched to in silico formalin-fixed paraffin-embedded specimens' reference sets. This platform consists of 274 000 probes including 74 somatic mutations from 9 genes (BRAF, KRAS, EGFR, IDH1, IDH2, PTEN, PIK3CA, NRAS, and TP53). The diagnosis of melanoma on SNPM was made on the basis of the 5 genomic regions probed for FISH and other statistically significant genomic aberrations seen in melanoma.

Results: In our validation study, with the independent use of the SNPM data (Figure 58), we were able to confirm melanoma in all the cases (n = 14) and rule out melanoma in 34 of 35 in the histologic mimics of melanoma, with overall test sensitivity of 100%, specificity of 97%, and a negative predictive value of 100%. In addition, we confirmed the BRAF V600E mutation in 8 of 8 cases.

Conclusions: Here, we describe a powerful technology for confirming/ruling out melanoma in histologically difficult cases. We anticipate that this approach of obtaining high-resolution data from a formalin-fixed paraffin-embedded specimen sample at a reduced cost will facilitate diagnosis of melanoma, which was not previously possible.

Dr Kolhe has served as a consultant for Illumina, Qiagen, BMS, and Asuragen. Dr Kolhe also received honorarium from Agenda.

Unusual Metastatic Melanoma Mimicking Melanocytoma: Value of Molecular Analysis in Confirming Diagnosis
(Poster No. 125)

Yasna Chaudhary, MD (yasna.chaudhary@hotmail.com); Christina Kovacs, MD; Alkaroo Frometa, MD; Robert W. Allan, MD. Department of Pathology, Brandon Regional Hospital, Tampa, Florida.

Differentiating between a benign/locally aggressive meningeal melanocytoma and malignant melanoma metastatic to the meninges may be a challenging task, requiring a combination of histologic and clinical features. It is particularly challenging in cases of a solitary meningeal mass. We report the case of an 81-year-old man who presented with altered mental status, headache, nausea, and vomiting and was found to have an isolated 3.2-cm posterior right temporal lobe mass by head computed tomography. A biopsy was performed, and histologic sections demonstrated an atypical melanocytic proliferation. Immunohistochemistry confirmed a melanocytic neoplasm (S100+, HMB-45+, Melan-A+). Given the solitary nature and absence of history of cutaneous or other primary site melanoma, the differential diagnosis included solitary metastatic melanoma to the meninges and meningeal melanocytoma. As there are distinct molecular findings between melanocytoma (mutations in NRAS, GNA11, GNAQ) and metastatic melanoma (BRAF, KIT mutations), we used a panel of molecular studies by next-generation sequencing and FISH tests to aid in the distinction. The melanocytic tumor showed mutations in BRAF (NP_004324.2: p.Val600Lys), KIT (NP_000213.1:p.Gly565Glu), PIK3CA (NP_006209.2: p.Glu542Lys), TP53 (NP_000537.3:p.Arg175His), and TER1 promoter (~146C>T). FISH studies showed monosomy 10 with resultant PTEN deletion. These alterations are typically seen in metastatic melanoma, while alterations associated with melanocytoma (NRAS, GNA11, GNAQ) were not identified. The differential diagnosis between a primary meningeal melanocytic tumor (melanocytoma) and solitary meningeal metastatic melanoma may be challenging. This report highlights how molecular testing is useful in difficult cases not only diagnostically but also to guide subsequent therapy.

Alanine Aminotransferase Results Differ by Analyzer Manufacturer in a National Integrated Health Setting, 2012–2017
(Poster No. 126)

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Context: Alanine aminotransferase (ALT) is used in clinical care, based on the degree of ALT abnormality. Little is known about the performance of various chemical analyzers in ALT determination.

Design: The College of American Pathologists (CAP) requires clinical laboratories to test standardized samples as part of quality control procedures. From 2012–2017, a total of 80 standardized ALT samples were tested in 223 laboratories within the Department of Veterans Affairs (n = 22,950 individual CAP test results). We performed additional analysis on CAP samples <50 U/L, since they are typically considered to be in the normal ALT range by most laboratories.

Results: CAP samples averaging 21 to 268 U/L were tested by using analyzers from Beckman (38%), Siemens (25%), Abbott (14%), and Vitro/Ortho (12%). We found a mean difference of 12.4 U/L (SD = 3.6) per sample between the highest and the lowest analyzers. In the subgroup analysis of the 10 samples that were <$50 U/L, the mean differences were 15.6 U/L (SD = 1.8). In the 5 samples <35 U/L, the mean difference was 16.2 U/L (SD = 1.2). Vitro/Ortho gave consistently higher readings than other analyzers. Using a mixed-effects model, we
found that analyzers by different manufacturers had an independent effect on ALT values, both overall, in samples <50 U/L, and in samples <35 U/L (P = .001). This finding was independent of effect of year (P = .62; Figure 59).

Conclusions: Chemical analyzers by 4 major manufacturers produce different results over a wide ALT range. Furthermore, between-analyzer differences in the low ALT range are significant enough to impact clinical decision-making. Interpretation of ALT values should be made in the context of the analyzer.

To Determine Negative Predictive Value of Xanthochromia
(Poster No. 127)
Apeksha Agarwal, MD (Agarwalal@uthscsa.edu); Wieslaw Furman-ga, MD. Department of Pathology, University of Texas Health Science Center, San Antonio.

Context: Xanthochromia is the pigmentation of cerebrospinal fluid caused by subarachnoid hemorrhage. Subarachnoid hemorrhage is a medical emergency characterized by bleeding in the subarachnoid space and high mortality rate of 50%. Sensitivity of computed tomography (CT) scan declines after 12 hours from symptom onset but increases for xanthochromia test.

Design: This is a retrospective study in which 48 cases were included during a 2-year period for which CT scan and cerebrospinal fluid for xanthochromia testing were performed. Xanthochromia testing was done by spectrophotometry on tube numbers 1 and 4 for detection of “hemorrhagic bilirubin” at a wavelength of 440 to 460 nm. Results of head CT scan, xanthochromia test, time since development of symptoms, and final diagnosis were reviewed.

Results: Of the 48 cases, 2 were indeterminate, 1 was positive, and 45 were negative for xanthochromia. Both indeterminate cases were negative for intracranial bleed on head CT scan. The case positive for xanthochromia showed a ruptured anterior communicating artery on head CT scan. The test has a sensitivity of 100%, specificity of 95.74%, and negative predictive value of 100% with an accuracy of 95.83%.

Conclusions: Spectrophotometry is more sensitive and specific for detection of bilirubin-related cerebrospinal fluid discoloration than visual evaluation. Visual evaluation cannot distinguish bilirubin from other causes of pigmentation. Our study demonstrates that spectrophotometric testing of cerebrospinal fluid rules out intracranial bleeding older than 12 hours with a 100% of negative predictive value.

Prognostic Significance of Oligoclonal Protein Band and Ig Isotype Switching in a Patient With Multiple Myeloma After Autologous Hematopoietic Stem Cell Transplant
(Poster No. 128)
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Neoplastic proliferation of plasma cells in multiple myeloma is generally associated with excess production of a monoclonal protein of constant heavy chain isotype with light-chain restriction. Multiple Ig isotypes and isotype switching are uncommon events even after multiple treatments and are of uncertain clinical significance. We present a case of a 71-year-old woman with IgA k myeloma, Durie-Salmon stage III disease with hypercalcemia, anemia, and bone disease with 45% plasma cells in the marrow and 1p deletion by FISH. The patient underwent myeloablative conditioning and autologous stem cell transplant. Patient was monitored by serum immunosubtraction cancer zone electrophoresis (ISE), serum free light chain analysis, and urine protein immunofixation electrophoresis for relapse according to the standard monitoring protocol. The patient achieved remission after transplant and showed severe hypogammaglobulinemia on serum protein electrophoresis and ISE. Urine protein electrophoresis did not show causes of proteinuria or light chains. However, 6 months after her transplant, she displayed an IgG k and lambda monoclonal protein on ISE (Figure 60, A through D) and a lambda light on urine protein electrophoresis with normal k/lambda ratio. With the presence of this Ig switching, she continues to remain in remission with normal laboratory parameters. Presence of heavy and light chain Ig isotype switching is a rare phenomenon that can represent a good prognostic feature in patients with multiple myeloma who are undergoing stem cell transplant. Patients exhibiting this feature should be followed up from the time of the appearance of these monoclonal proteins to better understand the prognostic significance of these proteins.

The 99th Percentile of Cardiac Troponin I: Comparison Between Blood Donors and Patients Admitted to Emergency Department With No Previous History of Cardiac Disease
(Poster No. 129)
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Context: Chest pain is the second most common chief complaint among adults presenting to emergency department across the United States. The 99th percentile of cardiac troponin I (cTn I) in the healthy population is the cutoff level used for identifying acute myocardial infarction. However, the definition of healthy population is not clear while it has an important role in decision-making regarding further observation or early discharge of admitted patients.

Design: We evaluated the admission cTn I levels in 50 patients who presented to the emergency department with and without chest pain as the main chief complaint and identified those with no previous history of chest pain or abnormal cTn I levels (n = 39). Blood samples of 50 blood donors were used as the control group. The 99th percentile of cTn I levels is calculated in each group.

Results: The 99th percentile of cTn I is 0.062 µg in the blood donor group and 0.457 µg in patients admitted to the emergency department with no previous history of chest pain or abnormal troponin levels.

Conclusions: The 99th percentile of cTn I is significantly lower in the donor group, who are routinely considered a healthy population, than in admitted patients to the emergency department with no previous history of cardiac disease. The donor group may not be an appropriate representative of the normal population. Defining cTn I cutoff levels based on this group may lead to admission of suspicious patients for a longer duration and bring a larger financial burden to the health system while it can be avoided.

Laboratory Considerations in the Diagnosis of Tick-Associated Meat Allergy: The Effect of Interferants on IgE α-Gal Results
(Poster No. 130)
Jennifer Ju, MD (jy3bjy@hsmail.mcc.virginia.edu); Barbara Murphy; Walter Oliveira; Lidong He, PhD; Joseph Wieneck, PhD. Department of Pathology, University of Virginia, Charlottesville.

Context: Recent studies have shown that bites from lone star ticks can result in meat allergies due to IgE sensitization to galactosyl-α-(1,3)-galactose (α-gal) present in mammalian tissue. Specific IgE testing against α-gal, using cetuximab (which contains α-gal, Bristol-Myers Squibb, New York, New York) bound to streptavidin ImmunoCAP (anti-α-gal-IgE-ImmunoCAP, Phadia, Portage, Michigan), is created and offered at our institution. Our study seeks to examine the effect of hemolysis, hyperbilirubinemia, and hypertriglyceridemia on anti-α-gal-ImmunoCAP testing.

Design: We designed our study by following Clinical Laboratory Standards Institute EP7-A2 clinical laboratory guidelines. Increasing concentrations (low, mid, high) of hemolysate, unconjugated bilirubin, and triglyceride (Sun Diagnostics, New Gloucester, Maine) were spiked in residual serum below or above the anti-α-gal-IgE-ImmunoCAP

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cutoff (0.35 kUA/L). As a comparison, a commercially available, promae ImmunoCAP against dust mite (anti-D pteronyssinus-IgE- ImmunoCAP, Phadia) was also evaluated. All specimens were analyzed on a Phadia250 instrument in triplicate and acceptable tolerance limits were set at 10%.

**Results:** Samples above the anti-a-gal-IgE-ImmunoCAP and anti-D pteronyssinus-IgE-ImmunoCAP with a primer had no effect on results for samples spiked up to our highest concentrations (hemoglobin, 0.8 g/dL; unconjugated bilirubin, 40 mg/dL; and triglyceride, 800 mg/dL). Similar results were obtained for samples below the anti-D pteronyssinus-IgE cutoffs for all interferences. However, samples below the anti-a-gal-IgE cutoff were impacted by a midconcentration hemoglobin of 0.4 g/dL. All unconjugated bilirubin and triglyceride concentrations studied did not impact anti-a-gal-IgE-ImmunoCAP results.

**Conclusions:** Hemolysis impacts anti-a-gal-IgE-ImmunoCAP results below the cutoff in comparison to the other interferences studied. Additional caution is necessary in this range for anti-a-gal-IgE-ImmunoCAP testing methodology.

**Better Managed Follow-ups After Post Vasectomy Spermogram by Flow Cytometry: A First Retrospective Study**

(Poster No. 131)

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**Context:** Vasectomy success (VS) is usually confirmed by postvasectomy spermogram analysis (PVSA) when VS. sperm concentration $\leq 100$ 000 sperm/mL and no motility is detected. We developed a PVSA by flow cytometry (cfPVSA). Samples for which sperm concentration was $\leq 5000$ sperm/mL by cfPVSA never contain living spermatozoa. This cutoff allowed for samples to be refrigerated and transported to the laboratory within 48 hours, since no motility/viability analysis is needed.

**Design:** The goals were to determine how many patients require only one cfPVSA to confirm VS when only the 5000 cutoff is used and whether the sperm concentration at first cfPVSA (1cfPVSA) can predict the second cfPVSA (2cfPVSA) result. The study was based on the review of 2243 1cfPVSA, their outcome, and the follow-up tests that were performed on these patients.

**Results:** Eighty patients (80.2%) showed a concentration $\leq 5000$ sperm/mL at 1cfPVSA. The 2cfPVSA confirmed VS in 52% of the patients. When the result of the 1cfPVSA is between 5000 and 10 000 sperm/mL, the likelihood that a 2cfPVSA will confirm VS is 84% and decreases as sperm concentration for the 1cfPVSA increases until the probability falls to 20% (CVi) at a concentration of 1cfPVSA is $\geq 100$ 000 sperm/mL.

**Conclusions:** VS can be confirmed routinely with only 1 cfPVSA. A 2cfPVSA will confirm VS in selected patients, based on the 1cfPVSA result. Analysis involving viability assessment that requires sample to be produced at the laboratory can be recommended by the physician when the likelihood determined that a 2cfPVSA confirms VS is too low.

Dr. Massicotte and Boilard are shareholders of Nasci Biologie Médicale Inc.

**Monitoring Analytic Performance of Immunoassays Using a Sigma-Metric Approach Based on Biological Variation Specifications**

(Poster No. 132)

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**Context:** Sigma-metric is a quality tool to assess analytical method performance based on precision, bias, and allowable total error (aTE). The objective of this study was to determine and monitor the sigma-metric of various tumor marker immunoassays, based on biological variation (BV) specifications of within-subject BV (CVi) and between-subject BV (CVg).

**Design:** Sigma-metric (Sigma = [aTE (%) – Bias (%)]/[CV (%)]) was calculated for CA 125, CA15-3, CEA, AFP, CA19-9, and thyroglobulin immunoassays for a period of 7 months (March–September 2018). Assays were performed on a Cobas 6000 (Roche Diagnostics, Indianapolis, Indiana) or a UniCel-Dx800 (Beckman Coulter Inc, Brea, California).

Analytical imprecision (%CVa) was estimated from internal quality control material. Analytical bias was estimated by comparison to BioRad Unity peer group interlaboratory reports. Analytical method performance was monitored by using the BV specifications criteria for aTE. Imprecision and bias performance were estimated by using %CVa/CVi and %Bias/(CVi + CVg)1/2 ratios, respectively.

**Results:** CA125 and CA 125 performed on the Cobas 6000 showed world-class performance with mean sigma values of 6.2 and 7.5, respectively. CEA, AFP, CA19-9 and thyroglobulin performed on the UniCel-Dx800 showed between marginal to excellent performance with mean sigma value ranging from 3.4 to 5.8. The imprecision ratio (%CVa/CVi) of Roche and Beckman immunoassays was optimal to minimal. The bias ratio (%Bias/(CVi + CVg)1/2) was optimal for Roche, while optimal to desirable for Beckman immunoassays.

**Conclusions:** The sigma-metric based on BV specifications is an alternative and objective quality tool that can be used to monitor tumor markers’ immunoassay performance.

**A Comparative Study for Determining Isatuximab Interference in Myeloma Patients Using Immunoanalysis Electrophoresis and Immunosubtraction**

(Poster No. 133)

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**Context:** A comparative study for determining isatuximab (CD38 monoclonal antibody in phase III trial) interference from endogenous monoclonal antibodies associated with myeloma.

**Design:** Determination of isatuximab is dose dependent; a pooled normal serum was used for spiking studies. The analytical sensitivity results were compared by using serum protein electrophoresis, immunosubtraction (IS), and immunofixation electrophoresis (IFE). We also spiked isatuximab into patient’s serum with known endogenous IgG κ disease; comigration of the endogenous IgG κ and isatuximab pattern was also characterized by free light chains, serum protein electrophoresis, IFE and IS measurements.

**Results:** Serum protein electrophoresis and IS results showed a quantifiable M-protein in βγ region (βγ-bridge) at 1 mg/mL of isatuximab concentration. At 0.6 mg/mL of isatuximab concentration, a faint band was visually observed on IFE and a clear visible peak was noticed in the pre-γ region of IS. Isatuximab (0.6 mg/mL) was also spiked into patient’s serum with known IgG κ disease and results are variable. In 3 patients, isatuximab comigrated with endogenous IgG κ and they were not differentiated by IFE. In the other 2 patients, they were well separated and this may be an attribute of clonal variability. On the other hand, isatuximab was well differentiated from endogenous IgG κ in all the patients (n = 5) by IS.

**Conclusions:** Although IS and IFE have similar sensitivity for isatuximab, IS has the ability to distinguish therapeutic interference of isatuximab from endogenous IgG κ, whereas IFE suffers from specificity when endogenous IgG κ and isatuximab comigrate.

**Capillary Dry Blood Spots to Determine Serum Testosterone Levels: A Way to Rethink Sample Collection in Routine Clinical Chemistry**

(Poster No. 134)

Tami Nguyen, BS (tamin05@gmail.com); Kaiinda DeSilva, BS; Siobhan McKinney, BS; Charles Salley, MD; Mariko Nakano, PhD. Department of Toxicology, Molecular Testing Labs, Vancouver, Washington.

**Context:** Capillary dry blood spots (cDBS) have been used in neonatal screening for decades but recent demand for direct-to-consumer tests have seen cDBS gain popularity. However, implementation of cDBS as a surrogate for serum is still debatable. Particular challenges to address include analytical sensitivity, lack of reference ranges, and clinical interpretation of DBS results. This study aimed to determine if cDBS was a comparable specimen to venous serum (VS) by comparing testosterone levels in VS, vDBS, and cDBS.

**Results:** Serum protein electrophoresis and IS results showed a quantifiable M-protein in βγ region (βγ-bridge) at 1 mg/mL of isatuximab concentration. At 0.6 mg/mL of isatuximab concentration, a faint band was visually observed on IFE and a clear visible peak was noticed in the pre-γ region of IS. Isatuximab (0.6 mg/mL) was also spiked into patient’s serum with known IgG κ disease and results are variable. In 3 patients, isatuximab comigrated with endogenous IgG κ and they were not differentiated by IFE. In the other 2 patients, they were well separated and this may be an attribute of clonal variability. On the other hand, isatuximab was well differentiated from endogenous IgG κ in all the patients (n = 5) by IS.

**Conclusions:** Although IS and IFE have similar sensitivity for isatuximab, IS has the ability to distinguish therapeutic interference of isatuximab from endogenous IgG κ, whereas IFE suffers from specificity when endogenous IgG κ and isatuximab comigrate.
Results: The calculated serum values from cDBS were comparable to VS values. The observed testosterone levels in cDBS were 93 to 988 ng/dL, and the error compared to serum was 10%. The correlation of DBS and serum values was linear in relationship with an $R^2 = 0.89$ (Figure 61).

Conclusions: Strong positive correlations between calculated and measured serum testosterone concentrations suggest that cDBS can be used to estimate serum testosterone levels. Therefore, DBS is a highly potentiated specimen for many blood chemistry assays and could significantly decrease the need for venous blood collection, especially for screening tests at home.

Anti-Müllerian Hormones in Dried Blood Spot as a Potential Biomarker for the State of Male Sexual Health
(Poster No. 135)
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Context: As males advance in age, they typically experience notable depressions in total testosterone. The mechanisms contributing to this deterioration are still not well defined. Monitoring via quantitative measurement maintains accuracy and is readily accessible when collected by dried blood spot (DBS) cards. Anti-Müllerian hormone (AMH) is expressed in Sertoli cells during male sex development. In this study, we elect AMH as a potential contributor to male sex hormone decline.

Design: Ninety-seven DBS samples were collected from males 20 years of age or older. AMH was measured by enzyme-linked immunosorbent assay, and dehydroepiandrosterone sulfate (DHEAS) and testosterone were measured by liquid chromatography–mass spectrometry.

Results: AMH decreased as male participants increased in age. AMH and DHEAS showed a significant depression in the 40- to 70-year age group (AMH, 57%; DHEAS, 59%) compared to the 20- to 39-year age group. AMH was correlated positively with DHEAS ($R^2 = 0.112$). AMH and testosterone levels were higher in age group 20 to 39 years (AMH, 49%; testosterone, 91%). AMH and testosterone exhibited positive correlation ($R^2 = 0.122$).

Conclusions: AMH and DHEAS were observed to correlate with levels of testosterone, which can be used as an additional indicator of male sexual health. Inhibition of the aromatase enzyme by AMH could restrict the conversion of testosterone to estradiol. Conversely, lack of inhibition could decrease testosterone. Because AMH reserves potential to act as a controller of androgen conversion, inhibition of the aromatase enzyme may provide an explanation for our results. We plan to follow up these data with quantitation of androstenediol, androstenedione, and estrogens.

A Novel Tricolor Immunohistochemical Assay to Determine HER2 and GRB7 Protein Expression
(Poster No. 136)
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Context: Growth factor receptor–bound protein 7 (GRB7) is a cytoplasmic ligand for a multitude of receptors involved in cell proliferation, migration, and angiogenesis. Of particular importance is the role it plays in activating human epidermal growth factor receptor 2 (HER2). Patients with a high expression of both HER2 and GRB7 have poor outcomes in overall survival, recurrence risk, and metastasis as compared to HER2 overexpression alone, with independent GRB7 overexpression having the poorest outcomes. Assessment of GRB7 overexpression, either concurrently or independently of HER2 overexpression in individual cells, may provide valuable insights into prognosis, treatment plans, and recurrence risk.

Design: To visualize overexpression levels of GRB7 and HER2 on a single slide, a dual immunohistochemical (IHC) assay was developed to stain GRB7 (abcam, Cambridge, United Kingdom) red and HER2 (Roche, Tucson, Arizona) green. Breast, gastric, and esophageal junction carcinomas were stained on Benchmark XT instruments (Roche).

Results: The dual IHC stain appears black in areas of both GRB7 and HER2 overexpression. Single and clusters of cells overexpressing GRB7 without concurrent HER2 overexpression were identified in HER2-amplified breast, gastric, and esophageal carcinomas, with gastric adenocarcinoma having the highest frequency of heterogeneous expression. Cases from all 3 tissue types expressed HER2 without concurrent GRB7 overexpression.

Conclusions: We successfully developed a tricolor IHC assay for HER2 and GRB7 proteins by using a red and green IHC detection system. This tricolor IHC assay would enable pathologists to visualize and quantify heterogeneous expression of both markers on a single slide, improving individualized prognosis accuracy and treatment plans.

Anti-N-Methyl-D-Aspartate Receptor Encephalitis Associated With Ovarian Teratoma
(Poster No. 137)
Azhar Saeed, MD, MSc (asaeed2@kumc.edu); Fred Papp, MD, PhD; Zhan Ye, MD, PhD. Department of Pathology, University of Kansas Medical Center, Kansas City.

Anti-N-methyl-D-aspartate receptor (NMDAR) antibody encephalitis is a recently described autoimmune disease. The diagnosis is confirmed by detection of IgG antibodies against the GluN1 subunit of the NMDAR receptor in serum or cerebrospinal fluid. This disease commonly affects women younger than 45 years and approximately half of patients have an underlying tumor, especially ovarian teratoma. While delayed diagnosis and treatment could cause progressive neurologic deterioration and even death, most patients return to baseline level of functioning after appropriate treatment. Outcome is usually better if treatment starts earlier; therefore, early and thorough diagnosis is critical. We report a case of a 27-year-old woman with past medical history of polycystic ovarian syndrome who initially presented at an outside institution with progressive neuropsychiatric symptoms.

Extensive testing revealed positive NMDAR antibody in serum (1:80) and cerebrospinal fluid (1:5). The patient was transferred to our institution in a catatonic state after failing to improve on immunomodulatory therapy. Plasmapheresis was started and further imaging of the abdomen and pelvis revealed a well-defined nodule in the left ovary, measuring 1.7 x 1.2 cm. A left oophorectomy was done and the final diagnosis of the ovary was mature ovarian teratoma with neuronal
elements and lymphoid infiltrates (Figure 62, A and B). The patient’s symptoms resolved quickly after the tumor removal and plasmapheresis. This case shed light on the importance of screening for an underlying neoplastic etiology associated with autoimmune encephalitis, especially in a young adult female with acute onset of neuropsychiatric symptoms.

Extended Stability of Immunoglobulin in Dried Blood Spots
(Poster No. 138)

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Context: Using dried blood spots (DBS) over serum has clinical advantages; it is less invasive, requires a minimal specimen volume, and is easy to collect. The accuracy of enzyme-linked immunosorbent assays (ELISAs) on DBS has been confirmed, yet the extended stability of immunoglobulins in DBS is not readily available. The aim of this study was to determine the stability of immunoglobulins in DBS for sexually transmitted diseases.

Design: Blood containing immunoglobulins against human immunodeficiency virus, hepatitis C, herpes simplex virus type 2, or syphilis was spotted on DBS cards, air-dried, and stored at −80°C. At various times, the DBS were thawed and analyzed with commercially available ELISA test kits (see Table).

Results: Regardless of the ELISA test, the immunoglobulins in DBS were readily detected for up to 17 months with little variability (3%–16%), which was compatible with the first 3 months (2%–18%). The ELISA results with extended storage fell within a range of the mean with 1 standard deviation calculated from the first 3-month period.

Conclusions: Immunoglobulin levels in DBS during the course of 17 months remained at stable levels for the duration of the study and fell within acceptable variations. The 3-month stability at room temperature has been established, and our study exhibited the stability up to 17 months at −80°C, which indicates a superior stability compared to serum. Increased use of DBS could benefit at-risk populations because it is cost-effective and can be collected privately, without a clinical visit.

List of Commercial Kits for Sexually Transmitted Diseases

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<tr>
<th>STI Target</th>
<th>Product Name</th>
<th>Source</th>
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<tbody>
<tr>
<td>Human immunodeficiency virus</td>
<td>GS HIV Combo</td>
<td>Bio-Rad Laboratories</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>Ag/Ab EIA</td>
<td>(Hercules, California)</td>
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<tr>
<td>Herpes simplex virus 2</td>
<td>Ortho HCV Version</td>
<td>Bio-Rad Laboratories</td>
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<tr>
<td>Syphilis</td>
<td>3.0 ELISA Test</td>
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<td>HerpeSelect 2 ELISA</td>
<td>Focus Diagnostics</td>
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<td>IgG</td>
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<td>Trinity Biotech</td>
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Cribriform-Morular Variant of Papillary Thyroid Carcinoma With Associated Familial Adenomatous Polyposis
(Poster No. 139)

Katherine Cochrane, MD (kcochrane@utmck.edu); George Sneed, DO. Department of Pathology, University of Tennessee at Knoxville.

Cribriform-morular variant is a rare, morphologically distinct subtype of papillary thyroid carcinoma that has been associated with sporadic or germline mutations of the APC gene. It is unique in its association with familial adenomatous polyposis (FAP), with approximately half of patients showing FAP. Histologic features include a distinctive papillary neoplasm showing solid and predominantly cribriform pattern with characteristic morules of solid whorls of cells without keratinization or psammoma bodies. We report a case of cribriform-morular variant of papillary thyroid carcinoma in a 41-year-old woman who presented to the hospital with neck enlargement and dysphagia. Ultrasonography demonstrated multiple hypoechoic nodules and subsequent fine-needle aspiration was considered for malignancy. A total thyroidectomy revealed a bilateral, multinodular, infiltrative, and angioinvasive tumor measuring up to 6.0 cm with areas of solid, cribriform, and squamous morular growth characteristic of cribriform-morular variant of papillary thyroid carcinoma (Figure 63). Tumor cells were positive for β-catenin, CK19, and TTF-1 with HMGB positive only in squamous morules. Colonoscopy showed multiple polyps and a mass suggestive of invasive adenocarcinoma. Total colectomy revealed a 2.9-cm exophytic mass of moderately differentiated adenocarcinoma with invasion into the muscularis propria, 3 positive lymph nodes, and approximately 330 sessile and pedunculated polyps consistent with a polyposis syndrome such as FAP. In 25% to 30% of cases, this distinct variant may provide the first indication of an underlying FAP, thus highlighting the importance of the role of the pathologist in recognizing this unusual entity and alerting the clinician to screen for colon cancer and exclude FAP.

Ectopic Adrenal Tissue in the Liver Masquerading as Hepatocellular Carcinoma
(Poster No. 140)

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The incidence of ectopic adrenal tissue in visceral organs, outside the kidney, is extremely rare. While ectopia of nodular adrenal tissue is frequently found in perirenal regions, and ectopia in more distant regions is found in male or female genitalia, only rare cases have been reported in the liver. We present a case of a 48-year-old woman with past medical history of psoriasis and Hashimoto thyroiditis. She presented with left upper quadrant abdominal pain. Liver transaminases and alkaline phosphatase were slightly elevated, both hepatitis B and hepatitis C virus tests were negative. Magnetic resonance imaging showed a 2-cm right hepatic lobe lesion highly suggestive of hepatocellular carcinoma (Figure 64, A) and 19-cm splenomegaly; carcinoembryonic antigen, carbohydrate antigen 19.9, and α-fetoprotein were normal. The patient had evidence of portal hypertension (platelets were 88 k/μL and esophagogastrectomy showed grade 1 varices). The patient underwent microwave ablation of the liver lesion with biopsy. Histopathologic examination revealed benign adrenal cortical tissue (Figure 64, B), which stained negatively for arginase (Figure 64, C), glypican 3, and hepatocytes but positively for Melan-A (Figure 64, D) and inhibin. The differential diagnosis included ectopic adrenal tissue versus inadvertently sampled adrenal cortex. Radiology
confirmed biopsy of the actual lesion. The background liver showed chronic hepatitis with severe fibrosis and early cirrhosis. Six weeks later, imaging showed no significant enhancement of the treated lesion. This case highlights the importance of considering ectopic adrenal tissue when evaluating liver lesions in order to avoid misdiagnosis as hepatocellular carcinoma.

**Pendred Syndrome: A Mimicker of Thyroid Carcinoma**  
(Poster No. 141)

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Pendred syndrome is an autosomal recessive disorder consisting of sensorineural deafness, enlargement of the vestibular aqueduct, and variable thyroid dysfunction ranging from congenital hypothyroidism to euthyroid goiter. Mutations in the SLC26A4 (solute carrier family 26A) gene on chromosome 7q22-31 result in a mutated gene product, pendrin, a transmembrane ion transporter. Defects in pendrin are associated with defective iodide organification in the thyroid gland and cochlear malformations. Diagnosis relies upon confirmation of inner ear abnormalities by computerized tomography or magnetic resonance imaging of the temporal bone, an abnormal perchlorate discharge test, the presence of hearing loss, and goiter. Detection of the mutated gene with molecular testing confirms the diagnosis. A 16-year-old boy presented for evaluation of an enlarged thyroid gland of 1 year in duration. The patient’s medical history included hypothyroidism at birth, congenital sensorineural deafness, and cerebral palsy with subsequent developmental delay. Family history revealed hypothyroidism in his mother and brother. Owing to compressive symptoms, total thyroidectomy was performed. The thyroid gland was enlarged. Sectioning revealed multiple well-defined rubbery nodules with homogenous yellow-brown appearance. The histologic examination showed multiple unencapsulated adenomatoid nodules with scattered atrophic follicles in the background. Follicular cells exhibited cytologic atypia with nuclear pleomorphism (Figure 65). The features indicated a dyshormonogenetic goiter. This patient’s clinical presentation and affected family members suggest a diagnosis of Pendred syndrome. A specific diagnosis for phenotypic Pendred syndrome is important for surgical planning for cochlear implant placement, genetic counseling, and engaging strategies to prevent further hearing loss.

**Metastasis of Breast Carcinoma to Thyroid Gland With Concurrent Papillary Thyroid Carcinoma**  
(Poster No. 143)

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Distant metastases from lobular carcinoma of the breast most commonly involve the lungs, bone, brain, and liver. The incidence of thyroid metastasis, however, is very rare. We describe a case of metastatic lobular carcinoma to the thyroid and to central neck lymph nodes in the setting of concurrent encapsulated papillary carcinoma. A 69-year-old woman with a history of invasive lobular carcinoma treated with resection and adjuvant chemoradiation 2 years prior presented with multiple thyroid nodules incidentally found on carotid ultrasonography. The dominant solid nodule measured 2.8 cm in the left lobe. The patient’s serum thyroid-stimulating hormone level was 0.498, and a family history of hypothyroidism was noted. The patient underwent fine-needle aspiration, which revealed intranuclear inclusions and nuclear grooves, suggestive of malignancy. Total thyroidectomy with central compartment dissection was performed. Gross examination revealed multiple lesions in bilateral thyroid lobes. Histologic examination of the thyroid and lymph nodes showed infiltrative plasmaocytoid tumor cells with immunohistochemical features (GATA3 and ER), supporting a carcinoma of breast origin. In addition, the diagnosis of primary carcinoma was confirmed as encapsulated papillary carcinoma. This case highlights synchronous spread of lobular breast carcinoma to the thyroid, mimicking thyroid carcinoma.

**Thyroid Carcinoma Metastatic to Central Nervous System: A 13-Year Retrospective Review**  
(Poster No. 142)

Christopher Knoeckel, MD, PhD; Bette K. DeMasters, MD; Carrie B. Marshall, MD (carriebmarshall@gmail.com). Department of Pathology, University of Colorado, Aurora.

**Context:** Several types of carcinomas frequently metastasize to the brain, but metastatic thyroid carcinoma rarely impacts the central nervous system (CNS). The diagnosis can be challenging, as the patient may have a remote history of thyroidectomy, often for unclear reasons, and a limited immunohistochemical panel workup, with a tumor positive for both keratin and TTF-1, which may erroneously lead to a diagnosis of lung adenocarcinoma as the primary site.

**Design:** Anatomic pathology databases were searched from January 1, 2006, to February 1, 2019, inclusively, to identify cases of thyroid carcinoma impacting the CNS by linking the terms thyroid and metastatic with brain or central nervous system.

**Results:** Twenty cases were identified. Thirteen of 20 cases were paraspinal lesions requiring neurosurgical intervention, affecting cervical (n = 4), thoracic (n = 7), and lumbar (n = 2) levels. Seven of the 20 cases were parenchymal lesions: 1, pituitary; 1, intraventricular; 2, frontal lobe; and 1 each in temporal, parieto-occipital, and occipital lobes. Carcinoma types included papillary (3), follicular (8), medullary (1), poorly differentiated (3), and anaplastic (5). Most patients were known to have thyroid carcinoma antecedent to developing CNS-impacting lesions, but primary tumor histology was seldom available for direct comparison. One patient had a 41-year interval from primary diagnosis to metastasis (Figure 66).
INSM1 Expression in Adrenal Pheochromocytomas

(Poster No. 144)

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Context: Insulinoma-associated protein 1 (INSM1) has been identified as a useful diagnostic marker of neuroendocrine differentiation in various sites. Characterization of its expression in pheochromocytomas has not been extensively studied. We examined the expression of INSM1 in adrenal pheochromocytomas and compared it to that of synaptophysin, chromogranin, and CD56.

Design: Cases of pheochromocytoma were selected from June 2015–December 2018. Twenty-two cases were identified and stained with synaptophysin, chromogranin, CD56, and INSM1. Immunohistochemical staining was scored by intensity (0–3+) and percentage (rare, focal 5%–50%, diffuse >50%). Any degree of staining was considered positive.

Results: All cases were positive for the 4 immunostains (Table). Synaptophysin showed diffuse cytoplasmic staining in all cases, most exhibiting 3+ intensity (20/22). Twenty-one of 22 cases showed diffuse, 3+ cytoplasmic staining for chromogranin, with 1 case showing focal staining. CD56 showed predominantly membranous staining with 21/22 showing diffuse staining with 2–3+ intensity. INSM1 showed nuclear staining and did not stain adrenal cortex. It was diffusely positive in 11/22 cases with the remaining cases showing rare or focal staining. The intensity of INSM1 staining was more often 1+–2+.

Conclusions: INSM1 is a sensitive marker for pheochromocytomas with distinct nuclear staining; however, the intensity and frequency of INSM1 staining tends to be focal and less intense. It may not be sufficient as a stand-alone marker of neuroendocrine differentiation in pheochromocytomas and may be of limited use in biopsy material in which pheochromocytomas are in the differential. INSM1 does not stain adrenal cortex, allowing distinction of cortical and medullary neoplasms.

Expression of Neuroendocrine Markers in Pheochromocytomas

<table>
<thead>
<tr>
<th>Markers</th>
<th>Frequency</th>
<th>Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>INSM1</td>
<td>Rare (2/22), focal (9/22), diffuse (11/22)</td>
<td>1+ (10/22), 2+ (5/22), 3+ (7/22)</td>
</tr>
<tr>
<td>Synaptophysin</td>
<td>Rare (0/22), focal (0/22), diffuse (22/22)</td>
<td>1+ (2/22), 2+ (0/22), 3+ (20/22)</td>
</tr>
<tr>
<td>Chromogranin</td>
<td>Rare (0/22), focal (1/22), diffuse (21/22)</td>
<td>1+ (0/22), 2+ (1/22), 3+ (21/22)</td>
</tr>
<tr>
<td>CD56</td>
<td>Rare (0/22), focal (0/22), diffuse (22/22)</td>
<td>1+ (1/22), 2+ (2/22), 3+ (19/22)</td>
</tr>
</tbody>
</table>

Incidental Metastatic Follicular Variant of Papillary Thyroid Carcinoma Presenting Initially as Renal Metastasis

(Poster No. 145)

Bahaeidin Youssef, MD1 (youssefb@mail.etsu.edu); Ghassan Tranesh, MD2; Jason T. Lewis, MD2; Haytham Helmi, MD2; Aziza Nassar, MD, 1 Department of Pathology, East Tennessee State University, Johnson City; Department of Pathology, University of Arizona, Tucson; Departments of Pathology and Transplant and Critical Care, Mayo Clinic, Jacksonville, Florida.

Thyroid cancers account for around 0.5% and 1.5% of all male and female cancers, respectively. Differentiated thyroid cancers include follicular and papillary subtypes; the latter is further subclassified into classical and follicular variants. They infrequently metastasize beyond the thyrocervical region. The most common sites for metastasis include bone, lung, and mediastinum. Renal metastasis is rare and often occurs in the setting of multifocal spread, even years after removal of primary thyroid cancer. We report a case of an 85-year-old woman who presented with a right-sided abdominal discomfort. Both the abdominal ultrasound and a computed tomography scan showed bilateral upper pole renal masses. Positron emission tomography scan confirmed the presence of bilateral hypermetabolic masses with increased radiotracer uptake. A percutaneous biopsy was performed and the microscopic examination showed bilateral renal metastasis by a low-grade follicular variant of papillary thyroid carcinoma (FVPTC). Tumor cells show positive immunoreactivity for TTF-1, thyroglobulin, CK7, PAX-8, and vimentin and negative racemase expression. She had a previous history of benign thyroid nodules 3 years prior to her current presentation. Neck ultrasound-guided biopsy revealed 2 nodules (0.5 and 0.4 cm) of papillary thyroid carcinoma within the right lobe and isthmus. The patient underwent total thyroidectomy and external beam radiation for both kidney masses, as she was a poor candidate for nephrectomy. Detection of renal metastasis is difficult, attributed to the inability of the metastatic lesions to trap iodide on iodine-131 scan. Ultrasound-guided fine-needle aspiration biopsy is very sensitive in detecting FVPTC, albeit the nuclear features are very subtle.

Anaplastic Thyroid Carcinoma Masquerading as Primary Squamous Cell Carcinoma

(Poster No. 146)

Stephanie L. Holdener, MD (stephanie.holdener@bcm.edu); Thomas Wheeler, MD; Nilanjana Sur, MD. Department of Pathology, Baylor College of Medicine, Houston, Texas.

Papillary thyroid carcinoma (PTC) is the most common malignancy of the thyroid, typically carrying an excellent prognosis. Conversely, anaplastic thyroid carcinoma (ATC) is the most aggressive thyroid malignancy accounting for approximately half of thyroid cancer deaths. ATC may give rise to squamous cell carcinoma (SCC), which rarely exhibits keratinization, and can be mistaken for primary SCC arising from adjacent structures or metastatic disease. We present a case of ATC masquerading as SCC during intraoperative consultation in a 78-year-old man who presented to an outside institution with dysphonia and was found to have a mediastinal mass with pulmonary metastasis. Lung wedge resection showed metastatic PTC with a squamoid focus, and the patient was referred for mediastinal tumor resection with adjuvant radioactive iodine. Intraoperative biopsy showed keratinizing SCC without features of PTC (Figure 67). The surgical team was conflicted, as the treatments vary dramatically between primary SCC and PTC. Given the outside report findings, en bloc resection was performed. Grossly, the 7.5-cm mass was invading the manubrium and involved the inferior thyroid follicles. Microscopic examination revealed ATC with squamous and adenosquamous components, a focus of classical PTC, and tall cell–variant PTC. A minute focus of residual thyroid tissue was identified. Thyroid markers (TTF-1, PAX-8) were partially retained in the anaplastic and squamous components. A BRAF V600E mutation was also detected. The thyroidectomy only had a focus of follicular–variant PTC. This case demonstrates how ATC with SCC can potentially lead to inappropriate treatment or lack thereof and highlights the importance of continual communication between team members.
Morphologically Benign Thyroid Tissue Presenting Years Later as Renal Metastasis: Role of Molecular Pathology

(Poster No. 147)

Diana Metry, MBChB1 (dmetry@augusta.edu); Saleh Heneidi, MD2; Won Lee, MD3; Paul Biddinger, MD1; Kolhe Ravindra, MD1; Rabii Madi, MD1; Sravan Kavuri, MD1.1 Departments of 1Pathology and 2Surgery - Urology, Medical College of Georgia - Augusta University, Augusta.

A 57-year-old woman presented with lower back and hip pain. Magnetic resonance imaging revealed a right kidney mass suggestive of malignancy. The patient underwent a partial nephrectomy, and pathologic examination revealed morphologically benign-appearing thyroid tissue constituting the mass (Figure 68, A). The mass was positive for TTF-1, PAX8 (Figure 68, B), thyroglobulin (Figure 68, C), while negative for HBME-1 (Figure 68, D). The patient’s past medical history was significant for a total thyroidectomy for multinodular goiter 7 years earlier. Previous thyroidectomy slides were re-examined, confirming the initial diagnosis of nodular hyperplasia. As ectopic thyroid tissue in kidney is extremely rare, molecular testing was performed on both specimens, revealing positivity for the same NRAS pQ61R c.182A>G gene mutation, suggesting that the thyroid lesion and right renal tumor were of the same origin. NRAS pQ61R c.182A>G is the most common driver mutation of somatic follicular thyroid carcinoma (70%) and follicular adenomas (55%). Interestingly, molecular analysis of the adjacent normal renal tissue revealed the same TP53 N235S mutation, consistent with germline mutation. However, NRAS mutation was clearly somatic, consistent with a clonal tumor. To the best of our knowledge we report the first case of a renal tumor composed of morphologically benign-appearing thyroid tissue but with molecular aberrations consistent with malignancy.

Massive Transfusion in Severe Trauma and the Use of Liquid Plasma

(Poster No. 148)

Andrea P. Ho, MD1 (andrea.ho@ucdenver.edu); Bethany E. Ho, BA2; Nanette D. West, BS, MBA2; Cheryl Phillips, RN, BSN2; Hana Hamdan, MD1.1 Department of Pathology, University of Missouri, Kansas City; 2Department of Medicine, University of Colorado School of Medicine, Centennial; 1Department of Pathology, Truman Medical Center, Kansas City, Missouri.

Context: Death from traumatic injury has increased 23% in the last decade with 20% to 40% of trauma deaths occurring after hospital admission owing to massive hemorrhage, and 25% of patients presenting with coagulopathy. Improved survival has been documented in institutions with massive transfusion protocols using prompt hemostatic support. Early administration of blood products in a 1:1:1 ratio of pRBCs to plasma to platelets establishes a ratio close to reconstituted whole blood. For blood banks to provide a balanced ratio of transfusion products, liquid plasma can be used.

Design: At an inner city hospital with a high incidence of trauma patients, a retrospective study was performed on massive transfusion protocols and the ratio of red blood cells to plasma used during those protocols. This institution introduced the use of liquid plasma in June 2016. This product permitted the hospital blood bank to equip the emergency room with 4 units each of O negative, O positive pRBCs, and liquid plasma for immediate use in the emergency room.

Results: Our study showed an increase in the number of massive transfusion protocols performed and a gradual decrease in the ratio of red blood cells to plasma ratio from 3:1 in 2014–2015 to 1.4:1 in 2017 (Table). This more equalized ratio resulted in a decrease in the mortality rate between 12 and 24 hours from 44% to 26%.

Conclusions: Using liquid, never-frozen plasma makes it possible for the blood bank to have plasma readily available for trauma victims. Providing the trauma services with readily accessible blood products encourages the use of an equalized blood product ratio.

Characterization of Blood Component Market Withdrawals: A 4-Year Review

(Poster No. 149)

Rachel Jug, MB BCh BAO (rachel.mattson@duke.edu); Gustaaf de Ridder, MD, PhD; Nicholas Bandarenko, MD; Jessica Poisson, MD. Department of Pathology, Duke Health, Durham, North Carolina.

Context: While lookback investigations follow specific US Food and Drug Administration requirements, the management of blood product market withdrawals from suppliers can vary widely. Follow-up data are limited, prompting this review of the types and reasons for recipient notification and their outcomes.

Design: A single institution retrospective review of market withdrawal and lookback files from 2012–2015 included product type, reason, notification, follow-up, and turnaround time. Descriptive statistics and χ² analysis were performed.

<table>
<thead>
<tr>
<th>Reason for Recipient Notification of Supplier Product Withdrawal</th>
<th>Total</th>
<th>Notified (%)</th>
<th>Tested (Notified)</th>
<th>% Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human leukocyte antigen antibodies</td>
<td>152</td>
<td>0 (0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Postdonation information</td>
<td>134</td>
<td>13 (10)</td>
<td>6</td>
<td>46</td>
</tr>
<tr>
<td>Other</td>
<td>95</td>
<td>8 (8)</td>
<td>3</td>
<td>38</td>
</tr>
<tr>
<td>False-positive infectious disease screen</td>
<td>78</td>
<td>11 (14)</td>
<td>8</td>
<td>73</td>
</tr>
<tr>
<td>Processing error</td>
<td>36</td>
<td>0 (0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Donor medication</td>
<td>34</td>
<td>0 (0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Donor high-risk behavior</td>
<td>34</td>
<td>15 (44)</td>
<td>8</td>
<td>53</td>
</tr>
<tr>
<td>Lookback</td>
<td>27</td>
<td>21 (78)</td>
<td>15</td>
<td>71</td>
</tr>
<tr>
<td>Postdonation illness</td>
<td>16</td>
<td>3 (19)</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>Travel</td>
<td>10</td>
<td>3 (30)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Infectious disease positive</td>
<td>3</td>
<td>2 (67)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Transfusion reaction</td>
<td>2</td>
<td>0 (0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>553</td>
<td>61 (11)</td>
<td>34</td>
<td>56</td>
</tr>
</tbody>
</table>

Results: For 4 years, 868/229 549 blood components (0.37%) were implicated in supplier notifications. Of these, 96.7% were market withdrawals and 3.1% were lookbacks. Plasma with antibodies to human leukocyte antigens was the most common reason for withdrawal (45%) followed by red blood cell withdrawal for postdonation or high-risk donor behaviors (28%; Table). Seventy-six recipient notifications were performed, 97% within 3 months of supplier notification date. Common reasons for recipient notification of market withdrawals were false-positive infectious disease tests and postdonation...
Direct Oral Anticoagulant Therapy Associated With Gastrointestinal Bleeding: Investigation of the Underlying Causes Responsible for This Complication

(Poster No. 150)

Mary Wyzykowski, MT (ming.xie@beaumont.org); Ming Xie, MD. Department of Pathology, Beaumont Health System, Troy, Michigan.

Context: Direct oral anticoagulants (DOACs) have gained wide use in prevention and treatment of thromboembolic diseases; however, both major and nonmajor bleeding events have been reported. Gastrointestinal (GI) bleeding is the most common bleeding complication in patients receiving DOACs.

Design: This study investigates the underlying local diseases responsible for DOAC therapy–related GI bleeding.

Results: There were 38 patients (16 males and 22 females); median age was 75 years (range, 58–90). All patients experienced DOAC therapy–related GI bleeding. All patients had GI specialist evaluation. Active hemorrhoid bleeding was found in 10 patients. Upper and/or lower GI endoscopic examination was performed in 33 patients (excluding 5 patients with hemorrhoid bleeding). Sixteen patients had endoscopic pathologic findings responsible for active bleeding and 12 had no evident active bleeding. The most common anatomic location of bleeding was duodenum (n = 7), followed by stomach (n = 5), colon (n = 3), and esophagus (n = 7). Pathologic findings were ulcer (n = 7), vascular diseases (n = 6), active inflammation with hemorrhage (n = 2), and Mallory-Weiss tear (n = 1). All patients, except 1, had anemia with hemorrhoid bleeding.

Conclusions: Most patients (26/38) with DOAC therapy–associated GI bleeding have identifiable bleeding causing local diseases in this study. Hemorrhoid bleeding was most common. Ulcerative and vascular lesions in duodenum and stomach account for most underlying diseases identified by endoscopy. Since GI bleeding is the most common bleeding complication and responsible for clinically significant anemia in some patients, a special GI evaluation may be considered before DOAC therapy, especially in patients with prior history of ulcerative and vascular diseases.

Implementation of STAT Pack to Guide Coagulation Testing in Massive Transfusion

(Poster No. 151)

Sepideh N. Asadbeigi, MD (sepidelah-asadbeigi@ouhs.edu); Faaria Gowani, DO; Stephanie Bates, MD. Department of Pathology, Oklahoma University of Health Sciences, Oklahoma City.

Context: Hemorrhage is the most common cause of death within the first hour of arrival to a trauma center. Most institutions activate massive transfusion protocols (MTPs), with varying ratios of blood products. However, laboratory tests, such as fibrinogen and thromboelastography (TEG), are not routinely included in the protocol. These labs ensure that blood products are not wasted, while also achieving rapid hemostasis.

Design: In an attempt to make ordering labs easier for clinicians, the new STAT pack protocol was implemented. The package included an insert with which labs to order, 1 EDTA tube, and 2 sodium citrate tubes. One pack was sent with every other round of blood products, so that posttransfusion labs could be easily collected. We gathered data on MTP laboratory usage from 2016 to 2017, and compared the rate of ordering TEG and fibrinogen before and after implementation of this new policy.

Results: Fibrinogen was ordered for 46% of the patients in 2016 and 42% of the patients in 2017. TEG was ordered for 43% of the patients in 2016 and 38% of the patients in 2017. The new policy did not increase the rate of laboratory coagulation testing.

Conclusions: Although the process of ordering laboratory tests during MTP was ostensibly improved, the rate did not increase. Multidisciplinary education does not appear to have increased compliance to national guidelines on performing coagulation studies. We strongly recommend work aids and ongoing education to improve the compliance.

Emergency Blood Product Practices in a Rural Referral Hospital

(Poster No. 152)

Ann McCord, BS; Stephanie Welsh, MLS; Eshan Sood; Adam Horn, MD (ahorn@marylanning.org). Department of Pathology and Laboratory Medicine, Mary Lanning Healthcare, Hastings, Nebraska.

Context: Our facility is a regional level 3 trauma center with a rural referral base where emergency blood use is neither a never-event nor frequent enough to be routine. To the best of our knowledge, benchmark data for emergency blood use in our type of facility do not exist. We sought to evaluate the frequency and content of emergency blood product orders.

Design: Records for emergency blood release during a 24-month period were reviewed. The time to release, nature of the order, products released, and final disposition of product were evaluated.

Results: A total of 22 emergency events occurred (17 emergency releases, 5 mass transfusion activations) out of 1818 total transfusion events (1.2%). One mass transfusion extended beyond the initial supply box. Seventy-nine percent of the requested product was transfused. Of the product transfused, 46 were packed red cells, 9, fresh frozen plasma; and 6, apheresis platelet doses. The average time to release was 11.5 minutes. One unit of plasma was given outside of a mass transfusion activation. Eleven events involved emergency department admissions, 45% of which were stabilized and transferred, with 1 also receiving plasma.

Conclusions: Emergency release utilization appeared appropriate and had a timely response. Mass transfusions were limited, as high-complexity patients were transferred. Minimal plasma use in transfer cases supports the addition of liquid plasma to our stock.

Massive Transfusion Protocol Activations in a Tertiary Care Medical Center: Where Are the Opportunities for Improvement?

(Poster No. 153)

Priscilla R. Powell, DO (priscilla.powell@bswhealth.org); Umaima Wajid, MD; Walter J. Linz, MD, MBA. Department of Pathology, Baylor Scott and White, Temple, Texas.

Context: Activation of a massive transfusion protocol (MTP) is labor and blood product intensive, and potentially dangerous as uncross-matched blood products are released for transfusion support. For the appropriate indication, (ie, trauma patient with uncontrolled blood loss) complex large volume transfusion support can be lifesaving. To minimize potential harm and cost, our single institution retrospective MTP review identified institutional opportunities to decrease unnecessary activations.

Design: We performed a single institution retrospective review of all MTP activations from 2016–2017. The institution is a tertiary care medical center with a level I trauma center. The number of activations, the indication for the activation, the location of the activation, and the number and type of blood products consumed or returned were recorded. Indications included nontrauma blood loss, gastrointestinal bleed, intraoperative blood loss, postoperative blood loss, non–blood loss-related emergency, and trauma. For each MTP request, 6 units of packed red blood cells, 4 units of plasma, and 1 single donor platelet were released.

Results: During 2016–2017, a total of 114 activations consumed 1314 products. Of 734 (37%) requested products were returned. Trauma accounted for 56% of activation indications. Seventy-eight percent of MTPs were activated in the operating room or emergency department. Of the 114 activations, at least 16 (14%) had a questionable indication.

Conclusions: Our study identified both MTP overactivation and excess product availability, requiring return of product and restocking. This finding translates not only to a potential area of cost and resource savings, but also, and more importantly, to an area for improving patient safety through avoidance of uncross-matched blood products.
P-Selectin Expression Assay in a Repeatedly SRA-Negative Patient With Heparin-Induced Thrombocytopenia

(Poster No. 154)

Kanika Taneja, MD1 (ktanejai@hfhs.org); Shannon Rodgers, DO2; Yaser Alkhatif, MD; Ieoma N. Onwubiko, MD, MPH3; Anand Padmanabhan, MD, PhD3; Zaher Otrock, MD, PhD1. Departments of 1Pathology and Laboratory Medicine and 2Oncology-Hematology, Henry Ford Health System, Detroit, Michigan; 3Blood Center of Wisconsin, Medical College of Wisconsin, Milwaukee.

The serotonin-release assay (SRA) is considered the gold standard test to diagnose heparin-induced thrombocytopenia (HIT). We discuss the utility of a P-Selectin expression assay (PEA) in diagnosing HIT in an SRA-negative patient. A 66-year-old man presented in October 2017 with cerebral infarction, managed with heparin with good response, who 1 week later presented with worsening neurological symptoms and radiologic evidence of new ischemic changes. His platelet count was low, and he was treated with apixaban. HIT antibody testing was positive; SRA was negative. He returned with worsening symptoms and workup revealed lower extremity deep venous thrombosis, bilateral pulmonary embolism, and renal and splenic infarcts. Repeated HIT antibody testing was positive with improvement in platelet count and no further episodes of HIT. Repeated HIT testing was negative. High clinical suspicion for HIT prompted us to investigate with the novel PEA. Platelet-activating HIT antibodies were detected in the PEA in the October specimen, at 42% (a positive result is ≥24%), which was confirmed by inhibition in the presence of high-dose heparin. PEA in December specimen was negative likely owing to the decrease in antibody titers (Figure 69). The patient was maintained on apixaban with improvement in platelet count and no further episodes of thrombosis. This case highlights the limitation of the gold standard SRA in HIT testing. PEA was instrumental in making the diagnosis of HIT, thus avoiding management with heparin.

Unreliable Clauss Fibrinogen Activity in a Middle-Aged Woman With Congenital Dysfibrinogenemia

(Poster No. 155)

Efrain A. Gutierrez-Lanz, MD (egutierrez@med.umich.edu); Shih-Hon Li, MD, PhD. Department of Pathology, University of Michigan, Ann Arbor.

Dysfibrinogenemia is a coagulation disorder characterized by a qualitative defect in fibrinogen or fibrin. Laboratory diagnosis is made via a widely accepted testing algorithm. This case illustrates the difficulty in using and interpreting follow-up testing, for which there is little published guidance. A 51-year-old woman, with no significant medical history, presented to the emergency department with a history of chest pain. Her fibrinogen was normal. Owing to the variability in Clauss fibrinogen activity on follow-up testing in this patient, it is recommended to perform prothrombin time and activated partial thromboplastin time on repeated testing. This patient’s fibrinogen activity was unreliable on multiple occasions, which was subsequently confirmed with the Clauss method. The patient was discharged in good condition. Three weeks later, the patient presented with acute upper extremity deep venous thrombosis and new pulmonary embolism. Repeated HIT testing was negative. High clinical suspicion for HIT prompted us to investigate with the novel PEA. Platelet-activating HIT antibodies were detected in the PEA in the October specimen, at 42% (a positive result is ≥24%), which was confirmed by inhibition in the presence of high-dose heparin. PEA in December specimen was negative likely owing to the decrease in antibody titers (Figure 69). The patient was maintained on apixaban with improvement in platelet count and no further episodes of thrombosis. This case highlights the limitation of the gold standard SRA in HIT testing. PEA was instrumental in making the diagnosis of HIT, thus avoiding management with heparin.

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Chronic ischemia caused by DPVD will lead to less of normal bowel movement, dilatation, necrosis, and perforation. It is important to be aware that long-term diabetic patients can have severe DPVD in mesenteric artery, which can lead to devastating consequences.

**Isolated Cardiac Sarcoidosis: A Rare Case Report**  
*(Poster No. 158)*

**Jana Tarabay, MD**† (jtarabay@uci.edu); Ifegwu Ibe, MD; Fritz Lin, MD; Ilab Alamri, MD; Beverly Wang, MD. Departments of *Pathology and Laboratory Medicine and Cardiology, University of California, Irvine, Orange.*

Isolemental cardiac sarcoidosis presenting with no evidence of extracardiac involvement has received special attention in diagnosis and management. Recent data suggest that patients with isolated cardiac sarcoidosis have a worse prognosis than patients with systemic involvement of sarcoidosis. Early recognition and initiation of therapy is therefore critical. Despite the new advances in cardiac imaging, isolated cardiac sarcoidosis remains a diagnostic challenge and a positive endomyocardial biopsy is still required. We report the case of a 43-year-old man, with history of beta-thalassemia, who presented to the emergency department with palpitations, chest pain, dyspnea, and tachypnea. Echocardiography showed severely reduced bilateral ventricular function, and cardiac magnetic resonance imaging confirmed nonischemic cardiomyopathy. A workup for infectious diseases was completely negative. He was subsequently diagnosed with biventricular heart failure of unknown etiology. Endomyocardial biopsy revealed frequent giant cells and noncaseating epithelioid granulomas without myocardial necrosis (Figure 71, A and B). Acid-fast bacteria and Gomori methenamine silver stains were negative. The overall histologic findings were consistent with cardiac sarcoidosis. Computed tomography scan of the chest showed no evidence of hilar lymphadenopathy. Clinically, there was no evidence of systemic involvement. Although prednisone therapy was initiated, the patient’s condition continued to deteriorate. An implantable cardioverter defibrillator was implanted, and the patient was placed on the heart transplant list. In summary, the rare presentation of isolated cardiac sarcoidosis can create diagnostic and therapeutic challenges and should be considered in the differential diagnosis of severe heart failure of unknown etiology.

**Comparison in Patients With Clinical and Morphologic Findings of Cardiac Sarcoidosis Severe Enough to Warrant Heart Transplant in Those With Versus Without Noncaseating Granulomas in the Explanted Heart (Burnt-Out Sarcoid)**  
*(Poster No. 159)*

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**Context:** Can cardiac sarcoidosis with heart failure severe enough to warrant orthotopic heart transplant (OHT) be present without noncaseating granulomas in the explanted heart? We studied clinical and morphologic features in patients with cardiac sarcoidosis, comparing gross morphology and clinical features of those with versus without noncaseating granulomas in the explanted heart.

**Design:** The study was conducted at Baylor University Medical Center in Dallas, Texas. From a total of 671 explanted hearts examined from 1993 to 2018, 25 (4%) had gross morphologic features characteristic of cardiac sarcoidosis. At the time of OHT, the patients ranged in age from 50 to 69 years with an average of 57 years. Cardiac sarcoidosis was diagnosed before OHT in 3 patients (12%), by percutaneous biopsy of the heart in 2 patients, and by examination of the “left ventricular core” in 1 patient who had a left ventricular assist device inserted.

**Results:** Of the 25 patients, 16 (64%) had typical sarcoid noncaseating granulomas in the explanted heart, and 9 (36%) had no granulomas in the explanted heart. Comparison of certain clinical and morphologic features in the group with versus the group without cardiac granulomas showed no significant differences.

**Conclusion:** Of patients with cardiac sarcoidosis severe enough to warrant OHT, some have typical noncaseating granulomas in the explanted heart and some do not. The clinical and gross morphologic features of those with and those without cardiac granulomas are similar.

**A Rare Case of Osseous Metaplasia in the Popliteal Artery**  
*(Poster No. 160)*

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Osseous metaplasia (OM) is defined as the transformation of uncalcified soft tissue to calcified osseous tissue via endochondral ossification. This rare phenomenon has been described in the endometrium, cervix, in ovarian tumors, and in medium- and large-caliber arteries. We report a case of osseous metaplasia in the popliteal
Giant Cell Myocarditis: A Case of a Rare and Aggressive Disorder With an Unusually Favorable Clinical Course

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Giant cell myocarditis (GCM) is a rare, rapidly progressive, and frequently fatal disease. We present a case of GCM that showed classic histopathologic findings but followed an unusually favorable clinical course. A 62-year-old woman presented with upper respiratory symptoms followed 3 weeks later by progressive dyspnea, night sweats, fever, and chest pain. She was diagnosed with acute heart failure and cardiogenic shock that was unresponsive to medical management, necessitating implantation of a left ventricular assist device (LVAD). Histopathologic examination of the cardiac tissue revealed prominent myocyte necrosis associated with a diffuse, serpiginous mixed interstitial inflammatory infiltrate (Figure 73, A) composed of numerous CD68+ multinucleated giant cells and histiocytes, abundant CD3+ T lymphocytes, and conspicuous eosinophils (Figure 73, B through D). An extensive clinical workup for infectious etiologies revealed an elevated parvovirus B19 IgM, but in situ hybridization for parvovirus and stains for fungi, acid-fast bacilli, Epstein-Barr virus, cytomegalovirus, and adenovirus were all negative. Despite the lack of a clear underlying etiology, the patient was started on steroids and cyclosporine. Given her poor prognosis, a heart transplant workup was also initiated. However, during the next 3 months, her cardiovascular status improved and repeated echocardiography showed nearly normal ventricular systolic function. The patient is now 11 months status post initial diagnosis and is living independently at home with her LVAD still in place and only mild heart failure symptoms. This degree of recovery is extremely rare and supports growing evidence that rapidly instituted cyclosporine-based immunosuppression can significantly improve transplant-free survival in patients with GCM.

Two Cases of Aortic Aneurysm in Patients With Loeys-Dietz Syndrome

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Loeys-Dietz syndrome is an autosomal dominant connective tissue disorder that is caused by mutations in the transforming growth factor β receptors 1 and 2. Clinical manifestations of Loeys-Dietz syndrome include hypertelorism, split uvula, cleft palate, tortuous arteries, and rapidly progressive aortic aneurysmal disease among others. We present 2 cases of Loeys-Dietz syndrome in patients that developed severe aortic dissection. The first case involves a 36-year-old man with a surgical history of multiple aortic dissection repairs who presented with severe acute on chronic aortic dissection requiring emergency aortic aneurysm repair. The second case involves a 30-year-old man with a history of severe aortic insufficiency and chronic aortic dissection who required surgical management after progression was noted on imaging studies. Histologic examination of the aortic walls showed a loss of elastic fibers in the media, which was demonstrated by Elastic Van Gieson and trichrome special stains (Figure 74, A through C, and D). Alcian blue staining showed myoid degeneration, and smooth muscle actin staining highlighted a proliferation of smooth muscle fibers. The patient in the first case succumbed to his disease just 2 days after his procedure, while the patient in the second case has shown no adverse effects 3 months following his procedure. Loeys-Dietz syndrome is a rare entity; however, it is increasingly recognized as a cause of connective tissue abnormalities and should be suspected in young patients with histologic evidence of elastic fiber degeneration in the aortic wall and may warrant further genetic testing.
and submitted as a “mass” for histopathology. Microscopic evaluation revealed a myxoid spindle cell lesion composed of primitive small spindle cells with entrapped myocardial fibers in a diffuse myxoid background and focal mild fibrosis. There was no significant cytologic atypia. Differential diagnosis includes jet lesion and cardiac myxoma. The patient’s clinical history, as well as the location and size of the lesion, suggests that this is most likely a reactive jet lesion due to high-to-low pressure blood shunt across the defect, striking the right atrial free wall. The diagnosis is confirmed by postsurgical endocardiogram at 6 months that showed normal right atrial thickness. This case nicely illustrates the importance of well-documented clinical history and echocardiogram findings for accurately diagnosing this rare cardiac lesion.

**Endocardial-Based Cardiac Hemangioma: A Diagnostic Challenge**

(Poster No. 165)

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Cardiac hemangioma is a rare benign tumor of the heart accounting for 2% to 3% of all primary cardiac tumors. It is usually asymptomatic and is diagnosed incidentally. This is a case report of a 14-year-old girl presenting with 1-month history of shortness of breath on lying down and 2 episodes of acrocyanosis. Cardiac MRI revealed a 2-cm broad-based intraventricular mass attached to the left ventricular endocardial surface. Echocardiogram showed a smooth-walled, homogeneous, echogenic mass. Tumor was excised and sent to pathology. Grossly, the lesion was 1.5 x 1.0 x 0.6-cm tan-white rounded rubbery soft tissue. Histologically, the tumor was composed of anastomosing vessels in a myxoid background. The vessel walls were variable, some very thin and composed solely of endothelium with basal lamina and others having 2 to 3 layers of spindle cell cuffing. At the base of the stalk, the vessels appeared to intermingle with the most superficial aspects of the attached myocardium. Calretinin was negative, anti-muscle-specific antibody (HHF-35) highlighted pericyte cuffs, and Alcian blue highlighted extensive myxoid matrix, supporting the diagnosis of myxoid hemangioma. Hemangiomas are rare benign tumors that can arise from any chamber of the heart. They can arise from endocardium or myocardium. Endocardium-based tumors tend to show abundant myxoid background, making the distinction from myxoma difficult, but the hemangioma lacks myxoma cells or ring structures. HHF-35 and calretinin can be used to differentiate between them.

**Mobile Applications in Pathology Practice**

(Poster No. 165)

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Of the 462 MAs that were retrieved from the search criteria, 285 (61.6%) were deemed relevant to the practice of anatomic and clinical pathology. We classified these MAs by their specific function into 4 categories as follows: (1) communication applications, 5 of 285 (1.8%), for example, FaceTime and WhatsApp; video live stream can be video-recorded on the mobile device camera; it can only measure whole numbers; see Figure 75 for a measurement of placenta by Measure app; (2) other applications (265 of 285, 93%), are for educational, business, and other purposes that can be of indirect use to pathologists. MAs represent a significant opportunity for the practice of pathology. A few but growing number of applications exist today, mostly geared toward productivity and communication. Future areas of study include faculty and trainee survey of the applications’ usage.

**Quantification of Estrogen Receptor Immunohistochemistry Using Whole Slide Imaging and Morphometric Image Analysis Software**

(Poster No. 166)

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Context: Biomarker quantifications are required for targeted therapy and/or disease prognosis. Visiopharm software is able to extract data from whole slide images (WSIs) and quantify biomarker immunohistochemistry (IHC). In this pilot study, we validated quantifying estrogen receptor (ER) IHCs from WSIs using Visiopharm.

Design: After institutional research board approval, 60 invasive breast carcinomas with ER IHCs were included. H&E and IHC slides were scanned at X40 with either Hamamatsu NanoZoomer XF 2.0 (Woburn, Massachusetts) or Philips IntelliSite (Andover, Massachusetts) scanners. Besides using Visiopharm’s preconfigured App for ER quantification, a customized App was built by fine-tuning color deconvolution, morphologic filters, and classification algorithms. Three approaches were performed, including (1) automatically selecting regions of interest (ROIs) and analyzing by using preconfigured application (App) (ROI-vApp); (2) manually selecting ROIs and analyzing by using customized App (ROI-cApp); and (3) manually selecting all invasive carcinoma areas and analyzing by using customized App (All-cApp). The data were compared with pathologists’ manual gold standard.

Results: Of the 462 MAs that were retrieved from the search criteria, 285 (61.6%) were deemed relevant to the practice of anatomic and clinical pathology. We classified these MAs by their specific function into 4 categories as follows: (1) communication applications, 5 of 285 (1.8%), for example, FaceTime and WhatsApp; video live stream can be video-recorded on the mobile device camera; it can only measure whole numbers; see Figure 75 for a measurement of placenta by Measure app; (2) other applications (265 of 285, 93%), are for educational, business, and other purposes that can be of indirect use to pathologists. MAs represent a significant opportunity for the practice of pathology. A few but growing number of applications exist today, mostly geared toward productivity and communication. Future areas of study include faculty and trainee survey of the applications’ usage.
readings (PathR). Figure 76 shows representative images from 2 cases with strong (top panel) or weak (lower panel) ER staining.

**Results:** All 3 Visiopharm approaches demonstrated excellent ER positivity concordance with PathR (ROI-vApp: 90%, ROI-cApp: 95%, All-cApp: 96.7%). The Pearson correlation coefficients (r) for ER H-scores were 0.9202 (ROI-vApp versus PathR), 0.9843 (ROI-cApp versus PathR), and 0.9918 (All-cApp versus PathR).

**Conclusions:** The Visiopharm readouts using All-cApp approach demonstrated the strongest correlation with PathR, but ROI-cApp approach showed comparable results with All-cApp approach. Therefore, designing a customized App in Visiopharm may provide better separation of desired data elements and thus render more robust and accurate results.

**Streamlined Software for Community Biorepositories** *(Poster No. 167)*

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**Context:** Community oncology programs could be a diverse source of biospecimens for cancer research but community biorepositories are limited by a lack of standardized specimen management software that is low cost and easy to use.

**Design:** The University of Virginia has extended the open source research data management system Caisis (caisis.org) to create biorepository software appropriate for use at community sites or mid-sized academic centers. Caisis is a Web-based ASP.NET application that can be installed on a single Windows server. The design of the biorepository module is informed by published best practices from the National Cancer Institute and International Society for Biological and Environmental Repositories, established data standards, and accreditation requirements from the College of American Pathologists.

**Results:** The system supports both protocol-driven specimen collection and archival biobanking. Comprehensive data (774 data elements) may be captured on research protocols, investigators, subjects, specimen, aliquots, derivatives, and processing events. Aliquots may be created in batches with inheritance of specimen features and events, and there is a full pathologic quality assurance workflow. Search may include clinical, specimen, or processing characteristics and may specify matching fluids, normal tissue, or derivatives. The inventory system supports storage and retrieval of aliquots in multiple container types. Aliquots may be assigned to collections that are included in packing lists and invoices for distribution.

**Conclusions:** This streamlined software is appropriate for community and mid-sized academic sites, incorporates biorepository best practices, and standard data elements, and is being released with documentation for free access as part of the Caisis open source distribution.

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**A Web-Based Tool for Generating Comprehensive Bone Marrow Report Amendments in Acute Myeloid Leukemia** *(Poster No. 168)*

**Brian Wong, MD** (brian.wong@ualberta.ca); Elena Turley, MD. Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Alberta, Canada.

**Context:** Recent American Society of Hematology/College of American Pathologists leukemia reporting guidelines strongly recommend integrating morphology and ancillary test results, which may require amendments. We anticipate the autopopulate feature will further increase pathologist efficiency in uncomplicated cases while minimizing potential typographic errors.

**Design:** The EZ-SMaRT amendment module facilitates AML classification according to the World Health Organization classification system and aligns with reporting guidelines. This EZ-SMaRT module efficiently generates standardized amended reports with pertinent ancillary studies. We anticipate the autopopulate feature will further increase pathologist efficiency in uncomplicated cases while minimizing potential typographic errors.

**Wisdom of the Crowds: Social Media Polls Demonstrate That Collectively Pathologists Identify the Correct Answer Better Than the Individual** *(Poster No. 169)*

**Patrick McIntire, MD** (pmcintire2@gmail.com); Ayse Irem Kilic, MD; Kamran Mirza, MD; Eva Wojcik, MD; Goliz A. Barkan, MD; Stefan Pambuccian, MD. Department of Pathology, Loyola University Medical Center, Chicago, Illinois.

**Context:** The ubiquitous use of social media by pathologists, especially the younger generation, makes it an ideal tool to conduct research studies. “Wisdom of the crowds,” that is, “the many are smarter than the few” contends that decisions made by groups are better than those by the members of the group. The aim of this study was to determine if this also holds true for pathology diagnoses.

**Results:** We created an amendment module that produces a standardized amended report with robust input options for frequently performed testing. The autopopulate feature autogenerates a diagnostic comment and highlights typical testing results for specific AML entities (Figure 77). Retrospectively generated EZ-SMaRT outputs aligned with the manually amended reports. A user feedback survey will be distributed later in the release cycle.

**Summary of Statistics Collected From the 15 Twitter Polls**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Average</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impressions</td>
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<td>3,834</td>
<td>1,102–11,757</td>
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<tr>
<td>Engagements</td>
<td>5462</td>
<td>364</td>
<td>123–929</td>
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<tr>
<td>Media engagements</td>
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<td>64–370</td>
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<tr>
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<td>94</td>
<td>15–236</td>
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<td>7–94</td>
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<td>16</td>
<td>6–46</td>
</tr>
<tr>
<td>Replies</td>
<td>59</td>
<td>4</td>
<td>1–10</td>
</tr>
</tbody>
</table>

**Design:** Two pathology trainees (PJ/MABK) conducted polls of difficult cases presented as 3 to 8 images and a case history vignette via Twitter from January 21, 2019, through March 1, 2019. For each case, any individual, regardless of training, was allowed to vote once during a 3- to 7-day period. All statistics were collected via Twitter. Terminology is as follows: “impressions,” times people saw this Tweet on Twitter; “total engagements,” times people interacted with this Tweet; “media engagements,” the number of clicks on your media; “detailed expands,”
the number of times people viewed details about this Tweet. Results were collected and basic statistical analysis was performed with Microsoft Excel.

**Results:** The polls included 6 surgical pathology cases and 9 cytology cases. A total of 57,504 impressions captured 902 votes (1.6%). The Table summarizes the results.

**Conclusions:** Of the 15 polls, the “crowd” identified the correct answer in 13 cases (86.7%) with an average of 54.9% (495/902) of the respondents selecting the correct answer. Thus, we found that the “crowd” was far more likely to select the correct answer than the individual.

**Pathology Review of Outside Material: Contribution to the Surgical Pathology Workload, Distribution by Subspecialty, and Frequency of Major Discrepancy in Diagnoses**

(Poster No. 170)

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**Context:** Outside surgical pathology cases are reviewed at our institution when either patients transfer their care or the original pathologist requests a second opinion. The aim of this study is to determine the relative workload the review of outside slides contributes to the surgical pathology service overall and by subspecialty, frequency of discrepant diagnoses, and the need for review of old cases at a tertiary care center.

**Design:** Outside surgical pathology cases referred to our academic medical center between January 1, 2018, and June 30, 2018, were identified and recorded by subspecialty to determine the number of slides reviewed and major disagreements with the referring pathologist. Current procedural terminology (CPT) codes were assigned similar to in-house cases for comparison of the workload.

**Results:** The highest number of slides and cases were reviewed by the breast (29.6%) and gastrointestinal (23.9%) services. When CPT codes were assigned similar to in-house cases, outside cases consisted of 14.0%, 27.6%, and 23.3% of the most common CPT codes (88305, 88307, and 88309, respectively). Genitourinary (GU) service had the highest total professional component, based on the assigned in-house CPT codes. Major disagreements in cases older than 1 year were similar to all cases (3.5%) and none of the 5 cases resulted in a change in treatment.

**Conclusions:** Review of outside slides contributes significantly to the surgical pathology workload. Breast and GU subspecialties have the highest workload by slide numbers and assigned in-house CPT codes, respectively. Review of old outside cases may not always be medically needed.

**Biomarker Testing Survey for Non-Small Cell Lung Cancer: The Role of PD-L1 Inhibitor Testing in Clinical Practice**

(Poster No. 171)

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**Context:** The list of approved immune-based biomarkers for non-small cell lung cancer (NSCLC) therapies is growing worldwide. They include EGFR gene mutations, ALK gene rearrangements, ROS1 gene rearrangements, BRAF (V600E) gene mutations, and PD-L1 expression. Immune checkpoint inhibitors targeting the PD1/PD-L1 axis represent a major paradigm shift in treating NSCLC and have shown their efficacy in selected population of patients.

**Design:** An online survey that included 20 questions regarding biomarker testing for NSCLC, with 8 regarding the use of PD-L1 testing, was sent to oncologists. Approximately 41 oncologists responded to the survey.

**Results:** Most clinicians (95.12%) perform PD-L1 testing at the time of diagnosis of NSCLC before initiating any therapy. In a limited sample, 97.56% of clinicians order PD-L1 as a first priority followed by EGFR and ALK. Gastric/GEJ, melanoma, and bladder carcinoma are the most common malignancies other than NSCLC for which clinicians order PD-L1 testing (18.6%, 13.95%, and 13.95%, respectively). Immunohistochemistry is the most common method used for PD-L1 analysis. Lack of tissue and reimbursement issues are the most common barriers that prevent clinicians from using PD-L1 testing (56.82% and 22.73%, respectively). The turnaround time for PD-L1 testing is about a week in most cases (36.36%); however, 22.73% of clinicians received the results in 2 days or less.

**Conclusions:** PD-L1, along with EGFR and ALK biomarkers, is the most common routinely performed testing at the time of diagnosis of NSCLC. PD-L1 is the top priority for most clinicians in setting of limited samples. Most clinicians get the results within a week.

**Highlighting the Importance of Real-Time Denial and Code-Revision Monitoring for Appropriate Medicare Reimbursement**

(Poster No. 172)

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**Context:** The Protecting Access to Medicare Act of 2014 (PAMA) will instigate drastic reimbursement cuts to the clinical laboratory fee schedule. To protect fair reimbursement for services, clinical laboratories must proactively monitor Medicare-related denials and coding revisions. Around this same time, the current procedural terminology (CPT) codes associated with next-generation sequencing underwent significant changes. In 2015, our laboratory began using the new CPT 81445 (targeted genomic sequence analysis panel). This has a clearly defined local coverage determination for our region and is reimbursed separately from the ambulatory payment classification rate associated with the outpatient encounter.

**Design:** Outpatient claims for CPT code 81445 were retrospectively reviewed. From 2015 to 2019, a total of 125 cases were sampled. Proportion of denials, associated International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes, and test utilization were reviewed.

**Results:** Our data showed a significant denial rate of 96.8% for this CPT code. The primary reason for denial was medical necessity (94.5%), duplicate order (5%), and billing error (0.5%). On review, the cancer diagnosis resulting from the diagnostic biopsy was not correctly associated with the CPT code in question, and occasionally the entire encounter was billed under ICD-10 code.

**Conclusions:** We expected an increase in reimbursement related to CPT code 81445 given the new fee schedule and defined approval indications, but this was strikingly incorrect. We discovered incorrect CPT-ICD10 code pairings, suboptimal CPT-service linkage, and a need for denial monitoring and specific code evaluation within the laboratory. A Lean-Six Sigma project to develop a more streamlined workflow to monitor denials and increase compliance has been initiated.