Abstracts and Case Studies From the College of American Pathologists 2014 Annual Meeting (CAP ’14)

Abstracts and case study poster sessions will be conducted during the 2014 College of American Pathologists Annual Meeting, which is scheduled for September 7 to 10, 2014. The meeting will take place at the Hyatt Regency Hotel, Chicago, Ill. The poster sessions will occur in the CAP ’14 Exhibit Hall. Specific dates and times for each poster session are listed below. Also shown before each poster session are the subject areas that will be presented during each session.

POSTER SESSION 100: MONDAY, SEPTEMBER 8, 2014
9:00 AM–12:15 PM
Gastrointestinal and Liver Pathology; Breast Pathology; Pulmonary and Mediastinal Pathology

A Case of Intraductal Tubulopapillary Neoplasm: A Rare Intraductal Neoplasm of the Pancreas With Foci of Invasion
(Poster No. 1)

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Intraductal tubulopapillary neoplasm (ITPN) of the pancreas is a rare tumor, accounting for less than 1% of pancreatic exocrine neoplasms. We report a case of a 74-year-old man with a mass in the pancreatic head. Imaging studies showed significant pancreatic ductal dilation with a nondilated common bile duct. Clinical suspicion was for an endocrine or acinar cell neoplasm. A pancreaticoduodenectomy was performed. Pathologic examination demonstrated a 6-cm, intraductal mass that protruded into the ampulla, not involving the intestinal mucosa. The mass showed tubulopapillae lined by dysplastic cells with eosinophilic cytoplasm without intracytoplasmic mucin and with rare foci of stromal carcinoma, consistent with ITPN with invasive carcinoma (Figure 1). Immunohistochemistry was focally positive for MUC1 and negative for MUC2, MUC5AC, endocrine, and acinar markers. The main differential diagnosis for ITPN is intraductal papillary mucinous neoplasm and pancreatic ductal adenocarcinoma. Intraductal tubulopapillary neoplasms are relatively indolent neoplasms, with significantly better prognosis than pancreatic ductal adenocarcinomas. The prognosis of noninvasive ITPNs is as favorable as noninvasive intraductal papillary mucinous neoplasms. Further investigation is needed to assess the comparative prognosis of invasive ITPN. This case demonstrates that ITPN can be reliably distinguished from other pancreatic neoplasms, but additional studies regarding prognosis in the setting of invasion are needed.

Widespread Breast Metastasis Discovered on Routine Colonoscopy
(Poster No. 2)

Reeba A. Omman, MD (romman@lumc.edu); Roberto G. Gamez, MD; Sherri L. Yong, MD. Department of Pathology, Loyola University Medical Center, Maywood, Ill.

Distant metastasis is the most common form of recurrence and the main cause of death in patients with breast cancer. The most common site for breast cancer metastasis is bone followed by visceral organs. It has also been shown that breast cancer metastasis to visceral organs has a shorter disease-free survival. This is a case of a 51-year-old woman with a history of infiltrating lobular carcinoma treated with a left modified radical mastectomy and axillary dissection. The tumor was a multifocal, 3.5 cm, infiltrating lobular carcinoma, grade III tumor that was estrogen and progesterone receptor positive but HER2/neu negative by fluorescent in situ hybridization. The tumor was a multifocal, 3.5 cm, infiltrating lobular carcinoma, grade III tumor that was estrogen and progesterone receptor positive but HER2/neu negative by fluorescent in situ hybridization. One of 19 lymph nodes was positive for tumor, and she was classified as pT2N1aMx, stage IIIA. She started chemotherapy, and her breast cancer follow-up was thereafter negative. However, routine screening colonoscopy done 4.5 years after completion of treatment showed a 3-mm cecal polyp. Microscopically, sections of the polyp demonstrated colonic mucosa with infiltrating, poorly differentiated, single cells in the lamina propria (Figure 2, a and b). The tumor cells stained positive for CK7 (Figure, c) and GCDFP-15 (focally) (Figure, d). The morphologic and immuno-histochemical pattern was consistent with metastatic lobular carcinoma. The patient has since had a positron emission tomography scan, which showed increased uptake in the porta hepatis lymph node and in the vertebral bodies. A computed tomography scan showed prominent lymphadenopathy in chest, abdomen, and pelvis. The patient has since been started on capecitabine. This case illustrates how asymptomatic, disseminated breast carcinoma can be discerned incidentally on routine colonoscopy.

Reprints not available.

MUC1 and negative for MUC2, MUC5AC, synaptophysin, and trypsin.
The ITPNs are grossly visible, intraductal tube-forming epithelial neoplasms with high-grade dysplasia and ductal differentiation without overt mucin production. They are immunoreactive for MUC1 and MUC6 and negative for MUC2, MUC5AC, endocrine, and acinar markers. The main differential diagnosis for ITPN is intraductal papillary mucinous neoplasm and pancreatic ductal adenocarcinoma. Intraductal tubulopapillary neoplasms are relatively indolent neoplasms, with significantly better prognosis than pancreatic ductal adenocarcinomas. The prognosis of noninvasive ITPNs is as favorable as noninvasive intraductal papillary mucinous neoplasms. Further investigation is needed to assess the comparative prognosis of invasive ITPN. This case demonstrates that ITPN can be reliably distinguished from other pancreatic neoplasms, but additional studies regarding prognosis in the setting of invasion are needed.

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Further investigation may be necessary for this conclusion. However, the low number of positive results suggests that expression of the studied biomarkers does not correlate with overall survival, and a cytoplasmic (IMP3 and CK19) or nuclear (S100P) stain in more than 10% of the tumor cells.

**Expression of S100P, IMP3, and CK19 in Hepatocellular Carcinoma**

(Poster No. 3)

Larry Zhao, MD (larry.zhao@umassmemorial.org); Otto Walter, MD; Xiaofei Wang, MD, PhD. Department of Pathology, University of Massachusetts Medical School, Worcester, Mass.

**Context:** S100P, IMP3, and CK19 have been found in other studies to be independent predictors of early tumor recurrence in hepatocellular carcinomas (HCCs) with poor prognoses. However, no study has analyzed the expression of the 3 markers together. In this study, the panel of 3 markers was examined and correlated with HCC stage, grade, and clinical outcome.

**Design:** Seventy cases of HCC from 2003 to 2012 were identified and retrieved from our archives. The specimens included cases with varying stages and grades: 22 stage I, 35 stage II, 13 stage III and IV cases; 14 were well-differentiated, 35 moderately differentiated, and 21 poorly differentiated tumors. All cases were stained with a monoclonal antibody for S100P, IMP3, and CK19 proteins, and the results were evaluated independently by 3 observers. A positive result was defined as a cytoplasmic (IMP3 and CK19) or nuclear (S100P) stain in more than 10% of the tumor cells.

**Results:** Significantly greater coexpression of these markers was found in stage III and IV tumors: 5/13 cases (38%) showed double or triple stain positivity versus 23% (5 of 22) in stage I and 26% (9 of 35) in stage II tumors (see Table).

<table>
<thead>
<tr>
<th>Stage</th>
<th>IMP3, No. (%)</th>
<th>S100P, No. (%)</th>
<th>CK19, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I, n = 22</td>
<td>6 (27)</td>
<td>6 (27)</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Stage II, n = 35</td>
<td>14 (40)</td>
<td>10 (28)</td>
<td>5 (14)</td>
</tr>
<tr>
<td>Stage III, n = 8</td>
<td>2 (25)</td>
<td>2 (25)</td>
<td>2 (25)</td>
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<tr>
<td>Stage IV, n = 5</td>
<td>5 (100)</td>
<td>3 (60)</td>
<td>4 (80)</td>
</tr>
<tr>
<td>Grade 1, n = 14</td>
<td>2 (14)</td>
<td>1 (7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Grade 2–3, n = 56</td>
<td>25 (45)</td>
<td>20 (36)</td>
<td>10 (18)</td>
</tr>
</tbody>
</table>

**Conclusions:** The panel of S100P, IMP3, and CK19 expression is positively correlated with the histologic grade and clinical stage. However, the low number of positive results suggests that expression of the studied biomarkers does not correlate with overall survival, and further investigation may be necessary for this conclusion.

**IgG4-Related Pseudotumor of the Colon Mimicking Colon Cancer in a Patient With a History of Inflammatory Bowel Disease**

(Poster No. 4)

Jordan Roberts, MD (jaroberts@tmhs.org); Jae Ro, MD, PhD. Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Tex.

Immunoglobulin G4–related disease is a tumefactive, fibroinflammatory process that has been described in numerous organ systems. The diagnosis IgG4-related disease relies on the presence of characteristic histologic findings, including a dense, lymphoplasmacytic infiltrate with elevated numbers of IgG4 immunopositive plasma cells, sclerotic fibrosis, focaly, with a storiform pattern and obliterator thrombophlebitis. Here, we report a case of IgG4-related pseudotumor of the colon mimicking colon carcinoma clinically. A 64-year-old man with a history of inflammatory bowel disease (IBD) underwent a surveillance colonoscopy, which showed a 3-cm sessile mass arising in the ascending colon. This mass was biopsied and showed ulceration and active colitis; however, no dysplasia or malignancy was seen. Because of the size of the mass and concern for cancer, the patient underwent a segmental colectomy. Microscopic examination of the mass showed a dense plasma-cell infiltrate with associated lymphocytes and eosinophils and extensive sclerotic fibrosis in the lamina propria and submucosa. No obliterator thrombophlebitis was seen. Immunostain for IgG4 showed numerous IgG4-positive plasma cells (>50 high power field) with an IgG4/IgG ratio greater than 40%, consistent with IgG4-related pseudotumor. No dysplastic changes or malignancy were seen. Serum IgG4 levels were not obtained. To our knowledge, an IgG4-related pseudotumor of the colon mimicking malignancy in a patient with history of IBD has never been described. Some studies have shown an increased incidence of IBD in patients with autoimmune pancreatitis (a prototypic IgG4-related disease). Further studies are needed to elucidate the possible relationship between IgG4-related disease and IBD (Figure 3).
Solid Pseudopapillary Tumor in Young Pediatric Male Patient Presenting With Abdominal Pain

(Poster No. 6)

Esther Yoon, MD1 (yoone@wcmc.com); Liying Han, MD2; Oliver Muensteroler, MD2; Samir Pandya, MD.2 Departments of 1Pathology and 2Pediatric Surgery, Westchester Medical Center, Valhalla, NY.

Solid pseudopapillary tumor (SPPT) of the pancreas is a distinct type of neoplasm that accounts for less than 4% of pancreatic tumors. It occurs predominantly in young females (female to male ratio, 10:1). It is exceedingly rare in males, and only a few cases have been reported in children. We are reporting a case of SPPT of the pancreas in a 15-year-old adolescent boy. Our patient was previously healthy before presenting to the hospital with moderate aching pain in right, lower quadrant for 4 days. Imaging studies showed a 9-cm heterogeneously enhancing, septated, peripherally calcified pancreatic tumor centered in the tail of the pancreas with preservation of the peripancreatic fat and pancreatic duct. Grossly, an intact mass with attached pancreatic tissue measured 10.0 x 8.0 x 6.0 cm and weighed 405.1 g. The lesion was multicystic and contained a friable, yellow, stellate lesion measuring 8.0 x 3.0 x 2.5 cm; 70% of the mass was hemorrhagic and necrotic. Microscopic examination showed pseudopapillae with hyalinized fibrovascular cores lined by several layers of bland fragile epithelial cells with clear to eosinophilic cytoplasm. There was an abundant amount of foam cells and clusters of cholesterol crystals in the tumors. Immunohistochemical studies revealed the tumor cells were positive for vimentin, β-catenin (nuclear staining), CD10 (cytoplasmic staining), CD56, and PR and negative for CD99. The morphologic features and immunohistological staining pattern support the diagnosis of SPPT of the pancreas. This case study emphasizes the importance of recognizing the SPPT of the pancreas in the pediatric population and increases awareness of appropriate treatment when necessary.

A Limited Immunohistochemical Panel for Subtyping Hepatocellular Adenomas in Routine Clinical Practice

(Poster No. 7)

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Context: There are 4 subtypes of hepatocellular adenomas (HCAs). Hepatocyte nuclear factor 1α-mutated (H-HCA) and those without known molecular abnormalities (unclassifiable HCA [UHCA]) have no known therapeutic import. β-catenin-mutated HCA (β-HCA) is resected because of its markedly elevated risk of hepatocellular carcinoma. Inflammatory HCA (IHCA) is associated with a systemic inflammatory syndrome that may be cured with resection. Definitive subtyping requires molecular studies, but immunohistochmistry is helpful in routine practice. This study evaluated whether HCAs could be divided into clinically relevant subgroups using only limited immunohistochmistry.

Design: Representative blocks from 41 HCA resections were immunostained against a panel including serum amyloid A (Dako, Carpinteria, Calif), glutamine synthetase (Biocare, Concord, Calif), and β-catenin (Cell Marque, Rocklin, Calif). Amyloid was scored as none/patchy or diffuse. Glutamine synthetase was scored as none/perivascular, maplike, diffuse, or uninterpretable. β-catenin was membranous or nuclear. Working diagnoses of β-HCA, IHCA, other HCA, focal nodular hyperplasia, and nondiagnostic were assigned using the diagrammed diagnostic algorithm.

Results: Sixteen IHCAs, 7 β-HCAs, and 18 other HCAs were diagnosed. No cases showed maplike glutamine synthetase staining denoting focal nodular hyperplasia or uninterpretable staining, as in some indeterminate lesions.

Conclusions: This panel successfully subtyped all cases as IHCA, β-HCA, or other HCA. None showed focal, nodular, hyperplasia-like, or uninterpretable patterns. Although HHCAs and UHCAs cannot be determined by this panel, subtyping them has no direct therapeutic impact. This study shows that HCAs can be subtyped in a clinically meaningful way with minimal immunostaining. Further study could determine whether this panel performs similarly on biopsies (Figure 5).

EZH2 Is a Useful Marker to Confirm Diagnosis of Colorectal Adenocarcinoma in Suboptimal Biopsy Specimens

(Poster No. 8)

Wewei Chen, MD, PhD1 (wchen25@buffalo.edu); Donghong Cai, MD, PhD.2 1Department of Pathology, University at Buffalo, NY; 2Department of Pathology, Chilton Hospital, Pompton Plains, NJ.

Context: The diagnosis of colorectal adenocarcinoma in biopsy specimens can be difficult if the specimens are suboptimal because of cautering artifacts, small sizes, and/or extensive necrosis. Overexpression of enhancer of zeste homolog 2 (EZH2) has been shown in colorectal cancer. We investigated whether EZH2 could be used as a tumor marker to aid in diagnosis of colonic adenocarcinoma in suboptimal biopsy specimens.

Design: EZH2 expression was studied by immunohistochemistry in 4 different conditions: normal colon, tubular adenoma, intramucosal adenocarcinoma, and invasive adenocarcinoma. The expression levels were qualitatively graded, and the overall percentage of positivity in glandular/tumor cells for each condition was calculated. Next, EZH2 expression was retrospectively investigated in cases where suboptimal
**Microfibrillar-Associated Protein 5 (MFAP5) Is Not Helpful in Differentiating Pancreatic Ductal Adenocarcinoma From Chronic Pancreatitis**

**(Poster No. 9)**

Wei Chen, MD, PhD1 (wei.chen2@osumc.edu); Benjamin Swanson, MD, PhD1; Mark Bloomston, MD2; Wendy Frankel, MD.1 Departments of 1Pathology and 2Surgical Oncology, Ohio State University Wexner Medical Center, Columbus, Ohio.

**Context:** Chronic pancreatitis (CP) may mimic pancreatic ductal adenocarcinoma (PDAC), creating a diagnostic challenge. MFAP5 is involved in elastic microfibril assembly and has been reported to show decreased expression in tumor stroma of prostatic and colonic cancer. It is helpful in the diagnosis of colonic adenocarcinoma. It is helpful in the diagnosis of colonic adenocarcinoma. It is helpful in the diagnosis of colonic adenocarcinoma. It is helpful in the diagnosis of colonic adenocarcinoma. It is helpful in the diagnosis of colonic adenocarcinoma. MFAP5 expression was assessed in CP and PDAC to determine whether it was useful in helping to differentiate the 2 entities.

**Design:** Ten CP and 29 PDAC resection cases were immunostained for MFAP5 (1:1500, Sigma-Aldrich, St. Louis, Mo). Staining intensity was graded as negative (0), weak (1), moderate (2), and strong (3). Staining score was calculated as the product of intensity and percentage of stromal positivity. Statistical analysis was performed using the Student t test.

**Results:** In CP and PDAC, patient age ranged from 26 to 55 years (mean, 42 [9] years) and from 30 to 78 years (mean [SD], 64 [12]), with male to female ratio of 2.3:1 and 1:6.1. Normal adjacent pancreas from these cases showed MFAP5 staining only in the thin fibrous septae between lobules, with no staining in pancreatic acini, ducts, or islets. The CP showed focal staining in the fibrotic stroma between atrophic acini and ducts, with a staining intensity similar to that of normal pancreatic septae. The PDAC showed focal, variable staining around tumor glands and in the desmoplastic stroma. The average staining score for PDAC (0.61 [0.80]) was not significantly different from CP (0.66 [0.29]) (P = .85).

**Conclusions:** Normal pancreatic tissue only expresses MFAP5 in the thin, fibrous septae between pancreatic lobules. Neither CP nor PDAC show significant differences in MFAP5 expression; therefore, MFAP5 is not helpful in distinguishing CP from PDAC.
study, we investigated the expression of more than 70 commonly used biomarkers in both esophageal and pancreatic ADCs. These immunomarkers included (1) various cytokeratins, (2) transcription factors/ nuclear staining markers (ER, p53, p63, p40, CDX2, SATB2, PAX8, TTF1, DPC4, SOX2, SOX10, HNF1B, GATA3, ERG, SALL4, OCT4, CDK4), (3) mucin genes (MUC1, MUC2, MUC4, MUC5AC, MUC6), and (4) tumor-associated proteins (β-catenin, cadherin-17, HBME1, mammaglobin, galectin-3, glypican 3, napsin A, TTF1, maspin, S100, S100P, P504S, melanoma markers, and more).

**Design:** Immunohistochemical evaluation of the aforementioned immunomarkers in 48 esophageal and 49 pancreatic ADCs on tissue microarray sections was performed and was recorded as positive if more than 5% of tumor cells stained.

**Results:** The immunostaining results from the selected immunomarkers and the comparison of their expression in esophageal and pancreatic ADCs are summarized in the Table. Expression of HepPar1, SALL4, and FLI1 was seen in 12.5%, 2%, and 6.4% of esophageal ADCs, respectively. Expression of ER, TTF1, arginase-1, PAX8, RCC, S100, uroplakin II, inhibin-α, OCT4, GATA3, glypican 3, and ERG was not observed in either esophageal or pancreatic ADCs.

**Conclusions:** Tissue-specific immunomarkers were not identified for either esophageal ADCs or pancreatic ADCs. However, the panel of immunomarkers in the Table is potentially useful in the distinction of these 2 entities.

### Summary of Useful Immunomarkers

<table>
<thead>
<tr>
<th>Marker</th>
<th>Esophageal ADC (n = 48), %</th>
<th>Pancreatic ADC (n = 49), %</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK17</td>
<td>6</td>
<td>61</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>CK20</td>
<td>48</td>
<td>12</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>CK903</td>
<td>33</td>
<td>63</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Cadherin-17</td>
<td>48</td>
<td>12</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>CDX2</td>
<td>43</td>
<td>16</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>MUC1</td>
<td>64</td>
<td>100</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>DPC4</td>
<td>0 (loss of expression)</td>
<td>50 (loss of expression)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>β-catenin</td>
<td>15 (nuclear stain)</td>
<td>0 (nuclear stain)</td>
<td>&lt;.05</td>
</tr>
</tbody>
</table>

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**Darling Disease Masquerading As Malignancy/ Disseminated Tuberculosis**

(Poster No. 13)

Jessica A. Kumar, DO, MPH1 (jessicakumardo@gmail.com); Edgar J. Morales, MD2; Joseph F. Tomasheski, MD, MD2; Department of Infectious Disease and HIV Medicine, University Hospitals Case Western Reserve University, Cleveland, Ohio; 2Departments of Pathology, MetroHealth Medical Center, Cleveland, Ohio.

Disseminated histoplasmosis (Darling disease) is often unrecognized in immunocompetent patients, leading to delays and inaccurate diagnosis. We present a case of a 74-year-old woman with previous exposure to *Mycobacterium tuberculosis* (TB) presenting with failure to thrive, cognitive decline, and ataxia. She developed a productive cough, dyspnea, nausea, and abdominal pain. Upon hospitalization, she became febrile, and an abdominal computed tomography (CT) scan showed pneumoperitoneum. An urgent exploratory laparotomy was performed, and she was found to have a jejunal perforation (45 cm from the duodenojejunal flexure) with multiple nodules throughout the small bowel, concerning for malignancy. The patient developed T-cell lymphopenia with normal immunoglobulins without evidence of TB. Histologically, the resected bowel showed acute necrotizing enteritis, perforation, and a dense histiocytic infiltrate with scattered, poorly formed granulomas and innumerable yeast forms within the histiocytes, consistent with histoplasma (Figure 7). Subsequently, her urine histoplasma antigen was found to be elevated (12.07 ng/mL), and bronchial washings revealed *Histoplasma capsulatum*, correlating with a chest CT finding of innumerable, milliary centriflobular nodules. Gastrointestinal histoplasmosis can manifest with protean symptoms. Diarrhea, dysphagia, abdominal pain, lever, weight loss, and less frequently, obstruction or perforation can mimic TB, inflammatory bowel disease, or carcinoma. As illustrated by this case, gastrointestinal involvement may be the presenting and dominant manifestation of disseminated histoplasmosis. Moreover, histopathologic identification of fungal organisms may be the initial clue to the diagnosis of this often-fatal disease.

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**Ciliated Hepatofugal Cyst: A Report of 2 Cases**

(Poster No. 14)

Katherine C. Bishop, BS1 (bishopk@wusm.wustl.edu); Carmen M. Perrino, MD2; Marianna B. Ruzinova, MD, PhD3; Elizabeth M. Brunt, MD2; 1School of Medicine and 2Department of Pathology and Immunology, Washington University, St Louis, Mo.

Ciliated hepatofugal cyst (CHFC) is a rare, cystic lesion that is most commonly identified in segment 4 of the liver and that arises from the embryonic foregut. The classic, histologic pattern comprises 4 distinct layers (inner ciliated epithelial lining, smooth muscle, loose connective tissue, fibrous capsule). Although rare, cases of metaplastic and even malignant transformation of the epithelial lining of CHFC have been described. We report 2 of our 6 cases of CHFC in the past 25 years, one with the classic morphology and a second with evidence of gastric metaplasia. The first case was discovered incidentally in a 67-year-old man. The second case occurred in a 42-year-old woman who experienced postprandial epigastric discomfort. Tumor marker serologies (CA 19-9, CEA) were performed, and results were within reference range. Both lesions, treated with complete surgical resection and located in the porta hepatis, were unilocular. The first lesion was 6.5 cm in greatest dimension, and microscopically, showed classic histology but with numerous mucin-containing goblet cells. The second lesion was 8.0 cm in greatest dimension and showed focal gastric foveolar metaplasia; selective immunohistochemistry was performed, and the epithelial lining was positive for keratin 7. Neither case had evidence of malignancy. In conclusion, CHFC is a rare diagnostic entity that should be considered in the differential diagnosis for cystic hepatic lesions, especially in segment 4. Although most reported CHFC cases are benign, metaplasia and even squamous cell carcinoma can occur, affecting clinical management by making complete surgical excision the recommended treatment.

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**Tissue Microarray Technology in Universal Screening of Lynch Syndrome**

(Poster No. 15)

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**Context:** Lynch syndrome is an autosomal-dominant disorder conveying increased risk for multiple primary cancers. Universal screening of tumors for Lynch syndrome by immunohistochemistry with mismatch repair proteins MLH1, MSH2, MSH6, and PMS2 may determine whether genetic testing is warranted. Immunohistochemistry can be costly and time-consuming; tissue microarrays (TMAs) provide an alternative to whole-tissue sectioning (WTS) by sampling multiple tumor cores. The TMAs conserve time, reagents, and archival tissue when many specimens are processed simultaneously. We investigated TMA and WTS concordance for mismatch repair proteins in colon cancer.

**Design:** Twenty colectomies for adenocarcinoma were retrospectively sampled, and 4 benign colons served as controls. Three 2-mm cores were punched from paraffin-embedded tissue per case. Our
Crownlike Structures in Peripancreatic Adipose Tissue in Patients With Pancreatic Ductal Adenocarcinoma

(Poster No. 16)

Deyali Chatterjee, MD1 (dchatter@bcm.edu); Aparna Balachandran, MD2; Priya R. Bhosale, MD2; Eric P. Tammi, MD2; Asif Rashid, MD, PhD3; Matthew H. Katz, MD4; Jason B. Fleming, MD4; Huamin Wang, MD, PhD3; Matthew H. Katz, MD4; James L. Abbruzzese, MD5; Robert A. Wolff, MD5; Jason B. Fleming, MD4; Huamin Wang, MD, PhD3.1Department of Pathology, Baylor College of Medicine, Houston, Tex; 2Department of Pathology, University of Texas Southwestern Medical Center, Dallas, Tex; 3Department of Pathology, University of California, San Francisco, Calif; 4Department of Pathology, University of Texas MD Anderson Cancer Center, Houston, Tex; 5Department of Pathology, University of Texas Southwestern Medical Center at Dallas, Dallas, Tex.

Context: Studies in mice and human mammary glands have shown that crownlike structures (CLSs) formed by macrophage infiltration surrounding a necrotic adipocyte correlate with the activation of NFκB, elevated aromatase levels, and elevated body mass index, and they have an important role in the development of breast cancer. Our study is the first to analyze CLS in peripancreatic adipose tissue in patients with pancreatic cancer.

Design: Our study population consisted of 84 patients with pancreatic ductal adenocarcinoma (PDAC) who underwent pancreatocoduodenectomy at MD Anderson Cancer Center (Houston, Texas). The representative areas of peripancreatic adipose tissue were selected and 5Gastrointestinal Medical Oncology, MD Anderson Cancer Center, Houston, Tex.

Conclusions: Current guidelines recommend screening all patients newly diagnosed with colorectal cancer for Lynch syndrome. Based on our findings, TMA technology offers a viable and economical alternative to WTS.

Results: The CLSs were present in 44 of 84 cases (52.4%), which correlated with total body fat and visceral adipose tissue content ($P = .03$ and $P = .02$, respectively). However, there were no correlations of CLS with any other parameter studied.

Conclusions: Although the presence of CLSs correlated with total body fat and visceral fat in cases of pancreatic ductal adenocarcinoma and unclear associations exist in the literature between obesity and pancreatic cancer, no correlation of the presence of CLS can be shown with the disease parameters.

An Unusual Pattern of CK7/20 Concordance Staining in a Case of Gastric Adenocarcinoma

(Poster No. 17)

Jesse C. Qiao, MD (qiao@uthscsa.edu); Nicole D. Riddle, MD. Department of Pathology, University of Texas Health Science Center at San Antonio, Tex.

A 77-year-old woman underwent an exploratory laparotomy (for reasons unknown to the pathologist) for peritoneal carcinomatosis. Biopsy of the pelvic sidewall is shown (Figure 9, A). Immunohistochemistry showed the malignant cells to be strongly and diffusely positive for cytokeratin 20 (CK20; Figure, B), negative for cytokeratin 7 (CK7, Figure, C). Although that immunoprofile suggests a colon cancer primary, we were later informed that the patient underwent an endoscopically guided biopsy of a gastric mass at another institution that revealed a poorly differentiated, signet-ring-type adenocarcinoma of the stomach. Given the additional clinicopathological features, we favored gastric primary. Gastric adenocarcinomas can present as either an intestinal type or a diffuse type (signet-ring cells), both with similar immunohistochemical staining patterns. However, unlike other malignancies, such as breast and colon cancer, CK7 and CK20 coordinate staining patterns are often heterogeneous for gastric adenocarcinomas of either subtype. CK7+/CK20+ and CK7-/CK20+ are the predominant patterns, followed by CK7-/CK20- (suggesting undifferentiation) and CK7+/CK20- (the least common pattern). Although the lack of uniform coordinate CK7/CK20 staining may reflect differences in intermediate filament expression in gastric adenocarcinomas, it may also be due to the lack of definitive cutoff percentages at which staining is classified as positive or negative. This case demonstrates a pitfall of relying on the utility of CK7 and CK20 staining to characterize gastric adenocarcinoma and its metastases. Clinical and histopathologic correlation is required to make an accurate diagnosis, including adequate discussion with the clinician if warranted.

CDH17 Is a Highly Specific Marker and Is a More-Sensitive Marker Than CDX2 and CK20 in Colon Cancer

(Poster No. 18)

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Context: Cadherin 17 (CDH17) is a cell-adhesion molecule expressed in the intestinal epithelium and transcriptionally regulated by CDX2. CDH17, belonging to the 7D-cadherin superfamily, represents a novel oncogene, which is involved in tumor invasion and metastasis. Recently, studies have shown CDH17 to be a highly specific marker for gastrointestinal epithelium, particularly the intestinal type.

Design: CDH17 rabbit monoclonal (RM), CDH17 mouse monoclonal (M), and CK20 and CDX2 antibodies were evaluated for specificity and sensitivity on (formalin-fixed, paraffin-embedded) tissue microarrays consisting of colon adenocarcinoma (n = 99), lung cancer (n = 71), ovarian cancer (n = 70), melanoma (n = 6), urothelial carcinoma (n = 20), prostate adenocarcinoma (n = 20), breast cancer (n = 13), lymphoma (n = 10), renal cell carcinoma (n = 12), and in normal tissues (n = 30). Antibody titers were optimized, and visualization was accomplished using a polymer-based detection system.

Results: CDH17 (M) and CDH17 (RM) stained 100% (99/99) of colon cancers, whereas CDX2 and CK20 stained 94% (93/99) and 92%
Recognizing malignancy-associated paraneoplastic syndromes. Demonstrates the importance of liver biopsy and the clinical relevance of tumors. The present case is the first of primary hepatic SCC with Cushing syndrome. There is only one prior report of Cushing syndrome with a primary hepatic neuroendocrine tumor, a carcinoid. The previously reported 14 cases of hepatic SCC showed a male predominance and age range of 51 to 89 years (mean, 68 years). There was typically a large, single tumor nodules in 0.2 to 6.0 cm of the liver, with no tumor of any other organs. The pituitary was unremarkable, and although the tumor failed to immunoreact for ACTH, the clinical course was consistent with SCC-associated Cushing syndrome. The immediate cause of death was Aspergillus-associated pneumonia, likely secondary to Cushing syndrome. The present case is the first of primary hepatic SCC with Cushing syndrome. There is only one prior report of Cushing syndrome with a primary hepatic neuroendocrine tumor, a carcinoid. The previously reported 14 cases of hepatic SCC showed a male predominance and age range of 51 to 89 years (mean, 68 years). There was typically a large, single liver mass, and the present case represents only the second in which the tumor presented with multiple tumor nodules. The prognosis is poor, with 67% dead of disease within an average of 10 months. This case demonstrated the importance of liver biopsy and the clinical relevance of recognizing malignancy-associated paraneoplastic syndromes.

Metastatic Neuroendocrine Carcinoma in a Patient With AIDS and Widespread Kaposi Sarcoma

Syncytial Variant of Nodular Sclerosis Classic Hodgkin Lymphoma of the Terminal Ileum in a Patient With Longstanding Crohn Disease

Conclusions: CDH17 is a highly specific and sensitive marker for colon cancer and may be used in combination with CDX2 and CK20 in tumors of unknown origin.

Dr Tacha is a shareholder in Biocare Medical.

Primary Hepatic Small Cell Carcinoma With Cushing Syndrome: A Case Report and Literature Review

Poster No. 19
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Small cell carcinoma (SCC) (grade 3 neuroendocrine carcinoma) arises in the lung in more than 96% of cases. Primary hepatic SCC is exceedingly rare, with only 14 previously reported cases. We report a 62-year-old man with symptoms suggestive of Cushing syndrome, with elevated serum adrenocorticotropic hormone (ACTH) and 24-hour urinary cortisol. Imaging suggested liver cirrhosis; however, biopsy showed SCC. Synaptophysin and chromogranin were positive, and cytokeratin 20, CDX2, napsin A, and TTF1 were negative. The patient expired 1 week later. Immunohistochemistry showed bilateral adrenal hyperplasia and innumerable tumor nodules in 0.2 to 6.0 cm of the liver, with no tumor of any other organs. The pituitary was unremarkable, and although the tumor failed to immunoreact for ACTH, the clinical course was consistent with SCC-associated Cushing syndrome. The immediate cause of death was Aspergillus-associated pneumonia, likely secondary to Cushing syndrome. The present case is the first of primary hepatic SCC with Cushing syndrome. There is only one prior report of Cushing syndrome with a primary hepatic neuroendocrine tumor, a carcinoid. The previously reported 14 cases of hepatic SCC showed a male predominance and age range of 51 to 89 years (mean, 68 years). There was typically a large, single liver mass, and the present case represents only the second in which the tumor presented with multiple tumor nodules. The prognosis is poor, with 67% dead of disease within an average of 10 months. This case demonstrated the importance of liver biopsy and the clinical relevance of recognizing malignancy-associated paraneoplastic syndromes.

Metastatic Neuroendocrine Carcinoma in a Patient With AIDS and Widespread Kaposi Sarcoma

Poster No. 20
Jong T. Kim, MD (jtkim1@ufl.edu); Andrea Duque, MD; William Clapp, MD. Department of Pathology, Immunology and Laboratory Medicine, University of Florida, Gainesville, Fla.

The spectrum of cancers in HIV-infected patients has changed in recent years with a decreasing incidence in AIDS-defining malignancies (ADCs) and a relative increase in non–AIDS-defining malignancies (NADCs). Among neuroendocrine tumors, although the incidence of Merkel cell carcinoma has increased more than 10-fold in patients with HIV infection, the occurrence of other neuroendocrine (NE) carcinomas in patients with AIDS is not well documented. We present a case of widespread metastatic NE carcinoma in patients with AIDS whose course was complicated by widespread Kaposi sarcoma, an ADC. Most cases of NE carcinoma involving the liver represent metastatic disease from an extrahepatic origin. Primary hepatic NE tumors are extremely rare. However, the clinical course and radiologic imaging (computed tomography/positron emission tomography scans) in our patient supported tumor involvement of the liver before the tumor involvement of other organs, such as the lung, pancreas, and heart. The carcinoma displayed a nested/organoid, trabecular, or diffuse growth pattern and consisted of intermediate-size, round-to-oval cells, with finely stippled nuclear chromatin. Mitotic figures averaged fewer than 2 per 10 high-power fields, and the Ki-67-labeling index was 7%. The tumor cells showed positive immunoreactivity for synaptophysin and chromogranin but were negative for CD20, CDX2, TTF1, and PAX8. The overall clinicopathologic findings are suggestive but not definitive for a primary hepatic, well-differentiated NE carcinoma. Our case study should contribute to raising awareness that the number and spectrum of distinct NADC associated with HIV infection is broadening.

A Case of Cronkhite-Canada Syndrome Without Polyposis and a Review of the Literature

Poster No. 22
Pingchuan Zhang, MD (pzhang@swmail.sw.org); Debby Rampise-la, MD. Department of Pathology, Scott and White Memorial Hospital, Temple, Tex.

Cronkhite-Canada syndrome (CCS) is a rare, noninherited disease associated with high morbidity and characterized by diffuse hamartomatous polyposis, diarrhea, weight loss, and ectodermal manifestations. We report an unusual case of CCS presented without polyposis. A 74-year-old, white man presented with altered sense of taste, abdominal pain, bloating, diarrhea, and marked weight loss (45 lbs [20.9 kg]) for 6 months. His past medical history was significant for hypothyroidism. Physical examination demonstrated onychodystrophy of finger and toe nails, cutaneous hyperpigmentation of palms, and alopecia. The esophagogastroduodenoscopy revealed severely thickened gastric folds...
and markedly edematous duodenal mucosa. Colonoscopy showed markedly edematous colonic mucosa with diverticulosis. Multiple biopsies were obtained from the stomach, duodenum, jejunum, terminal ileum, and colon. All of the biopsies showed marked, diffuse lamina propria edema. Prominent mucosal villous atrophy was particularly evident in the small bowel and duodenum. Focal acute enteritis and colitis were also seen. Immunohistochemical stains revealed an increase of immunoglobulin G4 (IgG4)-positive plasma cells in all biopsies (up to 20 per high-power field; Figure 10). Given the positivity of IgG4 and the good response to immunosuppressant therapy reported in the literature, the etiology of CCS is probably autoimmune related. Even without polyposis, the classic clinical presentations with the finding of diffuse gastrointestinal mucosal edema should raise the index of suspicion for the diagnosis of CCS.

A 7-Month-Old Infant With Inflammatory Fibroid Polyp of the Small Intestine

(Mohanad Shaar, MD; Stefan Pambuccian, MD. Department of Pathology, Loyola University Medical Center, Maywood, Ill.)

Since the first description of the entity in 1949 by Vanek, inflammatory fibroid polyps were only exceptionally reported in children. To our knowledge, no prior case diagnosed before the first year of age has been reported to date. We present a case of inflammatory fibroid polyp occurring in a 7-month-old, female infant who presented with acute abdomen and concern for intestinal obstruction. Emergency exploratory laparotomy revealed a mass at the distal jejunum/proximal ileum junction that was thought to represent a perforated Meckel diverticulum. The resected 3.7-cm segment of small bowel showed a 3.0-cm-long thickening of the wall with focal perforation. Histologic examination showed a proliferation of bland spindle cells infiltrating the full thickness of the bowel wall, focally extending to the mucosa and causing ulceration (Figure 11, A).

Cellularity was variable, with focal perivascular onion skinning (Figure, B). No necrosis and only occasional mitoses were seen. Focal lymphoid aggregates and interspersed eosinophils, mast cells, lymphocytes, and plasma cells were present (Figure, C). Immunohistochemistry showed strong reactivity of tumor cells with CD34 (Figure, D) and vimentin and low Ki-67 proliferation index (∼5%). There was no expression of smooth muscle antigen, ALK-1, desmin, myogenin, CD117, S100, and inhibin. No PDGFRα mutation was identified. This case stresses the importance of considering inflammatory fibroid polyp in the differential diagnosis of gastrointestinal tract spindle cell tumors, even in cases occurring in childhood or infancy.

Clinical and Histologic Correlation of KRAS and BRAF Mutated Colorectal Adenocarcinomas

(Yanelba Toribio, MD; Monica T. Garcia-Buitrago, MD. Department of Pathology and Laboratory Medicine, University of Miami Miller School of Medicine, Miami, Fla.)

Context: KRAS and BRAF mutated colorectal cancers (CRCs) have poor response to anti-EGFR therapy and worse survival. The aim of this study was to identify associations of KRAS and BRAF mutated CRCs regarding age, degree of differentiation, location, TNM, and microsatellite instability (MSI).

Design: We retrospectively analyzed data from 170 patients diagnosed with CRCs at the University of Miami/Jackson Memorial Hospital from 2008–2013. Ninety-three and 83 patients had KRAS and BRAF mutation analysis, respectively.

Results: KRAS-mutated CRCs occurred more in a younger subset of patients (43.2%, ≤50 years) in the right colon (52.8%) and showed low-grade differentiation (86.5%), higher T designation (89.5%), metastatic nodal disease (57.9%), distant metastasis (18.4%), and microsatellite stability (MS) (96.9%). BRAF wild-type CRCs occurred more in older patients (69.6%, >50 years), in the left colon (56.1%) and showed MSI (16.9%). BRAF-mutated CRCs occurred more in a younger subset of patients (47%, ≤50 years), in the right colon (75%), showed low-grade differentiation (100%), and MSS (100%). BRAF wild-type CRCs occurred more in older patients (66%, >50 years), in the left colon (56.2%), showed higher T designation (85.7%), metastatic nodal disease (51.9%), distant metastasis (11.7%), and MSI (11.6%).

Conclusions: Our analysis showed BRAF-mutated CRCs occurred more in a younger subset of patients and behaved less aggressively, whereas KRAS-mutated CRCs occurred more in a younger subset of patients and behaved more aggressively. Thus, KRAS and BRAF mutation could be predictive in identifying younger patients with more aggressive CRCs.

The Role of Lymphoglandular Complex in Human Noncancerous Mucosa and Adenocarcinoma of the Colon

(Michio Shimizu, MD, Saki Yajima, MD; Hiroshi Yamaguchi, MD; Koji Nagata, MD; Takahiro Hasebe, MD; Masanori Yasuda, MD. Department of Pathology, Saitama Medical University, International Medical Center, Saitama, Japan.)

Context: Lymphoglandular complex (LGC) is crypt epithelium within a lymphoid follicle, extending from the mucosa through the muscularis mucosae into the submucosa. We investigated the role of LGC in the human colon including normal and neoplastic colonic mucosa.

Design: We reviewed LGC in noncancerous colonic mucosa. This noncancerous mucosa was taken from the surgical negative margin of 46 resected cases of colon cancer. We evaluated the relationship between the incidence of LGC per one section and clinical information. Histologic features of LGC were also examined by using hematoxylin–eosin stain and immunohistochemistry. In addition, 6 cases with early adenocarcinoma of the colon involving LGC, all cases demonstrated so-called type 0, and most cases were well-differentiated tubular adenocarcinoma.

Results: Eleven LGCs were found of 82 sections examined in noncancerous mucosa. The incidence of LGC in noncancerous mucosa was 1 per 21-cm length in the ascending colon, 2 per 27-cm length in the transverse colon, 1 per 21-cm length in the descending colon, and 4 per 75-cm length in the rectum. Histologically, 2 types of LGC were found. One showed incomplete, thin muscularis mucosae, and the other revealed no muscularis mucosae. Regarding the cases of adenocarcinoma involving LGC, all cases demonstrated so-called type 0, and most cases were well-differentiated tubular adenocarcinoma.

Conclusions: In the human colon, one LGC can be seen per 22-cm length of the colon. Based on the review of cases of early stage colonic adenocarcinoma, LGC may be one of the important pathways of the direct invasion to the submucosa by cancer cells.

Rectal Adenocarcinoma With Prominent Rhabdoid Features: A Case Report and Review of the Literature

(Manoj Gadara, MD; Jonathan Earle, MD; Laila Maylor, PhD; William Sardella, MD; Saverio Ligato, MD. Departments of Pathology and Colorectal Surgery, Hartford Hospital, Hartford, Conn.)

Colonic adenocarcinoma with rhabdoid features is extremely rare, and only 10 cases have been previously reported in the literature. An 85-year-old man presented the present case with a large rectal mass. A biopsy revealed a neoplasm with epithelioid features. The patient underwent pelvic exenteration, and a 6.3 × 2.1 × 1.0-cm, ulcerated, necrotic mass, located in the anterior rectum was identified. Microscopically, a bi-phenotypic tumor composed of a glandular component (Figure 12, A1) and
of moderately differentiated adenocarcinoma (CK20+, CDX2+, CK7-, and preserved nuclear stain for INI [Figure, B1]), and a rhabdoid component (Figure, A2) of loosely cohesive, large epithelioid cells (CKMNF+, vimentin+, EMA+, CK+ and AE1/AE3+, and CK7-. CDX2- and loss of nuclear staining for INI [Figure, B2] with vesicular nuclei, prominent nucleoli, and significant amount of eosinophilic cytoplasm was identified. A histologic diagnosis of adenocarcinoma with rhabdoid features was made. No loss of expression of mismatch repair protein by immunohistochemistry or BRAF V600E gene mutation was identified. To date (11 months after surgery), our patient is alive and doing well without evidence of recurrent disease. Colon cancers with rhabdoid features are extremely rare and are not yet included in the most recent World Health Organization classification of large-bowel tumors. Such tumors have a very poor prognosis, proving fatal in 75% to 100% of patients within 6 months after having been diagnosed. Rhabdoid tumors should be considered in the differential diagnosis of malignant tumors involving the gastrointestinal tract.

**Spindle-Type Predominant GIST With a Minor Epithelioid Component Exhibiting PDGFRα Mutation: A Case Report and Review of the Literature**

(Yanelba Toribio, MD (yantoribio@gmail.com); Claudia P. Rojas, MD; Monica T. García-Buitrago, MD. Department of Pathology and Laboratory Medicine, University of Miami Miller School of Medicine, Miami, Fla.)

Gastrointestinal stromal tumors (GISTs) occur throughout the GI tract, mesentery, and omentum, but mostly arise from the stomach (60%) and small intestine (25%). Histologically, they are subtyped as spindle cell, epithelioid, or mixed types. Most GISTs tend to be positive for c-Kit (>95%), DOG1 (>95%), and CD34 (70%) by immunohistochemistry. Spindle-cell–type GISTs tend to be KIT mutated, whereas epithelioid-type GISTs are often PDGFRα mutated. Both components of a mixed-type GIST show the same receptor kinase-type mutation, relevant for therapy prediction to imatinib. We report a case of a 73-year-old woman who presented with abdominal discomfort and early satiety. Endoscopic ultrasound revealed a 1.4-cm submucosal gastric mass. Fine-needle aspiration was suggestive of GIST. A partial gastrectomy was performed. Pathologic examination revealed a 1.4-cm, well-circumscribed, submucosal mass. Histologically, it was a low-grade GIST, predominantly spindle with a minor epithelioid component. Immunohistochemistry revealed the epithelioid component was positive for PDGFRα and negative for c-Kit and CD 34, whereas the spindle component was positive for c-Kit, CD34, and weakly positive for PDGFRα. Both components were negative for DOG1. Mutational analysis revealed a D842V PDGFRα mutation. Identification of a GIST’s oncogenic mutation is crucial to identify patients who may be less responsive or resistant to imatinib therapy, that is, exon 9-KIT mutation, wild-type KIT, and D842V-PDGFRα mutation. Even though this GIST was predominantly spindle-type with a minor epithelioid component, it harbored a PDGFRα mutation. A combination of histomorphology and PDGFRα immunostaining is a reliable predictor of PDGFRα genotype in GIST, even in tumors with small epithelioid components (Figure 13).

**Colonic Reactive Angioendotheliomatosis-Like Lesion Mimicking Crohn Disease**

(Rahul Jawale, MBBS, MD (rahul.jawale@bhs.org); Amitabh Srivastava, MD. Department of Pathology, Brigham and Women’s Hospital, Boston, Mass.)

Primary neoplastic vascular lesions of the gastrointestinal tract (GIT) are rare. Tumorlike lesions of the blood vessels may mimic a primary neoplasm, and in some cases, the secondary mucosal changes associated with the lesion may be confused with a primary inflammatory disorder of the GIT. We present a case of reactive angioendotheliomatosis (RAE)-like lesion of the colon that was initially diagnosed as Crohn disease (CD). A 59-year-old man presented with diarrhea and abdominal pain of 6 month’s duration. A colonoscopy showed segmental ulceration involving the sigmoid colon. The clinical differential diagnosis was CD and ischemic colitis. Biopsies showed mucosal ulceration with no definite etiology, and the patient was treated with a presumptive diagnosis of CD. The pain persisted despite steroid and infliximab therapy for a year. A left hemicolectomy was eventually performed that showed mucosal ulceration and a transmural proliferation of capillaries in a lobular configuration that was centered around large veins in some areas. Epithelioid endothelial cells, foci of intravascular fibrin microthrombi, and intraluminal capillary tufts resembling glomeruloid bodies were present. There was no evidence of a chronic colitis, and no granulomas were identified. A review of patient history, symptoms, and clinical findings did not reveal evidence of a systemic disorder typically associated with RAE. The patient is asymptomatic in follow-up 6 months after surgery. Although RAE-like lesions involving the GIT are rare, secondary mucosal changes associated with this lesion may mimic a primary inflammatory disorder of the GIT such as CD.

**Follicular Pancreatitis: Yet Another Mimic of Pancreatic Cancer?**

(Rajib K. Gupta, MD (rajibgupta2011@gmail.com); Kurt T. Patton, MD; Stephen W. Behrman, MD, FACS; Bill H. Xie, MD. Department of Pathology and Surgery, University of Tennessee Health Science Center, Memphis, Tenn; Department of Pathology, Pathology Group of the Midsouth, Germantown, Tenn.)
Follicular pancreatitis is a recently described, histologically distinctive, lymphoplasmacytic pancreatitis, characterized by florid ductocentric lymphoid follicles, collagenous fibrosis, absent granulocytic epithelial lesions, and normal count of immunoglobulin G4 (IgG4)-positive plasma cells in pancreatic tissue, along with normal levels of IgG4 in serum. Both clinically and on gross examination, follicular pancreatitis has mimicked carcinoma of the head in reported cases. We report a 60-year-old, African-American man who underwent distal pancreatectomy. On gross examination, there was a $3 \times 2 \times 2.6$-cm, firm, discrete mass in the pancreatic tail, which, on frozen section and routine hematoxylin-eosin, revealed chronic pancreatitis with multiple ductocentric and lobulocentric lymphoid follicles, very focal storiform fibrosis, obliterator phlebitis, and occasional granulocytic epithelial lesions. Germinal center lymphocytes were negative for BCL2, and IgG4 plasma cells were not increased in the inflammatory infiltrate. Serum IgG4 was also within reference range. Although we cannot completely exclude an unusual variant of type 1 or type 2 autoimmune pancreatitis, the histopathologic features in our case favor follicular pancreatitis, the first such reported case arising in the tail of the pancreas. Awareness of this rare and benign mimic of pancreatic lesions. Germinal center lymphocytes were negative for BCL2, and IgG4 plasma cells were not increased in the inflammatory infiltrate. Serum IgG4 was also within reference range. Although we cannot completely exclude an unusual variant of type 1 or type 2 autoimmune pancreatitis, the histopathologic features in our case favor follicular pancreatitis, the first such reported case arising in the tail of the pancreas. Awareness of this rare and benign mimic of pancreatic cancer is important for surgeons, radiologists, and surgical pathologists alike because it could be treated conservatively and not with surgery (Figure 14).

Unique Case of An Extrahepatic Biliary Tree, Grade 2, Well-Differentiated Neuroendocrine Tumor

(Poster No. 30)

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A 29-year-old man presented with signs and symptoms of obstructive jaundice. Endoscopic cholangiopancreatography demonstrated a common bile duct stricture as well as a mass that appeared to compress the duct. The mass was resected and histologic examination revealed a well-differentiated neuroendocrine tumor with round nuclei with granular chromatin, abundant eosinophilic granular cytoplasm, and a portion of the cells had intracytoplasmic inclusions. Immunohistochemical examination revealed positive staining with synaptophysin and chromogranin. The inclusion stained strongly positive for Cam 5.2. Additionally the tumor had some higher-grade features, including focal punctuate necrosis, a Ki-67 index of 3%, and perineural invasion. Well-differentiated neuroendocrine tumors of the extrahepatic biliary tree are very rare, with only 150 cases reported. It is unclear how many of these prior cases may have had higher-grade features, and there are no well-accepted guidelines on how to stage these tumors. To our knowledge, this is the first reported case of a grade 2 extrabiliary neuroendocrine tumor in a patient with multiple endocrine neoplasia type 1 (Figure 15). The above authors are employees of the US Federal Government and the US Army and Air Force. The opinion(s) or assertion(s) contained herein are the private views of the authors and do not reflect the official policy or position of Brooke Army Medical Center, the US Army Medical Department, the US Army Office of the Surgeon General, the Department of the Army, Department of Defense, or the US government.

Diagnosis of Hepatocellular Adenomas on Biopsy: A Clinicoangiopathologic Experience in a Single US-Based Institution

(Poster No. 31)

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Context: Hepatocellular adenomas (HCAs) have recently been subclassified according to molecular analyses yielding diagnostic categories that can be assessed by immunostaining of tissue samples: inflammatory HCA (iHCA), confirmed by C-reactive protein (CRP) expression; HNF-1α-inactivated HCA (hHCA), confirmed by loss of liver fatty acid-binding protein (LFABP); and β-catenin mutated HCA (β-HCA) confirmed by nuclear β-catenin and increased glutamine synthetase (GS) expression. Definitive diagnosis on biopsies is becoming imperative because these subtypes have prognostic and management implications. We reviewed the epidemiologic and radiologic characteristics of biopsy-proven HCAs and analyzed the histopathologic features encountered.

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Design: We retrieved 16 in-house cases and 15 consult cases (all from New York state) diagnosed as HCA on biopsy from 2009 to 2013 from our institution’s database. Prebiopsy computed tomography/magnetic resonance imaging with contrast studies using Eovist and extracellular contrast media (ECCM) were obtained for the in-house cases. The radiologic, epidemiologic, and pathologic characteristics including immunohistochemistry were studied.

Results: Results are shown in the Table.

Conclusions: Our institution shows a marked predominance of iHCA (≈75% of classifiable HCAs), which may reflect this subtype’s association with metabolic syndrome and, therefore, be related to epidemic obesity in the United States. Radiologic features were not
Risk Stratification for Cancer in Barrett Esophagus by CDX2, c-Myc, p120ctn, and JAG1 Immunohistochemistry

Sara E. Ohanessian, MD1; Diphti M. Karamchandani, MD1; Arthur S. Berg, PhD2; Douglas B. Stairs, PhD1; Departments of 1Pathology and 2Public Health Sciences, Pennsylvania State University Milton S. Hershey Medical Center, Hershey, Pa.

Context: Barrett esophagus (BE) exhibits the potential to progress to esophageal adenocarcinoma (EAC) via an unpredictable metaplasia-dysplasia-carcinoma sequence. Currently, histologic assessment of BE biopsies remains the gold standard for surveillance. Detection of nondysplastic BE (BE-NDB) or low-grade dysplasia (LGD) necessitates repeated endoscopy because they pose a lower-risk of progression, whereas high-grade dysplasia (HGD) and EAC may warrant endoscopic ablative techniques and/or esophagectomy. Because histologic examination suffers from considerable interobserver variability, new diagnostic biomarkers are required to more accurately stratify cancer risk.

Design: One hundred and one samples of BE (25 BE-ND, 23 LGD, 24 HGD, and 29 EAC) were analyzed. Four putative protein biomarkers (c-Myc, CDX2, p120ctn, and JAG1) were examined via immunohistochemistry and semiquantitative scoring to assess differential expression.

Results: Nuclear expression of c-Myc and JAG1 were significantly stronger in HGD and EAC samples, compared with BE-ND and LGD (P < .001). p120ctn membrane and nuclear CDX2 expression were significantly decreased in HGD and EAC, compared with BE-ND and LGD (P < .001). The ROC area under the curve was 0.882, indicating that c-Myc, CDX2, p120ctn, and JAG1 are good indicators for risk stratification.

Conclusions: In an attempt to optimize proper treatment decisions for these patients, we show that the immunohistochemical expression of 4 genes (c-Myc, CDX2, p120ctn, and JAG1) can stratify patients into lower and higher risk status. These genes may be used as an adjunct to histologic assessment in challenging cases.

Metastatic Adenosquamous Carcinoma of the Esophagus: An Unusual Dimorphic Presentation of Tumor at a Metastatic Site

Nour Yadak, MD (nanamyadak@yahoo.com); Raghavendra Pillappa, MD; Nadeem Zafar, MD. Department of Pathology, University of Tennessee Health Science Centre, Memphis, Tenn.

Adenosquamous carcinoma of the esophagus is a rare variant of esophageal cancer with a highly aggressive biologic behavior, including frequent metastasis and poor survival. A 54-year-old man with a long-standing history of gastroesophageal reflux disease underwent distal esophagectomy for a suspected malignant stricture in the distal esophagus. At microscopy, a well-differentiated, invasive adenoscarci-

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Progression of Signet-Ring Cell Carcinoma In Situ of the Esophagus to Adenocarcinoma With Signet-Ring Cell Features in a Background of Barrett Metaplasia

(Poster No. 36)

Jessica P. Tracht, MD (ptracht@ubmc.edu); Dejun Shen, MD, PhD, Department of Pathology, University of Alabama at Birmingham, Ala.

Signet-ring cell (SRC) carcinoma in situ in the gastrointestinal tract is a rare and poorly defined entity with little pathologic documentation reporting progression to SRC carcinoma. Invasive esophageal adenocarcinoma with SRC features is associated with a diffuse growth pattern, advanced stage at presentation, and worsened prognosis. We present a case documenting the progression from adenocarcinoma in situ with SRC features in a background of Barrett metaplasia to invasive esophageal adenocarcinoma with SRC features in an obese 63-year-old, white man. The patient presented with an esophageal nodule diagnosed endoscopically as T1N0. Endoscopic mucosal resection was performed, revealing adenocarcinoma in situ with SRC features arising in metaplastic intestinal epithelium. Immunostain for type IV collagen was positive around the cancerous glands (Figure 16), supporting a diagnosis of carcinoma in situ with SRC features. A biopsy of a recurrent nodule during surveillance revealed adenocarcinoma in situ with SRC features, extending under the surface of the squamous epithelium. Because of this finding, the patient underwent another endoscopic resection with pathology revealing invasive, well-differentiated adenocarcinoma with SRC features. Rather than a diffuse growth pattern, the invasive adenocarcinoma with SRC features appeared well-differentiated and maintained glandular architecture, although the cancerous glands lacked surrounding type IV collagen by immunostaining. It is unclear whether this may represent signet ring carcinoma in situ in transition to invasive signet-ring cell carcinoma. This case represents a rare finding of signet-ring cell carcinoma in situ of the esophagus that progressed to invasive adenocarcinoma.

Gastroenteric Biopsies in Patients With Rare Immunodeficiency Syndromes: Two Case Reports and Literature Review

(Poster No. 37)

Yanli Ding, PhD, MD (yanli.ding@bmc.org); Michael O'Brien, MD; Qing Zhao, MD, Department of Pathology and Laboratory Medicine, Boston University, Boston, Mass.

Common variable immunodeficiency and immunoglobulin (Ig) A immunodeficiency are rare primary immunoglobulin deficiency in adults. Patients often present with chronic diarrhea, malabsorption, and persistent infections. Biopsies are the gold standard diagnostic means. We present gastroenteric biopsies from 2 patients, a 37-year-old Hispanic woman and a 28-year-old white man, both resembling Crohn disease and/or celiac disease clinically. The pronounced histologic findings in both patients were in the duodenum and included villous blunting and shortening; active neutrophilic duodenitis with chronic inflammation but no or few plasma cells in the lamina propria, and intraepithelial lymphocytes. The biopsy fragments were diffusely involved. No granuloma was seen in either patient. The differential diagnoses included Crohn disease, celiac disease, immunoglobulin deficiency syndrome, and autoimmune gastroenteropathy. Fecality of plasma cells in the lamina propria is a pathognomonic finding in patients with primary immunodeficiency syndrome. There is no skip lesion or focal enhanced gastroenteritis to suggest Crohn disease; no goblet cell depletion, significant intraepithelial lymphocytes, or severe inflammation in favoring autoimmune disease; and severe active inflammation with crypt abscesses are rarely seen in patients with celiac disease. Clinical serology tests showed significantly reduced immunoglobulin levels (IgA, 32 mg/dL; IgG, 494 mg/dL; IgM, <5 mg/dL) in one patient. The other patient had an IgA level of 9 mg/dL (other immunoglobulins not tested). Both patients were treated with antibiotics and symptomatically, and symptoms were significantly improved. Primary immunodeficiency syndrome is rare. Adding this entity into the differential diagnoses when considering Crohn, celiac, and autoimmune diseases is important. Serology tests can be used to confirm pathologic impression. Effective treatment includes antibiotics and immunoglobulin replacement.

An Unusual Case of Exclusive, Early Liver Metastasis From Adenoid Cystic Carcinoma of the Parotid Gland

(Poster No. 38)

Abul Ala Syed Rifat Mannan, MD1 (amannan@chpnet.org); Beverly Wang, MD2; Neil D. Theise, MD2; Songyang Yuan, MD, PhD2; Department of Pathology, St Luke's-Roosevelt Hospital Center, New York, NY; 2Department of Pathology, Beth Israel Medical Center, New York, NY.

Liver is an unusual metastatic site for adenoid cystic carcinoma (ACC) of the salivary gland. Most liver metastases originate from nonparotid ACCs. We report a rare case of isolated, early liver metastasis of ACC from the parotid gland. A 61-year-old woman presented with a right parotid mass for 6 months. A fine-needle aspiration biopsy was reported as a malignant salivary gland neoplasm. Right total parotidectomy with right neck dissection was performed. Macroscopy revealed a 3.2 × 1.9 × 1.4-cm, ill-defined, gray-white mass abutting the surface of the parotid gland. On microscopy, the tumor was composed of basolaid cells arranged in solid, trabecular, and focal cribiform patterns (Figure 17, A). There were brisk mitotic activities but no necrosis. A diagnosis of high-grade adenoid cystic carcinoma (pT3N0Mx) was rendered. The patient was subsequently treated with external beam radiotherapy. Eleven months later, follow-up positron emission tomography/computed tomography scan revealed a 3.5 × 3.5-cm, hypodense nodule in the left hepatic lobe. There were no lesions elsewhere in the body. A resection of the left lower lobe was performed. Microscopy confirmed a metastatic ACC. However, the tumor cells were more well differentiated (Figure, B). Comparison of the morphology of primary tumor and immunoreactivity for CD117 (Figure, C) and DOG1 (Figure, D) helped in establishing the diagnosis. Exclusive early hepatic metastasis of ACC from the parotid gland is very unusual. Liver metastases are usually associated with local recurrence or metastases to other organs. The present case highlights the unpredictable biologic behavior of ACC.

Enteric Myopathy in a Patient With Long-Term Duchenne Disease

(Poster No. 39)

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The patient was a 30-year-old man with history of Duchenne muscular dystrophy, chronic constipation, and possible inflammatory bowel disease who ultimately succumbed to septic shock following multiple abdominal surgeries. An autopsy was requested to characterize...
the extent of his infection and to rule out the possibility of pulmonary embolism. In addition to the diffuse skeletal muscle atrophy and fatty replacement expected in Duchenne muscular dystrophy, Masson trichrome stains showed diffuse atrophy and fibrosis of all layers of the small and large intestine musculature that raised the consideration of a Duchenne-related enteric myopathy, an entity that has been previously described in a single case report. Immunohistochemical stains for neuron-specific enolase, S100, and CDK17 performed on sections of bowel confirmed the presence of normal nerves and ganglion cells, ruling out an enteric neuroopathy, and the normal distribution of lymphocytes seen on CD45 immunohistochemical stains argued against an autoimmune process. The presence of marked fibrosis and smooth muscle atrophy in the enteric muscularis propria is consistent with previously reported findings in patients with intestinal pseudo-obstruction associated with Duchenne muscular dystrophy. Mucosal findings were nonspecific and could be consistent with chronic injury because of chronic ischemia, drug effect, chronic pseudo-obstruction stemming from enteric myopathy, or inflammatory bowel disease. Given the relatively long life span of this particular patient, our findings may highlight the natural long-term course of this disease and illustrate future challenges to clinicians as the average life expectancy of patients with Duchenne increases.

**Epstein-Barr Virus (EBV) Hepatitis and Metastatic Seminoma: A Diagnostic Pitfall**

(Poster No. 40)

Richa Jain, MD

A 46-year-old man presented with a 4-week history of fever, jaundice, sore throat, neck mass, and transaminitis. Computed tomography of the abdomen–pelvis revealed a 6-cm para-aortic mass with periportal lymphadenopathy and 2 pulmonary nodules. Biopsies of liver and the para-aortic mass were performed. The liver biopsy revealed intense portal and lobular inflammation with few well-formed granulomas. There were atypical Reed-Sternberg–like lymphoid cells in the portal tract along with CD3- and CD5-positive T cells. Blood flow cytometry was within reference range. The para-aortic mass revealed a lymph node infiltrated by large atypical cells with clear cytoplasm, round nucleus, and prominent cell borders. The neoplastic cells in the lymph node were positive for CD117 and PLAP, consistent with metastatic seminoma. Atypical cells in the liver were nonreactive for CD117, PLAP, CD15, and CD30. EBV-Monospot, HIV, HAV, HBV, and HSV results were negative; CMV was positive. Serum EBV IgM and EBER on the liver biopsy were positive. Tumor-infiltrating lymphocytes in seminoma were EBER2, but tumor cells were negative. Therefore, a final diagnosis of EBV hepatitis and metastatic testicular seminoma to the para-aortic lymph node was rendered. Our patient underwent radical orchectomy and chemotherapy. There was spontaneous resolution of systemic symptoms and neck mass. Both EBV hepatitis and its association with testicular cancer are exceedingly rare, and EBV hepatitis is a diagnostic pitfall because the atypical lymphoid cells seen on liver biopsy can easily be mistaken for lymphoma in the absence of clinical information and serologic findings.

**Primary Cystic Leiomyosarcoma of Duodenojejunal Junction**

(Poster No. 41)

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Primary leiomyosarcoma of the gastrointestinal tract is considered rare in the post–gastrointestinal stromal tumor (GIST) era. We report a case of a 54-year-old man presenting with a 1.7-cm, submucosal, partially cystic mass (Figure 18, A) causing intestinal obstruction of the duodenojejunal junction at the ligament of Treitz. Microscopically, the wall of the cyst was lined by interlacing fascicles of epithelioid to spindle cells having eosinophilic cytoplasm, cigar-shaped nuclei with moderate atypia (Figure, B), and a mitotic rate up to 5 high-power fields (Figure, C). Its submucosal location, histologic features, and muscular differentiation and given its immunoreactivity with both smooth muscle actin and desmin (Figure, D) and negative staining for GIST markers (CD117, DOG1, and CD34), neural marker S100, and vascular marker CD34, confirmed the diagnosis of a leiomyosarcoma. This tumor was somewhat peculiar given its anatomic location, size, and partially cystic nature. It is important to differentiate leiomyosarcoma in this setting from the more-common GIST because specific chemotherapy options are available for the latter. Despite the usual aggressive behavior and overall poor prognosis expected for an intestinal leiomyosarcoma, an excellent prognosis is expected for this patient given a relatively early detection (possibly attributable to its special anatomic location) and complete surgical resection without clinically detectable metastatic disease.

**Hyalinizing Cholecystitis With Features of IgG4-Related Disease: Coincidence or an Unrecognized Association?**

(Poster No. 42)

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Hyalinizing cholecystitis (HC), a recently described subtype of chronic cholecystitis, is characterized by dense, paucicellular to acellular, hyalinizing mural sclerosis. The lesion is rare, occurring in approximately 1.6% of cholecystectomy specimens. Immunoglobulin G4 (IgG4)-associated cholecystitis, a lesion in the spectrum of IgG4-related disease (IgG4-RD), is also a newly described variant of cholecystitis characterized by mainly extramural, lymphoplasmacytic inflammation; lymphoid follicles; storiform fibrosis; phlebitis; and
increased tissue IgG4+ plasma cells. Herein, we describe a case of a 76-year-old, asymptomatic, white man with a porcelain gallbladder discovered on ultrasound. The cholecystectomy specimen revealed characteristic features of hyalinizing cholecystitis with the additional aforementioned histopathologic features of IgG4-associated cholecystitis, including elevated IgG4 plasma cells (up to 30–50 per high-power field). Our patient also had a significantly elevated serum IgG4 level. To our knowledge, this association of HC with IgG4-RD has not yet been described in literature. Although it is difficult to draw any strong conclusions, our case suggests that some cases of HC may be the result of IgG4-RD. Moreover, because gallbladders are common specimens in surgical pathology laboratory, recognizing mural fibrosis of any extent accompanied by robust lymphoplasmacytic inflammation may serve as an important sentinel finding for patients at risk of developing systemic IgG4-RD (Figure 19).

Erdheim-Chester Disease Discovered as an Incidental Finding in Explanted Liver of a Patient With Hepatitis C Cirrhosis

(Poster No. 43)
Xiaoyan Liao, MD, PhD (xliao@ucsd.edu); Grace Y. Lin, MD, PhD. Department of Pathology, University of California, San Diego, La Jolla, Calif.

We report a case of Erdheim–Chester disease discovered incidentally in a 65-year-old man with end-stage liver disease secondary to hepatitis C cirrhosis requiring liver transplant. Our patient was first diagnosed with hepatitis C in 1993 and with cirrhosis in 2002. He was doing well until 2010 when he presented with ascites requiring frequent surgical intervention for paracentesis. Histologic examination of the explanted liver confirmed chronic hepatitis with bridging necrosis and advanced fibrosis bordering on cirrhosis. In addition, there were prominent foamy histiocytes on the capsular surface and in some portal areas associated with fibrosis. By immunohistochemical staining, those foamy histiocytes were strongly positive for CD68 and factor XIIIa but negative for CD1a and S100 (Figure 20). Mutations were discovered in the PDGFCRA, PTEN, and HNF1A genes. We noted that this patient also had symptoms of paraproteinemia with pancytopenia, and a bone marrow biopsy in 2012 demonstrated sheets of similar histiocytes that are rarely positive for factor XIIIa. Of interest, this patient’s magnetic resonance imaging and positron emission tomography scans showed increased heterogenous uptake in bilateral humeral and femoral diaphyses, which could be the skeletal manifestation of the same disease process. A diagnosis of Erdheim–Chester disease was thus rendered, with at least liver and bone marrow involvement. Erdheim-Chester disease is a very rare form of xanthogranulomatous, non-Langerhans cell systemic histiocytosis of unknown etiology that typically affects 50- to 70-year-old adults. Manifestations in skeletal and extraskeletal organs have been reported. This case highlights the importance of histologic examination with correlation of imaging and clinical presentations to identify this rare unique disease.

Cytokeratin (CK) Changes Induced by p120-catenin (p120ctn) Loss and Epidermal Growth Factor Receptor Overexpression in Esophageal Squamous Cell Carcinoma

(Poster No. 44)
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Context: Esophageal squamous cell carcinoma (ESCC) is a highly aggressive malignancy and its molecular pathogenesis is not well known because of the lack of models to study it. No comprehensive study has been done on keratin changes in ESCC. Epidermal growth factor receptor (EGFR) is commonly overexpressed and p120ctn down-regulated in ESCC. This study aims to investigate keratin changes induced by p120ctn down-regulation and EGFR overexpression in a 3-dimensional organotypic tissue culture system (OTC) and human ESCC.

Design: The OTC control samples and those with both p120ctn down-regulation and EGFR overexpression (PE) were obtained. Keratins were studied by immunohistochemistry (IHC) in 5 control and PE OTC samples, 10 human normal esophageal, and 24 ESCC specimens. Morphology (hematoxylin-eosin) was analyzed using ImageJ, and proliferation was quantified by Ki-67 immunohistochemistry (IHC).

Results: EGFR was overexpressed in 83% of ESCC samples, and p120ctn was down-regulated in 67%. The intersection of those genes (p120ctn down-regulation and EGFR overexpression) occurs in 63% of ESCCs. The IHC studies of keratin expression in human specimens showed that ESCCs retain K1 and K5, gain K8, and lose K4, K10, and K15. In our OTC system, PE samples showed significantly increased cellularity, nuclear size, and proliferation (all P < .05). Interestingly, they contained apparently transformed epithelium resulting in cellular invasion into the matrix (Figure 21). The IHC studies demonstrated similar keratin patterns between normal human esophagus and OTC controls and also between human ESCC and OTC PE samples.

Conclusions: The ESCCs retain K1 and K5, gain K8, and lose K4, K10, and K15. Our genetically modified OTC PE epithelium resembles human ESCC with similar morphologic changes and keratin patterns.

Colonic Malakoplakia Presenting as Lymphoma

(Poster No. 45)
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Malakoplakia is a rare, chronic, inflammatory condition characterized by the presence of aggregates of histiocytes known as von Hansemann histiocytes that contain intracytoplasmic targetoid bodies known as Michaelis-Gutmann bodies (MGB). Although originally and most commonly described in the genitourinary tract, in the past several years, malakoplakia has been described in several organs with increasing frequency, including colon, stomach, appendix, and prostate. The etiology of malakoplakia is poorly understood, but a deficient cellular immunity and phagocytic activity associated with infection or immunosuppression has been thought to be the underlying mechanism. Ultrastructurally, MGB have been shown to consist of partially digested and degenerated bacteria. We received 3 unusual specimens submitted as polyps on different occasions. All 3 specimens were predominantly lymphocytic tissue and thought to be suspicious for
lymphoma. On careful examination, we identified von Hansemann histiocytes and MGB within the lymphoid aggregates (Figure 22). Special stains like von Kossa, iron, and Fite highlighted abundant MGB to confirm our impression of malakoplakia. We would like to present these cases to emphasize that malakoplakia can be easily missed by pathologists if they are unaware of its presentation as polyps or raised lesions within the gastrointestinal tract because of its subtle presentation. These patients need to be diagnosed and thoroughly worked up to rule out any underlying infections or causes of immunodeficiency and to be treated by appropriate antibiotics to prevent the progression of the disease.

### Cytomegalovirus-Associated Pseudotumor Simulating Gastric Malignancy in a Patient With HIV-Negative, Nontransplant Recipient

**Poster No. 46**

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Although gastrointestinal cytomegalovirus (CMV) infection is more prevalent in immunocompromised patients, localization to the stomach, in particular the gastric antrum, is rare. To our knowledge, all cases of CMV-associated pseudotumors of the stomach reported in the literature were observed in patients with HIV or transplant recipients. We recently encountered an unusual case of a CMV-associated antral mass that mimicked a gastric malignancy by ultrasound and endoscopy in an HIV-negative, nontransplant recipient patient. A 72-year-old woman with a history of end-stage renal disease requiring dialysis and long-term treatment with prednisone and colchicine for gout presented with a recurrent upper gastrointestinal bleed requiring multiple blood transfusions. An upper endoscopy demonstrated an abnormal antral mass with a central depression suggestive of ulceration. Biopsies at that time were nondiagnostic. Subsequently, the patient underwent a subtotal gastrectomy. Histologic sections showed chronic active gastritis with a large area of ulceration, granulation tissue, and focal necrosis. Numerous CMV inclusions were seen on hematoxylin-eosin and immunohistochemistry. Interestingly, sodium polystyrene sulfonate crystals were identified within the granulation tissue. Subsequently, it was verified that the patient had been treated with Kayexalate in the recent past. Another interesting incidental finding in this case was the presence of foci of colchicine-induced mitotic arrest in the adjacent gastric mucosa. Our case demonstrates that CMV-associated pseudotumors should be considered in the differential diagnosis of all immunocompromised patients.

### Review of Radiologic and Histopathologic Features of Hepatic Echinococcal Cysts: Retrospective Study of 10 Years in an Urban Tertiary-Care Center

**Poster No. 47**

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**Context:** Echinococcal cyst (EC) or hydatid cyst is a parasitic infection caused by larval stage of the tapeworm *Echinococcus granulosus*. The infection is acquired by ingestion of parasitic eggs. This is a rare disease in developed countries. Although the diagnosis is made from a combination of clinical and radiologic presentations, the histopathology is not always representative because of chronic changes, such as fibrosis and calcification.

**Design:** From January 2004 to February 2014, all cases of EC were retrieved from our database. We reviewed the epidemiology, clinical presentation, and radiologic and histologic features. The slides were reviewed, and features were noted in an attempt to correlate helpful features that aid in the diagnosis.

**Results:** Eight cases of hepatic EC were identified. The age range was 41 to 77 years. Male to female ratio was 1:1. Six of 8 patients were Middle Eastern. Clinical features included abdominal pain (7/8), nausea and low appetite (3/8), and sepsis because of ruptured EC (2/8). The cyst size ranged from 3.4 to 13 cm. Histologic features noted were scolices and hooklet (4/8), laminated membranous structure with focal calcification (6/8), fibrotic and calcified cyst wall (2/8), and necrosis (3/8). All cases showed nonspecific inflammatory changes in adjacent hepatic tissue. Figure 23 shows the cyst wall with scolices.

**Conclusions:** Although a rare diagnosis, EC should be considered in the differential diagnosis of hepatic cysts if suspected clinically and radiologically, especially in the Middle Eastern population.

### Gastritis Cystica Profunda Arising Within Gastric Heterotopia in the Rectum: A Case Report of a Rare Condition Involving a Novel Location

**Poster No. 48**

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Gastritis cystica profunda (GCP) is a rare condition exhibiting cystic dilation and submucosal extension of gastric glands. It results from damage to the muscularis mucosa by factors such as chronic inflammation, ischemia, and previous surgery or biopsy. The compromised integrity of the muscularis mucosa allows these commonly hyperplastic and highly proliferative glands to migrate downward. A synonymous condition with displaced crypts occurs in the colon, termed...
Intraductal Tubulopapillary Neoplasm of Pancreas: A Rare Case Report With Initial Misdiagnosis on Fine-Needle Aspiration

(Poster No. 51)

Victoria B. Parker, DO (victoria.parker@hhchealth.org); Manoj Gadara, MD; Ana Yuil-Valdes, MD; Saievero Ligato, MD. Department of Pathology, Hartford Hospital, Hartford, Conn.

Intraductal tubulopapillary neoplasm of the pancreas (ITPN) represents less than 1% of exocrine pancreatic neoplasms, and the criteria for its diagnosis has only recently been established. Only a few studies have reported the cytologic findings for this neoplasm on fine-needle aspiration (FNA). We present a case that was initially misdiagnosed on ultrasound-guided, FNA as an intraductal papillary mucinous neoplasm and diagnosed on resection as ITPN. Here, we review the cytologic features of this neoplasm and highlight the diagnostic pitfalls during cytologic examination on endoscopic ultrasound FNA. The cytoarchitectural features identified in our case included a hypercellular aspirate with many branching, staghorn, tubular, and focally papillary clusters in a background of discohesive cells (Figure 24, a). High-power magnification showed uniform cells

demonstrating mild to moderate cytologic atypia, absence of intracellular mucin, and rare intracellular pseudoinclusions. Based on the presence of scant extracellular mucin (Figure, b) and papillary clusters, a diagnosis of intraductal papillary mucinous neoplasm was rendered; however, on histologic exam, an ITPN was diagnosed (Figure, c and d).

In retrospective review, the main cytologic features helpful for a correct diagnosis of ITPN are (in addition to already established criteria and the radiologic findings): (1) absence of intracytoplasmic mucin in the constituent cells, and (2) correct interpretation of the scant extracellular mucin as an expression of gastrointestinal contaminant and not as a constituent part of this neoplasm.

Intraductal Tubulopapillary Neoplasm of Pancreas: A Rare Case Report With Initial Misdiagnosis on Fine-Needle Aspiration

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(Poster No. 51)

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Intraductal tubulopapillary neoplasm of the pancreas (ITPN) represents less than 1% of exocrine pancreatic neoplasms, and the criteria for its diagnosis has only recently been established. Only a few studies have reported the cytologic findings for this neoplasm on fine-needle aspiration (FNA). We present a case that was initially misdiagnosed on ultrasound-guided, FNA as an intraductal papillary mucinous neoplasm and diagnosed on resection as ITPN. Here, we review the cytologic features of this neoplasm and highlight the diagnostic pitfalls during cytologic examination on endoscopic ultrasound FNA. The cytoarchitectural features identified in our case included a hypercellular aspirate with many branching, staghorn, tubular, and focally papillary clusters in a background of discohesive cells (Figure 24, a). High-power magnification showed uniform cells

demonstrating mild to moderate cytologic atypia, absence of intracellular mucin, and rare intracellular pseudoinclusions. Based on the presence of scant extracellular mucin (Figure, b) and papillary clusters, a diagnosis of intraductal papillary mucinous neoplasm was rendered; however, on histologic exam, an ITPN was diagnosed (Figure, c and d).

In retrospective review, the main cytologic features helpful for a correct diagnosis of ITPN are (in addition to already established criteria and the radiologic findings): (1) absence of intracytoplasmic mucin in the constituent cells, and (2) correct interpretation of the scant extracellular mucin as an expression of gastrointestinal contaminant and not as a constituent part of this neoplasm.

Intraductal Tubulopapillary Neoplasm of Pancreas: A Rare Case Report With Initial Misdiagnosis on Fine-Needle Aspiration

(Poster No. 51)

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Extramedullary Hematopoiesis as a Cause of Abnormal Liver Function Test in Posttransplant Liver

(Diviya Sharma, MD1 (sharmadi@ucmail.uc.edu); Stephen Zucker, MD; Shimul Shah, MD; Nadeem Anwar, MD; Baojin Fu, MD; Jiang Wang, MD, PhD.1 Departments of 1Pathology and Laboratory Medicine; 2Division of Digestive Diseases, Internal Medicine; and 3Division of Transplantation, Surgery, University of Cincinnati Medical Center, Cincinnati, Ohio.

Advances in surgical techniques and postoperative care have significantly improved patient outcomes after liver transplantation. Although posttransplant complications are markedly reduced, it remains an important factor in morbidity and mortality. Any dramatic or persistent increase in liver function tests (LFTs) after transplant mandates a series of diagnostic tests to evaluate the possibility of complications, such as rejection, ischemic injury, and infections. We report a case of a 68-year-old man who underwent liver transplant for alcoholic cirrhosis and had persistent elevation of liver enzymes starting 4 months posttransplant. Acute cellular rejection with progressive fibrosis was attributed as the cause of enzyme elevation at that time, and the patient was managed appropriately. At 8 months, however, his liver enzymes again started rising, and biopsy of the liver showed no evidence of acute cellular rejection but the presence of extramedullary hematopoiesis (EMH) (see Table). The histologic features of liver EMH include focal sinusoidal congestion, increased cellularity in sinusoidal spaces, and the finding of immature precursor cells and large atypical megakaryocytes (Figure 25, A and B). The liver enzymes trended down with supportive therapy. Such EMH in an allograft is a rare occurrence. Its pathophysiology remains unclear and could be attributed to expansion of quiescent liver-based hematopoietic progenitor cells in response to liver injury or because of hematopoietic microchimerism of donor origin. It is important to consider this entity as a cause of elevated liver enzymes after transplant in the absence of cellular rejection or other etiologies. The treatment is only supportive, and the liver functions stabilized spontaneously without intervention in this case.

Liver Function Test Trends Between 4 and 8 Months Posttransplant

<table>
<thead>
<tr>
<th>Liver Function Tests</th>
<th>4–5 mo</th>
<th>6–7 mo</th>
<th>8 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaline phosphatase</td>
<td>1301</td>
<td>305</td>
<td>984</td>
</tr>
<tr>
<td>Aspartate amino transferase</td>
<td>232</td>
<td>113</td>
<td>1398</td>
</tr>
<tr>
<td>Alanine transaminase</td>
<td>193</td>
<td>321</td>
<td>2570</td>
</tr>
<tr>
<td>Total protein</td>
<td>2.3</td>
<td>3.3</td>
<td>3.9</td>
</tr>
<tr>
<td>Albumin</td>
<td>5.1</td>
<td>6.2</td>
<td>6.0</td>
</tr>
<tr>
<td>Bilirubin total</td>
<td>2.4</td>
<td>0.6</td>
<td>0.7</td>
</tr>
<tr>
<td>Liver biopsy</td>
<td>Acute cellular rejection</td>
<td>Stage 2 Extramedullary hematopoiesis with no evidence of acute cellular rejection</td>
<td></td>
</tr>
<tr>
<td></td>
<td>p62</td>
<td>0.64</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Peculiar Filamentous Intranuclear Inclusion in Rectal Leiomyoma

(ABDUL ALA SYED RIFAT MANNAN, MD1 (amannan@chpnet.org); Beverly Wang, MD; Violette Ghali, MD; Jonathan Sarlin, MD; Jason Reidy, MS.2 1Department of Pathology, St Luke’s-Roosevelt Hospital Center, New York, NY; 2Department of Pathology, Beth Israel Medical Center, New York, NY.

Intranuclear inclusion is an enigmatic cytologic phenomenon, which appears as an optically clear nucleus on hematoxylin-eosin–stained sections. It can either be a true inclusion, or a pseudoinclusion. True inclusions result from intranuclear accumulation of viral particles, cytoplasmic materials, or nuclear laminas. Pseudoinclusions, on the other hand, represent invagination of cytoplasm into the nucleus. Here, we present a case of rectal leiomyoma with unusual intranuclear inclusions. A 56-year-old man with no significant past medical history presented to the gastroenterology clinic for cancer screening. A colonoscopy was performed, which revealed a 3-mm sessile rectal polyp that was biopsied. Microscopic examination revealed a submucosal leiomyoma, confirmed by immunoreactivity for caldesmon. A striking finding was the presence of optically clear nuclei in many of the tumor cells. Deparaffinized tissue was submitted for electron microscopic evaluation following standard procedure. Ultrastructural examination revealed electron-dense, intranuclear inclusions within the tumor cells, with peripheral displacement of the nuclear chromatin (Figure 26). These inclusions were composed of 8 to 10-nm-diameter fibrillar filamentous structures, which morphologically resembled intermediate filaments. The inclusions were devoid of any cytoplasmic organelle, indicative of pseudoinclusion. To our knowledge, this case represents the first report of the demonstration of true intranuclear inclusion in a leiomyoma, with ultrastructural resemblance to intermediate filaments. It highlights the utility of electron microscopy in differentiating true intranuclear inclusions from nuclear pseudoinclusions.

Expression of p62 and Ubiquitin in Liver Neoplastic and Nonneoplastic Disease: Correlation Between Visual and Automated Image Analytic Quantitation, Prognosis, and Outcome

(MARYAM ABDELGHANI, MD (maryam.abdelghani@emory.edu); Cynthia Cohen, MD; Charles K. Kovach, MD; Alton B. Farris, MD. Department of Pathology, Emory University Hospital, Atlanta, Ga.

Context: p62 and ubiquitin are associated with hepatocellular injury. We examined their expression in liver disease using immunohistochemistry, compared visual versus image analytic quantitation methods of immunostains, and examined correlation with outcome in hepatocellular carcinoma.

<table>
<thead>
<tr>
<th>Stain/Localization</th>
<th>Concordance</th>
<th>Correlation</th>
<th>Fisher</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>p62/cytoplasmic</td>
<td>87</td>
<td>0.76</td>
<td>&lt;.001</td>
<td>.57</td>
</tr>
<tr>
<td>p62/nuclear</td>
<td>66</td>
<td>0.33</td>
<td>.31</td>
<td>.26</td>
</tr>
<tr>
<td>Ubiquitin/nuclear</td>
<td>76</td>
<td>0.64</td>
<td>&lt;.001</td>
<td>.80</td>
</tr>
<tr>
<td>Ubiquitin/cytoplasm</td>
<td>68</td>
<td>0.29</td>
<td>&lt;.001</td>
<td>.23</td>
</tr>
</tbody>
</table>

* Linear regression r value, P < .001.
Intraductal Oncocytic Papillary Neoplasm of Pancreas: Report of a Case Associated With Multifocal, Clear Cell Renal Cell Carcinoma and Oncytoma

(Poster No. 55)

Tricia A. Murdock, MD (tricia.murdock@vtmednet.org); Maryam Zenali, MD. Department of Pathology, University of Vermont, Burlington, Vt.

Intraductal oncocytopapillary neoplasm (IOPN), a rare subtype of intraductal papillary mucinous neoplasm, was first described in a small case series in 1996. This tumor is typically composed of papillary projections with cuboidal cells and oncocytoplastic cytoplasm. The IOPNs generally have an indolent clinical course but can be associated with invasive foci and a more-aggressive prognosis. We present a case of a 77-year-old woman with a history of colon cancer, multifocal clear cell renal cell carcinoma of the right kidney, and oncocytoplasia of the left kidney. Upon surveillance for renal tumors, computed topography of the abdomen demonstrated abnormal soft tissue causing dilation of the pancreatic duct and ampulla. The patient underwent a Whipple procedure. Grossly, the tumor was tan-white and friable, encompassing 2.5 cm of the pancreatic duct (Figure 27, left, arrow at ampulla). It extended into the duodenal papilla with no definitive invasion. The entire pancreas and ampulla were submitted. Histologically, the tumor was a high-grade oncocytoplastic carcinoma, with a predominantly solid growth pattern, minor papillary components, and markedly pleomor- phic cells with medullary-like features (Figure, right, inset hematoxylin-eosin, original magnification ×20). Because of the history of colon and renal cell carcinomas, immunostaining performed proved the pancreatic tumor was an independent primary. This case illustrates a rare representation of the high-grade histologic spectrum of IOPN. To our knowledge, the association of this rare entity with clear cell and oncocytoplastic renal tumors has not been described. Whether they represent a spectrum of a syndromic process requires further investigation.

Can Esophageal Eosinophilia in Biopsies From Esophageal Strictures Predict the Diagnosis of Eosinophilic Esophagitis?

(Poster No. 56)

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Context: Eosinophilic esophagitis (EoE), gastroesophageal reflux disease (GERD), and proton-pump inhibitor-responsive eosinophilic esophagitis are the most common causes of isolated eosinophilic esophagitis (EE; ≥15 eosinophils/high-power field [eos/HPF]) on esophageal biopsy. Each may lead to stricture formation. We investigated whether EE in biopsies from esophageal strictures can predict the diagnosis of EoE.

Design: Two hundred forty-five cases with esophageal stricture biopsy were identified in our pathology database (January 1, 2005, to January 1, 2012). Nineteen of 245 (7.8%) stricture biopsy cases had 15 or more eos/HPF, 33 of 245 (13.5%) had 1 to 14 eos/HPF, and 193 of 245 (78.8%) had zero eosinophils. Seventy-one biopsies were studied: 52 that had any eosinophils on counting and 19 random biopsies from the remaining 193 with zero eosinophils. EE was defined as 15 or more eos/HPF. Histologic data were correlated with clinical and endoscopic findings. SPSS version 19 (IBM, Armonk, NY) was used for statistical analyses.

Results: Patients with 15 or more eos/HPF in stricture biopsies were (1) significantly more likely to have EoE, based on clinical and endoscopic findings, than GERD or other causes of stricture (P < .001; 15 of 19 patients [79%] with ≥15 eos/HPF); (2) significantly younger (48 years versus 63 years, P < .001); and (3) 5 times more likely to be males (95% confidence interval, 1.04–24.1) than patients with strictures caused by GERD or other conditions. The GERD-caused stricture was the most-common stricture in our study (40 of 71; 56.3%), and the prevalence of hiatal hernia was 68% to 71% across all groups.

Conclusions: Although our study is limited by the relatively few esophageal stricture biopsy cases with EE (≥15 eos/HPF) and warrants further studies, our data suggest that when EE in esophageal stricture biopsies, EoE is the most likely etiology.

Concurrent Occurrence of Microcystic Serous Cystadenoma and Intraductal Papillary Mucinous Neoplasm of Pancreas and Islet Cell Amyloidosis

(Poster No. 57)

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Microcystic serous cystadenomas (MSC) generally are solitary lesions. However, there have been reports associating serous cystadenomas with other pancreatic tumors. We report a case of a 75-year-old woman with history of type II diabetes who was found to have a cystic lesion in the tail of the pancreas. This asymptomatic patient was followed for 4 years with imaging studies. The last computed tomography scan showed increased size and morphologic changes of the mass. The Ca19-9 and CEA tumor markers were 71.7 U/mL and 2 ng/mL, respectively. Because of the high risk for malignancy, the patient underwent distal pancreatectomy with splenectomy. Grossly, the pancreas showed a 2.7 × 1.7 × 1.5-cm, white-tan, multicystic mass. Microscopically, there were multiple microcysts lined by a single layer of cuboidal cells with round, centrally located nuclei and clear cytoplasm with no atypia. Adjacent to this mass was a 1-cm cyst lined by columnar mucinous cells with elongated nuclei and foveolar appearance (Figure 28). An MSC and a branch-type intraductal papillary mucinous neoplasm (IPMN) with low-grade dysplasia, gastric-subtype, were diagnosed. Additionally, diffuse islet cell hyperplasia with amyloid deposition was identified. The amyloid showed apple-green birefringence on Congo red stain and was negative for amyloid A, k, l, and transthyretin, consistent with islet amyloid polypeptide. The case displays an unusual coexistence of MSC with branch-type gastric IPMN in the background pancreatic islet cell amyloidosis. The latter can be found in patients with type II diabetes. To our knowledge, there are only 2 previously reported cases of combined MCS and IPMNN in the literature.
Irisin: A Skeletal Muscle–Derived Factor With Tumor-Inhibitory Activity

Eva V. George, MD (evertes@ufl.edu); Chao Xie, BA; Hai Wang, MD; Lijun Yang, MD. Department of Pathology, University of Florida, Gainesville, Fla.

Context: Tumors rarely arise in, or metastasize to, skeletal muscle. However, the mechanisms underlying that phenomenon remain unclear. We propose that skeletal muscle secretes factors that inhibit tumor cell growth. Here, we focus on irisin, a recently discovered myokine released during exercise from skeletal muscle, which appears to protect against obesity-linked insulin resistance and to promote white-to-brown fat conversion. We hypothesize that irisin may also have antitumor activity. The observation that skeletal muscle is largely devoid of cancer and the link between exercise and decreased cancer incidence points toward irisin as a potential muscle-derived antitumor candidate. We hypothesize that irisin modifies tumor cell metabolism, decreasing glycolysis and increasing oxidative phosphorylation, thereby counteracting the Warburg effect.

Design: We sought to determine whether irisin inhibits tumor cell proliferation and to define the molecular pathways mediating its activity. Hepatocellular carcinoma cells (Hep-G2) and pancreatic adenocarcinoma cells (Panc-1) were grown in vitro and treated with or without irisin. Proliferation was measured using the MTT assay. Genes of interest were quantified by reverse transcription-polymerase chain reaction in tumor cells with and without treatment with irisin.

Results: Irisin, even at low concentrations, significantly inhibited tumor cell proliferation. Irisin appears to inhibit tumor cell growth by altering the transcription of hypoxia inducible factor 1α (HIF1A) and vascular endothelial growth factor A (VEGFA).

Conclusions: The results from this study suggest that irisin may have a role in the physiologic inhibition of tumor growth within the skeletal muscle microenvironment and, importantly, may represent a novel therapeutic strategy.

Neuromuscular and Vascular Hamartoma

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Neuromuscular and vascular hamartoma (NMVH) is very rare with only 20 cases reported in the English literature since its initial characterization by Fernando and McGovern in 1982. Whether this lesion is truly hamartomatous or represents a burnt-out phase of varying chronic pathologies is debatable. Examples of NMVH have been reported in the setting of diaphragm disease, Crohn disease, radiation, and ischemia. Herein, we present the case of a 73-year-old woman with partial small-bowel obstruction and a past surgical history notable for cholecystectomy and abdominal hysterectomy. A computed tomography scan revealed an ill-defined mass with the same density as muscle extending to the mesentery, generating the differential of lymphoma versus metastatic disease. Upon laparotomy, a 2.5-cm, constrictive, mural, and mesenteric mass was notable. The more-proximal bowel was dilated, and there were dense, serosal adhesions. Grossly, the transmural lesion had a tan-yellow cobweblike cut surface. Histologically, lesional tissue contained fascicles of smooth muscle, irregularly placed nerve bundles and thick-walled, elastic vessels haphazardly arranged within hypocellular fibrous bands and entrapped fat, consistent with NMVH. Yet, in contrast to findings commonly reported, the mucosa was not significantly altered. No stigmata of Crohn disease were observed, and the patient’s history was negative for chronic nonsteroidal antiinflammatory use, radiation, and hyperlipidemia. This case of NMVH is presented as a reminder of benign mass-forming lesions causing small-bowel obstruction and raises the potential chronic effect of abdominal serositis and adhesions as a plausible risk factor for the development of NMVH (Figure 29).

Versican in Colonic Adenocarcinoma: A Late Event in Cancer Progression

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Context: Tumor stroma has an important role in the progression and metastasis of colon cancer. Versican, a hyalectan regulator of cell adhesion, has been implicated in the development and progression of human cancers. The aim of our study was to describe the epithelial and stromal expression status of versican in nonneoplastic colonic mucosa, colonic adenoma, and colonic adenocarcinoma.

Design: A tissue microarray, containing 106 cases of colonic adenocarcinoma, 30 cases of adenoma, and 8 cases of nonneoplastic colonic mucosa, was used for this study. The epithelial and stromal versican expressions were assessed using immunohistochemistry. The data were statistically evaluated using the χ² test.

Results: Versican protein was overexpressed in the stroma adjacent to the infiltrating, malignant, colonic adenocarcinoma glands but not in the stroma surrounding the adenoma glands (P = .02) or the normal colonocytes (P = .05). We found no statistically significant differences in versican epithelial expression between nonneoplastic colonic mucosa, adenoma, and colonic adenocarcinoma (P > .05).

Conclusions: The data from the current study demonstrate elevated stromal expression of versican as a late event in the progression of colonic adenocarcinoma and could be further evaluated as a potential therapeutic target.
A Comparison of the World Health Organization (WHO) 2004 and 2010 Classification Systems in Pancreatic Neuroendocrine Tumors (PNETs)

(Poster No. 61)

James Casey, MD1 (james.casey@jeffersonhospital.org); Aakanksha Asija, MD2; Ashwin Sama, MD2; Jocelyn Andre Sendecky, MSPH, BS2; Nancy Lewis, MD3; Harish Laviu, MD3; Jordan Winter, MD3; Jonathan Brody, PhD4; Edith Mitchell, MD4; Charles Yeo, MD5; Anthony Prestipino, MD1; Madhavan Pillai, MD. Departments of 1Pathology, 2Medical Oncology, 3Pharmacology & Experimental Therapeutics, 4Kimmel Cancer Center, and 5Surgery, Thomas Jefferson University, Philadelphia, Pa.

Context: PNETs are rare tumors with multiple classification systems. We compared the WHO 2004 and 2010 classification systems in predicting mortality, metastasis, and associations with mortality.

Design: Pathologic parameters were reviewed, including nuclear grade, tumor size, mitotic count, perineural/lymphovascular invasion, Ki-67 positivity, and the presence of metastasis. These parameters were used to classify all tumors in both the WHO 2004 and WHO 2010 classification systems. The relationship between the WHO 2004 and WHO 2010 grading was investigated using an exact χ2 test. The WHO grade categorization was next explored by vital status to determine whether there was a difference in survival and metastasis by grading system.

Results: The WHO grades were significantly associated with one another (P < .001). As shown in the Table, both grading systems were strongly associated with predicting mortality; all cases of mortality were in the higher grades. The 2010 grades do slightly better than the 2004 grades do in predicting metastasis because metastases occur only in high grades (G2 and G3). Mitotic index was significantly different, with a median of 0 in live patients versus 15 in deceased (P < .001). This was similarly borne out in the survival analysis using Cox proportional model, where, for every one unit increase in mitotic index, there was about a one-third increase in the hazard of death (P = .001). There was no significant difference in survival by tumor size, comorbidities, or margins.

Conclusions: The WHO 2010 grading system is strongly associated with predicting mortality and performs better in predicting liver metastasis than the 2004 grading system does.

<table>
<thead>
<tr>
<th>Vital Status and WHO Grades</th>
<th>Alive/Censored (n = 43), No.</th>
<th>Deceased (n = 7), No.</th>
<th>P Value</th>
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</thead>
<tbody>
<tr>
<td>WHO 2004</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poorly differentiated endocrine carcinoma</td>
<td>0</td>
<td>4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Well-differentiated (WD) endocrine carcinoma</td>
<td>12</td>
<td>3</td>
<td></td>
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<tr>
<td>WD endocrine tumor (ET) with benign behavior</td>
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<td>0</td>
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<tr>
<td>WHO 2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G1</td>
<td>23</td>
<td>0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>G2</td>
<td>20</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>G3</td>
<td>0</td>
<td>6</td>
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</tbody>
</table>

Gastric Foveolar Adenocarcinoma Arising in a Patient With Muir-Torre Variant Lynch Syndrome

(Poster No. 62)

Kara M. Klingman, BA1 (kara.klingman@uvm.edu); Amy E. Noffsinger, MD2; Rebecca Wilcox, MD3. Department of Pathology and Laboratory Medicine, Fletcher Allen Health Care/University of Vermont College of Medicine, Burlington, Vt; 2Department of Gastrointestinal Pathology, Miraca Life Sciences, Irving, Tex.

Lynch syndrome predisposes individuals to developing cancer, with colorectal and endometrium cancer carrying the highest risk. Gastric cancer risk is not as well defined, making surveillance guidelines less straightforward. The Netherland’s Hereditary Cancer Registry documents gastric cancer risk as being 3.4 times higher in patients with Lynch syndrome, specifically those with MLH1 or MSH2 mutations, compared with their general population. Foveolar-type dysplasia is a morphologic subset of gastric dysplasia different from intestinal-type dysplasia in that its background mucosa generally lacks atrophy and intestinal metaplasia. Foveolar-type dysplasia has a documented association with FAP, and gastric foveolar carcinoma has a documented association with microsatellite instability; however, these microsatellite instability-associated foveolar gastric carcinomas showed hMLH1 promoter hypermethylation rather than familial microsatellite instability. We present a 61-year-old man with Muir-Torre variant Lynch syndrome who underwent endoscopic mucosal resection for a persistent gastric fundic lesion. Previous history included metachronous colon cancers (at age 45 and 59 years) and multiple sebaceous adenomas. MSH2 sequencing was positive for germline mutation e21del4. Histologic examination of the fundal mass revealed a welldifferentiated, intramusosal adenocarcinoma arising in a 1.3-cm, foveolar-type adenoma. The background gastric mucosa was normal without atrophy or intestinal metaplasia (Figure 30, a). There was loss of MSH2/MS6 protein expression by immunohistochemical staining with retained expression of MLH1/PM2 in the adenoma and adenocarcinoma (Figure, b). A geographically separate, foveolar-type adenoma with high-grade dysplasia was also removed at the time of the endoscopic mucosal resection. To our knowledge, this is the first documented case of gastric foveolar adenocarcinoma arising in a patient with Lynch syndrome.

Colon Small Cell Carcinoma: Immunohistochemistry Important for Diagnosis

(Poster No. 63)

Amy C. Laib, BA1; David S. Laib, MD2 (david.laib@osfhealthcare.org); Dian Feng, MD, PhD2; Edward Santos, MD. 1Department of Pathology, American University of the Caribbean Medical School, Dupe Coy, Saint Martin; 2Department of Pathology, OSF Saint Anthony Medical Center, Rockford, Ill.

Extrapulmonary small cell carcinomas are rare. A 66-year-old woman presented with obstructive symptoms of the gastrointestinal tract. Right hemicolectomy revealed a circumferential lesion that measured 5.6 × 4.5 × 3.8 cm, which extended to the radial resection margin. Microscopic examination showed a poorly differentiated malignancy composed of large nests of atypical, intermediate-sized, cohesive, round and spindled cells. These malignant cells showed cytologic atypia consisting of nuclear pleomorphism, hyperchromasia, and a granular chromatin pattern with occasional small nucleoli. Many mitotic figures were present, including atypical ones. Also present were necrosis, perineural invasion, and angiolymphatic invasion. No well-formed glands, dyskeratosis, or squamous pearls were present. No background adenomatous change was present. Immunoperoxidase stains revealed a poorly differentiated malignancy that was positive for synaptophysin and negative for chromogranin, CK7, CK5/6, and CK20. The tumor invaded through the full thickness of the colon wall into the surrounding fat, which contained tumor deposits. Metastases were found in 11 of 12 pericolic lymph nodes with matting. By computed tomography scan, metastases were present in the liver, pelvic peritoneum, mediastinum, appendix, and retroperitoneum. To exclude metastatic lung small cell carcinoma, TTF1 is helpful. With other concurrent tumor types, the small cell component determines the biologic aggressiveness of the tumor. Treatment includes excision, adjuvant radiotherapy for incompletely resected disease, and systemic chemotherapy. In conclusion, extrapulmonary small cell carcinoma is a rare, very aggressive malignancy, and immunoperoxidase stains are necessary for diagnosis.
Primary B-Cell Lymphoma of the Extrahepatic Bile Duct Mimicking Periductal Infiltrating Cholangiocarcinoma
(Poster No. 64)

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Primary extranodal non-Hodgkin lymphoma arising from the extra hepatic biliary tract is a rare phenomenon, with fewer than 20 cases reported in the literature. Most of the cases are diffuse large B-cell lymphomas, which account for 30% to 40% of all cases of lymphomas. Up to 40% of diffuse large B-cell lymphomas will initially present at extranodal sites, most commonly the gastrointestinal tract, and rarely, the biliary tree. Lymphomas account for approximately 1% of cases of biliary obstruction related to malignancy, and in most of those cases, the obstruction is extrinsic, related to enlarged lymph nodes in the area. We report the unusual case of a 46-year-old, previously healthy man who presented with acute postprandial right upper-quadrant pain unaccompanied by jaundice. Radiologic and gross images were strongly suggestive of a periductal infiltrating cholangiocarcinoma, but microscopic examination revealed a primary, diffuse large B-cell lymphoma arising in the extrhepatic bile ducts and extending in a periductal fashion into the intrahepatic bile ducts, thereby expanding the portal triads and inducing a histiocytic reaction. Although rare, primary extranodal B-cell lymphomas should be considered in the differential diagnosis of Klatskin tumors because that could dramatically change the course of management (Figure 31).

Intraductal Papillary Neoplasm of the Bile Ducts: Case Report of an Uncommon Tumor Variant and Review of the Literature
(Poster No. 65)

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Intraductal papillary neoplasm of the bile duct (IPNB) is an uncommon variant of bile duct carcinoma, recently recognized by the World Health Organization as precursor to invasive carcinoma. Its clinicopathologic features are still poorly defined, and its identification can represent a diagnostic challenge. We report a case of a 38-year-old woman with a history of choleodocholithiasis who presented in December 2012 because of alcoholic stools and jaundice. Blood workup was consistent with obstructive jaundice. A magnetic resonance cholangiopancreatography showed a common bile duct mass and 3 liver masses. The patient received preoperative chemotherapy, underwent a partial hepatectomy, and is currently receiving adjuvant chemotherapy. The liver showed a 1.5 × 1.5 × 1.0-cm, tan, friable, papillary mass at the right hepatic duct and common bile duct junction and 6 pale-tan, homogenous masses, ranging from 1.0 to 6.0 cm. Microscopically, a dilated bile duct showed an intraductal papillary mass adjacent to infiltrative adenocarcinoma. The papillary fronds had fine vascular cores and were lined by epithelial cells with different degrees of dysplasia and foveolar-like mucinous cytoplasm (Figure 32). By immunohistochemistry, the epithelium was positive for MUC5 and negative for MUC1, MUC2, and CDX2, which is consistent with gastric foveolar subtype of IPNB. We describe the histomorphology and immunohistochemistry of an IPNB with invasive adenocarcinoma in a young, female patient who is still alive after 15 months. Accurate distinction of this tumor from cholangiocarcinoma is necessary to recognize patients with better prognosis and to further investigate the natural history of this precursor of bile duct carcinoma.

Accuracy of Vascular Invasion Reporting in Hepatocellular Carcinoma Before and After Implementation of Subspecialty Surgical Pathology Sign Out
(Poster No. 66)

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Context: Hepatocellular carcinoma (HCC) is the most common, solid-organ malignancy in males worldwide, is increasing in incidence in the United States and other Western countries, and has high mortality (overall 5-year relative survival rate, 16%). The preferred treatment for small HCCs is liver transplantation. Pathologic factors associated with decreased survival in patients undergoing transplantation for HCC include size and number of tumors and the presence of vascular invasion (VI). In recent years, there has been a movement toward subspecialty sign out (SSSO) in surgical pathology. One study has suggested SSSO improves reporting accuracy of pleural invasion in lung cancer. We hypothesized that pathologists with special interest and training in liver pathology would be more likely to identify and report VI in HCC than would general surgical pathologists.

Design: We reviewed reports and hematoxylin-eosin–stained slides from 118 transplant hepatectomies with HCC; 89 cases before implementation of SSSO and 29 cases after SSSO implementation.

Results: Before SSSO implementation, 39 of 89 (44%) cases were reported as positive for VI; upon our review, 59 of 89 (66%) of the cases had VI. After SSSO implementation, 8 of 29 cases (28%) were reported as positive for VI; upon our review, 14 of 29 cases (48%) had VI. Before SSSO, the VI status of 69 of 89 cases (78%) was correct; after SSSO, VI status was correct in 23 of 29 cases (79%).

Conclusions: Overall reporting accuracy of VI in HCC remained constant before and after SSSO.

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Hemorrhagic Benign Pancreatic Cyst Masquerading as a Malignant Cystic Neoplasm on Radiograph: A Diagnostic Pitfall

(Poster No. 67)

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Mucinous pancreatic cystic neoplasm can be managed according to clinicoradiologic features. Patients with high-grade cytology on fine-needle aspiration or worrisome radiologic features can be managed conservatively. Here, we present a case of benign pancreatic mucinous cystadenoma that underwent extensive hemorrhage with radiologic features mimicking malignant transformation. The patient subsequently had an uneventful surgery. A 61-year-old woman was incidentally discovered to have a unicellular cyst in the tail of her pancreas in 2010 and had been followed since. On radiograph, the cyst had increased in size from 2.65 cm to 5 cm. Our patient did not have symptoms, except recent, mild upper left-quadrant abdominal pain. Magnetic resonance image showed a hemorrhagic cyst with internal debris. An enhancing mural nodule with stalk was also noted, raising the suspicion of mucinous cystic neoplasm that had undergone malignant transformation. Laparoscopic distal pancreatectomy and splenectomy were performed to reveal a 6 × 5 × 5-cm unicellular hemorrhagic cyst with thin cystic walls, chocolate-like fluid, and hemorrhagic debris. Microscopically, most of the cystic wall showed extensive histiocytic reaction with hemosiderin deposition. Focally, the cyst was lined by a single layer of cuboidal epithelium with no cystic atypia. The cyst was 4th-adenoma-like stroma, composed of abundant stromal cells, and progesterone receptors, suggestive of pancreatic mucinous cystadenoma. The lesion was sufficiently sampled, and no malignant tumor was identified. In summary, we present a benign pancreatic mucinous cystadenoma radiologically mimicking malignant transformation. Careful clinicoradiologic correlation is necessary to avoid misinterpretation and unnecessary surgery.

First Report of a Uterine Leiomyosarcoma Metastatic to the Tail of the Pancreas: A Case Report and Review of the Literature

(Poster No. 68)

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Pancreatic leiomyosarcomas are rare and may present a diagnostic challenge when a primary and metastatic lesion are differentiated. A 35-year-old woman with abnormal uterine bleeding underwent a hysterectomy that revealed a 13-cm leiomyosarcoma. Six years later, she presented with a pancreatic tail mass. The lesion was resected and diagnosed as a leiomyosarcoma. Histologically, immunohistochemical, and molecular studies confirmed the metastatic nature of the malignant neoplasm. We report the first case of metastatic leiomyosarcoma from a uterus primary to the tail of the pancreas. In addition, our case appears to be one of the few cases where pancreatic metastasis presented as an isolated incidence. We also review the literature pertaining to this topic and outline some of the strategies for differentiating between a pancreatic primary tumor and a metastatic tumor.

Gastric Medullary Carcinoma With SporadicMismatch Repair Deficiency and a TP53 R273C Mutation: An Unusual Case With Wild-Type BRAF

(Poster No. 69)

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Medullary carcinoma has long been recognized by the World Health Organization (WHO) as a distinct form of colorectal cancer that is associated with microsatellite instability and Lynch syndrome. Gastric medullary carcinoma, a very rare neoplasm, has recently been added to the 4th edition of the WHO classification of tumors. This tumor is highly sensitive for our nuclear expression in the 67-year-old man who presented with a gastric mass without evidence of other masses. A total gastrectomy revealed a well-demarcated but poorly differentiated carcinoma with organoid growth pattern, pushing borders, and abundant peritumoral lymphocytic response. The prior cytologic specimen was highly cellular with the immunohistochemical panel consistent with upper gastrointestinal/pancreaticobiliary origin. Overall, the histopathologic findings were consistent with gastric medullary carcinoma. A mismatch repair panel revealed loss of MLH1 and PMS2, and intact MSH2 and MSH6 expression, indicating a mismatch repair protein-deficient tumor. BRAF V600E immunohistochemical staining (VE1) and BRAF molecular testing were negative, indicating a wild-type gene. Tumor sequencing of MLH1 demonstrated a wild-type gene. Our standard molecular panel also identified a TP53 R273C mutation. With the patient’s advanced age, these findings are compatible with a sporadic tumor. Given that morphologically identical medullary tumors often occur in Lynch syndrome, it is possible that mismatch repair loss is an early event in sporadic tumors, with TP53 mutation being a late event. Despite having wild-type BRAF, this tumor is sporadic and unrelated to Lynch syndrome. This case report demonstrates that coordinate ancillary studies are needed to resolve sporadic versus hereditary rare tumors.

Surgical, Endoscopic, and Histologic Correlates and Challenges Linked to Inverted Appendiceal Stump

(Poster No. 70)

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Context: The diagnosis of inverted appendiceal stump may depend upon a combination of a history of prior appendectomy, endoscopic precise location (polyp at the appendiceal orifice), and histologically androgynous-like lymphoma. This case report presents the potential for endoscopic and histologic diagnostic oversight.

Design: We searched the clinical, endoscopic, and pathology databases for inverted appendiceal stumps in our medical center for a 10-year period (2003–2013). The electronic medical records and pathology findings were reviewed.

Results: Eight cases were identified (5 men, 3 women; age range, 37–61 years). Documented history of appendectomy was available in only 4 of 8 patients, all with open appendectomy and stump invasion. Five were asymptomatic patients presenting for colon cancer screening, 2 presented with hematochezia, and 1 with abdominal pain. Endoscopically inverted appendiceal stump was suspected in 6 of 8 cases. Pathologically, in 3 of 8 cases, deeper sections and immunostains were performed. None had ulceration, bleeding granuloma, or dysplasia.

Conclusions: Open appendectomy with operative invagination of the stump results in inverted appendiceal stump. It is an incidental finding. Endoscopists suspect this lesion based on its location but may remain diagnostically unsure and need to elicit history and details of appendectomy. The pathologic diagnosis is easier with a documented history of appendectomy and endoscopic suspicion of inverted appendiceal stump. Workup of these surgical and endoscopic correlates, histologic diagnosis is nonspecific or with Needless appraisals for a neoplastic mass or lymphoma.

Intracholecystic Papillary-Tubular Neoplasm Arising in Adenomyoma of the Gallbladder

(Poster No. 71)

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A 72-year-old man with a recent history of abdominal pain underwent a cholecystectomy for a clinical diagnosis of cholelithiasis with cholecystitis. The resected gallbladder had 3 choleliths and a 2.5-cm mural mass in the fundus. The fundic mural mass had features of an adenomyoma with glandular elements intermixed with proliferating bands of smooth muscle. The glandular elements included an intraluminal proliferation with papillary architecture having focal, mild to moderate dysplasia. The remainder of the gallbladder had features of chronic and subacute cholecystitis. The margins of resection and the single pericystic lymph node were not involved by tumor. The overall findings were interpreted as an intracholecystic papillary-tubular neoplasm (ICPN) with mild to moderate dysplasia, arising in an adenomyoma. There is not a consensus on classification of preinvasive neoplasms and papillary tumors in the gallbladder. A recent proposal

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Solid pseudopapillary tumor of pancreas (SPT) is an uncommon and enigmatic pancreatic neoplasm that occurs mainly in young women. Rare cases of extrapancreatic SPT have been reported. We present a case of SPT that posed a diagnostic challenge by presenting at an unusual location. A 32-year-old woman presented with dull, upper-abdominal pain for 3 months. Computed tomography scan revealed a well-defined heterogeneous mass in the subhepatic region between the head of the pancreas and the second portion of the duodenum. Radiologic features were suggestive of a gastrointestinal stromal tumor. The tumor was subsequently excised under general anesthesia. At operation, the tumor appeared to be adherent to the inferior surface of the head of the pancreas, but it could be easily separated from the pancreas. Macroscopically, the tumor was a well-circumscribed, hemorrhagic mass, measuring 10.0 × 8.0 × 3.0 cm. On microscopy, the tumor exhibited a predominant, solid growth pattern with focal pseudopapillary formation (Figure 34, A and B). The tumor cells were polygonal with abundant eosinophilic cytoplasm and round to oval nuclei with fine nuclear chromatin. There was no ectopic pancreas histologically. Immunohistochemistry showed strong expression of CD10, vimentin, CD56 (Figure, C) and α1-antitrypsin, whereas synaptophysin was focally positive. β-catenin immunostain showed strong nuclear expression (Figure, D). A final diagnosis of SPT was rendered. The SPTs occur as primary tumors outside the pancreas exceedingly rarely; only 12 cases have been reported in the English literature. Awareness of the existence of this tumor in extrapancreatic sites is essential to avoid misdiagnosis.

A Case of Schwannian Pseudohypertrophy of Muscularis Propria in Rectum

(Poster No. 74)

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Fibrosis as a response to change of milieu is not uncommon in the gastrointestinal tract, but fibrotic thickening limited to muscularis propria accompanied by an increase in Schwann cells has not been reported. We report a case of a 69-year-old woman who presented with irreducible segmental rectal prolapse and underwent resection. Grossly, the rectum demonstrated focal erosion and ulcer in the mucosa. There was hypertrophy-like thickening of the muscularis propria to 2 or 3 times the normal thickness in areas uninvolved by erosion or ulcer (Figure 35, A, arrow). Histologically, the thickened areas demonstrated fibrotic thickening (Figure, B, arrow, trichrome) that was limited only to the muscularis propria. The fibrosis (Figure, C, trichrome) nicely followed the distribution of the inner muscle layer and tapered off at the periphery without accompanying fibrosis in the surrounding tissue. Some bland spindle cells, reminiscent of Schwann cells, were present, and those cells were immunoreactive for S100 (Figure, D). Electron microscopy was
performed and features of Schwann cells were demonstrated in those cells. No increase in neurons or axons was demonstrated by immunohistochemistry for PGP9.5 or neurofilament proteins. We named this unique change schwannian pseudohypertrophy because this is not genuine hyperplasia or hypertrophy because of its lack of increase in cellularity or enlarged cell bodies. It is indeed a pseudohypertrophy because of fibrosis. This term also reflects the increase in Schwann cells. This type of change may be mistaken as a tumor of peripheral nerve origin in small biopsies and thus deserves recognition.

**Adenovirus-Associated Acute Appendicitis**  
(Poster No. 75)

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**Context:** Acute appendicitis (AA) is one of the most common causes of a abdominal surgery worldwide, occurring most frequently in those age 10 to 29 years. Adenovirus (ADV) is a rare but reported cause of AA in children. Annually, about 36 000 young, basic military trainees (BMTs) undergo initial training at Lackland Air Force based in Texas. One third develop an adenoviral upper respiratory tract infection (URI) during the 8.5 weeks of training. We hypothesized that ADV may be more frequently associated with AA in this population.

**Design:** This study involved a retrospective review of patient charts and existing pathologic tissue specimens of all BMTs who underwent appendectomy at the Wilford Hall Ambulatory Surgical Center from January 1, 2003, to May 31, 2011. Pathologic tissue from 114 BMTs was assayed by quantitative polymerase chain reaction (PCR) and immunohistochemical (IHC) staining for ADV.

**Results:** Adenovirus DNA was detected in 16 of 114 samples (14%) via PCR: ADV type 4 in 13 cases, ADV type B14 in 1 case, and nontypable ADV in 2 cases. The IHC was positive in only the ADV B14 case.

**Conclusions:** By using PCR, this study demonstrated an association between viruses and appendicitis higher than has been previously reported. Comparison of PCR to immunohistochemistry shows that routine pathology analysis may overlook evidence of viral causes.

**Newly Diagnosed Colonic Adenocarcinoma: The Presenting Sign in a Young Woman With Undiagnosed Crohn Disease in the Absence of Primary Sclerosing Cholangitis and a Normal Microsatellite Instability Profile**  
(Poster No. 76)

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Ulcerative colitis has long been established to pose an increased risk for the development of colonic adenocarcinoma, whereas Crohn disease has only recently been reported in some studies to pose a similar increased risk of colonic adenocarcinoma. We report a 33-year-old healthy woman with no documented past medical history and insignificant family history who presented with severe abdominal pain. She was taken to surgery for a perforated appendix and intraoperatively switched to a right hemicolecctomy because of the presence of a colon mass. Pathology revealed a poorly differentiated colonic adenocarcinoma extending through the muscularis propria and into the subserosal fat with metastases to 8 lymph nodes. In the background colonic mucosa, focal chronic-active colitis with marked crypt distortion, crypt abscesses, and reactive epithelial atypia was found. Upon further questioning, the patient reported loose, frequent stools since she was a teenager. The clinicians concluded that the patient had an undiagnosed Crohn disease without evidence of primary sclerosing cholangitis. Primary sclerosing cholangitis with associated inflammatory bowel disease results in much milder symptoms; these cases will often be undiagnosed and are associated with early colonic adenocarcinoma. The microsatellite instability profile showed normal immunohistochemical MLH1, MSH2, MSH6, and PMS2 protein expression, making Lynch syndrome unlikely. The etiology of this patient’s colonic adenocarcinoma is suspected to be related to the ongoing inflammation of the underlying inflammatory bowel disease. Newly diagnosed colonic adenocarcinoma in a young, healthy woman as the presenting sign for Crohn disease in the absence of primary sclerosing cholangitis is an extremely rare occurrence.

**Ossifying Colonic Adenocarcinoma: Case Report With Brief Review of Literature**  
(Poster No. 77)

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Within the gastrointestinal tract, osseous metaplasia is an extremely rare phenomenon. It represents dystrophic ossification and may occur in benign or neoplastic conditions. The cause of osseous metaplasia is controversial. Some authors think the best explanation for ossification in epithelial tumors is that it follows metaplasia of undifferentiated stromal tumors into osteoblasts. The first 2 cases of heterotopic ossification in a colorectal carcinoma were reported by Hasegawa in 1923. Very few cases of carcinoma with osseous metaplasia have been reported since. Of the cases of colon tumors, mucinous adenocarcinomas have been more frequently associated with rare cases of osseous metaplasia. We report a case of adenocarcinoma with osseous metaplasia of the cecum and ascending colon in a 55-year-old man. The patient was found to have a partially obstructing mass of the cecum. Grossly, the hemicolecctomy specimen (20 × 10 × 7 cm) revealed a fungating tumor mass in the cecum and ascending colon (6 × 5 × 5 cm). Cut surface showed tumor with hard bony areas and extension into the subserosal tissue. Histologically (Figure 36), the tumor was a well to moderately differentiated, invasive adenocarcinoma with prominent osseous metaplasia, which infiltrated the subserosa. One lymph node of 16 was positive for metastatic adenocarcinoma. Osseous metaplasia is generally a radiologic and histologic curiosity with an unknown significance. It is important to be aware of this phenomenon as being distinct from carcinosarcoma, which has a poorer prognosis.
Gastric Fibrin Cap Polyp Unrelated to Helicobacter Infection
(Poster No. 78)
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Cap polyposis is a rare, nonneoplastic condition characterized by multiple, distinctive, inflammatory polyps with fibrin caps most commonly occurring in the distal colon. Prior case reports and series have described an association with Helicobacter pylori infection and resolution of colonic lesions following eradication treatment. Gastric cap polyposes are extremely rare and, although the pathogenesis is poorly understood, an association with H. pylori infection has been proposed. Here, we describe a case of a solitary gastric fibrin cap polyp in a 50-year-old man with HIV presenting with abdominal pain, diarrhea, fever, and hypotension. Laboratory studies demonstrated elevated liver enzymes with decreased serum albumin and hemoglobin levels. The patient was found to have a common bile duct stone, and the gastric polyp was identified incidentally during therapeutic endoscopic retrograde cholangiopancreatography. The pedunculated polyp measured 5 cm and originated from the pylorus with prolapse into the duodenal bulb. Histopathologic examination of the polyp revealed markedly hyperplastic, elongated foveolar epithelium with underlying reactive glands, focal intestinal metaplasia, prominent smooth muscle bundles, and increased inflammatory cell infiltrates in the lamina propria. Notably, the surface of the polyp was extensively covered by a prominent fibrin cap comprising inspissated fibrin and protein with associated neutrophilic infiltrates and extravasated red blood cells. Immunohistochemistry for infectious agents, including H. pylori, CMV, and HSV, were negative. In addition, in situ hybridization for Epstein-Barr virus was negative. Therefore, we report a unique case of gastric fibrin cap polyp without concurrent H. pylori infection, possibly causing protein and red cell loss.

MCM7, a New Potential Index Marker, Significantly Correlated With Ki-67 Expression in Esophageal Squamous Cell Carcinoma, Adenocarcinoma, and Precancerous Lesions
(Poster No. 79)
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Context: Minichromosome maintenance (MCM) proteins have important roles in DNA replication. The deregulation of these proteins has been shown to contribute to tumorigenesis. This study compared MCM7 with Ki-67 expression in esophageal carcinoma and its precancerous lesions to determine their predictive value for the progression of esophageal disease.

Design: Esophageal tissue microarrays of 76 squamous epithelium, 58 columnar metaplasia, 38 Barrett esophagus, 21 low-grade dysplasia, 14 high-grade dysplasia, 108 adenocarcinomas, and 23 squamous cell carcinomas were immunohistochemically stained. Nuclear staining was considered positive. Percentage (0%–100%) and intensity (0–1) of positively stained cells were recorded. A P value of <.05 was considered significant.

Results: Immunohistochemical studies showed that all esophageal tissue types expressed both MCM7 and Ki-67 with strong intensity. The mean percentage for MCM7 and Ki-67 positivity progressively increased from squamous epithelium (8.9% and 5.5%, respectively), columnar metaplasia (18.7% and 3.6%), Barrett esophagus (57.6% and 6.9%), low-grade dysplasia (65.5% and 11.3%), high-grade dysplasia (73.3% and 27.7%), to adenocarcinoma (76.3% and 24.9%) and squamous cell carcinoma (87.4% and 36.1%). The increase in MCM7 and Ki-67 expression from columnar metaplasia and Barrett esophagus to adenocarcinoma, as well as from squamous epithelium to squamous cell carcinoma, was significant. MCM7 and Ki-67 expression was also significantly correlated (correlation coefficient, 0.61; P < .001). Neither MCM7 nor Ki-67 expression was significantly associated with esophageal adenocarcinoma survival (P = .88 and P = .34, respectively).

Conclusions: MCM7 and Ki-67 expression showed significant correlation and increase from benign esophageal lesions to carcinomas. MCM7 may serve as a promising proliferative index marker for differentiating esophageal lesions and evaluating disease progression.

High-Grade Leiomyosarcoma of the Liver in a 66-Year-Old Man
(Poster No. 80)
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We report here a case of high-grade leiomyosarcoma of the liver in a 66-year-old man. The patient had a history of Hodgkin lymphoma with chemotherapy and radiation when he was 16 years old. He presented with a history of abdominal discomfort, pain, and early satiety for 4 months. A computed tomography (CT) scan of the abdomen without contrast revealed a possible mass approaching 10 cm in the right lobe of the liver and a definitive mass (14 cm) in the left lobe. A CT-guided needle core biopsy of the left lobe of the liver demonstrated a spindle cell malignancy in a sheeitlike pattern with extensive hyalinization, degenerative changes, and necrosis. The tumor cells showed a fascicular configuration with a moderate amount of eosinophilic cytoplasm and pleomorphic and hyperchromatic nuclei. Scattered mitoses were present. Immunohistochemical staining exhibited positive reactivity for vimentin, desmin, caldesmon, and smooth muscle actin. c-Kit and DOG1 were equivocal. Pancytokeratin, S100, CD34, EMA, HMB45, cytokeratin OSCAR, myogenin, and myoD1 were negative. A diagnosis of high-grade leiomyosarcoma was rendered. The primary site may include the inferior vena cava and other great vessels in or near the liver. A positron emission tomography scan demonstrated hypermetabolic scattered activity seen in the hepatic lobe mass with a maximum standardized uptake value of 4.1 to 4.4. Bilateral pleural effusions were present. Cardiac system, gastrointestinal tract, and genitourinary system showed normal hypermetabolic activity. In conclusion, large high-grade leiomyosarcoma may exist in the liver, although it is rare. The patient is doing well with appropriate treatment.

Gastric Zygomycosis in a Previously Healthy 56-Year-Old Man
(Poster No. 81)
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Zygomycosis refers to infections caused by bread mold fungi of the Zygoomyco phylum. Infections generally occur in immunocompromised individuals. The following case is of a previously healthy 56-year-old man admitted to the hospital following a motor vehicle accident. During his hospitalization, there was a significant drop in hemoglobin, which led to an upper gastrointestinal endoscopy. The

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endoscopic revealed numerous, large, 30-mm, craterlike gastric ulcers with an adherent clot. Biopsies of the ulcer margins revealed broad papules, ribbonlike, slightly refractile fungal forms, which were highlighted with periodic acid–Schiff stain. A Gomori methenamine silver stain was negative. These forms were suggestive of zygomycetes.

A subsequent gastrectomy was performed that revealed similar findings. The patient experienced severe trauma, which may have contributed to the progression of his condition; however, this is an unusual presentation because the patient was previously healthy and did not illustrate any conditions that might compromise his immunity. The severity and rarity of this condition makes this a unique and intriguing case (Figure 37).

Evaluation of IMP3 Expression in Pancreatic Neuroendocrine Tumors (PNETs) and Its Significance

(Poster No. 82)

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Context: IMP3 is an oncofetal protein that has recently demonstrated diagnostic and prognostic value for various malignant tumors and been shown to be almost exclusively expressed in high-grade neuroendocrine tumors. The goal of this study was to examine the clinical outcome of a series of PNET cases and evaluate the potential of IMP3 as a biomarker.

Design: A prospectively maintained database of patients undergoing pancreatic resection for PNET from 1998 to 2013 was reviewed and evaluated for clinical outcome. IMP3 immunohistochemistry was performed on paraffin sections of the cases, and dark-brown cytoplasmic and/or membranous staining in more than 5% of tumor cells was considered positive.

Results: A total of 29 PNETs, including 17 cases of World Health Organization grade I and 12 cases of grade II tumors, were assembled. Mean follow-up period was 32 months. Of the 29 cases, 5 patients (17%) had evidence of active disease at the end of follow-up period. Of these 5 patients, 2 (40%) had liver metastases diagnosed at time of resection, 2 (40%) had disease recurrence with liver metastases at 8 and 38 months after resection, and 1 (20%) had local recurrence at 8 months postresection. IMP3 positivity was seen in 24 of 29 cases (83%), with 13 of these (54%) cases demonstrating strong and/or diffuse (>50%) positivity. IMP3 positivity did not correlate with local and/or metastatic disease recurrence (P = .45).

Conclusions: In contrast to previous studies of IMP3 in other neuroendocrine tumors, IMP3 positivity is observed in most of these low-grade PNETs. This finding suggests a possible divergent carcinogenic pathway for PNETs and warrants further investigation.

Stromal Immunoreactivity to Anti-Collagen Type XII Antibody Can Aid in the Distinction Between Invasive Adenocarcinoma and Benign, Misplaced Glands in Endoscopically Removed Colorectal Polyps

(Poster No. 83)

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Context: In large colorectal adenomas, the distinction between benign, misplaced glands and invasive adenocarcinoma is sometimes challenging. We investigated the expression characteristics of the tumor-associated matrix collagen type XII (colXIIa) within the periglandular submucosal stroma of colorectal adenomas with invasive cancer or benign misplaced glands and the diagnostic value of that marker in facilitating a correct diagnosis.

Design: Sixty-six endoscopically removed, paraffin-embedded colorectal polyps were stained with anti-collXIIa antibody (OncoMatrix, Bilbao, Spain). The polyps comprised 45 malignant polyps (MPs) with deeply invasive adenocarcinoma and desmoplastic stroma (including 5 with concurrent misplaced glands), 5 MPs with superficially invasive cancer and minimal desmoplastic stroma, 11 adenomas with benign misplaced glands only, and 5 conventional tubulovillous adenomas.

Results: Intracellular granular expression of colXIIa was observed either diffusely or focally in desmoplastic fibroblasts at the invasive cancer front in 80% (36 of 45) of the MPs. All 9 MPs containing a mucinous cancer component (100%) were immunoreactive. Expression was retained in 16 of 18 MPs (88.9%) despite the presence of significant electrocautery effect near the polypectomy margin. No staining was observed in 5 superficially invasive cancers, 16 adenomas with misplaced glands, and 5 tubulovillous adenomas.

Conclusions: ColXIIa antibody can assist in distinguishing the desmoplastic stroma associated with invasive adenocarcinoma from that associated with misplaced glands with a sensitivity and specificity of 72% and 100%, respectively. If applicable in the presence of electrocautery effects and mucinous differentiation, 2 factors that regularly interfere with conventional histologic assessment. However, it has little value in diagnosing early invasive cancers with limited desmoplastic stroma.

Incidental Findings in Gastric Sleeve Resections for Severe Obesity

(Poster No. 84)

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Context: In the past few decades, the prevalence of obesity has continued to increase, especially in developed countries. Comorbidities associated with obesity such as treatment complications are particularly important, and bariatric surgery has become an increasingly popular form of treatment. Review of these resections histologically is necessary as unexpected pathology may be found. However, to our knowledge, a large retrospective case review of sleeve gastrectomies has not been performed.

Design: We identified 343 bariatric gastric sleeve surgery cases performed at the University of Illinois Hospital and Health Sciences System from January 2009 to August 2013.

Results: The most frequent finding was gastritis (69%), including chronic inactive (73.8% of gastritis patients, 51% of total patients), chronic active (22.4%, 15.4% of total), acute-on-chronic gastritis (2.9%, 2.0% of total) and associated Helicobacter pylori infection (22.8%). Six patients (1.7%) had ulcers, with 2 having a known history of ulcers. Two patients (0.58%) had gastrointestinal stromal tumors. Other findings included an unknown recurrence of adenocarcinoma (1 patient), one polyp (1 patient), a gastric diverticulum (1 patient), mucosal and vascular congestion, intestinal metaplasia, hemorrhage, and pyloric stenosis (1 patient). Eighty-five patients (24.8%) had specimens negative for significant histopathologic changes.

Conclusions: In this case review, more than one-half of the patients had histopathologic findings, 24.8% of which were clinically significant. The histologic findings ranged from chronic inactive gastritis to gastrointestinal stromal tumor and adenocarcinoma. This review confirms the importance of examining these specimens histologically because clinically significant lesions may be found, and follow-up treatment may be necessary.

Synchronous Colon Adenocarcinomas in a Patient With Common Variable Immunodeficiency: Report of a Rare Case

(Poster No. 85)

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Common variable immunodeficiency (CVID) usually manifests with recurrent infections and autoimmune disorders. Approximately 15% of patients with CVID develop malignancies, most commonly lymphoma and gastric adenocarcinoma. Malignancy of the lower gastrointestinal (GI) tract is rare. One study documented 3 cases of solitary colon cancer among 476 patients with CVID. The rare case reports describe either neuroendocrine or adenosquamous colorectal carcinoma. We present a case of synchronous colon adenocarcinomas in a patient with CVID. A 52-year-old man with CVID, previously treated for enterocytitis as the lowest GI lesion by colonoscopy to evaluate long-standing diarrhea. Endoscopic biopsy of a broad-based polyp in the hepatic flexure revealed a moderately differentiated adenocarcinoma. The patient underwent subtotal colectomy. Grossly, there was a 3.6-cm exophytic mass in the midascending colon and a separate submucosal nodule located 3.0 cm distal to the first lesion. The terminal ileum was granular, and the involved colonic mucosa was erythematous and flattened. Histologically, the larger mass was a pT3, moderately differentiated adenocarcinoma with mucinous features. The smaller lesion was a...
pT2, moderately differentiated adenocarcinoma, measuring 2.0 cm microscopically. Immunohistochemical expression of MLH1, MSH2, MSH6, and PMS2 was retained in both tumors. Thirty-two lymph nodes were negative for metastatic carcinoma. Nonneoplastic ileum and colon demonstrated diffuse ileocolitis with intraepithelial apoptotic bodies, nodular lymphoid hyperplasia, and markedly decreased numbers of plasma cells, compatible with the diagnosis of CVID. To our knowledge, this is the first report of synchronous colonic adenocarcinomas in the setting of CVID.

Immunohistochemical Evaluation of c-Myc Expression in Carcinomas From Various Organs

(Footer No. 86)

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Context: c-Myc is a transcription factor and oncoprotein. As well established, the t(8;14) translocation is critical for the development of Burkitt lymphoma. In addition, c-Myc overexpression has been reported in other malignancies. In this study, we investigated c-Myc expression in a large series of carcinomas.

Design: Immunohistochemical evaluation of the expression of c-Myc (EP121 or Y69, Epitomics Inc, Burlingame, Calif) in 912 carcinomas on tissue microarray sections and 18 medullary carcinomas of the large intestine on routine tissue sections was performed. The staining intensity and distribution were recorded.

Results: Some of the results are summarized in the Table. One hundred percent of medullary carcinomas were positive for c-Myc. Papillary thyroid carcinomas, renal cell carcinomas, endometrial carcinomas, hepatocellular carcinomas, and pancreatic neuroendocrine tumors were negative for c-Myc.

Conclusions: These data suggest that (1) c-Myc can be useful in confirming a diagnosis of colorectal carcinoma because c-Myc overexpression is present in nearly 100% of colorectal carcinomas, including medullary carcinomas; and (2) c-Myc can be used in differentiating lung squamous cell carcinoma from lung adenocarcinoma. Additionally, a carcinoma with c-Myc overexpression may potentially respond to c-Myc-targeted cancer therapy.

Summary of c-Myc Immunostaining Results

<table>
<thead>
<tr>
<th>Tumor</th>
<th>c-Myc+ %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testicular tumors, n = 120</td>
<td>6</td>
</tr>
<tr>
<td>Lung ADC, n = 80</td>
<td>10</td>
</tr>
<tr>
<td>Lung SCC, n = 74</td>
<td>87</td>
</tr>
<tr>
<td>Follicular thyroid CA, n = 37</td>
<td>5</td>
</tr>
<tr>
<td>Colonic ADC, n = 82</td>
<td>99</td>
</tr>
<tr>
<td>Esophageal ADC, n = 48</td>
<td>42</td>
</tr>
<tr>
<td>Pancreatic ADC, n = 48</td>
<td>7</td>
</tr>
<tr>
<td>Urothelial CA, n = 43</td>
<td>2</td>
</tr>
<tr>
<td>Prostatic ADC, n = 96</td>
<td>26</td>
</tr>
<tr>
<td>Breast ductal CA, n = 46</td>
<td>7</td>
</tr>
<tr>
<td>Endocervical ADC, n = 25</td>
<td>56</td>
</tr>
<tr>
<td>Ovarian serous CA, n = 41</td>
<td>14</td>
</tr>
</tbody>
</table>

Abbreviations: ADC, adenocarcinoma; CA, carcinoma; RCC, renal cell carcinoma; SCC, squamous cell carcinoma.

Application of the 2010 World Health Organization Classification Can Classify Previously Uncategorized Hepatobiliary Tumors as Combined Hepatocellular-Cholangiocarcinoma Subtypes

(Poster No. 87)

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Context: The 2010 World Health Organization (WHO) liver tumor classification divides combined hepatocellular-cholangiocarcinoma (HCC-CC) into classic type and subtypes with stem cell features (SCFs). The HCC-CCs with SCFs include (1) typical subtype, showing clustered hepatocytes encircled by progenitor-like cells; (2) intermediate-cell subtype, composed of nested cells in desmoplastic stroma with both hepatocellular and cholangiocellular differentiation; and (3) cholangiolocellular subtype with small cells forming anastomosing tubules. This study examines whether the WHO definitions standardize classification of hepatobiliary neoplasms.

Design: One hundred hepatobiliary neoplasms, including hepatocellular carcinomas, cholangiocarcinomas, and primary hepatic tumors with mixed features, resected between January 2008 and September 2013 were retrieved from departmental files. Slides from 69 cases were available for review, and 3 more cases of primary hepatic tumors with mixed features were additionally included, totaling 72 cases for review. All hematoxylin-eosin–stained tumor sections were examined for combined HCC-CC morphology. Ten cases with combined features were found, including 7 originally reported using only descriptive terminology, and immunostained to further assess for SCFs (see Table). Ten and 9 pure hepatocellular and cholangiocarcinomas, respectively, were stained as controls.

Results: Tumors showing combined morphology included 2 combined HCC-CCs, classic type; 2 combined HCC-CCs with SCFs, cholangiolocellular subtype; and 6 combined HCC-CCs with SCFs, intermediate subtype. Immunostaining was confirmatory in the pure hepatocellular and cholangiocarcinomas and helped confirm the presence or absence of SCFs in combined HCC-CC (Table). Tumors with mixed features, including those reported descriptively, could be categorized by WHO criteria. Immunohistochemistry supported morphologic impressions. Overall, the WHO subtypes help to classify hepatobiliary tumors, eliminating variable descriptive terminology in reporting.

Immunostaining of Progenitor-Like Cells in Combined HCC-CC by Subtype

<table>
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<tr>
<td>CK7 (cytoplasmic)</td>
<td>Leica, Biosystems, Buffalo Grove, Ill 0 1 4/6</td>
<td>CK19 (cytoplasmic), Cell Marque, Rocklin, Calif 0 1 6/6</td>
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|                   | Leica, Biosystems, Buffalo Gro...
Role of hCAS in the Progression of Barrett Neoplasia

(Kun Jiang, MD, PhD (kun.jiang@moffitt.org); Daniel Cowden, MD; Mokenge P. Malafa, MD; Domenico Coppola, MD. Department of Pathology, H. Lee Moffitt Cancer Center, Tampa, Fla.

Context: The human cellular apoptosis susceptibility (hCAS) protein is involved in proliferation, apoptosis, invasion, and metastasis; it is a key player in cytoplasm-to-nuclear transport in various tumor cells. We hypothesized that hCAS expression may be altered during the progression of Barrett neoplasia.

Design: Fifty-nine esophageal resection specimens were reviewed and categorized to include Barrett mucosa (BE), low-grade dysplasia (LGD), high-grade dysplasia (HGD), and invasive adenocarcinoma (ICA); 10 BEs, 20 LGDs, 36 HGDs, and 59 ICAs were analyzed. hCAS was measured using a rabbit antibody (Spring Bioscience, Pleasanton, Calif.) and the Ventana Medical Systems (Tucson, Ariz.) automated immunostainer. hCAS overexpression and knockout cell lines were used as controls.

Results: Low expression (immunohistochemistry [IHC] score < 4) of hCAS was detected in all (n = 10) of the BEs (100%). Conversely, all but 1 (97.2%) HGDs and all (100%) ICAs demonstrated high hCAS (IHC score > 4). High score was noted in 12 LGD and low score was noted in 8 LGD cases. Statistical analysis was significant when P < .001; BE versus LGD (P < .001); BE versus HGD (P < .001); BE versus ICA (P < .001); LGD versus HGD (P < .001); and LGD versus ICA (P < .001). No significance was found between HGD and ICA (P > .30). Interestingly, hCAS was preferentially nuclear in BE but cytoplasmic and nuclear in LGD, HGD, and ICA.

Conclusions: hCAS is expressed early and across all stages of Barrett neoplasia. hCAS may represent a marker for early detection of dysplasia in Barrett esophagus. In addition, it may represent a new potential target for the prevention and treatment of Barrett neoplasia.

Olmesartan-Associated Celiac Disease Enteropathy in a Patient With Severe Diarrhea

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A 62-year-old woman with a history of hypertension presented with severe diarrhea. Endoscopic examination of the gastrointestinal tract revealed erythema of the sigmoid colon and rectum, and granularity in the second part of duodenum. Biopsies from left colon, rectum, and sigmoid colon were histologically unremarkable. Duodenal biopsies showed multifocal surface ulceration, villous blunting, and intraepithelial lymphocytosis (Figure 38, A). These changes were suspicious for celiac disease in a background of erosive injury. Serologic testing was suggested to exclude celiac disease, which turned out negative. The patient continued to have severe diarrhea and developed dehydration that required hospitalization. Review of the patient's medication revealed use of olmesartan for hypertension during previous 2 years, which was stopped as a probable cause of her symptoms. She recovered from diarrhea within 3 days of discontinuation. Repeat duodenal biopsy after 1 month showed histologic recovery (Figure, B). Olmesartan is an angiotensin II receptor antagonist that is used to manage hypertension. Olmesartan-associated celiac disease enteropathy has been rarely described in the past, and the underlying mechanism is unknown. However, the long delay between onset of therapy and the development of diarrhea suggests a role for cell-mediated immunity. Inhibition of transforming growth factor β has also been suggested as a possible mechanism. In summary, we present a unique case of olmesartan-associated celiac disease enteropathy in a patient with severe diarrhea. Pathologists and clinicians should consider this entity in the differential diagnosis when dealing with a case of seronegative celiac disease enteropathy.

A Unique Case of Primary Colonic Leiomyosarcoma Arising in a Preexisting Leiomyoma

(Sofia Garces, MD (sofia.garces@msmc.com); Robert Poppiti Jr, MD; Cristina Vincentelli, MD. Department of Pathology, Mount Sinai Medical Center, Miami Beach, Fla.

Primary leiomyosarcomas of the gastrointestinal tract are extremely rare and aggressive neoplasms. Malignant transformation of a leiomyoma is an exceedingly rare event that has only been reported in locations other than the gastrointestinal tract. We present the case of a 74-year-old woman with a 5-year-history of an intramural mass in the sigmoid colon that underwent sudden rapid growth. The resected colon revealed a 6.5 × 3.5-cm, well-circumscribed, white, rubbery intramural mass with focal hemorrhage. Histologically, the neoplasm was mainly composed of bland spindle cells showing smooth muscle differentiation. Sections from the hemorrhagic focus displayed malignant features, including hypercellularity, severe atypia, necrosis, and a high mitotic rate. An immunohistochemical panel was performed to rule out the possibility of a gastrointestinal stromal tumor. The neoplastic cells were positive for SMA, MSA, desmin, and caldesmon and were negative for CD117 and DOG1. Ki-67 showed a high proliferation rate in the hypercellular focus. Moreover, molecular analysis failed to detect mutations in the KIT or PDGFRA genes. The diagnosis of a leiomyosarcoma arising in a preexisting leiomyoma was made. To our knowledge, this is the first reported case of malignant transformation of a gastrointestinal leiomyoma. Sudden growth of a long-standing leiomyoma should raise concern for malignant transformation and must be followed by proper tissue sampling of different areas of the tumor. Furthermore, a complete immunohistochemical panel and molecular studies are essential to accurately differentiate a smooth muscle neoplasm from a gastrointestinal stromal tumor because of prognostic and therapeutic differences.

Esophageal Leiomyoma: A Rare Benign Intramural Tumor of the Esophagus

(Muhammad S. Khurram, MD (muhammad.khurram@stjohn.org); Daniel Ockner, MD; Basim Al-Khafaji, MD. Department of Pathology, St John Hospital and Medical Center, Detroit, Mich.

Leiomyomas of the esophagus are rare benign neoplasms that frequently cause symptoms, necessitating resection. We report a rare case of esophageal leiomyoma originating primarily from the lower esophagus. The patient was a 78-year-old woman with a 4-year history of gastroesophageal reflux disease, dysphagia, abdominal pain, and nausea, with computed tomography findings of thickening at the level of gastroesophageal junction and abnormal areas of calcification. An upper GI endoscopy showed submucosal thickening at the gastroesophageal junction, with a slightly tortuous esophagus and irregular Z line. The clinical impression was an esophageal mass. The fine-needle aspiration diagnosis was spindle cell neoplasm. Upon resection, the mass had a gray-white, whorled, and focally calcified cut surface. Microscopically it demonstrated mild cellular fascicles of smooth muscle with numerous foci of calcification without significant nuclear atypia, mitotic activity, or necrosis. Properly controlled immunohistochemical stains showed the spindle cells to be diffusely positive for smooth muscle actin; however, stains for CD117 and CD34 were negative. These histologic features and immunohistochemical profile confirm the diagnosis of a leiomyoma. Symptomatic and large leiomyomas should be treated surgically, whereas small, asymptomatic lesions may be managed by regular follow-up and repeated endoscopies.

Collision Lymph Node Metastasis of Bladder Urothelial Carcinoma and Colonic Adenocarcinoma

(Kailee Imperatore, MD (kailee.imperatore@msmc.com); Robert Poppiti, MD. Department of Arkadi M. Rywlin MD Pathology and Laboratory Medicine, Mount Sinai Medical Center, Miami Beach, Fla.

Reference:

Collision tumors are 2 malignant neoplasms from separate primary sites that meet and eventually intermingle. Collision tumor cases are rare, but even rarer are collision metastases in a lymph node. We report the case of a 75-year-old woman who presented with a 2-day history of worsening abdominal pain. Her history is significant for a recent right lower-extremity deep vein thrombosis, which led to pulmonary embolism. Imaging showed a pelvic mass encasing the distal small bowel, right external iliac vessels, and distal right ureter; multiple enlarged mesenteric lymph nodes; thickening of the right colon; and bilateral pulmonary nodules. Cystoscopy revealed a large mass; biopsies showed invasive, high-grade urothelial carcinoma. Two days later, palliative surgery was done to relieve the intestinal obstruction, which was thought to be caused by direct invasion of the bladder tumor. Multiple segments of bowel were resected revealing a 10.5-cm primary colon adenocarcinoma extending through the wall of the colon into the distal 2 tumor deposits in the peri-intestinal fat, one with adenocarcinoma (CK20+ and CK7+ and p63+) and one with urothelial carcinoma (CK7+ and p63+ and CK20+); and 3 of 19 lymph nodes with metastatic carcinoma, one with adenocarcinoma, one with urothelial carcinoma, and one with both adenocarcinoma and urothelial carcinoma. This case is unique in that it is the first reported case of a collision metastasis in a lymph node consisting of both urothelial carcinoma and colonic adenocarcinoma.

Low-Grade Breast Adenosquamous Carcinoma: A Case Illustrating the Potential Pitfall of Misdiaugnosing a Low-Grade Tumor (Low-Grade Adenosquamous Carcinoma) for a High-Grade Tumor (Breast Carcinoma of the Basal Subtype)

(Paper No. 93)

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Low-grade adenosquamous carcinoma (LGASC) of the breast is a rare variant of metastatic carcinoma. Given its triple negative ER, PR, and HER2 biomarker profile and positive expression for basal markers, this entity can be mistaken for ductal breast carcinomas of the basal subtype by histomorphology, especially if the squamous differentiation is subtle, as in the following case. It is important to differentiate between these 2 entities given the significantly different clinical behavior and treatment decisions. This case illustrates the pathology pitfall of misdiagnosing a low-grade tumor (LGASC) for a high-grade tumor of the basal subtype. A 63-year-old woman presented with an infiltrative breast mass. The excisional biopsy was diagnosed as invasive ductal carcinoma. The carcinomatous glands displayed a triple-negative biomarker profile. Additional positive expression for basal immunohistochemical markers (EGFR, keratin 5) resulted in initially classifying this tumor as ductal carcinoma of the basal subtype. Upon review of the tumor, the discrepancy between the tumor’s bland histomorphology and its TN biomarker and basal immunohistochemical profile was observed. Consequently, after immunohistochemical marker validation, the rare entity of LGASC was suspected and confirmed by demonstrating the characteristic pattern of concomitant immunohistochemical expression of keratin 5 and a spectrum of diffuse, discontinuous, and absent myoepithelial (p63) marker expression in the infiltrative glands. Although this rare carcinoma is triple negative and displays positive expression for basal markers, it is associated with a good prognosis and local, complete excision is usually curative, unlike other triple negative and basal marker-positive breast carcinomas.

Clinicopathologic Features of Fibroadenoma With Atypia and Carcinoma In Situ: A Single Institution Experience

(Paper No. 94)

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Context: Fibroadenoma (FA) is a common, benign, biphasic tumor arising from the terminal-duct lobular unit and demonstrating epithelial and stromal elements. Usual ductal hyperplasia commonly arises within FAs. Atypical proliferations, carcinoma in situ (CIS), and invasive carcinoma arising within FAs is rare. This study’s purpose was to assess the clinical findings and follow-up pathology in patients with FA associated with atypia or carcinoma.

Clinical Findings Associated With Fibroadenoma

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases, No.</td>
<td>30</td>
<td>5</td>
<td>7</td>
<td>n/a</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>41.73 (14.13)</td>
<td>43.20 (13.16)</td>
<td>51.43 (15.77)</td>
<td>.28</td>
</tr>
<tr>
<td>BIRADS score, mean (SD)</td>
<td>3.79 (0.86)</td>
<td>3.75 (0.50)</td>
<td>4.60 (0.78)</td>
<td>.08</td>
</tr>
<tr>
<td>Parity</td>
<td>1.4</td>
<td>1.3</td>
<td>1.86</td>
<td>.75</td>
</tr>
<tr>
<td>Family history of breast</td>
<td>No.</td>
<td>positive</td>
<td>No.</td>
<td>negative</td>
</tr>
<tr>
<td>cancer</td>
<td>4 (23)</td>
<td>2 (3)</td>
<td>0 (7)</td>
<td>.16</td>
</tr>
<tr>
<td>Oral contraceptive use</td>
<td>No.</td>
<td>yes</td>
<td>No.</td>
<td>no</td>
</tr>
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<td>6 (21)</td>
<td>0 (5)</td>
<td>0 (7)</td>
<td>.20</td>
</tr>
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Abbreviations: BIRADS, breast imaging reporting and data system; n/a, not applicable.

Design: The FAs diagnosed from 2007 to 2013 were reviewed and categorized as follows: group 1, FAs with usual ductal hyperplasia; group 2, FAs with atypical proliferations including atypical ductal hyperplasia, atypical lobular hyperplasia, and flat epithelial atypia; and group 3, FAs with ductal CIS or lobular CIS. Patients with a history of carcinoma were excluded. Patient history was reviewed.

Results: The clinical findings, as seen in the Table, were not significantly different between the 3 groups. However, the BIRADS score was notably higher in group 3. Within the 30 FA cases in group 1, one developed invasive carcinoma 12 months later. Group 2 had 5 FA cases, 3 of which included atypical ductal hyperplasia, whereas 2 included atypical lobular hyperplasia. Of the 7 FA cases in group 3, there were 3 with ductal CIS, 3 had lobular CIS, and 1 case had both.

Conclusions: Atypical proliferations and CIS are rarely detected within FAs. A higher BIRADS score might be a good screening indicator for cases in which there is concurrent atypia or carcinoma arising within a FA on follow-up pathology. This will warrant further follow-up with excision to confirm the diagnosis and exclude malignancy.

Bilateral Metachronous Phyllodes Tumor of Breast in a Patient With Crohn Disease

(Paper No. 95)

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Phyllodes tumor (PT) is a rare neoplasm accounting for about 1% of all breast tumors. Bilateral disease is even more infrequent. Patients with Crohn disease (CD) have a slight increase in extraintestinal malignancies, but currently no association between PT and CD has been reported. Although chronic immunosuppression is known to increase the risk of malignancy, very scant data exist on immunosuppression and development of breast fibroepithelial neoplasms. We present a case of bilateral metachronous PT in a 48-year-old woman with CD. At age 34 years, she had a right breast mass, which proved to be a low-grade, malignant PT on lumpectomy. Three years later, she developed unilateral recurrence and underwent total mastectomy. Microscopy showed a similar low-grade, malignant PT. The patient was also diagnosed with CD in her middle thirties. She was on immunosuppressive regimen, which included azathioprine and had a colectomy at age 41. At age 47 years, the patient developed a 7-cm mass in the contralateral breast and underwent lumpectomy. Microscopy showed high-grade malignant PT with subepithelial stromal condensation, atypical spindle stromal cells, 20 mitoses per 10 high-power field, and no stromal overgrowth. The tumor cells were negative for pankeratin, Cam 5.2, cytokeratin 5/6, p63, SM myosin, and CD10. Positive margins on lumpectomy led to subsequent mastectomy, which showed residual microscopic nodules with malignant periductal stroma. This report presents a rare case of association between CD, immunosuppression, and recurrent malignant PT.
Carcinoma-Associated Schistosoma: Report of 2 Cases

(Paper No. 96)
Rico P. Lasaca, MD (rplasaca@gmail.com). Department of Laboratory, St Paul’s Hospital, Tacloban City, Leyte, Philippines.

Schistosomiasis is considered one of the most common parasites afflicting humans globally. The relationship between carcinoma and the parasite is still controversial. We report 2 cases of cancer associated with Schistosoma sp. Case 1 involves a 73-year-old woman who underwent modified radical mastectomy. The resected lesion had invasive ductal carcinoma with several deposits of Schistosoma japonicum ova. Case 2 involves a 65-year-old man who underwent exploratory laparotomy (colon resection). Permanent sections of the second case disclosed a well-differentiated colonic adenocarcinoma with several ova deposits of Schistosoma japonicum. These cases are presented to contribute additional data to the available literature on the association of malignancy with an infectious parasitic process.

Correlation Between Magnetic Resonance Imaging (MRI) Findings and Gross and Microscopic Pathology in Breast Surgical Specimens After Neoadjuvant Therapy: A Review of 30 Cases

(Paper No. 97)
Kevin Neill, MD, MPH1; Cliff Bernstein, MD2; Jingqiu Liu, MD, PhD3; Sui Zee, MD3; Jules Cohen, MD2; Meenakshi Singh, MD2; Brian O Hea, MD4; Carmen Tornos, MD4. Departments of 1Pathology, 2Radiology, 3Medicine, and 4Breast Surgery, Stony Brook Medicine, Stony Brook, NY.

Context: Breast MRIs are often performed to evaluate the extent of disease before neoadjuvant therapy, after treatment, and before surgery to assess tumor response.

Design: We reviewed 30 breast specimens from patients who received neoadjuvant chemotherapy. Twenty-three patients underwent total mastectomy, and 7 patients had lumpectomies performed after the completion of therapy. Breast magnetic resonance imaging (MRI) was performed at baseline and preceding surgery. We compared the response to therapy based on MRI assessment with the findings on gross and microscopic examination of the surgical specimens. A copy of the MRI report was available at the time of grossing for correlation in all cases. Samples were taken from all areas of concern identified on MRI to correlate with histologic diagnosis.

Results: In 22 cases (73.3%), the MRI detected the presence of residual tumor with an accuracy of ±5 mm (14 cases) or the presence of a complete response confirmed by microscopic examination (8 cases). In 4 cases, the size of the residual carcinoma was overestimated on MRI by more than 1.5 cm (Table). In 4 cases, the size of the carcinoma was underestimated by MRI (Table).

Conclusions: An MRI is an accurate method of evaluating response to neoadjuvant chemotherapy in 73.3% of cases. In this study, overestimation of residual tumor by MRI was seen in 13.3% of cases (strongly associated with florid fibrotic reaction) and underestimation in 33.3% of cases. Underestimation by MRI in select cases may reflect the inherent limitations of identifying viable carcinoma in treated tissues on a microscopic level.

<table>
<thead>
<tr>
<th>Cases of Residual Carcinoma Overestimated and Underestimated on MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case No.</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Cases of residual carcinoma overestimated on MRI</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>Cases of residual carcinoma underestimated on MRI</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
</tbody>
</table>

Abbreviations: CR, complete response; DCIS, ductal carcinoma in situ.

Clinicopathologic and Immunohistochemical Characteristics of HER2+ Invasive Lobular Carcinoma

(Paper No. 98)
Ihab Lamzabi, MD (Ihab_Lamzabi@rush.edu); Aparna Harbhajanka, MD; Richa Jain, MD; Ritu Ghai, MD; Sahir Syed, MD; Paolo Gattuso, MD. Department of Pathology, Rush University Medical Center, Chicago, Ill.

Context: HER2 amplification is well studied in invasive ductal carcinoma of the breast. However, there is sparse literature regarding invasive lobular carcinoma (ILC) with HER2 amplification. The aim of this study was to investigate this subgroup of breast carcinomas.

Design: E-cadherin-ILCs were selected from 2000 to 2012. Retrospective analysis of variable clinicopathologic parameters and IHC stains for ER, PR, E-cadherin, HER2, MIB-1, and fluorescence in situ hybridization (FISH) for HER2 were retrieved from the surgical pathology files of 255 ILC cases. Additional immunohistochemistry markers, including p53, c-KIT, vimentin, p16, cyclin D1, and BCL2, were performed in 39 classic ILC (CILC) and 36 pleomorphic ILC (PILC) cases. SPSS software (IBM, Armonk, NY) was used for statistical analysis.

Results: A total of 255 cases of ILC were identified. Two hundred nineteen (86%) cases were CILC; 36 (14%) were PILC; 77 (30.2%) showed axillary lymph node metastases, 15 (5.88%) showed HER2 amplification by FISH analysis. Of which were pleomorphic and 10 were classical (P = .04). HER2 amplification was more frequently seen in elderly patients (P = .02). In comparison to HER2+ cases, HER2+ cases showed higher T stage (P = .04), higher recurrence rate (P = .04), more distant metastases (P = .04), less multifocality (P = .06), PR negativity (P < .001), higher MIB index (P = .006), and higher cyclin D1 expression (P = .001). Disease-free survival was lower in HER2 overexpressing ILC (P < .01).

Conclusions: The ILC with HER2 amplification showed distinct clinicopathologic and IHC characteristics, conferring an overall worsened prognosis. Interestingly, HER2-amplified cases show higher cyclin D1 expression, suggesting a possible induction by ERBB signaling pathway.

Correlation of Perineural Invasion and Lymphovascular Invasion With Clinicopathologic Parameters and Its Role as a Prognostic Factor in Patients With Invasive Lobular Breast Cancer

(Paper No. 99)
Aparna Harbhajanka, MD (aparna_harbhajanka@rush.edu); Ihab Lambzabi, MD; Richa Jain, MD; Sahr Sayed, MD; Jamie M. Slade, MD; Paolo Gattuso, MD. Department of Pathology, Rush University, Chicago, Ill.

Context: Lymphovascular invasion (LVI) is an important prognostic factor in patients with invasive breast cancer. Little is known about its correlation with other clinical and pathologic features of invasive lobular carcinoma (ILC). Prognostic value of perineural invasion (PNI) is unclear and controversial in breast cancer. The aim of this study was to analyze the prognostic significance of LVI and PNI in patients with ILC and to correlate it with clinicopathologic parameters to understand the biology of a tumor undergoing invasion.

Design: Two hundred sixty-two patients from 2000 to 2012 were reviewed for clinicopathologic parameters and immunohistochemical stains for ER, PR, E-cadherin, HER2, and MIB-1.

Results: Of 262 ILC cases, 14 (5.3%) and 30 (11.45%) showed PNI and LVI, respectively. Of the 14 patients with PNI, 5 (35.7%) had LVI. Both PNI and LVI were associated with higher T stage and positive lymph node status. The LVI was associated with the pleomorphic type (P = .02), a lack of vimentin (P = .06), a tumor size of 2 cm (P < .001), and positive lymph node status (P < .001), but not with ER, PR, HER2, MIB-1, or p53. The mean age was 65 years. The LVI was a significant independent prognostic factor for disease-free survival (DFS) (P < .002). Multivariate analysis revealed that LVI (P = .006) was an even better prognostic factor than positive lymph node status (P = .03). Perineural invasion was not a prognostic factor for DFS.

Conclusions: A LVI should be considered in the therapeutic strategy as a decision-making tool in the adjuvant chemotherapy setting. A PNI is a relatively rare histologic feature in ILC occurring less frequently than LVI. Tumor characteristics associated with PNI include higher T stage, positive lymph node status, and LVI. The role of PNI as a poor prognostic feature remains questionable.
Breast Carcinoma in Nonagenarians: An Institutional Experience
(Poster No. 100)
Ronald N. Araneta III, MD (ronaldaraneta@hhchealth.org); Mary Fiel-Gan, MD; Margaret Assaad, MD; Andrew Ricci Jr, MD. Department of Pathology, Hartford Hospital, Hartford, Conn.

Context: A number of breast carcinoma cases in the elderly are seen at our institution.

Design: Data of the Hartford Hospital Tumor Registry files from 2000 to 2012 of patients 90 years and older presenting with breast carcinoma were analyzed; histology, stage, and treatment modalities in this patient population were assessed.

Results: Sixty-one patients were retrieved from the registry files, with ages ranging from 90 to 103 years (mean, 94.2 years). Histology showed 6 in situ and 55 invasive (67.3% ductal [n = 37]; 9.1% lobular [n = 5]; and 23.6% mixed [n = 13]) carcinomas. Most tumors were positive for ER and PR, and 9 were positive for HER2-nu. See Table for stage and mode of treatment.

Conclusions: (1) There are a significant number of breast carcinoma cases in nonagenarians and above. (2) Most are invasive with some at advanced stage. (3) Many patients can tolerate surgical treatment, but fewer were given radiation, and none had chemotherapy; hormonal therapy was offered to node-positive patients. (4) Continued surveillance should be made among this patient population to catch breast carcinomas at an early, resectable stage. (5) Analysis of complications from treatment and survival data was compiled to determine success of therapy.

The Importance of Neuroendocrine Differentiation in Mammary Carcinoma
(Poster No. 101)
Ian-Marie Lano, MD (ali.saad@saskatoonhealthregion.ca); Louise Quenneville, MD; Ali G. Saad, MD. Department of Pathology, Saskatoon Health Region, Saskatoon, Saskatchewan, Canada.

Context: The significance of neuroendocrine (NE) differentiation in invasive mammary carcinoma (IMC) is controversial, in particular for those with <50% NE marker-positive tumor cells. We evaluate the clinicopathologic characteristics of IMC with NE differentiation with emphasis on those with <50% NE differentiation.

Design: A representative tumor section from patients with IMC was immunostained with synaptophysin. Cases with 50% or more synaptophysin-positive tumor cells were designated NE carcinoma (according to the World Health Organization), whereas those with less than 50% were designated IMC with NE features.

Results: A search of the electronic database in our center resulted in 88 cases of invasive breast carcinomas, 69 cases of IMC with NE features, and 81 patients with no NE expression (control group). These 3 groups were matched for age. Patients with less than 50% NE cells tended to show higher rates of HER2 amplification (P = .01) but no difference in tumor grade or stage when compared with the control group. When compared with the control group and the group with less than 50% NE cells, NE carcinomas showed higher tumor grade and stage and more-frequent negative hormone receptors and HER2 amplification.

Conclusions: This is the largest series of patients with IMC and NE differentiation. Of special interest, patients with IMC and NE features showed a high rate of HER2 amplification compared with the control group. This may explain, at least in part, the occasional aggressive behavior of these tumors. In line with other studies, NE carcinoma showed higher grade and stage compared with the control group.

Is Sentinel Lymph Node Frozen Section Examination for Diagnosis of Metastatic Breast Cancer Cost Effective?
(Poster No. 102)
Sadia Sultana, MD (sadia.sultana@bbsala.com). Department of Pathology, Baptist Health System, Birmingham, Ala.

Context: Intraoperative analysis of the sentinel lymph node (SLN) by frozen section (FS) allows for immediate axillary lymph node dissection (ALND) in cases of metastatic disease in patients with breast cancer. The aim of this study was to evaluate the benefit of intraoperative FS, reduce false-negative rates, and determine its cost effectiveness in the management of patients with breast cancer.

Design: A retrospective analysis of intraoperative lymph node FS on 233 patients between 2008 and January 2014 was performed. The FS diagnoses were compared with the final diagnoses (after additional levels and immunohistochemistry).

Results: The final diagnosis was positive for metastatic involvement in 80 cases. There were 65 true-positives (27.89%) with 51 containing macrometastases (Ma), 2 false-positives (0.9%), and 17 false-negatives (7.3%) with 14 having micrometastases (Mi) and isolated tumor cells (ITCs). Therefore, the false-negative rate was 20.73%. The SLN was negative in 153 cases.

Conclusions: In our community hospital, FS is associated with a high false-negative rate (20.73%). This raises the question of how to reduce the false-negative rate and increase the cost effectiveness of performing FS on SLN in the current health care era. An FS diagnosis is adequate to identify macrometastasis. However, formalin-fixed, paraffin-embedded sections and immunohistochemistry are superior for identifying micrometastasis and ITCs.

Sentinel Lymph Node Evaluation: A Prospective Comparison of Gross and Microscopic Intraoperative Examination
(Poster No. 103)
Daniel Olsen, MD (daniel.olsen@vtmednet.org); Donald Weaver, MD; Abiy Ambaye, MD. Department of Pathology, University of Vermont, Burlington, Vt.

Context: The sensitivity of detecting metastatic breast cancer in sentinel lymph nodes (SLN) using intraoperative cytologic examination (ICE) ranges from 36.5% to 95%; ICE may lead to increased detection of clinically insignificant micrometastases and isolated tumor cell clusters (ITCs). Intraoperative gross and microscopic examination (IGE) of SLNs may be an alternative strategy for preferentially detecting macrometastases (MM) now that completion axillary dissection (ALND) is being questioned for micrometastases and ITCs.

Design: We prospectively gathered IGE and ICE data during intraoperative SLN evaluation from 2005 to 2007. Each pathologist performed IGE of each SLN followed by microscopic examination using ICE. All SLNs were sectioned at 2-mm intervals, processed for permanent histologic examination (PHE), and examined using hematoxylin-eosin stains.

Results: Of a total of 565 SLNs from 175 consecutive, clinically node-negative patients were reviewed. Overall, detection sensitivity for IGE was 29% (9/31) and for ICE was 71% (22/31). The MM sensitivity for IGE and ICE were 44% and 89%, respectively. All 22 patients positive by ICE had immediate ALND. However, only 1 of 11 patients with positive SLN on ICE selected subsequent completion ALND (Table).

Conclusions: IGE has higher sensitivity than ICE for detection of any SLN metastases and or MM. Patients may not elect ALND even when MM is detected by PHE. Thus, ICE appears to be an option for patients reluctant to undergo immediate ALND for SLN micrometastases or ITCs. Although all patients with positive intraoperative SLNs underwent completion ALND (100%), only 1/11 (9%) underwent subsequent completion ALND when a positive SLN was identified on PHE.

Size of Sentinel Lymph Node Metastases on Intraoperative Gross (IGE), Intraoperative Cytology (ICE), and Permanent Histologic Examination (PHE)

<table>
<thead>
<tr>
<th>Metastases</th>
<th>Total, No.</th>
<th>IGE, No.</th>
<th>ICE, No.</th>
<th>PHE, No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrometastases</td>
<td>8</td>
<td>0</td>
<td>3</td>
<td>22</td>
</tr>
<tr>
<td>Micrometastases</td>
<td>16</td>
<td>3</td>
<td>3</td>
<td>22</td>
</tr>
<tr>
<td>Isolated Tumor Cells</td>
<td>19</td>
<td>9</td>
<td>4</td>
<td>31</td>
</tr>
</tbody>
</table>
**Autofluorescence Reduction and Cross-Talk Correction in a Whole-Slide Digital Pathology System**

*(Poster No. 104)*

James Mansfield, PhD, James Mansfield | Clifford Hoyt, PhD | Kent Johnson, PhD | Peter Miller, PhD | Department of Quantitative Pathology | PerkinElmer, Hopkinton, Mass.

For research applications in pathology and for fluorescence in situ hybridization imaging there is a growing need to scan an entire slide in fluorescence for digital archiving of ephemeral fluorescence and to enable digital analyses. However, fluorescence scanning has issues that have limited its practical use. One is interference from tissue autofluorescence. Formalin-fixed, paraffin-embedded tissues inherently have a strong, intrinsic autofluorescence signal that masks the fluorescent signal of interest and limits legibility. Another is fluorophore cross talk or bleed through, in which the signal from one fluorophore appears inappropriately in a neighboring fluorescence channel. Both problems can lead to incorrect slide assessment. We have developed a whole-slide scanning system that is able to unmix or separate tissue autofluorescence from real fluorophore signal by scanning one extra fluorescent channel using a novel spectral-signature development methodology. To develop the spectral signatures, a negative control sample was used to measure and ensure the autofluorescence spectrum and spectral signatures of the fluorophores were synthetically derived. Six breast cancer samples stained with DAPI, ER (FITC), and PR (Cy3) were scanned and compared with standard imaging methods. Whole-slide scanning with autofluorescence reduction produced images with markedly lower autofluorescence than standard imaging methods. Whole-slide scanning was able to scan an entire slide in a fraction of the time required with standard imaging methods.

**Utility of Immunohistochemical Markers in Irradiated Breast Tissue: An Analysis of the Role of Myoepithelial Markers, p53, and Ki-67**

*(Poster No. 106)*

Kaeley E. Anderson, BA | anderkae@ohsu.edu | Elizabeth M. Williams, MD | Megan L. Troxell, MD, PhD | Department of Pathology, Oregon Health and Science University, Portland, Ore.

**Context:** The diagnosis of recurrent/de novo carcinoma in a background of radiation atypia (RA) is difficult, especially on small biopsies. The utility and characteristics of immunostains for myoepithelial cells have not been previously studied in irradiated breast. We also explored the utility of the proliferative marker Ki-67 and the tumor suppressor protein p53 in discriminating RA from carcinoma.

**Design:** We identified 29 irradiated breast resection specimens with RA, +/− carcinoma in situ (CIS), and invasive carcinoma. Blocks were stained with antibodies to the myoepithelial proteins p63, smooth muscle myosin heavy chain, calponin, Ki-67, and p53. Nonirradiated breast tissue was also stained with Ki-67 and p53 (CIS, normal, contralateral).

**Results:** In irradiated breast, myoepithelial markers demonstrated abundant myoepithelial cells in all RA and nearly all CIS, with focal stain attenuation seen with smooth muscle myosin and calponin in CIS. As expected, myoepithelial cell staining was absent in invasive carcinoma. p63 staining revealed unique nuclear morphology in RA including multinucleation and nucleomegaly. p53 staining was increased in irradiated nonneoplastic breast when compared with controls ($\text{t}[43] = 2.66, P = .01$); however, irradiated CIS had lower p53 staining when compared with control CIS ($t[20] = 3.19, P = .005$) (Table).

**Conclusions:** Immunohistochemical staining for myoepithelial markers is a useful diagnostic adjunct in irradiated breast, with caveats similar to nonirradiated breast. Ki-67 is elevated in some cases of CIS as compared with RA, similar to nonirradiated breast. Surprisingly, CIS in irradiated breast had attenuated p53 staining as compared with nonirradiated CIS, which may indicate different activity of this tumor suppressor pathway postirradiation.

**Table:**

| Ki-67 and p53 in Irradiated Nonneoplastic Tissue and CIS Compared With Controls |
|---|---|---|---|
| Tissues, No. | XRT RA (Benign) | Control Benign | XRT CIS | Control CIS |
| Ki-67, % | 26 | 19 | 12 | 10 |
| p53, % | 12 | 2 | 14 | 23 |

**Unilateral Malignant Adenomyoepithelioma of the Breast With Contralateral Extensive Ductal Carcinoma In Situ**

*(Poster No. 107)*

Arch Pathol Lab Med—Vol 138, September 2014  Abstracts  e33
in situ with similar cytomorphology led us to the high-grade primary invasive ductal carcinoma diagnosis. Our case differs from the previously reported studies of primary invasive ductal carcinoma because we observe TTF1 positivity only in the invasive component and not in the in situ component of the tumor. This suggests that more research is needed to explain not only the occasional TTF1 positivity in primary invasive ductal breast carcinoma but also the different TTF1 reactivity that may occur in the invasive and in situ components of the tumor when it is high grade.

**Transgeln: A New Diagnostic and Prognostic Marker for Triple-Negative and Non–Triple-Negative Breast Cancers**  
(Poster No. 109)

**Deepthi Rao, MBBS\(^1\) (drao@kumc.edu); Bruce Kimler, PhD\(^2\); Warren Nothnick, PhD\(^3\); Marilyn Davis, BS\(^3\); Fang Fan, MD, PhD\(^2\); Ossama Tawfik, MD, PhD.\(^2\) Departments of \(^1\)Pathology and Laboratory Medicine, \(^2\)Radiation Oncology, \(^3\)Molecular Integrated Physiology and Pathology, Image Analysis and Cytodiagnostic Services, University of Kansas Medical Center, Kansas City, Kan.

**Context:** Triple negative (TN) breast cancers are aggressive, rapidly growing, hormonally nonresponsive tumors diagnosed at later stage with shorter overall survival. The TN tumors have recently been shown to be a molecularly, pathologically, and clinically heterogeneous subgroup of breast cancer. Although most TN tumors are of the basal type, many are not, making it difficult identifying target markers for effective treatment strategies. Transgeln (TGLN) is a 22-kDa actin-binding protein of the calponin family. It is one of the earliest markers of smooth muscle. TGLN has been shown to have important biology activities including regulating muscle contractility, cell migration, and lately as a tumor suppressor.

**Design:** TGLN expression was examined as a function of tumor size, grade, histologic type, lymph node (LN) status, overall survival, ER, PR, HER2, and Ki-67 in 101 tumors, including 34 luminal A, 28 luminal B, 4 HER2, and 34 basal types.

**Results:** TGLN positivity (defined as 2+ or 3+) was associated with more-aggressive tumors (18% of grade I tumors were TGLN\(^2\)-versus 5% of grade II tumors; P < .05). TGLN positivity correlated with high Ki-67 and with low ER and PR (P < .001) but was not associated with tumor size, patient’s age, or LN metastasis. There was a significant difference between TN (n = 35) and non-TN (n = 66) tumors in their relationship to TGLN positivity (74% versus 11%, respectively; P < .001).

**Conclusions:** TGLN appears to be a potentially excellent diagnostic and prognostic tumor marker of breast tumors. Our results suggest there may be value for using TGLN in stratification of patients and in selecting patients for treatment.

**Granular Cell Tumors of the Breast: A Clinicopathologic and Immunohistochemical Study**  
(Poster No. 110)

**Rohit I. Singh, MD (rohit_i_singh@rush.edu); Lauren E. Rosen, MD; Ihab Lamzabi, MD; Vijaya Reddy, MD; Pincas Bitterman, MD; Paolo Gattuso, MD. Department of Pathology, Rush University Medical Center, Chicago, Ill.

**Context:** Granular cell tumor (GCT) of the breast is a rare neoplasm affecting mostly premenopausal African-American women. Despite the benign nature of this tumor, it may mimic invasive breast carcinoma clinically and radiologically, making the diagnosis challenging.

**Design:** Twelve cases of GCT were identified (December 1992 to June 2013). Clinicopathologic data were reviewed, and immunohistochemistry for estrogen receptor (ER), progesterone receptor (PR), S100, and mammaglobin was performed on paraffin-embedded tissue.

**Results:** See Table. Six of the 12 women (50%) were white, 5 were African American (42%), and one was Hispanic (8%). Age at excision ranged from 20 to 78 years (median, 54.5 years). Right and left breasts were equally affected. Tumors ranged in size from 0.2 cm to 3.0 cm (average, 1.8 cm). Three patients had history of breast carcinoma, all occurring in the same breast as the GCT; one was synchronous and the other 2 metachronous. One patient developed recurrent GCT 4 years after the original tumor was excised. All cases of GCT were positive for S100 and negative for mammaglobin. One case showed focal positivity for ER and PR, whereas the others were negative.

**Conclusions:** GCTs can occur as synchronous or metachronous tumors with breast carcinoma; therefore, clinically and radiologically, they may mimic invasive carcinoma. Despite racial heterogeneity of our patient population, we encountered a greater number of GCTs.
cases in white women. These tumors have potential for local recurrence if incompletely excised. Mammaglobin, ER, and PR negativity, and S100 positivity are consistent with Schwann cell origin of GCT of breast.

<table>
<thead>
<tr>
<th>Clinicopathologic and Immunohistochemical Data of 12 Cases of Granular Cell Tumor of Breast</th>
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<tbody>
<tr>
<td><strong>Age, y/ Race</strong></td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>64/white</td>
</tr>
<tr>
<td>55/white</td>
</tr>
<tr>
<td>20/white</td>
</tr>
<tr>
<td>63/Hispanic</td>
</tr>
<tr>
<td>67/African-American</td>
</tr>
<tr>
<td>43/African-American</td>
</tr>
<tr>
<td>54/African-American</td>
</tr>
<tr>
<td>40/white</td>
</tr>
<tr>
<td>42/white</td>
</tr>
<tr>
<td>21/African-American</td>
</tr>
<tr>
<td>62/white</td>
</tr>
<tr>
<td>78/African-American</td>
</tr>
</tbody>
</table>

Breast Carcinoma in Young Women: A Correlation of Pathologic Features and Biomarkers

Payal Shrivastava, MD (payal.stva@gmail.com); Diganta Hazarika, MD; Mary Nandini Singh, MD. Department of Pathology, Health Care Global Oncology, Bangalore, India.

**Context:** Breast cancer in young patients is uncommon, yet of considerable interest because of its unfavorable prognosis and differences in tumor morphotype and biomarker expression profile compared with those in older women. This study sought to analyze the effect of age (<40 years versus >50 years) on histopathologic features and biomarker expression in patients with breast cancer. 

**Design:** One hundred patients with breast cancer (50 patients each in the young [<40 years] study group and older [>50 years] control group) were studied for histopathologic characteristics and biomarker (ER, PR, HER2/neu, EGFR, p53, Ki-67) expression. The χ² test, Shapiro-Wilk s test, and Mann-Whitney U test were used for statistical analysis. Statistical values of P < .05 were considered significant.

**Results:** The young age group showed significantly greater poorly differentiated, high-grade tumors (P = .03), and tumor necrosis (P = .04). Tumor type, tumor size, tumor location, and tumor stage (pTNM) did not differ significantly between the 2 groups. Biomarker analysis showed the younger age group had significantly greater ER+ tumors (P = .04), higher proliferation rate (Ki-67; P = .03), more triple-negative tumors (P = .02), HER2/neu overexpression and p53 and EGFR positivity were higher in the younger age group (although not statistically significant).

**Conclusions:** The current study indicates that breast cancer in young women exhibits a more-aggressive phenotype in tumor grade and biomarker profile. These tumors have greater hormone receptor–negative status, more triple negativity, and higher proliferation index than do those from the older age group.

Squamous Cell Carcinoma of the Breast

Payal Shrivastava, MD; Mary Nandini Singh, MD; Diganta Hazarika, MD. Department of Pathology, Health Care Global Oncology, Bangalore, India.

A 59-year-old woman presented with an abnormal mammogram. The mammogram showed a slightly irregular, mildly lobular, marginated nodule located in the upper, outer quadrant of her left breast. The nodule measured 7 × 5 × 5 mm. An ultrasound-assisted biopsy was performed and revealed a solid tumor composed of squamous cells in a background of keratin pearls. There were 20 mitoses per 10 high-power fields. Immunohistochemical staining showed diffuse (>90%) positivity for p63 and focal positivity for CK7. A diagnosis of squamous cell carcinoma, moderately to poorly differentiated, was rendered. ER, PR, and HER2/neu were negative. A wire-guided needle localization lumpectomy with sentinel lymph node biopsy was performed. The sentinel lymph node was negative. The lesion measured 8 × 7 × 6 mm within the left breast. All margins were negative. The patient was treated with adjuvant radiation therapy and was negative for recurrence at both the 6-month and 1-year follow-up appointments.

Liver Metastasis and Elevated Serum Chromogranin A Levels Prompt Reclassification of an Invasive Carcinoma of the Breast Diagnosed 2 Years Previously

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A 63-year-old woman with a history of right breast invasive ductal carcinoma, no special type, presented with upper-quadrant abdominal pain. Computed tomography revealed liver lesions suspicious for metastatic disease. Although serum CEA and CA 27.29 levels were elevated, supporting recurrent breast carcinoma, chromogranin A levels were also elevated, suggesting neuroendocrine malignancy. Biopsy of the liver lesions revealed a poorly differentiated carcinoma. A panel of immunohistochemical stains was ordered. Estrogen receptor, synaptophysin, and chromogranin were positive, CK7 and CA19.9 were focally positive, and progestrone receptor, HER2, CK20, TTF1, and CDX2 were negative. The primary breast carcinoma diagnosed 2 years previously was reviewed and demonstrated a poorly differentiated, invasive ductal carcinoma that was strongly hormone receptor positive and HER2 negative. At that time, the patient underwent right breast excision and sentinel lymph node biopsies. The invasive carcinoma measured 2.7 cm, with 2 foci of lymphovascular invasion, negative margins, and 2 negative sentinel lymph nodes. Oncotype DX recurrence score was 14 (low risk). The patient received adjuvant radiation and tamoxifen. Chemotherapy was offered, but the patient declined it at that time. Although the immunohistochemical profile of the metastatic carcinoma, primarily the estrogen receptor, CK7, and CK20 results, supported metastasis from a primary breast origin, chromogranin and synaptophysin immunostains were repeated on the breast primary for confirmation. The primary breast carcinoma showed 100% of tumor cells staining for synaptophysin and focal staining with chromogranin. The breast carcinoma was subsequently reclassified as invasive ductal carcinoma with neuroendocrine differentiation.
Loss of Myoepithelial Cell Markers in High-Grade Ductal and Pleomorphic Lobular Carcinomas In Situ

Paolo Cotzia, MD1; Laura Biederman, MD; Alessandro Bombonati, MD; Juan P. Palazzo, MD. 1Department of Pathology, Thomas Jefferson University Hospital, Philadelphia, Pa.

Context: The detection of myoepithelial (ME) cells has been studied in several breast lesions for evaluation of tumor invasion. However, little is known about these markers in mammary carcinomas in situ.

Design: To analyze the ME cells in ductal carcinoma in situ (DCIS), lobular carcinoma in situ (LCIS), and invasive carcinoma, immunohistochemical staining for p63 and calponin was performed in 70 cases of breast carcinoma (56 DCIS with and without invasion and 14 LCIS). Low- and high-grade DCIS as well as classic and pleomorphic LCIS were selected. Benign ducts were used as internal control.

Results: p63 showed decreased expression in ME cells in high-grade DCIS and DCIS associated with invasive ductal carcinoma. High-grade DCIS and DCIS associated with invasive carcinoma showed a marked reduction of calponin, and some cases showed absence of staining. In classic LCIS the expression of p63 and calponin was preserved. A reduction of p63 and calponin as well as complete loss of staining was seen in pleomorphic LCIS in the absence of invasive carcinoma. Most cases showed heterogeneity in the staining pattern with both antibodies.

Conclusions: When evaluating ME cells it is important to interpret the stains with attention to the histologic features of the lesion. High-grade DCIS and pleomorphic LCIS may lack expression of p63 and calponin. Decreased ME markers in the in situ lesions frequently precede the development of invasive carcinoma. The use of multiple ME markers is recommended given their heterogeneous and negative expression in high-grade in situ carcinomas.

Benign Breast Disease, Atrophy, and Subsequent Breast Cancer Risk Among African-American Women

Baraa Alish, MD; Michele Cote, PhD1 (mcoate@med.wayne.edu); Sudeshna Bandyopadhyay, MD; Julie Ruterbusch, MS; Quratalain Ahmed, MD; Haitham Arabi, MD; Emaan Abdulrahim, MD; Marlene Frost, PhD; Derek Radisky, PhD; Daniel Visscher, MD; Rouba Ali-Fehmi, MD. 1Department of Pathology, Wayne State University, Detroit, Mich; 2Department of Pathology, Mayo Clinic, Rochester, Minn; 3Department of Pathology, Mayo Clinic, Jacksonville, Fla; 4Department of Pathology, Mayo Clinic, Rochester, Minn.

Context: African-American (AA) women suffer from disproportionately high breast cancer mortality rates, yet the risk factors are not well characterized in this group. The presence of atrophy in benign tissue appears to be associated with breast cancer development; however, it is unknown to what extent those parameters can be directly applied to AA women.

Results: We identified 1428 benign breast biopsies from AA women from our pathology database. Women aged 18 to 85 years undergoing a breast biopsy from 1997 to 2000 were included. Lesions were classified based on DuPont and Page criteria. Presence of atrophy, apocrine metaplasia, ductal hyperplasia, lobular hyperplasia, cysts, duct ectasia, fibrosis, sclerosing adenosis, and degree of atrophy (0%, 1%–75%, >75%) was determined. Follow up for subsequent breast cancer was documented from the SEER database. We compared our cohort to a white cohort at the Mayo Clinic.

Conclusions: The protective effects of breast atrophy are evident in both AA and white women, despite the presence of other lesions that may be associated with increased risk of breast cancer.

Expression of SMURF2, a Ubiquitin Ligase, Is Decreased in Triple-Negative Breast Ductal Carcinoma

Ashley Flowers, MD1 (aflowers@sluhsc.edu); Hiroaki Kiyokawa, MD, PhD; Xin Gu, MD. 1Department of Pathology, Louisiana State University Health Sciences Center, New Orleans, LA.

Context: SMURF2 is a ubiquitin ligase involved in diverse biologic events, such as cell division, cell polarity, cell migration, and receptor signaling. Evidence suggests that SMURF2 is a tumor suppressor and has important roles in cancer development. This project examines immunohistochemical expression of SMURF2 in breast-infiltrating...
ductal carcinomas and analyzes correlations between SMURF2 expression and ER, PR, and HER2/neu status.

**Design:** Tissue from 51 cases of triple-negative infiltrating ductal carcinoma and 51 cases of receptor-positive infiltrating ductal carcinoma were analyzed. SMURF2 expression was detected by immunohistochemistry using polyclonal anti-SMURF2 antibody (Santa Cruz Biotechnology, Dallas, Tex). SMURF2 staining was scored as 1⁺, 2⁺, or 3⁺ according to the percentage of tumor cells staining and intensity of staining. The results were analyzed by a 2 sample proportion z test.

**Results:** The triple-negative cases had statistically significant decreased expression of SMURF2 compared with receptor-positive cases. When comparing unequivocal high SMURF2 expression (2⁺/3⁺), 80.4% of receptor-positive cases were unequivocally positive, whereas only 56.9% of the triple-negative cases displayed unequivocally positive staining (P < .05). In contrast, decreased SMURF2 expression (1⁺) was observed in 19.6% of receptor-positive cases compared with 43.1% of triple-negative cases (P < .05) (Figure 4). The triple-negative cases had statistically significant decreased expression of SMURF2 in tumor cells as associated with invasive breast cancers. We also report a new finding that expression is decreased more often in triple-negative breast carcinomas.

The Integrin α6β4 Is Elevated in Triple-Negative and HER2-Positive Breast Cancers

**Poster No. 119**

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**Context:** Integrins are heterodimeric proteins that bind extracellular matrices and contribute to cancer progression. Integrin α6β4 has been implicated in tumor development and invasion and is associated with aggressive behavior and poor prognosis in many human malignancies. Although integrin α6β4 can promote tumor progression, it relates to the different subtypes of human breast cancer is not well understood. Gene expression-profiling studies suggest that the integrin α6β4 is predominantly overexpressed in basallike breast cancer. Our goal was to examine integrin α6β4 expression across many samples and to characterize expression among different breast cancer subtypes.

**Design:** We analyzed expression of the integrin α6β4 in a breast cancer tissue microarray (N = 54) using immunohistochemistry for the integrin β4 subunit. We performed staining for ER, PR, and HER2 to allow for tumor subclassification. Staining was scored using a standard semiquantitative scale, and expression of the β4 integrin was compared between hormone receptor-positive, HER2-positive, and triple-negative breast cancers.

**Results:** As previously shown, we found that integrin β4 expression is elevated in triple-negative breast cancers when compared with hormone receptor–positive cancers (P = .02). Interestingly, we found that integrin β4 expression was elevated in HER2-positive tumors when compared with hormone receptor–positive tumors (P = .008). Although most hormone receptor–positive breast cancers had low integrin β4 expression, a small subset had high expression.

**Conclusions:** Expression of the integrin α6β4 is increased in triple-negative, HER2-positive, and a subset of hormone receptor–positive breast cancers.

Estrogen Receptor–Negative, Progesterone Receptor–Positive Breast Cancers: Clinicopathologic Characteristics and Outcome Correlation With Other Subsets

**Poster No. 121**

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**Context:** Estrogen receptor (ER) and progesterone receptor (PgR) in breast carcinoma are important prognostic indicators and predictors of response to hormonal treatment. Ambiguity surround whether ER−/PgR− phenotype exists as a distinct entity and whether PgR can independently predict response to hormonal treatment because some pathologic lesions, including HH, atypical HH, and HHM. We did not identify invasive components, which are rarely reported.

**Estrogen Receptor–Negative, Progesterone Receptor–Positive Breast Cancers: Clinicopathologic Characteristics and Outcome Correlation With Other Subsets**

Arch Pathol Lab Med—Vol 138, September 2014

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investigators regard ER status as the single most important therapeutic predictive factor, regardless of PgR status. We investigated ER+/PgR- breast cancers to answer the ambiguity surrounding this phenotype regarding its existence, as a predictor of response to hormonal treatment, and its prognostic effect if it truly does exist.

**Design:** We reviewed 314 archival-documented ER+/PgR- breast cancer diagnoses between January 1994 and July 2009. Repeat immunohistochemistry confirmed 92 cancers as ER+/PgR-. Clinicopathologic parameters, such as age, ethnicity, tumor size, histologic grade, subtype, associated ductal carcinoma in situ, lymphovascular invasion, and nodal status were evaluated between the groups and correlated using the chi2 test or the Fisher exact test. Survival outcomes were estimated with the Kaplan-Meier method and compared between groups using log-rank statistics.

**Results:** ER+/PgR- tumors accounted for 1.1% of all ER/PgR+ phenotypes. Compared with ER+ phenotypes, they exhibited different clinicopathologic features and poor survival similar to ER+/PgR- tumors.

**Conclusions:** ER+/PgR- breast cancers exist as a unique entity, albeit rare, and have poorer disease-free and overall survival, posing the question of whether they respond to conventional hormonal therapy. They are of little value in predicting response to hormonal treatment in ER+ breast cancers; therefore, routine testing of PgR may not be justifiable and remains debatable.

Quantitative Image Analysis of Ki-67 Immunohistochemistry Compared With Manual Pathologist Analysis in Breast Cancer

(Poster No. 122)

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**Context:** Image analysis (IA) is prevalent in pathology quantification. Determining Ki-67 percentage is complicated by tumor type, observer variability, bias, and workload.

**Design:** Spartanburg Medical Center reports 350 breast cancers annually. Biomarker reports from 2012 to 2013 identified 100 cases with Ki-67 results. Slides with controls were acquired on the authors’ microscopes and were analyzed from multiple fields of view using Applied Spectral Imaging (Carlsbad, Calif) pathology platform (GenASiS HiPath) with vendor-provided IA software algorithms for nuclear staining. Manual, semiquantitative pathologist analysis (MA) for cases scored between 1% and 14% and 15% or greater were compared with IA.

**Results:** Overall initial concordance between MA and IA was 91/100 cases (91%). The MA scored 35 cases as 14% or less, with IA concordance of 14% or less in 30/35 cases (86%). On review of the discordance between MA and IA, MA revised scoring of 4 cases to match IA scoring and brought concordance to 34/35 cases (97%). Of the 65 cases scored by MA as 15% or more, IA concordance of scoring was 61/65 cases (94%). The 4/65 cases (6%) in which there was discordance were all scored as 15% by MA and between 12% and 14% by IA. Final concordance was 95/100 cases (95%).

**Conclusions:** Overall high concordance of IA shows the value of the technology. As 4 MA cases were revised from a score of less than 15% to a score greater than 15%, combined with the slight difference in scoring contributing to instances of discordance in cases scored by MA as above 15%, IA is useful in borderline cases suggesting a role for IA in cases scored as 5% to 25%.

Dr Kaplan is a consultant for Applied Spectral Imaging.

Detection of a High-Grade Serous Carcinoma on a Breast Core Biopsy in a Subspecialty Practice Setting: Case Study and Review of the Literature

(Poster No. 123)

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It is important to identify extramammary cancers in the breast because their management and outcomes differ from a breast primary. Metastasis from an ovarian high-grade serous carcinoma can show overlapping morphologic and immunohistochemical features with a breast primary. This problem is heightened in the absence of any history and in a subspecialty practice setting. We report the detection of a high-grade serous carcinoma using morphologic clues and immunohistochemical panel in the absence of a known primary. An 82-year-old woman had a breast biopsy for abnormal densities on mammography. The slides showed a high-grade carcinoma associated with lymphocytic infiltration. No DCIS or normal breast parenchyma was identified. The tumor had a triple-negative morphology but was positive for ER and PR. Immunostains for mammoglobin and GATA-3 were negative. Because gynecologic tumors can also express ER and PR, WT1 and PAIX were subsequently ordered, and were strongly positive. This confirmed the diagnosis of a high-grade serous carcinoma of Mullerian origin. The morphologic and immunohistochemical mismatch in the absence of DCIS and normal breast parenchyma are clues to suspect a metastatic lesion. In the current literature, such cases have been diagnosed with an excision history or obvious papillary architecture. Our case is unique because it did not did not have a prior diagnosis or papillary architecture. In such situations, immunostains for GATA-3 and mammoglobin are useful as an initial assessment because metastasis of a high-grade serous carcinoma in the breast is a rare diagnosis.

Decreased Claudin 7 Expression Is Associated With Mammary Paget Disease

(Poster No. 124)

Jianhong Li, MD, PhD (jli@lifespan.org); Shaolei Lu, MD, PhD; Evgeny Yakirevich, MD, DSc; Yihong Wang, MD, PhD. Department of Pathology, Rhode Island Hospital, Brown University, Providence, RI.

**Context:** Mammary Paget disease is a rare form of breast cancer characterized by the invasion of epidermis by breast cancer cells, and its pathogenesis remains unclear. Dysregulation of claudins, tight junction membrane proteins, has been described in multiple malignancies, including breast cancer. We hypothesized that alteration in claudin expression may be involved in the development of Paget disease. We investigated expression of claudins 1, 3, 4, 7, and 8 in Paget cells in comparison with underlying ductal carcinoma in situ (DCIS) in this study.

**Design:** We identified 22 cases with both Paget disease and underlying DCIS from the Rhode Island Hospital. Paraffin-embedded tissue microarrays were analyzed for immunohistochemistry expression of claudins 1, 3, 4, 7, 8, HER2, and ER. Claudin immunoreactivity was assessed semiquantitatively and analyzed by chi2 test.

**Results:** All claudins demonstrated a membranous staining pattern in the nonneoplastic breast tissue, Paget cells, and underlying DCIS. The positivity of claudins ranged from 13.3% to 77% in Paget cells and 42% to 86% in DCIS. Claudin 7 was significantly decreased in Paget cells as opposed to DCIS (13.3% versus 40%; P = .02). Most DCIS (79%) and Paget cells (86%) were positive for HER2. All except one case were negative for ER expression.

**Conclusions:** The significantly decreased claudin 7 expression in Paget cells may be associated with the transition from DCIS to Paget disease to facilitate spread of the tumor cells to the epidermis.

Claudin Expression in Ductal Carcinoma In Situ (DCIS), Paget Cells, and Epidermis (* P = .02)

<table>
<thead>
<tr>
<th>Breast Cancer, No. (%)</th>
<th>ER</th>
<th>Claudin 1</th>
<th>Claudin 3</th>
<th>Claudin 4</th>
<th>Claudin 7*</th>
<th>Claudin 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCIS</td>
<td>17 (77)</td>
<td>4 (18)</td>
<td>13 (60)</td>
<td>17 (77)</td>
<td>9 (41)</td>
<td>6 (27)</td>
</tr>
<tr>
<td>Paget</td>
<td>19 (86)</td>
<td>3 (13.6)</td>
<td>10 (45)</td>
<td>15 (68)</td>
<td>3 (13.6)</td>
<td>3 (13.6)</td>
</tr>
</tbody>
</table>

**Immunohistochemical Characterization of Adenomyoepithelial Tumors of the Breast**

(Poster No. 125)

Wanhua Yang, MD, PhD (wYang9003@nyp.org); Paula Ginter, MD; Michaela Nguyen, MD; Justin Wells, MD; Sandra J. Shin, MD. Department of Pathology and Laboratory Medicine, NYP-Weill Cornell Medical Center, New York, NY.

**Context:** Adenomyoepithelial (AME) tumors are uncommon and can be difficult to recognize. Identifying their epithelial (E) and...
myoepithelial (M) components may be helpful using immunohistochemistry. However, such characterization has not been well studied.

**Design:** The diagnoses of 41 mammary AME tumors (17 benign, 16 atypical, 8 malignant) were confirmed, and tumor slides were stained for S100 protein, SMM, CK14, CK5, p63, K903, CK AE1/3, CK7, CAM 5.2, ER, PR, and HER2 using the Bond-Max Autostainer (Leica Microsystems, Bannockburn, Ill.). Staining results were recorded.

**Results:** Among benign tumors, only SMM and CK14 were restricted to the M component and CAM 5.2 and ER were restricted to the E component in all cases. Among atypical tumors, only p63 and CK14 were restricted to the M component and CAM 5.2 was restricted to the E component in all cases. Among malignant tumors, only p63 was restricted to the M component in all cases, whereas none were consistently restricted to the E component. For all groups, the remaining stains either showed staining in both components or were negative in some cases.

**Conclusions:** Some M and E markers were superior to others studied in their abilities to stain respective components in AME tumors. In benign and atypical tumors, CK14 and CAM 5.2 reliably stained the M and E component, respectively, which can be diagnostically useful. In malignant tumors, no single stain consistently stained its respective component; therefore, immunostains may be of limited utility in this subset of AME tumors.

**Concordance Between Core Needle Biopsy and Surgical Excision for Hormone Receptors and HER2 Status in Triple-Negative Breast Cancer**

(Jing He, MD1 (jiehe@utmb.edu); Melissa Van Dellen, MD; Ashley Moehring, BA; Sandra Hatch, MD; Mahmoud Eltorky, MD, PhD.1 Departments of Pathology, School of Medicine and 2Radiology, The University of Texas Medical Branch, Galveston, Tex.

**Context:** Breast cancer is the most common malignancy affecting women. Accurate and reliable determination of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2) status in breast cancer is crucial for therapeutic decision making. Whether surgical specimens can be replaced by core needle biopsy (CNB) specimens for assessment of hormone receptors (HRs) and HER2 in breast cancer is still debated. We explored the reliability of using CNB alone in the assessment of ER, PR, and HER2 in triple-negative patients.

**Design:** We retrospectively analyzed patients with paired CNB and resection specimens from 2004 to 2013. The patients with ER, PR, and HER2-triple negative specimens on CNB were included. ER, PR, and HER2 were tested on the resected tumor by immunohistochemistry (IHC). The patients with HER2 of 2+ or 3+ by IHC were further examined by fluorescence in situ hybridization. The patients with HER2 of 2+ by IHC were further examined by fluorescence in situ hybridization.

**Results:** Because heterogeneous antigen expression might be a cause for false-negative results on the CNB, we tested tumors with ER, PR, and HER2 negative biopsy results again on the surgical specimen. Our study demonstrated that concordance rates between CNB and surgical specimens were 100% for both HRs and HER2 testing. Tumor heterogeneity was not detected in our specimens.

**Conclusions:** The results of this study indicate that ER, PR, and HER2 from CNB provided results that accurately reflect the marker status of the tumor. Our data suggest that CNB is reliable for HR and HER2 determination and could replace excisional specimens for evaluation of HRs and HER2 triple-negative status.

**Distinctive Morphologic and Immunohistochemical Features of Apocrine Breast Carcinoma**

(Mohammed T. Lilo, MBChB (mllol1@hmi.edu); Rajni Sharma, PhD; Helen Fedor, BS; Pedram Argani, MD; Ashley Cimino-Matthews, MD. Department of Pathology, The Johns Hopkins Hospital, Baltimore, Md.

**Context:** Molecular studies show a subset of apocrine invasive carcinoma (AIC) phenotype as basallike triple-negative breast carcinomas (TNBCs). However, most AICs express androgen receptor (AR), which may be a viable therapeutic target in these tumors. Thus, AIC should be distinguished from nonapocrine TNBC. 5α-Reductase catalyzes bioactive androgens, but the exact relationships among tumor progression, AR, and androgen-producing enzymes in AIC is unclear.

**Design:** Tissue microarrays (TMAs) were constructed from 12 AICs and 12 apocrine ductal carcinoma in situ (ADCIS). The TMAs were labeled by immunohistochemistry for estrogen receptor (ER), progesterone receptor (PR), AR, HER2, EGFR, Ki-67, and 5α-reductase. The TMAs containing 32 nonapocrine, basallike TNBC (CK5/6+ or EGFR+) and 13 nonapocrine unclassified TNBC (CK5/6+ /EGFR+) were also labeled with AR.

**Results:** Eighty-three percent of AICs and 92% of ADCIS were AR+/ ER+ (96% of AICs and 45% of ADCIS demonstrated HER2 overexpression, and 60% AIC showed EGFR overexpression). The expression of HER2 or EGFR was mutually exclusive in AIC. Seventy percent of AICs and 64% ADCIS labeled for cytoplasmic 5α-reductase. The Ki-67 proliferation index was less than 10% in 50% of AICs, 10% to 20% in 30% of AICs, and more than 20% in 40% of ADCIS. The AR labeling was seen in 22% of basallike TNBCs and in 15% of unclassified TNBC.

**Conclusions:** A subset of triple-negative AIC shows EGFR labeling, consistent with a basallike phenotype. 5α-Reductase is expressed in most AICs and ADC, suggesting autocrine androgen synthesis in AIC, which may have therapeutic implications. A subset of histologically nonapocrine TNBC label with AR, suggesting these may be a phenotypically apocrine group and may respond to antiandrogen therapy.

**The Role of Cytokeratin OSCAR in the Diagnosis of Metaplastic Carcinomas of the Breast**

(Pallavi Kanwar Galera, MBBS (kanwar.p23@gmail.com); Ashraf Khan, MD; Dina Kandil, MD. Department of Pathology, UMass Memorial Medical Center, Worcester, Mass.

**Context:** Metaplastic breast carcinoma is a heterogenous group of tumors that diverge from conventional glandular differentiation. The metaplastic component can sometimes be focal or can present in a pure form posing diagnostic challenges. Metaplastic carcinomas are known to show focal or even negative immunostaining for some cytokeratins (CKs). Therefore, a panel of low- and high-molecular weight CKs is often needed to prove their epithelial origin. OSCAR is a relatively new anti-CK antibody with a broad spectrum of keratin reactivity.

**Design:** Thirty-one cases of metaplastic breast carcinoma diagnosed at our institution between 1998 and 2012 were retrieved. A representative slide was immunostained for CK–OSCAR, and compared with CK AE1/AE3, CAM 5.2, CK903, and CK5/6. Nineteen spindle cell lesions, including 6 malignant phyllodes, 10 borderline phyllodes, 1 inflammatory pseudotumor, 1 solitary fibrous tumor, and 1 nodular fasciitis, were used as controls.

**Results:** All 31 metaplastic carcinoma cases were positive for CK–OSCAR (31/31; 100%), compared with 28/31 (90%) for CK AE1/AE3, 21/31 (68%) for CK903, 19/31 (61%) for CAM 5.2, and 14/31 (45%) for CK5/6. All control cases were negative for CK–OSCAR.

**Conclusions:** Our data showed that CK–OSCAR is more sensitive than other CKs in identifying metaplastic breast carcinomas. Coupled with 100% specificity, CK–OSCAR may potentially be used in lieu of a panel of CKs to identify the epithelial origin of these tumors. This is particularly useful in limited core biopsy specimens to help guide treatment while simultaneously lowering the cost of testing.

**Predictive Factors Associated With Axillary Lymph Node Metastases of Low-Grade Breast Carcinomas**

(Amandeep Aneja, MD1 (amandeep.anuja@tuhs.temple.edu); Shobha Parajuli, MD; John P. Gaughan, MS, PhD, MBA; Xinmin Zhang, MD.1 Department of Pathology, Temple University Hospital, Philadelphia, Pa; 2Biostatistics Consulting Center, Temple University School of Medicine, Philadelphia, Pa.

**Context:** Axillary lymph node metastasis (ALNM) is the most significant prognostic factor for patients with breast cancer (BC), and low-grade BC (LGBC) has rare ALNM. However, it remains unknown which LGBC may metastasize to ALN.

**Design:** Thirty-two cases of LGBC between June 2005 and April 2013 were retrieved from the archives of our department. Medical records were reviewed, and pathologic slides were reevaluated for morphologic features; ER, PR, and HER2 status; and Ki-67 labeling index.

**Results:** Among the 32 cases, 16 had ALNM. Tumors with and without ALNM had a significant difference in Nottingham scores (3–5; P < .001), although individual assessment on tubular formation, nuclear pleomorphism, and mitosis showed no statistical difference. The ALNM was significantly associated with diminished or loss of PR expression (P
The agreement of Ki-67 assessments among the 3 evaluators was good (intrateric intraclass correlation coefficient, 0.797). A cut-point analysis using recursive partitioning indicated that a Ki-67 index of more than 10% was the most accurate value for predicting ALN metastasis. No significant differences were identified in size, lymphovascular invasion, ER, and HER2 status between the 2 groups.

Conclusions: Our study identified 3 pathologic factors to serve as potential predictors for ALNM of LGBC: higher Nottingham score, diminished or loss of PR expression, and Ki-67 labeling index of 10% or more. The findings could help to identify the subgroups that are likely to develop ALN metastasis and, therefore, may provide guidance to clinicians in choosing the appropriate postoperative therapeutic protocol for patients with LGBC.

Multiplexed Ion-Beam Imaging of 10 Markers in Human Breast Tumors Using Metal-Tagged Antibodies With Potential for Hectaplexing

(Poster No. 130)

Richard Levenson, MD; Michael Angelo, MD, PhD; Alexander Borowsky, MD, PhD; Sean Bendall, PhD; Yasodha Natkunam, MD; Chuck Hitzman, PhD; Scott Liu, PhD; Shuchun Zhao, BS; John Lowe, MD; Rachel Finck, BS; Matthew Hale, PhD; Garry Nolan, PhD.

Department of Pathology and Laboratory Medicine, UC Davis Medical System, Sacramento, Calif; Departments of Laboratory Medicine, Baxter Laboratory in Stem Cell Biology, Microbiology and Immunology, Pathology, Materials Science and Engineering and Microbiology and Immunology, Stanford University, Palo Alto, Calif; Department of Pathology, Genentech, South San Francisco, Calif.

Context: Existing immunohistochemical (IHC) methods rely on antibodies tagged with fluorophores or chromogenic enzyme reporters. Because of the potential for spectral and spatial overlap, it can be difficult to use more than a few probes simultaneously. Consequently, multiplexed IHC is not routinely employed in clinical settings. We have developed a novel method that images mass-tagged antibodies using secondary ion mass spectrometry (MS) with potentially better-than-light-microscope resolution.

Results: Comparison of HER2-, ER-, and PR-positivity demonstrates appropriate expression with respect to immunophenotypes established by conventional IHC staining performed in a clinical laboratory. Side-by-side comparison of MBI and quantitative imaging analysis of ER IHC in 9 breast tumors demonstrated robust agreement between the 2 methods in mean nuclear staining intensity and H score (r = 0.99, P < .001; and r = 0.99, P < .001, respectively).

Conclusions: A MBI analysis will generate highly multiplexed tissue-imaging results with sensitivity and resolution comparable to conventional IHC methodologies (Figure 43). This approach could provide new insights by integrating tissue microarchitecture with multiparameter cellular expression patterns for basic research, drug discovery, and clinical diagnostics.

Synchronous Occurrence of Primary Breast Adenoid Cystic Carcinoma and Invasive High-Grade Urothelial Carcinoma in a 75-Year-Old Man: Case Report and Review of the Literature

(Poster No. 131)

Divya Sharma, MD; Chengquan Zhao, MD; Jiang Wang, MD, PhD; Shaqifa Khan, MD; Lindsey Lowder, DO; Mingtu Zhou, Pathologist Assistant; Hua Tao Yang, MD, PhD.

Department of Pathology and Laboratory Medicine, University of Cincinnati Medical Center, Cincinnati, Ohio; Department of Pathology and Laboratory Medicine, Magee-Women’s Hospital, Pittsburgh, Pa.

Adenoid cystic carcinoma (AdCC) of the breast is a rare malignancy accounting for 0.1% of all breast carcinomas. In contrast to the aggressive nature of AdCC at other sites, AdCC of the breast has a favorable prognosis, low rate of lymph node involvement, and uncommon distant metastases. It is generally cured by simple mastectomy. Chemotherapy, radiation, and hormonal treatment are infrequently used. We report a rare case of primary breast AdCC in a 75-year-old man who presented with a subareolar, well-defined, 2.2-cm mass. Breast core biopsy showed invasive AdCC (Figure 44, A) with triple-negative phenotype (negative for ER, PR, and HER2/neu). The cells were positive for p63 (Figure, D), c-Kit (Figure, E), SMMHC, and E-cadherin. Ki-67 labeling index was 28% and Her2:CEP17 by fluorescence in situ hybridization (FISH) was not amplified (Figure, F). Our patient underwent total mastectomy (Figure, B, C). The AJCC pathologic staging was pT2 pN0 pM0. After 2 months of AdCC diagnosis, he was diagnosed with invasive high-grade papillary urothelial carcinoma of urinary bladder with lamina propria invasion. Transurethral resection of the bladder tumor showed 2 urothelial carcinomas. The first was 3 cm located at the bladder base and the second was 6 cm located at the posterior wall. He subsequently received local Bacillus Calmette-Guerin treatment and methotrexate/5-fluorouracil adjuvant chemotherapy. Patient is doing well without evidence of local recurrence or distant metastasis of either AdCC or urothelial carcinoma. The pathogenesis of synchronous occurrence of primary breast and urothelial carcinoma is uncertain.
Low-Grade Neuroendocrine Tumors of the Lung, Including Tumorlet, Typical, and Atypical Carcinoid: A Clinicopathologic Review

(Poster No. 132)

Lauren E. Rosen, MD1 (lauren_e_rosen@rush.edu); Chaohui Zhao, MD2; Paolo Gattuso, MD3; Humberto E. Trejo Bittar, MD (htotbittar@gmail.com); Marina Nikiforova, MD; Samuel A. Yousum, MD. Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pa.

Context: The clinical behavior of low-grade neuroendocrine tumors, including tumorlet, typical carcinoid (TC), and atypical carcinoid (AC) of the lung, is not firmly established. The aim of our study was to determine whether clinicopathologic features can be used to predict tumor behavior.

Design: We searched our surgical pathology records from 1993 to February 2013 for cases of low-grade neuroendocrine tumors. The following parameters were reviewed: age, sex, tumor size, location, lymph node status, and distant metastases. Lymph node involvement and distant metastases were considered markers of aggressive behavior. Data were analyzed with SPSS 20.0 (IBM, Armonk, NY) using the χ² test, binary logical regression, and multinomial logical regression. P < .05 was considered statistically significant.

Results: A total of 101 cases were identified (72 TCs, 17 ACs, 12 tumorlets). The female to male ratio was 1.7:1. Age ranged from 13 to 82 years, with a mean of 59 years. Fifty-nine tumors (58%) were central (50 TCs, 8 ACs, 1 tumorlet) and 42 (42%) were peripheral (22 TCs, 9 ACs, 11 tumorlets). The mean tumor size was 0.37 cm for tumorlets, 2.24 cm for TCs, and 2.99 cm for ACs. Lymph node status was assessed in 69 cases (68%) (71% TC, 88% AC, 42% tumorlet). Nine cases (13%) had lymph node metastases (35% AC, 4% TC). Two (2%) cases had distant metastases, both AC (12%).

Conclusions: Younger age (P = .02) was found to predict aggressive tumor behavior. Compared with TCs, ACs had an increase in aggressive behavior (P = .01) and were more likely to be located in the peripheral lung (P = .03) than TCs were. Sex, tumor size, and tumor location had no association with aggressive behavior.

KIT (CD117) Is Overexpressed in a Subset of Lung Adenocarcinomas: A Morphologic and Genetic Analysis

(Poster No. 133)

Humberto E. Trejo Bittar, MD (htotbittar@gmail.com); Marina Nikiforova, MD; Samuel A. Yousum, MD. Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pa.

Context: Lung carcinoma-related mortality is still the leading cause of cancer deaths worldwide; therefore, identifying potential pharmacologic targets is of great importance. KIT (CD117) is a receptor tyrosine kinase, and its role in lung cancer is controversial. Here, we aimed to correlate KIT-expressing carcinomas with their morphologic features and molecular alterations and identify potential predictors of the tumor KIT expression status.

Design: One hundred fifty-two surgically resected non–small cell lung carcinomas for which tissue was available for ancillary studies were analyzed. KIT (CD117) immunohistochemistry was performed and graded according to intensity (0–3†). Histomorphologic features were documented, including predominant growth pattern. KIT polymerase chain reaction sequencing was performed.

Results: A total of 42 KIT positive adenocarcinomas (ADC) (27.5%) were identified, 15 with weak (35.7%), 19 with moderate (45.2%), and 8 with strong (19.1%) staining patterns. KIT-positive ADC showed more acinar (48.9% versus 37%) and papillary (25.6% versus 14%) growth patterns. Invasive mucinous ADC showed less KIT expression than conventional ADC (7% versus 13%). All solid ADCs (6.4%), squamous

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**Summary of Selected Published Cases of Primary Breast Adenoid Cystic Carcinoma in Men**

<table>
<thead>
<tr>
<th>Source, y</th>
<th>Size, cm</th>
<th>Immu-no-histochemistry</th>
<th>Lymph Node/or Metastasis</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferlito and Di Bonito, 1974</td>
<td>Pealike nodule</td>
<td>None</td>
<td>None</td>
<td>No recurrence</td>
</tr>
<tr>
<td>Hjorth and Magnusson, 1977</td>
<td>2.0</td>
<td>None</td>
<td>None</td>
<td>No recurrence</td>
</tr>
<tr>
<td>Miliauskaus and Leong, 1991</td>
<td>3.8</td>
<td>Positive: vimentin, SMA, EMA, collagen type 4, laminin, negative: S100</td>
<td>None</td>
<td>No recurrence</td>
</tr>
<tr>
<td>Kshirsagar et al, 2006</td>
<td>6.0</td>
<td>Negative: ER, PR on recurrent chest wall nodules</td>
<td>3 axillary lymph nodes positive; recurrence within 2 y of refusal of radiation therapy</td>
<td>Recurrence</td>
</tr>
<tr>
<td>Liu et al, 2011</td>
<td>2.0</td>
<td>Positive: CK7, SMA, BCL2; negative: ER, PR, HER2, p53, EGFR, Toplil</td>
<td>None</td>
<td>No recurrence</td>
</tr>
<tr>
<td>Yoo et al, 2013</td>
<td>1.7</td>
<td>Positive: CK5/6, p53; negative: ER, PR, HER2/neu</td>
<td>Left axillary lymph node; cervical vertebrae; bone marrow</td>
<td>No recurrence</td>
</tr>
<tr>
<td>Present study</td>
<td>2.2</td>
<td>Positive: c-Kit, p63, SM, Myosin, E-cadherin; negative: ER, PR, HER2/neu, Ki-67, labeling index: 28%; HER2 FISH: negative</td>
<td>None</td>
<td>No recurrence</td>
</tr>
</tbody>
</table>
cell carcinomas (3.2%), and adenosquamous carcinomas (2.6%) were KIT negative. No mutations on KIT exons 9, 11, or 13 were identified. A representative KIT-positive ADC is shown (Figure 45).

Conclusions: KIT-expressing cases failed to show mutations in exons 9, 11, or 13, likely representing wild-type KIT overexpression. KIT-overexpressing ADCs display more papillary and acinar growth patterns, with all solid ADCs failing to overexpress KIT. Therapeutic strategies directed at KIT should be focused on posttranscriptional events.

Pathology of Swan-Ganz Catheter-Related Pulmonary Artery Rupture
(Poster No. 134)
Ya Xu, MD, PhD (yaxususa@yahoo.com); L. Clarke Stout, MD, Department of Pathology, University of Texas Medical Branch, Galveston, Tex.

Pulmonary artery rupture (PAR) is now an unusual complication of single Swan-Ganz catheter (SGC) diagnostic pulmonary wedge-pressure measurements. To our knowledge, detailed pathologic studies of such pulmonary artery ruptures have not been performed. This is a concern because safer methods may be available. The patient was a 75-year-old woman with recent-onset left ventricular failure because of progressive aortic stenosis. Shortly after wedge pressure measurement she coughed up 200 mL of blood followed later by a cardiac arrest despite vascular volume stabilization. At autopsy, small linear intimal fibrin deposits in a 1.6-cm segment of the left lower lobe lateral basal branch identified the possible pulmonary artery rupture. Complete 4-μm step cross-sections of this segment into 54 levels stained with hematoxylin-eosin, Movat pentachrome, and Masson trichrome stains revealed 12 total tears microscopically. Eleven were incomplete tears (0.05–2.5 mm wide and 0.3–6 mm long), and the 12th (6 mm long) was a penetrating tear. All tears had fractures of variable numbers of elastic lamina in a vertical line. No evidence of medial dissection was seen. Tears did not resemble aortic traumatic tears from 3 file cases. For controls, the same artery in the right lower lobe and lobar and main branches from both lungs were similarly stained. No other structural abnormalities were seen in the torn or control arteries. The large number of tears and their uniformity suggested a generalized wall weakness rather than a Swan-Ganz catheter or operator malfunction.

Interstitial Lung Disease With Anti-Ro/SSA Autoantibodies
(Poster No. 135)
Alexander A. Berrebi, MD (aberreb@umm.edu); Adina Pauk, MD; Allen P. Burke, MD, Department of Pathology, University of Maryland, Baltimore, Md.

Interstitial lung disease in patients with anti-Ro/SSA autoantibodies is most frequently seen in association with systemic lupus erythematosus, for which there are few histologically documented cases. We report histologic findings in 2 patients with undifferentiated connective tissue disease, anti-Ro/SSA antibodies, and respiratory disease at the initial presentation that led to death or transplantation. A 47-year-old man presented with 1 month of dyspnea and subsequent proximal muscle weakness. Serologic studies revealed anti-Ro/SSA autoantibodies and a diagnosis of undifferentiated connective tissue disease was rendered. Computed tomography (CT) scan demonstrated steroid-resistant, progressive, ground-glass and reticular densities. Wedge lung biopsies demonstrated capillaritis with acute lung injury. The patient initially responded to cyclophosphamide and methotrexate, but eventually died 2 months after admission. Autopsy demonstrated organizing diffuse alveolar damage with disseminated cytomegalovirus infection. Our second case involves a 32-year-old woman with a 6 month history of recurrent pneumonia who was admitted for progressive hypoxia and respiratory failure. Rheumatologic workup demonstrated anti-Ro/SSA autoantibodies and symptoms suggestive of Sjögren syndrome, prompting a diagnosis of undifferentiated connective tissue disease. Wedge lung biopsies showed organizing pneumonia and nonspecific interstitial pneumonia. The CT scan showed ground-glass and reticular densities suggestive of progressive fibrosis. The patient underwent bilateral lung transplant 14 months after initial evaluation with the explant showing nonspecific interstitial pneumonia, hypertensive arterial changes, and basilar honeycombing. These cases illustrate that progressive interstitial lung disease may occur in patients with anti-Ro/SSA autoantibodies, is histologically heterogeneous, and may be rapidly fatal, especially in the presence of vasculitis.

Eosinophilic Granulomatosis With Polyangiitis Concurrent With Primary Lung Adenocarcinoma: A Case Study and Review of the Literature
(Poster No. 136)
Xin Liu, MD, PhD (xliu.path@gmail.com); Vidya Nagrale, MD; David J. Stephen, DO; Steven Garzon, MD; John V. Groth, MD. Department of Pathology, University of Illinois at Chicago, Ill.

Eosinophilic granulomatosis with polyangiitis (EGPA/Churg-Strauss syndrome) is an uncommon systemic vasculitis first described by Drs Jacob Churg and Lotte Strauss in 1951. EGPA is currently defined by the American College of Rheumatology by having 4 or more of the following: (1) asthma, (2) eosinophilia (>15%); (3) neuropathy; (4) migratory or transient radiographic pulmonary findings of small centrilobular nodules, peripheral ground-glass opacities, consolidation, bronchial dilatation, wall thickening, and interlobar septal thickening; (5) paranasal sinus abnormality; and (6) a biopsy demonstrating necrotizing vasculitis, extravascular granuloma, and eosinophils. EGPA is currently classified as an antineutrophil cytoplasmic antibody-associated small-vascular vasculitis, along with microscopic polyangiitis and granulomatosis with polyangiitis. Recent studies suggest an increased cancer risk with microscopic polyangiitis and granulomatosis with polyangiitis; however, an increased cancer risk with EGPA has not been established, with 2 case reports of solid organ malignancies documented. We present a case of a 52-year-old woman with a history of asthma, chronic sinusitis/rhinitis, and peripheral eosinophilia who underwent a right upper lung lobectomy lymphadenectomy. This revealed a 2-cm, nonnecrotic invasive adenocarcinoma, acinar predominant, with concurrent abundant extravascular granulomas and eosinophils with eosinophilic and granulomatous small vessel vasculitis. Three thoracic lymph nodes demonstrated abundant extravascular nonnecrotizing granulomas and eosinophils. This allowed for the diagnosis of concurrent lung adenocarcinoma and previously undiagnosed EGPA. EGPA is a clinically challenging diagnosis to make and is underrecognized with disease onset lagging diagnosis by 12 years. This case highlights the third case of EGPA associated with solid organ malignancy and the first with lung adenocarcinoma (Figure 46).

Detection of Merkel Cell Polyomavirus in Lung Adenocarcinomas Carcinomas: Role of Immunohistochemistry
(Poster No. 137)
Humberto E. Trejo Bittar, MD (htotbittar@gmail.com); Sanja Dacic, MD, PhD; Liron Pantanowitz, MD. Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pa.

Context: Merkel cell polyomavirus (MCPyV) is an oncogenic DNA virus that causes Merkel cell carcinoma. Recently, MCPyV has been identified in other noncutaneous tumors including lung non–small cell carcinoma. However, the true role of this virus in lung carcinogenesis is unclear. We aimed to detect by immunohistochemistry the prevalence of MCPyV in a series of lung adenocarcinomas.

Design: Nuclear expression of the MCPyV large T-antigen was evaluated by immunohistochemistry (CM284 antibody) in formalin-fixed, paraffin-embedded lung adenocarcinomas of different histologic subtypes, grades, and mutation status using tissue microarrays.

Abstracts

e42 Arch Pathol Lab Med—Vol 138, September 2014
Results: A total of 90 lung adenocarcinomas were examined, 23 (25.6%) were wild-type, 18 (20%) harbored EGFR mutations, and 49 (54.4%) showed KRAS mutations. None of the tumors were positive for MCPyV T-antigen expression by immunohistochemistry.

Conclusions: These data suggest that lung adenocarcinomas do not harbor MCPyV. Further studies are needed to similarly evaluate other types of lung carcinomas and to correlate these data with molecular studies for MCPyV DNA integration.

Lung Sarcomatoid Carcinoma With Focal Chondroid Differentiation

(Poster No. 138)

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Sarcomatoid carcinoma of the lung with chondroid differentiation is rare. A 56-year-old man had a history of squamous cell carcinoma of the epiglottis treated with chemoradiation. Seven years later, the patient presented with a productive cough. A computed tomography (CT) scan revealed a 9.6-cm right-upper lobe mass with mediastinal lymphadenopathy. The preoperative right upper-lobe CT-guided needle biopsy and the lobectomy showed a poorly differentiated malignancy composed of cohesive nests of large, spindled cells having a high nucleus/cytoplasmic ratio, and hyperchromatic pleomorphic nuclei with prominent nucleoli, a moderate cytoplasm, atypical mitotic figures, and much necrosis. Also present were focal chondroid differentiation, and a metastasis to a sentinel parastrachial lymph node. This malignancy invaded the visceral pleura without going through it. This malignancy was different from the previously diagnosed epiglottis squamous cell carcinoma. Immunohistochemistry was positive for pankeratin at a low foci; negative were CK7, CK20, CD34, S100, desmin, MSA, PSA, TTF1, and calretinin. Additional positive immunohistochemical stains at the Mayo Clinic included CK5/6 and AE1/AE3 in some of the epithelioid cells. The Mayo Clinic final diagnosis was sarcomatoid carcinoma with a heterologous chondroid element (World Health Organization 2004 classification). In spite of treatment with surgery and postoperative radiation, this patient died 4 months after diagnosis. In conclusion, lung sarcomatoid carcinoma with chondroid differentiation is rare, very aggressive, frequently symptomatic, and usually locally advanced with higher rates of recurrence. Immunohistochemistry helps make the diagnosis.

Importance of Pulmonary Pathology Workup for Early Treatment of Complications in Patients With Hematopoietic Stem Cell Transplantation

(Poster No. 139)

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Context: Pulmonary complications, most not diagnosed antemortem, are the major cause of morbidity and mortality in recipients of hematopoietic stem cell transplantation (HSCT). Bronchoalveolar lavage (BAL), with or without transbronchial lung biopsy and video-assisted thoracoscopic surgical lung biopsy, may be needed when radiologic studies reveal no specific etiology. There are only a few studies on the pulmonary pathology findings after HSCT. In this retrospective study, we reviewed the pulmonary complications after HSCT at Tufts Medical Center (Boston, Mass) during the past 15 years.

Design: Archival pathology reports from 30 patients with previous history of allo/auto stem cell transplant were reviewed; this included 11 lung wedge biopsies, 42 bronchoalveolar lavages (BALs), and 4 autopsy reports from 15 women and 15 men with mean ages of 45 and 65 years, respectively.

Results: Pathology findings included chronic and/or acute inflammation caused by any of these organisms: Pneumococciardis (n = 1), Aspergillus (n = 4), herpesvirus simplex (n = 1), mycobacteria (n = 1), gram-positive or gram-negative rods/cocci (n = 3), Candida (n = 2), diffuse alveolar damage (n = 6), alveolar hemorrhage (n = 3), diffuse interstitial/alveolar wall fibrosis (n = 3), organizing pneumonia (n = 2), and constructive bronchiolitis obliterans and obliterative bronchiolitis (bronchiolitis obliterans). Two of the autopsy cases had leukemic infiltration suggesting relapse of the previously known, acute lymphoblastic leukemia.

Conclusions: The BAL and lung biopsy should be considered more often as diagnostic methods in pulmonary complications after SCT and be reviewed by a cytologist and surgical pathologist because most of the complications are treatable with timely proper diagnoses.

Diagnosing Indeterminate Lung Nodules in a Third-World Country: Impact of Radiologic, Anatomic, and Histopathologic Features

(Poster No. 140)

Azra Akhtar, MBBS (alameras@yahoo.com); Noreen Akhtar, MBBS. Department of Anatomic Histopathology, Shaukat Khanam Memorial Cancer Research Hospital, Lahore, Pakistan.

Context: Recent advances in imaging have improved the chances to detect small, indeterminate lung nodules. Determination of the underlying malignant or benign origin of lung nodules remains a challenge.

Design: We analyzed clinical data and computed tomography (CT) scan findings of 89 patients with lung nodules admitted to our institution (2008–2013). Clinical findings were correlated with histopathologic findings from the biopsies of these lung nodules. The size of nodule was correlated with radiologic size and divided into 4 categories as A, B, C, and D on the basis of size (0–5, >5–10, >10–15, and >15 mm, respectively). Pearson χ2 test was used to assess for differences across various subgroups, and a P value of <.05 was considered to be statistically significant.

Results: On CT scan, malignant, benign, or indeterminate nodules were reported in 82%, 6.7%, and 9.0% of patients, respectively. Most of the nodules were reported in the lower (48.3%) and upper lobes (36.1%). Most common reported diagnoses were squamous cell carcinoma (30.3%) and carcinoma (20.2%). Histopathologic review of these nodules revealed a malignancy in 56.2% of patients. The proportion of malignant cases based on size in the order of decreasing percentage was C (77.8%), D (76.2%), A (52.8%), and B (38.7%) (P < .05). The prevalence of malignancy in the larger nodules was higher (76.7%) versus smaller nodules (44.8%) (P < .05). Prevalence of malignancy was 65.0%, 69.2%, 83.3%, and 46% in patients with 1, 2, 3, or multiple lung nodules, respectively (P = .14). The CT scan was found to have 94% sensitivity and very low specificity (33.3%). The negative predictive value of the CT scan was high (81.2%) when correlated with histopathologic findings.

Conclusions: Larger lung nodules are more likely to be malignant irrespective of the number of nodules. The CT scan has a high sensitivity (94%) and high negative predictive value (81.2%) in initial assessment of indeterminate lung nodules.

Correlation of Immunohistochemical Stain for Pepsin on Transbronchial Biopsy With Pepsin Levels in Bronchoalveolar Lavage Fluid in Lung Transplant Patients

(Poster No. 141)

Sameer Al Diffalha, MD1 (saldiffalha@lumc.edu); Mohanad Shaar, MD1; Christopher Davis, MD2; Marco Fischella, MD2; Swati Mehrrota, MD2; Razan Wafai, MD1. 1Department of Pathology and 2Surgery, Loyola University Medical Center, Maywood, Ill.

Context: Gastroesophageal reflux disease (GERD) is a potential risk factor for allograft survival in patients with lung transplants. The GERD symptoms along with detectable pepsin in bronchoalveolar lavage (BAL) with patients to laparoscopic antireflux surgery. Immunohistochemical (IHC) detection of pepsin in laryngeal mucosa has been reported to be a sensitive and specific test for diagnosing laryngopharyngeal reflux (LPR). Our goal was to test the correlation between detectable BAL pepsin and pepsin IHC stain to further the possibility of using pepsin IHC stain in transbronchial biopsies from transplant patients as a marker for GERD.

Design: One hundred fifty-seven transbronchial biopsies obtained from 74 patients in 2009–2010 were selected. Paraffin sections were stained for pepsin using appropriate positive controls (stomach) and negative controls (lung from nontransplant patients). Slides were evaluated by 2 pathologists with consensus achieved on discrepant cases. Intracellular and extracellular positivity was recorded and compared with BAL pepsin levels (n = 65). Fischer exact test was used for statistical analysis; P value <.05 was considered statistically significant.
Results: Our results show that pepsin IHC staining did not correlate with BAL pepsin levels (see Table). Calculated $P$ value for intracellular and extracellular positivity was .67 and .42, respectively, which was not statistically significant.

Conclusions: The immunostain for pepsin was poorly reproducible in transbronchial biopsies with high interobserver and intraobserver variability. More so, there was no correlation between BAL pepsin levels and IHC staining pattern in transbronchial biopsies from transplant patients. We conclude that IHC stain for pepsin has no role in the diagnosis of GERD in transplant patients.

<table>
<thead>
<tr>
<th>Results of Pepsin Immunohistochemical Staining</th>
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<tbody>
<tr>
<td>n = 65</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Extracellular (+)</td>
</tr>
<tr>
<td>Extracellular (-)</td>
</tr>
<tr>
<td>Intracellular (+)</td>
</tr>
<tr>
<td>Intracellular (-)</td>
</tr>
</tbody>
</table>

Synchronous Small Cell Carcinoma and Typical Carcinoid Tumor in the Same Lung Lobe

(Poster No. 142)

Lifang Liu, MD (liulf@ucmail.uc.edu); Jiang Wang, MD. Department of Pathology, University of Cincinnati, Ohio.

Based on World Health Organization classification, primary pulmonary neuroendocrine carcinoma has 4 subtypes: typical carcinoid, atypical carcinoid, small cell carcinoma, and large cell neuroendocrine carcinoma. Synchronous lung neuroendocrine tumor in the same lobe has not been found in the literature, to our knowledge. Here, we present the case of a 71-year-old woman with a history of chronic obstructive pulmonary disease, hypertension, and congestive heart failure who came to the hospital for productive cough. She had smoked one pack of cigarettes per day for the past 58 years. Positron emission tomography–computed tomography identified a peripherally located 2.3 cm 3-cm lung wedge resection was performed. The 24-g, 10 $\times$ 5.7 $\times$ 3-cm lung wedge showed a gray nodular area (1.8 cm) in the pleura, which connected to a 2.3 $\times$ 1.9 $\times$ 1.2-cm, irregular, firm, pink-white lesion in the parenchyma. Microscopically, the lesion contained one larger mass (2.3 cm) and 3 well-circumscribed nodules (2–4 mm). The larger mass contained a sheet of small cells with minimal cytoplasm, salt-and-pepper chromatin, and without prominent nucleoli. Smudging cells, nuclear molding, and necrosis were present, and mitotic figure was high (Ki-67 > 95%).

Giant Solitary Fibrous Tumor of the Pleura With Parenchymal Lung Metastases: Comparison of Histologic Findings in the Primary and Metastatic Tumor

(Poster No. 143)

Adina T. Paulik, MD (adina506@gmail.com); Alexander A. Berrebi, MD; Allen P. Burke, MD. Department of Pathology, University of Maryland, Baltimore, Md.

The criteria for malignancy in solitary fibrous tumors (SFT) are necrosis, increased mitotic activity, and cellularity. Although recurrences are not unusual, distant metastases are uncommon. Histologic features of metastatic lesions have rarely been reported. We present a case of giant SFT with benign histologic features presenting with metastatic disease, which was also sampled histologically. A 74-year-old man with rheumatoid arthritis was found to have a right pleural-based mass obliterating the right lung. The upper lobe of the right lung was resected with a 26-cm encapsulated mass and demonstrated a separate 1.1 cm well-circumscribed intra-parenchymal mass. Extensive sampling of the 26-cm tumor demonstrated a SFT with rare mitotic activity, areas of relative acellularity, fibrosis, absence of necrosis, diffuse staining with CD34 and Bcl-2, negative staining for CD99, and a Ki-67 proliferative index of 17%. The 1.1-cm right upper-lobe mass revealed a monomorphic, cellular, spindle cell neoplasm with the same immunohistochemical profile, a mitotic index of up to 13 high-power fields, focal necrosis, and a Ki-67 proliferative index of 71%. The patient developed bilateral lung metastases with progression of disease on sunitinib and single-agent doxorubicin. He was discharged to hospice care 13 months after diagnosis and remains alive with disease 19 months after diagnosis. Our case illustrates that giant SFT with similar histologic features to benign SFT and without increased cellularity, necrosis, and mitotic activity, may undergo malignant transformation.

Pleuroparenchymal Fibroelastosis: A Report of the First 2 Cases Diagnosed at Autopsy

(Poster No. 144)

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Pleuroparenchymal fibroelastosis is a rare condition characterized by the proliferation of interstitial elastic fibers, predominantly subpleural and more commonly seen in upper lobes. The etiology is unknown, and no specific diagnostic criteria have been reported. Because the condition was initially characterized in 2004, only 25 cases have been described in the literature. Here, we report the first 2 cases in which diagnosis has
been made at the time of autopsy. One patient, a 58-year-old woman, carried a diagnosis of familial idiopathic pulmonary fibrosis made on imaging for 5 years before her final admission. The second case was an 87-year-old woman with multiple comorbidities residing at a long-term care facility who experienced a prolonged and progressive downhill course with no specific, acute event suspected at the time of her demise. In both cases, microscopy revealed a diffuse interstitial pneumonia characterized by a diffuse proliferation of predominantly elastic fibers (Figure 48). The more extensive nature of the parenchymal fibroelastosis in these cases, as compared with previously reported cases, is likely attributable to the longer duration of the disease. Additionally, the condition in these patients was discovered on autopsy when the entirety of both lungs could be histologically examined, rather than being limited to imaging and biopsy. Our findings suggest that pleuroparenchymal fibroelastosis may be a more diffuse condition than previously reported and that it must be considered in the differential diagnosis of fibrous interstitial pneumonia at the time of autopsy and in examination of explanted lungs.

**Primary Pulmonary Syncytial Sarcoma**

*(Poster No. 145)*

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Primary pulmonary synovial sarcoma accounts for less than 0.5% of lung tumors and has poor prognosis with overall 5-year survival rate of 50%. We present a case of primary pulmonary synovial sarcoma where initial diagnosis was difficult and missed and where the patient has shown a long survival. The patient is a 27-year-old woman who was recently found to have a 3-cm lesion in the left upper lobe (LUL) of lung. Histologic examination of a resected lesion showed high-grade malignant spindle cells with brisk mitotic activity and no necrosis. Initial differential diagnosis included small blue cell tumor and synovial sarcoma. The tumor cells were positive for vimentin, BCL2, CD99, and CD56, and focally positive for synaptophysin, epithelial membrane antigen, and inhibin. The tumor showed SYT-SSX2 translocation by reverse transcription-polymerase chain reaction, consistent with synovial sarcoma. Incidentally, this patient had a previous wedge resection of LUL approximately 12 years prior. Histologically, it showed a more benign appearing cellular spindle cell lesion devoid of necrosis or significant mitotic activity. Because of the unusual histology, it was sent to a pulmonary pathologist who diagnosed it as cystic synchyronal neoplasm, favoring low-grade malignancy. Retrospective testing detected presence of the same SYT-SSX2 translocation. This case is unusual in that the diagnosis of synovial sarcoma was difficult at the time of initial presentation because of the low-grade cytologic features. Although synovial sarcoma is believed to be a low-grade tumor, our patient is alive 14 years after initial presentation of this tumor, and the patient is doing well 2 years after the last recurrence.

**Pulmonary Smooth Muscle Tumors of Uncertain Malignant Potential: Possible Malignant Transformation From a Benign Metastasizing Leiomyoma?**

*(Poster No. 146)*

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Pulmonary smooth muscle tumors are not an uncommon finding in females with concomitant uterine leiomyomas. These have been previously described as benign, metastasizing leiomyomas in the literature. We present a case of a 58-year-old, HIV-positive woman who presented with multiple pulmonary nodules in the upper lobe of the right lung. Review of previous pathology revealed she had undergone total hysterectomy for a uterine leiomyoma 3 years prior. Histologically, the uterine tumor showed minimal atypia with rare mitosis (1/10 high-power field [HPF]) and no necrosis. There were 2 well-circumscribed nodules from the upper lobe of the right lung (1.3 and 0.5 cm) showing a tan-white, bulging, and whorled cut surface. These were composed of plump spindle cells admixed with scattered cleft-like spaces lined by cuboidal epithelium. The spindle cells exhibited mild to moderate atypia with increased mitosis (9/10 HPF) (Figure 49). Immunohistochemistry showed the spindle cells were positive for smooth muscle antigen and ER with 30%–67% positivity. HHV8, Epstein-Barr virus, and PR were negative. Controversy still exists as to whether these entities represent true metastatic lesions or are multicentric leiomyomatous tumors. There has been some recent evidence showing clonality in cases where both the pulmonary and uterine tumors are benign-appearing. In this particular case, the histology of the pulmonary and uterine tumors gives rise to the possibility of a metastasizing uterine leiomyoma with subsequent malignant transformation.

**Pulmonary Pneumocytoma: A Report of 2 Cases of a Rare Entity**

*(Poster No. 147)*

Jayalakshmi P. Balakrishna, MD (djayapanicker@yahoo.com); Arzu Buyuk, MD. Department of Pathology, St Luke’s Roosevelt Hospital Center, New York, NY.

Pulmonary pneumocytoma or sclerosing hemangioendothelioma is a rare neoplasm of the lung. This might cause diagnostic difficulty particularly in frozen sections. We present 2 cases of pulmonary pneumocytoma. The first case involved a 51-year-old woman evaluated for a lung mass. A left lower lobectomy was performed, which showed a mass with firm tan cut surfaces, extensive hemorrhage, and well-defined margins. The second involved a 42-year-old HIV-positive man found to have a mass in the right lung during a positron emission tomography/computed tomography evaluation for Hodgkin lymphoma. The mass was biopsied. Both cases on microscopy showed solid and admixed, cleftlike areas showing papillary architecture, extensive hemorrhage, and sclerosis. There were 2 types of cells; lining the spaces and papillary structures were cuboidal to flattened cells, and in the interstitium were oval to polygonal cells with clear cytoplasm and uniform nuclei. Immunohistochemical analysis revealed that the tumor cells were positive for thyroid transcription factor 1 and epithelial membrane antigen (EMA). Only the lining cells were positive for napsin A and cytokeratin 7. Ki-67 index was very low, and neuroendocrine markers were negative. Pulmonary pneumocytoma is rare, and it is important to differentiate it from other epithelial neoplasms particularly adenocarcinoma with lepidic growth pattern. Large cell size, hyperchromasia, pleomorphism, and mitotic activity helps in diagnosing adenocarcinoma whereas 2 cell populations, architectural patterns, and the positivity for EMA and selective staining of lining cells with napsin A are features helpful to make an accurate diagnosis of pulmonary pneumocytoma.

**Clinical Implication of Reclassification of Bronchioalveolar Carcinomas Based on the 2011 IASLC/ATS/ERS Classification of Lung Adenocarcinoma**

*(Poster No. 148)*

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Context: Per 2004 World Health Organization classification, bronchioalveolar carcinoma (BAC) is defined as a pattern of neoplastic cells growing along preexisting alveolar structures, where invasion of stroma, pleura, or lymphatic spaces is absent. However, per a new lung adenocarcinoma classification system proposed by the International Association for the Study of Lung Cancer, American Thoracic Society, and the European Respiratory Society, cases formerly classified as BAC were reclassified into adenocarcinoma in situ; minimally invasive
adenocarcinoma; lepidic predominant adenocarcinoma; adenocarcino-
ma, predominant invasive with some nonmucinous lepidic compon-
ent; or invasive mucinous adenocarcinoma. The new classification
clearly emphasizes the prognostic significance of histologic subtypes,
including a new micropapillary subtype.

**Design:** Eight cases previously diagnosed as pure BAC on resection speci-
men at our institution from 2002 to 2010 were reclassified, and the
cases were compared with at least 5 years of follow-up.

**Results:** Of those 8 cases, 3 were micropapillary predominant, 3
were lepidic predominant, 1 was invasive mucinous, and 1 was papillary
predominant. All of the patients with nonmicropapillary predominant
pattern are still alive and have had greater than 5-year survival. How-
ever, 2 of the 3 patients with micropapillary predominant pattern
expired at 40 months and 91 months after diagnosis. Those 2 patients
also had lymph node metastasis with micropapillary component at the
time of resection.

**Conclusions:** Our data confirmed recently published studies showing
micropapillary pattern is a pathologic marker of poor prognosis.
Those findings confirm that tumors which have been previously
diagnosed as BAC need to be evaluated with careful attention to the
new criteria because of the major clinical implications.

**A Novel Case of Pulmonary Veno-Occlusive Disease Following Orthotropic Liver Transplantation**

(Jennifer S. Woo, MD (JSWoo@mednet.ucla.edu); Haodong Xu, MD, PhD; Michael C. Fishbein, MD. Department of Pathology, David Geffen School of Medicine at UCLA, Los Angeles, Calif.

De novo pulmonary arterial hypertension (PAH) developing after
orthotropic liver transplantation is rare, with a total of 16 reported cases
since 1992. We present a case of a 49-year-old woman with a history of
autoimmune hepatitis 7.5 years after liver transplantation who
presented with shortness of breath. Although there was no evidence of
PAH before transplantation, transthoracic echocardiogram and right
heart catheterization on admission now showed severe PAH (right
tatral pressure, 19; mean pulmonary arterial pressure, 53). At autopsy,
histologic examination of the lungs showed severe-elastic–Vasa-
stain demonstrated thickened veins with intimal hyperplasia and near-
complete luminal obliteration within thickened interlobular septa.
Occasional arteriolarization of venules and intimal hyperplasia of small
arterioles were also identified. Overall, the findings are supportive of
the diagnosis of pulmonary veno-occlusive disease (PVOD) with
secondary hypertensive pulmonary angiopathy. To our knowledge, this
is the first reported incident of de novo PVOD arising after liver
transplantation. The PVOD is a rare cause of pulmonary hypertension,
which is morphologically characterized by an intimal proliferation of
septal veins and is often misdiagnosed as idiopathic PAH. Correct
diagnosis is critical because prostaglandins, a common treatment for
PAH, may cause pulmonary edema in PVOD. In this case report, we
review our current understanding of the pathogenesis of PAH and
PVOD in the posttransplant setting. We speculate that immunosup-
pressant therapy following transplantation may play a role in the
development of PVOD through vascular injury and endothelial
dysfunction.

**Mediastinal Alveolar Rhabdomyosarcoma of Solid Variant**

(Ijeundu Korie, BS†; David S. Laib, MD† (david.laib@osusharecare.
.org); Mete Korkmaz, MD. †Department of Pathology, American University
of the Caribbean Medical School, Cupe Coy, Saint Martin; Departments of Pathology and Oncology, OSF Saint Anthony Medical Center, Rockford, Ill.

The solid variant of alveolar rhabdomyosarcomas is rare. A 79-year-
old man presented with shortness of breath, cough, and difficulty
swallowing. Imaging studies revealed an anterior superior mediastinal
mass measuring 7 × 6.5 × 6 cm. This mass encased the innominate
artery and displaced the trachea. Microscopy showed desmoplastic large
cells with pleomorphic nuclei, chromatin crowded, prominent nucleoli,
invagination, necrosis, and brisk mitotic activity. By immunohistochemistry,
these malignant cells were positive for myogenin and desmin; negative
were muscle-specific actin, smooth muscle actin, CD45, cytokeratin
AE1/AE3, cytokeratin CAM 5.2, cytokeratin OSCAR, PSA, CDX2,
cytokeratins 5/6 and 7 and 20, calcitonin, EMA, CD99, S100, and
chromogranin. The Mayo Clinic consult diagnosis was alveolar
rhabdomyosarcoma of solid variant. Reverse transcription–polymerase
chain reaction performed at Mayo Clinic was negative for the PAX3-
FOXO1A and PAX7-FOXO1A fusion transcripts (80% sensitivity for
alveolar rhabdomyosarcoma). Alveolar rhabdomyosarcomas are more
commonly found in younger patients. Its skeletal muscle origin is
usually confirmed by a positive immunostaining for desmin. This
patient was treated with chemotherapy but died 7 months later, which
is characteristic of this tumor’s poor prognosis. In conclusion, alveolar
rhabdomyosarcomas of solid variant are rare, very aggressive malign-
ancies that can be diagnosed by immunohistochemistry and molecular
biology.

**Sebaceous Gland Carcinoma Presenting as An Airway Obstruction**

(David A. Cohen, MD (dacothen@tmhs.org); Eric Salazar, MD, PhD; Patricia Chevez-Barrios, MD; Roberto J. Barrios, MD; April Ewton, MD. Department of Pathology and Genomic Medicine, Houston Methodist, Houston, Tex.

Metastatic sebaceous gland carcinomas are extremely rare, and when
they do occur, the primary site is typically the eyelid adnexae or skin.
We report a case of a 57-year-old woman with a recent diagnosis of
lung cancer with metastases to the mediastinum and brain. No known
skin lesions were identified during her oncologic evaluation. She
presented with an acute airway obstruction and 100% occlusion of the
right mainstem bronchus. Sections of the obstructing tumor, removed
by bronchoscopy, showed a carcinoma characterized by lobulated cells
with foamy cytoplasm, marked nuclear pleomorphism, and abundant
collagogenous necrosis. Other areas of the tumor showed mucin-
producing glands. The mitotic count was 21/10 high-power fields with
atypical figures. The differential diagnosis initially included a squamous
infilrative carcinoma, a metastatic glandular type tumor, or a metastatic sebaceous gland carcinoma. Adipophilin (×40)
showed strong, dotlike staining of lipid globules and a focal vesicular
pattern (Figure 50, arrows) in a subset of foamy cells with membranous
staining for CAM 5.2 and CK7. The tumor cells were nonreactive for
TPH, PAX8, CD56, CK20, p40, and p63. Although the patient’s
presentation was advanced, the diagnosis of sebaceous gland carcinoma
was important because of its association with Muir-Torre syndrome.

In such a case, the metastases present in this patient most likely
represented an aggressive sebaceous gland carcinoma. Currently, the
tumor is being tested for microsatellite instability. The initial clinical
presentation also raises the possibility of a primary lung sebaceous
gland carcinoma, an entity with only one such case known in the
literature.

**Intrapericardial Mixed Germ Cell Tumor**

(Teklu B. Legesse, MD† (tlegesse@umm.edu); Daniel Fix, MD†; Aletta Frazier, MD; Allen Burke, MD. †Departments of Pathology and Radiology, University of Maryland Hospital, Baltimore, Md.

Intrapericardial germ cell tumors are exceedingly rare, and most of
the reported cases are teratomas. There are very few reports of
intrapericardial, malignant germ cell neoplasms and nearly all of them
are yolk sac tumors. We report an exceptionally rare case of
intrapericardial mixed germ cell tumor composed of a mature teratoma
and yolk sac tumor. The patient is a 22-month-old girl without
a significant past medical history who presented with a 1-week history
of upper respiratory symptoms and malaise. Serum α-fetoprotein was
elevated and magnetic resonance imaging evaluation revealed an
intrapericardial mass measuring 6.3 × 6.6 × 5.7 cm with cystic and
hemorrhagic changes involving the root of aorta. She subsequently
underwent surgical resection and gross examination of the specimen
demonstrated a pink-tan mass weighing 114 g and measuring 7.0 × 7.0 × 5.3 cm. Serial sectioning of the mass exposed an overall multi-loculated structure with multiple cystic cavities filled with a clear mucoid substance. Other areas were white to yellow-tan with punctate areas of hemorrhage and necrosis scattered throughout the mass. Histologic examination revealed cysts lined by a ciliated columnar epithelium with islands of mature cartilage and brain tissue consistent with a mature teratoma. A large part of the tumor was composed of cellular areas made of pleomorphic cuboidal cells with reticular, cystic, papillary, and solid growth patterns consistent with yolk sac tumor. After surgery, she underwent 6 cycles of chemotherapy and she remains disease free with no recurrence 2 years later.

**Pulmonary Adenoleiomyomatous Hamartoma: A Case Report of a Rare Presentation**

(Poster No. 153)

Yuna Gong, MD† (yuna.gong@umassmemorial.org); Marjan Mirzabeigi, MD†; Syed Quadri, MD‡; Steven Goodman, MD‡; Ashraf Khan, MD‡. Departments of †Pathology and ‡Surgery, University of Massachusetts Medical School, Worcester, Mass.

We report a rare variant of a pulmonary hamartoma with unusual adenoleiomyomatous features. This is a case of a 56-year-old woman with a solitary pulmonary nodule that increased in size for 3 years. She also reported unintentional weight loss (15 lb [6.8 kg]) and significant progressive dysphagia within the same period. A computed tomography scan of the lungs showed an 8-mm mass at the periphery of the right lower lobe with features suspicious for a primary lung cancer. Because of concerns of a malignancy, a wedge resection was performed. Gross examination of the lesion revealed a small, lobulated, and ovoid loculated structure with multiple cystic cavities filled with a clear mucoid substance. Other areas were white to yellow-tan with punctate areas of hemorrhage and necrosis scattered throughout the mass.

**Smooth Muscle Component**

The smooth muscle component was positive for calponin (Figure, C), positive for TTF1 (Figure, B), confirming the pulmonary origin, and the increased mitosis. No cartilage or adipose tissue was seen (Figure 51, A). The smooth muscle component also appeared benign with no cytologic atypia or increased mitosis. p63 and S100 stains demonstrated a pink-tan mass weighing 114 g and measuring 7.0 × 7.0 × 5.3 cm. Serial sectioning of the mass exposed an overall multi-loculated structure with multiple cystic cavities filled with a clear mucoid substance. Other areas were white to yellow-tan with punctate areas of hemorrhage and necrosis scattered throughout the mass. Histologic examination revealed cysts lined by a ciliated columnar epithelium with islands of mature cartilage and brain tissue consistent with a mature teratoma. A large part of the tumor was composed of cellular areas made of pleomorphic cuboidal cells with reticular, cystic, papillary, and solid growth patterns consistent with yolk sac tumor. After surgery, she underwent 6 cycles of chemotherapy and she remains disease free with no recurrence 2 years later.

**Primary Lung Carcinoma With Concomitant Granulomas: A Clinical and Histopathologic Challenge**

(Poster No. 154)

Lauren E. Rosen, MD (lauren_e_rosen@rush.edu). Department of Pathology, Rush University Medical Center, Chicago, Ill.

**Context:**

Granulomas have been sporadically described in neoplasia. When working on tumors of uncertain origin, lung adenocarcinomas (ADCs) are often a differential consideration. TTF1 and napsin A are relatively specific lung adenocarcinoma immunomarkers, expressed in approximately 75% of cases. Other organ-specific immunomarkers may infrequently be expressed in lung ADCs. To investigate the frequency of aberrant expression of other tissue-specific immunomarkers in lung ADCs, we evaluated the expression of more than 80 commonly used immunomarkers in lung ADCs, including (1) epithelial markers, (2) transcription factors/nuclear staining markers, (3) mucin genes, and (4) tumor-associated proteins, such as HBME1, calretinin, mammaglobin, GCDFP-15, uroplakin II, RCC, and actin. The association of granulomas with malignant lung tumors poses a challenge for clinicians in differentiating granulomas from tumor multifocality or regional lymph node metastases.

**Reevaluation of Expression of Immunomarkers in Lung Adenocarcinomas**

(Poster No. 155)

Haiyan Liu, MD (hliu1@geisinger.edu); Fan Lin, MD, PhD. Department of Laboratory Medicine, Geisinger Medical Center, Danville, Pa.

**Context:**

We performed a review of our surgical pathology records to evaluate the relationship between primary lung malignancy and granulomas.

**Design:**

From 1992 to August of 2013, 118 cases of lung granulomas were recorded. Cases associated with primary lung carcinomas were included. Histopathologic characteristics, topographic relationship of the granulomas to the tumors, and presence of microorganisms (assessed with PAS, GMS, fites) were reviewed.

**Results:**

Of the 118 cases, 29 (25%) were associated with lung carcinomas (16 adenocarcinomas, 8 squamous, 5 neuroendocrine). The female to male ratio was 1.6:1 with a mean age of 69 years. Ten of 29 granulomas associated with malignancy were caseating and 19/29 were noncaseating (16 sarcoïdlike, 2 hyalinated). Microorganisms were identified in 8/29 cases (5 histoplasma, 2 blastomyces, 1 aspergillus). Lymph node sampling was performed in 24/29 cases, of which 46% contained granulomas (6 calcified/hyalinated, 4 caseating, 1 sarcoïd-like). Lymph node metastases were present in 1/11 cases with lymph node granulomas (caseating).

**Conclusions:**

Twenty-five percent of lung granulomas were associated with malignancies. The most common malignancy associated with granulomas was adenocarcinoma (55%). The most common microorganism associated with malignancy was histoplasma. The presence of intratumoral and extratumoral, sarcoïdlike granulomas in association with lung malignancy may represent an immunologic host response against the tumor and may have an important role as a diagnostic marker for lymph node metastases.

**Summary of Immunostaining Results on Selected Immunomarkers**

<table>
<thead>
<tr>
<th>Immunomarkers</th>
<th>Positive Cases, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBME1</td>
<td>51</td>
</tr>
<tr>
<td>Calretinin</td>
<td>7</td>
</tr>
<tr>
<td>p40</td>
<td>1</td>
</tr>
<tr>
<td>p63</td>
<td>9</td>
</tr>
<tr>
<td>Arginase 1</td>
<td>1</td>
</tr>
<tr>
<td>HepPar1</td>
<td>8</td>
</tr>
<tr>
<td>Inhibinα</td>
<td>1</td>
</tr>
<tr>
<td>CDK4</td>
<td>35</td>
</tr>
<tr>
<td>CD138</td>
<td>59</td>
</tr>
<tr>
<td>pVHL</td>
<td>4</td>
</tr>
<tr>
<td>Mammaglobin</td>
<td>8</td>
</tr>
</tbody>
</table>

**Design:**

Immunohistochemical evaluation of the aforementioned immunomarkers in 84 lung ADCs on tissue microarray sections was performed, which were graded as positive when more than 5% of the tumor cells stained.

**Results:**

Expression of TTF1 and napsin A was seen in 81% and 75% of the cases, respectively. The aberrant expression of selected immunomarkers in lung ADCs is summarized in the Table. The expression of ER, GATA3, GCDFP-15, CDX2, SATB2, SALL4, OCT4, vimentin II, PAX8, RCC, ERG, PSA, D2-40, glypican 3, and melanoma markers (S100, MART-1, HMB-45, MITF, and SOX10) was not observed.
rarely expressed in lung ADCs. It is preferable to use a small panel of immunomarkers when working on a tumor of uncertain origin, especially if a lung primary is considered.

Concurrent Mediastinal Lymph Node Metastases From Carcinoma of the Lung and the Breast

(Jain Zhou, MD, PhD; Kerry Welsh, MD, PhD; Jing Liu, MD, PhD. Department of Pathology, University of Texas Medical School at Houston, Tex.)

Metastatic disease to mediastinal lymph node from extrathoracic neoplasms is an infrequent event. The most common extrathoracic primary cancers are genitourinary, head and neck, breast, and malignant melanoma. Concurrent metastasis from both lung and breast carcinoma have not been reported in the literature. A 59-year-old, white woman with past medical history of breast cancer in 1999 and adenocarcinoma of the right lung in 2011 underwent a positron emission tomography/computed tomography of the chest, which demonstrated an increased trace uptake activity of the pretracheal and paratracheal lymph nodes, concerning for lymph node metastasis. Biopsies of these 2 lymph nodes were performed. Microscopic examination of high right paratracheal lymph nodes revealed infiltration of malignant cells that were large and strongly and diffusely positive for CK7, TTF1, napsin, and E-cadherin; partially and weakly positive for ER; and negative for mammaglobin, CK20, PR, and GCDFP-15. The findings support the diagnosis of metastatic adenocarcinoma from a lung primary. Microscopic examination of the pretracheal lymph nodes showed nests of smaller tumor cells with small and relatively round nuclei. The tumor cells were strongly and diffusely positive for ER, CK7, and E-cadherin, and negative for TTF1, napsin, mammaglobin, CK20, PR, and GCDFP-15. The findings support the diagnosis of metastatic adenocarcinoma from a breast primary. The present report demonstrated the first case of concurrent mediastinal metastases from both intrathoracic and extrathoracic carcinomas, and careful evaluations of the histology of every lymph node with a panel of immunohistochemistry studies along with clinical history will lead to the correct diagnosis (Figure 52).

POSTER SESSION 200: MONDAY, SEPTEMBER 8, 2014, 12:45 PM TO 4:00 PM
Kidney and Genitourinary Pathology; Hematopathology; Transfusion Medicine and Coagulation

Malignant Leydig Cell Tumor of the Testis: A Case Report and Review of the Literature

(Elham Albalawi, MD; Daniel Rosen, MD. Department of Pathology, Baylor College of Medicine, Houston, Tex.)

Leydig cell tumors are rare benign sex cord-stromal tumors comprising 1% to 3% of all testicular neoplasms. Malignant transformation is very rare. Currently, no definitive early histologic criteria for malignancy exist. Therefore, metastasis is the only reliable criterion. We report a case of a 50-year-old man presenting with a 2-year history of left testicular mass. Initially, he complained of severe pain in the left testis, was given antibiotics, and was then lost to follow-up. A year later, he consulted because of discomfort. Ultrasound showed a 10-cm heterogeneous, left, soft tissue mass, and was lost to follow-up again. Recently, the patient referred for weight loss. Presurgical laboratory test showed high testosterone levels (10.1 ng/mL, range: 1.75–7.81 ng/mL). All other laboratory tests were within reference range. The left orchiectomy specimen showed a 10×8×8-cm, well-circumscribed, variegated testicular mass. Microscopically, polygonal cells with abundant granular acidophilic cytoplasm expanding the rete testis spaces without frank invasion were seen. Tumor necrosis, focal lymphovascular invasion, and lack of Reinke crystals were noted. Immunohistochemical stains showed strong stain for calretinin, vimentin, and inhibin and were negative for pancytokeratin, CD30, AFP, and CD117. Increased mitotic activity (15 mitosis per 10 high-power field) and Ki-67 proliferation index of 25%. Here, we report a rare case of malignant, Leydig cell tumor and review the published clinical and histologic criteria for malignancy.

Simple Tumor Enucleation, Without Hilar Vasculature Clamping, for Small Renal Cancers—Is it Feasible?

(Jingyang Feng, MD; Lu Wang, MD; Helyn Alvarez, BS; Haiyan Chen, MD, PhD; Gopal Gupta, MD; Maria Picken, MD, PhD. Departments of Pathology and Urology, Loyola University Medical Center, Maywood, Ill; Department of Pathology, Stritch School of Medicine, Maywood, Ill.)

Context: Small renal cancers are increasingly detected in aging patients with reduced nephron mass and vascular comorbidities, which put them at risk for loss of renal function requiring dialysis. A simple tumor enucleation without clamping of hilar vasculature may be applicable to small renal tumors, thus affording maximal nephron...
sparing as well as avoidance of ischemia because of clamping. However, despite generally excellent oncologic outcomes, concerns have been raised regarding the oncologic safety of such procedures.

**Design:** A total of 31 small renal tumors were removed by a simple enucleation between March 2012 and June 2013. We evaluated the gross and microscopic morphology of tumor pseudocapsule and correlated those with tumor size, nuclear grade, and tumor subtype.

**Results:** All pseudocapsules were smooth, focally semitransparent pseudocapsules, except for one specimen that became fragmented during evaluation via laparoscopic port. Microscopically, the pseudocapsules were composed of fibrous tissue and adjacent compressed renal parenchyma, frequently with sclerosed glomeruli and tubules. In 7 tumors, despite grossly intact appearance, microscopically, there were focal pseudocapsule penetration and positive margins. The presence of pseudocapsule penetration is significantly associated with tumor Fuhrman grade (Figure 53).

**Conclusions:** This study indicated that most small renal masses demonstrate a continuous, nonfenestrated, fibrous pseudocapsule. Pseudocapsule penetration represents an additional prognostic factor in patients with early stage renal cell carcinoma. Careful evaluation of the status of the pseudocapsule is important in patients treated with nephron-sparing procedures, in particular, enucleation.

**Metastatic Renal Cell Carcinoma With Immunohistochemical and Molecular Confirmation in the Absence of a Suspicious Renal Mass: Report of 2 Cases**

(Poster No. 3)

Protima Rayapati, MD (protima.rayapati@uky.edu); Matthew Purdom, MD; Dana Richards, MD. Department of Pathology and Laboratory Medicine, University of Kentucky, Lexington, Ky.

Metastases of renal cell carcinomas are frequently detected before the primary site is clinically apparent. After adequate imaging, however, metastatic disease in the absence of an identifiable suspicious renal mass is exceedingly rare with only 2 cases previously documented in the literature. Herein, we describe 2 cases of metastatic carcinoma that were morphologically and immunophenotypically compatible with metastatic renal cell carcinoma, without a suspicious renal mass by multiple imaging modalities. The first case involved a 77-year-old man with metastatic sarcomatoid carcinoma in the inferior pubic ramus of the pelvis and the second case involved a 55-year-old man with metastatic carcinoma with papillary features presenting as a retroperitoneal mass. Both patients had benign-appearing simple cysts within the kidneys but no suspicious masses by imaging. Both cases demonstrated positivity for pancytokeratin, vimentin, and renal markers PAX2 and PAX8. After the diagnoses were rendered, both cases were subsequently submitted for molecular testing for carcinoma of unknown primary (CancerTYPE-ID, bioTheranostics, San Diego, Calif), and were confirmed as consistent with renal primaries both with 96% probability. Throughout therapy, no obvious renal primary became apparent on imaging, including multiple computed tomography scans and one magnetic resonance imaging. To our knowledge, this is the first report of metastatic renal cell carcinoma in the absence of a suspicious renal mass that has been confirmed by molecular testing. Possible explanations for the findings include a primary that is occult by imaging because of its small size, tumor regression, or an entirely cystic primary resembling a benign cyst.

**Poststreptococcal Glomerulonephritis With Alveolar Hemorrhage: A Case Report and Literature Review**

(Poster No. 4)

Yanfei Huang, MD, PhD (huangy@ufl.edu); Dana Wakefield, MD; William Clapp, MD. Department of Pathology, Immunology and Laboratory Medicine, University of Florida, Gainesville, Fla.

Pulmonary-renal syndromes are a group of disorders characterized by acute glomerulonephritis and lung inflammation or hemorrhage. They can be life-threatening with 25–50% of mortality rate if not diagnosed and treated in time. The common causes include ANCA-positive small-vessel vasculitis, Goodpasture syndrome, and lupus erythematosus. Alveolar hemorrhage associated with poststreptococcal glomerulonephritis is extremely rare with 3 cases been reported in the literature. In our case, a 23-year-old man with a past medical history of morbid obesity and asthma presented to the emergency room with a sore throat, nonproductive cough, and shortness of breath. Chest x-ray showed bibasilar pleural-parenchymal disease. Further workup showed an elevated BUN and creatinine and positive antistreptolysin-O and anti-DNase-B antibody. A kidney biopsy revealed an acute endocapillary (exudative) proliferative immune-complex-mediated glomerulonephritis consistent with postinfectious glomerulonephritis. During admission, the patient had several episodes of hemoptysis. A bronchoscopy with bronchoalveolar lavage was performed. The aspirate was blood-tinged, and cytology results showed hemosiderin-laden macrophages. The patient was treated with high-dose systemic steroids and recovered quickly. Although the exact mechanism of alveolar hemorrhage in poststreptococcal glomerulonephritis is unclear, an experimental study suggested that an antibody against streptococcal cell membrane antigens might have an important role in the pathogenesis of the association. Uncontrolled observations in the previous reports suggested that high-dose systemic steroid therapy produced a prompt improvement in the nephritis associated with alveolar hemorrhage, which was also seen in our current case.

**GATA3, Thrombomodulin, and β-Catenin in the Diagnosis of Primary Adenocarcinoma of the Urinary Bladder**

(Poster No. 5)

Jayaalakshmi P. Balakrishna, MD1 (drjayapanicker@yahoo.com); Violette Ghali, MD,2 1Department of Pathology, St Luke’s Roosevelt Hospital Center, New York, NY; 2Department of Pathology, Beth Israel Medical Center, New York, NY.

**Context:** Primary adenocarcinoma of the urinary bladder is an exceedingly rare malignancy with a poor prognosis. Diagnosis of these may be a challenge and is of great clinical significance.

**Design:** Twelve cases of primary adenocarcinoma of the urinary bladder were reviewed. The diagnoses were clear cell adenocarcinoma (n = 2), mucinous adenocarcinoma (n = 2), signet ring cell adenocarcinoma (n = 1), poorly differentiated adenocarcinoma (n = 4), adenosquamous carcinoma with papillary features (n = 2), and urachal carcinoma with micropapillary and glandular features (n = 1). Immunohistochemical staining was performed with cytokeratins 7 and 20, CDX2, GATA3, thrombomodulin, Cad-17, 10-20k, and α-catenin.

**Results:** Of the 12 adenocarcinomas, 75% were positive for CK7, 50% were positive for CK20, and 25% were positive for both. GATA3 was positive in 66% of the cases. β-catenin showed diffuse strong membrane staining in all the 12 cases. All the cases were negative for thrombomodulin and only 1 case was positive for Uroplakin II. Cad-17 was positive in 50% of the cases whereas CDX-2 was positive in only 25% of the cases.

**Conclusion:** The immunophenotypic profile of adenocarcinoma is similar to conventional urothelial carcinoma in being positive for CK7 or both CK7 and CK20 and GATA3. They show membranous staining for β-catenin which is helpful to differentiate them from colonic primaries. They differ from those tumors in being negative for thrombomodulin and uroplakin II. Cad-17 can be expressed by primary adenocarcinomas and does not differentiate them from colonic metastasis. Also, CDX-2 can be expressed by a small percentage of these tumors, and is not helpful in differential diagnosis.

**Features of Intrapeudocapsular Vasculature in Small Renal Neoplasms: Critical Analysis of 178 Cases**

(Poster No. 6)

Lu Wang, MD1 (luwang@lumc.edu); Jingyang Feng, MD, PhD2; Helyn Alvarez, MD3; Gopal Gupta, MD3; Maria Picken, MD, PhD.1 Departments of1 Pathology, Stritch School of Medicine and 2Urology, Loyola University Medical Center, Maywood, Ill.

**Context:** Simple enucleation of small, nonhilar renal tumors maximally preserves nephrons and allows for zero warm-ischemia time because it can be done off clamp with apparently no significant bleeding. This study aimed to analyze the intrapeudocapsular vasculature of small renal tumors.

**Design:** Small renal tumors (<4 cm) surgically removed during 2002 to 2013 were reexamined with special attention to the intrapeudocapsular vasculature (diameter, ≥0.2 mm), and its relationship to tumor type and size. Student t test and χ² test were used for statistical analysis.

**Results:** We reviewed 178 surgically removed renal tumors. Most of the intrapeudocapsular blood vessels were small (<0.2 mm in diameter) or obliterated. A total of 335 intrapeudocapsular arteries (≥0.2 mm in diameter) were identified microscopically, with average outer and luminal diameters of 0.32 mm and 0.12 mm, respectively. Vascular compressions and prominent subintimal fibrosis contributed

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to lumen narrowing. Most arteries ran parallel to the pseudocapsule and rarely were perpendicular. Intrapseudocapsular veins were largely collapsed or obliterated. Chromophobe renal cell carcinoma (RCC) had the highest percentage of tumors with intrapseudocapsular arteries (88.89%), followed by oncocytoma (83.33%) and clear cell RCC (77.12%); Papillary RCC had the lowest percentage (51.52%). Arterial densities among different tumor types ranged from 2.29 to 2.64 arteries/tumor (P < .05). There were no significant differences in the size of arteries among different tumor types (P > .05).

**Conclusions:** Larger vessels are encountered infrequently within the tumor pseudocapsule, with the highest percentage found in chromophobe RCC and the lowest in papillary RCC. Both artery density and diameter were similar among different types of renal tumor.

**Urethral Enteric-Type Adenocarcinoma Mimicking Primary Clear Cell Adenocarcinoma: A Case Report With Evidence of Stepwise Pathogenesis**

*(Poster No. 7)*

Kristen E. Muller, DO\(^1\) (kristen.e.muller@hitchcock.org); Jason D. Peterson, MD\(^2\); Alan R. Schned, MD\(^3\); Jorge L. Gonzalez, MD\(^4\); John D. Seigne, MD\(^5\); Jason R. Pettus, MD\(^6\). Departments of \(^1\)Pathology and \(^2\)Urology, Dartmouth-Hitchcock Medical Center, Lebanon, NH.

Primary urethral adenocarcinoma is a rare entity, and little is known about its pathogenesis. Although many of these tumors are identified in association with intestinal metaplasia, the role of intestinal metaplasia in the pathogenesis has been debated. We report a case of a 71-year-old woman with a history of long-standing urethral diverticulum, complicated by urethral-vaginal fistula, who presented with hematuria. Cystoscopic biopsy of the trigone confirmed an unusual malignancy, originally favored to be clear cell (so-called mesonephric) adenocarcinoma. Subsequently, radical cystectomy and urethrectomy revealed a pT3b pNX pM0 adenocarcinoma of the proximal bladder and urethra. The dominant mass was composed of large cells with abundant clear cytoplasm arranged in mixed solid, tubular, and cribriform architecture (Figure 54, A). Scattered eosinophilic luminal secretions were present (Figure, B). Interestingly, sampling of the associated urethral diverticulum revealed a positive staining for PAS, CK7, a distal tubular marker, and phosphorylated-p70S6K (p-p70S6K, the main downstream signal of mTOR), and compared them to 10 cases of adult polycystic kidney disease (PKD). Numerous cysts of the pediatric kidney revealed an eosinophilic epithelial lining. Some of cysts contained glomerular structures. The cystic lining showed positive staining for PAX8. By contrast, the PKD cystic lining stained positively for CK7 and p-p70S6K, but negatively for PAS and KIM-1. These findings indicate that the TS-associated cysts arise from proximal renal tubules, whereas PKD cysts are derived from distal nephron tubules. Our recent study revealed upregulated mTOR in the cyst lining of PKD. TSC is the upstream inhibitor of mTOR pathway, and mutation of TS genes may result in upregulation of the mTOR pathway. In this pediatric cystic disease, positive p-p70S6K in the cyst lining is strongly suggestive of contributing to the upregulation of the mTOR pathway for cyst formation. In summary, TS-associated renal cysts are derived from proximal tubules, possibly through the activation of mTOR pathway.

**Florid, Diffuse, Leydig Cell Hyperplasia in the Setting of Burned-Out, Testicular, Mixed Germ Cell Tumor With Metastases: A Case Report With Cytology-Histology Correlation**

*(Poster No. 9)*

Whitney A. McCarthy, MD (wamccart@bcm.tmc.edu); Retty L. Cox, MD; Rodolfo Laucirica, MD; Jason E. Moss, MD. Department of Pathology & Immunology, Baylor College of Medicine, Houston, Tex.

Burned out testicular germ cell tumors are rare, representing involved primary tumors typically discovered during workup for metastatic disease with associated elevated serum tumor markers. Histologically, a hyalinized scar is seen, often with surrounding intratubular germ cell neoplasia. We report a 24-year-old man who presented with a 2-month history of cough, dyspnea, and intermittent testicular pain. Ultrasound revealed a 0.6 × 0.5 × 0.5-cm lesion within the right testis. Chest imaging revealed innumerable pulmonary nodules and diffuse lymphadenopathy. Serum tumor markers were elevated (AFP, 432.9 ng/mL; LDH, 2606 U/L; and β-hCG, 97 575 mIU/mL), and the patent underwent a radical orchiectomy. Upon examination there was a 0.5-cm multinodular mass surrounded by intratubular germ cell neoplasia and florid, diffuse, Leydig cell hyperplasia. Fine-needle aspiration of a left supraclavicular lymph node was performed, revealing a mixed germ cell tumor with embryonal carcinoma, seminoma, and chorionicarcinoma. Diffuse, Leydig cell hyperplasia in the setting of germ cell tumors is rare and is thought to be induced by markedly elevated serum β-hCG from a syncytiotrophoblastic component (possibly associated with chorionicarcinoma). To our knowledge, this case represents the first report of diffuse, Leydig cell hyperplasia with adjacent, burned-out, testicular germ cell tumor, metastatic chorionicarcinomatous elements, and elevated serum β-hCG.
Prostate Adenocarcinoma Expresses Neurotrophic Factors Inhibiting Tumor Innervation  
(Poster No. 10)

Dmitriy Gutkin, MD, PhD
(dmgutkin@hotmail.com); Galina Shurin, PhD; Michael Shurin, MD, PhD
Department of Pathology, VAMC Pittsburgh, Pa; Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pa.

Context: Although blood vessels were abundant in the tumor tissue, the neural structures were scarce compared with benign prostate tissue. Tumor-conditioned media of TRAMP-C2 and RM-1 murine prostate cancer cell line were added to the murine neuron cultures, and the morphology of the neurons was analyzed 60 hours later. The number of neurons, the number of cells with neurites, the number of neuritis per cell, the lengths of neurites, and the number of branching points per cell were calculated. Expression of NF genes in prostatic adenocarcinoma was evaluated by reverse transcription-polymerase chain reaction using specific primers.

Results: Although blood vessels were abundant in the tumor tissue, the neural structures were scarce compared with benign prostate tissue. Tumor-conditioned media of TRAMP-C2 and RM-1 murine prostate cancer cell line significantly inhibit the neurite growth and branching in mouse neuron cultures. The role of these elements in tumor growth and metastatic potential is under investigation.

Conclusion: Prostate cancer cells express NF factors that inhibit neurite growth and lead to hypoinnervation of the tumor mass. The role of this phenomenon in tumor growth and metastatic potential is under investigation.

An Unusual Composite Tumor: Chromophobe Renal Cell Carcinoma Associated With Foci of Collecting Duct-Type Carcinoma  
(Poster No. 11)

Lauren N. Pearson, DO (Lauren.Pearson@vtmednet.org); Maryam J. Zenali, MD. Department of Pathology & Laboratory Medicine, Fletcher Allen Health Care, Burlington, Vt.

We report the case of a 69-year-old woman who originally presented with an incidental renal mass, at the time diagnosed as oncocytoma by cytology and needle core biopsy. In less than 2 years, the mass doubled in size, raising concern for malignancy. Surgical management was pursued. The nephrectomy specimen contained a 6.0-cm, relatively circumscribed, tan-brown cystic and solid mass confined to the kidney. Upon microscopic evaluation, there were 2 morphologically distinct neoplastic populations. The tumor was predominantly composed of monotonous, eosinophilic cells with distinct cytoplasmic borders and rasinoid nuclei with a perinuclear halo, in keeping with chromophobe renal cell carcinoma. In the midaspect of the tumor, high-grade tubulopapillary foci with hobnail pleomorphic nuclei and extracellular lumen were present. Both components stained with CK7 and E-cadherin, while expectedly, only the collecting duct carcinoma stained with vimentin (Figure 55). As anticipated, Hale-Colloidal iron showed a differential pattern of staining in chromophobe renal cell carcinoma and collecting duct carcinoma. A few case reports of collision tumors involving chromophobe carcinoma are described in the English literature; the current case describes yet another extremely unusual variant. Awareness of these entities is of paramount importance in the determination of prognosis, management, and diagnosis of patients with chromophobe renal cell carcinoma. Detailed attention to the evolving clinical course and radiologic features as well as the adequacy of tumor sampling is critical as highlighted by the current case.

Two Cases of Clear Cell Papillary Renal Cell Carcinoma With Emphasis on Immunohistochemical Phenotype  
(Poster No. 12)

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Clear cell papillary renal cell carcinoma is a relatively new entity among renal epithelial neoplasms. Proper diagnosis can be challenging to the anatomic pathologist because of varying gross, histologic, and immunohistochemical presentations. We present 2 cases of clear cell papillary renal cell carcinoma with similar histology and immunohistochemistry. The first case is a 73-year-old man who presented with a 1.3-cm cystic renal mass. The second case is a 59-year-old man who presented with a 2-cm cystic renal mass. Macroscopically, both masses were cystic with no obvious malignant component. Histologically, the tumors were composed of cystic structures lined by cuboidal cells with clear cytoplasm. However, clear cell papillary renal cell carcinoma can present with solid, papillary, glandular, or cystic features. Immunohistochemistry performed on these cases showed positive reactivity to CK7 and CA IX and was negative for AMACR, CD10, and TFE3. It is important to effectively distinguish the immunohistochemical stains for clear cell papillary renal cell carcinoma from clear cell and papillary renal cell carcinoma because of vastly different prognoses and treatment modalities. Because clear cell papillary renal cell carcinoma is less aggressive than clear cell or papillary renal cell carcinomas, more conservative treatment can be employed. By diligent use of immunohistochemistry and histologic analysis, a correct diagnosis can be made to provide for better patient care.

Mucinous Tubular and Spindle Cell Carcinoma: A Case Report Associated With Nephrolithiasis  
(Poster No. 13)

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A 47-year-old man with a history of ureteric calculi presented with recurrent hematuria. Imaging investigation demonstrated the presence of a 2-mm right renal calculus and an incidental right upper-pole renal mass. The patient underwent a laparoscopic right nephrectomy. Grossly, the right upper pole contained a pale, white-tan, firm, well-circumscribed tumor measures 3.8 cm in greatest diameter. The tumor abutted the renal capsule but did not breach it or the renal calyces grossly. Histologically, sections demonstrated a well-circumscribed tumor situated in the renal cortex. The tumor was composed of tightly packed, ill-defined tubules with large areas of spindle cell formation. Both the tubular and spindle cell components demonstrated relatively low-grade cytology with predominantly small nuclei and rare mitotic figures. The spindled foci were associated with abundant mucinous material, confirmed as such with an Alcian blue stain. Immunohistochemical staining demonstrated positivity for racemase, CAM 5.2, EMA, and CK7. CD10 was weakly positive. Overall, histologic appearances and staining profile were most consistent with a mucinous tubular and spindle cell carcinoma of the kidney. Unusual features of this tumor included a prominent epithelioid component, areas of clear cell change, and occasional prominent nuclei within the epithelioid component (Fuhrman grade 3). However, there was no evidence of significant
mitotic activity or necrosis. The atypical foci all stained strongly for racemase and CK7.

**A Rare Case of Urachal Carcinoma Presenting as Umbilical Hernia**

*Poster No. 14*

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The urachus is an embryologic remnant that connects the umbilicus to the bladder. It regresses into the median umbilical ligament before birth. Urachal carcinoma is a rare, highly malignant tumor that requires clinical suspicion, imaging, and pathologic examination for appropriate diagnosis. It is slightly more common in males than females. It usually present with hematuria, symptoms of bladder irritation, abdominal pain, or as an abdominal mass. We present a case of a 50-year-old woman who was noted to have an umbilical hernia during breast reconstruction. The pathologic examination of the hernia sac revealed nests of pleomorphic, malignant cells with a high nuclear to cytoplasmic ratio, and hyperchromatic nuclei with prominent nucleoli. The tumor cells were positive for CK7, CDX2, CK19, and CEA, and were negative for mucin, uroplakin, p63, CK20, CA 125, CA 19-9, TTF1, ER, mammaglobin, CD56, and GCDFP-15. Based on the staining profile, a specific primary tumor could not be identified. Before clinical workup, the diagnosis was poorly differentiated metastatic carcinoma, and the differential diagnosis included upper gastrointestinal, pancreatic, cholangiocarcinoma, or colorectal cancer, among others, with recommendation for clinical correlation. Computed tomography and positron emission tomography scans revealed a heterogenous density at the umbilicus, which showed intense hypermetabollic activity and soft tissue thickening. Based on the radiologic, pathologic, and clinical findings, a diagnosis of urachal carcinoma, with no evidence of metastasis or spread beyond the umbilical area, was concluded. The patient currently awaits partial cystectomy, umbilicectomy with urachal remnant excision (Figure 56).

**MMP-26 May Detect Prostate Cancer Risk Regardless of Needle Biopsy Pathology**

*Poster No. 15*

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**Context:** Several molecular diagnostic approaches have been proposed to detect coexisting, unsampled prostate cancer in histologically negative biopsy cores, or urine. Most have relied on DNA promoter methylation, particularly that of GSTP1. Matrix metalloproteinase 26 (MMP-26) was reported as overexpressed in prostate cancer tissues, with peak expression in high-grade prostatic intraepithelial neoplasia. We compared these 2 alterations in prostate biopsy specimens.

**Results:** The Table shows the 12-part biopsy cases 1 and 2 with differing amounts and grades of cancer: 20% to 99% cancer in 5 cores, and 5% cancer in 1 core respectively. In case 3 with 14 cores of benign prostatic tissue, MMP-26 was positive in 3, suggesting increased risk. In another 2-core case of all benign prostatic tissue, the left midsample had the highest MMP-26 expression; at the 3-year follow-up biopsy, the left midsample was diagnosed with Gleason 3 + 3 = 6 cancer in 5% of the core.

**Conclusions:** In this pilot study, MMP-26 overexpression occurred more frequently than GSTP1 promoter methylation in prostate biopsies. Validation in a larger population with repeat biopsies is required.

**Immunohistochemical Expression of Folate Receptor α in Urothelial Carcinoma of Bladder**

*Poster No. 16*

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**Context:** Folate receptor α (FRA), a high affinity folate receptor, is a potential target used for folate-linked chemotherapy. Moreover, FRA expression is restricted to normal epithelial cells but upregulated in several carcinomas. Additionally, FRA expression is described as prognostic marker in some cancers. The goal of the present study was to evaluate the frequency of expression of FRA in urothelial carcinoma of bladder (UCB) and its prognostic significance.

**Design:** Tissue microarrays (TMA) were constructed using cystoprostatectomy specimens collected from years 1998 to 2016. Specimens were divided in 3 groups: (1) 10 patients with no bladder cancer, (2) 9 patients with UCB without metastasis, and (3) 45 patients with UCB with lymph node metastasis. Immunohistochemical stains were performed on TMA using mouse anti-FRA monoclonal antibody 26B3.P2. Stains were evaluated independently by 2 pathologists and scored 0 (negative), 1 (weak), 2 (intermediate), and 3 (strong) based on intensity of membranous staining. A sample was considered positive if 10% or more cells were stained for any intensity.

**Results:** None of the benign bladder cases were positive for FRA. Only one UCB without lymph node metastasis showed intermediate expression, compared with 9 of 45 (20%) of the UCB with lymph node metastasis; 3 of those showed strong positivity. In this group, expression was concordant between primary tumor and lymph node metastasis in 3 of 9 tumors.
Conclusions: In this study, FRA was positive in 18.5% of UCB. Those patients may benefit from FRA-targeted therapy. Additionally, FRA is more likely to be positive with metastatic disease (11% versus 20%).

Estrogen Receptor β in Urothelial Carcinoma With Lymph Node Metastases

(Poster No. 17)

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Context: Estrogen receptor β (ER-β), expressed in bladder cancer cell lines and many human bladder tumors, mediates the estrogen-induced G1/S transition in the cell cycle in urothelial cells. Although its role as a prognostic marker for urothelial carcinoma (UC) is controversial, ER-β inhibition with tamoxifen synergistically increases the cytotoxicity of chemotherapeutic agents in vitro, and clinical trials are evaluating its use in UC. To provide insight into this therapeutic strategy, we examined ER-β expression in cystectomy specimens.

Design: Cystectomy specimens from patients with UC metastatic to lymph nodes at the time of surgery, UC without metastases, or normal bladders were analyzed. Slides were examined by 2 pathologists and scored based on nuclear staining for ER-β. In addition to comparing ER-β expression among the cystectomy specimens, expression in lymph node metastases was compared with expression in the primary tumor.

Results: Nuclear ER-β expression was present in 79% of the normal bladders (11/14) and in 78% of the UC confined to the bladder (7/9), but only in 51% of the UC bladders with lymph node metastases (23/45). Within the lymph node metastases group, there was no significant difference in ER-β expression in the primary tumors (20/40) compared with the lymph node metastases (12/31).

Conclusions: Our result suggests that ER-β expression is a favorable prognostic marker, as its expression is lower in UC metastatic to lymph nodes. Because ER-β upregulation occurs in a large proportion of high-grade invasive bladder tumors and lymph node metastases, its inhibition may represent a novel modality for targeted therapy in advanced disease.

Polyomavirus-Associated, Poorly Differentiated Clear Cell Adenocarcinoma of the Urinary Bladder in a Kidney Transplant Patient

(Poster No. 18)

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Clear cell adenocarcinoma of the urinary tract is a rare neoplasm predominantly affecting the urethra and is more common in women. We report a case of 32-year-old man with a history of bilateral lung transplant for cystic fibrosis and kidney transplant for immunoglobulin A (IgA) nephropathy. Six years after the kidney transplant, he presented with dysuria, and cystoscopic examination showed a 4.5-cm mass in the bladder. Urinary bladder barbotage and biopsy was obtained. A concomitant plasma BK virus DNA polymerase chain reaction (PCR) showed 84 525 copies/mL. The histologic sections of the tumor showed poorly differentiated adenocarcinoma with tubulocystic, clear cell, and sarcomatoid differentiation, which was also observed in the bladder barbotage and the subsequent partial cystectomy specimen (Figure 57, A). Immunohistochemical stains are outlined as below: positive: SV40 (polyomavirus; Figure, B and inset), PAX8 (Figure, C), cytokeratin 5/6, and CD10 (Figure, D); negative: AMACR, PAX2, and CK7. Recent reports on clear cell adenocarcinoma of the urinary bladder raise the possibility of a renal tubular/mesonephric origin for some of these tumors. Rare reports of coexistence of polyomavirus-associated urothelial carcinoma of the urinary bladder with BK viruria have been published. Our case showed diffuse positivity for SV40 (polyomavirus) immunohistochemical stain in the tumor cells, whereas adjacent normal cells were negative. Additionally, BK virus DNA PCR was not detected after the tumor excision. To our knowledge, this is the first case of clear cell adenocarcinoma associated with polyomavirus. This case adds to evidence for the possibility of BK virus in the pathogenesis of bladder cancer, especially in immunosuppressed patients.

Not All Renal Masses Are Wilms Tumor in Patients With Prior Wilms Tumor History: Meet IgG4-Related Kidney Disease

(Poster No. 19)

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Wilms tumor is the most common renal tumor of childhood. Wilms tumor has the potential for both local and distant spread; approximately 5% to 10% of children present with bilateral or multicentric tumors. The most frequent sites of late recurrence are abdomen, lungs, and contralateral kidney. This is a case of an 11-year-old boy with left total nephrectomy for Wilms tumor 6 years previously, who presented with a new mass in his right kidney. Because of a high clinical suspicion of Wilms tumor recurrence, a partial nephrectomy was pursued. The specimen contained a 3-cm, circumscribed but unencapsulated, gray-tan, myxoid, somewhat lobulated mass that was histologically characterized by a florid tubulointerstitial nephritis predominated by plasma cells. Most lymphocytes were composed of T cells as shown by a
Angiomyolipoma With Regional Lymph Node Involvement in a Patient With Hemochromatosis: A Case Report and Literature Review

(Poster No. 20)

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Angiomyolipoma (AML) is a mesenchymal tumor belonging to a family of lesions characterized by proliferation of perivascular epithelioid cells, accounting for 1% of renal tumors. Conventional AMLs (nonnephthelioid type) are known to be benign, whereas epithelioid variants are known to be clinically more aggressive. Usually, AML occurs sporadically; however, when seen in familial syndromes, most commonly tuberous sclerosis, it tends to be bilateral and multifocal. A 54-year-old man with a history of hemochromatosis and no clinical evidence of tuberous sclerosis presented with a solitary left renal mass, extending into the perirenal fat. Subsequent radical nephrectomy revealed a 4.6-cm, lobulated, hemorrhagic mass involving kidney and perinephric adipose tissue. Histopathologically, a classic triphasic histology, composed of mature adipocytes, the most common variant was UCa with squamous differentiation. Most of the UCa had presented first or only at that site, and 67 (69%) were recurrences or concurrent to UCa elsewhere in the GU tract. Most of the UCa had conventional morphology, and the most common variant was UCa with squamous differentiation.

Conclusions: Our study shows that, unlike bladder UCa, most upper tract UCa are high grade and present with advanced pathologic stage. The interval from upper tract to bladder recurrence is significantly shorter than from bladder to upper tract UCa recurrence.
Immunohistochemical Distinction Between Metastatic Renal Cell Carcinoma to the Adrenal and Primary Adrenal Lesions

(Poster No. 23)

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Context: The morphology of clear cell renal cell carcinoma, when low grade, overlaps with normal adrenal and primary adrenal adenoma, when high grade, with carcinoma. We applied a panel of 10 antibodies to 62 cases to determine the optimal antibody panel to discriminate these entities.

Design: Resection specimens with established diagnoses from the past 18 years were available from Medical College of Wisconsin (28 cases) and Charles University Hospital (34 cases): 34 men and 28 women. As controls, 42 cases contained normal adrenal tissue. Areas of tumor or normal adrenal tissue were punched from paraffin blocks and assembled into tissue microarrays; duplicate spots represented each entity. Immunostains included CAM 5.2 (1:50, Becton Dickinson, Franklin Lakes, NJ), E-cadherin, p53, INI-1, and EMA. Cases were graded (0–4) based on nuclear atypia, mitosis, necrosis, and vascular invasion. The morphology of clear cell renal cell carcinoma, when high grade, overlaps with normal adrenal and primary adrenal adenoma, when low grade, overlaps with renal cell carcinoma. We applied a panel of 10 antibodies to determine the optimal antibody panel to discriminate these entities.

Results: Area-under-the-curve analysis (SAS Institute, Cary, North Carolina) ranked the significant markers for each entity (see Table). Logistic regression analysis disclosed that PAX8 nuclear reactivity plus absence of PAX8 cytoplasmic reactivity, discriminated renal cell carcinoma associated with very aggressive behavior and a dismal prognosis. These tumors remain relatively undercharacterized. The aim of our study was to use multiple immunohistochemistry antibodies as well as a targeted molecular analysis to compare the expression of proteins in the conventional carcinoma component versus the sarcomatoid/rhabdoid component of these tumors.

Design: Included in this retrospective study were 25 cases of sRCC. Representative areas of sarcoma and carcinoma were selected from each case and compiled into a tissue microarray. Immunohistochemical stains were performed at ARUP Laboratories (Salt Lake City, Utah) with commercially available antibodies for Pim1, Pim2, Pim3, phosphorylated mTOR, phosphorylated S6rib, PTEN, IMP3, β-catenin, E-cadherin, p53, INI-1, and EMA. Cases were graded (0–4) based on the percentage of cells positive for each antibody (0, <5%; 1, 5%–25%; 2, 26%–50%; 3, 51%–75%; 4, >75%). Scores of 2 or greater were considered positive. Molecular testing was performed on paraffin-embedded tissues from 6 samples using a Sequenom (San Diego, Calif) panel of 277 known mutations.

Results: The percentage of tumors with positive staining in conventional carcinoma areas compared with sarcomatoid/rhabdoid areas is provided in the Table. No targetable mutations were detected by the Sequenom panel.

<table>
<thead>
<tr>
<th>Stain</th>
<th>Carcinoma (n = 25), %</th>
<th>Sarcoma (n = 25), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIM1</td>
<td>14</td>
<td>18</td>
</tr>
<tr>
<td>PIM2</td>
<td>57</td>
<td>73</td>
</tr>
<tr>
<td>PIM3</td>
<td>5</td>
<td>18</td>
</tr>
<tr>
<td>Phos-mTOR</td>
<td>81</td>
<td>85</td>
</tr>
<tr>
<td>Phos-S6rib</td>
<td>76</td>
<td>82</td>
</tr>
<tr>
<td>INI-1</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>IMP3</td>
<td>43</td>
<td>64</td>
</tr>
<tr>
<td>PTEN</td>
<td>14</td>
<td>45</td>
</tr>
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</tr>
<tr>
<td>p53</td>
<td>5</td>
<td>18</td>
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<tr>
<td>EMA</td>
<td>48</td>
<td>41</td>
</tr>
</tbody>
</table>

Conclusions: Sarcomatoid and rhabdoid components appear to show increased Pim kinase, IMP3, and p53 expression when compared with the conventional renal cell carcinoma component. Expression of the aforementioned markers may contribute to disease progression and serve as a potential site for targeted therapy.

Primary Renal Angiosarcoma in a 44-Year-Old Man

(Poster No. 25)

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Angiosarcomas are one of the rarest forms of soft tissue neoplasms. They account for less than 1% of all sarcomas and have a predilection for skin and superficial soft tissue. We report a case of a 44-year-old man who presented with left flank pain of 2-week duration and 15-pound (6.8 kg) weight loss and fatigue for 2 months. A computed tomography scan of the abdomen and pelvis showed an enlarged diffusely heterogeneous mass involving the left kidney, which was considered compatible with renal cell carcinoma. A radical nephrectomy of the left kidney revealed an irregular hemorrhagic mass that extended through the renal capsule into perinephric fat. Microscopic examination revealed a high-grade spindle cell malignant neoplasm, which focally revealed a typical pattern of a high-grade angiosarcoma. Immunohistochemical stains confirmed the vascular nature of the
A 65-year-old man presented with loss of appetite and loss of weight. On physical examination, a palpable mass was noted in the right hypochondrium, which on computed tomography scan of abdomen and pelvis, was revealed to be a complex cystic mass measuring 23.0 × 14.5 × 14.2 cm, involving the entire right kidney. A radical nephrectomy was performed. Gross examination showed an encapsulated, multicystic tumor containing hemorrhagic fluid. On microscopy, the tumor had a tubulocystic appearance (Figure 61). The lining epithelium featured cuboidal, flat, and hobnail cells with eosinophilic cytoplasm and enlarged nuclei with prominent nucleoli. Focally (<5%), the tumor exhibited areas with papillary architecture. No foamy histiocytes or psammomatous calcifications were seen. Areas of necrosis were noted. No infiltrative growth pattern with stromal desmoplasia or sarcomatoid areas was seen. No lymphovascular emboli were present. Electron microscopy was performed on the tumor, and the tumor cells were shown to possess sparse, short microvilli as well as abundant mitochondria. Definite cytoplasmic interdigitation was not observed. The final diagnosis was that of a tubulocystic renal cell carcinoma. The patient developed metastasis within a year of diagnosis. We describe here a case report of such an entity with tumor necrosis, an unusual feature which may portend a more aggressive clinical course although that requires further study.

**Tubulocystic Renal Cell Carcinoma With Necrosis: An Unusual Feature in a Rare Tumor**

*(Poster No. 28)*

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Tubulocystic renal cell carcinoma is a rare subtype of renal cell carcinoma, in which necrosis has yet to be described. We describe a case in our institution of this tumor with this unusual histologic feature.

**Abstracts**

**Electron Microscopic Identification of Myeloid Bodies in Proximal Tubules Due to Aminoglycoside Toxicity: Old Finding and New Application**

*(Poster No. 29)*

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Electron microscopy is largely used to identify glomerular changes in renal biopsies, whereas renal tubular changes are usually not evaluated. Myeloid bodies are deposits in lysosomes within glomerular podocytes and are associated with Fabry disease. In the 1970s, animal studies revealed diffuse myeloid bodies in the proximal tubules resulting from nephrotoxicity secondary to gentamicin. Later, it was confirmed that myeloid bodies also developed in human renal biopsies following gentamicin therapy. We describe a case of tobramycin nephrotoxicity with myeloid bodies detected by electron microscopy. An 18-year-old man with acute lymphocytic leukemia, treated with chemotherapy, developed an infection and received treatment with tobramycin. Three days later, the patient developed acute kidney injury with a serum creatinine level up to 10 mg/dL. Renal biopsy showed 23 unremarkable glomeruli. The distal tubules had focal calcium phosphate deposits. The proximal tubules demonstrated moderate cytoplasmic osmotic vacuolization with mildly diminished brush borders and stained positively for kidney injury molecule 1 and strongly positive for lysosome, implying lysosome accumulation. Immunofluorescent staining was negative.
Electron microscopy of the glomeruli was unremarkable, but numerous myeloid bodies were visible in the cytoplasm of the proximal and distal tubular epithelial cells, each 1 nm in diameter. On ultrastructural examination, the myeloid bodies were essentially identical to those typically seen in the podocytes of Fabry disease. Our final diagnosis was acute tubular necrosis secondary to tobramycin toxicity. In this case, ultrastructural examination of the renal tubules provided the key diagnostic evidence.

**Sclerosing PEComa of the Kidney: Report of 2 Cases**

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Hornick and Fletcher described a variant of PEComa showing markedly hyalinized stroma with a striking predilection for the retroperitoneum of middle-aged women, for which they proposed the term sclerosing PEComa. In this study, we present 2 cases of sclerosing PEComas arising from the kidney. Clinical and radiologic findings were obtained from the institutional medical records. Immunohistochemistry was performed with the following antibodies: pancytokeratin, Melan-A, HMB-45, MITF, desmin, actin, and anti-PAX8. A 54-year-old woman and a 65-year-old woman presented with a 16.2 × 8.4 × 5.2-cm mass and a 7.1 × 3.5-cm masses in the retroperitoneum. Both patients underwent radical nephrectomy along with removal of the mass. Follow-up for 7 months and 4 months after surgery showed no evidence of recurrence or metastasis. The tumors were adherent to the renal cortex, were unencapsulated, sharply demarcated from the adjoining renal parenchyma, and were composed of epitheloid and spindle cells embedded in densely sclerotic stroma. The tumor cells were arranged angiocentrically around thick-walled blood vessels. Lipomatosous component was absent. No necrosis, pleomorphism, or increased mitoses were identified in these tumors. The tumor cells were diffusely positive for muscle markers (SMA and desmin) and melanoma markers (HMB-45 and MITF) and were negative for Melan-A and pancytokeratin. We report 2 cases of sclerosing PEComas arising from the kidney, indicating kidney as a possible site of origin for these tumors and reinforcing this entity as a relatively indolent neoplasm.

**A Rare Case of Granulomatous Glomerular and Tubulointerstitial Nephritis**

(Shohreh Eliazsadeh, MD (shohreh@uic.edu); Steven Garzon, MD; Sara Mossahebi, MD; 2 Department of Pathology and Laboratory Medicine, University of Illinois at Chicago, Ill; 3 Department of Surgery, Ferdows Surgical Center, Isfahan, Islamic Republic of Iran)

Nephrogenic adenoma (NA), also known as nephrogenic metaplasia, is a benign, rare lesion of the urinary system. The most common site of involvement is the urinary bladder. For pathogenesis, it has been considered to be metastatic in nature and to occur at sites that are exposed to injuries and irritation caused by stones, infections, and chronic catheterizations. Previous history of renal transplantation or identified on special stains. Immunofluorescence studies were negative for immunoglobulin (Ig) G, IgA, IgM, C3, and C1q deposits. The classic findings on renal sarcoid biopsy are noncaseating granulomas intersitial nephritis, giant cells, and normal glomeruli. Our case was unusual because, in addition to the tubulointerstitial damage, there was glomerular involvement and effacement by the sarcoid granuloma intensifying the renal function impairment with proteinuria.

**Nephrogenic Adenoma of the Bladder: A Mimicker of Carcinoma**

(Shohreh Eliazsadeh, MD (shohreh@uic.edu); Steven Garzon, MD; Sara Mossahebi, MD; 2 Department of Pathology and Laboratory Medicine, University of Illinois at Chicago, Ill; 3 Department of Surgery, Ferdows Surgical Center, Isfahan, Islamic Republic of Iran)
bacillus Calmette-Guérin therapy for urothelial carcinoma of the bladder was noted in 8% of patients. Conversely, some studies have shown the implantation of renal epithelium in the urinary tract as a potential cause of the lesion. Here, we report a rare case of a 61-year-old woman with a history of diabetes mellitus, diabetic nephropathy, and multiple urinary tract infections, presented with symptoms of bladder inflammation, dysuria, and hematuria. Ultrasonography showed a well-distended bladder with a slight thickening and trabeculation of the wall. The patient underwent cystoscopy and posterior bladder biopsy. Microscopic examination demonstrated a circumscribed proliferation of tubules in the lamina propria and cysts lined by cuboidal epithelial cells and focal hobnail features, consistent with diagnosis of nephrogenic adenoma. Immunohistochemical staining for cytokeratin-7, vimentin, P540S, and high–molecular-weight keratin were positive on the cells of the lesion, supporting the diagnosis. Nephrogenic adenoma frequently causes ureteral obstruction and imitates malignancy in the imaging or clinical setting. Furthermore, the immunoprofile and architectural pattern of nephrogenic adenoma overlaps significantly with malignant lesions in the differential diagnosis. Therefore, clinical correlation and thorough microscopic examination are vital for avoiding a misdiagnosis of carcinoma.

**Application of Aperio eSlideshare in Kidney Transplant Evaluation**

(Poster No. 34)

Woodlyne Roquiz, DO (wroquiz@lumc.edu); Ewa Byors, MD; Dariusz Byors, MD; Maria M. Picken, MD, PhD. Department of Pathology, Loyola University Medical Center, Maywood, Ill.

**Context:** Digital pathology has become a major platform in education and multicenter research. Digital imaging is progressively being incorporated into daily pathology practice and has been implemented in remote areas with limited access to pathologists. The aim of this study was to demonstrate the diagnostic accuracy of telepathology on kidney transplant biopsy specimens in both local and remote access modes.

**Design:** During a 20-day period, slides for kidney transplant cases were captured with the Aperio ScanScope CS2 (Leica, Buffalo Grove, Ill) whole-slide scanner at Loyola University Medical Center (LUMC). The slides were viewed virtually by a pathologist from a remote site using Aperio eSlideshare Web-based slide viewing/sharing platform. The pathologist had secure access to the LUMC Laboratory Information System. The glass slides were later viewed by light microscopy in a single-blinded fashion by 2 pathologists to evaluate for concurrence or discrepant findings with the originally reported results.

**Results:** Twenty cases were scanned, evaluated virtually, and a preliminary diagnosis was rendered. The mean observable time for scanning cases, uploading onto eSlideshare, and reporting results to the transplant team averaged 30 minutes. The mean observable time for the pathologist to come to the facility (especially during evening hours), retrieve the slides, and relay a diagnosis to the clinician was 2.25 hours. There was no diagnostic discrepancy on glass slide review.

**Conclusions:** The ability to view hematoxylin–eosin stain and immunohistochemistry side-by-side on one screen and accessibility via Internet to facilitate reduced turnaround time for diagnosis are just a few advantages we have discovered with the use of virtual microscopy over glass slides.

**Metastatic Renal Oncocytoma? A Unique Case With Morphologic Features Identical to Renal Oncocytoma With Liver Metastasis**

(Poster No. 35)

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The spectrum of renal oncocytes ranges from benign (oncocytoma) to those with malignant potential, such as eosinophilic variants of chromophobe and clear cell renal carcinoma; hybrid oncocytoctumor; papillary renal carcinoma, type II; and oncocytoctoid renal cell carcinoma after neoblastoma. We present a case of a renal oncocytoctoid in a 66-year-old man, with histologic features typical for an oncocytoctoma that was metastatic to the liver. The resection specimen as well as the prior biopsy revealed features diagnostic of renal oncocytoctoma in both the renal primary and the liver metastasis. Areas typical of chromophobe renal carcinoma or the hybrid oncocytoctoid tumor were not seen. The only feature not in keeping with a diagnosis of oncocytoctoma was positive immunostaining for CD10 in both the kidney tumor and liver metastasis. To our knowledge, a case with similar histologic and immunophenotypic findings has not been previously published. This case illustrates our expanding knowledge of the biologic heterogeneity of renal tumors with oncocytoctic features.

**A Biopsy-Based, 17-Gene Molecular Diagnostic Test Predicts Aggressive Prostate Cancer Despite Variability in Pathology Assessment**

(Poster No. 36)

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**Context:** The genomic prostate score (GPS) (Genomic Health, Redwood City, Calif), is a validated, biopsy-based predictor of adverse pathology (AP) at radical prostatectomy (RP). In the clinical validation study, central review of biopsy and RP pathology was performed by one uropathologist (J.S.). Given interobserver variability of pathologic interpretations, we assessed the ability of GPS to predict AP based on original diagnostic reads.

**Design:** Patients with RP and low or low-intermediate risk PCa from 1997–2011 were eligible. Original biopsy GPS score (GPS), RP GS, and pathologic T stage reflected diagnoses by more than 15 University of California, San Francisco, pathologists. The GPS was assessed from microdissected biopsy tumor tissue. The AP at surgery was defined as major pattern 4 or any pattern 5 and/or pT3 stage. Univariate and multivariable logistic regression models were used.

**Results:** Of 395 patients, 295 (75%) had biopsy GS 6 on original review and 301 (76%) on central review, 24% discordance. The GPS–predicted AP defined by central RP review after adjusting for central biopsy GS (GPS OR/20 units, 1.93; P = .001) or original biopsy GS (GPS OR/20 units, 1.98; P < .001). At RP, 123 (31%) and 66 (17%) patients had AP based on central and original review, respectively. Discordance for RP GS was 26% and for pT stage 14%. In univariate models, GPS was predictive of AP assessed by central (P < .001) or original (P < .001) RP review.

**Conclusions:** Discordances observed in pathology assessments are consistent with previous studies. The GPS is a robust predictor of AP despite differences in Gleason scoring and stage assessment. A recent study is a consensus of various companies, including Genomic Health, Inc, and has received grant/research support from Genomic Health, Inc, Myriad Genetics, the National Cancer Institute, and the Department of Defense. Dr Cooperberg is a consultant to various companies, including Genomic Health, Inc. Dr Carroll has received grant/research support from the National Cancer Institute, the Department of Defense, Abbott, Genomic Health, Inc, and Myriad. Dr Chan has received grant/research support from the Department of Defense. Ms. Cowan has received grant/research support from Abbott.

**Clear Cell Papillary Renal Cell Carcinoma Masquerading as a Renal Cyst: A Case Report of a Recently Recognized Unique Entity**

(Poster No. 37)

Shivali P. Marketkar, MD (smarketkar@lifespan.org); Mangray Shamal, MD; Evgeny Yakirevich, MD. Department of Pathology, Rhode Island Hospital, Providence, RI.

Clear cell renal cell papillary carcinoma (CPRCC) is a recently described entity with an immunohistochemical and genetic profile distinct from that of the conventional renal cell carcinoma and papillary carcinoma. It was originally thought to be associated with end-stage and acquired renal cystic disease, but the patients with CPRCC in the large recent series did not have end-stage renal disease. Characteristic histologic features of these tumors are clear cells with nuclei above the basement membrane that imparts an appearance similar to subnuclear vacuoles of early secretory pattern endometrium. Our case is a 55-years-old patient with a history of hypertension-induced renal failure, who
Kidney Neoplasm With Extensive Osteosarcomatous Differentiation: A Case Report Focus on Morphology, Immunohistochemistry, and Molecular Study

(Poster No. 38)

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Kidney neoplasm with osteosarcomatous differentiation is not uncommon. Once the differentiation is extensive, it is difficult to differentiate primary extraskeletal osteosarcoma from high-grade carcinoma with extensive sarcomatous differentiation, including renal cell or urothelial origin. A 69-year-old man, presented with left renal mass and hematuria. Imaging revealed a large, heterogeneous, poorly enhancing, calcified mass arising from the left kidney. Grossly, an ill-defined mass measuring 10.2 × 7.8 × 7 cm located in the midportion and lower pole of kidney, invading renal cortex, and medulla was noted. The cut surface was tan-grey, fleshy with areas of necrosis, hemorrhage, and myxoid degeneration. Some areas were hard to cut because of extensive calcification. Histopathologic examination revealed undifferentiated spindle cells with areas of well-defined islands of osteosarcoma and chondrosarcomatous differentiation comprising approximately 80% and 20%, respectively. Interestingly, glomerular-sparing pattern has been noted. Glomerular-sparing pattern can occur in urothelial carcinoma or collecting duct carcinoma. Cells with osteosarcomatous differentiation were negative for most of the stains, except for vimentin. A few tumor cells were positive for CK5/6, p63, and GATA3 and were negative for PAX8. We performed TERT promoter mutation analysis. TERT promoter mutation has been detected in 70% of the urothelial carcinoma but has not been detected in renal cell carcinoma or osteosarcoma yet. Our current case had a TERT promoter mutation, hence, also suggestive of urothelial carcinoma. Here, we describe a rare case of urothelial carcinoma with extensive osteosarcomatous differentiation to demonstrate our experience for a comprehensive diagnostic approach of morphology, immunohistochemistry, and molecular study.
Here, we present an autopsy case of a 68-year-old man who was admitted for sepsis and mental status change with a past medical history of diabetes, hypertension, and hyperlipidemia. The patient had intermittent hematuria and urinary tract infection in the previous 2 years with progressive bowel obstruction. He died soon after septic shock. Autopsy revealed a 10 × 10-cm solid mass with multifocal necrosis completely replacing the prostate and compressing the bladder at the level of the urethra and compressing but not infiltrating the wall of the rectum. Microscopically, the mass was composed predominantly of spindle cells in an interlacing fascicles pattern, intermixed with some large cells with bizarre nuclei (Figure 64). Immunostains showed positive staining for vimentin, smooth muscle actin and desmin, negative for prostate specific antigen, prostate-specific acid phosphatase, pankeratin, CD117, Ki-67 shows 25% positivity. No metastasis was found. Leiomyosarcoma of the prostate is a mesenchymal tumor originating from smooth muscles of the prostate. Typically, it is large and has metastasis upon diagnosis. The most common sites of metastasis are lung, liver, and bone. The differential diagnoses for a spindle cell tumor in the prostate also include cellular leiomyoma, gastrointestinal stromal tumor of rectum, stromal sarcoma or stromal tumors of uncertain malignant potential, sarcomatoid carcinoma, inflammatory myofibroblastic tumor, solitary fibrous tumor, and rhabdomyosarcoma, among others.

**Evaluation of Fluorescence in Situ Hybridization (FISH) for Deletion of Chromosome Arm 3p in the Workup of Renal Lesions**

(Poster No. 41)

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**Context:** Chromosome arm 3p deletion is a well-established, genetic alteration in clear cell renal cell carcinoma (RCC). We aimed to validate and assess the utility of interphase FISH for deletion 3p in formalin-fixed, paraffin-embedded tissues in various renal lesions.

**Design:** We used FISH to assess the ratio of 3p to 3q on formalin-fixed, paraffin-embedded tissue (deletion defined as a ratio ≤0.8). The following renal lesions were used for validation: 10 clear cell RCCs, 4 papillary RCCs, 3 chromophobe RCCs, 3 clear cell papillary RCCs, 5 oncocytomas, and 3 cortical cysts. The 3p FISH was subsequently available for clinical use and performed in 10 cases for 3 months.

**Results:** Deletion 3p was identified in clear cell RCC (70%), papillary RCC (25%), and oncocytoma (20%). Clear cell papillary RCC, chromophobe RCC, and simple cysts were negative for 3p loss. When comparing 3p deletion in clear cell versus non-clear cell RCC, sensitivity was 70%, specificity 82%, positive predictive value 78%, and negative predictive value 75%. In clinical practice, FISH was helpful in 50% of specimens: 4 resections with clear cell versus clear cell papillary RCC (loss detected in 1 diagnosed as clear cell RCC, remaining 3 clear cell papillary RCCs), and 1 bone biopsy of RCC, unresectable (loss detected, diagnosed as clear cell RCC).

**Conclusions:** Detection of chromosome arm 3p deletion with FISH may be a helpful adjunct molecular test in the workup of clear cell RCC, but its utility is limited given the presence of this genetic alteration in multiple renal lesions.

**Müllerian-Like Stroma in the Seminal Vesicle: Case Report and Literature Review**

(Poster No. 42)

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Müllerian remnants in male patients are most commonly testicular/paratesticular lesions with typical müllerian epithelium and are usually of minimal clinical significance. Several neoplasms are known to contain müllerian-like stroma, such as mixed epithelial and stromal tumors of the kidney and mucinous cystic tumors of the pancreas, which occur predominantly, but not exclusively, in women. We present an incidental finding of a focus of müllerian-like stroma in the seminal vesicle. The patient was a 62-year-old man who underwent a radical prostatectomy for prostatic adenocarcinoma, Gleason score 7 (3 + 4), which was confined to the prostate. He was not receiving hormonal treatment before surgery. A small focus (3 mm) of müllerian-like stroma was found in the left seminal vesicle. Histologically, the area showed spindly cells embedded in collagen bundles, reminiscent of müllerian stroma. Immunohistochemical studies (Figure 65) showed strong, diffuse positivity for ER (3+), PR (3+), and CD10 (3+) and strong, focal positivity for SMA (3+) and desmin (3+). An extensive literature search revealed 2 cases of müllerian tumors in the seminal vesicle, both diagnosed as adenosarcoma-like tumors. However, no references of müllerian-like stroma in either the prostate or the seminal vesicle were previously reported. To our knowledge, this would be the first case of a müllerian-like stroma described in the seminal vesicle. Whether this represents a true embryologic rest or a localized stromal reaction to hormones is unknown. Pathologists should be aware that such an entity can occur in the seminal vesicle and potentially give rise to rare neoplasms.

**Peritumoral Pseudocapsule Penetration as Prognostic Factor for Small Renal Tumor? Analysis of 161 Total and Partial Nephrectomy and Enucleation Specimens**

(Poster No. 43)

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**Context:** A pseudocapsule frequently surrounds renal cell carcinoma (RCC), especially tumors smaller than 4 cm in greatest dimension. The presence of a peritumoral pseudocapsule penetration (PSP) could represent the first pathologic evidence of the capacity of tumor cells to infiltrate and invade surrounding tissue and may represent an additional prognostic factor in patients with early stage RCC.

**Design:** Renal cell carcinoma was identified in 161 patients, and tumors ranged in size from 0.8 to 4.0 cm. We investigated 75 cases treated with total nephrectomy, 55 cases treated with partial nephrectomy, and 31 cases treated with tumor enucleation. Peritumoral capsule status was carefully analyzed by 3 pathologists and correlated with tumor nuclear grade. The unpaired Student t test and the χ2 test were used to evaluate the possible statistical correlation between the risk of PSP and a nuclear grade.

**Results:** In 109 RCC tumors (67.7%), the pseudocapsule was intact or with focal incomplete invasion into its layers, whereas in 52 (32.3%), there was a focal penetration into the adjacent parenchyma or perirenal fatty tissue. In the low (Fuhrman grade 1 and 2) nuclear grade group, 24 (24.5%) of the cases showed PSP, whereas there were 28 cases (50.9%) with high (Fuhrman grade 3 and 4) nuclear grade that showed PSP.

**Conclusions:** In this study, we found correlation between the PSP and a higher nuclear tumor grade, which suggests that PSP could represent an additional prognostic factor in patients with early stage RCC. Careful evaluation of the status of the pseudocapsule is important in patients treated with nephron-sparing procedures, in particular enucleation.

**Isolated Renal Metastasis From Neuroendocrine Tumor: How Rare is Rare?**

(Poster No. 44)

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Neuroendocrine tumors are epithelial neoplasms arising from neuroendocrine cells, most commonly in the gastrointestinal tract and the bronchopulmonary system. Primary neuroendocrine tumors of
and nests of moderately pleomorphic cells with eosinophilic granular cytoplasm, stippled nuclear chromatin, and a few mitoses. The tumor cells were positive for chromogranin, synaptophysin, and CD56 and had a Ki-67 of 18%. The morphologic and immunohistochemical features were consistent with that of the primary rectal mass, except for a new CD56 positivity and a higher proliferative index by Ki-67, indicating a more-aggressive behavior. Diagnosis of neuroendocrine tumor of the kidney, especially in a limited core biopsy sample can be challenging because of its rarity and unusual morphology (Figure 66).

Not All Gleason Grade 4 Prostate Cancer Is Alike: Differential CD44 Variant Expression Between Cribriform Pattern and Fused Small Acini

(Poster No. 45)

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Context: Recent articles have demonstrated that the presence and amount of cribriform (or large acinar) pattern as a component of prostate cancer confers a distinct disadvantage in outcome, making both PSA failure and metastasis after prostatectomy more likely. CD44 is a cell-stroma and cell-cell adhesion and signaling protein, and the standard isoform is decreased in prostate cancer, whereas variant isoforms are overexpressed because of aberrant mRNA splicing, including exons coding for CD44v7-10.

Design: We performed immunostaining for CD44 variant 7/8 (clone VFF-17, SeroTec, Raleigh, NC) at a 1:50 dilution with citrate retrieval, on 15 prostatectomy tissues. Other biomarkers with established relevance to high-grade prostate cancer, namely RBM3 (Abnova, Jhongli, Taiwan) and LIMK2 (Epitomics, Burlingame, Calif), both regulators of CD44; E-cadherin (Dako, Glostrup, Denmark), SPARC (Abnova), NSAI1-activated gene 1 (Upstate Biotechnology, Billerica, Mass), and telomerase (hTERT, Novus, Littleton, Colorado) were stained for in the same tissues.

Results: Diminished CD44v7 reactivity in cribriform acini as compared with water-fused small acini from the same case was noted in 13 of 15 cases (87%). The figure shows loss of cytoplasmic CD44v7/8 in the cribriform structure, particularly central cells, compared with fused small acini from the same slide (Figure 67). With other proteins, reactivity did not vary by Gleason 4 cancer pattern.

Conclusions: The finding of differentially expressed CD44 variants or other cell adhesion molecules may correlate with prostate cancer morphology. Further studies may suggest that the degree of cell dysdhesis, as manifested by CD44 or other adhesion markers, correlates with tumor growth morphology.

Ectopic Ureter Villous Adenoma in Zinner Syndrome

(Poster No. 46)

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Zinner syndrome is an uncommon congenital malformation of the mesonephric duct associated with abnormalities of the upper urinary tract and ipsilateral seminal vesicle resulting in renal agenesis, ipsilateral seminal vesicle cyst, and ejaculatory duct obstruction. Initial evaluation may lead to confusion with ureterocele; however, the constellation of findings is not associated with this entity. Intestinal-type villous adenomas of the genitourinary tract are uncommon with most of them occurring in the bladder and are hypothetically related to chronic inflammation (chronic urolithiasis or repeated infection). Meanwhile, intestinal-type villous adenomas of the upper urinary tract are very rare with very few cases described in the English literature. We present a case of Zinner syndrome associated with an ectopic ureter containing an intestinal-type villous adenoma. This 60-year-old man has a history of solitary right pelvic kidney and chronic kidney disease and a previous episode of urinary retention requiring catheterization. He subsequently presented with early morning obstructive voiding symptoms and constipation. Cystoscopy and intravenous-contrasted computed tomography of the abdomen and pelvis identified a large cystic pelvic structure in the lower anterior abdomen with an attached tubular structure on the anterolateral aspect that ended in a blind pouch consistent with ureterocele; however, the constellation of findings is not associated with this entity. Intestinal-type villous adenoma of the genitourinary tract and ipsilateral seminal vesicle cyst as well as the incidental finding of a villous adenoma in the ectopic ureter. To our knowledge, this represents the first described case of Zinner syndrome associated with a villous adenoma in an ectopic ureter and may represent a unique variation of Zinner Syndrome.

Primary Thyroidlike Follicular Renal Cell Carcinoma: Case Report of an Emerging Entity and Review of the Literature

(Poster No. 47)

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We report a case of a 34-year-old man with a past medical history of hypertension and hyperlipidemia, who was found to have an abnormal urinalysis during a routine checkup. Subsequent ultrasound revealed a left kidney tumor. Partial nephrectomy was performed revealing a well-
have shown that catenin accumulation and activation of T-cell factor (TCF) transcription associated with development of high-stage urothelial carcinoma. We hypothesized that overexpression of TCF was other components of the Wnt pathway may have a role in urothelial carcinogenesis. We analyzed 9 cystectomy specimens from patients diagnosed between 1998 and 2005 with urothelial carcinoma of various pT stages with lymph node metastases. Tissue microarray slides were developed and stained for either TCF1 or TCF4, 2 TCF family transcriptions factors. These slides were blindly reviewed by 2 pathologists and scored as 0 to 3+. Average scores greater than 1.5 were considered positive.

Results: TCF1 was highly expressed in 33% of pT1 to pT2 urothelial carcinomas and in 67% of pT4 to pT4 carcinomas. Overall, only 25% of lymph node metastases retained TCF1 expression. TCF4 expression was positive in 100% of cases with retention of high-stage urothelial carcinoma. No nuclear β-catenin was identified.

Conclusions: TCF1 overexpression is associated with the presence of higher pT-staged urothelial carcinomas. In addition, TCF4 expression appears to be highly expressed in urothelial carcinoma, regardless of pT stage. This is downstream player of the Wnt pathway, the TCF family of transcription factors is abundantly expressed in urothelial carcinomas despite low β-catenin nuclear expression and represents a potential target for therapeutic agents.

Malignant Mesothelioma of the Tunica Vaginalis Testis: Case Report and Diagnostic Challenges

Poster No. 49

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Malignant mesothelioma of the tunica vaginalis is an extremely rare tumor arising in about 0.3% to 5% of all malignant mesotheliomas. Diagnosis can be very challenging because of its nonspecific clinical manifestations and variable morphology. The patient was a 49-year-old man with osteogenesis imperfecta who presented with recurrent, long-standing, right hydrocele. His latest presentation was for right scrotal mass, and previous prostatic and gastric adenocarcinoma, was found to have a 2.4-cm right renal mass. Biopsy cores revealed benign renal parenchyma and biphasic lesion showing bland cystic epithelial structures surrounded by bland, dense spindle cells with scant cytoplasm and no polymorphism. Very rare mitosis was seen. The cystic epithelial cells stained positive for KIM-1, PA2X, and PA8X. The spindle cells stained positive for calretinin, SMA, and were weakly positive for EMA, but were negative for ER, PR, androgen receptors, CD34, CD117, HMB45, and pancytokeratins. As ER and PR are reported to be negative in 30% of MEST and the morphologic appearance of the lesion appeared bland, our molecular tests (subtyping assay and FISH) were surprisingly positive for X:18 translocation confirming synovial sarcoma diagnosis. Total nephrectomy was done and the resected tumor showed malignant cystic epithelial and spindle cell components, supporting a biphasic synovial sarcoma of renal primary. Retrospectively in our archive, several MESTs were seen and all had positive EMA staining in the spindle cells of the current core biopsy that reminded us of molecular tests. In renal core biopsies with biphasic features, several factors including gender (male), negative ER/PR stains, and positive EMA staining in spindle cells should showed tubulospirillary architecture, brisk mitotic activity with atypical mitoses, and extensive necrosis. No evidence of lymphovascular invasion was noted. The tests showed hypospermato genesis with a predominance of Sertoli cell–only pattern and no intratubular germ cell neoplasia (ITGCN). Immunostains were positive for calretinin, cytokeratin 7, cytokeratin 5/6, EMA, and focally, for WT1. The differential diagnosis included benign and malignant entities, including florid mesothelial hyperplasia, adenomatoid tumor, pseudotumor in the testis, serous papillary tumor, and testicular germ cell tumors. A careful multidisciplinary approach is needed to diagnose malignant mesothelioma of tunica vaginalis.

Low-Grade Urothelial Carcinoma With Intercalated Histiocytes, Mucoid Cytoplasmic Inclusions, and Intercellular Lumina: Case Report and Review of the Literature

Poster No. 50

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We present a histologic, immunohistologic, and ultrastructural analysis of a low-grade papillary urothelial carcinoma of the bladder with an abundant intercalated histiocyte population that contained mucoid cytoplasmic inclusions, had intercellular lumina, and produced mucin in the absence of glandular differentiation. The cytoplasmic inclusions were PAS–, mucicarmine–, Alcian blue–, and mucicarmine–, and had a histochemical profile of a weakly acidic mucin. Ultrastructural analysis revealed intracytoplasmic deposits of mucin, in histiocytes, and intercellular lumina, containing abundant mucin, and degenerating cells. MUC1 staining was positive on apical tumor cell surfaces and perinuclearly. There are few in the literature that describe intracelular mucoid appearing inclusions in urothelial neoplasms of the bladder. Those articles imply a relation between these mucoid deposits, high tumor grade, and glandular differentiation. None of those cases describe a histologic pattern of intercalated histiocytes containing mucoid material. Recognizing that a mucoid–appearing tumor could be something other than another adenocarcinoma of the bladder or a lower urinary tract neoplasm raises considerations that mucoid deposits in urothelial cancers is helpful for proper diagnosis. Furthermore, the contribution of intercalated histiocytes to the overall pattern of an epithelial neoplasm is an important histologic feature. This case report encourages the further study of 2 ideas. The first idea is why neoplastic urothelial cells produce abundant mucin in the absence of glandular differentiation and the second relates to the finding of MUC1 positivity and intercellular lumina; chiefly does its presence in low-grade urothelial tumors confer a more aggressive biologic behavior, as in other mucinous epithelial lesions.

Biopsy Identification of Renal Synovial Sarcoma

Poster No. 51

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We report a renal core biopsy with biphasic features mimicking mixed epithelial and stromal tumor (MEST). Special stains and molecular tests provided us with a definite diagnosis. An 82-year-old man, with previous prostatic and gastric adenocarcinoma, was found to have a 2.4-cm right renal mass. Biopsy cores revealed benign renal parenchyma and biphasic lesion showing bland cystic epithelial structures surrounded by bland, dense spindle cells with scant cytoplasm and no polymorphism. Very rare mitosis was seen. The cystic epithelial cells stained positive for KIM-1, PA2X, and PA8X. The spindle cells stained positive for calretinin, SMA, and were weakly positive for EMA, but were negative for ER, PR, androgen receptors, CD34, CD117, HMB45, and pancytokeratins. As ER and PR are reported to be negative in 30% of MEST and the morphologic appearance of the lesion appeared bland, our molecular tests (subtyping assay and FISH) were surprisingly positive for X:18 translocation confirming synovial sarcoma diagnosis. Total nephrectomy was done and the resected tumor showed malignant cystic epithelial and spindle cell components, supporting a biphasic synovial sarcoma of renal primary. Retrospectively in our archive, several MESTs were seen and all had positive ER/PR stains. It was the positive EMA in the spindle cells of the current core biopsy that reminded us of molecular tests. In renal core biopsies with biphasic features, several factors including gender (male), negative ER/PR stains, and positive EMA staining in spindle cells should...
Cell Cycle Progression Score Stratifies Prostate Cancer Risk and Significantly Modifies Treatment Decisions in Prostate Cancer

(Poster No. 52)

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Context: The cell cycle progression (CCP) test provides information on the risk of prostate cancer-specific disease progression and mortality when combined with standard clinicopathologic parameters. In this analysis, we evaluated how the CCP score modified AUA risk in results from commercial testing and queried clinicians’ judgment regarding the clinical utility of the CCP test.

Design: Myriad's laboratory database was evaluated for patients whose formalin-fixed prostate biopsy was tested with the CCP test and whose clinicopathologic data were provided by the ordering physician. A relative classification of cancer aggressiveness was used to interpret how a patient’s CCP score compared to other patient scores within the same AUA risk category. Clinicians ordering the CCP test commercially completed surveys regarding treatment decisions before and after receiving the CCP test result.

Results: Based on the CCP score, 29.1% of men had a less aggressive cancer compared to the clinicopathologic prediction while 26.3% of patients had a more aggressive cancer. One hundred fifty clinicians completed surveys on the influence of the CCP test in 305 cases. In 65% of cases, there was a change recorded between the therapy initially planned and the therapy actually selected. In 40% of cases, clinicians indicated they would reduce the intended therapeutic burden post-CCP test.

Conclusion: Over 50% of men tested commercially were assigned to a different risk category than predicted by clinicopathologic features alone. Based on the judgment of ordering physicians, the CCP test result led to major changes in treatment decisions with an increase in conservative management options.

Dr Crawford is a consultant to and has received grant/research support from Myriad Genetic Laboratories, Inc. Dr Shore is a consultant to and has received grant/research support from Myriad Genetic Laboratories, Inc. Dr Tward is a consultant to and has received grant/research support from Myriad Genetic Laboratories, Inc. Dr Scholz has received grant/research support from Myriad Genetic Laboratories, Inc. Authors Kunz, Moyes, Kaldate, Fitzgerald, Stone, and Brawer are shareholders in Myriad Genetics, Inc, or Myriad Genetic Laboratories, Inc.

Novel Label-Free Chemical Imaging for the Identification of Biomarkers of Diabetic Nephropathy Recurrence in Renal Transplant Patients

(Poster No. 53)

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Context: The main treatment for end-stage renal disease is kidney transplantation; however, close monitoring of posttransplant biopsies is required to identify subclinical complications. We identified biochemical markers using chemical imaging that were associated with recurrent diabetic nephropathy. Chemical imaging is an emerging approach to obtain images of the biochemical composition of tissue biopsies in a label-free fashion.

Design: A pilot study focused on identifying 8 patients with no evidence of diabetic nephropathy and 8 patients with advanced diabetic nephropathy. Serial sections were acquired and stained with PAS or imaged using chemical imaging. Infrared spectra were extracted to identify biomarkers associated with diabetic nephropathy progression. A second study identified 3 transplant patients who underwent very rapid recurrent diabetic nephropathy and 2 patients with no evidence of diabetic nephropathy at time of harvest.

Results: Biomarkers were identified that were changed in renal structures associated with the progression of diabetic nephropathy, including increased levels of glycation. These biomarkers were found to be increasing in the cohort of transplant patients that underwent rapid diabetic nephropathy recurrence. In addition, the early biopsy from the patients that underwent later diabetic nephropathy progression were biochemically different from the nonprogressive patients, suggesting that chemical imaging may identify prehistologic biomarkers that will predict outcome.

Conclusions: We have identified a number of biomarkers that are associated with the advancement of diabetic nephropathy and that we can track the early recurrence of diabetic nephropathy in surveillance biopsies. In addition, we have highlighted a biochemical signature that may be predictive of the later progression of diabetic nephropathy recurrence.

TGFβ1 and Foxp3+ Regulatory Cells in the Long-Term Tolerant Kidney Allografts in Rhesus Monkeys

(Poster No. 54)

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Context: The significance and role of mononuclear infiltrates in allograft with normal function and no rejection is largely unknown, and to date there is no histopathologic pattern associated with the development of transplantation tolerance.

Design: We analyzed kidney allograft biopsy tissue obtained from 5 rhesus monkeys (mean graft survival time 2287.25 days) that had enjoyed long-term normal kidney allograft function and were off all immunosuppression. Kidney biopsies were immuno labeled for the regulatory molecule TGFβ1 and for the nuclear transcription factor Foxp3 (a marker of naturally occurring T regulatory cells).

Results: TGFβ1+ cells localized primarily in the interstitium of long-term tolerant kidney allografts (0.75 cells/tubule versus 0.19 cells/tubule in biopsies with rejection (P < .001) and were remarkably absent in intragraft lymphoid aggregates. These cells coexpressed CD4, but not CD8 or Foxp3. In contrast, Foxp3+ cells that coexpressed CD4 but not TGFβ1 were found primarily in allograft lymphoid aggregates (34.1 cells/field in 10 high-power fields). PBMC from rhesus monkeys revealed a low response to donor antigen when tested with the ex vivo DTH in SCID mice (P < .05). The presence of intragraft Foxp3+ cells significantly correlated with donor DTH regulation (P < .05).

Conclusions: In this preclinical primate animal model, adaptive CD4+ TGFβ1+ Tregs and natural CD4+Foxp3+ Tregs occupy distinct niches in the allograft, and therefore may have different roles in the maintenance of transplantation tolerance. This is in contrast to murine animal models where regulatory cells diffusely infiltrate the allograft.

Elevated Caveolin-1 Expression in Squamous Cell Carcinoma of Bladder in Comparison to Urothelial Carcinoma

(Poster No. 55)

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Context: Caveolin-1 (Cav-1) is a component of caveolin proteins on cell membrane. It is involved in transportation of cholesterol. It is expressed in various normal tissues. Deregulated expression has been found in many tumors. Herein, we investigated expression of Cav-1 in urothelial carcinoma of bladder (UCB) and squamous cell carcinoma of bladder (SCCB) to determine differential expression.

Design: Tissue microarrays were constructed using cysctotye and cystoprostatectomy specimens from year 1981 to 2006. Specimens were divided into 4 groups: (1) 11 specimens with no bladder cancer, (2) 9 specimens with UCB without lymph node metastasis, (3) 45 specimens with UCB with lymph node metastasis, and (4) 35 specimens with...
SCCB with or without metastasis. Tissue microarrays were stained with monoclonal antibodies to Cav-1. Immunoreactivity was scored based on intensity as negative, weak, intermediate, and strong. Any staining is considered positive.

**Results:** In benign bladder tissue only 2 of 11 specimens showed weak staining for Cav-1. Three of 9 specimens (33%) with UBC without metastasis were reactive. In comparison, 52% of UCB with lymph node metastasis were positive. Almost all of SCCB (94%) showed at least some reactivity. Almost 70% of them showed intermediate to strong expression, while only 20% of the UCB were intermediate to strongly positive.

**Conclusions:** This study showed that Cav-1 is expressed in half of the UCB with metastasis. In comparison, 94% of all SCCB showed Cav-1 expression. Further studies are needed to demonstrate potential role of Cav-1 in bladder tumors with squamous differentiation and tumor progression.

**IGF1R Overexpression in Upper Tract Urothelial Carcinoma**

(Paper No. 56)

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**Context:** Insulin-like growth factor receptor-1 (IGF1R) is a transmembrane tyrosine kinase receptor. Its overexpression has been documented in several human cancers. We previously demonstrated IGF1R overexpression in invasive bladder carcinoma with a potential impact on prognosis. Given known biologic differences among upper and lower urinary tract urothelial carcinoma, we aimed to assess the expression status and prognostic significance of IGF1R in upper tract urothelial carcinoma (UTC).

**Design:** Two tissue microarrays were constructed with triplicate tumor and paired benign urothelium from 99 Japanese patients with nonmetastatic UTC who underwent radical nephroureterectomy with curative intent between 1997 and 2011. Membranous IGF1R staining was evaluated using immunohistochemistry (G11, Ventana Medical Systems), using a scoring method analogous to that for HER2 expression in breast carcinoma. The highest score was assigned in each tumor. IGF1R overexpression was defined as cases showing score $>1$. Correlation with pertinent clinicopathologic parameters and outcome was performed.

**Results:** IGF1R overexpression was observed in 70% of UTC; however, it did not correlate with any clinicopathologic parameter evaluated. UTC progression and disease-specific survival rates were 33% and 70% respectively. We found no association between IGF1R overexpression and UTC progression (HR: 1.3 [0.63–2.7], P = 0.57) or disease-specific survival (HR: 1.26 [0.57–2.75], P = 0.57).

**Conclusions:** A large proportion of UTC tumors demonstrate immunohistologic overexpression of IGF1R. This finding could have clinical implications given that IGF1R is therapeutically targetable. However, unlike the bladder counterpart, IGF1R overexpression in urothelial carcinoma of upper urinary tract does not appear to correlate with outcome; nonetheless, its biologic significance merits further assessment.

**False-Positive C4d Reactivity by Immunohistochemistry in Renal Allografts With Thrombotic Microangiopathy**

(Paper No. 57)

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Drug-induced thrombotic microangiopathy (TMA) can be difficult to distinguish clinically and pathologically from acute humoral rejection (AHR) in renal allografts. The presence of linear endothelial staining for complement (most notably C4d in peritubular capillaries) favors AHR over TMA. In reality, use of rabbit antithymocyte globulin (ATG), an immunosuppressive drug, may result in false-negative C4d immunoreactivity, secondary to damaged capillary walls. We reviewed an automated immunohistochemistry platform used in our laboratory for C4d, CMV, and SV40 (BK virus stain), coupled with an actual case of TMA in an allograft biopsy. Antibodies utilized in immunohistochemical stains include rabbit polyclonal anti-human C4d antibody and mouse monoclonal anti-CMV antibody. Importantly, the secondary antibody used is a cocktail of goat anti-rabbit and goat anti-rabbit antibody. The case mentioned showed TMA, morphologically favoring TTP/HUS. C4d stain was diffusely positive in peritubular capillaries, suggesting AHR. Unexpectedly, SV40 and CMV stains also showed diffuse immunoreactivity in peritubular capillaries. It is well known that circulatory components can be passively “trapped” in damaged vascular walls of TMA. These include cellular debris, thrombotic fibrinoids, and trapped rabbit ATG immunoglobulin, creating a false-positive C4d immunoreaction in peritubular capillaries. In the current scenario, the same staining pattern was shared by CMV and SV40, indicating false-positive results. This potential technical pitfall is of paramount importance for the practicing pathologist to interpret C4d stain in an allograft biopsy.

**Papillary Renal Cell Carcinoma With Clear Cell Features: Case Report and a Review of Literature**

(Paper No. 58)

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Although not recognized in the current World Health Organization classification of renal tumors, clear cell papillary renal cell carcinoma (CCPRCC) has been described as a unique entity since 2002. A variety of names has been proposed. Most common histopathologic features include clear cells organized in combination with cystic and focal to diffuse papillary arrangements. Consequently, the most frequently used nomenclature is CCPRCC. Although CCPRCC was initially diagnosed in end-stage renal disease, a few cases have been described involving otherwise normal kidneys. There are 4 neoplasms in the differential diagnosis with overlapping microscopic structures including papillary renal cell carcinoma (RCC), clear cell RCC, CCPRCC, and Xp11 translocation RCC. Here we report a unique case of a 49-year-old man without significant past medical history of renal disease who presented with 1 month of weak urinary stream, pelvic pain, and gross hematuria. Computed tomography scan demonstrated a cystic mass in the upper pole of the right kidney. The patient underwent a partial nephrectomy. Microscopically, the tumor consisted of papillary structures composed of cuboidal cells with slightly irregular nuclei and inconspicuous nucleoli. Small foci of clear cell changes were also noted. The specimen stained positively for RCC, CK7, and carbonic anhydrase. It was weakly positive for P504S and negative for CD10. While the morphology was compatible with papillary renal cell carcinoma, the staining features were consistent with CCPRCC. Strict adherence to immunohistochemical criteria and a thorough microscopic evaluation will reduce confounding factors in the diagnosis of papillary type renal cell carcinomas.

**P40 as a Basal Cell Marker in the Diagnosis of Prostate Glandular Proliferations: Relation With 34E12**

(Paper No. 59)

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**Context:** 34E12 is—similarly to p63—a standard marker of basal cells of prostate glands. These markers are used in the diagnosis of difficult atypical glandular proliferations of the prostate. p40 is an isoform of p63, and may be of diagnostic value in prostate pathology.

**Design:** We retrospectively evaluated the relation of 34E12 and p40 in 68 prostate biopsy specimens by immunohistochemistry using antibodies to 34E12 and p40 at the time of diagnosis for atypical glandular proliferations. Basal cell staining was classified as negative, partial (<60%), or diffuse (60%); irregular staining was defined as discordant staining patterns for p40 and 34E12.

**Results:** Of the acinar proliferations, 10% were negative for both markers; because of the limited amount of glands (<4) these cases were termed atypical small acinar proliferation. Partial staining for both markers was seen in 42% and diffuse staining in 46% of these cases. An irregular reactivity was noted in 1 case only (2%). Finally, these lesions were noted in the context of prostate atrophy, prostatic hyperplasia, inflammation, and oradenosis depending upon further histopathologic features. Out of 6 PIN lesions, 2 cases showed partial and 3 cases diffuse reactivity for both markers; 1 case stained irregular. All cases diagnosed as prostate carcinomas had no evidence of staining for either of the
markers; they were proven carcinomas on final prostatectomy specimens.

Conclusions: p40 expression is closely correlated to 34BE12 with respect to demonstration of basal cells of prostate glands, and may provide further information on the dignity of small glandular proliferations of the prostate.

Clear Cell Sarcoma of the Kidney in a Child With Fanconi Anemia

(Poster No. 60)

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Patients with Fanconi anemia subgroup D1, attributable to biallelic mutations in BRC2A2, have an increased risk of solid tumors. Tumors in the kidneys of these patients are almost exclusively Wilms tumors. We report the first recorded case of a clear cell sarcoma of the kidney in a patient with this cancer predisposition syndrome already presenting with acute myeloid leukemia. We emphasize the need for careful clinical observation in patients of this complementation group, given their higher risk for malignancy. This risk is likely the result of increased but nonspecific chromosomal instability, rather than as a consequence of abnormalities involving a specific genetic pathway.

Is There Any Relationship Between Tumor Size and Extrapseudocapsular Extension in Small Renal Cell Carcinoma?: Critical Appraisal of 156 Cases

(Poster No. 61)

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Context: Simple tumor enucleation has been proposed for surgical treatment of small-size nonhilar renal tumors. The adequacy of the surgical margin is still under debate, because of concerns for microscopic extrapseudocapsular tumor invasion. This study aimed to analyze the relationship between size of renal cell carcinoma (RCC) and extrapseudocapsular extension (EPE).

Results: A total of 156 surgically removed small RCCs were reviewed, including 39 (25.0%) 2.0–2.9 cm, and 59 (37.8%) 3.0–4.0 cm. The average thicknesses of the pseudocapsule of these 3 groups of RCC were 0.19, 0.20, and 0.24 mm, respectively (P = .05). The data did not show a positive correlation between EPE rate and tumor size; however, there was no statistically significant correlation.

Conclusions: In this study, the average thickness of the pseudocapsule of small RCC showed a tendency to increase with increasing tumor size; however, there was no statistically significant correlation. The EPE also failed to show any correlation with tumor size. Thus, tumor size in small RCC was independent of both pseudocapsule formation and tumor EPE.

Adenomatoid Tumor of the Adrenal Gland: Report of a Rare Case With Unusual Immunohistochemistry

(Poster No. 62)

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Adenomatoid tumor is the most common benign tumor of the epididymis and is comprised of mesothelial cells. There are only a handful of cases in the English literature of these tumors involving the adrenal gland. A 50-year-old man presented with a history of uncontrolled hypertension. Magnetic resonance imaging showed 2 masses in the right adrenal gland that were consistent with myelolipoma. A right total adrenalectomy was performed. Grossly, the adrenal gland had a large 7-cm well-circumscribed mass consisting of 2 separate parts: a 6.5-cm area of predominately adipose tissue, and a 4.5-cm pink-white firm, granular area. Surrounding the mass was a thin rim of normal golden adrenal gland tissue. On histology, the 6.5-cm mass was comprised of mature adipose tissue with hemorrhage, while the 4.5-cm mass had an infiltrative, tubular appearance without blood in the lumens of the tubules. Adjacent to the tubular mass was a 0.9-cm focus of hematopoietic tissue diagnosed as myelolipoma. The main differential for the tubular area was vascular lesion versus adenomatoid tumor, with histologic appearance favoring adenomatoid tumor and site favoring vascular lesion. The immunohistochemical panel performed showed the tumor cells to be positive for CD34, CK7, D2-40, and AE1/A3 while negative for calretinin, WT-1, CK5/6, CK20, factor VIII, and CD31. These results did not support a mesothelial origin nor did they support an endothelial origin for this tumor. Finally, electron microscopy was employed and demonstrated prominent microvilli and desmosomes, consistent with mesothelial cells and diagnosed as adenomatoid tumor.

High- and Low-Risk Urothelial Carcinomas: Are the IHC Expressions of P53, p21/p27, and p16 Pathways or FGFR3, HRAS, and Retinoblastoma Proteins Valuable Markers for the 2 Different Pathways?

(Poster No. 63)

Peter E. Stoemmer, PhD (Prof_Stoemmer@web.de); Patricia Torres-Galea, PhD. Department of Gemeinschaftspraxis Pathologische, Forschungslabor Pathologie, Augsburg, Germany.

Context: Urothelial carcinomas result via low-risk FGFR3 pathway or via high-risk pathways like p53 and p21 or via p16INK4a pathway. We conducted an IHC protein-level study of these oncogenes-suppressor proteins in relation to the morphologic behavior of tumor cells.

Design: Formalin-fixed, paraffin-embedded archival noninvasive and invasive urothelial tumors semiquantitatively were analyzed by IHC. Antibodies were p21WAF1Ab-5 HZ52 1:100; p27Kip1 SX53G8 1:50; p53 Ab8 DO-7 + BP53-12 1:250 (Medac, Germany); p16INK4a m16N4ka (mtm Heidelberg, Germany).

Results: For p53 tumor-suppressor protein, we found no low expression in normal urothelium and in pTaG1/G2, high expression in invasive carcinoma (and adjoining papillary noninvasive carcinoma).

For p16INK4a, normal urothelial cells were completely negative; in pTaG1a few, mostly basal tumor cells were reactive in cytoplasm and nucleus. Invasive carcinomas (pTaT1/2, G3) show intense reaction in nearly all tumor cells. p21 and p27 were tightly controlled by p53; in normal urothelium and pTaG1 there was high intranuclear expression; there was loss of staining in high-grade and invasive carcinomas. For FGFR3, no distinction between invasive and noninvasive tumor cells was possible (IHC). For HRAS and BRAF (nonmutated), there was high expression in noninvasive papillary carcinoma cells and low expression in invasive tumor cells.

Conclusion: Only p53, p16INK4a, and p21 can be used as markers for high-risk pathway in urothelium. Proteins characterizing the low-risk pathway are HRAS and BRAF nonmutated. The differences in the expression of these proteins may give hints for the pathway and with
Castlemann Disease Presenting as a Renal Mass: A Case Report and Literature Review

(Poster No. 64)
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A 45-year-old woman presented with a chief complaint of low back pain. Review of symptoms was positive for nausea, urinary urgency, and bladder incontinence. The differential diagnosis included musculoskeletal pain and urinary tract infection; however, despite therapy the symptoms persisted. Abdominal computed tomography, ordered for kidney stone protocol, revealed a 3-cm mass in the upper pole of the left kidney suspicious for renal cell carcinoma. The patient underwent a left nephrectomy. Gross inspection revealed a 3.5-cm firm, dark yellow lobate mass within the renal parenchyma, separate from the renal hilum. Microscopic inspection showed the mass to contain lymphoid tissue with numerous involuted follicles with occasional small, hyaline areas. Microscopy (EM) and/or direct immunofluorescence (DIF). Other 6 (4) 0 0 2

Diagnosis and Follow-up

Diagnosis Total No. of Patients (No. of Stable Patients) Patients on Dialysis Deceased Patients Patients Lost to Follow-up
Diabetic nephropathy 22 (12) 5 2 3
Immune complex–mediated nephropathy 5 (3) 2 0 0
Cryoglobulin deposits 1 (0) 0 1 0
IgA nephropathy 3 (1) 0 1 1
Allograft nephropathy 4 (2) 0 0 2
Focal segmental glomerulosclerosis 1 (0) 1 0 0
Other 6 (4) 0 0 2

Vascular Lesions in Renal Grafts: A Retrospective Study

(Poster No. 66)
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Context: Rejection in renal transplants is one of the major causes of graft loss. Intimal arteritis alone or accompanied by tubulointerstitial inflammation is a manifestation of acute T-cell–mediated rejection. We studied biopsies of transplanted kidneys performed either as part of a research protocol or for cause, in order to identify the presence of intimal arteritis. We examined laboratory results to determine the impact of vascular rejection on graft function.

Design: Renal transplant organ biopsies (n = 300) performed with an average of 5-year follow-up were examined for the presence of intimal arteritis. The presence and degree of tubulointerstitial inflammation was also scored along with the degree of tubular atrophy and interstitial fibrosis, as an indicator of graft dysfunction.

Results: Biopsies performed to assess for the cause of rising creatinine had a significantly greater number of cases of acute cellular rejection than those performed as part of a study protocol. A minority of cases had evidence of intimal arteritis with associated evidence of graft dysfunction. Only a fraction of blood vessels in each biopsy had intimal arteritis.

Conclusions: Intimal arteritis alone or accompanied by tubulointerstitial inflammation is a manifestation of acute T-cell–mediated rejection. This is a critical feature of renal transplant rejection that affects only a minority of vessels. Therefore, adequacy of the biopsy for sampling of blood vessels has a significant impact on obtaining valuable information for graft outcome.

Should Electron Microscopy and Direct Immunofluorescence Be Routinely Considered in Post-Kidney-Transplant Biopsies: A Retrospective Review and Prospective Follow-up in 211 Post-Kidney Transplant Biopsies With Electron Microscopy and Direct Immunofluorescence

(Poster No. 65)
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Context: Post-kidney transplant biopsies (ktx) are performed to rule out acute cellular rejection, which can be diagnosed by light microscopy alone. However, a few diagnoses can be reached only after electron microscopy (EM) and/or direct immunofluorescence (DIF).

Design: We reviewed all ktx biopsies from January 2010 to December 2012. There were a total of 460 ktx biopsies, out of which 211 had EM and DIF. The glass slides, EM images, and electronic medical record were reviewed for the indications for transplant and for follow-up (14–50 months).

Results: Forty-two of the 211 biopsies had significant findings for which EM and DIF were essential. The diagnosis and follow-up are as indicated in the Table.

Abstracts

Conclusions: There were significant diagnoses that could be reached only with the help of EM and/or DIF in 42 out of 211 cases. Recurrence of pretransplant pathologic processes was noted in 17 out of 42 cases that can only be diagnosed with the help of EM and DIF. The ancillary modalities appear to be justified in ktx.
Stem Cell Marker CD133 Helps to Confirm Clear Cell Papillary Renal Cell Carcinoma in Renal Core Biopsies (Poster No. 70)

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Context: Clear cell papillary renal cell carcinoma (CCP-RCC) is a rare type RCC which was only focally positive in other type RCCs. In this study, we report CD133 as a confirmatory marker for CCP-RCC in 4 renal core biopsies.

Design: Patients A–D were 2 men and 2 women, aged from 67 to 75 years old. All 4 patients underwent biopsies and subsequently nephrectomies. The biopsies of these masses were evaluated with immunostains including CK7, P504S, vimentin, and CD133, which was only focally positive in other type RCCs. In this study, we report CD133 as a confirmatory marker for CCP-RCC in 4 renal core biopsies.

Results: All 4 biopsies from patients A–D showed typical histologic features of CCP-RCC with an IHC pattern of CCP-RCC (CK7+, vimentin+, and P504S+). In addition, all 4 tumors also showed diffuse membranous positivity for CD133. The follow-up total or partial nephrectomy specimens of patients A–D showed tumors from 2.1 to 3.5 cm. Microscopically, CCP-RCC was confirmed in each case except one treated with cryoablation.

Conclusions: Diffuse membranous CD133 staining can be a helpful marker for confirming CCP-RCC. An accurate diagnosis of this tumor is of paramount importance for clinical management, because CCP-RCC has a better outcome than other types of RCC. As CCP-RCC in our series expressed CD133 in 100% of 20 cases and another stem cell marker OCT3/4 in 66.7% (12/18) cases with available tissue (no other types of RCC were OCT3/4 positive), we raise a possibility that CCP-RCC is a tumor with cancer stem cells.

The Cysts in Autosomal-Recessive Polycystic Kidney Disease Come From Distal Nephron Tubules (Poster No. 71)

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Typical cysts in autosomal recessive polycystic kidney disease (AR-PKD) are characterized by a cylinder pattern of long, narrow cysts. Although conventionally the cysts in AR-PKD are believed to come from distal nephron tubules (possible collecting ducts), one study demonstrated that early cysts in AR-PKD were derived from proximal tubules. We report a case of a 31-week-old female infant born with enlarged bilateral kidneys and liver surviving for 3 days with intubation. Autopsy revealed bilateral enlarged kidneys that distended the abdomen. Microscopically the kidneys revealed the typical cylindrical pattern of renal tubular cysts extending from renal surface to cortical...
medullary junction at arcuate artery level (Figure 71). The cylindrical cysts appeared to be present in medullary rays, compressing the labyrinth zone with glomerulur and their associated tubules. In addition, elongated cysts were also present in the medulla. All of the cylindrical cysts stained positively for cytokeratin 7 (distal tubular marker) but negatively for kidney injury molecule 1 (KIM-1, proximal tubular marker). KIM-1 showed positive staining in dilated, injured proximal tubules around glomeruli. This cytokeratin-7–positive and KIM-1–negative profile in the AR-PKD is similar to the adult type of PKD that we demonstrated in the past. Our study confirms that the typical cylindrical cysts in AR-PKD are most likely derived from distal nephron tubules (possibly collecting ducts due to a ureteric bud defect) in the medullary rays of cortex separating labyrinth zone with glomeruli. The dilated proximal tubules in AR-PKD are a transient, reactive change secondary to the distal cystic transformation.

Histologic Changes in the Prostate and Bladder Following Radiation Therapy for Prostate Cancer

(Poster No. 72)

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Context: Approximately 2.5 million men in the United States have been diagnosed with prostate cancer, many of whom were treated with radiation therapy (RT). While histologic changes such as fibrosis, acinar atrophy, epithelial atypia, and vasculopathy have been described in the past, our study reviews the spectrum of therapy-related changes, which are especially striking in the prostate. An awareness of these changes, particularly prostatic glandular atypia, may be helpful in avoiding overinterpretation.

**Clinical Characteristics**

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<th>Age, mean ± SD (n = 65)</th>
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<tr>
<td>Years from RT to surgery, mean ± SD (n = 61)</td>
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<tr>
<td>Type of RT (n = 65)</td>
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<tr>
<td>Brachytherapy</td>
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<tr>
<td>External beam</td>
<td>Combined 27.7%</td>
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<tr>
<td>Type of surgery (n = 65)</td>
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<td>Cystoprostatectomy</td>
<td>Prostatectomy 23.1%</td>
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<tr>
<td>Cystectomy 7.7%</td>
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</table>

First Detailed Study of Survival of Patients With Renal Cell Carcinoma in India

(Poster No. 73)

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Context: Renal cell carcinoma (RCC) accounts for 2% to 3% of all adult malignancies and approximately 90% of all renal malignancies. The rates of kidney cancers are high in developed countries and low in eastern countries and Africa. Our objective was to conduct a survival study among Indian patients who had nephrectomy for RCC, as there was a paucity of Indian studies in medical literature.

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>n (%)</th>
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<tr>
<td>Cystectomy 7.7%</td>
<td>69.2%</td>
</tr>
<tr>
<td>Prostatectomy 23.1%</td>
<td>65.1%</td>
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<tr>
<td>Cystoprostatectomy 69.2%</td>
<td>38.5%</td>
</tr>
<tr>
<td>External beam 38.5%</td>
<td>38.5%</td>
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<tr>
<td>Combined 27.7%</td>
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</tr>
</tbody>
</table>

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Metachronous Bilateral Testicular Seminoma Developing After an Interval of 31 Years

(Poster No. 74)

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Men diagnosed with testicular germ cell tumors are at higher risk for development of a second germ cell tumor in the contralateral testis. Metachronous bilateral testicular germ cell tumors usually occur within 5 years, with the longest interval documented at 21 years. Here, we report a case of a 63-year-old man previously diagnosed with testicular seminoma who developed testicular seminoma within the contralateral testis after an interval of 31 years. The patient was asymptomatic and found to have a right testicular mass on routine urologic exam. The patient had a left orchiectomy followed by radiation therapy 31 years ago for stage I testicular seminoma. Physical exam was pertinent for an enlarged, nontender right testicle without evidence of metastatic disease or lymphadenopathy. Serum ß-hCG (AFP, 3.2 µg/L) and chorionic gonadotropin (ß-HCG, 3 IU/L) were within normal limits. The surgery specimen revealed a 4.2 × 3.1 × 1.8-cm light yellow, firm, distinct mass in the subcapsular and medial portion of the right testicle without tumor involvement of tunica albuginea or the tunica vaginalis. Microscopic examination showed classic seminoma with venous/lymphatic tumor involvement. The tumor cells were positive for placental alkaline phosphatase (PLAP), focally positive for HCG, and negative for CD30 and AFP. No choriocarcinoma was identified by microscopy. The current case shows that contralateral testicular seminoma may occur at an advanced age, thus underscoring the importance of recommending lifelong follow-up for patients with testicular germ cell tumors.

Cisplatin-Induced Nephrotoxicity: Another Mimicker of Myeloma Cast Nephropathy
(Poster No. 75)

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True myeloma cast nephropathy is caused by precipitation of Bence Jones proteins with Tamm-Horsfall and other filtered proteins in the form of angulated and brittle casts. Myeloma-like cast nephropathy occurs occasionally with antibiotics, Waldenström macroglobulinemia, lymphomas, carcinomas, and recently in HIV patients. We report a 65-year-old man diagnosed with squamous cell carcinoma of tongue. He was treated with cisplatin, an immunosuppressive drug, in addition to radiation. He developed acute renal failure with oliguria and markedly elevated serum creatinine levels from baseline during the second chemotherapy cycle. The drug history was negative for NSAIDs. Emergent renal biopsy was performed and appropriately triaged. Hematoxylin and eosin-stained sections showed acute tubular injury and cast formation. The casts elicited a cellular reaction of macrophages and neutrophils, and morphologically mimicked myeloma casts. However, immunofluorescence microscopy failed to demonstrate monoclonal restriction. Under electron microscope (EM), irregular casts appeared dark blue in toluidine blue-stain section. They were composed of amorphous or granular material of low density admixed with scattered high electron-dense globules and membrane debris. The tubular epithelial cells showed vacuolization. EM of the glomeruli exhibited largely preserved foot processes with no evidence of immune complex or organized protein deposits. In addition, serum protein electrophoresis and immunofixation confirmed absence of monoclonal gammopathy. Myeloma-like cast nephropathy and true myeloma cast nephropathy pose similar destructive effects on renal parenchyma. Although cisplatin has a well documented nephrotoxic profile, we are reporting the first case of myeloma-like cast nephropathy with cisplatin.

Glomerular Sparing Pattern in Primary Kidney Tumors: Clinical, Morphologic, and Immunohistochemical Study
(Poster No. 76)

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**Context:** Glomerular sparing (GS) is defined as a unique growth pattern where tumor cells replace the majority of renal tubules and overgrow the glomeruli. However, no study has been reported. Here, we studied the clinical-pathologic and immunohistochemical features of primary kidney tumor with glomerular sparing pattern.

**Design:** The archives of Westchester Medical Center’s anatomic pathology department were searched for nephrectomy specimens from 2009 to 2013. All reports were reviewed, cases with tumor were selected, clinicopathologic information was collected, and cases were reevaluated with focus on glomerular sparing pattern. Immunohistochemical stains of Pax-8, p63, and INI-1 were performed.

**Results:** A total of 204 nephrectomy cases included 163 cases of renal cell carcinoma (RCC), 37 cases of urothelial carcinoma (UC), and 4 cases of others (Wilms tumor, primary diffuse large B-cell lymphoma, angiolipoma, rhabdoid tumor). Finally, we identified 7 cases: 2 cases of clear cell renal cell carcinoma (CCRCC), 2 cases of urothelial carcinoma (Figure 73, A), 1 case of collecting duct carcinoma (CDC, Figure, B), 1 case of diffuse large B-cell lymphoma (Figure, C) and 1 case of rhabdoid tumor (Figure, D). CCRCC and CDC were Pax8+ and P63-; UC were Pax8– and P63+; lymphoma was Pax8+; and rhabdoid tumor was INI1–.

**Conclusions:** Primary kidney tumors with glomerular sparing pattern are rare and incidence in our study is <4% (7/204). They are associated with RCC, UC, collecting duct carcinoma, lymphoma, and rhabdoid tumor. However, they are found with high-grade, large-size tumors and are typically located at the junction of the tumor and the surrounding renal parenchyma. Careful morphologic evaluation and immunohistochemical stains would be helpful for diagnosis.

Pure Testicular Embryonal Rhabdomyosarcoma, Diffuse Anaplastic Variant: A Case Report and Literature Review
(Poster No. 77)

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Pure testicular embryonal rhabdomyosarcoma is a rare tumor and recapitulates the phenotypic and biological features of embryonic skeletal muscle. The genitourinary system is involved in ≥28% of cases, with the urinary bladder, prostate, and paratesticular soft tissues as typical examples. We report a 17-year-old adolescent boy who presented with a right testicular mass for 5 weeks. Gross examination was remarkable for 6-cm heterogeneous mass with focal hemorrhage and necrosis. Microscopic examination of the tumor was remarkable for primitive spindle and epithelial atypical cells with hyperchromatic and numerous mitotic figures. There were extensive areas of anaplasia characterized by large pleomorphic cells with multinucleated nuclei and multinucleated giant cells. The neoplastic cells were positive for myogenin, myoglobin, actin, desmin, and vimentin. They were negative for inhibin, CD30, HCG, CK AE1/AE3, CD117, AFP, and PLAP. The Ki67 shows a very high proliferation rate. Since the introduction of current chemotherapy, modern radiotherapy, and improved surgical procedures, disease-free survival has improved from 20% to about 70%. Three factors influence the prognosis: histologic subtype, site, and stage. Rhabdomyosarcomas with diffuse anaplasia have a worse outcome. Regarding primary site, head and neck, genitourinary, and orbital lesions have a better overall prognosis. The lungs, lymph nodes, liver, and brain are the most common metastatic sites.
The Utility of Flow Cytometry of Bronchoalveolar Lavage in the Diagnosis of T and NK Cell Malignancies in Critically Ill Patients With Respiratory Symptoms

(POSTER NO. 78)

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The value of bronchoalveolar lavage (BAL) in the diagnosis of pulmonary diseases of diverse etiologies is widely accepted. Flow cytometry (FC) as an adjunct diagnostic tool for BAL specimens has not been adequately exploited. FC has numerous advantages, such as short turnaround time and the ability to differentiate reactive processes from hemato logic neoplasms. Here we describe 2 cases of critically ill patients presenting with primarily respiratory symptoms. FC analysis of the BAL fluid established an early diagnosis of hemato logic neoplasms. Cytospin of the BAL in case 1 demonstrated predominantly macrophages intermixed with mildly atypical lymphoid-appearing cells, which had NK cell immunophenotype by FC. A subsequent bone marrow biopsy showed subtle infiltration by neoplastic cells with abundant intermingled reactive histiocytes with hemophagocytosis. The neoplastic cells were positive for CD2, CD7, CD16, CD56, granzyme, and EBV by EBER ISH while negative for CD3, CD4, CD5, and CD8. These findings led to the diagnosis of aggressive NK cell leukemia with secondary hemophagocytic lymphohistiocytosis. Cytospin preparation of the BAL specimen in case 2 showed predominantly large, atypical cells with convoluted nuclei and prominent nucleoli in a background of polymorphous lymphocytes, intermixed with macrophages. FC showed CD4-positive T-cell population with loss of CD7 and coexpression of CD25. HTLV I/II serology was positive. The combined findings were consistent with the diagnosis of adult T-cell leukemia/lymphoma. FC of BAL fluid is a valuable diagnostic tool especially in the differential diagnosis of unexplained pulmonary infiltrates, providing an expeditious diagnosis of hemato logic malignancy.

Detection of a New Compound Heterozygote, Hemoglobin S and Hemoglobin Hekinan, in 4 Members of a Haitian American Family

(POSTER NO. 79)

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Context: Differential diagnoses for sickle cell disease in carriers for hemoglobin (Hb) S include a long list of Hb variants as well as thalassemias. We have evaluated a family with HbS and Hb Hekinan (a27; Glu-Asp), a rare a-chain variant reported in 8 publications. Both sickle solubility tests were positive without other genetic analysis, and HbA/HbS patterns using acid and alkaline pH electrophoresis. Both sickle solubility tests were positive without other hemato logic abnormalities identified. DNA sequencing confirmed a GAG-GTG mutation at codon 6 of the -globin gene for Hb S and a GAG-GAC mutation at codon 27 of the a2-globin gene for Hb Hekinan. So far no clinical symptoms associate with this combination.

Conclusions: The combination of Hb Hekinan and HbS hasn’t been published before. Also, there is no report of the a2-gene substitution at IVS-II-64 A to G either alone or in combination with Hb Hekinan. It’s fascinating that multiple female members in consecutive generations apparently all inherited the same hybrid variant.
Restaging positron emission tomography showed an excellent and near complete remission with only minimal residual disease (Figure 75).

Evaluation of Immunohistochemistry in Lymphomas With Crush Artifacts
(Poster No. 82)
Dalia Magdi Abdel Azim, MD, PhD (dazim@health.southalabama.edu); Jacek M. Polski, MD. Department of Pathology, University of South Alabama, Mobile.

Context: Crush artifacts are common in hematopathologic specimens, which can be diagnostically challenging. To assess the diagnostic utility of immunohistochemistry (IHC) in lymphomas with crush artifacts, we evaluated IHC performance in crushed lymphoma tissue.

Design: A pathology archives search for lymphomas with crush artifacts yielded 10 cases; including 8 diffuse large B-cell lymphomas, 1 classical Hodgkin lymphoma, and 1 anaplastic large cell lymphoma. The following IHC markers were assessed: CD20, CD79a, CD45, CD30, CD15, CD10, CD3, Bcl-2, Bcl-6, Ki-67, MUM1, CD99, Pax5, TdT, CD68, S-100, Cam5.2, vimentin, synaptophysin, NSE, ALK-1, TTF-1, EMA, κ, and λ. Qualitative and quantitative scoring (H score) was performed by 2 independent observers. Spearman correlation and χ statistic were used to determine correlation coefficients.

Results: There was a good initial interobserver agreement on noncrushed tissue IHC (91.8%, K = 0.84, H score correlation 0.93). Similarly good agreement existed on crushed tissue IHC (95.9%, K = 0.92, H score correlation 0.94). A good correlation was shown between average H scores for crushed versus noncrushed tissue IHC (0.92), and for qualitative scoring with full agreement for the majority of stains (86.3%). Markers that showed qualitative discordance were CD3, CD5, CD10, vimentin, MUM1, κ, and λ. False-positive results were commonly caused by inability to distinguish reactive T cells from crushed lymphoma cells. Some markers showed lower H scoring in crushed tissue, but with no qualitative discordance.

Conclusion: The data suggest that lymphomas with crush artifacts are still amenable to IHC analysis. Most markers were found to be reliable. Strong CD20 staining correctly predicted B-cell lineage of the crushed lymphoma cells.

Myeloid Antigen Expression Is Similar in Pediatric and Adult Acute Lymphoblastic Leukemia Patients
(Poster No. 83)
Zhihong Hu, MD, PhD (zhu1@lumc.edu); Reeba Omman, MD; Milind Velankar, MD; Ameet R. Kini, MD, PhD. Department of Pathology, Loyola University Medical Center, Maywood, Illinois.

Context: Acute lymphoblastic leukemia (ALL) is a rapidly fatal malignant neoplasm derived from lymphoid progenitor cells. Myeloid antigens are occasionally expressed in ALLs. One hypothesis is that differences in myeloid antigen expression may partly account for differences in prognosis between pediatric and adult ALL.

Design: The clinical and hematopathologic materials in ALL patients of the past 2 decades were retrospectively reviewed from a single institution. Patients were classified as pediatric group (<18 years at the diagnosis) or adult group (≥18 years at diagnosis). Differences between myeloid antigen expression in adult and pediatric populations were analyzed by using the χ² test. Survival analyses were performed for the pediatric and adult groups by the Kaplan-Meier method.

Results: A total of 177 ALL patients were included in the present study. There were 36 cases of T-ALLs, and 141 cases of B-ALLs (13 pediatric T-ALLs; 23 adult T-ALLs; 67 pediatric B-ALLs, and 74 adult B-ALLs). As has been widely shown, the pediatric ALL patients had significantly better prognosis than adult ALL patients. Although a slightly higher proportion of adult ALL cases showed myeloid antigen expression, this difference was not significant. In addition, there was no association of myeloid antigen expression with overall survival either in the pediatric or in the adult ALL patients (Figure 76).

Conclusion: There is no significant difference in myeloid antigen expression between pediatric and adult ALLs. The findings indicate that the relatively poor prognosis of adult ALLs is not associated with myeloid antigen expression.

Crystal Storing Histiocytosis Associated With Plasma Cell Neoplasms: Two Cases
(Poster No. 84)
Beenu Thakral, MD (beenuthakral@gmail.com); Laura Moench, MD; Robert W. McKenna, MD; Elizabeth Courville, MD. Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis.

Crystal-storing histiocytosis (CSH) is characterized by intracytoplasmic accumulation of crystallized immunoglobulins in histiocytes and is typically associated with disorders that express monoclonal immunoglobulins. We describe 2 cases of CSH associated with a plasma cell neoplasm (PCN). Case 1: A 43-year-old woman with stage IV chronic kidney disease due to renal tubular acidosis undergoing evaluation for kidney transplant was found to have a 0.2 g/dL serum IgD κ monoclonal protein. Bone marrow core biopsy showed numerous aggregated histiocytes with intracytoplasmic eosinophilic inclusions (Figure 77, A), prominent on the aspirate smears and present in histiocytes and plasma cells (Figure, B). Immunohistochemical stains identified 5%–8% κ monotypic plasma cells. No lytic lesions were seen on imaging. The patient was diagnosed with monoclonal gammopathy of uncertain significance (MGUS). Case 2: A 70-year-old man with a 1-year history of IgG κ MGUS with innumerable hypermetabolic osseous lytic lesions on imaging. Computed tomography guided biopsy of sacral lesion showed a proliferation of histiocytes with numerous intracytoplasmic rhomboid to needle-shaped crystals (Figure, C) and interspersed aggregates of κ restricted plasma cells by ISH (Figure, D).

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Subsequent iliac crest biopsy showed 10% κ-restricted plasma cells and numerous crystal-laden histiocytes. The patient was diagnosed with plasma cell myeloma. We have illustrated 2 cases of CSH associated with PCN, both with a prominent histiocytic component. In Case 1, the patient’s renal failure, with decreased clearance of monoclonal proteins, may have contributed to the presentation. Case 1 also illustrates CSH associated with IgD heavy chain, which has been rarely described.

**Atypical Blasts With Rosettelike Multinucleation and Abundant Vacuoles in Acute Myeloid Leukemia With Complex Cytogenetic Abnormalities With FLT-3 D835 Variant**

*(Poster No. 85)*

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A 28-year-old woman presented with hematemesis, chills, sweats, and profound weakness. Laboratory findings revealed hypercalcemia, elevated LDH, and pancytopenia. The bone marrow aspirate revealed 95% blasts with 2 distinct populations. While one subset of blasts had typical blast morphology, another subset showed large atypical blasts with irregular nuclear contours, prominent nucleoli, markedly vacuolated cytoplasm, and binucleation/multinucleation with rosettelike features. By flow cytometric analysis the blasts expressed dim CD4, CD13, CD15, dim CD33, CD36, dim CD64, and dim MPO without HLA-DR expression, findings diagnostic of AML with monocytic differentiation. No megakaryocytic differentiation was identified. Genetic studies revealed 5 clonal cell lines with complex cytogenetic abnormalities and FLT-3 D835 variant mutation without FLT-3 ITD, NPM1, and CEBPA. The patient underwent induction chemotherapy with CPI-613, cytarabine, and mitoxantrone. The blast population with conventional morphology showed a good response to induction chemotherapy. However, the atypical blasts were persistent in day 14 (nadir) marrow, suggesting resistance to conventional chemotherapy. There are scant reports on atypical morphology of blasts in the literature. Blasts with prominent nuclear invagination (cuplike nuclear indentation) have been reported in acute myeloid leukemia (AML) with FLT3 ITD and loss of HLA-DR expression or NPM1 mutation. Blasts with bilobed nuclei were reported in AML with t(16;16) (p13;q22) and monosomy 13 showing a new CBFB-MYH11 fusion transcript. In our case, the blasts were large in size and had highly convoluted nuclear outlines, rosettelike multinucleation, and abundant cytoplasmic vacuoles. To our knowledge, these findings have not been previously reported.

**Primary Myelofibrosis in a 3-Year-Old: A Rare Manifestation of a Predominantly Adult Entity**

*(Poster No. 86)*

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Primary myelofibrosis is characterized by a clonal proliferation of hematopoietic stem cells, associated replacement of bone marrow by fibrosis, and resultant extramedullary hematopoiesis. It is a relatively uncommon condition that is predominantly diagnosed in older adults. Exceedingly rare childhood cases have been documented. We report the case of a previously healthy 3-year-old girl who presented with fever, rash, and fatigue. Massive splenomegaly and pancytopenia were noted on initial evaluation. Extensive testing excluded immunologic, metabolic, and infectious processes. The peripheral blood had moderate anisopoikilocytosis with occasional dacrocyes and spherocytes. The bone marrow biopsy was hypocellular with hematopoietic elements comprising <1% of total marrow space. Sinusoids were markedly dilated in a whorled, fibrotic stroma. A reticulin stain confirmed myelofibrosis grade 3 (Figure 78). Cytogenetic studies revealed a normal karyotype. This case posed a diagnostic challenge given the rarity of primary myelofibrosis in this age group. Physical exam, hematologic analysis, and bone marrow features were instrumental in establishing this diagnosis. The patient received myeloablative therapy with a 10/10 HLA-matched, unrelated donor hematopoietic stem cell transplant, after which she developed acute graft-vs-host disease and numerous other complications. Although a bone marrow biopsy at 6 months showed no evidence of myelofibrosis, the patient continued to have a clinical decline and expired approximately a year after diagnosis.

**B-Cell Lymphoma With Extra MYC Signal—Is It Double-Hit Lymphoma?**

*(Poster No. 87)*

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Double-hit lymphomas (DHL) are defined as B-cell lymphoma unclassifiable with a chromosomal breakpoint affecting the MYC/B23 locus in combination with another rearrangement at (14;18)(q32;q21). However, we recently observed that 2 patients with an extra intact MYC signal in association with the t(14;18) demonstrated morphology similar to that of DHL. We evaluated the impact of an extra copy of MYC on the morphology, immunophenotype, and clinical course. The study group included 2 patients diagnosed with B-cell lymphoma unclassifiable demonstrating t(14;18) and an extra copy of MYC. FISH analysis was negative for MYC gene rearrangement in both cases. Tissue sections displayed proliferation of medium-sized lymphocytes, typical starry-sky appearance with rare cytoplasmic lipid vacuoles in case 1, and bands of sclerosis in case 2. Tumor cells were positive by immunohistochemistry for BCL2 and BCL6 in both cases and demonstrated Ki-67 at 95% in case 1 and 35% in case 2. Flow cytometry in both cases demonstrated light-chain-restricted CD20+ and CD10-positive neoplastic B cells, with negativity for CD19 in case 1. The patients were treated with different chemotherapy regimens and achieved complete remission. B-cell lymphoma with an additional copy of intact MYC may act as second hit in combination with t(14;18). They
Concordance of Interpathologist and Intrapathologist Diagnosis of Classical Hodgkin Lymphoma With the MultiOmyx HL Profile

(Poster No. 88)

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Context: The diagnosis of Hodgkin lymphoma is often difficult. We have developed a fluorescent hyperplexed methodology for paraffin-embedded sections that enables assessment of multiple antigens on a single section, with similar staining characteristics as standard immunohistochemical stains, and evaluation of specific cells (Multi-Omyx).

Design: Historical immunohistochemistry diagnoses were compared to MultiOmyx diagnoses, studying blinded cases consisting of 23 classical Hodgkin lymphomas, 29 other diagnoses, and 3 cases without an original diagnosis. One section from each specimen was probed with CD30, CD15, CD45, Pax5, CD20, CD79a, OCT2, Bob1, and CD3 antibodies. Three independent pathologists viewed each biomarker as a grayscale image, an overlay of multiple biomarkers, or as a pseudodiagnosis in conjunction with clinical and pathologic findings of double-hit lymphoma.

Results: Of the 52 diagnosed cases 45 (87%) showed complete concordance among all pathologists with the historical diagnosis. Analysis of one discordant case raised doubt to the validity of the historical diagnosis. Review of the other discordant cases showed them to be diagnostically challenging and open to multiple interpretations. Average pairwise agreement among the pathologists was 93% \((k = 0.85)\). High intrapathologist agreement was also found.

Conclusions: A concordance study of multiple pathologists showed excellent agreement for diagnosis of Hodgkin lymphoma (Table). MultiOmyx is performed on a single section and provides images similar to standard immunohistochemistry stains, and therefore is useful in cases with rare Hodgkin cells or small samples. This novel methodology is practical for routine diagnosis, and will be further validated as an aid to the improved diagnosis of Hodgkin lymphoma.

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Sequential Occurrence of Primary Mediastinal Lymphoma and Nodular Sclerosis Classical Hodgkin Lymphoma: Clonal Relationship and Implications for Management

(Poster No. 90)

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Primary mediastinal diffuse large B-cell lymphoma (PMBCL) and classical Hodgkin lymphoma, nodular sclerosis subtype (cHL-NS), have overlapping clinicopathologic and genetic features. Rarely, synchronous or metachronous PMBCL and cHL-NS occur. These are not technically “mediastinal gray zone lymphomas” as defined by the 2008 WHO classification, but likely represent a related process. Our 22-year-old patient presented with night sweats, cough, and weight loss. Imaging revealed a 16-cm mediastinal mass. Biopsy showed a monotonous population of large lymphoid cells that were strongly positive for CD20 and CD79a, with weak focal CD30 staining and compartmentalizing fibrosis (Figure 79, left). The patient was diagnosed with diffuse large B-cell lymphoma, and treated with rituximab, cyclophosphamide, vincristine, and prednisone (R-CHOP). The mediastinal mass initially decreased in size, but follow-up imaging showed progressive disease;
this was treated with proton beam therapy. The patient subsequently developed cervical lymphadenopathy, concerning for a secondary malignancy. Biopsy showed a nodular infiltrate of small lymphocytes, eosinophils, and large atypical cells with polylobated nuclei and prominent nucleoli. These cells expressed CD15 and CD30, and were negative for CD20, consistent with cHL-NL (Figure, right). Molecular studies for immunoglobulin heavy-chain rearrangement demonstrated a clonal peak at 323 bp in the IGH framework 1 reaction in both biopsy specimens, suggesting a clonal relationship between the 2 processes. Though the individual biopsies yielded 2 different diagnoses, the overall findings were consistent with recurrence of the patient’s original lymphoma rather than a second primary, making the patient eligible for autologous stem cell transplant.

Primary Cervical Lymphoma Complicated With Bilateral Obstructive Uropathy

(Poster No. 91)

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Primary lymphomas of the female genital tract are uncommon and pose a diagnostic challenge if their existence is not suspected, especially in young and immunocompetent patients. A 22-year-old previously healthy woman presented to our institution with complaints of crampy abdominal pain and heavy menstrual periods for 2 months. She was found to have acute renal failure (creatinine 5.2 mg/dL). Computed tomography scan revealed markedly thickened cervix with bilateral obstructive hydronephrosis. Renal radionuclide scan showed absent left renal function. Serum creatinine normalized subsequent to percutaneous nephrostomy tube placement. Magnetic resonance imaging showed a 6.1 × 4.1-cm cervical malignancy extending to the pelvic sidewall continuous with the left side of the sigmoid colon with bulky internal iliac adenopathy. Cervical cone biopsy revealed diffuse infiltration of the cervix, complexified with bilateral obstructive ureteral obstruction. Biopsy of the supraclavicular lymph node showed capsular invasion with a nodular infiltrate of small lymphocytes, centroblasts that were CD20 + /CD10 – /BCL2 – /BCL6 – , and CD30–. Also present were eosinophils, and large atypical cells with polylobated nuclei and prominent nucleoli. These cells expressed CD15 + /CD30 + and negative for CD3, CD45, and ALK-1. Also present were small lymphocytic nodules containing predominantly small lymphocytes with irregular cleaved nuclear contours and few transformed centroblasts that were CD20+/CD10–/Bcl2+. Flow cytometric analysis also identified a CD19–, CD20–, CD10–, and A+, light-chain–restricted B-cell population. This finding supports the diagnosis of composite lymphoma: nodular sclerosis classical Hodgkin lymphoma and low-grade follicular lymphoma. Even though it is rare, the possibility of composite lymphoma should be considered in patients who present with AIHA.

The Clinical Significance of Quantitative Analysis of Neoplastic B Cells of Follicular Lymphoma With Flow Cytometry

(Poster No. 93)

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Context: Follicular lymphoma is a low-grade B-cell lymphoma. The prognosis is closely related to the grade and extent of the disease. Lymph nodes involved by follicular lymphoma often have variable numbers of neoplastic B cells in a background of residual benign B and T cells. The clinical significance of this variability is unclear.

Design: The flow cytometric data of 98 previously diagnosed follicular lymphoma cases were retrospectively analyzed. These cases included 42 men and 56 women with an age range of 31–88 years (n = 43 for stage I–II, n = 55 for stage III–IV; n = 70 for grade 1–2, n = 28 for grade 3). The percentages of neoplastic and nonneoplastic B cells were enumerated based on antigen expression pattern and light-chain restriction.

Results: The average total B cells of total lymphocytes was about the same between the group with stage I–II disease and the group with stage III–IV disease (44.5% versus 48.1%, P = .3). The average neoplastic B cells of total B cells in the group with stage III–IV disease was significantly higher than in the group with stage I–II disease (87.4% versus 75.9%, P = .003). The clinical significance of this variability is unclear.

Conclusions: It appears that increased percentage of neoplastic B cells in the lymph node with follicular lymphoma is associated with clinical disease progression. Flow cytometry analysis of this parameter may help with further risk stratification of follicular lymphoma.

Initial Presentation of HIV/AIDS: Rectal Mass

(Poster No. 94)

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The patient, a previously healthy 39-year-old man, presented for a swollen mass around his rectum. Examination showed no obstruction, fistula, weight loss, fever, or other pertinent positives. Physical exam identified a 1-cm erythematous rectal mass. Initial labs revealed human immunodeficiency virus (HIV) positivity with CD4 count of

Composite Hodgkin Lymphoma and Follicular Lymphoma Presenting as Autoimmune Hemolytic Anemia

(Poster No. 92)

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Composite lymphoma, a rare entity, is described as the presence of 2 or more distinctive morphologic and immunophenotypic types of lymphomas in a single anatomic site. The association between autoimmune hemolytic anemia (AIHA) and lymphoproliferative disorders is well established. However, AIHA as the initial presentation of a patient with composite lymphoma has not been reported previously. We describe a case of a 70-year-old man who presented with AIHA at our institution. Peripheral smear revealed spherocytes consistent with hemolysis. Bone marrow biopsy performed for delineation of a lymphoproliferative process as a cause of hemolysis was negative and showed a hypercellular marrow with erythroid hyperplasia. Further clinical workup revealed a supracavitary and retroperitoneal lymphadenopathy. Biopsy of the supracavitary lymph node showed capular and intranodal sclerosis with a nodular proliferation containing Reed-Sternberg cells amidst a reactive background of lymphocytes, histioocytes, eosinophils. The Reed-Sternberg cells were positive for CD15 and CD30 and negative for CD3, CD45, and ALK-1. Also present were small lymphocytic nodules containing predominantly small lymphocytes with irreglar cleaved nuclear contours and few transformed centroblasts that were CD20+/CD10–/Bc12+. Flow cytometric analysis also identified a CD19–, CD20–, CD10–, and A+, light-chain–restricted B-cell population. This finding supports the diagnosis of composite lymphoma: nodular sclerosis classical Hodgkin lymphoma and low-grade follicular lymphoma. Even though it is rare, the possibility of composite lymphoma should be considered in patients who present with AIHA.
B-Lymphoblastic Lymphoma of the Lesser Sac Mimicking Retropertitoneal Neuroblastoma Tumor

(Krisnapal Boon-Unge, MD (kboonunge@chla.usc.edu); Sheng-mei Zhou, MD, Paul Pattengale, MD. Department of Pathology and Laboratory Medicine, Children’s Hospital Los Angeles, Los Angeles, California)

Neuroblastoma and Wilms tumor are the 2 most common tumors in children presenting with abdominal mass. Lymphoblastic lymphoma is a common pediatric malignant neoplasm. However, primary lymphoblastic lymphoma involving the lesser sac and pancreas is extremely rare. To the best of our knowledge, there is no documented case in literature to date. We report a 36-year-old previously healthy girl presented with a 3-week history of increasing abdominal girth, intermittent abdominal pain, and early satiety. Computed tomography scan of chest/abdomen/pelvis revealed a large heterogeneous mass measuring 12.2 × 10.8 × 10 cm in the left abdomen crossing the midline and encasing the aorta with the characteristics most compatible with a neuroblastoma. There was no evidence of intrathoracic involvement. Operative finding was a large soft mass arising from a lesser sac of the left abdomen. There was no attachment to the stomach wall. Biopsy showed a small round blue cell neoplasm infiltrating pancreatic tissue. The neoplastic cells had oval to round hyperchromatic nuclei, inconspicuous nucleoli, and scant eosinophilic cytoplasm. Mitoses and apoptotic bodies were readily identified. Immunohistochemical staining revealed that the tumor cells were positive for CD45, CD79a, CD5, CD10, and FLI-1, but negative for CD3, PG-P9.5, tyrosine hydroxylase, CD56, and CD99. Systemic workup showed no bone marrow or central nervous system involvement.

The final diagnosis was primary abdominal B-cell lymphoblastic lymphoma, Stage III. The patient underwent 1 month induction chemotherapy with complete clinical resolution. Though primary abdominal lymphoblastic lymphoma is extremely rare, increased awareness of this entity may help avoid delay in diagnosis/misdiagnosis.

CD5-Negative Marginal Zone—Like Mantle Cell Lymphoma: A Rare Case Report

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Mantle cell lymphoma (MCL) is an uncommon and aggressive B-cell lymphoma, comprising 5%–10% of non-Hodgkin lymphoma in the United States. The 5-year overall survival is less than 30% and most patients present with late stage disease. Neoplastic cells are typically monomorphic small to medium-sized lymphocytes with sparse cytoplasm and irregular nuclei. Centroblasts and immunoblasts are usually absent. Other rare variants with distinct morphologic features have been recognized, including blastoid and pleomorphic variants. Classically, the neoplastic cells are positive for B-cell markers in addition to CD5, BCL2, and cyclin-D1. Cytogenetic translocation t(11;14) is characteristic. We report a rare case of MCL with histologic features similar to marginal zone lymphoma (MZL) that is CD5 negative. To our knowledge, only a few similar cases have been reported so far. A 74-year-old woman presented with right lower lobe lung mass. A wedge resection was performed, and sections demonstrate atypical dense lymphoid infiltrate of small to medium-sized lymphocytes with a moderate amount of clear cytoplasm admixed with plasmacytic immunophenotype with a high proliferation index via Ki-67 (≥90%). Core biopsy of the liver lesion showed additional involvement by PBL; however, bone marrow biopsy was negative. PBL is a proliferation of large atypical cells with a plasmacytic immunophenotype, typically seen in HIV and Epstein-Barr virus-positive individuals. PBL patients commonly present with advanced disease, having oral cavity or other mucosal surface masses. Morphologically, the disease varies from diffuse, cohesive cells resembling immunoblasts or carcinoma to cells with plasmacytic differentiation. Mitotic figures, apoptotic cells, and tingible body macrophages are common. Most cases have >90% Ki-67; stain positive for CD138, CD38, IRF4/MUM1, and Epstein-Barr virus; and are negative for CD45, CD20, PAX-5, and CD56. Most cases of PBL involve the upper aerodigestive tract in immunodeficient patients. Our patient presented with a rare location of involvement, but an otherwise classic presentation; he is receiving treatment for HIV and PBL.

Transformation of Extranodal Marginal Zone Lymphoma of Mucosa-Associated Lymphoid Tissue Lymphoma Into Diffuse Large B-Cell Lymphoma Associated With MYC Rearrangement

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MYC dysregulation in B-cell lymphomas is often associated with aggressive disease and unfavorable prognosis. We report a case of diffuse large B-cell lymphoma (DLBL) possibly transforming from a coexisting small B-cell lymphoma associated with MYC translocation. A 62-year-old man presented with a right orbital mass, which microscopically revealed 2 distinct atypical lymphoid nodules involving the glandular tissue. The larger nodule comprised large lymphocytes with high N:C ratio, vesicular nuclei, conspicuous nucleoli, and scant cytoplasm. These cells were positive for CD20, BCL6, MUM-1, and CD10, along with a near 100% Ki-67 proliferation rate. The second nodule consisted of sheets of small mature lymphocytes with focal monocytoid cell clusters, showing CD20, BCL2, CD43, and partial CD5 positivity, with a Ki-67 proliferation rate <10%. By flow cytometry the large cell population showed light-chain restriction, while the small B cells were λ restricted. Based on these findings, the diagnoses of DLBL with high-grade features and extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) were rendered. FISH studies demonstrated higher MYC gene rearrangement in DLBL than MALT area (33% versus 18%, respectively). B-cell immunoglobulin gene rearrangement study showed clonal pattern in both areas. Three of 5 clonal peaks were shared by both lymphomas, raising the possibility of a common initial clonal process. This case likely represents an ongoing transformation into large cell lymphoma with light-chain switch. Additional genomic testing is being performed to further understand the pathophysiology of such transformation in the presence of MYC translocation.

Parvovirus B19 Infection in a Chronic Myelogenous Leukemia Patient on Imatinib Therapy and Failed Allogeneic Bone Marrow Transplant

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Allogeneic bone marrow transplantation recipients are predisposed to common and opportunistic viral infections acquired from donors or community and from reactivation of latent viruses. Imatinib therapy also predisposes to viral infections due to defects in cell-mediated immunity. We present an unusual case of a 53-year-old man with chronic myelogenous leukemia (CML) diagnosed 18 years prior, allogeneic bone marrow transplant from HLA-matched sister 17 years back, on imatinib for 4 years who presented with WBC 20 × 10^9/L, hemoglobin 11.3 g/dL, and platelets 467 × 10^9/L and whose hemoglobin levels decreased to 8.4 g/dL within a month. Failed bone marrow transplant and diethylstilbestrol, M3 to 2nd phase, 18 months later. Microrna bone marrow biopsy (Figure 81) that had 10%–15% CD34+ blasts, severe myelofibrosis, and t(9;22) male karyotype with multiple cytogenetic abnormalities (normal female karyotype 8 years back). Severe erythroid hypoplasia, rare pronormoblasts with smudged
chromatin (Figure), and parvovirus B19 (PVB19) erythroid precursors by immunohistochemistry were present (Figure). Peripheral blood viral assay PCR should be performed and bone marrow biopsy for confirmation can be diagnostic. PVB19 PCR was positive. PVB19 is ubiquitous with 60%–90% seropositivity in adults. PVB19 is highly erythrotropic, causing cessation of erythropoiesis and transient aplastic crisis in hemolytic anemia patients and persistent infection and chronic anemia in immunosuppressed patients. High myeloid to erythroid ratio and decreased erythroid precursors are expected in CML and hemoglobin levels can fall in aggressive phase. High index of suspicion for PVB19 infection is required in such cases. Immunosuppressed patients may not produce PVB19 neutralizing IgG/IgM, complicating serologic test interpretations. Peripheral blood viral assay PCR should be performed and bone marrow biopsy for confirmation can be diagnostic.

CD5 Positive Intravascular B-Cell Lymphoma in a Patient With Wilson Disease
(Poster No. 99)
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Intravascular large B-cell lymphoma (IVLBCL) is a rare type of extranodal large B-cell lymphoma with aggressive clinical course. A 68-year-old man with past history of liver cirrhosis secondary to Wilson disease presented to the emergency department because of lethargy. The patient was found to have hepatic encephalopathy and renal failure (hepatorenal syndrome) and was admitted. Despite treatment, his conditions deteriorated and he expired. A complete autopsy was performed. No lymphadenopathy was grossly identified. Histologic examination confirmed liver cirrhosis. In addition, large atypical lymphoid cells were found within the lumina of small blood vessels in multiple extranodal sites: thyroid, gallbladder, lung, peripancreatic tissue, and omentum, with round to slightly irregular nuclei, prominent nucleoli, and scant cytoplasm. Immunophenotypically, the neoplastic cells were positive for CD20, CD5, CD30, PAX5, and MUM-1, and negative for CD3, CD10, CD138, BCL-6, and cyclin-D1. Ki67 stained approximately 60%–70% of neoplastic cells. Based on these findings, a postmortem diagnosis of IVLBCL was made. IVLBCL is characterized by selective intravascular growth of lymphoma cells. The clinical presentation is highly variable and depends on the organs involved, with the central nervous system and skin being the mostly affected sites. Owing to its rarity and nonspecific clinical manifestations, the diagnosis is often made postmortem. IVLBCL is a diagnostically challenging, highly aggressive lymphoma with poor prognosis that, in part, reflects frequent delays in diagnosis. In summary, we describe a rare case of CD5-positive IVLBCL, which is identified postmortem in a patient with Wilson disease.

Hereditary Pyropoikilocytosis: A Rare but Not an Uncommon Disease
(Poster No. 100)
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Hereditary pyropoikilocytosis (HPP) is a rare form of autosomal recessive red cell membrane defect that causes hemolytic anemia in infancy. The red cell fragmentation and poikilocytosis share the morphology similar to thermally damaged red cells. In HPP the red cells have increased osmotic fragility and the neonate can exhibit hyperbilirubinemia at birth, requiring exchange transfusion or phototherapy. We present a case of HPP in a child who was born to Kurdish parents as a second child. The baby was found to be pale shortly after birth. Complete blood count showed hemoglobin of 9.6 g/dL, which decreased in the next 3 hours. Reticulocytosis (16.5%) with normal mean corpuscular volume and total bilirubin and negative direct Coombs test were noted. The peripheral blood smear revealed marked anisopoikilocytosis with bizarre red blood cell forms including microspherocytes. The white blood cells and platelets were unremarkable. The patient’s 7-year-old brother was also diagnosed with a hemolytic anemia in infancy, and was evaluated in another hospital. Following splenectomy at age 5 years the need for red blood cell transfusions decreased. These findings are consistent with HPP. Our patient is now 17 months old without organomegaly and has required a total of 6 units of packed red cell transfusions. Although HPP is rare, it should be included in the differential diagnosis for a hemolytic anemia in a neonate.

Differentiating Between Malignant Erythroid Proliferations and Recovering Marrows Utilizing CD105
(Poster No. 101)
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Two patients, one having undergone treatment for acute T-lymphoblastic leukemia, the other with a history of polycythemia vera, had bone marrow specimens submitted for analysis by multidimensional flow cytometry. Both showed an elevated level of immature nucleated erythroid progenitors (12%, and 30% respectively, normal <2% of nucleated cells). Upon further evaluation of the maturational patterns the case with a history of acute leukemia showed normal erythropoiesis, albeit at an elevated rate (Figure 82, B). Meanwhile, the case with a history of polycythemia vera showed dyserythropoiesis, including clonal growth consistent with acute erythroid leukemia (Figure, C). The primary differentiating relationship involved CD105, an antigen present on immature erythroid progenitors. Unlike normal specimens (Figure, A) or the first case when compared to an antigen present on mature nucleated erythroid progenitors (CD235a, CD71, or CD36) the patient does not show the normal pattern of maturation. Cytogenetic analysis of the second specimen revealed a complex result including clonal growth consistent with acute erythroid leukemia. The primary differentiating relationship involved CD105, an antigen present on immature erythroid progenitors. Unlike normal specimens (Figure, A) or the first case when compared to an antigen present on mature nucleated erythroid progenitors (CD235a, CD71, or CD36) the patient does not show the normal pattern of maturation. Cytogetic analysis of the second specimen revealed a complex result with abnormalities of chromosomes 2, 5, 7, 9, 12, 13, 15, 16, 17 (including loss of the TP53 gene), 19, 21, and 22, validating the flow cytometric findings. Thus we were able to differentiate between a bone marrow recovering from treatment, with increased but normal erythropoiesis, from a case with malignant dyserythropoiesis. These 2 cases demonstrate that CD105 is a valuable tool for the assessment of nucleated erythroid progenitors, and when utilized can allow for the correct identification of dyserythropoiesis in cases in which it would not otherwise be possible.
Correlation of CD117 and CD34 Expression With International Prognostic Scoring System in Bone Marrow Biopsies of Patients With Myelodysplastic Syndromes

(Poster No. 102)

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Context: CD34 and CD117 are used to determine blast counts of patients with myelodysplastic syndromes (MDS). Our study examines the relationship of CD34 and CD117 expression by immunohistochemistry to the International Prognostic Scoring System (IPSS).

Design: Bone marrow biopsies of 51 MDS patients and 17 with staging bone marrow were reviewed and IPSS was calculated. CD34 staining of control patients was not examined. Positivity was determined by counting 500 cells and was expressed as percentage. CD117 was considered positive upon identification of membranous and faint cytoplasmic staining, while dark, homogenous staining of the whole cell including the nucleus was excluded. Positive CD34 staining showed cytoplasmic pattern.

Results: MDS patients comprising 28 males and 23 women were examined, mean age 74.9 years (range, 50–95 years). Percentages of CD34 and CD117 staining increased as the risk scores rose. CD117 positivity increased sharply between intermediate 1 (I1) and 2 (I2) (P < .05) while differences between I2 and high risk (HR) was not significant (P = .88). The difference in CD34 expression between LR and I1 was not significant (P = .75). It was significant between I1 and I2 and between I2 and HR (P < .05).

Conclusions: The CD34 and CD117 correlations show statistically different blast populations, possibly explained by CD34/CD117+ blast compartment occurring in MDS of intermediate grade. Increased CD117 expression was more likely to have cytogenetic abnormalities. This mechanism may account for dysplasia seen in MDS. CD117 antigen expression may serve as an additional prognostic factor for patients with MDS.

Peripheral T-Cell Lymphoma in 2 Patients With a Long-Standing B-Cell Chronic Lymphocytic Leukemia: Atypical Richter Transformation?

(Poster No. 103)

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The occurrence of T-cell lymphoma in patients with chronic lymphocytic leukemia (CLL) is extremely rare. We describe 2 cases of peripheral T-cell lymphoma (PTCL) in patients with CLL. We searched our surgical pathology electronic database for cases with PTCL and CLL from 2002 through 2012. Clinical and pathologic data were retrieved as well as the results of the ancillary studies. We identified 2 cases (1 man and 1 woman) with CLL diagnosed at the ages of 55 and 60, and PTCL diagnosed 12 and 10 years later, respectively. Both cases had leukemic involvement and extensive bone marrow (BM) infiltration by CLL, deletion of chromosome 13, typical CLL markers, and, in the woman’s case, atypical expression of CD25. The former patient’s CLL had bright expression of CD38 and Zap70. The PTCL in the female patient presented with knee mass and was CD3, CD4, CD2, and CD7 positive with TCR α/β and EBV expression and negativity for CD56/57 and CD8. The second case, PTCL presented as abdominal pain with gastrointestinal and BM involvement. The PTCL was CD3 and CD8 positive and CD4, CD5, and CD30 negative with significant chromosomal abnormalities. We reported 2 patients with long-standing CLL that developed PTCL and 1 of whom had EBV-infected neoplastic cells. The development of this neoplasm might be due to insufficient number of viable cells. The patient responded poorly to chemotherapy, and stem cell transplant is currently being considered. To our knowledge, we report the first case of hairy cell variant of splenic B-cell lymphoma with coexisting plasma cell myeloma (Figure 83).

Hairy Cell Leukemia Variant Coexistent With Plasma Cell Myeloma

(Poster No. 104)

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The hairy cell leukemia variant entity is a rare disease, accounting for approximately 0.4% of chronic lymphoid malignancies and 10% of all conventional hairy cell leukemia cases. We report the case of a 61-year-old man who presented with anxiety and depression after years without medical care. He was found to have extensive lymphadenopathy, splenomegaly, and an IgG λ monoclonal protein by serum electrophoresis. Examination of the peripheral blood smear showed anemia and absolute lymphocytosis with morphologic features of hairy cell leukemia: small mature lymphocytes with cytoplasmic projections and prolymphocyte-like nuclei. The cells marked as positive for CD19, CD20, CD11c, HLA-DR, and IgG/K/A and negative for CD103 and CD25 by flow cytometry. A bone marrow biopsy revealed hypercellular marrow, trilinear hematopoiesis, and abnormal interstitial/sinusoidal lymphoid infiltrate representing 10–15% of marrow cells. These cells were CD20 positive by immunohistochemistry. Also present, representing 20%–30% of marrow cells, was a population of plasma cells positive for CD138 and λ light chain by mRNA in situ hybridization. Flow cytometric analysis of the bone marrow aspirate revealed a mature lymphocyte population marking similar to what was seen in the peripheral blood sample, diagnostic of the hairy cell variant of splenic B-cell lymphoma. The plasma cell population could not be further characterized because of insufficient number of viable cells. The patient responded poorly to chemotherapy, and stem cell transplant is currently being considered. To our knowledge, we report the first case of hairy cell variant of splenic B-cell lymphoma with coexisting plasma cell myeloma (Figure 83).

Hemoglobin Southwestern: A Novel β-Globin Variant (Arg40Thr) Associated With Mild Erythrocytosis

(Poster No. 105)

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Hemoglobinopathies are caused by globin gene mutations that affect the structure and/or production of globin proteins. While the majority of hemoglobin (Hb) variants produce no clinical manifestations, a minority of variants are of clinical significance, including those that alter oxygen affinity. We describe a novel Hb variant in the αβ contact region of the β-globin protein. Blood from an 8-month-old Hispanic...
male infant with Cornelia de Lange syndrome was submitted for abnormal Hb identification. Basic hematology, high-performance liquid chromatography (HPLC), isoelectric focusing (IEF), and bidirectional DNA sequencing of the entire β-globin gene (HBB) were performed. The variant Hb eluted in the HbA window with a quantity of 41.6% by HPLC. IEF demonstrated migration in a position anodal to ("faster than") HbA. DNA sequencing demonstrated a previously undescribed mutation in HBB (c.122 G→C het) with a predicted amino acid substitution of threonine for arginine at codon 40 (Arg40Thr). The hemolytic parameters were notable only for elevations in the red blood cell count, 5.83 × 10¹²/L; Hb, 15.7 g/dL; and hematocrit, 46.2%. The amino acid substitution of this new variant, Hb Southeastern (Arg40Ser) occurs in the same position as the known variants Hb Austin (Arg40Ser) and Hb Athens-GA (Arg40Lys), both of which show increased oxygen affinity. The α₂β₂ contact is involved in the reversible transition from the oxy to the deoxy tetrameric configuration. Hemoglobin variants with mutations involving the α₂β₂ contact characteristically show alterations in oxygen affinity and demonstrate the importance of this contact in Hb function.

**JAK2-Positive Myeloproliferative Neoplasm Concomitant With Marginal Zone Lymphoma**

(Poster No. 106)

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Polycythemia vera is a chronic myeloproliferative neoplasm (MPN) characterized by increased red blood cell production. Almost all cases are associated with gain-of-function mutation of the Janus 2 kinase (JAK2) gene. Without therapy, the natural progression of MPN includes the development of myelofibrosis or acute leukemia. The coexistence of MPN and lymphoproliferative neoplasm is rare without prior history of chemotherapy or radiation. We present a case series of 2 patients with rare coexistence of MPN and marginal zone lymphoma (MZL). The first case is a 73-year-old man who presented with abdominal pain, diarrhea, and weight loss. Laboratory findings revealed slightly increased hemoglobin levels and computer tomography scan showed splenomegaly. The second case is a 66-year-old man who presented with elevated hemoglobin and white blood cell levels. In both cases, bone marrow biopsy combined with flow cytometry revealed MPN (polycythemia vera) with concomitant MZL. Molecular analysis detected JAK2 V617F mutation in both cases. Only a few cases of the concurrent MPN with non-Hodgkin lymphoma have been reported. The pathophysiologic mechanism of coexistence of MPN and non-Hodgkin lymphoma as well as JAK2 involvement in the process is not clear. To our knowledge, this is the first case series presenting an association between JAK2 mutation–positive MPN and MZL.

**Diagnostic Challenge: Biphenotypic Blast Phase of Chronic Myelogenous Leukemia as Initial Presentation Versus De Novo Mixed-Phenotype Acute Leukemia**

(Poster No. 107)

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Mixed-phenotype acute leukemia with BCR-ABL1 translocation is a rare subtype of acute leukemia with poor prognosis. On the other hand, chronic myelogenous leukemia patients may present initially in blast phase; a portion of these patients show biphenotypic differentiation. It is important to distinguish de novo mixed-phenotype acute leukemia from chronic myelogenous leukemia in blast phase. We report a 60-year-old man with no history of a myeloproliferative disorder who presented with symptoms of deep vein thrombosis. Peripheral blood smear revealed marked leukocytosis with left-shifted maturation and 30% circulating blasts. The blasts showed dimorphic morphology, including both larger-sized “myeloid” blasts and smaller-sized “lymphoid” blasts. Bone marrow (BM) biopsy showed 39% blasts and 32% maturing myeloid cells. The blasts had both B and myeloid differentiation. Cytogenetics revealed BCR-ABL1 translocation as the sole abnormality in 94% of the cells. After induction chemotherapy, day 21 BM was hypercellular with no excess blasts. No biphenotypic blasts were detected in either peripheral blood or the marrow. FISH revealed 1% of total cells with BCR-ABL1 translocation. Empirically, many features of our case are suggestive of chronic myelogenous leukemia in blast phase, including (1) left-shifted in peripheral blood, (2) a significant component of maturing myeloid cells in BM, (3) the diagnostic BM showing higher percentage of BCR-ABL1 translocation than the blast percentage (94% versus 39%), (4) BCR-ABL1 translocation as the sole cytogenetic abnormality, and (5) postinduction hypercellular BM. However, the observation of minimal residual BCR-ABL1 in postinduction marrow argues otherwise, as suggested by some publications.

**CD8⁺ Cytotoxic Peripheral T-Cell Lymphoma, Not Otherwise Specified, in a Young Child: Case Report and Literature Review**

(Poster No. 108)

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Peripheral T-cell lymphoma, not otherwise specified (PTCL, NOS), is a mature T-cell lymphoma that very rarely occurs in children. The immunophenotype in nodal cases is usually CD4⁺/CD8⁺. We report a highly unusual and diagnostically challenging case of PTCL, NOS exhibiting a cytotoxic phenotype in an 8-year-old boy with massive lymphadenopathy without constitutional symptoms. Initial biopsy of the axillary lymph node demonstrated morphologic features resembling nextrizing lymphadenitis with paracortical expansion by polymorphous T cells associated with prominent karyorrhexis (Figure 84, A–C).

Persistence and progression of the lymphadenopathy led to a repeat biopsy of the right cervical lymph node. The atypical T cells demonstrated partial down-regulation of the CD7 pan-T-cell antigen by flow cytometry and immunohistochemistry. The vast majority of the T cells in the paracortex were CD8⁺/TIA-1⁺ cytotoxic T cells (Figure, D). T-cell receptor (TCR) gene rearrangement was positive for clonal T cells in both biopsies. A diagnosis of PTCL, NOS was made and confirmed by an outside expert on the repeat biopsy because of the clinical progression of the lymphadenopathy, the expansive proliferation of atypical T cells, and the consistently clonally rearranged T cells. The unusual presentation of PTCL, NOS in this 8-year-old child illustrates the broad differential diagnoses of persistent massive lymphadenopathy in pediatric patients. Furthermore, polymorphous nodal T-cell proliferation exhibiting a CD8⁺ cytotoxic immunophenotype and associated necrotizing changes should not exclude a diagnosis of PTCL, NOS. Published cases of childhood PTCL, NOS in the literature will be reviewed.

**An Indolent Case of Extranodal NK/T-Cell Lymphoma, Nasal Type: Does It Represent a Separate Entity?**

(Poster No. 109)

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Extranodal natural killer (NK)/T-cell lymphoma, nasal type, is most commonly an aggressive form of non-Hodgkin lymphoma derived from NK or T cells infected with the Epstein-Barr virus. The disease usually relapses or progresses despite aggressive treatment. Median survival time is reported as 12.5 months, while survival time for patients with a disseminated leukemic picture is less than 6 months. A protracted disease course is extremely rare and in this report we describe such a case. A 78-year-old woman presented with a 14-month history of nasal wall swelling. Computerized tomography demonstrated periorbital cellulitis. Limited response to antibiotics over the following 2 months prompted a nasal wall biopsy. Histology showed a mostly perivascular and adnexal nodular, small lymphocytic infiltrate. Flow cytometry demonstrated a large population of NK cells accounting for 80% of lymphocytes. A diagnosis of extranodal NK/T-cell lymphoma, nasal type, was made and subsequent bone marrow examination showed bone marrow involvement. Because of the patient’s age and comorbidities, no systemic chemotherapy was initiated. Three months after the diagnosis, the patient is currently tolerating local radiotherapy well and has no major clinical problems related to the disease. The indolent clinical behavior of extranodal NK/T-cell lymphoma, nasal type, in this case is unusual and underscores the need to study the pathogenetic mechanisms and prognostic factors of a much larger cohort. With such an indolent behavior, these cases raise the question of whether it is the same disorder as the aggressive counterpart needing aggressive therapy or if local therapy may be adequate.

### Blastic Plasmacytoid Dendritic Cell Neoplasm With t(11;19)(q23;p13.3); MLL-ENL, a Diagnostic Challenge

*(Poster No. 110)*

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Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare myeloid neoplasm with an immunophenotype (IP) of CD56+, CD123+, and HLA-DR+, which is variably overlapped with acute myeloid leukemia (AML). MLL rearrangement is a recurrent genetic abnormality in AML. Herein, we reported a case of BPDCN in a 41-year-old man with t(11;19)(q23;p13.3); MLL-ENL, which posed a diagnostic challenge to distinguish from AML. The patient presented with a recurrent disease with pancytopenia and extensive bone marrow infiltration of medium-sized, lymphoid-appearing cells with irregular nuclei and scant agranular cytoplasm. Flow cytometric (FC) and immunohistochemical (IHC) analyses revealed an IP of CD3+, CD4+, CD13+, CD14+, CD15+, CD19+, CD33+, CD34+, CD56+, CD64+, CD68+, HLA-DR+, TCI-1+, MPO+, lysozyme+, and TdT+. Notably, CD123 expression was variable, positive by FC and IHC with a clone of 7G3 (BD Biosciences), but negative by IHC with a clone of 6H6 (Cell Marque). Cytogenetic and FISH studies revealed a complex karyotype with t(11;19)(q23;p13.3); MLL-ENL fusion. Given the characteristic morphologic and IP features, including lack of myeloperoxidase and lysozyme, this case was diagnosed as BPDCN with an unusual t(11;19)(q23;p13.3); MLL-ENL. To the best of our knowledge, this is the only second such case in the literature. Our case underscores the importance of a comprehensive immunophenotypic analysis in establishing diagnosis, in particular the awareness of novel observation of variable CD123 expression by IHC using different clones. Furthermore, our case suggests that MLL rearrangement is a rare but recurrent genetic abnormality in BPDCN, and may play an important role in disease pathogenesis.

### Three Cases of Acute Promyelocytic Leukemia With Cryptic t(15;17) Identified Only by RT-PCR

*(Poster No. 111)*

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Context: We report 3 cases of “cryptic” acute promyelocytic leukemia (APL) showing morphologic features concerning for APL, but having normal karyotype and fluorescence in situ hybridization (FISH) studies, which were positive for the PML-RARA fusion by reverse transcriptase polymerase chain reaction (RT-PCR).

Design: Three patients were identified at presentation of APL. Two cases had circulating abnormal promyelocytes with dense cytoplasmic granulation, Auer rods, and faggot cells, consistent with the hypergranular variant. In the third case, abnormal promyelocytes showed lobulated and bilobed nuclei with only rare faggot cells identified, consistent with the hypergranular variant. Cytochemical myeloperoxidase was strongly positive in all cases. Flow cytometry studies showed bright CD33 and dim to negative CD34 and HLA-DR. In all cases, conventional karyotyping and FISH for t(15;17) using the LSI PML/RARA dual color, dual fusion probe system from Vysis was ordered. Because of strong morphologic suspicion for APL, RT-PCR using primers to detect all 3 gene fusion transcripts (bcr-3, bcr-1, and bcr-2) was also performed.

Results: In all cases, routine karyotyping and FISH did not demonstrate abnormalities. In the 2 cases with hypergranular morphology, RT-PCR was positive for the bcr-1 form PML-RARA transcript. The hypogranular case was positive for the bcr-3 form.

Conclusions: When morphologic and flow cytometry immunophenotyping are strongly suggestive of APL despite normal cytogenetics and FISH, a cryptic t(15;17) translocation detectable only by PCR should be considered. Negative FISH studies may occur when miniscule insertions do not hybridize with available FISH probes. RT-PCR offers a sensitive methodology to identify specific breakpoints.

### Unusual Association of Inflammatory Pseudotumor of the Spleen and Idiopathic Thrombocytopenic Purpura

*(Poster No. 112)*

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Inflammatory pseudotumor of the spleen (IPTS) is a rare benign lesion of uncertain etiology. Only 5 cases have been reported in association with idiopathic thrombocytopenic purpura so far. Herein, we describe the case of a 65-year-old woman with a history of idiopathic thrombocytopenic purpura that was found to have an IPTS mimicking splenic hamartoma on preoperative imaging studies. Following splenectomy, the spleen measured 11.0 × 8.5 × 5.0 cm and weighed 149 g. Grossly, a 6.2 × 5.8 × 4.5-cm well-circumscribed tan-yellow firm nodular mass was identified adjacent to the splenic capsule (Figure 85). Microscopic examination revealed the presence of a mixture of fibroblast-like spindle cells, small lymphocytes, plasma cells, histiocytes, nonnecrotizing granulomata, and a central area of necrosis with occasional neutrophils (Figure). Immunostaining for CD20 and CD3 showed scattered B and T lymphocytes. CISH for k(15) revealed polyclonal plasma cells. The spindle cells were positive for desmin, muscle-specific actin, CD68, CD31, and S100, and negative for CD34, CD1a, CD21, CD23, and ALK. Ki-67 was positive in approximately 30% of the cells. A reticulin stain showed a disorganized vascular bed.
pattern. EBER was positive in many tumor cells (Figure) but completely negative in the normal splenic parenchyma. To our knowledge, the identification of Epstein-Barr virus in IPTS with idiopathic thrombocytopenia purpura has not been previously described. The exact relationship between IPTS and idiopathic thrombocytopenia purpura and the role of Epstein-Barr virus in its development are yet to be investigated.

Multicentric HHV–8–Positive Castleman Disease and Kaposi Sarcoma as the Presenting Sign of Undiagnosed HIV Infection

(Poster No. 113)

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Multicentric Castleman disease (MCD) is a rare lymphoproliferative disorder associated with human herpesvirus 8 (HHV-8) and human immunodeficiency virus (HIV). In comparison to the benign, localized lymphoid hyperplasia first described by Castleman in 1956, HHV–8–associated MCD is characterized by multifocal involvement and severe constitutional symptoms. In addition, HIV-positive patients with MCD frequently develop Kaposi sarcoma (KS) during the course of their disease. We report a case of concurrent MCD and KS in a 59-year-old man, presented with fever, weight loss, cervical lymphadenopathy, anemia, and thrombocytopenia. Imaging studies showed abdominal, pelvic, and mediastinal lymphadenopathy and splenomegaly, causing clinical concern for lymphoma. Lymph node biopsy showed features suggestive of the plasma cell variant of Castleman disease, and a focal, subtle atypical vascular proliferation concerning for Kaposi sarcoma (Figure 86). Based on these findings, testing for HIV and HHV-8 was recommended. Dual infection by HIV and HHV-8 was confirmed, with viral loads of 108,000 and 603,000 copies/mL, respectively. Immunohistochemical staining for HHV8 was positive in the atypical vascular proliferations (Figure) and in scattered lymphoid cells. A diagnosis of HIV infection presenting with multicentric Castleman disease and Kaposi sarcoma was made. This case stresses the importance of considering MCD in the differential diagnosis for patients with B symptoms and lymphadenopathy. Careful assessment for subtle evidence of Kaposi sarcoma in lymph nodes showing features of MCD should also be performed, even in patients without a known history of HIV.

Hypercalcemia in a Case of Classical Hodgkin Lymphoma With Abundant Histiocytes

(Poster No. 114)

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Hypercalcemia is rare in Hodgkin lymphoma, with only a few cases reported in the medical literature. Herein, we report the case of a 78-year-old woman who presented with nonspecific gastrointestinal symptoms, dehydration, and weakness and was found to have a renal calculus and diffuse lymphadenopathy on imaging studies. Laboratory testing revealed hypercalcemia (12.0 mg/dL; reference range [RR], 8.5–10.5 mg/dL), normal phosphorus (2.9 mg/dL; RR, 2.5–4.9 mg/dL), normal parathyroid hormone (15 pg/mL; RR, 14–72 pg/mL), normal parathyroid hormone-related protein (<3 pmol/L; RR, 0.0–4 pmol/L), elevated vitamin D (122 ng/mL; RR, 30–80 ng/mL) and acute renal failure (BUN 33 mg/dL; RR, 6–24 mg/dL; creatinine 1.4 mg/dL; RR 0.6–1.3 mg/dL). Microscopic examination of an axillary lymph node biopsy revealed effacement of the lymph node architecture by a diffuse infiltrate rich in histiocytes (Figure 87) with confluent nonnecrotizing granulomata, small lymphocytes, plasma cells, neutrophils, fibroblasts, and scattered Hodgkin cells (including Reed-Sternberg cells and other Hodgkin cell variants; Figure). By immunohistochemistry, the Hodgkin cells were positive for PAX-5 (weak), CD15, and CD30 and negative for CD20 and CD45. The morphologic and immunohistochemical findings supported the diagnosis of mixed cellularity classical Hodgkin lymphoma. Several mechanisms of hypercalcemia of malignancy have been described. In this case, we hypothesize that the pathogenesis of hypercalcemia may have involved the conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D by the 1-a-hydroxylase expressed in the histiocytes, in a fashion similar to that described in sarcoidosis. Therefore, the association of classical Hodgkin lymphoma with abundant histiocytes and hypercalcemia may warrant future investigation.

C–MYC Expression in Diffuse Large B-Cell Lymphoma and Its Prognostic Significance: Single-Institution Experience

(Poster No. 115)

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Context: Diffuse large B-cell lymphoma (DLBCL) is the most common aggressive lymphoid malignancy. Patients with DLBCL have markedly different treatment outcomes, suggesting a need for reliable prognostic factors. C–MYC is an oncoprotein implicated in pathogenesis of a variety of lymphomas. In this study we evaluated C–MYC expression detected by in-house immunohistochemistry (IHC) technique as a prognostic marker in DLBCL.

Design: A tissue microarray, containing 79 cases of DLBCL diagnosed between 1999 and 2008, was analyzed by IHC for C–MYC (ab 32072; Abcam, Massachusetts). C–MYC overexpression was defined as strong staining of >30% of lymphoma cells. The results of staining were correlated with overall survival, IPI score, and DLBCL subtype (germinal center versus nongerminal center as per Hahn algorithm), and Ki67 expression. χ2 test was used to analyze the results.

Results: C–MYC was expressed in 16 of 79 cases (60.1%) and 26 cases (33%) showed its overexpression. C–MYC expression did not correlate with overall survival, IPI, or DLBCL subtype (P = .58, P = .97, P = .94, respectively). Moreover, there was no correlation between C–MYC overexpression and overall survival when groups with and without rituximab in the therapeutic regime were analyzed separately (P = .68, P = .21, respectively). Interestingly, there was correlation between Ki-67 and C–MYC overexpression (P < .001). Combined Ki-67 and C–MYC overexpression did not carry prognostic significance (P = .78).

Conclusions: Although C–MYC is an important player in the pathogenesis of lymphomas, the results of our study are in concert with...
other reports demonstrating that C-MYC overexpression assessed by IHC does not carry prognostic significance in DLBCL.

**Epstein-Barr Virus–Associated Atypical B-Cell Lymphoproliferation in Adult T-Cell Lymphoma/Leukemia: A Diagnostic Dilemma**  
(Poster No. 116)

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Atypical small to medium-sized CD4 node biopsy with immunohistochemistry confirmation, which showed gene rearrangement study. This prompted review of the original lymph loss of CD7. Monoclonality was confirmed by T-cell receptor (TCR) revealed an abnormal T-cell population, small to medium in size, with presented with recurrent disease. Restaging bone marrow biopsy was negative for involvement. Complete remission was rendered initially. Bone

**Disease: A Case Report of an Unusual Tumor With Review of the Literature**  
(Poster No. 118)

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Castleman disease is an uncommon form of lymph node hyperplasia. It commonly involves the mediastinum but can also involve extrathoracic sites, including the neck, axilla, pelvis, and retroperitoneum.

The stroma-rich variant of Castleman disease of the hyaline-vascular type (CDHV) is a rare entity that shows overgrowth of a variety of stromal cells in the expanded interfollicular area. We report here a case of a 20-year-old woman who presented with nausea, vomiting, and a syncopal event. An ultrasound revealed a 5.6-cm right retroperitoneal mass. An excisional biopsy showed a lobulated lymph node architecture effaced by sheets of spindled and ovoid cells forming fascicles in a storiform pattern. At the periphery and interspersed between the spindled cells were residual lymphoid follicles with regressive changes and multi-germinal center pattern. Sclerotic vessels with hyaline walls radially penetrate the germinal centers, reminiscent of the features of hyaline-vascular Castleman disease. The interfollicular spindle cells were positive for smooth muscle actin, and they were negative for CD21, CD34, CD117, CD163, ALK-1, HHV-8, and S-100 proteins. This case was diagnosed as a stromal-rich variant of Castleman disease. This is a rare entity that shows overgrowth of stromal cells in the widened interfollicular area. Clinically, it usually presents as an asymptomatic, solitary nodule that predominantly develops in the retroperitoneum. This stromal-rich lesion is typically hyperplastic and clinically benign, and it must be distinguished from neoplastic stromal proliferation such as follicular dendritic cell tumor or vascular neoplasm associated with Castleman disease because of its potential for recurrence and metastasis (Figure 88).

A Case of Pediatric Interfollicular Hodgkin Lymphoma  
(Poster No. 119)

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In addition to representing a rare variant of Hodgkin lymphoma, interfollicular Hodgkin lymphoma displays subtle histologic findings, which may closely resemble follicular hyperplasia. Herein, we describe an illustrative case demonstrating interfollicular Hodgkin lymphoma as well as benign follicular hyperplasia in a 6-year-old girl. The patient presented to the university otolaryngology department complaining of painless swelling of the right posterior cervical chain. Previously, local practitioners had placed the patient on antibiotics without improvement. A complete blood count was unremarkable. Imaging revealed bilateral multilevel cervical lymphadenopathy. A right level 5 cervical lymph node was removed, which demonstrated preserved nodal architecture with expansion of the interfollicular zones by epithelioid histiocytes and eosinophils. Within these zones, Reed-Sternberg cells were seen (Figure 89) as highlighted by CD15 and CD30 immunostains. While dimly positive in the Reed-Sternberg cells, PAX-5 was strongly positive in the follicular and interfollicular B-cells. This case was diagnosed as interfollicular Hodgkin lymphoma, and the patient was started on chemotherapy. After 4 cycles of chemotherapy, positron emission
tomography scan and computed tomography showed persistent lymphadenopathy and hypermetabolic activity. A right cervical lymph node excision again displayed preserved architecture with expansion of the interfollicular zones. However, no Reed-Sternberg cells or variants were seen, as confirmed by the absence of CD15, CD30, and PAX-5 expression. The reactive follicular and interfollicular hyperplasia depicted the second lymph node excision without involvement by Hodgkin lymphoma. We also challenged pancreatic insulin expression of the case.

Conjunctival Myeloid Sarcoma as an Initial Presentation of Relapsed Chronic Myelogenous Leukemia

(Poster No. 120)

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Myeloid sarcoma is an exceedingly rare presentation of neoplastic immature myeloid cells. The conjunctival myeloid sarcoma is exceedingly rare with only a few cases reported in the literature. We report a case of conjunctival myeloid sarcoma as the initial presentation of relapsed chronic myelogenous leukemia (CML). A 36-year-old man presented with a left eye lesion that was first noticed 3 months ago. His past medical history was significant for CML that was initially diagnosed 11 years ago and treated with imatinib since then. He was compliant with his drug therapy. The biopsy of the eye lesion revealed a diffuse proliferation of immature mononuclear cells with dispersed nuclear chromatin and prominent nucleoli. Immunohistochemistry, the atypical cells expressed CD34, CD117, CD79a (weak, focal), CD79a (weak, focal), and CD45 (variable), and were equivocal for CD34. They were negative for myeloperoxidase, muramidase, Tdt, CD3, CD10, CD20, CD99, pancytokeratin, and S-100. A limited panel by flow cytometric analysis revealed approximately 15% CD34-positive blasts. The combined morphologic and phenotypic findings were consistent with myeloid sarcoma. The subsequent bone marrow aspirate smears revealed normocellular marrow with 28% myeloid blasts with the same immunophenotype. The peripheral blood showed mild thrombocytopenia with no circulating blasts. The diagnosis of acute myeloid leukemia was rendered. Skin biopsies from the shins revealed leukemia cutis. Myeloid sarcomas most commonly involve periboneal structures, lymph nodes, soft tissues, and skin. This case highlights the need to be aware that myeloid sarcomas can occur anywhere in patients with CML or other myeloid neoplasms.

Acute Myeloid Leukemia With Mutated NPM1 With Morphologic and Immunophenotypic Features Mimicking Acute Promyelocytic Leukemia (APL)

(Poster No. 121)

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NPM1 mutation occurs in about one-third of adult acute myeloid leukemias (AML). AML with mutated NPM1 frequently shows myelomonocytic or monocytic features, presents in adults with normal cytogenetics, and in the absence of a FLT3-ITD mutation has good response to induction chemotherapy and favorable prognosis. We report an unusual case of AML with mutated NPM1 composed of promyelocytes by morphology and immunophenotypic features for either PML-RARA or other RARA gene rearrangement, with an aggressive clinical course and death from severe coagulopathy. A 66-year-old woman presented with fatigue, fever, rapid onset anemia, leukocytosis, and thrombocytopenia. A bone marrow biopsy showed 80% promyelocytes. Flow cytometry demonstrated predominantly immature granulocytic precursors at promyelocyte stage (CD10-, CD11b-, CD13+, CD16-, CD15+, CD33+, CD34-, CD117 partial, and HLA-DR-). However, FISH analysis utilizing a PML-RARA dual-color, dual-fusion probe and a RARA gene rearrangement probe and PCR for PML/RARA fusion transcript were negative. A MDS FISH panel was negative. Culture of leukemic cells revealed a normal female karyotype. The specimen was positive for NPM1 gene mutation and negative for FLT3-ITD mutation. The patient was initially treated with ATRA based on a presumptive diagnosis of APL. There was no overt clinical or hematologic response. Induction chemotherapy (7 + 3) was started 3 days after ATRA treatment. The patient responded with improved white cell count. Unfortunately, she died from persistent DIC 13 days later. To our knowledge, this is the first case of AML with NPM1 mutation presenting with severe coagulopathy and promyelocytic morphology and immunophenotype mimicking APL.

Anaplastic Lymphoma Kinase–Positive Diffuse Large B-Cell Lymphoma Presenting as a Subglottic Mass: A Challenging Diagnosis in the Head and Neck

(Poster No. 122)

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Anaplastic lymphoma kinase (ALK)–positive diffuse large B-cell lymphoma (DLBCL) is an extremely rare lymphoma representing less than 1% of DLBCL. Approximately 50 cases have been reported in the literature. ALK-positive DLBCL primarily involves the lymph nodes and typically presents as a mediastinal mass. Extranodal involvement of the head and neck is extremely rare, with a few reported cases in the nasopharynx and the tongue. Here we report a case of ALK-positive DLBCL presenting as an intraluminal laryngeal mass. The patient is a 60-year-old white man with a rapidly enlarging subglottic mass. Biopsy of the lesion was performed that showed a proliferation of large lymphocytes with abundant cytoplasm and a plasmablastic/immunoblastic morphology. Immunostains showed the malignant cells to be diffusely positive for CD45, CD138, CD10, MUM-1, and EMA. In addition, ALK-1 exhibited the classic strong granular cytoplasmic staining pattern. In situ hybridization essays revealed a λ light-chain restriction. EBER was negative. The cells were negative for CD30, CD15, CD20, CD56, myeloperoxidase, bcl-2, and PAX-5. CD3 stained reactive background T cells only. Ki-67 fraction was 80%. In addition, Lu-5 (cytokeratin) and S100 were negative. In the head and neck and oral cavity, where plasmablastic lymphoma is more common, a tumor with plasmablastic differentiation should be tested for ALK-1 and in situ hybridization tests should be performed to rule out the presence of EBV in order to avoid misdiagnosis of ALK-negative DLBCL as plasmablastic lymphoma.

A Composite Lymphoma Case of Diffuse Large B-Cell Lymphoma (DLBCL) and Mantle Cell Lymphoma (MCL)

(Poster No. 123)

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The patient is a previously healthy 67-year-old man who presented with fatigue, weight loss and leukocytosis. A computed tomography scan showed diffuse lymphadenopathy and an inguinal lymph node biopsy was subsequently obtained. The lymph node architecture was completely effaced by 2 components. The first component, comprising 70% of the lymph node, was a diffuse lymphoid infiltrate of large, pleomorphic cells with prominent nucleoli, suggestive of diffuse large B-cell lymphoma (DLBCL). These cells were positive by immunohistochemistry for CD20, BCL-2, and MUM-1 and negative for CD10, BCL6, and cyclin D1. The other 30% of the lymph node was composed of a distinct population of atypical, small-medium cells that stained positively for CD20, CD5, cyclin D1, and Sox 11, which raised the question of a concurrent mantle cell lymphoma (MCL). Fluorescent in situ hybridization confirmed an IGH/CCND1 fusion, indicating the classic t(11;14)(q13;q32) of MCL in this separate focus, but not in the focus of DLBCL. The patient was diagnosed with composite lymphoma and eventually underwent chemotherapy with remission by PET/CT imaging and is currently planning autologous stem cell transplant. Composite lymphomas (CL) are rare, comprising <1% of all lymphomas. The number of cases with MCL as a component is even more limited, with only 2 previously described cases of MCL and DLBCL. Our case highlights the importance of using multiple modalities to diagnose rare entities like CL because treatment is usually targeted to the more aggressive component of the CL and may be related to overall patient prognosis.
Marginal zone lymphoma (MZL) is a mature B-cell neoplasm composed of malignant cells resembling marginal zone lymphocytes. MZL, regardless of type (extranodal, splenic, or nodal), is considered indolent undergoing occasional transformation into diffuse large cell lymphoma. We discuss a case of MZL with an unusually aggressive clinical behavior. A 53-year-old man presented to a different institution with leukopenia, microcytic anemia, and leukoerythroblastosis. Bone marrow aspirate and biopsy demonstrated a subclone of small-to-medium-sized B cells with monocytoid appearance, which were positive for CD20, PAx5, Bcl-2, MUM1, and Ki-67 (20%) and negative for CD5, CD10, CD23, Bcl-1, CD43, TRAP, and annexin A1. The diagnosis of MZL was made and the patient underwent chemotherapy. The patient relapsed after the success of chemotherapy, was supported with bone marrow biopsy. One year later, multiple skin lesions were noted although they were not biopsied. One month subsequently, radiologic imaging showed progressive disease involving right iliac bone extending into the paraspinal muscles and the lung. The patient was admitted to our institution with a pathologic fracture of the femur. The fracture site, skin lesions, and bone marrow showed lymphomatous infiltrate similar in morphology and immunophenotype to previously diagnosed neoplasm, including Ki-67 positivity of 20% of cells. FISH, not previously performed, demonstrated a gain of chromosome 18/18q BCL2 region. RICE therapy showed an appropriate response and will be followed by stem cell transplant. This case of MZL demonstrates a particularly aggressive biology of what by morphology, immunophenotype, and proliferation index was expected to be an indolent lymphoma.

Primary Cutaneous CD4-Positive Small/Medium T-Cell Lymphoma With an Associated Clonal B-Cell Proliferation

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The concomitant presence of a clonal B-cell lymphoid proliferation and a cutaneous T-cell lymphoma is highly unusual. A 52-year-old man presented with a singular 1.5 × 1.2-cm pink, non-tender nodule on the left parietal scalp region. There were no other skin lesions, lymphadenopathy, or B symptoms. The skin biopsy had a dense nodular and diffuse proliferation of predominantly small to medium-sized lymphoid cells extending throughout the dermis and adjacent subcutaneous fat, without epidermotropism. By immunohistochemistry, there was a predominant CD3+, CD5+, bcl2- T-lymphoid population, in their large majority CD4+, admixed with a smaller subset of scattered CD8+ T cells. There was also a large CD20+ B-lymphoid population, coexpressing bcl2 and negative for CD10, CD5, bcl, and cyclin D1. The proliferation rate reached 40%–50%. Molecular studies detected the presence of T-cell receptor beta and gamma rearrangements and immunoglobulin heavy-chain gene rearrangements. A diagnosis of primary cutaneous CD4-positive small/medium T-cell lymphoma with an associated clonal B-cell proliferation was rendered. A computed tomography scan did not detect lymphadenopathy or hepatosplenomegaly. The patient underwent radiation therapy and remains free of disease 6 months after diagnosis. Clonal B-lymphoid populations have been previously reported in association with peripheral T-cell lymphomas, but only in association with cutaneous T-cell lymphomas. This case illustrates how the presence of numerous B cells can complicate the diagnosis of a T-cell lymphoma and may potentially lead to misdiagnosis if clonality is not assessed in both T- and B-cell lines.

Two Occurrences of Acute Lymphoblastic Leukemia With Concurrent Diffuse Bone Marrow Reticulin Fibrosis in Adults

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Acute lymphoblastic leukemia (ALL) with concurrent diffuse bone marrow reticulin fibrosis is rare. Most of the studies with this association are done in children. Studies in adults are limited because of very low occurrence, small sample size, and technical difficulties due to dry tap. Hence it remains difficult to determine the prognostic significance of this association in adults. We report 2 additional occurrences to support further studies on the prognostic significance of

An Exon 13 JAK2 (G571S) Mutation Resulting in Erythrocytosis

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The V617F mutation in exon 14 of JAK2 is seen in 95% of polycythaemia vera patients, with exon 12 mutations in approximately 4% of the patients. We report a 49-year-old woman with persistently elevated hemoglobin level (16.8 g/dL), and normal white blood cell and platelet counts. Her bone marrow was normocellular (50%) with trilineage hematopoiesis (myeloid to erythroid ratio = 3:2:1). There was no dysplasia in the myeloid or erythroid series. Megakaryocytes were normal in number with no clustering. Although rare hypolobated megakaryocytes were present, most of the megakaryocytes displayed normal morphology. Molecular testing (RT-PCR amplification followed by sequencing) of exons 12 and 14 of JAK2 detected a mutation. We report 2 additional cases of the V617F mutation and exon 12 mutations were not detected. The patient’s hemoglobin level has been controlled through monthly phlebotomies.

Transformation From Acute Myeloid Leukemia With Maturation to Pure Erythroid Leukemia

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Relapsing acute myeloid leukemia (AML) typically retains the same phenotypes. We describe a case of AML with maturation relapsing to pure erythroid leukemia. A 67-year-old man was initially diagnosed with AML with maturation. Bone marrow aspirate at diagnosis showed 50% myeloblasts with typical myeloblast morphology. The blast population was positive for CD34, CD13, CD33 (dim), CD117, CD38, and HLA-DR on flow cytometry, and negative for CD4, CD14, CD64, CD11b, CD15, MPO, CD11b, and all T-cell markers. The cytogenetics study was normal on the original bone marrow aspirate. The patient initially achieved remission after induction chemotherapy but developed leukemia relapse 13 months later. The relapsing leukemia cells showed similar morphology and immunophenotypic features to the initial diagnostic cells. The patient was subsequently placed on 2 courses of chemotherapy. A JAK2 G571S mutation was detected 13 months after diagnosis and 13 months after the patient presented with many blasts in peripheral blood. Bone marrow aspirate revealed markedly increased erythropoiesis composed mostly of early normoblasts (73%), many with basophilic and vacuolated cytoplasm. Immunophenotyping of these blasts showed positive for CD71 and negative for all T-cell markers, B-cell markers, CD13, CD33, CD34, CD64, MPO, CD117, glycoprophrin A, and TdT. Immunohistochemistry studies showed positive staining for PAS and glycoporphrin A (30%–40%), scattered positive staining for CD117 and MPO, and negative staining for CD34. Cytogenetics study revealed a tetrasomy 8 clone. The results are consistent with pure erythroleukemia, which supported clonal evolution. To the best of our knowledge, this is the first report of clonal conversion from AML with maturation to pure erythroid leukemia.

Marginal Zone Lymphoma: Aggressive Behavior of a Normally Indolent Neoplasm

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Excellent Response to Bendamustine-Rituximab Therapy in the First Reported Case of Adolescent Extramedullary Marginal Zone Lymphoma With γ Heavy Chain Disease (γHCD)

(Br. No. 130)

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Extramedullary marginal zone lymphoma (EMZL) is an extremely rare diagnosis in children. Most cases are localized with excellent prognosis. Advanced stage EMZL in adults is considered incurable, although prolonged remission may occur after multi-agent chemotherapy. γHCD is a rare disease of adults with no comparable reports nor consensus recommendations for therapy in children. We report the first pediatric case of advanced-stage EMZL and γHCD who presented with a 3-month history of weight loss and respiratory compromise secondary to enlarged tonsils and adenoids. Positron emission tomography–computed tomography scans revealed extensive disease in the head/neck region, mediastinum, lungs, and inguinal region. Tonsils and salivary gland demonstrated morphologic and immunophenotypic features of EMZL. Immunohistochemistry identified a subset of plasma cells and plasmacytoid lymphocytes expressing IgG heavy chain and lacking light-chain expression. Serum protein immunofixation study identified an aberrant IgG band. Gene rearrangement studies were negative. Bone marrow was not involved. The rare association of advanced stage EMZL and γHCD and the paucity of data in young patients make it impossible to predict the ultimate prognosis for this patient and raise the question of need for prolonged maintenance therapy. The combination of bendamustine and rituximab is an excellent option for treatment of patients with advanced disease EMZL. It is imperative to further delineate treatment protocols for diseases that are more common and/or have poor prognoses in the adult population but may be amenable to treatment in the pediatric patient.

Angiomyomatous Hamartomas of Multiple Lymph Nodes, Clinically Concerning for Malignancy: Clinicopathologic Correlation and Review of the Literature

(Br. No. 131)

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Angiomyomatous hamartoma of the lymph node is characterized by a benign vascular and smooth muscle proliferation with unknown etiology. Angiomyomatous hamartoma was first described by Chan et al in 1992 and to date there are only 31 reported cases. We describe a 63-year-old man who presented with fever and left leg edema. Blood work revealed pancytopenia, and a positron emission tomography scan was performed that showed 2 hypermetabolic lymph nodes, one in the left inguinal region and the second in the left deltoid region, both concerning for malignancy. The patient ultimately expired because of sepsis, and an autopsy was performed. Grossly, both lymph nodes showed leukocytosis (38.5 x 10^3/L) and severe thrombocytopenia (7 x 10^3/L) with absolute lymphocytes (33.9 x 10^3/L) and severe thrombocytopenia (7 x 10^3/L). Peripheral blood showed 75% blasts. Subsequent bone marrow biopsy showed markedly hypercellular marrow (80%) with B-cell ALL (90% blasts) and moderate to marked diffuse reticulin fibrosis. Blast population expressed CD19, CD20, and CD10. Genetics were positive for Bcr-Abl. Both cases were treated with standard ALL chemotherapy (hyper-CVAD) and subsequent bone marrow biopsies showed suppression of marrow reticulin fibrosis with remission of ALL (Figure).
measured 3.0 × 2.0 × 1.0 cm and had a gray-tan cut surface. Histologically, the parenchyma was mostly replaced by fibrous tissue with an extensive vascular proliferation, spindle cell bundles, and multiple small foci of adipocytes (Figure 91, A). Immunohistochemical analysis showed strong desmin and smooth muscle actin positivity in the spindle cells, confirming they were smooth muscle fibers (Figure, B, C). Also, CD34 highlighted the extensive vascular proliferation (Figure, D) and HMB-45 was negative, ruling out angiomylipoma. Although angiomatousomatous hamartoma of a lymph node is a rare entity, it is important to be recognized by both clinicians and pathologist as benign lesions that may mimic malignancy. To the best of our knowledge this is the first case of angiomatousomatous hamartoma affecting more than 1 lymph node and the first case to involve a lymph node in an upper extremity.

**Burkitt Lymphoma in a 67-Year-Old Man With a History of HIV**

(Poster No. 132)

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We report here a case of Burkitt lymphoma in a 67-year-old man with a history of HIV. The patient presented with worsening body pains involving the head, neck, shoulders, trunk, and legs. His HIV was stable on antiretroviral therapy. He also had a history of splenectomy from a motor vehicle accident years ago. No significant family history of cancer was seen. His blood test showed anemia, thrombocytopenia, and elevated abnormal lymphocytes. Bone marrow biopsy exhibited sheetlike monotonous intermediate-sized atypical lymphocytes with a starry-sky pattern. Frequent mitoses and apoptosis were identified with tingible body macrophages throughout. Immunohistochemical staining of these tumor cells was positive for CD3, CD10, CD19, CD20, CD22, and CD34. The Ki-67 proliferation index was 99% proliferation rate. Negative were EBV, TdT, BCL-2, CD3, CD34, c-KIT, and cyclin D1. Flow cytometry detected a monoclonal B-cell population with a diffuse proliferation of large atypical cells. The tumor cells were positive for CD20, bcl-2, and bcl-2, and negative for CD3, CD5, TdT, and CD30. The Ki-67 proliferation index was 80%–90%. Flow cytometry showed a population of large cells expressing CD10, CD19, CD20, CD22, and CD34, without coexpression of surface immunoglobulin, CD34, and CD15. Cytogenetics showed a near-tetraploid karyotype with 1 X chromosome attached with material of unknown chromosomal origin at the q28 band region. losses of chromosome 1, 4, and 6, and t(13;14)(q13;q32), the latter confirmed by fluorescent in situ hybridization (FISH). Furthermore, FISH has confirmed the disruption of IGHG1 and FOXO1 (Figure 92): but no RBl disruption was found. FOXO1 is a transcription factor that may act as a tumor suppressor. Misregulation/ mutations of FOXO1 have been implicated in multiple cancers, including rhabdomyosarcoma, breast and colon cancers, multiple myeloma, B-CLL, CML, Hodgkin lymphoma, and a few cases of DLBCL; however, disruption of FOXO1 due to t(13;14) has not been reported in DLBCL. To our knowledge, this is the first report of t(13;14) involving FOXO1 in DLBCL.

**Nodular Lymphocyte Predominant Hodgkin Lymphoma With Late Bone Marrow Involvement; Recurrent Versus Transformed Lymphoma**

(Poster No. 133)

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Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) represents approximately 5% of all Hodgkin lymphomas. It is more frequent between the ages of 30 and 50. Extranodal involvement is very rare, with the exception of splenic disease (10%–15%). Transformation to large B-cell lymphoma (LBCL) has been reported in 3%–5% of the patients. Here we present a case of a 61-year-old man who came to our facility with a right axillary mass in 2009. The diagnosis of NLPHL was made on a lymph node biopsy. In 2011, a follow-up bone marrow biopsy revealed replacement of the normal hematopoietic elements by nodular sheets of lymphocytes, with a monotonous intermediate-sized atypical lymphocytes with a starry-sky pattern. Frequent mitoses and apoptosis were identified with tingible body macrophages throughout. Immunohistochemical staining of these tumor cells was positive for CD3, CD10, CD19, CD20, CD22, and CD34. The Ki-67 proliferation index was 80%–90%. Flow cytometry detected a monoclonal B-cell population with a diffuse proliferation of large atypical cells. The tumor cells were positive for CD20, bcl-2, and bcl-2, and negative for CD3, CD5, TdT, and CD30. The Ki-67 proliferation index was 80%–90%. Flow cytometry showed a population of large cells expressing CD10, CD19, CD20, CD22, and CD34, without coexpression of surface immunoglobulin, CD34, and CD15. Cytogenetics showed a near-tetraploid karyotype with 1 X chromosome attached with material of unknown chromosomal origin at the q28 band region. losses of chromosome 1, 4, and 6, and t(13;14)(q13;q32), the latter confirmed by fluorescent in situ hybridization (FISH). Furthermore, FISH has confirmed the disruption of IGHG1 and FOXO1 (Figure 92): but no RBl disruption was found. FOXO1 is a transcription factor that may act as a tumor suppressor. Misregulation/ mutations of FOXO1 have been implicated in multiple cancers, including rhabdomyosarcoma, breast and colon cancers, multiple myeloma, B-CLL, CML, Hodgkin lymphoma, and a few cases of DLBCL; however, disruption of FOXO1 due to t(13;14) has not been reported in DLBCL. To our knowledge, this is the first report of t(13;14) involving FOXO1 in DLBCL.

**Myeloid Antigen Expression in Lymphoid Blasts Does Not Impact Prognosis in Acute Lymphoblastic Leukemia**

(Poster No. 135)

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Context: In acute lymphoblastic leukemia (ALL), the proliferating lymphoblastic cells occasionally express myeloid antigens. The prognostic significance of myeloid antigen expression remains controversial.

Design: To better understand the role of myeloid antigens in the prognosis of ALL, we reviewed flow cytometry results and clinical data in ALL patients from 1995 to 2012. B-lineage and T-lineage ALL cases were included. ALLs were classified into 2 groups: with or without aberrant myeloid antigen expression, in which myeloid expression was defined for one or more of the myeloid markers (CD13, CD33, and CD117). Survival rates were compared in these 2 groups by Kaplan-Meier analysis.

Results: Aberrant myeloid antigens were expressed in 40 of 207 ALL patients (19.3%). The most frequent myeloid antigen in the lymphoid blasts was CD33 (13.5%), followed by CD13 (10.1%) and CD117 (1.9%). Based on the availability of outcome data, a total of 177 ALL patients were included in the survival analysis (F: 47.5%, M: 52.5%, age 0 to 82 years). B-ALL patients (n = 141) with and without myeloid antigen expression had no significant difference in overall survival. Similarly in the T-ALL patients (n = 36), there was no significant difference in overall survival between these 2 groups. Moreover, there was no association of relapse or disease persistence of ALL with myeloid antigen expression (Figure 93).

Conclusions: Expression of myeloid markers does not represent adverse prognosis in ALL patients. This finding suggests that myeloid-surface antigen expression can be excluded from the strategic considerations in ALL treatment planning.

A Rare Case of CD15-Expressing Nodular Lymphocyte Predominant Hodgkin Lymphoma

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Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) can be diagnosed by its characteristic morphologic and immunophenotypic features; however, variation in these features can make diagnosis of NLPHL difficult. We report a case of NLPHL with classical morphologic features and rare aberrant expression of CD15. The patient was a 42-year-old man presenting with progressive weakness, muscle wasting, and weight loss. Computed tomography revealed mesenteric and right axillary lymphadenopathy. An excision of the axillary lymph node revealed nodular effacement by predominantly small lymphocytes (that are predominantly B lymphocytes) with clustering of large pleomorphic, multi-lobulated lymphoma cells. These lymphoma cells were positive for CD45, CD20, PAX5, BCL6, OCT2, BOB.1, and CD15 (focal), but negative for CD30 and EMA (Figure 94). Epstein-Barr virus (EBER) in situ hybridization was negative. The lack of CD30 and EBER-encoded RNA coupled with the strong expression of B-cell markers excludes the diagnosis of classical Hodgkin lymphoma. CD15 expressing NLPHL has not been previously described by the World Health Organization; however, few cases have been reported in the literature. We emphasize the importance of recognizing this subset of CD15+ NLPHL because it could present as a diagnostic challenge, mimicking classic Hodgkin lymphoma.

Vision-Threatening Ocular Extramedullary Hematopoiesis in a Patient With a Myeloproliferative Neoplasm

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Extramedullary hematopoiesis (EMH) associated with myeloproliferative neoplasms (MPNs) usually involves the spleen, liver, and lymph nodes. Other sites of involvement are rare. Few cases of intraocular choroidal EMH have been reported in adults at autopsy or via enucleation. To our knowledge, we present the first case of intraocular choroidal EMH diagnosed by cytology. A 57-year-old man with chronic narrow angle glaucoma presented with acute angle-closure glaucoma. His history was significant for 1 year’s duration of JAK2 V617F-positive MPN, weight loss, hepatosplenomegaly, and inguinal lymph node EMH. Initial treatment of his acute glaucoma included laser peripheral iridotomy and steroids. The patient was then transferred to our facility, where ophthalmologic evaluation revealed bilateral elevated intraocular pressures, retinal detachments, and choroidal infiltrates. Immediate surgical intervention included pars plana vitrectomy and radial sclerotomy drainage. Choroidal effusion cytology revealed a neutrophilic infiltrate including immature forms and erythroid precursors. Rather than a reactive inflammatory process, these findings were most consistent with neoplastic EMH representing extension of this patient’s MPN. Subsequent cerebrospinal fluid analysis also showed a heterogenous myeloid population including eosinophils, basophils, and immature granulocyte forms including metamyelocytes and myelocytes. Bone marrow findings were consistent with myelofibrosis without increased blasts. Treatment included intrathecal methotrexate and prednisone. Sequential cerebrospinal fluid studies were negative and imaging demonstrated reduction of choroidal infiltrates. The patient was discharged in good condition. This exceptional case demonstrates the importance of ophthalmology and pathology in the multidisciplinary treatment of an emergent, sight-threatening EMH.

Mantle Cell Lymphoma After 10 Years’ History of Chronic Lymphocytic Leukemia: A Possible Intralineage Conversion in Small B-Cell Lymphoma

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A 50-year-old man presented with 3-year history of lymphocytosis and lymphadenopathy. Blood smear showed marked leukocytosis with absolute lymphocytosis. Bone marrow biopsy exhibited a diffuse, interstitial infiltration of small lymphocytes that were negative for cyclin D1 by immunohistochemistry. Flow cytometry revealed 65% λ light-
Primary Unilateral Testicular Diffuse Large B-Cell Lymphoma in a 3-Year-Old Boy

(Poster No. 139)

Kritsanapal Boon-Unge, MD (kboonunge@chla.usc.edu); Sheng-ming Zhou, MD; Paul Pattengale, MD; Meizhou Zhou, MD; Yves DeClerck, MD; Paul H. McCarthy, MD. 1 (kboonunge@chla.usc.edu); Sheng-ming Zhou, MD; Paul Pattengale, MD. 2 (kboonunge@chla.usc.edu); Sheng-ming Zhou, MD; Paul Pattengale, MD. 3 (kboonunge@chla.usc.edu); Sheng-ming Zhou, MD; Paul Pattengale, MD. 4 (kboonunge@chla.usc.edu)

Primary pediatric testicular diffuse large B-cell lymphoma (DLBCL) is extremely rare, with only 6 cases reported in literature. A 3-year-old boy with a history of mental delay associated with autism spectrum disorders and 6 weeks after a left hydrocele repair presented with a slightly enlarged left testicle. Incisional biopsy showed testicular tissue that was extensively infiltrated by a lymphomatous process with a diffuse growth pattern. The atypical cells were large with round nuclei, nuclear clefiting, vesicular chromatin, one to several prominent nucleoli, and moderate amounts of eosinophilic cytoplasm. Scattered small lymphocytes and histiocytes were seen. Mitoses were brisk (2–3/high-power field). Several vague nodules were present, suggesting colonization of preexistent germinal centers. Seminiferous tubules were intact and showed no evidence of lymphomatous infiltration. The atypical cells expressed CD20, CD45, CD79a, PAX-5, BCL-6, C-MYC (less than 40%), and Ki67 (70%) and were negative for CD3, CD5, CD15, CD30, BCL-2, CD10, MUM-1, Tdt, ALK, MYC, myeloperoxidase, marmaduke, AE1/AE3, PLAP, and EMA. CD21 immunohistochemistry highlighted disrupted colonized follicular dendritic cell networks. B-cell gene rearrangement study revealed a clonality of the immunoglobulin heavy-chain gene on chromosome 14. Systemic workup was negative for lymphoma. The final diagnosis was primary testicular DLBCL, germinal center immunophenotype, Murphy stage 1, group B (unresected). The patient was treated with rituximab and chemotherapy. Six months after treatment, left orchiectomy was performed and there was no evidence of residual tumor. Though primary pediatric testicular DLBCL is a very rare entity, it should be in the differential diagnosis of testicular mass.

Transformation of Follicular Lymphoma to Acute Lymphoblastic Leukemia With Novel Genetic Mutations

(Poster No. 140)

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Transformation from follicular lymphoma to B lymphoblastic leukemia/lymphoma is rare. While the specific roles of genetic mutations are yet to be elucidated, MYC/BCL-2 involvement in mature B-cell lymphoma is well documented, but ML1 rearrangement has only rarely been described. Cellular imaging on a 46-year-old man with a history of grade 2, λ restricted follicular lymphoma treated with 6 cycles of rituximab and bendamustine. Fifteen months after diagnosis he presented to the emergency department with epistaxis and excessive bleeding after teeth extraction. At presentation, the patient had the following blood counts: WBC 12,000/µL, hemoglobin 9.3 g/dL, and platelets 6000/µL. A marrow biopsy revealed diffuse involvement by acute B-cell lymphoblastic leukemia with the following immunophenotype: 63% blasts that expressed dim CD45, HLA-DR, CD38, dim CD19, CD10, dim CD22, CD79a, and cytoplasmic λ light-chain restriction. The cells were negative for CD34 and CD20. Immunohistochemical staining showed dim TdT expression. Cytogenetics revealed a complex, abnormal karyotype. Fluorescence in situ hybridization revealed rearrangement of MYC (77% of cells), a 14;18 translocation (74% of cells), and a rearrangement of the ALL, gene (74% of cells). The patient was treated with 3 cycles of hyper-CVAD, including 7 intrathecal methotrexate treatments. After 4.5 months, the patient is alive with plans for an allogeneic stem cell transplant. In a review of the literature, no published cases with both a “double-hit” BCL-2/MYC profile and a concurrent MLL gene rearrangement were found.

Hodgkin and Reed-Sternberg and Hodgkin- and Reed-Sternberg-Like Cells in Hodgkin Lymphoma, Non-Hodgkin Lymphoma, Reactive Lymphadenitis, and 2 Cases of Hodgkin Lymphoma, Small/Syncytiot Cell Variant

(Poster No. 141)

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Hodgkin lymphoma is characterized by scattered Hodgkin and Reed-Sternberg (HRS) cells in a background of mixed inflammatory cells. HRS cells are large mononucleated or multinucleated cells that typically express CD15, CD30, PAX5, and MUM1. The presence of HRS cells is not limited to Hodgkin lymphoma. Cells with similar morphology to HRS cells, called HRS-like cells, can be seen in CLL and lymphadenitis. On the other hand, Hodgkin lymphoma may present with HRS variants.

Design: We compared the morphology and IHC phenotype of HRS cells in Hodgkin lymphoma and HRS-like cells in CLL and lymphadenitis (Table).

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<th>IHC Phenotypes of HRS, Small Variant HRS, and HRS-Like Cells</th>
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Results: Similar to HRS cells, HRS-like cells were positive for CD15, CD30, MUM1, and PAX5 and were negative for CD20 and CD45. HRS-like cells express additional markers representing the disorders where they reside, such as CD5, CD23 in CLL. HRS-like cells can be positive for markers that HRS cells don’t express, such as BOB.1 and OCT-2. We also examined 2 cases of relapsed Hodgkin lymphoma with atypical HRS cells, which were medium-sized immunoblast-like (Figure 95); positive for CD30, MUM-1, CD15 (partial), and PAX5; negative for CD20, CD45, CD68, CD3, ALK-1, BOB.1, OCT-2, and with variable EBER expression. Thus, we propose there might be a small/syncytiot cell variant of Hodgkin lymphoma that has not been reported before.

Conclusions: The presence of HRS cells is not specific for Hodgkin lymphoma. HRS-like cells can be identified in other lymphoma and lymphadenitis. In addition, classical Hodgkin lymphoma may have a variant featuring small/syncytiot cells.
The Utility of \textit{BRAF} V600E Mutation-Specific Antibody VE1 for the Diagnosis of Hairy Cell Leukemia

(Poster No. 142)

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\textbf{Context:} \textit{BRAF} V600E mutation is a highly studied recurrent genetic abnormality present in essentially all cases of hairy cell leukemia (HCL) and is rare or absent in other indolent B-cell neoplasms. The aim of this study was to verify the utility of VE1 antibody in a cohort of HCL and its mimics in a North American sampling.

\textbf{Design:} We selected 89 cases of mature B-cell neoplasms; of these, 86 cases were formalin-fixed paraffin-embedded decalcified bone marrow core biopsies. The remaining 3 cases were lymph node/spleen. Immunohistochemistry was performed using the anti-\textit{BRAF} V600E (VE1) mouse monoclonal primary antibody (Ventana Medical Systems, Inc, Tucson, Arizona). \textit{BRAF} V600E mutation analysis was performed on selected HCL cases (Cobas 4800 BRAF V600 Mutation Test; Roche, Basel, Switzerland).

\textbf{Results:} \textit{BRAF} V600E expression was detected in 15 of 17 cases (88%) of HCL and 2 of 20 cases (10%) of CLL/SLL, and was not detected in the remainder of the mature B-cell neoplasms. The 2 negative cases of HCL were positive for \textit{BRAF} V600E mutations. The 2 positive CLL/SLL cases showed an atypical pattern with expression only in a minority of lymphoma cells, representing possibly reactive rather than neoplastic elements. The overall sensitivity of VE1 antibody in this HCL cohort is 88% and the overall specificity 97%.

\textbf{Conclusions:} Based on this selected series of cases, we conclude that with a sensitivity of 88% and specificity of 97%, immunohistochemistry using the VE1 antibody is a useful and convenient method for detecting \textit{BRAF} V600E in bone marrow biopsy specimens.

Primary Small Intestinal Hodgkin Lymphoma

(Poster No. 143)

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Primary gastrointestinal lymphomas are very rare and account for 1%-4% of all gastrointestinal tumors. The gastrointestinal tract, with an incidence of 0.5%, is rarely the primary site for Hodgkin lymphoma. Because of the rarity of Hodgkin lymphoma in this location, strict criteria for the diagnosis are used. We report a case of a 62-year-old man who presented with intermittent abdominal pain, nausea, and vomiting for 8 months’ duration. A computed tomography scan showed a 4.8-cm single jejunal mass and multiple pulmonary lesions, which were radiologically suspicious for metastatic disease. A small-bowel resection was performed and revealed a 5.0 × 4.0 × 1.5-cm tan-white, firm, obstructive mass within the jejunum. Microscopically, the bowel mucosa was ulcerated and showed a transmural infiltration by a mixed population of cells including lymphocytes, plasma cells, histiocytes, neutrophils, eosinophils, and malignant tumor cells suggestive of Reed-Sternberg cells. Immunohistochemistry showed that the malignant cells were positive for CD15 and CD30 and negative for CD3, CD20, and CD45, confirming that cells were in fact Reed-Sternberg cells. Based on histomorphology and immunohistochemistry, the diagnosis of Hodgkin lymphoma was established; however, the diagnosis of primary Hodgkin lymphoma is inferred because a single mass within the jejunum with multiple masses within the lungs was present on computed tomography scan at initial presentation. Although rare, Hodgkin lymphoma of the gastrointestinal tract has a good response to therapy and favorable prognosis in many cases (Figure 96).

BCR-ABL1–Negative Atypical Chronic Myeloid Leukemia With t(13;14)(q14;q24) and Progression to Myeloid Sarcoma

(Poster No. 144)

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Atypical chronic myeloid leukemia (aCML) is a rare chronic myeloproliferative/myelodysplastic neoplasm lacking BCR-ABL1 fusion gene and characterized in the World Health Organization 2008 classification by leukocytosis and dysgranulopoiesis, with or without dysplasia of erythroid and megakaryocytic lineages. A 27-year-old asymptomatic man presented with leukocytosis ([123.4 ± 10^9]/L) and neutrophilia (65%) with 1% immature neutrophil precursors and 1% blasts, subset of hypersegmented neutrophils, monosomy (2%), eosinophilia (8%), and basophilia (2%), with mild anemia (hemoglobin 12.5 g/dL), and with an adequate number of platelets (220 × 10^9/L). The hypercellular bone marrow had 0.6% blasts, neutrophilic hyperplasia (66.2%), eosinophilia (18.4%), and monocytosis (3.4%); mild dyserythropoiesis (<6% of erythroid precursors); and a subset of dysplastic megakaryocytes. The karyotype showed 46,XY,t(13;14)(q14;q24)(20)/46,XY(2), while FISH studies were negative BCR-ABL1 fusion, PDGFRα,
PDGFRB, FGFR3, CBFB, and del 13q14.3. Molecular studies were negative for JAK2V617 mutation and also negative for BCR-ABL1 fusion. The patient was treated with hydroxyurea and his CBC indices returned to reference ranges. After 13 months he developed lymphadenopathy and had 15-pound weight loss, and an enlarged 6 × 4 × 2.5-cm right groin lymph node showed myeloid sarcoma. His peripheral blood was remarkable for leukocytosis (73 × 10^9/L) and anemia (hemoglobin 11.1 g/dL) and the bone marrow aspirate had 10.4% blasts, neutrophilic hyperplasia (66.2%), eosinophilia (11.6%), monocytes (6.8%), and dysmegakaryopoiesis. The karyotype analysis showed 46,XY,t(13;14)(q14;q24)(20). While karyotypic abnormalities in BCR-ABL1-negative aCML have been reported, and its presence suggests a more aggressive clinical course.

Primary cardiac tumors are rare, with more than 90% being benign. Cardiac myxomas represent 84% of all cardiac tumors. While secondary involvement by disseminated lymphoma is fairly common, primary cardiac lymphoma accounts for roughly 2% of all primary cardiac neoplasms and <1% of extranodal lymphomas. We report the case of a 50-year-old man with chest pain. Echocardiography revealed an atrial mass. The specimen was a pedunculated, 7-cm, brown, gelatinous mass. Histologically, it showed the typical appearance of a cardiac myxoma and displayed positivity for calretinin, CD34, and S-100. However, the periphery of the lesion was composed of large, highly atypical lymphoid cells with abundant mitosis (Figure, B) that were positive for CD20 (Figure, C), CD30, BCL-2, and MUM-1 while negative for CD10, BCL-6, and ALK and demonstrated a high level of Ki-67 expression. The diagnosis of Epstein-Barr virus–positive diffuse large B-cell lymphoma arising within an atrial myxoma was made. Staging studies revealed no evidence of lymphoma elsewhere, indicating this to be a true primary cardiac lymphoma. Recently, it has been proposed that primary cardiac Epstein-Barr virus–positive diffuse large B-cell lymphoma of the immunocompetent patient is a distinct type of primary cardiac lymphoma arising in association with an underlying local pathologic process that generates an altered immune microenvironment conducive to lymphoma development. As evident in recent case reports, primary cardiac Epstein-Barr virus–positive diffuse large B-cell lymphoma appears to have an indolent clinical course; therefore, its recognition may be significant for therapeutic decisions and prognosis.

A Case of Primary Cardiac Epstein-Barr Virus–Positive Diffuse Large B-Cell Lymphoma Arising Within a Left Atrial Myxoma in an Immunocompetent Patient

(Poster No. 145)

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Primary cardiac tumors are rare, with more than 90% being benign. Cardiac myxomas represent 84% of all cardiac tumors. While secondary involvement by disseminated lymphoma is fairly common, primary cardiac lymphoma accounts for roughly 2% of all primary cardiac neoplasms and <1% of extranodal lymphomas. We report the case of a 50-year-old man with chest pain. Echocardiography revealed an atrial mass. The specimen was a pedunculated, 7 × 3-cm, brown, gelatinous mass (Figure 97, A). Microscopically, it showed the typical appearance of a cardiac myxoma and displayed positivity for calretinin, CD34, and S-100. However, the periphery of the lesion was composed of large, highly atypical lymphoid cells with abundant mitosis (Figure, B) that were positive for CD20 (Figure, C), CD30, BCL-2, and MUM-1 while negative for CD10, BCL-6, and ALK and demonstrated a high level of Ki-67 expression. The diagnosis of Epstein-Barr virus–positive diffuse large B-cell lymphoma arising within an atrial myxoma was made. Staging studies revealed no evidence of lymphoma elsewhere, indicating this to be a true primary cardiac lymphoma. Recently, it has been proposed that primary cardiac Epstein-Barr virus–positive diffuse large B-cell lymphoma of the immunocompetent patient is a distinct type of primary cardiac lymphoma arising in association with an underlying local pathologic process that generates an altered immune microenvironment conducive to lymphoma development. As evident in recent case reports, primary cardiac Epstein-Barr virus–positive diffuse large B-cell lymphoma appears to have an indolent clinical course; therefore, its recognition may be significant for therapeutic decisions and prognosis.

Therapy-Related T/Myeloid Mixed-Phenotype Acute Leukemia Following R-CHOP Chemotherapy for Primary Cutaneous Diffuse Large B-Cell Lymphoma

(Poster No. 146)

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Mixed-phenotype acute leukemia is a rare entity that accounts for 2%–5% of all acute leukemias. Therapy-related mixed-phenotype acute leukemia is an exceedingly rare hematologic neoplasm that accounts for less than 1% of acute leukemias. These leukemias are associated with alkylating agents and topoisomerase II inhibitors and have a poor prognosis. We describe a case of therapy-related mixed-phenotype acute leukemia following chemotherapy for primary cutaneous diffuse large B-cell lymphoma. The patient is a 63-year-old woman who presented with several large cutaneous nodules consistent with primary cutaneous lymphoma. Staging revealed no bone marrow involvement or extracutaneous involvement at the time of diagnosis. The patient was treated with systemic chemotherapy. She was in remission for 4 years when she presented with dyspnea, night sweats, weakness, and diffuse lymphadenopathy. Her presentation was initially concerning for recurrent lymphoma; however, flow cytometry of the peripheral blood revealed 10% CD34+ blasts suspicious for acute leukemia. A bone marrow biopsy and aspirate were performed, with flow cytometry showing 20% CD34+ blasts showing coexpression of CD117, bright CD7, cytoplasmic CD3, and myeloperoxidase (Figure 98, D). The bone marrow biopsy was hypercellular at 80%–90% and showed sheets of blasts (Figure, A). There was no evidence of her cutaneous B-cell lymphoma. Immunostaining of the bone marrow showed the tumor cells positive for CD34, CD117, CD3 (Figure, C), CD7, myeloperoxidase (Figure, B) and TdT and negative for CD5, CD20, and CD79a. Cytogenetics showed an abnormal 46,XX,t(8;12)(q22,p13) karyotype and normal AML/MDS FISH panels. Mutational analyses for NPM1 and FLT3 were negative.

Natural Killer–Cell Enteropathy: An Indolent Mimic of T-Cell Lymphoma

(Poster No. 147)

Amelia Fierro-Fine, MD (amelia-fierrofine@ouhsc.edu); Sarah Lindley, MD; Teresa Krauss, MD. Department of Pathology, University of Oklahoma, Oklahoma City.

A recently described benign entity, natural killer (NK)–cell enteropathy is significant for the risk of misdiagnosis as extranodal NK/T-cell lymphoma, peripheral T-cell lymphoma, or enteropathy-
associated T-cell lymphoma (type II) with subsequent overtreatment. We report a case of NK-cell enteropathy initially misdiagnosed as a peripheral T-cell lymphoma. A 55-year-old woman presented for routine screening colonoscopy, and was found to have a 7-mm, sessile rectal polyp. Biopsy showed a fairly well-circumscribed, submucosal population of large, atypical lymphoid cells with irregular nuclear contours, occasional prominent nuclei, and a moderate amount of clear cytoplasm, admixed with small lymphocytes and eosinophils (Figure 99). Immunohistochemical staining showed the atypical cells to be positive for CD2, cCD3, CD7, CD56, and CD45, with focal faint staining for CD8, and negative for CD4, CD5, CD20, CD30, CD68, CD1a, and S100. In situ hybridization for Epstein-Barr virus was also negative. A diagnosis of peripheral T-cell lymphoma was suspected, and the patient was referred to our hospital for treatment and bone marrow transplant evaluation. Staging workup, including a positron emission tomography scan and bone marrow biopsy, showed no evidence of disease. The overall clinical features, morphology, and immunophenotype were found to be compatible with NK-cell enteropathy. A colonoscopy 5 months later showed a single tubular adenoma; random biopsies revealed no atypical lymphoid infiltrates. NK-cell enteropathy is a rare and recently described, apparently benign lesion. Awareness of this lesion is essential to prevent misdiagnosis and unnecessary, potentially harmful therapies.

A Novel GATA-1 Mutation in a Neonate With Transient Myeloproliferative Disorder Without Down Syndrome

(Poster No. 148)

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Transient myeloproliferative disorder (TMD) occurs as a rare disorder in newborns with Down syndrome, mosaic trisomy 21, and occasionally in phenotypically normal infants. In addition to the association with trisomy 21, TMD is also associated with mutations in the GATA-1 gene. Subsequent to the resolution of TMD in 50% of patients will develop myeloid leukemia. We report a case of TMD with a novel mutation in the GATA-1 gene. A male neonate was found to have leukocytosis (52.9 × 10^9/L) with 50% myeloid blast forms. Fluorescence in situ hybridization on peripheral blood showed trisomy 21 restricted to the blast forms. He did not have constitutional trisomy 21, based on multiple constitutional cytogenetic studies and examination by clinical genetics. Sequencing studies performed on DNA isolated from a peripheral blood sample showed a frameshift mutation in the GATA-1 gene (c.148_149delCC) with predicted premature termination (p.Ser51ArgfsStop87). A diagnosis of transient myeloproliferative disorder spectrum with acute myeloid leukemia was made. The patient was treated with cytarabine and follow-up blood counts showed resolution of leukocytosis and a blast count of less than 0.5% at 1 month of age. At 6 months, the bone marrow showed 1% of cells with trisomy 21 by fluorescence in situ hybridization. The specimen was negative for the GATA-1 gene mutation. Follow-up at 2 years after diagnosis showed normal blood counts and no evidence of TMD. As previously reported, the trisomy 21 was confined to the blast cells, which harbored the novel mutation.

Minor B-Cell Clone Detected at Diagnosis of Chronic Myelogenous Leukemia Bcr-abl1 Positive—Herald of Imminent Accelerated Phase and Commitment to Blastic Transformation?

(Poster No. 149)

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Chronic myelogenous leukemia (CML), BCR-ABL1 positive, has a reported incidence of 3% of leukemias in the pediatric and adolescent population, with the majority of the patients presenting in chronic phase (CML-CP). Five percent of the patients present in accelerated phase or blast crisis. A 17-year-old male patient with a history of weight loss and fatigue developed priapism. He had leukocytosis (402.3 × 10^9/L), neutrophilia with shift towards immaturity and 2% blasts, monosomy, eosinophilia, and basophilia. The hypercellular aspirate had myeloid hyperplasia and 3% blasts. In the biopsy section were identified 10% PAX5+ and 5%–10% TdT+ and CD34+ nucleated cells. A minor clonal B-lymphoid population was detected by PCR and the karyotype showed t(9;22)(q34.1;q11.2)(20). He was treated with Gleevec, and a year later developed an accelerated phase, with a 46,X,Y(9;22)(q34;q11.1)(1)/46, idem, +21, +der(22)(9;22)(2)/46XY(17) karyotype and 16% bone marrow blasts. Five months later he developed blast crisis with 83.2% blasts in the aspirate, coexpressing CD79a, CD10, CD4, partial CD19, CD45, TdT, and CD34 and being negative for CD13, CD33, and cytoplasmic myeloperoxidase. Molecular studies detected a clonal B-lymphoid population with a band similar in size to the one detected in the diagnostic bone marrow. After induction chemotherapy (DF-05-001) and after reaching morphologic remission he underwent bone marrow transplantation. The unusual features of this case suggest that the clone responsible for blast phase may be present at the diagnosis of CML-CP, and may be missed if clonality is not assessed and the assumption of a population of hematogones is made.

Evolving Myelodysplastic Syndrome: A Potential Cause of Erythropoietin Resistance in Hypoproliferative Anemia of Chronic Renal Disease

(Poster No. 150)

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Myelodysplastic syndrome (MDS) with isolated del(5q) is characterized by anemia with or without slight thrombocytosis and isolated cytogenetic abnormality del(5q)(q13q33). Hypoproliferative anemia of chronic kidney disease (HACKD) is due to reduced production of erythropoietin by the kidney. Recombinant human erythropoietin (EPO) is standard of care for treatment of HACKD. We report 2 patients with HACKD who had received EPO for more than 12 months with initial optimal response. Gradually their baseline hemoglobin began to decline along with increasing MCV. We received specimens for MDS evaluation (peripheral blood smear, bone marrow aspirate, and biopsy with specimen for chromosomal analysis) on both patients. The blood smears showed macrocytic anemia with normal leukocyte and platelet counts. Their aspirate smears showed unremarkable erythroid and granulocytic maturation
and less than 5% blasts. The megakaryocytes were slightly increased with occasional hypolobate forms. The biopsies were normocellular and reflected the aspirate findings. Cyogenetic analyses showed del(5)(q31q33) in at least 2 cells. A diagnosis of “MDS with isolated del(5q)” was rendered in both patients. Based on this diagnosis, lenalidomide was added to EPO. Both patients with HACKD showed an excellent response with improvement in their baseline hemoglobin with normalization of MCV. In conclusion, declining hemoglobin with macrocytosis should raise the possibility of MDS in HACKD patients showing suboptimal response to EPO. An MDS evaluation as above should be performed. If a readily treatable MDS such as MDS with del(5q) is identified addition of a drug like lenalidomide may help reinstate response to EPO.

Mediastinal Lymph Nodes With Mesothelial Inclusions Mimicking Metastatic Carcinoma

(Poster No. 151)
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A 27-year-old previously healthy woman presented with a 2-month history of dyspnea at rest, peripheral edema, and chest palpitations. Upon hospital admission she developed superior vena cava thrombosis, recurrent bilateral chylothorax, and pericardial effusions, undergoing thoracic duct ligation and bilateral pleurodesis with no significant improvement. Radiologic workup revealed only enlarged level VII mediastinal lymph nodes, which were subsequently biopsied with a frozen section diagnosis of atypical cells of undetermined significance and permanent sections showing a nest of atypical nonhematolymphoid cells with a sinusoidal pattern of infiltration (Figure 100, A) and immunohistochemical phenotype characteristic of mesothelial cells: cytokeratin AE1/AE3 (Figure, B), cytokeratin 7, cytokeratin 5–6, calretinin (Figure, C), D2-40 (Figure, D), and mesothelin positive and CDX-2, CD20, CD34, CD31, and CD68 negative. A final diagnosis of benign mesothelial inclusions to lymph node was rendered. Patients with these types of processes have been reported in the literature as having a poor prognosis, especially ones with associated chylothorax and severe pleural or pericardial effusions. The majority of these patients have a coexistent malignancy, usually hematomylphoid, or an infectious process in the mediastinum. Although our patient has continued to develop recurrent pleural and pericardial effusions, no underlying malignancy or severe infection has been identified. Surgical pathologists should be aware of the presence of benign mesothelial cells within lymph nodes as an uncommon and underrecognized phenomenon, specifically at the time of frozen section, to avoid a misdiagnosis of metastatic carcinoma or mesothelioma.

A Unique Case of a Myelodysplastic/Myeloproliferative Neoplasm With Distinct Histiocytic and Dendritic Outgrowths

(Poster No. 152)
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Erdheim-Chester disease (ECD) and Langerhans cell histiocytosis (LCH) are rare histiocytic disorders. There are a limited number of case reports of patients with ECD in association with LCH. We report a case of a 61-year-old woman who presented with a trunk rash of several months duration, A skin biopsy showed a dermal infiltrate of histiocytic cells positive for CD68, S100, and CD1a, supporting the diagnosis of LCH (Figure 101, A). Several months later, she was hospitalized for hypernatremia due to diabetes insipidus, anemia, thrombocytopenia, and leukocytosis. A bone marrow biopsy showed a myeloid hyperplasia without definite dysplasia and large, atypical histiocytes showing erythropagocytosis and neutrophil emperipolysis (Figure, B). These histiocytes were positive for CD68 and negative for S100 and CD1a. The peripheral blood showed neutrophilia with hypogranular and hypersegmented forms and an absolute monocytes with immaturity, but no increase in blasts. An abdominal computed tomography showed soft tissue infiltration surrounding the aorta and kidneys. The patient’s history of diabetes insipidus, the radiographic findings of the aorta and kidneys, and morphologic findings of the bone marrow led to a diagnosis of ECD with evidence of an underlying myelodysplastic/myeloproliferative neoplasm. A subsequent duodenal biopsy revealed an infiltration of the submucosa by atypical histiocytes positive for CD68 and S100 but negative for CD1a (Figure, C). The patient expired within 1 month after diagnosis of ECD. We presented here a unique case of a patient with multisystem involvement by 3 different histiocytic proliferations with distinct morphologies and immunophenotypes and evidence of an underlying myeloproliferative/myelodysplastic neoplasm.

Performance of Published Algorithms in the Classification of Specimen Types for Coagulation Testing

(Poster No. 153)
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Context: Plasma is often separated from cells and transferred into transport tubes for coagulation testing. In this process, certainty about the specimen type is lost. A reference laboratory may generate spurious results unless it can identify inappropriate specimens. Published algorithms use calcium, sodium, and potassium (algorithm 1) or sodium and potassium (algorithm 2) to classify specimens as citrate plasma or other type.

Design: Calcium, sodium, and potassium were measured on 129 sodium citrate specimens and 43 EDTA specimens after completion of coagulation or hematology testing in Intermountain Central Laboratory. Tests results were obtained from a data warehouse for 4903 lithium heparin specimens and 10 096 serum specimens submitted for chemistry testing. Specimen types were classified by algorithms 1 and 2, and classifications were compared against actual specimen types.

Results: Both algorithms correctly classified all EDTA specimens as noncitrate plasma. Algorithm 1 correctly classified 100.0% of citrate specimens, 42.4% of lithium heparin specimens, and 97.9% of serum
specimens. Algorithm 2 correctly classified 99.8% of lithium heparin specimens and 100.0% of serum specimens, but only 3.1% of citrate specimens. Figure 102 shows the proportion of each specimen type classified as citrate plasma by each algorithm.

![Specimens Classified as Citrate Plasma](image)

Conclusions: Neither algorithm simultaneously classifies all specimen types correctly. Algorithm 1 lacks specificity, classifying a majority of lithium heparin specimens as citrate plasma. Algorithm 2 lacks sensitivity, placing most citrate specimens into the lithium heparin/serum category. Alternative algorithms must be developed to use chemistry values in the identification of inappropriate specimens for coagulation testing.

Privacy Protection in a National Red Blood Cell Antibody Registry

(Poster No. 154)

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Context: Patients are often seen at multiple hospitals. Undetectable red cell antibodies, population mobility, and limited information sharing increase the risk for hemolytic transfusion reactions. We developed an online HIPAA-compliant database of patient antibody histories allowing transfusion services to review records from other participating facilities. HIPAA privacy rules safeguard individuals' protected health information (PHI) while allowing the exchange of PHI for treatment purposes.

Design: To meet HIPAA’s “minimum necessary” standard, exported information is limited to patient demographics, positive antibody test results, transfusion history, and reactions. Accountability is ensured via detailed access logs, patient consent, RAAs, delineation of responsibilities, and liability protections for providers. The repository incorporates such HIPAA security measures as risk analysis, physical security, personnel policies, data encryption, and disaster recovery.

Results: Major health care systems’ privacy, legal, and risk management departments reviewed documentation and evidence of HIPAA compliance, and all approved their hospitals’ participation in the registry. Facilities reviewed patient consent forms and, except in states that require explicit notice of participation in EHRs, required no change to their consent processes. An independent IT security firm conducted penetration tests and verified that the repository complies with all of their recommended practices.

Conclusion: A nationwide antibody registry is permissible under HIPAA. A thorough and detailed approach to compliance has earned acceptance from health care providers. This paves the way for wider deployment to significantly improve patient care by reducing the risk of hemolytic transfusion reactions and by decreasing TAT and transfusion-associated costs.

Unusual Case of a Severe Hemolytic Transfusion Reaction Caused by Rh Incompatibility

(Poster No. 155)

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Transfusion of group O Rh+ red blood cells to Rh~ males is routinely utilized in emergency situations. Controversy exists over rates of alloimmunization, with reported rates of anti-D alloimmunization ranging from 0.6% to 8.6%, the greatest seen in healthy recipients and the lowest in immunosuppressed patients. Nonetheless, the development of a severe hemolytic transfusion reaction with intravascular hemolysis due to Rh incompatibility in this situation is rare and has seldom been reported. We report a case of a 69-year-old O Rh-negative man with no known serologic history who received an emergent massive transfusion of O–Rh+ units. The patient initially presented to a peripheral hospital with hematemesis and melena, hemoglobin of 9.7 g/dL, and INR 2.92. Within the first 5 days of admission he received 14 units of O Rh+ blood. He was subsequently referred to our hospital with hemoglobin of 7.4 g/dL and laboratory evidence of intravascular hemolysis (elevated LDH, indirect bilirubin, hemoglobinemia, and hemoglobinuria). Serologic investigations demonstrated jaundiced plasma, positive antibody screen, and a direct antiglobulin test for IgG and complement. Antibody panel and selective cell testing identified anti-D and anti-C alloantibodies in the plasma and the eluate. Anti-D titering revealed an IgM and IgG of 1:256 and >1:2048, respectively. Nonimmunologic causes of hemolysis had been clinically excluded. The severe hemolysis was attributed to the high-titer IgM and IgG anti-D and anti-C antibodies. Rh incompatibility in patients with multiple comorbidities may be severe; a high degree of suspicion should be maintained in such patients when transfusing Rh+ units.

Challenges in Providing Compatible Red Blood Cell Units for a Newborn With Life-Threatening Anemia and Hyperbilirubinemia Secondary to Antibody to U Antigen

(Poster No. 156)

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Anti-U is a rare red blood cell alloantibody found exclusively in African Americans lacking the high-frequency U antigen. It can cause hemolytic disease of fetus and newborn and hemolytic transfusion reactions. We report the case of an Rh-negative mother who presented for delivery with limited history of prenatal care. At birth, the baby’s hemoglobin was 4.9 g/dL and emergent transfusion with O Rh-negative blood was initiated, then aborted because of incompatibility. The baby typed as O Rh-positive with a positive direct antiglobulin test. A local reference laboratory reported the mother’s previous history as a Rh-negative with anti-D and anti-U following prior pregnancy and C-, E-, K-, P-+, S-, S~, U-negative phenotype. Current maternal sample revealed anti-U and anti-D with other alloantibodies ruled out. A local search for Rh-negative, U-negative units was unsuccessful. Intravascular immunoglobulin was infused. The decision was made to use mother as a source of D-, U-negative blood. The risk of incompatible ABO type was felt to be minimal in the neonate. The mother’s collected unit was leukoreduced, washed, irradiated, and aliquoted for the emergent transfusions. Despite a posttransfusion hemoglobin of 16.6, a rise of total bilirubin prompted importing a U−, D− unit for exchange transfusion. A second exchange was requested because of continued hyperbilirubinemia and a second unit from mother was obtained and prepared. The life-threatening anemia was resolved with maternal and compatible donor units, but the baby continued to have unexplained hyperbilirubinemia.
POSTER SESSION 300: TUESDAY, SEPTEMBER 09, 2014, 9:00 AM–12:15 PM

Autopsy and Forensic Pathology; Bone and Soft Tissue Pathology; Gynecologic and Placental Pathology; Head, Neck, and Oral Pathology; Cardiovascular Pathology

A Case of Unsuspected Hereditary Hemochromatosis and the Important Role of Autopsy

(Poster No. 1)

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Autopsy serves an important role in diagnosis and as a teaching tool for clinicians. The deceased was a 34-year-old man with history of heavy alcoholism (750 mL vodka per day) for the past 2 years. He presented to the emergency room because of fatigue, fever, and abdominal protrusion and pain. On physical examination generalized jaundice, bilateral pleural effusion, and ascites were identified. Serology was negative for HIV and hepatitis B and C. Radiology showed small liver and splenomegaly. The patient was admitted with diagnosis of alcohol-induced liver failure. Shortly after admission, he developed hepatic encephalopathy and quickly became unresponsive and coded. Autopsy confirmed clinical diagnosis of hereditary hemochromatosis.

Prussian blue iron staining revealed generalized iron deposition within heart, thyroid, skin, pancreas, testicle and pituitary (Figure, C and D). After further discussion with the family to exclude any secondary sources for the hemochromatosis, a quantitative liver iron study was done on paraffin-embedded liver tissue. This study demonstrated significant elevation of hepatic iron index at 9.8 μmol/g/y (normal <1.9 μmol/g/y). Given the absence of any secondary reason for hemochromatosis and hepatic iron index of >1.9 μmol/g/y, the diagnosis of hereditary hemochromatosis was confirmed, which was not the leading clinical diagnosis for his cirrhosis, and genetic counseling was done for the family. This case exemplifies the important role of autopsy in diagnosis, clinician education, and prognosis of surviving family members.

Death Due to Pulmonary Fat Embolism and Thromboembolism After Abdominal Surgery: An Unexpected Autopsy Finding

(Poster No. 3)

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A 72-year-old morbidly obese man with massive abdominal ventral hernia with small-bowel obstruction was transferred from an outside facility for treatment of small-bowel obstruction that did not resolve with conservative treatment. On the seventh day of hospitalization, after obtaining medical clearance, he underwent repair of the massive ventral hernia, subtotal colectomy, and pancreatectomy. After surgery, he was admitted to the surgical intensive care unit, where he began to clinically deteriorate, with hypoxia and hypotension requiring vaso-pressors. A computer tomography scan of the chest showed bilateral pulmonary emboli in the main pulmonary arteries with embolic extension into segmental arteries involving all lobes of both lungs. He continued to deteriorate and was placed on comfort care and died soon after obtaining medical clearance, he underwent repair of the massive ventral hernia, subtotal colectomy, and pancreatectomy. After surgery, he was admitted to the surgical intensive care unit, where he began to clinically deteriorate, with hypoxia and hypotension requiring vaso-pressors. A computer tomography scan of the chest showed bilateral pulmonary emboli in the main pulmonary arteries with embolic extension into segmental arteries involving all lobes of both lungs. He continued to deteriorate and was placed on comfort care and died soon after.

Autopsy and Forensic Pathology; Bone and Soft Tissue Pathology; Gynecologic and Placental Pathology; Head, Neck, and Oral Pathology; Cardiovascular Pathology

Rare Occurrence of Martinez-Frias/Mitchell-Riley Syndrome With Neonatal Hemochromatosis: A Second Reported Case

(Poster No. 2)

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Martinez-Frias Syndrome (MFS) is a rare, fatal, autosomal recessive disorder characterized by pancreatic hypoplasia, intestinal atresia, and gallbladder aplasia/hypoplasia, with or without tracheoesophageal fistula. A variant of this syndrome, Mitchell-Riley syndrome, has features of MFS with neonatal diabetes but without tracheoesophageal fistula. We report a 10-day-old female infant born at 39 weeks gestation with multiple congenital anomalies fulfilling the diagnostic criteria of MFS with neonatal hemochromatosis. To our knowledge, this association has been reported only once. Following vaginal delivery the infant was noted to be growth restricted and was transferred to the NICU for variable hypo-hyperglycemia control. Two days later she underwent repair of duodenal atresia and intestinal malrotation. She expired 10 days later from hypoxic-ischemic encephalopathy. At postmortem examination she demonstrated pallor, jaundice, small face and narrow chin, short nose with anteverted nares, down-slanting palpebral fissures, pancreatic hypoplasia with dispered islet cells (Figure 104, A), marked hepatic hemosiderosis (Figure, B), intestinal atresia, gallbladder aplasia, Meckel diverticulum, microcolon, and intestinal malrotation. Tracheoesophageal fistula was not identified. Whole genome microarray DNA analysis on peripheral blood detected a region of homozygosity at chromosomal band 1q15 to 1q22.33, containing the RFX6 gene, which has been associated with MFS. This gene has been found to affect the embryogenesis of anterior endodermal organs, pancreatic islets, and insulin production, with mutations causing small-bowel defects and neonatal diabetes, as seen in this case. Whether this gene is associated with neonatal hemochromatosis requires further study.
Case Report of a Rare Fatal Pulmonary Alveolar Proteinosis With Review of Literature
(Poster No. 4)
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Pulmonary alveolar proteinosis was first described by pathologists Rosen, Castlemain, and Liebow in the New England Journal of Medicine in 1958 as an accumulation of lipoproteinaceous material in the alveolar spaces with lack of fibrosis. This material was identified as surfactant by Larson and Gordinier in 1965. In recent years, approximately 240 case reports and a 410-case miniseries have been published in English literature. The disease is mainly considered an autoimmune process where inhibition of granulocyte-macrophage colony-stimulating factor (GM-CSF) by blocking autoantibodies results in the lack of surfactant clearance from the alveolar spaces. Pulmonary proteinosis can be secondary to diverse underlying disorders such as infections, hematologic malignancies, immunodeficiencies, or mutations in surfactant protein genes that lead to rare congenital disease presentations. Treatment mainly consists of repeated whole lung lavage or new GM-CSF therapies. Fatalities due to the pulmonary alveolar proteinaceous are even rarer. At the Wayne County Medical Examiner’s Office, we report a case of a 46-year-old woman who died of pulmonary alveolar proteinosis. Conversations with family members disclosed that she suffered from chronic respiratory issues since 2006 and had undergone multiple lung lavages, some of which resulted in respiratory difficulties. Salient findings at autopsy included heavy lungs with firm bilateral consolidation. Microscopic examination showed granular material filling the alveoli (Figure 105, A). Periodic acid-Schiff (PAS) stain showed increased staining in the larger aggregates (Figure, B). Special stains for microorganisms were negative.

Hunting for Immediate Cause of Death in a 75-Year-Old Man With Multiple Diseases
(Poster No. 5)
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It can be challenging to discern the immediate cause of death (COD) when a decedent has multiple coexisting severe diseases. Carefully checking the medical history and performing a full autopsy can avoid mistakenly overestimating contributing factors and missing the true COD. We report the autopsy of a 75-year-old man who died after 2 weeks of progressing confusion, difficulty walking, and delirium. Magnetic resonance imaging showed ischemic changes in the midbrain, basal ganglia, and periventricular and subcortical regions. He had just been discharged from a previous hospitalization for persistent hypertension. Prior history was notable for severe coronary artery disease, diabetes, hypertension, lung cancer status post pneumonectomy, and prostate cancer status post radiation therapy. The clinical findings strongly suggested cerebrovascular ischemia as the COD, but metastatic tumor could not be excluded. Initial autopsy findings confirmed severe coronary artery disease, with incidental findings of papillary thyroid carcinoma and papillary renal cell carcinoma, but no evidence of residual lung cancer or prostate cancer. Careful examination of the brain revealed several dusky areas in the left periventricular white matter and brainstem, as well as softening of the periaqueductal gray matter (Figure 106, A). Sections from those areas revealed large CD20+ atypical lymphocytes (Figure, B). Diagnosis of primary diffuse large B-cell CNS lymphoma was made and is considered to be the immediate COD. This case proved the necessity and importance of autopsy in decedents with multiple severe diseases because 3 malignant tumors, including the immediate COD, would have been missed without autopsy.

Intestinal Obstruction in an Infant due to Gastrointestinal Mucinous Hyperplasia Associated With Prostaglandin E2 Therapy
(Poster No. 6)
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Gastric antral and intestinal epithelial hyperplasia is known to occur with prostaglandin therapy. A florid hyperplasia causing intestinal obstruction has not been reported earlier, to the best of our knowledge. A 3-month-old male infant developed florid mucinous hyperplasia of the gastrointestinal tract that caused intestinal obstruction at 10 weeks of age. He had received prostaglandin-E2 since birth to keep the ductus arteriosus open because of pulmonary valve atresia. He underwent ileal resection with ileostomy and creation of mucous fistula for ileal perforation secondary to intestinal obstruction that resulted in 4 cm of bowel loss. He developed wound dehiscence of abdominal incision 10 days after the surgery, which required additional surgery. He was on ventilator support for 2 more weeks, after which life support measures were withdrawn. He received total parenteral nutrition throughout his life. At autopsy his intestines had mucinous and goblet cell hyperplasia, his stomach showed florid mucinous hyperplasia with cystic glandular dilation, and his appendix showed proliferation of mucinous glands with detached glands floating in a pool of mucin inside the appendiceal lumen. Pulmonary valve atresia, membranous ventricular septal defect, an aorta overriding interventricular septum, right ventricular hypertrophy, patent ductus arteriosus, diffusely hypoplastic pulmonary arteries, partially membrane protected patent foramen ovale, persistent left superior vena cava draining to coronary sinus, desquamative interstitial pneumonia, rudimentary/absent thymus, and asplenia were documented at autopsy. A peritoneal swab and aortic blood grew Stenotrophomonas maltophilia. This case is presented to highlight a rare life-threatening complication of lifesaving prostaglandin-E2 therapy. Surgeons should be aware of this rare possible complication.

A Unique Autopsy Case of Sudden Death in a Patient With Lipomatous Hypertrophy of the Interaltrial Septum and Mitral Valve Fibrotic Thickening Extending to the Conduction System Associated With Rhythm Disturbance
(Poster No. 7)
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Lipomatous hypertrophy of the interatrial septum (LHIS) is a rare cardiac tumor that can cause congestive heart failure, atrial fibrillation, supraventricular tachycardia, syncope and sudden cardiac death. This lesion has never been described in conjunction with mitral valve thickening and fusion of mitral valve chordae tendineae. We report a case of a 49-year-old woman with past medical history of bipolar disorder and systemic lupus erythematosus who presented for a surgical hernia repair. Two days after the uneventful procedure, she became delusional and agitated and there were concerns of a manic episode. She was
treated with olanzapine and haldol. Five days after surgery she suddenly collapsed, and after unsuccessful resuscitation efforts, she was pronounced dead. An autopsy was performed, using a modified Virchow approach. Significant gross anatomic findings included cardiomegaly, a $2.5 \times 2.2 \times 2.0$-cm unencapsulated mass confined to the interatrial septum, fused anterolateral papillary muscle, and a discrete focus of marked fibrosis of the adjacent endocardium extending to the mitral valve. Bilateral pulmonary congestion and edema were also noted. Microscopically, the mass was composed of mature adipose tissue consistent with LHIS. The mitral valve demonstrated moderate to marked fibrosis. Gross and histologic examination confirmed LHIS. However, the degree of mitral valve fibrosis extending to the conduction system was remarkable. Although more than 200 cases of LHIS have been reported, no previous case has been described in conjunction with a valvulopathy and endocardial fibrosis, which, in combination, likely led to this patient’s fatal arrhythmia.

Unique Adult Autopsy Case of Spontaneous Retroperitoneal Hemorrhage in a Patient With Hepatitis C Viral Infection

(Poster No. 8)

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We report a 68-year-old African American man with a past medical history significant for emphysema, hypertension, type II diabetes mellitus, and hepatitis C infection. The patient complained of worsening shortness of breath, chest pain, productive cough, and lower extremity edema. His symptoms began a few weeks prior to presentation and did not improve with the use of a nebulizer and prednisone. Admission examination revealed hypertension, tachycardia, tachypnea, diminished breath sounds, bilateral rhonchi, and bilateral pitting edema of the lower extremities. Laboratory examination revealed leukocytosis and mild hyperkalemia. After admission he complained of right leg pain and examination revealed abdominal ecchymosis followed by hypovolemic shock. Despite aggressive cardiopulmonary resuscitation, he expired. Autopsy findings directly related to his death included hepatic cirrhosis and a large right retroperitoneal hemorrhage measuring $21 \times 9 \times 9$ cm with extension into the proximal right lower extremity and adjacent pericolic adipose tissue. Hemorrhage was also identified within the right lower lobe of the lung with direct extension to the diaphragm. No bleeding site was identified despite thorough examination. This sudden, large hemorrhage explains the acute onset of hypovolemic shock prior to his death. Spontaneous retroperitoneal hemorrhage has been reported in association with anticoagulant therapy, cirrhosis, and trauma. Diagnosis of retroperitoneal hemorrhage is often difficult because of vague symptoms at presentation, especially in patients without a history of anticoagulant therapy or trauma. Cirrhosis has been implicated in some reports of spontaneous retroperitoneal hemorrhage. Delay in diagnosis can lead to significant morbidity and mortality (Figure 107).

Angiosarcoma Arising in an Abdominal Aortic Aneurysm After Endovascular Repair: A Case Report of Autopsy Findings and Literature Review

(Poster No. 9)

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Plastic polymers, including Dacron, have been found to induce sarcoma in 7% to 50% of exposures in animal studies. Although the same carcinogenic effect has not been found in humans, a small number of cases of sarcoma, a rare entity in the aorta, have been reported around previously placed vascular prostheses, raising the possibility of a carcinogenic effect. Herein, we present an autopsy case of an angiosarcoma arising in an abdominal aortic aneurysm (AAA) discovered at autopsy 4 years after aortic graft placement. The decedent was a 71-year-old man with a medical history of AAA status post endovascular repair 4 years prior and subsequent type IA and type II endoleak repair, who presented with a 2-week history of hematuria, flank pain, and a 75-80-lb weight loss. An angiogram revealed numerous perianeurysmal abnormal vessels, with possible connection to the right ureter, which were subsequently embolized. The patient continued to deteriorate with leukocytosis, coagulopathy, electrolyte abnormalities, and altered mental status, and expired 1 month after admission.

Encephalomyelitis Resulting From Chronic West Nile Virus Infection

(Poster No. 10)

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West Nile virus (WNV) is a mosquito-borne RNA flavivirus and human neuropathogen. The overall mortality rate for WNV disease is 2% to 7%. Most WNV-related mortality results from neurologic and respiratory complications. In patients with WNV encephalitis, the mortality rate ranges from 12% to 15%. In these patients, neuromuscular manifestations such as muscle weakness and respiratory failure are apparent manifestations predicting mortality. Peripheral axonal or demyelinating neuropathies such as Guillain-Barre syndrome (GBS) or encephalitis with poliomylitis-like syndrome have been reported in association with WNV infection. We report a fatal case of encephalomyelitis due to chronic WNV infection in a 21-year-old man who presented with muscle weakness progressing to ascending paralysis and respiratory distress requiring mechanical ventilatory support. He was diagnosed with acute motor axonal neuropathy, a GBS variant, and had a prolonged hospital course until he died 8 months after the onset of symptoms. Microscopic examination of the central nervous system samples collected during autopsy revealed meningoencephalomyelitis. Subsequent serologic testing revealed antibodies to WNV, and immunohistochemistry detected WNV antigens in neurons in multiple foci in the cerebrum, cerebellum, brainstem, and spinal cord. Myelitis and motor neuron degeneration in the spinal cord with subsequent atrophy in skeletal muscle were also observed. Our case exemplifies chronic WNV infection causing encephalomyelitis that manifested clinically as acute motor axonal peripheral neuropathy, WNV-associated encephalomyelitis along with peripheral neuropathy should be considered in a patient presenting with muscle weakness and paralysis.

Hepatic and Gastric Pathology Discovered at Autopsy in Neurofibromatosis Type 2

(Poster No. 11)

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Neurofibromatosis type 2 is a rare dominantly inherited cancer syndrome associated with multiple tumors of the nervous system, most commonly meningiomas and bilateral vestibular schwannomas, and uncommonly neurofibromas. We report a case of visceral involvement by neurofibromatosis type 2-related neoplasms identified at autopsy. The 20-year-old woman had presented with a 1-year history of unsteady gait and progressive hearing loss, and was found to have bilateral vestibular nerve root lesions and a large meningioma in the foramen magnum compressing the spinal cord. She died...
suddenly from intracranial hemorrhage approximately 1 week after staged resection of the foramen magnum meningioma. Autopsy identified additional meningiomas of the intracranial dura and spinal cord and schwannomas of multiple cranial and spinal nerve roots, including bilateral vestibular schwannomas. There were multiple cutaneous pleomorphic schwannomas. An unexpected finding was extensive irregular hepatic fibrosis with an unusual macroscopic growth pattern. A single submucosal pleomorphic schwannoma was present in the gastric fundus. To our knowledge, this hepatic and gastric pathology in neurofibromatosis type 2 has not been described in the literature (Figure 108).

Ehlers-Danlos With Periventricular Heterotopias (Type VIII): First Reported Autopsy Case Shows No Filaminopathy

(Poster No. 12)
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Ehlers-Danlos (ED) with periventricular heterotopias is a newly recognized form of ED disease, is X-linked, and is caused by a mutation in filamin A. Unlike other forms, a distinct central nervous system manifestation is associated with the condition. To date this has not been illustrated at autopsy, and specifically it is unknown if astrocytic filaminopathy inclusions occur. We report full autopsy findings on a 29-year-old man in whom this diagnosis was made postmortem. He had a history of multiple congenital heart malformations, requiring surgery at age 13 months. During childhood he suffered multiple gastrointestinal symptoms and rectal bleeds. Eight years before death he was clinically diagnosed with ED (abnormal scarring and hyperextensibility of lower extremities) in preparation for heart valve replacements. A skin biopsy showed normal collagen 3, ruling out ED type IV (vascular form). He eventually developed cardiomegaly, congestive heart failure, and pulmonary emboli and died despite aggressive medical therapy. Autopsy examination showed thin skin, severe cardiomegaly (800 g) with pulmonary hemorrhage, myoid degeneration of mitral and tricuspid valves, and abundant blood in stomach and small bowel. The brain showed bilateral frontal and pericentral region polygyria in a 6-layer on microscopy. Several small nodular periventricular heterotopias in the lateral ventricle were diagnostic for ED type VIII. Careful search showed no astrocytic inclusions of filamentopathies or small vessel abnormalities. We conclude that autopsy examination correctly identified the syndrome/genetic mutation in this patient.

A Fatal Gastrocardiac Fistula Following Esophagectomy With Gastric Pull-Through

(Poster No. 13)
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A 73-year-old man presented with hematemesis. He had a near-total esophagectomy and gastric pull-through for carcinoma 16 years prior. On admission, a bleeding source was not identified on esophagogastroduodenoscopy because of a large blood clot in the stomach. An abdominal aortogram showed no definitive evidence of an aortoenteric fistula and no active dye extravasation. Shortly after the aortogram procedure, the patient went into cardiac arrest and died approximately 36 hours after initial presentation. At autopsy, the gastric pull-through conduit was found to be adherent to the posterior surface of the pericardium; thus, during dissection it was preserved attached to the heart and pericardium and fixed en bloc in formalin. A 2.0 × 2.0-cm gastric ulcer was present in the body of the stomach. The ulcer base contained blood and necrotic material. A thrombus beneath the posterior mitral valve leaflet close to the interventricular septum was noted on dissecting the heart. Gentle probing confirmed a fistula communicating the gastric ulcer and left ventricular cavity through its posterior wall. Microscopic examination showed a benign peptic ulcer with chronic active inflammation and mixed inflammatory exudate in the interaction along the fistula. The superimposed mixed infection may be a contributory factor to fistula formation. There has been no report of successful treatment of a gastrocardiac fistula with the left ventricle and diagnosis of this rare variant of gastrocardiac fistula is primarily made at autopsy. This case serves to illustrate the continued utility of autopsy in the modern medical era.

A Rare Variant of Tracheoesophageal Fistula

(Poster No. 14)
Amanda K. Martin, MD, MPH (Amanda_Martin@urmc.rochester.edu); Philip J. Katzman, MD; Leon A. Metlay, MD. Department of Pathology and Laboratory Medicine, University of Rochester Medical Center, Rochester, New York.

Tracheoesophageal fistula is an abnormal communication between the esophagus and the trachea. Five types of tracheoesophageal fistula have been described in association with esophageal atresia, the most common of which is esophageal atresia with a distal tracheoesophageal fistula (84%). Here, we report a case of the rarest variant of tracheoesophageal fistula in a 35-week stillborn male infant. The mother, a 32-year-old gravida 2, para 1 Hispanic woman with past medical history significant for unspecified cardiac anomaly, immune thrombocytopenic purpura, and obesity, was followed closely throughout the pregnancy. Early ultrasounds revealed bilateral renal pyleactasis, hypoplastic nasal bone, and shortened femurs. Subsequent imaging studies revealed severe polyhydramnios and an absent stomach bubble. A fetal echocardiogram showed a structurally normal heart with a dilated coronary sinus, concerning for persistent left superior vena cava. Based on these findings along with a positive quad screen, the mother was offered amniocentesis, which was declined. At 35 weeks of gestation, the mother presented to our institution for induction of labor because of fetal death in utero diagnosed via ultrasound. During induction, the mother consented to amniocentesis. A stillborn male infant was delivered. Autopsy findings were significant for a fistulous connection between the trachea and the proximal portion of the esophagus along with a blind-ending distal esophageal stump. Cardiovascular anomalies were consistent with those identified on fetal echocardiogram. The remainder of both abdominal and thoracic examination was essentially normal. Approximately 1 week after the autopsy, the chromosomal analysis came back positive for trisomy 21.

Malignant Peritoneal Epithelioid Mesothelioma Diagnosed at Autopsy

(Poster No. 15)
Justus V. Philip, BS (justus.philip@rockets.utoledo.edu). Department of Pathology, University of Toledo Medical Center, Toledo, Ohio.

Malignant peritoneal mesotheliomas are rare aggressive tumors arising from the serosal surface of the peritoneum with a medium survival time of 6–12 months, making up only 20 to 33% of all mesotheliomas. Herein we report a case of a 67-year-old man admitted for septic shock and multiple organ dysfunction syndrome. Prior to admission the patient experienced several weeks of nausea, vomiting, numerous episodes of vaginal pain, and constipation. A chest x-ray revealed cardiomegaly, congestive heart failure, and necrotic material. A thrombus beneath the posterior mitral valve leaflet close to the interventricular septum was noted on dissecting the heart. Gentle probing confirmed a fistula communicating the gastric ulcer and left ventricular cavity through its posterior wall. Microscopic examination showed a benign peptic ulcer with chronic active inflammation and mixed inflammatory exudate in the interaction along the fistula. The superimposed mixed infection may be a contributory factor to fistula formation. There has been no report of successful treatment of a gastrocardiac fistula with the left ventricle and diagnosis of this rare variant of gastrocardiac fistula is primarily made at autopsy. This case serves to illustrate the continued utility of autopsy in the modern medical era.

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Diaphragmatic Paralysis in a Patient With Antisynthetase Syndrome: A Case Study at Autopsy and Literature Review

(Poster No. 16)

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Antisynthetase syndrome is a rare autoimmune disorder associated with autoantibodies to tRNA synthetase. It includes a constellation of clinical features including interstitial lung disease, inflammatory myopathy, inflammatory polyarthritis, Raynaud’s phenomenon, fever, and “mechanic’s hands.” Because of a low prevalence, a complete pathophysiologic disease process has yet to be characterized. We report a case of a 72-year-old woman with antisynthetase syndrome and positive anti-Jo1 serum antibodies, with onset of progressive muscle weakness for 1 year. She presented, unresponsive, to the emergency department and was admitted for hypercapnic respiratory failure. During her hospital course, she developed severe diaphragmatic paralysis requiring intubation, and, despite aggressive management, died 3 days postadmission. At autopsy, there was severe, multifocal pulmonary fibrosis with chronic inflammation, edema, and pleural effusions. Histologic examination of the diaphragm, psoas, and gastrocnemius muscles showed mild to moderate chronic inflammatory infiltrates with severe endomysial and perimysial fibrosis, degenerating/regenerating muscle fibers, and marked muscle atrophy, most pronounced in the diaphragm (Figure 109, A). Proximal muscle taken from the pectoralis, however, showed no myopathic changes. These findings suggest an antisynthetase-related myopathic paralysis rather than interstitial lung disease as the primary underlying cause of death. Postmortem immunohistochemical analysis, molecular studies, and literature review were performed.

Sudden Death With Myocardial Bridging in the Setting of Severe Atherosclerotic and Hypertensive Cardiac Disease

(Poster No. 18)

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Myocardial bridging, a developmental anatomic variation, proximally affects a single epicardial coronary artery branch that has normally derived from its aortic origin. Bridging is defined by a thick anomalous band of subepicardial myocardium overlying the arterial segment, referred to as the “tunneled artery,” usually the mid left anterior descending branch. According to Alegria et al, the tunneled segment may be compressed with each systole, and myocardial bridging has been clinically associated with angina, arrhythmia, depressed left ventricular function, myocardial stunning, early death after cardiac transplantation, and sudden death. We report sudden cardiac death in a 45-year-old man with past medical history of mild hypertension controlled by medication. At autopsy, findings were confined to the enlarged heart (771 g). In addition to concentric left ventricular hypertrophy (2 cm in thickness), microscopic patchy remote subendocardial fibrosis of the left ventricle papillary muscles and posterior wall was observed. No acute ischemic myocardial changes were identified. The aorta was of normal caliber with minimal atherosclerotic changes. Sectioning through the anterior descending artery documented a 0.6-cm segment running intramurally (beneath a 0.4-cm myocardial bridge; Figure 110, A and B). Marked atherosclerotic narrowing (greater than 80%; Figure, C) was present proximal to the stenosed intramural artery segment. The cause of death was attributed to complications of severe atherosclerotic and hypertensive cardiovascular disease, with myocardial bridging as a major contributing factor. Awareness of this anatomic variation is critical in the autopsy of sudden cardiac death cases.
after the onset of pneumonia. In summary, we presented an autopsy case with SM-caused hemorrhagic pneumonia, which is usually a fulminant and lethal complication associated with bone marrow failure secondary to hematologic malignancies.

Cardiac Metastasis of Cutaneous Squamous Cell Carcinoma in a Patient With Graft-Versus-Host Disease

(Poster No. 20)

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The 63-year-old man had a significant past medical history of follicular lymphoma (1996) treated with chemotherapy. He subsequently relapsed and was treated with allogenic bone marrow transplant (1997) resulting in chronic graft-vs-host disease (GVHD) of skin and lungs (1998). He was treated with immunosuppression therapy until spring 2010 and later with low dose Imatinib. He was diagnosed with cutaneous squamous cell carcinoma (SCC) of his left leg (June 10, 2011) with metastasis to left inguinal lymph nodes, prompting a left leg below knee amputation. The patient was admitted on December 17, 2012 for worsening shortness of breath, chest pain, low-grade fever, and altered mental status. The patient’s condition deteriorated and he died on January 10, 2013. His autopsy showed gross and microscopic evidence of metastatic SCC involving pericardium, right ventricle (Figure 1A and B), and left ventricle. Microscopic examination of interventricular septum showed another focus of metastatic SCC (Figure, C and D). Other gross and microscopic metastases were found in lymph nodes, chest wall, lungs and pleura, diaphragm, liver, kidneys, and adrenal glands. Metastatic tumors in the heart from SCC are rare but have been reported in immunocompetent and post-renal transplant patients. Most cases involve the pericardium, but rarely the myocardium or endocardium is involved. To the best of our knowledge, this is the first report of metastatic cutaneous SCC to the heart of a GVHD patient treated with immunosuppressive therapy.

Fatal Hemorrhagic Pneumonia Caused by Stenotrophomonas maltophilia in a Patient With Acute Myeloid Leukemia: An Autopsy Case Report

(Poster No. 19)

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Stenotrophomonas maltophilia (SM) is a nonfermenting gram-negative bacillus with emerging importance as a dangerous hospital-acquired opportunistic pathogen, causing pneumonia, sepsis, urinary tract or skin infection, and meningitis. Hemorrhagic pneumonia is one of the most severe SM infections. Although SM is very rare compared to other hemorrhagic pneumonia-causing pathogens such as invasive fungi, SM infection is usually lethal and shows resistance to multiple antibiotics. We report on a 46-year-old man with acute myeloid leukemia who developed chemotherapy-associated pancytopenia, hemorrhagic pneumonia, and acute respiratory failure as the immediate cause of death. Postmortem examination revealed both lungs to be wet, heavy, and hemorrhagic (2140 g left; 2280 g right). Microscopically there were diffuse intra-alveolar hemorrhage and fibrin exudate deposition, with parenchymal necrosis, consistent with hemorrhagic pneumonia (Figure 1A and B). Many bacilli were seen in both the interstitium and alveolar parenchyma; there was no acute inflammation in this immunosuppressed patient (Figure, B). There was no evidence of cytomegalovirus, herpes simplex virus, or fungal infection. Bone marrow aplasia was observed, explaining the lack of inflammation in the lungs. Postmortem culture of bilateral lung tissue obtained at autopsy revealed SM with multidrug resistance. The patient died shortly after the onset of pneumonia. In summary, we presented an autopsy case with SM-caused hemorrhagic pneumonia, which is usually a fulminant and lethal complication associated with bone marrow failure secondary to hematologic malignancies.

A Pediatric Autopsy Case of Necrotizing Enterocolitis With Systemic Gas Embolism

(Poster No. 21)

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Necrotizing enterocolitis (NEC) is the most common gastrointestinal emergency in premature infants and has a high morbidity and mortality rate. Multiple factors have been implicated in the pathogenesis of NEC: formula feeding, absence of enteral feeding, abnormal bacterial colonization of the immature gut, and hypoxia/hypoperfusion. Although radiologic findings of NEC include portal venous gas, only a few cases report systemic gas embolism. We present an autopsy case of a female infant with systemic gas emboli to the heart. The patient was an infant of a diamniotic-dichorionic twin pregnancy, delivered by Cesarean section at 28 weeks gestation because of severe intrauterine growth retardation and oligohydramnios. The infant was admitted to neonatal intensive care unit and thrived until day 65, when she became dyspneic and had a hematocrit of 22.8% requiring transfusion. Two hours after the transfusion, she acutely decompensated and demonstrated physical and radiologic findings of NEC. Despite maximum resuscitation efforts, the infant died. The family consented to an autopsy. The external autopsy findings were significant for generalized petechiae and purpura and protuberant abdomen. The internal examination revealed marked pneumatosis intestinalis. The ileum and jejunum had red/maroon discoloration with no evidence of perforation and microscopically showed transmural necrosis with gram-negative bacterial overgrowth. Gas bubbles were seen in the mesenteric vessels, coronary vein, and pulmonary artery. The death of this infant was attributed to the systemic gas embolism due to fulminant NEC. This case demonstrates the importance of thorough autopsy examination to elucidate the exact mechanism of death in infants with NEC.

Fatal Hepatic Vascular Malformation in a Third-Trimester Female Fetus

(Poster No. 22)

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The female fetus was delivered by forceps at 36 weeks gestation weighing 2395 g and with a birth length of 49 cm. She was noted to have two abdominal masses present at birth. During the neonatal period, workup of the fetal masses revealed a left hepatic cyst containing clear, straw-colored fluid and a right hepatic parenchymal mass. The right mass was noted to be well-circumscribed with a lobulated configuration and a heterogeneous echogenicity, and was thought to be a hemangioblastoma on ultrasound. The patient died at day 5 due to respiratory failure. At autopsy, two masses were seen in the liver, one in the right lobe and one in the left lobe. The right mass measured 5 × 4 × 3 cm and was thought to be a hemangioblastoma. The left mass was also located in the left lobe and measured 4.5 × 3 × 2.5 cm. Histologically, the right mass was a hamartoma. The left mass was a vascular malformation consistent with a parasanguineous malformation (hemangioma). At autopsy, a large arteriovenous malformation was noted in the liver and included the two masses described above. It involved the left lateral segment of the liver. Histology showed a distinct arteriovenous malformation with anastomotic channels and large, dilated vessels. The left liver lobe included the hepatic mass and the right lobe included the hemangioblastoma. The lesion had increased vascularity and was consistent with a vascular malformation. The infant died on day 5 due to respiratory failure secondary to the hepatic vascular malformation.
A stillborn female fetus, 25 weeks, 3 days gestation, was delivered to a healthy 26-year-old gravida 2 mother with regular prenatal care and a normal sonogram at 21 weeks gestation. At 25 weeks gestation, she felt decreased fetal movement, and ultrasound followed by fetal magnetic resonance imaging (Figure 113, A) revealed an 8.3-cm abdominal mass of uncertain origin with a differential including nephroblastoma, hepatoblastoma, and, because of the rapid change in size, a vascular lesion. The following day, she felt no fetal movement, and ultrasound diagnosed intrauterine fetal demise. Induction of labor and delivery followed the next day. Gross examination at autopsy revealed an 8-cm hemorrhagic, necrotic hepatic lesion (Figure, B), and no other congenital malformations. Histology with trichrome staining (Figure, C) showed the lesion consisted of haphazard, dilated vascular spaces with areas of hemorrhagic infarction. Immunohistochemistry was positive for CD31/34, confirming vascular origin, and negative for GLUT1 (Figure, D), classifying it as a vascular malformation rather than a hamangiomata. Congenital hepatic vascular malformations are rare, nonneoplastic entities with only a few hundred described. Unlike hemangiomomas, they do not regress spontaneously, respond to corticosteroids, or express GLUT1. Most present at birth and are resected without recurrence. This exceptional case suggests that an early third-trimester presentation, because of a faster proliferation, may herald a greater risk of infarction and intrauterine fetal demise. Better recognition of the behavior of hepatic vascular malformations in the third trimester would enhance prenatal counseling for these mothers.

**Pathology Uncovering the Mystery of Abdominal Pain of Unknown Origin**

(Melissa Straub [(Melissa.Straub@rockets.utoledo.edu); Amira Gohara, MD. Department of Pathology, University of Toledo College of Medicine, Toledo, Ohio.]}

A 51-year-old man with a history of back pain presented to the emergency department with worsening sharp, stabbing abdominal pain associated with nausea and no vomiting. Clinicians were suspicious of
choleCYStitis or appendicitis. Upon initial workup, a computed tomography scan revealed inflammatory changes with fluid in the right upper to lower quadrants. Subsequent scans showed no significant pathology within these organs. Lab workup the patient was anemic and had an increased total serum protein level (15.8 g/dL) as well as a markedly decreased serum albumin (2.8 g/dL). Urinalysis displayed a concentrated specimen (specific gravity 1.030) with elevated protein (300 mg) and microscopic hematuria with pyuria. Three days after admission, he patient rapidly decompensated with respiratory failure and experienced a cardiopulmonary arrest from which he could not be resuscitated. At autopsy, the patient was found to have multiple myeloma with amyloid deposition in the intestines, confirmed by special stains and electron microscopy.

**Amyloidoma: An Unusual Cause of Death**

(Poster No. 26)

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Amyloidosis is a group of various disorders in which there is extracellular deposition of abnormally folded insoluble protein that interferes with tissue function. Amyloidosis can be clinically classified as either localized or systemic and has been identified in almost every organ system. An amyloidoma is an uncommon occurrence in which localized depositions of amyloid leads to a pseudotumor. While gastrointestinal amyloidosis is quite common, amyloidomas of the gastrointestinal tract are quite infrequent, with only a few cases reported in the literature. We present a case of an 85-year-old man who presented to the emergency room with complaints of coffee-ground emesis, generalized fatigue, and shortness of breath. The patient expired within a day and a half from admission. Gross examination revealed a hemorrhagic mass located in the distal small intestine causing obstruction and diffuse hemorrhage with blood filling the lumen distal to the lesion. The obstruction led to severe bilateral aspiration pneumonia that progressed to sepsis. Microscopic examination of the mass revealed pale pink homogenious material with extensive hemorrhage and dense aggregates of lymphocytes. Congo red and crystal violet stains confirmed the diagnosis of amyloidoma. The amyloidoma in this case was associated with a localized low-grade B-cell lymphoma, extranodal marginal zone type. Amyloid deposits were not noted in any other sites at autopsy. To our knowledge, this is the first reported case of an intraluminal amyloidoma as a cause of death.

**Lung Adenocarcinoma Metastasis to Tunica Adventitia of Ascending Aorta: An Autopsy Case Report**

(Poster No. 27)

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We report an interesting case of a 53-year-old woman presenting with vague abdominal discomfort and no known history of cancer. On admission, her lab results included marked increased D-dimer, mildly elevated INR, and normal hematocrit and platelets. Chest x-ray revealed normal lung and heart findings with no pericardial or pleural effusions. Her condition soon deteriorated with rapidly increased INR and PTI and decreased hematocrit and platelet count. She expired 14 hours after her admission. The autopsy examination revealed 400 mL of blood in the pericardium, bilateral straw-colored pleural effusions (right 700 mL, left 550 mL), and 1000-ML straw-colored ascites. Thoracic examination of the heart and cardiac vasculature revealed a 2.0-cm hemorrhagic area at the anterior surface of the ascending aorta. We found one 2.0-cm subpleural firm nodule in the upper lobe of the left lung. Other gross abnormalities included enlarged subaortic and para-aortic lymph nodes. Microscopic examination revealed the nodule as a lung adenocarcinoma, mixed type, which stained positive for TTF1 and CK7 and negative for CK20 and WT1. The hemorrhagic area at the ascending aorta was discovered to be a metastatic adenocarcinoma focus with marked hemorrhage in the tunica adventitia. Extensive tumor thrombi were also noted in microvasculature of the lung pericardium, ascending aorta, and thymus. We conclude that the cause of death was cardiac tamponade, resulting from active bleeding from metastatic carcinoma foci at the tunica adventitia of the ascending aorta. The bleeding may have been precipitated by malignancy-related disseminated intravascular coagulation (Figure 115).

**The Cause of Death Is an Obscure Manifestation of Loeys-Dietz Syndrome**

(Poster No. 28)

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Loeys-Dietz syndrome is a connective tissue disease caused by mutations of the transforming growth factor β receptor genes that shares many of its pathologic manifestations with Marfan syndrome. Aortic root dilatation, mitral valve insufficiency, arachnodactyly, and pectus deformity are shared features, whereas a bifid uvula, arterial tortuosity, widely spaced eyes, and skin abnormalities are distinct features of Loeys-Dietz syndrome. Although the development of emphysematous bullae in the lungs occurs in both syndromes, the histopathology of this manifestation has been described only for cases of Marfan syndrome. We report a case of a 35-year-old man with Loeys-Dietz syndrome and a history of severe pulmonary manifestations that presented to the autopsy service. At autopsy, the pulmonary changes of Marfan syndrome–affected lungs, called distal acinar emphysema, were present by gross examination (bilateral emphysematous bullae) and by microscopy (paraseptal and subpleural hyperexpansion of alveoli and smooth muscle hyperplasia of membranes bronchioles). Other features seen in the lungs (diffuse mucostasis and diffuse and patchy muscular remodeling of alveolar septa) are unique to this case and suggest that the pulmonary pathology associated with Loeys-Dietz syndrome is distinct from that of Marfan syndrome. This case highlights the problematic nature of implicating an unfamiliar manifestation of a rare syndrome as the cause of death in the autopsy report.

**Current Cytology Examination Is Suboptimal for Microorganism Detection in Lung Transplant Patients**

(Poster No. 29)

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**Context:** Infection is one major complication of lung transplantation (tx). Special stains (GMS and PAS) and CMV immunohistochemical stain have been routinely performed to detect infectious pathogens in transbronchial biopsy (tx), bronchoalveolar lavage (BAL), and/or bronchial washing specimens; however, the efficacy of these microorganism detection methods is still controversial.

**Design:** To evaluate these pathogen detection methods, we retrospectively reviewed the lung tx patients who underwent autopsies from a single tx center in the past 2 decades (during 1992–2013). The microorganism detection methods were compared with regard to premortem transbronchial biopsy, BAL/bronchial washing cytology specimens, and tissue/BAL culture/PCR.

**Results:** A total of 82 autopsies were included in the present study. Forty-six patients died of infection/sepsis (bacteria/virus/fungus), of which 32 deaths (10 females, 22 males; age, 51.7 ± 2.26 years) were caused by virus/fungus. CMV was the main viral pathogen. Transbronchial...
chial biopsies were performed in 30 patients, with CMV detected in 10 patients (10 of 30). Of these 10 patients with CMV infection, cytologic examination was performed only in 5 patients, and none of them had (+) CMV diagnosis. Fungal organisms were detected in 5 patients in transbronchial biopsy, but none of them were detected by cytology. On the other hand, the sensitivity of CMV/fungus detection in tissue/BAL cultures or PCR was much higher than BAL/bronchial washing cytology examination (Figure 116).

Conclusions: Transbronchial biopsy and culture/PCR are more sensitive than BAL/bronchial washing cytologic examination to detect microorganisms. Cytologic examinations for microorganisms need to be further improved in lung tx patients.

A Novel Constellation of Congenital Cardiac Anomalies in the Setting of Monosomy X and 8p23.1 Duplication With Initial Presentation in Utero (Poster No. 30)

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Though monosomy X and 8p23.1 duplications have been well reported in conjunction with certain cardiac defects, we describe a case of a premature female newborn with a combination of monosomy X mosaicism and an 8p23.1 duplication on chromosomal microarray, with novel cardiac features previously unobserved in either entity. The mother is a gravida 6 para 5 with no family history of congenital heart defects. On sonogram, at approximately 19 weeks gestation, heart defects were detected and confirmed by prenatal fetal echocardiogram revealing a nonfunctional pulmonary valve with massive pulmonary artery dilation (Figure 117, A). An emergent Cesarean section was performed at 28 weeks gestation because of hydrops fetalis. Despite medical management, pulmonary hypertension persisted, the pulmonary artery continued to dilate (Figure, B), and the infant died at 45 weeks calculated gestational age. The heart anomalies confirmed at autopsy included severe pulmonary valve dysplasia and pulmonary arterial dilation (Figure, C and D), a bicuspid aortic valve, and dysplastic atrioventricular valves with shortened chordae tendineae and upwardly displaced papillary muscles. We are currently seeking chromosomal analysis to determine familial versus de novo 8p23.1 duplication, which has a phenotypic spectrum ranging from subclinical to more pronounced cardiac defects. In this novel case, we present a fatal constellation of cardiopulmonary manifestations uncommon to either 8p23.1 duplication or monosomy X mosaicism. In a literature review, the dysplastic pulmonary valve cusps and subsequent dilated pulmonary artery in utero are novel to these syndromes.

Senile Systemic Amyloidosis in an Elderly Patient Presenting With Gastrointestinal Bleeding (Poster No. 31)

Maryna Tarbunova, MD (maryna.tarbunova@jax.ufl.edu); Agnes Aysola, MD. Department of Pathology, University of Florida, Health Science Center, Jacksonville.

Amyloid is an abnormal protein made of continuous nonbranching fibrils in β-pleated conformation, which can accumulate in various tissues and organs insidiously. Senile systemic amyloidosis (SSA) is a common age-related amyloidosis that characterized by accumulation of transthyretin (TTR) predominantly in the heart. We report a case of an 83-year-old woman with history of hypertension, congestive heart failure, and restrictive lung disease, on coumadin therapy for pulmonary embolism, admitted with gastrointestinal bleeding. Despite stabilization of hemoglobin level, she developed progressive hypotension and died. Autopsy revealed significant cardiomegaly (750 g). The sigmoid colon had a hemorrhagic segment with several diverticula. The heart microscopically showed extensive, diffuse, homogenous deposits compressing the myocardial fibers. They are strongly positive with Congo red staining and give apple-green birefringence under polarized light. The lung sections microscopically showed massive diffuse and nodular alveolar-septal thickening by waxy, acellular amyloid deposits. Section of the hemorrhagic colon revealed diverticulosis and amyloid depositions in the vessels walls. The diagnosis of SSA is problematic secondary to lack of specific clinical symptoms or biomarkers. SSA is an acquired late-onset disease affecting patients in their 70s and 80s. However, 4% of the black population in the United States is a carrier of mutant allele of TTR, leading to deposition of mutant TTR mainly in the heart. In our case, congestive heart failure, restrictive lung disease, and gastrointestinal bleeding were the manifestations of an unsuspected SSA. Our case indicates that SSA should be in the differential diagnoses when evaluating cardiopulmonary symptoms in elderly patients (Figure 118).
Unexpected Findings of a Young Sickle Cell Patient Who Died Suddenly
(Poster No. 32)

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We present a 24-year-old woman with a history of numerous admissions for sickle cell disease complications who presented to the emergency room with shortness of breath exacerbated by hot weather. Chest computed tomography scan showed new bilateral and diffuse pulmonary ground-glass opacities, and she was diagnosed with acute chest syndrome. Pulmonary artery pressure was measured for the first time and was found to be severely elevated at 82 mm Hg. Her hospital course was characterized by continued hypoxia. On the 12th day of admission, she died suddenly with severe hypoxia. Autopsy revealed chronic thromboembolic pulmonary hypertension with embolic foreign body granulomatosis. Pulmonary foreign bodies are birefringent, located mostly within the arterial walls, and few within organized thrombi; their morphologies and special staining profiles are those of talc and microcrystalline cellulose. Elastic van Gieson stain shows rupture of the elastic laminae associated with foreign body granulomatosis within multiple arteries. Additionally, both kidneys show collapsing glomerulopathy. The patient denied intravenous drug abuse; therefore, we believe this patient was crushing her prescription hydromorphone and diphenhydramine tablets order to intravenously inject aqueous suspensions of its contents via her indwelling peripherally inserted central catheter line. Sudden death due to embolic foreign body granulomatosis in sickle cell patients has rarely been reported. Collapsing glomerulopathy has rarely been reported in human immunodeficiency virus–negative sickle cell patients but is a well-known result of intravenous drug abuse. After extensive literature search, these 2 lesions have never been reported within the same patient.

Metastatic Merkel Cell Carcinoma to the Brain With Diffuse Involvement of Ventricular System: An Autopsy Report
(Poster No. 33)

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Merkel cell carcinoma is a rare aggressive primary neuroendocrine carcinoma of the skin. Merkel cell carcinoma is known for its local recurrences. Metastasis to brain is rare and the intraventricular growth pattern has not been reported to our knowledge. The decedent was a 98-year-old woman who presented with acute delirium and confusion. She passed away 2 days after admission because of cardiopulmonary arrest. She had a history of Merkel cell carcinoma 4 years ago on the right index figure that was resected. Laboratory testing revealed severe hyponatremia (118 mmol/L), inappropriate elevation of urinary sodium (194 mmol/L), hypocalemia (7.2 mg/dL), and hypokalemia (3.2 mmol/L). The cerebrospinal fluid cytology was positive for malignant cells and brain. Magnetic resonance imaging showed diffuse intraventricular nodularity with focal outcropping into adjacent white matter. At autopsy, gross findings included diffuse tan-white coating on the inner surface of ventricular cavities with focal extension into the surrounding white matter (Figure 119). Multiple metastatic foci were identified on the spleen capsule. Microscopic evaluation showed ill-defined nodules that were composed of monotonous small round cells with vesicular nucleus and dusty granular chromatin (Figure, inset). Frequent mitoses and extensive necrosis were also observed. Immunohistochemical stains revealed tumor cells positive for EMA, pan–CK, CD56, CK20, and NSE and negative for GFAP, CD45, HMB45, and CD99. The case is interesting because of these unique findings: intraventricular growth pattern mimicking primary neurologic disease, and electrolyte imbalance as a part of paraneoplastic syndrome.

Unknown and Unsuspected Systemic Amyloidosis: Cause of a Lethal Complication of Cardiac Catheterization
(Poster No. 34)

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Amyloidosis is a protein-misfolding disease where fibrils deposit in tissues and organs causing damage and organ failure. Here we report a unique autopsy case of previously unknown and unsuspected systemic amyloidosis predisposing to a lethal complication during cardiac catheterization. A 79-year-old man with history of aortic stenosis, coronary artery disease, and complete AV block requiring a pacemaker was admitted to hospital for shortness of breath at rest for 6 weeks. He was diagnosed with congestive heart failure, which was attributed to a disconnected lead of his pacemaker. He was discharged home after a revision of his pacemaker. One day antemortem, he presented to hospital because of continuous shortness of breath. A cardiac catheter procedure was performed to evaluate his aortic stenosis. During the procedure, he became hypotensive with altered mental status. Using pericardiocentesis, 300 mL of blood was removed. He died shortly thereafter. At the autopsy, a left ventricular wall transmural defect (0.1 × 0.1 cm) was identified, resulting in hemopericardium (250 mL blood). Histologically, severe systemic amyloidosis (confirmed by Congo red, identified as AA type) was demonstrated involving the heart, lung, kidney, stomach, pancreas, and thyroid. The heart was very floppy and fragile because of diffused involvement by amyloid. This unexpected situation contributed not only to his severe heart failure and AV block, but also to the lethal consequence during the cardiac catheterization. In summary, although rare, systemic cardiac amyloidosis should be considered in the differential diagnosis in elder patients with heart failure, and extreme caution needs to be taken during a cardiac procedure.

Tumor-to-Tumor Metastasis With Pancreatic Neuroendocrine Carcinoma Metastatic to Well-Differentiated (Intramucosal) Adenocarcinoma of Rectum
(Poster No. 35)

Eunice K. Choi, MD (ekchoi@tmhs.org); Suzanne Crumley, MD; Hidehiro Takei, MD; Jae Y. Ro, MD, PhD. Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Texas.

Tumor-to-tumor metastasis is a rare occurrence and to our knowledge, a pancreatic neuroendocrine carcinoma metastasizing to rectal cancer has not been reported in the literature. We report the first case of pancreatic neuroendocrine carcinoma as a donor tumor metastasizing to a well-differentiated (intramucosal) adenocarcinoma of the rectum, a recipient tumor. A 47-year-old man with history of high-grade dysplastic polyph of the rectum presented with an encehphalopathy. The clinical diagnosis of the patient was acute hepatic encephalopathy, and liver transplant workup was initiated. On abdominal magnetic resonance imaging, his liver showed multiple lesions. The biopsy of these lesions was diagnosed as adenocarcinoma, favor cholangiocarcinoma. The patient expired 10 days after the admission and autopsy was performed. There was no previous history of malignancy. Gross examination during the autopsy showed a 7-cm

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yellow-tan mass abutting the body and head of the pancreas. Also, a 3-cm tan-brown fungating mass was identified in the rectal mucosa. Microscopic examination of the pancreatic mass showed high-grade neuroendocrine carcinoma. Multiple liver nodules were also metastatic neuroendocrine carcinoma from the pancreas, and not a cholangiocarcinoma. The rectal mass was a tubulovillous adenoma with multiple foci of well-differentiated (intramucosal) adenocarcinoma. Within the rectal tumor, there was diffuse infiltration of neuroendocrine tumor cells, morphologically similar to the cells in the pancreatic neuroendocrine carcinoma. Immunohistochemistry confirmed the presence of 2 separate tumors involved in a tumor-to-tumor metastasis. This autopsy reports a unique case of tumor to tumor metastasis with pancreatic neuroendocrine carcinoma and well-differentiated (intramucosal) rectal carcinoma.

Cacophony of Development: Limb–Body Wall Complex
(Poster No. 36)

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Limb–body wall complex is a rare, sporadic developmental disorder that manifests as diverse developmental abnormalities and limb defects. The term limb–body wall complex was introduced in 1987 by Van Allen et al. The etiology and pathogenesis are unknown; however, several theories related to early amnion rupture, vascular disruption, and embryonic dysgenesis have been proposed to explain this syndrome. We report an immature male fetus, born at 28 weeks, to a 24-year-old G1 P0 mother whose pregnancy was complicated by prolonged premature rupture of membranes and fetal anomalies detected on prenatal ultrasound. External examination demonstrated multiple developmental anomalies including complete loss of the right arm, sternum, and scapula, thoracoabdominoschisis with evisceration of abdominal contents, asplenia, club feet, dextroesotrosis, syndactyly of the left hand, facial clefting, cleft palate and lip, and an atrial septal defect. Neuropathologic abnormalities included encephalocoele, abnormalities in the development of midline structures, neuronal migration disorders, aqueductal atresia/stenosis with hydrocephalus, agenesis of the corpus callosum, and abnormalities of cerebellar development. Histopathologic examination of the placenta was notable for degeneration of the amnion and fibrotic nodules on the subamniotic connective tissue. This case illustrates a spectrum of abnormal developmental abnormalities consistent with limb–body wall complex and a placental finding that has not been previously described. This disorder demonstrates a highly variable phenotype, one that likely represents a multifactorial pathogenesis.

A Rare Case of Wolman Disease Presenting as Hydrops Fetalis
(Poster No. 37)

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Wolman disease is a rare autosomal recessive inborn error of metabolism resulting in the deposition of fat in multiple organs. This occurs because of total lack of the enzyme lysosomal acid lipase. There is massive accumulation of cholesterol esters and triglycerides in the spleen, liver, bone marrow, small intestine, adrenal glands, and lymph nodes. Mutations in chromosome 10q23 are usually seen. Wolman disease is estimated to occur in 1 in 350,000 newborns. We report a rare case of Wolman disease in a full-term male neonate presenting as hydrops fetalis. The parents of the baby were genetically related. The abdomen was distended, liver was enlarged and firm, and cut surface was yellow and greasy. Spleen was enlarged, firm, and reddish yellow. Thymus was not identified; adrenal was symmetrically enlarged and gritty. Histologic examination of the liver showed vacuolations in Kupffer cells and hepatocytes. There was periductular and periportal fibrosis. Oil red O stain was positive in the vacuolated cells. Adrenals showed areas of calcification and vacuolation. Spleen shows features of extramedullary hematopoiesis. One of the tests showed adrenal rest with vacuolation. In view of the clinical presentation, histopathology, and special stain, a diagnosis of Wolman disease was rendered. The differential diagnosis is cholesterol ester storage disease, which presents much later, is clinically milder, has a benign course, and only involves GIT and liver. Prenatal diagnosis is possible by assaying enzyme levels in cultured chorionic villi and amniocytes. Wolman may present as hydrops fetalis and a perinatal diagnosis is possible (Figure 120).

A Rare Case of Metastatic Oropharyngeal Squamous Cell Carcinoma With Cardiac Involvement: An Autopsy Report
(Poster No. 38)

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Distant metastasis of head and neck cancer is not commonly seen, and therefore, the finding of cardiac metastasis in such cases is exceedingly rare. Of neoplasms with cardiac metastases seen at autopsy, oropharyngeal cancer ranks near the end of the list with a frequency of only 1%. We present a case of a 60-year-old man with oropharyngeal squamous cell carcinoma treated with chemoradiation, with metastases to the left lung and kidney. He presented with severe dyspnea and was found to have a low-voltage EKG, which spurred further evaluation with an echocardiogram, discovering a large mass involving the right ventricle. The patient succumbed to his disease within 2 days of this finding and an autopsy was performed. The metastatic disease was more extensive than previously thought, with masses identified in bilateral lungs, kidneys, and adrenals, as well as the heart. Of particular interest was the cardiac metastasis, which consisted of a white-tan mass with focl of hemorrhage and necrosis, mainly occupying the right ventricle wall and chamber (Figure 121, A), which was consistent with metastatic squamous cell carcinoma on histologic sections (Figure B). P16 immunostain was performed and was negative, which corresponded with the original biopsy. Review of the literature only shows 4 cases.
of head and neck cancer with cardiac metastases that were discovered premortem, highlighting the rarity of this case. Additionally, this case displays the prognostic importance of assessing P16 status in head and neck cancers, as HPV-negative patients often display a worse disease course than their HPV-positive counterparts.

**Autopsy Diagnosis of a Case of Intrauterine Meconium Aspiration Syndrome**  
(Poster No. 39)  
Weihong Li, MD (weihong.li@utoledo.edu); Amira Gohara, MD. Department of Pathology, University of Toledo Medical Center, Toledo, Ohio.

The pathogenesis of meconium aspiration syndrome (MAS) is complex and incompletely studied. The incidence of MAS is reported as 1.8% in a study of 162,075 term infants born between 1997 and 2007. A 36-year-old, 39 weeks pregnant woman presented for not feeling fetal movement for 24 hours. She denied any leaking of fluid or vaginal bleeding. Intrauterine fetal demise was confirmed by ultrasound. Labor was induced and a stillborn male infant was delivered. Gross exam revealed meconium-stained placenta, with centrally located umbilical cord revealing thromboemboli in 2 vessels near the placenta. Microscopic examination confirmed thrombosis in umbilical cord vessels, focal fibrinoid necrosis, and attached blood clots on the peripheral placenta surface, consistent with ischemic changes of the placenta. Fetal lungs (right, 36 g; left, 27 g) were grossly unremarkable. The parenchyma was soft and pale. Microscopic examination showed meconium-stained amniotic fluid filled in the alveolar space and airways. Multiple petechial hemorrhages consistent with hypoxia were present on the visceral pleural surfaces. The cause of the baby’s death can be attributed to hypoxia secondary to intrauterine aspiration of meconium stained amniotic fluid, which involved intrauterine passage of meconium, aspiration, pulmonary disease, hypoxemia, and fetal demise. The most probable scenario of the tragic events could be that thrombosis in the umbilical cord put the fetus in distress; then the fetus passed meconium into the amniotic fluid; while straining to pass the meconium, he took a gasp and aspirated meconium-stained amniotic fluid into his lungs, which led to his intrauterine demise.

**Is Autopsy a Dying Medical Discipline or an Integral Part of Patient Care?**  
(Poster No. 40)  
Zarine Kamaluddin, MD (zarine.kamaluddin@utoledo.edu); Amira Gohara, MD. Department of Pathology, University of Toledo Medical Center, Toledo, Ohio.

Autopsy is the most reliable and comprehensive way to evaluate a clinician’s diagnosis after death of the patient. Herein, we present a case where the correct diagnosis was provided after autopsy. An 89-year-old man with Alzheimer dementia presented to the emergency room with severe abdominal pain, coffee-ground vomitus, hypotension, and tachycardia. The computed tomography (CT) revealed multiple air-fluid levels and thickening of the small-bowel wall, attributed to obstruction and infectious process, respectively. A calcified mass was noticed that was unchanged from a previous CT report. He was transferred to the medical intensive care unit, where aggressive fluid resuscitation, vasopressors, and antibiotics were started. Surgery was not indicated because of multiple comorbid conditions. The patient had a history of coronary artery disease and atrial fibrillation. The patient’s blood pressure and heart rate progressively deteriorated. Two days later, he succumbed to sepsis. The autopsy findings revealed the presence of a purulent ascites, peritonitis, and small-bowel perforation due to obstruction from a well-differentiated mucinous adenocarcinoma of the ascending colon with adenocarcinomatosis of the omentum and metastasis to the lung. Other findings included pleural effusion, aspiration pneumonia, severe coronary artery disease, and a calcified granuloma of the mesentry. The malignant tumors were totally unsuspected during the clinical course, underscoring the utility of autopsy. An argument can, therefore, be made that gaps in clinical knowledge and diagnosis are best filled through a medical autopsy despite the era of increasingly sophisticated technologies.

**Synovial Sarcoma Presenting as an Obstructing Thyroid Mass**  
(Poster No. 41)  
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The majority of synovial sarcomas occur in the extremities, while a primary occurrence in the mediastinum is rare. Here we present a case of a 79-year-old man who was found to have an obstructing thyroid mass with symptoms of stridor, worsening shortness of breath, and voice change. Computed tomography showed extension of the mass to involve the trachea. Preoperative fine-needle aspiration of the mass revealed a malignant spindle cell neoplasm. The patient was taken to the operating room for thyroid lobectomy. Intraoperative frozen section consultation of the mass was inconclusive, with sarcoma in the differential. The permanent sections showed a spindle cell neoplasm that was positive for EMA and BCL2. Fluorescence in situ hybridization (FISH) analysis showed t(X;18), confirming the diagnosis of synovial sarcoma. Postoperative positron emission tomography–computed tomography showed possible residual disease in the thyroid lobectomy bed and metastatic disease in the lungs. The prognosis of thyroid synovial sarcoma is associated with a high risk for local and metastatic relapses. This case highlights the importance of including synovial sarcoma in the differential of thyroid masses, as mediastinal synovial sarcomas are associated with a worse prognosis unless a complete resection can be achieved.

**Proximal-Type Epithelioid Sarcoma With Angiomatoid Features Presenting as a Prevertebral Mass**  
(Poster No. 42)  
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Proximal-type epithelioid sarcoma is a rare and aggressive neoplasm that usually affects the axial skeleton of older individuals and primarily occurs in the pelvis, perineum, pubic region, and vulva. Rare variants of this entity have been reported. We describe an unusual case of proximal-type epithelioid sarcoma presenting as a prevertebral thoracic mass in a 44-year-old man. Image-guided fine-needle aspiration (FNA) of the mass demonstrated clusters of neoplastic cells with moderately abundant cytoplasmic cytoplasm and vesicular chromatin, as well as spindled cells (Figure 122, A). The pathogenesis of meconium aspiration syndrome (MAS) is complex and incompletely studied. The incidence of MAS is reported as 1.8% in a study of 162,075 term infants born between 1997 and 2007. A 36-year-old, 39 weeks pregnant woman presented for not feeling fetal movement for 24 hours. She denied any leaking of fluid or vaginal bleeding. Intrauterine fetal demise was confirmed by ultrasound. Labor was induced and a stillborn male infant was delivered. Gross exam revealed meconium-stained placenta, with centrally located umbilical cord revealing thromboemboli in 2 vessels near the placenta. Microscopic examination confirmed thrombosis in umbilical cord vessels, focal fibrinoid necrosis, and attached blood clots on the peripheral placenta surface, consistent with ischemic changes of the placenta. Fetal lungs (right, 36 g; left, 27 g) were grossly unremarkable. The parenchyma was soft and pale. Microscopic examination showed meconium-stained amniotic fluid filled in the alveolar space and airways. Multiple petechial hemorrhages consistent with hypoxia were present on the visceral pleural surfaces. The cause of the baby’s death can be attributed to hypoxia secondary to intrauterine aspiration of meconium stained amniotic fluid, which involved intrauterine passage of meconium, aspiration, pulmonary disease, hypoxemia, and fetal demise. The most probable scenario of the tragic events could be that thrombosis in the umbilical cord put the fetus in distress; then the fetus passed meconium into the amniotic fluid; while straining to pass the meconium, he took a gasp and aspirated meconium-stained amniotic fluid into his lungs, which led to his intrauterine demise.

**Is Autopsy a Dying Medical Discipline or an Integral Part of Patient Care?**  
(Poster No. 40)  
Zarine Kamaluddin, MD (zarine.kamaluddin@utoledo.edu); Amira Gohara, MD. Department of Pathology, University of Toledo Medical Center, Toledo, Ohio.

Autopsy is the most reliable and comprehensive way to evaluate a clinician’s diagnosis after death of the patient. Herein, we present a case where the correct diagnosis was provided after autopsy. An 89-year-old man with Alzheimer dementia presented to the emergency room with severe abdominal pain, coffee-ground vomitus, hypotension, and tachycardia. The computed tomography (CT) revealed multiple air-fluid levels and thickening of the small-bowel wall, attributed to obstruction and infectious process, respectively. A calcified mass was noticed that was unchanged from a previous CT report. He was transferred to the medical intensive care unit, where aggressive fluid resuscitation, vasopressors, and antibiotics were started. Surgery was not indicated because of multiple comorbid conditions. The patient had a history of coronary artery disease and atrial fibrillation. The patient’s blood pressure and heart rate progressively deteriorated. Two days later, he succumbed to sepsis. The autopsy findings revealed the presence of a purulent ascites, peritonitis, and small-bowel perforation due to obstruction from a well-differentiated mucinous adenocarcinoma of the ascending colon with adenocarcinomatosis of the omentum and metastasis to the lung. Other findings included pleural effusion, aspiration pneumonia, severe coronary artery disease, and a calcified granuloma of the mesentry. The malignant tumors were totally unsuspected during the clinical course, underscoring the utility of autopsy. An argument can, therefore, be made that gaps in clinical knowledge and diagnosis are best filled through a medical autopsy despite the era of increasingly sophisticated technologies.
epithelioid sarcoma with angiomatoid features. The presence of ectatic vascular spaces in this rare variant could be misinterpreted as angiokeratoma. Shown in the Figure are a high-power image of epithelioid and spindle tumor cells (Pap stain) (A); a high-power image highlighting angiomatoid spaces (H&E stain) (B); tumor cells are pancytokeratin positive (C); and loss of INI 1/BAF47 nuclear positivity in tumor cells (D).

**Pleomorphic Angiomatoid Fibrous Histiocytoma: Report of a Case With EWSR1 Gene Rearrangement**

(Poster No. 43)
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Angiomatoid fibrous histiocytoma (AFH) is a rare soft tissue tumor mainly occurring on the extremities of children and young adults. It is considered a tumor with intermediate malignant potential. Histologically, AFH is composed of pseudovascular spaces with bland spindle and/or round cell proliferation surrounded by a dense lymphoid cuff and a peripheral fibrous pseudocapsule. The pleomorphic variant is exceedingly rare; only a few cases have been reported in the literature. Herein we report a case of left-arm mass in a 14-year-old boy that was initially mistaken for sarcoma. Sections showed solid sheets of spindle cells with highpleomorphic nuclei, vesicular chromatin, and a sclerotic background. The tumor was surrounded by dense chronic inflammation with lymphoid follicles. A solitary cleftlike cystic space with surrounding hemosiderin was noted. Occasional mitoses were identified (1/10 high-power fields); however, there was no evidence of necrosis. The tumor cells were positive for desmin, EMA, CD99 (weak), and CD34 (focal), but negative for cytokeratin, S100 protein, and SMA. Molecular cytogenetic analysis with a DNA probe specific for the EWSR1 gene region of 22q12 revealed that a significant number of cells (77.5%) had a split of the gene indicative of rearrangement. Despite the pleomorphic cytology, this variant of AFH does not carry a worse prognosis. It should be considered in the differential diagnosis of pleomorphic spindle cell lesions in children and young adults. Other differentials include pleomorphic undifferentiated sarcoma, atypical fibrous histiocytoma, atypical fibroxanthoma, and rhabdomyosarcoma. In difficult cases, immunohistochemical studies and FISH can be helpful.

**Thoracic Vertebrae Osteoblastoma With a Secondary Aneurysmal Bone Cyst Causing Neurologic Symptoms in an 11-Year-Old Girl**

(Poster No. 44)
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Osteoblastoma is a rare benign bone tumor comprising less than 1% of bone tumors, with sporadic secondary aneurysmal bone cyst formation. We present an interesting case of an 11-year-old girl with no significant past medical history who presented with lower extremity weakness and increasing gait instability. Imaging studies revealed an epidural mass extending from the T7–8 intervertebral disc to the T9–10 intervertebral disc, causing moderate to severe spinal cord stenosis. Given the location of the mass, the radiologic differential diagnosis consisted of a schwannoma, neuroblastoma, epidural meningioma, or cavernous hemangioma. Preliminary diagnosis was most consistent with an epidural mass extending from the T7–8 intervertebral disc to the T9–10 intervertebral disc, causing moderate to severe spinal cord stenosis. The tumor was surrounded by dense inflammatory infiltrate and hemosiderin. Occasional mitoses were identified. The presence of ectatic vascular spaces in this rare variant could be misinterpreted as angiosarcoma. Immunohistochemical analysis showed positive staining for CD99, CD34, and EMA. Molecular cytogenetic analysis showed a split of the EWSR1 gene region of 22q12 revealed that a significant number of cells (77.5%) had a split of the gene indicative of rearrangement. Despite the pleomorphic cytology, this variant of AFH does not carry a worse prognosis. It should be considered in the differential diagnosis of pleomorphic spindle cell lesions in children and young adults. Other differentials include pleomorphic undifferentiated sarcoma, atypical fibrous histiocytoma, atypical fibroxanthoma, and rhabdomyosarcoma. In difficult cases, immunohistochemical studies and FISH can be helpful.

**Low-Grade Spindle Cell Neoplasms With RB Loss in Unusual Locations**

(Poster No. 45)
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Cellular angiofibroma (CA), spindle cell lipoma (SCL), and mammary-type myofibroblastoma (MFB) all have overlapping morphologic, immunohistochemical, and molecular findings. Low-grade spindle cell neoplasms with features of these tumors but occurring in unusual locations are difficult to classify. We present 2 cases of low-grade spindle cell neoplasms with features of CA, SCL, and MFB, thereby broadening the spectrum of these tumors. We report 2 cases of low-grade spindle cell neoplasm: (1) a 47-year-old man with a 5.9-cm perirectal mass and (2) a 23-year-old man with a 5.0-cm thigh mass. Both cases showed morphologic similarities to CA, SCL, and mammary-type MFB. Both stained for CD34; the perirectal mass showed loss of 13q14 (RB1) by FISH. Immunohistochemical stains for RB showed loss in both tumors. These cases belong to this family of tumors of CA, SCL, and MFB. This report demonstrates the utility of the RB immunohistochemistry and FISH in making the diagnosis when these tumors present in unusual locations.

**Melanocytic Neuroectodermal Tumor of Infancy: A Case Report and Review of the Literature**

(Poster No. 46)
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This rare tumor of neural crest origin typically presents during the first year of life and most commonly arises in the maxilla, with few cases reported in other parts of the body. Herein we report a case of a 4-month-old, full-term, healthy female infant with a 3.2-cm complex mass with sclerotic edematous edges. An excisional biopsy of the mass revealed a biphasic tumor composed of larger epithelioid cells containing variable amounts of melanin.
highlighted by Fontana-Masson stain admixed with smaller neuroblast-like cells. The larger epithelioid cells were positive for cytokeratin, CD99, and HMB45 immunostains, whereas the smaller cells were positive for synaptophysin and chromogranin. Additional immunostains (CD45, desmin, MyoD1, WT1, and S100) were all negative in both cell types, excluding other differential diagnoses. Although the majority of these tumors follow a benign course, high rates of local recurrence have been reported and metastases are known to occur, and ≥10 mitoses/10 high-power fields in posttreatment resections. Only tumor viability and mitotic rate on resection retained significance in the multivariate model adjusted for tumor size, tumor location, and metastatic status. The chemotherapy response score outperformed percentage residual viable tumor in predicting prognosis in both training and validation cohorts (Figure 125).

Conclusions: The amount of residual viable tumor and its proliferative activity posttherapy are independent measures of chemotherapeutic efficacy and strongly associated with survival outcome. Based on this finding, we developed and validated a grading system for routine clinical use.

Sarcomatous Brain Metastases: A Single Institution, 28 Years of Experience

(Poster No. 48)

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Context: Brain metastasis from sarcomas is rare and limited information is available. We examined pathologically confirmed sarcomas brain metastases diagnosed over a period of 28 years.

Design: This is a single-institution retrospective study of 112 cases of brain sarcoma metastasis. Clinical records were reviewed for demographic, clinical, pathologic, and survival data (Table).

Results: Undifferentiated sarcoma was the most common source (28%) followed by alveolar soft part sarcoma. Most common primary location was the extremities (50.0%). The majority were adults (89%) with a mean age of 35.7 years. Headache was the common presenting symptom. Most showed an evidence of prior metastatic disease to other sites (73%). Median time to brain metastasis was 2.1 years (range: 0.03–16.70 years). Most of the metastatic foci were parenchymal (92%), nonhemorrhagic (70%), and singular (78%). Half the tumor deposits were in the frontal lobes. Thirty-one percent of brain metastases recurred, all within 5.8 years. Of the patients, 76% succumbed to the disease, with a mean survival time of 1.37 years. No difference in survival was noted between hemorrhagic versus nonhemorrhagic (P = .22), single versus multiple (P = .72), or primary soft tissue versus bone sarcomas (P = .97). No effect on survival when surgical resection was combined with radiotherapy and/or chemotherapy (P = .19).

Conclusions: Brain metastasis is a late event in sarcoma clinical progression. In our study, undifferentiated sarcomas were the most common source of brain metastasis followed by alveolar soft part sarcoma. The majority of cases showed evidence of prior metastatic disease. Surgical resection is employed to manage symptoms, but prognosis remains dismal.
Osteochondroma of the Lumbar Spine: A Common Tumor but Rare Location
(Poster No. 49)
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Osteochondroma is the most common benign tumor of the bone, with a strong predilection to the metaphysis of the long bones. However, solitary osteochondroma of the spine is rare, consisting of 1%–4% of all reported cases. The cervical and upper thoracic vertebrae are the predominant spinal levels involved, and the lumbar segment is much less commonly affected. We report a case of a 24-year-old man who presented with persistent low back pain for several weeks with no radicular symptoms. A computed tomographic scan of the spine showed a bony expansile, noninfiltrating mass of the right L4 lamina extending into the posterior paraspinal musculature. There was preservation of the normal lumbar lordosis without cortical destruction of vertebral bodies. The mass did not extend into the epidural spaces or neural foramina. The radiologic findings were compatible with osteochondroma. The mass was resected and the patient was symptom free. Gross examination revealed a 5.3 × 4.1 × 2.0 cm, tan-white, bony mass with irregular edges. Microscopic examination demonstrated a benign osteo-cartilaginous tumor comprising of a cartilaginous cap surrounded by a thin rim of perietoal connective tissue and foci of enchondral ossification. Cellular atypia, necrosis, and mitotic activity were absent on histology. Histopathologic findings and the radiographic evidence were consistent with osteochondroma. Radiologic-pathologic evaluation is critical for diagnosis and guiding treatment of these tumors, as clinical symptoms of spinal involvement can be inconspicuous and nonspecific. Additionally, up to 5% of osteochondromas can evolve into chondrosarcoma.

Emerging Immunohistochemical Markers for Malignant Peripheral Nerve Sheath Tumor
(Poster No. 50)
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Context: Malignant peripheral nerve sheath tumor (MPNST) is an uncommon aggressive sarcoma that usually arises in association with nerve tissue. Morphologically, MPNST demonstrates variable histologic patterns rendering distinction from other sarcomas, particularly undifferentiated or unclassified pleomorphic sarcomas (UPS), challenging. Currently, the diagnosis is based on clinical evidence of neurofibromatosis type 1 disease or clinical evidence of neural origin along with the finding of usually high-grade sarcoma that often shows patchy S100 protein expression. We attempted to identify a panel of immunohistochemical markers that can aid in the diagnosis of MPNSTs and allow it to be robustly distinguished from the UPS category.

Design: Previously constructed tissue microarrays (TMAs) for MPNST and UPS were stained for S100 protein, PGP9.5, CD56, and podoplanin. Staining for additional markers including NFI is currently in progress. The TMAs included 109 MPNST and 233 UPS tumor tissues. Statistical analysis was conducted using SPSS 21 software.

Results: Both PGP9.5 and S100 protein showed a higher percentage of expression in MPNST compared to UPS (P = .03, P < .001, respectively). CD56 was more highly expressed in MPNST compared to UPS but failed to demonstrate statistical significance (P = .19). Podoplanin, however, showed a significantly higher expression in UPS compared to MPNST (P = .005; Figure 126).

Conclusions: The diagnosis of MPNST routinely includes a panel of immunohistochemical markers that are characteristic of this tumor and help exclude histologic mimics including UPS. We suggest that along with S100 protein, other markers such as PGP9.5 and podoplanin could also be considered.

Terminal Deoxynucleotidyl Transferase Immunostaining of Sarcomeres in Rhabdomyosarcoma
(Poster No. 51)
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Although skeletal muscle differentiation with sarcomeres is fundamental in the diagnosis of rhabdomyosarcoma, this feature is not always present. The diagnosis is made following multiple immunostaining including desmin and myogenin. We encountered a case of alveolar rhabdomyosarcoma that was evaluated with multiple immunostains prior to diagnosis including terminal deoxynucleotidyl transferase (TdT) to rule out lymphoblastic lymphomas/acute leukemia, which demonstrated positive immunoreactivity for TdT. We retrospectively analyzed a second case of poorly differentiated rhabdomyosarcoma for immunostaining with TdT. Anti-TdT rabbit polyclonal antibody was used in both cases and they were stained using Ventana ultra automated immunostainer. With hematoxylin and eosin stain, while the alveolar rhabdomyosarcoma revealed very rare and faint impression of sarcomeres (Figure 127, A), the latter were not identifiable in poorly differentiated rhabdomyosarcoma. Both rhabdomyosarcoma subtypes showed positive immunostaining of distinct sarcomere bands with TdT (Figure, B). Mild diffuse cytoplasmic staining of tumor cells was also noticed with few streaks of developing sarcomere bands. Normal skeletal muscle sarcomeres at the periphery of tumor in one case also showed positive staining for TdT. As TdT cross reacts with sarcomeres of rhabdomyosarcoma and normal muscle, diagnostic pitfalls during flow cytometry should be avoided. Because the reactivity of TdT is cytoplasmic in rhabdomyosarcoma compared to nuclear in leukemia, this could be of diagnostic value. TdT is a DNA polymerase located in the cell nucleus that catalyzes the polymerization of deoxynucleotides; why this stains sarcomeres in the cytoplasm is unknown at this time.

Decubital Ischemic Fasciitis/Atypical Decubitus Fibroplasia: A Pseudosarcomatous Lesion Commonly Presenting as Sarcoma
(Poster No. 52)
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Ischemic fasciitis is a type of reparative/regenerative process, occurring primarily in physically debilitated or immobilized elderly patients. It consists of a fascia-based fibroelastic and myofibroelastic proliferation and is part of the pseudosarcomatous lesions group, which also includes nodular fasciitis, proliferative fascitis, and proliferative myositis. The
pathogenesis consists of intermittent ischemia leading to necrosis and breakdown, followed by a regenerative, reparative process. The lesion can be overdiagnosed as sarcoma clinically, cytologically, and even histologically. While histomorphologically similar to nodular fascitis, it can be misdiagnosed as epithelioid sarcoma, myxofibrosarcoma, or myxoid liposarcoma. An 85-year-old woman presented with a 5-cm, ill-defined, painless, firm mass involving the right arm deep subcutis, muscle, and fascia, without skin ulceration. The mass was noted 3 weeks earlier, when the patient became bedridden after a complicated hip replacement. An atypical spindle cell lesion was diagnosed on core biopsy. The lesion displayed lobular configuration, fibrinoid necrosis, and prominent myxoid stroma, rimmed by ingrown, ectatic, thin-walled vascular channels (Figure 128, upper images, low power). Atypical, enlarged, degenerated stroma, rimmed by ingrown, ectatic, thin-walled vascular channels displayed lobular configuration, fibrinoid necrosis, and prominent myxoid atypical spindle cell lesion was diagnosed on core biopsy. The lesion was followed up with no signs of recurrence 6 months after excision.

Epithelioid Hemangioma of the Penis
(Poster No. 53)

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Penile epithelioid hemangioma is a rare vascular tumor that is characterized by tumefactive proliferation of epithelioid endothelial cells and inflammatory infiltrate with lymphocytes and eosinophils. We present a case of penile epithelioid hemangioma. A 41-year-old man presented with a painful nodule on the penis. Physical examination revealed a 0.8-cm erythematous lesion on the dorsal base of the shaft of the penis. Histopathology showed a well-circumscribed vascular proliferation (Figure 129, A and B; low- and high-power view of the lesion). The vascular spaces were lined by plump epithelioid endothelial cells with enlarged nuclei and distinct nucleoli. Background inflammatory cells included lymphocytes and eosinophils. Differential diagnosis included epithelioid hemangioendothelioma and epithelioid hemangioma. The endothelial cells do not have the characteristic hyaline connective tissue matrix, definite hyaline globules, or severe nuclear atypia suggestive of epithelioid hemangioendothelioma. Immunohistochemical stains demonstrated that tumor cells showed strong expression of CD34 and minimal expression of CD31. Ki-67 expression confirmed low proliferation rate. Final diagnosis was penile epithelioid hemangioma, completely excised. The patient was followed up with no signs of recurrence 6 months after excision.

Histologically, penile epithelial hemangioma shows characteristic features of epithelioid appearance of endothelial cells with inflammatory infiltration of lymphocytes and eosinophils. The epithelioid endothelial cells have no nuclear atypia and low proliferation rate. Penile epithelioid hemangioma is a benign lesion. Complete local excision with periodic follow-up is the optimal management.

Spindle Cell Lipoma, Low-Fat Variant With Marked Myxoid Change: A Diagnostic Implication
(Poster No. 54)

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Mesenchymal tumors may undergo a wide range of degenerative changes that obscure key diagnostic histopathologic features and may lead the weary pathologist awry. Examples include myxoid change, pseudoangiomatous change, fibrosis, and cystic change. Additional confounding factors include overrepresentation of one or more tissues within a lesion and an unusual anatomic location. We present a diagnostically challenging case of a 44-year-old man with a slowly enlarging breast mass. At surgery, a 4.5 × 4.5 × 3.0-cm circumscribed mass was excised. The cut surface was tan-white and mucoid. Microscopically, it revealed a hypocellular spindle cell proliferation within abundant Alcian blue–positive myxoid stroma and scant adipocytes (<10%). The short, monomorphic spindle cells had blunted ends. Pseudovascular spaces were present, and collagenous fibrosis formed some pseudovascular structures. Our differential diagnosis included superficial angiomyxoma, neurofibroma, mammary-type myofibroblastoma, and low-grade sarcoma. By immunostains the spindle cells were CD34 positive and negative for S100 protein, desmin, and smooth muscle actin. Masson trichrome highlighted some “ropy collagen” throughout. A diagnosis of low-fat spindle cell lipoma with marked myxoid change was rendered. As illustrated, it is important to remember when faced with an unusual mesenchymal tumor in an unusual location that shows myxoid or other degenerative changes that extreme care must be taken to establish the diagnosis, accounting for factors that cloud the picture. Fortunately, creating a broad differential diagnosis, paying attention to key diagnostic features, and prudently using special stains and immunohistochemistry will reward the surgical pathologist with the correct diagnosis and afford the patient the appropriate prognosis.
Lipomembranous dystrophy (lipomembranous fat necrosis) is a rare distinctive type of ischemic fat necrosis that most commonly occurs in the subcutaneous fat of the lower extremities of adult women in the setting of panniculitis or venous stasis. We present 2 cases of lipomembranous dystrophy with prominent amyloid deposition, a previously unreported finding in this lesion. Two patients (a 79-year-old man and an 81-year-old woman) presented with a single, palpable, firm subcutaneous abdominal wall mass (2 and 4.3 cm, respectively). Histologic sections revealed classic features of lipomembranous dystrophy but with additional, intermixed waxy eosinophilic material. Congo red stains revealed extensive amyloid deposition in both cases. Von Kossa stains demonstrated calcium deposits. Feathery membranes in microsections were PAS positive. Patient history included diabetes mellitus and hypertension in both with no history of amyloidosis or myeloma. Bone scans were negative for tumor but suggested Paget disease in the male patient. The female patient had a history of multiple abdominal surgeries. Five additional cases of dermal lipomembranous dystrophy secondary to panniculitis were negative for amyloid deposition by Congo red staining. A review of the medical literature revealed no reports of concurrent, intermixed amyloidosis and lipomembranous dystrophy. Deep nodules of lipomembranous dystrophy may contain amyloid protein. This is a previously unreported finding. Extensive amyloid mixed with lipomembranous fat necrosis does not seem to be associated with paraneoplastic causes of amyloid deposition such as myeloma; however, data are limited. This unique hybrid lesion histologically overlaps lipomembranous dystrophy and amyloidoma.

Calcifying Fibrous Tumor of the Jejunum: A Case Report of a Rare Entity and Literature Review

(Poster No. 56)
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Calcifying fibrous tumor (CFT) is a rare benign lesion characterized by a hypocellular, densely hyalinized fibrous tissue and dystrophic and/or psammomomatous calcifications. Usual sites of involvement include soft tissue, abdominal cavity, and rarely gastrointestinal tract, especially small bowel. To our knowledge this is the first case of CFT arising from the jejunal wall. Herein, we report a case of a 33-year-old man presenting with lower abdominal pain. Imaging revealed a partially calcified nonenhancing lesion in the abdominal cavity. Grossly, the tumor was 4.5 cm, firm, tan-red, and well-circumscribed. Microscopically, the lesion was unencapsulated with marked fibrous adhesions and many reactive fibroblasts on its serosal surface. Centrally it showed a bland paucicellular spindle cell proliferation, hyalinized stroma with thick-walled blood vessels, abundant dystrophic calcification, few psammoma bodies, and scattered lymphocytes. Immunohistochemically, the tumor was positive for vimentin, but negative for CD117, S100, CD34, smooth muscle actin, desmin, DOG-1, ALK-1, and CAM 5.2. Ki-67 was positive in 50% of tumor cells. The resection specimen confirmed the diagnosis, with 3 of 3 positive lymph nodes. Multiple pulmonary nodules have been detected 3 months after identification of lytic bone lesions. Expression of SPARC has been reported in some soft tissue sarcoma cases, but has not been studied in epithelioid angiosarcoma of bone. When the resection specimen was examined immunohistochemically, there was strong and diffuse staining for SPARC (Figure 130). This finding could suggest new therapeutic options for further consideration.

Myoepithelioma of Bone

(Poster No. 58)
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Myoepitheliomas are unusual tumors resembling salivary gland mixed tumors and showing myoepithelial differentiation. Initially described in salivary glands and later in soft tissue, myoepitheliomas arising in bone have been rarely reported. Herein we present 2 cases of myoepithelioma arising primarily in bone. Hematoxylin and eosin slides, ThinPrep prepared fine-needle aspiration slides, and a battery of immunostains were reviewed. The patients were both males, 70 and 58 years old, with tumors arising in the left proximal humerus and left iliac bones, respectively. The tumors were 11.2 and 12.0 cm in greatest dimension. One tumor showed solid sheets and cords of cells with clear cytoplasm. The fine-needle aspiration of the tumor exhibited cells with clear cytoplasm, enlarged hyperchromatic nuclei, and increased nuclear to cytoplasmic ratio. The other tumor showed similar architecture but with more eosinophilic cytoplasm and focal keratin pearls (Figure 131). Both tumors had a chondromyxoid background and did not show any significant nuclear atypia or increased mitosis. Immunostains showed positive staining for smooth muscle actin, desmin, and S100 in the myoepithelial component of both tumors. The primary epithelial component was negative for S100 and desmin and strongly positive for cytokeratin. CD34 was positive in both tumors. These findings support the belief that myoepitheliomas are neoplasms arising from myoepithelial cells rather than from the myoepithelial component of mixed tumors.

Primary Epithelioid Angiosarcoma of Bone With Robust Cell Cycle Progression and High Expression of SPARC: Therapeutic Implications

(Poster No. 57)
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Epithelioid angiosarcoma is a very rare variant of angiosarcoma and it rarely involves bone as a primary site. SPARC (osteonectin) is a secreted protein that is acidic and cysteine-rich and binds albumin. Expression of SPARC in tumors has been correlated with sensitivity to albumin-bound paclitaxel, particularly in the context of robust cell cycle progression into the mitotic phase. We report a 62-year-old man who presented with lower extremity pain and was found to have lytic bone lesions involving the lower end of femur and upper end ofibia and fibula. The differential diagnoses after computed tomography–guided core biopsy included metastatic carcinoma, epithelioid sarcoma, and malignant epithelioid vascular lesion. Open biopsy showed epithelioid angiosarcoma involving lamellar bone with focal areas of epithelioid hemangioendothelioma. The mitotic figures were 19 per 10 high-power fields in the most mitotically active area. The tumor cells were positive for pancytokeratin, CAM 5.2, vimentin, CD31, CD34, and factor VIII. Ki-67 was positive in 50% of tumor cells. The resection specimen confirmed the diagnosis, with 3 of 3 positive lymph nodes. Multiple pulmonary nodules have been detected 3 months after identification of lytic bone lesions. Expression of SPARC has been reported in some soft tissue sarcoma cases, but has not been studied in epithelioid angiosarcoma of bone. When the resection specimen was examined immunohistochemically, there was strong and diffuse staining for SPARC (Figure 130). This finding could suggest new therapeutic options for further consideration.
both tumors to be positive for S100 and cytokeratin AE1/AE3. Other myoepithelial markers such as SMA, calponin, and GFAP were negative. Fluorescent in situ hybridization (FISH) on both tumors exhibited an intact EWSR1 gene. The histologic descriptions and immunohistochemical staining pattern of these 2 tumors confirms the diagnosis of a myoepithelioma arising in bone. It is important to include this rare category of tumors in the differential diagnosis of epithelioid-appearing tumors in bone, and not to confuse them with metastasis.

Primary Synovial Sarcoma of the Pleura: A Case Report and Literature Review

(Paper No. 59)

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Synovial sarcoma is a rare soft tissue malignancy. However, it has remained as a diagnostic challenge, because of its diverse biological behavior and variable anatomic sites. We present the case of a 16-year-old girl who had right-sided chest pain for 5 years and was managed conservatively as costochondritis. Recently, the nature of her chest pain changed abruptly, resulting in difficulty in breathing. A computed tomography scan of the chest showed a pleura-based soft mass (Figure 132, A). Positron emission tomography imaging showed hypermetabolic activity. A computed tomography-guided biopsy of this lesion was nondiagnostic. The patient subsequently underwent thoracotomy with excision of the mass. Gross evaluation showed a tan-red and hemorrhagic background (Figure, B and C). The lesion consisted of alternating hypercellular and hypocellular myxoid areas. The spindle cells were arranged as interlacing fascicles in the hypercellular areas, with over 5 mitoses/10 high-power fields. The extensive hemorrhage appears to obscure areas of necrosis. Immunohistochemically, tumor cells showed diffuse positivity for TLE-1 (Figure, D), vimentin, RCL-1, CD56, and smooth muscle actin; focal positivity for epithelial membrane antigen, AE1/AE3, CAM5.2, CK7, CD99, and calretinin; and negativity for CD34, S100, ALK-1, p53, and HMB45. Ki67 was moderately increased. The morphology and immunohistochemical profiles are consistent with monophasic type synovial sarcoma. Translocation between chromosome X and 18 using fluorescence in situ hybridization confirmed the diagnosis.

Transformation of Schwannoma Into Malignant Rhabdoid Tumor in a Patient With Germline SMARCBI/INI-1 Mutation

(Paper No. 60)

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Patients with germline SMARCBI/INI-1 mutation are predisposed to either malignant rhabdoid tumors in childhood or schwannomatosis as adults. We previously reported the occurrence of both schwannomatosis in adults and malignant rhabdoid tumors in children within a single family with a germline duplication of exon 6 of SMARCBI/INI1. Herein, we report the transformation of a neuroblastoma-like schwannoma into a high-grade sarcoma with rhabdoid features in a 29-year-old man in this family. The patient developed a rapidly growing mass involving the right sciotic, tibial, and peroneal nerves. Grossly, the tumor was 20.0 cm, tan-pink, soft, and gelatinous with scattered calcifications. Microscopically, it was a high-grade sarcoma, arising from a neuroblastoma-like schwannoma, and showed sheets of small round blue cells with primitive nuclei, prominent nucleoli, and scant amphophilic cytoplasm. Rare neoplastic cells displayed rhabdoid morphology. Immunohistochemistry showed complete loss of INI-1 in the sarcoma, whereas the precursor schwannoma showed patchy loss of INI-1. S100 stain showed strong nuclear reactivity in the schwannoma. The sarcoma cells were locally positive for EMA and negative for S100, desmin, FLI-1, CD99, CD45, CD34, CD31, AE1/AE3, and CAM 5.2. Subsequently, the patient developed multiple vertebral and paravertebral metastases with more prominent rhabdoid features (Figure 133) and diffuse loss of INI-1. The sarcoma showed no specific line of differentiation but demonstrated rhabdoid morphology, suggesting that adults with familial schwannomatosis are at risk for malignant rhabdoid tumors, similar to related children in these families. We suggest close surveillance in adults with germline SMARCBI/INI-1 mutation.

Myxoinflammatory Fibroblastic Sarcoma—A Rare Tumor With Unusual Histomorphology: Report of a Case and Review of the Literature

(Paper No. 61)

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Myxoinflammatory fibroblastic sarcoma (MIFS) is a recently recognized low-grade sarcoma, generally located in extremities. Clinically, MIFS is significantly difficult to distinguish from benign lesions. Histologically, it mimics inflammatory reactive changes. Pathologists should be aware of this entity to avoid diagnostic errors as benign conditions. We present this case of a 39-year-old woman who had a long-standing painless right forearm mass. Recently she developed pain and decreased mobility of the right hand. Imaging studies suggested a benign cystic lesion. Surgical biopsy showed a low-grade spindle cell myxoid lesion. Grossly, the excision specimen was an ill-defined 6-cm mass, infiltrating the subcutaneous tissue and focally involving the tendons close to the wrist joint. Microscopically, the mass demonstrated alternating hyaline, fibrous, and myxoid areas in variable proportions (Figure 134, A). There were different types of tumor cells, including large spindle cells (Figure, B), large polygonal

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and bizarre ganglion-like cells with large inclusion-like nucleoli (Figure, C), and large bubbly multivacuolated lipoblast-like cells (Figure, D). The tumor cells were positive for vimentin and focally positive for CD34, while negative for epithelial and lymphoid markers. After differentiated from potential soft-tissue mimics, such as nodular and proliferative fasciitis and inflammatory myofibroblastic tumor, it was diagnosed as MIFS. The excision margins were negative, except for one small tumor focus near the margin. Six months later, the patient experienced recurrence at the excision site. After re-excision, imaging follow-up every 6 months for 2 years revealed no evidence of recurrence or metastasis. MIFS should be identified early and resected with wide margins.

![Image](image_url)

**Atypical Fibrous Histiocytoma of Bone**

(Poster No. 62)

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Context: Benign FH (BFH) of bone is rare. It has a wide age distribution and may involve any bone but most commonly the diaphysis of long bones. BFH is usually a well-defined, radiolucent medullary defect without matrix mineralization, and histologically is composed of fibrohistiocytic cells arranged in a storiform pattern admixed with foam cells and multinucleated giant cells. Malignant FH of bone occurs usually in older adults. It demonstrates aggressive features radiographically and often appears as a pleomorphic sarcoma histologically. In rare cases the cells of FH lesions may exhibit nuclear atypia intermediate between these entities, thus justifying the term atypical fibrous histiocytoma (AFH), but no consensus has been reached as to the degree of atypia for which a diagnosis of low-grade atypical fibrous histiocytoma (AFH), but no consensus has been reached as to the degree of atypia for which a diagnosis of low-grade malignancy should be rendered.

Design: We present 3 cases of unusual FH lesions of bone involving the cortex of the femoral diaphysis or tibial epiphysis of middle-aged adults to outline these lesions.

Results: Focal reactive bone formation/mineralization was present in both cortical lesions, of which one showed soft tissue extension. Moderate nuclear atypia was seen in the epiphyseal lesion. One patient had multiple recurrences, in which smooth muscle differentiation became evident.

Conclusions: There is a group of FH lesions of bone that are histologically more worrisome than typically seen in BFH, and may occur in unusual sites including the cortex and epiphysis, with or without worrisome features. Further, various lineages of differentiation may appear in recurrences. These lesions should be classified initially as AFH until long-term follow-up can determine their biologic potential.

**Lessons Learned: Unusual Initial Clinical Presentations of EWSR1-Rearranged Tumors**

(Poster No. 63)

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EWSR1-rearranged tumors encompass the Ewing family of tumors, including Ewing sarcoma/primitive neuroectodermal tumor, Askin tumor, and desmoplastic small round cell tumor. While the majority of these tumors present in the early decades of life, involving the musculoskeletal system and peritoneal surfaces, occasional cases do occur. We present 2 cases of atypical EWSR1 tumors that serve as reminders to keep these entities in the differential at all times. Case 1: A 40-year-old man presented with lower back pain and muscle weakness. Imaging demonstrated a circumscribed mass in the femoral nerve clinically thought to be an MPNST. Biopsy revealed a small round cell tumor within the nerve positive for CD99 and CD56. Ewing sarcoma was suspected and confirmed through RT-PCR demonstrating the EWS-FHL1 gene rearrangement. This case is unusual given the primary location of the tumor. Case 2: An 87-year-old woman presented with flank pain. A destructive and lytic 10-cm mass involving the 10th rib was found and thought to represent metastasis or myeloma. Histology demonstrated a small blue cell tumor positive for CD99. EWSR1 rearrangement was identified and a diagnosis of Ewing sarcoma was rendered. This case is unique because of the age of the patient and axial skeletal system distribution. Regardless of age or clinical presentation, pathologists should always keep EWSR1-rearranged tumors in the differential when evaluating small round cell neoplasms. In cases where EWSR1 are considered, FISH and RT-PCR provide an invaluable set of tools for diagnosis (Figure 135).

**Amyloidoma of the Thigh Associated With Localized B-Cell Lymphoproliferative Process**

(Poster No. 64)

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Amyloidoma is a solitary tumourlike deposit of amyloid. Amyloidoma of soft tissue most commonly occurs in the mediastinum and abdomen. Extremities are an unusual site with most cases composed of the AA amyloid. Localized tumors involve the AA amyloid deposition with associated local B-cell lymphoproliferative disorder (LPD) is rare. A 90-year-old woman with diabetes, hypertension, and hyperlipidemia presented with a mass in her left thigh mimicking sarcoma. Physical examination was otherwise unremarkable. Magnetic resonance imaging revealed the mass to be located in the subcutaneous adipose tissue with no extension into muscle or bone. Excision revealed a distinct subcutaneous mass with a tan/yellow cut surface, measuring 4 cm in greatest dimension. Microscopically the mass was composed of nodular deposits of amyloid with associated multinucleated giant cells, fibrosis, and patchy lymphoplasmacytic infiltrates. Immunohistochemistry revealed that the lymphocytes were mostly CD20+ B cells admixed with CD138+ λ monoclonal plasma cells. Flow cytometry revealed λ monoclonal B cells. Amyloidoma in the soft tissues of the thigh with associated localized B-cell LPD is highly unusual. The presence of monoclonal B cells and plasma cells is most consistent with AL amyloid. B-cell LPDs with associated AL amyloid deposition are usually disseminated, systemic processes. Our patient did not have clinical features of systemic involvement and serum protein studies did not show...
significant dysproteinemia or M component, making the precise categorization of this LPD using the WHO 2008 classification scheme difficult. Additional studies of more patients may help to clarify the nature and clinical significance of amyloidoma associated with a localized B-cell LPD.

**Vasculitis/Perivasculitis and Vascular Damage in Large Tumors of Adipose Tissue: Increased Frequency and Extent in Atypical Lipomatous Tumors/Well-Differentiated Liposarcomas Versus Large Lipomas**

(Poster No. 65)

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**Context:** Mesenchymal tumors may elicit a systemic inflammatory response. Inflammation within fatty tumors and its potential significance have not been systematically investigated. We compared the prevalence of one type of inflammation, perivascular inflammation, and evidence of prior inflammation, vascular damage, in atypical lipomatous tumors/well-differentiated liposarcomas (ALT/WDL) and large lipomas.

**Design:** Cases of ALT/WDL and lipoma (>10 cm) for which all slides were available for review were retrieved. Tumor size, immunohistochemistry, karyotype, patient demographics, and clinical history were obtained. Follow-up was obtained for ALT/WDL cases. Presence and extent (number of blocks) of lymphoplasmacytic perivascular or vascular inflammation and presence of vascular damage (fibrinoid necrosis, intimal edema and hyperplasia, medial hypertrophy and hyalinization, and thrombus formation) were recorded for each case. Inflammation and damage associated with ischemia, necrosis, or biopsy site changes were excluded.

**Results:** Perivascular/vascular inflammation was identified in 31 of 36 ALT/WDL (86%, avg. 5.6 blocks affected) and 8 of 28 lipomas (29%, avg. 1 block affected). Vascular damage was observed in 14 ALT/WDL (2 without inflammation) and 2 lipomas (1 without inflammation). Follow-up data were available for 26 patients, 8 of whom had recurrent disease. There was no association between recurrence and vasculitis or vascular damage. Vasculitis and vascular damage were not significantly related to tumor size, location, patient demographics, or presence of necrosis.

**Conclusions:** Perivascular/vascular inflammation and vascular damage occur with increased frequency and extent in ALT/WDL compared to lipomas, suggesting a preferential hyperimmune response. These changes do not appear to be related to recurrence. Further study is warranted.

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**Solid Variant of Angiomatoid Fibrous Histiocytoma: Is It More Common Than We Think?**

(Poster No. 66)

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Angiomatoid fibrous histiocytoma (AFH) is a slow-growing, distinctive tumor of uncertain histogenesis, usually arising in the extremities or neck of children and adolescents, characterized by histiocytic cells with pseudoangiomatoid spaces, fibrous pseudocapsule, and lymphocytic cuff. The solid variant is rare and often underrecognized because of the absence of characteristic pseudoangiomatoid spaces. We report 2 cases of the solid variant in 2 boys, 8 and 15 years old, who presented with slow-growing, dermal-based masses on the chest wall and thigh, respectively. Grossly the lesions were nodular, with tan-yellow fleshy cut surfaces. Microscopically, the characteristic findings of an AFH were noted, although pseudoangiomatoid spaces were absent. One of the tumors showed focal cytologic atypia and germinal centers, mimicking a lymph node (Figure 136, A and B). Wide excisions revealed no residual tumor and both patients are free of recurrences or metastases 6 months postdiagnosis. The differential diagnosis was broad and included lymph node metastasis of epithelial or soft tissue origin, Kaposi sarcoma, and spindle cell lesions, such as nodular or proliferative fasciitis. The solid variant of AFH may be an underrecognized and challenging diagnosis that may occur with greater frequency than reported and should be considered in the differential diagnosis of a well-defined, dermal-based, histiocytoid proliferation without blood-filled pseudocystic spaces. These cases illustrate the importance of recognizing the classic and uncommon features of AFH and the spectrum of features seen in the solid variant to prevent a misdiagnosis or an erroneous diagnosis of lymph node metastasis.

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**Combined Erdheim-Chester Disease and Langerhans Cell Histiocytosis With BRAF V600E Mutation**

(Poster No. 67)

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A 76-year-old woman with osteoarthritis was found to have bilateral symmetric mixed lytic–sclerotic intramedullary infiltrates of the tibial metaphyses on x-ray. Core biopsy was initially interpreted as nonspecific chronic inflammation. Subsequent left total knee arthroplasty demonstrated a subchondral sparing proximal tibial medullary infiltrate of finely vacuolated CD68+, CD21+, CD1a-, S100- histiocytes, lacking granulomatous organization or emperipolesis characteristic of ECD. T lymphocytes and Touton giant cells were intermixed. Five percent of the infiltrate showed aggregates of histiocytic cells morphologically and immunophenotypically characteristic of Langerhans cells (S100+, CD1a+, and CD21+, CD68+) with associated T lymphocytes and eosinophils (Figure 137). The Langerhans cell aggregates were associated with areas of bone resorption. **BRAF V600E mutation was demonstrated by real-time PCR in DNA extracted from the nondecalcified core biopsy that, upon review, contains an Erdheim-Chester disease (ECD) infiltrate but no Langerhans cells. ECD is a rare systemic histiocytosis. Data are largely derived from case reports. Since the 1980s a relationship between ECD and Langerhans cell histiocytosis (LCH) has been emerging, with reports of concurrent or sequential ECD and LCH, and few reports, like ours, of combined ECD-LCH. In 1992 Reid demonstrated that both CD1a-positive dendritic cells and CD1a-negative macrophages can be derived from the same single cell culture of CD34-positive progenitor cells from adult human bone marrow. It has recently been shown that LCH and ECD show a similar high prevalence of **BRAF V600E mutation, 57% and 54% respectively. With increased understanding we may find that combined ECD-LCH is the norm rather than the exception.**
High-Grade Follicular Dendritic Cell Sarcoma—An Unlikely Mimic of Carcinoma: Report of 2 Cases  
(Poster No. 68)
Matthew Bernstein, MD (mbernstein@gru.edu); Michael Toscano, MD; Natasha Savage, MD; Suash Sharma, MD. Department of Pathology, Medical College of Georgia, Georgia Regents University, Augusta.

Follicular dendritic cell sarcoma (FDCS) is a rare tumor of adults involving nodal or extranodal sites, with an erroneous histologic diagnosis reported in 18.6% of cases. In one of our cases, a 67-year-old woman presented with a 4-cm neck mass that doubled in size in 2 months. An outside fine-needle aspiration was reported as “poorly differentiated carcinoma.” The resected 4.0-cm submandibular mass appeared encapsulated, composed of epithelioid and spindled cells in sheets and clusters interspersed with reactive lymphoid cells. Neoplastic cells exhibited moderate pleomorphism, nuclei, high mitotic activity (20/10 high-power fields) and 1% necrosis. Despite weak pankeratin staining, membranous immunopositivity for CD21 and CD23 was diagnostic of FDCS. Twenty lymph nodes from a neck dissection were negative, CD21 and CD23 positivity favored FDC sarcoma over histiocytic or interdigitating cell sarcoma. Over a 2-year follow-up, the tumor was negative.

Epithelioid Inflammatory Myofibroblastic Sarcoma Mimicking a Benign Inflammatory Process  
(Poster No. 70)
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Epithelioid inflammatory myofibroblastic sarcoma (EIMS) is a recently described variant of inflammatory myofibroblastic tumor with a predictably poor prognosis. Cases presented in its initial description were originally thought to represent a number of malignant neoplasms before their true nature was established. We report a case of EIMS that was originally felt to represent a benign inflammatory process in a 69-year-old man. After presenting with complaints of abdominal pain and a significant unintentional weight loss, the patient was found to have a 6.4-cm pericolic mass on computed tomography. A percutaneous biopsy was obtained and although a diagnosis of sarcomatoid carcinoma was initially considered, upon review the biopsy material was felt to represent a benign inflammatory process. Within 3 months of the initial biopsy the mass dramatically increased in size and the patient was referred to our institution for surgical management. Grossly, the tumor consisted of a 21.2-cm white-tan, multilobated, fleshy to myxoid mass that was adherent to portions of the colon, pancreas, and spleen. Histologically, it consisted of predominately epithelioid cells deposited in a variably myxoid stroma with an accompanying mixed inflammatory infiltrate. Tumor cells were found to be immunoreactive for ALK-1 with a distinctive nuclear membrane pattern of reactivity. The presence of an ALK gene rearrangement was confirmed by FISH and the diagnosis of EIMS was made. This case represents only the second report of EIMS since its description and underscores the importance of considering this entity when evaluating material that appears otherwise inflammatory in nature.

Benign Osteoblastic Tumor of the Third Distal Phalanx in the Left Foot of an 11-Year-Old Girl  
(Poster No. 69)
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Osteoid osteoma and osteoblastoma are benign bone-forming tumors with similar morphology but different growth potentials. Osteoid osteoma may be present in a patient for several years; however, the lesion seldom exceeds 1 cm in greatest diameter. The term osteoblastoma is usually applied if a lesion of similar morphology is greater than 2 cm in diameter. We present a case of benign osteoblastic tumor occurring in the distal third phalanx of the left foot in an 11-year-old girl. Imaging studies showed soft tissue proliferation with minimal sclerosis and global enlargement of the third distal phalanx with absent physes. Osteoblastoma versus glomus tumor was suspected clinically based on the imaging results. Histologic examination of the amputation specimen showed a fairly well-circumscribed tumor pushing into the medullary cavity; it was composed of woven bone spicles or trabeculae lined by a single layer of osteoblasts. The tumor showed rich vascularity with osteoblasts and scant osteoclast-like giant cells (Figure 138, A and B). The lesion measured 0.4 cm in greatest dimension. By size definition, our case favored an osteoid osteoma; however, by involvement of the medullary cavity and the size ratio of the tumor to small phalanx bone (1:3), the lesion more closely resembled an osteoblastoma. There is a need for discussion about other factors especially in the small bones regarding not only size criteria for distinguishing osteoid osteoma from osteoblastoma. A review of the literature found 3 articles reporting osteoblastoma in the phalanges (A in the toe, B in the fingers).

Desmoid Tumor (Abdominal Fibromatosis) Presenting as an Incisional Hernia  
(Poster No. 71)
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Desmoid tumors are soft tissue tumors of intermediate (locally aggressive) malignant potential. Originating from a clonal myofibroblastic proliferation in the fascia and muscle aponeurosis, these locally aggressive fibromatoses often occur at sites of local trauma and can recur even if completely excised. Mutations in genes expressing β-catenin, adenomatosis polyposis coli, or other proteins affecting β-catenin complex regulation, either occurring sporadically or as part of a genetic syndrome such as familial adenomatous polyposis, contribute to their development. Here, we report a desmoid tumor presenting as a midline incisional hernia. An 88-year-old man with a history of multiple tumors in various body sites, including colon cancer for which a partial colectomy was performed through a midline incision 3 years prior, presented with what appeared to be a nonreducible incisional hernia. During surgical repair, instead of an abdominal wall defect, a mass was discovered. Histologic examination revealed cytologically bland spindle cells arranged in storiform and herringbone patterns forming a dense collagenous stroma entrapping skeletal muscle. The cells showed nuclear positivity for β-catenin, which distinguishes desmoid tumors from other fibroblastic and myofibroblastic tumors. Other negative stains confirmed the diagnosis. Given the cancer history, this diagnosis suggested a possible genetic mutation, prompting clinicians to further investigate family history and consider genetic testing. Although the patient ultimately declined. This case not only highlights the importance of considering desmoid tumor when confronted with soft tissue tumors with a history of surgical trauma, but also emphasizes considering genetic testing that may affect tumorigenesis of other organs.
**HMB-45–Negative Solitary Mesenteric Lymphangioleiomyoma**

*(Poster No. 72)*

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Lymphangioleiomyomas are typically associated with lymphangioleiomyomatosis, a multisystem disease, affecting predominantly women in the reproductive period. We present a case of a 44-year-old woman with pain in the left upper quadrant of the abdomen. The computed tomography scan of the abdomen and pelvis showed a large left abdominal and pelvic mass encasing mesenteric vessels and causing displacement of the bowel loops to the right. Grossly, the specimen consisted of a segment of bowel with a 20-cm tan-brown and cystic mass arising from the mesentery and containing milky fluid. The histologic findings were typical of lymphangioleiomyoma and included a ramifying network of lymphatic spaces lined by a single layer of endothelium surrounded by fascicles and bundles of abnormal smooth muscle–like cells (LAM cells), occasional lymphoid follicles, and congested vascular spaces. However, HMB-45 staining, which is typically positive in the tumor cells, was negative. Most commonly, this disease process involves the lungs, which were not involved in our patient. Extrapulmonary lymphangioleiomyomas are rare and mainly occur in the pelvis, mediastinum, and retroperitoneum. The mesentery as an involved site of extrapulmonary lymphangioleiomyomas is an extremely rare location. Only 4 cases of mesenteric lymphangioleiomyoma have been described in the literature (Table); of these 2 also had pulmonary involvement. Our case is unique in that it is not only the largest solitary mesenteric lymphangioleiomyoma, but it is also the first report of an HMB-45-negative lymphangioleiomyoma involving the mesentery.

**Clinicopathologic Findings of Mesenteric Lymphangioleiomyomas**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age, y</th>
<th>Size, cm</th>
<th>Association</th>
<th>HMB-45</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11</td>
<td>8</td>
<td>None</td>
<td>Positive</td>
</tr>
<tr>
<td>2</td>
<td>43</td>
<td>8</td>
<td>Pulmonary lymphangioleiomyomatosis</td>
<td>Positive</td>
</tr>
<tr>
<td>3</td>
<td>51</td>
<td>15</td>
<td>Pulmonary lymphangioleiomyomatosis, angiomyolipomas</td>
<td>Positive</td>
</tr>
<tr>
<td>4</td>
<td>47</td>
<td>17</td>
<td>None</td>
<td>Positive</td>
</tr>
<tr>
<td>Our case</td>
<td>44</td>
<td>20</td>
<td>None</td>
<td>Negative</td>
</tr>
</tbody>
</table>

**Pleomorphic Sarcoma of the Ovary With Fast Growing Metastases Into Right Ventricle and Lungs**

*(Poster No. 73)*

Mayes Dormosh, M.D (mdormosh@drexelmed.edu); Andrie Plagov, MD; Jianping Lin, MD; Bethany L. Mapow, DO. Department of Pathology, Drexel University/Hahnemann Hospital, Philadelphia, Pennsylvania.

We report a 69-year-old woman who presented with a large left pelvic mass occupying the pelvis. Preoperative studies including chest x-ray and electrocardiography did not reveal any evidence of metastatic disease. An extensive resection was performed including exploratory laparotomy, bilateral salpingo-oophorectomy, omentectomy, and pelvic and aortic lymph node dissection. No evidence of metastatic disease or lymphadenopathy was identified during the surgery. Pathologic evaluation of the mass revealed a pleomorphic sarcoma arising from a mature cystic teratoma. Six weeks later, the patient complained of progressively worsening shortness of breath on exertion. Radiologic imaging revealed multiple solid and ground-glass nodules scattered throughout the lungs bilaterally. Transthoracic echocardiography was performed, revealing a large mass occupying the right ventricle of the heart. Three days later she experienced respiratory distress, pulseless electrical activity, and death. Significant autopsy findings included a large infiltrative tumor within the heart measuring 7.5 × 5.5 × 4.5 cm occupying the entire right ventricular cavity, extending into the right atrium with obstruction of the tricuspid valve. Histopathologic examination confirmed metastatic undifferentiated pleomorphic sarcoma involving the heart and lungs. It is likely that the tricuspid valve obstruction and invasion of the interventricular septum caused conduction defects and rhythm disturbances, leading to a fatal cardiac arrhythmia. In this case, we report that metastatic sarcoma can develop without any obvious symptoms and present at advanced stage in a very short period of time (Figure 139).

**High-Grade Osteosarcoma of the Mandible in a Patient With History of Irradiated Tonsillar Carcinoma: A Serious Rare Radiation-Induced Complication**

*(Poster No. 74)*

Claudia Ormenisan, MD (claudiaormenisan@yahoo.com); Raafat Makary, MD, PhD. Department of Pathology, University of Florida Jacksonville.

Postirradiation osteosarcoma (PIO) is a rare but serious long-term complication of high-dose irradiation for cancer therapy (latency period up to 53 years, mean of 10–20 years) with estimated risk of 0.03%–0.8%. The prognosis is dependent on site and resectability, with the least favorable prognosis in craniofacial sites. Most have poor prognosis because of their aggressive nature, recurrence, and rapid tumor spread. We report a case of PIO of the mandible in a 63-year-old man who had a history of squamous cell carcinoma of the right tonsil, treated with radiation therapy in 2002. He presented in 2013 with right mandibular tenderness, right V3 hypesthesia, and trismus. Computer tomodesitometry showed a lytic lesion in the right mandibular ramus and an ill-defined soft tissue mass along the floor of the mouth. The patient underwent right hemimandibularctomy, mandibular reconstruction bar, fibula myo-osseous adiposofascial free flap, neck dissection, and full-thickness skin graft. Grossly the tumor (5.5 × 2.6 × 2.3 cm) had hard bony, gray chondroid, and soft tissue areas with necrosis (Figure 140, A...
and B). Histologically the tumor revealed variable histologic patterns of conventional high-grade osteosarcoma, including chondroblastic, osteoblastic (Figure, C), epithelioid, and malignant fibrous histiocytoma-like patterns with brisk abnormal mitoses >50 mitoses/high-power field (Figure, D), necrosis, and lymph-vascular and perineural invasion. He currently received chemotherapy (cisplatin and adriamycin). Although rare, the possibility of PIO should be considered in the field of radiation therapy and mandates long-term follow-up for early diagnosis and treatment, as PIO tends to be more aggressive compared to the primary osteosarcoma.

Radiation-Induced High-Grade Myxofibrosarcoma (Myxoid MFH) of Chest Wall in a Patient With History of Breast Carcinoma: An Aggressive Tumor With Important Treatment Implications
(Poster No. 75)
Rafat Makary, MD, PhD; Claudia Omnenisian, MD (claudiaomnenisian@yahoo.com). Department of Pathology, University of Florida Jacksonville.

Radiation-induced sarcomas (RIS) are rare complications of radiotherapy in the irradiated field after several years of latency (range, 2.5–57.8 years). Sarcoma in itself is a rare malignancy and RIS accounts for 0.5% to 5.5% of all sarcomas. The prognosis of RIS is poor and treatment is challenging because RIS are usually high-grade aggressive sarcomas diagnosed at advanced stage. Undifferentiated pleomorphic sarcoma, also known as malignant fibrous histiocytoma (MFH), is one of the main histologic types of RIS and may display pleomorphic-storiform, giant cell, inflammatory, or myxoid patterns. We report a case of radiation-induced high-grade myxofibrosarcoma (also known as myxoid MFH) in the chest wall in a 77-year-old woman. The patient was diagnosed with stage IIIA (T3N1bM0) left breast carcinoma (1985) treated with lumpectomy followed by radiotherapy. She had a recurrence in the axillary tail (2000), treated with radical mastectomy and postoperative radiotherapy. In 2008 she presented with a large chest wall tumor with destruction of fifth left rib. She underwent excision of the chest wall tumor with reconstruction and latissimus dorsi flap. Grossly, the excised tumor (7.0 × 2.7 × 2.2 cm) was rubbery white-tan, with focal necrosis and hemorrhage (Figure 141). Histologically, the tumor showed markedly pleomorphic undifferentiated sarcoma with a myxoid background and brisk abnormal mitoses (Figure, B and C). The tumor cells were negative for desmin, pancytokeratin (AE/AE3), Melan A, HMB-45, and S100, with focal scattered SMA positivity. RIS, although rare, is an increased potentially fatal risk and is radiation-dose dependent, mandating careful, long-term follow-up for early detection and treatment.

Atypical Lipomatous Tumor With Myopericytoma/Myofibroma-Like Differentiation
(Poster No. 76)
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Atypical lipomatous tumors (ALT) are well known for having heterologous components. However, an ALT with myopericytoma/myofibroma-like differentiation has not been previously reported. Here we report such a case as the first one in English literature. A 68-year-old man presented with a painful left thigh mass recaitrant to nonoperative treatment. An en bloc resection was performed and a 12 × 8.2 × 3.6-cm mass was removed. Grossly, the mass appeared as an unremarkable adipose tissue containing a 3.5 × 2.0 × 1.8-cm white-tan firm irregular fibrous area. Histologically, the fibrous area resembled myopericytoma/myofibroma, being composed predominantly of perivascular smooth muscle cells arranged in nodules around hyalinized cores. The remainder of adipose tissue showed minimal atypia but variably increased cell size. FISH using a dual-color break-apart probe for the DDT3 (CHOP) locus on 12q13 showed amplification of the telomeric end of the probe only. This region encompasses the CDK4 gene. Subsequent FISH with MDM2 probe on 12q15 also showed amplification. Therefore, a diagnosis of ALT with myopericytoma/myofibroma-like differentiation was rendered. The heterologous component was not high grade, with less than one mitotic figure per 10 high-power fields. In myopericytoma/myofibroma, a translocation (t(7,12)) had been reported. It causes the fusion of ACTB (β-actin) and GLI-1 (glioma-associated oncogene homolog-1). Presumably the fusion gene results in upregulation of GLI-1 and tumor formation. The GLI-1 gene is located in 12q13, the centromeric side of the DDT3 probe. In our case, whether GLI-1 is coamplified or translocated as a secondary event needs to be further investigated.

Amyloidoma of Bone Associated With Chronic Renal Failure and Hemodialysis
(Poster No. 77)
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Amyloidomas of bone are rare lytic lesions due to amylloid deposition. Dialysis related amyloidosis associated with β2 microglobulin deposition has an ostearticular predominance. Described here is an 86-year-old woman with a radiologic “cystic” femoral head lesion who presented after a traumatic fall. Her past medical history is significant for end-stage renal disease, previous diagnosis of membranous glomerular nephritis currently on dialysis, and chronic mycobacterium avium intracellulare pneumonia on treatment. The femoral head contained a 1.5-cm discrete grey rubbery lesion, which microscopically was composed of pink amorphous material associated with scattered histiocytes and rare multinucleated giant cell histiocytes. There was associated destruction of lamellar bone and thinning of adjacent cortical bone, but no frank fracture. The adjacent and distant marrow contained normocellular hematopoietic elements, with all cell lines showing normal maturation. Plasma cells were present in normal numbers and polyclonal, confirmed by CD138, κ, and λ immunohistochemical stains. Lymphocytes were CD3-positive T cells and rare PAX5-positive B cells, without abnormal CD43 expression. The lesion stained strongly positive for CD19, confirming the diagnosis of an amyloidoma. IHC performed on peptides extracted from the bone lesion by microdissec- tion from the paraffin block via liquid chromatography–tandem mass spectrometry detected a peptide profile consistent with β2-microglobulin–type amyloid deposition. This unusual case demonstrates the pathology of amyloidoma of bone in the setting of dialysis and the need for awareness of the entity to enable correct diagnosis and the potential treatment with novel therapies.

Mesenteric Fibromatosis Presenting as Ureteral Obstruction and Hydronephrosis
(Poster No. 78)
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Fibromatosis is a benign, locally invasive tumor that tends to recur. It is seen more commonly in the abdominal wall or in the extremities, usually in older individuals. There is a known association with familial polyposis coli, previous trauma, and hormonal imbalance. Very rarely, mesenteric fibromatosis in younger patients can grow retroperitoneally and encompass the ureter, causing hydronephrosis. Distinguishing this lesion from other fibrosing processes that occur in this location, such as idiopathic retroperitoneal fibrosis, may be difficult clinically. We describe a case of a sigmoid colon mesenteric fibromatosis, which
Myxoid AFH should be included in the differential in a case of myxoid morphologic mimics when there is a predominant myxoid stroma. A plasmacytic infiltrate should be used to differentiate AFH from its pseudocystic spaces, distinct pseudocapsule, and peripheral lymphoplasmacytic cuff. Immunohistochemical studies showed focal positivity for desmin and EMA and diffuse positivity for pankeratin and progesterone receptor; focally positive for pankeratin and desmin; and weakly positive for synaptophysin. The tumor was positive for CD10, vimentin, WT-1, estrogen receptor, and progesterone receptor; focally positive for pankeratin and desmin; and weakly positive for synaptophysin. The tumor was negative for CD117/c-kit, S100, CDX2, mammoglobulin, GCDFP15, and TTF-1. Ki67 analysis showed that the proliferation fraction was 10%–20%. The morphologic and immunohistochemical findings were consistent with a low-grade endometrial stromal sarcoma. In February 2012, the patient underwent total hysterectomy and bilateral salpingo-oophorectomy in our hospital. A second tumor was identified involving the right ovary without capsular involvement, and was positive for CD10 but negative for caldesmon and CD117/c-kit. The tumor morphology was similar to the endometrial stromal sarcoma diagnosed in the mass excised from the colon. There was no evidence of endometrial stromal sarcoma involving the uterus. Overall, our findings are most consistent with 2 separate foci of endometrial stromal sarcoma involving the right ovary and sigmoid colon that most likely arose from foci of endometriosis (Figure 142).

Myxoid Stroma in Angiomatoid Fibrous Histiocytoma: A Diagnostic Pitfall

Cardiac Papillary Fibroelastoma of Pulmonary Valve: A Case Report and Review of Literature

Myxoid Stroma in Angiomatoid Fibrous Histiocytoma: A Diagnostic Pitfall

Coexistent Abdominal Fibromatosis (Desmoid Tumor) and Endometriosis: An Exceedingly Rare Case Report and Review of Literature
scans demonstrated a right rectus sheath mass. Intraoperative pathology assessment was performed, and a diagnosis of endometriosis was rendered. Histologic examination of the permanent sections showed florid endometriosis with cicatricial fibrosis admixed with bundles of spindle cells infiltrating skeletal muscle fibers (Figure 143). Based on the microscopic findings, the differential diagnosis was scar endometriosis versus coexistent endometriosis and abdominal wall fibromatosi.

The diagnosis of fibromatosis was confirmed by diffuse nuclear positivity of the spindle cells for β-catenin by IHC staining. Deep fibromatoses are clonal myofibroblastic proliferations that are prone to aggressive local recurrences. Virtually all deep fibromatoses have somatic β-catenin or adenomatous polyposis coli (APC) gene mutations leading to intranuclear accumulation of β-catenin. To the best of our knowledge, this is the first reported case of coexistent fibromatosis and endometriosis. Considering the impact of the correct diagnosis on patient management and the potential for a missed diagnosis of fibromatosis in a background of florid endometriosis with cicatricial fibrosis, one should be aware of this possibility and the utility of β-catenin IHC staining in difficult cases.

Placental Alkaline Phosphatase in Benign and Malignant Endometrium: Detection and Diagnostic Potential

(Haiyan Chen, MD, PhD; Jingyang Feng, MD; Ian Hughes, MD; Stefan Pambuccian, MD; Xiuzhen Duan, MD, PhD). Department of Pathology, Loyola University Medical Center, Maywood, Illinois.

Context: Placental alkaline phosphatase (PLAP) is a membrane-bound glycosylated dimeric enzyme. It is expressed in some types of normal tissue including placenta and neonatal testis. It is also present in certain types of germ cell tumors, especially seminomas. One study using a cultured cell line demonstrated that PLAP is expressed in endometrial carcinoma cells, but not in normal endometrial cells. To our best knowledge, the immunohistochemical (IHC) profile of PLAP in human benign and malignant endometrial tissues has not been studied.

Our study was to assess the IHC staining pattern of PLAP in benign, hyperplastic, and malignant endometrium.

Design: Four endometrial categories were included in this study, including normal endometrium (n = 67), simple hyperplasia (n = 14), complex hyperplasia (n = 8), and endometrial carcinoma, endometrioid type (n = 41). Immunostain of PLAP using anti-PLAP mouse monoclonal antibody (clone 8A9, Leica) was performed for all the cases with proper positive and negative controls. The results were interpreted by 2 attending pathologists and the data were analyzed. A positive immunostaining result was defined as strong membranous and cytoplasmic staining of at least 10% of epithelial cells. Weak staining, less than 10% positivity in epithelial cells, or only apical staining were interpreted as negative.

Results: See Table.

| The Results of IHC Stains of PLAP in the 4 Endometrial Categories |
|------------------|-----------------|-----------------|-----------------|-----------------|
|                  | Negative <40%   | Positive >40%   | Overall Positivity, % |
| Benign           | 0               | 0               | 0               |
| Simple hyperplasia| 14              | 0               | 0               |
| Complex hyperplasia| 2              | 3               | 75              |
| Endometrial cancer, endometrioid type | 22             | 8               | 11              |

Conclusions: 1. Our study demonstrated that normal endometrium and simple hyperplasia do not express PLAP. 2. PLAP was only identified in complex hyperplasia or endometrial carcinoma. 3. The
differential expression of PLAP in simple and complex (atypical) hyperplasia could reflect their different molecular pathways. PLAP cannot be used as a marker to differentiate complex hyperplasia from endometrial cancer.

Significance of Extramedullary Hematopoiesis in Uterus

(Poster No. 86)

Deepthi Hoskoppal, MD (dhoskopp@uthsc.edu); Raghavendra Pillappa, MD; Louisa Balaz, MD. Department of Pathology and Laboratory Medicine, University of Tennessee Memphis.

Extramedullary hematopoiesis is the production of myeloid and erythroid progenitor cells outside the bone marrow. It is commonly found in liver and spleen. Less than 5% occurs in other organs, including thoracic spinal region, lymph nodes, visceral surfaces and lung. Its presence in uterus is extremely rare and may be associated with myelofibrosis, chronic myeloproliferative disorders, and other hematologic malignancies. A 48-year-old woman presented with irregular uterine bleeding of 6 months’ duration. Imaging revealed uterine fibroid and myometrium showed benign leiomyoma with granulation tissue. Also seen were clusters of erythroid precursors and immature granulocytes in the lesion. At low-power magnification, these small hematopoietic clusters may be overlooked as lymphocytes or histiocytes. Immunostains for CD43 was strongly positive; myeloperoxidase was weakly positive and CD34 was negative. The histologic and immunohistochemical findings were consistent with extramedullary hematopoiesis. Complete blood workup revealed no hematologic abnormalities. Clinically, complete blood workup will assist us to identify underlying hematologic malignancies, even though the vast majority of cases are associated with chronic anemia. Presence of benign isolated foci with no comorbid hematologic disorders should not warrant extensive hematologic workup. The uterine extramedullary hematopoiesis etiology is unclear. Few hypotheses suggest that in leiomyoma, hypoxia may stimulate differentiation of mesenchymal stem cells into hematopoietic cells, which could be aberrantly activated by estrogen signaling pathways. In conclusion, extramedullary uterine hematopoiesis may be in response to diverse changes in the microenvironment.

Invasive Mixed Endocervical and Intestinal Type Adenocarcinoma of the Uterine Cervix in a Patient With Peutz-Jeghers Syndrome

(Poster No. 87)

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Peutz-Jeghers syndrome is a rare autosomal-dominant disorder characterized by the development of hamartomatous gastrointestinal polyps, mucocutaneous melanin deposition, and increased cancer risk. Female patients with this syndrome are at an increased risk for the development of gynecologic malignancies. The cumulative risk for cervical cancer in these patients is 10%, with the most common being adenoma malignum. We describe a case of endocervical adenocarcinoma in a 40-year-old woman with history of Peutz-Jeghers syndrome with STK11 gene mutation. She was followed with pelvic sonography, annual endometrial biopsies, and annual Pap smears in order to screen for gynecologic malignancies. A majority of cases are associated with chronic anemia. Presence of benign isolated foci with no comorbid hematologic disorders should not warrant extensive hematologic workup. The uterine extramedullary hematopoiesis etiology is unclear. Few hypotheses suggest that in leiomyoma, hypoxia may stimulate differentiation of mesenchymal stem cells into hematopoietic cells, which could be aberrantly activated by estrogen signaling pathways. In conclusion, extramedullary uterine hematopoiesis may be in response to diverse changes in the microenvironment.

Clinical Presentation of Uterine Serous Carcinoma in an Urban Setting—A Shift in Paradigm?

(Poster No. 88)

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Context: Emerging evidence has linked obesity with type II endometrial carcinoma, specifically uterine serous carcinoma (USC). The purpose of this study is to evaluate morbidly obese patients with USC.

Design: Women with USC diagnosed from 1996 to 2013 at a single institution were identified in our pathology database. Electronic medical records were reviewed for clinicopathologic information. A pathologist reviewed cases to confirm USC diagnosis. Patients were stratified based on their BMI. Morbidly obese (BMI = 40 kg/m²) patients were compared to those with normal BMI (25 kg/m²).

Results: Included in the study were 140 cases of USC. Seventeen patients (12%) had BMI 25 kg/m² and 27 (19%) had BMI 40 kg/m². Median age at presentation was 70 and 64 years respectively (P = .04). Median survival was 28 months in normal BMI and 21 months in morbidly obese. Majority of the morbidly obese women (78%) presented with early-stage disease at diagnosis (FIGO stage I and II) compared to 35% with normal BMI (P = .01). The background endometrium was predominantly atrophic in both BMI categories, with the only exceptions being 1 normal-BMI and 5 morbidly obese patients, all of whom had proliferative endometrium (P > .05). Other clinicopathologic parameters were not statistically significant (Table).

<table>
<thead>
<tr>
<th>Clinical and Pathologic Parameters</th>
<th>BMI 25 kg/m² (N = 17)</th>
<th>BMI 40 kg/m² (N = 27)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), y</td>
<td>70 (54–91)</td>
<td>64 (40–81)</td>
<td>.04</td>
</tr>
<tr>
<td>Race, %</td>
<td></td>
<td></td>
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<tr>
<td>Black</td>
<td>9 (54)</td>
<td>20 (74)</td>
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<td>White</td>
<td>4 (23)</td>
<td>6 (22)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>4 (23)</td>
<td>1 (4)</td>
<td></td>
</tr>
<tr>
<td>FIGO stage, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>5 (29)</td>
<td>19 (71)</td>
<td>.01</td>
</tr>
<tr>
<td>II</td>
<td>1 (6)</td>
<td>2 (7)</td>
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<tr>
<td>III</td>
<td>7 (41)</td>
<td>4 (15)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>4 (24)</td>
<td>2 (7)</td>
<td></td>
</tr>
<tr>
<td>Early stage (I, II)</td>
<td>6 (35)</td>
<td>21 (78)</td>
<td></td>
</tr>
<tr>
<td>Late stage (III, IV)</td>
<td>11 (65)</td>
<td>6 (22)</td>
<td></td>
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<tr>
<td>Background endometrium, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrophic/nonproliferative</td>
<td>16 (94)</td>
<td>22 (81)</td>
<td>.38</td>
</tr>
<tr>
<td>Proliferative</td>
<td>1 (6)</td>
<td>5 (19)</td>
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<td>Lymphadenectomy, %</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>11 (64)</td>
<td>16 (59)</td>
<td>.76</td>
</tr>
<tr>
<td>No</td>
<td>6 (36)</td>
<td>11 (41)</td>
<td></td>
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<tr>
<td>Lymph node status, %</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Positive</td>
<td>4 (24)</td>
<td>4 (15)</td>
<td>.67</td>
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<td>Negative</td>
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<tr>
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<td>6 (35)</td>
<td>11 (42)</td>
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<tr>
<td>LVSI, %</td>
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<td></td>
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<tr>
<td>Positive</td>
<td>12 (59)</td>
<td>14 (52)</td>
<td>.34</td>
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<tr>
<td>Negative</td>
<td>5 (41)</td>
<td>13 (48)</td>
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<tr>
<td>Survival status, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No evidence of disease</td>
<td>3 (18)</td>
<td>2 (7)</td>
<td>.87</td>
</tr>
<tr>
<td>Alive with disease</td>
<td>9 (53)</td>
<td>19 (70)</td>
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<tr>
<td>Died of disease</td>
<td>2 (12)</td>
<td>0 (0)</td>
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<tr>
<td>Died of other cause</td>
<td>0 (0)</td>
<td>1 (4)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>3 (17)</td>
<td>5 (19)</td>
<td></td>
</tr>
<tr>
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<td>21 (78)</td>
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</tr>
<tr>
<td>Died</td>
<td>2 (12)</td>
<td>1 (4)</td>
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</tr>
<tr>
<td>Unknown</td>
<td>3 (17)</td>
<td>5 (18)</td>
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</tbody>
</table>

Conclusions: Morbidly obese women with USC appear to present at an earlier age and earlier stage compared to normal-BMI women. This may represent differences in accessing medical attention by the 2 groups, resulting in earlier detection. Larger studies are needed to understand the impact of obesity in USC.
Significance of Papillary Proliferation in Endometrial Biopsies: A Clinical Implication

(Poster No. 89)

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Papillary proliferations without malignant nuclear features are less common, can pose a significant challenge in endometrial biopsy interpretation, and can be confused with papillary metaplasia, endometrial hyperplasia, or low-grade serous papillary carcinomas. In the last decade, only 2 papers are published in the literature. We present 2 cases of papillary proliferation with follow-up. A 46-year-old woman presented with abnormal uterine bleeding. The endometrial biopsy showed simple papillae with fibrovascular cores, occasional branching, localized proliferations covered by epithelial cells with bland nuclear features, and mild atypia. Later, subsequent biopsy showed benign secretory endometrium. The second patient was a 52-year-old woman who presented with excessive menstruation. The endometrial biopsy showed simple papillary clusters with minimal atypical cells, followed by hysterectomy demonstrated disorganized proliferative endometrium. None of our patients developed hyperplasia or carcinoma on follow-up. Both patients had localized simple papillae without diffuse proliferation or complex papillae. Mitoses, psammoma bodies, hobnail cells or solid growth pattern were absent. Significant architectural complexity and proliferation has been associated with increased risk of hyperplasia (30%) and endometrioid carcinoma (13%), as reported by Philip PC et al. Hence the distinction between simple and complex papillary proliferation may be difficult in small endometrial samples. Additional tissue consideration for curettage may be helpful to stratify these patients and avoids the risk of unnecessary treatment. Because of persistent disease, follow-up is required to ascertain complete removal of the lesion. In conclusion, papillary proliferations are uncommon lesions, and with simple papillary pattern on an adequate sample are associated with uneventful outcome.

“Pseudomyxoma Endometrii”: Endometrial Deposition of Acellular Mucin from a Low-Grade Appendiceal Mucinous Neoplasm as a Rare Mimic of Myxoid Endometrial Stromal Tumor

(Poster No. 90)

Kristin C. Shaw, BA (kristin.shaw@som.umaryland.edu); Dina Kokh, MD; Paul N. Staats, MD; Paul N. Staats, MD. Department of Pathology, University of Maryland School of Medicine, Baltimore.

Low-grade appendiceal mucinous neoplasms (LAMN) are commonly associated with deposition of mucin, with or without admixed low-grade epithelium, on peritoneal surfaces (pseudomyxoma peritonei). We describe a very rare presentation of LAMN, as extensive mucin deposition within the endometrium of a 43-year-old woman that was mistaken for a primary uterine myxoid neoplasm. The patient underwent endometrial curettage for infertility, which demonstrated abundant myxoid/mucinous material interspersed with small vessels, bland eosinophilic spindled cells, scattered foci of typical endometrial stroma, and occasional endometrioid glands. Immunohistochemical staining showed CD10-positive endometrial stroma and actin-positive eosinophilic spindled cells. The lesion was interpreted as “mucoid/mucinous neoplasm, most likely of smooth muscle/endometrial stromal origin.” Subsequent laparotomy revealed peritoneal mucin in the anterior cul-de-sac and a dilated appendix. Pathologic examination confirmed appendiceal LAMN, multifocal peritoneal mucinosis, and anterior cul-de-sac and a dilated appendix. Pathologic examination of the lesion was interpreted as bland eosinophilic spindled cells, scattered foci of typical endometrial stroma. The lesion was interpreted as mucin rather than myxoid stroma. This is evidenced readily mistaken for a primary uterine myxoid neoplasm, particularly myxoid endometrial stromal tumor. A key to diagnosis is recognition that the material is mucin rather than myxoid stroma. This is evidenced by the absence of embedded stromal cells and presence of myofibroblastic stromal and vascular infiltration associated with organization. Epithelium containing goblet cells is an important clue if present. The presence of rare endometrial glands within the entrapped endometrial stroma suggests that the latter is entrapped rather than neoplastic stroma.

Primary Ovarian Diffuse Large B-Cell Lymphoma in a 15-Year-Old Girl

(Poster No. 91)

Pallavi Khattar, MD (khattarpwcmc.com); Liying Han, MD, PhD; Humayun Islam, MD, PhD. Department of Pathology, New York Medical College at Westchester Medical Center, Valhalla.

Ovarian involvement by non-Hodgkin lymphoma (NHL) is usually secondary, occurring as a part of systemic disease. Primary involvement of ovary by NHL, especially in young patient, is extremely rare. Here we report a rare such case of primary ovarian diffuse large B-cell lymphoma (DLBCL). A 15-year-old girl with no significant past medical history presented with abdominal pain and mild hypertension. Laboratory workup revealed normal findings except very high serum LDH (1245 U/L) and increased CA-125 (934.8 U/mL). Imaging showed very large lobulated heterogeneous pelvic mass of possible ovarian origin. Bilateral salpingo-oophorectomy was performed. Grossly, right and left ovarian masses measured 22 × 13 × 7 and 16 × 11 × 6 cm, weighing 1877 and 540 g, respectively. The external surfaces of both were tan-white and vaguely nodular with intact capsule. Cut section was tan and fleshy with patchy yellowish necrotic areas. Microscopic examination showed diffuse proliferation of large atypical lymphoid cells with areas of necrosis almost entirely replacing the ovaries. Focal residual ovarian tissue with extensive surrounding ovarian and mesenteric fat deposition was also present. The diagnosis of primary diffuse large B-cell lymphoma of ovarian origin was made.

Utility of Stromal P16 Expression for Distinction of Endometrial Polyp With Atypical Hyperplasia From Atypical Endometrial Hyperplasia and Carcinoma: A Case Report and Review of Literature

(Poster No. 93)

Reza Nejati, MD (rnejati@uthsc.edu); Pillappa Raghavendra, MD; Nadeem Zafar, MD; Louisa Balazs, MD. Department of Pathology, University of Tennessee, Memphis.

Mammary-like glands, formerly referred as an ectopic breast tissue, can be found in the skin of the anogenital area. Mammary-like glands can undergo all benign and malignant changes identical to those in the breast. Ductal and lobular carcinoma, mucinous adenocarcinoma, phyllodes tumors, and fibroadenoma have all been reported in the literature. Less than 30 cases of invasive mammary-like carcinoma have been described to date, with only a few reports of ductal carcinoma in situ. We report a case of ductal carcinoma in situ arising from mammary-like glands of vulva in a 40-year-old woman. The patient presented with a 2-year history of an enlarging superficial nodule within the central-medial aspect of the right labium majus. A needle biopsy revealed a well-differentiated papillary adenocarcinoma, followed by wide local excision. Final pathology showed mass forming lesion measuring 1 cm, composed of dilated ducts lined by markedly atypical epithelium in a papillary configuration; however, no evidence of invasion was present, as demonstrated by preservation of p63-positive myoepithelial layer. The ductal epithelium showed positive staining for estrogen and progesterone receptor and GCDFP-15, supporting mammary phenotype. Given the noninvasive nature of the lesion, the patient was instructed to follow up in 3 months. Carcinoma arising in mammary-like tissue of the vulva is rare and it must be distinguished from other cutaneous and adnexal carcinomas. Because of rarity of this tumor, there are no treatment and follow-up recommendations, and they are extrapolated from breast cancer guidelines.
Endometrial polyp is a common gynecologic lesion. Although the histopathologic diagnosis of an endometrial polyp on a hysterectomy specimen is straightforward, it can be difficult to differentiate a polyp from endometrial hyperplasia or a fragmented biopsy or curettage specimen. The diagnosis can be particularly challenging in endometrial polyp cases with complex or atypical hyperplasia. As Winkler et al have reported, endometrial polyps are commonly diagnosed as endometrial hyperplasia. Recently, stromal p16 expression has been proposed as a useful marker for the diagnosis of endometrial polyp. According to a study by Suzuko Moritani et al, stromal p16 expression was seen in 31 cases of endometrial polyps (89%), but in only 1 case of endometrial hyperplasia (3%). We present a case of endometrial polyp in a 45-year-old woman with features of complex atypical hyperplasia, originally thought to be a possible endometrial atypical hyperplasia. In this case, we utilized p16 immunostain to confirm our diagnosis. The stromal cells were strongly positive for p16 IHC stain. We also reviewed p16 immunostain in previously diagnosed cases of atypical endometrial hyperplasia (2 cases) and endometrial carcinoma (3 cases). As the aforementioned study has described, in contrast to endometrial polyp, the stromal cells were only focally or weakly positive in all 5 endometrial hyperplasia or carcinoma cases we reviewed. In summary, p16 immunostain is a possible useful tool to make the correct diagnosis in difficult endometrial polyp cases that are associated with malignancy or atypical hyperplasia.

The Increasing Frequency of Bilateral Salpingectomy in Patients With Benign Gynecologic Conditions

(Boster No. 94)

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Context: At our tertiary academic center we are seeing increased numbers of bilateral salpingectomy (BS) specimens from patients with benign gynecologic conditions who are not at increased risk of ovarian or fallopian tube (FT) cancer. Our aim was to quantify the recent increase in BS rate in non-high-risk patients and consider how this has impacted workload in the pathology laboratory.

Design: Our database was searched for all hysterectomies performed from January to June 2007 and July to December 2012. Exclusion criteria included clinical history of gynecologic malignant and premalignant lesions, abnormal mass, BRCA mutation, and strong family history of breast or ovarian cancer. Reports were reviewed to determine hysterectomy indications, pathology identified in uterus and FTs, and number of FT blocks submitted.

Results: Of the 142 hysterectomies from 2007, 38 cases had BSs (26.8%). Of the 131 hysterectomies from 2012, 52 had BSs (39.7%). This increase in BS rate was statistically significant (P = .03, Fisher exact test). The number of FT blocks submitted per hysterectomy was 38% greater in 2012 (0.87) than in 2007 (0.63). The most common indications were symptomatic uterine fibroids and uterine prolapse. The FT pathology identified included paratubal cysts, salpingitis, endometriosis, plical fibroids, adenomyosis, hydrosalpinx, serous borderline, and Krukenberg tumor. No serous tubal intraepithelial carcinomas or serous tubal intraepithelial lesions were found.

Conclusions: The FT theory of ovarian serous carcinogenesis has impacted the management of non–high-risk gynecologic patients and increased the number of FT slides being reviewed by pathologists. No serous tubal intraepithelial lesions or serous tubal intraepithelial carcinomas were identified in these non–high-risk patients.

Ovarian Ectopic Pregnancy in a Patient With Previous Bilateral Salpingectomies

(Boster No. 95)

Eric L. Cochran, MD1 (eric.cochran@downstate.edu); Sadia Khan-daker, MD2; Mohamed Abdulla, MD1. Departments of 1Pathology and 2Gynecology, Kings County Hospital, Brooklyn, New York.

Ectopic pregnancy in the ovary is one of the rarest forms of extrauterine pregnancy and its pathogenesis is not well understood. Risk factors include endometriosis, pelvic inflammatory disease, and intrauterine contraceptive devices. We present a case of a 32-year-old woman with multiple adhesions and abdominal pain. Her β-human chorionic gonadotropin was elevated (880 mIU/mL) and sonogram showed intrauterine hemorrhage with a left ovarian complex mass. The patient underwent exploratory laparotomy with excision of the left ovarian tissue. Within the removed tissue, trophoblasts were identified inside a hemorrhagic ovarian corpus luteum cyst of early pregnancy consistent with a diagnosis of ovarian ectopic pregnancy. Interestingly, she had previously undergone bilateral salpingectomies for ectopic pregnancies on 2 different occasions, once in the right fallopian tube (2007) and once in the left fallopian tube (2009). It is rare for patients to have multiple ectopic pregnancies and when it happens a reproductive abnormality is typically identified. The rare occurrence of pregnancy in the ovary suggests that with potential for recurrence previous tubal ectopic pregnancies may have played a role through the inflammation and promotion of adhesions that kept the ovary in proximity to the remnant portion of the fallopian tube. Spontaneous recanalization may have allowed for fertilization of an ovum that either: (1) remained in the ovary or (2) was pushed back towards a corpus luteum cyst. The pathogenesis of ectopic extrauterine pregnancies remains poorly understood; however, prior salpingectomy for previous ectopic pregnancies appears to be an important risk factor.

Influence of Vascularity and Immunohistochemical Expression of Clotting and Angiogenesis Factors on Risk of Venous Thromboembolism in Cancer Patients

(Poster No. 96)

Cory J. Broehm, MD1 (cbroehm@salud.unm.edu); Li Luo, PhD2; Ian Rabinowitz, MD2; David Garcia, MD3; Therese Bocklage, MD, Department of 1Pathology and 2Internal Medicine, Hematology and Oncology, University of New Mexico School of Medicine, Albuquerque; 3Department of Clinical and Translational Science Center, University of New Mexico Health Sciences Center, Albuquerque; 4Department of Medicine, Division of Hematology, University of Washington School of Medicine, Seattle.

Context: Venous thromboembolism (VTE) occurs in patients with all types of cancer. Causes and predisposing factors are largely unknown. We evaluated vascularity and expression of clotting and angiogenesis factors by immunohistochemistry in tumors of cancer patients with and without VTE to determine associations with thrombosis development.

Design: Cases from 30 cancer patients with VTE and 30 cancer patients without VTE were retrieved and matched for age, gender, tumor category (primarily gynecologic, breast, male genitourinary, gastrointestinal, and skin), and tumor grade. Microarrays were prepared, consisting of 2-mm punches from center and edge (where available) of formalin-fixed paraffin-embedded tumor sections taken from each patient. Microarrays were stained with H&E and antibodies to the clotting factors noncryptic tissue factor (L. Vijaya Rao, University of New Mexico) and cryptic tissue factor (Santa Cruz Biotechnology, Dallas, Texas) and the angiogenesis drivers VEGF1 and VEGF2 (Dako, Carpinteria, California) and Vessel counts were scoring for presence, extent, and intensity of antibody staining for each punch was performed by 2 pathologists blinded to clinical data and thrombosis outcome.

Results: Statistical analysis revealed no association of development of VTE with patient age or gender, tumor type, or tumor grade. Vascularity and expression and intensity of staining of cryptic and noncryptic tissue factor, VEGF1, VEGF2, and VEGF2 did not show a significant association with VTE (P > .05).

Conclusion: In this study, VTE in cancer patients was not associated with increased vascularity or increased expression of cryptic or noncryptic tissue factor, VEGF1, or VEGF2, as measured by immunohistochemistry.

Adult Ovarian Granulosa Cell Tumor With Anaplastic Features

(Poster No. 97)

Maryna Tarbunova, MD (maryna.tarbunova@jax.ufl.edu); Raafat Makary, MD. Department of Pathology, University of Florida, Health Science Center, Jacksonville.

Ovarian granulosa cell tumors are rare sex-cord neoplasm derived from granulosa cells. Adult granulosa cell tumor (AGCT) is a low-grade neoplasm with potential for recurrence and metastases and overall good prognosis. These tumors are composed of small, bland, polygonal monomorphic cells with prominent grooves (“coffee bean”) arranged in different patterns and low mitotic count (rarely >1-2/10 high-power fields). We report a rare case of adult granulosa cell tumor with anaplastic features. A 41-year-old woman presented with abdominal pain. Magnetic resonance imaging showed a large complex mass in the left ovary. The removed mass (19 × 18 × 11 cm) was well-encapsulated, soft, fleshy, and gray-tan with solid, cystic, and necrotic areas with hemorrhage on cut surface (Figure 144). Histologically the
tumor architecture was consistent with that of AGCT (microfolliculosis with Call-Exner bodies, macrofolliculosis, insular, trabecular, watered-silk, cystic, and solid patterns). However, tumor cytomorphology was unusual for the high-grade nuclear atypia, marked pleomorphism, brisk and abnormal mitoses (up to 16 mitoses per 1 high-power field), necrosis, and lack of prominent nuclear grooving. The tumor was positive for inhibin, calretinin, CD56, and CKAE1/AE3 (punctate pattern), weakly positive for EMA in rare cells, and negative for CK7, synaptophysin, and chromogranin. The tumor histology and immuno-stain profile were consistent with the diagnosis of AGST (pT1aNx) with synaptophysin, and chromogranin. The tumor histology and immunohistochemistry were consistent with the diagnosis of AGCT (pT1aNx) with synaptophysin, and chromogranin.

The age range of patients was 50–90 years (median 65). The common clinical presentation was postmenopausal bleeding. Serous carcinoma was confined to polyps in 20 cases (16%). The preoperative EMB/EMC diagnoses are shown in the Table. 75% of cases had abundant material for diagnoses while 25% had a very limited sample, causing diagnostic difficulty. In the latter scenario, the most useful histologic features predictive of serous carcinoma included glandular cells with marked nuclear pleomorphism, tight papillae structure, and necrotic debris. Positive p53 immunostain was observed in one third of the cases. The most common pitfalls included (1) incorrectly designating samples as nondiagnostic, (2) mistaking them as reactive atypia, and (3) misclassifying them as low-grade endometrioid adenocarcinoma owing to the villoglandular architecture (10% of cases).

Conclusions: Our study demonstrated that certain histologic features are highly predictive of malignancy, including rare pleomorphic cells, small papillae, and necrotic debris. In an otherwise scant endometrial sample, these are strong indicators for serous carcinoma in postmenopausal bleeding patients.

### Table: Preoperative EMB/EMC Diagnoses for Patients With Serous Carcinoma

<table>
<thead>
<tr>
<th>EMB/EMC Dx Cases, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-grade carcinoma or serous carcinoma 94 (75)</td>
</tr>
<tr>
<td>Endometrioid adenocarcinoma (grade 1 or 2) 10 (8)</td>
</tr>
<tr>
<td>Atypical complex hyperplasia 2 (2)</td>
</tr>
<tr>
<td>Rare atypical cells present 14 (11)</td>
</tr>
<tr>
<td>Insufficient tissue for diagnosis 3 (2)</td>
</tr>
<tr>
<td>Benign 2 (2)</td>
</tr>
</tbody>
</table>

### Evaluation of Histologic Features Predictive of Serous Carcinoma in Scant Endometrial Samples: A Study of 125 Patients

(Poster No. 99)

Parvian Ahmadi Moghaddam, MD (parvian.ahmadi@moghadam@umassmemorial.org); Ali Sakhdari, MD, MSc.; Dina Kandil, MD; Yuxin Liu, MD, PhD. Department of Pathology, University of Massachusetts, Worcester.

Context: Endometrial serous carcinoma tends to occur in elderly patients. When encountering scant endometrial biopsy/endometrial curettage (EMB/EMC) samples, diagnosing this entity can be a challenge. We studied 125 cases with the goal of finding histologic features highly predictive of serous carcinoma in scant samples.

Design: The demographic features of 125 patients were collected. Specimens from their preoperative EMB/EMC as well as postoperative hysterectomy slides were reviewed.

Results: The age range of patients was 50–90 years (median 65). The common clinical presentation was postmenopausal bleeding. Serous carcinoma was confined to polyps in 20 cases (16%). The preoperative EMB/EMC diagnoses are shown in the Table. 75% of cases had abundant material for diagnoses while 25% had a very limited sample, causing diagnostic difficulty. In the latter scenario, the most useful histologic features predictive of serous carcinoma included glandular cells with marked nuclear pleomorphism, tight papillae structure, and necrotic debris. Positive p53 immunostain was observed in one third of the cases. The most common pitfalls included (1) incorrectly designating samples as nondiagnostic, (2) mistaking them as reactive atypia, and (3) misclassifying them as low-grade endometrioid adenocarcinoma owing to the villoglandular architecture (10% of cases).

Conclusions: Our study demonstrated that certain histologic features are highly predictive of malignancy, including rare pleomorphic cells, small papillae, and necrotic debris. In an otherwise scant endometrial sample, these are strong indicators for serous carcinoma in postmenopausal bleeding patients.

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</tr>
</tbody>
</table>

### Malignant Mixed Müllerian Tumor of the Fallopian Tube With Synchronous Serous Adenocarcinoma of the Uterine Cervix

(Poster No. 98)

George A. Tijonas, MD (g.tijonas@med.miami.edu); Mehrdad Nadji, MD. Department of Pathology, Jackson Memorial Hospital, Miami, Florida.

A 61-year-old woman presented to the emergency department with vaginal bleeding. She gave the history of pelvic pain and intermittent postcoital bleeding of 6-month duration. She underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, and pelvic and para-aortic lymph node excision. Microscopic examination revealed a low-grade papillary serous adenocarcinoma of the cervix, 4.0 × 2.0 cm, that invaded the cervical wall to a depth of 0.9 cm. The endometrial cavity was not involved (pT1b1). Bilateral ovaries and peritoneal biopsies, and omentum were negative. The patient was treated with postoperative radiation and combination chemotherapy of carboplatin and taxol. She is free of disease at 6-month follow-up. MMMT of the fallopian tube is an uncommon tumor, with about 80 cases reported in the literature. To evaluate the prognosis of AGCT and MMMT, we examined the cases.

### Cervical Uterine Epithelioid Sarcoma, Proximal Type: An Unusual Location for a Rare Tumor

(Poster No. 100)

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Epithelioid sarcoma is an unusual malignant mesenchymal neoplasia with epithelioid appearance that accounts for 0.6% to 1% of the sarcomas. There are 2 subtypes, the classic seen in adolescents or young adults located in the extremities, and the proximal type that is seen in older patients located in the deep soft tissues of pelvic girdle, perineum, and genital area with more aggressive course. We report a 23-year-old woman who presented with abnormal vaginal bleeding and a mass protruding through the cervix that was initially misdiagnosed as hemangiopericytoma. Later on the cervical mass recurred and an epithelioid malignant neoplasm that was positive for EMA and AE1/ AE3 and negative for smooth muscle markers, HMB-45, p16, HMWK, and p63 with loss of INI-1 expression was consistent with epithelioid sarcoma of the proximal type. Imaging studies did not show evident mass. To our knowledge this is the third case of primary epithelioid sarcoma involving the cervical uteri.
Benign Cystic Mesothelioma Associated With Ipsilateral Renal Agenesis in an Adult Male
(Poster No. 101)

Diana Murro, MD1 (diana.murro@rush.edu); Aparna Harbhajanka, MD1; Brett Mahon, MD1; Daniel Deziel, MD, MD2. Departments of 1Pathology and 2Surgery, Rush University Medical Center, Chicago, Illinois.

Benign cystic mesothelioma (BCM) is a rare peritoneal lesion that usually occurs in reproductive-age females with a history of abdominal surgery or other source of injury. Reports of estrogen and progesterone receptor expression in these cells may explain a predilection for women, and regression after tamoxifen treatment has been reported. BCM cases in males are very rare. We describe an unusual case of BCM associated with ipsilateral renal agenesis in a 26-year-old man without any prior surgical history. The cyst lining stained positively for cytokeratin 5, Wilms tumor-1, epithelial membrane antigen, and estrogen and progesterone receptor receptor, and negatively for PAX8, supporting the diagnosis of BCM. No recurrence was noted at 3-week follow-up. Though previous studies have tested specimens from both sexes for hormone receptor expression, no other cases involving men have been reported with estrogen receptor and progesterone receptor positivity. Only 3 cases of BCM associated with various congenital renal anomalies have been reported, and all occurred in pediatric patients. To the best of our knowledge, this is the first report of BCM associated with ipsilateral renal agenesis in an adult male. Such a case suggests the presence of congenital anomalies should be considered in patients with BCM, and previous studies have postulated that BCM may have a developmental origin.

Umbilical Cord Hemangioma Versus Other Vascular Lesions: A Comparative Clinicopathologic Study
(Poster No. 102)

Xiaoyan Liao, MD, PhD (xliao@ucsd.edu); Mana Parast, MD, PhD. Department of Pathology, University of California, San Diego, La Jolla.

Umbilical cord tumors are extremely rare. Hemangioma of the umbilical cord is a benign vascular tumor associated with congenital anomalies and increased perinatal mortality. Differential diagnoses include angiomyxoma, hematoma, and aneurysm. We report a case of umbilical cord hemangioma and a case of umbilical cord organizing hematoma/dissecting aneurysm to compare these 2 entities clinically and histologically. The case of umbilical cord hemangioma was diagnosed in a full-term female neonate born to a 31-year-old G1P0 mother with umbilical cord hemorrhage discovered on prenatal sonography. Surgical repair of the omphalocoele after birth identified an urachal cyst tracing down to the bladder. Histologic examination revealed a 3-veined umbilical cord associated with small capillary-type vascular proliferation positive for factor VIII immunostaining, consistent with hemangioma (Figure 145, A). In the second case, a large umbilical cord mass with a highly vascular solid cord partially clinically suggestive of hemangioma or angiomyxoma was discovered on prenatal ultrasonography in a 42-year-old G4P2 mother with elevated amniotic fluid AFP level. Other abnormalities in the fetus detected by ultrasonography included the absence of bladder, hypoplastic lower extremities, enlarged heart, and separation of amnion from chorion. Fetal demise occurred at 21 weeks. Histologic examination revealed small pools of blood in the umbilical cord dissecting through the Wharton jelly with no endothelial lining (Figure, B), as confirmed by negative factor VIII staining. This led to a diagnosis of organizing hematoma or dissecting aneurysm, instead of hemangioma. Our work highlights the importance of histopathologic examination in correlation with ultrasound imaging and clinical presentations.

Malignant Mixed Mullerian Tumor of the Ovary Arising in a Background of Atypical Endometriosis
(Poster No. 103)

Atin Agarwal, MD (aagarwal@bcm.edu); Nishant Tiwari, MD; Ramya Masand, MD. Department of Pathology, Baylor College of Medicine, Houston, Texas.

Malignant transformation, particularly carcinomas, arising in endometriosis is extremely rare and usually occurs after estrogen replacement therapy. We present the case of a 53-year-old woman with history of increasing abdominal girth of 6 months’ duration. Past history was significant for abdominal hysterec-tomy and unilateral salpingo-oophorectomy for symptomatic endometrioid uterus. Computed tomography scan of the abdomen revealed a complex cystic lesion with a mural nodule in the pelvis. She underwent exploratory laparotomy with excision of the mass, staging biopsies, and omentectomy. Pathologic findings demonstrated a 720-g, 20×16×6.5-cm mass that was predominantly cystic with mucoid, necrotic contents, and a 6-cm friable mural nodule. Microscopy revealed a carcinosarcoma arising in an endometriotic cyst with atypical lining epithelium. The tumor was composed of homologous sarcoma (80%) and undifferentiated carcinoma (20%). A microscopic focus of metastatic carcinoma was found in the omentum. The patient had an unremarkable postoperative course and is currently undergoing 6 cycles of chemotherapy. It is estimated that up to 1% of women with endometriosis will develop endometriosis-associated neoplasms (EANs), most being carcinomas. Although ovary is the most common site for EAN, carcinosarcoma arising in an endometriotic ovarian cyst is extremely uncommon. Our patient had no previous history of endometriosis or unopposed estrogen use, a known risk factor for development of endometriosis and EAN. In summary, we report a carcinosarcoma arising in atypical endometriosis of the ovary with no known estrogenic stimulus, which to our knowledge has not been reported previously in the literature.

ARID1A Expression in Uterine Carcinosarcomas
(Poster No. 104)

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Context: ARID1A is a novel tumor suppressor in endometrial carcinoma. However, its role in malignant mullerian mixed tumor (MMMT)/carcinosarcoma is unclear. This study characterized the expression of ARID1A in uterine carcinosarcomas.

Design: Immunohistochemistry using an ARID1A antibody was performed on 54 cases of carcinosarcomas.

Results: Of these, 47 cases showed strong and diffuse ARID1A expression (high expression), and 7 cases showed lost or low expression (low expression), in which both carcinomatous and sarcomatous components showed low expression. Of the cases with high expression, 21 had higher tumor stages (T2-T4) and 26 had lower tumor stages (T1); of the cases with low expression, 6 had homologous sarcomatous component, but is not correlated with lymphovascular invasion, lymph node metastasis, or tumor stage.

Conclusions: ARID1A is lost or has low expression in some MMMT cases, in which both carcinomatous and sarcomatous components showed low expression. The low expression of ARID1A is correlated with homologous sarcomatous component, but is not correlated with lymphovascular invasion, lymph node metastasis, or tumor stage.

Monoclonal PAX-8 in Mucinous Ovarian Tumors: A Study of 59 Cases of Primary and Metastatic Tumors
(Poster No. 105)

Chengbao Liu, MD1 (chengbao.liu@stonybrookmedicine.edu); Bryan Harmon, MD; Kenneth Shroyer, MD, PhD1; Mallory Korman, BS1; Sonya Hwang, MD; Michael Pearl, MD; Melissa Henrietta, MD; Carmen Tornos, MD1. Departments of 1Pathology and 2Gynecology, Stony Brook University Hospital, Stony Brook, New York.

Monoclonal PAX-8 in Mucinous Ovarian Tumors: A Study of 59 Cases of Primary and Metastatic Tumors
**PAX8 Immunohistochemical Staining in Mucinous Neoplasms Involving Ovary: A Critical Evaluation Including Comparison of Monoclonal Versus Polyclonal Antibodies**

(Poster No. 107)

Seema Khutti, MD (sdkhutti@yahoo.co.in); Pamela Necomb, BA, HT; Jason Burghardt, HT; Srinivas Mandavilli, MD. Department of Pathology, Hartford Hospital, Hartford, Connecticut.

**Context:** Distinction of primary mucinous tumors of ovary (PMO) from metastatic carcinoma involving ovary (MCO) is challenging. Immunohistochemical (IHC) stains including PAX8 have been recently used to aid in differential diagnosis. The aims of this study were (1) to evaluate PAX8 IHC expression in MCO particularly from the lower GIT; and (2) to compare staining patterns of the monoclonal (MC) versus polyclonal (PC) antibody (AB).

**Design:** From the pathology database we retrieved 25 MCOs (2 stomach, 1 jejunum, 7 appendix, 10 colon, and 5 clinically unknown but suggestive of primary GIT, on the basis of other IHC findings), 10 PMOs, and 1 primary mucinous carcinoma of ovary. PAX8 IHC staining using MC and PC AB was performed and nuclear staining was evaluated.

**Results:** One of 25 MCOs showed PAX8 nuclear positivity (50%) and 1 case of primary ovarian mucinous carcinoma was negative. Endocervical type of PMO showed diffuse strong staining, and the intestinal-type PMO showed variable degrees of staining (Table).

**Conclusion:** (1) Most MCOs (96%) were negative for PAX8 and the 1 positive case showed less than 5% staining. (2) The sensitivity of PAX8 for diagnosing PMO is low (63.6%), particularly in the intestinal-type PMO, but any nuclear positivity is strongly suggestive of this diagnosis over MCO. (3) PC AB for PAX8 is very difficult to assess owing to the background cytoplasmic staining, unlike the MC AB, which can be evaluated without ambiguity even on low-power microscopic evaluation.

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**Limited Endometrial Samples From Patients ≥60 Years of Age: A Study of 1780 Cases**

(Poster No. 106)

Ali Sakhdari, MD, MSc (ali.sakhdari@umassmemorial.org); Par- nian Ahmadi Moghaddam, MD; Dina Kandil, MD; Yuxin Liu, MD, PhD. Department of Pathology, University of Massachusetts, Memorial Medical Center, Worcester.

**Context:** Postmenopausal bleeding is highly suggestive of endome-trial adenocarcinoma. Elderly patients generally yield limited samples from endometrial biopsy or curettage. To date, there are no published diagnostic criteria for adequacy of endometrial samples, especially regarding those from the elderly. We studied 1780 endometrial samples from patients ≥60 years with the aim of establishing the lower limit of adequacy. We followed up these patients for 1 year to determine the risk of missing malignancy in limited endometrial samples.

**Design:** Our institute database (2005–2010) was searched. The patients’ follow-up data were extracted from medical records. Histologic slides were reviewed.

**Results:** Of the samples, 267 (15%) were classified as nondiagnostic; 979 (55%) as atrophic; 214 (12%) as proliferative, hyperplastic, or polyp; and 320 (18%) as malignant. The nondiagnostic samples ranged from 0 to 10 atrophic endometrial strips. Subsequently, 96 patients (36%) with nondiagnostic samples underwent a second biopsy and 18 (7%), a hysterectomy. Malignancy was detected in 10% of them. Among 979 atrophic samples, 84% were composed of 10 to 30 endometrial strips and 16% of >30 strips. None of these patients developed endometrial cancer within the 1-year follow-up. Among 320 malignant cases, 75% had abundant material for diagnoses, while 25% had very limited sample, causing certain diagnostic difficulty.

**Conclusion:** Our study proposes ≥10 PAX8 mononal antibody endometrial strips as the lower limit of adequate sample for elderly patients. Samples consisting of ≥2 strips should be sufficient in the diagnosis of benign or malignant conditions. Samples <10 strips cannot confidently exclude malignancy. In such cases, repeating the sampling procedure is warranted.

**Human Papilloma Virus mRNA In Situ Hybridization: A Novel Approach to Differentiating Cervical and Endometrial Adenocarcinoma on Cervical Biopsy**

(Poster No. 108)

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**Context:** The presence of adenocarcinoma on cervical biopsy can pose a dilemma for the pathologist: did the cancer arise in the cervix or did it arise in the endometrium and “fall” to the cervix? In cases of ambiguous morphology, polymerase chain reaction for human papili- loma virus (HPV) and immunohistochemical stains are techniques commonly used to answer the question of tumor origin. However, polymerase chain reaction is expensive and requires fresh tissue, while multiple immunohistochemical stains are costly and often inconclusive. HPV mRNA in situ hybridization (ISH) is a potential highly sensitive and specific and cost-effective method for differentiating cervical adenocarcinoma, which is commonly HPV related, from endometrial adenocarcinoma, which is not.

**Design:** An in-house 5-year retrospective search for cervical biopsy cases with a diagnosis of adenocarcinoma of unclear origin was performed. All cases had subsequent resection specimens in which the...
A Case of Uterine Lipofuscinosis in a Patient With Progressive Cerebellar Ataxia and Dystonia

(Poster No. 109)

Lifang Liu, MD (liuf@ucmail.uc.edu); Ady Kendler, MD. Department of Pathology, University of Cincinnati, Ohio.

Lipofuscinosis is a rare condition with excessive accumulation of lipopigments (lipofuscin) in tissue. More commonly, it is seen in neuronal cells (neuronal ceroid lipofuscinosis). Rare cases of lipofuscinosis in liver, intestine (brown bowel syndrome), and kidney have been found in literature. Here we report a case of lipofuscinosis in the uterus. A 36-year-old woman with progressive dystonia and cerebellar ataxia for the past 23 years and menorrhagia and dysmenorrhea for the past 12 years had a hysterectomy. Grossly, the uterus (72 g, 8.5 cm) showed marked brown discoloration in the endomyometrium. Microscopically, the light brown green granular pigments are seen in smooth muscle cells. Adenomyosis and endometriosis were ruled out. Iron and copper special stains are negative. Uterine lipofuscinosis is extremely rare. By literature search, to date, only 2 cases have been reported: I is related to vitamin E deficiency and I is associated with brown bowel syndrome and Friedreich ataxia. The etiology of uterine lipofuscinosis remains unclear. It may be related to vitamin E deficiency, which leads to mitochondrial myopathy in smooth muscle cell, which may explain at least partially the intestinal symptoms in brown bowel syndrome and menorrhagia. Vitamin E deficiency can be secondary to malabsorption. However, isolated vitamin E deficiency was also reported in a case with progressive spinocerebellar syndrome, which was improved upon the correction of the deficiency. This patient had no gastrointestinal symptoms and there is no serum vitamin E report so far. Serum vitamin E level should be recommended (Figure 146).

Adenocarcinoma In Situ of Cervix Versus Tubal Metaplasia: p16 Immunohistochemical Staining Pattern Not Useful Anymore

(Poster No. 110)

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Context: p16 immunostain positivity is a known helpful tool in differentiating between cervical adenocarcinoma in situ (strong diffuse) and its histopathologic mimic, tubal metaplasia (weak or strong focal). The objective of this study was to determine any overlap between the staining patterns of these 2 entities.

Design: In this IRB-approved HIPAA-compliant retrospective study (September 2011–September 2013), 132 cervical samples (biopsies, LEEP, and hysterectomies) with p16 staining were retrieved. These were reviewed in consensus by 2 pathologists. Cases in which diagnosis of AIS or tubal metaplasia could be confidently made were included in the study. Indeterminate cases and all other diagnoses were excluded. Subsequently, the same pathologists, in random order, reviewed p16 slides for all included cases and classified them as diffuse or focally positive, strong or weakly positive, and negative. Correlation with the histopathologic diagnosis was made. Rate of strong diffuse positivity in AIS and tubal metaplasia was compared by using Fisher exact test.

Results: Of 132 patients (cervical sampling, p16 performed), 17 had tubal metaplasia and 10 had AIS. Of these 17 cases of tubal metaplasia, p16 positivity was strongly diffuse in 5 (29.4%), strongly focal in 3 (17.6%), and negative in 9 cases (53%). None of them showed weak diffuse or weak focal positivity. All 10 cases (100%) of AIS showed strong diffuse p16 positivity. Also, AIS more frequently showed strong diffuse p16 positivity ($P < .001$).

Conclusion: Significant proportion of cases of tubal metaplasia showed strong and diffuse p16 positivity. It is important to consider this benign mimic while assessing p16-positive cervical samples.

Benign Multicystic Peritoneal Mesothelioma Presenting as an Adnexal Mass and Mimicking Diffuse Intra-abdominal Malignancy

(Poster No. 111)

Amber A. Berning, MD (amber.berning@ucdenver.edu); Miriam D. Post, MD. Department of Pathology, University of Colorado, Aurora.

Benign multicystic peritoneal mesothelioma (BMPM) is a rare intra-abdominal neoplasm with a strong predilection for females of reproductive age, and is more common in patients with prior abdominopelvic operations, endometriosis, or pelvic inflammatory disease. Although generally indolent, there is a high local recurrence rate with incomplete excision, and rare cases of malignant transformation have been reported. BMPM often presents with abdominal or pelvic pain and is most commonly discovered incidentally on imaging studies. We report 2 cases of women who presented with adnexal masses, and upon exploratory laparotomy, were found to have diffuse, small, cystic nodules throughout the abdomen. Intraoperatively, these lesions were concerning for a malignant process, although frozen section revealed multiple bland-appearing cysts. Final pathology revealed multiple peritoneal cysts lined by 1 to several layers of bland mesothelial cells lacking complex architecture, mitotic activity, or infiltration, diagnostic for BMPM. One patient had a concurrent mucinous borderline tumor, while the other patient’s sole disease process was BMPM. Both patients are currently alive and following up with surgical oncology. Although BMPM is rare, it should be considered in the differential diagnosis of adnexal masses. While the diffuse nature of the disease may mimic intra-abdominal spread of a malignant neoplasm, classical staging procedures for ovarian malignancies are not indicated. It is therefore important to differentiate BMPM from other lesions, as BMPM has the tendency to recur if incompletely excised and may require additional treatment such as cytoreductive surgery and peritonectomy.

PAX8 and PAX2 Expression in Benign and Glandular Cervical Lesions

(Poster No. 112)

Pallavi Khatkar, MD1 (kkhattarp@wcmc.com); Puneet Bedi, MD2; Living Han, MD, PhD3; Minghao Zhong, MD, PhD. 1Department of Pathology, New York Medical College at Westchester Medical Center, Valhalla; 2Department of Internal Medicine, Lincoln Medical and Mental Health Center, Bronx, New York.

The objective of this study was to determine any overlap between the staining patterns of these 2 entities.
Leiomyosarcoma of the Broad Ligament: A Rare Highly Malignant Tumor

Context: PAX8 and PAX2 are transcription factors critical to Mullerian system organogenesis and are commonly expressed in ovarian and uterine epithelial neoplasms. However, the immunohistochemical (IHC) results published on PAX8 and PAX2 expressions in uterine cervical lesions are more variable and difficult to interpret owing to the limited number of cases that have been investigated. Therefore, we systemically evaluated the expression of PAX8 and PAX2 in different cervical lesions.

Design: We collected cases of cervical adenocarcinoma in situ (n = 11), invasive adenocarcinoma (n = 8), squamous cell carcinoma in situ (n = 15), and invasive squamous cell carcinoma (n = 27). PAX8 and PAX2 IHC stains were used on tissue microarray sections and results were evaluated for nuclear expression.

Results: PAX8 was positive in 11 of 11 adenocarcinomas in situ (100%) and 5 of 8 invasive adenocarcinomas (62.5%), whereas PAX8 was focally weakly positive in 2 of 11 adenocarcinomas in situ (18.18%) and 0 of 8 adenocarcinomas (0%). Both PAX8 and PAX2 were completely negative in all squamous cell carcinomas in situ and squamous cell carcinomas. In benign epithelium and lesions, PAX8 and PAX2 were positive in all glandular components and negative in squamous component.

Conclusions: (1) PAX8 and PAX2 were positive only in benign and neoplastic glandular component; and negative in benign and neoplastic squamous component. (2) PAX2 expression was lost in most cervical glandular neoplasms, which still retained PAX8 expression. PAX8+/PAX2- can be a useful immunoprofile in distinguishing benign and malignant cervical glandular lesions. (3) In all instances, the immuno-reactivity for PAX8 was stronger than that for PAX2, and no case that reacted only for PAX2 was observed.

Umbilical Artery Thrombosis and Vascular Smooth Muscle Necrosis With Associated Single Umbilical Artery in a Live Birth

Context: Cases of normal myometrium (n = 24), uterine leiomyoma (n = 37), and uterine leiomyosarcoma (n = 16) were included. Immunostaining for MITF was performed by using a mouse monoclonal antibody (clone C5/DS, Ventana) with proper positive and negative controls. For the purpose of this study, a positive result was defined as nuclear staining of at least 10% of total relevant cells. The slides were read by 2 attending pathologists and the data were analyzed with Fisher exact test.

Results: See Table. The difference between the MITF immunostain positivity of benign cases (normal myometrium or leiomyoma) and uterine leiomyosarcoma was statistically significant (P < .001). We did not identify any significant histologic differences between uterine leiomyosarcomas that did express MITF and those that did not.

Conclusions: We found that MITF is consistently expressed in normal myometrium and uterine leiomyomas, while its expression is lost in most uterine leiomyosarcomas. Our data indicated a limited diagnostic usefulness for MITF in the differential diagnosis between uterine leiomyomas and leiomyosarcomas.

| Results of IHC Stains of MITF in the 3 Uterine Myometrial Categories |
|-----------------------------|---------------------|-----------------|
|                            | Negative | Positive | Positivity, % |
| Normal myometrium           | 1        | 23       | 96            |
| Uterine leiomyomas          | 3        | 34       | 92            |
| Uterine leiomyosarcoma       | 12       | 4        | 25            |

Presence and Potential Diagnostic Utility of Microphthalmia-Associated Transcription Factor Staining in Normal Myometrium, Uterine Leiomyoma, and Leiomyosarcoma

Context: Microphthalmia-associated transcription factor (MITF) plays a key role in melanocytic differentiation and has been used for more than 10 years as a melanoma marker. MITF is also expressed in a variety of normal tissues (eg, muscles of the stomach and colon), as well as in some tumors (eg, angiomylipoma). However, its expression in normal myometrium, uterine leiomyoma, and uterine leiomyosarcoma has not been well studied. Our study aimed to assess the MITF immunohistochemical (IHC) staining profile in normal myometrium, uterine leiomyoma, and uterine leiomyosarcoma, and evaluate its potential diagnostic utility in myometrial neoplasms.

Results: See Table. The difference between the MITF immunostain positivity of benign cases (normal myometrium or leiomyoma) and uterine leiomyosarcoma was statistically significant (P < .001). We did not identify any significant histologic differences between uterine leiomyosarcomas that did express MITF and those that did not.

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| Results of IHC Stains of MITF in the 3 Uterine Myometrial Categories |
|-----------------------------|---------------------|-----------------|
|                            | Negative | Positive | Positivity, % |
| Normal myometrium           | 1        | 23       | 96            |
| Uterine leiomyomas          | 3        | 34       | 92            |
| Uterine leiomyosarcoma       | 12       | 4        | 25            |
were congested and spongy with a 0.6-cm solid tan subchorionic lesion. Umbilical cord was 60 × 1.0–1.1 cm, left-hypercoiled. Microscopic examination exhibited a single occulsive UA thrombus with complete vascular smooth muscle necrosis consistent with thrombosis remote to delivery (Figure 147). A mural thrombus was embedded deep into a large chorionic plate vessel wall. Multifocal avascular villi and prominent syncytial knotting and basophilia were observed. Several mechanisms have been implicated: cord pathology (knots, hypercoiling, prolapse, funisitis), fetal thrombophilia, and meconium-induced vascular necrosis; however, oftentimes the etiology is unknown. Antenatally, such lesions can be clinically silent, and thus careful pathologic examination may be the only method to identify UAT.

**Multifocal Serous Carcinoma of the Cervix and Fallopian Tube in a Patient With Turner Syndrome**

(Poster No. 116)

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Patients with Turner syndrome are at increased risk for gonadoblastoma, cancers of the uterine corpus, and other nongynecologic neoplasms. To date, there are no reports of Turner syndrome associated with cervical carcinoma or serous carcinoma of the fallopian tube in the English literature. We report a case of multifocal serous carcinoma of the cervix and fallopian tube in a patient with a confirmed diagnosis of Turner syndrome. The patient was a 46-year-old woman taking combined oral contraceptives who presented with pelvic pain. Pelvic ultrasonography revealed a small uterus and bilateral complex adnexal masses. The patient underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy with radical tumor debulking. The hysterectomy specimen consisted of uterus and bilateral fallopian tubes. The ovaries were absent, and a disrupted cystic mass was present on the posterior surface of the uterus. The entire cervix, lower uterine segment, and endometrium were submitted for histologic examination. Sections showed serous intraepithelial carcinoma and invasive poorly differentiated serous carcinoma of the endocervix and left fallopian tube (Figure 148), with involvement of the left fallopian tube serosa and uterine serosa. The endometrium was atrophic and no ovarian tissue was identified. Metastatic tumor was present in the omentum and colon. The tumor was immunoreactive with WT-1 and ER, and negative for PR, EGFR, and CEA. The tumor cells were completely negative for p53, suggesting p53 mutation. The patient was treated with 6 cycles of carboplatin and taxol and has no evidence of disease at 11 months after surgery.

**Papillary Cystadenocarcinoma of Ovary With Sarcoma-Like Mural Nodules**

(Poster No. 117)

Jayalakshmi P. Balakrishna, MD; Jonathan Sarlin, MD. 1Department of Pathology, St Luke's-Roosevelt Hospital Center, New York, New York; 2Department of Pathology, Beth Israel Medical Center, New York, New York.

Mural nodules in ovarian tumors are very rare. They are described in benign, borderline, and malignant tumors. Most common association is with mucinous borderline tumors. The mural nodules can be of sarcomatous, sarcoma-like, carcinosarcoma-like, and anaplastic carcinoma types. Most of the nodules are carcinomatous and sarcoma-like. We report a case of high-grade papillary cystadenocarcinoma with serous and mucinous differentiation and sarcoma-like mural nodules containing osteoclast-like giant cells. A 23-year-old woman underwent surgery for pelvic mass. The removed adnexal mass was 25 cm in diameter with predominantly cystic structure. There was a 10-cm-diameter hemorrhagic solid mass floating within the cystic cavity, with attachment to the cyst wall. There were multiple smaller nodules with similar gross appearance attached to the wall. Microscopically, the cystic tumor showed papillary areas with high-grade cytology, foci of stromal invasion, and necrosis. There were areas of mucinous, serous, and squamous differentiation. The free-floating mass and attached mural nodules showed a spindle cell lesion with numerous osteoclast-like multinucleate giant cells and foci of necrosis and hemorrhage. These nodules did not show stromal or vascular invasion or atypical mitotic activity. Mural nodules are a rare occurrence in ovarian tumors. The accurate diagnosis of this entity is important, since the sercomatous and anaplastic carcinomatous nodules show poor prognosis, and sarcoma-like mural nodules show better prognosis. Carcinomatous and sarcomatous nodules can be differentiated by immunohistochemical analysis and sarcoma-like nodules are differentiated by their characteristic lack of vascular or stromal invasion.

**Ovarian Serous Carcinoma Arising in Micropapillary-Cribriform Serous Borderline Tumor: Low-Grade Serous Carcinoma With Nuclear Pleomorphism or True Transformation to High-Grade Serous Carcinoma?**

(Poster No. 118)

Whitney A. McCarthy, MD (wamccart@bcm.tmc.edu); Ramya P. Masand, MD. Department of Pathology & Immunology, Baylor College of Medicine, Houston, Texas.

**Context:** Low-grade serous carcinoma (LGSC) arising in micropapillary/cribriform serous borderline tumor (MSBT) displays behavior intermediate between LGSC and high-grade serous carcinoma (HGSC). LGSC and HGSC arise from different molecular pathways and represent 2 different tumor types; the molecular origins of MSBT are not definitively known. We present the cases of 3 women with LGSC/MSBT with nuclear pleomorphism, evaluate p53 and p16 immunostains in these tumors, and look at patient outcomes.

**Design:** Three cases of LGSC/MSBT with focal HGSC were identified. Diagnosis was based on the criteria established by Malpica et al; nuclear pleomorphism is the primary diagnostic criterion, and mitotic count is secondary. p53 and p16 immunostains were used. Clinical information was obtained from patients' charts.

**Results:** Tumors in these patients showed increased nuclear pleomorphism (HGSC) that was multifocal and contiguous with LGSC. However, mitotic rate in pleomorphic areas was similar to adjacent LGSC. Patchy p53 and p16 staining was seen throughout. Patients had optimum debulking. For 2 patients, disease recurred within 1 month of resection; 1 has no evidence of disease.

**Conclusions:** We present 3 cases of LGSC/MSBT with focal increased nuclear pleomorphism. The immunostaining patterns suggest that areas of nuclear pleomorphism are not HGSC but rather LGSC with nuclear pleomorphism. Thus, nuclear pleomorphism does not seem to warrant the diagnosis of HGSC in these tumors. The tumors in this small cohort tend to recur early with the chemoresistance of an LGSC, suggesting an intermediate behavior and prognosis. Molecular studies are needed to further characterize the genetic aberrations in these tumors of young women.

**Vanishing Endometrial Cancer in Hysterectomy Specimens: A Myth or a Fact**

(Poster No. 119)

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**Context:** Occasional cases of endometrial cancer (EC) diagnosed on biopsy have no residual cancer (RC) identified in the hysterectomy specimen. The incidence of these cases is not well studied. The aim of our study was to analyze this “vanishing cancer” phenomenon.
Design: Cases of EC on dilation and curettage and biopsy with no RC on hysterectomy were identified. The endometrium was entirely submitted in each case. Clinicopathologic variables analyzed included patient demographics; tumor type, grade, and stage; biopsy method; treatment; surgical procedure; recurrence; and disease-specific survival.

Results: We identified 24 biopsies of EC with no RC on hysterectomy specimen. The median age of patients was 58.5 years (32–76 years). Of the 24 patients, 15 (62.5%) had endometrioid, 6 (25%) serous, 1 (4.2%) clear cell, 1 (4.2%) serous intraepithelial carcinoma and 1 (4.2%) low-grade adenosarcoma. Of the endometrioid carcinoma cases, 12 (50%) were FIGO grade I, 2 (8.3%) were grade II, and 1 (4.2%) was grade III. Eighteen of 24 patients underwent dilation and curettage and 6 had endometrial biopsy as primary procedure. Median follow-up was 8.8 years (SD = 0.617 year). Two patients with serous carcinoma underwent adjuvant chemotherapy. One patient died of disease. This patient was diagnosed as having FIGO grade II endometrioid carcinoma, later developed recurrence, and died within 31 months of diagnosis (Table).

Conclusions: The inability to identify cancer in a hysterectomy specimen for biopsy confirmed that carcinoma does not indicate technical failure, as all cases in our cohort underwent complete endometrial sampling and evaluation. Although there is no standard treatment for patients with vanishing endometrial cancer, the prognosis is excellent.

<table>
<thead>
<tr>
<th>Histology</th>
<th>n = 24, No. (%)</th>
<th>TAH/BSO Only, No. (%)</th>
<th>TAH/BSO With Pelvic, Para-aortic LN, and Omental Biopsy, No. (%)</th>
<th>TAH With Pelvic or Para-aortic LN Only, No. (%)</th>
<th>Adjuvant Therapy</th>
<th>Recurrence</th>
<th>DOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>EM ca (FIGO 1)</td>
<td>12/24 (50)</td>
<td>9/12 (75)</td>
<td>2/12 (16.7)</td>
<td>1/12 (8.3)</td>
<td>0</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>EM ca (FIGO 2)</td>
<td>2/24 (8.3)</td>
<td>2/2 (100)</td>
<td></td>
<td>0</td>
<td>Yes, 1/2 (50)</td>
<td>Yes, 1/2 (50)</td>
<td>No</td>
</tr>
<tr>
<td>EM ca (FIGO 3)</td>
<td>1/24 (4.2)</td>
<td>1/1 (100)</td>
<td></td>
<td>0</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Serous ca</td>
<td>6/24 (2.5)</td>
<td>3/6 (50)</td>
<td>3/6 (50)</td>
<td>2/6 (33.3)</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Clear cell ca</td>
<td>1/24 (4.2)</td>
<td>1/1 (100)</td>
<td></td>
<td>0</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Serous intraepithelial ca</td>
<td>1/24 (4.2)</td>
<td>1/1 (100)</td>
<td></td>
<td>0</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Adenosarcoma low grade</td>
<td>1/24 (4.2)</td>
<td>1/1 (100)</td>
<td></td>
<td>0</td>
<td>No</td>
<td>No</td>
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</tr>
</tbody>
</table>

A Pure Sex Cord Proliferation Arising in 46,XY Dysgenic Gonads
(Poster No. 120)

Alexander A. Berrebi, MD (aberrebi@umm.edu); Paul N. Staats, MD. Department of Pathology, University of Maryland Medical Center, Baltimore.

Patients with 46,XY complete gonadal dysgenesis (Swyer syndrome) are externally and internally female with dysgenic streak gonads. The disorder is often due to a mutation in the SRY gene on the Y chromosome, which is responsible for the initiation of male sex determination. The gonads are composed of fibrous stroma without sex cord development or germ cells. There is a significant risk of developing neoplasia within these gonads. Gonadoblastoma is the most commonly reported benign tumor, while germ cell tumors, especially dysgerminomas, are the most common malignant tumors. We present a case of a previously unreported sex cord proliferation in the streak gonads of a patient with Swyer syndrome. A 13-year-old patient with Swyer syndrome and a SRY gene mutation underwent surgical exploration that revealed bilateral small streak gonads and an undeveloped uterus. Microscopically, numerous small, simple, hollow tubules were dispersed throughout the fibrous stroma of the left and right streak gonads. The tubules were lined by columnar cells with minimal cytoplasm and bland, oval nuclei, with no appreciable mitotic activity. The tubular cells were positive for inhibin, confirming a sex cord derivation. Germ cells were not identified histologically or by placental alkaline phosphatase immunostain. The proliferations are favored to be hamartomatous owing to their bilaterality, distribution, and intermingling with gonadal fibrous tissue, but a benign neoplastic origin cannot be excluded. This case highlights a unique finding in streak gonads, not previously reported in the medical literature, which may pose a diagnostic dilemma (Figure 149).

Primary Intraosseous Malignant Myoepithelioma of Mandible With EWSR1 Translocation: A Case Report and Review of the Literature
(Poster No. 121)

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Myoepithelial cells have a unique potential for divergent differentiation along both epithelial and mesenchymal lineages. Outside the salivary gland, myoepithelial tumor (MET) is a newly introduced
processes, the pathogenesis of which has yet to be elucidated. One theory postulates a connection with a traumatic or scanning process; this same reactive mechanism—namely, an exaggerated response by follicular dendritic cells to tissue injury—is believed by some to contribute to the reactive mechanism—namely, an exaggerated response by follicular dendritic cells to tissue injury—is believed by some to contribute to the pathogenesis of which has yet to be elucidated.

**Hyaline Vascular Castleman Disease Associated With a Calcifying Fibrous Pseudotumor in a Pediatric Neck Mass**

(Poster No. 122)

Nicole R. Dominiak, MD¹ (dominiak@musc.edu); David LeBel, MD²; Samuel Oyer, MD²; David R. White, MD²; Michael J. Caplan, MD.¹ Department of Pathology and Laboratory Medicine and ²Otolaryngology Head & Neck Surgery, Medical University of South Carolina, Charleston, South Carolina.

Castleman disease (CD), although well-described, remains a relatively rare lymphoproliferative disorder. There is a known association of CD with exposure to human herpesvirus-8 and HIV. Histologically, CD is divided into the hyaline vascular, plasma cell, transitional/mixed, and plasmablastic subtypes. The hyaline vascular subtype is by far the most common variant, typically presenting as a unicentric mass involving the lymph nodes of the mediastinum, neck, abdomen, or axilla. We present the case of a 9-year-old boy with a slowly enlarging, radiologically heterogeneous, 10-cm neck mass. Upon resection of the mass, classic features of hyaline vascular CD were observed to be enveloped by a densely sclerotic zone punctuated by scattered dystrophic calcifications. The lesion was ultimately diagnosed as hyaline vascular CD associated with associated calcifying fibrous (pseudo) tumor. While CD has been associated with other neoplastic entities, its association with calcifying fibrous pseudotumor has only rarely been reported in the literature. Calcifying fibrous pseudotumors are exceptionally rare, benign soft tissue established history of trauma or surgical intervention; thus, the stimulus in this child remains unknown (Figure 151).

**Metastatic Papillary Thyroid Carcinoma With Anaplastic Transformation Presenting as a Retroperitoneal Mass**

(Poster No. 123)

James P. Solomon, MD, PhD¹ (jsolomon@ucsd.edu); Fang Wen, MD, PhD²; Lily J. Jih, MD.¹ ¹Department of Pathology, University of California, San Diego; ²Department of Pathology, VA San Diego Healthcare System, San Diego, California.

Associated with poor prognosis, anaplastic transformation of papillary thyroid carcinoma (PTC) is a rare event that usually occurs within the thyroid or cervical lymph nodes. Here, we report a case of anaplastic transformation within a retroperitoneal metastasis of PTC in a patient 30 years after thyroidectomy. A 64-year-old man presented with a symptomatic 20-cm abdominal mass. He had a long history of PTC, with initial diagnosis and total thyroidectomy in 1985, bilateral neck dissection in 1999, and resection of a left axillary metastasis in 2005. Fine-needle aspiration of the retroperitoneal mass at an outside institution showed a papillary neoplasm positive for TTF-1 and thyroglobulin, consistent with metastatic PTC. The resection, however, was mostly necrotic, and extensive sampling of viable areas showed sheets of undifferentiated cells and no papillary architecture. The malignant cells had abundant granular eosinophilic cytoplasm; eccentric, vesicular nuclei; and prominent nucleoli. The cells were diffusely positive for AE1/AE3, variably positive for TTF-1, and negative for thyroglobulin. Many were also positive for p53, which is often seen after anaplastic transformation. A battery of stains ruled out metastases from other sites, and given the longstanding history of PTC, the diagnosis of anaplastic transformation of PTC was made. Anaplastic transformation of PTC in metastatic sites is exceedingly rare, only previously documented in a few case reports (<10). Only 1 of these reports described anaplastic transformation in a retroperitoneal metastasis, with other reported sites including the submandibular gland, the soft tissue of the shoulder, and the lungs.

**Interobserver Variability in the Classification of Extracapsular Extension in Metastatic p16⁺ Oropharyngeal Squamous Cell Carcinoma**

(Poster No. 124)

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**Context:** Extracapsular extension (ECE) in nodal metastases is an adverse prognosticator in head and neck squamous cell carcinoma (SCC). We previously developed a system for ECE classification in oropharyngeal SCC (ÖPSSC). The purpose of this study was to discern the degree of interobserver variability in ECE classification in p16⁺ ÖPSSC and then to compare our system.

**Design:** From a database of 50 p16⁺ ÖPSSC, 50 nodal metastasis slides were randomly selected. Five head and neck pathologists from different institutions read them twice, first by their own standards as ECE present or absent, and second by using our system: grade 0 (no ECE), 0c (no ECE; cells limited to node with thickened capsule), 1 (ECE; nodal tissue present but cells infiltrate beyond capsule), and 2 (soft tissue metastasis; no residual nodal tissue). For each slide, the pathologists agreed in 55% (n = 44). In the second round, at least 4 pathologists agreed on presence (0 or 0c) or absence (1 or 2) of ECE in 76% (n = 38), and all 5 agreed in 66% (n = 33). χ² value was 0.635 (95% CI: 0.4719–0.7833), indicating substantial agreement. Difference in χ² between the 2 rounds was 0.127 (95% CI: 0.0013–0.2642). The lower limit of this CI is >0, representing significant improvement in agreement.
Conclusions: There is significant interobserver variability in ECE assessment in p16+ OPSCC. A defined classification system improves agreement.

Follicular Center Cell Lymphoma Arising in Warthin Tumor
(Poster No. 125)
Abha Soni, DO (abhasoni@uabmc.edu); Deniz Peker, MD. Department of Pathology, University of Alabama in Birmingham.

Warthin tumor is a benign cellular proliferation of the parotid salivary ducts that are entrapped within the intraparotid lymphoid stroma. Rarely, lymphoma can arise in Warthin tumor; fewer than 20 cases in English literature have been reported. This is the case report of a 62-year-old woman with left parotid gland swelling and enlarged lymph nodes on the left lateral aspect of her neck that persisted for several years. Histologically, the parotidectomy specimen showed characteristic features of Warthin tumor associated with lymphocytic infiltrate composed of monotonous population of small cleaved cells with features of follicular center lymphocytes predominantly forming closely packed follicles. The lymphoma cells were reactive with CD20, PAX5, and CD10, with a low (20%) Ki-67 proliferative rate, and negative for CD3 and CD5 via immunohistochemistry. A diagnosis of low-grade follicular lymphoma (WHO grade I/III) was rendered on the basis of these histomorphologic and phenotypic features. This is an unusual presentation of tumor exhibiting 2 histologically distinct neoplasms: lymphoma and Warthin tumor. One of the most accepted theories explains that the pathogenesis is due to heterotopic salivary ducts that are entrapped within the intraparotid and periparotid lymph nodes. This tissue, when induced immunologically, can undergo reactive and malignant transformation.

Mycobacterium avium Infection of Nasal Septum in a Diabetic Adult
(Poster No. 126)
Liyan Xu, BM, MS (liyanlxu@creighton.edu); Nicholas Dietz, MD; Elza Matrova, MD; Niru Nahar, MBBS. Department of Pathology, Creighton University, Omaha, Nebraska.

A 69-year-old man with diabetes mellitus was admitted with a 2-month history of left lateral frontal headache. The pain was fluctuating and partially relieved by pain medications. He also had complaint of chronic cough, but the chest x-ray was unremarkable. Intrasal nasal examination revealed a sessile polypoid lesion (1.5 cm in diameter) on the right anterior nasal septum. Bilateral turbinate showed atrophic changes. A biopsy was performed. The gross examination revealed tan-yellow polypoid soft tissue fragments. Microscopic examination showed stratified squamous epithelium overlying numerous foamy histiocytes with admixed inflammatory cells. An acid-fast stain highlighted numerous bacilli within the foamy histiocytes. There was no evidence of caseating granulomas. Biopsy tissue culture was positive for Mycobacterium avium. As the patient’s incision had healed well, no antibiotics were initiated. The patient was followed up at 6 months with intranasal examination showing a scar without evidence of a mass or other abnormality. M avium complex is an unusual cause of extrapulmonary infection, with most examples presenting in immunocompromised adults. The current case illustrates both an atypical anatomic location, the nasal cavity, and an often overlooked cause of immune compromise, diabetes mellitus. Chronic inflammation with foamy histiocytes should prompt consideration of M avium complex, especially in patients with diabetes mellitus. Acid-fast bacilli on stains and growth on culture can be used to confirm the diagnosis of M avium infection (Figure 152).

Unusual Granulomatous Vocal Cord Nodules: Two Rare Cases
(Poster No. 127)
Melissa Guzzetta, DO (melissaguzzetta@gmail.com); Alice Laser, MD; Leonard Kahn, MD. Department of Pathology, Hofstra North Shore-LIJ Health System, New Hyde Park, New York.

The most common vocal cord lesions are vocal cord nodules/polyps. Both occur as the result of vocal cord irritation, can be bilateral or unilateral, and can develop anywhere along the vocal cords. These lesions show little variation grossly. They are identified grossly as white or gray protuberances covered by intact squamous epithelium and may be sessile or pedunculated. Histopathologically, the most distinctive feature is myxoid stromal change with fibrin deposition. The differential diagnoses include recurrent laryngeal papillomatosis, contact granuloma, ulcer, amyloidosis, myxoma, hemangioma, granular cell tumor, paragangliomas, and squamous cell carcinoma. We present 2 unusual cases of vocal cord nodular granulomatous lesions. The first involves a 66-year-old woman who presented with 1.5 years of hoarseness and hilar adenopathy. On biopsy, there were well-defined, noncaseating granulomas that were negative for microorganisms when stained with acid-fast bacilli and Grocott methenamine silver, consistent with sarcoid granulomas (Figure 153, A). The second case involves a 49-year-old woman with known history of rheumatoid arthritis who presented with a left vocal cord nodule. On biopsy, there were multiple foci of fibrinoid necrosis surrounded by palisading histiocytes and multinucleated giant cells. There was an associated lymphoplasmacytic connective tissue infiltrate. These findings, taken in conjunction with the patient’s history, were quite typical of rheumatoid nodule of the vocal cord (Figure, B). A review of the literature shows few reported cases of these lesions, since they are rare and unusual in this particular location.

Kikuchi-Fujimoto Disease: A Clinicopathologic Study
(Poster No. 128)
Abul Ala Syed Rifat Mannan, MD1 (amannan@chpnet.org); Songyang Yuan, MD, PhD2; Thomas Vurgese, MD, MRCP.1,2Department of Pathology, St.-Luke’s Roosevelt Hospital Center, New York, New York; 1Department of Pathology, Beth Israel Medical Center, New York, New York; 2Department of Medicine, Al Jahra Hospital, Jahra, Kuwait.

Context: Kikuchi-Fujimoto disease (KFD) is a rare benign, self-limiting cervical lymphadenitis of unknown etiology. The present study was aimed at analyzing the clinical and laboratory parameters of KFD.

Design: We analyzed 10 cases of KFD at a multispecialty hospital in Kuwait during a 9-year period (2000–2009). Patients belonged to different nationalities, including 2 Kuwaitis, 3 Indians, 3 Egyptians, and 2 Filipinos. The clinical presentations, laboratory parameters, and histopathologic features of lymph node biopsy were reviewed.

Results: The mean age of the patients was 36.5 years (range, 13–49 years). The male to female ratio was 1:4. All patients had cervical lymphadenopathy at presentation, most commonly involving the posterior cervical group, accompanied by fever. Prominent laboratory
Gnathic, Intraosseous (Central) Sebaceous Adenocarcinoma of Salivary Gland Differentiation (Poster No. 129)

Sohail Qayyum, MD1 (sqayyum1@uthsc.edu); Deepthi Hoskoppal, MD2; Yeshwant B. Rawal, BDS, MDS, MS, MD.1 2Department of Pathology, University of Tennessee Health Science Center, Memphis; 1Department of Diagnostic Sciences & Oral Medicine, College of Dentistry, University of Tennessee Health Science Center, Memphis.

Primary intraosseous salivary malignancies are rare. Adenoid cystic adenocarcinoma, adenocarcinoma NOS, acinic cell adenocarcinoma, and epithelial-myoepithelial carcinoma have all been reported within the jaws, but the mucoepidermoid carcinoma is by far the most common tumor in this setting, accounting for 2% to 4% of all mucoepidermoid carcinomas. Sebaceous adenocarcinoma has never been reported in this location. Here, we document a sebaceous adenocarcinoma of the maxilla in a 56-year-old woman presenting with a painful swelling of the right face. Computed tomography scans showed a large mass in the left nasal cavity and extending into the contralateral nasal cavity. Biopsy showed moderately to poorly differentiated sinonasal mucinous adenocarcinoma with a histologic appearance of colonic adenocarcinoma, which has a CD70+, CDX2+, villin+, and variable for CK7. K-ras mutation has been reported in 15% of cases. The 5-year-survival rate is approximately 40%, with most deaths occurring within 3 years. Here we are presenting the case of a 67-year-old woman with a moderately to poorly differentiated sinonasal mucinous adenocarcinoma with a histologic appearance of colon adenocarcinoma, which has a CD70+, CD20 and CDX2 negative immunoprofile. The patient presented with a 3-month history of nasal obstruction, pain, and anosmia. She had no history of exposure to chemicals or other agent. Computed tomography scan showed a large mass in the left nasal cavity and extending into the contralateral nasal cavity. Biopsy showed moderately to poorly differentiated sinonasal mucinous adenocarcinoma. Surgical resection of the mass was performed and followed by radiation and chemotherapy. Several months later, she presented with multiple liver metastasis. We are reporting this case because of its interesting immunophenotype and histologic appearance and the rarity of this cancer especially in females.

MicroRNA Expression Profiling of Papillary Thyroid Carcinomas (Poster No. 132)

Seema Sethi, MD1 (dssethi7@gmail.com); Fazlul Sarkar, Ph.D1; Shadan Ali, MS2; Rajani Suresh, BS2; Paul Tranchida, MD3; Wael Sakr, MD3; Tamar Giorgadze, MD, PhD.1 2Department of Pathology, Wayne State University, Detroit, Michigan; 3Department of Pathology, New York-Presbyterian Hospital/Weill Cornell Medical College, New York, New York.

Context: MicroRNAs (miRNAs) are small endogenous molecules involved in the posttranscriptional regulation of genes. Papillary thyroid carcinoma (PTC) is the commonest thyroid cancer with rising incidence in the United States. Its incidence and mortality differ by race, with the increasing burden occurring among African Americans. We hypothesize that in PTC (1) identification of altered miRNAs can improve diagnosis,
prognosis, and treatment; and (2) differentially expressed miRNAs by race would help in overcoming race disparities.

**Design:** RNA was extracted from PTC (n = 27; 16 white Americans + 11 African Americans) and normal thyroids (n = 27). miRNA expression profiling was performed by using microfluidic biochip microarrays (LC Sciences). Data were statistically analyzed by using the Student t test.

**Results:** Of the 2555 miRNAs profiled, PTC revealed overexpression of miR-146, miR-221, miR-222, miR-31, and miR-4267 and low expression of miR-138, miR-451, and miR-143, compared to normal thyroid (P < .001). In African Americans there was upregulation of miR-31 and in white Americans there was upregulation of miR-4267 (Figure 155) with down-regulation of miR-138 (P < .001).

**Conclusions:** Overexpression of miR-146, miR-21, miR-221, miR-222, miR-31, and miR-4267 and low expression of miR-138, miR-451, and miR-143 can serve as a molecular "signature" for PTC. Upregulation of miR-31 in African Americans and down-regulation of miR-138 with upregulation of miR-4267 in white Americans could explain race disparities in PTC. Our findings may have significant clinical impact, since these can be used to improve diagnostic accuracy; determine prognosis; and with the use of antagonirs (chemically modified oligonucleotides), serve as novel targets for therapy to achieve the goals of precision medicine.

**Histopathology of Lemierre Syndrome**

**Poster No. 133**

Stell D. Patadji, MD (patadjsid@upmc.edu); Alka Palekar, MD; Liron Pananowitz, MD. Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania.

Lemierre syndrome is caused by a necrotizing infection of the head and neck. This can become complicated by septic thrombophlebitis with ensuing sepsis. The histopathology of this forgotten syndrome has previously not been well characterized. We describe the case of a 20-year-old man who developed a left tonsillar abscess, septic thrombophlebitis of his left jugular vein, and septic shock. *Fusobacterium* was isolated from his blood cultures. The patient underwent internal jugular vein excision. Grossly, the vein was occluded by clot and the thickened blood vessel wall was adherent to adjacent soft tissue. Microscopic examination showed an organizing thrombus with acute and chronic inflammatory cells (Figure 156, A). The wall of the vein was also infiltrated by acute and chronic inflammatory cells (Figure, B; higher magnification). Circumferential granulation tissue with fibrosis extended from the media into perivascular soft tissue. Masson trichrome and Verhoeff-Van Gieson elastic stain showed interruption of the vessel wall with inflammation and fibrosis. Intramural granulation tissue was highlighted by using CD31, CD34, and FLI-1 immunostains. Smooth muscle actin stained proliferating myofibroblasts and CD68-admixed histiocytes. No organisms were identified with special stains, perhaps because the patient was previously treated with antibiotics. As depicted in this case, the histopathology of Lemierre syndrome is characterized by septic thrombophlebitis. Albeit rare, this is an important diagnosis because these necrotizing infections of the head and neck can have a lethal outcome.

**Papillary Thyroid Carcinoma, Follicular Variant, Arising Within a Thyroglossal Duct Cyst**

**Poster No. 134**

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The incidence of carcinoma arising in a lingual thyroid is very rare, less than 1%, with approximately 45 reported cases since its first discovery in 1910. To date, fewer than 5 cases of papillary thyroid carcinoma, follicular variant, arising from a lingual thyroid have been reported in the literature. We report the case of a 23-year-old woman who presented with a right neck mass and a hyoid mass of 10 years’ duration with a slow growth rate. The right neck mass was excised and consisted of a 2.6-cm cystic mass filled with spongy brown material. Microscopic examination showed benign ectopic thyroid tissue with cystically dilated colloid follicles, fibrosis, hemosiderin-laden macrophages, and aggregates of foreign body cells with cholesterol clefts. Interestingly, there were a few small foci of cells with papillary nuclear features, but this was favored to represent degenerative atypia. However, the possibility of a metastatic carcinoma was not entirely excluded. The hyoid mass was excised and consisted of a 4-cm, lobulated, pink-tan rubbery mass with attached hyoid bone. Microscopic examination showed papillary thyroid carcinoma, follicular variant, 1.7 cm, involving the hyoid bone and adjacent skeletal muscle (Figure 157). The tumor was admixed with ectopic thyroid tissue and surrounded by a thick fibrous capsule. The patient subsequently underwent a total thyroidectomy, in which no focus of carcinoma was identified. We present a detailed examination of our case and literature review.

**Intranaal Parotid Nonsebaceous Lymphadenoma**

**Poster No. 135**

Matthew F. Raines, MD (matthew.f.raines.mil@mail.mil); Thomas A. Adams, MD; Mikelle L. Kernig, DDS, MS. Department of Pathology, San Antonio Uniformed Services Health Education Consortium, Fort Sam Houston, Texas.
We present the case of a 58-year-old man with a history of pancreatic neuroendocrine tumor who presented with presyncope. A magnetic resonance imaging of the brain showed no intracranial abnormalities and an incidentally noted enlarged upper right cervical lymph node. A follow-up computed tomography and magnetic resonance imaging showed a heterogeneous, 2.4-cm, well-circumscribed right parotid mass with radiographic features of a pleomorphic adenoma (benign mixed tumor). The patient was asymptomatic with no facial pain or numbness and was unaware of the lesion. A fine-needle aspiration showed basaloid epithelial cells with a prominent lymphoid component, which was favored to be a low-grade parotid neoplasm. Given the low-grade impression based on imaging and fine-needle aspiration, the nodule was removed conservatively without sacrificing facial nerve branches (superficial parotidectomy). The resection specimen was well circumscribed and encapsulated, grossly resembling a lymph node. Microscopically, it was an encapsulated, well-circumscribed nodule that was removed conservatively without sacrificing facial nerve branches (superficial parotidectomy). The resection specimen was well circumscribed and encapsulated, grossly resembling a lymph node. We present a case of nonsebaceous lymphadenoma that demonstrates associated lymphoid proliferation, lacking features of a lymph node.

**Distant (Liver) Metastasis in a Patient With Recurrent Middle Ear Adenoma: Case Report and Review of Literature**

(Rong Shen, MD, MS; P. Holmes, MD; Norio Azumi, MD, PhD; Metin Ozdemirli, MD, PhD; Bhaskar Kallakury, MD; Department of Pathology, Medstar Georgetown University Hospital, NW Washington, DC.)

Middle ear adenomas (MEAs) are rare neoplasms of the middle ear, which are generally considered to be benign. Surgical excision is the standard therapy and generally considered curative. Local recurrence has been reported in 12% to 22% of the cases and is thought to be related to conservative initial excision. There are very few reported cases of regional metastasis after years of disease and only 1 case of visceral metastasis. We report a case of distant metastasis of MEA to the liver. A 52-year-old man presented with left ear fullness and hearing loss in 2009 and had a mass lesion filling the space around the ossicles without osseous erosion. Biopsy specimens obtained at 2 outside institutions diagnosed this lesion as MEA. Subsequently, patient had multiple local recurrences until 2011 and underwent both diagnostic and curative surgical procedures at our institution. Each time the diagnosis of recurrent MEA was confirmed on the characteristic morphology and supported by immunohistochemistry findings. Four-and-a-half years after the original presentation, multiple liver lesions measuring up to 4.5 cm were incidentally discovered on computed tomography scan. A core biopsy of the hepatic lesion showed monomorphic plasmacytoid neoplastic cells with eosinophilic cytoplasm, and immunohistochemistry studies confirmed positivity for cytokeratin, synaptophysin, chromogranin, CD56, and 10% proliferation index by Ki-67, identical to known previous profile, indicative of metastatic MEA. This rare case of hepatic metastasis of MEA is indicative of malignant potential of this lesion, which thus far has been generally considered a relatively benign neoplasm.

**Tumor Biology Clues Learned From Tridimensional (3-D) Morphologic Study of Squamous Cell Carcinoma**

(Dibson D. Gondim, MD; Dikson D. Gondim, MD; Jens Enemark, MD; Ulf-Henrich Braumann, PhD; Jens-Peer Kuska, PhD; Virgilia Macias, MD; Andre Kajdacy-Balla, MD, PhD; Department of Pathology and Laboratory Medicine, Indiana University School of Medicine, Indianapolis; Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, Missouri; Department of Pathology, Obstetrics and Gynecology and Interdisciplinary Centre for Bioinformatics, University of Leipzig, Germany; Department of Pathology, University of Illinois at Chicago.)

**Context:** Conventional histology cannot demonstrate the natural 3-D behavior of tumors. Is an isolated cluster of cells ("island") next to the primary tumor a metastasis or a fingerlike projection of the tumor? Do we frequently underdiagnose perineural invasion because we only see a tangential cut of it? Do we frequently underdiagnose vascular invasion because we do not see endothelial cell nuclei at a given level? Very few efforts have been made to understand the biological meaning of the patterns in a tridimensional context.

**Design:** One case of squamous cell carcinoma (SCC) of the tongue with a markedly dispersed invasion pattern composed of "islands" that were more than 1 mm away from the invasion front was serially sectioned to obtain 50 slides at 15-μm intervals. Images of 12 cases of SCC of the uterine cervix (90-500 slides each case) with different invasion patterns were also reviewed.

**Results:** The "islands" were interconnected with each other and with the main tumor mass mostly, and the "islands" were actually interconnected represented lymphovascular invasion and were initially inconspicuous, but clarified when the vessels were followed in the "lost dimension," the z-axis. Some of the "islands" actually were tangential cuts of tumor encapsulating a nerve.

**Conclusion:** The cases of SCC studied had apparent "islands" that were actually interconnected tumor. The presence of tumor "islands" located far away from the invasion front may represent an additional clue for diagnosing perineural invasion or lymphovascular invasion.

**Crohn Disease: An Unusual Cause of Sinonasal Granulomatous Disease**

(Sheva Khalafbeigi, MD; Shevakhalafbeigi@centura.org; Daniel C. Mayes, MD; Thomas A. Dalsaso, MD; Department of Pathology, Penrose Hospital, Colorado Springs, Colorado; Head & Neck Surgery, Ear, Nose & Throat of Colorado Springs, Colorado.)

A 27-year-old woman presented with sinus symptoms, intermittent epistaxis, and discomfort. Significant past medical history includes Crohn disease. Examination showed a nasal septal perforation as well as bilateral turbinate hypertrophy. A partial reduction of the inferior turbines was performed. Histopathologic examination shows sinonasal mucosa with prominent involvement by granulomatous inflammation. The submucosa is expanded by noncaseating granulomas composed of both mononuclear histiocytes and multinucleated, Langhans-type giant cells. The granulomas are dispersed within a dense lymphoplasmacytic infiltrate. Special stains for microorganisms are negative (acid-fast [Ziehl-Neelsen], Gomori methenamine silver, Brown and Brenn; Figure 159). Vasculitis is not observed. Many patients with Crohn disease have extraintestinal manifestations, but sinonasal involvement has been reported in only 8 patients, including this case. Studies of sinonasal symptoms in patients with Crohn disease suggest that the prevalence may be much higher than currently appreciated. Presenting symptoms in histologically documented cases have included chronic sinonasal congestion, nasal obstruction, intermittent epistaxis, and septal perforation. Histopathologic findings are nonspecific; the findings reported in this patient are characteristic. The differential diagnosis includes infectious disorders, various forms of vasculitis, lymphoma, trauma, cocaine use, and sarcoidosis. The diagnosis requires a high index of suspicion, and correlation with the clinical, imaging findings, and other laboratory findings. Perhaps underrecognized,

Abstracts
Crohn disease should be considered in the differential diagnosis of granulomatous sinonasal disease.

A Case of Mammary Analog Secretory Carcinoma of Salivary Gland With High-Grade Histology
(Poster No. 139)
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Mammary analog secretory carcinoma (MASC) of salivary gland is a recently recognized malignancy that strikingly resembles secretory carcinoma of the breast in histology and bears the same balanced translocation of (12;15)(p13;q25) that creates a ETV6-NTRK3 fusion. MASC occurs most commonly in parotid and uncommonly in minor salivary glands, has low-grade histology, and follows a relatively benign course. Metastasis to lymph node is uncommon and high-grade histology is only rarely reported. MASC is often confused with acinic tumor and adenocarcinoma not otherwise specified and less commonly with other salivary gland tumors. Here we report a rare case with high-grade histology and metastasis to cervical lymph nodes. The tumor occurred in the hard palate of a 41-year-old adult and confirmed with ETV6-NTRK3 translocation. It was histologically composed of a minor glandular component with pale eosinophilic secretion (Figure 160, A and B) commonly seen in MASC and a dominant solid component with mitotically active (arrows in Figure, D) solid cell nests separated by fibrovascular septa. Both components had enlarged nuclei with prominent nucleoli. Expression of cytokeratin 7 and 8/18 was patchy in the glandular component but diffuse in the solid component. Both components were diffusely immunoreactive for S100 and vimentin but negative for calponin, cytokeratin 5/6, epithelial membrane antigen, GCDFP-15, and p63. The solid component has higher Ki-67 labeling index. This case emphasizes the importance of molecular pathology in distinguishing this tumor from other high-grade tumors of salivary gland.

Spindle Cell Carcinoma of the Tongue (Poster No. 140)

Zengshan Li, MD, PhD1; John Gooey, MD2; Charles K. Allam, MD1; Qin Huang, MD, PhD1 (qin.huang@va.gov). Departments of Pathology and ENT Surgery, VA Boston Healthcare System, West Roxbury, Massachusetts.

Context: Spindle cell carcinoma of the tongue (SpCC) has not been well studied.

Design: This is a retrospective case series.

Results: Four SpCC cases were identified among 97 tongue squamous cell carcinomas (SCCs) during a 10-year period at VA Boston Healthcare System. All patients were men with a median age of 65.4 years (range, 58–75 years). Tumors were polypoid and ulcerated with a mean size of 23.6 mm (range, 2–76 mm). By histology, neoplastic cells showed both SpCC and SCC components. Two tumors exhibited a predominant SpCC component intermingled with foci of SCC with or without keratin pearls. Other 2 contained near-equal amount of SpCC and SCC components with separate basaloid SCC and glandlike features. Focal SCC in situ was seen in 2 tumors. Neoplastic spindle cells showed moderate pleomorphism in a myoid stroma with variable collagenous fibrosis. The transition between SpCC and SCC components was evident in all 4 tumors. Focal osteoid and chondroid metaplasia were noted in 2. Focal skeleton muscle infiltration was found in 3 and intranuclear invasion in 1. By immunohistochemistry, neoplastic spindle cells were diffusely immunoreactive to vimentin in 4 tumors and focally to p40 in 2, but negative to EMA. Ki-67 reactivity was noted in 20% to 80% of spindled cells. None were immunoreactive to p16 in both SCC and SpCC components. Median survival after resection was 14 months (range, 1–35 months) in the SpCC group, significantly shorter than 34 months (range, 1–116 months, P < .05) in the SCC group.

Conclusion: SpCC is a rare variant of tongue SCC, and is not related to HPV infection, but with a dismal prognosis.

Anaplastic Lymphoma Kinase–Positive Large B-Cell Lymphoma Presenting in the Tonsil: An Unusual Tumor in an Unusual Location
(Poster No. 141)
Ioannis Ioannidis, MD (ioannidis@health.southalabama.edu); Erin Racz, MD1; John J. Nelson, MD; Jack Polski, MD; Javier Laurini, MD. Department of Pathology, University of South Alabama, Mobile.

Anaplastic lymphoma kinase (ALK)–positive large B-cell lymphoma is a neoplasm composed of monomorphic large immunoblast-like B cells, with occasional plasmablastic differentiation, characteristically showing granular cytoplasmic expression of ALK-1. Considered a subtype of diffuse large B-cell lymphoma, it is extremely rare, with only approximately 40 cases reported so far. The tumor usually presents in lymph nodes or as a mediastinal mass and only rarely does it involve extranodal sites such as nasopharynx, tongue, stomach, bone, and soft tissue. A 51-year-old man was noted to have asymmetric tonsillar enlargement and underwent bilateral tonsillectomy. The specimens were grossly unremarkable and completely submitted for evaluation. Morphologically, a neoplastic proliferation composed of large polygonal cells with abundant eosinophilic cytoplasm with prominent nucleoli was noted to focally involve the right tonsil. The tumor effaced the lymphoid tissue and partially displayed a sinusoidal pattern of growth. The neoplastic cells were positive for CD45, EMA, CD79a, CD4, CD138, and MUM-1 and negative for CD20, CD3, cytokeratin, and melanoma-associated markers. Furthermore, the tumor cells revealed strong and diffuse granular cytoplasmic positivity for ALK-1 and showed monotypic cytoplasmic expression of κ light chains. To our knowledge, this is the first case of ALK-positive large B-cell lymphoma presenting in the tonsil and highlights the need of including this entity in the differential diagnosis of tonsillar neoplasms to avoid misdiagnoses.
Parathyroid Lipoadenoma: An Entity Linking to Multiple Endocrine Neoplasia?  
(Poster No. 142)

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Parathyroid lipoadenoma is an extremely rare cause of hyperparathyroidism. There were fewer than 50 cases reported in the English literature, none of which was associated with multiple endocrine neoplasia (MEN). Reporting bias may exist owing to its rarity and the limited number of case reports. The characteristic histologic feature of parathyroid lipoadenoma is an increased parathyroid parenchymal mass with abundant stromal fat in a patient with primary hyperparathyroidism. The paradoxical increase in stromal fat poses significant challenges in preoperative imaging and intraoperative frozen diagnoses. We report 2 cases involving elderly women (58 and 66 years old) who underwent parathyroidectomy for primary hyperparathyroidism. Gross examination revealed completely and partially encapsulated masses weighing 2.64 and 5.07 g, respectively. Histologically, the masses, with thin rims of normal parathyroid (Figure 1A, A), are composed of abundant mature adipose tissue (30% and 40%, respectively) and follicular pattern predominant chief cells intermingled with nested and abundant mature adipose tissue (30% and 40%, respectively). The first patient had a concurrent incidental finding of stage IV thyroid carcinoma, in the context of a family history of MEN type II. The second patient has a rather strong family history of hyperparathyroidism clinically suggestive of MEN. In summary, we present 2 cases of parathyroid lipoadenomas in the context of a family history of MEN, suggesting an association of this rare tumor to MEN syndrome. A large-scale study needs to be conducted to confirm this correlation.

Oncocytic Mucoepidermoid Carcinoma Arising Within Warthin Tumor of the Parotid Gland  
(Poster No. 145)

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Oncocytic salivary gland carcinomas are uncommon salivary gland neoplasms, among which the oncocyic variant of mucoepidermoid carcinoma (OMEC) is very rare. We report a case of OMEC arising in a Warthin tumor of the parotid gland. A 66-year-old man had a 6-month history of left neck mass, which on fine-needle aspiration showed rare atypical cells. Computed tomography scan showed a 4.4 × 4.4-cm enhancing mass in the right kidney with possible extension to the renal vein concerning for renal cell carcinoma. A core biopsy with touch preparations was performed, which demonstrated highly cellular smears with pseudoglandular formation around metachromatic material; the cell block contained the classic cribriform architecture of ACC. The patient underwent neoadjuvant chemotherapy. Although late metastases are common for ACC, metastases to the kidney remain profoundly rare. ACC also shares a similar predilection for venous involvement with renal cell carcinoma, but the distinctive histologic features permit diagnosis even by minimally invasive methods.

Carcinosarcoma of the Parotid: Investigating Its Biology With Morphoproteomics  
(Poster No. 143)

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Carcinosarcoma of the parotid is a rare biphasic malignant neoplasm composed of both carcinomatous and sarcomatous components, and represents approximately 0.4% of all malignant salivary gland neoplasms. We report the case of a 55-year-old man who presented with progressive left ear pain, facial twitching, facial weakness, and an enlarging left facial mass. Computed tomography scan and magnetic resonance imaging of the neck and temporal bone was remarkable for an infiltrative, heterogeneously enhancing mass within the parotid gland with involvement of the tip of the left mastoid temporal bone and left level II lymph nodes. Subsequently, the patient underwent left total parotidectomy with neck dissection. Histopathologic evaluation of the tumoral tissue revealed a high-grade, mixed epithelial and mesenchymal malignant tumor, most consistent with a carcinosarcoma of the parotid. We performed morphoproteomic analysis on the surgical specimen to further characterize the biology of the tumor. Immunohistochemical stains were significant for secreted protein acidic and rich in cysteine (SPARC); glioma-associated oncogen protein 2 (Gli2); and phosphorylated signal transducer and activator of transcription (p-STAT3 [Tyr705]) positivity in the carcinomatous and malignant mesenchymal components. These aforementioned markers have been linked to the epithelial-mesenchymal transition in which epithelial cells lose their characteristics and phenotypically become mesenchymal cells. This finding allows us to further understand the biology of the 2 cellular components of the carcinosarcoma as having a monoclonal origin. Herein, we described a rare case of carcinosarcoma of the parotid and investigated its biology through the use of morphoproteomics.

Metastatic Adenoid Cystic Carcinoma to the Kidney  
(Poster No. 144)

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Adenoid cystic carcinoma (ACC) is an uncommon malignancy that arises in several sites, most commonly the salivary glands, and frequently exhibits an indolent but persistent pattern of growth. We present the case of a patient with incidentally identified metastatic ACC to the kidney decades after the initial diagnosis. A 62-year-old woman with history of left parotidectomy and radiation for ACC 22 years prior, status post right upper and middle lobectomies for metastatic ACC 4 years prior, presented for routine follow-up. A computed tomography scan demonstrated a 4.4 × 4.4-cm enhancing mass in the right kidney with possible extension to the renal vein concerning for renal cell carcinoma. A core biopsy with touch preparations was performed, which demonstrated highly cellular smears with pseudoglandular formation around metachromatic material; the cell block contained the classic cribriform architecture of ACC. The patient underwent neoadjuvant chemotherapy. Although late metastases are common for ACC, metastases to the kidney remain profoundly rare. ACC also shares a similar predilection for venous involvement with renal cell carcinoma, but the distinctive histologic features permit diagnosis even by minimally invasive methods.
Warthin tumor, which contains low-grade mucocoeleiform carcinoma with oncocytic features. The differential diagnoses of OMEC include other salivary oncocytes neoplasms, which usually can be differentiated by immunostains. Positive p63 and presence of mucocytes are the features of OMEC. In conclusion, it is important to recognize OMEC and distinguish this entity from other high-grade oncocytes carcinoma, since OMECs are usually a low-grade malignancy with low recurrence rate after complete excision (Figure 162).

B-Cell Lymphoma of the Ear in a 71-Year-Old Man
(Poster No. 146)

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B-cell lymphoma of the ear is rare. We report here a case of low-grade B-cell lymphoma of the right ear in a 71-year-old man. His past medical history is significant for rheumatic fever, splenomegaly, mitral valve replacement, and long-term use of anticoagulation. This patient presented with bilateral ear lobe redness, swelling, and pain. By clinical impression, the lesion could be a polychondritis. Thus, a punch biopsy was performed to rule out polychondritis. The ear skin showed a dense dermal infiltrate of monomorphic small lymphocytes with a gray zone separating the epidermis from the dermis. No lymphoid follicles were seen. Most of the small lymphocytes were CD20+, and CD43+, cyclin-D1, IgD, and neoplastic B-cells were negative for CD3, CD5, CD10, CD23, Bcl-6, and they exhibited jk. Most of the small lymphocytes were CD43+, and CD45+. They were interspersed with CD20+, CD5+, and CD45+ T-cells. The immunophenotypic profile in conjunction with morphology, supported a diagnosis of low-grade malignant lymphoma of B-cell phenotype. The possibility of polychondritis was ruled out. No other places of lymphoma involvement have been discovered in this patient so far. Thus, this is a primary cutaneous lymphoma, mostly likely a cutaneous marginal zone lymphoma. This patient is doing well with appropriate treatment.

A Rare Case of Respiratory Epithelial Adenomatoid Hamartoma
(Poster No. 147)

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Respiratory epithelial adenomatoid hamartoma (REAH) is a rare lesion of the sinonasal tract and nasopharynx. The case described here is from a 71-year-old man who presented with sneezing, anosmia, and nasal block. Endoscopic examination revealed bilateral nasal polyps. On surgical operation, multiple polyps were arising from nasal septum and all sinuses. The clinical diagnosis was bilateral sinonasal polyps and inverted papilloma. Microscopic examination revealed REAH with irregular glandular proliferation composed of widely spaced, small to medium glands lined by multilayered, ciliated respiratory epithelium.

The glands were in direct continuity with surface epithelium in some areas. Characteristic stromal hyalinization was present with envelope of glands by a thick, eosinophilic basement membrane (Figure 163). Multiple sinonasal polyps were also present. A search of medical literature showed approximately 54 cases of REAH, including the 31 cases first described by Wenig and Heffner in 1995. REAH preferentially involves 1 side of the posterior nasal septum but can occur at other sites also. The etiology of REAH is unknown but appears to be associated with inflammation and polyposis. REAH appears to be a benign lesion, since no recurrence or metastasis has been reported. Surgical excision is the treatment of choice. However, some studies suggest that REAH may be associated with sinonasal adenocarcinoma.

Myxofibrosarcoma of Sinonasal Tract
(Poster No. 148)

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Myxofibrosarcomas are the most common sarcomas in adults but predominantly arise in lower limbs of the elderly. The myxofibrosarcoma is characterized by predominantly myxoid morphology with rare fibrous areas. Myxofibrosarcoma is considered to be synonymous with low-grade myxoid malignant fibrous histiocytoma and has relatively good prognosis with a locally aggressive clinical course and rare distant metastases. Here we report a rare case of a myxofibrosarcoma arising in the sinonasal tract. The patient is a 60-year-old man, presented with chronic nasal obstruction and mild chronic discomfort in the area. Surgical resection was performed with no prior biopsy. The histologic examination of the lesion showed the classical histology of relatively bland spindle cells in myxoid background growing in a herringbone and microcystic pattern with rare focal areas of collagen deposition. The tumor behavior was graded intermediate with FNCLCC scoring of a “low-grade” sarcoma. The histologic differential diagnosis on a small specimen from sinonasal tract can include nodular fasciitis, spindle cell lipoma, nerve sheath myxoma (neurothekeoma), low-grade fibromyxoid sarcoma, myxoid liposarcoma, and extraskeletal myxoid chondrosarcoma. Most head and neck fibrosarcomas are associated with a favorable outcome (5-year survival: 75%). Recurrences are common (up to 60%), usually due to surgical difficulty and anatomic complexity of the sinonasal tract. Distant metastasis is uncommon (15%). The most common sites of distant metastasis are lung and bones. A poor prognosis is related to male patients, large tumors, advanced tumor stage (multiple sites involved), a high histologic grade, and positive surgical margins.

Sinonasal Eosinophilic Angiocentric Fibrosis
(Poster No. 149)

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Eosinophilic angiocentric fibrosis (EAF) is a rare benign condition. EAF is a tumefactive lesion of the orbit and upper respiratory tract, with progressive upper airway obstruction in association with submucosa inflammation, fibrosis, and tumoralike growth. Histologic features include different stages of fibrosis, inflammatory cell infiltration with predominance of eosinophils, lymphocytes, and plasma cells. The distinctive morphologic feature is the perivascular fibrosis (“onion skinning”). The fibrosis in EAF has various appearances as the disease progresses. Predominant fibrotic tissue with minimal onion skinning, as seen in our present case, represents an early stage of the disease course. Biopsy from the nasal cavity of our 36-year-old male patient is composed of
multiple fragments of fibrous tissue with inflammatory cell infiltrate including eosinophils, plasma cells, and lymphocytes. Small foci of characteristic “onion skinning” are appreciated with careful evaluation of the specimen. The ratio of IgG4 to IgG by immunohistochemical study is 0.18. This case represents another example of the unique and characteristic histologic picture of this rare entity, which will serve to increase the awareness of the entity and lead to the correct diagnosis. In addition to our case, in line with the previous 3 reported cases, demonstrates a possible IgG4 involvement in the pathogenesis of EAF (Figure 164).

**Splenic Lymphangiomia: An Extremely Rare Condition of Spleen**

(Poster No. 150)

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Splenic lymphangiomia is the malformed development of lymphatic channels in spleen, which is extremely rare, usually an incidental finding. Here we report a case of this entity. The patient was a 51-year-old woman with a complaint of abdominal pain for 1 year. The ultrasonography showed a cystic mass in spleen with increasing size on follow-up. A subsequent splenectomy was performed. Gross examination revealed a mass in the upper pole of spleen measuring 4.7 x 4 x 3.2 cm. The mass had a red-tan cut surface with central fibrosis. Microscopically, the mass was composed of abundant small spaces lined by scattered cells, which were plump or slightly attenuated. The spaces contained homogenous pink material without red cells or other blood elements. The central portion of the lesion showed fibrosis, degenerative change, hemorrhage, and hemosiderin-laden macrophages. There was no significant cytoplasmic atypia, active mitosis, or tumor necrosis identified. The lesion was intervening with benign splenic tissue at periphery without infiltrative pattern. Immunostains showed that the lining cells of the spaces were strongly and diffusely positive for CD31 and D2-40, and negative for CD68, confirming the diagnosis of splenic lymphangiomia. The differential diagnoses will be discussed, including littoral cell angioma, heman gioma, and low-grade angiosarcoma. Awareness of this entity and appropriate application of immunohistochemistry are essential to assure the correct diagnosis.

**A Novel Association of Biventricular Cardiac Noncompaction and Diabetic Embryopathy**

(Poster No. 151)

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Diabetic embryopathy (DE) refers to a constellation of congenital malformations arising in the setting of poorly controlled maternal diabetes. Cardiac abnormalities are the most frequently observed findings in this syndrome, with a 5-fold risk over normal pregnancies. While a diverse spectrum of cardiac defects has been documented, cardiac noncompaction morphology has not been associated with this syndrome. In this report, we describe a novel case of biventricular cardiac noncompaction in a neonate born to a mother with diabetes. The patient was a late preterm female neonate with nonspecific facial dysmorphism, caudal regression syndrome, bilateral bilateral lungs, multiple cardiac septal and arch defects, heterotaxy with left atrial isomerism, as well as biventricular cardiac noncompaction. Gross examination of both ventricles demonstrated marked spongy myocardium (Figure 165, A and B). Histologic sections by Masson trichrome staining showed increased myocardial trabeculation greater than 50% left ventricular thickness and greater than 75% right ventricular thickness, consistent with noncompaction morphology (Figure, C and D). Additionally, noncompaction was noted on postdelivery echocardiogram (Figure, E). The pathogenesis of DE and cardiac noncompaction are not well understood. DE may arise secondarily to cellular organelle stress in a hyperglycemic environment in utero. Cardiac noncompaction, commonly seen isolated to the left ventricle, has been associated with a number of genetic defects that arrest normal embryologic compaction of the developing myocardium. In this case, we postulate that the development of noncompaction morphology may also arise as a result of metabolic derangements secondary to gestational hyperglycemia, perhaps through epigenetic modification of genes critical for normal myocardial compaction.

**Diffuse Eosinophilic Arteritis Associated With Late In-Stent Thrombosis**

(Poster No. 152)

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Drug-eluting stents are associated with a low risk of late stent thrombosis (LST) related to delayed intimal healing. In a proportion of LST cases an allergic reaction to the polymer is the cause, but diffuse arteritis has not been previously reported. We present a case of LST caused by hypersensitivity documented at autopsy in a 50-year-old woman. The patient had a non-ST elevation acute myocardial infarction treated with drug-eluting (everolimus) Promus Element stent (Boston Scientific, Natick, Massachusetts) 5 months before cardiac arrest and death. Prior conditions included chronic obstructive lung disease, obesity, nonalcoholic liver disease, cigarette smoking, and hypertension. Medications before death included aspirin and prasugrel. Autopsy findings demonstrated moderate coronary disease involving the right, left anterior descending, and left circumflex arteries. The heart was moderately enlarged by concentric left ventricular hypertrophy (480 g). The stent, located in the proximal right coronary artery, was occluded by fibrin thrombus, macrophage giant cells, and chronic inflammation. The epicardial arteries (sectioned serially at 5-mm intervals) demonstrated diffuse eosinophilic and chronic inflammatory infiltrate most prominent in the adventitia, followed by the intima. There was minimal medial inflammation and no macrophage giant cells remote from the stent. The myocardium showed patchy areas of ischemia, but no transmural infarct. The cause of death was attributed to LST. Our case illustrates that LST, when caused by an allergic reaction to the polymer, may result in a diffuse eosinophilic perivascularitis and intimitis.

**Left Atrial High-Grade Pleomorphic Undifferentiated Sarcoma Masquerading as Atrial Myxoma: A Rare Entity**

(Poster No. 153)

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Pleomorphic undifferentiated sarcoma is a rare tumor that typically affects the extremities or retroperitoneum and represents less than 3% of cardiac tumors with a male predominance. We report a case of high-grade pleomorphic undifferentiated sarcoma arising from the left atrial septum. A 70-year-old woman with a past medical history of
Eosinophilic Coronary Periarteritis With Arterial Dissection: The Mast Cell Hypothesis

Rakesh Mandal, MBBS, MS, MPH (rakeshmandal@hotmail.com); Erin G. Brooks, MD; Robert F. Corliss, MD. Department of Pathology, University of Wisconsin, Madison.

A subset of coronary arterial dissections is associated with eosinophilic coronary periarteritis (ECPA); however, the pathogenesis of the process remains unclear. Mast cells normally reside in coronary arterial adventitia and are known mediators of eosinophilic inflammation and necrosis. The neoplastic cells were positive for immunohistochemical stains CD68 and vimentin, with rare cells staining for smooth muscle actin and muscle-specific actin. They were negative for pan-cytokeratin, S100, myogenin, desmin, and Melan-A. These findings supported the diagnosis of high-grade pleomorphic undifferentiated sarcoma. Surgical margins were free of involvement, but the lesion came to within 2 mm of the inked resection margins. Surgical resection with wide margins is the treatment of choice; however, owing to the location of the tumor, further excision was impossible. Prognosis for this lesion is generally poor with metastases commonly to the bone, kidneys, lung, lymph nodes, or skin. Sadly, the patient died of unknown causes 5 months after her surgery.

Immunohistochemical Evaluation of Ber-EP4, MOC-31, TAG-72, and CEA in Various Carcinomas

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Context: Ber-EP4, MOC-31, TAG-72, and CEA are the commonly used immunomarkers to identify carcinomas (CAs), especially in cytologic specimens; however, data were inconsistent. In this study, we evaluated their expressions in CAs from various organs.

Design: Immunohistochemical evaluation of the expressions of Ber-EP4 and MOC-31 ( DakoCytomation, Glostrup, Denmark), TAG-72 (Cell Marque, Rocklin, California), and CEA (BioGenex, San Ramon, California) was performed on 797 CAs on tissue microarray sections. The staining results were recorded.

Results: The positive staining results (%) and the total number of cases for each entity (N) are summarized in the Table. MOC-31 had the highest sensitivity (74%) and TAG-72 the lowest (18%). Urothelial CAs showed the lowest expression of all 4 markers. CEA was often expressed in colorectal, pancreatic, and endocervical adenocarcinomas; in contrast, it lacked or had low expression in ovarian serous CAs, and endometrial and prostatic ADCs.

Conclusions: Our data suggest that (1) MOC-31 and Ber-EP4 are reasonably sensitive markers for CAs and should be used as the first choice; (2) TAG-72 has very limited utility owing to its low sensitivity; (3) CEA is sensitive for adenocarcinomas of colon, pancreas, and endocervix; however, it has limited utility for ovarian serous CA, and...
Secondary Neoplasms of the Salivary Glands: A Review of 6 Cases

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Context: Secondary neoplasms of the salivary glands are uncommon. Head and neck cutaneous squamous cell carcinoma and malignant melanoma make up 80% to 85% of metastatic tumors to the major salivary glands. The most common distant primary sites include the lung, kidney, breast, and colon.

Design: Among 242 salivary gland fine-needle aspiration specimens at our institution between 1997 and 2014, we identified 6 cases that were either suggestive of or diagnosed as secondary neoplasms of the salivary glands. All initial diagnoses were rendered on salivary gland fine-needle aspiration cytology. The diagnoses were correlated with the site of primary tumor when available (3 of 6 cases).

Results: In our case series, secondary salivary gland neoplasms were identified more in men (men to women ratio = 4:2), with the average age at diagnosis being 72 years (58-84 years). In 2 cases, the site of primary tumor was definitively identified; these were squamous cell carcinomas metastatic from the tongue. In 2 cases, metastatic cholangiocarcinoma and metastatic lung carcinoma were highly suggested on the basis of morphology and immunohistochemistry studies. In the remaining 2 cases, the site of primary tumor could not be definitively identified. Of these, 1 case was diagnosed as metastatic poorly differentiated small cell neuroendocrine tumor; the other case was found to be highly suggestive of nasopharyngeal carcinoma.

Conclusions: Noncutaneous secondary neoplasms, although uncommon, should be considered in the differential diagnosis of malignant salivary gland neoplasms. This is the first case of renal mucinous tubular and spindle cell carcinoma in a patient with colon adenocarcinoma.

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Ber-EP4, No. (%)</th>
<th>MOC-31, No. (%)</th>
<th>TAG-72, No. (%)</th>
<th>CEA, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung, ADC</td>
<td>46 (54)</td>
<td>54 (64)</td>
<td>16 (19)</td>
<td>58 (68)</td>
</tr>
<tr>
<td>Breast, IDC</td>
<td>98 (56)</td>
<td>111 (63)</td>
<td>20 (11)</td>
<td>19/43 (44,2)</td>
</tr>
<tr>
<td>Breast, ILC</td>
<td>30 (38)</td>
<td>31/40 (78)</td>
<td>9 (12)</td>
<td>38 (49)</td>
</tr>
<tr>
<td>Pancreatic ADC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esophageal ADC</td>
<td>41 (87)</td>
<td>46 (98)</td>
<td>21 (45)</td>
<td>45 (96)</td>
</tr>
<tr>
<td>Gastric ADC</td>
<td>35 (83)</td>
<td>42 (91)</td>
<td>20 (43)</td>
<td>33 (72)</td>
</tr>
<tr>
<td>Colorectal ADC</td>
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<td>12 (67)</td>
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<td>10 (56)</td>
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<td>38 (100)</td>
<td>13 (34)</td>
<td>38 (100)</td>
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<td>40 (69)</td>
<td>16 (28)</td>
<td>9 (16)</td>
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<tr>
<td>Endocervical ADC</td>
<td>23 (78)</td>
<td>30 (100)</td>
<td>8 (27)</td>
<td>26 (87)</td>
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<td>Inv UCA</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Prostatic ADC</td>
<td>24 (29)</td>
<td>20 (25)</td>
<td>6 (8)</td>
<td>24 (30)</td>
</tr>
<tr>
<td>Total</td>
<td>543 (67)</td>
<td>565/759 (74)</td>
<td>146 (18)</td>
<td>309/664 (47)</td>
</tr>
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</table>

Abbreviations: IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; Inv, invasive.

A Splenule Disguised as a Pancreatic Mass—Endoscopic Ultrasound-Guided, Fine-Needle Aspiration Cytology Raises the Curtain and Steals the Show: Review of Cytologic Features and Differential Diagnoses

Jaya Bajaj, MD (jaya.eworks@gmail.com); Oana C. Rafael, MD; Ion Chiosea, MD; Mohamed Aziz, MD. 1Department of Pathology, NSLIJHS/HOFSTRA North Shore- LIJ School of Medicine, Lake Success, New York; 2Department of Pathology, NSLIJ–Lenox Hill Hospital, New York; 3Department of Transfusion Medicine, National Institutes of Health, Bethesda, Maryland.

Intrapancreatic accessory spleens (IPAS) are rarely encountered in endoscopic ultrasound-guided, fine-needle aspirations (EUS-FNA). However, as incidentally discovered IPAS can radiologically mimic a pancreatic neoplasm, a definitive diagnosis made by EUS-FNA can avert an unnecessary surgical intervention or additional radiologic studies. A follow-up computed tomography scan showed a 3.2-cm hyperdense cystic renal mass. Cytology smears revealed crowded clusters and sheets of cells with round nuclei and pinpoint nucleoli associated with mucinous material in the background (Figure 167). On cell block these cells were arranged in a tubular pattern. Core biopsy revealed several small fragments of tumor cells with uniform low-grade nuclei that formed microacinar and nested patterns. Tumor cells were positive for PAX8, CK7, and AMACR, and negative for CD10. This immunophenotype, along with morphology, was consistent with the diagnosis of mucinous tubular and spindle cell carcinoma. As this is a rare newly described entity, limited experience with renal mucinous tubular and spindle cell carcinoma may pose a diagnostic challenge on FNA, particularly in the presence of a second malignancy, for which the differential diagnosis includes metastasis to the kidney. To our knowledge, this is the first case of renal mucinous tubular and spindle cell carcinoma in a patient with colon adenocarcinoma.
A 77-year-old African American woman with a history of diverticulitis and thyroid cancer was found to have a pancreatic tail mass (18 x 13 mm) on computed tomography. She underwent EUS-FNA to rule out an endocrine neoplasm. Cytology slides showed a mixed population of inflammatory cells present both embedded in a vascular meshwork and loosely dispersed throughout the aspirate smears. We did not observe the presence of large platelet aggregates, a feature recently described in IPAS. Immunocytochemical analysis on cell block material showed lack of staining for synaptophysin, chromogranin, CD56, CAM 5.2, CK7, and CK20, and a mixed B- and T-cell population without evidence of a lymphoproliferative process. Ki-67 showed low proliferation (<10%). The primary cytologic differential diagnosis was neuroendocrine neoplasm, as the typically dispersed, predominantly single-cell population of inflammatory cells seen in IPAS can be mistaken for a monotonous population of neuroendocrine cells. The neoplastic cells of PanNET, however, typically have more cytoplasm than inflammatory cells, show eccentric round to oval nuclei, and finely dispersed chromatin. The differential diagnosis also included solid pseudopapillary neoplasm, but its blood vessels are typically larger than in IPAS and form fibrovascular cores surrounded by uniform epithelioid cells. Recognizing the cytologic features of IPAS on EUS-FNA and correct classification is important to avoid unnecessary surgery (Figure 168).

The median number of urine cytologies before a positive cytology finding was 2.0 (Figure 169). The median time from the initial negative to the first observed positive cytology finding was 1.4 months (IQR: 5.0 months). The median time from the first negative cytology finding until positive biopsy finding was 5.5 months (IQR: 11.0 months). Only 62 subjects (34.4%) had conversion from negative to positive cytology finding in the past 2 years. We explored patterns of conversion from a negative initial urine cytology finding to a positive finding on either subsequent cytology or biopsy as a benchmark for surveillance in the diagnosis of urothelial carcinoma. The median number of urine cytologies before a positive cytology diagnosis was 2.0 (Figure 169). The median time from the initial negative to the first observed positive cytology finding was 1.4 months (IQR: 5.0 months). The median time from the first negative cytology finding until positive biopsy finding was 5.5 months (IQR: 11.0 months). Only 62 subjects (34.4%) had conversion from negative to positive urine cytology finding.
findings confirmed the presence of invasive lobular carcinoma. Metastatic melanoma of the breast is an uncommon finding but must be considered in cases with cytomorphic features of melanoma presenting in breast cytology specimens. Despite the recent history of melanoma in our patient, it was important to consider the possibility of recurrence or metastasis from a prior carcinoma (endometrial or lobular).

**Lobular Carcinoma of the Breast Presenting as a Metastatic Melanoma to the Axilla on Fine-Needle Aspiration and Core Biopsy: Report of a Case and Review of the Literature**  
(Poster No. 8)

Tamar C. Brandler, MD, MS (tbrandler@nshs.edu); Hua Guo, MD; Fatima-Zahra Jelloul, MD; Mohamed S. Aziz, MD. Department of Pathology, Hofstra North Shore-LIJ School of Medicine, Lake Success, New York.

An 84-year-old woman with a history of infiltrating lobular carcinoma (status post right mastectomy) and endometrial adenocarcinoma presented for excision of a right upper back, irregular, multifocal, pigmented lesion. The lesion was diagnosed as malignant melanoma extending to the lateral margin. Two weeks later, she returned to the hospital with a right axillary mass. Sonography demonstrated a 1.5-cm region of ill-defined mixed echogenicity corresponding with a firm palpable right axillary nodule. The patient underwent a fine-needle aspiration and core biopsy of the right axillary soft tissue with the preprocedure differential diagnosis of melanoma, scar tissue, and carcinoma. Cytology slides revealed a hypercellular specimen with numerous malignant single cells and rare crowded groups displaying anisonucleosis, eccentric nuclei, dark dense cytoplasm, and small conspicuous nucleoli. The core biopsy showed an infiltrating solid tumor composed of single malignant cells with eccentric nuclei. These findings were highly suggestive of melanoma.

The case was diagnosed as cytomorphologically consistent with malignant neoplasm with immunostains pending for further characterization (Figure 173, A and B). Immunocytochemistry results were negative for S100, HMB-45, Melan-A, and E-cadherin, with positive staining in AE1/AE3 cytokeratin (Figure 173, C), high-molecular-weight cytokeratin 903, and estrogen receptor (>90%) (Figure 173, D). These findings confirmed the presence of invasive lobular carcinoma.

**Metastatic Melanoma of the Breast Presenting as a Lobular Carcinoma (status post right mastectomy) and endometrial adenocarcinoma**

**Diagnostic Pitfalls of Effusion Cytology for Early Diagnosis of Primary Pleural Angiosarcoma: Two Case Reports**  
(Poster No. 10)

Rajeswari Nagarathinam, MD (rajeswari74@yahoo.com); Donna K. Russell, MEd, CT(ASCP)HT; Zhongren (David) Zhou, BM, PhD. Department of Cytopathology, University of Rochester Medical Center, Rochester, New York.

Primary pleural angiosarcoma (PPA) is rare and often presents as pleural effusion without other symptoms, which makes effusion cytology diagnosis very important. We present 2 cases of PPA in which...
atypical cells were first identified in effusion cytology. Our first case involved a 31-year-old man with chest pain who developed pleural effusion. Fluid cytology revealed single and clusters of large cells with nuclear abnormalities and benign-appearing mesothelial cells (Figure 173, A and B). The negative-for-malignancy finding was diagnosed in an outside hospital, since the cells of interest were negative for Ber-EP4 on immunohistochemistry. Later, pleural biopsy and additional immunohistochemistry panel for fluid showed that the atypical cells were positive for CD31 and CD34, consistent with angiosarcoma (Figure, C and D). Diagnosis of PPA was established after clinically ruling out other primaries. Our second case involved a 65-year-old woman who presented with left pleural effusion and had past history of breast cancer. Single and irregular clusters of atypical cells were identified on fluid cytology with final diagnosis of atypical cells. Imaging revealed pleural mass and biopsy showed angiosarcoma with expression of CD31 and CD34. In both our patients with PPA, pleural effusion was the early presenting symptom and the definite diagnosis was established by biopsies after atypical cells were first identified on fluid cytology. Immunohistochemistry panel in effusion cytology usually includes mesothelial and epithelial cell markers. We report these 2 cases to emphasize the importance of identifying atypical cells by using adjunctive endothelial markers for an early diagnosis of PPA.

**Spermatogenesis Status in Azoospermic Patients Diagnosed by Testicular Fine-Needle Aspiration and Their Clinical Predictors**

(Poster No. 11)

Sohaib H. Abu-Farsakh, MD1 (f1lab@yahoo.com); Hussam Abu-Farsakh, MD.2; Department of Pathology, King Hussein Cancer Center, Amman, Jordan; 3Department of Pathology, First Medical Lab, Amman, Jordan.

**Context:** Fine-needle aspiration of testis (FNAT) is important in detecting sperm in azoospermic patients before their assisted reproduction techniques.

**Design:** A total of 2038 azoospermic patients were examined for the presence of sperm by performing FNAT from 10 sites (5 from each testis). Spermatogenesis status was reported as obstructive azoospermia (OA), hypospermatogenesis (HS), spermatogenesis arrest at spermatid stage (SATS), spermatogenesis arrest at spermatocyte stage (SACS), or Sertoli cell only (SCO). Testicular size was recorded as follows: normal testicular size (NTS), intermediate size (ITS), and small size (STS). Data regarding varicocele, body mass index, smoking history, family history, and hormonal status (FSH and AMH) were recorded.

**Results:** Thirty-eight percent of azoospermic patients were found to have sperm. Testicular size was noted as follows: 43% NTS, 39% ITS, and 18% STS. Fifty-two percent of patients with NTS had sperm, 33% of patients with ITS had sperm, while only 16% of those with STS had sperm. Patients with NTS and normal FSH and AMH levels (total of 83 cases) have the following spermatogenesis status: OA 25%, HS 47%, SATS 14%, SACS 12%, and SCO 2%. Patients with NTS, and normal FSH and AMH levels had a 72% chance of having sperm, while patients with less-than-normal testicular size, high FSH level, and low AMH (118 patients) level had a 19% chance of having sperm (P < .001), consistent with Ewing/PNET sarcoma. Molecular studies demonstrated Ewing sarcoma gene translocation, t(11;22)(q24;q12), confirming the diagnosis. In summary, FNAT is a quick procedure that may be used in the diagnosis of Ewing sarcoma. As in our case, accurate diagnosis can be made in deep-seated tumors by procuring adequate material under radiologic guidance.

**A Case of Peripheral T-Cell Lymphoma With Unusual Presentation in a HTLV-II–Positive Patient**

(Poster No. 13)

Tahereh Dadfarnia, MD1 (tdadfarnia@mednet.ucla.edu); Trisha M. Parekh, MD; You-Wen Qian, MD, PhD; Tarek M. Elghetany, MD; Vicki Schnadig, MD; Ranjina Nawgiri, MD.2 Department of Pathology, Olive View-UCLA, Los Angeles, California; Departments of Internal Medicine and Pathology, University of Texas Medical Branch, Galveston; 2Department of Pathology, Baylor College of Medicine, Houston, Texas.

Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS) is a rare neoplasm that typically presents as generalized lymphadenopathy. PTCL-NOS presenting as malignant ascites is rare. A 61-year-old African American man with past medical history of HCV, cryoglobulinemia, and cryptococcal pneumonia was admitted for dyspnea on
showed an abnormal T-lymphocyte population expressing CD4, CD5, weak surface CD3, but no expression of CD7. Polymerase chain reaction studies of ascitic fluid detected a clonal T-lymphocyte population with T-cell receptor γ gene rearrangement. Serologic testing for human T lymphotrophic virus (HTLV) was positive for HTLV II, and Western blot confirmed antibodies against HTLV II antigens. Subsequent bone marrow biopsy revealed lymphomatous involvement. Immunostaining with CD30 and ALK-1 immunostaining was negative. This case was classified as PTCL-NOS. PTCL-NOS can have an unusual clinical presentation, such as ascites and pleural effusion, and may also occur as a complication of immunodeficiency state. Cytomorphology may mimic adult T-cell lymphoma/leukemia. Further studies are needed to determine if HTLV II viral infection is associated with PTCL.

**Bacterial Vaginosis: Revisited in Liquid-Based Papanicolaou Smears**

(Julie Chepovetsky, MD (julie.chepovetsky@nyumc.org); Huimiao Jiang, MD; Aylin Simsr, MD; Wei Sun, MD. Department of Pathology, NY University Medical Center, New York, New York.)

*Abstracts*

**Context:** Bacterial vaginosis (BV) is the most common cause of vaginitis, frequently disregarded but with far-reaching clinical complications including increased susceptibility to sexually transmitted diseases. In recent years with the launch of the Vaginal Microbiome Project and culture-independent techniques for identifying microbiota, the identification of BV has gained in importance. We sought to study the incidence of BV in liquid-based Papanicolaou (Pap) smears and its correlation with Neisseria gonorrhoeae (NG), Chlamydia trachomatis (CT), and human papilloma virus (HPV) infection, and presence of squamous intraepithelial lesion (SIL).

**Design:** We performed computerized searches in our information system on liquid-based cervical Pap smears received between January 2012 and August 2013. A total of 22,063 Pap smears were identified, of which 1928 contained a shift in vaginal flora. Of 810 cases reviewed, 100 cases with additional molecular NG/CT testing, 400 cases with additional molecular HPV testing, and 210 cases with LSIL and HSIL were evaluated.

**Results:** A shift in vaginal flora was identified in 46% of NG/CT-positive cases as compared to 10% of NG/CT-negative cases (P < .001). However, no significant difference was noted in the presence of shift in vaginal flora in the HPV-positive cases (15.5%) as compared to the HPV-negative cases (9%) or in the cases with and without SIL.

**Conclusions:** A strong correlation is present between shift in vaginal flora identified in the Pap smear and NG and CT infection. No significant association was noted between shift in vaginal flora and HPV infection or squamous intraepithelial lesions.

**Cytomorphologic Features of “Intrathyroid Follicular Lesion” of Parathyroid Origin**

(Shobha Parajuli, MD (Shobha.Parajuli@tuhs.temple.edu); Heba Y. Durra, MD; Xinmin Zhang, MD; Varsha Manucha, MD. Department of Pathology, Temple University Hospital, Philadelphia, Pennsylvania.)

**Context:** Intrathyroidal parathyroid adenoma/hyperplasia is rare but a challenging lesion to distinguish from a follicular neoplasm of thyroid origin on cytology especially when submitted as “thyroid FNA.”

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(Xiaoyan Zhou, MD (xyzhou112@hotmail.com); Shikha Bose, MD. Department of Pathology, Cedars Sinai Medical Center, Los Angeles, California.)

**Abstracts**

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**Cytomorphologic Features of “Intrathyroid Follicular Lesion” of Parathyroid Origin**

(Shobha Parajuli, MD (Shobha.Parajuli@tuhs.temple.edu); Heba Y. Durra, MD; Xinmin Zhang, MD; Varsha Manucha, MD. Department of Pathology, Temple University Hospital, Philadelphia, Pennsylvania.)

**Context:** Intrathyroidal parathyroid adenoma/hyperplasia is rare but a challenging lesion to distinguish from a follicular neoplasm of thyroid origin on cytology especially when submitted as “thyroid FNA.”
Design: We present 3 cases of intrathyroid parathyroid adenoma/hyperplasia diagnosed on fine-needle aspiration (FNA). All 3 lesions underwent FNA on the basis of ultrasonographic suspicion of follicular neoplasm of thyroid origin. In the first case, initially diagnosed as suggestive of follicular neoplasm on the basis of cytomorphicologic features, the patient underwent total thyroidectomy that revealed a parathyroid adenoma in a normal thyroid. Cytologic features of these cases were retrospectively reviewed at the time of cytohistologic correlation. Subsequently, the other 2 cases were diagnosed as parathyroid adenoma/hyperplasia on the basis of cytologic features and confirmed by immunohistochemistry (negative TTF-1 and positive PTH stain), thereby avoiding thyroid surgery.

<table>
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<th>Clinical Informationa</th>
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Abbreviations: ESRD, end-stage renal disease; FNA, fine-needle aspiration; USG, ultrasonogram.

Conclusions: Presence of crowded, uniform cells arranged in thick trabeculae on “thyroid FNA” should raise a suspicion of parathyroid origin that can be easily confirmed by immunohistochemistry, thereby avoiding unnecessary thyroidectomy.

Fine-Needle Aspiration Biopsy Diagnosis of Oncocytic Carcinoma of the Pancreas

(Poster No. 17)

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1Department of Pathology, Peking Union Medical College Hospital, Beijing, China; 2Department of Anatomic Pathology, Moffitt Cancer Center, Tampa, Florida.

Oncocytic carcinoma is a very rare type of pancreatic adenocarcinoma, associated with intraductal papillary oncocytic neoplasm of the pancreas. It harbors genetic changes distinct from those of pancreatic ductal adenocarcinoma. Therefore, correct preoperative diagnosis is important in this era of personalized medicine. Here we report a case of oncocytic carcinoma diagnosed at Moffitt Cancer Center and discuss the cytologic and histologic features, differential diagnosis, utility of ancillary studies, and the recently updated knowledge about this entity. A 65-year-old woman presented with a mass in the head of the pancreas that was biopsied by fine-needle aspiration on 2 separate occasions. The smears were hypercellular with necrosis. The malignant cells showed oncocytic cytoplasm or less visible cytoplasm with rounded nuclei and prominent nuclei or rounded nuclei with pale chromatin, focal intranuclear inclusions, and grooves. The cells were arranged in crowded groups, irregular sheets, and papillary clusters (Figure 178, A). Oncocytic carcinoma diagnosis was rendered on the basis of these distinct cytomorphicologic features. Subsequent pancreateoduodenectomy demonstrated an invasive oncocytic carcinoma with an intraductal component involving the main pancreatic duct (Figure, B through D). The carcinoma was negative for HER2/neu, AFP, HepPar, CDX2, CD56, synaptophysin, and chromogranin by immunohistochemistry. This case demonstrates that oncocytic carcinoma can be diagnosed preoperatively by fine-needle aspiration biopsy on the basis of its unique cytomorphicologic features. The differential diagnosis includes other neoplasms occurring in the pancreas with oncocytic features, particularly neuroendocrine tumors. Ancillary studies are beneficial for a definitive diagnosis. This carcinoma variant lacks the KRAS mutations common to pancreatic ductal adenocarcinomas.

Utilization of MicroRNA Analysis to Differentiate Autoimmune Pancreatitis From Pancreatic Malignancy: Single Case Demonstration

(Poster No. 18)

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Autoimmune pancreatitis (AIP) is a benign entity that may resemble pancreatic malignancy clinically and radiologically. Accurate preoperative diagnosis is important to avoid unnecessary resection, since steroid is the treatment of choice for AIP. Studies regarding microRNA (miR) expression patterns to differentiate benign and malignant pancreatic lesions have been frequently reported. However, its utility to rule out pancreatic malignancy in fine-needle aspirates of patients with AIP has not been studied. We report the case of a 59-year-old woman with recurring abdominal pain and 1-week history of diarrhea, nausea, and jaundice who was evaluated for pancreatic mass. Endoscopic ultrasonography revealed a 37×35-mm mass in the head of pancreas, which was concerning for malignancy. Endoscopic ultrasound-guided, fine-needle aspiration revealed no definitive evi-
CDX2 in Metastatic Prostatic Adenocarcinoma—Potential for Diagnostic Dilemma: Report of 2 Cases

(Poster No. 19)

Oana C. Rafael, MD1 (orafael@nshs.edu); Oksana Yaskiv, MD1; Eugene Santagada, BA1; Pamela D. Unger, MD.1 1Department of Pathology, North Shore Long Island Jewish-Lenox Hill Hospital, New York, New York; 2Department of Pathology, North Shore Long Island Jewish Hospital/Hofstra School of Medicine, Lake Success, New York.

Diagnosis of metastatic prostatic adenocarcinoma is generally straightforward, using hematoxylin-eosin and immunohistochemistry. CDX2 is commonly positive in colorectal cancer and not usually associated with prostate cancer. However, a subset of mucinous/signet-ring prostate carcinomas can show reactivity. Colorectal carcinoma is in the differential diagnosis of metastatic/prostate adenocarcinoma. A positive CDX2 finding without a known history of prostate carcinoma and lack of prostate-specific antigen (PSA) staining can present diagnostic difficulties. We present 2 cases of metastatic nonmucinous prostate carcinomas with diffuse CDX2 positivity. Case 1 involved an 86-year-old man with elevated PSA levels who had transrectal ultrasound-guided biopsies, which showed extensive prostatic adenocarcinoma, predomnantly Gleason pattern 4+4. A CT of the chest, abdomen, and pelvis a year later showed extensive metastatic disease and no gastrointestinal tract lesions. A supraclavicular mass was biopsied, showing metastatic prostatic adenocarcinoma. CDX2 (Figure, C) and P504S stains were positive, while PSA and PAP were negative (Table). Immunohistochemistry of the original prostate biopsy (Table) showed strong diffuse positivity for PSA and CDX2 focal positivity (Figure, D). Pathologists need to be aware of possible CDX2 staining in prostate carcinoma, especially in metastatic disease. This unusual finding in conjunction with other immunohistochemistry and clinical history is crucial in establishing the correct diagnosis.

Suboccipital Malignant Solitary Fibrous Tumor Diagnosed on Fine-Needle Aspiration and Core Biopsy: Report of an Uncommon Tumor in a Rare Location and Review of the Literature

(Poster No. 20)

Tamar C. Brandler, MD, MS (tbrandler@nshs.edu); Jaya Bajaj, MD; Ryan Brenkert, SCT, MB; Mohamed S. Aziz, MD. Department of Pathology, Hofstra North Shore-LIJ School of Medicine, Lake Success, New York.

A 61-year-old man presented with an enlarged suboccipital heterogeneous soft tissue mass in the suboccipital region that had increased in size from 6.8 to 9.8 cm as compared with 6 months prior. The possibility of a soft tissue sarcoma was raised. Therefore, the patient underwent a fine-needle aspiration and core needle biopsy of the mass. Cytology slides showed sheets, clusters, and single cells with bland cytomorphic features and prominent plasmacytoid morphology (Figure 180, A through C). The core biopsy showed solid sheets of plasmacytoid-like cells with bland cytomorphology, predominantly in perivascular arrangements. Rare mitoses and no necrosis were noted. The differential diagnosis included solitary fibrous tumor (SFT), PEComa, and hemangioendothelioma owing to the perivascular arrangement of bland cells, nerve sheath tumors as well as smooth muscle tumors, melanoma and even squamous cell carcinoma. An extended immunocytochemistry panel was performed for tumor characterization. The only antibodies with strong/positive staining were CD34 and CD99 (Figure, D) with focal weak/positive chromogranin staining. Negative stains included S100, HMB-45, Melan-A, EMA, AE1/AE3, CAM 5.2, HMW-Ck903, p40, CD31, GFAP, CD163, desmin, SMA, and synaptophysin Ki-67 (< 2%). A diagnosis of low-grade mesenchymal neoplasm, hemangiopericytoma/SFT was made. Excision of the entire mass revealed the final diagnosis of malignant SFT. In cytology it is crucial to correlate the cytomorphic features with the clinical presentation and the radiologic findings. Although uncommon, SFTs should be included in the differential diagnosis of suboccipital masses in adults. Our case report adds to the very limited existing literature on cytologic diagnosis of SFT.
Malignant Pulmonary Neoplasm With Papillary Features, Not Otherwise Specified—Does It Belong to the Current Lung Tumor Classification? Report of 2 Unusual Cases

Oana C. Rafael, MD1 (orafael@nshs.edu); Frank Breuer, MD2; Swathi Ratkal, MBBS; Mohamed Aziz, MD.1 1Department of Pathology, North Shore Long Island Jewish-Lenox Hill Hospital, New York, New York; 2Department of Pathology, North Shore Long Island Jewish Hospital/Hofstra School of Medicine, Lake Success, New York.

Malignant pulmonary neoplasm with papillary features, not otherwise specified (NOS), is not part of the current classification of lung tumors; however, such cases do appear in daily practice. A 37-year-old woman presented with chest pain. Imaging revealed a large left lung mass, and a computed tomography–guided fine-needle aspiration followed. Smears and cell block showed a neoplasm with prominent papillary architecture, bland-looking columnar cells with increased nuclear to cytoplasmic ratio, regular nuclei, and inconspicuous nucleoli (Figure 181, upper images). Differential diagnosis included sclerosing hemangioma, papillary adenoma, adenocarcinoma, and papillary metastatic neoplasm. Immunohistochemical stains supported lung origin and excluded metastatic thyroid carcinoma (Table). The absence of a dual-cell population pointed to a well-differentiated adenocarcinoma. The MiB-1 (Ki-67) showed intermediate proliferation rate (10%–20%). In a second case a 53-year-old woman presented with dyspnea and a subphrenic/pleural mass. Cytopathology specimen showed a malignant neoplasm with papillary features. Immunohistochemistry suggested a poorly differentiated carcinoma, and pulmonary, mesothelial, renal, gastrointestinal, or mullerian primaries were excluded (Table). Another fine-needle aspiration and biopsy performed 1 month later recapitulated the initial hypercellular specimen: groups, sheets, clustered or single malignant cells, with enlarged nuclei and prominent nucleoli, vacuolated cytoplasm, and atypical mitoses (Figure, lower images). The proliferation index was 10% to 20%.

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<td>53 yo F</td>
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In both of these instances the final diagnosis was malignant neoplasm with papillary features, NOS. These cases underscore the invaluable help of immunohistochemistry in challenging situations. With continued reporting of additional similar cases, their classification as a separate entity may be warranted.

A Unique Case of Fibrolamellar Hepatocellular Carcinoma Presenting With Altered Mental Status and Elevated Liver Enzymes Diagnosed by Cytology of Peritoneal Fluid

Robert G. Atienza, MD (robbie.atienza@yahoo.com); Gail Prado, MD; Rajiv Pulinthananthu, MD. Department of Pathology, Saint Barnabas Medical Center, Livingston, New Jersey.

Fibrolamellar hepatocellular carcinoma (FL-HCC) is a rare malignant primary liver neoplasm that typically arises in young individuals lacking a background of chronic liver disease and other risk factors for hepatocellular carcinoma. Distinct pathologic features include presence of tumor cells with deeply eosinophilic cytoplasm and macronucleoli surrounded by abundant fibrous bands. On immunohistochemistry, FL-HCC shows both hepatocellular and bile duct differentiation. Metastasis significantly influences patient survival. The overall 5-year mortality rate for patients without metastasis at time of presentation is 86%, whereas it is 39% in cases with metastasis. We report the case of a 25-year-old white woman with history of deep venous thrombosis and without known chronic liver disease who presented with altered mental status. Liver enzymes (AST/ALT) were markedly elevated; CT scan revealed a 13×9-cm mass with focus of calcification in the left lobe of the liver and diffuse ascites. Ascitic fluid yielded dyshesive large tumor cells with abundant eosinophilic/oncocytic cytoplasm and large prominent nucleoli. Immunohistochemical stains were positive for CK7, EMA, and HepPar1, consistent with a metastatic FL-HCC. To our knowledge, this is the first documented FL-HCC that presented with altered sensorium and elevated liver enzymes. Metastatic FL-HCC can pose several diagnostic challenges owing to its uncommonness and the wide range of differential diagnoses. Extensive effort should be made in evaluating the patients’ demographic and clinical history, as well as laboratory and radiologic findings. Awareness of this tumor with emphasis on cytologic features, along with aid of immunohistochemical stains, is the key in clinching a diagnosis (Figure 182).

Retrospective Correlation of Cervical Biopsy Involved by Myelosarcoma With a Concurrent Cervical Papanicolaou Smear

Angelica Padilla, MD (angeliacapilllmd@gmail.com); Binara Assylbekova, MD, Lei Chen, MD, PhD; Natalia Golardi, MD. Department of Pathology and Laboratory Science, University of Texas Health Science Center Houston.

Myeloid sarcoma is a tumor of immature myeloid cells at an extramedullary site and often occurs in patients with a history of acute myeloid leukemia, myeloproliferative disorder, or myelodysplastic syndrome. Rarely, it can manifest initially as an isolated mass. Myeloid sarcoma involving the gynecologic tract is uncommon and manifestation as an isolated mass of the gynecologic tract is rare. We present the case of a 49-year-old woman who presented with menometrorrhagia. On imaging an endophytic mass within the cervix extending into the lower uterus measuring 7.2 × 8.4 × 6.3 cm was identified. The CBC
showed anemia with hemoglobin of 5.7 with normal differential. A Papanicolaou (Pap) smear revealed atypical cells of undetermined squamous significance. Bone marrow biopsy is currently pending and will be performed. A cervical biopsy was obtained. Hematoxylin-eosin--stained sections revealed cervical stroma with diffusely infiltrating large neoplastic cells with high nucleus to cytoplasmic ratio and immature chromatin. Rare scattered atypical megakaryocytes were identified. The tumors cells were diffusely and strongly positive for CD43, CD68, CD117, and myeloperoxidase; weakly positive for CD45; and negative for CD34, CD30, CD56, CD138, B-cell, T-cell, epithelial markers, and neuroendocrine markers. The morphologic findings and immunohistochemical profile were diagnostic of myeloid sarcoma. Retrospectively, the Pap smear identified abundant immature cells of myeloid origin. Few cases of well-documented cervical myeloid sarcoma as an isolated mass have been reported in the literature. Cytologic diagnosis of cervical myeloid sarcomas in asymptomatic patients without history or simultaneous involvement by acute myeloid leukemia can be challenging.

Metaplastic Carcinoma of the Breast Diagnosed by Fine-Needle Aspiration Biopsy: Diagnostic Pitfalls in Cytopathology
(Poster No. 24)
Elina Shustef, DO (elina.shustef@gmail.com); Jose Mantilla, MD; Laleh Hakima, DO; Esther Adler, MD; Samer Khader, MD. Department of Pathology, Albert Einstein College of Medicine, Montefiore Medical Center, New York, New York.

Metaplastic carcinoma of the breast is a rare, highly aggressive variant of ductal carcinoma. This heterogeneous neoplasm is characterized by the presence of adenocarcinoma admixed with squamous and/or mesenchymal components, and presents several diagnostic challenges in fine-needle aspiration cytology. We report a case of metaplastic carcinoma with chondroid differentiation in an 88-year-old woman with a left breast mass originally diagnosed as phyllodes tumor by fine-needle aspiration. The cytologic diagnosis was based on the finding of abundant atypical stromal cells admixed with scattered aggregates of epithelial cells and chondroid matrix. Subsequent excision revealed a highly cellular neoplasm with extensive chondroid differentiation and associated ductal carcinoma in situ, which was categorized as metaplastic carcinoma. Upon careful retrospective review, the cytology revealed epithelial atypia, most compatible with the diagnosis of metaplastic carcinoma (Figure 183).

Herpes Simplex Viral Cytopathic Changes Detected by Urine Cytology
(Poster No. 25)
Timothy Vandenboom, MD1 (tvandenboom@lumc.edu); Guliz A. Barkan, MD; Umesh Kapur, MD.1 Department of Pathology, Loyola University Medical Center, Maywood, Illinois; Department of Pathology, Silver Cross Hospital, New Lenox, Illinois.

Urinary tract cytopathology is a key component of the hematuria workup and surveillance of urothelial carcinoma. When reviewing these specimens, rarely infectious agents could be encountered. We present a rare finding of cellular changes consistent with herpes simplex virus (HSV) infection in a bladder barbotage specimen collected from a 68-year-old woman with recurrent urinary tract infections resulting in multiple hospital admissions. The patient had a past medical history of chronic kidney disease and was taking immunosuppressive agents owing to her liver transplant for alcoholic cirrhosis. Urology was consulted for cystourethroscopy to evaluate her bladder and upper urinary tract and placement of a suprapubic catheter. Cytomorphologic examination of the bladder barbotage specimen revealed an unexpected finding of multinucleated cells with glassy intranuclear inclusions, molding of nuclei, and margination of chromatin. This finding was consistent with the viral cytopathic effects of HSV (Figure 184, A) and was further supported by a positive HSV stain on the cell block section (Figure, B). Biopsies were obtained as well, but were negative for HSV.

Without cytologic examination of our specimen, the asymptomatic HSV infection in our immunosuppressed patient may have otherwise gone unnoticed, which may have presented in the future with dissemination and potentially devastating consequences. Therefore, our case highlights the vast importance of urine cytopathology in the identification and management of disease, including infectious agents such as HSV. Our case also displays the sampling advantage of urine cytology, as biopsies are only a focal sampling and failed to yield the HSV infection recognized in our bladder barbotage specimen.

Colonic Adenocarcinoma Metastatic to the Thyroid Gland Diagnosed by Fine-Needle Aspiration Biopsy
(Poster No. 26)
Malekh Alshaikhmohamed, MD (Malekh.Alshaikhmohamed@bcm.edu); Rodolfo Lauricica, MD. Department of Pathology & Immunology, Baylor College of Medicine, Houston, Texas.

Secondary tumors involving the thyroid gland may result from direct extension or hematogenous dissemination. Primary malignancies that directly involve the thyroid arise from the pharynx, larynx, trachea, esophagus, or adjacent cervical lymph nodes. Common sites of metastatic disease include the kidney, lung, uterus, and melanoma. We report the case of a 54-year-old woman with a past history of colon cancer. She presented to our clinic with a thyroid mass involving her right lobe. A fine-needle aspiration biopsy (FNAB) was performed and several smears and cell block material were obtained for analysis. The air-dried smears were stained with a modified Giemsa stain. The alcohol-fixed material was stained with the Papanicolaou method. The cell block material was sent for routine histology. All the immunohistochemical markers used in this case were stained via the avidin-biotin-complex method. The smears showed abundant neoplastic tissue associated with a necroinflammatory background. The tumor cells had large hyperchromatic nuclei with a vesicular chromatin pattern and prominent nucleoli. The tumor cells were positive for CEA, CK20, and CDX-2 and negative for CK7 and thyroglobulin. The morphology and immunohistochemical findings, coupled with the clinical history, were diagnostic for metastatic colonic adenocarcinoma...
involving the thyroid gland. FNAB provides a rapid and cost-effective means to evaluate not only primary but also metastatic lesions involving the thyroid gland.

**High-Grade Malignant Germ Cell Tumor With Initial Presentation as Metastatic Liver Lesions: Case Report and Literature Review**

(Poster No. 27)

Constantinos Coutouvelis, CT(ASCP)1 (ccoutouve@nshs.edu); Andry Markov, CT(ASCP)2; Oana C. Rafael, MD3; Mohamed Aziz, MD1,2 Department of Pathology, North Shore Long Island Jewish Health System Laboratories, Lake Success, New York; 2Department of Pathology, North Shore Long Island Jewish Health System-Lenox Hill Hospital, New York, New York.

Metastatic germ cell tumors (MGCTs) are relatively uncommon, but represent 1% to 5% of all GCTs. MGCTs are found in a variety of anatomic locations, but most commonly affect the mediastinal, retroperitoneal, and sacrococcygeal region, and other areas of the head and neck region. Fine-needle aspiration biopsy (FNAB) was performed on 2 male patients, ages 24 and 48 years, who both presented with multiple liver lesions and mediastinal masses. Neither patient had a prior history of malignancy or any scrotal or testicular masses. Cytology smears showed 3 mitoses per 10 high-power fields, and focal spindling of cells. Necrosis could not be evaluated in the limited sample. These features can be seen in up to one-third of epithelioid hemangioendotheliomas, which show atypical histologic features and confer with a more aggressive course. All hepatic and epithelial markers were negative (Hep-Par1, TTF-1, AE1.3, CK7, CAM 5.2, EMA), while mesenchymal and vascular markers were strongly positive (vimentin, CD31, CD34, factor VIII) (Figure, D). The morphologic and immunohistochemical features prompted the diagnosis of malignant epithelioid hemangioendothelioma. Our case showed predominantly low proliferation (<10% nuclear staining), with focal nodular areas showing high proliferation. Angiosarcoma also expresses endothelial markers, but it is more destructive and often has a greater degree of nuclear atypia and mitosis. This diagnosis may represent a morphologic continuum with epithelioid angiosarcoma.

**Cytologic Features and Genomic Profile of Renal Cell Carcinoma With Rhabdoid Features Diagnosed by Endobronchial Ultrasound-Guided Fine-Needle Aspiration Biopsy**

(Poster No. 29)

Wei Xie, MD, PhD1 (wxie1@bcm.edu); Bettye Cox, MD1; Nimesh R. Patel, MD1; Marilyn M. Li, MD2; Rodolfo Lauzirica, MD1 Departments of 1Pathology and Immunology and 2Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas.

Renal cell carcinoma (RCC) with rhabdoid features is a rare subtype of RCC. The rhabdoid features are suggestive of high histologic grade and pathologic stage, aggressive behavior, and poor prognosis. Endobronchial ultrasound (EBUS)–guided fine-needle aspiration (FNA) is an effective tool to aid in the diagnosis of lesions unable to be biopsied by other radiologic means. A 36-year-old man presented to the hospital with neck pain for 1 month. A computed tomography scan showed multiple lesions including 2 infiltrative masses in the C6 vertebral bodies, a heterogeneous mildly enhancing mass in the superior pole of the right kidney with internal necrosis, and hilar lymphadenopathy. EBUS-guided FNA was performed on the 10R superior pole of the right kidney with internal necrosis, and hilar lymphadenopathy. The smear showed abundant eosinophilic cytoplasm with focal cytoplasmic vacuolization. The cells showed marked nuclear atypia, mitotic activity > 3 mitoses per 10 high-power fields, and focal spindling of cells. Necrosis could not be evaluated in the limited sample. These features can be seen in up to one-third of epithelioid hemangioendotheliomas, which show atypical histologic features and confer with a more aggressive course. All hepatic and epithelial markers were negative (Hep-Par1, TTF-1, AE1.3, CK7, CAM 5.2, EMA), while mesenchymal and vascular markers were strongly positive (vimentin, CD31, CD34, factor VIII) (Figure, D). The morphologic and immunohistochemical features prompted the diagnosis of malignant epithelioid hemangioendothelioma. Our case showed predominantly low proliferation (<10% nuclear staining), with focal nodular areas showing high proliferation. Angiosarcoma also expresses endothelial markers, but it is more destructive and often has a greater degree of nuclear atypia and mitosis. This diagnosis may represent a morphologic continuum with epithelioid angiosarcoma.
showed a somatic (mosaic frame shift) mutation of VHL c.349delT. A subsequent biopsy of the C6 vertebral lesion also showed features of RRCC. To our knowledge, this is the first report of RRCC diagnosed by EBUS-guided FNA. RRCC should be considered in the differential diagnosis of an FNA specimen composed entirely of cells with rhabdoid morphology.

Cytologic Diagnosis of Intrapancreatic Accessory Spleen During Intraoperative Consultation

(Poster No. 30)

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Accessory spleens are found in approximately 10% of the population, 17% of which occur in the tail of the pancreas. Intrapancreatic accessory spleens are usually found incidentally on computed tomography (CT) imaging and may mimic a malignant pancreatic neoplasm. We report a case of intrapancreatic accessory spleen with emphasis on cytologic material obtained at the time of intraoperative consultation. A 58-year-old white man presented with symptoms of heart failure. An abdominal CT scan demonstrated an incidental solid, enhancing mass in the tail of the pancreas. A laparoscopic distal pancreatectomy and splenectomy was subsequently performed. The surgical specimen was received for intraoperative consultation. Within the pancreas was a well-circumscribed, 2.6-cm, red-brown homogeneous mass. Scrape cytology demonstrated hypercellular smears with cohesive, papillary groups of bland, epithelioid cells with round to oval nuclei, associated with traversing vessels; a heterogeneous lymphoid population of cells was noted in the background. Permanent sections show histologic features of splenic parenchyma and a diagnosis of intrapancreatic accessory spleen was rendered. The use of scrape cytology can be a fast and effective way of identifying both endothelial and hematopoietic elements when intrapancreatic accessory spleen is in the differential diagnosis of a pancreatic mass (Figure 187).

HIV-Associated Primary Effusion Lymphoma: An Exceedingly Rare Entity in the Cerebrospinal Fluid

(Poster No. 31)

Sarika Jain, MD1 (sainsp@upmc.edu); Alka Palekar, MD2; Sara Monaco, MD3; Fiona Craig, MD1; Ghassan Bejjani, MD2; Liron Pantanowitz, MD1. Departments of Pathology and 2Neurosurgery, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania.

Primary effusion lymphoma (PEL) in patients with human immunodeficiency virus (HIV) infection may involve pleural, pericardial, and peritoneal cavities. PEL involving cerebrospinal fluid (CSF) is exceedingly rare, and to our knowledge only 2 cases have been reported. These cases are challenging because they can be of the null-cell type. We report a case of a 61-year-old man with AIDS who presented with hallucinations, confusion, and an unsteady gait. Brain imaging studies showed findings suggestive of multiple prior subarachnoid hemorrhages, hydrocephalus, and leptomeningeal/periventricular enhancement (Figure 188, A). CSF cytology demonstrated large malignant cells with pleomorphic nuclei (Figure, B and C). These large cells were positive for CD45 (LCA) and LNA-1 (HHV8) (Figure, D) but negative for pankeratin, CK7, CK20, and TTF-1. Flow cytometry showed a null-cell phenotype of the large CD45(dim)-positive cells with CD38 coexpression. The diagnosis of HHV8-positive large cell lymphoma consistent with PEL was made. The patient was discharged with home hospice. This case highlights that albeit very rare, PEL should be included in the differential diagnosis when large atypical cells are encountered in CSF of HIV-positive patients, even when these patients do not have a history of lymphoma. As in this case, ancillary studies are needed to make a definitive diagnosis of PEL in CSF cytology.

Reed-Sternberg Cells in Bronchoalveolar Lavage: An Unusual Presentation of Classical Hodgkin Lymphoma

(Poster No. 32)

Brett M. Lowenthal, MD (blowenthal@ucsd.edu); Xiangdong Xu, MD, PhD; Lily J. Jih, MD. Department of Pathology, University of California San Diego Medical Center and Veterans Affairs Medical Center of San Diego, La Jolla, California.

It is quite unusual for classical Hodgkin lymphoma to initially present with pulmonary symptoms. Diagnosis of classical Hodgkin lymphoma by cytology could be very challenging owing to the rarity of Reed-Sternberg cells. Reed-Sternberg cells can be confused with reactive pneumocytes, reactive bronchiolar epithelium, poorly differentiated carcinoma, or even melanoma. We report the case of a 27-year-old man with no significant past medical history who presented with cough, progressive dyspnea, minimal hemoptysis, night sweats, and a 15-lb weight loss during the previous 7 months. A chest computed tomography revealed extensive bilateral upper lobe consolidations with bilateral hilar lymphadenopathy. A bronchoscopy was performed to reveal extrinsic compression and edema of the bronchi in bilateral upper lobes, in addition to 2 left-sided endobronchial sessile nodules. Papanicolaou-stained bronchoalveolar lavage and endobronchial brushing revealed scattered large atypical cells in a background of neutrophils, eosinophils, and lymphocytes. These large atypical cells have 1 to multiple convoluted nuclei with open reticulated chromatin, prominent nucleoli, and moderate cytoplasm. The concurrent biopsy of the endobronchial nodules revealed many Reed-Sternberg cells and Hodgkin cells with an immunophenotype consistent with classical Hodgkin lymphoma. Follow-up positron emission tomography demonstrated additional lymphadenopathy involving the mediastinum, the neck, and the paratracheal region. With the unusual pulmonary presentation, this case demonstrates the importance of considering classical Hodgkin lymphoma in the differential diagnosis for young patients with pulmonary consolidations and lymphadenopathy.
Atypical Liquid-Based Surepath Urine Samples: Revision of a “Waste Basket” Category According to the Ongoing Proposed Paris System for Reporting Urine Cytologies

(Mauricio Palau, MD

Atypical Liquid-Based Surepath Urine Samples: Revision of a “Waste Basket” Category According to the Ongoing Proposed Paris System for Reporting Urine Cytologies

(Mauricio Palau, MD)

Mauricio Palau, MD (mauricio.palau@fsfb.org.co); Luz Andrea Hermández Sánchez, BS; Jenny Saavedra Martínez, BS; Diana Milena Bermudez, BS; Nathalie Giselle Ruiz Sánchez, BS; Yubelly Avello Malaver, BS; Paula Andrea Rodríguez Urrego, MD. Department of Pathology, University Hospital Fundacion Santa Fe de Bogota, Colombia.

Context: During IAC 2013 held in Paris the need for a standardized reporting system for urine cytologies (UCs) was discussed and currently the Paris system is being evaluated and is under consideration for international consensus.

Design: All the UCs received in a period of 18 months were analyzed, and all categorized as atypical were revised and when necessary reclassified according to the proposed Paris system as follows: I, unsatisfactory; II, benign; III, urothelial atypia of undetermined significance; IV, urothelial atypia suggestive of high grade; V, positive for low-grade urothelial carcinoma; VI, positive for high-grade urothelial carcinoma; and VII, other neoplasias. Correlation with biopsies was performed when available.

Results: A total of 589 UCs with 68% (402) categorized as negative, 31% (181) categorized as atypical, and 1% (6) categorized as positive, were received (Table). The revised diagnostic category for the atypical cases showed that 32% of the cases were reclassified as negative and 6% as positive. None of the cases was placed under category V and 9% were reclassified as category IV. Twenty-four cases had follow-up biopsy with 8 concordant cases, 9 partial concordance (classified as III or IV but positive for carcinoma), and 9 discordant cases (classified as III or IV but final diagnosis was negative).

Conclusions: We agree with the urgent need to implement a standardized system for reporting UCs to decrease the number of cases placed in the “waste basket” atypical category; contribute to clinical diagnosis and follow-up; and finally, set clear findings to minimize interobserver interpretation among pathologists.

Diagnostic Categories Comparison After Reclassification

<table>
<thead>
<tr>
<th>Diagnostic Categories</th>
<th>Initial Category, No. (%)</th>
<th>Reclassification After Paris System, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unsatisfactory</td>
<td>Paris I 0 (0)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Negative</td>
<td>Paris II 402 (69)</td>
<td>459 (77)</td>
</tr>
<tr>
<td>Atypical</td>
<td>Paris III, IV 181 (31)</td>
<td>113 (19)</td>
</tr>
<tr>
<td>Positive</td>
<td>Paris V, VI, VII 6 (1)</td>
<td>16 (2)</td>
</tr>
<tr>
<td>Total</td>
<td>589 (100)</td>
<td>589 (100)</td>
</tr>
</tbody>
</table>

Utility of Cellient Cell Block and IMP3 Immunohistochemistry in the Diagnosis of Malignant Pleural Effusions

(Amy G. Zhou, MD; Ryan Brenkert, MS, SCT(ASCP)

Atypical Liquid-Based Surepath Urine Samples: Revision of a “Waste Basket” Category According to the Ongoing Proposed Paris System for Reporting Urine Cytologies

(Mauricio Palau, MD)

Utility of Cellient Cell Block and IMP3 Immunohistochemistry in the Diagnosis of Malignant Pleural Effusions

(Amy G. Zhou, MD, Amy.Zhou@umassmemorial.org; April Y. Hou, Andrew Fischer, MD; Zhong Jiang, MD. Department of Pathology, University of Massachusetts, Worcester; Department of Biology, Brandeis University, Waltham, Massachusetts.

Context: The Cellient automated cell block system with alcohol-fixed samples uses vacuum-assisted filtration to rapidly process small cytology samples for histologic sectioning. IMP3 is an oncofetal protein expressed in many malignant tumors, and is often used to distinguish benign from malignant tissue. We investigate whether IMP3 immunohistochemical staining of Cellient cell blocks is useful in the diagnosis of malignant pleural effusions.

Design: IMP3 immunohistochemistry was performed on 90 patients with Cellient cell blocks of pleural fluid specimens collected between 2008 and 2013, previously diagnosed as benign (n=50) or malignant (n=40) effusions. The malignant effusions include 20 lung cancers (non-small cell atypical, n=17; small cell carcinomas, n=3), 17 breast carcinomas, 5 ovarian carcinomas, 4 adenocarcinomas from the gastrointestinal system, and 3 metastatic carcinomas of unknown origin.

Results: IMP3 protein was only observed in the cytoplasm of metastatic malignant cells. None of the 50 benign effusions showed any positive staining for IMP3. Twenty-five of 40 patients (60%) were found to have IMP3 expression in their malignant effusions. IMP3 was positive in 12 of 17 non–small cell carcinomas of the lung (71%), 2 of 3 small cell carcinomas of the lung (67%), 1 of 8 breast carcinomas (13%), 4 of 5 ovarian carcinomas (80%), 2 of 4 gastrointestinal system carcinomas (50%), and 3 of 3 metastatic carcinomas of unknown origin (100%).

Conclusions: IMP3 staining of Cellient cell blocks is a useful adjunct to cytology to establish a definitive diagnosis of malignant pleural effusion. This technique is particularly helpful in distinguishing reactive mesothelial cells from malignancy in limited cytology specimens when a conventional cell block cannot be used.

Dr. Fischer is an inventor of Cellient cell block technology, and he receives royalties for sales of Cellient products, Hologic Corporation.

Malignant Myoepithelial Tumor of Soft Tissue

(Myoeptihelial Carcinoma) of the Left Foot Metastatic to Ipsilateral Inguinal Lymph Node Diagnosed by Fine-Needle Aspiration and Core Biopsy: Case Report of a Rare Neoplasm With an Uncommon Metastatic Site

(Ryan Brenkert, MS, SCT(ASCP)

Malignant Myoepithelial Tumor of Soft Tissue

(Myoeptihelial Carcinoma) of the Left Foot Metastatic to Ipsilateral Inguinal Lymph Node Diagnosed by Fine-Needle Aspiration and Core Biopsy: Case Report of a Rare Neoplasm With an Uncommon Metastatic Site

(Ryan Brenkert, MS, SCT(ASCP))

A 10-year-old girl presented with an enlarged left foot soft tissue mass as well as an enlarged inguinal lymph node on the ipsilateral side. Magnetic resonance imaging showed a 3.0 x 1.9 x 3.3-cm left foot superficial soft tissue mass and computed tomography scan showed a 2-cm enlarged inguinal lymph node. A core needle biopsy of the foot mass, as well as fine-needle aspiration of the lymph node, was performed. Cytology showed small round blue cells arranged in nests and lobules with round to elongated nuclei, and variable amounts of eosinophilic cytoplasm, indistinct cell borders, and plasmacytoid morphology in a background of abundant hyalinized chondromyxoid stroma (Figure 189, A and B, Papanicolaou-stained slides; C and D, core biopsy). Occasional mitoses were identified and there was no necrosis.

Tumor cells were positive for pankeratin AE1/AE3, CAM 5.2, EMA, caldesmon, calponin, and S100, while negative for desmin, GFAP, myogenin, SMA, p63, HMB-45, and HER2/neu. Nuclear positivity was retained in the INI1 stain. Fluorescence in situ hybridization study demonstrated a rearrangement of the EWSR1 gene. Given the age of the patient, clinical history, cytomorphology, and ancillary testing, a diagnosis of malignant myoepithelial tumor of soft tissue (myoeptihelial carcinoma) was rendered. Myoeptihelial carcinoma is a rare tumor with an aggressive clinical course and it can mimic small blue round cell tumors. EWSR1 gene rearrangement can be demonstrated in these tumors. Myoeptihelial carcinoma should be kept in mind in the differential diagnosis of soft tissue tumors.
Comparison of Cytologic and Subsequent Surgical Diagnoses of Urothelial Carcinomas Using a 4-Tiered Diagnostic Template

(Poster No. 36)

Jason M. Rarick, MD (jason.rarick@UHhospitals.org); Jay K. Wasmann, MD; Greg T. MacLennan, MD; Michael W. Claire, MD; Philip E. Bomeis, DO. Department of Pathology, University Hospitals Case Medical Center, Cleveland, Ohio.

Context: We recently instituted a 4-tiered diagnostic template for urine cytology and sought to validate it. The 4 categories used are abbreviated as follows: benign (UC1); clusters of urothelial cells without atypia favor a reactive process (UC2); clusters of urothelial cells with atypia cannot rule out a neoplasm (UC3); and positive for malignancy (UC4).

Design: We identified all voided urine cytology specimens from March 2010 to December 2012 that had corresponding surgical pathology follow-up within 1 year. A compilation of the cytologic and surgical pathology diagnoses was then compared for concordance rates in the following surgical diagnostic categories: negative for malignancy/ benign (NILM); PUNLMP/low-grade urothelial neoplasm (LGUN); high-grade urothelial neoplasm/urothelial carcinoma in situ (HGUN); and metastatic adenocarcinoma (MA).

Results: A total of 1245 urine cytology reports were identified within the time frame with the following diagnoses: 679 UC1 (55%), 355 UC2 (29%), 194 UC3 (16%), and 6 UC4 (0.5%). Of the 1245 urine cytology reports identified, 97 (7%) had surgical follow-up. Of these 97 urine cytology reports, the following diagnoses were noted: 30 UC1, 24 UC2, 39 UC3, and 4 UC4. See the Table for breakdown comparison of cytologic and subsequent surgical diagnoses.

Conclusions: As expected there is an increased percentage of low-grade and high-grade urothelial carcinomas with the higher urine diagnostic categories. Interestingly though, a considerable increase in low-grade urothelial carcinomas are diagnosed on follow-up for the UC3 versus the UC2 category (41% versus 26%). The data suggest that the UC3 category is more sensitive in identifying urothelial neoplasms than UC2.

<table>
<thead>
<tr>
<th></th>
<th>NILM, No. (%)</th>
<th>LGUN, No. (%)</th>
<th>HGUN, No. (%)</th>
<th>MA, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UC1</td>
<td>18 (60)</td>
<td>9 (30)</td>
<td>3 (10)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>UC2</td>
<td>12 (52)</td>
<td>6 (26)</td>
<td>5 (22)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>UC3</td>
<td>13 (33)</td>
<td>16 (41)</td>
<td>9 (23)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>UC4</td>
<td>1 (25)</td>
<td>0 (0)</td>
<td>2 (50)</td>
<td>1 (25)</td>
</tr>
</tbody>
</table>

Whole Slide Imaging in Gynecologic Cytology: Are We Ready for Prime Time?

(Poster No. 37)

Sara Makhdoum, MD1 (saramakhdoum@hotmail.com); Woodlyne Roquiz, DO;2 Eva Wojcik, MD.1 Department of Pathology, King Khalid University Hospital, Riyadh, Saudi Arabia; 2Department of Pathology, Loyola University Medical Center, Maywood, Illinois.

Context: We report the effect of dynamic virtual microscopy on screening and diagnostic accuracy in gynecologic (GYN) cytology.

Design: Ten ThinPrep GYN cytology slides were evaluated by using 2 viewing methods: virtual microscopy (VM) and glass slides. The slides were scanned with Aperio ScanScope CS2, eSlide Manager Web-based program, and ImageScope downloadable slide-viewing interface. Diagnostic accuracy and speed were assessed after a significant time delay by 1 observer between the following groups: unscreened (virtual [VUS] and glass [GUS] slides) and prescreened (virtual [VPS] and glass [GPS] slides). The glass slides were prescreened by a cytopathologist. Time to diagnosis (TTD) was measured in all viewing methods.

Results: VUS slides yielded a correct diagnosis in 90% of cases, whereas GUS, VPS, and GPS each yielded a correct diagnosis in 80% of cases. The following average TTD values were noted: VUS (9.34 minutes); GUS (5.28 minutes); VPS (2.59 minutes); and GPS (1.42 minutes) (Figure 190). TTD, using both viewing platforms, demonstrated statistical significance (P < .005). The most significant limitation identified was the inability to focus on 3-D cell clusters. Other limiting variables included operator experience, freezing of the computer during image manipulation, haziness/artifacts that delay interpretation, and the limited screen size on the Web-based format.

Importance of Routine Cytohistologic Evaluation in a Case of Peritoneal Mesothelioma as a Secondary Malignancy

(Poster No. 38)

Raghavendra Pillappa, MD1 (raghavendrapillappa@gmail.com); David Spencer, MD.2 Department of Pathology and Laboratory Medicine, University of Tennessee Health Science Center, Memphis; 2Department of Pathology and Laboratory Medicine, Trumbull Laboratories, Germantown, Tennessee.

We report an unexpected case of peritoneal mesothelioma diagnosed on cytology. Routine examination of an “abdominal mass” in a 54-year-old man was initially reported as adenocarcinoma because of its gland-forming nature. Several weeks after the diagnosis, the medical oncologist asked for a review of the case and possible tissue of origin testing, since the tumor had not responded to therapy. On review, the second pathologist found a low-grade, focally papillary neoplasm with cuboidal-like epithelioid cells. Additional information that the patient had a remote history of metastatic testicular germ cell tumor (type unknown to oncologist) prompted immunohistochemistry on the residual tissue in the cell block. Significant positivity with D2-40 and calretinin but negativity for PLAP, CD30, and BerEp4 supported a second review impression of mesothelioma. There was no history of asbestos exposure. This case illustrates the importance of the pathologist regarding any subsequent opportunity at evaluation of the tumor as being as important as the initial review. Incomplete or erroneous initial history is not uncommon and often yields an incomplete or erroneous pathologic diagnosis. In retrospect, initial clues to the correct diagnosis included cuboidal-like cells with low-grade nuclei and focal papillary formation. Paradoxically, the subsequent remote history of metastatic germ cell tumor in the abdomen was misleading. Mesothelioma often shares D2-40 positivity with malignant germ cell tumor. Despite marked advances in testing for malignant neoplasms, routine cytohistologic evaluation remains crucial for proper diagnosis of malignant neoplasms.

Pseudomyxoma Peritonei: Secondary to Appendiceal Tumor or to a Synchronous Tumor in Appendix and Ovary?

Case Presentation and Review of Literature

(Poster No. 39)

Fatima-Zahra Jelloul, MD (fjelloul13@nshs.edu); Taisia Vikutskovski, DO; Maruf Chowdhury, SCT; Mohamed S. Aziz, MD. Department of Pathology, Hofstra North Shore-LIJ Medical School, New Hyde Park, New York.
Pseudomyxoma peritonei is a rare condition characterized by the accumulation of abundant mucinous material within the peritoneal cavity associated with neoplastic mucinous epithelium. The appendix has been implicated as the primary site in most cases; however, association with neoplastic lesions of other sites, including the ovary, has also been reported. Pseudomyxoma peritonei can present with simultaneous appendiceal and ovarian tumors. Cytokeratins CK7 and CK20 are useful immunohistochemical markers for determining the primary site. Ovarian neoplasms are usually CK7 positive and might be CK20 positive or negative. Metastases of intestinal origin are generally CK7 negative and CK20 positive. We present the case of a 59-year-old woman with a history of ruptured mucinous appendiceal tumor 2 years prior who recently presented with 2 months of abdominal pain and bloating. Computed tomography scan showed an 18-cm cystic pelvic mass, large volume ascites, and diffuse omental nodular masses. Cytology examination of radiologically guided fine-needle aspiration of the omentum showed mucinous glandular epithelium with low-grade mucinous neoplastic features in a background of abundant mucinous material (Figure 191, A and B). No evidence of invasion was seen owing to the absence of stroma. The epithelial cells were positive for CK20 (Figure, C), CDX2 (Figure, D), CEA, and AE1/AE3; they were negative for CK7, PAX-8, and ER (0% nuclear staining). A secondary mucinous tumor of appendiceal origin was favored and the tumor was classified as a low-grade mucinous tumor. Our case report adds to the limited existing literature on cytologic diagnosis of pseudomyxoma peritonei.

GATA3 Expression in Metastatic Urothelial Carcinoma in Fine-Needle Aspiration Cell Blocks

Anne Hoffa, MD (ahoffa@emory.edu); Harold C. Sullivan, MD; Cynthia Cohen, MD; Momin T. Siddiqui, MD. Department of Pathology and Laboratory Medicine, Emory University, Atlanta, Georgia.

Context: GATA-binding protein 3 (GATA3) is a zinc finger transcription factor with high affinity for urothelial tissue and is a promising immunohistochemical marker in detection of urothelial carcinomas (UCs). We studied its utility in diagnosis of metastatic UC.

Design: This study was performed on cell blocks of fine-needle aspirates from 25 cases of metastatic UC in patients with previous high-grade UC of the urinary bladder. Metastatic sites include lymph nodes, pelvic wall, lung, liver, and mesentery. Immunohistochemical staining with the following reagents was performed: GATA3 (L50-823 clone, Dako), cytokeratin 7 (OB-TL12/30 clone, Dako), and CDX2 (Dako, Carpinteria, California), uroploidin (AU1 clone, Fitzgerald Industries, Acton, Massachusetts), cytokeratin 7 (OB-TL12/30 clone, Dako), and cytokeratin 20 (Ro20.8 clone, Dako). Ten cell blocks with malignant melanoma were negative controls.

Results: The pattern of GATA3 staining was intensely nuclear within the metastatic cells (Table). Sensitivity (92%) and specificity (100%) were high for GATA3 as well as the positive predictive value (100%) and negative predictive value (83.3%) for metastatic UC.

Conclusions: GATA3 has high sensitivity and specificity for detection of metastatic UC, with expression as a strong nuclear stain in tumor cells, and is comparable to cytokeratin 7. It can thus be used for detecting small amounts of metastatic UC in cell blocks as part of an immunohistochemical panel.

Antibody Marker Expression in Metastatic Urothelial Carcinoma

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Positive, No.</th>
<th>Negative, No.</th>
<th>Percentage Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>GATA3</td>
<td>23/25</td>
<td>2/25</td>
<td>92</td>
</tr>
<tr>
<td>Thrombomodulin</td>
<td>20/25</td>
<td>5/25</td>
<td>80</td>
</tr>
<tr>
<td>Uroploidin</td>
<td>0/25</td>
<td>25/25</td>
<td>0</td>
</tr>
<tr>
<td>Cytokeratin 7</td>
<td>23/25</td>
<td>2/25</td>
<td>92</td>
</tr>
<tr>
<td>Cytokeratin 20</td>
<td>7/25</td>
<td>18/25</td>
<td>28</td>
</tr>
</tbody>
</table>

Fine-Needle Aspiration Cytology of Metastatic Papillary Renal Cell Carcinoma of the Midsternal Soft Tissue

Huiying Wang, MD1 (hyw16@hotmail.com); Antonio Subietas-Mayol, MD2; Fidelina Desoto, MD.1 2Department of Pathology, SUNY Downstate Medical Center, Brooklyn, New York; 1Department of Pathology, Veterans Affairs New York Harbor Healthcare System, Brooklyn Campus, Brooklyn.

Approximately 25% of renal cell carcinomas develop metastases at the time of diagnosis. In many cases, they often involve the lung, liver, bone, brain, and adrenal gland. Subcutaneous soft tissue metastases are extremely unusual. A 57-year-old man presented to our hospital with a midsternal mass under the skin that has been progressively enlarging for 4 months. Chest computed tomography showed a large soft tissue mass arising from the inferior sternum with erosion of the bone and extending into the epicardial fat. Fine-needle aspiration of the chest wall mass was performed and cytology examination showed clusters of cells with eccentrically located nucleus and foamy vacuolated cytoplasm. The nuclei were large, atypical with prominent nucleoli. Sheets of cells were arranged in a papillary configuration in the cell block. Immunohistochemical staining was performed on sections of the cell block and showed positivity for pan-cytokeratin, PAX8, and AMACR, which favored the diagnosis of papillary renal cell carcinoma. Further radiologic studies revealed a 4.7×5.6×5-cm solid exophytic lesion arising from the lower pole of the left kidney. The findings emphasized a cautious approach in interpreting cytologic findings in aspirates with unusual cell features. Further workup using selective immunohistochemical stains can be useful in resolving the diagnostic challenge of diagnosing metastatic malignant tumors before the primary site has been found.

Adequacy of Formalin-Fixed, Paraffin-Embedded Cytology Specimens for Next-Generation Sequencing With the Ion Torrent PGM: A 10-Month Experience at a Tertiary Care Center

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Context: Cytology specimens, and in particular, fine-needle aspirations (FNAs) are widely used for diagnosing a variety of primary and metastatic cancers. Historically, the amount of DNA in cytology specimens was often inadequate for sequential single-gene testing. Recently, the introduction of next-generation sequencing (NGS) technologies has allowed simultaneous analysis of multiple genes in DNA extracted from formalin-fixed, paraffin-embedded (FFPE) cell
blocks. The aim of this study was to assess the adequacy of diagnostic cytology specimens for mutation analysis by NGS.

**Design:** Consecutive NGS reports on diagnostic cytology specimens from May 2013 to February 2014 were reviewed. DNA was extracted from FFPE tumor tissue and sequenced with the Ion Torrent Personal Genome Machine (PGM) for the 50-gene AmpliSeq Cancer Hotspot panel. Up to 10 ng of extracted DNA was used in preparation of libraries for sequencing. We excluded NGS performed on core-needle biopsy, excisional biopsy, and resection specimens.

**Results:** Across specimen types, most FFPE cell blocks were adequate for NGS (94%) (Table). Currently, most NGS is performed on cytology specimens diagnostic of adenocarcinoma or poorly differentiated carcinoma of the lung (61 of 69; 88% of specimens). As such, 62% of the specimens tested were endobronchial ultrasound-guided FNAs (EBUS-FNAs).

**Conclusions:** Our results indicate that most cytology specimens contained sufficient DNA for NGS. This supports continued routine molecular testing of cytology specimens, using NGS.

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Total No.</th>
<th>Adequate No.</th>
<th>Adequate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBUS-FNA</td>
<td>43</td>
<td>40</td>
<td>93</td>
</tr>
<tr>
<td>Fluid</td>
<td>13</td>
<td>13</td>
<td>100</td>
</tr>
<tr>
<td>CT-FNA</td>
<td>5</td>
<td>4</td>
<td>80</td>
</tr>
<tr>
<td>EUS-FNA</td>
<td>4</td>
<td>4</td>
<td>100</td>
</tr>
<tr>
<td>Brushings/washings</td>
<td>2</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td>BAL</td>
<td>2</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>69</td>
<td>65</td>
<td>94</td>
</tr>
</tbody>
</table>

Abbreviations: BAL, bronchoalveolar lavage; EBUS, endobronchial ultrasound; EUS, endoscopic ultrasound.

**Metastatic Monophasic Synovial Sarcoma to the Thyroid Gland, Originally Diagnosed as Medullary Carcinoma**

(Poster No. 43)

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Synovial sarcomas are malignant soft tissue tumors usually arising in deep soft tissue of the extremities. Synovial sarcomas of the head and neck region are rare, arising in approximately 5% of cases. We present a case of synovial sarcoma originally diagnosed as medullary carcinoma of the thyroid on fine-needle aspiration (FNA). A 41-year-old man presented with several weeks of dysphonia and a left thyroid mass. An FNA of the thyroid nodule showed a cellular smear composed of clusters and loosely cohesive oval to spindle-shaped cells with irregular nuclear borders, fine chromatin pattern, and inconspicuous nucleoli (Figure 192). A diagnosis of medullary carcinoma was rendered. During the patient’s total thyroidectomy, the mass was found to be arising from the cervical esophagus and involving the thyroid, pharynx, and trachea. Microscopic examination of the esophageal tumor revealed a densely cellular proliferation of spindle cells with finely granular chromatin, inconspicuous nucleoli, abundant mitoses, and foci of necrosis. The tumor cells were positive for BCL2 and vimentin and negative for thyroglobulin, calcitonin, TTF-1, CD117, desmin, myogenin, synaptophysin, chromogranin, and LCA. CK AE1/AE3, CK8/18, and EMA showed sparse positive tumor cells. Fluorescence in situ hybridization demonstrated translocation (X;18)(p11;q11), supporting the final diagnosis of synovial sarcoma. The patient underwent a laryngopharyngoesophagectomy with subsequent adjuvant therapy and is currently disease free. Metastatic synovial sarcoma to the thyroid gland can be a challenging task on FNA material because of its rarity and may show cytologic features resembling a primary spindle cell–type medullary carcinoma.

**A Leopard Doesn’t Change Its Spots—Granulosa Cell Tumor Metastatic to Clavicle 20 Years Later, A Cytology Diagnosis to Remember: Case Report and Literature Review**

(Poster No. 44)

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Ovarian granulosa cell tumor (GCT) is the most common malignant sex cord–stromal tumor, representing 2% to 3% of all ovarian cancers. It has a good prognosis and recurrences tend to be late (from 5 to 20 years), usually in the abdomen, pelvis, or lymph nodes. Metastases to liver, lung, kidney, and heart have been reported. Bone metastases are extremely rare and reflect hematogenous spreading. A 60-year-old woman was found to have an isolated lytic lesion in the right clavicle. A PET/CT scan showed an FDG-avid, destructive lesion in the medial right clavicle (Figure 193, A). A CT-guided fine-needle aspiration was performed. Cytopathology revealed aggregates of neoplastic cells arranged singly and in large sheets, with overlapping round-oval nuclei, many with nuclear grooves, high nuclear to cytoplasmic ratio, and increased mitotic activity, in a bloody background consistent with a metastatic tumor (Figure, B and C). The striking cytomorphic characteristics prompted “directed” questioning and the patient reported a remote history of GCT 20 years earlier. Our case showed similar cytomorphic features to the original tumor and the immunoprofile (Table; inhibin, Figure, D) confirmed the diagnosis of metastatic GCT. The proliferation index was 10%. There are only a few GCTs with bone metastases reported in the literature and, to the best of our knowledge, this is the first reported clavicle metastasis. This case highlights the importance of maintaining a high index of suspicion for unusual metastases during long-term follow-up in patients with previous GCT.

**Summary of Immunohistochemical Features**

<table>
<thead>
<tr>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibin (Figure, D); AE1/AE3, CK7, CAM 5.2, WT1, vimentin, SMA, CD99, S100, synaptophysin</td>
<td>p40, EMA, CD56, desmin, CD31, myogenin</td>
</tr>
</tbody>
</table>

1Department of Pathology, North Shore Long Island Jewish Hospital/ Hofstra School of Medicine, Lake Success, New York.
Unusual Metastatic Presentation of Submandibular Gland Adenoid Cystic Carcinoma to the Lung, Diagnosed by Fine-Needle Aspiration Cytology: Case Report and Review of the Literature

(Poster No. 45)

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A 50-year-old Hispanic man with no smoking history presented with shortness of breath, and imaging studies demonstrated 3 lung nodules, the largest measuring 3.4 x 2.9 cm. The possibility of metastatic disease versus multifocal primary lung cancer was raised. Fine-needle aspiration biopsy of 1 of the lung nodules showed small, monotonous basaloid cells with scant cytoplasm, and naked, stripped nuclei. The cells were also arranged in pseudoglandular clusters and as small sheets surrounding metachromatic hyaline material with isolated mitoses. Necrosis was absent (Figure 194, A [Diff-Quick]; B through D, Papanicolaou stain). The differential diagnosis included a basal cell neoplasm; low-grade polymorphous adenocarcinoma; mucoepidermoid carcinoma; and less likely, a primary lung carcinoma. The striking cytomorphic characteristics of the cytology smears prompted “directed” history, and the patient volunteered a remote history of adenoid cystic carcinoma (ACC) of the right submandibular gland. Correlative review of the salivary gland tumor and current cytology allowed the diagnosis of metastatic ACC to the lung. ACC is uncommon, accounting for only approximately 15% to 20% of all salivary gland malignancies, with most occurring in the minor salivary glands. It originates from the exocrine mucous glands. Despite its current classification with the salivary gland tumors, it is known to arise in any site where mucous glands exist. Slow local growth with local spread and perineural invasion are the hallmarks of this entity, rendering metastasis to the lung an unlikely occurrence and exceptionally rare.

Erdheim-Chester Disease Mimicking CLIPPERS

(Poster No. 47)

Kelly S. Mrachek, MD1 (kellymarrachek@centura.org); Seth C. Lummus, DO2; Denise A. Darnell, MD2; B. K. Kleinschmidt-DeMasters, MD2.1 Department of Pathology, Penrose Hospital, Colorado Springs, Colorado; Departments of 2Pathology and 2Neurology, University of Colorado, Aurora.

CLIPPERS (chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids) was coined in 2010 for a new, clinically and radiologically distinct, pontine-predominant encephalomyelitis first encountered in 8 patients. The condition has been increasingly reported since then, with more than 22 publications to date (JNEN. 73(3):272–277). Diagnosis is based largely on stereotypic neuroimaging features of symmetric, curvilinear, multifocal gadolinium enhancement within the pons, with variable extension into other sites. Reports since then of patients with similar neuroimaging features but...
other diseases (central nervous system [CNS] lymphoma, postvaccination, small vessel vasculitis) has led to confusion as to whether this is a single disease or an unusual pattern possible in several different conditions. We report the first case of Erdheim-Chester disease (ECD) of the CNS mimicking CLIPPERS. A 59-year-old woman presented with seizures, followed by a slow, stepwise, 2-year progression of weakness, and ataxia. Syndromes and radiographic abnormalities were initially steroid responsive. Neuroimaging showed numerous, mildly enhancing, predominantly T2/FLAIR hyperintense lesions in the midbrain, cerebellar hemispheres, mesiotemporal lobes, and right centrum semiovale, with pontine involvement the most striking (Figure 195). Extensive diagnostic evaluation for inflammatory, vascular, infectious, paraneoplastic, and malignant etiologies was negative. Brain biopsy demonstrated non-Langerhans CD68+ CD1a- histiocytosis. Bone scan showed heterogenous uptake involving bilateral distal femurs and tibias, consistent with ECD. This case adds to the growing list of different diseases with CLIPPERS-like neuroimaging findings and further raises the possibility that anatomic features within the basis pontis itself, and not a specific disease entity, predispose it to this curvilinear neuroimaging pattern.

Brain Stones Within the Pediatric Population Are Associated With a Variety of Entities

(Poster No. 48)

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Context: Extensive calcifications occurring within the central nervous system have diverse etiologies including infections, dystrophic mineralization after pediatric ischemic events, therapy-induced necrosis, and tumors. Single large cohesive calcifications are, however, usually confined to neoplasms. Recently, a series of 4 low-grade pediatric gliomas with massive calcifications was reported from St. Jude’s Hospital; these were inconsistent with any previously codified tumors in the current WHO 2007 classification that can be associated with large calcifications. The authors proposed a new entity, massively calcified low-grade glioma (MCLGG), for these supratentorial tumors with well-circumscribed margins, no contrast enhancement, microscopic large concentric calcifications, noninfiltrative borders, and an absence of ependymal or neuronal differentiation. Other reports have not yet appeared.

Design: To provide possible independent validation of the existence of MCLGGs, files of the authors (B.K.D., M.H.) were searched for pediatric brain lesions with large calcifications on neuroimaging occurring between 2007 and 2014.

Results: Massive calcifications on neuroimaging were identified in 5 patients and proved to be of widely varying types, including 1 each of ganglioglioma, atypical choroid plexus papilloma, supratentorial ependymoma, and cortical tuber, although 1 did in fact prove to be MCLGG. Electron microscopy and extensive immunohistochemistry in the MCLGG further negated diagnostic consideration of other tumor types.

Conclusions: Massive single calcifications (“brain stones”) are uncommon pediatric brain lesions of diverse pathogenesis. We provide an additional case of MCLGG and support the idea that these could be codified as a unique tumor entity in the future.

Sudden Visual Loss: A Rare Complication of Intracranial Solitary Fibrous Tumor

(Poster No. 49)

Sania Shuja, MD, PhD (sania.shuja@jax.ufl.edu); Yi Zhuang, MD, MS; Raafat Makary, MD, PhD. Department of Pathology, University of Florida, College of Medicine-Jacksonville.

Solitary fibrous tumors (SFTs) are mesenchymal tumors usually occurring extracranially. Rarely, they may occur intracranially as dural-based tumors radiologically resembling meningiomas. Visual loss secondary to intracranial SFT is an extremely rare occurrence. We report the case of a 26-year-old white man with SFT in the lefttemporoparietal occipital region with sudden visual impairment in both eyes. He presented with a 1-year history of left-side predominant frontal headaches, not associated with nausea or vomiting, and 4 months history of sudden complete visual loss in the right eye and profoundly decreased vision in the left eye. On examination, he had bilateral papilledema, worse on the right optic disc than on the left. He was referred to the emergency department. Magnetic resonance imaging revealed a giant multilobated temporoparietal enhancing mass (7 cm) with central cavitation/necrosis (Figure 196, A and B). Computed tomography angiogram revealed that the mass traversed the left leaf of the tentorium and insinuated itself into the left lobe of the cerebellum. Microscopic examination revealed spindle cell tumor with variably collagenous stroma, and thin-walled vessels, some resembling “staghorn” appearance (Figure, C and D). Mitoses were inconspicuous. The tumor cells stained positively for CD34 and BCL-2 (Figure, E and F), and negatively for EMA, consistent with the diagnosis of SFT. Visual loss persisted after surgery. SFTs are rare dural-based tumors of unpredictable behavior that may show histologic resemblance to meningiomas. Multilobated appearance of a dural-based mass should raise consideration of SFT. Early diagnosis and treatment are necessary to prevent irreversible complications as happened in our case.

Melanoma in the Third Eye: Differentiating Between Primary and Metastasis

(Poster No. 50)

Nicole Dominiazi, MD1 (dominiak@musc.edu); Michael Timothy Smith, MD1; Maria Spampinato, MD; William Vandergrift III, MD2; Cynthia T. Welsh, MD.1 Departments of 1Pathology and Laboratory Medicine, 2Radiology, and 3Neurosurgery, Medical University of South Carolina, Charleston.

Pineal gland tumors account for only 0.4%-1% of all intracranial neoplasms. Malignant melanomas in the pineal region are very rare, with primary lesions being exceedingly so. Seventeen cases of pineal malignant melanomas have been reported since 1999. Melanocytes are commonly known to exist in the skin, eyes, and mucosal sites, but they also exist in the leptomeninges of the central nervous system. Primary pineal melanomas most likely arise from these cells within the leptomeninges surrounding the gland, which invade and replace the normal tissue. Metastases within the central nervous system are not uncommon from many systemic malignant neoplasms; however, the pineal region is one of the rarest sites, accounting for less than 4% of all brain metastases. We compare 2 cases of malignant melanoma found in the pineal region: one a primary lesion, the other a metastasis. Both patients were males presenting with mental status changes who were found to have pineal masses on imaging. Both lesions were resected and diagnosed as malignant melanoma. Differentiating between primary and metastatic melanoma proves to be problematic if a corresponding cutaneous, mucosal, or ophthalmologic lesion is not known. Are there any other reliable methods, either radiologically,
Intravascular Lymphoma Diagnosed by Nerve Biopsy

(Poster No. 51)

John S. Van Arnam, MD, MS (john.vanarnam@gmail.com); Anne F. Buckley, MD, PhD. Department of Pathology, Duke University, Durham, North Carolina.

Intravascular lymphoma is a rare form of lymphoma that can present with variable symptoms. We present the case of a patient with significant weight loss, lower extremity weakness, and negative findings on extensive workup who was diagnosed with intravascular lymphoma on nerve biopsy. A 75-year-old man presented with 1 year of progressive lower extremity weakness, gait disturbance, muscle wasting, and frequent falls, along with fever, chills, night sweats, and an unintentional 60-lb weight loss. Initial evaluation and treatment included brain MRI, PET CT, antibiotic trials, upper GI endoscopy, and MRCP. He had EEG changes consistent with a neurodegenerative condition, and EMG/NCS demonstrated features of axonal loss. He underwent nerve and muscle biopsy to evaluate his progressive weakness. The muscle biopsy demonstrated fiber type grouping indicative of denervation. The sural nerve biopsy showed large lymphocytes with prominent nucleoli in vascular spaces; these cells stained for CD45 and CD20, indicating a diagnosis of intravascular large B-cell lymphoma. Nerve involvement is a pattern of the “Western type” of intravascular B-cell lymphoma, an aggressive malignancy frequently associated with neurologic symptoms and skin manifestations. Although rare, intravascular lymphoma represents an important entity in the differential diagnosis for a chronically ill patient with vague neurologic symptoms (Figure 197).

A Rare Case of Cerebral Autosomal Dominant Arteriopathy With Subcortical Infacts and Leukoencephalopathy (CADASIL) With Glioblastoma Multiforme

(Poster No. 52)

Rashna Clubwala, MD1 (rclubwala@lifespan.org); Edward Stopa, MD1; Stephen Salloway, MD, MS2; Suzanne de la Monte, MD, MPH1. Departments of 1Pathology and 2Neurology, Rhode Island Hospital, Providence.

CADASIL is a rare inherited arteriopathy that involves the brain and is caused by Notch3 mutations on chromosome 19. Arterial wall thickening due to mural degeneration, deposition of granular material, and fibrosis leads to transient ischemic attacks, infarcts, and dementia. We report an unusual case of a 59-year-old man with stable late-stage CADASIL in which a superimposed glioblastoma multiforme (GBM) was discovered on autopsy. To date, only 2 such cases have been reported. The decedent was aphasic and wheelchair bound at baseline. He developed new onset weakness, decreased eye contact, and died 11 days after discharge. Microscopic examination revealed multifocal cavitated and partially hemorrhagic lesions in frontal, parietal, and occipital deep and periventricular white matter, basal ganglia, and thalamus, and a large GBM involving the inferior frontal, left temporal, and posterior parietal regions, periventricular white matter, corpus callosum, and rostral brainstem. Histopathology demonstrated characteristic arteriopathy of CADASIL involving leptomeningeal, basal ganglia, and white matter vessels, with severe chronic ischemic leukoencephalopathy, cavitated infarcts, and hemorrhages. Electron microscopy demonstrated granular osmiophilic material surrounding smooth muscle cells. The GBM infiltrated structures damaged by CADASIL lesions, and also regions that were relatively spared. Accelerated neurologic deterioration in a patient with stable deficits from CADASIL should raise suspicion about a superimposed disease process. Although cancer rates are increased (8%) in people with CADASIL, GBMs account for 4% of those malignancies. Therefore, this case is highly unusual. A gain-of-function effect of Notch3 mutations could mediate the increased rates of CADASIL-associated malignancies, including GBM.

Uncommon Presentation of Epstein-Barr Virus–Associated Smooth Muscle Tumors as Intracranial Masses

(Poster No. 53)

Varsha Podduturi, MD (varsha.podduturi@gmail.com); George J. Snipes, MD, PhD. Department of Pathology, Baylor University Medical Center, Dallas, Texas.

Epstein-Barr virus–associated smooth muscle tumors (EBV-SMTs) are often benign mesenchymal lesions found commonly in various organs in immunosuppressed patients with solid-organ transplant or HIV/AIDS; however, these are rare in the central nervous system (CNS). We present 2 cases of EBV-SMT in the CNS. The first case involved a 46-year-old man with HIV presenting with dizziness for 1 week. Cranial MRI showed an enhancing dural-based mass along the left tentorium monitored by serial imaging. Thirteen months later, he had a complaint of right-sided hearing loss. Imaging found a new separate extra-axial dural-based mass in the right middle cranial fossa, and resection was performed. Biopsy showed spindle cells with rounded and tapered nuclei and eosinophilic cytoplasm forming a storiform and fascicular pattern and sporadic mitotic figures. Tumor cells were immunoreactive for smooth muscle actin and muscle-specific actin. In situ hybridization for EBV RNA showed focal nuclear positivity. The second case involved a 48-year-old man with HIV/AIDS with persistent headaches. Cranial MRI revealed a heterogeneously enhancing extra-axial mass within the right middle cranial fossa. Three months later, right temporal lobe resection was performed. Biopsy showed a moderately cellular spindle cell neoplasm with fascicular architecture and foci of necrosis (Figure 198). MIB-1 index measured 5% to 10%. Tumor cells were strongly positive for muscle-specific actin and smooth muscle actin. In situ hybridization confirmed EBV-encoded RNA in
most tumor cells (Figure). These 2 cases highlight uncommon presentations of EBV-SMT, an entity that should be included in the differential diagnosis of intracranial lesions in immunosuppressed patients.

**Titinopathy and Muscular Dystrophy Testing in the Pediatric Population**

(Poster No. 54)

Vidya Mehta, MS1; Diep Tran, BS1; Tim Lotz, MD2; Adekunle M. Adesina, MD, PhD1 (aadesina@email.emory.edu); Departments of Pathology and Pediatric Neurology, Texas Children’s Hospital, Houston.

**Context:** Titinopathy represents a hereditary myopathy with mutation in the titin gene. It presents as an autosomal dominant form of distal myopathy (tibial muscular dystrophy), while homozygotes present with the more severe limb girdle muscular dystrophy 2J. Rare autosomal dominant forms of the disease include myofibrillar myopathy with early respiratory failure.

**Design:** We sought to determine the frequency of abnormalities of titin expression by immunofluorescence in a cohort with clinical suspicion of myopathy for whom a muscle biopsy was done and to correlate the findings with other associated genetic analyses performed.

**Results:** A total of 75 consecutive pediatric muscle biopsy specimens were stained with antibody to titin. A total of 6.7% (5 of 75) of muscle biopsies showed lack of expression of titin, consistent with homozygous mutation of titin gene. A subset (13) also had whole exome sequencing. This subset showed 23.1% (3 of 13) having demonstrable titin mutation, with 2 identified as compound heterozygotes and 1 patient showing a homozygous mutation. The 2 compound heterozygotes had normal expression of titin on immunostaining. Muscle biopsy studies in the compound heterozygotes showed only mild myopathic changes with multiple foci of myofibrillar disruption and Z-band streaming on electron microscopy. In contrast, the patient with homozygote mutation showed florid dystrophic myopathy.

**Conclusions:** These findings are consistent with the presence of an identifiable subgroup of heterozygote mutants with a true recessive immunophenotype mimicking the mouse mdm model of titinopathy. The high frequency of titinopathy in the entirely unselected group highlights the need for inclusion of titin in the muscular dystrophy protein panel screening in the pediatric population.

**Fusobacterium necrophorum Brain Abscess Initiated a Diagnosis of Diabetes Mellitus**

(Poster No. 55)

Kristina Gvozdan, MD (kgvozdan@uic.edu); Tushar N. Patel, MD; Tibor Valey-Nagy, MD, PhD. Department of Pathology and Laboratory Medicine, University of Illinois at Chicago-University of Illinois Hospital and Health Science Systems, Chicago.

**Fusobacterium necrophorum** is a rare cause of brain abscess relative to the more common **Fusobacterium nucleatum**. While the former has been noted to occur predominantly in young and healthy individuals, the latter has been identified in the elderly in association with multiple comorbidities. We present the case of a 59-year-old patient who was admitted with a 2-day history of right hemiparesis, slurred speech, and headache, with MRI findings of left frontal lobe rim-enhancing lesion suggestive of high-grade glioma. Her blood glucose level was 302 mg/dL on admission. Subsequent craniotomy and histopathologic examination revealed necrotizing acute and chronic inflammation consistent with organizing abscess. Microbiologic culture grew *F. necrophorum*. To our knowledge, this is the only described case of *F. necrophorum* brain abscess to reveal a secondary diagnosis of diabetes mellitus, which has not been previously identified as a risk factor for development of invasive disease by the bacterium. We herein review the pathogenic mechanisms of *F. necrophorum* with a focus on immune system derangement in diabetics as a potential predisposing factor for brain abscess development by the pathogen.

**Metastatic Renal Cell Carcinoma to the Brain: A Clinicopathologic Analysis of 10 Cases**

(Poster No. 56)

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**Context:** Few large series have been published in pathology literature, analyzing the clinicopathologic features of patients with metastatic renal cell carcinoma (RCC) to the brain.

**Design:** Ten patients with metastatic RCC to the brain were identified from 2006–2013. Multiple clinicopathologic parameters were analyzed, including location, focality, and size of brain metastases.

**Results:** Ten patients with a mean age of 58 years were identified; 5 were male and 5 were female. All cases were metastatic clear cell RCCs with sarcomatoid differentiation (Fuhrman nuclear grade 4) in 3 of 10 cases and Fuhrman nuclear grade 3 in 7 of 10 cases. In 4 of 10 patients, brain metastasis was diagnosed before the renal primary. In 9 of 10 patients, brain metastases were located in the left hemisphere. The metastatic tumor was unifocal in most cases (8 of 10) with a mean size of 2.2 cm.

**Conclusions:** This is one of the largest studies to date on the clinicopathologic findings of patients with metastatic RCC to the brain. Clear cell RCC is the most common variant of RCC to metastasize to the brain. A solitary brain mass on imaging does not exclude metastatic RCC. Molecular studies of this specific subset of tumors may have a role in identifying patients at increased risk of developing brain metastasis.

**Angiomatoid Fibrous Histiocytoma of the Brain**

(Poster No. 57)

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Angiomatoid fibrous histiocytoma (AFH) is a soft tissue sarcoma of low malignant potential that only rarely recurs or metastasizes. It is most frequently encountered in the extremities of children and young adults. We recently encountered a 13-year-old girl with a frontal mass that showed a nodular neoplasm surrounded by dense lymphoplasmacytic inflammation and fibrosis. It displayed solid and microcystic architecture, containing round to oval epithelioid or syncytial-like cells with abundant pale cytoplasm, and monomorphic nuclei with scattered intranuclear inclusions. Immunohistochemistry showed florid desmin and patchy EMA and SMA positivity. Fluorescence in situ hybridization was positive for EWSR1 rearrangement, supporting the pathologic impression of AFH. To our knowledge, this is only the second confirmed primary intracerebral AFH in the literature. Greater clinical experience is needed to predict the behavior of AFH in this location (Figure 199).

**Primary Brain Tumors Associated With Rosai-Dorfman–Like Histiocytic Lesions: Report of 2 Cases**

(Poster No. 58)

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Primary Intraosseous Calvarial Meningioma—A Rare Lesion: Report of 2 Cases With Brief Review of Literature
(Poster No. 60)

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Primary intraosseous calvarial meningiomas (PCIOMs) are rare lesions. PCIOMs are thought to arise from ectopic meningeal/arachnoid cells entrapped in cranial sutures during molding of the head at birth or as result of trauma. We report 2 cases of PCIOM with brief literature review. The first case involved a 63-year-old man with a history of prostate cancer with intermittent dizziness, left eye blurred vision, and negative for CD1a. Case 2 involves a 78-year-old man with JAK2-positive myelofibrosis who presented with proptosis and orbital, temporal lobe, and meningeal lesions. The temporal lobe lesion was glioblastoma. The orbital and meningeal lesions were a histiocytic proliferation with similar findings as case 1 and consistent with a RDD-like histiocytic lesion. While the pathogenesis and significance of any possible association is not certain, this report of RDD-like histiocytic lesions and primary CNS tumors suggests that a RDD-like histiocytic lesion should be considered when an inflammatory process in proximity to a primary brain tumor is identified.

Seventeen-Year Survival After Multiple Recurrences and Repeated Resections for Pituitary Carcinoma: A Case Report and Review of the Literature
(Poster No. 59)

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Pituitary carcinoma is an extremely rare malignancy. There are fewer than 200 well-documented cases so far. The diagnosis requires either discontinuous intracranial spread or systemic metastasis. The clinical features of pituitary carcinomas are highly variable, but overall they are due to the mechanical pressure to surrounding tissues and/or to the effects of excessive hormonal secretion. Mass effect includes impairment, headache, hearing loss, ataxia, and motor dysfunction. Most reported pituitary carcinomas are hormonally active, with ACTH- and gonadotropin-secreting tumors being the most common type. Pituitary carcinomas are generally associated with poor prognosis despite multiple therapies. Patients with systemic metastases and intracranial spread have median survival of 12 months and 2.6 years, respectively. We present a rare case of a patient who survived at least 17 years with recurrent pituitary carcinoma. A 55-year-old man underwent endonasal transphenoidal resection of a pituitary adenoma in 1996. He developed multiple recurrences of the pituitary lesion and intracranial metastases since 1998. After multiple tumor resections, 2 well-circumscribed tumors (2.4 × 2.7 cm, 6.0 × 2.6 cm) in the left cerebral hemisphere and multiple spinal metastases were identified in 2013. Pathology from a left-sided temporoparietal craniotomy revealed a highly cellular neoplasm with uniform round nuclei, salt-and-pepper chromatin pattern, brisk mitotic activity, and relatively small amounts of cytoplasm. Tumor cells were positive for synaptophysin and chromogranin by immunostaining, and focally positive (50%) for p53 and Ki-67. The patient remains alive in March 2014 with residual metastatic disease.

A Practical Approach to the “ABC” Scoring System for the Neuropathologic Assessment of Alzheimer Disease
(Poster No. 61)

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Alzheimer disease (AD) neuropathologic change is currently evaluated by using an “ABC” score that derives from 3 separate 4-point scales: amyloid-β (Aβ) plaques (A0-A3), Braak/neurofibrillary pathology stage (B0-B3), and neuritic plaque score (C0-C3). The combination of an ABC score receives a descriptor of “not,” “low,” “intermediate,” or “high” AD neuropathologic change, providing guidance for clinicopathologic correlation. We report a practical approach to the “ABC” score system in 15 cases of AD examined in our institution during 2012–2013. Upon exclusion of other causes of neurodegenerative dementia by immunomorphologic methods, including primary tauopathies (frontotemporal dementia) and synucleopathies (diffuse Lewy body disease), our workflow focuses on (1) delineation of amyloid plaque score based on the distribution of cortical and subcortical Aβ deposits by immunohistochemistry, including diffuse plaques (Aβ deposits without dystrophic neurites) and neuritic plaques (Aβ deposits with dystrophic neurites) per original Thal phases (Neurology. 2002;58:1791); (2) determination of anatomically defined Braak stage of neurofibrillary pathology by immunohistochemistry using monoclonal antibody AT8 to hyperphosphorylated tau protein (phospho-tau), including phospho-tau (≥1) neurofibrillary tangles, pretangle neurons, neurtight threads, and dystrophic neurites of neuritic plaques (Acta Neuropathol. 2006;112:389); and Allocortical/mesolimbic areas include anterior and posterior hippocampus with subiculum, entorhinal cortex, and transentorhinal region. Neocortical areas include fusiform, superior tempo-
High-Grade Fibrosarcoma of the Brain in a Patient With Neurofibromatosis

(Poster No. 62)

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Fibrosarcoma is a malignant mesenchymal neoplasm that shows a predilection for the deep soft tissues of the trunk and extremities. Primary fibrosarcoma of the central nervous system is extremely rare with fewer than 50 cases reported in the literature. Our case is a unique presentation of primary fibrosarcoma of the brain arising in a patient with neurofibromatosis type I. The patient, a 78-year-old woman with neurofibromatosis type I and a remote history of stroke, presented with slurred speech, frontal headaches, insomnia, and dyspnea. MRI revealed a dural-based mass in the left parietal region of the brain, invading the adjacent parenchyma. Histologic evaluation of the mass revealed hypercellular areas composed of markedly pleomorphic cells arranged in a storiform configuration with hemorrhage and necrosis. Mitotic figures including atypical forms were readily identified. The neoplastic cells were positive for vimentin and negative for GFAP. The tumor cells were negative for BER-EP4, HMB-45, MART-1/Melan-A, CD68, EMA, S100, actin, desmin, and CAM 5.2. The presence of fibrosarcoma in the genetic background of neurofibromatosis is quite unique, and an association of the tumor with this genetic disease cannot be completely excluded. Further molecular and genetic studies might contribute in investigating the pathogenetic association among the 2 entities.

Disseminated Well-Differentiated Choroid Plexus Carcinoma

(Poster No. 63)

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Choroid plexus carcinoma is an uncommon papillary neoplasm that usually occurs in the ventricular system in children; it has poor overall outcome. We report the case of a 70-year-old man who was evaluated for progressive left-sided hearing loss. The follow-up MRI revealed multiple intra-axial and extra-axial, supratentorial and infratentorial minimally enhancing lesions, including small lesions at the level of foramen magnum causing crowding of the cerebellar tonsils with deformity of cervicomедullary junction. Biopsy specimen was obtained from the lesion of foramen magnum, which showed complex solid and focally papillary neoplasm lined by multiple layers of epithelioid cells with moderate increased nuclear-cytoplasmic ratio, hyperchromatic nuclei, and moderate pleomorphism, clear to eosinophilic cytoplasm, and increased mitotic activity, reaching up to 5 mitoses per 10 high-power fields. Necrosis was not identified (Figure 201, A and B). Immunohistochemical stains showed that the tumor cells were strongly and extensively positive for vimentin, S100 protein (Figure, C) and synaptophysin (Figure, D), with patchy expression of pancytokeratin in a cytoplasmic paranuclear ball-like pattern. Small subsets of tumor cells were positive for GFAP. The tumor cells were negative for BER-EP4, MOC-31, and EMA. Ki-67 stain showed foci of increased proliferation (up to 8%). These findings are more consistent with a diagnosis of well-differentiated choroid plexus carcinoma, given the extensive solid growth, degree of hypercellularity and pleomorphism, and proliferative activity. Clinical presentation of CPC as a multifocal lesion in brain parenchyma and spine is very unusual, and possibility of metastatic papillary tumor from elsewhere should be considered and ruled out, particularly in an elderly individual.

A Postmortem Investigation of Marchiafava-Bignami Disease in a Woman With Numerous Endocrine Pathologies

(Poster No. 64)

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Marchiafava-Bignami disease is a rare neurologic condition with an undetermined pathogenesis that causes degeneration and demyelination of the corpus callosum. Classically, this disease has been described in malnourished male alcoholics, though a handful of cases have also been reported in nonalcoholic patients with alternate diseases. We present the case of a 56-year-old alcoholic woman with a history of Cushing disease, Grave disease, type II diabetes mellitus, hypertension, chronic kidney disease, chronic obstructive pulmonary disease, osteoporosis, chronic back pain, and opioid dependence. This patient’s neurologic symptoms began at age 37 years with an insidious onset of loss of balance, dizziness, dysarthria, and memory loss. Imaging performed at that time revealed a cerebellar hemangioma and a cyst in the parahippocampal region. Her symptoms progressed during 2 to 3 years and then stabilized, yet she continued to suffer from short-term memory loss. When diagnosed with Cushing disease at age 52 years, additional brain imaging was ordered to evaluate for a pituitary lesion. In addition to revealing a slightly asymmetric pituitary gland, imaging displayed abnormally enhancing lesions within the corpus callosum. The patient eventually died of a myocardial infarction at age 56 years. Postmortem examination of her brain revealed a severe central atrophy of the corpus callosum (Figure 202), with preservation of the anterior and posterior genus. Microscopy showed extensive gliosis and...
degeneration of the corpus callosum consistent with a diagnosis of Marchiafava-Bignami disease. Immunohistochemistry and special staining highlighted several histologic features of the disease, including demyelination, axon loss, inflammation, and collagen deposition.

Sacrococcygeal Teratoma With Medulloepithelioma/ Central Primitive Neuroectodermal Tumor (PNET)

(Poster No. 65)

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Sacrococcygeal teratomas (SCTs) associated with malignant germ cell components are well described, but somatic malignancy is extraordinarily rare. Malignant non–germ cell components documented in the literature include carcinoma, neuroblastoma, rhabdomyosarcoma, liposarcoma, chordosarcoma, nerve sheath tumor, and ependymoma. We report the rare occurrence of a central PNET with features of medulloepithelioma/ependymoblastoma arising in an SCT. A 1-year-old girl without significant past medical history presented to the emergency department with a 1-week history of abdominal distension, constipation, and urinary retention. Pelvic CT and MRI revealed a large midline solid and cystic presacral mass with fat, interpreted as an Altman type IV sacrococcygeal teratoma encasing the rectum and causing bladder outlet obstruction. Serum α-fetoprotein, HCG, and LDH levels were normal. CT-guided fine-needle aspiration and core biopsy revealed a cellular blue cell neoplasm forming tubules, papillary structures, perivascular rosettes, and true rosettes resembling CNS medulloepithelioma/ependymoblastoma. Mitoses, necrosis, and apoptosis were prominent. The tumor was immunoreactive for CD99, CD56, GFAP, NF, synaptophysin, CAM 5.2, and EMA (dot pattern).

The tumor was interpreted as a central PNET arising in a teratoma. A diagnosis of central PNET arising in a teratoma was made (Figure 203).

Inflammatory Breast Cancer Involving Cerebral Vasculature

(Poster No. 67)

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A 52-year-old woman with inflammatory breast cancer, a rare breast cancer subtype, presented for neuropathology assessment of the brain as part of a complete autopsy examination. Microscopic examination showed acute hypoxic/ischemic injury within the medial and lateral occipital lobes, left parietal lobe, right frontal lobe, and right front lobe. The small capillaries of the brain contained pleomorphic, atypical cells. These atypical cells were strongly positive for pancytokeratin, CK7, EMA, and CAM 5.2, consistent with intravascular involvement by the patient's known inflammatory breast cancer. CK20, ER, PR, and mammoglobin were negative. No metastatic carcinoma was present in the surrounding brain tissue. The inflammatory breast carcinoma metastatic to spleen was negative for ER and PR and had only rare, focal staining for mammoglobin. This pattern of cerebral intravascular involvement has not been reported in inflammatory breast cancer. It is important to recognize, as involvement of the small cerebral vessels without metastatic deposits in the surrounding tissue is a subtle finding. An awareness of this pattern of metastatic spread is essential as it could contribute to the cause of death in patients with inflammatory breast carcinoma.

Neurodegeneration With Brain Iron Accumulation: An Autopsy Case Report With Unusually Colorful Findings

(Poster No. 68)

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Neurodegeneration with brain iron accumulation (NBIA) is a rare disorder, with fewer than 100 cases in the entire literature. It is broadly characterized by extrapyramidal symptoms, dementia, and iron deposition in the basal ganglia. NBIA is clinically and genetically heterogeneous, but only in extremely rare cases does it present in adulthood. We report the case of a 72-year-old woman who died of shock secondary to chronic rheumatoid arthritis; neurologic evaluation was limited owing to severe encephalopathy. She had a history of depression and possible wide-based gait, but no other overt neurologic symptoms. In fact, she was employed as a teacher and apparently functional and living independently. On autopsy, however, gross examination showed dramatic and symmetric blue discoloration of the bilateral basal ganglia. Microscopy showed pigment deposition and axonal spheroids in the caudate nuclei, putamina, and to a lesser extent in the globus pallidus. There was also severe degenerative gliotic rarefaction in the globus pallidus and decreased neurons, neuronal hypopigmentation, axonal spheroids, and increased extracellular
pigment deposits in the substantia nigra. Perls Prussian blue revealed the presence of iron within the pigment deposits and axonal spheroids.

Other more common neurodegenerative disorders can also demonstrate brain iron accumulation, but the pattern of iron deposition helps in making a diagnosis of NBIA. There are currently no definitive therapeutic options, but animal studies and early clinical trials in iron chelation therapy are ongoing and may show promise (Figure 204).

A Case of Recurrent Embryonal Tumor With Abundant Neuropil and True Rosettes With Unusual Histopathology (Poster No. 69)
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Embryonal tumor with abundant neuropil and true rosettes (ETANTR) is a rare, aggressive, infantile or childhood malignancy that most commonly presents in the cerebral hemispheres. Histologically, it is characterized by zones of primitive neuroepithelial cells, abundant neuropil islands, and multilayered ependymoblastic rosettes, whereas genetically it is characterized by focal amplification of a microRNA cluster at chromosome 19q13.4. We report on a 3-year-old girl who presented with a history of weight loss, vomiting, difficulty ambulating, and a large nonenhancing mass in the posterior fossa. The tumor consisted of an embryonal neoplasm with small cell phenotype and scattered islands of neuropil, but no ependymoblastic rosettes were identified (Figure 205, A). The tumor cells demonstrated diffuse immunoreactivity for synaptophysin and very high Ki-67 labeling index (Figure, B). A diagnosis of medulloblastoma was made and the patient was treated per standard protocol. Owing to radiologic progression, the tumor was resected again 7 months later. The recurrent tumor demonstrated increased differentiation characterized by low cellularity (Figure, C), and low Ki-67 labeling index (Figure, D). Fluorescence in situ hybridization on the primary and recurrent tumor detected an amplification at 19q13.4 (Figure, D, inset), and a diagnosis of ETANTR was favored. The patient died 6 months later. This case highlights the need to consider ETANTR in the differential diagnosis of embryonal tumors in the posterior fossa. Furthermore, it demonstrates the utility of fluorescence in situ hybridization for the miRNA locus at 19q13.4 for distinguishing ETANTR from other embryonal neoplasms in cases lacking ependymoblastic rosettes.

An Unusual Case of Recurrent Pituitary Carcinoma (Poster No. 70)
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Pituitary carcinomas are extremely rare and represent only 0.1% of pituitary tumors. The diagnosis requires the presence of metastatic disease, as histologic features alone are nondiagnostic. Death often occurs within 1 year of diagnosis, especially for patients with metastases outside the central nervous system. In our case, a 52-year-old male with a 13-year history of a recurrent growth hormone–secreting pituitary adenoma was found to have invasive pituitary carcinoma and was treated with surgical resection, radiation, and temozolomide. Growth hormone and insulin-like growth factor-1 levels were initially suppressed but rose again. Two years later, imaging revealed metastatic disease in the left temporal lobe, right dura, and left cervical lymph nodes. Pathology revealed pleomorphic, growth hormone–reactive tumor cells with a proliferative index of 33%. He was treated with bevacizumab and is alive and well. However, recent imaging 8 months later reveals new cerebral cortex and thoracic spine metastatic disease.

A Hypermelanotic Malignant Proliferating Trichilemmal Cyst/Tumor (Poster No. 71)
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Proliferating trichilemmal cysts are benign, longstanding cutaneous lesions that are commonly found on the scalp of elderly women. Malignant transformation occurs rarely, manifesting clinically as a sudden increase in size. Concomitant melanocytosis within these lesions is extremely rare. We report an unusual case of a malignant proliferating trichilemmal cyst/tumor excised from a 60-year-old man who had complaint of a sudden increase in the size of a painless left flank mass he stated had been present for 20 years. On histology, the tumor was composed of proliferating keratinocytes admixed with heavily pigmented dendritic melanocytes and an extensive blood vessel network. The epithelial component consisted of well-circumscribed lobules with areas of benign morphology typical for proliferating trichilemmal cyst/tumor. Adjacent areas show keratinocytic pleomorphism and proliferation with an invasive pattern, indicating malignant transformation. This is supported by a heterogenous p53 immunocytochemical staining pattern from weak in benign areas to strong in areas with an invasive pattern. The melanocytes show benign morphology and stain positively for Mart-1 and S100 antigens. The extensive intratumoral benign melanocytosis and pigmentation indicates a unique tumoral microenvironment that promotes the proliferation of melanocytes and their melanogenic activity, likely induced by factors produced by keratinocytes. CD34 stains demonstrate an extensive blood vessel network with reduced expression in areas of tumor stromal fibroplasia. Our case report provides an unusual example for, and will contribute to, future studies on the pathophysiology of malignant transformation of proliferating trichilemmal tumor and on
the microenvironmental regulation of melanocytes and their interaction with tumor keratinocytes.

**Primary Cutaneous Mucoepidermoid Carcinoma Occurring in a Renal Transplant Patient**

(Poster No. 72)

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Mucoepidermoid carcinomas arising from skin are exceptionally rare tumors, although, they account for 25% to 30% of malignant tumors arising in major and minor salivary glands. We describe a primary cutaneous mucoepidermoid carcinoma arising on the right face in a 66-year-old man. The patient had a history of renal transplant and had more than 100 cutaneous nonmelanoma skin cancers during the past 2 years. The tumor was 4 × 3 cm in maximum dimension with overlying ulceration. Histologically, the dermal tumor was composed of lobules of large polygonal cells with vesicular nuclei and prominent nucleoli. Focal surface epidermal connection, clear cell change, prominent mucinous differentiation, and dyskeratosis were present. Immunohistochemical staining showed positivity for EMA, CK5/6, CK34 BE12, and p63. MAK6 immunostain highlighted the epidermal component, while focal positivity for CEA and Ber-EP2 was seen. A mucicarmine stain highlighted the mucinous component, which formed an integral part of the tumor. The differential included a direct extension of an underlying mucoepidermoid carcinoma of the parotid gland or a cutaneous metastasis of it. However, in our case, the tumor was limited to the skin and deep dermis with no involvement or infiltration of the underlying parotid gland. These findings were consistent with primary cutaneous mucoepidermoid carcinoma arising in the setting of solid organ transplant with immunosuppression. Posttransplant malignancies behave in a more aggressive fashion and carry a poor prognosis. This lesion has a morphologic overlap with squamous cell carcinoma with clear cell change and sebaceous carcinoma. Distinguishing it from a mucoepidermoid carcinoma originating from the salivary glands could be problematic (Figure 206).

**Sebaceous Carcinoma of the External Auditory Canal: A Case Report With Review of the Literature**

(Poster No. 73)

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Sebaceous carcinoma is a rare and aggressive epidermal adnexal tumor occurring most frequently in the eyelids. It is extremely rare for this tumor to present in the external ear canal. Here, we report a case of sebaceous carcinoma in the external auditory canal with a review of the literature. A 49-year-old man had complaints of a painfully obstructing mass with bleeding and drainage in the external auditory canal. The lesion was described as 2 masses located in the posterior-inferior aspect of the external auditory canal; one was pedunculated and polypoid and the other more solid. Microscopically, the lesion consisted of dermal nests of basaloid cells (Figure 207) that appeared to bud off of the overlying epithelium. The nests had prominent retraction artifact but did not have peripheral palisading. There were mature vacuolated sebocytes scattered throughout the lesion. The basaloid cells showed strong diffuse nuclear positivity for p63 and strong diffuse cytoplasmic staining for CAM 5.2. The vacuolated sebocytes showed strong cytoplasmic staining for EMA (inset) and membranous vesicular staining with adipophilin. This pattern of staining with adipophilin, a protein on the surface of intracellular lipid droplets, is sensitive and specific for sebaceous carcinoma in this context. On follow-up, the excision of this lesion was negative for residual carcinoma. There have been fewer than 10 reports of sebaceous carcinoma arising in the external auditory canal. It is important to distinguish this entity from the much more common squamous and basal cell carcinomas because of its higher rate of recurrence, distant metastasis, and mortality.

**Automated Multiplexed Immunoprofiling of Melanoma Fresh-Frozen, Paraffin-Embedded Tissue Using PD-L1 and Lymphocyte Markers, Including Spatial-Phenotypic Characterization**

(Poster No. 74)

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**Context:** Recent successes with PD-L1 drugs and adoptive immunotherapy demonstrate the potential efficacy of leveraging the immune system to fight cancer. However, host-tumor interaction is complex and difficult to characterize with immunohistochemistry or flow cytometry. Capturing spatial relationships of immune phenotypes in and around tumor is enabled by multiplexed immunofluorescence labeling and multispectral imaging, potentially forming the basis of assays to guide therapy and monitor response.

**Design:** To demonstrate this new capability, we used a curated melanoma tissue microarray obtained from a cohort of ipilimumab-treated patients. A multiplexed immunofluorescence staining protocol was used for PD-L1, CD8, CD34, and FOXP3, with DAPI counterstain. The staining method used sequential tyramide signal amplification and
Antibody stripping. Analysis consisted of automated multispectral imaging and pattern recognition-based image analysis, in a workflow guided and reviewed by pathologists (Figure 208). Method validation consisted of comparing data collected this way and data from semiautomated analysis of serial sections stained with conventional immunohistochemistry.

**Results:** Results demonstrate reliable detection and phenotyping of lymphocytes in heterogeneous clinical samples, with high signal-to-background and precise measurements of PD-L1 and FOXP3 per-cell expression and of CD8+ cell density in intratumoral and extratumoral compartments. Percentage agreement, tabular data, and maps of cell phenotypes and expression level will be presented.

**Conclusions:** We believe we have demonstrated a new capability for elucidating the intricacies of cancer immune response, for research and potentially for clinical use, with a workflow that is automated by computer and amenable to present practices where results require review by a pathologist to assure data quality.

**Assessing Excision Margins in Basal Cell Carcinomas: A 3-Year Audit in a Small Hospital**

(Poster No. 75)

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**Context:** A 3- to 4-mm margin in basal cell carcinomas (BCCs) is generally quoted as adequate clearance in the transverse plain, based on the assumption that all specimens are uniform ellipse excisions. Specimens from the head and neck region have different shapes. We devised differential painting of margins and different way of assessing all margins to reduce false-negative clear margins, especially in clinically ill-defined BCCs with multifocal or adenoid growth patterns. The audit set out to determine (1) the rate of incompletely excised BCCs compared to an average of 7% in published literature. It is important to have a comprehensive method of assessing resection margins to ensure accurate reporting.

**Results:** Between 2011 and 2013, 1032 BCCs were diagnosed in the department and 165 (16%) had positive margins; 107 (65%) were reexcised, and 54 (50%) had residual disease in the reexcision specimen.

**Conclusions:** The audit detected a high rate (16%) of incompletely excised BCCs compared to an average of 7% in published literature. However, the rate of residual BCC of 50% is comparable to the 45% and 54% reported in other studies. It is important to have a comprehensive method of assessing resection margins to ensure accurate reporting.

**Alkaptonuria: A Case Report With Diagnostic Challenge**

(Poster No. 76)

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Alkaptonuria is a rare autosomal recessive metabolic disorder caused by deficiency of homogentisic acid (HGA) oxidase, the only enzyme capable of catabolizing HGA. Deficiency of this enzyme leads to excess HGA, which deposits in the connective tissue. We present a case of a 64-year-old woman who was referred to the dermatology clinic for a full body mole check and skin cancer screening. Clinically she had blue/gray pigmentation of the external ear and sclera. She also had a dented papule on the left cheek with punctate gray pigmentation, which was biopsied. Histopathologic examination showed a benign dermal nevus and nonpolarizable, yellow-brown, irregularly shaped fibers. Subsequent organic acid screen showed markedly elevated urinary HGA, diagnostic of alkaptonuria. On specific inquiry, the patient revealed she had a history of bilateral Achilles tendon rupture, black urine, arthritis, and external ear discoloration for many years. The pigmented material was then considered to be HGA deposition within the dermal collagen fibers. However, without the appropriate clinical data and confirmatory laboratory findings, the pigmented fragments on skin biopsy represented a diagnostic challenge. Measures such as low protein diet and ascorbic acid supplementation will slow down the disease progression and potential complications later in life; however, there is no definitive treatment for the disease. We emphasize the prompt recognition of the clinical signs and symptoms as well as the importance of the microscopic findings.

**Cutaneous Myeloid Sarcoma Masquerading as Drug Eruption: Potential Diagnostic Pitfall in Patients With Acute Myeloid Leukemia**

(Poster No. 77)

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Classically, myeloid sarcoma presents as single or multiple tumors in the skin, mucous membranes, genital tract, or testis and exhibits a diffuse tumor infiltrate on histologic examination. We present the case of a 38-year-old man with a history of refractory acute myeloid leukemia (AML) who presented with bilateral lower lobe infiltrates on chest x-ray, concerning for infection. The patient was empirically treated for infectious causes during his course of high-dose cytarabine and clofarabine therapy. On day 9 of chemotherapy, further levels are assessed if there is no residual BCC in the reexcision specimen.
the patient developed pruritus and erythema at the PICC line. The rash spread to the back and chest and was refractory to antihistamines and brief discontinuation of classically offending agents (cytarabine). On day 11 of high-dose cytarabine and clofarabine therapy, a biopsy was performed. Microscopic examination revealed a relatively subtle superficial and focally deep, perivascular infiltrate of large atypical cells with irregular vesicular nuclei with prominent nucleoli (Figure 210). Immunohistochemically, these large cells lacked CD56 expression, expressed myeloperoxidase, lysozyme, and CD163; CD117 was focally expressed in few large cells. The phenotype was similar to the original leukemic immunophenotype from a previous bone marrow biopsy. We present a unique case of early, nontumoral cutaneous myeloid sarcoma in a patient treated for recurrent AML presenting as a rash consistent with a drug eruption. Although exceedingly rare, leukemia cutis can clinically mimic benign skin conditions.

**p16 Immunostain Does Not Distinguish Verruca Vulgaris From Seborrheic Keratosis**

(Poster No. 78)

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**Context:** Verruca vulgaris (VV) often resembles irritated seborrheic keratosis (SK) clinically and histopathologically. There was controversy concerning the role of human papillomavirus (HPV) in some forms of SK. Recent studies showed HPV-6 in some vulvar SK but not in nongenital SK. HPV infection has been shown to be associated with overexpression of p16. The purpose of this study was to investigate the role of p16 immunohistochemical staining in differentiating nongenital irritated and clonal SK from VV.

**Design:** We identified 21 cases of nongenital SK and 23 cases of VV. p16 expression was evaluated by immunohistochemistry with score 0 (no expression), 1 (1%–10% expression), 2 (>10%–50% expression), and 3 (>50% expression).

**Results:** In the nongenital SK group, 10 of 21 (48%) showed p16 expression from weak to strong staining, compared to the verruca group, which showed p16 expression in 15 of 23 (65%). Comparing lesions with strong expression, 11 of 23 VVs (48%) stained strongly with p16 versus 5 of 21 SKs (24%). However, 3 of the strong-staining SKs exhibited clonal morphology.

**Conclusions:** Although this study demonstrates that p16 positivity was more frequent in VV than in SK, this finding was not statistically significant. Thus, p16 cannot be used to distinguish VV from SK in cases of overlapping morphology. Of interest is the strong positivity of clonal SKs, raising the possibility that these lesions may have altered morphology secondary to HPV infection. It also raises the possibility of more prevalent HPV infection in squamous lesions of the skin than currently appreciated.

**Microcystic Adnexal Carcinoma: Case Report of a Rare Tumor and Review of the Literature**

(Poster No. 79)

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Microcystic adnexal carcinoma is a rare neoplasm, typically involving the midface of young, middle-aged, or elderly women. It has a tendency toward persistent local recurrence, but not to metastatic deposits. A synonym of these tumors is sclerosing syringomatous carcinoma or sclerosing sweat duct carcinoma, which encompasses not only the neoplastic epithelia but also makes reference to the stromal desmoplasia, which is a frequent concomitant of these tumors. A 74-year-old woman presented with a slow-growing, crusty, painless, plaquelike lesion in the left upper cheek. Pathologic examination of the incisional biopsy showed nests and cysts of cytologically uniform, squamous cells randomly dispersed in a dense edematous collagenous stroma (Figure 211, A through D). In some areas, branching of tubular structures and aggregations of neoplastic cells gave comallike shapes. The microcysts contained lamellated keratinaceous-like material resembling hair matrix, and some areas demonstrated extensive squamous metaplasia. Moderately differentiated squamous cell carcinoma in the superficial layers was seen merging into a syringomatous carcinoma focally. Perineural invasion was present. Immunohistochemical analysis was consistent with syringomatous carcinoma (positive for p63, CK5/6, CK14 and questionable positive reaction with MUC1; negative for S100, calponin, actin, and mucin). Seven months later, the patient experienced recurrence at the same site. Excisional biopsy revealed recurrence of the same tumor. Nine months later, the patient experienced another local recurrence. She declined any further surgery. Radiotherapy of the involved area was performed, and the patient was lost to follow-up. We present this case report of this rare tumor and we provide literature review.
A Clinically Validated Gene Expression Score Impacts Diagnosis and Management Recommendations of Melanocytic Lesions by Dermatopathologists

(Poster No. 80)

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Context: Many studies have documented suboptimal accuracy and reproducibility in the diagnosis of melanocytic lesions by histopathology, even by experienced dermatopathologists. Therefore, adjunctive methods that provide objective and reliable data have been sought. Recently, a 23-gene expression signature has been clinically validated to improve reproducibility in the diagnosis of melanocytic lesions by histopathology. The goal of this study was to quantify the impact of this test on diagnosis and management recommendations made by dermatopathologists.

Design: Representative sections of difficult-to-diagnose melanocytic lesions encountered during routine dermatopathology practice were submitted for gene expression testing. Samples were accompanied by a survey documenting the physician’s pretest diagnosis, level of diagnostic confidence, further evaluation to be performed, and recommendations for management. After receiving the gene expression score for the lesion, the survey was repeated. Changes between the pretest and posttest surveys were analyzed.

Results: Completed pretest and posttest surveys were available for 687 cases submitted by 42 dermatopathologists during a 15-week period. When the gene expression score was provided, diagnosis was revised in 18.1% of cases and management recommendations were revised in 37.1% of cases. Overall, availability of the gene expression score increased the pathologists’ diagnostic confidence by 45.2%.

Conclusions: The gene expression score impacts diagnosis and management recommendations by dermatopathologists confronted with diagnostically challenging melanocytic lesions. Integration of this assay into current practice has the potential to improve patient care by allowing more definitive diagnoses and management recommendations for melanocytic lesions.

All authors are shareholders in Myriad Genetic Laboratories, Inc.

A Rare Case of Cutaneous Angiomyolipoma of the Ear

(Poster No. 81)

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Cutaneous angiomyolipoma (CAML) is a rare benign mesenchymal tumor, which is distinct from its renal counterpart in terms of sex predominance, clinical association, and HMB-45 immunoreactivity. To date, only 23 cases of CAML have been reported in the English literature. Here we report a case of CAML that presented as a swelling on the right ear. A 36-year-old man with no significant past medical history presented with a solitary, pea-sized, painless nodule on his right ear lobe for the past 6 months. There were no clinical features of tuberous sclerosis. On examination, there was a rubbery, movable, skin-colored nodule on the right ear lobe that measured 20 mm in diameter. The nodule was completely excised. Microscopy revealed a well-circumscribed tumor, spanning the dermis and subcutis, composed of an admixture of mature adipocytes, thick-walled ectatic blood vessels, and bundles of smooth muscles (Figure 212). Cellular pleomorphism and mitotic figures were absent. Immunohistochemistry highlighted the smooth muscle bundles with desmin, and the adipose tissue with S100 protein. The cells were uniformly negative for HMB-45 and Melan-A. We present this case to emphasize the uniqueness of CAML from a clinical and immunophenotypic standpoint. Unlike its renal counterpart, CAML shows a male predominance, is not associated with tuberous sclerosis, and is consistently negative for HMB-45.

NRAS-Mutant Metastatic Verrucous Melanoma in a 3½-Year-Old Girl

(Poster No. 82)

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Low suspicion and atypical histologic features of childhood melanoma may lead to misdiagnosis or delay in diagnosis. A 3½-year-old girl was referred with a diagnosis of malignant melanoma of uncertain origin after biopsy of a right neck mass. There was no family history of melanoma or other skin cancers. Other than 2 hyperpigmented, benign-appearing nevi on her neck, measuring less than 0.2 cm, there were no other skin lesions. Past history revealed that the patient had a pigmented lesion on her scalp since birth, which grew to 2.5 cm, bled once, and was excised at the age of 2 years in a community hospital. The pathology was reported as benign pigmented intradermal indeterminate congenital nevus. The excision site showed a 4×5-cm well-healed flat scar. Rereview of the slides demonstrated a cellular melanocytic neoplasm with an exophytic and papilliferous growth pattern. There were diffuse melanocytes dispersed along the dermal-epidermal junction and in the dermis with focal extension into the subcutaneous fat. Nuclear enlargement, pleomorphism, focal prominent nucleoli, increased mitoses, angiotropism, and neurotropism were noted. The tumor cells were positive for S100 and HMB-45. The rendered diagnosis was verrucous melanoma, with Breslow thickness of 6.07 mm and Clark level V. A Q61K NRAS mutation was detected. Array-based comparative genomic hybridization showed a total of 17 chromosomal gains. Staging studies revealed lung, liver, and bone metastasis. The melanoma did not respond to iplimumab but had a short-lived partial response to trametinib. Increased awareness of this rare entity may help avoid misdiagnosis.

Recurrent Morpheic Basal Cell Carcinoma With Distant Bony Metastasis

(Poster No. 83)

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While basal cell carcinoma is the most common cancer, the mortality is extremely low owing to its usual slow growth and very low metastatic potential. We report the case of a 51-year-old man with infiltrative basal cell carcinoma of the left cheek diagnosed in 2009 who subsequently presented in 2013 with right hip pain and a pathologic fracture of the right ischium due to metastatic seeding. The patient had undergone primary excision and superficial parotidectomy with facial nerve preservation in 2011 with reexcision 2 months later owing to initially positive margins. In November 2013, the patient was admitted for right hip pain and local recurrence of his left cheek basal cell carcinoma. The patient underwent wide local excision of the facial lesion with resection of a portion of the parotid duct and facial nerve; the resection demonstrated a morpheic pattern with perineural invasion. Imaging of the pelvis showed a pathologic fracture of the right ischium, and biopsy of the lesion revealed metastatic basal cell carcinoma with identical morphology and staining to the resected facial lesion (Figure 213).
Basal cell carcinoma metastases to bone are a rare occurrence: in metastatic cases, however, the skin lesions tend to be large and established, and the metastases multiple. In 2011, our patient’s lesion measured approximately 6 × 5 cm and the most recent imaging from 2013 has not revealed additional metastases. The relevance of the histologic subtype and presence of perineural invasion regarding metastatic potential warrant further investigation.

A Rare Cutaneous Collision Tumor

(Poster No. 84)

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A collision tumor (CT) is defined as 2 or more histologically distinct neoplasms coexisting in the same anatomic location. They are diagnostically challenging when they involve a combination of 2 malignant tumors, each with its own prognosis, treatment, and ability to metastasize. We present a rare collision tumor composed of a basal cell carcinoma (BCC) and an atypical fibroxanthoma (AFX). A 64-year-old white man presented for evaluation of a bleeding growth on his right temple that had grown larger in the past 3 months. Examination revealed a 3.5-cm pink, nearly irregularly shaped plaque with light brown crust along the edges. A hyperpigmented focus was noted at the interior aspect of the plaque with overlying erosions. The mass consisted of 2 histologically distinct tumors. The first tumor demonstrated nodular and cystic islands of basaloid cells with peripheral palisading and focal epidermal-stromal clefting (strongly positive for Ber-Ep4). Colliding with the first tumor was an infiltrating spindle cell proliferation with cells demonstrating marked pleomorphism with hyperchromasia, abundant eosinophilic cytoplasm, prominent nucleoli, and 1 to 4 mitoses per high-power field. The case was diagnosed as a CT composed of AFX and BCC. Because the tumor was broadly transected at the base, the more aggressive undifferentiated pleomorphic sarcoma could not be ruled out. Although BCCs are common components of collision tumors, AFX is rarely reported. Awareness of this entity is paramount, as a wider margin or excision and/or more frequent and extensive workup and follow-up may be needed than for a routine case of BCC.

Congenital Pigmented Epithelioid Melanocytoma: A Rare Case Report

(Poster No. 85)

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Pigmented epithelioid melanocytoma is a low-grade variant of melanoma with the potential for lymph node metastasis. To our knowledge, only 3 cases of congenital pigmented epithelioid melanocytoma have been reported in the literature. Herein, we present a case of a 5-month-old girl who was born cesarean section owing to failure of descent secondary to a large scalp mass. At initial presentation, the mass had doubled in size since birth. Physical examination showed a 6.0 × 6.0 nontender lesion on the vertex of the scalp with dark crusting under the skin and 2.0-2.0-cm overlying ulcerated area. Computed tomography scan revealed a 5.3 × 5.8 × 6.0-cm, hyperdense, heterogeneous scalp mass. Upon surgical excision, the mass measured 54 g, characterized as a 5.3 × 5.0 × 4.7-cm markedly pigmented lesion. Microscopic examination, using both H&E-stained and bleached sections, showed confluent sheets of heavily pigmented epithelioid melanocytes with variable cellularity, marked nuclear pleomorphism, phenotypic heterogeneity, and sclerosis of the dermal collagen. The melanocytes, though focally abutting the epidermis, did not appear to be arising from the epidermis. There was focal ulceration of the overlying epidermis, and the tumor cells extended to the surgical margin. Necrosis was present and mitoses were approximately 1 to 2 per high-power field. Array comparative genomic hybridization (CGH) showed loss of chromosomes 1p36.33-p35.3, 1q32.1-q44, and 17q11.1-24.2. A diagnosis of severely atypical pigmented epithelioid cell melanocytic proliferation of indeterminate malignant potential was rendered. No recurrence has been observed to date during her 6-month follow-up.

An Unusual Presentation of Disseminated Cryptococcosis in an Immunocompetent Host

(Poster No. 86)

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Cryptococcus neoformans is an encapsulated yeast that most commonly infects the immunocompromised but is rare in immunocompetent hosts. We report a case of disseminated cryptococcosis in an immunocompetent 58-year-old man who presented with acute renal failure, a 22-lb weight loss, a daily fever for the past month, and a 1-day history of intermittent, sharp, left-sided chest pain. Two weeks before presentation, the patient was prescribed an unknown antibiotic for a urinary tract infection. The patient continued to have symptoms, so his primary care physician prescribed him ciprofloxacin. Two days later, the patient developed polymorphic pink papules with hemorrhagic crusts on his face. Initially, blood cultures were negative, and he was treated with corticosteroids and dialysis for kidney failure. Incidentally, a computed tomography scan revealed cirsiorh of unknown origin. Five days after presentation, he became encephalopathic. Laboratory results showed a leukocytosis and ammonia; empiric antibiotics were started. A small right pleural effusion also developed. Three days later blood cultures grew yeast; and micafungin was started. A punch biopsy of the papules, performed on day 7, showed an ulcerated lesion with many yeasts resembling Cryptococcus and demonstrated by PAS, although mucicarmine and Mart-1 did not highlight the yeast forms. A tissue culture of the papules, a bronchial alveolar lavage, and the final blood culture grew C. neoformans. The patient died 11 days after admission. This case demonstrates the necessity of increased awareness of cryptococcosis manifestations and the gravity of early workup of dermatologic manifestations of disease.

Syringocystadenocarcinoma Papilliferum With Squamous Differentiation and Focal Invasive Squamous Cell Carcinoma

(Poster No. 87)

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Syringocystadenocarcinoma papilliferum is a rare neoplasm of apocrine glands and is the malignant counterpart of the more common benign syringocystadenoma papilliferum. Adenocarcinoma in situ and/or invasive adenocarcinoma is the most common malignant pattern. Squamous differentiation in the invasive component is rare, being reported in only 5 cases. We report a case of syringocystadenocarcinoma papilliferum in which there was squamous differentiation with focal invasive squamous cell carcinoma. An 86-year-old man presented with an 11-month history of a firm, pale brown, slightly variegated, painless nodule on the left elbow. The excision specimen showed a mixed solid and cystic epithelial tumor in the dermis and subcutis with focal connection to the epidermis. The cystic component was lined by a veritable field of mildly atypical rounded or squamous epithelial lining. There were some papillary projections into the cystic lumen that had a connective tissue core with an abundant chronic mononuclear inflammatory cell infiltrate including plasma cells. In one area of the tumor, an invasive squamous cell carcinoma was present. The epithelium lining of the cystic spaces was positive for cytokeratin 7 and cytokeratin 19. The portion with squamous cell carcinoma was negative with those 2 markers. CEA showed variable luminal staining of the epithelium lining the cystic spaces. p63 highlighted the dysplastic and nondysplastic squamous epithelium. There was absence of...
myoepithelial cells in the area of dysplastic squamous epithelium. Overall, the features were consistent with a background syringoystadeno-adenoma papilliferum that has prominent squamous metaplasia with a focal area of invasive squamous cell carcinoma.

**Animal-Type (Pigment-Synthesizing) Malignant Melanoma With Multiple Metastases to Brain**

(Poster No. 88)

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Animal-type melanoma or pigment-synthesizing melanoma is a rare subtype of malignant melanoma (MM) that shows excessive melanin production, resembling tumors reported in grey horses and laboratory animals. Only a limited number of cases in humans are on record, which suggests less aggressive behavior than conventional MM. We report a case of animal-type MM of the toe that led to multiple metastases in the brain. A 54-year-old woman with past history of MM of the toe presented with left-sided weakness and hemiplegia. MRI revealed multiple hemorrhagic lesions, with the largest lesion (3.5 cm) adjacent to the motor cortex. Bifrontal craniotomy was performed and jet black soft issue was received. Touch preparation revealed heavily pigmented cells, excessive black pigment in the background, and few atypical neoplastic cells (Figure 214, A). Microscopic examination of tissue revealed mostly heavily pigmented, round to spindled cells with cyttoplasm filled with abundant coarse melanin granules that obscured the nuclei, and pigment-laden macrophages with excessive extracellular brown pigment (Figure, B and C). Melanin bleaching helped in uncovering the cytologic atypia (Figure, D). Abundant melanin synthesis and lack of histologic features indicative of aggressive biologic behavior (mitoses, lymphovascular invasion) distinguish this variant from conventional MM. Local spread, recurrence, and satellitoses are more common than metastatic spread. The biologic behavior of pigment-synthesizing melanoma remains in question owing to a limited number of reported cases. Our case emphasizes that, owing to unpredictable behavior of this lesion, pigment-synthesizing melanoma should be treated in the same fashion as conventional MM.

**Syringofibroadenoma With Verrucous Carcinoma: Collision Tumor or Concurrence?**

(Poster No. 89)

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We report a case of a syringofibroadenoma on the foot of a 46-year-old woman who also had verrucous carcinoma in the same area. Our patient initially presented with a longstanding large, friable pigmented verrucoid lesion on the posterior aspect of the right calcaneus. Connected to it and extending onto the dorsolateral aspect of the foot was a flatter, nonfriable version of the same lesion that measured 7 × 3 cm. Neither one was painful or infected. The verrucoid lesion was excised and proved to be verrucous carcinoma on microscopic examination. The lesion on the dorsolateral foot was excised 6 months later and showed a broad epidermal proliferation with anastomosing strands of epithelial cells and ductal differentiation in a fibrovascular stroma, consistent with eccrine syringofibroadenoma. No features of verrucous carcinoma were noted. To the best of our knowledge, the concurrence of a syringofibroadenoma and verrucous carcinoma has not been previously reported. Whether it is the so-called collision tumor or if the syringofibroadenoma developed as a reactive response to verrucous carcinoma is debatable. The biological behavior and pathophysiology of these lesions warrant further evaluation of similar cases.

**Merkel Cell Carcinoma With an Unusual Immunoprofile**

(Poster No. 90)

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Merkel cell carcinoma is a rare cutaneous neuroendocrine carcinoma with a highly malignant nature that mainly affects elderly white individuals. Immunohistochemical profiling plays an important role in making an accurate diagnosis in addition to the histopathologic features. Besides neuroendocrine markers, most Merkel cell carcinomas show a characteristic perinuclear dotlike expression pattern with CK20 immunostaining. Here we report the case of a 96-year-old woman presenting with a painless plaque, red to violaceous in color, located on the arm, that demonstrated an unusual immunohistochemical profile. The tumor exhibited a trabecular and lobular growth pattern and was composed of highly cellular and mitotically undifferentiated small round blue cells with numerous apoptotic bodies. The neoplastic cells were small to medium in size with scant rims of cytoplasm and hyperchromatic nuclei with a salt-and-pepper chromatin pattern or intranuclear inclusions. The neuroendocrine differentiation of tumor cells was evidenced by their diffuse immunoreactivity for synaptophysin, neuro-specific enolase, and weak reactivity for chromogranin. Tumor cells also showed perinuclear cytoplasmic staining for AE1/AE3 but no immunoreactivity was detected for CK7, CK20, thyroid transcription factor-1, p63, and S100 antigens. The clinical history, histologic features, and immunohistochemical profile were consistent with the diagnosis of CK7/CK20-negative Merkel cell carcinoma. Our data, together with previous reports of rare CK20-negative Merkel cell carcinomas, emphasize that caution should be taken in excluding the diagnosis of Merkel cell carcinomas on the basis of the absence of reactivity of tumor cells for CK20.

**Papillary Thyroid Carcinoma With a Prominent Adenoid Cystic Carcinoma-Like Growth Pattern**

(Poster No. 91)

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The variants of papillary thyroid carcinoma (PTC) are classified by the predominant histopathologic pattern. Morphologic changes outside the realm of currently recognized variants can occur. PTC with adenoid cystic carcinoma-like growth has been described, most likely representing morphologic change in follicular-derived carcinoma rather than a specific variant. Our patient is a 30-year-old woman who presented to our institution with a 3-month history of an enlarging thyroid mass. Fine-needle aspiration yielded cellular smears showing crowded follicular groups with dense intraluminal hyaline-like material (Figure 215, A). The follicular groups were composed of radially arranged overlapping cells with elongated oval nuclei with pale chromatin, nuclear inclusions, and nuclear grooves (Figure, B). Serum calcitonin was negative. The patient then underwent a right hemithyroidectomy. The specimen revealed a 2.8-cm tan-white, rubbery, well-circumscribed mass. Microscopic examination demonstrated a prominent cribriform architecture with dense intraluminal and stromal hyaline material (Figure, C) without morules. This pattern was admixed with clear cell, follicular, and classical patterns of PTC (Figure, D). The neoplastic cells demonstrated nuclear features seen in the fine-needle aspiration. By immunohistochemistry the neoplastic cells expressed thyroglobulin and TTF1, and were negative for calcitonin, nuclear β-catenin, and CEA. The hyaline material was positive for PAS and focally...
for thyroglobulin. Subsequent completion thyroidectomy with lymph node dissection was negative for PTC. This case demonstrates cytormorphologic and histopathologic features similar to those described in previously reported cases and represents an infrequently encountered growth pattern in PTC about which pathologists should be aware.

Results of SMAD4 Immunohistochemistry in Well-Differentiated Neuroendocrine Tumors Reflects Relative Specificity of Chromosome 18 Losses for Jejunoileal Origin

(Poster No. 92)

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Context: Several groups, using various genomic approaches, have reported the relative specificity of chromosome 18 losses in jejunoileal neuroendocrine tumors (NETs). The tumor suppressor gene SMAD4 resides at 18q, and SMAD4 immunohistochemistry (IHC) is commercially available. Although the described losses are not limited to SMAD4, we hypothesized that loss of the second allele, resulting in complete absence of protein expression, would be selected for in some tumors.

Design: SMAD4 IHC was performed on tissue microarrays and whole sections of 267 NETs from the following sites: lung, stomach, duodenum, pancreas (primary and metastatic), jejunileum (primary and metastatic), appendix, and rectum. Tumor staining was scored as intact (any definite nuclear/cytoplasmic staining) or lost (completely absent staining). Fisher exact test was used to compare proportional data with P < .05 considered significant.

Results: Loss of SMAD4 expression was seen in 35% and 38% of jejunoileal primaries and metastases, respectively, while it was only seen in 5% of pancreatic primaries and no pancreatic metastases (P < .001 for jejunoileal versus pancreatic; P = .83 for jejunoileal primaries versus metastases). Rates of loss at other sites ranged from 0% to 15%, as detailed in the Table.

<table>
<thead>
<tr>
<th>SMAD4 Loss by Anatomic Site</th>
<th>Site</th>
<th>Loss, %</th>
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<tbody>
<tr>
<td></td>
<td>Lung (n = 20)</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Stomach (n = 16)</td>
<td>0</td>
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<tr>
<td></td>
<td>Duodenum (n = 19)</td>
<td>11</td>
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<tr>
<td></td>
<td>Pancreas primary (n = 57)</td>
<td>5</td>
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<tr>
<td></td>
<td>Pancreas metastatic (n = 14)</td>
<td>0</td>
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<tr>
<td></td>
<td>Jejunileum primary (n = 66)</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>Jejunileum metastatic (n = 39)</td>
<td>38</td>
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<tr>
<td></td>
<td>Appendix (n = 19)</td>
<td>11</td>
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<tr>
<td></td>
<td>Rectum (n = 17)</td>
<td>0</td>
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Conclusions: Loss of SMAD4 expression is frequent in jejunoileal NETs, with similar rates in primary tumors and metastases, which correlates with chromosome 18 losses observed by genomic approach.

Adrenal Cystic Lesions: A Clinicopathologic Analysis of 18 Cases With Review of the Literature

(Poster No. 93)

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Context: Adrenal cysts are very uncommon lesions. Currently, cystic lesions of adrenal gland are more often discovered incidentally by radiologic studies or surgery for other reasons. The better understanding of cystic adrenal masses is necessary to recognize true adrenal cysts and differentiating them from neoplastic lesions by demonstrating foci of cystic changes.

Design: We studied macroscopic, immunohistologic findings, and radiology records of 18 patients with adrenal cysts from 2000 to 2013.

Results: We identified 18 patients; 10 pseudocysts, 4 epithelial cysts, and 4 endothelial cysts. Female to male ratio was 2:1. Adrenal glands weight ranged from 4.5 to 5300 g. Cyst size ranged from 1.2 to 31 cm. Six cases were symptomatic (4 of 4 endothelial cysts, 2 of 10 pseudocysts) and 12 were diagnosed incidentally (4 of 4 epithelial cysts, 8 of 10 pseudocysts). None of them were associated with tumor except 2 cases, which were associated with myelolipoma and PEComa. Two of 4 endothelial cysts were confirmed to be lymphangiomatous by D2-40, 1 hemangioma by CD34, and 1 PEComa by HMB-45, Melan-A, and SMA. All epithelial cysts were positive for CK8/18. Two of 4 cases were CK7 and CK19 positive and negative for calretinin and WT1, suggestive of intra-adrenal bile ductules associated with adrenohepatic fusion. Two were positive for calretinin and WT1, suggestive of mesothelial origin.

Conclusions: Adrenal cysts were pseudocysts, epithelial cysts, or endothelial cysts. None of them were malignant. Endothelial cysts were asymptomatic, while epithelial cysts were asymptomatic. Two of 4 epithelial cysts may have been derived from adrenohepatic fusion. It is important to correlate clinical, radiologic, and histologic features for appropriate management of cystic adrenal lesions.

Pure Leydig Cell Tumor With Broad Spectrum Isosexual Pseudoprecocious Puberty and Spermatogenesis

(Poster No. 94)

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Pediatric Leydig cell tumors are rare sex cord/stromal gonadal tumors that represent approximately 4% of prepubertal testicular tumors. Unlike in adults, most Leydig cell tumors in children present with pseudoprecocious puberty with varying degrees of sexual and physical development. Previous reports have documented sperm maturation up to the level of primary spermatocyte, and in some cases, limited to the seminiferous tubules adjacent to the tumor. We report the case of a 5-year-old boy who presented with broad spectrum isosexual pseudo-precocious puberty including mature spermatozoa in the lumen of the vas deferens. His earliest symptoms were noted 1 year before presentation as adultlike sweat and body odor. Six months later, he developed other features of male puberty. His serum gonadotropins were within normal prepubertal levels. A 1.0-cm red-brown solid tumor was excised by radical orchidectomy. Microscopy showed typical Leydig cells in a poorly circumscribed nodule that closely abuts the tunica albuginea. The remaining seminiferous tubules showed progressive sperm maturation and there were free-floating spermatozoa in the lumen of the vas deferens. Immunostains showed strong and diffuse positivity for α-inhibin and calretinin in the tumor cells. This degree of sperm maturation in childhood cell tumors has not been previously reported in the literature and considering the small size of the tumor and relatively short duration of symptoms, it dissociates any positive correlation between size and functionality (Figure 216).
Use of Intraoperative Frozen Section and Fine-Needle Aspiration Biopsy for Thyroid Nodules

(Poster No. 95)

David Edwards, MD (birminghamdavey@gmail.com); Kim Parker, MD. Department of Pathology, Baptist Health System, Birmingham, Alabama.

Context: Thyroid nodules are a common disorder within the general population and can pose a diagnostic dilemma for the clinician, as only a small percentage of these nodules turn out to be malignant. Fine-needle aspiration biopsy (FNA) is used to identify those nodules that require surgical excision. Intraoperative frozen section (FS) is used to identify those nodules that are malignant and prevent a second operation for completion thyroidectomy. The recommendations for when to use FS vary widely and these are often based on FNA results. This retrospective review examines our experience with FS and FNA of thyroid nodules in a community-based hospital.

Design: Our review included 241 thyroidectomy cases from 2009–2013 where FS was obtained. If preoperative FNA was available, the results were recorded. Sensitivity and specificity were calculated for FS and FNA.

Results: Twenty percent of cases had a malignant diagnosis with most of these being papillary carcinomas (78%). The sensitivity for FS was 55% and the specificity was 99%. Eighty-five percent of cases had no preoperative FNA. Of those that did have an FNA, 30% were unsatisfactory. Sensitivity for FNA was 75% and specificity was 83%.

Conclusions: The sensitivity and specificity for FS fall within the range generally reported. However, it is suboptimal for detecting follicular carcinomas and microcarcinomas. Based on the FNA results, at our institution, the focus should be on emphasizing wider use of FNA and improving technique rather than implementing an algorithm for when to use FS, based on FNA results.

Thyroid Angiosarcoma in an African American Woman

(Poster No. 96)

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Angiosarcoma of the thyroid is a rare tumor reported most commonly in European Alpine regions. To our knowledge, fewer than 50 cases have been reported to date, with 3 documented cases from the United States. We report a case of thyroid angiosarcoma in an 89-year-old African American woman with longstanding multinodular goiter. The previously asymptomatic patient presented with recent rapid enlargement of her thyroid mass and left-sided neck pain. Computed tomography showed a large multinodular goiter with significant rightward tracheal displacement and esophageal compression. Fine-needle aspiration revealed markedly atypical epithelioid and spindle cells. The patient underwent subtotal thyroidectomy with left lateral neck dissection. Gross examination revealed an encapsulated, 11.0×8.4×8.2-cm tan-orange, predominantly hemorrhagic, necrotic nodule without grossly identifiable thyroid parenchyma. Initial histologic sections showed organizing thrombus with a rim of markedly atypical cells, worrisome for malignancy. A benign reactive process, secondary to previous fine-needle aspiration, was considered. Further sampling revealed nests of pleomorphic epithelioid cells with enlarged, hyperchromatic nuclei and irregular nuclear membranes forming atypical vascular spaces with increased mitoses. Tumor cells showed strong membrane reactivity for CD31, confirming the vascular nature of the lesion. Surrounding thyroid parenchyma showed multinodular goiter and lymphocytic thyroiditis. To our knowledge, this is the first reported case of thyroid angiosarcoma in an African American patient in the United States. This case emphasizes the potential diagnostic pitfalls that may be encountered in postaspiration lesions of the thyroid, and the importance of extensive sampling in such lesions (Figure 217).

An Unusual Presentation of Follicular Carcinoma of Thyroid Gland Metastatic to Thoracic Vertebrae

(Poster No. 97)

Muhammad S. Khurram, MD (Muhammad.Khurram@stjohn.org); Ahmad Ibrahim, MD; Robert Danforth, MD. Department of Pathology, St. John Hospital and Medical Center, Detroit, Michigan.

Follicular thyroid carcinomas usually have an indolent clinical course, with an excellent long-term prognosis. They have a propensity for vascular invasion. The most common site of metastases is lung. Only a few reports are available of fine-needle aspiration (FNA) biopsy findings from metastatic lesions of follicular thyroid carcinoma. We report an unusual presentation of follicular thyroid carcinoma metastasizing to thoracic vertebra. A 53-year-old woman presented with chronic back pain and shortness of breath. MRI showed pathologic compression fracture of T3. The patient had a previous biopsy of a left thyroid nodule that showed areas of atrophy and fibrosis, alternating with areas of hyperplasia. A CT-guided FNA of the destructive bony lesion involving the body of T3 vertebra was performed. The cytologic smears showed cohesive clusters of atypical round cells with nuclear overlapping. The cell block showed follicles with colloid. Property controlled immunohistochemical stains were used. The neoplastic cells were immunoreactive with thyroglobulin and TTF-1, confirming the diagnosis of metastatic carcinoma from thyroid gland. FNA is frequently indicated for evaluation of bone metastasis, as in this case, where distinct cytologic features can aid in identification of an unknown primary.

Evidence for the Cancer Progression Model in Proteus Syndrome: AKT1 and BRAF Somatic Mutations in Papillary Thyroid Carcinoma

(Poster No. 98)

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Proteus syndrome is a rare condition characterized by progressive, segmental overgrowth of connective tissues particularly affecting bone, skin, and blood vessels. It is caused by somatic mosaic mutation of the AKT1 gene. This gene encodes the AKT1 kinase, which regulates cell growth, apoptosis, and other processes. Activation of the AKT pathway also increases susceptibility to some tumors, for example, ovarian cystadenomas and monomorphic adenomas of parotid gland, both of which are part of the specific diagnostic criteria of Proteus syndrome. We present selected autopsy findings from a 21-year-old white woman with Proteus syndrome who was found to have multiple intracranial meningiomas, soft tissue vascular malformations, and a uterine leiomyoma. Additionally, the right thyroid lobe revealed papillary thyroid carcinoma, a tumor not previously described in this syndrome. Approximately 50% to 70% of papillary thyroid carcinomas demonstrate point mutations in BRAF, an oncogene associated with the RAS/MAPK signaling pathway, a finding that may have prognostic and therapeutic implications. AKT1 and BRAF mutation testing of the patient's normal and tumor thyroid was performed by sequencing or by mutation-specific restriction enzyme analysis. Two samples from papillary thyroid carcinoma demonstrated the p.Glu17Lys AKT1 mutation at levels of 30% and 8%, while uninvolved thyroid demonstrated no detectable AKT1 mutation. Additionally, the thyroid tumor samples had levels of the p.Val600Glu BRAF mutation that correlated with the AKT1 mutation levels, with uninvolved gland testing negative for BRAF. We suggest that the AKT1 and BRAF mutations synergized to support the malignant transformation of the thyroid.

**Black Thyroid Gland and Concurrent Thyroid Neoplasms: Coincidental or Significant?**

(Poster No. 99)

Eleanor R. Lewin, MD (elewin@tulane.edu); Philip J. Daroca, MD; Byron E. Crawford, MD. Department of Pathology, Tulane University School of Medicine, New Orleans, Louisiana.

**Context:** Black thyroid is an unusual but well-described finding in patients with a history of minocycline use; the medication reacts with black pigment not reported in the original diagnosis. We hypothesize that black thyroid as it relates to cancer risk will be discussed.

**Results:** We examined all thyroidectomies from 2007–2013 at our institution that had a diagnosis of “black thyroid” (n = 65). We plan to retrospectively examine thyroidectomy specimens with benign, non-neoplastic diagnoses from the past year and determine the proportion of these thyroids that contained black pigment not reported in the original diagnosis. We will compare benign to malignant thyroid specimens and determine whether there is a statistically significant original diagnosis. We will compare benign to malignant thyroid specimens and determine whether there is a statistically significant difference in the incidence of black thyroid between these groups.

**Design:** We examined all thyroidectomies from 2007–2013 at our institution that had a diagnosis of “black thyroid” (n = 65). We plan to retrospectively examine thyroidectomy specimens with benign, non-neoplastic diagnoses from the past year and determine the proportion of these thyroids that contained black pigment not reported in the original diagnosis. We will compare benign to malignant thyroid specimens and determine whether there is a statistically significant difference in the incidence of black thyroid between these groups.

**Conclusions:** The data analysis results and clinical significance, if any, of black thyroid as it relates to cancer risk will be discussed.

**Adrenocortical Carcinoma Arising in an Adrenal Rest**

(Poster No. 100)

Kristine M. Cornejo, MD (kcornejo@partners.org); Peter M. Sadow, MD, PhD. Department of Pathology, Massachusetts General Hospital, Boston.

Adrenocortical carcinomas arising from embryonic adrenal rests are rare, with only a handful of reported cases (12). We report a case of an adrenocortical carcinoma arising from an adrenal rest located between the bladder and prostate in a 51-year-old man. The patient presented after a year of rectal pain and constipation. Computed tomography scan revealed a 9-cm pelvic mass that appeared to arise within the soft tissue, displacing the prostate and bladder with narrowing of the rectal lumen, and suspected to be a sarcoma. The surgically resected specimen showed a well-circumscribed, partially encapsulated tumor measuring 10 cm in greatest dimension. Adrenocortical carcinoma histology revealed sheets and nests of high-grade pleomorphic tumor cells with abundant clear to vacuolated cytoplasm with areas of necrosis, a high mitotic index (>10 mitoses per 10 high-power fields), and foci suggestive of lymphovascular invasion. Adjacent adrenal cortical-type tissue was identified. Immunohistochemical stains revealed the tumor cells were weakly and focally positive for MITF, Melan-A, inhibin, and synaptophysin, and negative for CKA1E/AE3, HMB-45, calretinin, EMÃ, SMA, chromogranin, PAX8, MDM2, and CDK4. From the morphologic and immunohistochemical profile, we diagnosed this tumor as an adreno-cortical carcinoma arising in an adrenal rest. Both adrenal glands were identified and grossly unremarkable. To our knowledge, no such tumor has been previously described in this location.

**Paraneoplastic Diabetes in Intravascular Lymphoma**

(Poster No. 101)

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Paraneoplastic diabetes has rarely been reported in fibrosarcoma, mesothelioma, insulina, liver carcinoma, adrenal carcinoma, paracriatic carcinoma, renal cell carcinoma, and lung small cell carcinoma. A heretofore not previously described case of uncontrolled diabetes associated with equally rare intravascular lymphoma (IVL) is reported. A 71-year-old man with moderate dementia, uncontrolled type-2 insulin-dependent diabetes mellitus of recent onset, nephropathy, peripheral neuropathy, and a year earlier left nephrectomy for stage I pelvic urothelial cell renal carcinoma, was in his usual state of health up until 2 weeks before admission. Pertinent laboratory data were BUN 74, creatinine 2.28, estimated GFR 30, nonfasting glucose 170, and metabolic acidosis. His hospitalization went downhill for 4 days, and he ultimately died of 12-litrogen failure. The gross postmortem findings were nondiagnostic, but the microscopic results proved a multiorgan failure secondary to B-cell IVL. IVL is a malignant proliferation of lymphoid cells within vascular lumens with little or no parenchymal lesion. It affects fewer than 1 individual per 1 000 000 with some 300 cases reported to date. A B-cell immunotype is most common. The IVL cells lack CD18, resulting in defective adhesion to the endothelium, an inability to extravasate, and intravascular confinement. One notable aspect in the index IVL patient is the absent microscopic diabetes-related small artery disease and glomerulopathy. A paraneoplastic diabetes due to overproduction of CD44 antigen in IVL, which is a glycoprotein, is perhaps the basis for the uncontrolled hyperglycemia, excessive glucose byproducts, and metabolic acidosis on blood chemistry analysis.

**Systemic Quality Control for Scoring Lung Cancer Biomarkers**

(Poster No. 102)

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**Context:** Quality control is an important aspect of biomarker immunohistochemistry evaluation. However, few guidelines suggest best practice in the clinical or research settings. Here, we analyzed quality control data for lung cancer biomarker immunohistochemistry scoring in the Hirsch Biomarker Analysis Laboratory, University of Colorado.

**Design:** Protein expression was assessed in lung cancer specimens (N = 653 specimens) for each of 19 biomarker phospho- and biomarkers by using the H-score, a calculation of the percentage of cells labeled at different intensities. After the original scoring, 10% of cases for each project were independently reevaluated in a blinded fashion by the original scoring pathologist and an external pathologist. Original and new scores were compared and a consensus result was determined for discrepant cases.

**Results:** The immunostain intraclass correlation coefficients were 0.73 for all interobserver results, 0.73 for all intraobserver results, except for E-cadherin (0.57, Table). Analysis of the E-cadherin raw data revealed consistently lower H-scores for E-cadherin by 1 pathologist (mean = 207.5) compared with 2 other pathologists (means = 277.1 and 278.1). A consensus guide illustrating different intensities of E-cadherin staining was created to improve E-cadherin scoring.
Quality Communication in Surgical Pathology: The Importance of Effective Pathologist-Surgeon Communication During Intraoperative Consultation

(Marilyn A. Baird-Howell, MD1 (mbairdhowell@mfa.gwu.edu); Negin Shafizadeh, MD2; Samantha E. Easley, MD3.1 Department of Pathology, The George Washington University, Washington, DC; 2Department of Pathology, The George Washington University Hospital, Washington, DC.)

Context: Miscommunication accounts for approximately 80% of diagnostic and treatment errors. At our institution, face-to-face communication between surgeons and pathologists ensures positive patient outcomes.

Design: Pathology intraoperative consultation (IOC) forms and corresponding operative reports were reviewed for encounters between February 2012 and July 2012. Breast cancer cases were excluded. Data points recorded were presence or absence of IOC diagnoses in the operative report, diagnoses rendered by reviewing pathologist(s), diagnoses documented by surgeon(s), operating surgeon(s) subspecialty, and specimen type. The number and type of discrepancies (minor or major) between pathology and operative records were recorded. Discrepancies were classified as (1) intercategorical/major (benign to malignant, vice versa); (2) intracategorical/minor (change in tumor type).

Results: We reviewed 319 IOCs from 175 encounters. IOCs were most commonly requested for pulmonary (33%), thorinolaryngology (28.1%), and genitourinary (11.9%) procedures. Six of 319 IOCs (1.9%) were discrepant (0 major and 6 minor), occurring in otinolaryngology, pulmonary, and neurosurgical cases. Two of 6 discrepancies occurred during the same encounter. In one instance, the surgeon dictated the IOC diagnosis as “consistent with melanoma,” while the pathology IOC diagnosis was “malignant neoplasm, unlikely lymphoma.” In the remaining discrepant cases, the pathology IOC was dictated as “granulomatous inflammation” and interpreted by the operating surgeon(s) as “consistent with sarcoidosis.”

Conclusions: Our finding of a negligible discrepancy rate confirms that face-to-face communication during IOCs limits errors in transmission of diagnoses and ensures medical record accuracy. Review of IOC findings and final pathologic diagnoses dictated in operative reports is invaluable to an institution’s quality assurance program.

Use of Immunohistochemistry Study in Workup of Gastritis

(Larry Zhao, MD (larry.zhao@umassmemorial.org); Xiaofei Wang, MD, PhD; Otto Walter, MD. Department of Pathology, University of Massachusetts Medical School, Worcester.)

Context: The Gastrointestinal Pathology Society suggests the use of ancillary stains is on an as-needed basis for gastric biopsies submitted for identifying Helicobacter pylori, and “up-front” staining of all biopsy specimens is unnecessary. Currently, “up-front” Warthin-Starry (WS) stain is used in our laboratory. In this study, we explored the adaptability of the new recommendations in our laboratory.

Design: A total of 590 gastric biopsy specimens from 2011–2013 from our archives were retrieved and analyzed. Twenty cases (10 positive and 10 negative for H pylori) were selected from this group and given to 10 pathologists to evaluate blindly.

Results: Of the 590 total cases, 73 were identified H pylori on WS stains. The positive rates for 3 years were relatively low in our patient population (11.6%-12.8%). Of the 20 cases, in the 100 H pylori–positive calls (10 observers, 10 cases), 63 calls were made on H&E slides and 26 with IHC study. In the 100 negative calls, 68 calls were made on H&E and 31 with IHC study. Together, diagnosis was made correctly on 131 calls by just reviewing H&E slides. IHC study was needed on approximately only one-third (29%) of cases.

Conclusions: Most H pylori cases can be identified from just reviewing H&E slides in our laboratory. Approximately one-third of cases will need IHC study to help identify H pylori. The cost of IHC stain can be avoided in 70% of cases if it is done on an as-needed basis.
Conclusions: Specimen delay for processing in the urinalysis laboratory is critical for reporting urine microscopy results. Here we found that most of the delays (~50%) were due to preanalytic issues. The primary reason seemed to be transportation delay from the wards. Based on this analysis, measures will be taken to educate the transport personnel in the necessity for rapid delivery of these specimens.

Accuracy of Intraoperative Assessment of Depth of Myometrial Invasion in Endometrial Carcinoma

(Poster No. 107)

Toni Peters, MD (tpeters1@bidmc.harvard.edu); Mamta Gupta, MD, Department of Pathology, Beth Israel Deaconess Medical Center, Boston, Massachusetts.

Context: Myometrial invasion of 50% in endometrioid endometrial carcinomas (EMCs) is an indication for pelvic lymphadenectomy. Existing literature suggests a wide range of accuracy of intraoperative assessment in this setting. We evaluated the overall accuracy of this procedure at our institution and determined causes for discrepancy between intraoperative and final diagnosis.

Design: Pathology reports and H&E slides for all hysterectomies for EMCAs between 2003 and 2012 were reviewed to retrieve discrepant cases. Major discrepancy was defined as overestimation or underestimation of 50% myometrial invasion. Minor discrepancy was noted when an invasive carcinoma (within the critical threshold of <50% invasion) was diagnosed as noninvasive or vice versa.

Results: Intraoperative consultation was requested in 278 of 356 endometrioid EMCAs (78%). Depth of myometrial invasion was assessed by gross examination in 200 (72%) and by frozen section in 78 (28%) cases. Forty-seven of 200 cases (23%) evaluated by gross examination in 200 (72%) and by frozen section in 78 (28%) cases. Forty-seven of 200 cases (23%) evaluated by gross examination alone had discrepant results (14 [7%] major; 33 [16%] minor). Seven of 78 cases (9%) evaluated by frozen section had discrepant results (5 [6.5%] major; 2 [2.5%] minor). The sensitivity, specificity, PPV, and NPV of predicting >50% myometrial invasion were 76%, 95%, 70%, and 96% by gross examination alone, and 75%, 98%, 92%, and 94% by frozen section analysis, respectively.

Conclusions: Clinical significant discrepancies occur in approximately 7% of intraoperative consultations for depth of myometrial invasion in EMCAs. The specificity and PPV of frozen sections are superior to those of gross examination alone, and discordant frozen section results usually occur owing to sampling errors.

Focused and Ongoing Professional Practice Evaluations in Anatomic Pathology

(Poster No. 108)

Emily H. Glynn, MD (eglynn@uw.edu); Jonathan Henriksen, BA; Sher Ling Gan, JD; Sheila Mehr, MPH, HT(ASCP); Stephen Schmechel, MD, PhD; Suzanne Dintzis, MD, PhD, Department of Anatomic Pathology, University of Washington, Seattle.

Context: In 2008, the Joint Commission (TJC) introduced focused and ongoing professional practice evaluation (FPPE, OPPE) to objectively evaluate physician competence. Currently, there is limited guidance on implementing FPPE/OPPE within anatomic pathology. We aim to assess FPPE/OPPE in 4 institutions, develop an FPPE/OPPE policy by reconciling TJC requirements with existing pathology accreditation standards, and create an efficient OPPE data collection system.

Design: FPPE/OPPE policies of 4 affiliated institutions were compared. TJC standards were aligned with Washington State Department of Health medical test site standards and 2012 College of American Pathologists accreditation checklists. Based on these comparisons, an OPPE data collection system was created by using Access (Microsoft, Redmond, Washington).

Results: Significant variability in FPPE/OPPE policies existed across institutions and no institution’s policies were completely compliant with TJC requirements. Using the method described above, we created an FPPE/OPPE policy to assess pathologist competency. This incorporates 17 quality indicators organized into 4 categories: diagnostic accuracy, communication, turnaround time, and compliance. The data collected from these indicators are quantitative, unbiased, and easily standardized. In compliance with TJC, evaluation interval, thresholds for triggering FPPE, details and duration of FPPE, and core competencies defined were collected and retrieved from OPPE data, a database with entry forms designed for straightforward user interface was created by using Access.

Conclusions: These findings indicate that performance evaluation measures required for accreditation are variable in anatomic pathology departments affiliated with the same academic medical center. Future directions include adaptation of the data collection system developed here for efficient compliance with TJC requirements across institutions.

Implementing a Bar Code System for Labeling Surgical Pathology Blocks: Will It Decrease the Rate of Error?

(Poster No. 109)

Miglena Komforti, DO (miglena.dzahunovana@duke.edu); Alyssa Kraynie, MD; Endi Wang, MD, Department of Pathology, Duke University, Durham, North Carolina.

Context: Any surgical pathology laboratory is a complex system, where numerous opportunities for specimen mislabeling are created. In 2010, an article published by the College of American Pathologists stated that most errors occurred in the preanalytic phase. The aim of this study is to identify the most likely source of error, and to evaluate the outcome of implementing a bar code system.

Design: The steps of surgical specimen processing were outlined, and block labeling was identified as a major source of error. In July 2013, the surgical pathology laboratory of Duke University implemented a bar code system by which accession numbers are printed directly on the block rather than entered manually. The number of mislabeled blocks in the surgical pathology laboratory, but human error can still occur until complete automation and appropriate policies are put in place.

Conclusions: A bar code labeling system could decrease the incidence of mislabeled blocks in the surgical pathology laboratory, but human error can still occur until complete automation and appropriate policies are put in place.

<table>
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<th>Mislabeled Blocks During 6 Months After Bar Code Implementation</th>
<th>Month, Year</th>
<th>Mislabeled Blocks, Absolute No.</th>
<th>Mislabeled Blocks, %</th>
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</table>
**Immunohistochemical Approaches to Poorly Differentiated Tumors of Unknown Origins**

(Poster No. 110)

Anita Malek, MD (anita.malek@bmc.org); Qing Zhao, MD, PhD. Department of Pathology, Boston Medical Center, Boston, Massachusetts.

**Context:** Immunoperoxidase histochemical stain has been widely used as a tool in pathologic diagnosis since 1941. These stains become essential in poorly differentiated tumors or tumors of unknown origin. Few markers are organ specific. A combination of the markers is necessary in these cases to render diagnosis. This study attempts to summarize how immunohistochemical studies had been performed in such cases at 1 academic hospital from a quality control point of view. We propose a possible economic stepwise approach.

**Design:** We retrospectively reviewed 30 surgical specimens with diagnoses of poorly differentiated tumors or tumors with unknown primary (15 carcinomas and 15 sarcomas). All immunohistochemical stains (5 or more for each case) were reviewed and categorized into “necessary,” “unnecessary,” and “missing” by tumor morphology and corresponding clinical information.

**Results:** Our result shows that the average number of immunohistochemical stains used for carcinoma cases is 8, while for sarcomas it is 9. The average number of necessary markers would be 5 for carcinomas and 7 for sarcomas if we had applied the markers stepwise. The stepwise approach would help to cut down the cost for the hospital and insurance up to 29%.

**Conclusions:** (1) Immunohistochemical stains are essential in poorly differentiated tumors especially in tumors with unknown primary; (2) A stepwise immunohistochemistry panel approach would eliminate unnecessary markers and avoid missing essential ones; (3) A stepwise approach is financially wise given current health care reforms.

**Bone Marrow Biopsies Performed by Both the Powered OnControl Drill Device and the Jamshidi Needle Produce Adequate Specimens**

(Poster No. 111)

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**Context:** Adequate bone marrow (BM) biopsy and aspirate specimens are necessary to establish diagnosis in hematopoietic disorders. Traditionally, BM specimens were obtained by Jamshidi needle (or equivalents). Recently, a new Powered OnControl system was introduced. Studies comparing the 2 devices have shown conflicting results in terms of quality of specimen obtained. The aim of our study was to evaluate the adequacy and quality of the BM specimens, including biopsies and aspirates, obtained by the “Powered needle” and compare it with the manual Jamshidi needle procedure.

**Design:** Forty-four cases of BM biopsies and aspirates performed by Jamshidi needle and 31 with Powered needle device were analyzed retrospectively. All the BMs were reviewed by 2 pathologists (S.J., M.D.), who were blinded to the device used. Gross length of biopsy specimen before fixation, biopsy length after fixation, evaluable marrow length and total area, and fragmentation, aspiration, and marrow dropout artifacts were compared.

**Results:** See Table. The biopsies in the Powered needle group were performed by trained physician assistants (PAs). In the manual group, PAs performed 39 of 44 biopsies, while clinical fellows (trainees) performed 5 of 44 biopsies. There was no difference in the average evaluable marrow length (P = .36), average area of evaluable marrow (P = .62), and marrow dropout (P = .60). Aspiration artifact was minimal (<10%) in 31 of 44 in the manual group, and seen in only 6 of 31 in the Powered needle group (P < .001).

**Conclusions:** There is no significant difference in the biopsy size and quality of the BM obtained by the Powered needle device or manual device. Our study demonstrates that if trained personnel perform the procedure, both techniques provide adequate specimen of good quality.

**IgA Paraproteinemia in Multiple Myeloma Patient Can Interfere With Determination of Plasma Inorganic Phosphate When Using Beckman Coulter Analyzer**

(Poster No. 112)

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There are reports in the literature describing interference with phosphate concentration in serum samples of multiple myeloma patients with high paraprotein levels. Apparently, IgG and IgM paraproteins are the main source for interference; however, IgA paraproteins have been reported only rarely as a potential cause. We report the case of a 74-year-old man with a 10-year history of multiple myeloma and IgA paraproteinemia (Figure 219, A and B) who presented with new onset dizziness and frequent falls. His total protein level was 10.8 g/dL with IgA at 5.6 g/dL. Chemistry panel on Beckman Coulter DXC 800 analyzer revealed hypercalcemia, hypokalemia, and undetectable phosphate. Owing to possible IgA level interference with phosphate concentration, the sample was sent out and analyzed on the Vitros 5600 analyzer and the levels were also repeated after removal of IgA from patient’s serum sample by deproteinizing it with trichloroacetic acid (Figure, C). A basic metabolic panel was also performed along with the repeated analysis. The deproteinized serum sample was reanalyzed by using the same Beckman Coulter DXC 800 analyzer. The original serum sample was remeasured on the Vitros 5600 analyzer to compare the results. This analyzer uses dry chemistry, which is assumed to have minimal interference with paraproteins. The phosphate levels of IgA on the Beckman Coulter analyzer after deproteinization were comparable to those of the Vitros 5600 analyzer. Furthermore, the deproteinization did not interfere with the concentration of the remaining electrolytes. A study further investigating the cutoff point at which paraprotein level of concentration will cause interference with phosphate and other chemistry panel measurements is underway.

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**Comparison Results**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Jamshidi Needle</th>
<th>OnControl Drill</th>
</tr>
</thead>
<tbody>
<tr>
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<td>0.99 (0.1–2.2)</td>
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Evaluation of Biological Variation of Alkaline Phosphatase and γ-Glutamyltransferase From Serial Patient Measurements Supports ALP Only as a Primary Care Screening Test  
(Poster No. 113)  
Mireille M. Kattar, MD1 (Mireille.Kattar@albertahealthservices.ca); Adam R. Cembrowski, PhD2; Wendy Skoropadyk, MLT3; Andrea Kunst, MLT4; George S. Cembrowski, MD, PhD5. 1Department of Laboratory Medicine and Pathology, University of Alberta Hospital and Alberta Health Services, Edmonton, Alberta, Canada; 2Department of Laboratory Medicine and Pathology, University of Alberta Hospital and Alberta Health Services, Edmonton, Alberta, Canada; 3Department of Laboratory Medicine and Pathology, University of Alberta Hospital and Alberta Health Services, Edmonton, Alberta, Canada; 4Department of Laboratory Medicine and Pathology, University of Alberta Hospital and Alberta Health Services, Edmonton, Alberta, Canada; 5Department of Laboratory Medicine and Pathology, University of Alberta Hospital. Patient results that exceeded the upper 95th percentile limits (ALP > 110 U/L; GGT > 90 U/L) were excluded. A total of 3975 intrapatient pairs of ALP and 4474 pairs of GGT ordered between 0.5 days and 3.5 days and separated into 12-hour intervals (0–12, 12–24, etc) were analyzed. The standard deviations of differences (SDDs) of the paired results were calculated for each time interval (ALP range, 215–1652 pairs; GGT range, 323–1694 pairs). The graphs of SDDs versus time interval were linear. The y intercept, y0, provided by linear regression, represents the sum of s0 and short-term analytic variation (s0): y0 = s0 + s12. s0 was obtained from quality control data. Results: y0 and s0 for ALP and GGT were 7.6 and 7.4, respectively; and 5.15 and 4.8, respectively, corresponding to a biological variation of 9.9% and 14.4%. Conclusions: ALP’s lower biological variation supports ALP without GGT as a screening test for liver disease.

Do We Need a Free Testosterone Test With Every Total Testosterone Test?  
(Poster No. 114)  
Guo Zhu, MD1 (gzhu1@uthsc.edu); Judy Layden, MT2; Darlene Moore, MT3; Eugene S. Pearlman, MD. 1Department of Pathology, University of Tennessee Health Sciences Center, Memphis; 2Department of Pathology, Veterans Affairs Medical Center (VAMC), Memphis, Tennessee.  
Context: At the VAMC endocrinologists order a free testosterone test (FTest) at a reference laboratory (RL) with every total testosterone test (TTTest) done in-house. We wished to develop reflex criteria for FTTest. With an average request volume of 225 per month, the savings from an algorithmic approach could be significant. Design: Data on TTest and associated FTTest assays for the period April 15, 2012, to April 14, 2013, inclusively, were reviewed. TTest assays were done on the Vitros-5600 analyzer (OCID, Raritan, New Jersey) according to manufacturer’s directions. The manufacturer’s suggested reference interval (RI) (200–800 ng/mL) was adjusted to 210–793 ng/mL for our population by using a curve dissection method and Peakfit software (Systat, Santa Clara, California). FTTest was determined at an RL (Lab Corp, Raleigh, North Carolina). FTTest RIs were age dependent but FTTest < 6.3 pg/mL was below the lower limit of all RIs. Statistical analysis used nonlinear regression (Table Curve2D; Systat) and Student t test. Results: When FTTest (y) was plotted against TTest (x), a best-fit relationship was obtained with the following equation: FTTest = 1.28 + 0.16 [TTest/ln (TTest)] (n = 2638; r = 0.71 (P < .001)). Of 1745 values of FTTest 6.3 pg/mL, only 13 (0.75%) were associated with TTest concentrations ≤ 100 ng/mL; while of 893 FTTest values < 6.3 pg/mL, only 9 (1%) were associated with TTest values ≥ 600 ng/mL. Conclusions: Restricting FTTest assays to specimens with TTest assay results of 100 to 600 ng/mL would result in avoiding 459 send-out tests (18.2%) with an annual savings of $16 000 with a minimal decrease in sensitivity for the detection of hypogonadism.

The Success of Vitamin D Awareness in Geriatric Patients: A Step Closer but Not There Yet  
(Poster No. 115)  
Rita H. Khoury, MD (rkhoury@aculabs.com); B. P. Salmon, MS; Asha Gandhi, BS; Peter Gudaitis, BA; Dauna Gudaitis, BA. Aculabs, Inc. East Brunswick, New Jersey.  
Context: Vitamin D is known for its role in bone metabolism, cancer, autoimmune disorders, and many other conditions. The American Geriatrics Society released a new consensus statement to help physicians ensure that their geriatric patients are getting enough vitamin D to prevent the risk of falls and their related injuries.

Bio-Rad in2it Hemoglobin A1c Percentage Lot-Dependent Analytic Variation  
(Poster No. 116)  
Kavita R. Varma, MD (kvarma1@hfhs.org); Javier Arias-Stella III, MD; Frederick Meier, MD; Veronica Luzzi, PhD. Department of Pathology, Henry Ford Hospital, Detroit, Michigan.  
Context: In 2011, the American Diabetes Association included hemoglobin A1c% (A1c%) > 6.5% as diagnostic criteria for diabetes mellitus. To establish accuracy on a new lot of reagents, regulatory agencies require matrix-compatible material to be tested before using new lots of reagents on approved laboratory devices. Point-of-care (POC) devices are popular for diabetes risk assessment in outpatient settings; however, these devices may be waived from testing new lots using matrix-compatible material.

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(Poster No. 116)  
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Design: A total of 13 241 specimens collected from residents in long-term care facilities in 2013 were tested for vitamin D by using Roche Modular E. The patients were separated by severe deficiency, deficiency, insufficiency, and sufficient, and by age group. The results were compared to data obtained from 3612 specimens in 2009. Statistical analysis was performed with Analyse-it.

Results: In 2013, 29.3% of the patients had deficiency, 31.9% had insufficiency, and 38.8% had sufficient vitamin D levels. Severe deficiency is more common in people younger than 70 years. There was an increase of 21.3% and 16.5% in the sufficient level of vitamin D in the <50- and >60-year-old age groups, respectively, when compared to 2009; no improvement was found in the 51- to 80-year-old age group (Table). Conclusions: Most of the geriatric population has a vitamin D level below the normal level and almost one-third has insufficiency levels. The improvement in the vitamin D–sufficient population over the period tested maybe due to increased awareness of the importance of vitamin D in long-term care residents. More work is needed to improve vitamin D levels across all ages, and to achieve the goal set by the American Geriatric Society to reach the recommended level in more than 92% of older adults.

Bio-Rad in2it Hemoglobin A1c Percentage Lot-Dependent Analytic Variation  
(Poster No. 116)  
Kavita R. Varma, MD (kvarma1@hfhs.org); Javier Arias-Stella III, MD; Frederick Meier, MD; Veronica Luzzi, PhD. Department of Pathology, Henry Ford Hospital, Detroit, Michigan.  
Context: In 2011, the American Diabetes Association included hemoglobin A1c% (A1c%) > 6.5% as diagnostic criteria for diabetes mellitus. To establish accuracy on a new lot of reagents, regulatory agencies require matrix-compatible material to be tested before using new lots of reagents on approved laboratory devices. Point-of-care (POC) devices are popular for diabetes risk assessment in outpatient settings; however, these devices may be waived from testing new lots using matrix-compatible material.

Results: When repeated on a new lot of reagents, the linear regression showed very similar values of A1c% between the in2it and the Variant II HPLC methods in 2 independent comparisons (April 2012: y = 1.0042x – 0.5925; and December 2012: y = 1.0351x – 0.0753). However, in2it A1c% values obtained using lot No. 110 were 16% lower than Trinity Biotech HB 9210 assay values (y = 0.8389x – 0.22).
Conclusions: Users of POC devices are not required by current regulations to test matrix-compatible material every time a new lot of reagents is put into use. In this study, we demonstrated that failing to test new lot numbers in POC devices using matrix-compatible material may affect risk assessment or diagnosis of diabetes.

Evaluation of the BD Vacutainer Plus UA Preservative Tube for Urinalysis Testing of Outpatient Samples

(Poster No. 117)
Zhengtong Pei, MD (zhengtongpei@gmail.com); Selwyn J. Baptist, MD, Department of Pathology, St. Barnabas Medical Center, Livingston, New Jersey.

Context: Urine samples must be refrigerated or preserved if testing cannot be performed in 2 hours. The previous preserve tubes may cause false-positive results for bacteria and red blood cells. We evaluated the new BD UA Preservative Tube in samples up to 6 hours after collection. Our goals are (1) to identify the potential adverse impact of preservative particles; and (2) to evaluate the reliability of urinalysis results.

Design: Eighty-three urine samples from our outpatient department were randomly selected; aliquots of each sample in nonpreservative urine tube or new preservative tube were analyzed within 2 hours or up to 6 hours on the Bayer Clinitek Atlas automated urine dipstick chemistry analyzer coupled with the Sysmex UF 1000 automated urine particle analyzer. Eleven urine dipstick parameters (glucose, ketones, bilirubin, specific gravity, blood, pH, protein, urobilinogen, nitrite, leukocytes, and esterase) and 5 urine particle parameters (RBC, WBC, casts, epithelial cells, and bacteria) were compared.

Results: No significant differences were noted between results of urinalysis tests performed within 2 hours on specimens collected and transported in the current nonpreservative tube, and those collected and transported in the new preservative tube in 2 hours or up to 6 hours. No adverse impact of preservative particles on urinalysis results was noted and the preservative effectively preserved urine specimens for up to 6 hours.

Conclusions: The BD Vacutainer UA Preservative Tube has been improved to provide prolonged reliable preservation of urine specimens and reduce the major issue of false positives noted with tubes of the previous generation.

Hemoglobin A1c (HA1c): Does Methodology Make a Difference When Hemoglobin Variants Are Present?

(Poster No. 118)
Mary P. Gupta, MD1 (marypeyton@hotmail.com); Rachel Floyd, MT1; Chau Hoang, MT2; Eugene S. Pearlman, MD,2 1Department of Pathology, University of Tennessee Health Sciences Center, Memphis; 2Department of Pathology, Veterans Affairs Medical Center (VAMC), Memphis, Tennessee.

Context: At the VAMC it was standard protocol, when in-house HPLC (Tosoh, Grove City, Ohio) suggested a hemoglobin variant (HV), to send samples to a reference laboratory (RL; Lab Corp, Raleigh, North Carolina) for confirmatory study using immunoassay (IA). We wished to investigate the utility of this approach.

Design: HPLC and RL data were collected from 114 consecutive samples when HPLC suggested a HV. Two specimens were excluded given suspicion of a data entry or mislabeling error. Deming regression (DR) was used to compare the HPLC and IA results. Curve 3D software (Systat, San Jose, California) was used to measure levels of 25OHD in human blood (serum) samples by following manufacturer’s instructions and laboratory standards accepted by the College of American Pathologists.

Results: We performed 9226 tests in 2009 and 17 497 tests in 2012, showing a significant increase in both median and mean blood levels of 25OHD (median, 29.4–33.0 ng/mL; mean, 31.2–35.0 ng/mL; P < .001). Subjects with severe deficiency (25OHD levels < 10.0 ng/mL) declined significantly from 1.5% to 0.3% (P < .001). Subjects considered to have deficiency (25OHD levels < 20 ng/mL) declined from 17.6% to 9.9% (P < .001). Subjects with vitamin D levels < 30 ng/mL declined from 51.7% in 2009 to 39% in 2012 (P < .001).

Conclusions: Our analysis of 25OHD levels (2009–2012) shows a progressive, significant increase in vitamin D levels in our regional population, with greatest serum increase occurring in patients with deficiency. Statistically significant age- and sex-related variations with a consistent seasonal variation were also noted. We speculate that vitamin D supplementation reflects a social phenomenon in response to media publicity, professional acquaintance, and investigative endeavor despite published practice guidelines.

Estimation of Urine Osmolality From Urine Chemical Parameters: Can a Nonlinear Regression Equation Do Better?

(Poster No. 120)
Deepti Hoskoppal, MD1 (dhoskoppal@uthsc.edu); Victoria Anderson; MT1; Chau Hoang, MT; Eugene S. Pearlman, MD,2 1Department of Pathology, University of Tennessee Health Sciences Center, Memphis; 2Department of Pathology, Veterans Affairs Medical Center (VAMC), Memphis, Tennessee.

Context: While validating an osmometer (Advanced Instruments, Norwood, Massachusetts) recently acquired by the VAMC laboratory the question arose of the reliability of estimating urine osmolality from urine sodium, BUN, and creatinine and whether better estimation (higher correlation between estimated and measured osmolalities) could be achieved with nonlinear regression.

Design: Urine osmolality was measured by using our in-house osmometer, and urine chemistry variables were assayed on the Vitros-5600 analyzer (OCD, Rochester, New York) according to manufacturers’ instructions. Regression calculations were done by using TableCurve 3D software (Systat, San Jose, California). A multiplicative factor to convert osmolality to osmolality was estimated from the average concentration in 20 consecutive urine samples for which there was adequate specimen quantity to do requisitioned tests as well as osmolality and urine chemistries.

Results: The estimated osmolality to osmolality conversion factors were 1.0034, 1.00014, and 1.0024 L/kg solvent for BUN, creatinine, and sodium, respectively. The best-fit linear equation is given by the following: Z (est. Osmo) = 55 + 1.44 X + 1.24 Y [r2 = 0.951] where X = sodium and Y = [creatinine + BUN] osmolality. The best-fit nonlinear equation was obtained as follows: Z = 25.5 + 9.2 X/[LN. X] + 0.09 Y [r2 = 0.956]. Although the value of r2 is increased this does not reach the level of statistical significance [z = –0.15; P (2-tailed) = .88].

Conclusions: At physiologic concentrations the conversion of osmolality to osmolality and the use of nonlinear regression have little effect on the estimation of urine osmolality.
A Case of IgG4-Related Aortitis

(POSTER NO. 123)

Shivali P. Marketkar, MD (smarketkar@lfhs.org); Mark LeGolvan, DO. Department of Pathology, Rhode Island Hospital, Providence.

IgG4-related pancreatitis is a commonly described entity; however, IgG4-related aortitis is rare. It is one of the recent entities seen in the spectrum of IgG4-related disease and a newly recognized form of noninfectious aortitis. The histopathology is important in the diagnosis of the disease and is characterized by a lymphoplasmacytic infiltrate, storiform fibrosis, and obliterative phlebitis with increased IgG4-positive plasma cells and ratio of IgG4 to IgG plasma cells greater than 50 considered very suggestive of the disease. Our patient was a 50-year-old man who presented with the complaint of intermittent periumbilical pain for 2 years; the pain radiated to his back and groin bilaterally. The patient reported no fever or any symptom suggestive of an underlying infection. On imaging it was found that he had an aneurysm of the infrarenal aorta. The aneurysm histologically revealed sclerosing fibrosis, obliterative phlebitis, and increased IgG4 plasma cells (>60 per high-power field). Serology also identified increased values of IgG4. A confounding feature was noted with the growth of Streptococcus sanguis in only 1 of 2 retrospective culture isolates. Cultures from the aneurysm were negative for bacterial growth. There have been case studies with infectious aortitis associated with Staphylococcus aureus and increased IgG4-positive plasma cells; however, our case has all the pathognomonic features of IgG4-related aortitis but may have an associated S. sanguis infection, suggesting a possible inciting factor for the process. Further studies to correlate any connection between the 2 would be required.

Another Novel Mutation in LAMB2 Gene in Pierson Syndrome

(POSTER NO. 124)

Nizar Belgasem, MBBS, LMCC1 (nizarsaad@hotmail.com); Polycarp Erwiyo, MBBS, FMCPath2; Chitra Pushpanathan, MBBS, FRCP3; Darren Orielly, PhD4; David Price, BMEdSci, MD, FRSC5; Angela Pickles, MD, FRCP6; Dorothy Verona Bautista, BMEdSc, MD, FRCS6; Departments of 1Anatomical Pathology and 2Faculty of Medicine, Memorial University of Newfoundland, St. John’s, Newfoundland and Labrador, Canada. Departments of 3Pediatric Pathology, 4Diagnostic Radiology, 5Ophthalmology, and 6Pediatric Surgery, Jane-Way Children’s Health and Rehabilitation Centre, St. John’s, Newfoundland and Labrador, Canada.

Pierson syndrome (OMIM 609094) is an autosomal recessive disorder consisting of congenital nephrotic syndrome with diffuse mesangial sclerosis and distinct ocular anomalies including microcoria. Many patients die early, and those who survive tend to show neurodevelopmental delay and visual loss. It is caused by mutations in LAMB2, which encodes laminin β2, a basement membrane protein. Several LAMB2 mutations have been described in relation to the characteristic phenotype of Pierson syndrome. Here we report the case of a 1-month-old infant boy who presented with bilateral microcoria with esotropia and congenital nephrotic syndrome. Light microscopy of the kidney biopsy showed 65% to 70% of glomeruli displaying varying degrees of mesangial sclerosis. Electron microscopy showed significant effacement of the epithelial cell foot processes, glomerular capillary basement membrane lamellation, and very thin lamina densa. His genetic studies showed 2 predicted disease-associated heterozygous mutations: c.3904 C > T (p.R1302X) and c.1225 T > C (p.K408X). The sequence variants detected in this patient have neither been previously reported in the

Functionally Impaired, Maternally Derived Memory T-Cell Engraftment in an Infant Harboring a Novel IL-2 Receptor Common γ Chain (CD132) Mutation

(Poster No. 121)

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X-linked severe combined immunodeficiency develops in roughly 1:50 000 to 100 000 births, affecting males of virtually every ethnicity equally. The underlying defect is a functionally crippling mutation in the IL-2 receptor common γ chain (CD132) that is shared among immunoregulatory cytokines such as IL-2, IL-4, IL-7, IL-9, IL-15, and IL-21. As IL-7 and IL-15 are required for the maintenance of peripheral T cells and NK cells, aberrant signaling results in a numerical deficit of these key lymphocyte subsets. We recently evaluated a 6-month-old male infant with a recent onset of respiratory and middle ear infections that required intravenous antibiotics and ventilatory support at a community hospital. He also experienced persistent watery diarrhea for 5 weeks, and a preliminary immunologic workup revealed barely detectable serum immunoglobulins. At our institution he received a full immunologic workup that confirmed his hypogammaglobulinemia and detectable serum immunoglobulins. A stem cell transplant was performed that led to the numerical and functional restoration of normal immunologic parameters and resolution of clinical symptoms.

Performance Evaluation of IgG Subclasses on SPApplus Analyzer

(Poster No. 122)

Justin D. Richey, MD (jdrichey@iupui.edu); Michelle Zimmerman, MD. Department of Pathology and Laboratory Medicine, Indiana University School of Medicine, Indianapolis.

Context: The association between IgG subclass deficiencies and recurring and/or persistent bacterial infections involving respiratory and digestive tracts has increased demand for IgG subclass determination in children and adults. This study evaluates the performance of the SPApplus Analyzer compared to our current 72-hour radial immunodiffusion (RID) protocol.

Design: IgG subclass concentration on RID plates (Binding Site, Birmingham, United Kingdom) is determined by manually measuring the diameter of the lattice precipitin ring and plotting the squared diameter against the logarithm of the dilution factor. The association between IgG subclass deficiencies and infectious aortitis associated with Staphylococcus aureus and increased IgG4-positive plasma cells; however, our case has all the pathognomonic features of IgG4-related aortitis but may have an associated S. sanguis infection, suggesting a possible inciting factor for the process. Further studies to correlate any connection between the 2 would be required.

Conclusions: Binding Site’s IgG subclasses on the SPApplus Analyzer shows acceptable analytic performance.

Results: Within-run precision CVs (n = 20) using 2 levels of controls were as follows: IgG1, 1.75% and 6.33%; IgG2, 2.32% and 1.35%; IgG3, 2.70% and 1.74%; and IgG4, 1.58% and 1.47%. Between-run precision CVs (20 days) were as follows: IgG1, 2.02% and 2.60%; IgG2, 2.44% and 1.90%; IgG3, 2.21% and 1.86%; and IgG4, 1.67% and 1.94%. The assay showed good linearity with 8-point calibrators across a range of 5 to 3440 mg/dL for IgG1 with slope of 0.9654 and intercept of −11.677; 10 to 680 mg/dL for IgG2, slope 1.0147, intercept −1.7222; 2.0 to 95 mg/dL for IgG3, slope 0.9875, intercept 0.9400; 1 to 60 mg/dL for IgG4, slope 1.0242, intercept 0.4077. Method comparison results with patient samples to RID method gave Passing-Bablok regression for IgG1 (n = 42, 168–880 mg/dL) SPA = 0.9423[RID] + 33.5385; IgG2 (n = 42, 10–650 mg/dL) SPA = 0.9457[RID] + 4.0429; IgG3 (n = 39, 21–117 mg/dL) SPA = 0.9857[RID] + (−4.0857); and IgG4 (n = 40, 1–135 mg/dL) SPA = 0.8327[RID] + (−2.6204).

Conclusions: Binding Site’s IgG subclasses on the SPApplus Analyzer shows acceptable analytic performance.
More than 50% of melanomas harbor a single point mutation (V600E) in the kinase domain of the BRAF gene, resulting in constitutive activation of the MAP kinase pathway. The kinase loop in BRAF begins with Asp-Phe-Gly (DFG) (codons 594–596). Mutations in this region are rare. We report the presence of a G596R mutation in a metastatic melanoma in an 84-year-old woman and its possible association with her indolent clinical course. The patient had a clinical diagnosis of melanoma in 1974 and melanoma in her left forearm 25 years prior. She had no other health problems and refused to have a biopsy until she noticed a rapidly enlarging left submandibular lump 1½ years ago. A left subclavicular mass and hyperpigmented lesions in her left forearm and leg were also noted. Biopsies performed on both masses revealed metastatic melanoma (positivity for MART1). BRAF mutation analysis by Sanger sequencing identified a c.1786G>T, p.G596R mutation in exon 15. G596R mutation has only been reported in 2 cases of melanoma in current literature with no clinical information available.

This mutation is considered to be low activating, which means it activates the signaling pathway indirectly by binding and allosterically activating BRAF. Our patient has carried a clinical diagnosis of melanoma for more than 25 years. It seems that the G596R mutation is associated with the slow progression of her disease. It is unknown whether patients carrying this mutation will benefit from vemurafenib therapy. Our patient declined medical treatment.

Molecular Testing in Multiple Synchronous Lung Adenocarcinomas

Oana C. Rafael, MD
Department of Pathology, North Shore Long Island Jewish–Lenox Hill Hospital, New York, New York.

Discovery of driver mutations in pulmonary adenocarcinoma has revolutionized the field of thoracic oncology with major impact on therapy and diagnosis. Testing for EGFR, ALK, and KRAS mutations has become part of everyday practice. We report a case with multiple synchronous primary pulmonary adenocarcinomas in a 72-year-old woman with a previous history of smoking. The patient presented with cough and bilateral lung ground-glass opacities. A PET/CT scan showed no activity in mediastinal lymph nodes. She underwent a left upper lobe biopsy and a right upper lobe wedge resection. Pathology revealed 4 morphologically distinct adenocarcinoma foci, suggestive of synchronous primary lung tumors. Molecular testing demonstrated no mutation in the left tumor. Three different driver mutations were present in the right lung tumors: KRAS codon 12 G12D and G12V and EGFR exon 21 L858R mutation, confirming initial histologic impression. Subsequently, left upper lobe lobectomy showed 3 additional foci of adenocarcinoma with different morphologies, suggestive of synchronous primaries as well. No additional molecular testing was performed. Synchronous pulmonary adenocarcinomas are not uncommon; however, 4 or more synchronous tumors are rare. Distinguishing multiple lung tumors from intraoperative metastases remains a challenge in thoracic oncology with major implications for staging, prognosis, and treatment. Lung adenocarcinoma subclassification based on predominant and coexisting histologic patterns can greatly facilitate differentiation between intrapulmonary metastases and multiple synchronous tumors. Use of molecular profiling is recommended, since it further increases confidence in the diagnostic workup of multiple pulmonary adenocarcinomas and helps in guiding therapy.

MIR21 Is Differentially Expressed in the Lymphoid Tissue of Patients With Chronic Lymphocytic Leukemia

Olga Danilova, MD
Department of Pathology and 2Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire.

Context: MIR21 is highly expressed in peripheral blood chronic lymphocytic leukemia (CLL) cells. It activates PI3K/AKT signaling and directly targets p53 family member TAp63. However, there have been only a few reports regarding the prognostic significance of MIR21. There are also no data regarding MIR21 expression in the lymph nodes.

Results: RT-PCR was performed to quantify MIR21 in peripheral blood samples (N = 26) of previously untreated patients with CLL. A modified combined IHC-FISH was used to determine expression of...
MIR21 in lymph nodes (N = 26). B cells from normal donors and tissue of reactive tonsils were used as controls.

**Results:** MIR21 expression was elevated in 46% of CLL samples. It did not correlate with IG VH mutational status, ZAP-70 and CD38 expression, or cytogenetics by FISH, as well as time to first treatment. Surprisingly, we found that MIR21 was not expressed in most CLL lymph nodes. Of the 28 lymph nodes tested, 2 (7%) showed strong staining for MIR21, 9 (32%) demonstrated weak signal, and 17 (61%) were negative. By contrast, B cells in 2 of 4 normal tonsils demonstrated strong positivity for MIR21. Again, there was no correlation with prognostic markers.

**Conclusions:** Thus, here for the first time we successfully visualized MIR21 expression within the lymphoid tissue from patients with CLL; it ranged from undetectable to strongly expressed. This suggests that lymph node microenvironment may play a role in modulating MIR21. MIR21 expression needs to be studied in a larger cohort of patients with CLL, with paired peripheral blood and lymph node samples.

## Development of a New Triplex Assay for ER, PR, and HER2/neu in Breast Cancer Tissue

(Poster No. 130)

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**Context:** Breast cancer is the most common invasive cancer in women in the United States. Breast cancer biopsy specimens are routinely assessed for hormone receptor status (estrogen receptor [ER] and progesterone receptor [PR]) by immunohistochemistry (IHC) and human epidermal growth factor receptor 2 (HER2/neu) expression by IHC or amplification by fluorescence in situ hybridization in order to guide the choice of therapy. Currently, pathologists analyze ER-, PR-, and HER2/neu-stained slides, one at a time, unaided, evaluating visible antigen staining, giving approximate percentages of positive cells and degree of staining intensities.

**Design:** To overcome these limitations, we developed a novel histology expression analysis platform that is based on triplex tissue/cell immunostaining using hapten-coupled primary antibodies, a whole slide tissue scanner (Vala’s IC200Hist) with the capability of combined brightfield and fluorescence imaging, and digital image analysis software (CyteSeer). Breast cancer cell lines with different and known levels of ER, PR, and HER2/neu were prepared as paraffin-embedded cell microarrays to be used as on-slide standards for the patient tissue sample. Hematoxylin was used for counterstaining, providing the classic way to view the tissue.

**Results:** Biomarker expression is quantified automatically and objectively on a cell-by-cell basis in a manner that provides great guidance to clinicians to have the right diagnostic and the appropriate prognostic to improve the outcome of a patient with breast cancer.

**Conclusions:** Our methodology is reproducible, accurate, and beneficial for clinical purposes and also a useful tool for studying molecular events and processes in tumors that will increase understanding of the mechanisms underlying breast cancer.

## Periorcular Sebaceous Gland Carcinoma: Do Androgen Receptor (NR3C4) and Nuclear Survivin (BIRC5) Have a Prognostic Significance?

(Poster No. 131)

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**Context:** This study aimed to evaluate the expression of androgen receptor (AR) and nuclear survivin in periorcular sebaceous gland carcinoma and to determine if this expression is associated with histopathologic features, markers of apoptosis and proliferation, and with clinical outcomes.

**Design:** Retrospective and comparative case series of 56 patients. Immunohistochemistry was performed for AR, survivin, Ki-67, and p53. AR and nuclear survivin (NS) staining were scored for intensity and percentage expression to derive AR and NS scores, which were correlated with histopathologic features, clinical outcomes, proliferation index, and apoptosis.

**Results:** All patients expressed AR, p53, and Ki-67 in the nucleus of tumor cells. Twenty-four patients (43.6%) had a high AR score and 31 patients (56.4%) had a low AR score. Twenty-four patients (43.6%) expressed survivin in the nucleus of tumor cells. Nine patients (37.5%) had a high NS score and 15 (62.5%) had a low NS score. Patients with a high AR score and nuclear survivin had a greater recurrence (P < .005), greater regional lymph node metastasis (P < .001), higher expression of Ki-67 (P < .001 and P < .001, respectively), and a lower p53 expression (P < .005) (Figure 221).

**Conclusions:** Expression of AR significantly impacts prognosis and is thus a promising prognostic marker in periorcular sebaceous gland carcinoma.

## Orbital Pseudotumor With IgG4-Positive Plasma Cells: A Recently Recognized Entity

(Poster No. 132)

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Inflammatory pseudotumors account for approximately 10% of all tumors of the orbit. Infectious etiologies and lymphoma should be ruled out. We describe a case of suspected IgG4-related disease presenting as an orbital mass. A 39-year-old woman presented with a gradually enlarging mass in the right orbit. Imaging showed a heterogenous mass with focal calcification arising from the frontal sinus. During surgical excision, the mass (3.5 × 2 × 1.3 cm) was highly vascular. The differential diagnoses considered were hemangioma versus mucocele. Microscopy showed reactive follicular hyperplasia with a dense lymphoplasmacytic infiltrate, extensive fibrosis, focally storiform in pattern. Vasculitis was present without luminal obliteration. IgG4 and IgC immunostains showed an increase in IgG4 plasma cells, averaging 25 cells per high-power field (HPF) in 3 HPFs, with a ratio of IgG4 to IgG of 28%. Histochemical stains for fungus and acid-fast bacilli were negative. Histologic diagnosis suggestive of IgG4-related disease was rendered. Owing to the propensity for multiorgan involvement, systemic disease must be excluded clinically. Elevated serum IgG4 levels correlate with disease activity, but active disease may be associated with falsely low serum IgG4 levels, as reported by Khosroshahi et al (2014). Owing to serum IgG4 level variations, the initiation of glucocorticoid therapy should not be delayed. Clinical deterioration including proptosis, eyelid swelling, diplopia, and bilateral eye involvement has been reported in the literature. In conclusion, it is important to differentiate IgG4-related disease from orbital pseudotumors in view of clinical implications, with appropriate follow-up for development of systemic manifestations.

## Mucinous Carcinoma of Periorbital Region: A Mimicker, With Diagnostic Significance

(Poster No. 133)

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Primary mucinous carcinoma of periorbital region is rare. It is a low-grade malignancy with high recurrence rates and low metastatic potential. The recurrent tumor is usually locally destructive, and clinically can mimic a wide variety of nonneoplastic or neoplastic lesions. Owing to similar histology and rarity, the primary mucinous carcinoma of eye lid needs to be differentiated from metastatic mucinous adenocarcinoma. A 68-year-old woman presented with an asymptomatic slowly growing mass in the left periorbital region. Biopsy showed mucinous adenocarcinoma. Metastatic workup was negative for tumor elsewhere including breast. The mass (2.2 × 1.4 × 1 cm) was excised and submitted for histopathologic examination. Microscopy revealed dermal tumor, with uniform-appearing epithelial cell islands in mucin pools separated by thin fibrous septae. There was associated foreign body reaction due to mucin extravasation. Margins were positive for tumor. The mucin was mucicarmine, alcin blue (pH 2.5), and PAS-D positive. Immunohistochemistry revealed tumor cell positivity for CK7, AE1/AE3, estrogen receptor, progesterone receptor, GCDFP-15, CEA (focal), and EMA (minority). CK20, TTF-1, synaptophysin, and chromogranin immunostains were negative, which ruled out colon, lung adenocarcinomas, and neuroendocrine tumors. In view of histologic and immunohistochemical overlap, metastatic breast carcinoma is difficult to rule out completely owing to common eccrine/apocrine origin. Metastases to regional lymph nodes are reported in literature. Aggressive initial surgical treatment, Mohs micrographic surgery, or frozen section control of margins are useful to reduce the recurrence rate. However, prolonged follow-up is required owing to the high potential for late local recurrence.

Orbital Immunoglobulin G4–Related Disease: Clinicopathologic Features of a Novel Entity
(Poster No. 134)

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Context: Immunoglobulin G4–related disease (IgG4-RD) is a novel entity that is characterized by a diffuse or mass-forming inflammatory reaction with tissue infiltration by IgG4-positive plasma cells. The purpose of our study was to evaluate the clinicopathologic features of orbital IgG4-RD.

Results: Eleven patients (24%) fulfilled both criteria of IgG4-related disease (IgG4-RD group). Serum IgG4 was elevated in 8 patients of the IgG4-RD group and in 2 patients of the non–IgG4-RD group. Patients in the IgG4-RD group had a significantly higher rate of bilateral involvement (P < .001), dense fibrosis (P < .001), plasma cell infiltration (P < .001), and relapse after discontinuation of steroids (P < .005) (Figure 222).

Conclusions: IgG4-RD is a novel entity with distinct clinicopathologic features, prognosis, and management.

Bilateral IgG4-Related Dacryoadenitis Evolving Into an Extranodal Marginal Zone Lymphoma on One Side
(Poster No. 135)

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IgG4-related disease (IgG4-RD) is a novel entity that is characterized by mass-forming lesion, infiltration by IgG4-positive plasma cells, and sometimes elevated serum IgG4 levels. The exact relation between IgG4-RD and lymphoma is unknown. Rare reports in literature describe IgG4-positive plasma cells in a lymphoma. Even more rare is the evolution of IgG4-RD into a lymphoma. A 65-year-old woman presented with a bilateral lacrimal gland swelling of 3 months’ duration. Examination revealed bilateral proptosis. CT scan showed a homogenous mass involving both lacrimal glands. Incision biopsy of the right lacrimal gland showed features of IgG4-related dacryoadenitis. The left lacrimal gland showed a B-cell extranodal marginal zone lymphoma (MAL1-type) on a background of IgG4-related dacryoadenitis. Serum IgG4 levels were markedly elevated. This, according to the best of our knowledge, is just the fourth case of IgG4-RD evolving into a lymphoma.

Coats Disease: An Important Retinoblastoma Mimic
(Poster No. 136)

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Coats disease is a rare idiopathic disease of the retina that occurs primarily in young children, where proteinaceous exudates from abnormal vessels lead to retinal detachment. The common clinical presentation of Coats disease is a child with leukocoria, decreased visual acuity, strabismus, and retinal detachment; these features make it an excellent mimic of retinoblastoma. We describe 2 patients, a 22-month-old boy and a 23-month-old girl, who presented with leukocoria and decreased visual acuity. Clinical examination and imaging studies were consistent with an intraocular mass, and both were enucleated for presumed retinoblastoma. In each eye, gross examination demonstrated retinal detachment with a diffuse yellow exudative coagulum occupying most of the globe. Histologic analysis revealed diffuse intraretinal and subretinal eosinophilic exudates; dilated, tortuous, and thickened vessels; and numerous macrophages

Design: A retrospective review of 46 patients with nonspecific orbital inflammatory mass was performed. Immunostaining with CD138, IgG, and IgG4 was performed. Patients were divided into IgG4-RD and non–IgG4-RD groups on the basis of IgG4-IgG-positive cells and serum IgG4 titers.

Results: Eleven patients (24%) fulfilled both criteria of IgG4-related disease (IgG4-RD group). Serum IgG4 was elevated in 8 patients of the IgG4-RD group and in 2 patients of the non–IgG4-RD group. Patients in the IgG4-RD group had a significantly higher rate of bilateral involvement (P < .001), dense fibrosis (P < .001), plasma cell infiltration (P < .001), and relapse after discontinuation of steroids (P < .005) (Figure 222).

Conclusions: IgG4-RD is a novel entity with distinct clinicopathologic features, prognosis, and management.
with cholesterol clefts. There was no evidence of retinoblastoma or other malignancy in either case. Although preoperative imaging can often distinguish between Coats disease and retinoblastoma, it remains imperfect. Calcifications are often identified in cases of retinoblastoma, and their absence should lead to consideration of other possible diagnostic considerations. Recognition of this uncommon entity can help properly stratify risk of malignancy and also lead to the diagnosis of Coats disease at an earlier stage where intervention with laser photocoagulation or cryotherapy can be used in an attempt to arrest progression of the disease (Figure 223).

**Cerebral Chromoblastomycosis Caused by Fonsecaea pedrosoi**

(Poster No. 137)

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Dematiaceous fungi are rare causes of cerebral abscesses, and usually portend a poor prognosis, particularly in immunocompromised patients. Herein, we present the first reported case in the United States of cerebral chromoblastomycosis caused by *Fonsecaea pedrosoi*, confirmed by polymerase chain reaction. A 62-year-old man with hepatitis C, status post renal transplant, presented with acute onset of lower extremity weakness. Contrast computed tomography and magnetic resonance imaging showed multiple peripheral ring–enhancing lesions in the left basal ganglia, left frontoparietal lobe, and right frontal lobe. Biopsy of the left parietal lesion revealed dematiaceous fungi with granulomatous and acute inflammation. Hematoxylin-eosin–stained sections also showed medlar bodies with darkly pigmented walls and occasional transverse septae (Figure 224), highlighted by PAS and silver stains. *F. pedrosoi* was identified by polymerase chain reaction and DNA amplification. *F. pedrosoi* is more commonly a cause of cutaneous chromoblastomycosis in humid, tropical areas. Chromoblastomycosis usually enters skin or mucosa via traumatic implantation of fungal elements. While the point of fungal entry was unknown in our patient, he was immunocompromised and lived in Southern Louisiana, known for its warm, humid climate. The patient was treated with IV amphotericin B and discharged with oral voriconazole. Six months after discharge, the patient shows continual improvement in his symptoms with MRIs showing resolution of brain lesions. While *F. pedrosoi* is an exceedingly rare cause of cerebral abscesses, it should be considered in the differential etiology of fungal cerebral lesions in an immunocompromised patient.

**Organ Transplant–Associated Lymphocytic Choriomeningitis Virus Case Cluster**

(Poster No. 138)

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Lymphocytic choriomeningitis virus (LCMV) is a rodent-borne enveloped RNA virus belonging to the Arenaviridae family. LCMV infection is usually asymptomatic and not fatal. However, donor-transmitted LCMV infection in organ transplant recipients is associated with high mortality. We report a posttransplant LCMV case cluster in 3 allograft recipients from a common donor at our center in March 2013. The organ donor, a 49-year-old man, died from an intracerebral hemorrhage. Liver, both kidneys, and 1 cornea were transplanted. Three weeks post transplant, the solid organ recipients developed subacute symptoms of fever, diarrhea, wound breakdown, pancytopenia, elevated transaminases, mental status changes, and/or respiratory compromise. Given concern for a donor–derived infection, Organ Procurement and Transplantation Network/United Network for Organ Sharing and Centers for Disease Control and Prevention (CDC) were contacted. Specimens from each recipient tested positively for LCMV at CDC by serology, molecular analysis, and/or immunohistochemical stain on tissue. Donor aortic endothelial cells were positive for the same LCMV strain on molecular analysis. Although the patients were promptly treated with ribavirin, intravenous immunoglobulins, and by reducing immunosuppression, the liver recipient died, 1 kidney recipient lost the allograft, and both the kidney recipients also showed persistent mild memory defects. The cornea recipient was asymptomatic with negative diagnostic testing. This is the sixth transplant-associated LCMV case cluster reported worldwide. Previous reports involved 17 recipients and 14 deaths. Our series highlights how early diagnosis, using proper pathologic testing, led to prompt therapeutic intervention, which may have contributed to the more favorable outcome in the kidney transplant recipients (Figure 225).

**Babesia microti Infection: Two Case Reports and Review of the Literature**

(Poster No. 139)

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The incidence of *Babesia microti* infection has doubled in New York between 2004 and 2010. Hyperendemic areas include Shelter Island and the South Fork of Eastern Long Island. *Babesia* is transmitted via *Ixodes scapularis*, mainly between the months of June and November. Morphologically, *Babesia* is highly similar to *Plasmodium* species with the exception of the presence of extracellular forms, and intracellular merozoites arranged in tetrads (or “Maltese crosses”). We describe 2 local cases of *B. microti* infection in patients from Queens and Nassau County with no travel history to Eastern Long Island. The first involves a 45-year-old woman who presented with headaches, nausea, and fever. Our second case involves a 66-year-old man who presented with left-sided abdominal pain, fever, chills, and malaise. He noticed 2 tick
bites that he self-removed, but reported absence of rash. Physical examination showed splenomegaly and petechiae. Laboratory tests for both cases revealed severe thrombocytopenia, anemia, elevated lactate dehydrogenase levels, increased total bilirubin, and decreased haptoglobin. 

*Babesia* was identified on peripheral smear in both cases and confirmed by real-time polymerase chain reaction. Our first case was treated successfully with atovaquone/azithromycin/doxycycline regimen, while our second case was treated with atovaquone/azithromycin alone owing to doxycycline allergy. Babesiosis is becoming increasingly common in Long Island, outside established hyperendemic regions. There is heightened awareness of transfusion-transmitted babesiosis due to ineffective questioning method of prospective blood donors about history of babesiosis. It is particularly important to raise awareness of this infection in not typically endemic areas (Figure 226).

**Multidrug-Resistant*Helcococcus*-Like Organism Isolated From a Chest Abscess**

*(Poster No. 140)*

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*Helcococcus* is a genus of facultatively aerobic, gram-positive, catalase-negative cocci associated predominantly with wounds, but also prosthetic joint infections, bacteremia, and empyema. Standardized susceptibility testing methods have not been described for *Helcococcus* spp. Using nonstandardized methods, most isolates to date have displayed either no or single-antibiotic resistance. In early 2014 a case series was published describing the first known multidrug-resistant isolates (2 *Helcococcus kunzii*, 2 *Helcococcus sueciensis*, and 1 novel helcococcal isolate). We present an additional case of a *Helcococcus*-like organism that demonstrated multiple antibiotic resistance. A 31-year-old pregnant woman at 27 weeks gestation was referred to the dermatology clinic for a chest abscess associated with an epidermal inclusion cyst. Incision and drainage were performed and a swab specimen of purulent fluid was sent for culture. Gram stain showed gram-positive cocci in clusters. Culture grew pinpoint, grey, nonhemolytic colonies on chocolate agar at 48 hours. An API Strep system test (BioMerieux, Durham, North Carolina) failed to result in species identification in the commercial kit database. 16S rRNA gene sequencing of the isolate displayed 99% similarity to *H. sueciensis*, with 424 of 426 analyzed bases in alignment using the National Center for Biotechnology Information GenBank BLAST program to identify homologous sequences. Antibiotic susceptibility testing was performed by using the E-Test method (AB Biodisk, Piscatway, New Jersey). Vancomycin showed a minimum inhibitory concentration of 4 mg/mL, while penicillin G, trimethoprim-sulfamethoxazole, vancomycin, ciprofloxacin, and ceftriaxone all showed no zone of inhibition.

**Human Immunodeficiency Virus Type 1 Clade D-Transmitted/Founder Viruses Display Enhanced Macrophage Tropism That Maps to the Envelope Glycoprotein and Is Associated With Efficient CD4 Utilization**

*(Poster No. 141)*

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**Context:** Macrophages and related myeloid-derived cells are instrumental in human immunodeficiency virus type 1 (HIV-1) interaction of brain and have long been identified as potential reservoirs of systemic virus infection. A surprising finding of recent studies of HIV-1 transmission, however, is that transmitted/founder (T/F) HIV-1 clades B and C replicate poorly in primary human macrophages. Because clinical studies have reported an association between neuropathogenesis and HIV-1 clade D infection, we sought to characterize phenotypic properties of T/F clade D and A viruses, which cocirculate in East Africa.

**Design:** Here we evaluated viruses derived from a panel of 10 T/F clade A and D infectious molecular clones and Env-pseudotyped viruses derived from 23 T/F envelope clones, clade A (n = 13) and D (n = 10).

**Results:** Compared to clade A T/F viruses, clade D T/F viruses replicated more efficiently in primary human macrophages (P < .05). Macrophage tropism mapped to Env and was significantly associated with enhanced virus replication, sensitivity to sCD4, efficient utilization of low CD4 on target cells, and virus-cell fusogenicity (P < .05 for all comparisons).

**Conclusions:** These findings suggest that the enhanced neurovirulence associated with clade D infection is linked to phenotypic properties of HIV-1 clade D strains that enhance macrophage tropism from early in infection.

**Is It Time for a Pathology Objective Structured Clinical Examination?**

*(Poster No. 142)*

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**Context:** Objective structured clinical examinations (OSCEs) are widely used in graduate medical education, but not in pathology. Residency and fellowship programs will begin to use Milestones to document trainee progression this summer, and there are specific outcome measures that may be difficult to assess by traditional mechanisms such as subjective end-of-rotation evaluations and knowledge-based examinations; specifically, Milestones in the interpersonal communication skills and professionalism core competencies.

**Design:** The Pathology Milestones and literature available under the University of Washington institutional license pertaining to “OSCE” and “Pathology” were reviewed.

**Results:** A few pathology topics have been successfully integrated into nonpathology OSCEs, so inclusion of pathology trainees in existing clinical OSCEs is one option. Prospective topics include interpretation of morphologic, molecular, and ancillary studies and appropriate test selection. Stand-alone pathology OSCEs could include communication of autopsy findings, frozen section interpretations, clinical consultations, genomic data interpretation, blood utilization, and error disclosure.

**Conclusions:** Use of the Milestones in resident evaluation necessitates reappraisal of the repertoire of evaluation tools, and an OSCE is a reproducible method of evaluating resident performance across multiple core competencies. Barriers to local development of OSCEs include cost and the need for significant faculty development. Some degree of centralized development of OSCE scripts or templates could be considered to reduce costs; another alternative is interdepartmental collaboration capitalizing on existing institutional knowledge and resources. Savings derived from improved clinician understanding and utilization of pathology services and improved patient outcomes could justify subsidization of OSCE development at the national or state level.
The Utility of Virtual Specimens for Medical Student and Resident Education

(Poster No. 143)

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Context: Recent advances in imaging technology have allowed for 3-dimensional (3-D) rendering of objects using multiple 2-dimensional images. This technique was applied to gross pathology specimens to create 3 examples of true virtual specimens (Figure 227). A survey was sent out to pathology residents, fellows, and medical students to evaluate their opinion of the role of these virtual specimens in education.

Design: Three gross specimens were used for the study. A range of 19 to 39 photos were taken of each specimen from a variety of angles. These were converted into 3-D models by using Adobe 123d Catch software. Models were optimized and uploaded to an interactive viewing Web site (www.sketchfab.com). A survey was sent out that asked the opinions of the cohort regarding the educational utility of the virtual specimens.

Results: A total of 17 responses (8 residents, 5 medical students, 4 fellows) were received. All of the fellows and 88% of pathology residents agreed or strongly agreed that 3-D specimens would be useful in learning grossing techniques and as a learning tool for pathology courses. All of the medical students agreed or strongly agreed that 3-D specimens would be useful for learning anatomy and see a role for 3-D specimens in future medical education. All of the fellows and 75% of residents agreed or strongly agreed that 3-D specimens would be useful in presentations or conferences.

Conclusions: Virtual specimen construction is an effective tool for student, resident, and fellow education and has a role in the future of medical student and resident education.

An Assessment of Pathology Resident/Fellow Access to and Use of Technology: A Nationwide Survey

(Poster No. 144)

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Context: Current technologies, including digital slide scanners and handheld devices, can revolutionize clinical practice and resident education in pathology. The extent these technologies are used in pathology education is unknown. The purpose of this project is to determine the types of technologies used, usage amount, and how they are integrated into pathology residency/fellowship programs nationwide.

Design: A 40-question online survey for residents/fellows was developed and administered via REDCap (Vanderbilt University, Nashville, Tennessee) after institutional review board approval. Permission for resident/fellow participation was sought from program directors via e-mail.

Results: Fifty-two program directors (37%) gave permission for participation. A total of 171 responses were received (18% response rate). The Table shows respondents’ demographic data. Fifty-eight percent have access to digital slide scanners and 51% use telepathology; 17% use telepathology for education. Sixteen percent have access to asynchronous learning (video-recorded conferences). Few residents are provided electronic devices by their programs (laptop 22%, smartphone 0.5%, and tablet 12%). Most own personal devices (laptop 78%, smartphone 81%, and tablet 18%), which they use for professional work (75% use laptops for ≥1 hour per day, 57% use smartphones for ≥1 hour per day, and 52% use tablets for ≥1 hour per day). The most common laptop uses are e-mail, Internet searches, and scholarly efforts. The most common tablet uses are e-mail, e-books, and Internet searches. The most common smartphone uses are e-mail, phone calls, and texting.

Conclusions: Most residents/fellows have access to multiple technologies within their programs. Handheld devices (laptops, smartphones, and tablets) are rarely provided by programs. Opportunities for increased use of innovative technologies in pathology training programs exist.

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Primary Ewing Sarcoma of the Kidney: A Case Study and Review of the Literature

(Poster No. 145)

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Extraskelatal Ewing sarcoma may arise anywhere in the body; however, Ewing sarcoma of the kidney is rare. We report Ewing sarcoma with secondary genetic abnormality of trisomy 1 and gain of 1p36.1. The patient is a 15-year-old adolescent boy who presented with severe right-sided flank pain, hypertension, and hematuria. Computerized tomography revealed a large mass involving more than half of the right kidney. Nephrectomy was performed. Gross examination revealed a 10×10×9-cm mass consisting of tan-white lobulated cut surfaces with central necrosis. Microscopic analysis revealed a high-grade tumor composed of sheets of primitive small blue cells separated with fibrovascular cores. The nuclei were round; stippled chromatin was noted with scant cytoplasm. There were abundant mitoses and karyorrhexis. Immunohistochemistry showed that CD99, NSE, and INI-1 were positive; synaptophysin and CD56, focally positive; and FLI-1, diffusely positive. All keratin makers were negative. Cytogenetic analysis revealed abnormal karyotype, 47,XY,add(1)(p36.1),t(11.22)(q24;q21). The morphology, immunohistochemistry, and cytogenetics supported the diagnosis of Ewing sarcoma. Differential diagnosis in primary renal tumor in pediatric population includes Wilms tumor, clear cell sarcoma of kidney, neuroblastoma, and lymphoma. Molecular studies and immunohistochemistry play an important role in making a correct diagnosis. According to the literature, more than 80% of Ewing sarcomas express EWS–FLI-1 translocation. Previously reported secondary genetic abnormalities include trisomy 2, 5, 7, 8, or 12, deletions of 1p36, 9q12, 17p13; and gain of 1q. To the best of our knowledge, this is the first observation of secondary genetic abnormalities of gain 1p36.1 in primary renal Ewing sarcoma.

A Valuable Toolkit for Selecting a Whole Slide Imaging System for Diagnostic Pathology Use: Key Technical Features to Consider

(Poster No. 146)

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Features to Consider

- High quality of diagnoses
- Same results as 2D sections
- Faster diagnosis
- Enables teaching
- Reduces fatigue
- Enables research
- Enables remote consultation
- Enables remote teaching
- Enables medical record
- Enables audits
- Enables practice
- Enables protocol
Investigating the Progression of Liver Disease to Hepatocellular Carcinoma Using Label-Free Chemical Imaging

(Poster No. 148)

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Context: Currently, numerous vendors offer whole slide imaging (WSI) scanners/systems. As pathology laboratories are increasingly considering the acquisition of WSI systems, selecting an instrument to purchase is becoming challenging. Our intent was to identify key technical features that may help users appraise and compare various WSI systems in the marketplace to serve as a toolkit for helping in the selection process.

Design: During phase 1 of this study a list of key WSI scanner hardware and software features was composed. Features were categorized according to the digital imaging process (acquisition, archiving, and viewing). During phase 2, vendors marketing WSI scanners intended for pathology diagnostic use were requested to provide technical information about these key features for their scanners. This included 23 scanner models marketed by 11 vendors (3DHISTECH, Leica, Hamamatsu, Huren, Leica, Mikroskan, Olympus, Omnyx, Philips, Sakura, and Ventana).

Results: Identified key hardware features included (1) scanner physical properties (compact and light [10–11 kg] to large [up to 180 kg]; (2) slide handling (capacity ranging from 1 to 400 slides); (3) image acquisition (brightfield halogen or LED illumination offered by all vendors, dual brightfield and fluorescence in a single scanner offered by 4 vendors; and (4) image digitization (Z-stacking offered by many vendors). Key software features included image management, workflow management, and image analysis categories.

Conclusions: The list of key features identified in this study can serve as a useful toolkit to determine which WSI system is best suited for specific clinical needs (eg, cytopathology and workflows [eg, routine surgical pathology sign-out, consultations, frozen sections, or research]).

Laboratory Test Database Analysis Helps Clinicians Identify Clinical Gaps in Care and Improve Patient Outcomes

(Poster No. 147)

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Context: The Medivo Lab Value Exchange (LVX) database (Medivo Inc, New York, New York) includes laboratory tests conducted on more than 50 million patients by more than 200 000 physicians and offers a unique way of assessing testing rates, physician behaviors, and the impact of education.

Design: Three studies were conducted by using the LVX, looking at testing rates and results comparing case physicians (exposed to education on laboratory test analytics) versus control physicians (not exposed). Physicians included primary care clinicians and specialists, therapeutic areas included dyslipidemia, chronic myelogenous leukemia (CML), and gout.

Results: (1) Dyslipidemia: During 3 months, case physicians (N = 117) ordered significantly more low-density lipoprotein tests than control physicians (N = 116; 243 tests versus 313 tests; P = .02; 11% more on an annualized basis; (2) CML: During 12 months, analysis of BCR-ABL test results showed that 35% of patients with CML had not achieved major molecular response, suggesting a need for therapy change. Case physicians increased testing rates by 80% versus control physicians (1.8 versus 1.0 tests per year, P < .001); (3) Gout: Case physicians (N = 200) increased testing rates by 55% versus control physicians (N = 858); average 8.57 versus 5.52 (P < .001). Average serum uric acid levels in the case gout patient population fell from 7.27 mg/dL to 6.68 mg/dL (P < .001).

Conclusions: A national laboratory test database is a valuable tool to assess clinical gaps, impact changes in clinician behavior and outcomes. Physician educational initiatives based on laboratory test analytics can result in improved testing rates and better patient outcomes.

Crawl, Walk, Run: A Blood Center’s Perspective on Supporting Hospital-Based Patient Blood Management Initiatives

(Poster No. 149)

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Context: With the reduction in transfusion-transmitted infection and a relatively more secure blood supply, the focus of transfusion medicine has shifted to blood utilization. Clinical trials and comparisons to blood use and outcomes in other countries have demonstrated that there is unnecessary, inappropriate, and liberal use of blood and blood products in the United States. Recognizing these ongoing evolutionary shifts in health care, a multistate, regional blood supplier created a comprehensive approach to assist hospitals to effectively self-deploy patient blood management (PBM) programs.

Design: Based on common factors identified in hospitals able to successfully implement a PBM program, a systematic approach was developed to increase the likelihood that customers could successfully implement a PBM program addressing their goals for patient safety, cost savings, and operational efficiency.

Results: A 3-phased approach was developed: (1) Initial rollout. Create system-wide awareness of PBM rationale, develop common language, identify and define champions, stakeholders, potential barriers, and outcomes. Provide onsite assessment of laboratory and hospital processes, procedures, and governance. Help optimize blood committee. Introduce tools and provide basic education. (2) Next steps. Discuss outstanding issues, solidify champion and stakeholder support. Help roll out formal communications plan, initiate kick-off presentations, and identify early service-line education opportunities. Provide a formal plan. (3) Ongoing support. Support change through data, improve project management skills to overcome barriers, develop meaningful metrics, communicate and celebrate successes.

Conclusions: Hospitals can leverage blood center expertise to successfully implement a PBM program that improves transfusion practice and reduces costs. Once developed, the same approaches can be applied to other hospital-based patient safety initiatives.

Immunohistochemical Stain Utilization in a Medium-Sized Academic Center

(Poster No. 150)

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Context: Several studies have addressed the diagnostic utility of immunohistochemistry; however, few have focused on the patterns of usage in clinical practice. This study aims to determine factors influencing the use of immunohistochemistry stains (IHCs) in a busy academic practice with general sign-out.
**Design:** Surgical pathologist case volume was recorded during 6 consecutive months, excluding those performed per departmental protocol (sentinel nodes, breast markers, lymphoma/leukemia panels). Reported IHCS used on the remaining cases were categorized by organ system and specimen type (CPT codes). The following data points were recorded: pathologists’ volume per CPT codes, years of experience (0–4 years and ≥5 years), and subspecialty interest.

**Results:** A total of 997 IHCS were used. More than half (55.1%) were used on nonbiopsy specimens. Biopsy material (CPT 88305) represented 44.9% of all cases. IHCS were ordered with the most frequency on GU (20.7%), GI (14.4%), CNS (13.9%), soft tissue (12.8%), and lung (12.8%) cases. In every CPT group, pathologists with ≥5 years of experience ordered more IHCS than pathologists with 0 to 4 years of experience. Pathologists also ordered IHCS more frequently on cases in their subspecialty area, compared to their colleagues, exclusive of practice experience. Results are summarized in the Table.

<table>
<thead>
<tr>
<th>Case Defect</th>
<th>Issue</th>
<th>Root Cause</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Order entry</td>
<td>Patient denied specimen drawn</td>
<td>Incorrect identification at the time of</td>
<td>Test result</td>
</tr>
<tr>
<td></td>
<td></td>
<td>specimen collection</td>
<td>cancelled</td>
</tr>
<tr>
<td>2 Result display</td>
<td>Patient did not see reference</td>
<td>Unlike the hospital electronic medical</td>
<td>Display of</td>
</tr>
<tr>
<td></td>
<td>range for high sensitivity</td>
<td>record, the portal did not display</td>
<td>reference ranges</td>
</tr>
<tr>
<td></td>
<td>C-reactive protein assay</td>
<td>reference ranges</td>
<td></td>
</tr>
<tr>
<td>3 Test result</td>
<td>Patient questioned high level</td>
<td>As results of repeated evaluations were</td>
<td>Ordering</td>
</tr>
<tr>
<td></td>
<td>of testosterone</td>
<td>concordant, hormone supplementation was</td>
<td>provider</td>
</tr>
<tr>
<td></td>
<td>Analysis was repeated on the</td>
<td>considered as a possibility</td>
<td>notified for</td>
</tr>
<tr>
<td></td>
<td>same and a subsequent specimen</td>
<td></td>
<td>follow-up</td>
</tr>
<tr>
<td>4 Result display</td>
<td>Patient could not access CA-125</td>
<td>Results must be first reviewed by the</td>
<td>Ordering</td>
</tr>
<tr>
<td></td>
<td>results</td>
<td>ordering provider</td>
<td>provider</td>
</tr>
<tr>
<td>5 Result display</td>
<td>Patient could not access urine</td>
<td>Comprehensive drug results must be first</td>
<td>Ordering</td>
</tr>
<tr>
<td></td>
<td>drug screen results</td>
<td>reviewed by the ordering provider</td>
<td>provider</td>
</tr>
<tr>
<td>6 Order entry</td>
<td>Patient visit was registered</td>
<td>The registering staff were not adequately</td>
<td>Staff were</td>
</tr>
<tr>
<td></td>
<td>as inpatient encounter, and</td>
<td>oriented to policy regarding restricted</td>
<td>provided</td>
</tr>
<tr>
<td></td>
<td>thus the patient was unable</td>
<td>access to inpatient results</td>
<td>education</td>
</tr>
<tr>
<td></td>
<td>to access the result</td>
<td></td>
<td>on differences</td>
</tr>
<tr>
<td>7 Result display</td>
<td>Patient expressed dissatisfaction to the provider that the laboratory did not notify him of a hemolyzed specimen</td>
<td>Patient was not aware that the laboratory is not obligated to contact the patient for a hemolyzed specimen</td>
<td>Patient was advised of laboratory policy for handling hemolyzed specimens</td>
</tr>
</tbody>
</table>

**Conclusions:** The utilization pattern of IHCS in our study seems similar for both biopsies and resections. Although less experienced pathologists presumably need IHCS to support their diagnoses, we observed that more experienced pathologists supplement diagnostic work with IHCS at a higher frequency. Broader knowledge of diagnostic pitfalls and better understanding of tumor marker expression may explain this trend.

Direct Patient Access to Laboratory Test Results: Unanticipated Postimplementation Issues and Their Root Cause Analysis

(Poster No. 151)

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**Context:** A recent rule (amending CLIA regulations [42 CFR 493.1292(1)] and HIPPA Privacy Rule [45 CFR 164.524]) requires medical laboratories to provide patients, upon request, access to their completed test reports. Consequently, large health systems have started to offer direct access to their test results through online patient portals. However, the laboratory staff may face unintended and unforeseen operational scenarios, often brought directly to their notice by patients.

To better understand such scenarios, we analyzed individual issues brought to our laboratory’s attention.

**Design:** A prospective observational analysis of issues related to direct patient access to test results (including review of incident, root cause analysis, and follow-up) was performed during a period of 16 months (January 2013–March 2014) after the launch of online access in December 2012. Root cause analysis included review of electronic medical records and interviews with technical staff and ordering providers. Direct online patient access to laboratory results was through an online module (MyChart/Epic, Epic Systems Corporation, Verona, Wisconsin).

**Results:** A total of 7 issues were brought to the laboratory’s attention either by the patient (6 of 7 issues), ordering provider (1 of 7 issues), or through the institutional incident reporting system (1 of 7 issues) (Table).

**Conclusions:** Direct patient access to test results identifies process defects, both internal and external, to the laboratory (cases 1, 2, 6). Patients are often not aware of restrictions on release of sensitive test results (cases 4, 5). Close collaboration and improved communication between the laboratory and the ordering provider (cases 3, 7) is desirable when the patient encounters an unexpected test result.