Abstracts and Case Studies for the College of American Pathologists 2021 (CAP21) Annual Meeting

The following abstracts and case studies were accepted for the CAP21 Virtual Abstract Program. Shown before each poster session are the subject areas for that session.

**POSTER SESSION 1: SUNDAY SEPTEMBER 26, 2021**

**Gastrointestinal and Liver Pathology: Kidney and Genitourinary Pathology**

**Disease Anatomic Extent as Part of a Risk Stratification Model That Predicts Survival in Gallbladder Adenocarcinoma**

(Poster No. 1)

Haiyan Lu, MD, PhD1 (yanhailv@gmail.com); Breanna Perlmutter, MD; Robert Naples, MD2; Toms Augustin, MD2; Daniela Allende, MD1. Departments of 1Pathology and 2General Surgery, Cleveland Clinic Foundation, Cleveland, Ohio.

**Context:** Gallbladder adenocarcinoma has a poor overall survival (<5% at 5 years). We aim to design a risk-stratification model with novel and traditional features.

<table>
<thead>
<tr>
<th>Overall Survival in Patients With Gallbladder Adenocarcinoma With Different Pathologic Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gallbladder Adenocarcinoma (N = 57)</td>
</tr>
<tr>
<td>Pathologic Features</td>
</tr>
<tr>
<td>Disease extent</td>
</tr>
<tr>
<td>Focal</td>
</tr>
<tr>
<td>Diffuse</td>
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<tr>
<td>T stage</td>
</tr>
<tr>
<td>T1</td>
</tr>
<tr>
<td>T2</td>
</tr>
<tr>
<td>T3</td>
</tr>
<tr>
<td>Tumor grade</td>
</tr>
<tr>
<td>Well</td>
</tr>
<tr>
<td>Moderate to poor</td>
</tr>
</tbody>
</table>

**Design:** We retrospectively identified 57 gallbladder adenocarcinoma resection specimens from January 2009 through December 2017 at Cleveland Clinic Foundation. Clinical data were gathered and histologic features were obtained. Involvement by adenocarcinoma was defined as localized when a single anatomic region; remaining cases were considered diffuse. Kaplan-Meier analysis was used to estimate overall survival (OS) by using XLSTAT. Patients were risk-stratified by using 2 prediction models, and receiver operating characteristic curve and area under the curve (AUC) were used to compare the models. P < .05 was considered statistically significant.

Results: Of the 57 cases, 25 patients (43.9%) had localized disease at resection, whereas the rest had diffuse involvement of the gallbladder. The median follow-up was 29.7 months (range, 3.5–122 months). Twenty-six patients (45.6%) were dead from disease, with a median survival of 22.9 months (range, 3.8–61.5 months). Significant predictors of worse OS included diffuse involvement (P < .001), advanced stage (P = .02), and moderate to poor differentiation (P = .02). Lymphovascular invasion (LVI) showed a trend toward significance (P = .08). The risk-stratification model 1 (localized/diffuse extent of tumor, T stage, and tumor grade) provided better prediction for outcome (AUC = 0.721, P = .001) than model 2 (model 1 plus LVI) (AUC = 0.685, P = .009) (Table).

Conclusions: Diffuse involvement, advanced stage, and moderate to poor differentiation are independent prognostic factors of worse outcome in gallbladder adenocarcinoma. Our risk-stratification model (disease extent, T stage, and tumor grade) provides substantial prediction on outcome.

**The Impact of Pre-diagnostic Diabetic Status on the Survival of Patients With Pancreatic Ductal Adenocarcinoma**

(Poster No. 2)

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**Context:** Diabetes mellitus (DM) is a risk factor for pancreatic cancer, but its impact on postoperative outcomes remains controversial. It is unknown if prediagnostic diabetic status affects patient survival in tumors with any specific pathologic features.

**Design:** We retrospectively identified 507 patients with pancreatic ductal adenocarcinoma (PDAC) between January 2008 and December 2018 at Cleveland Clinic Foundation. Clinical data and pathologic features were compared between patients with and without DM prior to the diagnosis. Statistical analysis was performed using IBM SPSS Statistics 19. Overall survival was compared in DM and non-DM groups using Kaplan-Meier analysis in XLSTAT. P < .05 was statistically significant.

Results: In the cohort, 187 patients were diagnosed with DM prediagnostically and 320 patients stayed nondiabetic status prior to the diagnosis. Patients with DM tended to demonstrate worse overall survival (P = .06). In male patients, DM tended to negatively affect patients’ overall survival (P = .06). Among the pathologic features, DM status was significantly related to a worse survival in patients with poorly differentiated carcinoma (P = .03), lymphovascular invasion (P = .02), or lymph node metastasis (P = .045). In patients with pT1 tumors defined by AJCC 7th or AJCC 8th edition, DM was significantly associated with a worse survival (AJCC 7th, P < .001; AJCC 8th, P = .04). In patients with AJCC 8th T2 tumor, there was a tendency that DM negatively affected patients’ survival rate (P = .06) (Table).

Conclusions: Prediagnostic DM status is associated with worse survival in PDAC patients with poorly differentiated carcinoma, lymphovascular invasion, or lymph node metastasis. DM tends to negatively affect survival rate in male patients and in patients with pT1 and pT2 tumors (AJCC 8th).
Clinical pathological characteristics and associations of traditional serrated adenoma

(Poster No. 3)

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Context: Traditional serrated adenomas (TSAs) are the rarest of all the serrated polyps with distinctive endoscopically (“pine cone-like”) and histologic features. However, TSAs are underdiagnosed and the assessment of dysplasia in TSA is disputed. We retrospectively evaluated 62 TSAs to assess their clinicopathologic characteristics and associations.

Design: A review of our database from 2014 through 2020 found 62 TSAs. We retrospectively evaluated 62 TSAs to assess their clinicopathologic characteristics and associations.

Results: Most cases (59 of 62) were incidentally detected on screening colonoscopies. Polyps were 3-40 mm (mean, 26 mm). TSAs >10 mm were cold or hot snared and showed characteristic endoscopically (“pine cone appearance.” Fifteen patients (24%) had solitary TSA and the rest showed other conventional adenomas and/or SSAs (76%). The majority (85%) of TSAs were in the distal colon: sigmoid (21%), rectosigmoid (4%), and rectum (28%). All cases showed typical histologic features including eccrine crypt formation, slitlike saccations, elongated pine cone–like nuclei, and eosinophilic cytoplasm. Only 1 of 62 cases (1.6%) showed high-grade dysplasia.

Conclusions: TSAs are incidentally detected on screening colonoscopy and are often associated with other conventional polyps than solitary TSA. Most TSAs are located in the sigmoid colon and rectum. High-grade dysplasia appears to be quite rare, even in large TSAs. Multicenter long-term studies are needed to evaluate the true risk of colorectal carcinoma in these unique polyps.

Comparative analysis of intra-cholecystic “Pyloric gland adenoma” with luminal counterparts

(Poster No. 4)

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Context: Pyloric gland adenoma (PGA) is a rare neoplasm of the gastric mucosa, involved in the gallbladder (GB), main pancreatic duct, and duodenum. Intracholecystic lesions of >1 cm are identified as intracholecystic papillary-tubular neoplasms (ICPNs), and lesions <1 cm are referred to pyloric gland hyperplasia/metaplasia. Our study aims to compare groups of PGA/metaplasia (<1 cm) in the GB and the luminal counterpart.

Design: A retrospective study included cases of PGA or metaplasia at Mount Sinai West, New York, from January 1, 2000, to June 30, 2020. PGA cases in GB, >1 cm; ICPNs were excluded. Clinicopathologic parameters were analyzed, including age, gender, location of lesion, dysplasia, and the number of lesions (1/>1).

Results: Forty-five cases were included. Among them, 14 cases were from both GB and duodenum, and 13 were from the stomach only. The mean age of presentation was 73 years. The mean age of GB, stomach, and duodenum groups was 59, 85, and 70 years, respectively. Chronic cholecystitis was present in 85% of cases. All cases involving the GB were >0.3 cm, with 6 cases >0.5 cm and another 4 cases 0.3–0.5 cm.

Conclusions: According to our study, the terminology of “PGA” in the GB could aptly describe the lesions that are purely composed of pyloric glands in the GB, which may represent a true benign tumor rather than an inflammatory metaplastic process. “Adenoma” could be applied for mixed lesions, with overlapping morphology composed of an admixture of pancreaticobiliary and pyloric type, based on size or molecular signature.

Clinicopathologic features of PGA

(Table)

<table>
<thead>
<tr>
<th>Clinicopathologic Features</th>
<th>Gallbladder (n = 14)</th>
<th>Stomach (n = 13)</th>
<th>Duodenum (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, F:M</td>
<td>9:5</td>
<td>5:8</td>
<td>10:4</td>
</tr>
<tr>
<td>Age, median, y</td>
<td>59</td>
<td>85</td>
<td>70</td>
</tr>
<tr>
<td>No. of multiple lesions</td>
<td>1</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>No. with dysplasia</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

Gastric Amyloidosis Presenting as Gastrointestinal Bleeding: Case Report and Concise Review

(Poster No. 5)

Catherine E. Turner, MS (cet288@health.missouri.edu); Deepthi Rao, MD; Feng Yin, MD. Department of Pathology and Anatomic Sciences, University of Missouri–Columbia.

Amyloidosis defines a group of disorders characterized by extracellular protein deposition, such as AL, AA, ATTR, and AβM proteins. Clinical manifestations depend on the biochemical composition and site of deposition. Common sites include kidney, heart, and liver, but gastrointestinal amyloidosis is rare. The overall incidence of primary amyloidosis is 9 new cases per million persons, and involvement of gastrointestinal tract is exceptionally rare, with only an incidence of less than 1 per million. A 62-year-old man with past medical history of diverticulitis and colon resection presented to his physician with blood per rectum, unintentional weight loss, nausea, and vomiting for 1 month. He underwent esophagogastroduodenoscopy and colonoscopy. Biopsies of stomach and colon showed waxy, pale eosinophilic extracellular aggregates on microscopy (Figure 1.5, A), suggestive of amyloidosis, confirmed by Congo red staining (Figure 1.5, B) with apple-green birefringence in polarized light (Figure 1.5, C). These amyloid fibrils had a nonbranching, antiparallel twisted, β-pleated sheet configuration. Additional organ involvement was not found with imaging. This patient had no previous medical history of chronic inflammation, hematologic malignancy, renal disease, or family history, and the absence of risk factors suggested primary amyloidosis.

The patient’s k:α ratio and serum electrophoresis were unremarkable, proving primary amyloidosis. To our knowledge, this was the first ever reported case of gastric amyloidosis at University Hospital (Columbia, Missouri). Recognizing amyloidosis in a differential diagnosis is important, as early recognition of this disorder could prevent further complications for the patient, shorten time to diagnosis, and explore management options in an efficient manner.
Langerhans Cell Histiocytosis in Lower Gastrointestinal Tract Polyps With BRAF Testing

(Poster No. 7)

Eric Ollila, MD1 (eollila@uabmc.edu); Abzar Alghamdi, MD2; Sameer Al Diffalha, MD3; Samuel Borak, MD4.1 Department of Pathology, University of Alabama at Birmingham; 2Department of Pathology, University of Alabama at Birmingham, Montgomery. Langerhans cell histiocytosis (LCH) is a group of idiopathic disorders characterized by an abnormal proliferation of dendritic mononuclear cells that mostly involves the skin and bones. Involvement of the gastrointestinal tract by LCH is exceedingly rare, and few cases have been reported. Here, we present 2 cases of LCH with gastrointestinal involvement and BRAF testing. The first case involves a 51-year-old man who presented with intermittent abdominal pain. Five polyps were found on colonoscopy. Histopathologic examination revealed an infiltrate in the lamina propria consisting of small to intermediate-sized cells with variably irregular and focally reniform nuclei, with occasional nuclear grooves and mild amount of cytoplasm (Figure 1.7, A and B). Occasional mitotic figures and scattered eosinophils were present. These cells were immunohistochemically reactive with CD1a (Figure 1.7, C), S-100 (Figure 1.7, D), and CD43. BRAF testing was positive for the V600E mutation. The second case involves a 76-year-old woman who presented with a history of anemia and multiple episodes of C. difficile colitis that resulted in gastrointestinal distress and weight loss. Two polyps were found on colonoscopy. Histopathologic examination revealed active inflammation involving surface epithelium and underlying crypts surrounded by prominent histocytes. These cells were reactive with S-100 and CD1a. BRAF testing results were negative. Although involvement of the gastrointestinal tract by LCH is rare, it should be considered in the differential diagnosis when a histiocytic proliferation is present. To our knowledge, these are the first cases of lower gastrointestinal tract involvement in polyps by LCH with reported BRAF testing, which may prove helpful in diagnosis and treatment.

Disparity Between Endoscopic Findings and Graft-Versus-Host Disease Following Allogeneic Hematopoietic Stem Cell Transplantation

(Poster No. 6)

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Context: Gastrointestinal graft-versus-host disease (GVHD) poses a significant clinical and pathologic challenge following allogeneic hematopoietic transplantation. GVHD diagnosis requires clinical, laboratory, and histopathologic confirmation. Endoscopy has been fundamental in ensuring accurate diagnoses in numerous entities; however, an established correlation between endoscopic findings and GVHD remains undetermined.

Design: The endoscopic findings of 185 histopathologically confirmed GVHD and 11 viral enterocolitis cases were reviewed retrospectively.

Results: Among the 185 GVHD cases, 146 were grade 1, 26 were grade 2, 8 were grade 3, and 5 were grade 4. In the grade 1 cases, endoscopy was “normal” in 111 (76%) and abnormal in 35 (24%). Among the grade 2 cases, 21 were endoscopically “normal” (81%) whereas 5 appeared focally abnormal (19%). In the grade 3 cases, 6 (75%) were still considered “normal” and 2 abnormal (25%). Lastly, in the grade 4 cases a “normal” endoscopy was documented for 3 (60%), whereas an abnormal endoscopy was confirmed in only 2 (40%). Overall, endoscopic examination was “normal” in 141 of 185 GVHD cases (76%) and abnormal in only 44 (24%). Notably, in all 11 viral enterocolitis cases (7 cytomegalovirus and 4 adenovirus cases in which GVHD was clinically suspected), endoscopy was “normal.”

Conclusions: To summarize, neither a satisfactory endoscopic sensitivity nor specificity was observed in the 185 GVHD cases; therefore, no correlation can be established between endoscopic findings and histopathologic GVHD. Furthermore, endoscopic abnormalities are not only restricted to GVHD, but are also seen with infection, drug, and chemical-related injuries. Astute histopathologic inspection and ancillary tests remain the gold standard for discerning GVHD from its various mimickers.

Expression of Enhancer of Zeste Homolog 2 (EZH2) Protein and Its Association With Intracellular Signaling Molecules MYC, P-MAPK, and P-STAT3 in Colorectal Cancer

(Poster No. 8)

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Context: EZH2 is a histone methyltransferase associated with a poorer prognosis in several cancers. The regulation of EZH2 in colorectal cancer is unknown. Here we investigated EZH2 expression in colorectal cancer and its association with MYC, p-MAPK, and p-STAT3.

Design: One hundred fourteen colorectal cancer cases were collected. Immunohistochemical staining for EZH2, MYC, p-MAPK, and p-STAT3, potential regulators of EZH2, were performed using Fisher exact test and Pearson correlation coefficient by Graphpad Prism (San Diego, California).

Results: Eighty-six of 108 cases (79.6%) overexpressed EZH2. EZH2 overexpression was defined if ≥60% neoplastic cells exhibited moderate to strong staining. MYC was positive if ≥40% neoplastic cells displayed moderate to strong staining. Statistical analysis was performed using Fisher exact test and Pearson correlation coefficient by Graphpad Prism (San Diego, California).

Results: Eighty-six of 108 cases (79.6%) overexpressed EZH2. EZH2 overexpression was defined if ≥60% neoplastic cells exhibited moderate to strong staining. MYC was positive if ≥40% neoplastic cells displayed moderate to strong staining. Statistical analysis was performed using Fisher exact test and Pearson correlation coefficient by Graphpad Prism (San Diego, California).
three of 103 cases (61.2%) expressed MYC, whereas very few expressed p-MAPK (2 of 104) or p-STAT3 (1 of 106). Among EZH2-overexpressed cases, 59 of 82 (72%) coexpressed MYC. EZH2 expression correlated positively with MYC (P < .001) (Figure 1.8, C). MYC also showed a positive correlation with Ki-67 (P < .01) (Figure 1.8, D).

Conclusions: EZH2 overexpression is associated with more aggressive behavior in colorectal cancer, as indicated by the correlation with Ki-67 and tumor grade. Furthermore, MYC-related signaling, not p-MAPK or p-STAT3, might be involved in EZH2 regulation and correlated with tumor progression. Therefore, EZH2 and MYC could serve as potential prognostic and therapeutic targets for colorectal cancer.

Racial and Ethnic Disparities in Molecular Abnormalities and Pathological Findings of Colorectal Carcinoma

(Poster No. 9)

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Context: Although the national incidence of colorectal cancer (CRC) has decreased in recent years, it remains the fourth most common cancer in the United States. The objective of this study is to identify if there is a statistically significant difference in the pathologic and molecular findings of CRC by race and ethnicity at our institution.

Design: Patients with CRC resected from 2016 to 2019 were divided into 4 groups: white/non-Hispanic or Latino (N-HL), black/N-HL, Asian/N-HL, and other/N-HL. Risk factors, tumor location, grade, stage, size, invasion, and mutations were compared.

Results: A total of 138 patients were included. A higher percentage of the tumors were located in the rectum in Asians/N-HL and others/N-HL, compared to whites/N-HL and blacks/N-HL. Twenty-two patients (15.9%) had young-onset CRC. Most of the CRCs were microsatellite stable. Microsatellite-unstable cancer (50–59). Most cases were diagnosed at early stages in blacks/N-HL and whites/N-HL, whereas 36.4% of group 1 patients and 63.9% of group 2 patients were on a nonsteroidal anti-inflammatory drug (NSAID) prior to biopsy (P < .01), whereas 36.4% of group 1 patients and 63.9% of group 2 patients received PCR screening via rectosigmoidoscopy.

Regional Differences in Clinical Management of Patients With a Diagnosis of Chronic Active or Inactive Gastritis and Negative Helicobacter Immunohistochemical Stain

(Poster No. 10)

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Context: A preliminary study by our group suggested for patients with biopsy diagnosis of active or inactive chronic gastritis (CG) with a pattern that is highly suggestive of Helicobacter pylori (HP) infection but negative HP immunohistochemistry (IHC), a comment raising the possibility of HP infection can change the clinical management.

Regional Difference in Patient Management After Diagnosis of CG With Negative HP IHC

<table>
<thead>
<tr>
<th>Institution</th>
<th>Group 1 (Midwest or Northeast)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, No.</td>
<td>78</td>
<td>45</td>
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<tr>
<td>Mean age, y</td>
<td>50.6</td>
<td>61.6</td>
</tr>
<tr>
<td>Gender, M/F</td>
<td>41:37</td>
<td>18:27</td>
</tr>
<tr>
<td>On NSAID prior to biopsy, %</td>
<td>19.2</td>
<td>36.8</td>
</tr>
<tr>
<td>On PPI prior to biopsy, %</td>
<td>36.4</td>
<td>63.9</td>
</tr>
<tr>
<td>History of H pylori, %</td>
<td>47.4</td>
<td>21.6</td>
</tr>
<tr>
<td>Most common endoscopy finding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythematous mucosa, %</td>
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<td>42.2</td>
</tr>
<tr>
<td>Normal, %</td>
<td>19.2</td>
<td>20.0</td>
</tr>
<tr>
<td>Erosion/ulcer, %</td>
<td>19.2</td>
<td>6.7</td>
</tr>
<tr>
<td>Patients who received treatment, %</td>
<td>48.7</td>
<td>11.1</td>
</tr>
<tr>
<td>Patients who received treatment, %</td>
<td>14.1</td>
<td>6.7</td>
</tr>
<tr>
<td>Patients received fecal antigen test, %</td>
<td>15.4</td>
<td>13.9</td>
</tr>
</tbody>
</table>

Design: We conducted a retrospective comparative study of patients from an academic center in the South (group 1) to 3 centers in the Midwest/Northeast (group 2), all with a diagnosis of CG with negative HP IHC.

Results: A total of 19.2% of group 1 patients and 56.8% of group 2 patients were on a nonsteroidal anti-inflammatory drug (NSAID) prior to biopsy (P < .01), whereas 36.4% of group 1 patients and 63.9% of group 2 patients received PCR screening via rectosigmoidoscopy.
group 2 patients were on a proton pump inhibitor (PPI) prior to biopsy (P < .01). Group 1 patients more frequently had HP history (47.4% versus 21.6%, P < .01). After the diagnosis, 48.7% of group 1 and 11.1% of group 2 received treatment (P < .001). Of those treated, 14.1% and 6.7% received HP treatment, respectively (triple or quadruple therapy; P > .05). In cases with a comment in the pathology report raising the possibility of HP, patients from the South received HP treatment more often compared with cases without a comment (25.6% versus 2.6%, P < .01). This trend is similar for the Midwest/Northeast institutions (14.3% versus 0%, P = .06) (Table).

Conclusions: Our data suggest a regional difference in patient management after diagnosis of CG with negative HP IHC in that patients from the South were more frequently treated. A comment in the pathology report describing HP-pattern gastritis despite negative HP IHC increased HP treatment, especially in the South.

Colonic Mixed Neuroendocrine Non-neuroendocrine Neoplasm: A Rare Malignant Neoplasm

(Poster No. 11)

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Colonic mixed neuroendocrine-non-neuroendocrine neoplasms are a rare entity. The term has evolved with the World Health Organization adopting the current nomenclature in 2017. We present a case of a 59-year-old woman who presented with acute abdomen and a perforated viscus. Exploratory laparotomy revealed 2 right colon masses with tumors involving the peritoneum and pericolic fat. Histologic evaluation of the tumor identified 2 components, one forming 40%, consisting of sheets of poorly differentiated small hyperchromatic cells with conspicuous nuclei, admixed with a conventional colonic adenocarcinoma; both involved the full thickness of bowel wall and invaded into peri-colonic fibroadipose tissue. Strong positive staining of immunohistochemical markers synaptophysin, chromogranin, CD56, cytokeratin AE1/AE3, cytokeratin 20, and with focal positivity for CDX2 and negativity for TTF-1, was identified in the neuroendocrine component, whereas the conventional adenocarcinoma was positive only for Ber-EP4, CDX2, cytokeratin AE1/AE3, and cytokeratin 20. Additionally, Ki-67 showed 100% positive staining within the entire tumor. Subsequently, the patient developed seizures associated with brain metastasis and expired 2 months later. Mixed neuroendocrine-non-neuroendocrine neoplasms with a poorly differentiated neuroendocrine component are associated with an extremely poor prognosis with an average of 4.5-month survival in patients with stage 4. Mixed neuroendocrine-non-neuroendocrine neoplasm is a rare entity that requires diligent histologic evaluation to identify the neuroendocrine component histologically and immunohistochemically. Although the current criteria suggest a minimal 30% portion of each component, further clinical and histopathologic studies are required to validate these measures and establish appropriate therapy regimens.

Validation of the Current Histology Grading System in Appendiceal Goblet Cell Adenocarcinomas With Advanced Pathologic Stage

(Poster No. 12)

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Context: Appendiceal goblet cell adenocarcinoma (GCA) is a unique tumor composed of gobletlike cells. The 2019 World Health Organization criteria recommend a 3-tiered grading system based on proportion of low-grade and high-grade patterns. We aim to validate this grading schema with correlation to tumor stage, immunohistochemistry, and patient survival.

Design: All cases of GCA staged pT3 and above were retrieved (2005–2020). P values <.05 were considered significant.

Results: Our cohort consisted of 13 males and 12 females with median age of 62.5 years. Pathologically, 13 were pT3 and 12 were pT4, with 9 cases (36%) demonstrating lymph node and/or distant metastasis. Clinically, 15 (60%) were sites in more than one organ: stage II, 4 (16%) stage III, and 6 (24%) stage IV. Using the 3-tier grading system, 10 (40%) were G1, 7 (28%) G2, and 8 (32%) G3. Immunohistochemically, all cases were mismatch repair proficient. Loss of nuclear SMAD4 expression and occasional p53 expression occurred at equally low frequencies (n = 3, 12% each). Seven cases (28%) showed nuclear β-catenin positivity. The Ki-67 index (range, 1%–80%) were tiered into low (<5%, n = 8), intermediate (5%–20%, n = 10), and high (>20%, n = 7). Statistically, the histologic grade correlated with clinical stage (P < .001), but not with sex, age, Ki-67 index, or nuclear SMAD4/p53/β-catenin abnormalities. The histologic grade, T stage, lymph node, and distant metastases were associated with reduced survival (P < .05).

Conclusions: The current grading system for GCA correlated well with clinical stage and disease outcomes. A small percentage of GCA demonstrated nuclear SMAD4, p53, or β-catenin abnormalities, which did not correlate significantly with histologic grade, tumor stage, or patient survival.

Primary Pancreatic Signet Ring Cell Carcinoma in Patient With Lynch Syndrome

(Poster No. 13)

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Primary pancreatic signet ring cell carcinoma (PPS RCC) is a rare histologic variant of pancreatic ductal adenocarcinoma. We report a case of PPS RCC in a 52-year-old woman with a confirmed personal history of hereditary nonpolyposis colorectal cancer with MSH2 germline mutation. The patient had abdominal pain, and computed tomography showed a pancreatic body mass. Ultrasound-guided fine-needle aspiration (FNA) biopsy of the pancreas was nonconclusive. Cross-examination of the patient's distal pancreatectectomy specimen. Gross examination revealed a tan-white, poorly demarcated and unencapsulated mass located at the body, measuring 1.9 × 1.4 × 1.0 cm, and obstructing the pancreatic duct. Hematoxylin-eosin sections showed a polyoid mass occupying the pancreatic duct consisting of a predominant signet ring cell carcinoma. There was also some well-differentiated ductal adenocarcinoma component (20%). Because of the tumor obstruction of the pancreatic duct, distal pancreas showed extensive chronic pancreatitis. Immunostains showed the loss of MSH2 and MSH6 in the signet ring cell carcinoma with proper positive background staining. The patient did not have signet ring cell carcinoma in other parts of the gastrointestinal (GI) tract. Therefore, this is a primary signet ring cell carcinoma in a Lynch syndrome patient. The most common signet ring carcinoma site is the stomach and occasionally can be found in other parts of the GI tract, but pancreas is a rare place for the primary signet ring cell carcinoma. Lynch syndrome tends to be associated with poorly differentiated carcinoma, including signet ring cell carcinoma in colon, but has not been reported in pancreas. It imposes a diagnostic challenge for FNA cytology and frozen section if not aware of this rare variant.

Appendiceal Mucinous Neoplasm: Reflection on 20 Years of Experience at a Single Institution

(Poster No. 14)

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Context: During the past 3 decades, multiple diagnostic terms have been applied to the entity we now call low-grade or high-grade appendiceal mucinous neoplasm (LAMN/HAMN). We undertook this study to understand the rate of adoption of World Health Organization guidelines regarding the reporting of this entity in a community practice setting.

Design: We conducted a retrospective study of all the neoplastic appendiceal cases in a community hospital in Cleveland from 1999 to 2019. The cases were reviewed by 3 pathologists, including 1 gastrointestinal pathologist. In the cases of appendiceal mucinous neoplasm, we compared the terminology used at the time of diagnosis with contemporary nomenclature and grading.

Results: A total of 32 patients with appendiceal mucinous neoplasm were identified (LAMN [n = 3] and HAMN [n = 2]). 13 of these since 2010. Twenty-six of the cases (81.2%) would now receive another name, and of these, there were diagnostic discrepancies in 5 cases (19.2%) (Table). Anachronistic terminology continued to be used at least until 2019 (7 of 13 cases; 53.8%). None of these changes would have had an impact on the further management or clinical follow-up of the patients.

Conclusions: Despite frequent updates and consensus guidelines for pathologic assessment of appendiceal mucinous lesions, in the past 2 decades there has been considerable confusion around how these entities should be named and graded. Our findings suggest that...
Abbreviation: WHO, World Health Organization.

### Discrepancies in Terminology Between Original Pathology Report and WHO 2010 Recommendations

<table>
<thead>
<tr>
<th>Original Diagnosis</th>
<th>Diagnosis per WHO 2010</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucinous cystadenoma, mucocoele, and appendiceal mucinous tumor of uncertain malignant potential</td>
<td>Low-grade mucinous appendiceal neoplasm</td>
<td>21 (7 cases 65.6% since 2010)</td>
<td></td>
</tr>
<tr>
<td>Invasive mucinous appendiceal adenocarcinoma</td>
<td>Low-grade mucinous appendiceal neoplasm</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Low-grade mucinous appendiceal neoplasm</td>
<td>High-grade mucinous appendiceal neoplasm</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Tubular adenoma</td>
<td>Low-grade mucinous appendiceal neoplasm</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Invasive mucinous appendiceal adenocarcinoma</td>
<td>Invasive mucinous appendiceal adenocarcinoma and high-grade mucinous appendiceal neoplasm</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Invasive adenocarcinoma and goblet cell carcinoid</td>
<td>Goblet cell adenocarcinoma and low-grade mucinous appendiceal neoplasm</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

Abbreviation: WHO, World Health Organization.

**Cokeromyces recurvatus Incidentally Found in a Patient With Gastric Outlet Obstruction**

(Poster No. 15)

Bitania Wondimu, MD (bmw35@uw.edu); Benjamin Bradley, MD, PhD; Joshua Lieberman, MD, PhD; Seth Cohen, MD, MSc; Lynda Bui, MLS; Deepti Reddi, MD. Department of Pathology, University of Washington Medical Center, Seattle.

Isolation of *Cokeromyces recurvatus*, a dimorphic fungus in Zygomycete family, is equivocal because it is uncertain whether the organism is a pathogen or a tissue contaminant/colonizer. We report a case of *C recurvatus* present in a circumferential duodenal lesion. The patient is a 64-year-old man with medical history notable only for heavy consumption of edible marijuana, admitted with a 3-week history of left upper quadrant abdominal pain. Computerized tomography scan identified duodenitis with significant gastric outlet obstruction, confirmed by a partially obstructing nonbleeding duodenal ulcer on upper endoscopy (Figure 1.15, A). The histology showed variably sized spherical structures with bubbly internal contents and no nuclei, representing putative endospores were observed within the larger structures and in the exudate (Figure 1.15, B). Based on the histology, the differential diagnosis included *Coccidioides, Emmonsia, or Chrysosporium* species. Additionally, gastric biopsies revealed concurrent *Helicobacter pylori* gastritis. The fungus was identified as *C recurvatus* by broad-range fungal polymerase chain reaction performed on formalin-fixed, paraffin-embedded biopsy tissue, as well as morphology, DNA sequencing of the isolate, and cultures (Figure 1.15, C and D). The fungus was susceptible to a wide variety of antifungals; however, in the context of the *H pylori* infection, the patient was treated with amoxicillin and clarithromycin with improvement in his symptoms before hospital discharge. In literature review, 2 cases of *C recurvatus* were isolated from the colon in myeloma patients; this case highlights the unique clinical presentation in the small bowel in a patient with no underlying medical conditions.

**Metastatic Colonic Adenocarcinoma in a 12-Year-Old Female**

(Poster No. 16)

Sepideh Madahian, MD (Sepideh.madahian@umassmemorial.org); Richard Judelson, MD; Salwa Khedr, MD; Xiaoqin Zhu, MD. Department of Pathology, UMass Memorial Health Care, Worcester, Massachusetts.

Pediatric colorectal carcinoma is rare, comprising approximately 1% of pediatric neoplasms. Nonspecific symptoms and low awareness of the disease usually delays diagnosis, resulting in poor prognosis. We report a rare case of a 12-year-old female who presented with acute abdominal pain, bowel habit change, weight loss, and anemia. Abdominal computed tomography (CT) scan showed a 4.4-cm mass in the ascending colon, heterogeneous mass in the second/third portion of the duodenum, multiple liver hypodensities, stranding, and soft tissue thickening within the lower abdomen and scattered peritoneal nodules. During endoscopic ultrasound examination, a mass lesion was identified in pancreatic uncinate. Fine-needle aspiration of the pancreatic mass showed tumor cells positive for CK20 and CDX2 and negative for CK7 and HNF1b, most compatible with metastasis from a lower gastrointestinal primary. The colonic mass biopsy showed adenocarcinoma, arising in a background of tubular adenoma with high-grade dysplasia, positive for CK20 and CDX2 and negative for CK7 and HNF1b, consistent with colonic primary. Immunohistochemistry for DNA mismatch repair proteins was negative. Next-generation sequencing (NGS) detected *TP53* mutation. Gene copy number analysis showed gain (6 to 9 copies) of the *KRAS* (12p12.1) oncogene and deletion of the *TP53* (17q13.1) tumor suppressor. She started chemotherapy protocol (FOLFOXIRI + Bevacizumab) with interval improvement in disease on abdominal/pelvis CT scan. Because of nonspecific symptoms of pediatric colorectal carcinoma, clinicians should have a high index of suspicion to avoid diagnosis at an advanced disease stage with poor prognosis and outcomes.

**Recurrent Mucosal Schwann Cell Hamartoma: A 10-Year Follow-up Case Study**

(Poster No. 17)

Kevin Kuan, MD (kkuan@montefiore.org); Amarpreet Bhalla, MD. Department of Pathology, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, New York.

Mucosal Schwann cell hamartoma (MSCH) of the gastrointestinal tract is an uncommon entity that is usually an incidental finding from routine colonoscopy. It is a benign mesenchymal lesion that consists of poorly circumscribed spindle cells proliferation in the lamina propria. Hitherto, all the available literature suggests that the occurrence of MSCH is incidental, sporadic, and nonsyndromic, and that polyposity is curative. We present the first case of recurrent MSCH with a 10-year follow-up period. The patient is a 50-year-old woman who had a history of hypertension, obesity, and pituitary adenoma, Cushing

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syndrome, and Wolf-Parkinson-White syndrome status post ablation. The family history was noncontributory. The initial diagnosis of MSCH was made from colonoscopy procedure performed for abdominal pain. Subsequently, she has had 4 additional follow-up colonoscopy procedures and a total of 20 MSCH polyps were identified. These polyps were located from transverse to rectal sigmoid colon. They were all small sessile lesions (Figure 1.17, A) that range from 4 to 7 millimeters. On histologic examination, these polyps were composed of bland spindle cells within the lamina propria (Figure 1.17, B and C). Immunohistochemically, they were positive for S100 (Figure 1.17, D) and CD56, and negative for EMA, GFAP, CD117, chromogranin, and CD34. Although it is uncertain that the combination of the patient’s unusual clinical presentation is part of syndromic manifestation, the recurrence of multiple MSCH warrants further testing and close follow-up.

Recurrence of Granular Cell Tumor in the Esophagus With Multiple New Liver Lesions: Multifocal Disease Versus Metastasis?

(Author: Ayaz G. Kalsekar, MD (agkalsekar@houstonmethodist.org); Ahmed Shehabeldin, MD; Charlotte F. Kim, MD; Erin N. Vicknair, MD, Mary R. Schwartz, MD, Jae Y. Ro, MD, PhD. Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Texas)

Granular cell tumor (GCT) is an uncommon soft tissue tumor derived from Schwann cells that usually behaves in a benign fashion. GCT most commonly arises in skin, tongue, and gastrointestinal (GI) tract, with esophagus as the most common GI site. Hepatobiliary involvement can occur, although it is rare. Multifocal GCTs occur in about 10% of the cases; however, malignant GCTs are rare, accounting for approximately 0.5% to 2% of all GCTs. We present a 67-year-old woman who underwent a complete endoscopic resection of an esophageal GCT (Figure 1.18, A). Four years later, she presented with multiple liver lesions and a mass in an esophageal diverticulum that were biopsied and diagnosed as GCTs. Histologic examination of the previous resection specimen and the subsequent esophageal and liver biopsies (Figure 1.18, B) showed GCT with benign features (well demarcated, no nuclear atypia or tumor necrosis, and a mitotic count of <1/10 high-power fields). Immunohistochemical stains for S-100 (Figure 1.18, C) and CD68 (Figure 1.18, D) were immunoreactive in all the lesions, supportive of the diagnosis of GCT. Based on the benign histopathologic features, the presence of multiple liver lesions, and the rare occurrence of primary GCT in the hepatobiliary system, the liver lesions were interpreted as benign metastasizing GCT. We believe that the initial endoscopic resection may have inadvertently created iatrogenic spread of GCT via lymphovascular spaces to the liver. This phenomenon has been described in other tumors including benign metastasizing leiomyoma of uterus, giant cell tumor of bone, and pleomorphic adenoma of salivary glands.
pancreatitis (Figure 1.19, D). The patient recovered well from the surgery with no evidence of recurrence or metastasis 4 months later. Overall, our findings suggest that gangliocytic parangangioma, as well as other peripancreatic tumors, can be a rare cause of groove pancreatitis that mimics malignancies.

**Malignant Gastrointestinal Neuroectodermal Tumor With EWSR1 Gene Amplification: A Rare Case of a Rare Entity Lacking the Signature Gene Translocation**

(Poster No. 20)

**Omer A. Saeed, MBBS; Christopher Quinn, MD; Gail H. Vance, MD; Chen Zhang, MD, PhD; Departments of 1Pathology and Laboratory Medicine and 2Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis.

Malignant gastrointestinal neuroectodermal tumor (MGNECT) is a rare aggressive neoplasm with a dismal prognosis. There are fewer than 100 cases reported in the literature and most of them demonstrate translocation involving an EWSR1 gene with fusion partners of either ATFI or CREBI. Here we report a case of MGNECT lacking a EWSR1 gene translocation or rearrangement. The patient was a 43-year-old man who presented with symptoms of intestinal obstruction. An abdominal computed tomography scan showed findings compatible with proximal small bowel obstruction secondary to an enhancing mass measuring 3.9 cm and a left hepatic lobe mass measuring 4.6 cm. Exploratory laparotomy with small bowel resection and partial hepatectomy was performed. Grossly multiple submucosal masses, up to 3.5 cm, were identified in the small bowel, in addition to a 6-cm liver mass. Histologic examination showed a proliferation of malignant epithelioid and spindle cell cells with open chromatin and prominent nucleoli. The neoplastic cells were positive for SOX-10, S100, and synaptophysin, and focally positive for smooth muscle antigen. Stains for CD117, DOG-1, HMBS, Melan-A, and cytokeratin AE1/AE3 were negative. Fluorescence in situ hybridization testing with an EWSR1 break-apart probe showed EWSR1 gene amplification with no evidence of rearrangement. Although the current World Health Organization classification of gastrointestinal tumors indicates translocations involving EWSR1 gene as essential for the diagnosis of MGNECT, our case shows typical clinical, histologic, and immunohistochemical features of MGNECT, with unusual molecular findings involving the EWSR1 gene. To our knowledge, only one case of MGNECT with EWSR1 gene amplification has been previously reported.

**Differences in Vascular Patterns and Reticulin Staining Aid the Distinction Between Hepatoid Adenocarcinoma and Metastatic Hepatocellular Carcinoma**

(Poster No. 21)

**Yan Huang, MD; Carlos Castrodad-Rodriguez, MD; Kevin Kuan, MD; Preeti Malik, MBBS, MPH; Sun Chung, MD; Liang Liu, MD; Nicole Panarelli, MD; Amarnpreet Bhalla, MD. 1Department of Pathology, Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, New York; 2Department of Neurology, Harvard Medical School/Massachusetts General Hospital, Boston.

**Context:** Hepatoid adenocarcinoma (HAC) is a challenging diagnosis and is difficult to differentiate from metastatic hepatocellular carcinoma (mHCC). There is significant overlap in radiologic, serologic, and immunohistochemical profiles of the 2 tumors. Primary hepatocellular carcinomas often display reduced reticulin framework and diffuse positivity for CD34 within sinusoids. We hypothesized that these features would be retained in mHCC, but absent in HAC.

**Design:** The study included previously diagnosed mHCCs and HACs in our institution from 2018 to 2020. The clinical, radiologic, and follow-up data were documented. The hematoxylin–eosin and immunostained slides were reviewed. Reticulin and CD34 stains were performed. The patterns of both stains were analyzed in the 2 groups (Table).

**Results:** Six mHCCs and 5 HACs were identified. The architectural pattern in the mHCCs was solid, trabecular, and pseudoglandular. Reticulin stain outlined large vessels within the tumor but was absent amidst the tumor tissue. CD34 immunostain showed haphazardly arranged stromal blood vessels but lacked regular sinusoidal pattern.

**Conclusions:** Utilization of reticulin and CD34 stains is an economical and simple method, available in most laboratories, to differentiate mHCC from HAC. Retained delicate reticulin framework and organized sinusoidal CD34 staining are characteristic of mHCC but absent in HAC.

**Comparative Evaluation of Metastatic Hepatocellular Carcinoma and Hepatoid Adenocarcinoma**

<table>
<thead>
<tr>
<th></th>
<th>Metastatic Hepatocellular Carcinoma</th>
<th>Hepatoid Adenocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Age, y</td>
<td>50–93</td>
<td>40–76</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>5/1</td>
<td>3/2</td>
</tr>
<tr>
<td>Tumor side evaluated</td>
<td>Bone (4), retroperitoneal lymph node (1), lung (1)</td>
<td>Stomach (2), liver (2), adrenal glands (1)</td>
</tr>
<tr>
<td>Presumed site of primary tumor</td>
<td>Liver</td>
<td>Stomach, lung</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>4.3–9.1 cm</td>
<td>0.8–7.0 cm</td>
</tr>
<tr>
<td>Lymph node enlargement</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Arginase</td>
<td>Positive: 5; not performed: 1</td>
<td>Positive: 3; not performed: 2</td>
</tr>
<tr>
<td>HepPar</td>
<td>Positive: 4; negative: 2</td>
<td>Positive: 2; negative: 1; not performed: 1</td>
</tr>
<tr>
<td>Glypicin</td>
<td>Positive: 4; not performed: 2</td>
<td>Positive: 2; negative: 1; not performed: 2</td>
</tr>
<tr>
<td>TTF-1</td>
<td>Positive: 1; negative: 1</td>
<td>Positive: 2; negative: 1; not performed: 2</td>
</tr>
<tr>
<td>MOC-31</td>
<td>Not performed: 6</td>
<td>Positive: 3; not performed: 2</td>
</tr>
<tr>
<td>CDX-2</td>
<td>Not performed: 6</td>
<td>Positive: 2; negative: 1; not performed: 2</td>
</tr>
<tr>
<td>Reticulin framework within tumor cell groups</td>
<td>Present: 6; absent: 0</td>
<td>Present: 0; absent: 5</td>
</tr>
<tr>
<td>Organized CD34 sinusoidal staining</td>
<td>Present: 6; absent: 0</td>
<td>Present: 0; absent: 5</td>
</tr>
</tbody>
</table>

**A Pilot Study of a Universal Fibrosis Scoring System in Medical Liver Disease**

(Poster No. 22)

**Gabriel Lerner, MD; Sanjay Kakar, MD; Michael Torbenson, MD; Matthew Yeh, MD, PhD; Tsung-Teh Wu, MD; Dhanpat Jain, MD. 1Department of Pathology, Yale University, New Haven, Connecticut; 2Department of Pathology, University of San Francisco, California; 3Department of Pathology and Laboratory Medicine, Mayo Clinic Hospital–Rochester, Minnesota; 4Department of Pathology and Laboratory Medicine, University of Washington, Seattle.

**Context:** Evaluation of fibrosis is important for prognostication in medical liver pathology. Currently, many etiology-specific fibrosis scoring systems exist, making comparisons difficult. Thus, a need exists for a universal fibrosis scoring system (UFS). Our goal was to evaluate such a UFS.

**Design:** Ten biopsies from 8 diseases were selected, including viral hepatitis B (HBV), viral hepatitis C (HCV), autoimmune hepatitis, primary sclerosing cholangitis (PSC), primary biliary cholangitis (PBC), congestive hepatopathy, nonalcoholic steatohepatitis (NASH), and NASH with concurrent HBV or HCV. A UFS was designed using etiology-specific systems, including Blatts and Ludwig (viral, autoimmune hepatitis), Kleinermodeled Brunt (NASH), Dai (congestive hepatopathy), and Ludwig (PBC, PSC, Table). Hematoxylin and eosin, trichrome, and reticulin stains from
liver biopsies (>1 cm in length) were reviewed by 2 pathologists and scored by UFS and etiology-specific systems. In discrepant cases, consensus was achieved by second morphologic review.

**Results:** Fibrosis grading by UFS and etiology-specific systems showed high concordance across all entities, with 100% concordance (10 of 10 cases) in congestive hepatopathy, autoimmune hepatitis, NASH, PSC, HBV, and HCV. Concordance was lower in PBC (0.9; 9 of 10 cases) and NASH with concurrent HBV or HCV (0.9; 9 of 10 cases). The 2 discordant cases included HCV with concurrent NASH (Batts-Ludwig: 1; UFS: 2), and PBC (Ludwig: 1; UFS: 2).

**Conclusions:** Using UFS and etiology-specific systems, fibrosis grade shows high concordance across diverse hepatic disorders. Larger, prospective UFS studies are needed to assess observer variability and validate against clinical outcomes.

<table>
<thead>
<tr>
<th>Chronic Hepatitis (Batts-Ludwig System)</th>
<th>NASH (Kleiner-Modified Brunt System)</th>
<th>PBC and PSC (Ludwig System)</th>
<th>Congestive Hepatic Fibrosis (Dai System)</th>
<th>Proposed Universal Fibrosis Scoring System</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: No fibrosis</td>
<td>0: No fibrosis</td>
<td>0: No significant fibrosis</td>
<td>0: No significant fibrosis</td>
<td>0: No fibrosis</td>
</tr>
<tr>
<td>1: Portal fibrosis (fibrous portal expansion)</td>
<td>1: Perisinusoidal OR periportal: 1A: mild, zone 3, perisinusoidal 1B: moderate, zone 3, perisinusoidal 1C: portal/periportal</td>
<td>1: Portal: all disease activity confined to portal tracts; limiting plate intact</td>
<td>1: Central zone fibrosis only</td>
<td>1: Portal fibrosis without septa or with incomplete septa; mild or moderate pericentral or perisinusoidal fibrosis</td>
</tr>
<tr>
<td>2: Periportal fibrosis (periportal or rare portal-portal septa)</td>
<td>2: Perisinusoidal AND portal/periportal</td>
<td>2: Periportal; limiting plate disrupted by lymphocytic interface activity and/or ductular reaction; portal tracts have irregular shape</td>
<td>2A: Central zone and portal fibrosis with accentuation at central zone 2B: central zone and portal fibrosis withaccentuation at portal zone</td>
<td>2: Periportal fibrosis with few septa, portal and pericentral fibrosis; portal to portal bridging fibrosis with minimal lobular disarray; severe pericentral or sinusoidal fibrosis</td>
</tr>
<tr>
<td>3: Septal (fibrous septa with architectural distortion, no obvious cirrhosis)</td>
<td>3: Bridging fibrosis</td>
<td>3: Septa; fibrous septa (portal-portal bridging fibrosis)</td>
<td>3: Bridging fibrosis</td>
<td>3: Periportal fibrosis with numerous septa with obvious architectural distortion; porta-central bridging fibrosis; fibrosis with any evidence of regenerative nodules</td>
</tr>
<tr>
<td>4: Cirrhosis</td>
<td>4: Cirrhosis</td>
<td>4: Cirrhosis</td>
<td>4: Cirrhosis</td>
<td>4: Cirrhosis</td>
</tr>
</tbody>
</table>

**Expression of Aspartate B Hydroxylase in Gallbladder Adenocarcinoma**

(Poster No. 23)

Mehran Najibi, MD1 (mnajibikohneshshahri@lifespan.org); Rolf I. Carlson, BS2; Jack Wands, MD2; Dongfang Yang, MS3; Weibiao Cao, MD, PhD.1 Departments of Pathology and Medicine, Rhode Island Hospital-Brown University, Providence.

**Context:** Aspartate-β-hydroxylase (ASPH) is a transmembrane protein that catalyzes the hydroxylation of aspartyl and asparaginyl groups in the epidermal growth factor–like domains of membrane molecules. Previous studies revealed that ASPH is upregulated in several malignant neoplasms. However, the expression of ASPH in gallbladder adenocarcinoma remains unknown. In this study, we examined ASPH expression in gallbladder adenocarcinoma.

**Design:** Forty-one cases diagnosed from 2001 to 2017 were included. Slides were reviewed to select 3 cores for tissue microarray. Immunohistochemical staining for ASPH, PD1, PD-L1, CD3, and CD8 was performed. A combined score of intensity and extent was calculated and categorized as weak or strong staining (Figure 1.23, A and B).

**Results:** Strong ASPH staining was observed in 75.6% (31 of 41) of adenocarcinomas (P < .001), whereas only 18.8% (3 of 16) of adjacent benign tissues had strong staining. Eighteen of 20 poorly differentiated adenocarcinomas (90%) exhibited strong ASPH staining (P < .02), whereas 55% (11 of 20) of moderately and well-differentiated tumors showed strong staining. Seventeen of 31 high-stage tumors (stages 3 and 4) (54.8%) showed strong ASPH staining, which was significantly higher than that (10%, 1 of 10, P < .02) in low-stage (stages 1 and 2) tumors. Twenty-eight of 34 tumors with PD-L1–positive tumor-infiltrating lymphocytes (TILs) (82.4%) showed strong ASPH staining, which was significantly higher than that (42.8%; 3 of 7; P < .05) seen in tumors with PD-L1–negative TILs. However, there was no survival difference between weak and strong ASPH staining.

**Conclusions:** ASPH is highly expressed in gallbladder adenocarcinomas. Strong expression of ASPH is associated with higher tumor grade, tumor stage, and PD-L1–positive TILs. Our findings imply that ASPH may be a potential diagnostic and prognostic marker for gallbladder adenocarcinoma.

**Follicular Cholecystitis: A Rare Subtype of Chronic Cholecystitis Presenting as Mucosal Polyps of the Gallbladder**

(Poster No. 24)

Ahmed M. Alhusseiny, MD (ahmed.alhusseinymd@baystatehealth.org); Rahul Jawale, MD. Department of Pathology, Baystate Medical Center, Springfield, Massachusetts.

Follicular cholecystitis is a poorly characterized entity seen in approximately 2% of cholecystectomies. Since its initial description in the early 1900s, a limited number of cases have been analyzed to characterize this entity. We present a case of follicular cholecystitis presenting as multiple polypoid lesions of the gallbladder. A 71-year-old obese woman presented with 5 weeks of right upper quadrant abdominal pain. Ultrasound showed dilatation of the common bile duct, cholelithiasis without cholecystitis, and an 8-mm mucosal polyp. Computed tomography revealed dilatation of the common bile duct without distal obstruction. Laparoscopic cholecystectomy was performed that showed multiple mucosal polyps, the largest measuring 9 mm, with normal intervening mucosa. No choleliths were identified. The polyps were associated with well-formed lymphoid follicles; the

**Abstracts**

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A Rare Case of Disseminated Histoplasmosis Presenting With Widespread Gastrointestinal Tract and Soft Palate Involvement

(Poster No. 25)
Sanobar Yasmine Mohammed, MD (syanobar@uthsc.edu); Qandeel Sadiq, MD; Farhan Khan, MD. Department of Pathology, University of Tennessee Health Science Center, Memphis.

*Histoplasma capsulatum,* a thermally dimorphic fungus, is primarily found in Midwestern states. Immunocompromised patients are at risk of disseminated disease. Diagnosis of disseminated histoplasmosis requires a high index of suspicion. We report a case of disseminated histoplasmosis in an immunocompromised patient. A 59-year-old man presented with jaw pain, difficulty in swallowing, and weight loss for few months. HIV antibody was negative and CD4 count was 36. Computed tomography scan of the head showed thickening of the soft palate, near the uvula, concerning originally for squamous cell carcinoma. Patient also complained of diarrhea and black stools. Multiple gastrointestinal (GI) biopsies including duodenum and colon showed expansion of lamina propria by macrophages infected with fungal organisms. GMS special stain highlighted fungal organisms most compatible with histoplasma. Cytomegalovirus immunostain was negative and no microorganisms were identified on AFB special stain. The biopsy of the soft palate was negative for malignancy but showed histoplasmosis. The patient’s immunocompromised status predisposed to disseminated histoplasmosis in the soft and hard palate and the GI tract. This case study highlights the importance of a high index of suspicion for disseminated histoplasmosis in unusual sites, especially in immunocompromised patients without a prior history of pulmonary histoplasmosis.

Lymphocytic Gastritis: Clinical and Pathologic Presentation Vary With Age

(Poster No. 26)
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**Context:** Lymphocytic gastritis (LG) is an unusual pattern (present in less than 0.3% of gastric biopsies) of gastric mucosal damage characterized by increased intraepithelial lymphocytes (IELs; >25 per 100 epithelial cells in the gastric mucosa) and increased chronic inflammation in the lamina propria. LG is commonly associated with gluten-sensitive enteropathy, *Helicobacter pylori* gastritis, and nonsteroidal anti-inflammatory drugs. The clinical presentation of LG is variable, and the pathophysiology has yet to be elucidated. The aim of this study is to review and correlate the morphology of LG with the presence of comorbidities along with pathologic findings and age of presentation.

**Design:** We conducted a retrospective observational study of all patients diagnosed with LG via gastric biopsy at our medical center from 2002 to 2019. Thirty-eight patients with LG were identified and the data were stratified by age (<21 years, 22–59 years, and >60 years). Fisher exact tests were used to identify which categorical variables may correlate with increased IELs in the gastric mucosa. *P* < .05 was considered statistically significant.

**Results:** Increased IELs in patients >60 years were associated with a significantly higher probability of anemia/gastric bleeding, whereas increased IELs in patients <21 years were associated with a significantly higher probability of increased duodenum IELs and villus blunting.

**Conclusions:** Increased gastric IELs have significantly different clinical and pathologic associations dependent on age. These findings suggest that LG may have different etiologies dependent on age. Hence, morphologic diagnosis of LG should prompt different clinical and pathologic workup dependent on age.

Two Case Reports of Primary Anaplastic Large Cell Lymphomas of the Pancreas

(Poster No. 27)
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Primary pancreatic lymphoma is rare, and primary pancreatic anaplastic large cell lymphoma (ALCL) is extremely rare with fewer than 20 cases reported to our knowledge. ALCL is a type of T-cell lymphoma that can be divided into 2 subtypes based on anaplastic lymphoma kinase (ALK) expression: ALK-positive (ALK+) ALCL and ALK-negative (ALK-) ALCL. We report 1 case each of ALK+ and ALK-ALCL of primary pancreatic lesions. A 34-year-old woman presented with rapid-onset ascites and magnetic resonance imaging finding of ill-defined fullness in pancreatic head and neck. Fine-needle aspiration of the pancreatic mass (Figure 1.27, A) and subsequent small bowel biopsy (Figure 1.27, B) revealed large malignant cells with abundant cytoplasm and pleomorphic nuclei. Immunohistochemically, the tumor cells were CD30, CD4, and ALK positive but CD20 negative. Diagnosis of ALK+ ALCL was made. In another case, a 66-year-old woman presented with abdominal pain and jaundice. Computed tomography showed locally invasive hypoenhancing lesion in the pancreatic head. Fine-needle aspiration of the pancreatic lesion (Figure 1.27, C and D) revealed large...
malignant cells with abundant cytoplasm and pleomorphic, eccentric nuclei. Immunohistochemically, the tumor cells were positive for CD30 and CD4 but negative for CD20 and ALK. Diagnosis of ALK+ ALCL was made. ALK+ ALCL is more prevalent in young patients. In contrast, ALK− ALCL occurs most commonly in older adults. The clinical outcome of ALK+ ALCL with conventional therapy is generally poorer than that of ALK− ALCL.

**Hepatic Calcifying Nested Stromal Epithelial Tumor With Recurrence in a Transplanted Liver**

(Poster No. 28)

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Calcifying nested stromal-epithelial tumor (CNSET) is a rare liver neoplasm of debatable pathogenesis. It is primarily a pediatric tumor with female preponderance. An association of ectopic ACTH production, Cushing syndrome, Beckwith-Weidmann, and Klinefelter syndrome has been demonstrated in prior literature. We report a CNSET case with unique clinical, microscopic, and molecular features in a 17-year-old female who initially presented with liver failure and ultimately underwent liver transplantation. Gross examination of the resected native liver revealed a circumscribed calcified mass in the right lobe. Microscopic examination revealed a nested biphasic appearance composed of an epithelial and a stromal component (Figure 1.28, A) with calcification (Figure 1.28, B) and necrosis. A unique finding of the water-silk pattern of small blue cells (Figure 1.28, C) was identified in some tumor nests that was never described previously. The patient presented 3 years later with tumor recurrence in the transplanted liver and extensive metastasis. Recurrence in the transplanted liver has never been reported in previous literature. Biopsy from the recurrent tumor revealed similar morphologic findings. Immunohistochemistry revealed CD56, CDX2, β-catenin (cytoplasmic and nuclear) (Figure 1.28, D), WT-1 (nuclear), neuron-specific enolase (patchy), and CD99 positivity in the epithelial component and smooth muscle actin in the stromal cells, supporting our diagnosis. Our case also had a distinctive mutation profile involving CTNNB1, PIK3CA, and TERT promoter genes. The occurrence and accumulation of multiple mutations in our case may have contributed to the aggressive nature of this case.

**Sarcina Ventriculi in the Upper Gastrointestinal Tract: A Multicentric Study of 13 Cases**

(Poster No. 29)

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**Context:** Although the pathogenicity of Sarcina ventriculi (SV) in humans is still unproven, it has been associated with gastric outlet obstruction and emphysematous gastritis. We aim to further characterize the clinicopathologic features of SV in the largest yet reported case series.

**Design:** We searched for surgical pathology specimens carrying a diagnosis of SV from 2010 to 2020 at 2 institutions. Clinical and endoscopic findings were collected from medical records.

**Results:** Twelve upper gastrointestinal biopsies and 1 gastrectomy specimen were identified. The patients included 7 females and 6 males, with a mean age of 57 years. The most common symptoms were abdominal pain (n = 4, 31%), diarrhea (n = 3, 23%), nausea/vomiting (n = 2, 15%), dysphagia (n = 2, 15%), and reflux symptoms (n = 2, 15%). Most SVs were identified in the stomach or gastroesophageal junction (n = 10, 86%), with 2 (17%) in the esophagus and 1 (7%) in the duodenum. Endoscopically, the most common finding was retained food debris (n = 4, 31%), followed by erythema gastritis (n = 3, 23%) and ischemia/necrosis (n = 2, 15%). The most common clinical associations were gastroparesis (n = 8, 62%), diabetes mellitus (n = 8, 62%), gastroesophageal reflux disease (n = 5, 38%), and gastric outlet obstruction (n = 2, 15%). Two cases (15%) had concomitant Candida. Upon follow-up, 1 patient with gastric necrosis and suspected ischemia died of septic shock shortly after resection; the remaining 12 patients were alive.

**Conclusions:** Our study confirmed the frequent association of SV with gastroparesis and many other comorbidities, suggesting that it could be pathogenic. SV should be diligently searched for in upper gastrointestinal biopsies, particularly in those with ischemia or necrosis.

**Metastatic Colon Cancer to the Stomach: Report of a Rare Case**

(Poster No. 30)

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Colorectal cancer (CRC) is the most common malignancy arising from the gastrointestinal tract. Liver and lung are the most common sites of metastasis. Stomach is an exceedingly rare target for CRC. To our knowledge, there are only 5 cases of gastric metastasis from CRC published in the English literature. We present a 54-year-old man with a past medical history significant for colon adenocarcinoma (Figure 1.50, A), for which he underwent left hemicolectomy and received adjuvant chemotherapy. Immunohistochemically, the adenocarcinoma was positive for CK7 and CDX2 and negative for CK20. Molecular studies showed that the tumor cells harbored BRAF and PIK3CA mutations and did not have loss of mismatch repair proteins. Twelve months after the hemicolectomy, imaging studies revealed a 6-cm mass in the body of the stomach. Biopsy of the gastric mass showed that the tumor cells were morphologically similar to the colon adenocarcinoma. Notably, the tumor cells in the gastric mass displayed an immune-phenotyping profile similar to the colon adenocarcinoma (CK7+, CK20+, CDX2+). The patient underwent partial gastrectomy. Gross examination showed that the tumor was adherent to the supporting gastrocolic ligament.
of the gastrectomy specimen showed a 7-cm tan exophytic mass with central ulceration. Histology revealed an unremarkable gastric mucosa overlying the tumor (Figure 1.30, B). Morphologically, the tumor was identical to the colon cancer. SATB2, a highly specific nuclear marker for CRC, stained both colonic (Figure 1.30, C) and gastric (Figure 1.30, D) tumors strongly and extensively. This is a rare case of CRC metastatic to the stomach, in which the diagnosis is supported by SATB2 staining.

**Lanthanum-Induced Gastrointestinal Histiocytosis in the Setting of Recurrent Gastric Ulcers: Case Report and Review of the Literature**

*(Poster No. 31)*

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Lanthanum carbonate is a potent binder of dietary phosphate used to prevent hyperphosphatemia in patients with end-stage renal disease (ESRD). The resulting lanthanum-phosphate complex is highly insoluble and passes through the gastrointestinal (GI) tract with little absorption. However, recent case reports have described upper GI histiocytosis with intracellular lanthanum and phosphate accumulation in varied clinical and endoscopic settings. Here, we report a unique case of lanthanum-induced histiocytosis associated with recurrent gastric ulcers in a 62-year-old man with ESRD. Initial endoscopy for epigastric pain and melena revealed small nonbleeding gastric ulcers. Biopsies of the ulcer margin (Figure 1.31, A) and endoscopically normal duodenum (Figure 1.31, B) revealed histiocytic aggregates containing eosinophilic crystalloid material consistent with lanthanum. Following standard treatment, repeat endoscopy and gastric biopsies showed resolution of the ulcers and, interestingly, showed no evidence of lanthanum deposition. However, the patient subsequently presented with recurrent upper GI bleeding and multiple endoscopies revealed a large bleeding ulcer. Biopsies again showed lanthanum deposition at the ulcer margin (Figure 1.31, C) and in endoscopically normal mucosa (Figure 1.31, D). Of note, the patient reported avoiding nonsteroidal anti-inflammatory drugs after his initial presentation but remained on his original dose of lanthanum throughout this period. Gastric biopsies and serology were negative for *Helicobacter pylori* (ESRD). This case highlights a rare cause of GI histiocytosis and suggests a potential association between lanthanum deposition and formation of gastric ulcers. Although rare, recognition of lanthanum-induced histiocytosis is important as a reversible cause of GI injury in ESRD patients receiving lanthanum carbonate therapy.

1.31

**Unusual Giant Gastric Polyp in Juvenile Polyposis Syndrome**

*(Poster No. 33)*

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Juvenile polyposis syndrome (JPS) is a rare autosomal-dominant syndrome associated with mutations in the SMAD4 or BMPR1A genes. JPS is characterized by multiple hamartomatous polyps in the gastrointestinal (GI) tract, mainly in the colon and stomach. Patients are at increased risk of colon and stomach cancer. Clinically, JPS presents with hematochezia, diarrhea, and abdominal pain. Endoscopically, polyps range from small sessile nodules to pedunculated lesions large enough to prolapse rectally. Diagnosis of JPS requires at least 1 of the following: a minimum of 5 juvenile polyps (JPs) in the colon and/or rectum, multiple JPs in other parts of the GI tract, or a JP in a person with known family history of JPS. We present a 34-year-old woman who presented with abdominal pain and distension, and severe GI bleeding requiring transfusion. She was status post colectomy at age 11 and was now presenting with recurrent upper GI bleeding and multiple endoscopies revealed a large bleeding ulcer. Biopsies again showed lanthanum deposition at the ulcer margin (Figure 1.31, C) and in endoscopically normal mucosa (Figure 1.31, D). Of note, the patient reported avoiding nonsteroidal anti-inflammatory drugs after his initial presentation but remained on his original dose of lanthanum throughout this period. Gastric biopsies and serology were negative for *Helicobacter pylori* (ESRD). This case highlights a rare cause of GI histiocytosis and suggests a potential association between lanthanum deposition and formation of gastric ulcers. Although rare, recognition of lanthanum-induced histiocytosis is important as a reversible cause of GI injury in ESRD patients receiving lanthanum carbonate therapy.
because of her known SMAD4 mutational status and JPS family history. Imaging revealed a giant gastric mass and she underwent gastrectomy. Hundreds of polyps were present, the largest pedunculated and 17 cm in greatest dimension (Figure 1.33, A). Microscopically these were hyperplastic polyps with multiple cystically dilated crypts of foveolar-type epithelium and a milder degree of smooth muscle hyperplasia (Figure 1.33, B and C). The lamina propria was edematous with lymphoplasmacytic infiltrate and a few neutrophils. Focal low-grade dysplasia was identified (Figure 1.33, D) with elongated hyperchromatic pseud stratified nuclei. Our case highlights the importance of continued surveillance in JPS patients and necessity of extensive polyp sampling to identify dysplasia or carcinoma.

Postinfantile Giant Cell Hepatitis: A Rare Complication of Epstein-Barr Virus Infection

(Poster No. 34)

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Postinfantile giant cell hepatitis (PIGCH) is a rare and enigmatic inflammatory disease of the liver, characterized by the presence of enlarged, eosinophilic, and multinucleated hepatocytes in a background typically consisting of severe necroinflammatory stroma. Although only a handful of case reports are available in the literature, its exact pathogenesis remains elusive. Numerous factors, including various viral infections, medications, and even autoimmune conditions, have been associated and postulated as etiologic agents of PIGCH. Herein, we present an unusual case of PIGCH that is believed to be caused by autoimmune hepatitis secondary to a newly acquired Epstein-Barr virus (EBV) infection. The patient was a 56-year-old man with a history of HIV and HCV coinfection on antiviral therapy, HPV-associated squamous cell carcinoma of the tonsil, genital warts, and active cocaine user who presented to the emergency department because of abdominal pain and vomiting for several days. Preliminary test results revealed markedly elevated liver enzymes (ALT and AST >2000 U/L) and positive EBV serology, but HIV RNA was not detected. He was admitted for further evaluation and liver biopsy procedure was performed. Histologic examination of the collected liver tissue showed remarkable giant cell transformation of most hepatocytes, with associated active, chronic inflammation, florid ductular reaction, and bridging necrosis (Figure 1.34). Further serology testing also revealed elevated anti–liver-kidney-microsome antibody, supporting the diagnosis of autoimmune hepatitis with extensive giant cell transformation.

Clinical Implications of Microscopic Colitis–like Polyps

(Poster No. 35)

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Context: Microscopic colitis (MC) is generally identified on random colon biopsies performed for chronic diarrhea, but rarely incidental polyps have histologic features of MC. We compared patients with MC-like polyps (MCLPs) with control patients with conventional polyps to determine the implications of MCLPs.

Design: We searched medical records for patients without prior or concurrent MC who were found to have MCLPs. For each patient with MCLPs, 1 patient with conventional polyps was selected as a control. We reviewed histologic and clinicopathologic features of each MCLP and evaluated endoscopic and clinical findings for MCLP cases and controls.

Results: We identified 31 patients with MCLPs, with histologic features of collagenous colitis in 9 patients (29%) and lymphocytic colitis in 22 patients (71%). The MCLPs were unifocal in 13 patients (41.9%) and multifocal in 18 patients (58.1%). There was no difference in chronic diarrhea at time of procedure or on follow-up; at time of procedure 1 patient with MCLPs (5.6%) had chronic diarrhea compared with no patients in the control group (P = .44), and on follow-up 6 patients with MCLPs (28.6%) developed chronic diarrhea compared with 3 (10.3%) in the control group (P = .14). Of patients with follow-up biopsies, 1 patient with MCLPs (12.5%) and no control patients developed MC (P = .1).

Conclusions: MCLPs may be identified in asymptomatic patients and most patients do not develop chronic diarrhea, but there may be a trend for patients with MCLPs to develop diarrhea (29% versus 10% in controls). Thus, pathologists may suggest follow-up regarding chronic diarrhea in patients with MCLPs.

Correlation of Pre-operative Cytology With Malignant Histopathology of Pancreatoduodenectomy Specimens

(Poster No. 36)

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Context: Pancreatoduodenectomy (PD) is the standard of care for resectable pancreatic and peri-ampullary cancers. Abnormal imaging and fine-needle aspiration (FNA) lack 100% specificity in identifying malignancies. PD is a high-risk surgery with significant morbidity and mortality. We aimed to assess the cyto-histo correlation of PDs and explore parameters that increase the yield for a final malignant diagnosis.

Design: We studied 250 PDs performed at our institute during the last decade. A representative sample of the data is presented. We calculated mean with standard error for continuous data, whereas categorical data were expressed as percentages. Differences between groups were assessed using the χ² test. Data were analyzed using Stata v12.0.

Results: A total of 40 PDs were reviewed. Mean age was 65.7 ± 2.3 years. The predominant histopathologic diagnosis in resected specimens was malignancy (31 cases, 77.5%) followed by preneoplastic (12.5%) and benign (10%). Of the malignant cases, 87% strongly correlated with cytology (P < .001), 71% with gross findings (P = .03), 65% with imaging, and 55% with abnormal tumor markers (Figure 1.36). Among the 5 preneoplastic cases, 4 were either atypical or malignant on FNA, 4 had abnormal imaging results, and all 5 had abnormal gross findings. Of the 4 benign cases, 3 FNA results were
atypical/malignant, 3 were detected as “mass” on imaging, and 3 had ill-defined gross findings.

Conclusions: Our study demonstrates a strong positive correlation between the malignant histologic diagnosis with cytology and gross findings. It remains to be determined whether molecular genetics will add significantly to the predictive power of preoperative evaluation of PDs.

Novel Lifting Agent ORISE Granuloma: Report of 2 Cases

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The use of lifting agents in the performance of endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) of gastrointestinal neoplasms is an integral part of these new procedures. After injection for EMR or ESD procedures, these agents may remain in tissue for some time and may be found in subsequent surgical resections, where they can mimic other conditions. We report 2 cases where ORISE (Boston Scientific), a viscous gel lifting agent, was used in the setting of an incomplete (1 case) or aborted (second case) endoscopic submucosal dissection. Hematoxylin and eosin–stained sections demonstrated submucosal deposits of amorphous eosinophilic homogeneous material, mimicking amyloid (Figure 1.37, A through C). The material was neither refractile nor polarizable and was accompanied by a foreign body giant cell reaction. Because of the diagnostic consideration of amyloid, Congo red stains were performed on both cases, with negative results (Figure 1.37, D). It is important to be aware of the morphology of this new lifting agent for accurate diagnosis and to avoid the diagnostic pitfall of misinterpreting it as amyloid or other disease processes, with potential adverse clinical impact. This material can be definitively distinguished from amyloid by its nonreactivity on Congo red stain, familiarity with its histologic features, and recognition of its use in selected endoscopic resections.

Synchronous 2 Distinct Pancreatobiliary Tumors—Common Bile Duct Cholangiocarcinoma and Primary Pancreatic Ductal Adenocarcinoma

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Synchronous primary tumors of the pancreatobiliary system are extremely rare. We present a case of a 65-year-old man with a history of ulcerative colitis status post total proctocolectomy and metabolic syndrome who presented with jaundice and elevated liver enzymes. Computed tomography (CT) scan revealed biliary tract dilatation and an enhancing masslike lesion at the junction of the common hepatic duct and cystic duct with adjacent adenopathy. Endoscopic retrograde cholangiopancreatography demonstrated common bile duct (CBD) stricture, and bile duct brushing confirmed adenocarcinoma. In addition, CT scan revealed a separate 1.7-cm mass in the pancreatic body that was diagnosed as pancreatic adenocarcinoma by tissue biopsy. The patient underwent 6 months of chemotherapy followed by surgical resection. The resection specimen of CBD demonstrated moderately differentiated invasive adenocarcinoma (ypT1N0), with extensive low-grade and high-grade biliary intraepithelial neoplasia (BilIN), periductal concentric fibrosis, and diffuse chronic inflammation (Figure 1.38, A and B). The histologic findings, in conjunction with patient’s known history of ulcerative colitis, support the diagnosis of cholangiocarcinoma arising in primary sclerosing cholangitis with BilIN. The resected pancreas showed moderately differentiated adenocarcinoma (ypT1N0) in a background of low-grade pancreatic intraepithelial neoplasia (PanIN) and chronic pancreatitis (Figure 1.38, C and D). Subsequent molecular genetic analyses were performed to further delineate the nature of these 2 distinct neoplasms. The pancreatic adenocarcinoma showed KRAS p.G12V mutation while molecular signature of CBD adenocarcinoma is pending. This case provides a unique synchronous presentation of 2 distinct neoplasms within the pancreatobiliary system. Although this presentation is rare, it should be considered when assessing multiple pancreatobiliary lesions.

Metastatic Spindle Cell Hepatocellular Carcinoma: A Diagnostic Dilemma

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Spindle cell hepatocellular carcinoma (HCC) is very rare and has only been reported sporadically. Spindle cell HCC presenting with bone metastasis can cause a significant diagnostic challenge. We report a 67-year-old woman with a history of hepatitis C and well-differentiated HCC with bone metastasis.
HCC (Figure 1.39, A) in 2012. She was on regular monitoring until March 2020 with no recurrence. In November 2020, she had a sclerotic lesion in the left iliac bone. The lesion was biopsied and revealed a cellular bland spindle cell lesion (Figure 1.39, B) with a similar morphology as the metastatic spindle cell carcinoma. Albumin RNA in situ hybridization (ISH) was performed on the bone lesion and the spindle cells were diffusely positive for albumin RNA ISH (Figure 1.39, D), supporting the diagnosis of metastatic spindle cell HCC. The liver spindle cell HCC may be a new primary because the location and morphology are different from the 2012 well differentiated HCC, but a recurrent HCC with spindle cell morphology cannot be excluded. In conclusion, spindle cell HCC may present as a metastatic spindle cell lesion in bone and stain negative for glypican-3, hepar-1, arginase, and AFP may lead to misdiagnosis. Albumin RNA ISH is a more sensitive and specific marker and can be used for diagnosis of HCC in poorly differentiated or rare variants of HCC such as spindle cell HCC.

**Soft Tissue Metastasis From Gastric Carcinoma Mimicking Epithelioid Sarcoma**

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Soft tissue metastasis of gastric carcinoma is extremely rare. We report a 22-year-old man with abdominal fullness and nausea found to have an 11.8-cm right iliac bone and soft tissue mass, with osseous destruction. Extensive retroperitoneal lymphadenopathy was also identified. Differential diagnosis included primary sarcoma, lymphoma, and metastatic carcinoma. Fine-needle aspiration and core biopsy of the soft tissue mass was cellular with neoplastic cells arranged in clusters and singly, showing nuclear pleomorphism, irregular chromatin, prominent nucleoli, high nuclear to cytoplasmic ratio, and cytoplasmic vacuoles. Scattered intracytoplasmic pink globules were also present (Figure 1.40, A and B). Immunohistochemical stains showed the tumor to express cytokeratin AE1/3 and Cam5.2 (Figure 1.40, C), and to be negative for SOX10, S-100, ERG, myogenin, MyoD1, smooth muscle actin, desmin, CD99, GFAP, CD34, CD31, CD3, CD20, and CD30. The possibility of epithelioid sarcoma was raised, but the tumor cells showed retained INI1 expression (Figure 1.40, D). The patient quickly developed pleural effusion and a repeat biopsy of the iliac mass showed the tumor to express cytokeratin 7, cytokeratin 20, BerEP4, MOC31, and CDX2. The tumor was diagnosed as a poorly differentiated carcinoma of gastrointestinal origin (Figure 1.41, A). Histologic examination showed a hamartomatous polyp with arborizing smooth muscles extending from the muscular mucosa (Figure 1.41, B). The polyp was lined by nondonysplastic gastric antral and fundic gland lining mucosa. A 43-year-old man was admitted for small bowel obstruction. Diagnostic laparoscopy and enterotomy revealed intussusception of jejunum, with an associated polyp measuring 7.2 cm (Figure 1.41, A). Next-generation sequencing showed mutations of ERBB2 V777L and CDH-1 S337fs*3, splice site 1009-1G>A. Unfortunately, the patient died soon thereafter. Per literature review, this is one of the youngest patients identified with CDH1-mutated gastric carcinoma presenting with distant metastasis as the initial manifestation.

**Solitary Peutz-Jeghers–Type Polyp of Jejunum With Gastric Fundic and Antral Gland Lining Mucosa**

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Solitary Peutz-Jeghers–type polyp (PJP) is a rare lesion characterized by a hamartomatous polyp of the gastrointestinal tract in a patient without mucocutaneous pigmentation, family history of Peutz-Jeghers syndrome, or STK11/LKB1 mutations. These polyps can arise anywhere along the gastrointestinal tract and are characterized by arborizing smooth muscles lined by nondonysplastic mucosa. Although the lining mucosa is generally the same as the organ in which it arises, gastric pyloric and foveolar metaplasia have been reported in PJP arising in the small intestine. We present a case of a small intestinal PJP with gastric antral and fundic gland lining mucosa. A 43-year-old man was admitted for small bowel obstruction. Diagnostic laparoscopy and enterotomy revealed intussusception of jejunum, with an associated polyp measuring 7.2 cm (Figure 1.41, A). Histologic examination showed a hamartomatous polyp with arborizing smooth muscles extending from the muscular mucosa (Figure 1.41, B). The polyp was lined by nondonysplastic gastric antral and fundic gland mucosa. A 43-year-old man was admitted for small bowel obstruction. Diagnostic laparoscopy and enterotomy revealed intussusception of jejunum, with an associated polyp measuring 7.2 cm (Figure 1.41, A). Histologic examination showed a hamartomatous polyp with arborizing smooth muscles extending from the muscular mucosa (Figure 1.41, B). The polyp was lined by nondonysplastic gastric antral and fundic gland mucosa. A 43-year-old man was admitted for small bowel obstruction. Diagnostic laparoscopy and enterotomy revealed intussusception of jejunum, with an associated polyp measuring 7.2 cm (Figure 1.41, A). Histologic examination showed a hamartomatous polyp with arborizing smooth muscles extending from the muscular mucosa (Figure 1.41, B). The polyp was lined by nondonysplastic gastric antral and fundic gland mucosa.
terization of the lesion is underway. A diagnosis of solitary PJP of the small bowel with gastric antral and fundic gland mucosal lining was rendered. Although pyloric and foveolar metaplasia in PJP has been described, we believe this to be the first report of small intestinal PJP with gastric fundic gland mucosal lining mucosa.

**Extramucosal Anal Adenocarcinoma Arising From a Fistula Tract in a Patient With Longstanding Crohn Disease**

*(Poster No. 42)*

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Anal cancer accounts for 1% of all gastrointestinal malignancies in the United States. Although primary anal squamous cell carcinoma is well characterized, limited documentation of primary anal adenocarcinoma exists and its pathogenesis is not well understood, though it is hypothesized to arise in the setting of chronic inflammation and fistula tracts in the perianal region. We present a case of a 70-year-old man with a 24-year history of Crohn disease complicated by recurrent anal fistula formation, fistulotomy, and seton placement presenting with recurrent anal fistula, abscess formation, and rectal pain. No mucosal high-grade dysplasia or malignancy was identified on recent colonoscopy. Patient was found to have an atypical external opening on rectal examination under anesthesia, and a biopsy was sent for histopathologic evaluation. Microscopic examination revealed a poorly differentiated adenocarcinoma with mucinous features involving the perianal skin. Neoadjuvant chemoradiation therapy was initiated and abdominopelvic resection was performed post completion of neoadjuvant therapy. Resection specimen was sent to pathology for histopathologic evaluation, treatment response, and tumor staging. Gross examination revealed a large lobulated posterior perianal mass localized to the posterior anal canal, disrupting the internal/external anal sphincters and seton placement presenting with recurrent anal fistula, abscess formation, and rectal pain. No mucosal adenocarcinoma exists and its pathogenesis is not well understood, though it is hypothesized to arise in the setting of chronic inflammation and fistula tracts in the perianal region. We present a case of a 70-year-old man with a 24-year history of Crohn disease complicated by recurrent anal fistula formation, fistulotomy, and seton placement presenting with recurrent anal fistula, abscess formation, and rectal pain. No mucosal high-grade dysplasia or malignancy was identified on recent colonoscopy. Patient was found to have an atypical external opening on rectal examination under anesthesia, and a biopsy was sent for histopathologic evaluation. Microscopic examination revealed a poorly differentiated adenocarcinoma with mucinous features involving the perianal skin. Neoadjuvant chemoradiation therapy was initiated and abdominopelvic resection was performed post completion of neoadjuvant therapy. Resection specimen was sent to pathology for histopathologic evaluation, treatment response, and tumor staging. Gross examination revealed a large lobulated posterior perianal mass localized to the posterior anal canal, disrupting the internal/external anal sphincters and involving a right cutaneous anal fistula (Figure 1.42, A through D). Microscopic examination revealed an extramucosal, poorly differentiated adenocarcinoma with mucinous features arising from a preexisting fistula tract. Primary extramucosal anal adenocarcinoma is a rare entity with unusual presentation and no established therapeutic evidence-based algorithm. We report this case to highlight its occurrence in patients with long-standing Crohn disease and lack of mucosal malignancy on surveillance colonoscopy.

**Colonic Hemangioma Masquerading as Colonic Adenocarcinoma**

*(Poster No. 43)*

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Gastrointestinal tract hemangiomas can occur singly or multiply from the esophagus to the rectum. Colonic hemangiomas are an uncommon benign neoplastic proliferation of endothelial cells and often present as an incidental finding with spontaneous bleeding. We report a case of a 79-year-old man with a history of “known colorectal cancer,” unclear history of human immunodeficiency, and coronaryaropathy presenting with chronic fatigue. During hospitalization, the patient had several episodes of melena and hematochezia and was found to have severe iron-deficiency anemia. Upper endoscopy did not reveal a source of bleeding. On computed tomography scan and colonoscopy, the patient was found to have a partially obstructing, malignant-appearing, ulcerated mass localized to the splenic flexure of the transverse colon. The patient subsequently had an ileocolic resection. Gross examination revealed a 6.5-cm polypoid, partially circumferential mass. Microscopically, the lesion consisted of an ulcerative vascular lesion composed of thin-walled vessels involving the mucosa, submucosa, and pericolic tissue, mimicking a colorectal adenocarcinoma on imaging. The differential diagnosis included adenocarcinoma (clinically) and various vascular lesions (arteriovenous malformation, epithelioid hemangioendothelioma, Kaposi sarcoma, and angiosarcoma). The tumor was positive for CD31/CD34 (Figure 1.43, A through D), whereas it was negative for CAMTA1, FOSB1, had HHV8 and had a low proliferative index, supporting the diagnosis of hemangioma. Colonic hemangiomas have rarely been described in the literature. They can present with occult or acute bleeding and bowel obstruction mimicking a colorectal carcinoma. Colonic hemangiomas are often an incidental finding. There have been limited cases in the literature reporting overt gastrointestinal bleeding secondary to colonic hemangioma.

**Patients With Definite Distal Esophageal Adenocarcinoma Have Significantly Better Outcomes Than Patients With Carcinomas in Other Gastroesophageal Junction Regions: A Retrospective Study of 303 Consecutive Patients Treated in Boston**

*(Poster No. 44)*

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**Context:** Distal esophageal adenocarcinoma (EAC) is part of carcinomas in the gastroesophageal junction (GEJ) region with dismal prognosis and unknown mechanisms. Recently, the Cancer Genome Atlas (TCGA) published genomic profiles of those carcinomas in 5 groups but the prognostic significance of categorizing patients into these groups remains unclear.

**Design:** We followed the TCGA grouping criteria and retrospectively studied and statistically compared clinicopathologic and prognostic features of GEJ carcinomas in 5 groups of 303 consecutive patients treated at VA Boston during a 20-year period. The patients were grouped as G1, definite EAC (20.5%); G2, probable EAC (30.7%); G3, carcinoma straddling GEJ (13.9%); G4, probable proximal gastric carcinoma (27.7%); and G5, definite proximal gastric carcinoma (7.3%).

**Results:** More than 99% of patients were white men, with a mean age of 69.1 years and an average body mass index of 28.0. No significant difference was found in age, gender, ethnicity, body mass index, presence of cardiovascular diseases, diabetes, and history of tobacco/alcohol abuse among groups. Compared with patients in other groups, G1 patients showed significantly more frequent severe reflux disease, long-segment Barrett esophagus, common adenocarcinoma type, smaller tumor size, well-moderate differentiation, more stage I but
further stage III cases, scarcer lymphovascular invasion, fewer nodal and distant metastases, and significantly fewer overall disease-free and relapse-free survival. The 5-year overall survival rate was 41.3% in the G1 group, significantly higher than in other groups (17.2%; \(P < .001\)) (Figure 1.44, A through D).

Conclusions: With the TCGA grouping criteria, patients with definite EAC showed significantly better prognosis than those with carcinomas in other GEJ regions, suggesting different pathogenesis mechanisms.

Clinicopathologic Features of Esophageal and Esophagogastric Junction Gastrointestinal Stromal Tumors in the Targeted Therapy Era: An Institutional Review During an 18-Year Period (Poster No. 45)

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Context: Gastrointestinal stromal tumors (GISTs), usually gastric (60%–70%), arise throughout the gastrointestinal tract and comprise approximately 80% of mesenchymal GIST neoplasms. Esophageal GISTs are rare (0.7% of all GISTs); esophageal and esophagogastric junction (EGJ) GISTs have a reported incidence of 0.1–0.2/million patients. Given their rarity, we investigated their clinicopathologic features and frequency at our institution.

Design: Our pathology database was queried for GIST specimens from January 2003 through December 2020. The pathology reports and pertinent clinical notes were reviewed. Incidental microscopic lesions, so-called seeding GISTs, were excluded.

Results: A total of 1082 patients with 1458 GIST specimens (biopsies and resections) were histologically evaluated. Of these, 12 patients (1.1%; median age, 68.3 years [45–90 years]) with esophageal (n = 6, 50%) and EGJ (n = 6, 50%) GISTs were identified, with 16 specimens total, including 4 metastases (bone n = 1; liver n = 2, subcutaneous tissue n = 1) among 3 patients, and 1 recurrence (stomach). Two metastases were from the esophagus (1 liver, 1 bone) and 2 (1 liver, 1 subcutaneous tissue from same patient) from the EGJ. Primary tumors accounted for 0.8% of all specimens. There were 8 males (67%; median age, 67.5 years [49–73 years]) and 4 females (33%; median age, 74.5 years [62–90 years]). Primary site distribution between genders was as follows: esophageal, 4 males, 2 females; EGJ, 4 males, 2 females. Follow-up was available in 8 of 12 patients, none of whom died from their disease.

Conclusions: This further demonstrates the rarity of esophageal and EGJ GISTs, and the clinicopathologic features show low risk of aggressive or fatal disease. Whereas this subtype was often lethal in the past, it has a low risk for fatal disease in the targeted therapy era, even when metastatic.

Atypical Presentation of Aggressive Systemic Mastocytosis in a Pediatric Patient (Poster No. 46)

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Systemic mastocytosis (SM) in children is extremely rare and has a bimodal distribution. We report a case of aggressive SM with an atypical presentation in a 12-year-old girl. The patient had no significant past medical history and presented with 1-year duration of daily cramping abdominal pain, aggravated by eating. The condition was not relieved by proton-pump inhibitors. The patient underwent colonoscopy. The mucosa was edematous and friable with loss of vascular markings. Biopsies of all portions of colon were obtained. On microscopy, the biopsy fragments showed clusters and dense lamina propria infiltration consisting of mast cells with round-shaped nuclei and moderate amount of pale to clear cytoplasm. The background also showed numerous eosinophils. Immunohistochemical staining for CD117, mast cell tryptase (MCT), CD2, and CD25 highlighted increased numbers of neoplastic mast cells. KIT mutation testing was performed, and no pathogenic genetic alterations were detected. A subsequent bone marrow biopsy was performed that demonstrated mast cells in clusters adjacent to bony trabeculae, with spindled, round, and atypical morphology. Increased clusters of eosinophils were present around the atypical mast cells. Immunostaining for MCT and CD117 showed positive expression. By flow cytometry, atypical mast cells with aberrant expression of CD25 and CD2 and hematogone hyperplasia were identified. SM is a rare and heterogeneous disease characterized by the accumulation of abnormal mast cells in various tissues. Although cutaneous mastocytosis is the classical presentation in children, our case emphasizes the importance of considering SM in the differential diagnosis and further performing appropriate systemic screening in patients with atypical presentation.

Hammer is a consultant for Roche, Caris, and Foundation Medicine, and shareholder/owner for PathEdEx.

Biliary Atresia: A Biliary Cyst Distinct From Choledochal Cyst (Poster No. 47)

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Cystic biliary atresia (CBA) is a variant of biliary atresia characterized by a cystic dilation of atretic bile ducts. It comprises approximately 10% of biliary atresia cases and can mimic a choledochal cyst (CC) on imaging. Both disorders present in infancy with direct hyperbilirubinemia and a cystic structure near the hepatic hilum. A female neonate born at 36 weeks 2 days’ gestation was noted to have elevated direct bilirubin at birth. Ultrasound demonstrated a 3.1-cm cystic abnormality at the hepatic hilum, suspicious for CC. The patient was discharged but developed worsening jaundice and hepatomegaly. Repeat ultrasound at 4 weeks of age demonstrated enlargement of the cystic structure. Diagnostic cholangiogram found absence of bile duct communication and abnormal intrahepatic bile ducts concerning for CBA. Needle biopsy demonstrated obstructive pattern of cholestasis (Figure 1.47, A) and periporal fibrosis with focal bridging fibrosis. The patient underwent a hepatectomy with Kasai procedure at 6 weeks of age. The biliary remnants were examined in pathology. The gallbladder was atretic (Figure 1.47, B). The wall of the excised cystic lesion was thickened and demonstrated a luminal band of sclerosis (Figure 1.47, C). The portal plate showed numerous diminutive bile duct remnants associated with dense fibrosis (Figure 1.47, D). In summary, CBA may be challenging to differentiate from CC. CC demonstrates cholangiographic evidence of a patent biliary tree. Histopathologic features such as a luminal band of fibrosis/scarring and absence of epithelium are commonly seen in CBA when compared with CC. The distinction between CBA and CC is critical for appropriate and timely surgical management.
Ewing Sarcoma/Primitive Neuroectodermal Tumor of the Pancreas: A Rare Case in a Young Male
(Poster No. 49)
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Extraosseous Ewing sarcoma/primitive neuroectodermal tumor (ES/PNET) is a rare, aggressive malignant tumor that has been reported in various sites such as lungs, biliary tract, and kidney. ES involving pancreas is considered exceptionally rare. We report a case of primary pancreatic ES in a 33-year-old man. The patient had no significant past medical history and presented with severe abdominal pain, distention, and scrotum swelling. A subsequent computed tomography scan showed ascites, diffuse lymphadenopathy, and a 20 × 19 × 13-cm abdominal mass involving pancreas and multiple smaller tumors along the peritoneum. Both CEA and CA19-9 were within normal limits. Patient underwent exploratory laparoscopy and a biopsy was obtained. On microscopy, the tumor showed nests of small, round blue cells. Immunohistochemical staining was performed. Tumor cells were positive for CD99, FLI-1, CD200, and CD56 and negative for CK7, CK20, CK17, AE1/AE3, Cam 5.2, CDX2, S100, LCA, inhibin, CD117, DOG-1, β-catenin, progesterone, and CD10. Focal expression was noted with synaptophysin and chromogranin. Ki-67 showed proliferation index of 20.3%. Fluorescence in situ hybridization studies showed rearrangement of EWSR1 gene at 22q12 with FLI1 at 11q24 (t[11;22]). The diagnosis of extraosseous ES/PNET was rendered. Extraosseous ES involving pancreas is extremely rare, and similar morphology with small, round blue cells can be noted in a broad spectrum of tumors. But early recognition of ES/PNET can be critical to produce the best chance of survival with current treatment modalities. Therefore, our case emphasizes the importance of considering extraosseous ES/PNET in the differential diagnosis of pancreatic masses.

Neuroendocrine Carcinoma Originating From a Villous Adenoma With Squamous Morules
(Poster No. 50)
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Colorectal adenomas with squamous morules are a rare phenomenon described in the literature, with up to 0.4% incidence. Neuroendocrine carcinomas associated with adenomas have also been described, although they are extremely rare. Colonic adenoma with squamous morules can exhibit some degree of neuroendocrine differentiation, which has been defined as adenoma microcarcinoid. However, the presence of high-grade neuroendocrine carcinoma has not been reported before. We present a 64-year-old woman with a 3-cm polypoid lesion in the right colon not amenable to endoscopic resection. A right hemicolectomy was performed, and a 3.5-cm sessile polypoid lesion was found in the right colon. Hematoxylin-eosin slides showed a villous adenoma with high-grade dysplasia. In the base of the lesion, a high-grade, small cell neuroendocrine carcinoma, 0.9 cm in greatest dimension and limited to the submucosa, was also found.

Prostatic Adenocarcinoma Presenting as a Rectal Mass
(Poster No. 48)
Alwalid Ammoun, MD (alwalid.ammoun@uhhospitals.org); Min Cui, MD. Department of Pathology, University Hospitals Cleveland Medical Center, Cleveland, Ohio.

Rectal infiltration by prostatic carcinoma is an extremely rare presentation of advanced disease in the prostate. We report a case of an 80-year-old man with no history of malignancy presenting with change in bowel habits and weight loss. His serum carcinoembryonic antigen (CEA) level was elevated at 6.8 μg/L. Colonoscopy revealed a circumferential villous and fungating mass with near-complete obstruction in the rectum. Biopsies were taken for histologic evaluation. Representative sections were selected, paraffin embedded, and hematoxylin-eosin stained. Immunohistochemical studies (cytokeratin AE1/AE3, CK7, CK20, CDX-2, SATB2, NXX3.1, INSM-1, chromogranin, and synaptophysin) were also performed. Histologic examination showed glands/acini involving smooth muscle and infiltrating lamina propria of the rectum without overlying surface epithelial dysplasia (Figure 1.48, A). The tumor cells were positive for pancytokeratin AE1/AE3 (Figure 1.48, B) and negative for CK7, CK20, and neuroendocrine markers (INSM-1, chromogranin, synaptophysin). Both SATB2 (Figure 1.48, C) and CDX-2 showed weak and focal staining. The tumor cells were positive for pancytokeratin AE1/AE3 (Figure 1.48, D). The overall morphology and immunohistochemical profile were consistent with rectal involvement by prostatic adenocarcinoma. Review of literature shows infiltration of the rectosigmoid occurs in 4% of patients with prostatic adenocarcinoma, with only 40% of patients with a preceding diagnosis before the gastrointestinal presentation. In the literature, some patients underwent rectal resection because the preoperative diagnosis was primary rectal adenocarcinoma. Since prostate carcinoma may show weak nonspecific staining for markers of colorectal carcinoma (SATB2 and CDX-2), a high index of suspicion is required for correct diagnosis of the biopsy material to avoid inappropriate resection.
As an unusual feature the adenoma showed frequent squamous morules (Figure 1.50, B). Immunohistochemistry studies showed positive staining for synaptophysin (Figure 1.50, C) and chromogranin in the neuroendocrine carcinoma and negative in the squamous morules and the adenoma. Cytokeratin 20 and CDX2 (Figure 1.50, D) were negative in the neuroendocrine carcinoma and in squamous morules, and positive in the adenoma. With β-catenin there was positive nuclear staining in the neuroendocrine carcinoma and in the squamous morules, but not in the adenoma. Coexistence of positive nuclear expression for β-catenin in the neuroendocrine carcinoma and in the squamous morules may suggest a similar origin; however, molecular studies must be performed to confirm this hypothesis.

Benign Liver Cysts–Echinococcal Cysts: A Case Report and a Concise Review

(Poster No. 51)

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Various benign liver cysts are encountered in daily pathology practice, namely simple biliary cysts and congenital cysts. One of these that is rarely diagnosed in the United States is echinococcal cysts (ECs). ECs are usually found in immigrants from the Middle East, North Africa, or South America. They are often subclinical, but some patients develop hepatomegaly, abdominal enlargement, and ascites. Secondary infection may also develop. Ultimately, some patients experience liver failure, involvement of adjacent organs, and death. We describe a case of a 25-year-old man who presented with abdominal pain and nausea that worsened during several weeks. He grew up in Yemen and immigrated to the United States many years prior. Imaging studies showed left hepatic lobe with cystic lesions, which were partially exophytic and deformed the liver capsule (Figure 1.51, A). The left hepatic lobe was excised and sent for pathology. Grossing showed 2 cysts (6.5 and 3.5 cm) within the liver parenchyma; each was filled with several smaller “daughter cysts” (Figure 1.51, B). Histologic sections of the cysts revealed the inner layer of the cysts consisted of a thin lining of epithelial cells that gave rise to the “brood” capsules from which splanic or immature heads of adult worms develop. The outer cyst layers were composed of hyalinized material surrounded by fibrosis (Figure 1.51, C and D). The differential diagnosis includes amebic abscess, pyogenic abscess, and noninfectious processes. Recognition of these rare entities is crucial for optimal patient care and because of the high risk of death associated with cyst rupture.

FXYD2 Is a Novel and Specific Marker for Intrahepatic Cholangiocarcinoma

(Poster No. 52)

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Context: Adenocarcinoma of uncertain origin often presents as a liver mass and represents a frequent diagnostic challenge. In particular, adenocarcinomas originating in the upper gastrointestinal tract (GI), liver, extrahepatic biliary system, and pancreas demonstrate an overlapping morphology and immunophenotype that is difficult to distinguish in clinical practice.

Design: Sections from 69 tumors were evaluated with a panel of markers, including albumin in situ hybridization (ISH), FXYD2, DPC4, S100P, BAP1, CAV2, MUC5AC, IMP3, and K17. This cohort consisted of 19 intrahepatic cholangiocarcinomas (ICCs), 20 pancreatic ductal adenocarcinomas (PDACs), 15 upper GI adenocarcinomas (stomach, small intestine, and gastroesophageal junction), and 15 extrahepatic cholangiocarcinomas (ECCs), including both hilar and distal bile duct cholangiocarcinoma. DPC4 and BAP1 expression was scored as either retained or fully lost. The remaining markers were interpreted as positive if moderate to strong staining was present in at least 10% of tumor cells.

Results: FXYD2 expression was seen exclusively in ICC (63%), whereas albumin ISH labeling was significantly more common in, but not exclusive to, ICC (58%). Loss of DPC4 was only seen in ECC (40%) and PDAC (45%). S100P is expressed in all other tumors, but frequently lost in ICC. Results for BAP1, CAV2, MUC5AC, IMP3, and K17 were less discriminatory and are summarized in the Table.

Conclusions: FXYD2 shows higher sensitivity and specificity for identifying intrahepatic cholangiocarcinoma compared with albumin ISH in a limited cohort. The combination of DPC4 and FXYD2 may represent a diagnostically useful panel in differentiating adenocarcinomas of upper GI and pancreatobiliary origin.

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<th>Individual Stain and Panel Expression, Stratified by Tumor Location</th>
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A Case of Mixed Neuroendocrine-Nonneuroendocrine Neoplasm of the Gastroesophageal Junction Utilizing Endoscopic Submucosal Dissection: An Exceedingly Rare Site

(Poster No. 53)

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Neuroendocrine tumors of the esophagus are rare, comprising only 0.2% of cases. The most recent World Health Organization classification of 2019 defines mixed neuroendocrine-nonneuroendocrine neoplasms (MiNENs) as neoplasms in which both neuroendocrine and non-neuroendocrine components exceed 30%. Only 4 cases of MiNEN of the gastroesophageal (GE) junction are reported in the literature, and this is the second case report of the utilization of the endoscopic submucosal dissection technique. A 61-year-old man presented with dyspepsia and epigastric pain. Endoscopy revealed a medium-sized nonobstructing, fungating mass at the GE junction (Figure 1.53, A), which was initially
biopsied and diagnosed as invasive adenocarcinoma. Subsequently, the mass was resected with endoscopic submucosal dissection with negative margins. On histopathologic examination, the tumor showed a mixed tumor composed of adenocarcinoma (50%) and neuroendocrine carcinoma (50%) (Figure 1.53, B). The neuroendocrine component was strikingly positive for synaptophysin (Figure 1.53, C). Chromogranin, CD56, and Ki-67 (80%). MOC-31 was positive in both components (Figure 1.53, D). Our case was consistent with the aforementioned diagnostic criteria and was diagnosed as MiNEN. The patient was treated with adjuvant chemotherapy, including cisplatin and etoposide. This very rare case adds to the scant literature on this topic. The preoperative diagnosis of MiNEN is challenging until the final analysis of the resection specimen. Because of its uncommon presentation, little is known about the optimal management strategy, and more studies are needed to recommend new therapeutic approaches. Prognosis depends on the stage and tumor type, with a better prognosis for those tumors without distant metastatic involvement.

PD-L1 Expression in 2 Cases of Malignant Gastrointestinal Neuroectodermal Tumor in Young Adults

(Poster No. 54)

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Malignant gastrointestinal neuroectodermal tumor (GNET), also known as clear cell sarcoma of the gastrointestinal tract, is an extremely rare entity. We report 2 cases in small bowel of young adults. Our first case involves a 24-year-old man who presented with painless lower gastrointestinal bleeding. Imaging confirmed small bowel bleeding and Meckel scan was positive in the right lower quadrant. Our second case involves a 27-year-old man who presented with severe anemia, jejunal mass, and multiple pelvic masses. Both patients underwent segmental small bowel resection with frozen section revealing malignant neoplasm, “possibly stromal tumor.” Grossly the specimens demonstrated intramural masses, 4.5 and 4.7 cm, respectively, with fleshy cut surface, focally involving the mucosa and covered by serosa. Microscopically the tumors were located predominantly in the submucosa and muscularis propria; they displayed spindle cells in sheets, fascicles, and pseudovascular, with well-formed eosinophilic cytoplasm (case 1; Figure 1.54, A) and polygonal, epithelioid cells with clear cytoplasm, prominent nucleoli, and osteoclast-like giant cells (case 2; Figure 1.54, B). Immunohistochemical stains revealed tumor cells positive for S100, SOX10, and synaptophysin, and negative for HMB45, Melan-A, AE1/3, SMA, DOG-1, CD34, and CD117. Fluorescence in situ hybridization for EWSR1 translocation was positive, confirming the diagnosis of GNET (Figure 1.54, C). The tumor from case 2 expressed PD-L1 (22C3) with 15% tumor proportion score (Figure 1.54, D), whereas case 1 was negative. Our cases highlight the importance of including GNET in the differential diagnosis of gastrointestinal tumors in young patients. Immunohistochemistry and fluorescence in situ hybridization are crucial for differentiating GNET from other intramural tumors of the GI tract. PD-L1 expression in subset of GNET might provide a target for immunotherapy for aggressive cases.

Regression of Alcoholic Cirrhosis: Histological Evaluation of 2 Cases

(Poster No. 55)

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Cirrhosis is known to be a dynamic process in which regression is possible with appropriate therapy. Wanless et al described the histology of cirrhosis regression as the “hepatic repair complex” in 2000. Since that time, few reports have provided supportive evidence regarding alcoholic liver disease. The aim of this report is to describe 2 cases of diagnosed cirrhosis related to chronic alcohol use in which histologic evaluation after abstinence revealed regression of disease. A 33-year-old man with chronic alcohol consumption, F4 fibrosis on FibroTest, and an esophageal varix underwent liver biopsy 3 months after alcohol cessation. Microscopy showed preserved hepatic architecture with foci of hepatocellular regeneration and no bridging fibrosis or cirrhosis. Histology remains the gold standard for the diagnosis and understanding of the progression/regression of cirrhosis, yet it is rarely performed, especially in a setting of alcoholic liver disease. We provide 2 cases in which the histology supports regression of clinically diagnosed cirrhosis due to chronic alcohol use.

Acute Liver Failure Triggered by Therapeutic Dose of Acetaminophen in a Patient With Cystic Fibrosis

(Poster No. 56)

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Acetaminophen (APAP) toxicity is the most common cause of acute liver failure (ALF) in the United States. Even therapeutic doses can be hepatotoxic in susceptible individuals. Patients with cystic fibrosis (CF) often have glutathione deficiency and increased susceptibility to liver injury. Our case involves ALF in a 22-year-old man with CF (AP508/c.2657+5G>A) treated with tezacaftor/ivacaftor. Following an episode of binge drinking and unintentional ingestion of 2.5 g of APAP, the patient developed nausea and vomiting, with aminotransferases >7000, synthetic liver dysfunction, renal failure, and lactic acidosis. He was outside the therapeutic window for N-acetylcycteine and developed ALF. He underwent liver transplantation 6 days after the onset of symptoms. Microscopic evaluation of the explant liver showed extensive perivenular hepatocytic damage and inflammation (Figure 1.56, A) with a moderate amount (40%) of macrovesicular and
RNA was negative. Polymerase chain reaction for CD56, TIA-1, and perforin and negative for CD5, CD8, CD25, CD30, immunohistochemistry, the atypical cells were positive for CD3, CD7, with variable azurophilic cytoplasmic granules (Figure 1.57, B). By had ovoid to folded nuclei and moderate to abundant pale cytoplasm.

eroded colonic mucosa with dense infiltrate of mononuclear cells with anal verge, which was biopsied. Microscopic examination showed portion of tubulovillous adenoma with intramucosal carcinoma and CD34 (Figure 1.57, C and D). In situ hybridization for EBV-encoded RNA was negative. Polymerase chain reaction for TCR gene rearrangement failed because of insufficient DNA. The findings were most consistent with NK-cell enteropathy (NKCE). NKCE is a rare indolent lymphoproliferative disorder characterized by atypical proliferation of NK cells within the mucosa of the gastrointestinal tract in adults presenting with nonspecific abdominal symptoms. NKCE shows significant immunophenotypic overlap with extranodal NK/T-cell lymphoma, which may result in misdiagnosis and unnecessary investigation and treatment. In contrast to NK/T-cell lymphoma, NKCE is not associated with EBV and does not demonstrate clonal T cell gene rearrangements. Lymphomatoid gastropathy, an entity restricted to the stomach of Japanese patients, shares overall histologic, immunophenotypic, and clinical features with NKCE.

Clinical Occult Mixed Neuroendocrine-Nonneuroendocrine Neoplasm Masquerading as Perianal Extramammary Paget Disease: A Small Series

(Poster No. 58)

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Context: Extramammary Paget disease (EMPD) is a rare group of insidious yet challenging entities characterized by intraepithelial infiltration by mucin-rich signet ring-like neoplastic cells. It can be primary (skin intraepidermal) or secondary to skin adnexal adenocarcinomas or visceral malignancies. EMPD remains notorious for its underdiagnoses and recurrence following resections. EMPD associated with mixed neuroendocrine-nonneuroendocrine neoplasm (MINEN) has remained elusive and poorly understood clinically and pathologically.

Design: Review of the gastrointestinal archive identified 3 perianal EMPD cases that were originally diagnosed as skin adnexal primary, but progressed despite clinical interventions. Subsequently biopsies were performed, and systemic ancillary testing was conducted.

Results: All cases (79-year-old woman and 77- and 38-year-old men) showed intraepidermal spreading of Paget cells, additionally, the first 2 showed poorly differentiated mucinous carcinoma containing signet ring-like and polygonal cells with pink granular cytoplasm arranged in clusters, glands, and single files, whereas the third patient showed portion of tubulovillous adenoma with intramucosal carcinoma and EMPD involving adjacent anal mucosa. Immunostains revealed strongly positive synaptophysin, chromogranin A, INSM1, CDX2, and CK20, negative GATA3, and weak CK7 in both carcinomas and intradermal Paget cells of all cases, with amphicrine features. Combined, these findings uncovered an originally unsuspected MINEN-EMPD association. Two patients underwent FOLFOX chemotherapy followed by resection; no recurrence was detected more than 60 months later. The third patient is currently undergoing prechemotherapy followed by therapy imaging studies.

Conclusions: This study illustrates an underrecognized MINEN-EMPD association, highlighting the pivotal roles of systemic histomorphologic and immunohistochemical evaluation. Awareness of this differential diagnosis is essential for ensuring pathologic diagnosis and proper patient management.

Supplemental Studies Including Aberrant CD43 Expression as a Helpful Marker in Evaluation of Post-treatment Gastric MALT Lymphoma

(Poster No. 59)

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Context: Evaluation of posttreatment biopsies for gastric extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) is challenging given the morphologic and immunophenotypic overlap with gastritis and reactive lymphoid hyperplasia. The GELA histologic scoring system is commonly used. We hypothesized that immunohistochemical (IHC) and molecular methods may supplement hematoxylin-eosin evaluation of such cases.

Design: We reviewed 24 cases of gastric MALT lymphoma and follow-up biopsies diagnosed at our institution between 2008 and 2020. MALT lymphoma was diagnosed based on the World Health Organization classification. Potential useful markers for MALT lymphoma in pretreatment and posttreatment biopsies were evaluated including aberrant CD43 expression, presence of clonal plasma cells by microvascular steatosis (Figure 1.56, B). Ballooning degeneration and apoptotic hepatocytes (Figure 1.56, C) were present along with cholestasis (Figure 1.56, D). No fibrosis was identified on trichrome stain. These findings were consistent with drug/toxin injury in this patient with a history of CF and recent APAP use. This case suggests the possibility that CF patients are at increased risk for APAP-related hepatotoxicity compared with the general population. It is unknown whether this is due to glutathione depletion, underlying steatosis, concomitant medications, or other factors. The ubiquitous use of APAP in conjunction with the potential for morbidity in CF patients warrants further investigation with the goal of preventing further harm to this already vulnerable population.
A Case of Mucinous Adenocarcinoma Arising From Retrorectal Cystic Hamartoma

(Poster No. 60)

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Retrorectal cystic hamartoma or tailgut cyst is a rare congenital malformation that presents in the presacral space. Tailgut cysts arise from tailgut embryonic remnants and are more common in females. Malignant transformation of tailgut cysts is very rare. We report a case of an 83-year-old woman who presented with progressive pelvic pressure and elevated serum carcinoembryonic antigen levels. Imaging studies revealed a cystic mass with irregular wall thickening and enhancing solid component centered in the retrorectal/presacral space. The mass was resected, and the initial extensive samplings of specimen showed a multiloculated cystic structure with mucinous glandular epithelium as well as squamous linings. A focus of dysplastic columnar epithelium (Figure 1.60, A) was identified and therefore the entire specimen was submitted for histologic examination. The additional sections revealed few floating malignant epithelial cells within pools of extracellular mucin (Figure 1.60, B) as well as foci of invasive adenocarcinoma (Figure 1.60, C). Immunohistochemical stain for CK20 highlighted the neoplastic glands (Figure 1.60, D). The diagnosis of mucinous adenocarcinoma arising from a tailgut cyst was rendered. The carcinoma focally extended to the surgical resection margin and there was also acellular mucin present at the margin. Periodic postion emission tomography-computed tomography scans and serum carcinoembryonic antigen levels for assessing the treatment response and early detection of possible future recurrence were recommended. Although malignancy arising in tailgut cyst is very uncommon, this case demonstrates the importance of adequate samplings in these lesions to avoid missing an important diagnosis with significant impact on patient prognosis and follow-up.

Small Bowel Diverticulosis and Malrotation

(Poster No. 61)

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Diverticulosis of the small bowel is a rare entity; it is seen in approximately 1% of the population. It is commonly multiple and can vary from a few millimeters to several centimeters in size. Small bowel diverticulosis generally lacks a true muscular wall. The clinical picture may be an incidental finding without symptom, an acute complication, or chronic symptoms. A 65-year-old woman with past medical history of GERD presented with severe abdominal pain and was found to have small bowel diverticulosis complicated by diverticulitis and perforation. Computed tomography of abdomen with contrast also showed an unusual anatomic variant consisting of the ascending colon, terminal ileum, and cecum extending across the midline into the left upper quadrant. She underwent small bowel resection. Specimen received in pathology consisted of a segment of small bowel (44 cm) with more than 20 diverticula, the largest measuring 3.2 cm with focal exudate formation. Histology revealed diverticulosis, severe diverticulitis with abscess formation, and focal perforation. This case reports a jejunal diverticulosis associated with congenital dislocation of the terminal ileum, cecum, and ascending colon. The most common types of small bowel diverticula are congenital in origin and include Meckel diverticulum and duodenal diverticulosis. Less commonly, acquired cases of small bowel diverticulosis are encountered secondary to neuromuscular abnormalities. In this case, it is unclear if the diverticulosis is due to a congenital cause or acquired (Figure 1.61).

Primary Gastrointestinal Stromal Tumor of the Liver Presenting as a Cystic Mass

(Poster No. 62)

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Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal-origin tumors of the gastrointestinal tract. They commonly arise in interstitial cells of Cajal that have acquired receptor tyrosine kinase gene mutations, most commonly KIT or PDGFRA mutations. GISTs are most frequently located in the luminal gastrointestinal tract. Primary GIST of the liver is exceedingly rare, though metastatic spread of GIST to the liver is fairly common. We present a case of primary GIST of the liver in a patient with a large cystic liver mass. A 70-year-old woman presented with a 6-month history of abdominal pain and distention. Computed tomography scan revealed a cystic hepatic mass measuring 23 × 20 × 14 cm with an irregular thickened wall and septations replacing nearly the entire right lobe of the liver (Figure 1.62, A). A fine-needle aspiration was nondiagnostic with a mixture of erythrocytes, macrophages, and leukocytes. Resection was performed. Intraoperatively, 1.5 L of bloodlike fluid was drained from the mass and the cystic wall was submitted for pathology. Histologic examination revealed the wall consisted of GIST cells,
Steatohepatitic Variant of Hepatocellular Carcinoma in Pediatric Population Represents Distinct Clinicopathologic Entity

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Context: Steatohepatitic variant of hepatocellular carcinoma (SH-HCC) is a variant recapitulating steatohepatitis and often associated with metabolic syndrome. The demographics, risk factors, clinicopathologic characteristics, and prognosis of SH-HCC in the pediatric population are not well characterized, which may lead to underdiagnosis and ineffective treatment approaches.

Design: The pathology databases (2004–2021) of the participating institutions were searched for hepatocellular carcinoma with steatosis in the pediatric population. Cases for which histologic materials and follow-up information were available were included in the study. Slides were reviewed to satisfy SH-HCC criteria. Targeted next-generation sequencing was used for genomic analysis.

Results: Eight cases fulfilled the study criteria. Genetic information was available for case 1. The results are summarized in the Table. Important findings included the following: SH-HCC occurred predominantly in white boys 9.0 ± 7.1 years old. It was not associated with infectious hepatitis or metabolic syndrome. It often arose with a background of cirrhosis (63%) or steatosis (63%). At diagnosis, SH-HCC was predominantly confined to the liver, and AFP was increased in 50%. SH-HCC was refractory to chemotherapy but had favorable prognosis with surgical treatment. Histologically SH-HCC tended to be multifocal (89%) and well differentiated (G1) with bland features and very rare mitoses or lymphovascular invasion (13%). Genetic alterations in case number 1 included CTNNB1 in-frame exon 3 156-bp deletion and MAPK1 p.Glu322Lys missense variant.

Conclusions: Despite extreme infrequency, SH-HCC occurs in the pediatric population even in children without underlying liver disease. Strict diagnostic criteria and genetic profiling of this tumor is required to avoid unnecessary chemotherapy and develop effective targeted therapy of pediatric SH-HCC.

<table>
<thead>
<tr>
<th>Case No./Sex/Age, y/Ethnicity*</th>
<th>Etiologic Associations</th>
<th>At Diagnosis</th>
<th>Clinical Course, Outcomes</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/M/6/white Hispanic 9.0</td>
<td>Strong FH of metabolic syndrome</td>
<td>Liver confined; AFP 19.595 ng/mL</td>
<td>Neoadjuvant chemotherapy → OLT → chemotherapy and sorafenib → disease free (8 mo)</td>
<td>Native liver: multifocal SH-HCC, 10.5 cm, G3, LVI, 5% tumor necrosis (treatment effect)</td>
</tr>
<tr>
<td>2/M/6/white Hispanic 7.1</td>
<td>Possible toxin exposure in father</td>
<td>Liver confined; AFP 31.000 ng/mL</td>
<td>Lobectomy (60%) of liver → chemotherapy → disease free (5 mo, no appointments for 60 mo)</td>
<td>Right liver lobe: multifocal SH-HCC, 8.5 cm, G1, Background steatosis and fibrosis</td>
</tr>
<tr>
<td>3/M/3/white Hispanic 9.0</td>
<td>FH of DM</td>
<td>Extraliver extension, nonresectable; AFP 60.050 ng/mL</td>
<td>Neoadjuvant chemotherapy → radiation → death (5 mo after disease onset)</td>
<td>Biopsy: malignant hepatocellular neoplasm with steatosis, ballooning and fibrosis.</td>
</tr>
<tr>
<td>4/M/15/white Hispanic 10.5</td>
<td>Tyrosinemia, liver cirrhosis, obesity</td>
<td>Liver confined; AFP 150.58 ng/mL</td>
<td>OLT → recurrence (18 mo) and stomach DLBCL → s/p ablation (2 mo)</td>
<td>Native liver: multifocal SH-HCC, 2.1 cm, G2. Background steatosis and cirrhosis</td>
</tr>
<tr>
<td>5/M/4/white non-Hispanic 8.0</td>
<td>s/p Kasai procedure, liver cirrhosis</td>
<td>Liver confined; AFP 2 ng/mL</td>
<td>OLT → sorafenib → disease free (134 mo)</td>
<td>Native liver: multifocal SH-HCC, 3.8 cm, G1, Background steatosis and cirrhosis</td>
</tr>
<tr>
<td>6/M/24/white non-Hispanic 8.0</td>
<td>s/p Kasai procedure, liver cirrhosis, DM</td>
<td>Liver confined; AFP ND, incidental finding at OLT, but tumor AFP by IHC</td>
<td>OLT → disease free (2 mo, lost to follow-up)</td>
<td>Native liver: multifocal SH-HCC, 2.5 cm, G1. Background steatosis and cirrhosis; nonnecrotizing granulomas in HCC</td>
</tr>
<tr>
<td>7/M/7/white non-Hispanic 8.0</td>
<td>deletion in 2q13 with multiple abnormalities and liver cirrhosis</td>
<td>Liver confined; AFP ND, incidental finding at OLT, but tumor AFP by IHC</td>
<td>OLT → disease free (35 mo)</td>
<td>Native liver: multifocal SH-HCC, 1.8 cm, G1-G2. Background cirrhosis, ischemic injury</td>
</tr>
<tr>
<td>8/F/7/white Hispanic 8.0</td>
<td>s/p Kasai procedure, liver cirrhosis</td>
<td>Liver confined; AFP 1.67 ng/mL</td>
<td>OLT → disease free (27 mo). Note: retransplantation done because of rejection (no HCC in explant)</td>
<td>Native liver: unifocal SH-HCC, 3.6 cm, G1. Background cirrhosis</td>
</tr>
</tbody>
</table>

Abbreviations: AFP, α-fetoprotein; DM, diabetes mellitus; FH, family history; G1, well differentiated; G2, moderately differentiated; G3, poorly differentiated; IHC, immunohistochemistry; LVI, lymphovascular invasion; ND, not done; OLT, orthotopic liver transplantation; s/p, status post; +, positive; -, negative.

*7 patients were Florida residents.

*For multifocal tumors, size of the largest nodule is given.
Function of Enhancer of Zeste Homolog 2 (EZH2) Protein and Its Associated Intracellular Signaling Molecules P-ERK, MYC, and P-STAT3 in Pancreatic Cancer

(Poster No. 65)

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Context: EZH2, an important histone methyltransferase, has been shown to play an important role in tumorigenesis of various carcinomas and hematopoietic neoplasms. Here we investigated the expressions of EZH2 and its associated potential regulators p-ERK, MYC, and p-STAT3 in pancreatic cancer.

Design: Immunohistochemical staining for EZH2, p-ERK, p-STAT3, and MYC was performed in 41 pancreatic adenocarcinoma and 6 intraductal papillary mucinous neoplasm (IPMN) cases. Positive staining of neoplastic cells was scored. Statistical analysis was performed using Fisher exact test by Graphpad Prism (San Diego, California).

Results: Thirty-five of 41 cases of pancreatic adenocarcinoma (85.3%) showed strong EZH2 expression, whereas the low-grade IPMN showed no or very low EZH2 expression. Among pancreatic adenocarcinoma cases, 65.8% (27 of 41) showed strong p-ERK expression; 43.3% (16 of 37) showed strong MYC expression; and 47.2% (17 of 36) showed strong p-STAT3 expression (Table). Interestingly, EZH2 and p-ERK1/2 expression showed no significant association with tumor grades and lymph nodal metastasis, whereas MYC and p-STAT3 expression significantly increased in moderate to poorly differentiated carcinoma (P < .01). Further study of EZH2-positive cases showed 66% (23 of 35) coexpressed pERK1/2, 41% (13 of 32) coexpressed MYC, and 56% (19 of 34) coexpressed pSTAT3. MYC and/or pSTAT3 coexpression with EZH2 were significantly increased in the higher-grade tumors with or without metastasis and strongly associated with survival/prognosis (P < .01).

Conclusions: EZH2 is strongly expressed in advanced stage of pancreatic adenocarcinoma, indicating its oncogenic role in pancreatic cancer. MYC and/or pSTAT3 in association with EZH2 expression appears to play a critical role in driving tumor progression. These molecules may serve as prognostic biomarkers and therapeutic targets for advanced pancreatic cancer.

<table>
<thead>
<tr>
<th>EZH2, No. Positive Cases/Total (%)</th>
<th>p-ERK, No. Positive Cases/Total (%)</th>
<th>MYC, No. Positive Cases/Total (%)</th>
<th>p-STAT3, No. Positive Cases/Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1N (well-differentiated carcinoma without lymph node metastasis)</td>
<td>4/4 (100)</td>
<td>3/4 (75)</td>
<td>0/4 (0)</td>
</tr>
<tr>
<td>G1N (well-differentiated carcinoma with lymph node metastasis)</td>
<td>5/6 (83)</td>
<td>5/6 (83)</td>
<td>1/6 (17)</td>
</tr>
<tr>
<td>G2N (moderately differentiated carcinoma without lymph node metastasis)</td>
<td>9/11 (82)</td>
<td>7/11 (64)</td>
<td>7/11 (64)</td>
</tr>
<tr>
<td>G2N (moderately differentiated carcinoma with lymph node metastasis)</td>
<td>11/13 (85)</td>
<td>8/13 (61.5)</td>
<td>4/9 (44.4)</td>
</tr>
<tr>
<td>G3N (poorly differentiated carcinoma with lymph node metastasis)</td>
<td>6/7 (86)</td>
<td>4/7 (57.1)</td>
<td>4/7 (57.1)</td>
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</table>

Morphological Correlates of Tumor Mutation Burden in Colorectal Adenocarcinoma: A Tertiary Cancer Center Experience

(Poster No. 66)

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Context: Tumor mutation burden (TMB) is defined as the number of mutations per megabase region of tumor. Colorectal carcinoma (CRC) with low TMB is shown to have poor treatment response. Our study reports association of TMB with known morphologic prognostic factors of CRC.

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Swachi Jain, MBBS (sjain16@northwell.edu); Yonah Ziemba, MD; Taïsia Vitkovski, DO; Rebecca Thomas, MD; Arvind Rishi, MD.

Department of Pathology, Northwell Health—Long Island Jewish Medical Center, New Hyde Park, New York.

Context: Tumor mutation burden (TMB) is defined as the number of mutations per megabase region of tumor. Colorectal carcinoma (CRC) with low TMB is shown to have poor treatment response. Our study reports association of TMB with known morphologic prognostic factors of CRC.
**Design:** Retrospective review of 1374 primary CRCs was performed at a tertiary care center from 2016 to 2020. TMB analysis was done at Foundation Medicine, Cambridge, Massachusetts. The association of TMB with microsatellite (MS) status, nodal metastases, lymphovascular invasion (LVI), and tumor budding was studied and analyzed using χ² test. Cases with fewer than 12 mutations were classified as low TMB as per The Cancer Genome Atlas for CRC.

**Results:** Molecular analysis including TMB was requested in 8.6% of primary CRCs (n = 119), of which 80.6% (n = 96) had low TMB. Presence of low TMB (Table) was associated with a lower incidence of MS instability (2.1% versus 82.6%; P < .05), higher incidence of nodal metastases (82.29% versus 43.48%; P < .05), LVI (80.90% versus 43.48%; P < .05), and high tumor budding (31.11% versus 28.57%; P = .41). Mutation profiling of low-TMB cancers showed high frequency of mutations in TP53 and APC, followed by PIK3CA, SMAD4, SOX9, CTNNB1, FBXW7, and ARID1A.

**Conclusions:** Low TMB showed significantly high association with poor prognostic factors including MS instability, LVI, and regional nodal metastases. Our study suggests that routine TMB analysis of primary CRC may be helpful in predicting prognosis and personalize management. Further studies in mutation profiling may identify novel therapeutic targets that could improve survival in this subset of CRCs.

### Association of Tumor Mutation Burden in Colorectal Cancers With Prognostic Factors

<table>
<thead>
<tr>
<th></th>
<th>Low TMB, % (n = 96)</th>
<th>High TMB, % (n = 23)</th>
<th>P Value</th>
</tr>
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<tbody>
<tr>
<td>Microsatellite instability</td>
<td>2.1</td>
<td>82.6</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Nodal metastases</td>
<td>82.29</td>
<td>43.38</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td>80.90</td>
<td>43.48</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>High tumor budding</td>
<td>31.11</td>
<td>28.57</td>
<td>.41</td>
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**Expression of Immunohistochemical Markers (CD117, mCEA, and CD56) in Giardia lamblia Trophozoites**

(Poster No. 69)

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**Context:** Giardiasis is an infectious cause of diarrhea seen in 0.11% of duodenal biopsies. Duodenal biopsies demonstrate highest sensitivity (82.5%–100%) for diagnosis but can often be missed or misinterpreted on hematoxylin and eosin slides. Considering a low prevalence and simple treatment, we interpreted expression pattern of different immunohistochemical stains for the diagnosis of *Giardia lamblia*.

**Design:** Retrospective analysis of duodenal biopsies from January 2011 through January 2020 in our health system was performed. Seven cases of giardiasis were identified, and diagnosis was confirmed. Five cases had material remaining on the paraffin block, and the expression of CD117, monoclonal carcinoma embryonic antigen (mCEA), and CD56 was studied. Duodenal biopsies without giardiasis were paired as controls.

**Results:** CD117 stained the paired nuclei and apical cellular membrane of trophozoites in 4 of 5 cases (80%). Three of 5 cases (60%) were positive for mCEA and stained the paired nuclei. All cases were negative for CD56 stain. The lamina propria showed internal control staining of mast cell (CD117) and natural killer cells (CD56).

**Conclusions:** CD117 staining is currently the best immunohistochemical stain for diagnosis of giardiasis because of its consistent and typical staining pattern, followed by mCEA. Other stains need further studies to identify utility in daily practice. Frequent antigenic shifts can occur following interaction with the duodenal mucosa and treatment, which could explain the variable expression of markers. Routine staining of duodenal biopsies with CD117 in cases with high clinical suspicion and travel history should be encouraged to confirm the diagnosis and enhance patient care.

**A Case of Checkpoint Inhibitor–Induced Colitis in the Pediatric Population**

(Poster No. 70)

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Immune checkpoint inhibitors are immunotherapeutics with fewer side effects than chemotherapy. However, colitis is an important complication and has been described in adults; we present the first case in an adolescent male. An 18-year-old male with a history of Lynch syndrome and glioblastoma multiforme status post resection and radiation but without history of inflammatory bowel disease, transplant, and...
or infection presented with weeks of abdominal pain and bloody stools (more than 10 episodes per day). He had started PD-1 inhibitor (pembrolizumab) therapy 10 days prior. Clinical workup for infectious etiologies and inflammatory bowel disease were all negative. Endoscopy and colonoscopy visualized evidence of esophagitis, gastritis, duodenitis, and severe left-sided colitis. Consistently, biopsies showed mild to moderate acute and chronic inflammation in the esophagus, stomach, and duodenum; severe active colitis with ulceration, neutrophilic microabscesses, epithelial cell apoptosis, and necroinflammatory exudates in the transverse and descending colon; severe chronic active colitis with reactive atypia in the sigmoid colon and rectum; and no significant histopathologic abnormalities in the ileum and ascending colon. No granulomas, dysplasia, or viral inclusions were identified. There was no basal plasmacytosis or lymphoplasmacytic expansion of the lamina propria. Given both the history and clinicopathologic findings, this case most likely represented a side effect of the patient’s immunotherapy, though a remote possibility of early-stage Crohn disease cannot be completely ruled out. Because of these findings, the patient is undergoing reevaluation of his immunotherapy regimen. We present this case to raise awareness of this entity in pediatrics.

“Mesenteric Cyst”—Differential Diagnoses and Associated Uncommon Histologic Features

(Poster No. 71)

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Enteric duplication cysts are rare congenital abnormalities and are most often detected in the first few years of life. The most common involved site is ileum, but it can occur anywhere along the gastrointestinal tract. The presenting symptoms can be variable depending upon size and location of the cyst. We report an unusual presentation of a “mesenteric cyst,” the differential diagnoses, and associated uncommon histologic features. A 3-year-old girl presented to the emergency department with abdominal pain, vomiting, and low-grade fever. Imaging revealed a thick-walled cystic mass above the bladder with fluid-filled levels. On diagnostic laparoscopy, the cystic mass was noted within the mesentery of the terminal ileum. The resection specimen was a 4.2-cm unicystic cystic structure with predominantly smooth lining. The cyst wall exhibited mucosa, submu cosa, a well-defined muscularis propria with nerves and ganglion cells, and serosa. The lining epithelium was variable, predominantly demonstrating ciliated pseudostratified columnar epithelium. The organized muscular layer excluded an enterogenous cyst and mes en teric cyst, and a diagnosis of enteric duplication cyst was rendered, highlighting that assessment of ganglion cells in the muscular wall in a “mesenteric cyst” is essential. Several case reports have reported respiratory epithelium or foregut duplication cysts; however, ciliated epithelium in a midgut enteric duplication is very rare, and only a few cases have been reported. Albeit rare, given the advent of advanced imaging and laparoscopic surgery, these cases have frequently involved a surgical specimen and warrant an increased awareness of diverse microscopic findings.

A Granular Cell Tumor of the Rectum: A Very Rare Entity

(Poster No. 72)

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Granular cell tumor, also known as Abrikossoff tumor, is a soft tissue neoplasm arising from Schwann cells. Although it is predominantly a benign tumor, 1% of the cases are reported to be malignant. About 10% of the tumors develop in the gastrointestinal tract, with esophagus being the most common site and rectum being the rarest. We report a case of granular cell tumor in a 52-year-old man who presented to the gastroenterology clinic for screening colonoscopy. The patient denied any gastrointestinal-related complaints with no family history of colon cancer. Colonoscopy revealed a submucosal, smooth, yellowish 10-mm semisessile polyp in the rectum at 10 cm proximal to the anus, which was removed with a hot snare without complication (Figure 1.72, A). Histologic examination on low power showed a polyp with intact mucosa overlying a submucosal, poorly circumscribed unencapsulated tumor (Figure 1.72, B). On higher magnification, the tumor was composed of plump polygonal cells with abundant granular eosino-philic cytoplasm and small to large nuclei with vesicular chromatin (Figure 1.72, C). Immunohistochemical stains showed the neoplastic cells were diffusely and strongly positive for S100 (Figure 1.72, D) and negative for desmin, smooth muscle actin, c-kit, and CD34. Thus, the resected tumor was diagnosed as a benign granular cell tumor with uninvolved margins. It is important for pathologists to be aware of varying benign and malignant entities that show granular cell changes. Differential diagnoses include leiomyoma and leiomyosarcoma, gastrointestinal stromal tumor, melanoma, and metastatic renal cell carcinoma. Careful evaluation of clinical, histologic, and immunohis-tochemical findings should facilitate an accurate diagnosis.

Pancreatic Heterotopia of the Gallbladder

(Poster No. 73)

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Pancreatic heterotopia is aberrantly located pancreatic tissue having no vascular, neural, or anatomic connection to the normal pancreas. Commonly located in the stomach, it has also been reported in the small bowel, omentum, hepatobiliary system, spleen, and mediastinum. Involvement of the gallbladder is rare with reported incidence being 0.1%. Clinically it can present as acute and chronic cholecystitis and rarely an obstructing mass. We report a case of a 36-year-old man with a history of hyperlipidemia who presented with history of right upper quadrant abdominal pain and weight loss. Abdominal ultrasound demonstrated cholelithiasis and sludge within the gallbladder. Grossly, the gallbladder measured 8 × 3.5 × 3 cm and appeared distended with cholelithiasis. Microscopic examination revealed a focus of pancreatic heterotopia measuring 7 mm within the muscularis propria. It was composed of pancreatic acini, ducts, and islets and was classified as modified Heinrich type I. No dysplasia or malignancy was identified. The gallbladder was extensively sampled but no other foci of pancreatic heterotopia or other lesions were identified. Background gallbladder showed acute and chronic inflammation with focal intestinal metaplasia. Pancreatic heterotopia of the gallbladder is a very rare condition. It is important to recognize this entity to prevent overdiagnosis as a malignancy. Additionally, recognition is important to avoid potential complications and related pathologies.

Lifting Agent Granuloma— Gross Specimen, Frozen Section Analysis, Hematoxylin and Eosin Findings, and Immunohistochemical Phenotype

(Poster No. 74)

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We present the case of a 58-year-old woman with a lifting agent granuloma (LAG), a novel entity that occurs because of use of nonsaline compound for the purpose of lifting soft tissue at various anatomic locations.
RNA-Seq Analysis of Hepatocellular Carcinoma Liver Samples Identified Oxidative Phosphorylation as the Major Pathogenetic Feature

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**Context:** Dysregulation of mRNAs and associated genes plays critical roles in the etiology and progression of hepatocellular carcinoma (HCC). Previous transcriptomic studies of HCC have been largely focused on Asian populations based on microarray platforms. Next-generation-based RNA sequencing has provided an unparalleled power to comprehensively characterize HCC at the whole transcriptome level.

**Design:** We identified 17 fresh frozen HCC samples of white patients with paired nonneoplastic liver from our Biobank inventory. RNA-seq analyses were performed to identify genes, pathways, and functional terms differentially regulated in HCC versus normal tissues.

**Results:** At an FDR level of 0.1, a total of 13% (n = 4335) of transcripts were upregulated and 19% (n = 6454) down-regulated in HCC versus normal tissues, suggesting major transcriptomic dysregulation in HCC. Eighty-five KEGG pathways were differentially regulated (FDR < 0.1), with almost all pathways (n = 83) upregulated in HCC. Among the top upregulated pathways was oxidative phosphorylation (hsa00190) (FDR = 1.12 × 10^{-10}), which was confirmed by DAVID enrichment analysis using upregulated genes (Bonferroni corrected, P < 0.05). Consistent with oxidative stress, several DNA damage-related signals, for example, the upregulated hsa03420 nucleotide excision repair (FDR = 1.14 × 10^{-4}) and hsa04340 base excision repair (FDR = 2.71 × 10^{-4}), were observed. Additionally, among down-regulated genes (Bonferroni corrected, P < 0.05), terms related to cellular structures, for example, cell membrane (FDR = 3.05 × 10^{-4}) and cell junction (FDR = 2.41 × 10^{-4}), were highly enriched, suggesting a breakdown of cellular structure in HCC.

**Conclusions:** Our findings support oxidative phosphorylation and the associated oxidative stress damage as the major driving factor and pathologic feature in HCC.

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**Utilization of a Systematic Histopathology Protocol Led to the Discovery of High Prevalence of Eosinophilic Gastritis and/or Eosinophilic Duodenitis in Patients With Moderate-Severe Gastrointestinal Symptoms: Results From 2 Prospective Studies**

(Robert M. Genta, MD (rmgента@gastropath.com); Kevin O. Turner, DO; Margaret H. Collins, MD; Marjorie M. Walker, BMBS;)
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**Context:** Eosinophilic gastritis (EG) and/or duodenitis (EoD) are detected with increasing frequency. Although there are not yet consensus diagnostic criteria, recent prospective trials have used standardized diagnostic criteria for EG/EoD as agreed upon by the US Food and Drug Administration to evaluate novel therapies and study the prevalence of these diseases.

**Design:** We developed a pathology protocol to quantify eosinophilia in 8 gastric and 4 duodenal biopsies from subjects with moderate-severe gastrointestinal (GI) symptoms but no prior history of EG/EoD in 2 separate prospective studies (ENIGMA and AK002-019). Eosinophils were counted in 5 separate nonoverlapping high-power fields (hpf; 0.237 \( \text{mm}^2 \)) for each biopsy sample. Eosinophilia was defined as \( \geq 30 \) eosinophils in \( \geq 5 \) gastric hpf (EG), and/or \( \geq 30 \) eosinophils in \( \geq 3 \) duodenal hpf (EoD).

**Results:** Of 88 subjects biopsied in the ENIGMA study, 72 (82%) were found to have EG and/or EoD (Table). Furthermore, of 26 subjects biopsied in ENIGMA without a prior diagnosis of EG and/or EoD, 58% were found to have EG and/or EoD. Similarly, of 405 subjects in the AK002-019 study, most of whom (93%) were diagnosed as having functional GI disorders, 181 (43%) met histologic criteria for EG and/or EoD.

**Conclusions:** Systematic and intentional evaluation of gastric and duodenal eosinophilia in subjects with chronic, moderate-severe GI symptoms in 2 separate studies found 45% of patients without a previous diagnosis of EG/EoD met the histologic criteria for EG/EoD. Given the high diagnostic yield, a standardized biopsy and histopathology protocol is indicated to evaluate symptomatic patients for EG/EoD so that targeted therapies may be utilized.

<table>
<thead>
<tr>
<th>Rates of Discovery of EG and/or EoD in 2 Separate Trials of Patients With Gastrointestinal Symptoms</th>
<th>ENIGMA(^{a})</th>
<th>Prevalence(^{a})</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptomatic Patients (n)</strong></td>
<td>All Biopsied Patients, % (No.)</td>
<td>No Prior Diagnosis, % (No.)</td>
</tr>
<tr>
<td><strong>Who Meet Criteria</strong></td>
<td>(n = 88)</td>
<td>(n = 26)</td>
</tr>
<tr>
<td>EG and/or EoD</td>
<td>82 (72)</td>
<td>58 (15)</td>
</tr>
<tr>
<td>EG, with or without EoD</td>
<td>63 (45)</td>
<td>47 (7)</td>
</tr>
<tr>
<td>EG without EoD</td>
<td>14 (10)</td>
<td>20 (3)</td>
</tr>
<tr>
<td>EG with EoD</td>
<td>49 (35)</td>
<td>27 (4)</td>
</tr>
<tr>
<td>EoD, with or without EG</td>
<td>86 (62)</td>
<td>80 (12)</td>
</tr>
<tr>
<td>EoD without EG</td>
<td>38 (27)</td>
<td>53 (8)</td>
</tr>
</tbody>
</table>

\(^{a}\) Moderate to severe symptoms with \( \geq 30 \) eosinophils in 5 gastric high-power fields (hpf) (EG) and/or \( \geq 30 \) eosinophils in 3 duodenal hpf (EoD).

\(^{b}\) A total of 113 patients entered screening, 51 of which did not have a prior diagnosis of EG/EoD.

\(^{c}\) A total of 556 patients entered screening; all did not have a prior diagnosis of EG/EoD.

**Focal Nodular Hyperplasia Presenting in an Infant With Niemann Pick Disease**

(Christo No. 79)

Rocio López-Panqueva, MD\(^{1}\) (rocio.lopez@fsfb.org.co); Marcela Mejía-Arango, MD; Rafael García-Duperly, MD; Mónica Ortíz-Pereira, MD; Belen Mendoza de Molano, MD. 2Departments of 1Pathology and Laboratories, Surgery and 2Gastroenterology, Fundación Santa Fe de Bogotá/Universidad de los Andes, Bogota, Colombia; 3Department of Internal Medicine, Fundación Santa Fe de Bogotá, Bogota, Colombia.

**Context:** Inflammatory bowel disease (IBD) is a chronic immune-mediated illness with an increasing incidence in Latin America.

**Design:** Descriptive retrospective study of the demographic, clinical, and pathologic characteristics of patients with IBD at Hospital Universitario Fundación Santa Fe de Bogotá between 1996 and 2019. Pathologic and clinical characteristics were reviewed and compared with other institutions from Colombia.

**Results:** A total of 379 patients were included, 277 with ulcerative colitis (UC) and 102 with Crohn disease (CD). Gender, age at diagnosis, hospitalization rate, mortality, and surgery rate are shown in the Table. UC involvement was rectal (35.7%), descending colon (21.7%), and pancolitis (42.6%). A total of 35.4% of patients had clinically severe disease. Surgical intervention rate was significant (OR 3.70, \( P < .01 \)) and 13% of UC patients received biologic therapy. CD involvement was colonic (12.9%), ileocolic (43.6%), and right (43.6%). Clinicopathologic pattern was inflammatory (51%), stenosing (32%), and fistulizing (17%). Forty-five percent of the patients received biologic therapy and 55.9% surgical intervention. Perianal complications were the first indication. Sclerosing primary cholangitis was found in 4% (n = 15).2 of these patients developed colorectal carcinoma (OR 8.1; \( P = .008 \)). Sixteen of the IBD patients developed colorectal carcinoma, 13 with UC, and 3 with CD. Dysplasia was found in 7 patients with UC.

**Conclusions:** The characteristics of the patients with IBD diagnosed and treated at Hospital Universitario de la Fundación Santa Fe de Bogotá are, overall, consistent with the findings and literature from other institutions in Colombia. Further histopathologic, imagingology, and laboratory studies may increase our knowledge of the disease in our specific population.

### Demographic Characteristics (N = 379)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Ulcerative Colitis (n = 277)</th>
<th>Crohn Disease (n = 102)</th>
<th>Fisher ( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age at diagnosis</td>
<td>42 (7–91)</td>
<td>47 (12–86)</td>
<td>.02</td>
</tr>
<tr>
<td>(range), y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male, No. (%)</td>
<td>132 (47.7)</td>
<td>41 (40.6)</td>
<td>.24</td>
</tr>
<tr>
<td>Female, No. (%)</td>
<td>145 (52.3)</td>
<td>61 (59.4)</td>
<td>.24</td>
</tr>
<tr>
<td>Hospitalization rate, No. (%)</td>
<td>132 (47.7)</td>
<td>84 (82.3)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Mortality rate, No. (%)</td>
<td>2 (0.7)</td>
<td>1 (0.9)</td>
<td>1</td>
</tr>
<tr>
<td>Surgery, No. (%)</td>
<td>45 (16.2)</td>
<td>57 (55.9)</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

**Focal Nodular Hyperplasia Presenting in an Infant With Niemann Pick Disease**

(Poster No. 79)

Crystal Bockoven, MD (ckockedave@gmail.com); Roshan Mahabir, MD, MPH, PhD; Murad Alturtukistani, MD; Bruce Pawel, MD; Nick Shillingford, MD; Shengmei Zhou, MD; Ryan Schmidt, MD; Mika Warren, MD; Larry Wang, MD, PhD. Department of Pathology and Laboratory Medicine, Children’s Hospital of Los Angeles, California. A 20-month-old male with developmental delay and chronic vomiting presented with hepatosplenomegaly. He was also evaluated by medical genetics with concerns for lysosomal storage disease. He was referred to hepatology after laboratory workup showed elevated transaminases. A 4.5-cm liver mass was identified by ultrasound. Percutaneous liver biopsy showed nodular structures separated by fibrous septa containing reactive ductular structures. Normal portal triads were not appreciated. Immunohistochemical stain for glutamine synthetase showed a patchy, maplike staining pattern in the nodular areas, typical for focal nodular hyperplasia (FNH). Both the nodules and the background liver contained foamy cells with a soap bubble–like background. Normal portal triads were not appreciated. Electron microscopy demonstrated diffusely enlarged hepatocytes and Kupffer cells with numerous intracytoplasmic vacuoles containing lamellar material. Targeted exome sequencing showed compound heterozygous disease-causing missense variants in the SMPD1 gene. These findings were consistent with Niemann-Pick disease (NPD). FNH comprises approximately 2% of all pediatric liver tumors and can present at any age. There are very few reports of FNH in infancy in the English literature and no reports of FNH in NPD (PubMed and Google search). We report a rare case of FNH in infancy.
in the setting of NPD. Although rare in infancy, FNH can occur in the setting of other diseases, and care should be taken not to miss background liver disease.

**Eosinophilic Appendicitis: Report of a Series**  
*(Poster No. 80)*  

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**Context:** Eosinophilic appendicitis is not a well-defined entity. Rare reports can be found in the literature, but the exact etiology and significance are not clear. In this series we review our institutional experience with this entity.

**Design:** We searched the pathology laboratory information system (LIS) for the terms appendicitis and eosinophilia or eosinophilic. We also interrogated the LIS system for the number of appendices resected during the same time period.

**Results:** We identified 9 cases during the course of 50 years (1971–2021) where the diagnosis included the search terms. There were 13 766 appendectomies during the same period (0.02%). The patient ages ranged from 11 to 49 (average = 24.4) years; male to female ratio = 1.2%. Only one case had Enterobius vermicularis identified in the appendix. All cases showed increased mural eosinophils. Three cases showed acute inflammation, 1 case showed granulomatous inflammation, and 2 cases showed fibrosis. Three of the cases were grossly inflamed, but none of the cases showed perforation (Figure 1.80).

**Conclusions:** Eosinophilic appendicitis is rare in its pure form; it is occasionally associated with helminths infestation of the appendix. The clinical significance of mild forms of the disease is not clear; however, more severe forms do present with an appendicitis-like clinical picture. More attention is suggested for this entity as it may be underreported.

**An Unusual Presentation of Taxane Effect in Acute Cholecystitis After Exposure to Paclitaxel**  
*(Poster No. 81)*

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Taxanes (paclitaxel and docetaxel) are chemotherapeutic agents used to treat malignancies, including carcinomas of the esophagus, breast, and lung. These drugs target cells with high turnover and inhibit mitosis by interfering with microtubule breakdown during cell division. Documented side effects include myelosuppression, alopecia, arthralgia, myalgia, neuropathy, diarrhea, mucosal toxicity, and skin changes. We report a case of a 72-year-old woman who presented to the emergency department with abdominal pain, dizziness, nausea, and emesis during an 8-week chemotherapy regimen for invasive ductal carcinoma of the breast. Her last dose of paclitaxel was 4 days prior to presentation. Imaging revealed cholelithiasis with mild gallbladder wall hyperemia and thickening, compatible with acute calculus cholecystitis and she subsequently underwent cholecystectomy. Gross and microscopic examination of the gallbladder revealed hemorrhage and edema within the gallbladder wall with neutrophilic infiltration (Figure 1.81). The mucosal epithelium contained apoptosis and increased mitotic activity with numerous atypical ring mitoses. The gallbladder mucosa lacked significant cytoarchitectural complexity and nuclear hyperchromasia. The microscopic features of taxane effect are well described in the luminal gastrointestinal tract mucosa, but less commonly described in the biliary tree. This case represents an unusual finding of taxane effect in the gallbladder. The frequent atypical mitotic figures may lead to the misdiagnosis of high-grade biliary intraepithelial neoplasia (BilIN-3) or possible malignancy. Recognition of ring mitoses and correlation with the clinical history are imperative to arrive at the correct diagnosis. Additionally, this report supports acute cholecystitis as a rare side effect of paclitaxel therapy.

**Histopathologic Diagnostic Criteria for Eosinophilic Gastritis and Eosinophilic Duodenitis**  
*(Poster No. 82)*

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1Department of Pathology, UT Southwestern, Dallas, Texas; 2Department of Medicine, University of North Carolina, Chapel Hill; 3Cincinnati Center for Eosinophilic Disorders, Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio; Departments of 1Planning and Analytics and 4Clinical Development and Medical Affairs, Allakos, Inc, Redwood City, California; 5Department of Pathology, Inform Diagnostics, Irving, Texas.

**Context:** Eosinophilic gastritis (EG) and eosinophilic duodenitis (EoD) are diagnosed via endoscopy with biopsy and histopathologic detection of eosinophils in the stomach and duodenum. EG and/or EoD (EG/EoD) are more common than generally realized; however, lack of diagnostic guidelines, perceived rarity, and nonspecific clinical presentation contribute to their underdiagnosis. Standardized histopathologic criteria will improve detection of these diseases, thereby enabling patients to receive targeted treatment.

**Design:** Patients with moderate to severe gastrointestinal symptoms underwent endoscopy with systematic gastric and duodenal biopsy protocol (8 gastric + 4 duodenal) and histopathologic evaluation. At least 5 nonoverlapping high-power fields (hpfs) were evaluated per biopsy. Histopathologic criteria for EG was ≥30 eos/hpf in ≥5 gastric hpfs and for EoD was ≥30 eos/hpf in ≥5 duodenal hpfs. We analyzed diagnostic yields for EG/EoD and examined EG/EoD histopathologic diagnostic criteria using screening data from a randomized controlled trial of lirentelimab.

**Table: Results for Patients Evaluated**

<table>
<thead>
<tr>
<th>No. of hpfs (≥30 eos/hpf)</th>
<th>Gastric Biopsies Patients, No. (%)</th>
<th>Duodenal Biopsies Patients, No. (%)</th>
<th>Total, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>in 45 EG ± EoD</td>
<td>in 62 EoD ± EG</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(n = 329)</td>
<td>(n = 230)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>120 (36)</td>
<td>29 (13)</td>
<td>149 (27)</td>
</tr>
<tr>
<td>1</td>
<td>16 (5)</td>
<td>23 (10)</td>
<td>39 (7)</td>
</tr>
<tr>
<td>2</td>
<td>23 (7)</td>
<td>38 (17)</td>
<td>61 (11)</td>
</tr>
<tr>
<td>3</td>
<td>20 (6)</td>
<td>30 (13)</td>
<td>50 (9)</td>
</tr>
<tr>
<td>4</td>
<td>24 (7)</td>
<td>26 (11)</td>
<td>50 (9)</td>
</tr>
<tr>
<td>5</td>
<td>126 (38)</td>
<td>84 (37)</td>
<td>210 (38)</td>
</tr>
</tbody>
</table>

**Results:** Of the 88 patients evaluated, 72 met criteria for EG/EoD, including 15 of 26 (58%) with no prior diagnosis of EG/EoD. Morphologic abnormalities were present in 49% (22 of 45) of EG and 5% (3 of 62) of EoD patients. Eosinophilia was highly patchy; 41% of gastric biopsies (136 of 329) and 23% of duodenal biopsies (51 of 230) had 0 or 1 hpfs with ≥30 eos (Table). Evaluation of ≥5 nonoverlapping hpfs in ≥5 gastric and ≥4 duodenal hpfs was required to capture 100% of EG/EoD cases.

**Conclusions:** EG/EoD biopsies often showed patchy eosinophil distribution in otherwise normal- or almost normal-appearing gastric or duodenal mucosa, indicating that the careful high-power examination of ≥5 hpfs in all 12 biopsies is necessary to ensure detection.
Localised Amyloidosis of the Prostatic Urethra Mimicking Urothelial Carcinoma

(Poster No. 84)

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Amyloidosis is a disease characterized by extracellular deposition of amyloid protein fibrils in tissues and rarely involves the urethra, with fewer than 50 cases previously reported, and may mimic urothelial carcinoma at presentation. We report a 69-year-old man who presented to the emergency department with shortness of breath. An abdominal computed tomography scan demonstrated a right hydrourephrotic kidney and bladder largely occupied by a large, predominantly hyperdense lesion, presumed hematoma (Figure 1.84, A). Pan-cystoscopy revealed a 6-cm bladder mass involving the prostatic urethra displacing the right ureteral orifice, which was biopsied. Histologic examination showed large deposits of amorphous eosinophilic material associated with numerous osteoclast-type giant cells, with areas of calcifications and multifocal ossification (Figure 1.84, B through D). Amyloid deposits were confirmed by Congo red (Figure 1.84, D, inset) and sulfated Alcian blue stains. Light chromatophotot tandem mass spectrometry was performed and detected all types including serum amyloid P component, apolipoprotein A4, and apolipoprotein E; however, a specific amyloid type was indeterminate.

The patient had no history of gonorrhea. Further investigations for systemic amyloidosis were all negative. Amyloidosis of the urethra is extremely rare and may be either localized and idiopathic or a manifestation of systemic amyloidosis. Pathologists should be aware of this rare entity as this lesion may be indistinguishable from carcinoma, further emphasizing the importance of tissue diagnosis before definitive surgery. Long-term follow-up in the absence of symptoms may not be required.
High Intensity Focused Ultrasound Ablation for Prostate Cancer: A Retrospective Review of the Histological Characteristics and Clinicopathologic Correlates After Treatment

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Context: High-intensity focused ultrasound (HIFU) is a noninvasive treatment option used for localized prostate cancer or salvage surgery after failed radiation therapy. We report histologic findings in prostate needle biopsies following HIFU treatment.

Design: Between 2002 and 2020, 34 patients with localized prostate cancer underwent a single HIFU treatment. None had prior radiation therapy. We report histologic findings in prostate needle biopsies following HIFU treatment.

Results: Of the 15 patients, 5 were male and 10 were female, with ages ranging from 28 to 84 years (median, 52 years). Clinical presentation included adenocarcinoma (n = 10), preclinical Cushing syndrome (n = 4), and Carney complex (n = 1). The adenocarcinoma ranged from 0.7 to 12.5 cm (median 4.5 cm) and the gland weight ranged from 5.8 to 300 g (median 60 g). The clinicopathologic and radiologic features are summarized in the Table.

Conclusions: We provide a review of common histologic findings in prostatic biopsies after HIFU treatment. Particular attention should be placed on recognizing changes observed in both benign and malignant prostatic tissue. We propose reporting Gleason scores of posttreatment prostate cancer to provide information that will optimize patient management.

Pathologic Changes in Prostatic Tissue in Post-HIFU Needle Biopsies

<table>
<thead>
<tr>
<th>Benign Prostatic Tissue (n = 34) Present, No. (%)</th>
<th>Malignant Prostatic Tissue (n = 18) Present, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stromal compartment Fibrosis 34 (100) Perineural invasion 2 (11)</td>
<td></td>
</tr>
<tr>
<td>Eosinophils 17 (50) Angiolympathic invasion 0 (0)</td>
<td></td>
</tr>
<tr>
<td>Atypical fibroblasts 12 (35) Nuclear pyknosis 5 (28)</td>
<td></td>
</tr>
<tr>
<td>Chronic inflammation 21 (62) Nuclear enlargement 15 (83)</td>
<td></td>
</tr>
<tr>
<td>Acute inflammation 13 (38) Eosinophilic granular secretion 6 (33)</td>
<td></td>
</tr>
<tr>
<td>Calcification 4 (12) Corpora amylacea 0 (0)</td>
<td></td>
</tr>
<tr>
<td>Hemorrhage 8 (24) Cytoplasmic vacuolization 10 (56)</td>
<td></td>
</tr>
</tbody>
</table>

Benign glands

| Atrophy 33 (97) | Myointimal proliferation 3 (9) | Coagulation necrosis 25 (74) |

Mucinosis

| Corpora amylacea 26 (76) | Treatment-related atypia 0 (0) | Squamous cell metaplasia 1 (3) |

| Mucinous metaplasia 10 (29) | | |

Myelolipomatous Adrenal Adenomas: A Report of 15 Cases

Katrina Collins, MD1 (katcoll@iu.edu); Diana M. Oramas, MD2; Jeffrey Guccione, MD2; Khaled M. Elsayes, MD2; Mouhammed A. Habra, MD3; Miao Zhang, MD, PhD1; Liang Cheng, MD,1 Departments of 1Pathology, 2Pathology, 3Abdominal Imaging and 4Endocrine Neoplasia and Hormonal Disorders, The University of Texas MD Anderson Cancer Center, Houston; 3Department of Diagnostic and Interventional Imaging, The University of Texas Health Sciences Center at Houston.

Context: The presence of a myelolipomatous component of adrenal incidentalomas is a rare, but well-known, occurrence in both hyperplastic and malignancies. Although improved imaging modalities have increased detection, given the rarity of this lesion and nonspecific symptoms, these lesions can cause diagnostic uncertainty and can make subsequent management difficult. This study presents clinicopathologic features of pathologically proven cases of myelolipomatous adrenal adenomas with radiologic correlation.

Design: Fifteen myelolipomatous adrenal adenomas were retrieved from the files of the authors (1985 to 2020). Clinicopathologic and radiologic data were recorded for all cases.

Results: Of the 15 patients, 5 were male and 10 were female, with ages ranging from 28 to 84 years (median, 52 years). Clinical presentation included adrenal incidentaloma (n = 10), preclinical Cushing syndrome (n = 4), and Carney complex (n = 1). The adrenal tumors ranged from 0.7 to 12.5 cm (median 4.5 cm) and the gland weight ranged from 5.8 to 300 g (median 60 g). The clinicopathologic and radiologic features are summarized in the Table.

Conclusions: Myelolipomatous adrenal adenomas are rare, benign tumors, typically unilateral and hormonally inactive. They may be indistinguishable from a myelolipoma or carcinoma with a myelolipomatous component using conventional imaging techniques, resulting in a false clinical impression. It is important to appreciate that these tumors have been linked with endocrine syndromes, such as Cushing syndrome, and may have an underlying genetic cause.
Plasmacytoid Urothelial Carcinoma: Histomorphologic and Clinical Analysis

(Poster No. 88)

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Context: Plasmacytoid urothelial carcinoma (PUC) is a rare aggressive variant of invasive urothelial carcinoma (UC). A recent histologic categorization by Perrino et al divided PUC into classical, pleomorphic, and desmoplastic. We present our clinicopathologic experience with attention to the newly described subcategories.

Design: A search of our database yielded 39 patients with PUC, with 47 specimens during the last 20 years. Glass slides were reviewed for histomorphologic characterization. The clinical information was reviewed through chart abstraction.

Results: PUC showed male predominance (28:1 M:F) with mean age of 69 years (40–84 years). Clinical follow-up was available for 30 patients (median, 10 months; range, 1–36 months). Seventy-four percent (n = 29) of cases were stage ≥pT2, 44% (n = 17) had lymph node involvement, and 38.5% (n = 15) showed distant metastasis (see Table). Metastatic sites included small bowel, omentum, liver, lungs, bone, and peritoneum. The overall mortality rate was 18%. The most frequently seen histology was pleomorphic, often admixed with classical and/or desmoplastic subtypes. PUCs were commonly admixed with other UC variants (glandular and sarcomatoid) and associated with flat UC in situ (35%). PUC comprised ≥80% of tumor in 28% (n = 11), 50%–80% in 31% (n = 12), and <50% in 41% (n = 16) of cases.

Conclusions: PUC presents at advanced pathologic stage, with predisposition for nodal and/or distant metastasis. Awareness of the spectrum of histologic changes helps in recognizing this prognostically significant variant. The presence of abdominal visceral spread underlines PUC’s ability to cross fascial planes; the characteristics of UC at these sites could be an interesting future direction.

<p>| Adenoma Characteristics |
|-------------------------|---|---|---|---|</p>
<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Gross Examination</th>
<th>Macroscopic Fat on Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>61/F Cushing disease</td>
<td>Golden yellow with foci of hemorrhage and gray-tan tissue, numerous foci of calcification</td>
<td>Present, 1.6 cm</td>
</tr>
<tr>
<td>47/M Incidentaloma</td>
<td>Yellow, multifoliated</td>
<td>Present, 0.7 cm</td>
</tr>
<tr>
<td>52/M Incidentaloma</td>
<td>Yellow-golden brown with focal tan-pink discoloration areas</td>
<td>Present, 0.6 cm</td>
</tr>
<tr>
<td>50/F Incidentaloma</td>
<td>Red-tan to yellow-tan tumor with large areas of hyalinization and hemorrhage</td>
<td>Present, 1.1 cm</td>
</tr>
<tr>
<td>52/F Subclinical Cushing syndrome with history of bilateral macronodular hyperplasia</td>
<td>Yellow-golden brown with focal tan-pink discoloration areas</td>
<td>Present, 0.5 cm</td>
</tr>
<tr>
<td>72/F Incidentaloma</td>
<td>Orange-red with hemorrhagic areas</td>
<td>Present, 0.2 cm</td>
</tr>
<tr>
<td>70/M Incidentaloma</td>
<td>Dark red tissue and central gelatinous-appearing area</td>
<td>Not identified</td>
</tr>
<tr>
<td>84/F Incidentaloma</td>
<td>Yellow-black nodule compressing adrenal cortex</td>
<td>Present, 1.0 cm</td>
</tr>
<tr>
<td>59/F Subclinical Cushing syndrome</td>
<td>Variegated yellow to dark brown mass with rim of normal-appearing adrenal cortex</td>
<td>Present, 0.6 cm</td>
</tr>
<tr>
<td>53/F Incidentaloma</td>
<td>Well-circumscribed pale golden yellow mass with central fleshy area</td>
<td>Present, 0.7 cm</td>
</tr>
<tr>
<td>53/M Incidentaloma</td>
<td>Well-circumscribed homogeneous yellow mass</td>
<td>Present, 0.2 cm</td>
</tr>
<tr>
<td>46/F Incidentaloma</td>
<td>Tan to brown, soft, heterogeneous, well-delineated nodule</td>
<td>Not reported</td>
</tr>
<tr>
<td>28/M Carney complex with bilateral adrenal nodularity</td>
<td>Red, soft, heterogeneous, well-delineated nodule</td>
<td>Not reported</td>
</tr>
<tr>
<td>50/F Incidentaloma</td>
<td>Pale tan to yellow-orange to pink heterogeneous</td>
<td>Not reported</td>
</tr>
<tr>
<td>29/F Cushing disease</td>
<td>Gray-yellow to orange cortical nodule</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

Plasmacytoid Urothelial Carcinoma: Histomorphologic and Clinical Analysis

(Poster No. 88)

Melad N. Dababneh, MBBS1 (mdababn@emory.edu); Dylan Martin, MD; Mehmet A. Bilen, MD; Sara E. Wobker, MD, MPH; Lara R. Harik, MD; Departments of 1Pathology and Laboratory Medicine and 2Hematology and Medical Oncology, Emory University School of Medicine, Atlanta, Georgia; 3Department of Pathology, The University of North Carolina at Chapel Hill.

Context: Plasmacytoid urothelial carcinoma (PUC) is a rare aggressive variant of invasive urothelial carcinoma (UC). A recent histologic categorization by Perrino et al divided PUC into classical, pleomorphic, and desmoplastic. We present our clinicopathologic experience with attention to the newly described subcategories.

Design: A search of our database yielded 39 patients with PUC, with 47 specimens during the last 20 years. Glass slides were reviewed for histomorphologic characterization. The clinical information was reviewed through chart abstraction.

Results: PUC showed male predominance (28:1 M:F) with mean age of 69 years (40–84 years). Clinical follow-up was available for 30 patients (median, 10 months; range, 1–36 months). Seventy-four percent (n = 29) of cases were stage ≥pT2, 44% (n = 17) had lymph node involvement, and 38.5% (n = 15) showed distant metastasis (see Table). Metastatic sites included small bowel, omentum, liver, lungs, bone, and peritoneum. The overall mortality rate was 18%. The most frequently seen histology was pleomorphic, often admixed with classical and/or desmoplastic subtypes. PUCs were commonly admixed with other UC variants (glandular and sarcomatoid) and associated with flat UC in situ (35%). PUC comprised ≥80% of tumor in 28% (n = 11), 50%–80% in 31% (n = 12), and <50% in 41% (n = 16) of cases.

Conclusions: PUC presents at advanced pathologic stage, with predisposition for nodal and/or distant metastasis. Awareness of the spectrum of histologic changes helps in recognizing this prognostically significant variant. The presence of abdominal visceral spread underlines PUC’s ability to cross fascial planes; the characteristics of UC at these sites could be an interesting future direction.

![Table](https://via.placeholder.com/150)
intracellular \( \text{H}^+ \) ion for 1 extracellular \( \text{Na}^+ \) ion. In renal tubular cells, the reabsorption of NaCl is implemented by NHE3 isoform, which is regulated by NHE regulatory factor 1 (NHERF1). NHERF1 directly interacts with merlin, ezrin, radixin, and moesin proteins, which participate in cytoskeletal reorganization and signal transduction. In the normal proximal tubule, it is located in the apical zone, facilitating structural stability and ion exchange. Our aim was to characterize NHERF1 expression in renal cell carcinoma (RCC).

**Design:** Using immunohistochemistry, we analyzed the expression of NHERF1/EBP50 (ThermoFisher Scientific, Waltham, Massachusetts) on RCCs including papillary, chromophobe, and clear cell subtypes (21 cases [33%], 9 [14%], and 34 cases [53%], respectively). Twelve clear cell RCC (ccRCC) tumors were further analyzed by transmission electron microscopy.

**Results:** All neoplasia-transformed tubular cells, regardless of tumor grade and stage, had altered expression of NHERF1/EBP50. Changes ranged from complete absence to aberrant expression in the basolateral cell membrane or cytoplasmic locations. Among the subtypes, only ccRCC showed microlumen formation in singles or clusters as dot-shaped condensations of immunostaining at paranuclear, membranous, and submembranous sites. The latter 2 locations were common for Fuhrman grades 1 and 2. Ultrastructurally, the microlumens represented aggregates of microvilli surrounded by a monolayer membrane (Figure 1.89).

**Conclusions:** For ccRCC, the dysfunctional NHERF1 relocates inside the cell forming microlumens. It confirms significant changes in the intracellular environment, ionic imbalance, and may contribute to tumor progression, metastasis, and drug resistance requiring further analysis.

**The Clinical Utility of a 17-Gene Molecular Classifier Score in Men With NCCN Intermediate-Risk Prostate Cancer**

(Poster No. 90)

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**Context:** The Genomic Prostate Score (GPS, OncotypeDx, Genomic Health, Redwood City, California) is a 17-gene RT-PCR test on prostate biopsies that predicts risk of adverse pathology at prostatectomy and provides a posttest NCCN risk category. We have previously shown that cribriform pattern and higher percentages of Gleason pattern 4 are associated with higher GPS posttest NCCN risk category. In 2017, the test began subdividing the posttest intermediate NCCN risk category into intermediate favorable and intermediate unfavorable. We hypothesized that the intermediate unfavorable category would be associated with higher rates of cribriform pattern and higher average percentage Gleason pattern 4 than the intermediate favorable category.

**Design:** Prostate biopsies from our institution from October 2016 to December 2018 that had received a GPS and intermediate favorable or intermediate unfavorable posttest category were included. The slide from the block tested was rereviewed in a blinded manner for percentage Gleason pattern 4 and presence of cribriform pattern. GPS data were obtained from the medical record.

**Results:** There were 59 patients whose prostate biopsies underwent GPS testing and were assigned a posttest category of intermediate favorable (17 patients) or intermediate unfavorable (42 patients). Compared with patients in the intermediate favorable category, patients in the intermediate unfavorable category had higher GPS (29.5 versus 24.4, \( P = .02 \)), higher average percentage of Gleason pattern 4 (20.8% versus 10%, \( P = .002 \)), and higher rates of cribriform pattern (31% versus 6%, \( P = .04 \)).

**Conclusions:** NCCN posttest intermediate subcategory provided by GPS can be partially explained by careful histologic examination of prostate biopsy.

**Perinephric Myxoid Pseudotumor of Fat: A Rare and Emerging Entity**

(Poster No. 91)

Jessica Muldoon, MD (jlmuldoon@iu.edu); Katrina Collins, MD; Laura Warmke, MD; Muhammad Idrees, MD; Department of Pathology, Indiana University, Indianapolis.

Perinephric myxoid pseudotumor of fat is a newly described entity that may mimic fat-containing soft tissue tumors, such as well-differentiated liposarcoma or fibrosclerosing lesions associated with LG4-related disease. To our knowledge, a total of 12 cases were previously reported, of which 11 cases are from 1 case series (PMID 30826321). We presently report the 13th case. A 70-year-old woman with history of rheumatoid arthritis, diabetes mellitus type 2, and hypothyroidism presented with a long-standing abdominal mass and worsening abdominal distention and pain. Computed tomography imaging showed a large right retroperitoneal mass measuring 21 cm (Figure 1.91, A) as well as gallstones. Histologic sections showed a lipomatous lesion with focal myxoid change (Figure 1.91, B) and lymphoplasmacytic infiltrate (Figure 1.91, C and D). No atypical stromal cells characteristic of atypical lipomatous tumor/well-differentiated liposarcoma were identified. The presence of necrosis and lymphoplasmacytic infiltrate was concerning for LG4-related fibrosclerosing disease; however, immunohistochemistry showed IgG plasma cells were polyclonal with no increase in IgG4+ cells. MD22 immunohistochemical expression was negative. Fluorescence in situ hybridization study was performed and showed no evidence of MD22 gene amplification. Perinephric myxoid pseudotumor of fat is an extremely rare, fat-containing perirenal mass. The exact etiology is unclear but thought to result from perinephric fat irritation secondary to underlying nonneoplastic renal disease. Although this mass has imaging findings that overlap with liposarcoma, this lesion is favored to represent a pseudotumor of fat. MD22 amplification by fluorescence in situ hybridization can help to distinguish this benign lipomatous tumor from liposarcoma.
Leydig cell tumors represent 1%–3% of testicular neoplasms. The majority are benign; however, 5%–10% are malignant. Metastasis is the only criterion for malignancy. Benign perineural Leydig cells may be seen in extratesticular tissue. This finding may be challenging and lead to an incorrect diagnosis of malignant perineural invasion. We report a case of testicular Leydig cell tumor with benign perineural Leydig cells in the spermatic cord. We need to be aware of this phenomenon to avoid misdiagnosis. A 24-year-old man presented with a testicular mass. Imaging revealed a hypoechoic 1.6-cm mass of the left testicle (Figure 1.92, A). Imaging of the chest, abdomen, and pelvis showed no metastatic disease. Preoperative laboratory results were normal, including LDH 149 u/L, β-HCG <1.2 u/L, and AFP 1 ng/mL. Histology revealed the tumor had well-defined borders and was confined within the testicle (Figure 1.92, B). The neoplastic cells were bland looking with a single round nucleus and abundant eosinophilic cytoplasm (Figure 1.92, C). Present within the spermatic cord were small foci of cellular clusters within nerve that were morphologically similar to the tumor cells with bland cytology (Figure 1.92, D). Both tumor cells and cells within the nerve stained positive for inhibin, Melan-A, and calretinin. We conclude these were benign perineural Leydig cells mimicking malignant perineural invasion. The simultaneous occurrence of Leydig cell tumor and benign perineural Leydig cells in extratesticular tissue is uncommon but must be recognized. The tumor morphology and cytologic features were helpful in differentiating this benign perineural condition from the malignant Leydig cell tumor counterpart.

Malignancy Following Augmentation Cystoplasty: A Single Institution Experience

(Poster No. 93)

Aysha Mubeen, MD1 (aysha.mubeen86@gmail.com); Sofia Canete-Portillo, MD1; Soroush Rais-Bahrami, MD2; Pankaj Dangle, MD2; Cristina Magi-Galluzzi, MD1.1 Departments of 1Pathology and 2Urology, University of Alabama, Birmingham.

Context: Augmentation cystoplasty (AC) is a procedure where the bladder is anastomosed with segments of ileum, colon, or stomach in conditions like spina bifida, history of bladder exstrophy, or other neurogenic bladder etiology limiting bladder capacity and compliance. Limited literature is available on malignancy developing in AC because of the low incidence and long latency.

Design: We describe the clinicopathologic features of 5 patients who underwent AC at our institution and subsequently developed cancer in the augmented bladder.

Results: All patients were female; age at diagnosis ranged from 44 to 57 years. The histologic diagnoses were intestinal-type adenocarcinoma (n = 1), invasive high-grade papillary urothelial carcinoma (HGUPC) (n = 1), urothelial carcinoma in situ (CIS), (n = 1) and squamous cell carcinoma (SCC) (n = 2). Median latency period between AC and carcinoma diagnosis was 28.6 years (range, 15–52 years). Follow-up range was 2 to 80 months (mean, 29.9 months). The clinicopathologic features are summarized in the Table.

Conclusions: Many theories have been proposed for carcinogenesis in AC, including infection, chronic inflammation, interaction between 2 different epithelia, and altered bladder microenvironment. Close follow-up is necessary for an early diagnosis. Endoscopic detection of these tumors, however, can be challenging owing to the inflammatory changes. It is controversial if AC is an independent risk factor for bladder cancer development. Malignancy in AC is reported to have a poor prognosis. We conclude that malignancy in AC can have different histologic subtypes and arise after a long latency period.

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age at Augmentation, y</th>
<th>Underlying Disease/ Site of Malignancy</th>
<th>Latency Period, y</th>
<th>Diagnosis and Pathologic Stage</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>NB (spina bifida)/vesicostomy stoma</td>
<td>52</td>
<td>Intestinal-type adenocarcinoma</td>
<td>Urostomy re-excision</td>
</tr>
<tr>
<td>2</td>
<td>36</td>
<td>NB (spinal cord injury)/native bladder</td>
<td>15</td>
<td>Invasive HGUPC with glandular features and CIS (pT2 at least)</td>
<td>Re-TURBT; neoadjuvant chemo and cystectomy (planned)</td>
</tr>
<tr>
<td>3</td>
<td>28</td>
<td>NB (spinal cord injury)/native bladder</td>
<td>24</td>
<td>Poorly differentiated SCC (pT3a)</td>
<td>NED</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>NB (spina bifida/native bladder</td>
<td>29</td>
<td>Moderately differentiated SCC + CIS (pT4a)</td>
<td>Deceased (postoperative complications)</td>
</tr>
<tr>
<td>5</td>
<td>40</td>
<td>NB/native bladder</td>
<td>23</td>
<td>Urothelial CIS</td>
<td>Deceased (vaginal cancer)</td>
</tr>
</tbody>
</table>

Abbreviations: NB, neurogenic bladder; NED, no evidence of disease; TURBT, transurethral resection of bladder tumor.

Utility of P53 and Ki-67 Immunostaining in Balanitis Xerotica Obliterans (Lichen Sclerosus Et Atrophicus)

(Poster No. 94)

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Context: Balanitis xerotica obliterans (BXO)/lichen sclerosus et atrophicus (LSA) has an increased risk to develop differentiated penile intraepithelial neoplasia (d-PeIN) and squamous cell carcinoma (SCC). The aim of our study is to evaluate the utility of p53 and Ki-67 immunostains for BXO/LSA.

Design: From September 2018 to October 2020, all foreskin excisions from our institution were included. Immunostains for p53 and Ki-67 were reviewed and performed in selected cases.

Results: Among 180 patients (26 to 81 years of age with a median age at 46 years), 15 (8.3%) were diagnosed with BXO/LSA; 2 (13.3%) had dysplasia, including 1 (6.7%) with SCC; 13 (86.7%) had no dysplasia. p53 and Ki-67 immunostains were performed on 7 cases. Five cases showed mild atypia at basal layer, however, there was no significantly increased Ki-67 labeling, and p53 expression showed wild-type (normal) pattern in 4 cases. The hyperplastic changes of squamous
epithelium were noted, exhibiting increased Ki-67 index, and only 1 had increased p53 expression at basal layer without cytologic dysplasia. Severe dysplasia was seen in BXO/LSA lesion (Figure 1.94, A) in a 48-year-old patient with SCC. Increased Ki-67 index (Figure 1.94, B) and complete loss of p53 (Figure 1.94, C) were seen. The sensitivity and specificity of immunostains of p53 and Ki-67 for d-PeIN was 67% and 100%, respectively.

Conclusions: Our data demonstrate the importance of the utility of p53 and Ki-67 in BXO/LSA patients for detecting d-PeIN lesions.

A Rare Case of Primary Small Cell Carcinoma of the Urinary Bladder With Sarcomatoid Differentiation

Ahmed F. Lazim, MD (ahmed.lazim@tuhs.temple.edu); Salvatore Luceno, MD; Anu Peter, MD; Eli Balshan, MD. Department of Pathology, Temple University Hospital, Philadelphia, Pennsylvania.

Small cell carcinoma of the bladder (SCCB) is considered an aggressive, poorly differentiated extrapulmonary neuroendocrine tumor that comprises <1% of bladder tumors. The tumor is associated with a poor prognosis, high metastatic potential, a male preponderance, and a mean age of 78 years. Histologically, small cell carcinoma of the bladder is difficult to distinguish from small cell lung carcinoma (SCLC). However, unlike SCLC, it shares similar molecular alterations with urothelial carcinoma. Our case involves an 87-year-old man with a known medical history of hypertension, diabetes mellitus (II), intestinal diverticulitis, and renal caliculi. He presented with hematuria and a 7.5 × 4.8-cm lobulated left urinary bladder mass with perivesical soft tissue involvement (computed tomography abdomen/pelvis). A transurethral resection of the bladder tumor was performed. The tumor grossly involved (computed tomography abdomen/pelvis). A transurethral resection of the bladder tumor was performed. The tumor grossly involved (computed tomography abdomen/pelvis). A transurethral resection of the bladder tumor was performed. The tumor grossly involved (computed tomography abdomen/pelvis). A transurethral resection of the bladder tumor was performed. The tumor grossly involved (computed tomography abdomen/pelvis). A transurethral resection of the bladder tumor was performed. The tumor grossly involved (computed tomography abdomen/pelvis).

The specimen was processed routinely and a diagnosis of primary small cell carcinoma with focal areas of sarcomatoid differentiation was given. Histologically, small cell carcinoma of the bladder is difficult to distinguish from small cell lung carcinoma (SCLC). However, unlike SCLC, it shares similar molecular alterations with urothelial carcinoma. Our case involves an 87-year-old man with a known medical history of hypertension, diabetes mellitus (II), intestinal diverticulitis, and renal caliculi. He presented with hematuria and a 7.5 × 4.8-cm lobulated left urinary bladder mass with perivesical soft tissue involvement (computed tomography abdomen/pelvis). A transurethral resection of the bladder tumor was performed. The tumor grossly involved (computed tomography abdomen/pelvis). A transurethral resection of the bladder tumor was performed. The tumor grossly involved (computed tomography abdomen/pelvis). A transurethral resection of the bladder tumor was performed. The tumor grossly involved (computed tomography abdomen/pelvis). A transurethral resection of the bladder tumor was performed. The tumor grossly involved (computed tomography abdomen/pelvis). A transurethral resection of the bladder tumor was performed. The tumor grossly involved (computed tomography abdomen/pelvis). A transurethral resection of the bladder tumor was performed. The tumor grossly involved (computed tomography abdomen/pelvis).

Clinical-pathologic Features of PN and RN

<table>
<thead>
<tr>
<th>Clinicopathologic Features of PN and RN</th>
<th>Partial Nephrectomies, No. (%)</th>
<th>Radical/Total Nephrectomies, No. (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor Extent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limited to kidney</td>
<td>436 (95)</td>
<td>108 (57)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>(pT1, pT2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not limited to kidney</td>
<td>21 (5)</td>
<td>82 (43)</td>
<td></td>
</tr>
<tr>
<td>(pT3, pT4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Size, cm</td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&lt;7</td>
<td>429 (93.8)</td>
<td>107 (56.3)</td>
<td></td>
</tr>
<tr>
<td>≥7</td>
<td>28 (6.2)</td>
<td>83 (43.7)</td>
<td></td>
</tr>
<tr>
<td>Tumor Type</td>
<td></td>
<td></td>
<td>.09</td>
</tr>
<tr>
<td>CCRCC</td>
<td>291 (63.6)</td>
<td>109 (57.3)</td>
<td></td>
</tr>
<tr>
<td>PRCC</td>
<td>86 (18.8)</td>
<td>42 (22.1)</td>
<td></td>
</tr>
<tr>
<td>Chromophobe</td>
<td>38 (8.3)</td>
<td>11 (5.7)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>42 (9.3)</td>
<td>28 (14.9)</td>
<td></td>
</tr>
<tr>
<td>Follow-up</td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No evidence of disease recurrences and/or</td>
<td>335 (73.3)</td>
<td>107 (56.3)</td>
<td></td>
</tr>
<tr>
<td>Metastasis</td>
<td>31 (6.8)</td>
<td>59 (31)</td>
<td></td>
</tr>
<tr>
<td>N/A</td>
<td>91 (19.9)</td>
<td>24 (12.7)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: At our institution, PN is being performed more often on small tumors as compared with RN. The majority of PN tumors are being staged as confined to the kidney and these cases accounted for the majority of recurrences and/or metastasis seen in the PN group.
This result warrants attention and review as to whether pathologists are underrecognizing pertinent staging features for PN cases.

**PUNLMP Diagnosis in a General Surgical Pathology Sign-Out Setting: Institutional Experience Spanning 10 Years**

(Poster No. 97)

**Georges Tabet, MD** (georgetabet125@gmail.com); Aileen Grace Arriola, MD. Department of Pathology, Temple University Hospital, Philadelphia, Pennsylvania.

**Context:** Papillary urothelial neoplasm of low malignant potential (PUNLMP) is a diagnosis associated with significant diagnostic confusion. PUNLMP has been shown to have varied recurrence rates, poor interobserver agreement, and overlapping features with low-grade papillary urothelial carcinoma (LGUPC). Cases diagnosed as PUNLMP were examined.

**Design:** We identified all cases of PUNLMP between 2010 and 2020 from our institution. Data from electronic medical records were used to determine age, prevalence, history of bladder lesions, cystoscopy findings, recurrence, and progression. Fisher exact test was used to test for associations.

**Results:** PUNLMP cases were uncommon (only 25 diagnoses made during 10 years). The mean age was 65 (15 males, 10 females). Of the 25 cases, 11 (44%) had a history of bladder cancer whereas 14 (56%) did not. Most cases (n = 21; 84%) were viewed as papillary lesions on cystoscopy and the rest presented as erythematous mucosa. Overall, a total of 10 cases (40%) demonstrated either recurrence or progression on follow-up. In those who had a history of bladder cancer, no recurrence was documented, and nearly half progressed to LGPUC (n = 12). In those who had no history of bladder cancer were most likely nonrecurrent and nonprogressive.

**Conclusions:** Our findings suggest that PUNLMP cases at our institution might be overdiagnosed. History of bladder cancer can be a diagnostic pitfall for malignancy. We reviewed indeterminate urothelial diagnoses with respect to IDO expression. Additional larger studies are warranted, especially in relation to the expression of other immunotherapy biomarkers such as PD-L1.

**Table 1: Clinicopathologic Features in IDO-Positive and IDO-Negative Tumors**

<table>
<thead>
<tr>
<th>Clinicopathologic Feature</th>
<th>Positve (%)</th>
<th>Negative (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range), y</td>
<td>73.3 (42–94)</td>
<td>72.8 (62–93)</td>
<td>.82</td>
</tr>
<tr>
<td>Gender, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>20 (57.1)</td>
<td>7 (50)</td>
<td>.75</td>
</tr>
<tr>
<td>Female</td>
<td>13 (42.9)</td>
<td>7 (50)</td>
<td></td>
</tr>
<tr>
<td>Tumor grade, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>10 (28.6)</td>
<td>1 (7.1)</td>
<td>.14</td>
</tr>
<tr>
<td>High</td>
<td>23 (71.4)</td>
<td>13 (92.9)</td>
<td></td>
</tr>
<tr>
<td>Tumor size, mean (range), cm</td>
<td>3.9 (0.7–9.5)</td>
<td>3.6 (1.1–8.2)</td>
<td>.29</td>
</tr>
<tr>
<td>CIS, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>11 (31.4)</td>
<td>5 (35.7)</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>23 (65.7)</td>
<td>9 (64.3)</td>
<td></td>
</tr>
<tr>
<td>NA</td>
<td>1 (2.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neoadjuvant therapy, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4 (11.4)</td>
<td>1 (7.1)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>29 (82.9)</td>
<td>11 (78.6)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (5.7)</td>
<td>2 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Pathologic stage, No. (%)</td>
<td></td>
<td></td>
<td>.75</td>
</tr>
<tr>
<td>&lt;T2</td>
<td>20 (57.1)</td>
<td>7 (50)</td>
<td></td>
</tr>
<tr>
<td>≥T2</td>
<td>13 (42.9)</td>
<td>7 (50)</td>
<td></td>
</tr>
<tr>
<td>Lymph node status, No. (%)</td>
<td></td>
<td></td>
<td>.29</td>
</tr>
<tr>
<td>Positive</td>
<td>2 (5.7)</td>
<td>2 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>17 (48.6)</td>
<td>5 (35.7)</td>
<td></td>
</tr>
<tr>
<td>N/A</td>
<td>16 (45.7)</td>
<td>7 (50)</td>
<td></td>
</tr>
<tr>
<td>History of bladder cancer, No. (%)</td>
<td></td>
<td></td>
<td>.74</td>
</tr>
<tr>
<td>Yes</td>
<td>13 (37.1)</td>
<td>6 (42.9)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>21 (60)</td>
<td>7 (50)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (2.9)</td>
<td>1 (7.1)</td>
<td></td>
</tr>
</tbody>
</table>

**Indeterminate Urothelial Diagnoses in a General Surgical Pathology Sign-Out Setting: Institutional Experience Spanning 10 Years**

(Poster No. 99)

**Georges Tabet, MD** (georgetabet125@gmail.com); Aileen Grace Arriola, MD; Danial Mir, MD. Department of Pathology, Temple University Hospital, Philadelphia, Pennsylvania.

**Context:** Indeterminate urothelial diagnoses can be challenging because of the nature of management and frequency of surveillance performed for patients with bladder cancer. Several confounding factors, such as biopsy artifact, histology artifact, prior therapies, and infection, can lead to diagnostic pitfalls for malignancy. We reviewed indeterminate urothelial cases at our institution.

**Table 2: Clinicopathologic Features in IDO-Positive and IDO-Negative Tumors**

<table>
<thead>
<tr>
<th>Clinicopathologic Feature</th>
<th>IDO Positive (%)</th>
<th>IDO Negative (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range), y</td>
<td>73.3 (42–94)</td>
<td>72.8 (62–93)</td>
<td>.82</td>
</tr>
<tr>
<td>Gender, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>20 (57.1)</td>
<td>7 (50)</td>
<td>.75</td>
</tr>
<tr>
<td>Female</td>
<td>13 (42.9)</td>
<td>7 (50)</td>
<td></td>
</tr>
<tr>
<td>Tumor grade, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>10 (28.6)</td>
<td>1 (7.1)</td>
<td>.14</td>
</tr>
<tr>
<td>High</td>
<td>23 (71.4)</td>
<td>13 (92.9)</td>
<td></td>
</tr>
<tr>
<td>Tumor size, mean (range), cm</td>
<td>3.9 (0.7–9.5)</td>
<td>3.6 (1.1–8.2)</td>
<td>.29</td>
</tr>
<tr>
<td>CIS, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>11 (31.4)</td>
<td>5 (35.7)</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>23 (65.7)</td>
<td>9 (64.3)</td>
<td></td>
</tr>
<tr>
<td>NA</td>
<td>1 (2.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neoadjuvant therapy, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4 (11.4)</td>
<td>1 (7.1)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>29 (82.9)</td>
<td>11 (78.6)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (5.7)</td>
<td>2 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Pathologic stage, No. (%)</td>
<td></td>
<td></td>
<td>.75</td>
</tr>
<tr>
<td>&lt;T2</td>
<td>20 (57.1)</td>
<td>7 (50)</td>
<td></td>
</tr>
<tr>
<td>≥T2</td>
<td>13 (42.9)</td>
<td>7 (50)</td>
<td></td>
</tr>
<tr>
<td>Lymph node status, No. (%)</td>
<td></td>
<td></td>
<td>.29</td>
</tr>
<tr>
<td>Positive</td>
<td>2 (5.7)</td>
<td>2 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>17 (48.6)</td>
<td>5 (35.7)</td>
<td></td>
</tr>
<tr>
<td>N/A</td>
<td>16 (45.7)</td>
<td>7 (50)</td>
<td></td>
</tr>
<tr>
<td>History of bladder cancer, No. (%)</td>
<td></td>
<td></td>
<td>.74</td>
</tr>
<tr>
<td>Yes</td>
<td>13 (37.1)</td>
<td>6 (42.9)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>21 (60)</td>
<td>7 (50)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (2.9)</td>
<td>1 (7.1)</td>
<td></td>
</tr>
</tbody>
</table>
Design: We identified indeterminate urothelial diagnoses made at our institution (2010–2020). Cases with a descriptive diagnosis that included papillomas, hyperplastic, atypical, and dysplastic were included. PUNLMP cases were excluded. Data from electronic medical records were used to determine age, history of bladder lesions, cystoscopy findings, recurrence, and progression. Cases were stratified by history of bladder cancer. Fisher exact test was used.

Results: Overall, 49 cases were identified. The mean age was 67.58 (27 males, 21 females, 1 unknown). Twenty-two patients (44.9%) had a history of bladder cancer and 27 (55.1%) did not have any prior history of bladder cancer. A total of 5 cases (10.2%) demonstrated either recurrence or progression, with 1 recurrence and 4 progressions. All 5 cases with progression or recurrence had a history of bladder cancer. However, there was no significant difference in recurrence and progression when analyzing each diagnostic category separately (Table).

<table>
<thead>
<tr>
<th>Outcome Summary of Indeterminate Urothelial Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior History of Bladder Cancer &amp; No History of Bladder Cancer &amp; P Value</td>
</tr>
<tr>
<td>(n = 1) &amp; (n = 1) &amp;</td>
</tr>
<tr>
<td>Recurrence</td>
</tr>
<tr>
<td>Yes &amp; 0 &amp; 0</td>
</tr>
<tr>
<td>No &amp; 1 &amp; 1</td>
</tr>
<tr>
<td>Progression</td>
</tr>
<tr>
<td>Yes &amp; 1 &amp; 0</td>
</tr>
<tr>
<td>No &amp; 1 &amp; 1</td>
</tr>
<tr>
<td>Prior History of Bladder Cancer &amp; No History of Bladder Cancer</td>
</tr>
<tr>
<td>(n = 9) &amp; (n = 11) &amp;</td>
</tr>
<tr>
<td>Recurrence</td>
</tr>
<tr>
<td>Yes &amp; 1 &amp; 0</td>
</tr>
<tr>
<td>No &amp; 8 &amp; 11</td>
</tr>
<tr>
<td>Progression</td>
</tr>
<tr>
<td>Yes &amp; 2 &amp; 0</td>
</tr>
<tr>
<td>No &amp; 8 &amp; 11</td>
</tr>
<tr>
<td>Prior History of Bladder Cancer &amp; No History of Bladder Cancer</td>
</tr>
<tr>
<td>(n = 10) &amp; (n = 11) &amp;</td>
</tr>
<tr>
<td>Recurrence</td>
</tr>
<tr>
<td>Yes &amp; 0 &amp; 0</td>
</tr>
<tr>
<td>No &amp; 9 &amp; 15</td>
</tr>
<tr>
<td>Progression</td>
</tr>
<tr>
<td>Yes &amp; 1 &amp; 0</td>
</tr>
<tr>
<td>No &amp; 9 &amp; 15</td>
</tr>
</tbody>
</table>

Conclusions: Our findings show that cases with a de novo indeterminate urothelial diagnosis had different outcomes as compared with those cases with a history of bladder cancer. However, this difference was not found to be statistically significant when analyzing each diagnostic category separately, likely because of the small sample size. Hence, larger studies are warranted.

Donor-Derived Neuroendocrine Carcinoma Transmission to 2 Kidney Transplant Recipients Demonstrated by Short Tandem Repeat Analysis

(Poster No. 100)

Kotaro Takeda, MD1 (takedak18@ecu.edu); Rhonda Mittenzweig, MD2; Kim Geisinger, MD; Michael Datto, MD, PhD; Lorita M. Rebellato, PhD;1 Department of Pathology and Laboratory Medicine, East Carolina University and Vidant Medical Center, Greenville, North Carolina; 1Department of Pathology, Duke University Medical Center, Durham, North Carolina.

Kidney transplantation has improved the quality of life in patients with end-stage renal disease. However, transplantation is associated with an increased risk of malignancy, partially because of the need of chronic immunosuppression. One of the devastating scenarios is transmission of donor-derived cancers, which is frequently fatal. We report a case of lung cancer transmission from a deceased donor to 2 adult kidney recipients. Approximately 1 year after a vein transplant kidney transplantation, both recipients developed acute kidney failure. Computerized tomography for both recipients showed masses in the transplanted kidneys and innumerable masses in the livers. Pathologic examinations for both cases demonstrated high-grade neuroendocrine carcinoma with “mirror-image” histology in the transplant kidneys and liver metastases. Short tandem repeat (STR) analyses were performed to determine the origin of the tumors. STR analyses of both tumors were nearly identical to that of the donor, proving that both tumors were from the same donor. Immunohistochemical analyses showed that both tumors were positive for thyroid transcription factor 1, supporting a lung primary. One recipient died as a direct sequela to metastatic tumor, and the other required transplant nephrectomy and chemotherapy. STR analysis plays a crucial role for rapid and unequivocal determination of donor tumor transmission and significantly alters patient management, including reduction of immunosuppression and/or organ explant. Furthermore, it may spur investigation among other recipients of organs from the same donor. Awareness of this largely nonpreventable complication and prompt implementation of molecular testing if cancer transmission is suspected are critical for proper management of these patients.

Persistent Müllerian Duct Syndrome

(Poster No. 101)

Andriy Kostyuk, MD1 (andriykostyuk28@gmail.com); Maria Isabel Almira Suarez, MD2; Ali Azeer, MD. 1Department of Pathology, Medstar Georgetown University Hospital, Washington, DC; 2Department of Pathology, Children’s National Medical Center, Washington, DC.

A 1-year-old boy underwent a bilateral orchietomy for bilateral gonadal dysgenesis. The patient had an uncomplicated prenatal history. Postpartum evaluation revealed microepis without ambiguity and undescended tests. Ultrasound identified atrophic gonads in the inguinal canals (Figure 1.101, A). The karyotyping confirmed the presence of XY chromosomes, and the SRY gene was detected by fluorescence in situ hybridization. Laboratory testing showed increased follicle-stimulating hormone (FSH) and luteinizing hormone (LH), and undetectable testosterone, inhibin, and anti-Mullerian hormone (AMH) blood concentrations. The resection specimens contained benign atrophic testicular and para-testicular tissue (Figure 1.101, B) along with fallopian tube tissue (Figure 1.101, C). Undescended testes with Müllerian duct derivatives (Figure 1.101, D) have been associated with genetic abnormalities such as persistent Müllerian duct syndrome (PMDS). It is a rare autosomal recessive entity most commonly caused...
by mutations in the AMH gene (PMDS type 1) or the AMHR2 gene (PMDS type 2), responsible for AMH and AMH receptor 2 production, respectively. These 2 proteins induce regression of the Mullerian duct (the precursor to female reproductive organs), which develops as default in both fetus genders. Mutations in the AMH and AMH receptor 2 genes lead to Mullerian duct failure regression in males. As a result, the Mullerian duct persists to form a uterus and fallopian tubes. Pathologists should be aware of PMDS presentation and be able to correlate histologic findings with clinical, imaging, and genetic studies. It is essential to document every case of rare syndromes like this to continue to provide data that can be collected for further characterization and recognition.

**Post-pubertal Pure Yolk Sac Tumor of Testis: An Extremely Rare Entity**

(Poster No. 102)

Simmi Patel, MD† (patels@upmc.edu); Swati Satturwar, MD‡; Dayne P. Ashman, MD§; Gabriela Quiroga-Garza, MD. †Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; ‡Department of Pathology, University Hospitals Cleveland Medical Center, Cleveland, Ohio.

**Context:** Postpubertal pure yolk sac tumors (YSTs) are an extremely rare type of malignant germ cell tumor (GCT) that accounts for <1% of testicular GCTs. Their clinical behavior is aggressive compared with the more common prepubertal counterpart. The aim of this study was to analyze clinical presentation, histomorphologic spectrum, ancillary tests, and clinical outcomes in a case series of this entity.

**Design:** A retrospective review of 3 cases of postpubertal pure YST of testis was performed. Data collected for each patient included demographics, clinical presentation, serum markers, radiology and pathologic findings, treatment, and clinical outcomes.

**Results:** The Table summarizes the results of this study. One patient presented with metastatic disease at the time of diagnosis. All patients presented with testicular mass with or without associated pain and elevated serum α-fetoprotein level. Median age at presentation was 25 years (range, 25–27 years). Histologic patterns and features were germ cell neoplasia in situ (n = 3), reticular/microcystic (n = 3), solid (n = 2), glandular, papillary, cystic (n = 1) and angio-lymphatic invasion (n = 3). Fluorescent in situ hybridization test performed on case 2 showed presence of isochromosome 12p. Case 1 showed metastatic disease on follow-up.

**Conclusions:** Diagnosis of postpubertal pure YST remains challenging because of the variety of morphologic patterns seen in YSTs. Extensive sampling along with use of ancillary tests is the key to the correct diagnosis. In our case series, 2 of the 3 patients had metastatic disease at or after the diagnosis, confirming the aggressive nature of this rare entity.

### Summary of Pathology Findings in a Case Series of Postpubertal Pure Yolk Sac Tumor

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y/sex</td>
<td>25/M</td>
<td>25/M</td>
<td>27/M</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td>Testicular pain and mass for 2 months</td>
<td>Testicular swelling for 1 year, weight loss, weakness</td>
<td>Nontender testicular mass</td>
</tr>
<tr>
<td>Scrotal ultrasound and other imaging</td>
<td>Left testicle, solid mass (5.8 × 4.5 × 4.0 cm)</td>
<td>Left testicle, heterogenous mass (16.8 × 12.6 × 12.3 cm)</td>
<td>Right testicle, heterogenous hypoeochic solid mass (5.2 × 3.5 × 4.5 cm)</td>
</tr>
<tr>
<td>Pretreatment serum markers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AFP</td>
<td>406 ng/mL</td>
<td>2282 ng/mL</td>
<td>214 ng/mL</td>
</tr>
<tr>
<td>LDH</td>
<td>234 IU/L</td>
<td>697 IU/L</td>
<td>150 IU/L</td>
</tr>
<tr>
<td>HCG</td>
<td>&lt;0.5 mIU/mL</td>
<td>2.0 mIU/mL</td>
<td>3 mIU/L</td>
</tr>
<tr>
<td>Treatment</td>
<td>Orchietomy followed by chemotherapy</td>
<td>Orchietomy and chemotherapy</td>
<td>Orchietomy</td>
</tr>
<tr>
<td>Gross</td>
<td>Tan-gray to white, well circumscribed firm mass measuring 5.8 × 4.5 × 4.0 cm</td>
<td>Heterogenous, tan-white to tan-yellow, glistening to dull soft to rubbery, focally hemorrhagic, centrally necrotic mass measuring 22.5 × 15.5 × 11.5 cm</td>
<td>Heterogenous tan-white, solid mass measuring 7.0 × 4.8 × 4.8 cm</td>
</tr>
<tr>
<td>Histologic patterns and features</td>
<td>Reticular/microcystic, papillary with focal solid areas with Schiller-Duval bodies, focal necrosis, and germ cell neoplasia in situ present</td>
<td>Glandular, papillary, solid, perivascular, macrocystic with focal reticulocytic/ microcystic with Schiller-Duval bodies, eosinophilic globules, basement membrane-like material deposits, focal necrosis, and germ cell neoplasia in situ present</td>
<td>Reticular/microcystic with Schiller-Duval bodies, germ cell in situ present</td>
</tr>
<tr>
<td>AFP</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>AE1/AE3 (cytokeratin)</td>
<td>+</td>
<td>+</td>
<td>Not available</td>
</tr>
<tr>
<td>SALL4 (Sal-like protein)</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Glypican-3</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>OCT 3/4</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>CD30</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>CD117</td>
<td>+</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>FISH</td>
<td>Not performed</td>
<td>Isochromosome 12p</td>
<td>Not performed</td>
</tr>
<tr>
<td>Pathologic and clinical stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posttreatment serum markers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up imaging</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcome</td>
<td>Alive at 1.5 years after diagnosis, metastasis to lung and periaortic lymph nodes</td>
<td>Alive at 7 months, metastasis to lungs</td>
<td>Complete remission (&gt;6 months)</td>
</tr>
</tbody>
</table>

Abbreviations: AFP, α-fetoprotein; FISH, Fluorescent in situ hybridization; HCG, human chorionic gonadotropin; LDH, lactate dehydrogenase.
**Mucinous Tubular and Spindle Cell Carcinoma With Unusual Features**  
(Poster No. 103)

Aysha Mubeen, MD1 (aysha.mubeen86@gmail.com); Shuko Harada, MD1; Charles Peyton, MD2; Eddy Yang, MD, PhD2; Haider Mejbel, MD3; Cristina Magi-Galluzzi, MD.1 Departments of 1Pathology, 2Urology, and 3Radiation Oncology, University of Alabama at Birmingham.

Mucinous tubular and spindle cell carcinoma (MTSCC) is a rare subtype of renal cell carcinoma. Typically, it affects young adults with female predominance, and demonstrates indolent behavior. We report a case of locally advanced MTSCC with necrosis. A 61-year-old woman presented with a large renal tumor with mass effect on inferior vena cava. A 20.6-cm yellow-tan mass with hemorrhage and necrosis replaced most of the nephrectomy specimen. Microscopic examination revealed a mixture of tubular and spindle components in mucinous stroma. The tubules were lined by cuboidal cells with low-grade nuclei and scant cytoplasm; spindle cells had similar cytologic features (Figure 1.103, A). Tumor necrosis represented 15% of the lesion (Figure 1.103, B); sarcomatoid features were not present. Tumor extended into hilar fat (pT3a). Differential diagnoses were excluded by ancillary studies. Neoplastic cells were positive for PAX8 (Figure 1.103, C), CK7 (Figure 1.103, D), AMACR, and CD10 (focal), and negative for cathepsin K and CDKN2A/B. Since alterations have been reported in locally advanced/metastatic MTSCC, we assessed cyclin D1 protein expression as a surrogate marker and found no overexpression. Presence of unusual features in MTSCC (necrosis, solid or sarcomatoid growth, mitotic activity, vascular invasion, advanced stage) can pose diagnostic challenges. Our case showed necrosis and hilar fat invasion, features frequently associated with aggressive behavior. Additional molecular analysis is ongoing. Close follow-up is recommended.

**Primary Alveolar Soft Part Sarcoma of the Prostate: Report of a Deceptive Case**  
(Poster No. 105)

Parnaz Daneshpajounejad, MD (daneshp@penmedicine.upenn.edu); Casey Morrison, MD, Kumarasen Cooper, MD, PhD; Lauren Schwartz, MD; Xiaofeng Zhao, MD; Paul Zhang, MD; Priti Lal, MD. Department of Pathology, Hospital of the University of Pennsylvania, Philadelphia.

A 30-year-old never-smoker man presented with hematuria, dysuria, and constipation at an outside hospital and was diagnosed and treated for recurrent urinary tract infection. Because of continued symptoms, he underwent transurethral resection of bladder lesion (TURBT) and was diagnosed with urothelial carcinoma, AJCC stage pT2. Subsequently, he was transferred to the University of Pennsylvania. In-house radiology workup revealed a large vascular mass involving prostate pushing against bladder base. Prostate needle biopsies performed in house revealed an epithelioid neoplasm with nested growth pattern composed of cells with moderate amount of eosinophilic cytoplasm, mildly pleomorphic nuclei, and occasional prominent nucleoli (Figure 1.105, A). The differential diagnosis included carcinoma, sarcoma, and paraganglioma. Accordingly, a wide panel of keratins (Figure 1.105, B; negative AE1/3), along with S100, chromogranin, and synaptophysin, were negative. ERG and CD31 highlighted an extensive vascular network. Focal positivity for smooth muscle antigen prompted a TFE immunostain (Figure 1.105, C) and TFE3 break-apart fluorescence in situ hybridization assay, which were positive (Figure 1.105, D). Subsequently, using custom BAC probes, presence of an ASPSRC1 gene rearrangement was demonstrated. The outside hospital TURBT was reviewed and the diagnosis corrected to alveolar soft-part sarcoma (ASPS). Taking all the above findings together, the final diagnosis was ASPS with involvement of bladder. The patient was found to have bilateral lung metastases and was started on pazopanib and close...
follow-up for possible brain metastasis. ASPS is a rare soft tissue tumor that primarily involves the extremities, and to the best of our knowledge this is only the third case report of primary prostatic ASPS.

**The Significance of Immunohistochemical Workup in the Diagnosis of Renal Oncocytic Neoplasms on Core Biopsies at a Single Institution**

*(Poster No. 106)*

Liping Wang, MD, PhD (liping.wang@bswhealth.org); Ruth Asirvatham, MD; Adam Johnson, MD; Lina Liu, MD. Department of Pathology, Baylor Scott & White Health, Temple, Texas.

**Context:** Diagnosing renal oncocytic neoplasms on biopsy remains challenging because of morphologic overlap with other entities. We retrospectively reviewed cases of oncocytic neoplasms and compared histologic diagnosis, immunophenotype, and clinical follow-up.

**Design:** We conducted a 5-year retrospective review of our database’s renal oncocytic neoplasms on core biopsies. All biopsies were stained with a minimum immunopanel of CK7, CD117, and vimentin. Additional stains, including AMACR, CAIX, and CK20, were performed if necessary. Clinical follow-up was assessed through EMR.

**Results:** Forty-eight renal oncocytic neoplasms were reviewed, including 46 core biopsies and 2 core biopsies with subsequent resection. At the time of original diagnosis, 32 cases (32 of 48; 67%) were diagnosed as low-grade oncocytic neoplasm. After the minimum immunopanel, 16 of 32 cases were classified as classic oncocyotma and 3 cases as RCC. With additional stains, 2 cases of RCC (2 of 32; 6.3%) were subtyped as papillary RCC, oncocytic variant; and the other RCC (1 of 32; 3%) remained unclassified. Four of 32 CK7+/CD117+ cases (12.5%) were recognized as low-grade oncotypic tumor (LOT) of kidney. Nine of 32 cases with equivocal staining (CD117+<5% or CK7+ 50%–80%) could not be further characterized. Clinical follow-up showed lung metastasis in 1 papillary RCC, oncocytic variant. No other cases showed recurrence/metastasis. Of note, in the remaining 16 of 48 cases, the original diagnosis remained unchanged following additional workup.

**Conclusions:** A select immunohistochemistry panel (CK7, CD117, vimentin) can identify malignancies and classic oncocyotma that would otherwise receive an uncertain diagnosis. In addition, our study helps to recognize an emerging entity, LOT of kidney.

**Prostatic Basal Cell Carcinoma With ATM Deletion**

*(Poster No. 107)*

Daniel Neelon, MD1 (daniel.p.neelon.mil@mail.mil); Michael Goold, MD;1 Sean Baraniak, MD;1 Joel Moncur, MD, PhD;2 1Department of Pathology, Walter Reed National Military Medical Center, Bethesda, Maryland; 2Department of the Director, The Joint Pathology Center, Silver Spring, Maryland.

An 84-year-old man underwent transurethral resection of the prostate for prostate enlargement. Microscopically, 98% of the tissue was stained by infiltrated, anastomosing nests of basaloid cells with peripheral palisading in a desmoplastic stroma (Figure 1.107, A). The neoplastic cells were moderately pleomorphic with scant cytoplasm and prominent nucleoli. Perineural invasion and abundant mitotic figures were present. Necrosis was absent. Immunohistochemistry revealed strong nuclear p63 staining (Figure 1.107, B), diffuse cytoplasmic BCL-2 staining, and focal positivity with CK903 and NXX3.1. GATA3 expression was limited to benign urothelial cells lining the prostatic urethra and urethral ducts. The proliferative index was high (Ki-67 approximately 20%; Figure 1.107, C). The neoplastic cells were negative for prostate-specific antigen (Figure 1.107, D), PSAP, ERG, AMACR, CK20, and HER2, supporting the diagnosis of prostatic basal cell carcinoma (PBCC). Next-generation sequencing demonstrated deletion of ATM (ataxia-telangiectasia, mutated), which encodes a protein kinase that regulates DNA damage response. PBCC represents less than 0.01% of prostate carcinomas, and only 104 cases have been reported. Radical prostatectomy is often pursued because of lack of proven efficacy of chemotherapy. There is no standard treatment. PBCC’s molecular mutational landscape is ill defined. One other author has reported an ATM mutation, suggesting that the PARP inhibitor olaparib may be considered for targeted therapy. Furthermore, a recent report demonstrated a favorable response to olaparib in a patient with BRCA2-mutated PBCC. PARP inhibitors can effectively treat prostatic adenocarcinomas with mutations in genes involved in homologous recombination. Further investigation may demonstrate that PARP inhibitors could also be indicated for PBCCs with mutations affecting homologous recombination.
prominent nucleoli. The neoplasm was positive for CD117 and negative for CK7, CAIX, ALK, and vimentin, an immunohistochemical phenotype frequently seen in renal oncocytomas. Interestingly, there were increased mitoses, with scattered atypical mitotic figures (Figure 1.108, B). Ki-67 was mildly increased at 5%–10% (Figure 1.108, C). Additionally, many of the capillaries in the tumor were filled with sickled red blood cells (Figure 1.108, D). This case illustrates an unusual atypical oncocytic tumor that has not been described in a patient with sickle cell trait.

**Primary Signet Ring Cell Adenocarcinoma of the Urinary Bladder Following Nephrogenic Adenoma**

(Poster No. 109)

Margarita Loxas, BS1 (margarita.loxas@creighton.edu); Xing Zhao, MD2; Neil Alouch, MD3; Poonam Sharma, MBBS,2 School of Medicine and 1Department of Pathology, Creighton University, Omaha, Nebraska.

Signet ring cell adenocarcinoma arising from the urinary bladder is uncommon, comprising less than 1% of primary bladder malignancies. In addition to their rarity, the reported cases exhibit varying immunohistochemical profiles, making them diagnostic dilemmas. We present a 34-year-old paraplegic man with a history of transurethral resection of prostate adenomas. The patient subsequently developed biopsy-proven poorly differentiated, infiltrating adenocarcinoma with signet ring features. An in situ adenocarcinoma component (Figure 1.109, A) was identified as well. The nephrogenic adenoma possibly underwent malignant transformation into this adenocarcinoma. Upon radical cystoprostatectomy, the bladder was invaded by metastatic adenocarcinoma, with areas of hemorrhage and necrosis. The tumor stained positively for AE1/AE3, CK7, CDX2, GATA-3 (patchy), and negatively for PSA, CK20, and p40. β-catenin exhibited cytoplasmic staining (Figure 1.109, D). The majority of reported primary bladder adenocarcinomas demonstrate both CK20 and CK7 expression, with ours staining positively only for CK7. CDX2, which stained positive in our case, is also a marker of interest in this malignancy, but studies have provided inconsistent results in its positive predictive value. β-catenin has been looked at as a potential differentiator between colonic and bladder adenocarcinoma, showing cytoplasmic staining in primary bladder tumors versus nuclear staining in primary colonic adenocarcinomas. This aligns with our findings.

**A Rare Case of a Sarcomatoid Tumor of the Prostate**

(Poster No. 110)

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Sarcomatoid carcinoma of the prostate is an extremely rare malignancy with a very poor prognosis and represents less than 1% of all prostate neoplasms. Histologically and/or immunohistochemically this entity demonstrates epithelial and mesenchymal differentiation. Most of the patients have a prior diagnosis of prostatic adenocarcinoma. We report a case of a 78-year-old man who was diagnosed with prostatic adenocarcinoma in 2003, underwent brachytherapy in 2005, and was diagnosed with recurrent prostatic ductal adenocarcinoma in 2019 that was treated with radiation and androgen deprivation therapy. One year later, he presented with hematuria, a normal PSA value of 0.2 ng/mL, and computed tomography (CT) scan showing a large complex prostatic mass invading the bladder and seminal vesicle. A transurethral resection of prostate and bladder was performed. Histopathologic examination of the entire tissue showed a malignant sarcomatoid tumor with predominant osteosarcoma and chondrosarcoma components. No prostatic adenocarcinoma or benign prostatic tissue was identified. Immunohistochemical stains did not show any evidence of prostatic epithelial differentiation. A repeat CT scan 3 months later showed the tumor almost doubled in size. The patient was transferred to hospice care and died a few months after diagnosis. In our case, since the patient did not undergo a radical prostatectomy, the entire tumor could not be examined so there was no way to differentiate between sarcomatoid carcinoma and secondary postradiation sarcoma. One important takeaway from this case is that sarcomatoid overgrowth in sarcomatoid carcinoma may be misdiagnosed as sarcoma of the prostate, since the sarcomatoid component may represent up to 99% of the tumor.
Special stains of periodic acid–Schiff with diastase and von Kossa were performed, as well as immunohistochemical stains with IgG and IgG4.

**Results:** All 3 cases showed elevated prostate-specific antigen with imaging findings suspicious for malignancy. On resection, histiocytic infiltration with Michaelis-Gutman bodies was identified (Figure 1.111, A and B). Positive staining for von Kossa (Figure 1.111, C) and periodic acid–Schiff-diastase special stains were seen, consistent with prostate malakoplasia. One of these cases demonstrated chronic sclerosing inflammation with >50 IgG4 plasma cells per 1 high-power field and IgG4/IgG ratio >40%, consistent with IgG4-RSD (Figure 1.111, D).

**Conclusions:** The findings of simultaneous prostate malakoplasia and IgG4-RSD may represent a concordance of 2 disease processes, or more likely a common biologic or immunologic mechanism of both disease processes. Malakoplasia is treated with antibiotics whereas IgG4-RSD is treated with steroids, and as such the concordance of both disease processes may present a clinical dilemma. The clinical significance of increased IgG4 plasma cells in association with malakoplasia is not well defined and awaits further study.

**The Clinical Significance of Cribriform Pattern 4 in Prostate Biopsies: Our Institution Experiences**

(Poster No. 113)

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**Context:** Prostatic carcinoma (PCa) with cribriform Gleason pattern 4 (CP4) on radical prostatectomy (RP) is generally considered more aggressive and associated with a higher stage on RP and biochemical recurrence. The significance of CP4 on needle biopsy (NBx) is not extensively correlated with subsequent RP findings.

**Design:** All NBx with the diagnosis of PCa grade group (GG) 2, 3, or 4 between 2007 and 2014 were initially included and were reviewed by a genitourinary pathologist. Any amount of CP4 was labeled as positive for CP4. Pathologic findings on the corresponding RP specimens, including Gleason score, pTN stage, and percentage of prostate tissue involved, were obtained from the pathology reports. The χ² and Fisher exact test were used to analyze data.

**Results:** Of 144 patients evaluated, 46 had CP4 on their biopsies, whereas 98 had no evidence of CP4 on their biopsies. Patients with CP4 were significantly more likely to have higher-grade disease (odds ratio = 9; confidence interval, 3–26.8; P < .001). There was no significant difference between the 2 groups in terms of lymph node involvement, percentage of prostate tissue involved by tumor, or biochemical recurrence (Table).

**Conclusions:** Our study supports the general consensus that CP4 is associated with a more aggressive disease. This is important especially for patients with PCa GG2 with low percentage of Gleason pattern 4, as active surveillance is currently a management option for these patients at multiple institutions. The presence of any cribriform pattern 4 may be used as an exclusion criterion for active surveillance protocols.

**Histopathology and Biochemical Recurrence Data of the Study Population**

<table>
<thead>
<tr>
<th>Study Groups</th>
<th>Cases With Cribriform Morphology on Biopsy</th>
<th>Cases With No Cribriform Morphology on Biopsy</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall number</td>
<td>46</td>
<td>98</td>
<td>.001</td>
</tr>
<tr>
<td>Grade on radical, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade GG5</td>
<td>5 (10.9)</td>
<td>2 (2.04)</td>
<td>.06</td>
</tr>
<tr>
<td>Grade GG4</td>
<td>10 (21.7)</td>
<td>3 (3.06)</td>
<td>.06</td>
</tr>
<tr>
<td>Grade GG3</td>
<td>15 (32.6)</td>
<td>27 (27.6)</td>
<td>.06</td>
</tr>
<tr>
<td>Grade GG2</td>
<td>16 (34.8)</td>
<td>65 (66.3)</td>
<td>.06</td>
</tr>
<tr>
<td>Grade GG1</td>
<td>0</td>
<td>1 (1.00)</td>
<td>.06</td>
</tr>
<tr>
<td>Pathologic T stage, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T4a</td>
<td>1 (1.0)</td>
<td>13 (13.0)</td>
<td>.06</td>
</tr>
<tr>
<td>T4b</td>
<td>5 (6.2)</td>
<td>65 (66.3)</td>
<td>.06</td>
</tr>
<tr>
<td>Median tumor volume in radical prostatectomy (≥10%), No. (%)</td>
<td>55 (56.1)</td>
<td>.20</td>
<td></td>
</tr>
<tr>
<td>Biochemical recurrence, No. (%)</td>
<td>17 (17.3)</td>
<td>.99</td>
<td></td>
</tr>
</tbody>
</table>

**Newly Emerging Renal Tumors: A Presentation of 2 Cases**

(Poster No. 114)

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Recently described rare renal tumors that have not yet been added to the World Health Organization (WHO) classification present diagnostic difficulties, and several of these tumors have a favorable prognosis. We present 2 such cases: 1 case each of eosinophilic solid and cystic renal tumor (ESCRT), and biphasic squamous alveolar renal tumor (BSART); the latter may represent a subtype of papillary renal cell carcinoma. ESCRT has indolent behavior in most patients and is a member of the oncocytic renal neoplasms category, along with clear cell RCC, eosinophilic chromophobe RCC, oncocytoma, translocation-associated RCC, SDH-deficient RCC, and epitheliod angiomylipoma. A 59-year-old woman presented with an incidental 5.1-cm exophytic, well-demarcated left renal mass. Microscopically, solid, alveolar, and focally cystic patterns were present with voluminous granular eosinophilic cytoplasm (Figure 1.114, A) with rare pink cytoplasmic granules (Figure 1.114, B), enlarged irregularly contoured nuclei, and occasionally prominent nucleoli. Immunohistochemistry was positive for PAX8, focal CK7, and CK20, and negative for pancytokeratin, CD117, and...
A Case Series of Mixed-Grade Papillary Urothelial Carcinomas of the Renal Pelvis and Ureter

(Meagan Chambers, MD, MS, MSc1 (MeaganMD@UW.edu); Jonathan Wright, MD2; Michael Haffner, MD, PhD3; Nicholas Reder, MD, PhD4; Maria Tretiakova, MD, PhD5; Funda Vakar-Lopez, MD6; Lawrence True, MD7 Department of Pathology; Urology, and Fred Hutchinson Cancer Center, University of Washington, Seattle.

Context: Though most papillary urothelial carcinomas are graded either low or high grade, a minority are mixed grade, being composed of predominantly low-grade cells with a minor high-grade component. Prior analyses of these mixed-grade lesions have focused on the bladder. We present a series of mixed-grade papillary carcinomas of the upper urinary tract with a focus on clinical course and outcomes.

Design: Pathology records between 2009 and 2021 from our hospital were searched for diagnoses of papillary carcinomas of the ureter. Predominantly low-grade cancers with <10% of a high-grade component and >2 months follow-up were included. Exclusion criteria included a prior or concurrent high-grade diagnosis including carcinoma in situ.

Results: Twenty-seven cancers met inclusion criteria: M:F, 4:1; average age, 68 years, with median follow-up 22.3 months (range, 2.4–87 months). At diagnosis, 8 cancers (30%) invaded the lamina propria/subepithelial connective tissue and 1 invaded the muscularis (3.7%). Nineteen patients (70%) underwent nephroureterectomy. Recurrences occurred in those without resection (n = 2) and 1 status post ureterectomy with negative margins. There were 3 cases of fatal metastases, 2 in patients with nephroureterectomy with negative margins.

Conclusions: In this series, mixed-grade non–muscle-invasive cancers arising in the ureter/renal pelvis had a range of outcomes including fatal metastatic disease despite nephroureterectomy. This stands in contrast to these lesions in the bladder, where they appear to have a more indolent course. This may reflect difficulty in sampling, diagnosis, and/or treatment.

DNA Sequencing Profile of Micropapillary Urothelial Carcinoma

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Context: Micropapillary urothelial carcinoma (MPUC) is a distinct morphologic variant associated with aggressive behavior. Knowledge of the molecular profile of MPUC is limited, and to the best of our knowledge no DNA sequencing data have yet been published on MPUC.
Collision Tumors of Kidney: A 5-Year Single-Institutional Experience

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Context: Collision tumor is an uncommon entity characterized by 2 histogenetically and histologically different tumors “colliding” within a single mass. Although previously considered rare, collision tumors have been increasingly recognized in the kidney; more than 20 cases have been reported in the English literature. Here, we describe 6 additional cases of renal collision tumors at our institution within the past 5 years.

Design: Kidney tumors composed of more than 2 histotypes were selected from our institutional archives from 2015 to 2020. Cases of metachronous or synchronous tumors without collision, tumor-to-tumor metastasis, and hybrid oncocytoma-chromophobe renal cell carcinoma (RCC) were excluded.

Results: Six cases were reviewed. The patient ages at presentation ranged from 55 to 78 years, and the tumor sizes ranged from 1.4 to 8 cm (mean, 3.8 cm). The major tumor components were oncocytoma (n = 3), urothelial carcinoma (n = 1), chromophobe RCC (n = 1), and acquired cystic disease–associated RCC (n = 1). The minor components were mucinous tubular and spindle cell carcinoma (n = 2), type 1 papillary RCC (n = 1), clear cell papillary RCC (n = 1), tubulocystic RCC (n = 1), and papillary adenomatosis (n = 1) (see Table). To detect collision tumors, generous sampling, particularly from areas with distinctly different gross appearances, is highly recommended. In addition, for an unequivocal diagnosis of collision tumor, dedifferentiation, hybrid tumors, secondary degenerative changes, and tumor-to-tumor metastasis should be excluded. Molecular studies may be required to further elucidate the histogenetic origins of collision tumors.

Conclusions: Renal collision tumors are recognized more frequently than previously documented. To detect collision tumors, generous sampling, particularly from areas with distinctly different gross appearances, is highly recommended. In addition, for an unequivocal diagnosis of collision tumor, dedifferentiation, hybrid tumors, secondary degenerative changes, and tumor-to-tumor metastasis should be excluded. Molecular studies may be required to further elucidate the histogenetic origins of collision tumors.

Summary of 6 Renal Collision Tumors

<table>
<thead>
<tr>
<th>Age, y/</th>
<th>Total Size, cm</th>
<th>Major Component</th>
<th>Minor Component</th>
<th>Proportions of Major/Minor Component, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>76/M</td>
<td>2</td>
<td>Oncocytoma</td>
<td>Type 1 papillary renal cell carcinoma</td>
<td>75:25</td>
</tr>
<tr>
<td>74/F</td>
<td>4.5</td>
<td>Oncocytoma</td>
<td>Mucinous tubular and spindle cell carcinoma</td>
<td>80:20</td>
</tr>
<tr>
<td>70/M</td>
<td>2.9</td>
<td>Oncocytoma</td>
<td>Mucinous tubular and spindle cell carcinoma</td>
<td>90:10</td>
</tr>
<tr>
<td>78/M</td>
<td>8</td>
<td>Urothelial carcinoma</td>
<td>Clear cell papillary renal cell carcinoma</td>
<td>95:05</td>
</tr>
<tr>
<td>71/F</td>
<td>3.7</td>
<td>Chromophobe renal cell carcinoma</td>
<td>Tubulocystic renal cell carcinoma</td>
<td>80:20</td>
</tr>
<tr>
<td>55/M</td>
<td>1.4</td>
<td>Acquired cystic disease–associated renal cell carcinoma</td>
<td>Papillary adenomatosis</td>
<td>70:30</td>
</tr>
</tbody>
</table>

Although angiosarcoma can rarely arise from the urinary tract, morphologically uniform urothelial carcinoma with partial vascular phenotype has not been reported. A urinary bladder tumor was discovered in a 64-year-old man without prior radiation history after presenting with hematuria. A muscle-invasive urothelial carcinoma was diagnosed at an outside hospital. The patient underwent radical cystectomy following preoperative adjuvant chemotherapy. A 3-mm tumor of small blue cell morphology with no cytokeratin and GATA3 expression was identified in the resected specimen. No residual conventional urothelial carcinoma was identified. The patient subsequently developed diffuse peritoneal tumor spread. The peritoneal...
tumor demonstrated classical angiosarcoma morphology with atypical vascular spaces (Figure 1.119, A) and expression of all vascular markers. When the tumor in the preoperative transurethral resection was retrospectively studied, a second tumor cell population was revealed. In contrast to the associated conventional urothelial carcinoma (Figure 1.119, B), which expressed GATA3 (Figure 1.119, C) and was negative for all vascular markers, the second tumor cell population (10% of the tumor), although morphologically similar to intermixed conventional urothelial carcinoma (with no atypical vascular spaces) (Figure 1.119, B), expressed vascular markers including ERG (Figure 1.119, D) but was negative for GATA3. We believe the tumor is best classified as urothelial carcinoma (with no atypical vascular spaces) (Figure 1.119, B), although morphologically similar to intermixed conventional carcinoma with primary angiomatous differentiation based on the intimate association between conventional and vascular components and indistinguishable morphology between them. Our case demonstrated a challenge in diagnosis and ominous clinical outcome because of its resistance to urothelial carcinoma chemotherapy. Further molecular studies are warranted to understand the pathogenesis of the entity and identify druggable targets for management.

Correlation of Preoperative Studies With Extraprostatic Extension of Prostatic Carcinoma in Radical Prostatectomies: A Retrospective Study

(Poster No. 120)

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Context: Prostate carcinoma (PCa) is the second leading cause of cancer and of cancer death in US men. Primarily, its diagnosis is made on needle biopsies, which dictates the treatment choices. Radical prostatectomy (RPC) is followed by a significant decline in mortality in confined diseases; however, overall prognosis is reduced with locally advanced disease. Extraprostatic extension (EPE) in RPC is a strong prognostic factor. No single parameter can accurately predict EPE in RPC. The purpose of our study is to correlate preoperative studies with adverse histologic finding of EPE in RPC, and their value in guiding treatment.

Design: Following IRB approval, retrospective review of electronic medical records was performed to identify patients who underwent RPC for PCa. Our study group included PCa patients with and without EPE. Correlation studies were conducted on preoperative parameters including serum prostate-specific antigen (PSA) levels, PIRADS score, and biopsy findings including Gleason score (GS), quantitative tumor volume (TV), perineural invasion (PNI), and tumor in fibroadipose tissue (TFAT), with resection findings.

Results: One hundred three patients (65 EPE, 38 without EPE; average age 59 years [range, 42–73 years]; PSA 16.8 ng/mL [range, 0.6–89.7 ng/mL]) were identified. Ninety-eight corresponding biopsies were obtained. Correlation studies between preoperative parameters and resection findings are shown in the Table. Significantly increased incidence of EPE (P < .05) was noted with: PIRADS score >4; biopsy findings of TV >50%, GS, PNI, and TFAT. P value for >4 ng/mL PSA was .05.

Conclusions: This study suggests that a multi-parametric approach is essential for staging of RPC in patients with apparently localized cancer, which also helps direct the treatment strategy.

| Distribution of Preoperative Parameters With Presence and Absence of EPE in RPC (N = 103) |
|---------------------------------|---------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                 | Overall | EPE, No. (%) | No EPE, No. (%) | P Value         |
| Preop PSA level (ng/mL)         |         |               |                 |                 |
| <4                              | 9 (11.1) | 3 (5.88)      | 6 (20.0)        | .05             |
| >4                              | 72 (88.9) | 48 (94.12) | 24 (80.0)      |                 |
| PIRADS score                    |         |               |                 | .01             |
| 5                               | 25 (40.98) | 20 (57.14) | 5 (19.24)      | .01             |
| 4                               | 24 (39.35) | 10 (28.57) | 14 (53.85)     |                 |
| <3                              | 12 (19.67) | 5 (14.29)  | 7 (26.91)      |                 |
| Biopsy tumor volume             |         |               |                 | .02             |
| <50%                            | 70 (71.43) | 38 (63.00) | 32 (84.00)     |                 |
| >50%                            | 28 (28.57) | 22 (37.00) | 6 (16.00)      |                 |
| Biopsy Gleason score/grade group|         |               |                 | .001            |
| Grade 1 (3 + 3 = 6)             | 5 (5.10) | 2 (3.30)      | 3 (7.89)       | .001            |
| Grade 2 (3 + 4 = 7)             | 48 (48.98) | 24 (40.00) | 24 (63.16)     |                 |
| Grade 3 (4 + 3 = 7)             | 14 (14.29) | 6 (10.00)  | 8 (21.05)      |                 |
| Grade 4 (4 + 4 = 8, 3 + 5 = 8) | 13 (13.28) | 12 (20.00) | 1 (2.63)       |                 |
| Grade 5 (4 + 5 = 9, 5 + 4 = 9) | 18 (18.35) | 16 (26.70) | 2 (5.26)       |                 |
| Biopsy PNI                      |         |               |                 | .03             |
| Present                         | 41 (41.83) | 32 (49.23) | 9 (27.00)      | .03             |
| Tumor in fibroadipose tissue    |         |               |                 | .03             |
| Present                         | 9 (9.18)  | 9 (13.84)    | 0 (0.00)       | .03             |

Myoid Gonadal Stromal Tumor

(Poster No. 121)

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Myoid gonadal stromal tumor (MGST) is a rare pure stromal neoplasm of the testis, classified as a newly emerging entity in the 2016 World Health Organization (WHO) classification. MGST is hypothesized to arise from peritubular myoid cells, although its histogenesis remains unknown. We present a case of a healthy 33-year-old man who presented for evaluation of azoospermia. Scrotal ultrasound demonstrated an incidental, 1.1-cm hypoechoic mass in the superior pole of the right testis with prominent vascularity, which also helps direct the treatment strategy.
suspicious for a neoplasm. Right testicular nodulectomy was performed and gross examination demonstrated a well-circumscribed, homogenous, tan lesion. Microscopically, the lesion was composed of bland spindle cells with elongated nuclei and inconspicuous nucleoli, ectic vascularule, and variable amount of collagen deposition, and lacked necrosis, abnormal mitoses, and lymphovascular invasion. Our differential diagnoses included leiomyoma, testicular fibrothecoma, granulosa cell tumor, unclassified sex-cord stromal tumor, and MGST. The lesional cells demonstrated strong, diffuse S100 staining, coexpression of SMA, strong SF-1 nuclear staining (Figure 1.121), and lack of h-caldesmon and inhibin immunoreactivity. The morphology and immunophenotype of the lesion were consistent with diagnosis of MGST. There have been <16 cases of MGST reported in the literature. The unifying diagnostic criteria consist of pure spindle cell lesion without atypia/sex-cord differentiation, and coexpression of S100, SMA, and SF-1 immunostaining. Treatment involves nodulectomy or partial orchectomy. No cases of metastasis or recurrence have been reported in the literature. In summary, MGST is a newly emerging indolent spindle cell neoplasm of the testis and correct diagnosis is essential for appropriate patient care.

**Enteric-Type Adenocarcinoma Presenting as a Very Late Relapse of Testicular Cancer at Site of Metastasis: Report of 2 Cases**

(Poster No. 122)

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Somatic transformation of germ cell tumor (STGCT) occurs in 3%–6% of primary testicular nonseminomatous GCTs, in 8% of postchemotherapy retroperitoneal lymph node dissection (RPLND), and in 20% of late relapse cases. Very late relapse (>5 years after diagnosis) is very rare. We present 2 cases of STGCT that presented as recurrent retroperitoneal abscess and solid cystic abdominal mass 18 and 15 years postorchectomy, RPLND, and chemotherapy for testicular cancer diagnosed at 30 and 34 years of age, respectively (Table). For the first case, the initial biopsy revealed abscess and repeat biopsy revealed dysplastic enteric-type glands. Extensive workup for the origin of the tumor was negative. Subsequent resection revealed an enteric-type adenocarcinoma, negative for SALL4, but positive for i12p by fluorescent in situ hybridization (FISH). In our second case biopsy showed an adenocarcinoma, confirmed on surgical resection with subsequent i12p positivity. Only case 1 received chemotherapy; the patient developed metastatic disease to neck lymph nodes and abdominal recurrence within 6 months, which was treated with surgical resection, and is disease free 1 year later. The second patient is doing well at 1-year follow-up. Besides remote history, a completely different histology and atypical presentation at an older age increase the chances of late diagnosis or misdiagnosis of a late relapse and STGCT. This case report signifies the importance of keeping STGCT in the top differential diagnosis and including i12p analysis up front in a patient with history of testicular tumor, however remote it is and even if histology of primary tumor is unknown.

<table>
<thead>
<tr>
<th>Summary of 2 Cases</th>
<th>Case 1</th>
<th>Case 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at diagnosis</strong></td>
<td>30</td>
<td>34</td>
</tr>
<tr>
<td><strong>Histology of testicular cancer</strong></td>
<td>Unknown</td>
<td>Mixed germ cell tumor: embryonal, choriocarcinoma, and yolk sac tumor</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Orchiectomy, chemotherapy with cisplatin, etoposide, and bleomycin</td>
<td>Orchiectomy, RPLND, chemotherapy with bleomycin, etoposide, and platinum</td>
</tr>
<tr>
<td><strong>Relapse</strong></td>
<td>18 years later</td>
<td>15 years later</td>
</tr>
<tr>
<td><strong>Presentation at time of diagnosis</strong></td>
<td>7-cm heterogeneous right retroperitoneal mass</td>
<td>37-cm large complex abdominal mass with cystic components</td>
</tr>
<tr>
<td><strong>Transabdominal biopsy diagnosis</strong></td>
<td>First—abscess</td>
<td>Well-differentiated adenocarcinoma with abundant mucin production</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Surgical resection</td>
<td>Surgical resection</td>
</tr>
<tr>
<td><strong>Immunophenotype</strong></td>
<td>Positive CK20, CDX2</td>
<td>Positive CK20 and CDX-2</td>
</tr>
<tr>
<td><strong>Negative</strong></td>
<td>CK7, CD30, SALL4, OCT 3/4</td>
<td>CK7</td>
</tr>
<tr>
<td><strong>Isocromosome i(12p) on FISH</strong></td>
<td>Positive in 78% of cells</td>
<td>Positive in 38% of cells</td>
</tr>
<tr>
<td><strong>Final diagnosis</strong></td>
<td>Somatic transformation in a metastatic testicular germ cell tumor</td>
<td>Somatic transformation in a metastatic testicular germ cell tumor</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>FOLFOX: colon-specific chemotherapy</td>
<td>No chemotherapy; follow-up with CT CAP</td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td>Metastatic disease to neck lymph nodes in 6 months, recurrent abdominal disease, undergoes resection, continues to be followed up</td>
<td>CT CAP × 2: negative for recurrence; 1 year follow-up</td>
</tr>
</tbody>
</table>

Abbreviations: CT CAP, computed tomographic chest abdomen pelvis; FISH, fluorescent in situ hybridization; FOLFOX, 5-fluorouracil, leucovorin, and oxaliplatin; RPLND, retroperitoneal lymph node dissection.

**Vasitis Nodosa With Extensive Perineural Invasion and CA19-9 Positivity**

(Poster No. 123)

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Vasitis nodosa is a benign proliferation of the vas deferens epithelium, usually secondary to trauma or obstruction. This is commonly seen in the setting of prior vasectomy, occurring in approximately 50%–60% of patients presenting for vasovasostomy. Vasitis nodosa can have a variety of histologic characteristics that may be concerning for metastatic carcinoma, including infiltrative growth with perineural and vascular invasion and cytologic atypia with prominent nuclei. We present a case of a 37-year-old man with prior vasectomy who underwent vasovasostomy. Histologic examination of the discarded vas segments revealed a proliferation of infiltrative
ductules with and without sperm. The cells had enlarged nuclei and prominent nucleoli (Figure 1.123, A). Extensive perineural invasion was noted (Figure 1.123, B). The ductules demonstrated PAX-8 and AMACR positivity with loss of basilar p63. Ductules were negative for PSA and CDX-2. Interestingly, the tubules showed cytoplasmic and membranous staining for CA19-9 (Figure 1.123, C), which has not previously been described. CA19-9 was negative in the normal vas epithelium (Figure 1.123, D). CA19-9 is typically used as a marker for pancreatobiliary and gastrointestinal cancers. Levels may also be elevated in the urine of patients with urothelial carcinoma, benign ureteropelvic junction obstruction, or autosomal-dominant polycystic kidney disease. We hypothesize that CA19-9 levels may be elevated in some patients postvasectomy, which may explain the positive staining within the vasitis nodosa. CA19-9 staining of vasitis nodosa is a potential pitfall in rare cases of pancreatobiliary and gastrointestinal metastases to the male genitourinary tract.

A Rare Case of Clear Cell Renal Cell Carcinoma With Necrotizing Granulomatous Inflammation (Poster No. 124)

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A granulomatous reaction is a form of chronic inflammation composed of T lymphocytes and macrophages with or without necrosis. Clear cell renal cell carcinoma (RCC) associated with granulomatous reaction is a rare pathologic finding with only a few cases published in the literature. Among these few cases, the majority showed non-necrotizing granulomatous reaction and only few showed granulomatous reaction with small foci of coagulative necrosis. We present a case of clear cell RCC with multiple intratumoral necrotizing granulomas. A 43-year-old man with no known history of tuberculosis or sarcoidosis was noted to have suprapubic pain and nocturnal incontinence. The patient had a computed tomography scan of the abdomen and pelvis with intravenous contrast that showed a 4-cm hypervascular, enhancing, intrarenal mass. The patient underwent a biopsy of the right renal mass, which was consistent with clear cell RCC. A right partial nephrectomy was performed. Microscopic examination showed classic clear cell RCC with multiple necrotizing granulomas (Figure 1.124). AFB and GMS stains were negative. The patient has been followed up in our hospital for the last 5 years with no evidence of metastasis or recurrence. Studies suggest that granulomatous reaction is caused by a T-cell–mediated reaction against tumor antigens that may be secondary to antigen shedding or an immune reaction against the tumor. Necrotizing granulomas in clear cell RCC are a rare finding that pathologists should be aware of after excluding bacterial or fungal infections.

Renal Mucormycosis—A Rare, Life-Threatening Infection in a Renal Transplant Patient With Concurrent Marijuana Use (Poster No. 125)

Kayla Hoerschgen, MD (kayla.hoerschgen@usd.edu); Ashwyna Sunassee, MD. Department of Pathology, University of South Dakota Sanford School of Medicine, Sioux Falls.

Mucormycosis is a serious fungal infection that typically affects immunocompromised patients. We present a case of disseminated mucormycosis infection in a 34-year-old man with a history of marijuana use and focal segmental glomerulosclerosis who underwent living unrelated kidney transplant. After his transplant, he developed recurrent focal segmental glomerulosclerosis. Two months later, he developed pleuritic chest pain, and imaging revealed a ground glass opacity with a surrounding dense consolidation within the right upper lobe, concerning for an angioinvasive fungal infection. During the hospitalization, his creatinine increased, and a biopsy of the allograft kidney demonstrated acute tubulointerstitial nephritis, acute vasculitis, and glomerular intracapillary fibrin thrombi with angioinvasive Mucorales fungal infection. The patient subsequently underwent transplant nephrectomy. Grossly, the allograft was pale white to dusky tan-red with poorly delineated cortical medullary junctions. Microscopic examination revealed necrotic tubules with a dense neutrophilic infiltrate, multinucleated giant cells (Figure 1.125, A and B), and ribbonlike, aseptate hyphae (Figure 1.125, C). Gomori methenamine silver stain highlighted the fungal elements (Figure 1.125, D), which are morphologically consistent with Mucorales. Review of the literature revealed that the infectious rate posttransplant is approximately 2%–14%, with disseminated disease having a mortality rate of 76%. However, the literature does not show a consistency in presenting symptoms and few case reports have been published demonstrating marijuana use as a cause of pulmonary mucormycosis or even disseminated disease. The purpose of our case report is to add knowledge to the presenting symptoms and investigate the association of marijuana use with pulmonary and disseminated mucormycosis.
Primary Adenocarcinoma of the Urinary Bladder: A Rare Malignancy and Diagnostic Dilemma
(Poster No. 126)

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Adenocarcinoma of the urinary bladder is a rare neoplasm, representing <2% of urinary bladder malignancies. A 59-year-old African American hypertensive male presented with painless hematuria and symptomatic anemia. A computed tomography scan revealed a markedly enlarged prostate gland, associated with a bladder mass, causing significant bilateral hydronephrosis. Transurethral resection of the bladder tumor revealed invasive adenocarcinoma with signet ring cells. Transurethral resection of the prostate showed prostatic adenocarcinoma with direct invasion of the prostatic stroma by invasive adenocarcinoma arising in the bladder. Immunostain performed on the bladder revealed positive CK20 (cytoplasmic), CDX2 (nuclear), villin (cytoplasmic), and β-catenin (cytoplasmic) and negative CK7, GATA3, PSA, PSAP, and NKX3.1. No histologic features of conventional high-grade urothelial carcinoma and lack of expression of GATA3 and CK7 rule against high-grade urothelial carcinoma with divergent differentiation. These aggregate findings support the diagnosis of primary adenocarcinoma of the urinary bladder. Lack of PSA, PSAP, and NKX3.1 expression rules against prostatic origin. Cytoplastic β-catenin does not favor colorectal origin. Radial cystoprostatectomy revealed a ulcerated mass measuring 7.0 × 5.5 × 2.5 cm involving the base of the bladder directly extending into the base of the prostate and diffusely infiltrating the prostatic stroma. There was diffuse thickening of the bladder wall with sparing of the dome. Histologic findings in the radical prostatectomy were similar to the features as described above. This rare tumor can be a diagnostic dilemma with adenocarcinomas in adjacent organs; therefore, clinical information, imaging, histology, and immunohistochemical correlation is essential to render a correct diagnosis.

Squamous Cell Histology of Tumors of Upper Urinary Tract: A Clinicopathologic Study of Pure Squamous Cell Carcinoma and Extensive Squamous Differentiation of Urothelial Carcinoma
(Poster No. 127)

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Context: Squamous cell histology in tumors of the upper urinary tract is rare. Pure squamous cell carcinomas of the upper urinary tract are even rarer, and most of the knowledge about these tumors is derived from isolated case reports.

Design: We searched pathology databases in 2 institutions for pure squamous cell carcinomas and extensive (>50%) squamous differentiation in urothelial carcinomas and found 6 cases of pure squamous cell carcinoma and 4 cases of extensive squamous differentiation in urothelial carcinomas. The clinicopathologic details of these cases were studied.

Results: The patients’ mean age at diagnosis was 67 years (range, 33–93 years); 5 were women, and 5 were men. Patients usually presented with renal mass (n = 5) and hydronephrosis (n = 5). The mean tumor size was 4.9 cm (range, 1.5–10.0 cm). Of the 6 pure squamous cell carcinomas, 5 occurred in the renal pelvis and 1 in the ureter. Of the 4 cases of extensive squamous differentiation, 2 were in the renal pelvis, 1 in the upper pole, and 1 in the midureter. Lymph node metastases were not found in any of the cases with submitted lymph nodes. One patient had a tumor recurrence after a few months and died. One patient developed a high-grade urothelial carcinoma of the bladder 1 year later.

Conclusions: Tumors with squamous cell histology usually present at higher stage and older ages with an equal incidence in both sexes. In our limited study, most patients responded well to treatment and, barring 1 patient, survived.

A Case of AL Amyloidosis Confirmed by Liquid Chromatography Tandem Mass Spectrometry With Negative Immunofluorescence Finding
(Poster No. 128)

Yuan Huang, MD, PhD (huang2y@ucmail.uc.edu); Diping Wang, MD, PhD. Department of Pathology, University of Cincinnati Medical Center, Cincinnati, Ohio.

Immunofluorescence microscopy of kidney biopsy specimens is one of the primary tools in the diagnosis of AL amyloidosis. However, cases of AL amyloidosis with negative immunofluorescence staining for κ and λ light chains are not uncommon. We present a case of amyloidosis with negative immunofluorescence finding from a 69-year-old white man. He presented with stage 3 chronic kidney disease with nephrotic range proteinuria, previously diagnosed with monoclonal gammopathy of undetermined significance. Both serum and urine protein electrophoresis showed IgG λ monoclonal gammopathy. His bone marrow biopsy showed approximately 8% λ-restricted plasma cells. Kidney biopsy revealed mesangial expansion by amorphous acidoophilic material that stained weakly for PAS, negative for Jones silver, and positive for Congo red. In addition, the amyloid deposits involved the renal interstitium, many arterioles, and small interlobular arteries. Immunofluorescence staining by the standard method in our laboratory showed negative results for IgG, IgM, C3, and C1q, with IgA, κ, and λ highlighting tubular casts without light-chain restriction (Figure 1.128, A and B). Electron microscopy showed characteristic nonbranching, randomly oriented fibrils measuring 9–11 nm in thickness. The result of liquid chromatography tandem mass spectrometry performed at Mayo Clinic on microdissected areas of the paraffin-embedded tissue was consistent with AL-type amyloid deposition. AL amyloidosis is usually associated with systemic disease due to an underlying clonal plasma cell proliferation/β-cell lymphoma. It is crucial to differentiate AL amyloidosis from other types because of its distinct management. Liquid chromatography tandem mass spectrometry is proven to be helpful in this differentiation, especially in immunofluorescence-negative AL amyloidosis cases.

Distinguishing Benign and Malignant Oncocytic Tumors Using Deep Learning Algorithm
(Poster No. 129)

Andrei Kapustin, BS1; Karen Fang, MD2; Maria Tretiakova, MD, PhD1 (mariast@uw.edu).1Graduate School of Arts and Science, New York University, New York, New York; 2Department of Laboratory Medicine and Pathology, University of Washington, Seattle.

Context: Convolutional neuronal networks are a powerful deep learning (DL) tool increasingly utilized in tumor subtyping. Differentiating oncocytoma (ONC) and malignant counterpart chromophobe renal cell carcinoma (ChRCC) remains one of the most challenging areas in uropathology because of overlapping morphology. We aimed to create a DL classifier for accurate differentiation of benign ONC from ChRCC.

Design: Eighty ONC and 175 CHRCC tumors (60% classic and 40% eosinophilic) including historic cases with immunohistochemical and molecular confirmation of diagnoses, diagnostic cases from 2010 to 2020, and ChRCC cases from the Genome Atlas Data Portal were used. Cases were randomly assigned to either training (69%), validation (15%), or test set (16%). A total of 9263 digital images captured at ×20 magnification or selected from ×20 whole scanned images were split into 4 equal parts, resized to 320 × 180, and used for training several DL models. The best results were achieved with a custom ResNet-like model and further optimized.

Results: The best DL model achieved accuracy of 0.96, precision of 0.96, recall of 0.98, and AUC of 0.99 at a probability threshold of 0.6 (Figure 1.129). We then evaluated the model on a final held-out testing...
cohort with 90.4% accuracy for predicting benign ONC and 92% malignant ChRCC. Additionally, we tested the model on previously unseen cohort of hybrid tumors from Birt-Hogg-Dube patients or sporadic cases (n = 38, 477 images). Hybrid tumors were classified as benign in 92.7% of cases.

Conclusions: Our DL algorithm allowed accurate distinction between ONC and ChRCC, warranting further analysis of differentiating histopathologic features for diagnostic purposes. Novel finding of hybrid tumors classified as overwhelmingly benign by DL model supports their indolent behavior.

An International Validation Study of Automated Cancer Detection in Prostate Biopsies
(Poster No. 130)

Yuri Tolkach, MD;1 (yuri.tolkach@gmail.com); Vlado Ovtcharov;2 Alexey Pryalukhin, MD;3 Wolfgang Hulla, MD; Marie-Lisa Eich, MD; Peter Caie, PhD;2 Eric Runde, MSME;1 Reinhard Büttner, MD.1
1Department of Pathology, University Hospital Cologne, Germany; 2Department of Pathology, University Hospital Cologne, Germany; 3Indica Labs, Albuquerque, New Mexico.

Context: Digital pathology provides an opportunity for computational analysis of histologic slides and the standardized automation of some pathologic tasks. The reporting of prostate cases is time-consuming because of the large number of slides per case. In this retrospective study, we validate a deep learning–based tool for prostate cancer detection from patient biopsy samples.

Design: A prostate cancer deep learning–based detection tool was previously developed and implemented in HALO AI and HALO AP software (Indica Labs, Albuquerque, New Mexico). Two external validation cohorts of patients with multifocal prostate biopsy were analyzed from 2 high-volume pathologic institutes: cohort 1/dataset 1 (Cologne, n full cases = 57) digitized by Hamamatsu S360 scanner; cohort 2 (Wiener Neustadt, n full cases = 57) digitized by Hamamatsu S360 scanner (dataset 2) and Leica GT450 scanner (dataset 3).

<table>
<thead>
<tr>
<th>Metrics of Prostate Cancer Detection Accuracy in Patient Biopsy Samples</th>
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<tbody>
<tr>
<td>Dataset (No. Tumor Cores/ No. Cores)</td>
</tr>
<tr>
<td>--------------------------------------</td>
</tr>
<tr>
<td>Dataset 1 (320/1220)</td>
</tr>
<tr>
<td>Dataset 2 (176/693)</td>
</tr>
<tr>
<td>Dataset 3 (173/667)</td>
</tr>
<tr>
<td>Pooled (669/2580)</td>
</tr>
</tbody>
</table>

Results: Similar high-accuracy metrics were received for all 3 datasets, implying good generalization among cases from different institutes and digitized by different scanner systems (Table, without any forms of normalization). Several cores were detected where tumor was missed by pathologists (cohort 1: n = 7; cohort 2: n = 5). The average analysis time was 1 min/core in cohort 1, and 2 min/core for cohort 2.

Conclusions: The prostate cancer detection tool reported high accuracy for prostate cancer detection in biopsy cases during external validation independent of the institute or scanner used. It is fully integrated into Indica Labs' digital pathology platform and can assist pathologists in the form of prescreening or quality control during analysis of prostate biopsy cases.

De Novo Collecting Duct Carcinoma in a Transplant Kidney With Distant Metastasis
(Poster No. 131)

Mohamed A. Yakoub, MD (mohamed.a.yakoub@gmail.com); Ding Wang, MD, PhD. Department of Pathology, University of Cincinnati Medical Center, Cincinnati, Ohio.

Collecting duct carcinoma (CDC) is a rare type of renal cell carcinoma with aggressive behavior. De novo renal cell carcinomas in transplanted kidneys have been reported sporadically with incidence of about 0.5%, but reports of CDC in renal allograft are extremely rare. Cases presetting with distant metastasis have not been described before. We report a case of a 37-year-old woman with history of end-stage renal disease status post kidney-pancreas transplant and longtime BKV nephropathy. She presented 5 years later with an anterior abdominal mass. Biopsy showed metastatic undifferentiated high-grade carcinoma composed of highly pleomorphic cells, frequent mitoses (Figure 1.131, A), and positivity for CK7, P53, and PAX8. Suspicion for renal origin was raised. Subsequent imaging revealed a mass in the kidney transplant and retroperitoneal, pelvic, and mesenteric lymphadenopathy. The kidney mass biopsy confirmed the diagnosis of poorly differentiated CDC, showing tubular architecture, brisk mitoses, apoptosis, prominent nuclear atypia, and mixed inflammatory infiltrate (Figure 1.131, B and C). Comparative review with the prior abdominal biopsy showed identical features, confirming metastatic CDC. Tumor cells showed focal GATA-3 and CK7 positivity. SV40, a marker frequently used for BKV infection, showed positive nuclear staining (Figure 1.131, D), however, BKV RNA in situ hybridization was negative. Expression of BKV antigen was identified in tumor cells with no evidence of BKV RNA, raising a possible connection between CDC tumorigenesis and history of longtime BKV infection.

Heavy Metals in Prostate Tissue and Time to Biochemical Recurrence After Radical Prostatectomy
(Poster No. 132)

Virgilia Macias, MD1 (vmacias@uic.edu); Andrey G. Sarafanov, PhD; Todor I. Todorov, PhD; José A. Centeno, MD; Marion A. Gray, PhD; Ujilla Sheikh, MD, MSc; Batool H. Huzafa, MD; André Kajdacsy-Balla, MD, PhD;1 3Department of Pathology, University of Illinois at Chicago; 2Department of Biophysical Toxicology, Environmental and Infectious Disease Sciences, Armed Forces Institute of Pathology, Washington, DC; 3Office of Regulatory Science, Center for Food Safety and Applied Nutrition, Food and Drug Administration, College Park,
Our previous publication showed that low concentrations of iron and zinc in normal prostate tissue adjacent to tumor were associated with biochemical recurrence after prostatectomy.

**Context:** We are now presenting information on time to recurrence comparing patients in the lowest and the highest quartiles of iron and zinc concentrations using the same prostatectomy samples. The metal levels were obtained by inductively coupled plasma mass spectrometry from formalin-fixed, paraffin-embedded normal-appearing areas of prostate tissue adjacent to prostate cancer. Measurements were analyzed by log-rank test of time to recurrence, and Kaplan-Meier curves of the 20 cases of lowest quartile of metal ion concentration with those in the highest quartile.

**Results:** There was a trend but no statistical significance for faster time to recurrence in subjects with lower iron or zinc levels.

**Conclusions:** In contrast to prognosis for recurrence, time to recurrence is not influenced by low iron or zinc levels. The small number of subjects in our present study may not be sufficient for a definitive conclusion.

**Malignant Solitary Fibrous Tumor in a Kidney of a 67-Year-Old Woman**

(Poster No. 133)

Kaia M. Erickson, MD (kmerickson11122@gmail.com); Ashwyna Sunassee, MD; Ryan Askeland, MD. Department of Pathology, Sanford USD Medical Center, Sioux Falls, South Dakota.

Solitary fibrous tumor (SFT) is a mesenchymal fibroblastic neoplasm with prominent staghorn branching vessels, a “patternless” pattern, and characteristic immunostaining pattern of CD34, BCL-2, and STAT-6 positivity. It is typically benign unless there is necrosis, size greater than 10 cm, and increased mitoses. We present a case of malignant solitary fibrous tumor in a 67-year-old woman who initially presented with a 20-pound weight loss during several months, night sweats, and abdominal pain. Computed tomography (CT) of the abdomen showed a large heterogeneously enhancing right renal mass. She underwent a nephrectomy, revealing a 25.0 × 17.3 × 13.3-cm kidney entirely effaced by a tan-pink homogeneous mass with focal areas of necrosis. Microscopic examination revealed a spindle cell tumor with staghorn vasculature (Figure 1.133, A), necrosis (Figure 1.133, B), and up to 4 mitotic figures per 10 high-power fields. Immunohistochemical stains performed revealed the neoplastic cells were positive for STAT6 (Figure 1.133, C) and CD34 (Figure 1.133, D) and focally positive for BCL-2. The presence of necrosis, increased mitoses, and large tumor size are features described in solitary fibrous tumors that exhibit malignant behavior. This is an unusual case because solitary fibrous tumors make up only about 2% of soft tissue tumors. Among those, there have only been fewer than 100 cases reported in the kidney, with even fewer demonstrating histologic features suggestive of malignant behavior.
Correlation Between Sonographically Measured Endometrial Thickness and Histopathological Findings in Premenopausal and Postmenopausal Women With Abnormal Uterine Bleeding (Poster No. 1)

Jwan A. Alallaf, MD1 (Jwan.al-allaf@tmcm.org); Ethar Al-Husseinawi, MD; Kamani M. Lankachandra, MD; Evanthia Omoscharka, MD. 1Department of Pathology, University of Missouri, Kansas City; 2Department of Pathology, University of Kansas, Kansas City.

Context: Abnormal uterine bleeding (AUB) can be due to a wide spectrum of gynecologic and nongynecologic causes. The differential diagnosis includes benign and malignant causes. This study aims to analyze correlation of endometrial biopsy (EMB) and Papanicolaou smear results with ultrasound-measured endometrial thickness (ET) in women with AUB.

Design: A retrospective chart review was conducted on patients who presented to our institution from July 1, 2019, to July 1, 2020, for EMB. Patients with history of AUB and ET on ultrasonography were included. Two groups were identified: premenopausal and postmenopausal. Age, parity, body mass index (BMI), and use of hormonal therapy were recorded. The result of EMB was divided into normal (secretory, proliferative phase, and atrophic endometrium), abnormal (endometrial polyps, endometrial hyperplasia, endometrial cancer, and endometritis), and others (insufficient for diagnosis).

Results: A total of 59 patients were included: premenopausal women (47%) and postmenopausal women (52%). Normal EMB was found in 42%, and 47% of the patients had abnormal EMB. Endometrial polyps represented most abnormal findings (35.9%) especially in premenopausal patients, and atrophy represented most normal findings (27.7%), specifically in postmenopausal patients. Endometrial hyperplasia without atypia (5.1%), and endometrial cancer (3.1%) only presented in the postmenopausal group. BMI was high in all patients with endometrial cancer. Pap smear was normal in 73% of patients, and benign endometrial glands were identified in 8.4% of patients (Table).

Conclusions: Increased ET associated with AUB is mostly due to benign lesions of the uterus. EMB is the gold standard method for diagnosis of endometrial pathology. Radiologic and pathologic correlation is recommended for better patient outcome.

Demographic Distribution of Patients Included in the Study

<table>
<thead>
<tr>
<th>Characteristic (mean ± SD)</th>
<th>Pre menopause</th>
<th>Post menopause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y (54.78 ± 15.99)</td>
<td>28 (47%)</td>
<td>31 (52%)</td>
</tr>
<tr>
<td>Parity null 8 (13%)</td>
<td>49 (82%)</td>
<td>53 (88%)</td>
</tr>
<tr>
<td>Gravid parity (&gt;5)</td>
<td>3 (5%)</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>BMI (33.76 ± 11.88)</td>
<td>28 (47%)</td>
<td>31 (52%)</td>
</tr>
<tr>
<td>Pre menopause</td>
<td>28 (47%)</td>
<td></td>
</tr>
<tr>
<td>Post menopause</td>
<td>31 (52%)</td>
<td></td>
</tr>
<tr>
<td>Hormonal therapy</td>
<td>16 (27%)</td>
<td></td>
</tr>
</tbody>
</table>

Evaluation of Immunotherapeutic Vulnerability Indicators Indoleamine-2,3-Dioxygenase, Programmed Death-Ligand 1, and Mismatch Repair Protein Expression in Uterine Carcinosarcomas (Poster No. 2)

Joseph D. Coppock, MD, PhD (jdc5xc@virginia.edu); Taylor M. Jenkins, MD; Annie M. Mills, MD. Department of Pathology, University of Virginia, Charlottesville.

Context: Uterine carcinosarcomas are biphasic epithelial and mesenchymal malignancies. Therapy includes surgery +/- chemotherapy and/or radiation. High rates of recurrence and metastasis necessitate improved nonsurgical approaches. Indoleamine-2,3-dioxygenase (IDO) catalyzes the rate-limiting step in tryptophan metabolism. IDO can be upregulated by cancer cells, depleting microenvironment tryptophan, inhibiting regulatory T-lymphocyte activation/expansion, and impairing cytotoxic T-cell response. Inhibitors are under investigation for various cancers; however, expression is not well studied in carcinosarcoma, particularly with attention to PD-L1 and mismatch repair (MMR) status.

Design: Whole sections of formalin-fixed, paraffin-embedded tissue from 42 uterine carcinosarcomas with available MMR protein, PD-L1, and p53 expression status were evaluated. Hematoxylin-eosin diagnosis was confirmed. IDO expression was determined by immunohistochemistry (1:2000, HPA-023072, Sigma Prestige). At least 1% IDO tumoral staining was considered positive.

Results: Two cases were reclassified as dedifferentiated carcinoma, based on lack of mesenchymal differentiation. Seventy-five percent (30/40) of confirmed carcinosarcomas (Figure 2.2, A) demonstrated ≥1% IDO expression (Figure 2.2, B), including a single MMR-deficient carcinosarcoma. Only 4 cases showed >30% expression. Expression was most prominent within well-differentiated epithelial components. Seventy percent (21/30) of IDO-positive cases also expressed PD-L1 (CPS >1) (Figure 2.2, C), while 87% (26/30) demonstrated abnormal p53 expression. Both tumors reclassified as dedifferentiated carcinoma were IDO-positive (3% and 30%), PD-L1-positive, and MMR-deficient.

Conclusions: Most uterine carcinosarcomas express IDO, suggesting immunotherapy targeting IDO may have promise in this difficult-to-treat tumor type, potentially in combination with PD-1/PD-L1 axis inhibitors. Of note, dedifferentiated carcinomas may be misclassified as carcinosarcoma and appear particularly enriched for IDO expression, but also for other indicators of immunotherapeutic vulnerability including PD-L1 expression and MMR deficiency.

Limited Application of Silva System in Biopsies to Predict Clinical Behavior for Usual Type Endocervical Adenocarcinoma (Poster No. 3)

Yun Wang, MD1; Yafei Qi, MD; Rui Bi, MD, PhD; Ming Li, MD, PhD; Jinhang Li, MD; Ruby Chang, MD1 (rubyjchang@hotmail.com); Wenzhen Zheng, MD1. 1Department of Pathology, The First Medical Center of Chinese PLA General Hospital, Beijing, China; 2Department of Pathology, Sheng Jing Hospital of China Medical University, Shenyang, China; 3Department of Pathology, Fudan University Shanghai Cancer Center, Shanghai, China; 4Department of Pathology, UT Southwestern Medical Center, Dallas, Texas.

Context: Silva pattern–based system (PBS) for usual-type endocervical adenocarcinoma (uEAC) relies on pattern of invasion (POI) and lymphovascular invasion and offers valuable information as to risk of nodal metastasis and therapeutic options after surgery. Ideally, the most valuable time in applying PBS should be in the preresection specimen—the cervical biopsy, which can be used to guide surgeons in selecting optimal surgical procedures. We investigated the role of PBS in cervical biopsies by focusing on biopsy tumor size in relation to POI assessment in a multi-institutional study.

Design: A total of 397 paired biopsy resections of uEACs were included. POI as well as tumor size was evaluated. Standard statistical analyses were performed.

Abstracts
Ectopic Pregnancy Occurring in a Cesarean Section Scar

Saman S. Karimi, MD, MS (skarim27@uic.edu); Grace Guzman, MD. Department of Pathology, University of Illinois at Chicago.

In the United States, ectopic pregnancy (EP) accounts for 2% of all pregnancies and 3%–6% of pregnancy-related mortality. EP can occur in the ampulla of the fallopian tube (most commonly), myometrium, cervix, ovaries, and abdomen, among others. We present a case of a 32-year-old woman (gravida 7, para 2, 1,3-3) at 7 weeks and 3 days' gestational age with history of 3 cesarean-section deliveries. Ultrasound imaging demonstrated an antverted uterus with a gestational sac in the anterior portion of the uterine isthmus and a thin layer of myometrium between the gestational sac and the urinary bladder. After an unsuccessful attempt of moshetorexate injection of the gestational sac to induce abortion, the patient elected to have a gravid hysterectomy, unsuccessful attempt of methotrexate injection of the gestational sac. The specimen was sent to pathology for histopathologic evaluation.

### Identification of Pattern of Invasion Is Directly Related to the Biopsied Tumor Size

<table>
<thead>
<tr>
<th>Biopsy Tumor Size, cm</th>
<th>N</th>
<th>Identified Pattern of Invasion at Biopsy</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cases</td>
<td>397</td>
<td>144</td>
<td>36.27</td>
</tr>
<tr>
<td>&lt;=0.2</td>
<td>35</td>
<td>2</td>
<td>5.71</td>
</tr>
<tr>
<td>0.2–0.4</td>
<td>99</td>
<td>18</td>
<td>18.18</td>
</tr>
<tr>
<td>0.4–0.6</td>
<td>114</td>
<td>34</td>
<td>29.82</td>
</tr>
<tr>
<td>0.6–0.8</td>
<td>80</td>
<td>35</td>
<td>43.75</td>
</tr>
<tr>
<td>&gt;0.8</td>
<td>69</td>
<td>55</td>
<td>79.71</td>
</tr>
</tbody>
</table>

### Results:

POI was evaluable in 253 (64%) and assessable in 144 (36%) biopsy specimens. Tumor size on biopsy ranged from 0.1 to 2 cm (average, 0.6 cm). Most biopsy tumor sizes were 0.8 cm or less (83%).

### Conclusions:

Although Silva PBS offers valuable prognostic information with regard to risk of nodal metastasis, its applicability for triaging patients into low nodal metastasis group, before surgical resection and on cervical biopsies, is limited. This is likely secondary to small sample size limiting accurate POI assessment.

### Ectopic Pregnancy Occurring in a Cesarean Section Scar

**Poster No. 4**

**Saman S. Karimi, MD, MS (skarim27@uic.edu); Grace Guzman, MD. Department of Pathology, University of Illinois at Chicago.**

In the United States, ectopic pregnancy (EP) accounts for 2% of all pregnancies and 3%–6% of pregnancy-related mortality. EP can occur in the ampulla of the fallopian tube (most commonly), myometrium, cervix, ovaries, and abdomen, among others. We present a case of a 32-year-old woman (gravida 7, para 2, 1,3-3) at 7 weeks and 3 days’ gestational age with history of 3 cesarean-section deliveries. Ultrasound imaging demonstrated an antverted uterus with a gestational sac in the anterior portion of the uterine isthmus and a thin layer of myometrium between the gestational sac and the urinary bladder. After an unsuccessful attempt of methotrexate injection of the gestational sac to induce abortion, the patient elected to have a gravid hysterectomy, an unsuccessful attempt of methotrexate injection of the gestational sac. The specimen was sent to pathology for histopathologic evaluation.

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### A Subset of Vulvovaginal Fibroepithelial Polyps With Stromal Atypia Shows Deficiency of Retinoblastoma by Immunohistochemistry

**Poster No. 5**

**Salam Ashour, MBBS (ashours@ccf.org); Daniel Roberts, MD; Jesse McKenney, MD; Amy Joehlin-Price, MD. Department of Pathology, Cleveland Clinic Foundation, Cleveland, Ohio.**

**Context:** Vulvovaginal fibroepithelial polyps (FEPs) occasionally demonstrate stromal atypia resembling that seen in pleomorphic lipomas (PLs) and cellular angiofibromas (CAF s) with atypia. PLs and CAFs are often diagnosed by retinoblastoma (Rb) immunohistochemistry as reported as fairly sensitive and specific. Because of the morphologic overlap, we investigated whether FEPs with stromal atypia could be Rb-deficient.

**Design:** Departmental FEPs were reviewed for stromal atypia. Monoclonal anti-Rb immunohistochemistry (IHC) (clone G3-245, BD Biosciences) was performed. Nuclear Rb expression was scored by 3 pathologists according to a prior publication. Cases were considered deficient if 2 of 3 pathologists scored the FEP as deficient. For the remaining cases, median or consensus scores were recorded.

### Results:

Twenty-eight patients with a median age of 51 years (range, 25–72) had FEPs with stromal atypia in the vagina (n = 13, 46%), vulva (n = 12, 43%), perineum (n = 2, 7%), and cervix (n = 1, 4%). Rb IHC identified 5 cases (18%) with consensus Rb deficiency. The remaining 23 cases showed consensus or median scores of 1+ (n = 9, 32%), 2+ (n = 3, 11%), 3+ (n = 5, 18%), or 4+ (n = 6, 21%) (Table).

### Conclusions:

FEPs with stromal atypia may show Rb deficiency, suggesting that Rb loss needs to be interpreted in the context of clinicopathologic findings and is not entirely specific to the PL/CAF family of tumors.

### Scoring of Rb IHC in 28 FEPs

<table>
<thead>
<tr>
<th>Rb Score</th>
<th>Definition</th>
<th>Cases (n = 28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deficient</td>
<td>&lt;10% of cells showed nuclear staining</td>
<td>5 (18%)</td>
</tr>
<tr>
<td>1+</td>
<td>10% to 25% nuclear staining</td>
<td>9 (32%)</td>
</tr>
<tr>
<td>2+</td>
<td>&gt;25% to 50% nuclear staining</td>
<td>3 (11%)</td>
</tr>
<tr>
<td>3+</td>
<td>&gt;50% to 75% nuclear staining</td>
<td>5 (18%)</td>
</tr>
<tr>
<td>4+</td>
<td>&gt;75% nuclear staining</td>
<td>6 (21%)</td>
</tr>
</tbody>
</table>

Abbreviations: FEPs, fibroepithelial polyps; IHC, immunohistochemistry; Rb, retinoblastoma.

### Endocrine Cell Micronests in an Ovarian Mucinous Borderline Tumor: A Potential Diagnostic Pitfall for Microinvasion

**Poster No. 6**

**Katrina Collins, MD (katcoll@iu.edu); Sheila Segura, MD; Michael Hwang, MD. Department of Pathology, Indiana University, Indianapolis.**

The occurrence of endocrine cell micronests in ovarian tumors is rare. To our knowledge, there are only 3 prior cases reported to date, 2 occurring in an ovarian mucinous cystadenoma and 1 in an ovarian mucinous borderline tumor. This is a case of a 27-year-old woman who presented with a 1-month history of abdominal pain and fullness. Imaging studies revealed a large multiloculated cystic and solid mass measuring 23.9 cm, occupying most of the pelvis and abdomen, concerning for a primary ovarian malignancy. The patient underwent a right salpingo-oophorectomy with appendectomy. Histologic sections from the ovary showed a multiloculated, cystic, and focally solid mass lined by gastrointestinal-type mucinous epithelium with variable degrees of proliferation (Figure 2.6, A), accounting for greater than 10% of the epithelial volume. In addition to the mucinous epithelial component, there were several foci of bland, monotonous epithelioid cells in the context of epithelial degeneration or a true neoplasm is uncertain. Progression related to this neuroendocrine cell proliferation is...
unlikely and the recognition of this phenomenon holds more diagnostic value than prognostic significance, as it could be confused with microinvasion.

Histologically Pleomorphic Variant of High Grade Endometrial Stromal Sarcoma With Novel YWHAE Gene Amplification May Portend Poor Prognosis

(Poster No. 7)

Asad Ullah, MD (aullah@augusta.edu); Diana Kozman, MBCH; Samantha Mattox, DO; Pramila Moideen, MD; Tiffany Javadi, MD; Saleh G. Heneidi, MD; Natasha M. Savage, MD; Joseph White, DO.

Department of Pathology, Medical College of Georgia – Augusta University, Augusta.

High-grade endometrial stromal sarcomas (HG-ESS) can be subclassified on the basis of YWHAE or BCOR molecular findings, each with characteristic histologic features. In general, fusion-associated malignancies have a more uniform and less pleomorphic appearance. We report a case of HG-ESS without characteristic YWHAE or BCOR fusions, but instead with a novel YWHAE gene amplification. We conducted a thorough literature review looking for YWHAE amplifications or pleomorphic variants of HG-ESS. Additionally, The Cancer Gene Atlas (TCGA) and cBioPortal data were explored for YWHAE gene–associated uterine tumors in 259 patients. The HG-ESS with YWHAE gene–amplified tumor at our institution showed tongue-like destructive myometrial invasion with extreme nuclear pleomorphism and innumerable atypical mitoses. One of 259 cases from TCGA data was found to also have a YWHAE gene amplification, showing similar morphology, with extreme pleomorphism and was signed out as carcinosarcoma with heterologous elements. Review of the literature found a single case with a pleomorphic HG-ESS with negative fluorescence in situ hybridization but positive RT-PCR results, potentially making a third case of HG-ESS with YWHAE amplification. We describe a potential new subclass of HG-ESS, a pleomorphic variant with YWHAE gene amplification. YWHAE–amplified ESS appears to behave aggressively, most likely indicating a poorer prognosis. Given these findings, YWHAE gene–amplified tumor with pleomorphic morphology needs further exploration.

Epithelioid Trophoblastic Tumor: An Exceedingly Rare Entity and Diagnostic Challenge

(Poster No. 8)

Fahd Hussain, MD (fhussain@umc.edu); Ayush C. Srivastava, MD; William P. Daley, MD; Veena Shenoy, MD. Department of Pathology, University of Mississippi Medical Center, Jackson.

Epithelioid trophoblastic tumor (ETT) is a rare pathologic entity with very few cases reported in the English literature. We present a case of a 47-year-old woman diagnosed with ETT who presented with dyspnea and chest pain. On imaging, multiple lesions in the lungs, liver, and a large necrotic pelvic mass were identified. The patient underwent endometrium, lung, and liver biopsies followed by hysterectomy. The hysterectomy specimen revealed an ill-defined, fungating, necrotic hemorrhagic mass in the uterus (Figure 2.8, A). Microscopic examination revealed nests of uniform chorionic-type intermediate trophoblasts often surrounding a small blood vessel. Tumor cells showed round nuclei and focal cytoplasmic clearing in a background of extensive necrosis and eosinophilic hyaline material (Figure 2.8, B). Lung and liver biopsies showed histologic findings consistent with metastasis from endometrial primary. The tumor cells were positive for broad spectrum cytokeratin (Figure 2.8, C), inhibin (Figure 2.8, D), p63, CD10, and PLAP with a Ki-67 proliferative index of 30%–40%. ETT is a rare gestational trophoblastic tumor arising from chorionic-type intermediate trophoblasts. Patients usually are of reproductive age and present with vaginal bleeding. The most common primary site is the uterus, followed by the cervix. Poor prognostic factors include tumor extension beyond the uterus, age >40 years, interval from prior pregnancy of >2 years, and mitotic counts of >5/10 high-power fields. The differential diagnosis includes choriocarcinoma, placental site trophoblastic tumor, placental site nodule, and cervical squamous cell carcinoma. The patient received adjuvant chemotherapy; however, her disease progressed, and she died 24 months after her diagnosis.

Carcinosarcoma Arising in the Uterine Cervix

(Poster No. 9)

Jordan Steinberg, MD1 (jsteinberg3@northwell.edu); Sarah Werner, MD2; Hossein Hosseini, MD2; Doaa Morrar, MD3; Ryan Desjean, MD3.

Departments of 1Pathology and Laboratory Medicine and 2Obstetrics and Gynecology, Lenox Hill Hospital, New York, New York.

Carcinosarcoma, or malignant mixed Müllerian tumor (MMMT), is an uncommon diagnosis comprising 3%–4% of uterine malignancies. They contain both epithelial and stromal components. Typically, carcinosarcoma of the cervix results from local extension of a uterine primary rather than primary cervical tumor. There are fewer than 50 reported cases of cervical primaries. In one series of primary cervical
tumors, carcinosarcomas represented 5/1583 tumors or 0.003%. When the tumor is confined to the cervix, establishing the site of origin is academic. However, when the uterus is involved, immunohistochemistry should be used. Estrogen receptors and progesterone receptors stain strongly with endometrial primaries and are weakly positive in those from the cervix. Staining with monoclonal CEA favors a cervical origin. p16 is strong and diffuse with cervical tumors but patchy and weak in endometrial ones. We present a case of a 65-year-old woman who underwent a hysterectomy for a cervical mass. It measured 1.5 x 1.3 x 0.6 cm and was confined to the cervix. Histologically the epithelial component showed complex, disordered glands with cribriforming (Figure 2.9, A). The cells were pleomorphic, with hyperchromatic vesiculated nuclei, chromatin margination, and prominent nucleoli (Figure 2.9, B). The stromal component showed dark, spindled cells with areas of myxoid change. The epithelial component stained with pancytokeratin and vimentin (Figure 2.9, C). ER and PR were weakly positive, and monoclonal CEA was negative (Figure 2.9, D). These findings are consistent with a cervical primary. Our case represents 1 of only 50 cases of this entity. We submit this case study to expand on the limited data available for this entity.

**Papillary Thyroid Carcinoma Arising in Familial Struma Ovarii**

(Poster No. 10)

Dhuha Al-Sajee, MD, PhD1 (dhuha.al-sajee@medportal.ca); Ipshita Kak, FRCP; JEM Young, FRCP.1 Departments of 1Pathology and Molecular Medicine and 2Head and Neck Service, St Joseph’s Health Care, McMaster University, Hamilton, Ontario, Canada.

The occurrence of familial ovarian teratomas in twins, triplets, and successive generations in female patients raises a possibility of genetic correlation. When a mature teratoma is composed entirely or more than 50% of thyroid tissue, it is classified as struma ovarii. None of the reported familial ovarian teratomas to date showed a struma ovarii component. We present a case of an asymptomatic 68-year-old woman who was followed up with imaging for renal stones. CT showed an enlarged and complex left ovarian lesion. Pathologic examination revealed a mature cystic teratoma with a major component of thyroid tissue with a 0.4-cm follicular variant of papillary thyroid carcinoma. No further treatment was initiated. During follow-up, our patient volunteered that her sister, at 65 years old, also had thyroid tissue within an ovarian tumor. Review of the sister’s specimen revealed benign thyroid tissue in a left ovarian teratoma (struma ovarii). We are unaware of any known genetic links for struma ovarii and our patient had no offspring. Similar to many reports of teratoma and familial teratomas, no genetic studies offered for our cases. Although the follow-up period of 6 months in both cases was insignificant, familial teratomas occurring in children and younger women have a higher chance of recurrence, bilaterality, and secondary malignancies. We therefore recommended ovarian screening of the sister’s only daughter who is now 30 years old. We also recommend additional gross sampling of mature cystic teratoma, especially in familial cases, to exclude associated malignancies.

### Clear Cell Carcinoma and Borderline Mucinous Tumor of the Ovary: A Case Report of a Rare Mixed Epithelial Ovarian Tumor and Review of the Literature

(Poster No. 11)

Roselyne Choiniere, MD (roselyne.choiniere@usherbrooke.ca); Philippe Echelard, MD; Perrine Granger, MD. Department of Pathology, University of Sherbrooke, Québec, Canada.

Mixed epithelial ovarian tumors (MEOTs) are characterized by the coexistence of at least 2 distinct histologic subtypes in a single lesion. We present a case of MEOT and a review of the literature of all published cases of MEOT with mucinous and clear cell components. A 58-year-old, gravida 0, menopausal South American woman presented with lower abdominal pain and an ovarian mass with thick septations. Gross section showed a 1.5-cm yellow nodule protruding from one of the septations. It consisted of solid nests of clear cells with significant nuclear atypia and vesiculated nuclei, chromatin margination, and prominent nucleoli (Figure 2.9, B). The stromal component showed dark, spindled cells with areas of myxoid change. The epithelial component stained with pancytokeratin and vimentin (Figure 2.9, C). ER and PR were weakly positive, and monoclonal CEA was negative (Figure 2.9, D). These findings are consistent with a cervical primary. Our case represents 1 of only 50 cases of this entity. We submit this case study to expand on the limited data available for this entity.

### Reports of MEOTs Involving Clear Cell and Mucinous Tumors

<table>
<thead>
<tr>
<th>Source (y)</th>
<th>Age, y, Side, and Size</th>
<th>IHC in Mucinous Component</th>
<th>IHC in Clear Cell Component</th>
<th>Follow-up Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choiniere (2021)</td>
<td>58, left, 15 cm</td>
<td>AE1/AE3, WT1, p53 wild type, p16 heterogeneous, Napsin, ER, PR, P504S, MMR intact, PTEN intact</td>
<td>AE1/AE3, WT1, p53 wild type, p16 heterogeneous, Napsin, ER, PR, P504S, MMR intact, PTEN lost</td>
<td>10 mo, no recurrence or metastasis</td>
</tr>
<tr>
<td>Mackenzie (2015)</td>
<td>NR, NR, NR</td>
<td>WT1, p53 wild type, p16, HNF1B, TFF3, VIM, ARID1A, PR</td>
<td>WT1, p53 wild type, p16, HNF1B, TFF3, VIM, ARID1A, PR</td>
<td></td>
</tr>
<tr>
<td>Shang (2011)</td>
<td>57, left, 16 cm</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Allende (2010)</td>
<td>54, right, 20 cm</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Raj (2009)</td>
<td>48, left, 13 cm</td>
<td>Alcian blue, PAS-D, CK7, CK20, ER, PR</td>
<td>Alcian blue, PAS-D, CK7, CK20, ER, PR</td>
<td></td>
</tr>
<tr>
<td>Wani (2009)</td>
<td>59, left, 4.7 cm</td>
<td>ER, HNF1B, Laminin</td>
<td>ER, HNF1B, Laminin</td>
<td>11 mo, no recurrence or metastasis</td>
</tr>
<tr>
<td>Uddin (2007)</td>
<td>45, right, 9.5 cm</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Dutt (2000)</td>
<td>57, left, 24 cm</td>
<td>PAS and Alcian blue</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

Abbreviations: MMR, DNA mismatch repair (MLH1/PMS2/MSH2/MSH6); NR, not reported.

a Two cases in this study. Both cases showed the same IHC profiles. One case was initially diagnosed as mucinous tumor and Brenner tumor on morphology and was reclassified as mucinous tumor and CCC after IHC.
b McCluggage (2001) considered that the mucinous areas were mucinous metaplasia in an endometriotic cyst.
Primary Adenoid Cystic Carcinoma of Bartholin Gland: A Rare Malignant Tumor

(Poster No. 12)

Samreen Fathima, MBBS (samreen1608@gmail.com); Metin Punar, MD. Department of Pathology, Baylor University Medical Center, Dallas, Texas.

Primary carcinoma of Bartholin gland is a rare malignant tumor arising from the posterior half of the vulvar region. Adenoid cystic carcinoma (ACC) of Bartholin gland is a distinctive entity of vulvar malignancy, accounting for 10%–15% of Bartholin gland carcinomas. We report a case of a 46-year-old woman, with pain in the right vulvar region. Ultrasound imaging revealed a 1.4 × 0.6 × 0.6-cm, fluid-filled cyst. The patient was taken for marsupialization of the Bartholin gland cyst. Intraoperatively, a 3.0-cm firm, irregular mass in the area of right Bartholin gland was discovered and portions of it were biopsied. Microscopic examination showed multiple fragments of tissue with an epithelial proliferation with lobular architecture and infiltrative with a cribriform pattern with lymphohytic host response (Figure 2.12, A). Immunostaining showed cytokeratin 7 positivity in lobular areas, while its expression was lost in some of the nested areas (Figure 2.12, D). The smooth muscle actin (Figure 2.12, C), P63, and S100 were positive in the tumor. Ki-67 showed varying staining pattern (1%–2%) in well-preserved lobular areas and up to 20% focally in solid/cribriform areas with lymphocytic response. CD117 was positive (Figure 2.12, B). A diagnosis of adenoid cystic carcinoma (ACC) of Bartholin gland is a distinctive entity of vulvar malignancy, accounting for 10%–15% of Bartholin gland carcinomas. Only 1/15 patients had pelvic LNM. Six patients had recurrences post treatment (Table).

Conclusions: Silva pattern C was associated with higher stage at presentation and increased recurrences; however, pattern A and pattern B tumors were not exempt from extranodal metastasis and recurrences. Silva system, although reliable in predicting risk of nodal disease, is not a good predictor of extranodal disease and development of recurrences. Interestingly, only 1 patient with distant metastasis had nodal metastasis, suggesting nonlymphatic modes of spread (vascular, trans-tubal) are involved in metastases in these cases.

Correlation Between Silva Pattern of Stromal Invasion and Endocervical Adenocarcinoma With Extra-Nodal Metastasis and Recurrence

(Poster No. 13)

Hanna Siatecka, MD1 (siatecka@bcm.edu); Anthony B. Costales, MD2; Ramya P. Masand, MD.1 Departments of 1Pathology & Immunology and 2Division of Gynecologic Oncology, Dan L. Duncan Comprehensive Cancer Center, Baylor College of Medicine, Houston, Texas.

Context: Silva invasion pattern-based classification system of stromal invasion stratifies endocervical adenocarcinomas into 3 categories: pattern A (nondestructive invasion) not associated with lymph node metastasis (LNM), pattern B (limited destructive invasion) usually without LNM, and pattern C (diffuse destructive invasion) associated with LNM in 25% of cases. This system was developed to avoid unnecessary lymphadenectomy in low-risk patients, regardless of stage. In this study, we evaluated Silva pattern of invasion in endocervical adenocarcinomas with extranodal/distant metastasis.

Design: Patients with endocervical adenocarcinoma from 2010–2018 were retrospectively identified. Patients with extranodal/distant metastasis were included in the study. Data were collected from the electronic medical records and slides were reviewed.

Results: Forty-seven patients with a mean age of 49 years (range, 34–67 years) with endocervical adenocarcinoma were identified. Of the 15 patients with extranodal metastasis/recurrences, 14 were HPV related and 1 was non–HPV related. Silva system included pattern A (1), pattern B (4), and pattern C (10). Lymphovascular invasions were noted in 1 pattern B and 3 pattern C cases. Nine patients presented with metastatic disease. Only 1/15 patients had pelvic LNM. Six patients had recurrences post treatment (Table).

Conclusions: Silva pattern C was associated with higher stage at presentation and increased recurrences; however, pattern A and pattern B tumors were not exempt from extranodal metastasis and recurrences. Silva system, although reliable in predicting risk of nodal disease, is not a good predictor of extranodal disease and development of recurrences. Interestingly, only 1 patient with distant metastasis had nodal metastasis, suggesting nonlymphatic modes of spread (vascular, trans-tubal) are involved in metastases in these cases.

Clinical and Pathologic Features of Ovarian Anastomosing Hemangiomas (n = 12)

(Poster No. 14)

Austin McHenry, MD (austin.mchenry@yale.edu); Natalia Buza, MD. Department of Pathology, Yale University School of Medicine, New Haven, Connecticut.

Context: Anastomosing hemangioma (AH) is a recently described vascular neoplasm consisting of thin-walled, irregularly anastomosing vessels lined by endothelial cells with hobnail morphology and minimal atypia cuffed by pericytic supportive cells. While initially identified in the male genitourinary tract, AH has since been reported in multiple sites. Very few cases have been documented in the female genital tract. Of those reported, nearly all occur within the ovary, with the largest series to date including 6 patients.

Design: In this study, we identified 12 cases of AH of the ovary from our institutional archives between 2005 and 2020 (Table). All cases were...
unilateral, occurred at the ovarian hilum, and contained a vaguely lobulated architecture with sinusoidal-like vessels lined by hobnail epithelial cells with minimal to no cytologic atypia.

**Results:** A rim of luteinized cells with abundant, eosinophilic cytoplasm and round, centrally placed nuclei surrounding the hemangiomata was present in 9/12 cases, of which the volume of luteinized cells relative to the hemangiomata mass ranged from 2%–30%. Hilus cell hyperplasia, true with definable Reinke crystals was observed in 3 of these 9 cases, and all tumors with luteinized cells contained numerous eosinophilic, globular intracytoplasmic inclusions. Interestingly, the 3 cases without luteinized cells were exclusively intravascular lesions.

**Conclusions:** Awareness of this rare benign entity in the ovary is essential, as its association with stromal luteinization or hilar cell hyperplasia (often exuberant) may be misinterpreted as a steroid cell tumor, Leydig-cell tumor, or as a mixed stromal-vascular tumor.

### Chemoradiation-Induced Osseous Metaplasia in Endometrioid Adenocarcinoma

**(Poster No. 15)**

**Rosemary Mattaino, DO, MS** (rosemary.mattaino@uvmhealth.org); Agnes Balla, MD, MHS; Martin C. Chang, MD, PhD. Department of Pathology and Laboratory Medicine, The University of Vermont Medical Center, Burlington.

Osseous metaplasia within the endometrium is rare, with most reported cases citing incidental intrauterine bone seen in the setting of infertility or postpartum endometriosis. Proposed mechanisms include heterotopia, dystrophic/metastatic calcifications, ossification of postabortal endometriosis, metaplasia in healing tissue, and prolonged estrogenic therapy after abortion. We report a case of endometrial osseous metaplasia in a patient treated nonsurgically with chemoradiation for low-grade endometrial adenocarcinoma. A posttreatment biopsy was reviewed. A 55-year-old gravida 0, para 0 woman with a medical history of type 1 diabetes, hypertension, hyperlipidemia, and elevated body mass index (BMI) of 57 kg/m² presented to the emergency department with severe lower abdominal pain and vaginal bleeding. Pelvic magnetic resonance imaging revealed heterogenous masses in the endometrium, cervix, and left ovary. Histopathologic examination showed endometrial adenocarcinoma, endometrioid type, FIGO grade 1. She was clinically stage IIA, NO, M0. The patient was not a candidate for surgery and was referred for chemoradiation. She received concurrent external beam radiation with weekly carboplatin and paclitaxel. Posttreatment imaging showed stable disease. Two years after initial diagnosis a transvaginal ultrasonograph showed existing tumor in the uterus and bilateral ovarian masses. A dilation and curettage specimen showed persistence of endometrial adenocarcinoma, endometrioid type FIGO grade 1 with associated abundant osseous metaplasia without evidence of osteosarcoma (Figure 2.15). To our knowledge, this is the first case of benign osseous metaplasia arising in a low-grade endometrioid adenocarcinoma treated nonsurgically with chemoradiation and may provide further clues to the pathogenesis of this entity.
receptor, progestin receptor, and vimentin. This staining pattern supports the diagnosis, as the immunophenotypic features are identical to that of colonic epithelium. These lesions pose a diagnostic challenge, as they are identical to their intestinal counterpart with the possibility of malignant transformation. As this is an extremely rare lesion, very little is known about its pathogenesis and clinical progression; therefore, treatment guidelines have not yet been solidified and pose a challenge for clinicians. With the ability for malignant transformation, long-term follow-up of these patients is strongly advised.

**Cytology-Histology Correlation of Endocervical Adenocarcinoma In Situ From Papanicolaou Smear to Hysterec- tomy: A Series of 74 Cases**

(Poster No. 18)

Natalia Lashmanova, MD (natalia_m_lashmanova@rush.edu); Ankica Braun, MD; PaoloGattuso, MD; Lei Yan, MD, PhD. Department of Pathology, Rush University Medical Center, Chicago, Illinois.

**Context:** The incidence of adenocarcinoma of the cervix has increased during the past 3 decades. Endocervical adenocarcinoma in situ (AIS) is not always identified on cervical Papanicolaou (Pap) smear cytology. We retrospectively reviewed endocervical AIS cases diagnosed on Pap smears, cervical biopsy and/or endocervical curettage, loop electrosurgical excision procedure (LEEP), and hysterectomy specimens.

**Design:** Endocervical AIS cases diagnosed from August 2005 to January 2019 were retrieved from our institution’s databases and reviewed.

**Results:** A total of 74 patients with endocervical AIS were identified. The mean age at diagnosis was 39.9 years. About 66% of the AIS cases were not detected on screening Pap smears but were diagnosed during histologic examination of the surgical specimens. Only 10.8% of patients had a definitive diagnosis of AIS on Pap smears. Other abnormal glandular cytology included atypical glandular cells of undetermined significance (16.2%), atypical glandular cells favor neoplastic (5.4%), and suspicious for malignancy (1.3%). AIS was diagnosed in 31/42 cervical biopsies/curettages with 17 cases as incidental finding and 14 cases confirming previous abnormal glandular cytology (Table). Additionally, AIS was identified in 51/53 LEEP’s. About 41.5% of LEEP’s had a previous diagnosis of AIS and 54.7% of the cases were incidental finding and 14 cases confirming previous abnormal glandular cytology.

**Conclusions:** Our study demonstrated relatively low sensitivity of Pap smear tests in preoperative diagnosis of AIS, thus a thorough clinicohistologic evaluation for any atypical glandular cells on cytology is recommended.

**Comparison of Papanicolaou Smear Cytology, Biopsy and/or Endocervical Curettage, and Cervical Conization**

<table>
<thead>
<tr>
<th>Diagnostic Abnormalities</th>
<th>Positive Cases/Procedures Done</th>
<th>Sensitivity</th>
<th>% With Prior Glandular Abnormality</th>
<th>% Without Prior Glandular Abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papanicolaou smear</td>
<td>25/74</td>
<td>34%</td>
<td>-</td>
<td>100%</td>
</tr>
<tr>
<td>Biopsy/endocervical curettage</td>
<td>31/42</td>
<td>73.8%</td>
<td>45.2%</td>
<td>54.8%</td>
</tr>
<tr>
<td>Combined cytology and biopsy/endocervical curettage</td>
<td>41/72</td>
<td>56.8%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Conization</td>
<td>51/53</td>
<td>96.2%</td>
<td>41.5%</td>
<td>54.7%</td>
</tr>
</tbody>
</table>

**A Multi-institutional Study of Malignant Mixed Müllerian Tumor of the Ovary: Clinicopathologic Characteristics and Outcome Descriptors**

(Poster No. 19)

Evi Abada, MD, MS; Haidy Elazzamy, MD; RamiMusallam, MD; Hyejeong Jang, MS; Seongho Kim, PhD; Ziad Fehmi; Haya Batah, BS; Joseph Trak, MD; LamiaFathallah, MD; Sudeshna Bandopadhay, MD; RoubaAli-Fehmi, MD.

Departments of 1Pathology and 2Surgery, Wayne State University School of Medicine, Detroit, Michigan; 3Department of Pathology, Ascension St. John Hospital, Detroit, Michigan; 4Department of Oncology-Biostatistics Core, Karmanos Cancer Institute, Detroit, Michigan; 5Department of Biomolecular Science, University of Michigan, Ann Arbor, Michigan.

**Clinicopathologic Characteristics of Ovarian Carcinosarcoma**

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>N = 33</th>
<th>Overall Survival, P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis, median (range), y</td>
<td>68 (27–85)</td>
<td>.12</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>23 (70)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>6 (18)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>4 (12)</td>
<td></td>
</tr>
<tr>
<td>Histopathologic characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epithelial components</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serous</td>
<td>15 (45)</td>
<td></td>
</tr>
<tr>
<td>Other epithelial components</td>
<td>18 (55)</td>
<td></td>
</tr>
<tr>
<td>Mesenchymal components</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homologous</td>
<td>15 (45)</td>
<td></td>
</tr>
<tr>
<td>Heterologous</td>
<td>18 (55)</td>
<td></td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>12 (36)</td>
<td>.002</td>
</tr>
<tr>
<td>Absent</td>
<td>21 (64)</td>
<td></td>
</tr>
<tr>
<td>Lymph node metastasis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>7 (21)</td>
<td>.02</td>
</tr>
<tr>
<td>Absent</td>
<td>26 (79)</td>
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</tr>
<tr>
<td>Necrosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>17 (52)</td>
<td>.29</td>
</tr>
<tr>
<td>Absent</td>
<td>16 (48)</td>
<td></td>
</tr>
<tr>
<td>State of the endometrium</td>
<td></td>
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</tr>
<tr>
<td>Benign endometrium</td>
<td>32 (97)</td>
<td>.93</td>
</tr>
<tr>
<td>Cancer (endometrioid endometrial adenocarcinoma)</td>
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<td></td>
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<tr>
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<tr>
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<td>.03</td>
</tr>
<tr>
<td>Late stage (3A, 3B, 3C, 4B)</td>
<td>28 (85)</td>
<td>.03</td>
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<td>Menopausal status</td>
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<tr>
<td>Premenopausal</td>
<td>3 (9)</td>
<td>.54</td>
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<tr>
<td>Postmenopausal</td>
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</tr>
<tr>
<td>Parity</td>
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<tr>
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<td>23 (70)</td>
<td>.02</td>
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<tr>
<td>Nulliparous</td>
<td>10 (30)</td>
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<td>History of breast cancer</td>
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<tr>
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<td>.51</td>
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<tr>
<td>Absent</td>
<td>29 (88)</td>
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<tr>
<td>Family history of other malignancies</td>
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<tr>
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<td>10 (30)</td>
<td>.07</td>
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<tr>
<td>Absent</td>
<td>23 (70)</td>
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<tr>
<td>Comorbidities</td>
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<tr>
<td>Diabetes</td>
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<tr>
<td>Present</td>
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<td>Absent</td>
<td>30 (91)</td>
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<tr>
<td>Hypertension</td>
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<tr>
<td>Present</td>
<td>18 (55)</td>
<td>.44</td>
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<tr>
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<td>15 (45)</td>
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<tr>
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<tr>
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<td>.11</td>
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<tr>
<td>Absent</td>
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Context: Malignant mixed Müllerian tumor, which is also known as ovarian carcinosarcoma, is a rare and aggressive tumor of the ovary consisting of both epithelial and mesenchymal components, with a very poor prognosis. We aimed to study the clinicopathologic characteristics and outcome of this disease in our patient population.

Design: This was a retrospective study between 1990 and 2020. Histologic slides were reviewed for variables including tumor morphology, lymphovascular invasion, necrosis, and lymph node metastasis. Additional clinical data were obtained from electronic medical records. Univariable Firth Cox proportional hazard regression analysis was used to determine the association between several clinicopathologic variables and survival outcomes.

Results: Thirty-three patients were included in the study. Twenty-three (70%) were white, 6 (18%) Black, and 4 (12%) belonged to other ethnicities. The median age at diagnosis was 68 years. The median tumor size was 10 cm. All tumors had high-grade histology. Heterologous histology was seen in 18 cases (55%). Most patients (85%) had late-stage (III and IV) disease. All patients received standard treatments with tumor debulking and chemotherapy including carboplatin, ifosfamide, and paclitaxel in various combinations. Lymphovascular invasion, lymph node metastasis, parity, and advanced-stage disease were associated with worse overall survival. The 5-year overall survival was 71.08% (95% CI, 31.85%–81.95%). Patient characteristics including comorbidities and histopathologic descriptors are summarized in the Table.

Conclusions: Malignant mixed Müllerian tumor of the ovary is an aggressive disease, based on our results, lymphovascular invasion, lymph node metastasis, parity, and advanced-stage disease are associated with worse overall survival.

Inflammatory Myofibroblastic Tumor of the Placenta With Subsequent Successful Pregnancy and Benign Hysterectomy: A Case Report With 34 Month Follow-up (Poster No. 20)

Cooper Schwartz, BA1 (cooper_schwartz@brown.edu); Fusun Gundogan, MD, 2; Kamaljeet Singh, MD, 3; J. K. Schoolmeester, MD, 4; Natalie Banet, MD, 5; School of Medicine, Warren Alpert Medical School of Brown University, Providence, Rhode Island; Departments of 2Pathology and Laboratory Medicine and 3School of Medicine, Warren Alpert Medical School of Brown University (Women and Infants Hospital), Providence, Rhode Island; 2Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota.

Inflammatory myofibroblastic tumors (IMTs) are rare neoplasms of the gynecologic tract, predominantly in the myometrial wall. However, some cases have been reported in association with the placenta. Like those in other organs, IMTs of the placenta are characterized by molecular abnormalities, most commonly ALK gene rearrangements, and are often positive for ALK immunohistochemically. Though the clinical behavior of placental IMTs has so far proven benign, a successful intrauterine pregnancy with subsequent negative hysterectomy following a placental IMT has not been documented. We present a case study of a 27-year-old patient who was noted to have a 2-cm nodule attached to the extraplacental membranes (Figure 2.20, A). It was well circumscribed (Figure 2.20, B) and showed a “tissue culture” appearance, with alternating hypercellular and hypocellular areas with interspersed myoid matrix (Figure 2.20, C). Nuclear atypia and mitotic activity were minimal, inflammatory cells were present, and isolated cells showed decidualization (Figure 2.20, D). ALK was negative by immunohistochemistry and no ALK gene rearrangement was noted. The patient received no further treatment. After 31 months, the patient experienced a normal delivery in a pregnancy complicated by gestational diabetes. No longer desiring fertility, the patient elected to have a hysterectomy to confirm the absence of IMT at 34 months, and the uterus was unremarkable. This case provides insight into possible outcomes for patients with a rare tumor who may desire future fertility and may otherwise be advised to undergo hysterectomy in the setting of an unclear clinical course.

Pleomorphic Rhabdomyosarcoma of Uterine Corpus in an Adult (Poster No. 21)

Maryam Aghighi, MD (maryam.aghighi@gmail.com); Dionnee James, MD; Rajiv Pulimithanathu, MD. Department of Pathology, Rutgers Health-St Barnabas Medical Center, Livingston, New Jersey.

Pure rhabdomyosarcomas are part of heterologous sarcomas, which are primary to the uterus, together with other sarcomas of chondroid, adipocytic, and osteoid differentiation. They are further subclassified into embryonal, alveolar, and pleomorphic subtypes. Of these 3 categories, pleomorphic rhabdomyosarcomas are exceptionally rare. A 63-year-old postmenopausal woman presented with a 3-month history of vaginal bleeding and abdominal cramping. CT showed an enlarged uterus measuring 15.7 × 10.2 × 11.1 cm. The endometrium was thickened, measuring 6.9 cm with areas of hyperdensity. The patient underwent hysterectomy with bilateral salpingo-oophorectomy and lymph node dissection. Gross examination revealed a bulky uterine mass measuring 11 cm with >50% myometrial invasion (Figure 2.21, A), areas of necrosis, cervical stromal involvement, and lymph node metastasis. Histologically, the lesional cells showed a mixture of loosely cohesive round cells in sheets, spindled cells arranged in broad fascicles, and rhabdomyoblastic and markedly pleomorphic cells (Figure 2.21, B). Patchy areas of coagulative necrosis, myxoid change, and lymphovascular invasion were present. Mitosis averaged 34 per 10 hps. Desmin, myoD1 (Figure 2.21, C), myogenin (Figure 2.21, D), p53, vimentin, synaptophysin, and CD56 showed diffuse positivity. Cytokeratins were negative. There was no rearrangement of the JAZF1, PHF1, or YWHAE gene regions by fluorescence in situ hybridization. The diagnosis was rendered as pleomorphic rhabdomyosarcoma. In conclusion, our differential diagnosis included malignant mixed Müllerian tumor and endometrial stromal sarcoma with rhabdomyomatous differentiation; however, there was no evidence to support these diagnoses by immunohistochemistry and molecular studies. Pleomorphic rhabdomyosarcoma of the uterus is rare and portends a poor prognosis. Adequate sampling and a multidimensional approach should be especially emphasized to avoid a misdiagnosis.
Bilateral Squamous Cell Carcinoma Arising in Mature Cystic Teratoma

(Poster No. 22)

S. Shawn Liu, MD, PhD (ssliu@health.southalabama.edu); Mohamed A. Masoud, MD; Mingxia Shi, MD, PhD. Department of Pathology, University of South Alabama, Mobile.

Malignant transformation of mature cystic teratomas of the ovary is rare and only occurs in 1%–2% mature teratomas. Squamous cell carcinoma (SCC) accounts for approximately 80% of malignant transformation of mature teratoma in current literature. We reported the case of a 57-year-old woman with left and right ovarian masses measuring 11 cm and 4.5 cm, respectively. Grossly, the bilateral ovarian masses were cystic and solid, containing sebaceous content and hair with multiple gray-white firm mural nodules. Microscopic examination revealed bilateral ovarian invasive SCC, moderately to poorly differentiated, and arising in mature cystic teratoma. The malignant epithelial cells were diffusely positive for immunostains of p63 and CK5/6. Metastases of the SCC involving peritoneum, uterine, and small bowel were histologically demonstrated. SCC of the ovary can be pure de novo or arise in teratoma, squamous metaplasia of endometriosis, and endometrioid carcinoma. Perioperative diagnosis and management of SCC arising in teratoma is a clinical challenge owing to rarity and vague symptoms. It is important to thoroughly sample solid components of teratomas for malignancy. The prognosis of this lesion is related to the tumor size and patient age. Large mature cystic teratoma with solid components in elderly patients should be an alert for transformation of malignancy and followed up closely for metastasis.

Ovarian Serous Borderline Tumor and Recurrent Colonic Villous Adenomas in a Patient With Rett Syndrome

(Poster No. 23)

Anoshia Afzal, MD (anoshia-afzal@ouhsc.edu); Maria Kamal, MD; Lewis Hassell, MD. Department of Pathology, University of Oklahoma Health Sciences Center, Oklahoma City.

Rett syndrome is a neurodevelopmental disorder characterized by early normal growth followed by progressive developmental delay, motor function loss, and intellectual disability secondary to brain growth failure. Rett syndrome is caused by mutation in the methyl CpG binding protein 2, or MECP2 gene. Although a genetic disorder, less than 1% of Rett syndrome cases are inherited. One prior case of colon cancer has been reported in a patient with Rett syndrome, highlighting a possible association with colon cancer. We report a case of a 41-year-old woman with Rett syndrome who developed simultaneous colon (3 cm) and ovarian (16 cm) tumors as detected on body tomography. Her right ovary showed a stage 1a serous borderline tumor (Figure 2.23, A). Mismatch repair protein expression was intact and p53 showed missense phenotype. CK Oscar and CK 8/18 were reactive to PAX8 and CK7. P16 showed strong diffuse reactivity with multiple white-tan, whorled, firm intramural nodules measuring 0.5 to 1.5 cm in the greatest dimension. Microscopically, the cervical mass showed spindle cells separated by marked edema, abundant myxoid stroma, and prominent vascularity. However, in less edematous regions reasonable fascicular pattern of leiomyoma was appreciated. Spindle cells were reactive to ER/PR and desmin and were nonreactive to CD34 and S100 immunostains, suggestive of leiomyoma. Degenerative changes in the leiomyoma are not infrequent. However, predominant myxoid and edematous changes make recognition of fascicular patterns difficult and may be confused with other myxoid cervical lesions like superficial angiomyxoma. Careful microscopic examination and ancillary immunohistochemistry help in definite diagnosis.

Primary Cervical Leiomyoma With Marked Hydrophobic Changes: A Diagnostic Pitfall

(Poster No. 24)

Qandeel Sadiq, MD (qsadiq@uthsc.edu); Farhan Khan, MD. Department of Pathology, University of Tennessee Health Science Center, Memphis.

Primary cervical leiomyoma is an uncommon benign smooth muscle tumor of the uterine cervix. Secondary hydrophobic changes may pose significant diagnostic challenges. We report a case of a 48-year-old African American woman who presented with a complaint of a protruding mass from the vagina. Magnetic resonance imaging revealed the mass arising from the anterior portion of the cervix and protruding through the vagina. No uterine prolapse was noted and there was no evidence of a rectocele or enterocele. Cervical mass biopsy revealed squamous epithelium, endocervical mucosa, and fibromuscular stroma. No evidence of neoplasm or atypia was found. A hysterecomy with bilateral salpingectomy was then performed for a complete evaluation. On gross examination, a 6.2 × 5.5 × 1.0-cm tan-pink polypoidal cervical soft tissue mass was identified with multiple tan-pink, rubbery cut surfaces, and multiple cystic cavities containing gelatinous material. The uterine cavity was remarkable for multiple white-tan, whorled, firm intramural nodules measuring 0.5 to 1.5 cm in the greatest dimension. Microscopically, the cervical mass showed spindle cells separated by marked edema, abundant myxoid stroma, and prominent vascularity. However, in less edematous regions reasonable fascicular pattern of leiomyoma was appreciated. Spindle cells were reactive to ER/PR and desmin and were nonreactive to CD34 and S100 immunostains, suggestive of leiomyoma. Degenerative changes in the leiomyoma are not infrequent. However, predominant myxoid and edematous changes make recognition of fascicular patterns difficult and may be confused with other myxoid cervical lesions like superficial angiomyxoma. Careful microscopic examination and ancillary immunohistochemistry help in definitive diagnosis.

Uterine Carcinosarcoma Presenting as a Bladder Mass

(Poster No. 24)

Qandeel Sadiq, MD (qsadiq@uthsc.edu); Farhan Khan, MD. Department of Pathology, University of Tennessee Health Science Center, Memphis.

Uterine carcinosarcoma is an aggressive neoplasm, associated with metastatic disease at the time of initial presentation in 60% of patients. We report a case of a 64-year-old woman who presented with worsening renal function. Imaging revealed bilateral hydronephrosis and an enlarged uterus. Bilateral ureteral stent placement was done. A 2 × 4-cm sessile, nonpapillary friable bladder mass was resected. Histology showed a high-grade malignant neoplasm with extensive pleomorphism, and atypical mitotic figures involving the muscularis propria. The overlying urothelium was uninvolved, suggestive of extension from the adjacent site and/or metastasis. Urothelial markers were negative. Pelvic ultrasonography revealed a 6.6-cm hypoechogenic mass in the uterine fundus. Hysteroscopy and dilation and curettage showed a fixed palpable mass extending from the lower uterine segment to the parametrium bilaterally. Microscopic examination showed a high-grade biphasic malignant neoplasm composed of fragments of the malignant spindle to oval cells with focal rhabdoid differentiation. Scant admixed fragments of high-grade malignant epithelial cells with papillary architecture suggestive of serous carcinoma were noted. Both bladder and endometrial tumors were immunophenotypically similar. Tumor cells were reactive to PAX8 and CK7. P16 showed strong diffuse reactivity and p53 showed missense phenotype. CK Oscar and CK 8/18 were reactive in the carcinoma component. Desmin and myogenin highlighted focal rhabdomyoblastic differentiation, suggesting carcinosarcoma of the endometrium with heterologous elements and metastasis to the bladder. Urothelial neoplasms are heterogeneous with divergent epithelial and mesenchymal differentiation. Careful morphologic and immunohistochemical evaluation is required to rule out metastatic uterine malignancy, particularly in patients with radiologically evident uterine mass.

Abstracts
Endometrioid Carcinoma Exhibiting Microcystic, Elongated, and Fragmented (MELF) Pattern of Myoinvasion and Occult Lymph Node Metastasis Detected With Ultrastaging

(Poster No. 26)

Dokpe Emechebe, MBBS (Dokpe.emechebe@downstate.edu); Juan Coca Guzman, MD; Daniel Levitan, MD; Kristina Loukeris, MD. Department of Pathology, SUNY Downstate Health Sciences University, Brooklyn, New York.

Early-stage, FIGO grade 1 endometrioid endometrial carcinomas have a favorable prognosis. However, a minority of patients with early-stage, low-grade disease will have a more aggressive clinical course. Studies have shown that some patterns of myometrial involvement, such as the microcystic, elongated, and fragmented (MELF) type of myoinvasion, are associated with increased risk of lymphovascular space invasion (LVSI) and lymph node metastasis. We report a case of a 55-year-old woman who underwent resection and sentinel lymph node sampling for a low-grade endometrioid endometrial carcinoma. Sections revealed a FIGO grade 1 endometrioid carcinoma (Figure 2.26, A) associated with a MELF pattern of myoinvasion (Figure 2.26, B, arrow) and LVSI (Figure 2.26, B, inset). Sentinel lymph nodes appeared negative for carcinoma on initial microscopic evaluation of hematoxylin–eosin (H&E)–stained tissue. Ultrastaging was performed, which included review of a deeper H&E section as well as immunohistochemical staining for pancytokeratin (AE1/AE3). Keratin cocktail highlighted isolated tumor cells within the subcapsular sinus of one of the pelvic lymph nodes (Figure 2.26, C). Review of the initial H&E slide revealed relatively bland, intranodal histiocytoid tumor cells (Figure 2.26, D, circle). Our case reaffirms the diagnostic pitfall associated with endometrioid endometrial carcinomas with a MELF pattern of myoinvasion and underscores the utility of immunohistochemistry in revealing occult lymph node metastases in this context.

SMARCA4-Deficient Undifferentiated Uterine Sarcoma

(Poster No. 27)

Hula Taha, MD (hula.m.taha@uth.tmc.edu); Lan Zheng, MD; Shaimaa Elzamly, MD; Meaad Shitawi, MD; Tianhua Guo, MD; Songlin Zhang, MD; Nidhi Tandon, MD. Department of Pathology, University of Texas, Health Science Center, Houston.

SMARCA4 is a member of SWI/SNF complex whose inactivation is the leading oncogenic event in a variety of tumor types. Recently, SMARCA4 inactivation has been anticipated as a driven mutation in a rare subset of uterine sarcoma (SDUS). Here, we report a case of a 29-year-old woman who presented with vaginal bleeding and abdominal pain. Imaging showed a 4.8-cm uterine mass, 11.8-cm left adnexal mass, abdominal carcinomatosis, and ascites. Endometrium biopsy showed sheets of undifferentiated pleomorphic-epithelioid cells with scant cytoplasm, round to oval nuclei, prominent nucleoli, abundant mitotic figures, and necrosis. No definitive gland formation or squamous differentiation was identified. Immunohistochemical stains showed tumor cells were positive for pancytokeratin (rare cells), CAM 5.2 (rare cells), synaptophysin (weak, diffuse), CD56 (patchy), SALL4, p53 (wild-type), p16 (patchy), and cyclin D1. They were negative for PAX8, ER, PR, desmin, SMA, chromogranin, CD45, S100, and OCT4. They showed loss of SMARCA4 staining (Figure 2.27, A through D), and intact DNA mismatch repair staining (MLH1, MSH2, MSH6, PMS2). Molecular study revealed only SMARCA4 somatic mutation. A final diagnosis of SDUS was made. The patient died 14 weeks after the biopsy. SDUS is a newly described entity with aggressive clinical behavior. It has some overlapping morphologic and immunohistochemical features with undifferentiated/dedifferentiated endometrial carcinoma. Moreover, about 30% of the undifferentiated endometrial carcinomas can have SMARCA4 mutation. SDUS usually occurs in younger patients and is clinically more aggressive, is typically microsatellite stable, and demonstrates fewer genetic abnormalities. Recognition of the SDUS entity is clinically important for targeting therapies and for consideration of germline mutation test.

Herpesvirus Infection Masquerading as a Neoplasm in an HIV-Positive Patient: A Potential Diagnostic Pitfall

(Poster No. 28)

Kaitlyn Levet, MD (levet@bcm.edu); Julie Youngs, MD; Claire Hoppenot, MD; Ramya Masand, MD. Department of Pathology and Immunology, Baylor College of Medicine, Houston, Texas.

Herpesvirus infection in healthy and immunocompromised patients is fairly common and typically presents as clusters of fluid-filled blisters that heal by crusting. They usually heal spontaneously with resolution hastened by antiviral therapy. However, occasionally, especially in HIV patients, unusual presentations may be seen. We present such a case of a 55-year-old HIV-positive woman who presented with a growing pruritic, 5-cm firm and friable clitoral hood mass. Initial biopsy as well as subsequent wide local excision was read as ulcerated and inflamed fibroepithelial polyp. Within 2 weeks, 4 new similar lesions were noted in the vulva, prompting review of pathology. On review, sections demonstrated a polyoid exophytic growth with acanthotic overlying epidermis and abundant plasma cell–predominant inflammation interspersed with collagen bundles. The surface epithelium was focally ulcerated with associated acute inflammation. Within the ulcerated areas were scattered enlarged squamous cells demonstrating characteristic herpesvirus viral cytopathic effect positive by pan-herpesvirus immunostain. Significant regression of the new lesions was noted within weeks of antiviral therapy. Exophytic vegetative lesions in response to herpesvirus in the anogenital region in HIV patients are presumed to be the result of an impaired immune response. The tumor-like appearance clinically with prominent pseudopseudothelomatous hyperplasia seen histologically, especially with enlarged regional lymph nodes, can lead to an erroneous diagnosis of malignancy. Awareness of this clinical presentation and microscopic appearance with appropriate use of immunostains is important to prevent misdiagnosis as other neoplastic lesions, and for prompt institution of antiviral therapy.
Overgrowth of Rhabdomyosarcomatous Element Mimicking a Primary Sarcoma in a Sertoli-Leydig Cell Tumor of the Ovary in an Adolescent Girl: An Unusual Presentation
(Poster No. 29)
Prachi, MD (prachipath123@gmail.com); Hema M. Aiyer, MD. Department of Pathology and Blood Bank, Dharamshila Narayana Superspeciality Hospital, New Delhi, India.

Here we highlight the possibility of heterologous sarcomatous elements being present in Sertoli-Leydig cell tumors (SLCTs) and multiple recurrences presenting with a dominant sarcomatous element capable of being misinterpreted as a primary sarcoma in the absence of clinical history and findings. SLCTs constitute 0.5%–1% of all ovarian tumors and can be benign or malignant. We present a rare case of recurrent SLCT with concurrent heterologous rhabdomyosarcomatous component in a 14-year-old girl who presented with a heterogeneous mass of either ovarian or mesenteric origin on imaging. Her tumor markers (AFP and inhibin) were elevated. Post resection the pathologic findings were consistent with poorly differentiated SLCT, stage IA. She underwent 4 cycles of bleomycin, etoposide, cisplatin regimen and the tumor markers returned to a normal range. After 2 years, a follow-up positron emission tomography showed a complex abdominopelvic mass measuring 19.9 × 16.4 × 7.8 cm, abutting the retroperitoneum. Pathologic findings were consistent with a poorly differentiated SLCT with predominant rhabdomyosarcomatous differentiation–embryonal type and she was put on VAC regimen. After completion of chemotherapy, she was found to be in complete remission on imaging. After 1 year, a repeated contrast-enhanced CT showed a recurrent complex abdominopelvic mass. On radical hysterectomy and excision, the abdominopelvic mass revealed a predominantly rhabdomyosarcomatous differentiation–embryonal type and she was on surveillance with cystoscopy and computed tomography imaging, which showed disappearance of the bladder mass but her bilateral ovarian masses, which were clinically thought of as metastases, failed to respond. Hence, the patient underwent hysterec- tomy with bilateral salpingo-oophorectomy, which showed malignant and borderline Brenner tumors in the left and right ovaries, respectively (Figure 2.30, A and B). She was on surveillance with cystoscopy and computed tomography imaging, which showed disappearance of the bladder mass but her bilateral ovarian masses, which were clinically thought of as metastases, failed to respond. Hence, the patient underwent hysterec- tomy with bilateral salpingo-oophorectomy, which showed malignant and borderline Brenner tumors in the left and right ovaries, respectively (Figure 2.30, C and D). In our case scenario there was a clear difference in treatment responsiveness between the Brenner tumors and recurrent invasive uterine carcinoma of the urinary bladder, though they had similar histomorphologic features. Also, the malignant Brenner tumor had borderline areas favoring an ovarian primary over a metastasis, supporting that these 2 tumors may represent distinct tumor entities. It is very important to delineate these uterine-looking coincidental tumors. This may aid us in adopting an appropriate treatment strategy. In the future, more studies are needed to establish any possible link in their pathogenesis and to prove if they have any impact on prognosis.

Bilateral Brenner Tumors of the Ovary in Association With Recurrent Invasive Urothelial Carcinoma of Urinary Bladder: Metastases or Ovarian Primaries?
(Poster No. 30)
Vijaya Kadam Maruthi, MBBS1 (vkadamma@buffalo.edu); Devi Jeyachandran, MD2; Mohamed Mokhtar Desouki, MD.2 1Department of Pathology, Buffalo General Hospital, University at Buffalo, New York; 2Department of Pathology, Roswell Park Comprehensive Cancer Center, Buffalo, New York.

Brenner tumors are very rare epithelial tumors of the ovary with a handful of cases associated with urothelial tumors of the urinary tract. We present the first case in the literature describing borderline and malignant Brenner tumors of both ovaries in association with muscle-invasive urothelial carcinoma of the bladder, and recurrence in the urinary bladder. A 74-year-old woman underwent neurectomy for ureteral invasive urothelial carcinoma (Figure 2.30, A) on biopsy with subsequent chemotherapy for the recurrence in the urinary bladder (Figure 2.30, B). She was on surveillance with cystoscopy and computed tomography imaging, which showed disappearance of the bladder mass but her bilateral ovarian masses, which were clinically thought of as metastases, failed to respond. Hence, the patient underwent hysterec- tomy with bilateral salpingo-oophorectomy, which showed malignant and borderline Brenner tumors in the left and right ovaries, respectively (Figure 2.30, C and D). In our case scenario there was a clear difference in treatment responsiveness between the Brenner tumors and recurrent invasive uterine carcinoma of the urinary bladder, though they had similar histomorphologic features. Also, the malignant Brenner tumor had borderline areas favoring an ovarian primary over a metastasis, supporting that these 2 tumors may represent distinct tumor entities. It is very important to delineate these uterine-looking coincidental tumors. This may aid us in adopting an appropriate treatment strategy. In the future, more studies are needed to establish any possible link in their pathogenesis and to prove if they have any impact on prognosis.

Incidental Intravascular Large B-Cell Lymphoma in the Background of an Extensive Cervical High-Grade Squamous Intraepithelial Lesion During Pregnancy
(Poster No. 31)
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Intravascular large cell lymphoma is an aggressive rare subtype of lymphoma confined to the intravascular space, most commonly of B-cell origin. We present the case of a 31-year-old pregnant woman (gravida 1, para 0) with a history of a first-trimester Papanicolaou test positive for high-grade squamous intraepithelial lesion (HSIL) and HPV 16–positive cotest. Follow-up colposcopic biopsies showed persistent HSIL. A loop electrosurgical excision procedure was performed at 25 weeks’ gestation, showing extensive HSIL involving endocervical glands (Figure 2.31, A) and a focal intravascular atypical lymphoid population, characterized by cells of large nuclear size, open chromatin, and scant cytoplasm (Figure 2.31, B). These atypical lymphocytes were in stark contrast to surrounding reactive inflammatory cells centered around HSIL. The atypical cells were positive for CD20 (partial) (Figure 2.30).
2.31, C), CD30, PAX5, MUM1, BOB1, CD138 (partial), and c-MYC, with increased Ki-67 index (>90%) (Figure 2.31, D), and negative for CD3, CD5, CD10, ALK, BCL1, BCL2, BCL6, EBER-ISH, HHV8, and TdT. B-cell gene rearrangement studies detected IgH gene clonality. Fluorescence in situ hybridization studies were negative; however, malignant cell numeration was minimal on the tissue sections submitted. These findings are characteristic of intravascular large B-cell lymphoma. To our knowledge, this is the first report of an intravascular large B-cell lymphoma diagnosed during pregnancy in the context of HSIL and highlights pitfalls in overlooking a rare lymphoid neoplasm when evaluating a squamous lesion containing background inflammation. Care must be taken to evaluate morphology of the inflammatory infiltrate and scrutinize that which does not fit benign patterns or cytology, especially when clinical history is not characteristic.

Metastatic Uterine Leiomyosarcoma to the Breast
(Poster No. 32)

Fahd Hussain, MD (fhussain@umc.edu); Anu Abraham, MD; Tejal Patel, MD; Veena Shenoy, MD. Department of Pathology, University of Mississippi Medical Center, Jackson.

Breast metastases from nonmammary malignancies are rare, constituting approximately 2% of all breast malignancies. Very few cases of uterine leiomyosarcoma metastasizing to the breast have been reported in the English literature. Leiomyosarcoma is an aggressive soft tissue sarcoma derived from smooth muscle cells. The most common primary site is the uterus. We present a case of a 66-year-old woman who presented with a palpable mass at the inferior aspect of her left breast. Four years prior, the patient underwent a hysterectomy for uterine leiomyosarcoma, followed by adjuvant chemoradiotherapy. On physical examination, a 3-cm tender mass was identified in the left breast and was resected. Gross examination revealed a firm, tan-pink, centrally hemorrhagic mass. Microscopic examination revealed a cellular spindle cell lesion arranged in fascicles with prominent cigar-shaped nuclei, high mitotic activity, and areas of necrosis (Figure 2.32, A and B). Immunohistochemical stains showed the tumor cells to be positive for caldesmon (Figure 2.32, C), smooth muscle actin, and desmin (Figure 2.32, D) and negative for broad-spectrum cytokeratin, consistent with the diagnosis of metastatic leiomyosarcoma. Uterine leiomyosarcoma is a highly aggressive neoplasm with an increased rate of recurrence and metastases due to its propensity for hematogenous spread. The most common site of metastases is the lung followed by peritoneum, bone, and liver. However, breast metastasis is extremely rare. Metastatic disease should be considered in the differential diagnosis in a patient with breast mass, particularly if there is a history of extramammary malignancy.

Uterine Adenosarcoma With Sarcomatous Overgrowth: A Case Report Highlighting the Importance of Recognition and Diagnosis for Future Treatment Guidance and Prognosis
(Poster No. 33)

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Uterine adenosarcoma with sarcomatous overgrowth (ASSO) is a rare gynecologic malignancy. Adenosarcoma is a biphasic mesenchymal tumor composed of benign epithelium and malignant stroma. Poor prognostic factors include sarcomatous overgrowth (defined as presence of pure sarcoma comprising at least 25% of the tumor), high mitotic rate, myometrial invasion, necrosis, and metastases. We report a case of uterine ASSO in a 62-year-old woman. The patient presented with difficulty urinating and 2 episodes of postmenopausal vaginal bleeding. Pelvic examination and CT of the abdomen/pelvis demonstrated an enlarged uterus with a mass protruding from the endocervix. The patient was admitted for complete surgical resection. A total hysterectomy and bilateral salpingo-oophorectomy specimen was submitted for pathologic examination. Grossly, a tan-pink, rubbery, nodular mass (12.0 × 10.0 × 7.0 cm) protruded from the lower uterine segment with 2 additional polypoid lesions (2.3 and 1.8 cm) identified. Microscopically, the biphasic tumor was composed of benign endometrial-like glands and sarcomatous stroma (Figure 2.33, A) with a predominance of the mesenchymal stromal component (>75%) (Figure 2.33, B). Pathologic diagnosis was ASSO with variable cellularity, mild to moderate atypia, and focal myometrial invasion. The rarity of adenosarcoma makes the discussion of prognosis difficult, although it is certain that the presence of sarcomatous overgrowth is unfavorable. There are limited data to help guide treatment, and thus therapy is not...
well defined. Standard of care is complete surgical resection and the role of adjuvant therapy is still being delineated. This case highlights the importance of recognition and accurate pathologic diagnosis of ASSO to further characterize effective treatments and prognosis.

A Multifactorial Review of Placentas From Mothers With Coronavirus Disease 2019 (COVID-19)

(Poster No. 34)

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Context: The effects of COVID-19 are a continuous and evolving focus of research. Yet, data from gynecologic pathology are scant. This study reviews findings of placental pathology, placental weight, and mode of delivery in patients with COVID-19 versus healthy control group.

Design: Nineteen placentas from women with COVID-19 from April 2020 to December 2020 were retrieved from our institution’s pathology database and compared clinicopathologically with a control group (139 placentas).

Results: The group of women with COVID-19 at delivery consisted of 11 patients with minimal symptoms, 4 patients had moderate to severe symptoms, and the remainder were diagnosed before antepartum. Sixteen patients delivered at term and 3 patients delivered preterm. Seven patients had vaginal deliveries and 12 had cesarean sections (P = .15). One placenta showed accelerated villous maturation (P = .12), congested blood vessels in fetal membranes (P = .12), vasculitis (P = .32), decidual thrombotic vasculopathy (P = .12), intervillous thrombus (P = .40), and delayed villous maturation (P = .54). Two placentas demonstrated small for gestational age (P = 1), large for gestational age (P = 1), chorangiosis (P = .34), villous edema (P = 1), and infarct (P = .30). Five placentas had acute chorioamnionitis (P = .07) and 6 placentas had calcifications (P = .46). Increased intervillous fibrin deposition was detected in 8 placentas (P = .002) (Table). The mean placental weight of the COVID-19 placentas was 475.26 ± 101.06 g and in the control group it was 449.18 ± 119.64 g, P = .37.

Conclusions: Our results suggest a significant increase in intervillous fibrin deposition in placentas from COVID-19 patients. There is no significant difference in other clinicopathologic findings. However, our sample size is limited, and larger studies will be needed to report definitively.

Histologic Findings Found Among COVID-19 Mothers and Their Noninfectious Counterparts

<table>
<thead>
<tr>
<th>Histopathologic Findings</th>
<th>Placentas From Mothers With COVID-19 (19)</th>
<th>Control Group (139)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accelerated villous maturation</td>
<td>1</td>
<td>0</td>
<td>.12</td>
</tr>
<tr>
<td>Congested blood vessels in fetal membranes</td>
<td>1</td>
<td>0</td>
<td>.12</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>1</td>
<td>2</td>
<td>.32</td>
</tr>
<tr>
<td>Thrombotic vasculopathy in decidua</td>
<td>1</td>
<td>0</td>
<td>.12</td>
</tr>
<tr>
<td>Intervillous thrombus</td>
<td>1</td>
<td>3</td>
<td>.40</td>
</tr>
<tr>
<td>Delayed villous maturation</td>
<td>1</td>
<td>5</td>
<td>.54</td>
</tr>
<tr>
<td>Small for gestational age</td>
<td>2</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Large for gestational age</td>
<td>2</td>
<td>19</td>
<td>1</td>
</tr>
<tr>
<td>Chorangiosis</td>
<td>2</td>
<td>8</td>
<td>.34</td>
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<tr>
<td>Villous edema</td>
<td>2</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Infarct</td>
<td>2</td>
<td>7</td>
<td>.30</td>
</tr>
<tr>
<td>Acute chorioamnionitis</td>
<td>5</td>
<td>15</td>
<td>.07</td>
</tr>
<tr>
<td>Calcifications</td>
<td>6</td>
<td>58</td>
<td>.46</td>
</tr>
<tr>
<td>Increased intervillous fibrin deposition</td>
<td>8</td>
<td>16</td>
<td>.002</td>
</tr>
</tbody>
</table>

Operating Characteristics of TP53 Sequencing as a Surrogate for P53 Immunostaining in Endometrial Cancer

(Poster No. 35)

Pooja Khonde, MD (k.pooja@wustl.edu); Jan Hagemann, MD, PhD. Department of Pathology and Immunology, Washington University, St. Louis, Missouri.

Context: In the ProMisE TCGA-based molecular classification of endometrial cancers, p53 immunohistochemistry (IHC) is the gold standard for assigning cases to the p53-abnormal group. We asked whether TP53 mutation is a reliable surrogate for p53 IHC, and whether the mutation type predicts the p53 staining pattern.

Design: We retrieved hysterectomy cases for endometrial cancer that had undergone TP53 sequencing in a 5-year period. For each case, we performed or retrieved p53 IHC. IHC results were classified as normal, abnormal/gain, or abnormal/loss.

Results: In 46 of 49 cases that met inclusion criteria, TP53 status by sequencing (wild type versus mutated) matched the status by gold standard IHC (normal versus abnormal) (Table). All 24 of 24 cases with a pathogenic sequence variant had abnormal IHC. A total of 20 of 21 cases with missense mutation (including 2 with concurrent frameshift) had abnormal/gain IHC, but 1 carcinosarcoma with p.R273H showed abnormal/loss IHC. Three of 5 cases with frameshift showed abnormal/loss IHC; the other 2 were the ones with concurrent missense mutation and had abnormal/gain IHC. Among 25 cases with wild-type TP53, 22 had normal IHC, but 3 had abnormal IHC: a carcinosarcoma with abnormal/loss IHC, a POLE-mutated carcinosarcoma, and a serous carcinoma with abnormal/gain IHC.

Conclusions: TP53 sequencing was 94% accurate for predicting p53 IHC status for purposes of the ProMisE classifier. TP53 mutation was 100% predictive of abnormal p53 IHC. There were 3 false negatives, but sequencing by a panel approach would have identified 1 as a POLE tumor. Relying on sequencing alone would have assigned 2 of 49 cases (4%) to the incorrect ProMisE group, notwithstanding their high-risk histology.

Three Cases of Clear Cell Carcinoma Arising Within Endometrial Polyps

(Poster No. 36)

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Clear cell carcinoma (CCC) of the endometrium is rare, especially when arising in endometrial polyps. Two cases of postmenopausal women with CCC arising in endometrial polyps are presented below. A 68-year-old woman (patient 1) and a 57-year-old woman (patient 2) both presented with postmenopausal bleeding. Ultrasonography

<table>
<thead>
<tr>
<th>TP53 Sequencing</th>
<th>p53 IHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mutant</td>
<td>Abnormal</td>
</tr>
<tr>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>Wild type</td>
<td>3</td>
</tr>
</tbody>
</table>

A Rare Case of Primary Ovarian Leiomyoma

Varsha Prakash, MD (vprakash@umc.edu); Vijay Kumar, MD; Veena Shenoy, MD, Department of Pathology, University of Mississippi Medical Center, Jackson.

Leiomyoma, though a common benign tumor in the uterus, occurs rarely in the ovary and accounts for only 0.5%–1% of all benign ovarian neoplasms. Recent advances in anaplastic biomarkers as well as a better understanding of the clinical behavior have led to the development of a molecular classification of endometrial stromal tumors, including the development of a rare phenotype of this neoplasm known as leiomyoma with unique histologic features. This case describes a rare ovarian leiomyoma with unique histologic features, including prominent smooth muscle cell proliferation, positive for smooth muscle actin, desmin, calretinin, and CD10 and negative for melan A, HMB-45, CD34, D2-40, and Wilms tumor gene. The clinical course is described, highlighting the importance of this condition.
tumors. Ovarian leiomyomata are typically unilateral and most common amongst premenopausal women. A 37-year-old woman presented with menorrhagia, dysmenorrhea, and dyschezia. Ultrasonography showed a solid right adnexal mass. The patient underwent a right salpingo-oophorectomy. On gross examination, the ovary revealed a firm, tan-white whorled nodule measuring 3.5 cm in greatest dimension. Microscopic examination showed a well-circumscribed spindle cell lesion composed of intersecting fascicles of smooth muscle cells with blunted, cigar-shaped nuclei and eosinophilic cytoplasm (Figure 2.39, A and B). Mitotic activity, necrosis, and nuclear pleomorphism were not identified. Immunohistochemistry showed the neoplastic cells to be positive for desmin (Figure 2.39, C and D) and caldesmon (Figure 2.39, D) and negative for inhibin. Primary ovarian leiomyoma is a rare benign tumor, usually detected incidentally during pelvic examinations. While most patients are asymptomatic, some present with dysmenorrhea and dyschezia. Giant ovarian leiomyoma can present with ascites, hydrenephrosis, or elevated CA 125. Ovarian leiomyomas may arise from smooth muscle cells in hilar blood vessels or ovarian ligaments, multipotential cells in ovarian stroma, or undifferentiated germ cells. Leiomyoma should be considered in the differential diagnosis of solid ovarian masses in middle-aged females. Ancillary studies are important for differentiation from other primary ovarian neoplasms, like sex cord–stromal tumors. The patient has been asymptomatic and doing well since surgery.

A Rare Case of Multi-phenotypical Cervical Cancer
(Poster No. 40)
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Carcinomas composed of multiple types are unusual. The mixture of small cell neuroendocrine carcinoma, adenocarcinoma, and squamous cell carcinoma is rare. We present a rare case of high-grade human papillomavirus (HPV)–associated multiphenotypic carcinoma of the uterine cervix with squamous, glandular, and small cell neuroendocrine components in a 68-year-old woman presenting with postmenopausal bleeding. The tumor was immunophenotyped and analyzed. Microscopically, sections of the biopsies showed a morphologically heterogeneous tumor composed of 3 different components of squamous (Figure 2.40, A, right side), adenocarcinoma (Figure 2.40, B), and small cell neuroendocrine carcinoma (Figure 2.40, C). Two additional tumor components were also identified. One was p40 and p63 positive basal pemphigus vulgaris-associated component (Figure 2.40, C), which was suggestive of an HPV-infected reserve cell population. The other had mixed features between neuroendocrine carcinoma and adenocarcinoma, which we referred to as the “intermediate” component. It showed cells with the cytology of neuroendocrine small cell carcinoma but with limited neuroendocrine marker positivity. The intermediate component itself had 2 subsets, one which showed wild-type p53 expression (Figure 2.40, A, left side) and the other that showed p53 overexpression (Figure 2.40, D). The former had more rudimentary glands and the latter had rosette structures. All components were diffusely positive for p16. We evaluated an unusual case of HPV-associated multiphenotypic cervical carcinoma. We favor the origin of the tumor components to be originally derived from a reserve cell population/populations. However, further tumor component selective differentiation appears possible considering the intermediate component identified in this case.

Prognostic Histologic Factors in Uterine Carcinosarcomas in Caribbean Women
(Poster No. 41)
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Context: Uterine carcinosarcoma is a rare biphasic neoplasm consisting of malignant epithelial and sarcomatous elements. Carcinosarcomas are overrepresented, understudied, and associated with worse outcome among women of color in the United States, many of whom have Caribbean ancestry. Prognostic histologic factors of carcinosarcomas have never been studied among Caribbean women despite its overrepresentation. We performed this study to identify the prognostic significance of epithelial and sarcoma predominance in uterine carcinosarcomas in Caribbean women.

<table>
<thead>
<tr>
<th>Uterine Carcinosarcomas Stratified by Epithelial and Sarcoma Predominance</th>
<th>Epithelial-Predominant</th>
<th>Sarcoma-Predominant</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>9</td>
<td>14</td>
<td>&gt;.05</td>
</tr>
<tr>
<td>Pathologic stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized (n = 25)</td>
<td>2 (22%)</td>
<td>10 (71%)</td>
<td>.03</td>
</tr>
<tr>
<td>Advanced (n = 21)</td>
<td>7 (78%)</td>
<td>4 (29%)</td>
<td>.03</td>
</tr>
</tbody>
</table>

Design: We identified 53 uterine carcinosarcomas (9 biopsy and 44 hysterectomy specimens) from patients from institutions in Trinidad. Tumors were evaluated for extent of epithelial and sarcomatous components, histologic subtype, necrosis, lymphovascular invasion, and tumor histology within lymphovascular spaces. Epithelial predominance was defined as >90% neoplastic epithelium and sarcoma predominance, and >90% sarcomatous differentiation. Relationships between these histologic features and pathologic stage were assessed.

Results: Two of the 9 biopsy cases had concurrent pathologically confirmed intra-abdominal metastases, thus considered stage IVB and included in analysis. There were slightly more localized than advanced tumors. There were 9 epithelial-predominant tumors (20%) and 14...
sarcoma-predominant tumors (30%). There was a higher proportion of epithelial-predominant tumors than sarcoma-predominant tumors in the advanced-stage cohort, while conversely sarcoma predominance was overrepresented in the localized tumor cohort (Table). Necrosis, histologic subtype, and presence of heterologous elements had no prognostic significance.

**Conclusions:** Epithelial predominance is associated with advanced stage in uterine carcinosarcomas in Caribbean women, suggesting its poor prognostic significance. This should prompt further study into both treatment and prognosis of carcinosarcomas in women of color.

**Clinicopathologic Features and Outcomes of Endometriosis-Associated Ovarian Tumors: A Multi-institutional Study**

(Poster No. 42)

Michelle S. Lin, MD1 (mslin@houstonmethodist.org); Ramya P. Masand, MD2; Cagla Benkli, MD2; Hanna Siatecka, MD2; Jim W. Hsu, MD, PhD3; Shilpa Jain, MD2; Michael T. Deavers, MD.1 1Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Texas; 2Department of Pathology and Immunology, Baylor College of Medicine, Houston, Texas.

**Context:** Past studies have suggested that endometriosis-associated ovarian tumors (EAOTs) may represent a distinct subset of ovarian tumors with unique clinicopathologic characteristics; however, the prognostic significance of EAOT is unclear. The aim of our study was to characterize the clinicopathologic features of EAOT, particularly in comparison to ovarian tumors not associated with endometriosis (non-EAOT).

**Design:** An institutional database search for ovarian epithelial borderline tumors and carcinomas from 2015-2020 was conducted. Clinicopathologic parameters including age, histotype, stage, and follow-up outcomes were recorded.

**Results:** Eighty-one cases of EAOT and 302 cases of non-EAOT were identified (Table). The mean age at diagnosis of patients with EAOT was significantly younger than patients with non-EAOT (52.5 versus 58.9 years). Histotypes of EAOT were enriched for endometrioid carcinoma (32.1% versus 3.3%) and clear cell carcinoma (28.4% versus 3.6%). A higher proportion of patients with EAOT presented with early-stage (FIGO stage I-II) disease (74.4% versus 56.3%), and a higher proportion were alive without disease at last follow-up (73.2% versus 55.8%). However, when stratified by stage and histotype, there was no significant difference in the outcomes of patients with EAOT and non-EAOT.

**Conclusions:** EAOTs tend to present at a younger age and earlier stage, with relatively good clinical outcomes. However, when controlling for stage and histotype, the difference in outcomes between EAOT and non-EAOT was eliminated. This suggests that endometriosis does not confer an independent prognostic advantage to patients with EAOT, and that positivity for EAOT in non-EAOT may be related to favorable histologies and detection at earlier stages of the disease.

**Accuracy of Frozen Sections on Hysterectomy Specimens: A 10-Year Study in a Safety Net Hospital**

(Poster No. 43)

Hamza Ashmila, MD (hamza.ashmila@tuhs.temple.edu); Saad Tarafid, MD, MBA, FCAP, FIAC. Department of Pathology, Temple University Hospital, Philadelphia, Pennsylvania.

**Context:** The frozen section (FS) is routinely used for treatment planning of endometrial cancer, including evaluating the depth of invasion and lymph node metastasis. The literature on the accuracy of FS for surgical staging of endometrial cancer is varied, with concordance rates between FS and paraffin sections for the depth of myometrial invasion ranging from 72% to 95%. We wanted to evaluate the accuracy of FS in our safety net hospital, including the impact of restricted access to health care and advanced-stage presentation of our unique patient population.

**Design:** We retrospectively analyzed 273 uterine FS specimens obtained at our institution between 2010 and 2019. Cases were retrieved from the departmental laboratory information system. Results were tabulated and analyzed with Excel. Intraoperative FS diagnosis was compared to final diagnosis for accuracy of diagnosis and the depth of myometrial invasion.

**Results:** The overall concordance rate was 87.9% (240/273). The concordance rate for the depth of invasion was 92% (252/273). The concordance rate for the depth of invasion was 96% (262/273). All of the discrepant cases (12.1% [33/273]) were underestimates.

**Conclusions:** In this study, FS is highly accurate for determining the depth of myometrial invasion, higher than that reported in previous studies. Only a few cases were upstaged owing to a higher depth of invasion on final pathology. Discrepancy due to underestimates calls for more representative sampling during intraoperative consultation. FS can be used reliably to guide surgical staging of endometrial carcinoma in underserved populations.

**Case of Unusual Mesothelial Inclusions in the Ovary: Rare Morphologic Mimickers of Malignancy in Gynecologic Specimens**

(Poster No. 44)

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Unusual mesothelial inclusions are benign findings rarely observed in gynecologic specimens that can be mistaken for neoplasia or metastatic disease. Mesothelial hyperplasia can occur as a reactive change in the ovary independently of neoplastic processes; however, its morphologic characteristics effectively mimic adenomatoid tumor and, to a lesser degree, metastatic mesothelioma or adenocarcinoma. The incidental discovery of mesothelial inclusions during the evaluation of tissue for existing or suspected malignancy further lends to the likelihood of misinterpreting this benign finding. Although unusual mesothelial inclusions have not been directly associated with gynecologic malignancy, a possible association with endometriosis has been suggested in the literature. The patient in this case is a 60-year-old woman diagnosed with endometrial adenocarcinoma and adenomyosis status post total hysterectomy with bilateral salpingo-oophorectomy. Histochemical examination of the left ovary demonstrated nested aggregates of cuboidal cells with scattered central lumina and a focal pseudo-infiltrative pattern. Immunohistochemical staining was remarkable for calretinin, CK7, and WT1 positivity with focally positive D2-40. Inhibin, EMA, CK5/6, and PAX8 were negative, thereby demonstrating an appropriate staining pattern for mesothelial cells. Although adenomatoid tumor was considered, the lack of a mass lesion was most consistent with unusual mesothelial inclusions rather than a neoplasm.
Sarcomatoid Squamous Cell Carcinoma of the Cervix  
(Poster No. 45)  
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Department of Pathology, Walter Reed National Military Medical Center, Bethesda, Maryland;  
Department of Pathology, Uniformed Services University of the Health Sciences, Bethesda, Maryland.

Sarcomatoid squamous cell carcinoma of the cervix is a very rare histologic variant of squamous cell carcinoma. We report a case of an 84-year-old woman who initially presented to the emergency department with a prolapsed 8-cm cervical mass on vaginal examination. An initial excisional biopsy showed sheets and short fascicles of malignant spindle cells positive for CD10, while negative for SMA, desmin, and AE1/AE3. The patient underwent a total vaginal hysterectomy with bilateral salpingo-oophorectomy. Gross examination revealed a fungating, friable mass arising from the central anterior ectocervix. Histologic examination revealed extensive high-grade squamous intraepithelial lesion (HSIL) (Figure 2.45, A) with underlying sheets and fascicles of neoplastic spindle cells (Figure 2.45, B) exhibiting nuclear pleomorphism, vesicular chromatin, and increased mitotic figures in a background of prominent geographic necrosis. By immunohistochemistry, the areas of HSIL were strongly positive for p16 (Figure 2.45, C), CK5/6, p40, and p63. Additionally, the neoplastic spindle cells were strongly positive for p16 (Figure 2.45, D) and CD10, with weak and focal positivity for smooth muscle myosin heavy chain. Wild-type p53 expression was also observed. They were negative for SMA, CD34, CK8/18, CK7, CK903, ER, PR, desmin, PAX8, and CK5/6. HPV ISH was negative in both the HSIL and spindled cell components. Next-generation sequencing on the biopsy material revealed TERT and LAT1 mutations in addition to a JUN copy number gain. RNA expression was negative. This case highlights an uncommon histologic variant of cervical squamous cell carcinoma and its dysplasia-carcinoma sequence from intraepithelial dysplastic lesions to sarcomatoid squamous cell carcinoma.

Vaginal Dermatofibrosarcoma Protuberans With Fibrosarcomatous Changes  
(Poster No. 46)  
Valentina Zanfagnin, MD; Tiffany Lee, DO; Chen Zhengshan, MD, PhD; Cleandrea R. Williams, MD; Tiannan Wang, MD, PhD; Saloni Walia, MD. Department of Laboratory Medicine and Pathology, University of Southern California, Los Angeles.

Dermatofibrosarcoma protuberans (DFSP) represents a rare skin neoplasm, and the vulva is the most common primary site of origin in the gynecologic tract. Recently, DFSPs with fibrosarcomatous change and characteristic COL1A1-PDGFB fusion have also been described arising in the cervix and corpus uteri. We present the case of a 46-year-old woman who was found to have a rapidly growing lesion arising from the posterior vaginal fornix. Grossly, the tumor was a well-circumscribed, firm tan-white lesion measuring 56 × 45 × 34 mm, while histologically it was composed of spindle cells with a predominant fascicular growth pattern (Figure 2.46, A). The cells showed moderate nuclear atypia, indistinct cell borders, increased mitotic activity (41/10 high-power fields), and focal necrosis. No characteristic vascular pattern was noted. Immunohistochemistry showed rare tumor cell positivity for CD34 (Figure 2.46, B) and negativity for Melan-A, HMB-45, CD31, desmin, S100, CK5/6, p63, synaptophysin, CD99, TLE1, and pancytokeratin. Pan-trk immunohistochemical stain was equivocal and noncontributory. Cytogenetic studies confirmed COL1A1-PDGFB fusion and absence of SYT-SSX1, SYT-SSX2 translocation. DFSPs with fibrosarcomatous change are locally aggressive and have a metastatic potential; the patient was referred for adjuvant treatment with radiotherapy and targeted therapy (imatinib). To our knowledge, this is the first described case of fibrosarcomatous DFSP arising in the vagina. This diagnosis can be challenging; however, it should be part of the differential diagnosis when working up spindle cell tumors of the vagina. Molecular studies represent a fundamental tool in the diagnostic and therapeutic process of the individualized medicine era.

Mesonephric-like Carcinoma of the Endometrium Presenting as an Endometrial Polyp  
(Poster No. 47)  
Jana Tarabay, MD; Sonia Veran-Taguibao, MD; Mahra Noorbakhsh, MD; Samira Mortazaee, MD; Ted Farzaneh, MD. Department of Pathology and Laboratory Medicine, University of California, Irvine, Orange.

Mesonephric-like carcinoma (MLCa) of the endometrium represents less than 1% of endometrial carcinomas and unlike mesonephric carcinoma of the cervix, it lacks any association with mesonephric remnants. Morphologically, it shares similar architectural patterns with
endometrial adenocarcinoma with glandular or tubular pattern as the most frequent form observed in both entities. The presence of intraluminal eosinophilic secretions, immunohistochemical and genetic profile, and the tumor location aid toward the correct diagnosis. Hereby, we report the first case of an endometrial MLCa arising from an endometrial polyp. A 68-year-old woman presented with postmenopausal vaginal bleeding managed with an endometrial biopsy reported as endometrial endometrioid adenocarcinoma, FIGO grade 1. A hysterectomy was subsequently performed. Gross pathologic examination revealed a 3-cm polypoid, focally hemorrhagic mass in the endometrial cavity. Microscopically, the polyp revealed crowded atypical glands with tubular, papillary, and cribriform architecture (Figure 2.47, A). The neoplastic glands were lined by cuboidal cells with angulated vesicular nuclei, occasional nuclear grooves, and scant amphophilic cytoplasm. Some glands contained dense intraluminal eosinophilic secretions (Figure 2.47, B). Immunohistochemistry revealed nuclear reactivity for PAX8 (Figure 2.47, C), TFF-1 (Figure 2.47, D), and GATA-3, with focal staining for CD10 and calretinin. ER and PR were negative. The overall findings were diagnostic for endometrial MLCa. MLCa is a rare variant of endometrial carcinoma. It is most likely of Mullerian origin but shows morphologic, immunohistochemical, and molecular features of mesonephric carcinoma. Considering the aggressive behavior of MLCas, distinction of this entity is extremely important for clinical purposes. Therefore, one should be aware of this distinct entity.

Dichorionic Twin Pregnancy With a Complete Hydatidiform Molar Placenta Previa and Coexisting Fetus

(Poster No. 48)

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Twin pregnancy consisting of complete molar pregnancy and a coexisting normal fetus is an obstetric rarity with an incidence of approximately 1/100,000 pregnancies. It is associated with severe maternal and fetal complications. Most end in spontaneous abortion with less than a 40% chance of live birth. We report a case of twin pregnancy with a histopathologically proven complete mole and coexistent fetus. A 26-year-old gravida 2, para 1 woman presented with abdominal pain and vaginal bleeding. Serum β-hCG was >1,000,000 IU/mL. An ultrasonograph revealed a twin pregnancy with molar previa and coexistent fetus with 2 separate placentas (Figure 2.48, A). She underwent emergent dilation and evacuation. Macroscopic examination of the products of conception showed hemorrhagic tissue fragments admixed with a substantial amount of molar tissue (vesicles) and fetal tissue. Histology showed normal chorionic villi (Figure 2.48, B) and separate molar tissue with diffuse villous enlargement, hydropic changes, cistern formation, trophoblastic hyperplasia, and stromal mucin (Figure 2.48, C). Immunohistochemical stain for p57 was negative in villous cytotrophoblasts and stromal cells (Figure 2.48, D). A diagnosis of dichorionic twin pregnancy with complete hydatidiform mole and a coexisting fetus was confirmed. Twin pregnancy with complete mole and a coexisting fetus is rare and the majority of such pregnancies are usually terminated. Management with a viable fetus and coexistent mole is difficult and often requires complex, multidisciplinary care. Close follow-up with clinical evaluation and serial serum β-HCG is essential for diagnosing and treating persistent trophoblastic disease.
Strumal carcinoid is an unusual ovarian teratoma characterized by the presence of thyroid tissue with a carcinoid tumor. The carcinoid component is a well-differentiated neuroendocrine tumor with an excellent prognosis. We report a case of a 60-year-old nulliparous woman who presented with complaints of a decrease in appetite, urinary frequency, and left lower extremity edema. Ultrasonography showed a large multicystic pelvic lesion occupying almost the entire pelvis and measuring $24 \times 14 \times 20$ cm with internal debris concerning for either uterine or ovarian cystic carcinoma. Magnetic resonance imaging confirmed it to be an ovarian lesion. Laboratory investigation revealed elevated CA 125 (105 U/mL) and CEA (6.4 ng/mL). The patient underwent surgery. Intraoperative consultation confirmed teratoma with a prominent neuroendocrine component. Grossly, a $17 \times 14 \times 4$ cm left ovarian multicystic mass was identified. Sectioning revealed a partially solid and partially cystic mass containing clear, bloody, and mucoid fluid in different cysts. Histopathology showed foci of ectopic thyroid tissue with colloid-filled follicles admixed with foci of well-differentiated neuroendocrine tumor, grade 1 (carcinoid) displaying insular and trabecular patterns with dense stromal hyalinization consistent with the diagnosis of strumal carcinoid (monodermal teratoma). Thyroid transcription factor (TTF-1) and thyroglobulin immunostains highlighted ectopic thyroid tissue, and synaptophysin highlighted a neuroendocrine component. Strumal carcinoids are almost invariably benign and pathologic staging is not warranted. The treatment of strumal carcinoid is salpingo-oophorectomy. Papillary thyroid carcinoma may rarely arise in strumal carcinoids.

**Enteric-Type Bartholin Gland Adenocarcinoma: A Case Report and Literature Review of a Rare Vulvar Adenocarcinoma**

**Poster No. 52**

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Primary adenocarcinomas of the Bartholin gland are exceptionally rare. Enteric-type adenocarcinoma is an extremely rare variant and only 4 cases of this histologic subtype have been reported in the literature. Criteria for the diagnosis of primary Bartholin gland carcinoma (BGC) were initially described by Honan in 1897 and later revised by Chamlian and Taylor to include the following: (1) the tumor involving the area of the Bartholin gland is histologically compatible with the origin from the Bartholin gland; (2) areas of apparent transition from normal elements to neoplastic ones are found in the histologic study; and (3) there is no evidence of primary tumor elsewhere. Herein we report a case of a 57-year-old postmenopausal woman who presented with occasional vaginal spotting for 6 months. A firm, red, and fixed lesion at the right posterior fourchette was identified. The patient underwent a right radical vulvectomy with bilateral inguinal lymph node dissection after the diagnosis of adenocarcinoma was confirmed by biopsy. Gross examination showed an ulcerated, hemorrhagic mass with healed-up borders. Histologically, the neoplastic glands were lined by tall columnar eosinophilic cells with focal goblet cells reminiscent of intestinal differentiation. The tumor met the criteria for BGC diagnosis, and the immunohistochemical profile (positive for CK7, CK20, CEA, CDX2, and CA 19-9) of the tumor was identical to that reported previously for this enteric variant. Finally, other primary sites were excluded. We present this case to improve awareness of this diagnostically challenging enteric variant of Bartholin gland adenocarcinoma.

**A Report of Undifferentiated Carcinoma Arising From Cervical Endometriosis**

**Poster No. 53**

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Undifferentiated carcinoma is a rare and aggressive neoplasm. It mainly involves the endometrium and is defined as a malignant epithelial tumor without evidence of either glandular or squamous differentiation. There are no case reports in the literature that focus on undifferentiated carcinoma arising from cervical endometriosis because of the extremely rare incidence rate. We report a case of a 48-year-old woman who presented with complaints of a decrease in appetite, urinary frequency, and left lower extremity edema. Ultrasonography showed a large multicystic pelvic lesion occupying almost the entire pelvis and measuring $24 \times 14 \times 20$ cm with internal debris concerning for either uterine or ovarian cystic carcinoma. Magnetic resonance imaging confirmed it to be an ovarian lesion. Laboratory investigation revealed elevated CA 125 (105 U/mL) and CEA (6.4 ng/mL). The patient underwent surgery. Intraoperative consultation confirmed teratoma with a prominent neuroendocrine component. Grossly, a $17 \times 14 \times 4$ cm left ovarian multicystic mass was identified. Sectioning revealed a partially solid and partially cystic mass containing clear, bloody, and mucoid fluid in different cysts. Histopathology showed foci of ectopic thyroid tissue with colloid-filled follicles admixed with foci of well-differentiated neuroendocrine tumor, grade 1 (carcinoid) displaying insular and trabecular patterns with dense stromal hyalinization consistent with the diagnosis of strumal carcinoid (monodermal teratoma). Thyroid transcription factor (TTF-1) and thyroglobulin immunostains highlighted ectopic thyroid tissue, and synaptophysin highlighted a neuroendocrine component. Strumal carcinoids are almost invariably benign and pathologic staging is not warranted. The treatment of strumal carcinoid is salpingo-oophorectomy. Papillary thyroid carcinoma may rarely arise in strumal carcinoids.

**Strumal Carcinoid of the Ovary Presenting as a Large Pelvic Mass**

**Poster No. 51**

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Ovarian Sertoli Cell Tumor: Diagnostic Dilemmas in Histopathology and Immunohistochemistry

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Ovarian Sertoli cell tumor (SCT) is an uncommon gynecologic neoplasm. Overlapping histologic features and immunohistochemical staining patterns with similar-appearing sex cord–stromal tumors and non–sex cord-stromal tumors occasionally make unequivocal classification of SCT challenging. In problematic cases, therefore, rational interpretation of immunohistochemistry, along with clinicopathologic findings, contributes to diagnostic validity. A 60-year-old postmenopausal woman with a history of breast cancer presented with an increasing left adnexal mass. Ovarian neoplasm-specific tumor markers were normal, and the patient underwent surgical management. Pathologic examination of the specimen revealed a 4.2 cm left ovarian mass with intact capsule, lobulated solid yellow cut-surfaces, and absence of necrosis and hemorrhage. Microscopic evaluation (Figure 2.54, A) revealed a well-demarcated neoplasm comprising predominantly solid and hollow tubules with dispersed solid nests and cordlike patterns and intervening fibrous stroma. The tubules were lined by cuboidal cells with eosinophilic luminal secretions. Cytologically, the cells demonstrated minimal atypia and mitoses with scant pale eosinophilic cytoplasm, and granular chromatin. The differential diagnosis included sex cord–stromal tumor and carcinoid tumor. Immunohistochemistry demonstrated diffusely positive SF-1 and inhibin (Figure 2.54, B and C), compared to chromogranin (Figure 2.54, D) and synaptophysin, favored SCT, a less aggressive tumor, over carcinoid tumor. SCT is a diagnosis of exclusion; because of its rarity, it remains understudied. Further comparative studies are warranted for distinguishing SCT from carcinoid tumor.

Case of the Vanishing Endometrium

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Pseudomyxoma peritonei is a clinical term used to define a low-grade mucinous neoplasm involving the peritoneum. While some cases can arise from ovaries, urachus, or the pancreatobiliary system, 95% of cases have an appendiceal origin. This carcinoma bears high risk of metastasis to peritoneal and pelvic organs while also having the unique ability to recolonize the endometrium. We report a case of a 58-year-old woman presenting with a 2-month history of lower abdominal pain and distention. Transvaginal ultrasonography showed a 15-cm left adnexal mass that was treated with surgical debulking. The histologic findings were consistent with pseudomyxoma peritonei diffusely involving the appendix, and a diagnosis of low-grade mucinous appendiceal neoplasm was made. Sections from the uterus showed that the neoplasm had completely replaced the endometrial lining (Figure 2.55, A). The diagnosis was confirmed with immunohistochemical staining, which supported the intestinal phenotype of low-grade mucinous appendiceal neoplasm. The endometrium displayed (Figure 2.55, A through D) neoplastic cells positive for CDX2 (Figure 2.55, D) and CK20 (Figure 2.55, C), focally weak positivity for CK7, and was entirely negative for PAX8 (Figure 2.55, B). Appendiceal primary neoplasm has the ability to recolonize the endometrial lining. The lack
of associated tubal features, ciliated epithelium, and our given immunostaining pattern further strengthen the diagnosis. Accurate assessment of morphology and precise immunohistochemical staining are therefore vital to confirm such occurrences. With the absence of any histologic features supporting endometrial carcinoma, metaplasia, and cervical neoplasia, it is necessary to be aware of this finding when reviewing endometrial biopsies showing mucinous features.

Juvenile Granulosa Cell Tumor in a Young Girl With Gender Dysphoria

(Poster No. 56)

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Juvenile granulosa cell tumor (JGCT) is a rare type of granulosa cell tumor that occurs predominantly in children and young adults. JGCT occurring in prepubertal children typically presents with isosexual pseudoprecocity. We present a case of unilocular juvenile granulosa cell tumor presenting in a teenage female patient with gender dysphoria, an unusual circumstance that, to the best of our knowledge, has rarely been published. The patient presented with delayed secondary sexual characteristic, mild signs of virilization, and abdominal distension for 2 months. The patient reported sporadic menstruation since age 11 years with leg and facial hair that became prominent in the previous 3 years.

The patient had not taken any hormonal therapy. Imaging showed a large (26 cm) well-circumscribed homogeneous cystic lesion with a thin enhancing wall located centrally in the abdomen and pelvis, which abutted and flattened the ovary. It was thought to be a benign cyst. Laboratory testing revealed elevated inhibin B. The patient underwent ovarian-sparing right cystectomy. The tumor was composed of 1 large unilocular cyst, lined by a layer of stratified granulosa cells. Occasionally, small cords or groups of tumor cells within the stroma were noted. Many tumor cell groups had basophilic fluid. The nuclei of tumor cells were generally round to oval with hyperchromatic chromatin and rare nuclear grooves. Call-Exner bodies were inconspicuous but present. Scattered stromal Leydig cells were noted. Next-generation sequencing (TruSight Tumor 15) was negative for FOXL2 and other mutations. This is a rare case with complicated management and many ethical considerations.

A Challenging and Rare Case of Female Adnexal Tumor of Probable Wolffian Origin With Malignant Features

(Poster No. 57)

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Female adnexal tumor of probable Wolffian origin (FATWO) is an extremely rare tumor arising from remnants of the Wolffian duct. The most common location is the broad ligament, although the ovary and fallopian tubes can be affected. We report a case of 72-year-old woman with an 18-cm right adnexal mass detected on ultrasonography. The patient underwent total hysterectomy with bilateral salpingo-oophorectomy. Grossly, the entire right ovary was replaced by a lobulated solid to cystic lesion. Microscopically, the mass had lobular architecture composed of solid cords of tumor cells exhibiting round nuclei and pale chromatin. Slender and scattered tubules containing eosinophilic intraluminal secretions (Figure 2.57, A). A high mitotic index (>15/10 HPF) was seen, unusual for FATWO (Figure 2.57, B). Focal areas exhibited endometrioid glandular differentiation (Figure 2.57, C). Immunohistochemistry revealed the tumor cells to be strongly CD10 (Figure 2.57, D) and CD117 positive and variable for PAX-8, ER, PR, CK7, EMA, and p16. Based on the morphology, high mitotic index and immunohistochemistry profile, a diagnosis of FATWO with malignant features was made. Ovarian FATWO may histologically resemble entities such as well-differentiated endometrioid adenocarcinoma, granulosa cell tumor, Sertoli–Leydig tumor, and clear cell carcinoma, which makes this entity a true diagnostic challenge. Treatment consists primarily of surgical excision and close follow-up. The prognosis of FATWO is generally good; however, the clinical course when malignant features are present remains unknown owing to the rarity of this entity. It is important to consider FATWO in locations outside the broad ligament and to assess thoroughly for aggressive features to avoid potential diagnostic pitfalls.

Adenomyomas of the Endocervical Type: A Rare Incidental Finding in the Cervix

(Poster No. 58)

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Adenomyoma of endocervical type (AE) is a rare benign mixed epithelial and mesenchymal tumor of the female genital tract first described in the uterine corpus in 1896. AE is extremely uncommon in the cervix. Few cases were reported in middle-aged women that typically presented with polypoid masses and/or vaginal bleeding. We present the case of a 74-year-old woman with AE arising in the cervix, incidentally found after a hysterectomy with bilateral salpingo-oophorectomy for an ovarian mass diagnosed as mucinous cystadenoma. The cervix was expanded by an intramural 3.8-cm tan-white whorled well-defined lesion. Microscopically, the lesion demonstrated interfacing fascicles of smooth muscle (SM) with neurtllemmoma-like areas and a focus of bland endocervical-type mucinous glands rimmed by fibrous stroma, which in turn was enveloped by SM fascicles (Figure 2.58, A and B). No mitotic activity or atypia was noted in the epithelial or the SM component. Immunohistochemistry demonstrated estrogen receptor-positive glands and stromal cells (Figure 2.58, C) and a thin rim of CD10+ fibrous stroma surrounding the glands (Figure 2.58, D). Previous studies described the epithelial component as variably sized glands arranged in lobular configurations containing occasional papillary infoldings. The glandular lining was described as endocervical type with rare tubal, mesonephric, or endometrioid epithelium surrounded by endometrioid-type stroma reported in few cases. SM
was the predominant stromal component, with few reports of a thin rim of periglandular fibrous stroma. SM atypia was also described. Although rare, recognition of AE is important, as it can be confused with other biphasic cervical tumors including adenomyomas of (usual) endometrioid type, lobular endocervical glandular hyperplasia, adenofibroma, adenocarcinoma, and adenoma malignum.

**Molecular Evidence for Epithelial Origin of Mixed Epithelial–Germ Cell Ovarian Neoplasms**  
(Poster No. 59)  
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Ovarian germ cell tumors (GCTs) account for 2–3% of malignant ovarian neoplasms in Western countries and typically occur within the first 2 decades. When presenting later in life, GCTs may be associated with epithelial malignancies. In these circumstances, it has been theorized that these tumors may originate from a somatic, rather than germ cell origin, especially in the postmenopausal setting; however, the true derivation is not fully understood. Our database was searched for primary ovarian GCTs associated with a malignant epithelial component in patients >35 years of age, from 2006 to 2021. For each case, slides were reviewed, and targeted next-generation sequencing (NGS) was used to identify and compare gene mutation variants in morphologically distinct components. Two cases were identified. Patient A was 58 years old, with choriocarcinoma and minor component of mucinous adenocarcinoma; and patient B was 43 years old, with yolk sac tumor and minor component of endometrioid adenocarcinoma. The morphologically distinct areas in each case showed disparate staining patterns; however, NGS demonstrated identical mutation variants within both the germ cell and epithelial components. Variants in *CDKN2A*, *PIK3CA*, *PIK3R1*, and *TP53* were present in patient A’s tumor, while patient B’s tumor showed *CTNNB1*, *PIK3R1*, and 2 *PTEN* variants. These mutational patterns are similar to those seen in pure epithelial counterparts, suggesting somatic derivation of the germ cell component. These rare tumors portend a worse prognosis than pure GCTs, and understanding their origin has clinical and therapeutic implications.

**Angioleiomyoma: A Rare Variant of Uterine Leiomyoma**  
(Poster No. 60)  
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Angioleiomyoma (vascular leiomyoma) is a mesenchymal tumor composed of a variable number of smooth muscle cells swirling around thick-walled blood vessels. It can occur anywhere in the body, most commonly on extremities, but only a few cases of uterine angioleiomyoma are reported in the literature. We report a case of uterine angioleiomyoma in a 45-year-old woman who presented with chronic pelvic pain, dyspareunia, and abnormal uterine bleeding. Ultrasonography showed a 2.7-cm subserosal fibroid arising from left uterine fundus. She underwent a hysterectomy for continued symptoms despite medical management. Grossly, a 2.7-cm bulging left fundal hemorrhagic mass was identified with a maroon cut surface showing vascular lumina. Histologically, the tumor was composed of variably dilated thick and thin-walled vascular channels with scant spindle cells swirling around them. No cytologic atypia, mitotic activity, or necrosis was identified. A differential diagnosis of angioleiomyoma, vascular malformation, PEComa, and myopericytoma was considered. The spindle cells were diffusely strongly positive for smooth muscle actin, desmin, and h-caldesmon immunohistochemical stains, confirming the cells were smooth muscle in origin and supporting the diagnosis of angioleiomyoma. Uterine leiomyomas can have varied clinical presentations and can cause severe intraoperative hemorrhage. Awareness of this entity is important for managing physicians to avoid complications and for pathologists to be knowledgeable of this leiomyoma variant. This rare variant is not included in World Health Organization classification of uterine neoplasms and should be recognized as a separate variant of leiomyoma under the category of uterine mesenchymal neoplasms (Figure 2.60).

**Xanthogranulomatous Inflammation of the Uterus Presenting as a Mimicker of Malignancy**  
(Poster No. 61)  
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Xanthogranulomatous inflammation involving the female genital tract is very rare. We report a case of a 73-year-old woman who presented with diarrhea, constipation, and abdominal pain. Surgical history was significant for salpingectomy for tubal pregnancy. A C1 of the abdomen showed an enlarged, heterogeneous uterus; and magnetic resonance imaging showed a bicornuate uterus with a multilobulated, enhancing centrally necrotic uterine mass in the left endometrial cavity, measuring 4.7 cm, extending into the adjacent pelvic fat, highly concerning for malignancy. A subsequent positron emission tomography scan showed fluorodeoxyglucose avidity with a standardized uptake value max of 19.6. Robotic hysterectomy with bilateral salpingo-oophorectomy and lymph node biopsy were performed. Gross examination of the uterus showed a tan-yellow serosal indurated discoid mass measuring 4.3 cm on the posterior-lateral side. Serial sections revealed a yellow-orange lobulated noncircumscribed, nonencapsulated mass that abutted the serosa with a central area of necrosis confined to the myometrium. Microscopic examination revealed extensive histiocytic proliferation and lymphoplasmacytic infiltration diffusely involving the uterine corpus. Multifocal histiocytic proliferation also involved endometrial mucosa. Histiocytic/cytoid follicular dendritic cell neoplasm was excluded with a battery of immunohistochemical stains. AFB, GMS, Gram, and Von Kossa stains were negative. Polymerase chain reaction testing was negative for *Tropheryma whippelii* organisms. ALK-1 immunostain was negative. Immunostain demonstrated focal increase in absolute IgG4-positive plasma cells (focally >50/1 high-power field) with focal IgG4/IgG ratio more than 40%, raising a possibility of IgG4-related disease. Of note, the serum IgG4 level was normal (23.1 mg/dL). Here, we present a case of xanthogranulomatous inflammation of the uterus, a rare entity and mimicker of malignancy.

**Arteriovenous Malformation of the Uterus**  
(Poster No. 62)  
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Arteriovenous malformation (AVM) is a vascular lesion most frequently encountered in the brain, lungs, colon, and soft tissues of the extremities. It is a rare entity, however, in the uterus where it can cause abnormal and even life-threatening uterine bleeding. Here, we present the case of a 41-year-old gravida 6, para 6 woman with abnormal uterine bleeding resulting in a hemoglobin of 10.2 g/dL. On gross examination, the uterus was enlarged, measuring 17.5 × 12 × 10 cm, with a pronounced globoid appearance and bogginess on palpation. The cut surface was hemorrhagic and notable for numerous, tortuous vascular lumina of variable size. Abnormal vasculature was grossly apparent throughout the entire myometrium but was found to...
be most prominent in the lower uterine segment of the anterior wall. Microscopic examination revealed an admixture of malformed vascular structures composed of arteries, veins, and capillaries. Vessels showed prominent dilation and tortuosity with abrupt variation in thickness of the media and elastic lamina, as highlighted by Van Gieson stain. Unlike most other organ systems where AVM is generally considered a congenital lesion, uterine AVM is more often an acquired lesion following pregnancy or instrumentation, including curettage and cesarean section. Upon further review of the patient’s history, her final delivery was via cesarean section, after which she developed abnormal uterine bleeding. We present this case as a reminder to consider AVM as an unusual cause of abnormal uterine bleeding as it may be easily overlooked, even by the experienced pathologist.

Flow Immunophenotypic Analysis of Plasma Cells in AL Amyloidosis

(Poster No. 63)

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Context: AL amyloidosis (AL) is a rare plasma cell neoplasm that is characterized by the production of a fibrillar protein with the potential for systemic accumulation. We analyzed the immunophenotypic profile of AL plasma cells in AL and multiple myeloma (MM) to determine if any distinguishing properties could be identified.

Design: Flow cytometry was performed on bone marrow aspirates of 30 patients with AL and 45 patients with MM and assessed for the presence or absence, and expression level, of the following antigens: CD45, CD19, CD20, CD38, CD138, CD56, CD117, κ, and λ (surface and cytoplasmic).

Results: As expected, the percentage of clonal plasma cells was lower in AL (1.14%) than MM (15.8%) (P < .001). Residual polytypic plasma cells were also present in a greater proportion of AL cases (24/30) than MM cases (10/45) (P < .001). CD38 was positive in all cases; however, the mean fluorescence intensity was greater in the AL group (191,297) than the MM group (128,594) (P < .001). CD56 also displayed a difference in expression, with lower expression levels seen in AL (11,359) than MM (17,905) samples (P = .004). This association was independent of the frequency of clonal plasma cells.

Conclusions: Our studies demonstrate that AL differs from MM notably in both CD38 and CD56 expression intensity. These findings may explain the excellent response of AL patients to anti-CD38 therapy. In addition, given the roles of CD38 and CD56 in cell signaling and adhesion, it is possible these differences contribute to the variation in natural behavior observed between these entities.

Immunohistochemistry for P53 as a Screening Method for TP53 Mutational Analysis in High-Grade Myeloid Neoplasms

(Poster No. 64)

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Context: TP53 mutational status in acute myeloid leukemia (AML) is prognostic and may lead to alternative induction therapy; therefore, rapid assessment is necessary for precision treatment. We investigated whether p53 immunohistochemistry (IHC) can accurately predict TP53 mutations to enable quicker therapeutic decision-making.

Design: We searched cases of high-grade myeloid neoplasms with TP53 pathogenic or likely pathogenic mutations from our archives (2016–2019). Control samples included TP53-negative AML marrows (12 cases) and negative lymphoma staging marrows (6 cases). TP53 IHC was performed on both cases and controls. Two pathologists scored these cases; 2+ or more nuclear staining was considered positive.

Results: The TP53-mutated group comprised 54 samples from 48 patients with 62 pathogenic or likely pathogenic TP53 mutations. One case was excluded owing to little to no marrow space for evaluation. Most TP53-mutated cases (85.0%, 39/47) expressed p53 by IHC, and there were 2 truncating, 1 in-frame insertion, and 43 missense mutations in these TP53-mutated p53 IHC-positive cases. Among the 8 TP53-mutated IHC-negative cases, there were 7 truncating and 1 splice-site mutations. TP53 staining was negative in all control samples.

Conclusions: In this cohort of high-grade myeloid neoplasms, p53 immunopositivity correlated with TP53 mutational status, especially missense mutations, with excellent specificity. Truncating TP53 mutations explain most TP53-mutated IHC-negative cases impacting the sensitivity of IHC. This study demonstrates that p53 IHC can be used as a rapid initial screen for TP53 mutations, allowing quicker treatment decisions for most patients; however, not all patients will be identified so follow-up molecular studies will also be required.

Hemophagocytic Lymphohistiocytosis (HLH) as a Complication of Orthotopic Liver Transplant

(Poster No. 65)

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Hemophagocytic lymphohistiocytosis (HLH) is a severe systemic inflammatory syndrome, usually secondary to acute viral infections, or less frequently in association with a subset of neoplastic processes. We report the case of a 53-year-old man with primary sclerosing cholangitis, status post orthotopic liver transplant. The patient presented to the emergency department with abnormal liver function tests and supratentorial tachyarrhythmias. During his hospitalization, his condition acutely declined with the development of fever, multiorgan dysfunction, seizures, and pancytopenia. Laboratory tests revealed marked hyperferritinemia (>15,000 ng/mL) and hypertriglyceridemia (>420 mg/dL). All serologic, CSF, and culture studies demonstrated lack of bacteria, viral, and systemic fungal infections. A bone marrow biopsy was performed and demonstrated an aplastic marrow with numerous mature histiocytes, and focal hemophagocytosis. CD163 immunostaining demonstrated an increased number of infiltrating histiocytes (Figure 2.65 A through C). Consistent with the clinical microbiology studies, GRAM, AFB, and GMS immunostains performed on the bone marrow biopsy did not demonstrate morphologic evidence of infectious microorganisms. The patient fulfilled clinical criteria for HLH (meeting ≥5 diagnostic criteria for this entity), and HLH-directed therapy was initiated. Owing to the absence of a definitive infectious etiology, the development of HLH was likely triggered by liver transplant. HLH is a rare complication of orthotopic transplants, with few cases reported in the literature. The mechanism for HLH development in patients with orthotopic transplants is not well understood, although it has been hypothesized to be associated with graft dysfunction. This case emphasizes that occurrence of HLH in posttransplant patients can occur, in the absence of acute infection or malignancy.

High Correlation Is Observed Between the Incidence of TP53 Mutation and Deletion of 5q in Myelodysplastic Syndromes Patients

(Poster No. 66)

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Context: Myelodysplastic syndromes (MDS) comprise a group of clonal hematopoietic stem cell disorders with cytopenia and myeloid lineage dysplasia. MDS with del(5q) is known for its relatively benign course. TP53 mutation in MDS with del(5q) mutation has a worse prognosis than MDS with del(5q) with wild-type TP53. Here, we have investigated the incidence of different gene mutations observed in MDS with del(5q) and the correlation between TP53 mutation and del(5q).
Design: We retrospectively analyzed the cytogenetic, fluorescence in situ hybridization, and gene expression data, including a 40-gene myeloid panel of 290 MDS patients.

Results: Thirty-one patients (10.7%) met the criteria of MDS with del(5q). TP53 mutation is found in 35 patients (12.07%). Female predominance was observed in MDS with del(5q) patients (female to male ratio = 2.4) and in MDS patients with TP53 mutation (female to male ratio = 1.7). The incidence of TP53 mutation was highest in MDS with del(5q) patients (Figure 2.66, A). Forty percent of patients with TP53 mutation showed del(5q) with or without other karyotypic abnormalities. No patients with TP53 mutation showed isolated karyotypic anomaly other than del(5q). Forty-eight percent of MDS patients with TP53 mutation showed complex karyotype (MDS-CK), with more than half of them comprising del(5q) (Figure 2.66, B).

Conclusions: Our study shows that the incidence of TP53 mutation in MDS patients has a high correlation with 5q-deletion, with or without additional chromosomal anomaly. Given the better prognosis of MDS with del(5q) and a worse prognosis of MDS with TP53 mutation, the coexistence of these 2 traits possibly warrants a separate MDS subclassification with the del(5q) category.

TAFRO Syndrome-like Bone Marrow Morphology in a Patient With POEMS Syndrome

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POEMS syndrome is characterized by polyneuropathy, organomegaly, endocrinopathies, monoclonal gammopathy, and skin lesions. The bone changes associated with an essential mixed plasma cell dyscrasia are typically sclerotic. Although reticulin fibrosis may be observed, the fibrosis is classically associated with plasma cell infiltrates and shows a paratrabeclar distribution. Other disorders that may be associated with POEMS syndrome include Castleman disease, papilledema, edema, keratoconus, and thrombocythemia. Here we describe a patient with well-established POEMS syndrome with bone marrow findings that are more typically associated with TAFRO syndrome (thrombocytopenia, anasarca, bone marrow fibrosis, renal disease, and organomegaly).

Complete medical history in this patient includes Castleman disease, congestive heart failure, type II diabetes, splenomegaly, hypothyroidism, and renal insufficiency. He was treated with steroids, splenic embolization, rituximab, and melphalan, followed by stem cell transplant. The bone marrow showed minimal involvement by a plasma cell dyscrasia (<5% clonal plasma cells distributed as single interstitial cells, and small perivascular aggregates) in a hypercellular bone marrow for age (80% cellularity) with atypical megakaryocytic dysplasia (lobulated and the chromatin is hyperchromatic. In Figure 2.67, B, the incidence of TP53 mutation was highest in MDS with del(5q) patients (Figure 2.66, A). Forty percent of patients with TP53 mutation showed del(5q) with or without other karyotypic abnormalities. No patients with TP53 mutation showed isolated karyotypic anomaly other than del(5q). Forty-eight percent of MDS patients with TP53 mutation showed complex karyotype (MDS-CK), with more than half of them comprising del(5q) (Figure 2.66, B).

B-lymphoblastic Lymphoma With Atypical Presentation and Aberrant Expression of BCL-6

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B-lymphoblastic lymphoma (B-LBL) is a precursor B-cell lymphoid neoplasm presenting in extramedullary sites such as lymph nodes and skin, and patients may be asymptomatic. Rare cases have been reported that present as lytic bone lesions. BCL-6 expression is predominantly seen in mature B-cell neoplasms of germinal center origin. There are some studies showing BCL-6 expression in B-lymphoblastic leukemia, mainly in cases with t(11,19), but there are almost no studies regarding expression of BCL-6 in B-LBL. We report a case of B-LBL presenting...
with lytic bone lesions and BCL-6 expression. A 35-year-old man underwent CT scan for persistent lumbar pain, which showed lytic lesions at L4. The blood count was normal except for anemia (9.8 g/dL). L4 biopsy showed diffuse infiltrate of intermediate to large lymphoid cells with dispersed chromatin, round to irregular nuclear contours, and inconspicuous nucleoli (Figure 2.69, A). The cells were positive for PAX-5, CD20 (subset), CD10, TdT (Figure 2.69, B), BCL2, and BCL-6 (Figure 2.69, C) but negative for CD45, CD5, cyclin D1, MUM-1, CD15, CD30, and MYC. Similar results were observed from the mesenteric lymph node biopsy. Flow cytometry from the node showed abnormal B cells positive for CD19, CD20, CD23, and CD11c (subset). Fluorescence in situ hybridization studies were negative for KMT2A, BCL6, MYC, and BCL2 rearrangements. This case reports the interesting and rare presentation of B-LBL as a lytic bone lesion along with aberrant expression of BCL-6. Recognition of it is important as it can mimic “double hit” B-cell lymphoma with TdT expression.

### A Rare Case of Bone Marrow Biopsy Simultaneously Involved by Both Follicular Lymphoma and Plasma Cell Neoplasm

(Poster No. 70)

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Follicular lymphoma (FL) is a common non-Hodgkin B-cell lymphoma known for its indolent clinical course. Plasma cell neoplasm (PCN) of the bone marrow most commonly presents as myeloma with multifocal disease and organ damage. The simultaneous occurrence of FL and PCN is an extremely rare phenomenon. Here, we report a case of a 61-year-old man with concurrent FL and PCN both in bone marrow involvement. The patient presented to the clinic for a routine check-up where an incidental lymphocytosis (WBC ¼ 16 K/μL, lymphocytes ¼ 67.7%) was found on peripheral blood examination. Peripheral blood flow cytometry detected a population of monoclonal B cells with λ restriction. No peripheral lymphadenopathy was found on clinical examination. A radiology check-up found an isolated 1.3-cm lymph node in the mesentery. The bone marrow biopsy showed FL with the interstitial arrangement (about 30% of total cellularity) and the presence of a λ-restricted neoplastic plasma cell population consistent with PCN (about 15%–20% of total cellularity). Cytogenetic and fluorescence in situ hybridization (FISH) studies of the bone marrow showed t(14;18)(q32;q21), consistent with FL. In addition, t(11;14) was detected in the plasma cells. The distinct cytogenetic features and light-chain restriction (λ-restricted FL, cytoplasmic κ-restricted PCN) confirm that the 2 neoplasms arose from separate clones, with the Table summarizing immunohistochemical and cytogenetic features of these 2 neoplasms. To our knowledge, this is the first case of simultaneous occurrence of FL and PCN, both involving bone marrow.

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<tr>
<th>Comparative Immunohistochemical and Cytogenetic Features of FL and PCN</th>
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<td><strong>Follicular Lymphoma</strong></td>
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MYC Expression Is Associated With P53 Expression and TP53 Aberration and Predicts Poor Overall Survival in Acute Lymphoblastic Leukemia/Lymphoma

(Poster No. 71)

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**Context:** Acute lymphoblastic leukemia/lymphoma (ALL/LBL) is a malignancy that primarily occurs in children with overall cure rates of 85% to 90%. However, the overall survival rates of adult patients are only 40% to 50%. While TP53 mutations in ALL/LBL have been reported in multiple studies, there are limited data on p53 protein expression and its association with MYC expression and their prognostic role in ALL/LBL patients.

**Design:** We identified 177 ALL patients including 12 cases of mixed phenotype acute leukemia, 8 cases of therapy-related B-ALL, 131 cases of B-ALL, and 34 cases of T-ALL during 2003 to 2019. We retrospectively assessed p53 and MYC expression by immunohistochemistry and correlated MYC expression with p53 expression and TP53 aberration.

**Results:** Expression of p53 and MYC was present in 10.7% and 28.8% of ALL cases (n ¼ 19 and n ¼ 51), respectively. MYC expression was significantly associated with p53 expression and TP53 aberration (P ¼ .001 and P ¼ .01). p53 expression and MYC expression...
showed an adverse impact on overall survival (OS) in ALL patients ($P < .05$). MYC and p53 dual expression, as well as combined MYC expression and TP53 aberration, showed negative impact on OS in ALL patients.

**Conclusions:** MYC expression associates with p53 overexpression, TP53 aberration, and poor OS in ALL patients. MYC and p53 may work synergistically to confer a negative impact on survival in ALL patients.

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**Searching for the Culprit: Bone Marrow Metastasis From a Small Cell Neuroendocrine Carcinoma of Unknown Primary: A Rare Presenting Feature**

(Poster No. 72)

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Although bone marrow metastasis is frequently encountered with disseminated solid tumors, it is an uncommon event as a presenting sign especially with an unknown primary. In 3%–4% of patients with metastatic carcinoma, the primary site is unknown at the time of presentation. The incidence of cases presenting as bone marrow metastasis with an unknown primary is rarer still. We report a case of a 61-year-old man presenting with primary bone marrow and lymph node metastasis as the first manifestation of an occult primary tumor. On PET-CT, there was increased uptake in the supraclavicular, infraclavicular, and mediastinal lymph nodes along with marrow uptake in the axial and appendicular skeleton and a patchy consolidation in the left lung, likely inflammatory. A bone marrow biopsy was performed with a clinical impression of hematologic malignancy and was suggestive of a malignant round cell tumor with evidence of associated fibrosis in the marrow (Figure 2.72, A). Subsequently, the patient underwent a cervical lymph node biopsy displaying similar findings (Figure 2.72, B). An exhaustive panel of immunohistochemical markers revealed reactivity for pancytokeratin, synaptophysin (Figure 2.72, C and D) with a high Ki-67. CD3, CD20, CD34, CD68, CD79a, CD117, CD163, MPO, PAX-5, TdT, TTF-1, and chromogranin-A were negative. Based on the aforementioned morphologic and immunohistochemistry findings, a diagnosis of metastatic small cell neuroendocrine carcinoma was rendered. However, the primary tumor remained essentially unknown. The patient was subsequently given an empirical therapy and he later passed away. The patient underwent a cervical lymph node biopsy and an exhaustive panel of immunohistochemical markers revealed reactivity for pancytokeratin, synaptophysin (Figure 2.72, C and D) with a high Ki-67. CD3, CD20, CD34, CD68, CD79a, CD117, CD163, MPO, PAX-5, TdT, TTF-1, and chromogranin-A were negative. Based on the aforementioned morphologic and immunohistochemistry findings, a diagnosis of metastatic small cell neuroendocrine carcinoma was rendered. However, the primary tumor remained essentially unknown. The patient was subsequently given an empirical therapy and he later passed away.

Conclusions: These tumors pose a diagnostic dilemma and are of therapeutic interest. The patient subsequently received empirical therapy and later passed away. The patient subsequently received empirical therapy and later passed away.

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**Heterogeneity of Minimal/Measurable Residual Disease (MRD) Practices in Adult B-Cell Precursor Acute Lymphoblastic Leukemia (B-ALL) Underscores the Need for Further Standardizing MRD Sample Collection and Reporting: Results of a US-Based Survey**

(Poster No. 73)

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**Context:** Understanding minimal/measurable residual disease (MRD) testing practices will identify gaps limiting widespread adoption of MRD testing in B-ALL.

**Design:** Sixty-minute interviews were conducted in April 2020–June 2020 with hematopathologists (PATHs) (community n = 29, academic n = 6) and hematologists/oncologists (HEME/ONCs) (community n = 31, academic n = 7) in the United States.

**Results:** PATHs play a central role in MRD assessment. HEME/ONCs (71%) typically performed bone marrow (BM) collection in community-based practices versus nurse practitioners/physician assistants in academia (99%). In community practices, MRD methodology was primarily decided case-by-case by PATHs (90%); in contrast, 85% of academic practices had standardized protocols. Flow cytometry was the most commonly used method for MRD detection in both settings. In community practices (Figure 2.73), few respondents (PATHs: 38%; HEME/ONCs: 16%) identified the initial pull as the optimal sample for MRD testing; 28% of PATHs had encountered samples suboptimal for MRD testing owing to hemodilution. For MRD assessment in community practice, most PATHs (59%) sent samples to commercial reference laboratories, and 28% had MRD tests performed in-house. Most community PATHs (73%) noted the lack of guidelines to standardize MRD results’ reporting, indicating that evidence-based guidelines would be valuable. Engagement of the transplant (hematopoietic stem cell transplant) team occurred before induction in academia but usually after receiving MRD results in the community.

**Conclusions:** Heterogeneity in BM collection and lack of reporting guidelines underscore some of the challenges in MRD standardization. Initiatives supporting education and harmonization of best practices for collection (technique and sample handling) and standard reporting could significantly improve MRD assessment and precision care for B-ALL patients.

All authors are shareholders in Amgen.

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**Disseminated Mycobacterium tuberculosis: An Unusual Presentation and Complication**

(Poster No. 74)

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Hemophagocytic lymphohistiocytosis (HLH) is a rare, potentially fatal, systemic hyperinflammatory syndrome with exacerbated and
uncontrolled activation of histiocytes and lymphocytes against mature cells. Secondary HLH can occur in association with a myriad of underlying infections or malignancies. We present the case of a 38-year-old male prisoner with poorly controlled diabetes and no known other medical conditions. He was referred to our emergency department with a 3-week history of worsening malaise, weight loss, fever, bruising, and shortness of breath. Imaging showed pneumomediastinum, a lung nodule, and adrenal mass. Biopsy of the lung nodule revealed acid-fast bacilli. Furthermore, bone marrow biopsy showed foci of necrosis with associated acid-fast bacilli (Figure 2.74, A and B) and hemophagocytosis highlighted by CD163 stain (Figure 2.74, C and D); consequently, secondary HLH was suggested. Hence, laboratory results were reviewed and found to satisfy 5 of the 8 secondary HLH criteria. Moreover, ferritin was >10,000 ng/mL, which has been suggested to be highly suggestive of HLH. The patient was given anti-MAC therapy. Unfortunately, the patient’s status declined rapidly; he developed multiorgan failure and succumbed to the disease. Later, his culture confirmed Mycobacterium tuberculosis. In conclusion, we presented a rare and challenging case of secondary HLH associated with disseminated M tuberculosis. A high index of suspicion is required for early diagnosis and treatment, and pathologists should be aware of M tuberculosis’ association with secondary HLH.

Primary Mediastinal Large B-Cell Lymphoma in a 15-Year-Old Adolescent Male: A Rare Case Report With Complex Genomic Findings Refractory to Standard Therapy and Review of the Literature

(Poster No. 75)

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Primary mediastinal large B-cell lymphoma (PMBL) is a rare form of large B-cell lymphoma and approximately 20% to 50% of patients show persistent disease even after the standard therapy. There are limited data on genetic alterations associated with aggressive behavior. We report a case of PMBL in a previously healthy 15-year-old adolescent who presented with a cough, shortness of breath, weight loss, and a new heart murmur. CT scan revealed a 16.7-cm mass in the anterior diastinum, a lung nodule, and adrenal mass. Biopsy of the lung nodule confirmed M tuberculosis for early diagnosis and treatment, and pathologists should be aware of M tuberculosis’ association with secondary HLH.

Atypical Fluorescence In Situ Hybridization Patterns Are Associated With Aggressive Disease in Large B-Cell Lymphoma

(Poster No. 76)

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Context: Large B-cell lymphomas (LBCLs) that harbor MYC rearrangements concurrent with BCL2 and/or BCL6 rearrangements (so-called double-hit and triple-hit lymphomas) are aggressive lymphomas with a poor prognosis. Fluorescence in situ hybridization (FISH) signal patterns are sometimes atypical and include copy number alterations (CNAs) (gains or losses of the whole gene, or the 5’ or 3’ region). There remains uncertainty about whether these genetic findings impact patient outcome.

Design: We examined 34 cases of LBCL with atypical FISH patterns (28 with available follow-up information). These were classified into 1 of 3 categories. Category 1 (n = 12) included cases with atypical FISH patterns consistent with gene rearrangement. Category 2 (n = 10) included cases with CNAs, but no gene rearrangements. Category 3 (n = 10) included cases with typical gene rearrangements and CNAs. We also evaluated 27 control cases (non-double- or triple-hit cases).

Statistical analysis was performed by using Fisher exact test.

Results: Aggressive disease was defined as having partial remission after initial chemotherapy, relapse, or death. Aggressive disease was found in 22/28 patients with atypical FISH patterns (79%) and 8/27 patients in the control group (30%). The difference between the groups was statistically significant (P = .001). When each category was compared to the control group, there was also a statistically significant difference (category 1, P = .009; category 2, P = .001; category 3, P < .001).

Conclusions: Our results suggest that LBCL patients with atypical FISH patterns have more aggressive disease than patients with no rearrangements. These patients should be identified and may require more intense chemotherapy regimens.

A aberrant CD79a expression in AML with an unusual (6;21) translocation and RUNX1 rearrangement

(Poster No. 77)

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Ablarent expression of B-cell antigens in acute myeloid leukemia (AML) is associated with t(6;21)/RUNX1T1-RUNX1 and with RUNX1 mutations. The modified RUNX1 in conjunction with secondary mutations in signaling pathways causes the aberrant B-cell antigen expression in myeloid blasts. Here, we report a case of CD79a expression in therapy-related AML with t(6;21) (q13;q22) and RUNX1 rearrangement. A 73-year-old man with prior chemotherapy for Hodgkin lymphoma presented with new onset leukocytosis (WBC: 12.4 x 10^9/mL, 80% blasts). Flow cytometry revealed positive for CD34, CD117 (bright), HLA-DR, CD13, CD33, and MPO (subset). Immunohistochemical analysis of the core biopsy revealed expression of CD34, CD117, lysozyme, MPO (subset), and aberrant CD79a (dim) on the blasts. Karyotype findings were 46, XY, t(14;16)(q10;q22),-7[7]/46,XY[5]. Fluorescence in situ hybridization analysis detected -8 and extra RUNX1 signals, consistent with RUNX1 rearrangement. Molecular analysis revealed Nras G12D and U2AF1 Q157P. In this case, aberrant CD79a expression was seen in the context of a complex karyotype including t(6;21)(q13;q22) involving RUNX1. In contrast to AML with t(6;21), which is typically de novo disease with a favorable prognosis, this unusual t(6;21) was detected in the therapy-related setting. Absence of immunohistochemistry (IHC)–detected Pdx-5 is not atypical, as Pdx-5 is more widely expressed than is detectable by IHC. The 6q13 region can be involved in rearrangements, for instance with...
the MLL gene. Thus, aberrant B-cell marker expression in AML with RUNX1 rearrangement is not limited to t(8;21)/RUNX1T1-RUNX1, but can also be detected with alternate RUNX1 rearrangements.

**Rare Case of CD3+ T-Cell Larger Granular Lymphocytic Leukemia: A Diagnostic Pitfall**

(Poster No. 78)

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Large granular lymphocytic (LGL) leukemias are rare indolent leukemias and are further subclassified as T-cell LGL and chronic lymphoproliferative disorder of NK cells. T-cell LGL leukemias are almost always positive for surface CD3 in contrast to NK-cell LGL leukemias, which are usually negative. We present a rare case of surface CD3+ T-cell LGL leukemia. A 58-year-old man with a history of chronic hepatitis C status post treatment was found, 2 years prior, to have persistent lymphocytosis at an outside hospital and was reportedly diagnosed with NK-cell LGL leukemia. His current absolute lymphocyte counts at our institution were 8.4–10×10^9/L. A repeated peripheral blood flow cytometry at our institution demonstrated 45% cells expressing CD16+/CD56+ and CD3 (surface) (Figure 2.78). A follow-up bone marrow biopsy was performed, and a similar atypical lymphoid population was detected by flow cytometry. He had normal cytogenetics and negative in situ hybridization for EBER. However, T-cell clonality studies performed at our institution identified a monoclonal T-cell population, which supports a diagnosis of T-cell LGL leukemia. This case highlights a diagnostic pitfall in diagnosing LGL leukemia with routine flow cytometry panels in which the killer-cell immunoglobulin-like receptor isoforms are not included. A CD16+/CD3+ cell population does not rule out rare cases of T-LGL leukemia that have CD3+ expression. This case further substantiates the paramount importance of TCR rearrangement analysis especially in nonconventional cases for an accurate diagnosis of T-LGL.

**Results:** Immunohistochemical analysis showed numerous CD16+/CD3+ histiocytes (Figure 2.79, B) with high expression of PD-L1 (Figure 2.79, C), variable expression of IL-6/signal transducer and activator of transcription (STAT3) pathway, and mild expression of COX-2; however, vitamin D receptor (VDR) expression was constantly bright (up to 3+) (Figure 2.79, D).

**Conclusions:** Our study reveals unique findings of vitamin D pathway as the first report in KFD. It indicates the most likely factor influencing the development of KFD is vitamin D pathway. This study further illustrates the role of M2 polarized macrophages and raises the possibility of the application of a VDR inhibitor as a targeted therapy in a subset of KFD patients as indicated.

**Unusual Presentation of Myeloid Sarcoma at the Spine**

(Poster No. 80)

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Myeloid sarcoma is a rare extramedullary solid tumor composed of immature myeloid precursor cells, most commonly associated with acute myelogenous leukemia. We present the case of a 27-year-old man with acute spinal cord compression. The patient had no significant past medical history and presented with lower back pain and bilateral leg weakness associated with difficulty walking. Magnetic resonance imaging of the spine showed a new lumbar spine mass with cauda equina syndrome. Decompressive laminectomy of L3 with an open biopsy of the tumor was performed. Morphologically, the tumor was composed of monomorphic cells with enlarged nuclei, delicate chromatin, moderately prominent nucleoli, and often with prominent nuclear folds (Figure 2.80, A). There was a moderate amount of cytoplasm lightly amphiphilic to chromophobic. The tumor cells were immunoreactive for CD45, CD43, S100, vimentin, myeloperoxidase (Figure 2.80, C), and cMYC, and weakly stained for CD33 and CD117 (Figure 2.80, B). The cells were negative for cytokeratins AE1/3, CD34, and CAM 5.2, lysozyme (equivocal), SALL4, and EBER ISH. Fluores-
ence in situ hybridization was positive for PML/RARA gene rearrangement (Figure 2.80, D). A diagnosis of myeloid sarcoma was made. Subsequent bone marrow biopsy showed no involvement of marrow by the disease and PML/RARA rearrangement was negative in marrow, confirming the absence of marrow involvement. Presentation of acute promyelocytic leukemia as a myeloid sarcoma without any bone marrow involvement and as a spinal mass is very rare. Spinal cord compression from myeloid sarcoma as the initial presentation of disease is extremely rare and should be considered as a differential in patients with similar presentation.

An Unusual Case of ALK-Negative Lymphoma With a DNMT3B Mutation in a 10-Year-Old Child

(Poster No. 81)
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ALK-negative anaplastic large cell lymphoma (ALCL) is defined as a CD30+ T-cell neoplasm with variable morphologic and immunohistochemical presentations, creating a diagnostic challenge in hematopathology, and they constitute <5% of ALCLs in children. We report a case of a 10-year-old boy presenting with a large anterior mediastinal mass and bilateral pleural effusions. A core needle biopsy of the mediastinal mass showed medium to large atypical lymphoid cells with an increased amount of cytoplasm in a background of active inflammation and intestinal metaplasia. The immunoperoxidase studies marked neoplastic cells as B cells and were negative for CD5 and CD10, positive for CD43, with CD15 and CD45, and were FLAER-negative. A subsequent bone marrow core biopsy demonstrated a CD30+ lymphoproliferative neoplasm. A molecular study for B-cell and T-cell clonality revealed a polyclonal rearrangement pattern. Further analysis with next-generation gene sequencing revealed a DNMT3B mutation. The DNMT3B gene mutation results in epigenetic disruptions associated with tumorigenesis. ALK-negative ALCL has been connected to multiple genes, including MYC, TNFRSF8, TMOD1, IRF4, and DUSP22; however, the DNMT3B mutation has never been demonstrated in ALCL before. This creates a unique opportunity to review a rare case to expedite future diagnostics. Similar to this case, a minority of ALCL cases are ALK-negative, and T-cell receptor gene rearrangements are absent. The molecular application of molecular testing, the histologic features of ALCL remain vital in making the diagnosis.

Helicobacter heilmannii–Associated Extra Nodal Marginal Zone Lymphoma of Mucosa-Associated Lymphoid Tissue (MALT)

(Poster No. 82)
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Helicobacter pylori is the dominant human gastric pathogen, and only about 0.5%–0.6% of infections have been associated with Helicobacter heilmannii (HH). HH is generally found in primates, cats, and dogs. It is known to cause mild chronic gastritis and is rarely associated with peptic ulcer. Here we report an unusual case of a 74-year-old woman with a longstanding history of heartburn and iron deficiency anemia (IDA), with a subsequent diagnosis of HH-associated MALT lymphoma. Her initial esophagogastroduodenoscopy (EGD) was negative in 2011. Given her persistent IDA, it was recommended that she undergo a follow-up EGD in 2016. The patient declined the procedure and was taking H2 blockers. Owing to persistence of IDA, EGD was performed in January 2021, which showed a large area of erosive, edematous changes on the anterior gastric body. The biopsy revealed lamina propria infiltration by monomorphic population of predominately small lymphoid cells with an increased amount of cytoplasm in a background of active inflammation and intestinal metaplasia. The immunoperoxidase studies marked neoplastic cells as B cells and were negative for CD5 and CD10, positive for CD43, with CD3 predominance. The CD3 predominance was also seen in associated plasma cells. Clonal immunoglobulin gene rearrangement was detected. An H pylori stool antigen was negative. Hematoyxlin-eosin staining and subsequent immunostaining for Helicobacter showed strong coarse-lamellar-like organisms, morphologically consistent with HH. Although an extremely rare occurrence, our case emphasizes that gastric extranodal marginal zone lymphoma may arise in patients with HH infection. Appropriate treatment of HH infection may lead to complete remission of MALT lymphoma.

Paroxysmal Nocturnal Hemoglobinuria in an Essential Thrombocythemia Patient Diagnosed After COVID-19 Vaccination

(Poster No. 83)
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Paroxysmal nocturnal hemoglobinuria (PNH) is a rare hemolytic and prothrombotic disorder, occurring in 1–10 per million and can arise de novo or in the setting of bone marrow failure disorders, such as aplastic anemia, myelodysplastic syndrome, or primary myelofibrosis. Episodes of hemolysis may be triggered by various infections or inflammatory stimuli, and some report hemolysis after receiving the influenza vaccination. Here we report a case of PNH in a patient with essential thrombocytopenia (ET) after a recent COVID-19 vaccination. We report a case of a 74-year-old man with ET and PNH presenting with worsening anemia after receiving his second COVID-19 vaccination. Laboratory studies revealed pancytopenia (Hb: 6.4 g/dL, WBC: 3.78 × 10^3/L, platelets: 124 × 10^3/L), elevated LDH, low haptoglobin levels, and negative direct antiglobulin test. Reticulocyte count, bilirubin, iron, vitamin B12, and folate levels were normal. The patient was transfused. Flow cytometry analysis performed on peripheral blood showed a significant population of granulocytes (76.75%) and monocytes (93.15%) that were FLAER-negative. Approximately 1.0% of RBCs were CD59− and PNH was diagnosed.
This is a rare case of PNH that developed in a patient with ET after a COVID-19 vaccination. This case study suggests that PNH can arise in patients with myeloproliferative neoplasms (MPNs) and emphasizes the possibility that the immune response to vaccines can incite hemolysis in these patients who might not otherwise be diagnosed with PNH. Further investigation is necessary to elucidate the clonal evolution of PNH in MPN and the role of vaccinations in identifying these PNH patients.

A Comprehensive Analysis of Cytopenias and Bone Marrow Histology in Patients With a History of Metabolic and Bariatric Surgery

(Poster No. 84)

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Context: Following bariatric and metabolic surgery (BMS) patients may develop cytopenia(s) despite adequate micronutrient levels and undergo bone marrow biopsies to exclude primary bone marrow disorders.

Design: Clinical, histopathologic, and laboratory findings of patients with unexplained cytopenia(s) and history of BMS were reviewed.

Results: All patients (28 F, 11 M) were anemic, and 39% had macrocytic anemia despite no vitamin B12 or folate deficiencies. Myelodysplastic syndrome (MDS) or clonal cytopenia of unknown significance (CCUS) were diagnosed in 3 (8%) and 2 (5%) patients, respectively. Of patients without MDS/CCUS, 53% (16/30) had multiple cytopenias. Macrocytic anemia was present in significantly more patients with isolated anemia than patients with multiple cytopenias (63% versus 11%, P = .003). Rare/mild erythroid and megakaryocytic dysplasia (<10% of cells) was identified in 50% of cases with isolated anemia but just 22% of multiple cytopenias (P = .047). Patients with multiple cytopenias were more likely to have biopsy-proven fatty liver disease than those with isolated anemia (61% versus 17%, P = .02). Next-generation sequencing (NGS) for myeloid neoplasms was performed in 6 patients and aided in the diagnosis of 2 cases each of MDS and CCUS (Table). Folate, vitamin B12, and ferritin levels were frequently normal until 2017, when her total white cells became significantly elevated (5 l/100 K) and rose to 100 l/100 K in 2018 with worsening splenomegaly. Two bone marrow examinations in 2018 revealed del(5q) and acquisition of \( JAK2 \) V617F mutation. Deep sequencing targeting 50 cancer-associated genes was retrospectively performed on the sequential bone marrow specimens, which showed acquisition of \( JAK2 \) mutation in 2018 concordant to the acute worsening of leukocytosis and otherwise stable mutation pattern observed as CMML since 2010 (Table). The patient was treated with, and responded to, \( JAK2 \) inhibitor ruxolitinib. This case is unique because of the following: (1) \( 5q \) deletion is rarely reported in CMML. Similar to myelodysplastic syndrome with isolated del(5q), CMML carrying del(5q) as the sole cytogenetic abnormality may have a relatively indolent course. Interestingly, the fluorescence in situ hybridization probe for \( 5q \) deletion used in myelodysplasia is negative, suggesting a potentially different truncating site in this case. The efficacy of lenalidomide in treating CMML with del(5q) is questionable. (2) We showed the likely driving role of \( JAK2 \) mutation in 2018 in an asymptomatic patient who responded to \( JAK2 \) inhibitor ruxolitinib. This is further supported by the patient’s response to \( JAK2 \) inhibitor.

Molecular Characterization and 10-Year Follow-up of a Case of Chronic Myelomonocytic Leukemia With Del(5q) and \( JAK2 \) Mutation

(Poster No. 85)

Ranran Zhang, MD, PhD 1 (ranran.zhang@aspirus.org); Molly A. Accola, PhD 2; David T. Yang, MD 3; Ron J. Kirschling, MD. 3 Departments of 1Pathology and 2Oncology-Hematology, Aspirus Riverview Hospital, Wisconsin Rapids, Wisconsin; 3Department of Pathology and Laboratory Medicine, University of Wisconsin, Madison.

We report a unique case of chronic myelomonocytic leukemia (CMML) with del(5q) and \( JAK2 \) V617F mutation. The patient presented with anemia, thrombocytopenia, and monocytosis in 2009, and was observed as CMML since 2010 after bone marrow examination that showed a normal female karyotype. The patient remained asymptomatic until 2017, when her total white cells became significantly elevated (27 K/μL) with more than 10 K/μL monocytes, which continued to rise to >100 K/μL in 2018 with worsening splenomegaly. Two bone marrow examinations in 2018 revealed del(5q) and acquisition of \( JAK2 \) V617F mutation. Deep sequencing targeting 50 cancer-associated genes (Ion AmpliSeq Cancer Hotspot Panel v2, Thermo Fisher Scientific) was retrospectively performed on the sequential bone marrow specimens, which showed acquisition of \( JAK2 \) mutation in 2018 concordant to the acute worsening of leukocytosis and otherwise stable mutation pattern characteristic to CMML since 2010 (Table). The patient was treated with, and responded to, \( JAK2 \) inhibitor ruxolitinib. This is unique because of the following: (1) \( 5q \) deletion is rarely reported in CMML. Similar to myelodysplastic syndrome with isolated del(5q), CMML carrying del(5q) as the sole cytogenetic abnormality may have a relatively indolent course. Interestingly, the fluorescence in situ hybridization probe for \( 5q \) deletion used in myelodysplasia is negative, suggesting a potentially different truncating site in this case. The efficacy of lenalidomide in treating CMML with del(5q) is questionable. (2) We showed the likely driving role of \( JAK2 \) in leukocytosis of \( JAK2 \) CMML by sequential deep sequencing. This is further supported by the patient’s response to \( JAK2 \) inhibitor.

### Diagnostic Utility of Myeloid Neoplasm Next-Generation Sequencing Testing

<table>
<thead>
<tr>
<th>Age, Sex</th>
<th>Cytopenia(s)</th>
<th>Dyspoietic Lineage, Blast Count Percentage</th>
<th>Variant Tier Classification, Gene, Mutation (VAF%)</th>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>55, F</td>
<td>Macrocytic anemia, thrombocytopenia</td>
<td>Dysmegakaryopoiesis, 1%</td>
<td>TIER III SMC1A p.L123F (50.4%)</td>
<td>MDS-SLD (IPSS-R 3)</td>
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<td>75, M</td>
<td>Macrocytic anemia, neutropenia, thrombocytopenia</td>
<td>Rare dysmegakaryopoiesis, 2%</td>
<td>TIER II TET2 p.Q1548* (35.8%), TIER II ZRS2 c.203+1G&gt;A (70.7%), TIER III TET2 p.V1718L (49.1%)</td>
<td>CCUS</td>
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<tr>
<td>60, M</td>
<td>Normocytic anemia, neutropenia, thrombocytopenia</td>
<td>Rare dysmegakaryopoiesis, 1%</td>
<td>TIER II SRSF2 p.P95L (27.3%), TIER II TET2 p.R1440Ts<em>38 (29.9%), TIER III TET2 p.Q1523</em> (46.8%), TIER III GATA2 p.S148G (48.7%)</td>
<td>CCUS</td>
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<tr>
<td>49, F</td>
<td>Normocytic anemia, neutropenia</td>
<td>Dysmegakaryopoiesis, rare dyserythropoiesis, 1%</td>
<td>TIER I IDH1 p.R132H (46.6%), TIER II SRSF2 p.P95_R102del (40.7%)</td>
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### Mutation Profile

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<th>Gene</th>
<th>Protein</th>
<th>2010 Allele Frequency, %</th>
<th>2018-Bone Marrow-1 Allele Frequency, %</th>
<th>2018-Bone Marrow-2 Allele Frequency, %</th>
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<td>JAK2</td>
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<td>P95H</td>
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Undiagnosed Metastatic Carcinoma Presenting as Thrombotic Thrombocytopenic Purpura

(Poster No. 86)

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Microangiopathic hemolytic anemia, characterized by thrombocytopenia, hemolytic anemia, schistocytes, and microthrombi-related organ dysfunction, is seen in a variety of diseases including thrombotic thrombocytopenic purpura (TTP) and disseminated intravascular coagulation. Microangiopathic hemolytic anemia secondary to disseminated intravascular coagulation has been well described in association with carcinomas, especially with metastatic carcinoma. We present a case of a 66-year-old morbidly obese woman who presented with dyspnea and dizziness and no history of malignancy. Complete blood count showed anemia and thrombocytopenia with schistocytes on peripheral blood smear (Figure 2.86, A and B). Serum lactate dehydrogenase was markedly elevated with low serum haptoglobin and mildly elevated creatinine. Prothrombin time was mildly prolonged with elevated D-dimer. Partial thromboplastin time, fibrinogen, and fibrin degradation products were all normal. The patient was managed with plasmapheresis for TTP; however, the anemia and thrombocytopenia worsened. A bone marrow biopsy was performed to evaluate the persistent cytopenia. The biopsy showed replacement of the marrow by metastatic carcinoma, consistent with breast primary (Figure 2.86, C, pancytokeratin immunostain). Our case highlights an unusual TTP-like clinical feature as the initial presentation of undiagnosed metastatic carcinoma. Most cases of malignancy-associated hemolytic anemia have classic features of disseminated intravascular coagulation. TTP-like clinical presentation as the initial manifestation of an undiagnosed metastatic carcinoma is rare.

Widely Infiltrative Skull Base Mature B-Cell Lymphoma With Intracranial Extension

(Poster No. 87)

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Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) is the most common leukemia in adults in Western countries, accounting for approximately 25% to 35% of all leukemias in the United States. CLL/SLL involves the blood, bone marrow, and secondary lymphoid tissues. Extranodal involvement occurs in small subset of cases. Skull base CLL/SLL with intracranial extension is rare. We report a case of a 49-year-old woman presenting with left eye pain and binocular double vision of 1-week duration. Neuroimaging of her brain showed a widely infiltrative skull base mass centered over clivus (5.0 cm × 4.2 cm × 2.4 cm), involving bilateral cavernous and sphenoid sinuses, pituitary gland, pituitary stalk, and abutting optic chiasma (Figure 2.87, A). Past medical history was significant for chronic lymphocytic/prolymphocytic leukemia, diagnosed 4 years prior, treated with chemotherapy (rituxan and ibrutinib) and radiotherapy for an extradural intraspinal mass with T1-T2 cord compression. Cytogenetic workup revealed 11q deletion. Histopathologic examination of the skull base lesion biopsy showed a dense small atypical lymphoid infiltrate with clumped chromatin and pale staining areas of proliferation centers (Figure 2.87, B). The proliferation centers consisted of larger lymphoid cells, prolymphocytes, and paraimmunoblasts (Figure 2.87, C). Immunohistochemical staining of lymphoid infiltrate was positive for CD20, PAX-5, CD5, and LEF-1 (Figure 2.87, D). These findings were consistent with skull base and intracranial involvement from the patient’s known history of chronic lymphocytic leukemia/prolymphocytic leukemia. The patient is currently undergoing radiation therapy. Skull base involvement with intracranial extension is rarely seen in CLL/SLL. Early detection and treatment are associated with better outcome.

A Unique Case of Granular B-Cell Acute Lymphoblastic Leukemia With Del(9q)

(Poster No. 88)

Shuchi Zinzuwadia, BS; Shweta S. Zinzuwadia, BS; Maryam Raouf, MD; Rita Gupta, MD; Ameet R. Kini, MD, PhD (akini@lumc.edu). Department of Pathology, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois.

We report a case of a middle-aged man who presented with weight loss, headaches, and fatigue. A CBC showed a hemoglobin of 7.9 g/dL, a white cell count of 6.6 k/μL, and a platelet count of 30 k/μL. A bone marrow sample was obtained and showed numerous large immature cells (68% on a 500-cell differential count) containing nuclei with dispersed chromatin and the presence of nucleoli. These cells had moderate to abundant cytoplasm with numerous azurophilic granules. While the morphologic features suggested a myeloid malignancy, flow cytometry showed a lymphoid blast population with expression of dim CD45, CD19, dim CD10, CD34, CD22, CD33, CD38, cytoplasmic CD79a, and TdT. These blasts were negative for myeloperoxidase. Cytochemical stains for myeloperoxidase were also negative in the
biphasic myeloma. The patient is a 57-year-old woman with a history of left flank pain who underwent laminectomy for an extradural T11-T12 spinal canal lesion. Serum protein electrophoresis revealed immunoglobulin G, 783 g/dL; and κ free light chains, 2.52 mg/dL. Staging bone marrow biopsy showed normal hematopoiesis. Positron emission tomography scan revealed a 0.7 × 0.5-cm soft tissue nodule in the inferior aspect of the left breast, along with lesions involving the axial and proximal appendicular skeleton. Histology of the spinal canal and breast lesions demonstrated plasmacytoid cells with blastoid morphology (Figure 2.89, A). The cells were immunoreactive for CD38 (Figure 2.89, B) and B-cell markers, CD20, PAX5, CD79a, bcl-2, bcl-6, CD41, CD61, CD13, CD33, CD34, CD117. The neoplastic cells were negative for CD19, CD56, CD45, ALK-1, cyclin D1, and EBER. Flow cytometry detected an abnormal plasma cell population (85.6%) with equivocal light-chain restriction, and expression of both κ and λ light chains by immunohistochemistry and in situ hybridization (Figure 2.89, C and D). Molecular studies detected a clonal B-cell population with no significant MYD88 variants. Clinically, the patient achieved complete response with a revidrim, velcade, and dexamethasone regimen. This rare case highlights the challenges in detection of biphenotypic atypical myeloma for appropriate clinical management.

A Case of “RAM” Phenotype Acute Myeloid Leukemia With Associated CBFA2T3-GLIS2 Fusion and Weak to Moderate CD3 Expression by Flow Cytometry

(Poster No. 90)

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A 1-year-old female infant presented with otitis media and fever and, despite antibiotic and steroid therapy, developed a cough and shortness of breath. Her peripheral blood was notable for leukocytosis (neutrophilia, eosinophilia, lymphocytosis, and monocytosis) and 13% blasts. The hypercellular marrow aspirate had 62.4% blasts, eosinophilia, and decreased normal hematopoiesis. Bone marrow aspirate sample flow cytometry detected 29% blasts coexpressing CD34, CD117, CD53 (mod), bright CD56 and partial CD123, CD13, CD9, and CD38 expression, with weak to moderate cytoplasmic CD35 expression, and negative for CD45, HLA-DR, CD1a, TdT, surface CD3, CD2, CD7, CD4, CD5, CD8, CD10, CD303, CD57, CD11b, CD235a, CD41, CD61, monocytic (CD11c, MO2, CD36, CD14), and B-cell (CD20, CD22, CD79b, with CD19) expression noted in a very small subset, below the 20% positivity cutoff markers. CBFA2T3-GLIS2 fusion transcripts were detected by RT-PCR analysis. TCR β and γ gene rearrangements were not detected by PCR. The karyotype was 47,XX,-11[4]/46,XX[16]. This is a rare case of acute leukemia with associated CBFA2T3-GLIS2 fusion, immunophenotypically most compatible with an acute myeloid leukemia with a “RAM” phenotype despite its unusual weak to moderate expression of cytoplasmic CD3. An early T-cell precursor lymphoblastic leukemia was raised in the differential diagnosis, but lack of CD2 and CD7 and bright CD56 expression makes this later diagnosis less likely. AML with “RAM” phenotype (bright CD56, dim to negative CD45 and CD38, HLA-DR negative) has been reported with a median age of 9.8 years. Diagnosis of 1.26 years is associated with inv(16)(p13.3q24.3) and CBFA2T3-GLIS2 fusion protein.

Bone Marrow of Blastic Plasmacytoid Dendritic Cell Neoplasm Mimicking Acute Leukemia

(Poster No. 91)

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Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is an exceedingly rare, highly aggressive hematologic malignancy with poor prognosis, arising from precursors of plasmacytoid dendritic cells. BPDCN typically presents skin-limited lesions, often with or without bone marrow (BM) involvement and leukemic dissemination. We report a case of BPDCN in a 21-year-old man who initially developed multiple bruise-like brown to violaceous skin nodules (Figure 2.91, A) and rapidly progressed into disseminated leukemia within a 4- to 6-month period. Skin punch biopsy revealed dermal dense monomorphic tumor cell infiltrate composed of medium-sized cells resembling lymphoblasts. The BM aspirate showed similar atypical blasts in sheets with angulated nuclei, fine chromatin, scant agranular cytoplasm, 1 to several small nucleoli, and brisk mitotic figures (Figure 2.91, D). The marrow core biopsy displayed diffuse atypical blasts nearly completely enfacing the hypercellular marrow (Figure 2.91, B). The tumor cells are

Biphenotypic Atypical Plasma Cell Myeloma With Blastoid Morphology

(Poster No. 89)

Jason J. Siu, MD, PhD1 (jjsiu@uw.edu); Daniel Gallego, MD, MD2; Daniel Martig, MD3; Kerstin Edlefsen, MD4; Lorinda Soma, MD5; Jonathan Fromm, MD, PhD3; Andrew Cowan, MD6; Deepti Reddi, MD, MD.1 Department of Laboratory Medicine and Pathology, University of Washington, Seattle; 2Department of Medical Oncology, Seattle Cancer Care Alliance, Seattle, Washington.

Plasma cell myeloma is a proliferation of plasma cells that are monoclonal as based on immunoglobulin expression. There are rare cases of biphenotypic myeloma by electrophoresis, flow cytometry, or in situ hybridization. Here we report biphenotypic atypical myeloma with blastoid morphology that showed light-chain restriction by electrophoresis, flow cytometry, or in situ hybridization. The morphologic features of granular ALL can lead to a mistaken diagnosis of AML and therefore careful phenotypic analysis is essential (Figure 2.88).
positive for CD4 (Figure 2.91, C, right), CD56 (Figure 2.91, C, left), and CD123 (not shown); and negative for CD3, PAX5, CD34, TdT, and myeloperoxidase. Flow cytometric analysis from the aspirate demonstrated characteristic CD4, CD56, and CD123 coexpression in the blast cells. It is suggested the most common chromosomal deletions are those involving 5q, 12p13.1-p13.2/CDKN1B, 13q13.1-14.2/RB1, 6q, 15q, 9p21.3/CDKN2A/CDKN2B, and 7p12.2/IKZF1. Among these, the biallelic loss of 9p21.3 indicates a more aggressive course. Significant heterogeneity in clinical presentation and immunophenotypic profile makes BPDCN challenging to diagnose. Immunophenotyping and differentiating from other hematologic malignancies with cutaneous manifestations, including myeloid sarcoma, are essential. Allogeneic stem cell transplant may result in prolonged remissions in adults.

Pediatric Type Follicular Lymphoma: A Persistent Diagnostic Challenge
(Poster No. 92)
Sarvenaz Karamooz, MD (sarvenaz.karamooz@bswhealth.org); Eduardo Castro, MD. Department of Pathology, Baylor Scott and White, Temple, Texas.

Pediatric-type follicular lymphoma (PTFL) is a distinct variant of follicular lymphoma (FL) with limited-stage presentation and excellent response to surgical resection. Herein, we share our diagnostic challenges regarding a 11-year-old boy who presented for evaluation of a slowly growing, nontender, 3-cm firm mass subjacent to the left parotid gland. Two attempts at diagnosis with a fine-needle aspiration and a core biopsy yielded nondiagnostic material. The patient underwent a parotidectomy and excisional lymph node biopsy for definitive diagnosis. Hematoxylin-eosin stains showed an enlarged lymph node with markedly expanded, convoluted germinal centers (Figure 2.92, A), composed of enlarged atypical cells with predominantly centroblastic morphology (Figure 2.92, B). The germinal centers were negative for Bcl-2 (Figure 2.92, C) and positive for Bcl-6 (Figure 2.92, D). The B lymphocytes in the germinal centers were also positive for CD20 and CD10, and negative for CD5 and cyclin D1. Ki-67 shows a high proliferative index in the germinal centers with some evidence of polarization. Flow cytometric analysis showed k-predominant/restricted CD10+ B lymphoid cells. On this basis, the diagnosis of PTFL was rendered. Six months after surgical resection, the patient showed no evidence of disease recurrence. PTFL is a clinically indolent subtype of FL with distinctive pathologic features. Follicular proliferation with effacement of the lymph node architecture and high-grade morphology are characteristic. Given its morphologic features and immunohistochemistry, definitive diagnosis and distinction from florid follicular hyperplasia can be especially challenging. For this reason, surgical resection or a large sample is often required to evaluate architecture.

Survival Analysis of Primary Cutaneous Follicle Center Lymphoma: Lessons Learned From the National Cancer Institute Database
(Poster No. 93)
Kate Yu, MD, PhD (kateyumd06@gmail.com); Pooja Devi, MD. Department of Pathology, Robert Wood Johnson Barnabas Health Care System-Saint Barnabas Medical Center, Livingston, New Jersey.

Context: Primary cutaneous follicle center lymphoma (PCFCL) is the most common cutaneous B-cell lymphoma. We aimed to investigate the changing incidence of PCFCL during the past 10 years and factors influencing survival in PCFCL.

Design: The National Cancer Institute Surveillance, Epidemiology and End Results database from 18 registries was queried for all patients with PCFCL from 2006 to 2015. We included only PCFCL-specific death cases. Age-adjusted incidence rates per 100,000 population were calculated using the 2000 US census data. Kaplan-Meier analysis was used to estimate the survival and Cox regression models were used to calculate hazard ratios.

Results: A total of 1317 patients with PCFCL were identified, including 1014 males (77%), and 1225 (93%) were white. The most common cases were found among ages 45–54 years and the least common, among those younger than 10 years. California had the highest number of cases. Head and neck was the most common primary site, followed by the trunk. Most cases presented at Ann Arbor stage I, followed by stage IV. The incidence rates per year have increased from 0.0089 in 2006 to 0.016 in 2015. Multivariate Cox regression model showed that hazard ratios were statistically significant in the white race, males, Ann Arbor IV, no surgery, and having either radiotherapy or chemotherapy.

Conclusions: The incidence of PCFCL has increased in the past 10 years in the United States. Survival is decreased for patients with unfavorable prognostic factors including increased age, male, black race, and advanced lymphoma stage. Cancer-directed surgery has a better outcome than treatment with radiation or chemotherapy.

Burkitt Leukemia/Lymphoma: A Rare Presentation With Acute Appendicitis and Acute Kidney Injury
(Poster No. 94)
Vijay Kumar, MBBS, MD (vkumar4@umc.edu); Hardik Sonani, MBBS; Hansini Lahrwani, MBBS; John Lam, MD. Department of Pathology, University of Mississippi Medical Center, Jackson.

Appendicitis is the most common cause of an acute abdomen. An appendicular neoplasm is an incidental finding found in approximately 1% of appendectomies. Lymphoma arising from the appendix is extremely rare and is found in 0.015% of all appendicular specimens. Burkitt lymphoma (BL) is B-cell lymphoma characterized by its aggressive nature, translocation, and dysregulation of the c-Myc gene. If bone marrow analysis shows greater than 25% Burkitt blasts, it will be called Burkitt leukemia. The treatment approaches for Burkitt leukemia...
and lymphoma are similar. A 15-year-old male presented with clinical suspicion of acute appendicitis (Figure 2.94, A) and also showed right hydropneumosis and hydronephrosis due to ureteral compression by the enlarged appendix. The renal function panel showed increased creatinine level, and a renal biopsy revealed acute interstitial nephritis. The patient underwent laparoscopic appendectomy. Microscopic examination showed dense diffuse infiltration of medium-sized atypical lymphoid cells with few scattered macrophages creating a vague starry sky appearance (Figure 2.94, B). The atypical lymphoid cells were positive for CD20 (Figure 2.94, C), CD79a, CD10 (Figure 2.94, D), BCL-6, Ki-67 (100%), and 2.94, B). The atypical lymphoid cells were positive for CD20 (Figure 2.94, C), CD79a, CD10 (Figure 2.94, D), BCL-6, Ki-67 (100%), and diffuse infiltration of medium-sized atypical lymphoid cells with few scattered macrophages creating a vague starry sky appearance (Figure 2.94, B). The atypical lymphoid cells were positive for CD20 (Figure 2.94, C), CD79a, CD10 (Figure 2.94, D), BCL-6, Ki-67 (100%), and negative for BCL-2. Fluorescence in situ hybridization was positive for IGH-ATMC (8;14) fusion. The diagnosis of BL was made. The subsequent bone marrow biopsy demonstrated heavy (>90%) marrow infiltration by Burkitt blasts. Histopathologic investigations demonstrated Burkitt leukemia with isolated extranodal involvement of the appendix. The patient was subsequently started on a chemotherapy regimen. This case shows the extremely important role of clinical history, histopathologic examination, immunohistochemistry, and molecular analysis in the management of incidental diagnosis of Burkitt leukemia/lymphoma.

Prognostic Value of CD4, CD8, PD-1, and PD-L1 in T-Cell/ Histiocyte-Rich Large B-Cell Lymphoma and Nodular Lymphocyte-Predominant Hodgkin Lymphoma

(Poster No. 95)

Mohammad M. Al-Attar, MD (mohammad.al-attar@umass memorial.org); Karen Dresser, BS; Jacob R. Bledsoe, MD. Department of Pathology, University of Massachusetts Medical School, Worcester.

Context: T-cell/histiocyte-rich large B-cell lymphoma (TCHRLBCL) consists of atypical B-cells in a background of T cells and histocytes. Most TCHRLBCL cases are rich in background CD8 T cells, but recent studies have demonstrated cases with background CD4 T-cell predominance and abundant PD-1-positive cells, highlighting possible biological similarities between TCHRLBCL and nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL). We explore the clinicopathologic characteristics of TCHRLBCL and NLPHL, including PD-1 and PD-L1 expression, background T-cell types, and prognostic value of such findings.

Design: Immunohistochemistry for CD4, CD8, PD-1, and PD-L1 was performed on 17 NLPHL and 6 TCHRLBCL cases. PD-1 and PD-L1 expression was assessed on both neoplastic and background inflammatory cells and scored by staining intensity and frequency. Background T cells were scored as CD4 or CD8 predominant. Clinicopathologic characteristics were collected from medical records. Statistics were performed via Fisher exact test and survival by the Kaplan-Meier method.

Results: Clinical and immunophenotypic findings are summarized in the Table. Compared to NLPHL, TCHRLBCL showed a trend toward inferior overall survival (P = .06); there was no significant difference in overall or relapse-free survival between CD4 and CD8-predominant TCHRLBCL.

Conclusions: A subset of TCHRLBCLs demonstrates prominent background CD4+ cells including some cases with abundant PD-1–positive T cells, similar to NLPHL. A CD4 or PD-1-predominant background does not preclude the diagnosis of TCHRLBCL. Larger studies are needed to evaluate the clinical significance of these findings and whether CD4-predominant TCHRLBCL shares clinical features with NLPHL. Both NLPHL and TCHRLBCL have a high rate of PD-L1 expression, and checkpoint inhibition may be useful in these cases.

**Clinical and Immunophenotypic Characteristics of Studied Cases**

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<th>Lymphoma Type</th>
<th>TCHRLBCL</th>
<th>NLPHL</th>
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<tbody>
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<td>17</td>
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<tr>
<td>Median age at diagnosis</td>
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<td>60</td>
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<tr>
<td>Cases with CD4-predominant inflammatory, male to female ratio</td>
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<td>11:6</td>
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<td>Cases with CD4-predominant inflammatory background</td>
<td>3 (50%)</td>
<td>17 (100%); P = .01</td>
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<tr>
<td>Cases with CD8-predominant inflammatory background</td>
<td>3 (50%)</td>
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<td>Cases with frequent background PD-1-positive cells/total number of cases</td>
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<td>15 (88%; P = .05)</td>
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<td>Cases with PD-L1 expression in lymphoma cells/total number of cases</td>
<td>4/5 (80%)</td>
<td>15 (88%)</td>
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<td>PD-L1-positive background cells</td>
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An Unusual “Polyclonal” B-Cell Population Due to Two Underlying Clones: A Diagnostic Pitfall

(Poster No. 96)

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Flow cytometry provides a robust method to identify B-cell lymphoproliferative disorders by assessment of κ:λ light-chain ratios. A normal κ:λ ratio is approximately 1.5:1, and ratios that are <0.5 and >3 are considered to be evidence of B-cell clonality. We report a case of a middle-aged man who presented with absolute lymphocytosis. The patient did not report fever, weight loss, or night sweats. Physical examination did not reveal lymphadenopathy or any other significant findings. Flow cytometry revealed a B-cell population with expression of CD19 and CD20 with a κ (Figure 2.96, A) to λ (Figure 2.96, B) ratio of 2.5:1, suggestive of a polyclonal lymphocytosis. However, all the B cells expressed dim CD20 with coexpression of CD5 (Figure 2.96, C) with virtually no normal B cells. In addition, examination of a peripheral blood smear (Figure 2.96, D) demonstrated the presence of small lymphocytes with minimal cytoplasm and nuclei with dense chromatin.
in a “soccer-ball” pattern, reminiscent of chronic lymphocytic leukemia. For further analysis, conventional cytogenetic and fluorescence in situ hybridization (FISH) studies were performed that exhibited 2 distinct clones. The first clone revealed an interstitial deletion in 13q, t(1;2), and t(6;6). The second clone revealed trisomy 12. The presence of these 2 clonal populations likely corresponds to the appearance of the “normal” k2 ratio as demonstrated by flow cytometry. This case illustrates the importance of a comprehensive analysis including morphologic examination, and if necessary, cytogenetics and FISH studies to arrive at the correct diagnosis.

**Lymph Node Biopsy Showing Concurrent Features of In Situ Follicular Neoplasia/Partial Involvement by Fl and Garden-Variety Follicular Lymphoma**

(Poster No. 97)

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A 71-year-old man presented with increasing pain in his abdomen and back. A computed tomography scan revealed retroperitoneal lymphadenopathy. Excisional biopsy revealed 1 lymph node, 0.9 x 0.6 x 0.3 cm, which was submitted in 2 blocks. Block 1 (Figure 2.97, A, H&E) revealed reactive architecture with multiple secondary follicles of varying sizes with polarized mantle zones, and germinal centers containing tingible body macrophages, separated by abundant interfollicular space with patent sinuses, supporting reactive features. Block 2 (Figure 2.97, C, H&E) showed similar morphology, although there were focal areas of effaced nodal architecture, confluence of lymphoid follicles, and sparse intervening interfollicular space. Some of the follicles were poorly formed, with less defined mantle zones, and nonpolarized germinal centers lacking tingible body macrophages, supporting lymphoma. Immunohistochemical stains showed that the germinal center B cells in both blocks coexpressed CD10, Bcl-6, and Bcl-2 (Bcl-2 immunohistochemistry stain shown in Figure 2.97, B and D). This case showed concurrent features of in situ follicular neoplasia/partial involvement by FL and garden-variety follicular lymphoma in the same lymph node—findings that provide insight into the biology of the neoplastic cells. The presence of these 2 clonal populations likely corresponds to the appearance of the “normal” k2 ratio as demonstrated by flow cytometry. This case illustrates the importance of a comprehensive analysis including morphologic examination, and if necessary, cytogenetics and FISH studies to arrive at the correct diagnosis.

**Adult T-Cell Lymphoma/Leukemia With T-Helper Follicular (Tfh) Immunophenotypic Features**

(Poster No. 98)

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Adult T-cell lymphoma/leukemia (ATLL) is a mature T-cell neoplasm caused by human T-cell leukemia virus, type 1 (HTLV-1). It has a broad spectrum of cytologic and morphologic features. Immunophenotypically, the neoplasm is CD4+, CD25+, and CD7+. We present a case of ATLL with T-helper follicular (Tfh) immunophenotypic features. A 71-year-old woman presented with weight loss, night sweats, diffuse lymphadenopathy, leukocytosis, and hypercalcemia. A cervical lymph node excision revealed sheets of small-medium lymphocytes with coarse chromatin, inconspicuous nucleoli, and scant cytoplasm. The neoplastic cells were immunopositive for CD3, CD4, CD25 (weak), Bcl-6, and PD-1, while negative for CD7, CD8, and CD10. There were scattered cells positive for Epstein-Barr virus in situ hybridization (EBER). CD21 highlighted small residual dendritic meshes. Flow cytometry analysis of the peripheral blood identified abnormal T cells positive for cytoplasmic CD3, CD4, CD5, and negative for CD2, CD3 (surface), CD7, CD16, CD25, CD30, and CD56. A bone marrow biopsy showed disease involvement. Targeted sequencing studies showed CCND3, SLCAB1, and TP53 mutations, which have been described in ATLL. Mutations in CD38, ETS1, and PRMT1 were also reported. HTLV-1 serology and polymerase chain reaction (PCR) testing were positive, confirming the diagnosis of ATLL. PD-1 expression has been reported in ATLL; however, BCL6 expression, alone or concurrently with PD-1, has not been described. Here, expression of BCL6 and PD-1 raises a concern for T-cell neoplasm with Tfh origin, but was excluded on the basis of HTLV-1 PCR and supported by molecular genetic studies. This case highlights the immunophenotypic spectrum of ATLL, which can be a potential diagnostic pitfall.

**Rare Presentation of B-Lymphoblastic Leukemia/ Lymphoma With Intussusception in an Older Adult**

(Poster No. 99)

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B-lymphoblastic leukemia/lymphoma (B-ALL/LBL) is a neoplasm of B-cell precursor lymphoid cells. B-LBL constitutes about 10% of LBLs in most age groups, and almost all are of T-cell lineage. B-ALL/LBL is primarily a disease of children with 64% of B-LBLs in patients <18 years. In older adults it is an extremely rare occurrence. We present a case of a 46-year-old man with no pertinent medical or surgical history who presented with severe abdominal pain, nausea, and emesis. An abdominal CT was suggestive of strangulation of the distal small bowel and ischemia, showed extensive matted lymphadenopathy in the mesentery, and multiple left suprarenal periaortic nodes measuring up to 1.1 cm. A bowel resection was performed and there was an ileocolic intussusception with the right colon filled with the intussuscpted terminal 20 cm of ileum (Figure 2.99, A). Opening the specimen revealed a submucosal ileal mass that measured 3 x 2.2 x 1.3 cm (Figure 2.99, B) with a well-circumscribed, tan-white cut surface. Histologic examination showed a diffuse infiltrate composed of small and medium-size cells extending through the ileal wall from mucosa to subserosa (Figure 2.99, C), with irregular nuclear contours, open chromatin, inconspicuous nucleoli at the correct diagnosis.
(Figure 2.99, D), occasional mitoses, and frequent apoptotic bodies. Flow cytometry revealed 29% blasts expressing CD19, CD10, dim partial CD20, CD38, cCD79a, dim CD22, and nTdT consistent with B lymphoblasts, and corresponding to the diagnosis of B-ALL. BCR/ABL translocation by fluorescence in situ hybridization was not detected. Cytogenetics analysis showed a normal male karyotype 46,XY. B-ALL/ LBL is rare in older adults and can involve nodal and extranodal sites; however, the gastrointestinal tract is rarely compromised, with few cases reported in the literature.

**Aberrant CD3 Expression in Plasmablastic Lymphoma in the Context of Monomorphic Post-transplant Lymphoproliferative Disorder: A Diagnostic Pitfall**  
(Poster No. 100)

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Immunohistochemistry with various B- and T-cell antigens is paramount in diagnostic classification, management, and prognostication of lymphomas including posttransplant lymphoproliferative disorders (PTLDs). Lineage misclassification of high-grade lymphomas due to aberrant lineage marker expression can pose a diagnostic challenge, sometimes leading to a misdiagnosis. We report a case of a 63-year-old woman with a history of kidney transplant who presented with abdominal pain and anemia. Upper gastrointestinal endoscopy revealed a 7-mm erythematous, friable, nodular lesion in the duodenum, which was subsequently biopsied. Microscopic examination of the biopsy showed diffuse infiltrates of large, pleomorphic discohesive tumor cells within the lamina propria, distorting the villous architecture (Figure 2.100, A). Tumor cells have round nuclei, open chromatin, prominent nucleoli at least in a subset, and abundant eosinophilic cytoplasm. Immunohistochemistry showed the neoplastic cells to be strongly positive for CD3 (Figure 2.100, B), CD138 (Figure 2.100, D), and MUM1. They were negative for B-cell lineage-associated markers, CD20 (Figure 2.100, C), PAX5, and CD79a and all other T-lineage markers (CD2, CD4, CD8, CD5, and CD7). Tumor cells were negative by in situ hybridization. Clonal immunoglobulin IGH rearrangement was positive and T-cell rearrangement was negative, excluding a T-cell lineage. Aberrant CD3 expression in plasmablastic lymphoma is uncommon and can lead to erroneous diagnosis of peripheral T-cell lymphoma or extranodal NK/T-cell lymphoma without careful morphologic assessment, a high degree of suspicion, incorporation of additional B- and T-cell markers, and genetic studies. In the context of PTLD, this is the first report of CD3 expression in plasmablastic lymphoma.

**Chronic Myeloid Leukemia With Cutaneous Manifestation in an Adolescent Patient**  
(Poster No. 101)

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Chronic myeloid leukemia (CML) is rare among children, accounting for 2% of leukemias in patients younger than 15 years and 9% between 15–19 years of age, with an annual incidence of 0.6–1.0 and 2.1 per million, respectively. Its clinical presentation is usually more aggressive than that in adults. Lymphadenopathy and cutaneous or other tissue infiltration is uncommon; when present, accelerated or blast phases are suspected. We present a case of a 16-year-old male diagnosed with CML with cutaneous manifestations. The patient presented with a palpable abdominal mass. Initial workup revealed WBC count >428 K/μL with 2% blasts, Hb of 8.6 g/dL, elevated uric acid and lactate dehydrogenase, hepatomegaly, and massive splenomegaly. Fluorescence in situ hybridization (FISH) on peripheral blood demonstrated BCR/ABL1 rearrangement in 195/200 scored cells (97.5%). Bone marrow biopsy showed 100% cellularity with absolute myeloid hyperplasia, absolute erythroid hypoplasia, and an increased number of small megakaryocytes (Figure 2.101, A and B). Altogether, these findings were consistent with a diagnosis of CML. Furthermore, a 1.3-cm nodule on the right lateral hip was noted. Core needle biopsy showed fibroadipose tissue infiltrated by mature neutrophils forming microabcesses, eosinophils, and infrequent immature forms (Figure 2.101, C and D). Flow cytometry identified 1% CD34+ myeloblasts and FISH confirmed BCR/ABL1 rearrangement. The findings were concerning for CML subcutaneous involvement and possible accelerated phase. However, the possibility of passive tissue infiltration by circulating neoplastic myeloid cells in a patient with hyperleukocytosis could not be excluded, posing a challenge in determining disease progression. This case shows the difficulties in evaluating extramedullary involvement in CML.
formation on peripheral blood smear. Serum protein electrophoresis showed an IgM monoclonal protein (4.2 g/dL) with marked suppression of polyclonal γ globulins. CT scans showed enlarged mediastinal, hilar, upper abdominal, and retroperitoneal lymph nodes. No lytic lesions were seen on bone survey. Subsequent bone marrow biopsy showed hypercellular marrow with sheets of small lymphoid cells with lymphoplasmacytoid morphology (80%). They were positive for CD20, CD10, CD200 (subpopulation), PD-L1 (subset), and negative for CD56 and CD117. Concurrent flow cytometry immunophenotyping showed a minute population of γ-restricted monotypic B cells (CD5−/CD10+) (Figure 2.102, A through D) besides an overwhelmingly predominant population of γ-restricted monotypic plasma cells with partial expression of B-cell antigens. The working diagnoses included IgM plasma cell myeloma (PCM) with or without concurrent lymphoplasmacytic lymphoma (LPL), and CD5− mantle cell lymphoma with exuberant plasmacytoid differentiation. Subsequent fluorescence in situ hybridization studies detected t(11;14) (CCND1-IGH) rearrangement. Molecular NGS testing was negative for MYD88 mutations. The overall features favored a diagnosis of IgM PCM with a concurrent CD5−/CD10− lymphoproliferative disorder (non-LPL). There can be significant pathologic overlap between IgM PCM and lymphoplasmacytic lymphoma, with rare cases of composite conditions making it even more complicated; and henceforth careful bone marrow assessment is required, coupled with molecular and cytogenetic analysis.

Atraumatic Splenic Rupture With Lipogranuloma Formation in a Patient With Recent History of SARS-CoV-2 Infection

(POSTER NO. 103)
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Literature reports have shown that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections affect multiple organ systems, leading to systemic consequences due to inflammation, thrombosis, and hemorrhage. In the spleen, white pulp atrophy, red pulp hypercellularity, and sinus congestion. However, in this case of SARS-CoV-2-related splenic rupture, prominent lipogranuloma formation, a phenomenon not typically present in other cases of virus-associated splenic rupture, was additionally noted. Lipogranuloma formation has previously been reported in association with splenic rupture and is known to occur in the spleen owing to infection or systemic inflammatory diseases, possibly as a consequence of immunologic stimulation. It has been hypothesized that immunologic stimulation may contribute to splenic rupture, and, in this case, immunologic stimulation by SARS-CoV-2 infection may have contributed to splenic rupture. Atraumatic splenic rupture and lipogranuloma formation secondary to SARS-CoV-2 infection are unique findings, and further research to elucidate the mechanism of lipogranuloma formation and its association with splenic rupture is warranted.

Lymphocytic-Variant of Hypereosinophilic Syndrome Progressing to T-Cell Lymphoma

(POSTER NO. 104)
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Lymphocytic variant of hypereosinophilic syndrome (L-HES) is a rare subtype of hypereosinophilic syndrome characterized by reactive eosinophilia and aberrant or clonal T cells. We report a case of a 63-year-old woman who presented with diffuse musculoskeletal pain and recurrent fever with persistent eosinophilia for 11 months. Extensive workup revealed negative blood cultures, and bone marrow biopsy showed no lymphadenopathy. Flow cytometry of peripheral blood demonstrated an aberrant T-cell clone, which was confirmed with a clonal T-cell receptor (TCR) γ gene rearrangement demonstrated by polymerase chain reaction (PCR). Karyotype was normal and fluorescence in situ hybridization was negative for rearrangement of PDGFRα, PDGFRβ, and FGFR-1. BCR-ABL and JAK2V617F were absent by PCR. Bone marrow biopsy revealed hypercellular marrow with marked eosinophilia. CD3+ T cells demonstrated an aberrant phenotype, double positive for CD4 and CD8, negative for TdT and CD1a. The morphology and immunophenotypic and molecular studies support the diagnosis of L-HES, with concurrence by outside expert opinion. Three months later, the patient presented with severe anemia. On imaging, numerous ill-defined intraperitoneal and retroperitoneal soft tissue nodules and hepatosplenomegaly were noted. Core biopsy of the liver revealed diffuse involvement of hepatic sinusoids by T-cell lymphoma positive for CD3, CD4, and CD8, and negative for granzyme, CD5, CD30, and CD20, best classified as peripheral T-cell lymphoma, not otherwise specified (NOS). This case serves to raise awareness of L-HES as a rare subtype of hypereosinophilic syndrome and emphasize its uncertain biologic behavior, in this case as a harbinger to development of overt T-cell lymphoma.

Bone Marrow Classic Hodgkin Lymphoma in HIV-Positive Patients Frequently Demonstrating Hemophagocytic Lymphohistiocytosis Symptoms

(POSTER NO. 105)
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Context: Classic Hodgkin lymphoma (CHL) usually involves lymph nodes and rarely bone marrow (BM). In HIV-positive patients, primary bone marrow CHL is seldomly reported. The clinicopathologic features of CHL involving BM in HIV-positive patients have not been well characterized.

Design: We retrospectively reviewed the cases of CHL involving BM in HIV-positive patients from January 2000 through October 2020 in a single health care center, including 23 HIV-positive patients (20 men, 3 women; median age, 42 years [range, 24–62 years]) with CHL involving BM.

Results: Seventeen patients (73.9%) had systemic disease, and 6 (26.1%) had BM disease only. Histologic examination showed lymphoma cells amidst mixed inflammatory infiltrate, including numerous histiocytes and mature lymphocytes in BM. The lymphoma

Abstracts
cells were positive for CD30, PAX5 (dim), and MUM-1, and negative for CD3, CD20, and CD79a in all 23 cases examined. Epstein-Barr virus stain was positive in the lymphoma cells in 14/16 cases (87.5%). All 6 patients with primary bone marrow CHL presented with “hemaphagocytosis” symptoms such as fever, pancytopenia, splenomegaly, and markedly elevated ferritin levels. With a median follow-up of 16.4 months (range: 0.4–182.7), the median survival for patients with systemic CHL involving BM was 60.4 months, which was not significantly different from patients with primary bone marrow CHL (P = 0.6).

Conclusions: In summary, CHL involving BM tends to present with “hemaphagocytosis” symptoms. HIV-positive patients have a higher incidence of primary bone marrow CHL, indicating that the diagnosis of CHL involving BM should be considered among HIV-positive patients. Furthermore, HLH should be investigated and treated in HIV-positive patients with CHL involving BM.

Equivocal Use of Flow Cytometry in the Initial Diagnosis of Myeloproliferative Neoplasms: A Multi-Institutional Study

(Poster No. 106)

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Context: While flow cytometric immunophenotyping (FCI) plays an important role in the diagnostic workup of many hematopoietic malignancies, its role in the diagnosis of myeloproliferative neoplasms (MPNs) is not well established. To this end, we investigated the utility of FCI in the initial diagnosis of suspected MPNs.

Design: A retrospective review of 212 bone marrow biopsies obtained at 4 institutions from 2013 to 2021 for suspected MPN (neutrophilia, polycythemia, thrombocytosis, and/or eosinophilia) was performed. Cases with a known history of a hematopoietic malignancy were excluded.

Results: Of 212 total cases, final diagnoses included nonneoplastic (23%), myeloproliferative neoplasm, unclassifiable (22%), chronic myelogenous leukemia, chronic phase (20%), essential thrombocytopenia (17%), polycythemia vera (9%), primary myelofibrosis (8%), chronic myelogenous leukemia, accelerated phase (0.5%), and myeloid/lymphoid neoplasm with PDGFRα rearrangement (0.5%). The most common molecular findings included BCR/ABL gene fusion (21%), JAK2 mutations (34%), and CALR mutations (8%). Eighty-one percent of cases had normal flow cytometry, 3% had blasts between 2%–3%, 3% had blasts between 3%–6%, and 15% of cases showed other nonspecific abnormalities, to include most commonly myeloblasts with aberrant CD7 expression, granulocytes and/or monocytes with CD16 expression, granulocytes with loss of CD16, myeloid hyperplasia, and T cells with aberrant loss of CD2.

Conclusions: In all cases, the final diagnosis was ultimately made through morphologic, molecular, and cytogenetic testing, independently of FCI findings. Deferring FCI from the initial diagnostic workup of MPNs would save the institutions involved $91,885, $29,325, $17,595, and $11,730 annually, in addition to costs associated with further workup of incidental findings.

Peripheral T-Cell Lymphoma, Not Otherwise Specified, of the Base of Tongue in a Patient With Active HIV Infection

(Poster No. 107)

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B-cell lymphomas are the second most common malignancy in patients with human immunodeficiency virus (HIV) infection, accounting for almost 90% of all lymphoma cases in HIV-positive patients. T-cell lymphomas (TCLs), in contrast, are considerably rare, more so in HIV patients. Unlike B-cell lymphomas, a strong causal association does not exist between HIV infection and TCL. According to the World Health Organization, only few rare TCL cases have been reported, mainly mycosis fungoides, anaplastic large-cell lymphoma, and nasal-type NK/T-cell lymphoma. We present a case of a 68-year-old immunosuppressed patient, secondary to active HIV infection (HIV-RNA polymerase chain reaction quantification: 685 copies/mL, absolute CD4 cells: 104 cells/mm³), with a discrete enlarging mass in the anterior submandibular region of 1-month duration. Computed tomography scan of the neck revealed a 3.5-cm solid midline submandibular mass, right tongue base mass, and left posterolateral oropharyngeal fullness concerning for neoplasm. Under direct laryngoscopy, biopsies were taken and sent for histopathologic assessment. Microscopic evaluation revealed sheets of medium to large cells with pleomorphic, irregular, hyperchromatic nuclei; prominent nucleoli; and frequent atypical mitotic figures. Neoplastic cells were positive for CD45, CD3, CD5 (weak expression), CD30, and CD43 (weak expression) (Figure 2.107) and were negative for CD8, CD10, BCL6, CD34, TDT, ALK-1, EMA, Granzyme-B, CD56, and PAX-5. Epstein-Barr virus-encoded RNA (EBER) in situ hybridization was negative. Microscopic and immunohistochemical findings supported a diagnosis of peripheral TCL, not otherwise specified (PTCL, NOS). This case highlights the fact that, although very rare, PTCL, NOS can occur in HIV patients. More research is needed in establishing causal association between HIV and TCLs.
identified as well. The presence of hematopoietic precursors outside the bone marrow is compatible with EMH, which rarely occurs in the retroperitoneal/perinephric space. In adults, EMH warrants further hematologic workup.

### Atypical Plasma Cells With Unique Cytoplasmic Crystalline Inclusions in Breast Cancer Status Post Chemoradiotherapy

**Poster No. 109**

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Intracytoplasmic crystalline inclusions are uncommon but well-documented findings in lymphoplasmocytic proliferative disorders, and rarely in reactive plasma cell infiltrate. Here we report a case of a 70-year-old woman with breast invasive ductal carcinoma, status post lumpectomy and chemoradiotherapy, who underwent right mastectomy for recurrence. Sections of the specimen showed prior excision scar with extensive atypical plasma cell infiltration. These cells were oval to spindle shaped with eccentric nuclei and bright eosinophilic cytoplasm containing abundant elongated and needle-shaped crystalline inclusions that were arranged in fan/broom shapes and parallel arrays (Figure 2.109, A). They were positive for CD138 (Figure 2.109, B), CD38, CD79a (Figure 2.109, C), IgG, \(\lambda\)-light chain (Figure 2.109, D), Mum-1, and CD56, while negative for \(\kappa\)-light chain, IgA/D/M, desmin, and CD68. The crystalline inclusions were composed of \(\lambda\)-restricted immunoglobulin. No remarkable history or laboratory evidence of lymphoproliferative or plasma cell disorder in this patient was noted. A diagnosis of atypical plasma cells with cytoplasmic crystalline inclusions was made. Various forms of intracytoplasmic crystalline inclusions have been reported in reactive or neoplastic plasma cells, including rod shaped, Auer rod-like, rectangular, cylindrical, and rhomboid. There were only 2 cases demonstrating needle-shaped crystals arranged in fan shapes and parallel arrays like our case, but the plasma cells were polyclonal and reactive, and the crystals did not stain for immunoglobulin. In our case, it is unclear whether the development of this atypical monoclonal plasma cell is associated with chemoradiotherapy. Proper immunohistochemical studies play an important role in making the distinction and follow-up is recommended.

### Post-transplant Lymphoproliferative Disorder of the Central Nervous System, Manifesting as Epstein-Barr Virus (EBV\(^+\)) Diffuse Large B-Cell Lymphoma

**Poster No. 110**

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Posttransplant lymphoproliferative disorders (PTLDs) are lymphoproliferations that develop owing to immune suppression in a recipient of a solid organ or stem cell allograft. Most PTLDs are associated with Epstein-Barr virus (EBV) infection. The central nervous system (CNS) is rarely involved, either as the only site of disease or in association with multiorgan involvement. We report a case of a 60-year-old woman who presented with diplopia, blurring of the left eye, and intermittent headaches for 4 weeks. Her past medical history was significant for a liver transplant 6 years prior for acute liver failure of undetermined etiology. On imaging, multiple lesions in the brain were noted. A biopsy of the right frontal lobe revealed variable numbers of large, transformed cells and Hodgkin-like cells positive for CD20, PAX5, CD30, CD15 (occasional), BCL6, and MUM-1 in a polymorphous background of small T cells, B cells, plasma cells, and histiocytes (Figure 2.110). In situ hybridization for EBV (EBER) was positive in neoplastic large B cells (Figure 2.110). The morphologic and immunophenotypic features establish the diagnosis of monomorphic posttransplant lymphoproliferative disorder (M-PTLD), manifesting as EBV\(^+\) diffuse large B-cell lymphoma (DLBCL). This case is a rare example of PTLD primary to the CNS and illustrates 2 important points: PTLD of the CNS is typically EBV\(^+\), whereas primary DLBCL of the CNS is typically EBV\(^-\); and despite the morphologic appearance of large B cells in a polymorphous background, EBV\(^+\) DLBCL in the transplant setting is classified by the World Health Organization Classification of Tumors of Haematopoietic and Lymphoid Tissues as a form of monomorphic PTLD.
Clinical Utility of Molecular Profiling in Characterization, Diagnosis, and Prognosis of Pediatric Non-Hodgkin Lymphomas: A Single-Center Experience
(Poster No. 111)

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Context: Non-Hodgkin lymphomas (NHLs) account for 7% of childhood cancers in the developed world. The clinical utility of next-generation sequencing (NGS) is not well established in pediatric NHL patients when compared to the more common precursor lymphoblastic leukemia/lymphomas.

Design: The NGS heme panel sequenced DNA (406 genes), RNA (265 genes), and introns (31 gene rearrangements). We retrospectively reviewed the salient molecular profiles of 14 pediatric patients (<21 years) from 2017–2020, wherein NGS results helped characterize/establish definitive diagnoses.

Results: The cohort was composed of 32 pediatric NHL cases, including B-cell NHL: 2 diffuse large B-cell lymphomas (DLBCLs); 1 EBVþ DLBCL; 1 ALKþ large B-cell lymphoma (LBCL); 2 LBCLs with IRF4 rearrangement; 4 pediatric-type follicular lymphomas (PTFLs); 3 primary mediastinal large B-cell lymphomas (PMBLs); 8 Burkitt lymphomas (BLs); 2 aggressive B-cell lymphomas; T-cell NHLs: 8 ALKþ anaplastic large cell lymphomas (ALCLs); and 1 CD30þ lymphoproliferative disorder. NGS was performed in 43% of total cases: 100% of LBCLs with IRF4 rearrangement, 75% of PTFL cases, and 66% of PMBL cases. NGS helped establish ALKþ ALCL, small cell variant diagnosis in a child who presented with cerebrospinal fluid involvement. While 1 BL case lacked an identifiable MYC rearrangement by fluorescence in situ hybridization, it was detected by NGS in addition to CDKN2A ID3, and TP53 mutations, the latter being associated with poor outcomes. PMBLs had high TMB values (15–23 Muts/Mb), while ALKþ ALCLs had the lowest (1 Muts/Mb). All NHL cases were microsatellite instability (MSI) stable (Table).

Conclusions: NGS profiling can help resolve pediatric lymphoma diagnoses, besides furthering understanding of its biology, and increasingly provides prognostic/predictive information.

### Molecular Findings in Our Pediatric NHL Cohort (by Next-Generation Sequencing)

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<thead>
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<th>Age</th>
<th>Sex</th>
<th>Gene Mutation/Rearrangement</th>
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<td>5</td>
<td>Burkitt lymphoma</td>
</tr>
<tr>
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<td>2</td>
<td>Burkitt lymphoma</td>
</tr>
<tr>
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<td>1</td>
<td>ALKþ anaplastic large cell lymphoma (small cell variant)</td>
</tr>
<tr>
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<td>NPM1-ALK fusion</td>
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<tr>
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<td>ALKþ anaplastic large cell lymphoma</td>
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Macrocytic Anemia Due to “Whippit” Abuse: An Uncommon Etiology Requiring High Clinical Suspicion
(Poster No. 112)

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We present the case of a 57-year-old man with a history of thrombocytopenia, myeloproliferative neoplasm, previously treated with hydroxyurea, who presented with worsening macrocytosis. A bone marrow aspirate and biopsy were performed to assess for disease progression. Examination of his peripheral smear showed a macrocytic anemia (hemoglobin of 13.1 g/dL and mean corpuscular volume of 129.5 fL), absolute neutropenia (neutrophils of 1.7 K/μL) with frequent hypersegmented neutrophils (Figure 2.112, A), absolute lymphocytopenia (0.7 K/μL), and marked thrombocytosis. The biopsy showed a normocellular marrow with megakaryocytic hyperplasia with focal clustering (Figure 2.112, B), and aspirate smears showed adequate erythroid and granulocytic precursors with megaloblastoid changes (Figure 2.112, C and D). While an MPL exon 10 mutation and the marrow findings supported a diagnosis of essential thrombocythemia, it...
did not explain the patient’s severe macrocytosis and megaloblastoid changes. Initial review of the patient’s history revealed no apparent etiology for the macrocytic anemia. However, careful reexamination of the history revealed the patient frequently used “whippets” recreationally. Whippets are small, compressed cartridges of nitrous oxide used as propellants for whipped cream. The cartridge is attached to an inflatable object (usually by use of a balloon inflator) and the gas is subsequently inhaled. Whippit abuse can lead to nitrous oxide toxicity, an uncommon but a known cause of macrocytic anemia. Severe neurologic consequences such as ataxia and myeloneuropathy can also occur. When an apparent etiology for macrocytic anemia cannot be elucidated, whippit abuse should be considered, as removal of the agent and vitamin B12 supplementation can lead to clinical improvement for patients.

Unusual Presentation of Cyclin D1 Expression in a Case of Follicular Lymphoma That Transformed to an Epstein-Barr Virus (EBV)–Positive Diffuse Large B-Cell Lymphoma

(Poster No. 113)

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We present the case of a 68-year-old man with a history of follicular lymphoma diagnosed 17 years prior who presented with new lymphadenopathy. A lymph node biopsy revealed 2 morphologically distinct populations. The first population (Figure 2.113, A) had small lymphadenopathy. A lymph node biopsy revealed 2 morphologically similar lymphoma diagnosed 17 years prior who presented with new lymphadenopathy. Fluorescence in situ hybridization (FISH) revealed IGH/BCL2 fusion (63%, 82%), BCL6 rearrangement (97%, 90%), and trisomy 11 (12%, 28%) in the small and large cell populations, respectively, while trisomy 8 (48%) was only seen in the large cells. Cyclin D1 rearrangement was absent. Immunoglobulin heavy chain framework II gene rearrangement studies identified a clonal peak at 204 nucleotides in both populations. The differential diagnosis included cyclin D1–positive mantle cell lymphoma versus follicular lymphoma transforming to EBV-positive diffuse large B-cell lymphoma. However, the presence of the mantle zone, IGH/BCL2 and BCL6 rearrangements, and the absent cyclin D1 rearrangement supported follicular lymphoma. The presence of trisomy 11 in a subset of cells may explain the partial cyclin D1 overexpression observed. To avoid an incorrect diagnosis when cyclin D1 expression is observed in part of the lymphoma cells, FISH analysis is critical.

Circulating Nucleated Red Blood Cells: Pathologic or Commonplace?

(Poster No. 114)

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Context: Beyond the neonatal period, the finding of nucleated red blood cells (nRBCs) in the peripheral blood has traditionally been considered pathologic and associated with poor clinical outcomes. Historically, the presence of nRBCs in the peripheral blood was evaluated manually by a medical laboratory technologist. Recent technologic advances have led to the use of automated hematology analyzers. Reported values of nRBCs above the established reference range of 0.0% in our laboratory had increased since moving from manual counts of nRBCs in the peripheral blood to the automated counts. We hypothesized that hematology analyzers are more sensitive to the presence of nRBCs, leading to an increase in the number of referrals for manual counts.

Design: We performed a retrospective analysis of 66,498 healthy patients from outpatient clinics who received a complete blood count (CBC, blood film, platelet count, and differential). We evaluated the initial and follow-up CBC results and classified patients as having normal results, mild (0.0%–0.9%), or marked (>0.9%) nRBCs.

Results: Two of these patients had a low level of nRBCs within their peripheral blood. Based on statistical analysis of these results, our upper limit of normal could be reasonably updated to 0.10%.

Conclusions: Increasing the reference range of nRBCs has allowed us to better serve our patients by decreasing the constellation associated with discovering an abnormal laboratory value, and anecdotally decreased the number of subspecialty hematology referrals.

NPM1 and SF3B1 Mutations in a Case of Chronic Myeloid Neoplasm With Myelodysplastic/Myeloproliferative Neoplasm (MDS/MPN)–like Features and Hypereosinophilia

(Poster No. 115)

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Mutation of the NPM1 gene in chronic myeloid neoplasms is extremely uncommon, whereas it is one of the most commonly mutated genes in acute myeloid leukemia (AML), accounting for 20%–30% of cases. NPM1 mutation has been seen in approximately 2% of myelodysplastic syndrome (MDS) cases, and 3% of myelodysplastic/myeloproliferative neoplasm (MDS/MPN) cases. Mutation of the SF3B1 gene is extremely uncommon.

NPM1 gene mutation in nonacute myeloid neoplasms is associated with an aggressive clinical course with relatively rapid progression to acute myeloid leukemia within 12 months, whereas mutation in AML is associated with a more favorable
prognosis. We report a case of a 70-year-old patient initially presenting with ring sideroblasts and myelodysplastic features with marked eosinophilia. The patient’s initial bone marrow biopsies from 2010 and 2016 had shown persistently increased ring sideroblasts (>20%), and hypercellular marrow with mild dysmegakaryopoiesis and minimal dyserythropoiesis. Somatic mutation analysis was not performed at the time. Subsequent biopsy from 2020 showed hypercellular marrow with markedly increased eosinophils (Figure 2.115, A and B) at different stages of maturation, 8% myeloblasts, marked erythroid hypoplasia with ring sideroblasts (Figure 2.115, C), dysgranulopoiesis, and dysmegakaryopoiesis, and mild myelofibrosis. Karyotype, PDGFRB and FGFR1 gene rearrangements, and BCR-ABL1 fusion gene analysis were negative. The next-generation sequencing (NGS) panel showed 2 pathogenic mutations in NPM1 (c.863_864insCCTGp.Trp288Cysfs*12 VAF, 52%) and SF3B1 (C.1997A>Gp.Lys666Arg). So there was disease progression from a borderline, low-grade MDS to high-grade myeloid neoplasm with MDS/MPN-like features, eosinophilia, and mutated NPM1. At 7 months of follow-up, the patient did not have the conversion to AML and had a normal eosinophil count.

Chronic Lymphoproliferative Disorder of Natural Killer (NK) Cells Presenting as Asymptomatic Lymphocytosis and Circulating Smudge Cells

((Poster No. 116)

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Chronic lymphoproliferative disorder of natural killer (NK) cells is a rare 2016 World Health Organization provisional entity that can often be difficult to diagnose. We present a case of a 79-year-old man who was admitted to the hospital with a hip fracture. On admission he was found to have a lymphocyte count of 23 k/μL. The blood smear showed many smudge cells that were small to intermediate-sized lymphocytes with scant cytoplasm and clumped chromatin on an albumin smear. He had a complex autoimmune history of antiphospholipid syndrome, immune thrombocytopenia, and autoimmune hemolytic anemia. Clinical management included a splenectomy 2 years before the current admission. The spleen showed sinusoidal involvement by an expanded, atypical T/NK-cell population, which was observed. Given the new lymphocytosis, a bone marrow biopsy was performed. Flow cytometry studies demonstrated the same T/NK-cell population as the prior spleen specimen with expression of CD2, CD5, dim CD16, and partial CD57. They showed no expression of surface or cytoplasmic CD3, CD4, CD7, CD8, or CD56. The marrow showed interstitial infiltration by these cells, which are difficult to evaluate without immunohistochemical stains. Molecular studies for αβ and γδ T-cell receptor gene rearrangement were negative, and a STAT3 Y640F mutation was detected. Despite some of the atypical phenotypic expression of the NK cells by flow cytometry studies, the combination of the clinical history, marrow morphology, as well as the molecular studies, supports a diagnosis of chronic lymphoproliferative disorder of NK cells.

Utility of Cytogenetic Studies in the Detection of Residual Acute Leukemias in the Era of Measurable Residual Disease Testing

(Poster No. 117)

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Context: Though not currently required to designate complete remission as defined by an international working group, cytogenetic studies are commonly performed in surveillance bone marrow biopsies (BMBs) for acute leukemia. In the present study, we investigate the utility of cytogenetic analysis in the detection of residual disease in acute leukemia.

Design: We performed a retrospective review of all follow-up BMBs for acute leukemia with associated cytogenetic studies from 2009 to 2021.

Results: Of 404 follow-up BMBs, initial diagnoses included acute myeloid leukemia (51%), B-lymphoblastic leukemia (38%), T-lymphoblastic leukemia (7%), acute myelomonocytic leukemia (2%), multilineage acute leukemia (1%), and blast phase of prior myelodysplasia (0.75%). Cytogenetic abnormalities were present at diagnosis in 71% of cases. Residual disease was identified by morphology and/or flow cytometry immunophenotyping (FCI) in 24% (9/404), by measurable residual disease (MRD) testing in 32% (13/41), and by cytogenetics in 25% (101/404). Cytogenetic abnormalities consistent with residual disease were identified in 90% of cases, which were otherwise negative by morphology and FCI, including 7% (2/27) of cases that included MRD testing.

Conclusions: While morphology, FCI, and MRD testing were sufficient for the detection of residual disease in most cases, cytogenetic analysis detected evidence of residual disease, even in some cases negative by MRD. Performance of cytogenetic studies in all cases with known cytogenetic abnormalities is useful, even with concurrent MRD testing.

Anaplastic Lymphoma Kinase–Positive Large B-Cell Lymphoma (ALK LBCL) Presenting as an Abdominal Mass in the Pediatric Age Group

(Poster No. 118)

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ALK-positive large B-cell lymphoma (LBCL) is a rare, aggressive neoplasm of ALK-positive monomorphic immunoblast-like B cells with plasma cell phenotype. Diagnosis of ALK LBCL can be challenging because of its rarity, unique morphologic characteristics, and unusual immunophenotypic features (negative or weakly positive for usual B-cell lineage markers, despite being a B-cell lymphoma). It accounts for <1% of cases of diffuse large B-cell lymphomas (DLBCLs) with one third of cases occurring in the pediatric population. We present a case of a 9-year-old boy with abdominal pain. A computed tomography scan showed a lobulated retroperitoneal mass measuring 9 × 7 cm. The core biopsy showed sheets of dispersed large cells with vesicular chromatin, prominent nucleoli, and plasmablastic to immunoblastic morphology. The neoplastic cells were positive for CD45, EMA, BOB1, O bottoms, 2 ALK (cytoplasmic and golgi), CD13, MUM1, CD117, CD79a (weak and patchy), CD4, and showed λ light-chain restriction by in situ hybridization. The cells were negative for CD20, CD3, CD30, S100, and cytokeratin AE1/AE3, and EBER. Additional analysis showed t(2;17) CLTC-ALK fusion, confirming the diagnosis of ALK-positive LBCL. ALK LBCL is an aggressive disease with poor response to standard chemotherapy. However, limited literature suggests that its occurrence in the pediatric population and the presence of the localized disease is associated with longer survival. Fifteen months after diagnosis and treatment, the patient is disease-free. It is important to further explore...
the clinicopathologic features of ALK LBCL to ensure the awareness and accurate diagnosis of this unique entity, especially in lieu of its potential aggressive course and unfavorable outcome.

**Follicular Lymphoma Transformation to High-Grade B-Cell Lymphoma With BCL2, MYC Rearrangement, and Tdt Expression: A Rare Presentation and Aggressive Clinical Course**

(Poster No. 119)

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Transformation of follicular lymphoma to high-grade B-cell lymphoma with BCL2 and MYC gene rearrangement and Tdt expression is extremely rare. An 89-year-old man with a history of follicular lymphoma (Ann Arbor stage I) presented with generalized pain, weight loss, fatigue, and no palpable lymphadenopathy. Peripheral blood showed hemoglobin 9.7 g/dL, leukocyte count 5.4 K/mcl, and platelets 112 K/mcl. LDH was 1250 U/L. Abdominal ultrasonography and magnetic resonance imaging (MRI) without contrast showed hypoechogenic lesions in the liver and diffuse retroperitoneal lymphadenopathy. The MRI also demonstrated multiple lesions in spine, sacrum, and posterior ribs. Iliac bone marrow biopsy was hypercellular (90%), infiltrated by enlarged lymphocytes with blastic appearance. Flow cytometry showed monoclonal B-cell population expressing CD10, CD19, CD20, CD38, and k-light chain restriction. Immunohistochemical stains showed the neoplastic cells were positive for CD10, CD19, BCL2, and MUM1 (>90%), with partial expression of CD79a, and BCL6. Ki-67 was >90%. Fluorescence in situ hybridization showed MYC and BCL2 gene rearrangement. Cytogenetics showed complex abnormal karyotype with t(14;18) and abnormalities of 8q. Liver biopsy showed B-cell neoplasia with similar morphology to bone marrow and focal Tdt expression. According to the World Health Organization 2016, the preferred diagnosis in this situation would be bone marrow involvement by B-lymphoblastic lymphoma/leukemia. However, recent literature on this entity suggests a term of follicular lymphoma transformation to high-grade B-cell lymphoma with Tdt expression. This entity has a dismal prognosis with resistance to most conventional chemotheraphy regiments. The treatment options were discussed with the patient who had an Eastern Cooperative Oncology Group (ECOG) Performance Status 3 and agreed to hospice care.

**CD5+ Lymphoplasmacytic Lymphoma With Concurrent AL-Type Amyloidosis**

(Poster No. 120)

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Lymphoplasmacytic lymphoma (LPL) is 1 of 2 prototypic low-grade B-cell lymphomas that are typically CD5/Cd10+. Most cases of AL-type amyloidosis show no overt plasma cell (PC) myeloma or B-cell lymphoma. Although not routinely tested, CXCR4 mutations are present in 30%-35% of LPLs. Accumulating evidence shows that presence of CXCR4 mutation and/or associated amyloidosis portends higher disease activity and decreased overall survival, respectively. We present a case of a 66-year-old man with hyperviscosity and recent spinal surgery, admitted, with rapidly progressive weakness, for bone marrow biopsy and treatment of hyperviscosity syndrome (IgM = 2159 mg/dL [normal range, 40–230]). Flow cytometry (FC) of his BM aspirate revealed CD5+/CD10- λ-restricted monocytic lymphocyte (Figure 2.120, A and B) with no definitive PCs seen. Hematoyxlin-eosin of BM core biopsy (Figure 2.120, C) showed hypercellular marrow with extensive lymphoplasmacytic infiltrate. Most lymphoid cells were positive for CD20 (not shown). Although no PCs were detected by FC, A. (Figure 2.120, C inset) and k in situ hybridization and CD138 immunohistochemistry (not shown) revealed ~20% Λ-restricted cells with lambda light chain expression (not shown). Additionally, Congo red-positive amyloid (Figure 2.120, D) was confirmed to be AL (λ)-type by liquid chromatography mass spectrometry. Next-generation sequencing showed presence of MYD88 (L265P), CXCR4 (S342*), and TP53 (R273C). This is an interesting case with several unique features. First, the monotypic B cells are positive for CD5, not typically observed in LPLs; second, there is concurrent AL-type amyloidosis; third, besides commonly encountered MYD88 mutation, the case also harbors CXCR4 mutation. The presence of coexisting amyloidosis, and CXCR4 and TP53 mutations, will undoubtedly affect this patient’s prognosis as shown by previous studies.
cells that overexpress the interleukin-3 receptor subunit α (CD123). BPDCN predisposes the patient to leukemia transformation and may present in association with other myeloid neoplasms. Though the disease involves multiple sites, the most common initial presentation is skin manifestations. Microscopically, BPDCN has a diffuse monotonous infiltrate of medium-sized blasts resembling either myeloblasts or lymphoblasts. Immunohistochemically, the tumor cells express CD4, CD43, CD45RA, CD56, CD123, CD303, TCL1A, CD2AP, and SPIB. Among these, CD4, CD56, CD123, and Tdt are expressed relatively consistently. Tdt and CD123 show strong positivity, while CD4 and CD56 may show variable intensity. Here we present a relatively rare entity within this uncommon neoplasm with myeloid cells that do not express CD43. As this neoplasm was previously called CD4+ NK leukemia and CD4+ CD56+ hematodermic neoplasm/tumor, a CD4+ presentation can make the diagnosis challenging. This atypical presentation of a rare malignancy has implications in multiple subspecialties within pathology, namely dermatology and hematopathology, and this case highlights the difficulty in diagnosing an abnormal presentation of a rare entity.

**IGH-MYC–Positive Aggressive B-Cell Lymphoma With Precursor B-Cell Phenotype With Predominant Leptomeningeal Involvement**

(Poster No. 123)

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We report the case of a 54-year-old woman who presented with worsening bilateral leg weakness. Magnetic resonance imaging (MRI) identified an enhancing soft tissue mass, from T7 to S1 with cord compression and cauda equina nerve root thickening, diffuse leptomeningeal infiltrate with diffuse cranial nerve thickening, communicating hydrocephalus, without a primary brain neoplasm. Positron emission tomography confirmed the MRI findings with an intense FDG-avid intrathecal mass extending from T7 to S1, bilateral anterior emission tomography showed no other lesions or lymphadenopathy. A skin punch biopsy demonstrated a diffuse, sheetlike infiltrate of large atypical lymphoid cells. Arachnoid and lumbar nerve biopsies identified a dense infiltration of medium-sized to large lymphoid cells with round to oval nuclei, apoptotic cells, and increased mitotic activity with a high proliferation rate (95%, MIB1); and approximately 30% were TdT positive, and negative for CD20, bcl2, bcl6, cyclin D1, CD5, CD31, CD21, CD99, CD34, CD56, myeloperoxidase, WT1, and SI100. An EBER in situ hybridization stain was negative. IGH-MYC rearrangement was detected by fluorescence in situ hybridization (FISH). bcl2 and bcl6 rearrangements were not detected by FISH. The findings are in keeping with an IGH-MYC–positive aggressive B-cell lymphoma with precursor B-cell phenotype with predominant leptomeningeal involvement. While systemic lymphoma and primary diffuse large B-cell lymphoma of the CNS can involve the leptomeninges, an aggressive B-cell lymphoma with primary leptomeningeal involvement remains extremely rare.

**Acute Myeloid Leukemia With Myelodysplasia-Related Changes Harboring RAN-Binding Protein 2 (RANBP2)–Anaplastic Lymphoma Kinase (ALK) Fusion Gene: Case Report and Review of the Literature**

(Poster No. 124)

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**ALK** rearrangement has been described in the realm of anaplastic large cell lymphoma, inflammatory myofibroblastic tumor, neuroblastoma, and carcinomas. However, **ALK** rearrangements in myeloid neoplasia are extremely rare. Herein, we report a case of acute myeloid leukemia (M5(ML)) with myelodysplastic (partial) and changes consistent with RANBP2-ALK fusion. A 77-year-old woman with multiple comorbidities presented with abdominal pain, night sweats, and splenomegaly. Peripheral blood revealed marked monocytosis with atypical morphology and a small blast population. Bone marrow was markedly hypercellular with blasts and equivalents (21%) showing monocytic differentiation by morphology (Figure 2.124 A), and immunophenotype with cytochemical expression of myeloperoxidase (Figure 2.124, B). Atypical monocytosis and dysgranulopoiesis were appreciated. Flow cytometry revealed a small myeloid blast population and a prominent population in the monocytic gate with expression of MPO, CD64, CD14 (partial), CD13, CD15 (partial), CD11b, and CD16 (partial). Karyotype revealed 46,XX,?inv(2)(p11.2q21),-7[18]/46,XX[2]. Targeted massively parallel sequencing (FoundationOne Heme, Cambridge, Massachusetts) showed RANBP2-ALK fusion as the sole pathogenic molecular alteration. Immunohistochemically, the myelomonocytic population showed ALK expression (Figure 2.124, C) on the nuclear membrane and cytoplasm. CD30 highlighted very rare, scattered cells. The patient died of refractory disease after 10 months of treatment with azacitidine and venetoclax. Advanced age and comorbidities prevented intensive chemotherapy. RANBP2-ALK fusion is rare in myeloid neoplasms and was reported in AML with monocytic differentiation and juvenile myelomonocytic leukemia. It is frequently associated with monocytic differentiation, monosomy 7, and dismal prognosis. Additional studies are warranted for better understanding of the independent impact of RANBP2-ALK fusion on the etiopathogenesis of myeloid neoplasia and utility of crizotinib treatment.

**Primary Cutaneous Anaplastic Large Cell Lymphoma With aberrant CD20 Expression: A Rare Immunophenotypic Finding Presenting a Potential Diagnostic Pitfall**

(Poster No. 125)

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CD20 is commonly used to ascertain B-cell lineage in cutaneous lymphoid infiltrates; however, CD20 expression very rarely occurs in cutaneous T-cell lymphomas. Previously reported cases of CD20+ cutaneous T-cell lymphoma include mycosis fungoides and peripheral T-cell lymphoma unspecified. Here we describe a unique case of primary cutaneous anaplastic large cell lymphoma with strong and diffuse expression of CD20, which can be a diagnostic pitfall. A 42-year-old woman presented with a 2-cm violaceous, indurated nodule on the right thigh, which had enlarged during the course of a couple of months. She had no clinical findings of mycosis fungoides and PET/CT imaging showed no other lesions or lymphadenopathy. A skin punch biopsy demonstrated a diffuse, sheetlike infiltrate of large atypical lymphoid cells within the dermis. The tumor cells were diffuse and strongly positive for CD20 and MUM1 with dim CD3 expression, raising consideration of primary cutaneous diffuse large B-cell lymphoma, leg type; however, there was also diffuse expression of CD30, CD4, CD2, and CD5, with loss of CD7. The cells were negative for additional B-cell markers PAX-5 and CD79a. ALK-1 was also negative. Overall, morphologic and clinical findings were most consistent with primary cutaneous anaplastic large cell lymphoma. Aberrant immunophenotypic expression is not uncommon amongst hematolymphoid malignancies and can pose a significant diagnostic pitfall when limited panels are initially used to evaluate lesions. To our knowledge, this is the first reported case of strong, diffuse CD20 expression in primary cutaneous anaplastic large cell lymphoma.

**Systemic Mastocytosis With an Associated Hematological Neoplasm (SM-AHN): A Case Presentation With Literature Review for a Rare Entity**

(Poster No. 126)

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Mastocytosis is characterized by clonal neoplastic proliferation of mast cells and has 3 main variants: cutaneous mastocytosis, systemic
mastocytosis, and mast cell sarcoma. A 45-year-old woman presented with pancytopenia and high fever for 3 months. The bone marrow biopsy was markedly hypercellular with interstitial immature infiltrate, perivascular and paratrabecular spindled and atypical mast cell infiltrate (hypogranular with Giemsa stain). The immunohistochemistry showed 30%-40% cells positive for CD34 and CD117 (dim); and 40% mast cells positive for CD25 and CD117, and negative for CD2. The flow cytometry revealed a population of myeloblasts (positive for HLA-DR, CD34, CD117 [dim], and MPO) and a separate aberrant mast cell population (positive for CD25, bright CD123, and CD117). The molecular study showed the presence of KIT D816V mutation, confirming the diagnosis of systemic mastocytosis with an associated hematologic neoplasm (SM-AHN), which was acute myeloid leukemia in this case. SM-AHN is a rare entity that requires fulfillment of criteria for systemic mastocytosis and associated hematologic neoplasm for its diagnosis. As per the literature, chronic myelomonocytic leukaemia is the most common associated neoplasm with this entity, though in our case the associated neoplasm was acute myeloid leukemia. This entity poses diagnostic challenges and is associated with high-risk disease. With the limited data, splenomegaly, elevated alkaline phosphatase, and mutations in SRSF2/ASXL1/RUNX1 are considered as adverse prognostic markers in patients with systemic mastocytosis. We recommend that correlation of different techniques should be used for the proper diagnosis and characterization of the disease. This rare entity should be reported to clearly define its pathogenesis and prognostic implications.

A Pediatric Case of Erdheim-Chester Disease

(Poster No. 127)

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Erdheim-Chester disease (ECD) is a rare, systemic form of non-Langerhans cell histiocytosis of unknown etiology. It primarily affects adults, but rare pediatric cases have also been diagnosed. Virtually any organ or tissue can be infiltrated by ECD and some patients may not have typical bilateral and symmetric involvement of long bones. Mutation of BRAF V600E has been found in more than 50% of cases and it can be detected by immunohistochemistry. We report a case of a 9-year-old boy with a clinical history of Langerhans cell histiocytosis (LCH). He presented an infiltrative lesion in the frontoparietal region with skull and bilateral orbit involvement. Histology showed diffuse infiltration by histiocytes, some with single small nuclei and foamy cytoplasm, and others with eosinophilic cytoplasm. A few Touton-like giant cells were observed, and fibrosis and lymphocytes were also present (Figure 2.127). On immunohistochemistry studies, the histocytes were positive for CD68, CD163, and BRAF protein, and negative for CD1a, S100, CD21, and CD23. BRAF V600F mutation testing was positive. With these findings, the diagnosis of pediatric ECD was suggested. Recently a classification system has been proposed, with ECD and LCH included in the L group. Both diseases share common properties and overlap can occur in up to 12% of ECD cases. This association was presented in this case. The rarity of the disease can make the diagnosis challenging. Therefore, a multidisciplinary approach with radiologic and histopathologic criteria is required. Furthermore, the presence of BRAF mutation can be useful to confirm difficult cases.

Chronic Myelocytic Leukemia With Erythro-leukemic Blast Crisis

(Poster No. 128)

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Here we report the case of a 56-year-old man who presented to his primary care office with rapid onset symptoms of dorsalgia with lower extremity paresthesia, weight loss, fevers, chills, and night sweats. Magnetic resonance imaging incidentally identified diffuse abnormal marrow signal throughout the lumbar spine and additional areas of soft tissue densities within the epidural spaces. CT of the chest, abdomen, and pelvis identified splenomegaly and scattered lytic bone lesions. The peripheral blood smear revealed a leukocytosis with a left shift and occasional blasts. Flow cytometry, on whole blood, revealed a granulocytic left shift with 0.5% circulating blasts. These results prompted a bone marrow biopsy to be performed, which demonstrated hypercellularity (95%), with increased erythroblasts, myeloblasts, and mild erythroid dyspoiesis. Immunohistochemistry for CD71 identified a significant erythroid population in the marrow as well as a prominent CD34+ myeloblast population. Flow cytometry performed on the bone marrow detected 33.9% large myeloblast population. Bone marrow cytogenetic analysis revealed a complex karyotype. BCR/ABL1 fluorescence in situ hybridization was positive for gene rearrangements. Molecular studies, performed on whole blood, revealed a t(9;22) BCR-ABL1 major p210 fusion. This is an unusual case because the peripheral blood initially favored an erythroid leukemia morphologically; however, upon additional testing, the BCR/ABL1 translocation was discovered, revealing the origin of erythroid leukemia to be from chronic myelocytic leukemia. Chronic myelocytic leukemia with erythroid crisis is a rare entity with only a few reported cases of transformation of underlying chronic myelocytic leukemia to acute erythroid leukemia.

Cost Analysis of Orchiectomy Specimens From Patients With Gender Dysphoria

(Poster No. 129)

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Context: Hormonal therapy followed by orchiectomy is an integral part of management of gender dysphoria. The orchiectomy specimens from these patients are routinely subjected to histopathologic evaluation. The histopathologic findings are usually hormonal therapy related and are consistent and uniform. We intended to perform a cost analysis of these specimens.

Design: Orchiectomy specimens from patients with gender dysphoria received at our institution from February 2019 to February 2021 were included in the study. Data including patient age, weight of the testicles, number of tissue sections, processing cost, and histologic findings were collected.

Results: A total of 66 specimens were identified. Mean age of the patients was 35.9 ± 14.2 years. Mean weight of the testes were 28.1 ± 8.8 g (right) and 27.8 ± 9.4 g (left). Histologic evaluation showed hyalinization around seminiferous tubules and diminished/absent spermatogenesis in most cases. No tumor or unexpected findings were identified in any case. Mean number of tissue sections submitted per case was 5.7 ± 1.2. The estimated cost of processing, including technician labor, was $41.75 per specimen.

Conclusions: Orchiectomy specimens from patients with gender dysphoria almost always demonstrate hormonal therapy effects and chances of discovering any incidental finding of clinical significance are negligible. Diligent gross inspection and minimal tissue sampling with additional sampling reserved for gross abnormality can adequately document the histologic findings in a cost-effective manner.

How Much Time Do General Surgical Pathologists Spend on Diagnostic Data Entry?

(Poster No. 130)

Zhenhong Qu, MD, PhD (zqu@oakland.edu); Lanjing Zhang, MD; Xianzhong Ding, MD, PhD; Kausar Jabbar, MD. 1Department of Pathology, William Beaumont Hospital, Troy, Michigan; 2Department
of Pathology, Princeton Medical Center, Plainsboro, New Jersey; 2Department of Pathology, Loyola University Medical Center, Maywood, Illinois.

**Context:** As many pathology institutions have eliminated transcription service by office assistants, pathologists assume the task of diagnostic data entry (DDE) into pathology reports in the laboratory information system. This is not a trivial undertaking, yet tangible data are lacking on how much DDE adds to the workload of pathologists. Without such data, it is very difficult to assess the financial benefit of such a task shift and establish benchmarks.

**Design:** Four practicing pathologists covering a general surgical pathology service in 3 institutions with different laboratory information systems were selected for their dominant DDE method (speech recognition, pre-text, or manual typing) to generate greater than two-thirds of their pathology reports. In each sign-out session, the starting and ending times of the session were recorded. An online stopwatch was used to collate the DDE time for each surgical case during the session. Time for other activities, such as case information retrieval, slide review, and filling out a synoptic report, was not counted.

**Results:** Time for DDE, out of a total of 156 hours of consecutive sign-out sessions, was recorded. Judging by the ratio of “slides/specimen part/case,” the specimen-type mix appears typical of the general pathology service of a tertiary health care center. The results summarized in the Table demonstrate that pathologists spent >24.8% of sign-out time for DDE (median, 28.5%; quartile, 25.7%–29.5%).

**Conclusions:** With about 28.5% sign-out time devoted to DDE, the established workload of pathologists should be recalibrated. Since 1 full-time transcriptionist can cover DDE for 4–5 pathologists, the financial benefit of shifting DDE to pathologists should be reassessed.

<table>
<thead>
<tr>
<th>Pathologist</th>
<th>Main DDE Method</th>
<th>Total DDE Time, Mean, %</th>
<th>SD</th>
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<tr>
<td>1</td>
<td>Speech recognition</td>
<td>68.82</td>
<td>24.83</td>
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<tr>
<td>2</td>
<td>Pre-texted</td>
<td>31.51</td>
<td>28.78</td>
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<tr>
<td>3</td>
<td>Pre-texted</td>
<td>48.50</td>
<td>29.74</td>
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<tr>
<td>4</td>
<td>Manual typing</td>
<td>7.20</td>
<td>28.29</td>
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<tr>
<td>Combined</td>
<td></td>
<td>156.03</td>
<td>29.07</td>
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</tbody>
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**Optimizing Fluorescence In Situ Hybridization Test Utilization in Unsorted and CD138-Enriched Samples of Plasma Cell Myeloma at Diagnosis Versus Persistent/Relapsed Disease**

(Poster No. 132)

Priyatharsini Nirmalanantham, MD (Priyatharsini.Nirmalanantham@UHhospitals.org); Howard Meyerson, MD; Ehsan Malek, MD; Shashirekha Shetty, PhD. Department of Pathology, Case Western Reserve University/University Hospitals, Cleveland, Ohio.

**Context:** Fluence in situ hybridization (FISH) testing on enriched CD138⁺ plasma cells assists in identifying genetic abnormalities for risk stratification in multiple myeloma. Limited specimens are often encountered, precluding evaluation using all the desired probes. Therefore, to optimize test utilization, we assessed FISH detection rates among unsorted and CD138-enriched samples.

**Design:** A total of 439 patients with a plasma cell neoplasm (257 unsorted, 182 CD138-enriched) were examined by FISH for abnormalities of 3, 7, 11, 14, 16, 17, CKS1B, IGH, T(4;14), and T(14;16). The frequency of T(11;14), T(6;14), and T(14;16) upon reflex testing at diagnosis was 46%, 16%, and 6%, respectively, versus 33%, 11%, and 11% in P/R disease.

**Conclusions:** Differences between enriched and unsorted cases at diagnosis and persistent and relapse (P/R) disease were assessed.

<table>
<thead>
<tr>
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<th>Main DDE Method</th>
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<td></td>
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<td>29.07</td>
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**Intriguing Simultaneous Intestinal Spirochetosis and Lymphocytic Colitis in an 80-Year-Old Man With Heavy-Chain Gamma Globinemia**

(Poster No. 131)

Daniela Pereira, MD (danielavpereira@gmail.com); Kun Jiang, MD, PhD. 1Department of Pathology, Instituto Português de Oncologia de Lisboa Francisco Gentil, Lisbon, Portugal; 2Department of Pathology, Moffitt Cancer Center, Tampa, Florida.

Intestinal spirochetosis and lymphocytic colitis are both rare clinical encounters in patients diagnosed with neoplastic diseases. The pathogenesis of lymphocytic colitis is not well understood, and although a possible role of pathogenic microorganisms has been proposed, there are no reports on simultaneous spirochetosis and lymphocytic colitis in a single patient in the English literature. When managing patients with neoplasms history, “nonmalignant” findings should not be missed or omitted; therefore, to optimize patient care. An 80-year-old man with heavy-chain γ globinemia not requiring systemic therapy reported several months of diarrhea with intermittent abdominal cramping refractory to lifestyle changes. Clinically enterocolitis was suspected and a colonoscopy was performed. The colonoscopy was remarkable; hence random biopsies were obtained. Microscopic examination identified architecturally intact colonic mucosa with diffuse regeneration, intraepithelial lymphocytosis, and peculiar “false brush border,” and goblet cell–sparing basophilic epithelial fringe. Findings suggest coexisting lymphocytic colitis and spirochetosis (Figure 2.131, A and B). Subsequent immunohistochemistry (Figure 2.131, C) and special stains (Figure 2.131, D) confirmed both entities and excluded the hypothesis of amyloidosis. The patient was managed accordingly, with quick resolution of his symptoms. This unique case highlights the importance of timely recognition of rare diseases in ensuring proper patient management.

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**Abstracts**

**Arch Pathol Lab Med**

**SESSION 2**
Cytogenetic Abnormalities in Sorted and Unsorted Samples of Newly Diagnosed Versus Persistent/Relapsed

<table>
<thead>
<tr>
<th>FISH Probes</th>
<th>Newly Diagnosed Category</th>
<th>Persistent/Relapsed Category</th>
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<tbody>
<tr>
<td></td>
<td>Sorted Samples</td>
<td>Unsorted Samples</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CK15B (1q21)</strong></td>
<td>39/60 (65%)</td>
<td>36/72 (50%)</td>
</tr>
<tr>
<td><strong>Hyperdiploidy (chromosomes 3, 7, 11)</strong></td>
<td>36/60 (60%)</td>
<td>30/72 (42%)</td>
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<tr>
<td><strong>IGH rearrangement</strong></td>
<td>28/60 (47%)</td>
<td>21/71 (30%)</td>
</tr>
<tr>
<td><strong>TP53 deletion</strong></td>
<td>3/60 (5%)</td>
<td>13/72 (18%)</td>
</tr>
</tbody>
</table>

Coronavirus Disease 2019 (COVID-19): The Impact on Breast Cancer Management in an Inner-City Hospital (Poster No. 133)

Gabriela M. Oprea-Ilies, MD1 (goprea@emory.edu); Michel Attieh, MD1; Stefan E. Pambuccian, MD2; Geoffrey Smith, MD3; Evin H. Gulbahce, MD4 1Department of Pathology, Emory University, Atlanta, Georgia; 2Department of Pathology, Loyola University Chicago Stritch School of Medicine, Chicago, Illinois; 3Department of Pathology, ARUP Laboratories, Salt Lake City, Utah.

Context: The COVID-19 pandemic has impacted the diagnosis and surgical management of malignancies, including breast cancer. Hospitals developed a rapid and unprecedented reorganization of surgical units to ensure optimal care for patients with respiratory distress. Access-to-care delays resulting from the pandemic may negatively impact early diagnosis, potentially reducing survival. In this study, we assessed the impact of COVID-19 on breast carcinoma management in a busy inner-city hospital.

Design: We searched our files for breast carcinoma diagnosed in our busy inner-city cancer center. A period spanning from February to March was evaluated comparing 2019 to 2020. Matched pairs analysis of identical months in 2019 and 2020 was performed in SAS JMP Pro v15.2.0.

Results: We studied 273 female patients with a mean age of 60 years (range, 26–97). Seventy-two percent (185) of specimens studied were biopsies. The 1-sided paired t test P value in the matched pairs analysis (n = 273 cases received between February and August 2019 and 2020) is statistically significant (P = .02) for a reduction in case volume from 2019 to 2020. The reduction is most apparent in the months in the middle of the study period (April to July) (Figure 2.133).

Conclusions: There was a significant decrease in breast carcinoma patients being evaluated in our institution. Best management of breast cancer during pandemics must be determined.

Utility of Grocott Methenamine Silver and Acid-Fast Bacillus Staining in Surgical Pathology (Poster No. 134)

Fahd Hussain, MD (fhussain@umc.edu); Varsha Prakash, MD; Imran Ajmal, MD; Varsha Manucha, MD; Veena Shenoy, MD. Department of Pathology, University of Mississippi Medical Center, Jackson.

Context: Grocott methenamine silver (GMS) and acid-fast bacilli (AFB) were performed to identify fungal and mycobacterial organisms, respectively. In this study we investigated the value of these stains in surgical pathology and the impact on cost and turnaround time.

Design: For a period of 1 year, all surgical pathology cases with AFB and GMS stains were retrieved. The major histologic finding was noted, and results of the stains were compared with the culture results.

Results: Grocott and AFB were performed on 222 specimens from 207 patients. Of these, 71 (32%) were from the lung and 62 (30%) from lymph nodes (mediastinal and cervical). Eighty-three cases (40%) showed granulomatous inflammation (32 necrotizing and 51 non-necrotizing). In the remaining cases, stains were performed owing to either clinical request or the presence of nonspecific inflammation. GMS was positive in 10 specimens (4.5%), of which 3 were culture positive. AFB was positive in 2 specimens (0.45%), of which 1 was culture positive (Figure 2.134). Of the 11 cases with positive results, 10 showed necrotizing granulomas. The cost incurred for AFB stains was $1985.50 and for GMS it was $10,718. The average turnaround time was increased from a few hours to a day, depending on the time the stains were ordered.

Conclusions: AFB and GMS stains were positive in only 5.4% of cases, all with necrotizing granulomatous inflammation. In the context of increasing cost of health care and low positivity rate, our results question the practice of ordering AFB and GMS in the absence of necrosis or granulomas.
Primary Intranodal Epithelioid Hemangioendothelioma With Molecular Confirmation

(Poster No. 1)

Jennifer Vazzano, DO, MS (jennifer.vazzano@osumc.edu); O. Hans Iwenofo, MD. Department of Pathology, The Ohio State University, Columbus.

Epithelioid hemangioendothelioma (EHE) is a vascular tumor with indolent biology, characterized by reciprocal t(1;3)(p36.6;q25) with resultant WWTR1-CAMTA1 gene fusion in the majority of cases, regardless of anatomic location. Primary intranodal EHE is very rare. We report a case in a 54-year-old man with persistent left groin mass with discomfort. Computed tomography of the abdomen and pelvis showed a minimally enlarged inguinal lymph node measuring 1.1 cm with no other masses or lymphadenopathy. Positron emission tomography imaging and magnetic resonance imaging of the abdomen showed no evidence of malignancy nor abdominal or pelvic metastases. Histologically, sections showed an epithelioid vasoformative neoplasm, centrally necrotic, involving a lymph node (Figure 3.1, A). The cells were arranged in anastomosing cords with intracytoplasmic lumens (“resembling signet ring cells”). There were no high-grade features or cellular anaplasia (Figure 3.1, B). By immunohistochemistry, the tumor cells were positive for vimentin, CD31, ERG, and CAMTA1 (Figure 3.1, C); focally positive for CD34; and negative for AE1/3, CAM 5.2, CK7, CK20, desmin, actin, HMB-45, and S-100. Ki-67 proliferation index was estimated <1%. Molecular confirmatory studies including next-generation sequencing revealed the presence of WWTR1-CAMTA1 gene fusion, and multiplex morphometric fluorescence in situ hybridization for CAMTA1 (in chromosome band 1p36.23) and WWTR1 (in chromosome band 3p25.1) showed fusion signals consistent with (1;3) translocation (Figure 3.1, D), cognate for diagnosing EHE. We highlight a rare epithelioid vascular neoplasm in a primary lymph node location exhibiting morphologic mimicry with metastatic carcinoma with treatment and prognostic implications. Careful attention to the histopathologic features will facilitate appropriate workup and prevent unnecessary excessive treatment.
Melanoma With Rhabdomyoblastic Differentiation: Case Report and Review

(Poster No. 4)

S. Shawn Liu, MD, PhD1 (ssliu@health.southalabama.edu); Zan Ahmed, MD1; Brian E. Persing, MD2; Zachary Trisel, MD2; Carlos A. Galliani, MD1; Annabelle L. Fonseca, MD2; Pallavi A. Patil, MD1
Departments of 1Pathology; 2Mitchell Cancer Institute and 3Surgery, University of South Alabama, Mobile.

Melanoma is notoriously difficult to prognosticate, a great mimicker, and biologically capricious, with potential for metastatic dormancy. We report a 56-year-old woman with metastatic melanoma that disseminated after a quiescent 15-year interval. Biopsy of a suspected abdominal wall abscess revealed a primitive tumor with rhabdomyoblastic differentiation (Figure 3.4, A). Immunohistochemically, the neoplastic cells expressed myogenin (10%), desmin (10%; Figure 3.4, B), S-100 (40%), SOX10 (30%), sparse HMB45 (<1%) and Melan-A (<1%). Tumor cells were negative for CK AE1/AE3, CAM5.2, CK34E12, p63, CD68, and CD117. A positron emission tomography scan revealed multiorgan metastases. A key medical antecedent of melanoma removed 15 years earlier surfaced. Brain metastasis showed large cells with abundant cytoplasm (Figure 3.4, C) positive for SOX10 (Figure 3.4, D), HMB45, Melan-A, and S100, which were negative for rhabdomyoblastic differentiation. Abdominal wall and brain metastases showed BRAF V600E mutation, and melanosomes by ultrastructural examination. This case emphasizes that morphologic identification of tumor type helps to determine first-line treatment in sarcomas. Whereas in melanomas identification of BRAF proto-oncogenic mutation in well-differentiated subtypes may present a viable systemic treatment alternative to cytotoxic and immuno-oncology–based regimens, divergent differentiation in melanomas is a therapeutic challenge as these subtypes are often resistant to molecular targeted therapy. The degree of divergent differentiation may determine alternative regimens. The behavior of melanomas with rhabdomyoblastic differentiation is not known. Melanomas with rhabdomyoblastic differentiation tend to be aggressive with a high mortality rate.

Extranuchal-Type Fibroma in a Patient With Gardner Syndrome

(Poster No. 5)

Mehenza A. Hanbazazh, MD (mehenza_hanbazazh@hotmail.com); Taylor Pickens, MD; Diana Morlote, MD; Shuko Harada, MD; Isam-Edin Eltoum, MD, MBA. Department of Pathology, University of Alabama at Birmingham, Birmingham.

Nuchal-type fibroma is a rare benign tumor arise in posterior neck and upper back and consists of spindle cells and thick collagen fibers. Nuchal-type fibroma in nonnuchal site (extranuchal-type fibroma) is a histologically similar lesion in patients with familial adenomatous polyposis (FAP)/Gardner syndrome. It tends to occur at young age, with more frequent recurrence and in unusual or multiple sites. We report a case of extranuchal-type fibroma in a patient presented with multiple rectal polyps and underwent completion proctectomy. The patient had an early diagnosis of FAP and history of colectomy. Gross examination reveals a 3.4-cm firm, white, fibrotic nodule located within mesentery attached to ileum (Figure 3.5). Histopathologically, the lesion was peculiar and consisted of bundles of collagen fibers and spindle cells infiltrating the mesenteric fat and entrapping numerous nerve twigs (Figure 3.5, B), representing the coexistence of traumatic neuroma features. Modified Masson trichrome illustrates the collagenous nature of the lesion and the entrapped nerves. Elastic tissue stain highlights delicate elastic fibers. By immunohistochemistry, the spindled fibroblasts were CD34 positive (Figure 3.5, C) with scattered nuclear β-catenin positivity (Figure 3.5, D), indicating active adenomatous polyposis coli (APC)–Wnt pathway. Genetic analysis showed an intronic pathogenic mutation in APC gene (c.1409-1G>A). Our case strengthens the association between extranuchal-type fibroma and Gardner syndrome. Such lesions should raise the suspicion or might even be the initial event in Gardner syndrome detection. Furthermore, it demonstrates the risk of developing the fibroma at a previous surgical site, which might explain the traumatic neuroma features.

A Case Report of Lipoblastoma Reminiscent of Myxoid Liposarcoma Resolved by Molecular Testing

(Poster No. 6)

Qing Wei, MD, PhD1 (qwei@uabmc.edu); Geling Li, MD, PhD2; David R. Kelly, MD, PhD2.1 Department of Pathology, University of Alabama at Birmingham; 2Department of Pathology and Laboratory Medicine, Children’s of Alabama, Birmingham.

Lipoblastoma predominantly occurs in infants, especially males with an age of less than 3 years. We report a lipoblastoma morphologically overlapping with myxoid liposarcoma. A 9-month-old girl presented with a left axillary mass. Surgical excision revealed a single edematous tan fleshy mass, measuring 4.5 cm in the greatest dimension. Sections showed a lipomatous lesion with both hypocellular and cellular areas and a vaguely lobular appearance with incomplete fibrous septa. The lesional cells consisted of monomorphic, stellate or fusiform-shaped cells and lipoblasts with a peripheral concentration of mature adipose cells. The background showed prominent myxoid stroma with enriched plexiform vasculature. Rare mitoses were recognized (Figure 3.6, A through D). The differential diagnoses include lipoblastoma versus low-grade myxoid liposarcoma. Myxoid liposarcoma rarely occurs in children younger than 10 years. However, pure morphologic diagnosis of this case is still challenging. DDIT3 FISH study demonstrated no rearrangement of DDIT3 gene region. NGS sarcoma panel identified HAS2-PLAG1 fusion, which confirmed the diagnosis of lipoblastoma. In summary, when lipoblastoma is difficult to distinguish with myxoid liposarcoma by morphology, molecular testing is essential to resolve the issue.

Abstracts
Clinicopathologic Features of 4 Cases of BCOR-CCNB3–Positive Sarcomas
(Poster No. 7)

Bharat Rekhi, MD, DNB, MCAP; Vaibhavi Vengurlerkar, MSC; Omshree Shetty, PhD. Department of 1Surgical Pathology, Division of Molecular Diagnostics and Translational Medicine and 2Division of Molecular Diagnostics and Translational Medicine, Tata Memorial Hospital, Mumbai, India.

Context: Sarcomas with BCOR genetic alterations have been included in the recent WHO classification of soft tissue and bone tumors. Currently, there is a single reported study from our country on inclusion of 4 additional such cases.

Design: Nine cases of undifferentiated round to spindle sarcomas were tested for BCOR-CCNB3 fusion by reverse transcriptase–polymerase chain reaction. All these tumors were negative for EWSR1 rearrangement and a single case also for SS18 rearrangement by fluorescence in situ hybridization.

Results: Four tumors occurred in 3 boys (13-year-old, 7-year-old, and 16-year-old) and a single woman (37-year-old), in tibia, femur, temporal region, and thigh, respectively. Histopathologically, tumors were composed of round (n = 4), polygonal (n = 2), to spindle cells (n = 2) in a myxoid matrix (n = 3) with interspersed thin-walled vessels (n = 4) and focal necrosis (n = 2) (Figure 3.7, A and B). Immunohistochemically, tumor cells displayed dotlike reactivity for MIC2/CD99 (4 of 4); positivity for SATB2 (3 of 4) (Figure 3.7, C and BCOR (2 of 2) (Figure 3.7, D); focal positivity for EMA (1 of 3); and negativity for desmin (0 of 4) and WT1 (0 of 3). Therapeutically, 2 patients underwent neoadjuvant chemotherapy (99% response and 78% response), followed by surgical resection. Two patients were offered palliative radiotherapy, in view of metastasis at presentation and lack of resectability. Three patients developed lung metastasis and a single patient developed local recurrence.

Conclusions: Certain morphologic features, such as spindle and polygonal cells, in addition to round cells, along with myxoid stroma, intervening vessels, dotlike immunoreactivity for MIC2, lack of EWSR1 rearrangement, and intraosseous location, constitute diagnostic clues for BCOR-CCNB3–positive sarcomas. SATB2 and BCOR are useful immunostains for triaging such cases for BCOR-CCNB3 fusion testing.

Foreign Body Granuloma Secondary to Leuprorelin Acetate Injections (Lupron)
(Poster No. 8)

Madeleine Opsahl, DO (madeleine.opsahl@phhs.org); Helena Hwang, MD. Department of Pathology, University of Texas Southwestern Medical Center, Dallas.

Leuprorelin (also known as leuprolide) acetate (LPA) is a gonadotropin-releasing hormone agonist indicated for the palliative treatment of advanced prostatic cancer. Depending on the formulation, LPA can be administered subcutaneously or intramuscularly. A very rare side effect of LPA is foreign body granuloma formation at the site of injection. We report a case of a 67-year-old man with a history of metastatic prostate cancer who was found with LPA granulomas. The patient was discovered to have a 2.2-cm masslike region of enhancement as well as enhancing indistinct striated regions of the left gluteus maximus on surveillance magnetic resonance imaging. An ultrasound-guided core biopsy was performed and showed an exuberant granulomatous reaction with epithelioid histiocytes, multinucleated giant cells and lymphocytic infiltrate (Figure 3.8, A). Distinct round clear vacuoles of varying size were seen in the multinucleated giant cells (Figure 3.8, B). No polarizable material was seen. The patient had been receiving 45-mg intramuscular LPA injections (Lupron Depot) every 6 months for 7 years. Lupron Depot consists of LPA in a suspension with lyophilized microspheres. LPA granulomas are hypothesized to be secondary to the substances used in LPA suspensions; however, a reaction to LPA itself cannot be excluded. Most of the few LPA granulomas that have been reported in the literature have been subcutaneous. Our case is extremely rare, not only because it is a case of LPA granuloma, but also because of its intramuscular location.

Localized Subcutaneous Cryptococcal Infection in a Patient With Myelodysplastic Syndrome
(Poster No. 9)

Katherine A. Weng, MD, PhD (katherine.weng@nyulangone.org); Jianhong Zhou, MD. Department of Pathology, NYU Langone Health, Mineola, New York.

Cryptococcosis is a rare fungal infection caused by Cryptococcus species, which are accountable for opportunistic infections in immunocompromised patients. Cryptococcal infections commonly involve the pulmonary and central nervous system. It is very rare to have localized subcutaneous involvement without evidence of disseminated disease. We report a case of localized cryptococcal subcutaneous abscess in a patient with myelodysplastic syndrome with recent transformation to acute myeloid leukemia. The patient presented with a subcutaneous abscess on his left hand. An excisional biopsy was performed. Hematoyxlin and eosin stain revealed subcutaneous tissue with extensive mass-forming acute and chronic inflammation, abscess formation, and scattered fungal organisms, indicative of Cryptococcosis species. Grocott silver stain was positive for fungal organisms. No disseminated Cryptococcus infection was identified. The patient was started on fluconazole 400 mg daily for 6 months. At 1-month follow-up, the patient remained afebrile without any signs or symptoms of
systemic Cryptococcus infection. This case signifies that although rare, localized subcutaneous Cryptococcus infection does occur. An excision biopsy is essential to evaluate for fungal organisms. Cryptococcus can be inconspicuous without immunohistochemistry. In immunocompromised patients, the yeast forms are usually surrounded by minimal edema without surrounding inflammatory or granulomatous response. In immunocompetent patients, the granulomatous reaction may obscure the microorganisms. In summary, with the prevalence of diseases leading to weakened immune system, physicians should be adept at recognizing the predisposing factors that place patients at risk for localized Cryptococcus infection to ensure efficient diagnosis and treatment.

Paratesticular Ectomesenchymoma in a 1-Year-Old Boy
(Poster No. 10)

Muhammad Ahmed, MD1 (muhammad.ahmed@yale.edu); Edwin Partovi, MD2; Marianne Casilla-Lennon, MD3; William Laskin, MD1; Raffaella Morotti, MD1; Departments of 1Pathology and Laboratory Medicine and 2Urology, Yale–New Haven Hospital, New Haven, Connecticut.

Malignant ectomesenchymoma is a rare, predominantly pediatric, tumor exhibiting both mesenchymal (usually embryonal rhabdomyosarcoma) and neuroectodermal elements (usually ganglion cells, neuroblastoma, ganglioneuroblastoma, or ganglioneuroma). Cases tend to arise in the paratesticular region in males. The rhabdomyosarcoma component dictates treatment; thus, identifying and subtyping this component is imperative. We report a case of a paratesticular ectomesenchymoma in a 1-year-old boy who presented with right testicular swelling. Ultrasound was remarkable for a 3.9-cm solid intrascrotal mass. He underwent a radical orchiectomy, which revealed a 4-cm, solid, tan-white, lobulated mass completely encasing the testis (Figure 3.10, A). Microscopic examination revealed a highly cellular tumor with sheets of small, rounded cells with high nucleocytoplasmic ratios exhibiting rhabdomyosarcomatous differentiation (Figure 3.10, B). Interspersed mature ganglion cells were identified amongst solid and spindled foci (Figure 3.10, C). Immunohistochemical staining for desmin was diffusely positive in the rhabdomyosarcomatous component (Figure 3.10, D), whereas patchy, strong myogenin positivity was observed. SI00 was focally positive. The FOXO1 gene rearrangement was not identified, supporting classification as the embryonal subtype of rhabdomyosarcoma. Cytogenetics showed an abnormal hyperdiploid clone with extra copies of chromosomes 2, 5, 8, 10, and 11. Tumor profiling revealed somatic variants in HRAS and p53. The p53 variant necessitated augmentation of the patient’s treatment regimen. Pathologists should remember that although pure rhabdomyosarcoma, specifically the spindle cell variant, commonly occurs in the paratesticular region, malignant ectomesenchymoma must also be considered in the differential as it has its own specific histology and known association with HRAS mutations.

Pre-sacral Myelolipoma
(Poster No. 11)

Kevin Mijares, MD (kevmijaresmd@gmail.com); Binny Khandakar, MBBS, MD; Abdelsalam Sharabi, MD. Department of Pathology, Icahn School of Medicine at Mount Sinai West/Morningside, New York, New York.

Myelolipoma is a benign neoplasm of mature fat and hematopoietic progenitors. It is commonly found in the adrenals, comprising 6%–16% of incidentalomas on computed tomography or magnetic resonance imaging (MRI). These are rare tumors with <1% incidence reported in autopsy series. Rarely, it can involve extra-adrenal sites, such as pre-sacral. Only 41 cases of pre-sacral myelolipomas have been reported since 1933. Given its retroperitoneal location, important differential diagnoses are liposarcoma or lymphoma. The patient was a 76-year-old woman with chronic low back pain. MRI revealed 5.6-cm and 2.1-cm pre-sacral fat-containing masses. Computed tomography scan (Figure 3.11, A) revealed ill-defined borders, concerning for sarcoma. Intraoperative findings show a firm, rubbery, somewhat encapsulated left-sided mass between the sacrum and mesorectum and a second soft lesion on the right adjacent to the first. Flow cytometry was submitted intraoperatively. Grossly, lesions were pink-tan and fleshy. Microscopically, these consisted of adipose tissue and bone marrow progenitors composed of megakaryocytes, differentiating myeloid elements, and erythroid islands (Figure 3.11, B through D). Flow cytometry revealed 85% viability, unremarkable B (19%) and T cells (64%), without evidence of non-Hodgkin lymphoma. A diagnosis of extra-adrenal myelolipoma was rendered. Myelolipoma occasionally can be extra-adrenal. In contrast to adrenal myelolipomas, pre-sacral myelolipomas usually have no hemorrhage or associated endocrine abnormality. Etiology of myelolipoma is poorly understood. The risk of recurrence is minimal. Although myelolipoma is rare, it is important to be aware of, as it would come as a rare differential diagnosis for fat-containing retroperitoneal and pre-sacral lesions.

Granular Cell Tumor of Inguinal Region
(Poster No. 12)

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Granular cell tumor (GCT) is a predominantly benign tumor derived from Schwann cells of the peripheral nerve fibers. Although this tumor can be found in virtually any body site, the most frequent sites are skin and subcutaneous tissue of head and neck region, followed by chest wall and arm. GCTs in groin are extremely rare. We here present a case of granular cell tumor of soft tissue, located in the inguinal region. A 59-year-old woman with a history of breast cancer and eyelid mucosa-associated lymphoid tissue lymphoma presented with right inguinal mass that was painless and slowly growing for approximately 1 year. Magnetic resonance imaging demonstrated a right inguinal ovoid 1.4 ×
0.9-cm small mass with speculated borders. An excisional biopsy was performed. Immunophenotyping of a portion of the mass by flow cytometry did not show evidence of non-Hodgkin lymphoma. A 1.4-cm gray firm mass was identified grossly. Microscopically, the neoplasm was nonencapsulated with irregular borders, composed of nests and cords of plump cells with abundant eosinophilic granular cytoplasm and central small nuclei. The tumor cells were positive for S100, SOX-10, PAS, and PAS-D and negative for CD68. These findings are consistent with granular cell tumor (Figure 3.12). Granular cell tumors in the inguinal region are rarely observed. Differentiating them from other inguinal lesions, such as lipoma, fibroma, fibrolipoma, dermatofibroma, or hamartoma, should always be considered. Broad surgical excision to obtain negative margins should be the therapeutic goal in all cases of GCT, as positive margins are highly correlated with recurrence of the lesion.

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 Extraskeletal Myxoid Chondrosarcoma of Bone, Osseous Myxochondroid Sarcoma/Chordoid Sarcoma of Bone, With Variant TAF15-NR4A3 Fusion: Report of an Eighth Case With 5-Year Follow-up (Poster No. 14)

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Extraskeletal myxoid chondrosarcoma (EMC) is a rare soft tissue sarcoma of uncertain differentiation primarily occurring in the deep soft tissue musculature of the extremities in older patients. The majority of EMC’s harbor an EWSR1-NR4A3 fusion, whereas rare non-EWSR1 fusions have been reported. Tumors identical to EMC have rarely been reported in bone, previously assigned various rubrics such as “osseous myxochondroid sarcoma” or “chordoid sarcoma of bone.” To our knowledge, there are only 2 small series of 2 cases and 5 cases, respectively, discussing this phenomenon. We report the eighth case of a 40-year-old man who presented with a 17-cm lytic mass centered in the left iliac wing and showing destructive soft tissue extension by CT (Figure 3.14, A). Surgical resection was performed, and gross evaluation showed this tumor emanating from the bone on cross-sectioning analysis. Histologically, the tumor grows in cords and chains, often creating a lacelike appearance. Close inspection shows scant eosinophilic cytoplasm and monotonous round to somewhat spindled nuclei without nuclear pleomorphism (Figure 3.14, B and C). Molecular analysis showed a variant TAF15-NR4A3 gene fusion of EMC. Five-year follow-up includes locoregional recurrences 3 and 5 years postoperatively as well as recent lung metastases status post metastasectomy (Figure 3.14, D) and is currently NED. This case is valuable given its extremely unusual presentation in bone and its variant fusion status, and it highlights the indolent but clearly malignant behavior of this rare translocation sarcoma.
Chondroid Lipoma of the Retroperitoneum
(Poster No. 15)

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Chondroid lipoma is a rare benign adipocytic tumor with unusual histopathologic features that can mimic malignant soft tissue neoplasms. We report a case of chondroid lipoma arising in the retroperitoneum, a location that has not been previously documented in the literature. A 20-year-old man presented with a right lower quadrant abdominal mass. Magnetic resonance imaging demonstrated a 2.4-cm heterogeneously enhancing mass along the right paracolic gutter. The patient underwent laparoscopic excision; intraoperatively, the mass was identified retroperitoneally at the level of the anterior superior iliac spine. On gross examination, the cut surface was tan-white to yellow and cystic. Microscopically, the mass appeared well circumscribed with lobules delineated by fibrous septa. It was composed of an admixture of mature adipocytes, multivacuolated lipoblast-like cells, and nests of epithelioid cells with vacuolated to eosinophilic cytoplasm within a chondromyxoid matrix (Figure 3.15, A through C). MDM2 amplification by FISH was negative. Targeted next-generation RNA sequencing revealed a C11orf95-MKL2 fusion, a recurrent translocation identified in chondroid lipomas. Initially, the retroperitoneal location of our case raised the differential diagnosis of well-differentiated liposarcoma, a more common adipocytic tumor encountered at that site. The circumscription of the mass, unique morphologic characteristics, and results of molecular testing were all supportive of a diagnosis of chondroid lipoma. Thus, our case highlights the importance of recognizing the morphologic features of this rare, benign entity to direct appropriate follow-up ancillary testing and avoid misdiagnosis as a more aggressive tumor.

A 72-Year-Old Patient With Intraabdominal Sclerosing Epithelioid Fibrosarcoma Sarcomatosis
(Poster No. 17)

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Sclerosing epithelioid fibrosarcoma (SEF) is a rare, unique variant of fibrosarcoma that has a wide variety of histopathologic findings. This frequently leads to a diagnostic dilemma, but distinction is important because it is malignant and portrays an aggressive clinical course. We present an interesting case of a 72-year-old man with no significant past medical history. He presented with symptoms of an upper respiratory tract infection. A computerized tomography scan performed as a part of the workup incidentally revealed innumerable omental and mesenteric nodules and masses (Figure 3.17, A). Clinical findings were concerning for lymphoma or metastatic carcinoma. Surgical resection of a trampoline. Magnetic resonance imaging revealed a heterogeneous, likely pleural-based mass measuring 6.4 × 5.1 × 5.1 cm in the right hemithorax extending into the right axillary region (Figure 3.16, D). Three days after her initial visit, she underwent a right chest wall needle biopsy, which revealed BCS (Figure 3.16, A and B) with nuclear CCNB3 positivity on immunohistochemistry (Figure 3.16, C). The occurrence of this sarcoma in our patient is unusual, as BCS generally shows a male predilection (M:F ratio: 4.5:1), with some of the studies showing male predominance of 86% to 90% and most cases occurring between 10 and 20 years of age (median, 15.5 years old). Accurate diagnosis of this family of sarcoma is important because the prognosis is similar to that of ES and better than that of CIC-rearranged sarcomas.

BCOR-Altered Sarcoma in a 7-Year-Old Girl: A Rare Presentation of a Rare Sarcoma
(Poster No. 16)

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Sarcomas with BCOR genetic alterations includes tumors with both BCOR gene fusions, of which BCOR-CCNB3 is the most common (approximately 90% of cases), and BCOR internal tandem duplications. This family of sarcomas is rare, occurring less commonly than Ewing sarcoma (ES); one study identified 27 cases of ES for every case of BCOR-CCNB3 sarcoma (BCS). BCS was first described by Pierron et al in 2012. It often presents with pain and swelling and occurs more commonly in bone than in soft tissue (ratio: 1.5:1), with a predilection for pelvis, lower extremity, and paraspinal region. We report a 7-year-old girl who presented to the emergency department with right upper back and right posterior shoulder pain after she fell backwards on a
the nodules revealed a dense lymphocytic infiltrate admixed with epithelial cells with neighboring areas consisting of similar cells surrounded by a densely sclerotic matrix. There were also other areas of the tumor that showed a proliferation of cytologically bland spindle cells in a predominantly fibrous background and with focal myxoid areas (Figure 3.17, B through D). Most of the histopathologic findings were consistent with a low-grade fibromyxoid sarcoma (LGFMS), however with areas of overlapping morphology with sclerosing epithelioid fibrosarcoma. Immunohistochemical stains were only positive for MUC4 and focally positive for EMA in the tumor cells. Additional molecular studies were performed that showed an EWSR1 positivity and negative FUS fusion rearrangements. Overall, the findings were consistent with sclerosing epithelioid fibrosarcoma. Thus, we present a unique and unusual case of an elderly patient with diffuse intraabdominal sarcomatosis of SEF resembling LGFMS, with only a few cases being described in the literature.

**Unique NTRK3 Fusion in a Spindle Cell Sarcoma**  
(Poster No. 18)  
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NTRK3 gene encodes the NT-3 growth factor receptor, the tropomyosin receptor kinase TrKc, a member of the neuroepithelial tyrosine receptor kinase family, which includes TRKA, TRKB, and TRKC. TrKc signaling leads to activation of RAS-MAPK and PI3K-AKT pathways. NTRK gene fusions are actionable genetic events that are responsive to TRK kinase inhibitors, hence making their detection routine is to be prioritized clinically. NTRK3 fusions are rare in sarcomas. There are sufficient clinical and preclinical data to indicate that NTRK fusions predict sensitivity to TRK inhibitors such as larotrectinib, entrectinib, belizatinib, and PLX7486. Larotrectinib showed remarkable and durable efficacy in locally advanced and metastatic solid tumors harboring NTRK fusion. Entrectinib, which is active against NTRK fusions as well as fusions involving ROS1 and ALK has also shown to be greatly effective in recent clinical trials. The efficacy of entrectinib has resulted in its subsequent fast-track approval by the Food and Drug Administration. Although fusion partners like ETV6, MYO5A, and MYH9 have been documented, MEF2A as a fusion partner of NTRK3 appears to be a rarity. We present a case of a 41-year-old man who was diagnosed with spindle cell sarcoma of right forearm. His tumor was found to have a NTRK3 fusion and was treated with entrectinib. He had a poor response and subsequently died from pulmonary complications related to metastases to the lungs. The fusion partner MEF2A has not previously been reported and may be related to being refractory to therapy and the poor outcome.

**Consecutive Lesions of Desmoplastic Fibroma and Langerhans Cells Histiocytosis in Skull Bone**  
(Poster No. 19)  
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Desmoplastic fibroma are locally aggressive benign bone tumors with a high rate of recurrence. In the English literature only 20 cases have been reported in cranial bone. In adults, the Langerhans cell histiocytosis is also rare (about 1 to 2 cases/million/y). Bony involvement occurs in about 78% of patients, which may represent as an incidental finding on imaging, or may produce bone pain. Prognosis depends on initial presentation (isolated lesion, less than 5% mortality, versus widespread disease, 50% mortality). We present a case of a 20-year-old man with 1-month history of headache, showing a 13-mm focal, well-defined fibroosseous lesion in the left parietal skull bone by neuroimaging. Excision of the lesion showed paucicellular spindle cell tumor within a collagenous stroma, consistent with intraosseous desmoplastic fibroma (Figure 3.19, A and B). Follow-up neuroimaging (5 months later) showed a new 9-mm enhancing lesion with punctate area in the left frontal bone. The excised new bone lesion showed eosinophilic microabscesses and histiocytic proliferation with coffee bean–grooved nuclei (Figure 3.19, C), diffusely positive for CD1a (Figure 3.19, D) and S-100 and patchy positive for CD68. The diagnosis of Langerhans cell histiocytosis with eosinophilic microabscesses was given. Partial excision of dura mater was focally involved by the tumor. CD1a immunostain was performed on the left parietal lesion of desmoplastic fibroma, which was negative. The follow-up with whole-body positron emission tomography scan showed no evidence of residual/recurrent metabolically active neoplasm.

**Clear Cell Chondrosarcoma Presenting as a Destructive Rib Mass in a Patient With Multiple Hereditary Exostoses: A Rare and Unexpected Finding**  
(Poster No. 20)  
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Multiple hereditary exostoses (MHE) is an autosomal-dominant condition characterized by patients who develop multiple benign osteochondromas and caused by mutations in the EXT1 or EXT2 genes, respectively. Patients with MHE develop these tumors at an early age; the tumors continue to grow until skeletal maturity with the closure of the growth plates. Malignant transformation of an osteochondroma into ACT/CS1 occurs in less than 5% of cases, whereas higher-grade (grade 2 or 3) or dedifferentiated chondrosarcoma is very rare (<10% of malignancies). Clear cell chondrosarcoma is a rare chondrosarcoma subtype typically presenting in epiphyseal locations of long bones in older adults. Occasionally, foci of conventional chondrosarcoma may be seen in clear cell chondrosarcoma; however, it is unusual to find clear cell chondrosarcoma admixed with conventional chondrosarcoma. Herein, we report a case of a 61-year-old man with MHE presenting with a destructive rib mass on computed tomography (Figure 3.20, A). Surgical resection revealed a 6.4-cm cartilaginous mass destroying the rib without a definitive osteochondroma stalk (Figure 3.20, B). Histologic examination revealed predominantly grade 2 conventional chondrosarcoma; however, numerous foci of clear cell chondrosarcoma were identified throughout the specimen, demonstrating pale eosino-
Primary Dedifferentiated Chordoma of the Nasopharynx
(Poster No. 22)
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Chordomas are malignant neoplasms with notochordal differentiation, a high rate of local recurrence, and frequent metastasis. Most chordomas (approximately 95%) are intraosseous tumors involving the axial skeleton, with the base of skull/crvice, vertebral bodies, and sacrococcygeal bones most commonly affected. The nasopharynx is a very rare location for chordoma to arise, with only a handful of cases reported in the literature: 1 chondroid chordoma and 20 conventional chordomas. Most dedifferentiated chordomas are diagnosed postdiagnosis or as a recurrence, and not as a primary diagnosis. We report a dedifferentiated chordoma arising in the extraosseous nasopharynx. To our knowledge, this is the first reported case of dedifferentiated chordoma arising in this location. We present an 85-year-old man with a past medical history of asthma, chronic lymphocytic leukemia, gastroesophageal reflux disease, hypertension, and hyperlipidemia, who presented with nose bleeds. Positron emission tomography/computed tomography imaging demonstrated a 3.8 × 2.8-cm FDG-avid, ill-defined soft tissue mass arising in the right posterior nasopharynx. The patient then underwent nasal endoscopy, at which time a biopsy was obtained that showed a biphasic tumor composed of the conventional chordoma (Figure 3.22, A) and the dedifferentiated high-grade spindle cell components (Figure 3.22, B). Both cytokeratin (Figure 3.22, C) and brachyury (Figure 3.22, D) were strongly expressed in the conventional chordoma component with absent to attenuated staining in the dedifferentiated component. The tumor was subsequently resected; however, the patient passed away less than a year after diagnosis because of complications related to chronic lymphocytic leukemia.

Case of an Infantile Mesenchymal Tumor With Novel SQSTM1-MET Fusion
(Poster No. 23)
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Fusion sarcomas in the pediatric population are emerging as distinct entities with impactful therapeutic implications. We report a case of a 6-month-old girl with a soft tissue mass of her left occipital scalp. Imaging demonstrated diffuse soft tissue thickening extending from the left temporal region inferiorly to the left occipital bone. Microscopic examination of an incisional biopsy showed features suggestive of fibrous hamartoma of infancy, but insufficient for definitive diagnosis (Figure 3.23, A). To further characterize the lesion, molecular testing was performed on the biopsy tissue in tandem with additional surgical intervention. Evaluation of histologic sections of the 4.5-cm resected mass revealed morphologic findings not represented in the prior biopsy, including paucicellular zones of spindled to epithelioid cells forming cords within a chondromyxoid stroma (Figure 3.23, B). Other areas showed infiltrative fascicles of spindle cells within a collagenized matrix...
with whorled growth around vessels (Figure 3.23, C). Immunohistochemical studies showed the tumor cells to have focal and variable positive staining for SMA, S-100, desmin, and CD34. Stains for MSA and pan-TRK were negative. Next-generation sequencing of the biopsy tissue identified a novel SQSTM1-MET fusion. Gene fusions between SQSTM1 and NTRK1 as well as between TFG and MET have been reported previously in pediatric mesenchymal tumors. It is plausible that the gene fusion seen in this case, though previously not described, may represent a clinically targetable alteration. This case report illustrates a novel SQSTM1-MET fusion tumor, expanding the spectrum of fusions seen in pediatric mesenchymal tumors.

Chondrosarcoma in Childhood—An Uncommon Tumor: Case Report and Literature Review

(Poster No. 24)

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Chondrosarcomas in young patients are uncommon with approximately 0.3 cases per million. Patients with multiple osteochondromatosis have a 5% increased risk of developing chondrosarcomas. We present a 12-year-old girl with personal and family history of multiple osteochondromatosis with an 18-day history of subacute pain in the lower left limb associated with paresthesia; magnetic resonance imaging showed an iliac and sacral mass with extension to left gluteal region approximately 60 × 85 mm. Two intralesional resections were performed with a diagnosis of atypical chondroid tumor/chondrosarcoma grade I. During follow-up there was evidence of multiple residual lesions and neuropathic pain, without response to radiation. She underwent a left hemisacrectomy and revealed a lobed and infiltrative mass of 13.5 cm predominantly in the sacrum, with extension to iliac bone and adjacent soft tissues (Figure 3.24, A). Histologically, a chondroid lesion was identified consisting of irregular cartilage lobes with areas of necrosis (Figure 3.24, B and C), high cellularity, and atypical chondrocytes, with irregular and hyperchromatic nuclei, binucleation, and up to 2 mitoses in 10 high-magnification fields (Figure 3.24, D), with foci of compromise of the margins of section. The diagnosis of grade 2 chondrosarcoma was made. Because of the paucity of data on chondrosarcomas in young individuals, the principles of treatment are similar to adult patients. Chondrosarcomas are resistant to chemotherapy and relatively radioresistant, although radiotherapy can be useful for palliation; therefore, surgery is the only reliable treatment that predicts prognosis and recurrence. Overall disease-free survival of 89% at 5 years has been reported in young patients.

Dedifferentiated Liposarcoma With a Striking Desmoid-Type Fibromatosis-like Morphology: A Clinical, Radiologic, and Pathologic Pitfall on Biopsy

(Poster No. 25)

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The retroperitoneum is the most common site for dedifferentiated liposarcoma (DDLPS) at 10:1; however, other sites, including the extremities, show wide clinical, radiologic, and morphologic presentations. Classically, DDLPS shows a nonlipogenic pleomorphic spindle cell sarcoma juxtaposed to a well-differentiated adipocytic component. The extent of dedifferentiation is variable. Transition is usually abrupt but may be gradual. Furthermore, in some cases, a well-differentiated component is hard to identify. The “dedifferentiated” component often assumes an array of morphologies, most of which are high grade; however, in recent years, a low-grade component has been increasingly recognized. This so-called low-grade DDLPS may show mild cytologic atypia and mitotic activity reminiscent of desmoid-type fibromatosis. We report a 40-year-old woman who presented with a firm 8-cm thigh mass with irregular infiltrative borders on magnetic resonance imaging resembling desmoid-type fibromatosis or nodular fasciitis (Figure 3.25, A). A biopsy showed relatively bland spindle cells arranged in fascicles in the background of mature adipose tissue, somewhat resembling desmoid-type fibromatosis (Figure 3.25, B). However, careful close inspection revealed subtle nuclear atypia and mitotic activity, clues of a more sinister
Ewing Sarcoma With EWSR1-ERG Fusion Mimicking Neuroendocrine Carcinoma: An Alarming Diagnostic Trap

With Tips to Avoid This Pitfall

(Poster No. 26)

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Ewing sarcoma (ES) is a small round sarcoma occurring most often in children and young adults as primary bone tumor; however, 12% of cases occur in extracellular sites. Nearly all ESs harbor an EWSR1-FLI1 (90%), EWSR1-ERG (5%) or, rarely, variant FEV-ETS family gene fusions. Immunohistochemically, ES shows strong and diffuse membranous expression of CD99 as well as nuclear expression of NKX2.2. Rarely, neuroendocrine expression can be seen, but keratin expression is very unusual. The combination of aberrant neuroendocrine and keratin expression can lead to significant diagnostic difficulty and undesirable patient outcomes. We report a case of a 28-year-old man presenting with a 12-cm intra-abdominal soft tissue mass of the right lower quadrant. A core needle biopsy showed primitive small round blue cells with monotonous nuclei and fine chromatin (Figure 3.26, A). Immunohistochemistry showed expression of keratin and synaptophysin, raising the possibility of neuroendocrine carcinoma (Figure 3.26, B and C); however, NKX2.2 was also strongly positive in a nuclear fashion (Figure 3.26, B). Subsequent molecular analysis identified an EWSR1-ERG fusion, supporting our diagnosis of ES. This case illustrates the wide clinical and immunohistochemical spectrum of ES, which could have easily led to a misdiagnosis of neuroendocrine carcinoma. Therefore, recognition by the astute pathologist of these diagnostic pitfalls and performing CD99, NKX2.2, and, when appropriate, molecular analysis, should lead to the correct diagnosis in nearly all cases.

Myxofibrosarcoma (MFS) comprises a spectrum of malignant fibrolastic neoplasms with variably myxoid stroma, nuclear pleomorphism, and distinctive curvilinear vascular pattern. MFS is common in the elderly, especially in sun-damaged sites. MFS is a specific diagnosis; however, it is also a morphologic pattern that can be seen in dedifferentiated liposarcoma, pleomorphic liposarcoma (PLS), intimal sarcoma, various high-grade sarcomas, carcinomas, germ cell tumors, and even melanomas. Therefore, MFS is a specific diagnosis but also a pattern, a diagnosis of exclusion. PLS is the rarest type of liposarcoma, occurring most commonly in older adults in the deep soft tissues of the extremities. The diagnosis of PLS requires the identification of pleomorphic lipoblasts, which may be very focal, requiring careful inspection and adequate tissue sampling. We report a case of a 53-year-old man presenting with a large mediastinal mass. A core needle biopsy showed an overtly malignant neoplasm growing within a prominent myxoid stroma containing delicate branching vasculature (Figure 3.27, A and B). Extensive immunohistochemical analysis did not reveal any specific line of differentiation. Therefore, malignant spindle cell neoplasm with myxofibrosarcoma-like features was diagnosed. Subsequent resection showed a myxofibrosarcoma-like pattern; however, now sheets of pleomorphic lipoblasts were identified (Figure 3.27, C and D). MDM2 analysis (to exclude homologous lipoblastic differentiation in DDLPS) was negative. The final diagnosis of PLS with MFS-like pattern was provided. The value of this case highlights the pitfalls of an MFS-like pattern on biopsy, the need to identify pleomorphic lipoblasts in PLS (which can be absent on biopsy), and its unusual presentation as a mediastinal mass.
Addition to Careful, Extensive Microscopic Examination of Leiomyosarcoma: Can Fumarate Hydratase Testing Help in use of ancillary studies when the radiologic impression is not typical.

This case illustrates the importance of careful histologic evaluation and diagnosis, and positive USP6 rearrangement supported our impression. The degree of infiltration into the normal myometrium was minimal (a few millimeters). The tumor was positive with SMA and desmin. The combination of large size, 10 mitoses per 10 high-power fields in the most active high-power fields, rare atypical mitoses, incipient tumor necrosis, and diffuse cellular atypia lead to a diagnosis of low-grade leiomyosarcoma. We discuss the differential diagnosis in this case, which included, among others, fumarate hydratase (FH)-deficient uterine leiomyoma, which was ruled out through histologic features, as well as the diffuse, strong FH positivity in the tumor, consistent with reported FH preservation in leiomyosarcomas.

Hybrid Sclerosing Epithelioid Fibrosarcoma/Low-Grade Fibromyxoid Sarcoma Presenting as a Skull-Based Mass: A Rare Sarcoma in an Unusual Site

Poster No. 31

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Sclerosing epithelioid fibrosarcoma (SEF) is a rare fibroblastic sarcoma characterized by epithelioid fibroblasts arranged in cords and nests embedded in a densely sclerotic hyalinized stroma. A subset of SEFs are morphologically and molecularly related to low-grade fibromyxoid sarcoma (LGFMS). Furthermore, SEF and LGFMS exist as both pure and hybrid tumors, respectively. We report a case of a 47-year-old woman presenting with a slowly growing skull-based mass over 3 years’ duration, eventually leading to neurologic symptoms. A computed tomography demonstrated a 3-cm mass centered in the temporalis muscle and eroding into the dura (Figure 3.31, A). Surgical excision showed a deceptively bland and variably cellular tumor composed of spindled and epithelioid cells arranged in cords in a densely sclerotic background. In addition, several areas of the tumor showed classic LGFMS morphology of bland spindle cells growing in alternating zones within a fibromyxoid stroma (Figure 3.31, B and C). Metaplastic bone was also present. Immunohistochemistry for MUC4 showed strong and diffuse expression (Figure 3.31, D). The histologic features and immunophenotype support the diagnosis of hybrid SEF/LGFMS. Molecular analysis is currently underway. Despite their rarity, soft tissue sarcomas including SEF/LGFMS are an important differential diagnosis in unusual slow-growing tumors of the skull base. Finally,
Respectively its deceptively bland morphology, these tumors often pursue an aggressive clinical course; therefore, accurate pathologist recognition and judicious use of MUC4 is needed. It is currently unknown if hybrid tumors behave differently from pure SEFs; however, this case highlights the importance in recognizing morphologic variants that may have clinical impact.

**Recurrent PIK3CA H1047R-Mutated Infiltrative Facial Lipomatosis**

*(Poster No. 32)*

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PIK3CA-related overgrowth spectrum (PROS) encompasses a group of rare clinical entities that cause asymmetric, patchy overgrowth of mesodermal tissues, including fat, blood vessels, skin, and nervous tissues, among others. It is caused by postzygotic mosaic-activating mutations in the PIK3CA gene. We hereby report a case of an 8-year-old boy with recurrent lipomatosis of the scalp and nose. At presentation, head and face computed tomography scan showed an enlarging soft tissue lesion measuring 9.7 × 7.4 × 3.1 cm in the forehead toward the right side extending to the parietal scalp. The lesion was characterized primarily by fat signal, with areas of soft tissue signal in the periphery, traversing the fatty component. Intraoperatively, the mass was noted to infiltrate the muscles, skin, and galea, and it was removed via piecemeal approach (Figure 3.32, A and B). Microscopically, the mass consisted predominantly of mature adipose tissue with irregular thin and thick fibrous septa, compatible with infiltrative facial lipomatosis (Figure 3.32, C). Genetic profiling of the excised tissue revealed mutation in the PIK3CA H1047R gene, supporting the diagnosis of PROS. Although PIK3CA is a well-known cancer driver, hotspot mutations are increasingly being identified in benign skin and soft tissue overgrowth. Although there are no sufficient data about an increased risk of PIK3CA-associated adult cancers among PROS patients, cooperating mutations might still contribute to cancer development in this population of patients. Besides surgical debulking, novel therapeutic agents such as Alpelisib (PI3K inhibitor) continue to be trialed in patients with PROS to prevent future recurrence.

**Hemangioma or Vanishing Bone Disease? The Importance of Clinical Correlation in Gorham-Stout Disease**

*(Poster No. 33)*

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Gorham-Stout disease (GSD) is a rare, aggressive disorder of unknown etiology characterized by massive bone resorption in conjunction with vascular or lymphatic vessel proliferation. It typically occurs in the young, usually affecting the mandible, pelvis, or shoulders, but may present in any age and location. We present the case of a 56-year-old woman presenting with neck pain. Computed tomography and magnetic resonance imaging demonstrated multiple lytic bone lesions throughout the cranial vault, skull base, odontoid process, vertebral, and proximal humerus. Initial workup (iliac crest marrow biopsy, C2 vertebral biopsy of the largest 1.8-cm lesion) was unrevealing. She underwent frontal bone craniotomy, which showed thickened woven lamellar bone with irregular cement lines, areas of marrow replaced by dilated vascular channels lined by bland endothelium, and areas of fibrosis and punched-out bony trabeculae lined by osteoclasts. A diagnosis of hemangioma was rendered with comment for consideration for GSD and craniofacial angiomatosis, 2 histologically indistinct entities. Definitive diagnosis of GSD depends on temporal clinical, pathologic, and radiologic correlation, and the differential diagnosis is vast and includes malignancy, metabolic disease, and genetic disorders. Awareness of this rare disease is lacking, and in this case, it was suggested by pathology. The distinction between angiomatosis and GSD is difficult, and in both, the bland histology is easily overlooked. Further recognition of and research into GSD may offer invaluable insight into the interplay among vascular, lymphatic, and bony tissues. We hope that this case will bring further awareness to this disorder.

**Immunoglobulin G4–Related Disease in Rosai-Dorfman Disease: A Small Case Series From One Institution**

*(Poster No. 34)*

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**Context:** Increased immunoglobulin G4 (IgG4)–positive plasma cells are a frequent finding in Rosai-Dorfman disease (RDD), raising a possibility that RDD can be a spectrum of IgG4-RD. However, its significance has been debated because such finding was not consistently accompanied by other clinical features of IgG4-RD. We report 4 RDD cases that fulfilled the histologic criteria of IgG4-RD at our institution in the recent 5 years.

**Design:** Thirteen RDD cases were found at our institutional archive from 2015 to 2020. Three cases did not have increased plasma cells. Six cases had increased plasma cells but did not have enough numbers (>50 IgG4-positive cells/high-power field) and proportions of IgG4-positive cells (>40% of IgG-positive cells or total plasma cells). At last, the remaining 4 cases met the histologic consensus criteria for IgG4-RD.

**Results:** The age of the patients ranged from 40 to 81 years (mean, 54.3 years). Three of the patients were female and the other was male. The sites of presentation were arm, gluteal, presacral soft tissue, and
nal cavity. All 4 cases showed storiform fibrosis (Figure 3.34, A), obliterative thrombophlebitis (Figure 3.34, B), significantly increased IgG4-positive plasma cells (Figure 3.34, C), and S100-positive histiocytes with emperipolisis (Figure 3.34, D); however, none had systemic manifestations of IgG4-RD nor increased IgG4 serum levels.

Conclusions: IgG4-RD is a relatively recently described entity whose clinical aspects are not fully elucidated. Our series indicate that RDD may have disproportionately higher chances to have morphologic features of IgG4-RD without systemic manifestations. Therefore, further clinical, radiologic, and serologic studies are required to secure the diagnosis of IgG4-RD in RDD.

An Inflammatory Myofibroblastic Tumor With Misleading ALK Protein Expression

(Poster No. 35)

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Inflammatory myofibroblastic tumor (IMT) is a tumor of intermediate biologic potential that can arise in any location but has a predilection for the lungs of young patients. Characterized by a proliferation of myofibroblasts accompanied by a lymphoplasmacytic infiltrate, its nonspecific histology can make distinguishing IMT from other spindle cell lesions a challenge. More than 50% of IMTs harbor ALK gene rearrangements and frequently stain positive for anaplastic lymphoma kinase (ALK1). Therefore, immunohistochemical (IHC) staining for ALK1 is usually performed when IMT is in the differential diagnosis. Below, we describe a potential pitfall of this approach. An otherwise healthy 17-year-old girl presented with chronic hemoptysis during a 3-year period. Bronchoscopy revealed a 1-cm mass of the right upper lobe bronchus that was biopsied. The mass was histologically consistent with IMT (Figure 3.35, A and B). An ALK1 IHC stain performed with appropriate controls was negative (Figure 3.35, C); however, subsequent FISH testing demonstrated an ALK1 gene rearrangement (Figure 3.35, D). Crizotinib therapy was initiated and yielded a significant clinical response. Despite the strong association between ALK fusions and IMT, there are few data on the concordance rate between IHC and molecular results in this entity. One study indicates that more than 10% of ALK-rearranged IMTs may be ALK1 IHC negative, but this finding may be clone specific. Accepting a negative IHC result without confirmatory molecular testing can both be diagnostically misleading and deprive a patient of tyrosine kinase inhibitor therapy. Further studies into the sensitivity of ALK1 IHC assays among ALK rearranged IMTs is needed.

Cervical Spine Chordoma: A Rare Entity

(Poster No. 36)

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Chordoma is a rare primary malignant bone tumor (1%-5%) with notochordal differentiation, which generally arises from the axial skeleton. In the head and neck, the clivus is the most common site. Vertebral and soft tissue chordomas are rare. We present a case of a 61-year-old man who presented with mild chronic neck pain, intermittent numbness, and tingling of bilateral hands for 2 years. He subsequently underwent anterior cervical disectomy. During the surgery, a cystic mass arising from the right neural foramina at C5-C6 level with extravasated mucin was seen, which was resected. Grossly, the specimen consisted of multiple pieces of tan-brown soft tissue measuring 0.6 cm in greatest dimension. Histology revealed large epithelioid cells in a predominantly syncytial arrangement with eosinophilic and vacuolated cytoplasm and moderate atypia in a myxoid background (Figure 3.36, A). Differential diagnoses included chordoma, chordosarcoma, chordoid meningioma, cystic schwannoma, and metastatic adenocarcinoma. On immunohistochemistry, the tumor cells expressed epithelial membrane antigen (Figure 3.36, B), pancytokeratin AE1/AE3 (Figure 3.36, C), vimentin, and brachyury (Figure 3.36, D), and were negative for S-100, consistent with chordoma. Brachyury has been shown to be the most specific immunomarker for chordoma. In patients with vertebral body masses, chordoma should be considered a differential diagnosis. Findings of the gross examination and immunohistochemical studies can aid in arriving at the correct diagnosis.

Ancient Schwannoma of the Orbit With a Unique Immunohistochemical Profile

(Poster No. 37)

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Schwannomas (or neurilemomas) are benign, slow-growing tumors arising from Schwann cells within the peripheral nervous system, often in young to middle-aged patients. They may undergo degeneration over time that can mimic the histopathologic changes normally associated with malignancy. Here we present a case of an orbital ancient schwannoma in a 45-year-old man with a long-standing history of a retro-orbital mass. The lesion arose from a local nerve and was circumscribed with a fibrous, focally discontinuous capsule surrounding fascicles of spindle cells arranged in alternating cellular areas (Antoni A) and hypocellular, dis cohesive areas (Antoni B). Nuclear palisading and Verocay bodies were present. The spindle cells had ovoid to tapered nuclei with occasional hyperchromatic pleomorphic forms. Scattered intranuclear inclusions were present with inconspicuous nucleoli and infrequent mitoses. Areas containing thick-walled, hyalinized blood vessels were seen as well as thin-walled, ectatic vessels. Several areas of microcystic/reticular pattern were
identified along with large cystically dilated spaces with a pseudoepithelial lining of Schwann cells. The spindle cells demonstrated strong, diffuse positive staining with S100 and SOX10 by IHC, and staining for D2–40 (podoplanin) was stronger in the cellular Antoni A areas surrounding the larger cystic spaces. These features have resulted in the misdiagnosis of these lesions as malignant. These IHC findings may be useful for identification in the future (Figure 3.37).

**NKX3.1 Biomarker Expression in Male Breast Cancer**

**Poster No. 38**

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**Context:** Male breast cancer is rare. The majority is invasive ductal carcinoma (IDC) with >90% ER+, approximately 80% PR+, 5% HER2+, and 1% ER+/PR-/HER2+. This ER/PR positivity rate is higher in male breast cancer than in female cases. NKX3.1 is a tumor suppressor gene regulated by androgens in the prostate. A prior study reports NKX3.1 expression in female breast cancer than in female cases. NKX3.1 is a tumor suppressor gene expressed in the rare entity of male breast cancer.

**Results:** In a retrospective analysis of male breast cancer cases 2013–2019, 9 cases were identified, all IDC. Three patients had history of prostate adenocarcinoma (30%) where NKX3.1 may be utilized to help determine primary versus metastasis. All cases were stained with hematoxylin-eosin. Receptor studies, NKX3.1, and androgen receptor immunohistochemistry were performed.

All cases were ER+ (100%), 8 PR+ (88%), 7 HER2+ by IHC (77%), 1 equivocal (11%), and 1 positive (11%). One was amplified and 8 nonamplified by HER2 IHC/ISH (88%). All cases were AR+ (100%). Two showed patchy positive NKX3.1 (22%); the remaining cases were negative (78%). Androgen receptor immunohistochemistry stains showed moderate to strong diffuse positivity with an average H-score of 230 (Table).

<table>
<thead>
<tr>
<th>Case No.</th>
<th>ER/PR IHC</th>
<th>HER2 IHC/ISH</th>
<th>AR/AR H-Score</th>
<th>NKX3.1 IHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>++</td>
<td>~/nonamplified</td>
<td>+300</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>++</td>
<td>~/nonamplified</td>
<td>+195</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>++</td>
<td>equivocal/noramplified</td>
<td>+180</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>++/++</td>
<td>~/nonamplified</td>
<td>+245</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>++/++</td>
<td>~/nonamplified</td>
<td>+190</td>
<td>–</td>
</tr>
<tr>
<td>6</td>
<td>++/++</td>
<td>~/nonamplified</td>
<td>+180</td>
<td>–</td>
</tr>
<tr>
<td>7</td>
<td>++/++</td>
<td>~/nonamplified</td>
<td>+290 (patchy)</td>
<td>–</td>
</tr>
<tr>
<td>8</td>
<td>++/++</td>
<td>+/amplified</td>
<td>+300 (patchy)</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>++/++</td>
<td>~/nonamplified</td>
<td>+190</td>
<td>+</td>
</tr>
</tbody>
</table>

**Conclusions:** Studies have reported NKX3.1 expression in female breast carcinomas. This study examines NKX3.1/AR expression in comparison with ER/PR/HER2 status in male breast cancers. In our study, NKX3.1 negativity was reliable in differentiating primary breast versus metastasis; however, patchy positive staining was seen in 2 of 9 cases. Diffuse AR/ER expression was seen in all cases, which correlates with the results of other studies (>90% ER/AR+). Further evaluation among additional specimens is needed to ensure the utility of NKX3.1 expression in the rare entity of male breast cancer.

**Rosai-Dorfman Disease of the Breast: Report of 4 Cases**

**Poster No. 39**

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**Context:** Rosai-Dorfman disease (RDD) is an uncommon histiocytosis typically presenting with lymphadenopathy and less commonly with extranodal involvement. Breast involvement of RDD is very unusual.

**Design:** We searched our institutional database of all breast cases from 2010 to 2020 and identified 4 cases of RDD of the breast. Hematoxylin-eosin-stained slides with associated ancillary studies, clinical history, imaging findings, and clinical follow-up data were reviewed. Immunohistochemistry studies including OCT2, a novel marker for monocye-macrophage phenotype of RDD, were performed on all 4 cases.

**Results:** All patients were black women ranging from 15 to 57 years of age. Patients presented with unilateral, unifocal (3 of 4) or multifocal (1 of 4) masses (Figure 3.39, A) confined to the breast, ranging from 13 to 31 mm, with BI-RADS category of 4 (3 of 4) or 5 (1 of 4). All 4 cases showed similar morphology with sheets of large histiocytes displaying emperipolysis with associated fibrosis and dense lymphoplasmacytic infiltrate (Figure 3.39, B). The histiocytes coexpressed CD68, S100 (Figure 3.39, C), and OCT2 (Figure 3.39, D), and were negative for CD1a and AE1/AE3 (4 of 4). Flow cytometry (1 of 4), k/x in situ hybridization (2 of 4), and IgG4/IgG immunohistochemistry (1 of 4) failed to reveal lymphoma or IgG4-related disease. No microorganisms were identified on AFB and GMS stains (3 of 4). Complete excision was performed in all 4 patients and no patient had recurrence during follow-up (3 to 128 months).

**Conclusions:** RDD rarely involves the breast. Histopathology in conjunction with ancillary studies, including the novel monocye-macrophage marker OCT2, is essential for accurate diagnosis and optimal clinical management. Patients with RDD of the breast have an excellent prognosis after complete excision.

**Low Estrogen Receptor–Positive Invasive Breast Carcinoma: Comparing a Large Academic Hospital With an Urban Public Hospital**

**Poster No. 40**

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**Context:** Testing for expression of estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor 2 receptor (HER2) is required for invasive, recurrent, and metastatic breast cancer.
cases. Cases with 1%–10% ER$^+$ malignant cells are reported as low ER positive (LER$^+$) with a comment per 2020 ASCO/CAP update. In this study, we compare data from a large academic hospital, the Emory Healthcare system (EHC), with that of Grady Memorial Hospital (GMH), an urban public hospital, for LER$^+$ invasive breast carcinomas (IBCs).

**Design:** The electronic medical records at GMH were searched for cases of IBC (2015–2018). ER and HER2 immunohistochemistry (IHC) and HER2 FISH amplification results were collected. ER and HER2 IHC percentage positivity, stain intensity, tumor grade, size, stage, and treatment were further evaluated for the years 2017 and 2018. EHC data were extracted from Redcap Database for the period January 2000–March 2020.

**Results:** Of 177 (GMH) and 2848 (EUC$^+$) ER$^+$ cases, 6 (5.4%) and 35 (1.23%) were LER$^+$, respectively (Table). The majority of LER$^+$ (>70%) received chemotherapy. A minority (approximately 35%) received hormonal therapy. At GMH, there was a statistically significant difference in histologic grade and tumor size ($P < 0.006$) between LER$^+$ and high-ER$^+$ cases. 100% of LER$^+$ cases were grade 3 with median tumor size of 2.9 cm, whereas only 29% of high-ER$^+$ cases were grade 3 and with a median tumor size of 1.8 cm.

**Conclusions:** Low ER-positive cases make up <5% of ER-positive cases. The majority of LER$^+$ cases are grade 3 and received chemotherapy. A minority received hormonal therapy.

**Distribution of Predictive Markers in IBC**

<table>
<thead>
<tr>
<th>Hospital (No. of Cases)</th>
<th>ER$^+$</th>
<th>LER$^+$</th>
<th>HER2$^+$</th>
<th>TN$^+$</th>
</tr>
</thead>
<tbody>
<tr>
<td>GMH (450)</td>
<td>351</td>
<td>3.4% (6/177)</td>
<td>11.8% (53)</td>
<td>16.9% (76)</td>
</tr>
<tr>
<td>EUH (4115)</td>
<td>2848</td>
<td>1.2% (35/2848)</td>
<td>15.8% (650)</td>
<td>15.7% (464)</td>
</tr>
</tbody>
</table>

Abbreviations: EUH, Emory University Hospital; GMH, Grady Memorial Hospital; TN, triple negative.

**Evaluating Analytical Agreement of Ki-67 Laboratory-Developed Tests With the MonarchE Clinical Trial Assay in Hormone Receptor-Positive (HR$^+$), Human Epidermal Growth Factor Receptor 2-Negative (HER2$^-$) Breast Carcinoma**

**Poster No. 41**

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**Context:** Lack of standardization of Ki-67 assessments and scoring methods, as highlighted by the International Ki-67 in Breast Cancer Working Group, has limited the use of Ki-67 immunohistochemistry in breast cancer management. Using a cutoff of $\geq 20\%$ to identify high-Ki-67 tumors in patients with HR$^+$, HER2$^-$, node-positive, high-risk early breast cancer, the MonarchE phase 3 trial (NCT03155997) showed the spindles and metastatic bone formation with osteoclast-like giant cells. Immunohistochemically, the spindle cells were negative for cytokeratin; diffusely positive for p63; negative for ER, PR, and HER2 (triple negative); and wild type for p53, and had an intermediate to high Ki-67 proliferation index (20%–30%). With moderate suspicion of metastatic carcinoma, a lumpectomy was subsequently performed. The excision specimen revealed an organized ossifying lesion lacking osteoblast atypia and peripheral spindle cells with occasional mitotic activity (Figure 3.42, A and B). All cytokeratin immunohistochemical stains were again negative and, after consultation with the soft tissue pathology department, a diagnosis of reactive spindle cell lesion was favored. Spindle cell lesions of the breast are rare entities in which cellular atypia cannot reliably be used to distinguish between benign and malignant tumors. In addition, osseous metaplasia is most often seen in malignant lesions in the breast, having only ever been reported in 2 other benign cases in the literature. This accentuates the importance of a broad differential diagnosis, comprehensive immunohistochemical panel, and expert consultation when atypical spindle cells with metastatic bone formation are observed in core needle biopsies in order to avoid the diagnostic pitfall of metastatic carcinoma.

**Use of Pan-TRK Immunohistochemistry to Identify a Secretory Carcinoma of the Breast in a 72-Year-Old Woman**

**Poster No. 43**

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Secretory carcinoma is a rare subtype of invasive breast carcinoma with an excellent prognosis. It was initially described in pediatric patients but can occur in adults, including occasional older patients. It is characterized by ETV6-NTRK3 translocation, resulting in the overexpression of a tropomyosin receptor kinase (TRK) C fusion protein. We present the case of a 72-year-old woman with a BI-RADS 4 left breast mass identified on screening mammography. Biopsy of the mass showed a low-grade neoplasm with microcystic architecture (Figure 3.43, A) and prominent dense eosinophilic intraluminal secretions (Figure 3.43, B). ER was only weakly positive (1+–20%) and PR and
HER2 were negative. Immunohistochemistry for pan-TRK (Ventana, EPR17341) showed strong, diffuse expression (Figure 3.43, C), as did S100 immunostaining. Fluorescent in situ hybridization using the Vysis ETV6 dual-color break-apart probe showed ETV6 disruption in 90% of cells (Figure 3.43, D), confirming the presence of an ETV6-NTRK3 translocation. This case demonstrates the value of pan-TRK immunohistochemistry in identifying these rare but prognostically significant tumors, particularly among older patients, in whom the diagnosis may be less expected. Pan-TRK immunohistochemistry may be especially useful in low-grade–appearing but hormone receptor–weak or –negative tumors, as most triple-negative breast cancers are generally higher grade, whereas most low-grade invasive ductal carcinomas have strong estrogen receptor expression.

**PD-L3 and PD-L1 Expression in Metaplastic Breast Carcinoma**

*(Poster No. 44)*

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**Context:** The majority of metaplastic breast cancers (MBCs) are ER/PR/HER2 triple negative. Immunochemistry provides a potential breakthrough in breast cancer treatment. PD-L3 is a promising target for emerging drug enoblituzumab. Our goal was to study PD-L1 and PD-L3 expression in MBC.

**Design:** A database search was performed, and 15 cases were identified. Upon review, 8 cases were classified as MBC and 7 as invasive ductal carcinoma (IDC). Immunohistochemistry (IHC) was performed using anti–PD-L1 (22C3) and anti–PD-L3 antibodies. PD-L1 and PD-L3 expression was evaluated in MBC, IDC, and nonneoplastic breast tissue. Expression in >1% of tumor cells was interpreted as positive for both markers. IHC scores were calculated by multiplying the percentage of the positive tumor cells by a degree of intensity (1, weak; 2, moderate; 3, strong).

**Results:** PD-L3 was expressed in 7 MBCs (87%) (Figure 3.44, D). Both metaplastic component and epithelial component showed strong staining in neoplastic cells. All 7 IDCs (100%) were positive for PD-L3. The mean PD-L3 IHC score in IDC was lower than that in MBC. Both IDC and IDC had higher PD-L3 expression compared with that of nonneoplastic breast tissue (Fisher exact test, P < .01). PD-L1 was positive in 3 MBCs (37%) and 2 IDCs (30%) (Figure 3.44, C).

**Conclusions:** Our study demonstrates that PD-L3 is expressed in the majority of MBC, indicating a possible role of anti–PD-L3 drugs. In MBC, PD-L3 exhibited high levels of expression in both metaplastic and epithelial components of the tumor. PD-L1 is expressed in a smaller fraction of MBC than PD-L3.

**GATA3 Expression in Breast Carcinoma Post–Neoadjuvant Chemotherapy and in Metastatic Setting**

*(Poster No. 45)*

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**Context:** GATA3 is used in immunohistochemistry panels to determine the primary site of metastatic carcinoma when breast origin is possible. The retention of GATA3 expression in breast carcinoma after chemotherapy or metastasis has not been well characterized.

**Design:** In 14 cases of breast carcinoma, GATA3 immunohistochemistry was performed on tumors before and after neoadjuvant chemotherapy. A search for GATA3-negative distant/extranodal metastatic breast carcinoma was performed, and GATA3 was performed on the corresponding primary tumors.

**Results:** Of 14 cases studied before and after neoadjuvant chemotherapy, 13 cases were positive in both specimens and 1 was negative in both specimens. Of 142 metastases, 138 were GATA3 positive and 4 GATA3 negative. Of the 4 GATA3-negative cases, 3 of the corresponding primary tumors were GATA3 negative and 1 was GATA3 positive. This patient presented with diffuse liver metastases and bone lesions. Prior to chemotherapy, biopsies of the liver metastasis and primary breast primary were both GATA3 positive. After 8 months of weekly paclitaxel, a liver biopsy revealed tumor with the same receptor profile (estrogen and progesterone receptor positive, HER2 negative) but negative GATA3. She died of disease 8.5 months after initial diagnosis.

**Conclusions:** In most cases chemotherapy does not alter GATA3 expression, and GATA3 testing of metastases is useful to suggest breast origin. Lack of GATA3 expression in metastatic breast carcinoma is uncommon and usually reflects absent expression in the primary tumor rather than loss. Loss of GATA3 expression post–neoadjuvant chemotherapy or in metastatic breast carcinoma is rare and may indicate an aggressive tumor with poor prognosis.

**Tubular Adenoma With a Concurrent Fibroadenoma: A Rare Disease With a Rare Occurrence**

*(Poster No. 46)*

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Tubular adenoma (TA) of the breast is one of the rarest benign neoplasms. There are only a handful cases of TA with concurrent fibroadenoma reported in literature. We present a case of tubular adenoma with a concurrent fibroadenoma of the breast in a 24-year-old woman. She presented with a right breast mass of 1 year’s duration. Physical examination showed a superficial, firm, and mobile well-circumscribed mass 4.0 cm in size at the 12-o’clock position. Ultrasound showed a well-defined oval hypoechoic mass with acoustic shadowing measuring 4.4 cm x 2.7 cm centered at the 12-o’clock position. After 3 months she underwent surgical excision of
the mass. Tissue received was fixed in neutral buffered formalin and embedded in paraffin for routine histologic examination. Grossly, the specimen consisted of one piece of white soft tissue measuring 4.5 × 4.0 × 2.0 cm with white homogenous cut surfaces. Microscopic examination showed 2 separate patterns: a well-circumscribed lesion composed of closely packed uniform small tubules with minimal intervening stroma. The tubules were lined by epithelial cells and myoepithelial cells as highlighted by P63 immunohistochemical stain. At the periphery of the tubular adenoma there were areas composed of compressed ducts showing typical fibroadenoma features with demarcated borders between the 2 patterns. The presence of tubular adenoma and fibroadenoma in the same breast supports a common pathogenesis. Further clonal analysis is required to prove the association.

Retrospective Review of All Breast Pathology Consult Cases at the Cleveland Clinic in 1 Year: What Do Pathologists Struggle With the Most?

(Poster No. 47)

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Context: To identify the most common reasons for consultation to the Breast Pathology Service at the Cleveland Clinic.

Design: The anatomic pathology database CoPath Plus (Sunquest Information Systems, Tucson, Arizona) was searched for all breast consultation cases in 2019, excluding in-house cases and cases of patients who were transferring care.

Results: A total of 553 cases met the criteria. Submitting institutions included a variety of academic and private practices. For each case, the paperwork from the submitting institution was reviewed to identify the specific question, subsequently classified into 14 categories (Table). The reason for consultation request was not provided for 78 cases (14%). In this category, a review of the outside diagnoses where applicable and those rendered at the Cleveland Clinic showed the top 5 reasons for consultation were likely the need to document a second pathologist’s review of a verified diagnosis (19%), assistance with subtype classification (15%) and presence of (micro-) invasive carcinoma (10%), evaluation of lymph node metastasis and distinction between hyperplasias (9%) each: florid, atypical lobular, and atypical ductal hyperplasia), and reaching the diagnostic threshold for ductal carcinoma in situ (5%).

<table>
<thead>
<tr>
<th>Summary of All Cases Into Categories</th>
<th>No. of Cases</th>
<th>Percentage</th>
<th>Mean Age, y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not provided</td>
<td>78</td>
<td>14.1</td>
<td>60.3</td>
</tr>
<tr>
<td>ADH versus DCIS</td>
<td>78</td>
<td>14.1</td>
<td>60.1</td>
</tr>
<tr>
<td>Other</td>
<td>64</td>
<td>11.6</td>
<td>60.6</td>
</tr>
<tr>
<td>Papillary lesion</td>
<td>59</td>
<td>10.7</td>
<td>61.9</td>
</tr>
<tr>
<td>FEL</td>
<td>59</td>
<td>10.7</td>
<td>41.3</td>
</tr>
<tr>
<td>Small focus of invasion</td>
<td>56</td>
<td>10.1</td>
<td>63.5</td>
</tr>
<tr>
<td>Atypia, don’t know how to classify</td>
<td>41</td>
<td>7.4</td>
<td>54.1</td>
</tr>
<tr>
<td>Spindle cell lesion</td>
<td>37</td>
<td>6.7</td>
<td>57.5</td>
</tr>
<tr>
<td>ADH versus FEA</td>
<td>28</td>
<td>5.1</td>
<td>53.3</td>
</tr>
<tr>
<td>Clinician request</td>
<td>16</td>
<td>2.9</td>
<td>56.8</td>
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<tr>
<td>Vascular lesion</td>
<td>14</td>
<td>2.5</td>
<td>63.1</td>
</tr>
<tr>
<td>CSL</td>
<td>13</td>
<td>2.4</td>
<td>60.8</td>
</tr>
<tr>
<td>Patient request</td>
<td>7</td>
<td>1.3</td>
<td>50.7</td>
</tr>
<tr>
<td>Second pathologist review</td>
<td>3</td>
<td>0.5</td>
<td>57.3</td>
</tr>
<tr>
<td>Total</td>
<td>553</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ADH, atypical ductal hyperplasia; CSL, complex sclerosing lesions; DCIS, ductal carcinoma in situ; FEA, flat epithelial atypia; FEL, fibroepithelial lesions.

Conclusions: We show the practicing pathologist most commonly struggles with classifying atypical precursor lesions specifically when small and focal or bordering on intraductal carcinoma (32%; 174 of 553). The second most common challenge, perhaps due to the burden this diagnosis bears, is diagnosing (micro-) invasive carcinoma (18%; 99 of 553). As such, our data support the continued need for rigid and clear criteria regarding atypical hyperplasia and intraductal carcinoma of the breast.

Point-Based Weighted Diagnostic Scale for Histopathologic Assessment of Mammary Cellular Fibroepithelial Lesions

(Poster No. 48)

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Context: Classification of cellular fibroepithelial lesions (cFELs) on breast core needle biopsies (CNBs) can be challenging. cFELs are usually excised and reclassified as either phyllodes tumors (PTs) or fibroadenomas (FAs), which differ in their clinical management. We set out to develop a point-based weighted diagnostic scale (WDS) with the purpose of improving cFEL classification on CNBs.

Design: Breast CNBs diagnosed as cFELs between January 2000 and December 2019 and their corresponding excisions were identified. Histologic slides were reviewed by 2 pathologists and 2 trainees using a predetermined score (PDS) of 11 histologic parameters (Table). A WDS was developed using the mean PDS based on the excisions and was then applied to CNBs to categorize cFELs as FA, PT, or undetermined (UD). Sensitivity, specificity, positive and negative predictive values (PPV, NPV), and the diagnostic accuracy index (DAI) were calculated.

Results: A total of 33 patients were identified, with an average age of 48 years (range, 22–82 years). Most cFELs were classified as FAs on excisions (72.7%; 24 of 33), whereas 27.3% (9 of 33) were diagnosed as PTs. The mean PDS was 16.25 (12.25–20.5) for PT, 6.9 (2.75–9) for FA and 10.2 (9.11–25) for UD. The WDS was 0–4.9 for FA, >5–11.25 for PT, and 9–11.25 for UD, with 33.3% sensitivity, 100% specificity, 100% PPV, 82.6% NPV, and 84% DAI. The WDS correctly identified 79.2% (19 of 24) of FAs but only 22.2% (2 of 9) of PTs on CNBs.

Conclusions: The WDS accurately classified 63.6% (21 of 33) of cFELs on CNBs with 100% specificity and 100% PPV; 57.6% (19 of 33) of patients could have been spared surgery.

Summary of Histologic Parameters

1. Permeative borders
2. Stromal cellularity
3. Stromal nuclear atypia
4. Stromal mitoses per 10 high-power fields
5. Stromal heterogeneity
6. Stromal involution
7. Stromal fragmentation
8. Stromal expansion
9. Stromal myxoid change
10. Leaflike architecture
11. Epithelial hyperplasia

Clinicopathologic Features of Female Mammary Carcinoma in Patients 30 Years Old or Younger

(Poster No. 49)

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Context: Female breast carcinoma is the most common malignancy in women. The peak age at diagnosis is in the 60s, whereas the incidence in patients <40 years old is 2%–7%. We reported the clinical, pathologic, prognostic markers, treatment, and prognosis of breast carcinoma in patients 30 years or younger, nonpregnant women.

Design: We searched our database (2000–2019) for breast carcinoma in <30-year-old nonpregnant women. Detailed clinicopathologic features were reviewed.

Results: Eighty-five patients with breast carcinoma were identified. The mean age at diagnosis was 26 years. Of these, 71 were invasive ductal carcinoma, 10 ductal carcinoma in situ, 2 lobular carcinoma in situ, 30 years old or younger.
situated, 1 invasive lobular, and 1 metaplastic carcinoma. Fifty-five patients had palpable breast mass. 73.2% were grade 3, 25.6% were grade 2, and 1.2% were grade 1. 73.9% were stages higher than T1b. Estrogen receptor (ER) and progesterone receptor (PR) were expressed in 73.4% and 59.5% of cases, respectively. HER2/neu was amplified in 29.3%; 79.3% had a proliferative index \( >20 \); 19.3% had BRCA mutation, of which 45.3% were triple negative. ER and PR were expressed in 85.7% and 76% of BRCA-negative patients, respectively. Of patients with invasive carcinoma, 40.3% had positive axillary lymph nodes. Of invasive carcinoma patients, 27.8% received neoadjuvant chemotherapy, followed by surgery. The remaining 72.2% received adjuvant chemotherapy. Follow-up revealed that 9 died from their disease, 36 were alive, and 40 patients were lost to follow-up.

Conclusions: Younger patients are more likely to have palpable masses and high-grade and high-stage tumors. BRCA-negative patients are more likely to express hormone receptors. BRCA-positive patients are likely to be triple negative.

Analytic Comparison Study of an IUO Ki-67 Clinical Trial Assay on Dako Omnis and Dako Autostainer Link48 (ASL48)

(Poster No. 50)

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Context: The monarchE trial assessed patient samples for Ki-67 expression using an assay that was developed and validated on Dako Omnis (Agilent technologies). The current study measures concordance rate test results from the clinical trial assay run on the Dako Omnis instrument and the Dako Autostainer Link48 (ASL48).

Design: Forty archival breast cancer specimens with a range of Oncotype DX breast recurrence scores were selected. An unstained slide of each was stained with Dako clinical trial assay reagents on the Dako Omnis (Agilent technologies). The current study measures concordance rate test results from the clinical trial assay run on the Dako Omnis instrument and Dako Autostainer Link48 (ASL48).

Results: Average percentage negative agreement (ANA), average percentage positive agreement (APA), and overall percentage agreement (OA) were calculated with corresponding 2-sided 95% percentile bootstrap CIs. Pairwise comparisons from the interinstrument study resulted in 322 total concordant outcomes (244 negative and 78 positive), with a total of 38 discordant outcomes. ANA, APA, and OA point estimates were 92.8%, 80.4%, and 89.4%, respectively. A Bland-Altman plot was used to visualize potential bias between the paired samples, in which no significant difference was observed. The cases scored via the Omnis instrument were on average 0.7% lower than those scored with the ASL48 (Pearson correlation coefficient = 0.908; Figure 3.50).

Breast Adenoid Cystic Carcinomas (Total Cases = 11)

<table>
<thead>
<tr>
<th>Clinicopathologic Variables</th>
<th>No.</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset, y (range, 48–99)</td>
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<td></td>
</tr>
<tr>
<td>( \leq 55 )</td>
<td>4</td>
<td>36.4</td>
</tr>
<tr>
<td>( &gt;55 )</td>
<td>7</td>
<td>63.6</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Laterality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>7</td>
<td>63.6</td>
</tr>
<tr>
<td>Left</td>
<td>4</td>
<td>36.4</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Presentation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lump</td>
<td>1</td>
<td>11.1</td>
</tr>
<tr>
<td>Screening</td>
<td>8</td>
<td>88.8</td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Morphologic patterns</td>
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<td></td>
</tr>
<tr>
<td>Cribriform/trabecular pattern</td>
<td>10</td>
<td>76.9</td>
</tr>
<tr>
<td>Solid pattern</td>
<td>2</td>
<td>15.4</td>
</tr>
<tr>
<td>High-grade transformation</td>
<td>1</td>
<td>7.7</td>
</tr>
<tr>
<td>Tumor size, mm (range, 6–38)</td>
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<td></td>
</tr>
<tr>
<td>( \leq 20 )</td>
<td>4</td>
<td>40</td>
</tr>
<tr>
<td>( &gt;20 )</td>
<td>1</td>
<td>60</td>
</tr>
<tr>
<td>Total</td>
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<td></td>
</tr>
<tr>
<td>Tumor grade</td>
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<td></td>
</tr>
<tr>
<td>1</td>
<td>4</td>
<td>44.4</td>
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<tr>
<td>2</td>
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<td>Total</td>
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<tr>
<td>Tumor stage (pT)</td>
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</tr>
<tr>
<td>1b</td>
<td>3</td>
<td>30</td>
</tr>
<tr>
<td>1c</td>
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<tr>
<td>Total</td>
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<tr>
<td>Tumor necrosis</td>
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<td>Present</td>
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<tr>
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</tbody>
</table>

Conclusions: The concordance study demonstrates there is no inherent bias between the Dako Omnis instrument and the Dako ASL48 instrument.

Downs-Kelly is a consultant with Eli Lilly. Badve has received grant or research support from Agilent Technologies and is a paid speaker for Agilent Technologies.

Clinical Pathologic Characteristics of Adenoid Cystic Carcinoma of the Breast: Ten Years of Experience From a Single Cancer Institution

(Poster No. 51)

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Context: Adenoid cystic carcinoma (ACC) is a rare malignant breast tumor that is typically ER−, PR−, and HER2−, with an indolent and favorable clinical course. Our goal is to characterize the clinicopathologic features and outcome of breast ACCs with an emphasis on breast biomarker expression.

Design: All breast ACCs for the period 2010–2020 were retrieved. Clinical and pathologic characteristics including follow-up data were analyzed.

Results: We identified 11 cases of breast ACCs (Table). In our cohort, breast ACC usually presented in older age groups as low-
intermediate-grade tumors with negative axillary lymph nodes. Nine of 11 ACCs were triple negative for ER, PR, and HER2. In 1 patient, the tumor was ER− (Allred score 3), PR−, and HER2−. A second case had ER− (Allred score 4), PR−, and HER2− on the biopsy; however, the excision had positive final surgical margins and showed ER+, PR+, and HER2−. This patient had a local recurrence and distant lung metastasis, both 13 years after the initial diagnosis with triple-negative biomarkers on the metastasis. A third case with triple-negative biomarkers and positive final surgical margins had 3 distant metastases to the lung, 6, 8 and 13 years after the initial diagnosis.

**Conclusions**: Despite the fact that breast ACC is an indolent disease, positive margin is strongly considered a predictive factor for local recurrence and distant metastasis. Expression of ER and/or PR may be associated with aggressive behavior and distant metastasis.

**Cytokeratin 7- and HER2-Negative Mammary Paget Disease Without an Underlying In Situ and Invasive Carcinoma: Report of a Rare Case**

(Mariam Ratiani, MD (maratiani@mcw.edu); Ayesha Farooq, MD; Julie M. Jorns, MD; Yuri Sheinin, MD. Department of Pathology, Medical College of Wisconsin, Milwaukee)

Paget disease (PD) of breast accounts for 1%–3% of all breast carcinomas. It can affect both women and men and usually presents with eczematoid changes of nipple areola complex, ulceration, crusting, discharge, or bleeding. It is known to be associated with carcinoma in situ or invasive carcinoma in the underlying breast. Tumor cells are usually positive for CK7, GATA3, HER2, and ER. We report a case of a 74-year-old African American woman who presented with a lesion on the right areola. A biopsy of the lesion demonstrated a pagetoid intraepithelial neoplasm, suggesting a differential diagnosis of mammary Paget disease and pagetoid Bowen disease. Excision of the mass showed large neoplastic cells in the nipple epidermis spanning at least 2.0 cm. The cells had enlarged ovoid nuclei with prominent nucleoli, nuclear pseudoinclusions, periductal stromal condensation, and variable degree of periductal stromal condensation, increased cellularity, and mitotic figures. Although a diagnosis of juvenile fibroadenoma was considered, the prominent leaflike architecture and periductal stromal condensation are features consistent with phyllodes tumor.

**Conclusions**: Any prior history of breast high-risk lesion or breast carcinoma should factor heavily toward surgical excision of a benign intraductal papilloma even in the absence of atypia at the time of biopsy.

**Synchronous Bilateral Benign Phyllodes Tumor of the Breast in a 17-Year-Old Female**

(Changzhao Li, MD, PhD (changzhaoi@creighton.edu); Matthew Morgan, MD; Catherine Stooz, MD. Department of Pathology, Creighton University, Omaha, Nebraska)

Phyllodes tumors are uncommon biphasic lesions accounting for 1% or less of all primary breast tumors. These lesions generally occur in middle-aged or elderly women. Synchronous bilateral benign phyllodes tumors in a young patient are extremely rare. We report a case of synchronous bilateral benign phyllodes tumor of the breast in a 17-year-old girl. The patient presented to the breast health clinic with bilateral breast masses. Gray-scale and color Doppler sonographic images demonstrate circumscribed round and ovoid hypoechoic masses within both breasts (Figure 3.54, A and B). Morphologically these lesions appeared like fibroadenomas; however, they exhibited some degree of posterior acoustic enhancement, as well as interval growth of the left mass, and thus biopsy was recommended. The biopsy specimen from both right and left breast demonstrated a fibroepithelial lesion with a predominately intracanalicular growth pattern, leaflike architecture, variable degree of periductal stromal condensation, increased stromal cellularity, and mitotic figures. Although a diagnosis of juvenile fibroadenoma was considered, the prominent leaflike architecture and periductal stromal condensation are features consistent with phyllodes.

**Factors Influencing Benign Intraductal Papillomas Upgrade Rates: A 20-Year Review**

(Robert Pantaleon Vasquez, MD (robert.pantaleon@gmail.com); Swati Bhardwaj, MD; Nebras Zeinazoun, MD; Melissa Alexander, MD; Adriana Corben, MD; Shabnam Jaffer, MD. Department of Pathology, The Mount Sinai Hospital, New York, New York)

Context: In recent years, the surgical management of intraductal papillomas without atypia has been questioned. Our goal was to identify potential factors that could influence the decision-making process.

Design: Using our pathology database, we retrospectively identified 922 benign intraductal papillomas diagnosed on core needle biopsy that subsequently underwent excision from 2000 to 2020. Medical history, radiologic correlation, and histopathologic findings were recorded and analyzed to identify potential factors contributing to upgrade rates.

Results: The overall upgrade rate on excision was 138 of 922 (14.96%). Upgrade rates to high-risk lesions including atypical lobular hyperplasia, lobular carcinoma in situ, and atypical ductal hyperplasia were 122 of 922 (13.23%). Upgrade rates to carcinoma in the form of ductal carcinoma in situ or invasive carcinoma were 16 of 922 (1.73%). Patients with no prior history of high-risk lesion or breast carcinoma (n = 793) had an upgrade rate to atypia/carcinoma of 101 of 793 (12.73%) compared with patients with a prior history of either high-risk lesion or breast carcinoma (n = 129), which had a significantly higher (unpaired t test, P < .001) upgrade rate to atypia/carcinoma of 37 of 129 (28.68%). In our study, patients with a history of benign ipsilateral or contralateral intraductal papilloma(s) (n = 138) showed an upgrade rate to atypia/carcinoma (17 of 138; 12.31%) similar to those with no prior history of high-risk lesion or carcinoma.

Conclusions: Any prior history of breast high-risk lesion or breast carcinoma should factor heavily toward surgical excision of a benign intraductal papilloma even in the absence of atypia at the time of biopsy.
Salivary Gland–Type Tumors of the Breast: A Retrospective Review of 101 Cases From a Single Institution

(Poster No. 56)

Lauren A. Duckworth, MD (duckwol@ccf.org); Roshan Bhattarai, MD; Erinn Downs-Kelly, DO; Patrick J. McIntire, MD; Miglena K. Komforti, DO. Department of Pathology and Lab Medicine Institute, Cleveland Clinic Foundation, Cleveland, Ohio.

**Context:** Salivary gland–type tumors (SGTTs) are rare entities in the breast that have histologic, and where applicable, molecular findings similar to their salivary gland equivalents. The morphologic characteristics of these lesions are highly variable, and a single entity may range from low grade to areas of dedifferentiation. The purpose of this study was to document our cohort of SGTTs of the breast at a large tertiary academic center, including relative incidence and pathologic variables.

**Design:** The anatomic pathology database CoPath Plus (Sunquest Information Systems, Tucson, Arizona) was searched for all SGTTs of the breast from 2000 to 2020.

**Results:** The final cohort consisted of 101 cases from 82 patients. The majority of the tumors were malignant (60 of 101; 59.4%), followed by benign (31 of 101; 30.7%) and atypical (11 of 101; 10.9%). Adenomyoepithelial (AME) was the most common SGTT (42 of 101; 41.6%) followed by adenosalveolar carcinoma (AdCC) (38 of 101; 37.6%), bilateral salivary gland adenocarcinoma tumors not further classified (6 of 101), epithelial–myoepithelial carcinoma (3 of 101), carcinoma with myoepithelial differentiation (3 of 101), secretory carcinoma (2 of 101), carcinomas with acinic cell differentiation (2 of 101), myoepithelioma (2 of 101), pleomorphic adenoma–like tumor (2 of 101), carcinoma ex pleomorphic adenoma (1 of 101), and mucoepidermoid carcinoma (1 of 101). The 42 AME tumors identified were further categorized into benign, atypical, and malignant (Table).

**Conclusions:** In our cohort, SGTTs of the breast were most commonly classified as malignant, with AdCC most frequently identified. The most common benign tumor was AME. The morphology in this cohort included those that fell within diagnostic categories recognized by the WHO, whereas a subset (21%) was diagnosed more descriptively, highlighting the challenge to accurately classifying these lesions.

Downs-Kelly is a consultant for Lilly Oncology.

### Characteristics of AME

<table>
<thead>
<tr>
<th>Grade</th>
<th>ER</th>
<th>PR</th>
<th>HER2</th>
<th>FISH</th>
<th>Other Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>+</td>
<td>+</td>
<td>2.9</td>
<td>NOS</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>+</td>
<td>+</td>
<td>1.7/2.1</td>
<td>NOS</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>+</td>
<td>+</td>
<td>2.5</td>
<td>Sclerosis</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>+</td>
<td>+</td>
<td>2.1</td>
<td>Mucinous</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>+</td>
<td>+</td>
<td>2.3/2.1</td>
<td>Mucinous</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>+</td>
<td>+</td>
<td>2.6/2.3</td>
<td>Mucinous and anaplastic lymphocytes</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>+</td>
<td>+</td>
<td>2.3</td>
<td>Anaplastic, tumor infiltrating lymphocytes</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>+</td>
<td>+</td>
<td>2.4</td>
<td>NOS</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>+</td>
<td>+</td>
<td>2</td>
<td>NOS</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>+</td>
<td>+</td>
<td>2.1</td>
<td>Tumor infiltrating lymphocytes</td>
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<tr>
<td>Poor</td>
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<td>4.8</td>
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<td>–</td>
<td>2.4</td>
<td>Extensive necrosis, tumor infiltrating lymphocytes</td>
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</tr>
<tr>
<td>Poor</td>
<td>–</td>
<td>–</td>
<td>2.1</td>
<td>Extensive necrosis, tumor infiltrating lymphocytes</td>
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</tr>
</tbody>
</table>

Abbreviations: AdCC, adenoid cystic carcinoma; ADH, atypical ductal hyperplasia; AME, adenomyoepithelioma; DCIS, ductal carcinoma in situ; EMC, epithelial–myoepithelial carcinoma; IDC, invasive ductal carcinoma.

### Counting Mitotic Figures in Phyllodes Tumor: A Survey Report

(Poster No. 57)

Ali R. Samani, BSc; Samieh Khosravinia, MD; Amir Samani, MD (amirsamani@hotmail.com). 1Department of Research, Amir Samani Medicine Professional Corporation, Toronto, Ontario, Canada; 2Department of Pathology, Humber River Hospital, Toronto, Ontario, Canada.

**Context:** Phyllodes tumors are malignant breast lesions that are considered as biphasic neoplasms with a stromal component and a proliferating epithelial component. The malignant potential of phyllodes tumors is related to tumor size, mitotic activity, and the presence of associated collections of blood and lymphatic fluid. Mitotic figures are an important criterion for malignancy in phyllodes tumors.

**Objective:** To document the mitotic figures per 10 high-power fields in 101 phyllodes tumors from a single institution to evaluate if these lesions are truly classified as malignant.

**Methods:** Using the pathology database from 2016 to 2020, we identified all cases of IBC that were HER2 1+ by IHC and reflexly evaluated IBCs that are HER2 (1+ to 2+) by IHC. At our institution, because of oncologists’ request, we also reflexly evaluate IBCs that are HER2 2+ by IHC. With the exception of 15 cases, FISH results were negative (HER2: CEP17 ratio <2.0). Histologic features of these 15 cases are described in the Table.

**Results:** 15 cases were HER2 1+ by IHC but amplified on FISH. We reviewed the histologic features of cases that were HER2 1+ by IHC, but positive on FISH.

**Conclusions:** IBCs that are HER2 1+ by IHC but amplified on FISH do exist, as seen in approximately 1% of our series. All IBCs were ductal, mostly poorly differentiated (73%), and 66.7% were ERþ, PRþ. The biopsy from the right breast mass demonstrates up to 5 mitotic figures/10 high-power field, which would otherwise qualify for borderline phyllodes tumor in older patients (Figure 3.54, C and D). However, studies have shown that benign phyllodes tumors in young patients can present with increased mitotic index. In summary, we report an extremely rare case of synchronous bilateral benign phyllodes tumor of the breast in a young female. Increased mitotic count should not preclude a diagnosis of benign phyllodes tumor in this population.

**Breast Cancers That Are HER2 FISH Amplified but 1+ by Immunohistochemistry—Do They Truly Exist?**

(Poster No. 55)

Swati Bhardwaj, MBBS, MD (swati.bhardwaj@mountsinai.org); Melissa Alexander, MD; Nebras Zeizafoun, MD; Shabnam Jaffer, MD. Department of Pathology, Molecular and Cell Based Medicine, Icahn School of Medicine at Mount Sinai Hospital, New York, New York.

**Context:** By College of American Pathologists and American Society of Clinical Oncology guidelines, invasive breast cancers (IBCs) that are HER2 equivocal (2+) by immunohistochemistry (IHC) need to be further evaluated by FISH. These guidelines do not mandate FISH evaluation of IBCs that are HER2 (1+) by IHC. At our institution, because of oncologists’ request, we also reflexly evaluate IBCs that are HER2 1+ on IHC by FISH.

**Design:** Using the pathology database from 2016 to 2020, we identified all cases of IBC that were HER2 1+ by IHC and reflexly evaluated IBCs that are HER2 (1+ to 2+) by IHC. At our institution, because of oncologists’ request, we also reflexly evaluate IBCs that are HER2 2+ by IHC. With the exception of 15 cases, FISH results were negative (HER2: CEP17 ratio <2.0). Histologic features of these 15 cases are described in the Table.

**Conclusions:** IBCs that are HER2 1+ by IHC but amplified on FISH need to be further categorized into benign, atypical, and malignant (Table).
neuroendocrine carcinoma (Figure 3.59, A through C). Neuroendocrine carcinoma combined with a contiguous component of small cell mainly composed of organoid nests of large cell neuroendocrine underwent radical mastectomy for a 2-cm breast mass. The tumor was small cell or large cell. We report the first case of combined NEBC with So far, in the literature, cases of NEBC have only presented as either Arch Pathol Lab Med

The latest WHO classification recommends making published reports lack uniformity as the diagnostic criteria have been repeatedly revised. The question was figures in phyllodes tumor? Do you use hot spot or not? We recorded TAT for cases in which HER2 FISH testing with IRB approval. A search was performed on in-house cases from 2018 to 2020. We recorded TAT for cases in which HER2 IHC was performed first followed by FISH. Although in the original paper (tori.seasor@hsc.utah.edu); Rachel Factor, MD. Department of Pathology, University of Utah, Salt Lake City;

The 2018 American Society of Clinical Oncology/College of American Pathologists guideline updated the algorithm for how to treat FISH-equivocal cases (groups 2–4), incorporating immunohistochemistry (IHC) as a subsequent test. If IHC is equivocal, representative areas are circled and FISH is repeated. Although this may provide diagnostic resolution, it seemingly adds time to these cases. We investigated the turnaround time (TAT) of equivocal FISH cases, comparing with cases where IHC was performed first. This was a retrospective pilot study at an academic center with IRB approval. A search was performed on in-house cases from 2018 to 2020. We recorded TAT for cases in which HER2 FISH testing was equivocal, requiring IHC. We compared the TATs of this cohort with cases in which HER2 IHC was performed first, followed by FISH.

The purpose was to look at a limited number of cases initially. There were 15 FISH equivocal cases reflexed to IHC. There were 13 cases in which HER2 IHC was equivocal and reflexed to FISH. The average number of days to obtain a final HER2 result in the FISH first cohort was 8.5 (range, 2 to 12). One case was excluded because of an exceptionally long TAT. The average number of days for the HER2 IHC first group was 3.8 (range, 2 to 7).

When performed as the initial test, HER2 FISH-equivocal cases can significantly delay the time to arrive at a final HER2 result, which can impact patient care.

The First Case Report of Primary Breast Combined Small Cell and Large Cell Neuroendocrine Carcinoma

Roselyne Choiniere, MD (roselyne.choiniere@usherbrooke.ca); Martin Chevrier, MD, BSc; Sameh Geha, MD. Department of Pathology, University of Sherbrooke, Quebec, Canada.

Neuroendocrine breast carcinomas (NEBCs) are uncommon and published reports lack uniformity as the diagnostic criteria have been repeatedly revised. The latest WHO classification recommends making a diagnosis of neuroendocrine neoplasm when morphology and diffuse expression of neuroendocrine markers represent >90% of the tumor. So far, in the literature, cases of NEBC have only presented as either small cell or large cell. We report the first case of combined NEBC with both small and large cell components: a 40-year-old woman who underwent radical mastectomy for a 2-cm breast mass. The tumor was mainly composed of organoid nests of large cell neuroendocrine carcinoma combined with a contiguous component of small cell neuroendocrine carcinoma (Figure 3.59, A through C). Neuroendocrine ductal carcinoma in situ was identified at the center of the large cell component, supporting a breast origin. Numerous lymphovascular invasions were identified without lymph node involvement with ultrataging. The large cell component showed strong expression of ER 3+, PR 3+, Ki-67 80%, synaptophysin (Figure 3.59, D), chromogranin, and CD56 along with GATA3 and mammaglobin, additional arguments for a primary breast origin. HER2 was negative. The small cell component exhibited positivity for synaptophysin (Figure 3.59, D), chromogranin, CD56, Ki-67 100%, and TTF-1, whereas ER, PR, HER2, CK7, mammaglobin, GCDFP-15 were negative. In addition, as expected of most small cell carcinomas and many large cell neuroendocrine carcinomas, our tumor showed Rb loss and p53 mutation (null type). Positron emission tomography was negative. To our knowledge, this is the first case of combined NEBC of the breast.

The Expression Patterns of Epithelial to Mesenchymal Transition–Related Markers in the Different Molecular Subtypes of Breast Cancer and Their Relation to the Tumor Immune Microenvironment

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Given the mounting interest in the use of immunotherapy for the treatment of subsets of breast cancer patients, it is of major importance to understand the fundamental tumor characteristics that dictate the intertumor heterogeneity in immune landscapes. The epithelial to mesenchymal transition (EMT) is an important phenomenon, which causes perturbations in the tumor microenvironment (TME). We sought to investigate EMT, in the different molecular subtypes of breast cancer, as it relates to the inflammatory infiltrate in the TME.

We studied the protein expression patterns of EMT-related markers (Snail, Twist, ZEB1, N-cadherin, E-cadherin, GRHL2, and EpCAM) by immunohistochemistry in 144 cases of invasive breast cancer. The inflammatory infiltrate in the TME was assessed semi-quantitatively on hematoxylin and eosin–stained sections. A χ² test (α = .05) was used to correlate between each of the EMT-related markers (negative or positive) and immune infiltrate abundance. The transcript expression patterns of the EMT-related markers were studied by conducting in silico analysis on publicly available data sets (University of California Santa Cruz Xena Cancer Genomics platform).

Breast cancer molecular subtypes showed distinct transcript and protein expression patterns of EMT-related markers. The inflammatory infiltrate was more intense in poorly differentiated carcinomas and triple-negative carcinomas where the protein expression of N-cadherin and EpCAM was upregulated (P < .001), whereas that of E-cadherin and GRHL2 was down-regulated (P = .001).
Conclusions: The EMT signature, associated with the molecular subtypes of breast cancer, might influence the immune response in the TME and hence may play a role in determining tumor aggressiveness as well as predicting response to treatment and prognosis.

Performance Analysis of Pathologists’ Assistants in Macroscopic Examination of Breast Specimens at a Cancer Center

(Zena Jameel, MD (zena.jameel@moffitt.org); Karen Coley, PA; Warren Gloria, PA; Marlin Rosa, MD. Department of Pathology, H. Lee Moffitt Cancer Center, Tampa, Florida.

Context: Pathologists’ assistants (PAs) play an important role in the daily operations of pathology departments. Their role includes research, teaching, management, and most importantly the examination and processing of a variety of surgical specimens. Quality grossing is a key part of the diagnostic process. Breast specimens are notoriously difficult to gross because of their fatty nature, complexity, and fixation guidelines. The purpose of this study was to evaluate the most common problems and discrepancies encountered by pathologists after breast cancer specimens have been grossed by PAs.

Design: Evaluations of PAs’ gross quality and completeness performed by the signing breast pathologist were collected between January 2020 and February 2021. Recorded problems/discrepancies were classified as major or minor according to the possible impact on patient management, impact of error on specimen integrity, and if the only slide with tumor was compromised because of poor fixation or fragmentation.

Results: We identified 1646 cases with submitted breast gross correlation events during the study period. Of these, 112 cases were flagged as discrepant (6.8%). Sixty-two cases (55%) constituted minor discrepancies and 50 cases (45%) constituted major discrepancies (Table). The most common major problems were inadequate sampling, margins, and incomplete gross description.

Conclusions: Our results show that in our setting, PAs provide high-quality grossing with only 3% of major errors in grossing complex breast specimens. Our findings will be used to educate PAs and other trainees about areas of improvement. To our knowledge, this is the first study to evaluate PAs’ performance in grossing complex breast pathology specimens.

Evaluations of PAs’ Gross Quality and Completeness

<table>
<thead>
<tr>
<th>Areas of Discrepancy</th>
<th>Major, No. (%)</th>
<th>Minor, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sampling</td>
<td>14 (28)</td>
<td>22 (35)</td>
</tr>
<tr>
<td>Fixation</td>
<td>3 (6)</td>
<td>14 (23)</td>
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<tr>
<td>Margins</td>
<td>9 (18)</td>
<td>4 (6.5)</td>
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<tr>
<td>Map/diagram</td>
<td>1 (2)</td>
<td>4 (6.5)</td>
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<tr>
<td>Incomplete gross description</td>
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<td>5 (8)</td>
</tr>
<tr>
<td>Inking</td>
<td>0 (0)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Incomplete workup</td>
<td>0 (0)</td>
<td>1 (1.5)</td>
</tr>
<tr>
<td>Multiple</td>
<td>16 (32)</td>
<td>4 (6.5)</td>
</tr>
<tr>
<td>Undocumented</td>
<td>0 (0)</td>
<td>5 (8)</td>
</tr>
</tbody>
</table>

Incidental Squamous Cell Carcinoma in Epidermal Cyst Associated With Implant Capsule

(Reza Nikfar, MD (rezanikfarmedical@gmail.com); Carlos Aneses, MD; Saeed Bajestani, MD. Department of Pathology, Moffitt Cancer Center, Tampa, Florida.

We report a case of a 61-year-old woman with history of bilateral breast augmentation done in 2000 with a transaxillary approach using a saline textured implant in the submuscular position. The patient now presented with an open wound in the inferior left breast with orange serosanguinous drainage. The medical impression was an exposed and infected breast implant, and she was placed on antibiotics. The breast implants were removed; however, she continued to have serosanguinous drainage exuding from the wound, for which a left breast capsulectomy was performed. Microscopic examination revealed an invasive squamous cell carcinoma in association with an epidermal cyst. Cyst lining showed verrucous changes. Overlying skin did not show any dysplasia or malignancy. The extent of invasions and margin status could not be determined because of the specimen being received in fragments. Squamous cell carcinoma arising from an epidermal cyst is a rare occurrence with an incidence range of 0.011% to 0.045% in the literature. This case illustrates the importance of having a high level of suspicion in patients presenting with unusual symptoms or nonhealing wounds for both surgeons and pathologists alike. These cases should be dealt with as potentially malignant for margin status and staging purposes, which both have important treatment implications for the patient.

Metastatic Small Cell Lung Cancer to Breast Mimicking Primary Breast Neuroendocrine Carcinoma

(Bing Han, MD1 (hanbing6611@gmail.com); Agustin C. Garcia, MD; Saeed N. Bajestani, MD. Departments of Pathology and Medicine, Louisiana State University Health Sciences Center New Orleans; Department of Pathology, H. Lee Moffitt Cancer Center, Tampa, Florida.

Small cell carcinoma of the lung with breast metastasis is rare and can mimic a primary high-grade neuroendocrine carcinoma of the breast. We report a case of a 62-year-old woman found to have an 11-mm, well-circumscribed left breast mass by screening mammography. Ultrasound-guided biopsy showed high-grade invasive neuroendocrine carcinoma with necrosis. The carcinoma cells were positive for synaptophysin, CK7, and TTF-1, and negative for GATA3, GCDFP-15, EBER, PR, CK20, and chromogranin. The high probability of metastasis from an occult lung primary was raised by the pathologist, and additional workup was recommended. Subsequently, imaging studies revealed a large lung mass and masses in her liver, pancreas, and left adrenal gland. Biopsies from the lung and adrenal gland showed identical histomorphology and immunohistochemical staining pattern. After clinical/radiologic correlation, the diagnosis of small cell carcinoma of the lung with widespread metastases was established. Small cell carcinoma of the lung is morphologically indistinguishable from the small cell variant of breast neuroendocrine carcinoma, yet the treatment implications differ vastly between the two. TTF-1 expression in breast neuroendocrine carcinoma has been reported, but not as diffusely and strongly as seen in lung small cell carcinoma. GATA3 expression is more commonly seen in breast neuroendocrine carcinoma than in pulmonary small cell carcinoma. In conclusion, it is crucial to exclude metastasis and Merkel cell carcinoma in cases with histomorphologic features of neuroendocrine carcinoma in breast biopsy specimens. Clinical-radiologic correlation and a limited panel of immunostains might help to establish the correct diagnosis (Figure 3.63, A and B, hematoxylin-eosin; C, synaptophysin; and D, TTF-1).

Wide-Field Optical Coherence Tomography Imaging May Improve the Workflow of Routine Cavity Margin Assessment in Breast-Conserving Surgeries

(Adriana Corben, MD; Shabnam Jaffer, MD; Twisha Oza, MD; Jessica Beyda, MD; Christina R. Wetz, MD; Elisa R. Port, MD; Beryl
Augustine, PhD\(^1\) (baugustine@perimetermed.com); Hank Schmidt, MD, PhD.\(^3\) Department of Pathology, Molecular and Cell Based Medicine, \(^1\)Icahn School of Medicine and \(^3\)Surgery, Mount Sinai New York, New York; \(^2\)Department of Clinical Research, Perimeter Medical Imaging AI, Toronto, Ontario, Canada.

**Context:** Routine cavity shave margins (CSMs) have been shown to lower re-excision rates in breast-conserving therapy (BCS). Additional research has demonstrated that fewer shaves, focused on regions of oncologic interest only, reduce the time and cost of pathology assessment compared with routine margins. The objective of this study was to assess wide-field optical coherence tomography (WF-OCT) imaging of routine CSMs as a screening tool to reduce the number of blocks for pathology processing.

**Design:** This was a prospective, single-center study of 35 women with invasive or in situ carcinoma who underwent BCS with CSMs. Using an investigational WF-OCT imaging system, CSMs were imaged immediately prior to standard histologic processing to provide 2-dimensional, cross-sectional, high-resolution (approximately 15 \(\mu\)m) images of the CSMs to a 2-mm tissue depth. WF-OCT image data were reviewed by a pathologist and correlated with final histopathology.

**Results:** WF-OCT was performed on 135 CSMs obtained from the 35 subjects. Of the 135 CSMs, only 4 were positive for residual malignancy on final histology. An average of 8 blocks per margin shave were generated in this study, resulting in 1080 total processed blocks for final pathology.

**Conclusions:** Assessment of WF-OCT of CSMs prior to processing demonstrated 82% concordance with final pathology, demonstrating a high degree of accuracy across multiple malignancy types. In the future, focused blocking and review strategy, directed using WF-OCT screening data, may be able to reduce the processing burden of final CSM pathology.

Augustine is a shareholder in Perimeter Medical Imaging AI. Schmidt is a consultant with Perimeter Medical Imaging AI.

**Amyloid Tumor of the Breast, a Mimicker of Fat Necrosis**

(Marcela Mejia-Arango, MD; Javier Baena-Del Valle, MD. Department of Pathology and Laboratories, Fundación Santa Fe de Bogotá, Colombia.)

Amyloidosis of the breast, although rare, has been described in the literature. When presenting as a single mass, it has been called amyloid tumor. It can be primary or secondary to systemic amyloidosis. We present the case of a 56-year-old woman with a nodular, hypoechoic, circumscribed mass of the breast, with scattered calcifications on mammography and ultrasound. Clinically, fat necrosis was suspected. The patient was taken to US-guided biopsy with a pathologic diagnosis of fat necrosis. A simple resection of the mass was performed. Hematoxylin-eosin slides showed extensive replacement of the stroma by eosinophilic material, with condensation around blood vessels, and acinar and ductal structures (Figure 3.65, A and B). In the adipose tissue, the picture was reminiscent of fat necrosis. Congo red stain for amyloid protein revealed abundant congophilic material (Figure 3.65, C), apple-green birefringent under polarized light (Figure 3.65, D). Further hematologic studies showed a normal bone marrow, but a monoclonal peak in serum. Other studies did not reveal signs of systemic amyloidosis. We present a case of an amyloid tumor of the breast presenting as fat necrosis, clinically and in an initial biopsy. Although a rare entity, it must be considered in the differential of fat necrosis, as well as other benign mass-forming lesions of the breast. Because some of the cases represent secondary involvement by systemic amyloidosis, complete hematologic and other studies are always warranted.

**Autopsy-Proven T Lymphocyte–Mediated Myocarditis as a Complication of SARS-CoV-2 Infection**

(Juanita E. Ferreira, MD (jefe2310@uky.edu); Autumn Hammonds, DO; William O’Connor, MD; Gregory Davis, MD; Derek Allison, MD. Department of Pathology and Laboratory Medicine, University of Kentucky, Lexington.)

Infection with SARS-CoV-2, the virus causing coronavirus disease 2019 (COVID-19), has been shown to bind to cells via ACE-2 receptor, which is expressed in many tissue types including the lungs, kidneys, and heart. More specifically, ACE-2 receptor is widely expressed in cardiomyocytes, coronary endothelial cells, and fibroblasts. Though several cases of clinically diagnosed COVID-19–associated myocarditis have been reported, autopsy-proven cases with detailed histopathologic descriptions are rare. We report findings on autopsy from a 62-year-old woman with a past medical history of COVID-19, who was diagnosed with COVID-19, succumbed to the disease 126 days after initial presentation, and was found to have histopathologic evidence of T lymphocyte–mediated myocarditis. At the time of autopsy, SARS-CoV-2 testing was negative, and the 420-g heart was of normal configuration and without any valvular abnormality. There was an increase in the right ventricular midtransverse diameter (4.0 cm), biventricular hypertrophy, and coronary sinus dilatation. Microscopically, hematoxylin and eosin staining of the left ventricle showed interstitial edema and a low-grade mononuclear infiltrate (Figure 3.66, A). The right ventricle showed individual necrotic myocytes with contraction band necrosis (Figure 3.66, B), CD68 positivity with diffusely moderate pericapillary staining, and CD3 positivity highlighting 10–15 T lymphocytes per \(\times 20\) field (Figure 3.66, C and D). This case highlights the importance of autopsy studies in diagnosing SARS-CoV-2–associated myocarditis as a complication of COVID-19 infection and may provide further insight as to the pathogenesis of myocardial injury.

**Anaplastic Pleomorphic Xanthoastrocytoma With Widespread Visceral Metastases and Therapy-Related Acute Myeloid Leukemia: An Autopsy Study**

(Nilesh Kapoor, BA\(^1\) (nilesh.kapoor@osumc.edu); Suzanna Logan, MD, PhD\(^2\); Christopher R. Pierson, MD, PhD\(^2\); Archana Shenoy, MD.\(^3\) Department of Pathology, The Ohio State University College of Medicine, 2Icahn School of Medicine and 3Surgery, Mount Sinai New York, New York.)

**Abstracts**

Arch Pathol Lab Med
Anaplastic pleomorphic xanthoastrocytoma (PXA) has a grade III tumor designation in the 2016 World Health Organization classification of central nervous system tumors. PXAs comprise less than 1% of astrocytic tumors and have a less favorable prognosis when anaplastic features are present. Recurrence has almost always been limited to the CNS. We thus present the case of a 13-year-old boy with anaplastic PXA who developed multiorgan metastases and eventually succumbed to his tumor burden. His primary tumor was diagnosed and resected at age 5. One year later, he developed local recurrence, which was treated with chemotherapy. About 5 years later, he presented with widespread extracranial metastatic disease. A familial mutation analysis was performed at this time and returned positive for a likely pathogenic TP53 germline mutation. Following multiple courses of radiation and chemotherapy, his clinical course was further complicated by therapy-related acute myeloid leukemia of erythroid lineage. Despite multiple therapies, he eventually developed progressive multiorgan dysfunction and asystole. Autopsy confirmed widespread metastases of anaplastic PXA characterized by giant, pleomorphic cells with vesicular nuclei and large, prominent nucleoli. Gross metastases were noted in the chest wall (Figure 3.67, A), bilateral lungs, liver (Figure 3.67, B; leukemia depicted on the left), spleen (Figure 3.67, C), and left kidney. Microscopic examination also confirmed pituitary (Figure 3.67, D), lymph nodal, and bone marrow metastases. Notably, there was no recurrence in the brain on autopsy. In summary, anaplastic PXA is a rare astrocytic tumor with potential for visceral spread, indicating a possible distinct tumor biology amongst central nervous system tumors.

A Rare Pediatric Case of Disseminated Coccidioidomycosis
(Poster No. 68)
Kareem Meiklejohn, MD (karleen.mm@gmail.com); Richard Sobonya, MD. Department of Pathology, University of Arizona, Tucson.

Coccidioidomycosis, also known as valley fever, is a lung infection caused by inhaling the spores of fungi of the genus Coccidioides, which lives in the dirt and is found throughout the southwestern United States and in certain regions of Mexico and South America. As a lung infection, coccidioidomycosis may be asymptomatic or flulike, and most patients recover without persistent disease. Disseminated coccidioidomycosis, defined as spread outside the lungs, occurs in less than 1% of cases. Risk factors for dissemination in adults include men, the extremes of age, and an immunosuppressed state. The literature is less clear for disseminated pediatric cases, especially infants, but most patients survive after a long treatment course. We present an unusual case of fatal seronegative disseminated coccidioidomycosis in a former 25-week premature infant at 7 months of age who had bronchopulmonary dysplasia, pulmonary hypertension, and no known immunosuppressive conditions. The patient presented initially with worsening rhinovirus infection and negative Coccidioides serologies. Respiratory status declined and blood cultures returned positive for Coccidioides species. The patient subsequently succumbed to multiorgan failure. At autopsy, the infection was found to extensively involve the lungs, thymus, and mediastinal lymph nodes, as well as the kidneys, liver, pelvic lymph nodes, larynx, spleen, and cerebellum. The most common locations of spread in pediatric cases are typically the skin, meninges, and musculoskeletal sites, but other sites, such as intra-abdominal organs as seen in our case, have been rarely documented and are typically associated with high titers on serologic studies (Figure 3.68).

Fatal Gastrointestinal Bleed From Gastric Pancreatic Heterotopia in the Setting of Alcohol Use Disorder
(Poster No. 69)
Stephanie Dreikorn, MD (sdreikorn@dbs.lacounty.gov); Kenechukwu Ojukwu, MD; Nadia Nashi, MD; Ping Ji, MD. Department of Pathology, Harbor-UCLA Medical Center, Torrance, California.

Pancreatic heterotopia (PH) has an incidence of 0.5% to 13% in autopsy studies. We describe a rare case of fatal hemorrhage from PH in a 34-year-old woman with a history of alcohol use disorder, chronic pancreatitis with pseudocyst, and portal vein thrombosis. She presented with hematemesis, melena, and fatigue for 1 month, and was hemodynamically stable with an initial hemoglobin of 7.4 g/dL. Computed tomography scan showed a left pleural effusion, questionably gastric wall thickening, and pancreatic calcifications. Hemoglobin decreased to 5.9 g/dL within 24 hours, requiring transfusion. Recurrent episodes required repeated transfusions. Esophagogastroduodenoscopy revealed only a 1-cm clean-based ulcer in the antrum (Figure 3.69, A). Repeated blood cultures were negative. Four days after admission, the patient's condition deteriorated because of hypotensive multiorgan dysfunction resulting in cardiac arrest, and she did not regain consciousness during the hospital course of 35 days. Complete autopsy
revealed an antral stomach ulcer overlying a hemorrhagic, necrotic, clot-filled 6 × 4.5 × 3-cm mass (Figure 3.69, B and D). Histology showed islet nests and duct pattern of ectopic pancreas with multiple nerve fibers, extensive fibrosis, and hemorrhage consistent with acute hemorrhagic pancreatitis within the heterotopic tissue (Figure 3.69, C). Liver cirrhosis and splenomegaly with minimal esophageal varices were the only other significant autopsy findings, with the cause of death to be blood loss from alcohol-induced acute pancreatitis located in gastric PH. This is a very rare complication of a known anatomic anomaly only revealed with an autopsy, as a cause of cryptic massive gastrointestinal hemorrhage.

**Fatal ANCA-Negative Microscopic Polyangiitis**

(Poster No. 70)

Andrew Kobalka, MD (akobalk@rockets.utoledo.edu); Amira Gohara, MD. Department of Pathology, The University of Toledo Medical Center, Toledo, Ohio.

We present a 53-year-old man who died from ANCA-negative microscopic polyangiitis. The patient presented to the emergency department with a diffuse throbbing headache for several days, a fever of 101°F (38.3°C), vomiting, diarrhea, body aches, and chills. During his 19-day hospital course, he received extensive workup and empiric treatment for infectious, autoimmune, and metabolic causes of his condition, without clinical benefit. On the eighth day, an electroencephalogram revealed severe encephalopathy. His creatinine rose to 2.82 mg/dL on the 13th day. On the 17th day, he was unresponsive to pain with no cough or gag reflex, and a do-not-resuscitate comfort care order was completed. Notably, although treatment included multiple antiviral and antimicrobial drugs including acyclovir, vancomycin, ceftiraxone, and meropenem, steroids were not administered. Further, premortem and postmortem serology for p-ANCA and c-ANCA was negative. Cultures of blood, cerebrospinal fluid, and urine were negative for bacteria and fungus. At autopsy, microscopic sections revealed widespread vasculitis. Intramural cardiac vessel inflammation led to ischemic injury of the interventricular septum of about 4 to 7 days' duration. Vasculitis involving perivascular area, endothelium, and adventitia was found in all 3 major coronary arteries (Figure 3.70, A). Four-chamber–dilated cardiomyopathy, cardiomegaly (530 g), left ventricular hypertrophy (2.2 cm), and severe pulmonary edema and vasculitis were seen. Vasculitis was also found in the kidneys (Figure 3.70, B), liver, esophagus, colon, and bladder. Vasculitis in the brain and brain stem led to focal hypoxic damage (Figure 3.70, C and D).

Pneumocystis jiroveci Pneumonia Mimicking Inherited Surfactant Deficiency in an Infant With Hyper IgM Syndrome: An Autopsy Report

(Poster No. 71)

Juhi D. Mahadik, MD1 (juhi.mahadik@bcm.edu); Ernestina Melic-off-Portillo, MD2; Nahir Cortes-Santiago, MD2; Kalyani R. Patel, MD.3

1Department of Pathology and Immunology, Baylor College of Medicine, Houston, Texas; Departments of 2Pediatrics-Pulmonary and 3Pathology and Immunology, Texas Childrens Hospital, Baylor College of Medicine, Houston.

A 7-month-old, former 33-weeks, male infant with progressive respiratory failure, admitted for suspected interstitial lung disease, continued to deteriorate and died within a week of admission. Antemortem targeted next-generation sequencing was negative for an inherited disorder of surfactant metabolism (SFTPBP, SFTPC, ABCA3, NKX2-1, and FOXL1 genes). Whole exome sequencing revealed a hemizygous pathogenic variant in CD40 ligand, the most common cause of hyper IgM syndrome, a primary immunodeficiency disorder. Limited autopsy (lungs only) showed intra-alveolar eosinophilic, granular, proteinaceous, frothy material (Figure 3.71, A), both PAS-D sensitive (inset) and resistant with type II pneumocyte hyperplasia (Figure 3.71, B). Methenamine silver stain showed intra-alveolar 5–6-μm round to cup-shaped cysts of *Pneumocystis jiroveci* (Figure 3.71, C). Electron microscopy (EM) revealed numerous abnormal lamellar bodies with central/centric electron-dense inclusions with a fried egg appearance within the cytoplasm of type II pneumocytes (Figure 3.71, D), with several normal forms (arrow). These EM findings are seen in surfactant dysfunction due to ABCA3 deficiency, for which the patient had tested negative. Both histology and EM findings could be explained by *Pneumocystis* infection, one of the most common opportunistic infections in patients with hyper IgM syndrome. Animal studies have shown that *Pneumocystis* can alter the expression of genes for surfactant proteins B and C and cause their deficiency. Studies from human patients have shown altered composition of surfactant in bronchoalveolar lavage fluids. The characteristic histology and EM findings mimicked a surfactant disorder. The case is unique and invites further research into the pathophysiology of *Pneumocystis*-induced surfactant dysfunction.

Multicentric Infantile Myofibromatosis: An Unusual Presentation

(Poster No. 72)

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Infantile myofibromatosis (IM) is a benign mesenchymal disorder characterized by the proliferation of myofibroblasts. Despite its being the most common fibrous tumor of infancy, the multicentric form with visceral involvement is extremely rare, and usually fatal. In all reported cases of multicentric form, the skin and subcutaneous tissue is inevitably involved. Our case is a 4-week-old term female infant with intrauterine growth restriction who presented with 1 episode of vomiting and was noted to have multiple bone fractures concerning for nonaccidental trauma. She had an echocardiogram done 2 weeks earlier that showed severe right ventricular hypertrophy. Shortly after admission, she developed shock unresponsive to vasopressors and hydration. Postmortem examination revealed a small infant with...
normal skin and physical appearance; however, multiple organs had nodular lesions, including bilateral adrenal glands, cerebellum, heart, liver, ovary, pancreas, and psoas muscle. Microscopically, the lesions showed a biphasic pattern composed of myoid nodules separated by more cellular zones containing a hemangioepicytoma-like vascular pattern and no increase in mitotic activity or nuclear pleomorphism. Immunohistochemically, the tumor cells were positive for SMA and vimentin and negative for desmin, myogenin, S-100, and CD34. In addition, ETV6 (12p13.2) rearrangement was negative. The final diagnosis was multicentric IM with visceral involvement. Although IM almost universally presents with skin lesions, our case presented without skin involvement. Therefore, a clinician should be aware of this misleading clinical presentation of IM. In conclusion, we present a challenging case of multicentric IM with visceral involvement, which initially presented with bone fractures and no skin lesions.

Acute Pulmonary Hemorrhage From Disseminated Kaposi Sarcoma: Autopsy Findings in a 20-Year-Old Patient With Recent Human Immunodeficiency Virus Diagnosis

(Wenjing Qiu, MD (wqiu1@lsuhsc.edu); Richard Vander Heide, MD, PhD, MBA. Department of Pathology, LSUHSC School of Medicine, New Orleans, Louisiana.

Kaposi sarcoma (KS) is an AIDS-defining cancer but is usually limited to the skin and treatable if detected early. We report a case of a 20-year-old HIV+ African American male who died of acute pulmonary hemorrhage secondary to disseminated KS 2 years after his initial HIV diagnosis despite a favorable systemic and immune system status (CD4 >150 cells/ml). The patient was diagnosed with HIV+ in 2018, but he refused therapy. He was diagnosed with KS involving the right thigh (T1OS1) 4 months prior to his terminal admission (11/20) (Figure 3.73, A). He presented with a 1-day history of hemoptysis and hematemesis and died 16 days later. An autopsy was performed. Gross examination revealed multiple hemorrhagic areas involving both lungs associated with severe pulmonary hemorrhage and 1250 mL serosanguinous fluid in the right thorax (Figure 3.73, B). Additional lesions were identified in the gastrointestinal system, appendix, liver, spleen, and bladder. Microscopically all lesions consisted of atypical spindle cell proliferation with slitlike vascular spaces that stained positive for HHV-8, CD31, and CD34, confirming a diagnosis of KS (Figure 3.73, C and D). The patient presented 4 months prior to death with a favorable AIDS-related KS score. Five-year relative survival rate for localized KS was noted in 1 case. A well-known, albeit rare complication of influenza is the alteration of metabolic pathways, leading to severe microvesicular steatosis of liver, confirmed by oil red O and toluidine blue stains. Pathologic findings are summarized in the Table. Severe microvesicular steatosis in the myocardium, which were stained with oil red O. Representative sections of all organs were microscopically examined. Both of the patients had a past medical history of hypertension and presented with severe flulike symptoms: fatigue, subjective fever, chills, and myalgia (in one case). Rapid influenza diagnostic tests were positive in both. Tracheal swabs revealed positivity for influenza A H1 virus by polymerase chain reaction assay. The average disease duration time after the onset of symptoms was 7 days. External examination of 1 case showed marked anasarca. Internal examination of both cases showed tracheal mucosal hemorrhage/congestion, marked congestion of the lungs, and cardiomegaly. Microscopy demonstrated microvesicular steatosis in the myocardium in both cases, confirmed by oil red O and toluidine blue stains. Pathologic findings are summarized in the Table. Severe microvesicular steatosis of liver, confirmed by oil red O, was noted in 1 case. A well-known, albeit rare complication of influenza A virus infection is the alteration of metabolic pathways, leading to severe microvesicular steatosis of liver.
An Unusual Presentation of Chronic Myeloid Leukemia in a 40-Year-Old Woman

(Poster No. 76)

Elisabeth Miller, MD (em2sz@virginia.edu); Elizabeth Courville, MD. Department of Pathology, University of Virginia, Charlottesville.

Chronic myeloid leukemia (CML), a myeloproliferative neoplasm defined by the presence of the fusion oncoprotein BCR-ABL1, is primarily composed of proliferating granulocytes localized to the peripheral blood, bone marrow, spleen, and liver. Most patients with CML are diagnosed in the chronic phase with typically an insidious onset. In this autopsy case study, we present a patient who presented with extensive soft tissue infiltration by CML but without demonstrable sheets of blasts. A 40-year-old woman was admitted with 5 months of progressive shortness of breath, dizziness, blurry vision, and headaches. Testing revealed a leukocytosis of 374 k/uL. Flow cytometry of peripheral blood demonstrated 5% circulating myeloid blasts, and genetic testing confirmed the presence of the BCR-ABL1 fusion oncoprotein. During her hospital course, her oxygen saturations progressively decreased, and despite intubation, she quickly decompensated. On autopsy, there was hepatosplenomegaly, fibrinous pericarditis, and a thickened diaphragm adherent to the liver. Although microscopic examination showed a proliferation of myeloid cells in the bone marrow, there was also an extramedullary proliferation and infiltration of myeloid cells of the diaphragm (Figure 3.76, A), pericardium (Figure 3.76, C), spleen, liver, peri-adrenal fat (Figure 3.76, D), and parametrium. Neither an increased population of blasts nor sheets of blasts were seen by hematoxylin–eosin–stained sections of involved tissue or CD34 immunohistochemical staining of the diaphragm (Figure 3.76, B) or bone marrow. Soft tissue infiltration from CML is typically seen in the blast phase, but this young patient presented with an unusual form of CML in which maturing myeloid cells infiltrated various soft tissues.

Summary of Pathologic Findings

<table>
<thead>
<tr>
<th>Case</th>
<th>1</th>
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<tbody>
<tr>
<td>Lung weight, combined, g</td>
<td>2495</td>
<td>1890</td>
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<tr>
<td>Tracheal mucosal congestion and hemorrhage</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Intra-alveolar hemorrhage</td>
<td>+</td>
<td>-</td>
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<tr>
<td>Parenchymal necrosis, lungs</td>
<td>–</td>
<td>+</td>
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<tr>
<td>Heart weight, g</td>
<td>517</td>
<td>415</td>
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<tr>
<td>Myocardial interstitial hemorrhages</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Epicardial petechiae</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Microvesicular steatosis, heart</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Microvesicular steatosis, liver</td>
<td>–</td>
<td>+</td>
</tr>
</tbody>
</table>

Transplacental Transmission of SARS-CoV-2

(Poster No. 77)

Harsimar Kaur, MBBS (hkaur14@jhmi.edu); Michelle Olson, MS, PA; Mark Hopkins, MD; Heba Mostafa, MBCh, PhD; Jody E. Hooper, MD. Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, Maryland.

SARS-CoV-2 is mainly transmitted through respiratory droplets. There is limited knowledge regarding the risk of vertical transmission in pregnancy. We present the autopsy findings of a fetus demise in utero secondary to maternal COVID-19. A young multigravida female presented in the third trimester with complaints of no fetal movement. Her prenatal course was notable for a COVID-19 diagnosis 19 days prior to presentation with only mild symptoms. After confirmation of fetal death in utero, she was admitted for induction. Her intrapartum course was notable for thrombocytopenia, elevated LFTs, and elevated PT and D-dimer with concern for disseminated intravascular coagulopathy versus HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome. After delivery, a complete fetal autopsy was performed. The main autopsy findings were in the placenta, which demonstrated chronic histiocytic intervillitis with extensive trophoblastic necrosis. The presence of SARS-CoV-2 was confirmed in both the placenta and a fetal throat swab using RT-PCR, and an RNA in situ hybridization assay for SARS-CoV-2 was positive in placental syncytiotrophoblast, confirming transplacental spread of the virus. These findings add to the growing evidence that the transplacental transmission of SARS-CoV-2 infection is a rare yet possible event with adverse fetal outcomes and may influence the obstetric management of SARS-CoV-2 infected pregnant patients.

Left Internal Mammary Artery Bypass Graft Dissection Detected at Autopsy

(Poster No. 78)

Annie E. Abraham, MD (Annie.Abraham@baystatehealth.org); Roxanne Florence, MD. Department of Pathology, University of Massachusetts Medical School–Baystate, Springfield.

Left internal mammary artery (LIMA) graft dissection is a very rare complication in patients who have undergone coronary artery bypass grafting (CABG) that can occur during subsequent arteriography or spontaneously. The few previously described LIMA graft dissections were detected during life and successfully treated, primarily with angioplasty and stent placement. We present what to the best of our knowledge is the first report of a LIMA graft dissection discovered at autopsy. The patient was an 82-year-old man with a complex medical history including remote myocardial infarction and ischemic cardiomyopathy who presented with left facial and arm numbness. A transient ischemic attack was suspected. Lateral ST depression in leads I and aVL on electrocardiogram and an elevated troponin level of 0.29 ng/mL were additionally present. He was managed medically but because of
subsequent chest pain, arrhythmias, and further troponin elevations he underwent emergent cardiac catheterization. CABG was performed with a LIMA graft to the left anterior descending artery and 3 saphenous vein grafts for severe multivessel coronary artery disease. On postoperative day 2 the patient became hypotensive while conversing with a nurse and rapidly progressed to asystole. Resuscitative attempts were unsuccessful. Cause of death at autopsy was attributed to a spontaneous dissection of the LIMA graft with true lumen compression (Figure 3.78, A and B). Myocardial infarcts 5–10 days and 2–6 weeks in age were also identified. Pathologist awareness of this very rare cause of death in CABG patients is important to accurately determine the cause of death at autopsy.

**Multiorgan Involvement of COVID-19–Induced Cardiomyopathy After Viral Clearance in an Autopsy Case**

(Poster No. 79)

**Luna Li, MD, PhD** (lunali@pathology.arizona.edu); **Ryan P. Bruhns, MD**; **Ty W. Abel, MD, PhD**. Department of Pathology, University of Arizona, Tucson.

Coronavirus disease 2019 (COVID-19) is reported to cause pneumonia, acute respiratory syndrome, renal failure, and death in severe cases. We report an autopsy case of a 58-year-old woman with history of myocarditis and pericarditis 6 years prior to her most recent presentation for chest pain. Imaging showed pneumonia and pericarditis, and EKG showed no signs of ischemia. Troponin was elevated at 295 ng/L. Echocardiogram showed near normal left ventricular ejection fraction (LVEF). Two days later, she experienced worsening symptoms and persistently elevated troponin. Emergent left heart catheterization showed patent coronaries, but severely reduced LVEF (10%–20%). She developed metabolic acidosis and was started on extracorporeal membrane oxygenation. COVID-19 SARS-CoV-2 RNA was detected 3 times during the course of the admission but became negative after 2 weeks. During the subsequent 10 days, she encountered multiorgan dysfunction and became unresponsive, with imaging showing anoxic brain injury. At autopsy, skin desquamation and bullae were noted, affecting 22% of body surface area (Stevens-Johnson syndrome/toxic epidermal necrolysis complex). Necrosis of multiple fingers and toes was noted. Severe, bilateral pulmonary edema and hemorrhage were observed. The left cardiac ventricle was remarkable for scattered petechial hemorrhage. Microscopically, acute paucicellular pan-epidermal necrosis of the skin was noted. The left ventricle demonstrated interstitial fibrosis and chronic inflammation involving the pericardium and myocardium. In the lung, organizing and acute pneumonia were seen in a background of hemorrhage and edema. The liver showed cholestasis and ischemic changes. The left kidney showed focal infarction and glomerulosclerosis. This case highlights the development of irreversible, multiorgan dysfunction related to COVID-19, despite viral clearance (Figure 3.79).

**Cannabis and Cocci: Autopsy Findings of Florid, Multiorgan Disseminated Coccidioidomycosis**

(Poster No. 81)

**Jack P. Guccione, MD** (jgucci@uci.edu); **Joaquin Ponce Zepeda, MD**; **Suvarna A. Deshmukh-Rane, MD**. Department of Pathology and Laboratory Medicine, UC Irvine Medical Center, Orange, California.

Fulminant, disseminated coccidioidomycosis with multiorgan involvement is reported in a 63-year-old man with a history of cannabis farming. Initially, he presented with innumerable pulmonary miliary opacities on chest computed tomography scan (Figure 3.81, B). Physical examination revealed numerous plaquelike nonhealing skin lesions on the face, hands (Figure 3.81, C), and abdomen that developed during the course of months, concerning for a fungal process. HIV testing and tuberculin tests were negative. Initial fungal serology and blood cultures were also negative. The patient’s condition deteriorated, and he expired overnight. An unrestricted autopsy confirmed numerous white nodules involving all lung lobes (Figure 3.81, A), liver, and spleen. Gross autopsy findings revealed abdominal organs to be severely adhered to a thickened and diffusely nodular omentum with enlarged mediastinal and abdominal lymph nodes. Microscopy showed innumerable, intact, and ruptured spores of coccidioidomycosis involving all lung lobes, spleen, lymph nodes, omentum, bowel serosa, liver, gallbladder, adrenal gland, thyroid gland (Figure 3.81, D), prostate gland, and skin. Disseminated coccidioidomycosis is a rare sequela of a coccidioidomycosis infection. Coccidioides immitis spores are endemic to...
Agnathia-Otocephaly Complex With Short Lower Limbs: A Rare Case Report

(Poster No. 83)
Fnu Sameeta, MD1 (fsameeta@health.southalabama.edu); Elizabeth Manci, MD; Departments of 1Pathology and 2Pediatric Pathology, University of South Alabama, Mobile.

Agnathia–otocephaly complex (AGOTC, MIM 202650) is an extremely rare anomaly. About 135 cases have been reported since the first description 251 years ago. Study of new cases will better define this condition. A 103-g, 18-week gestational age, nonviable female fetus was born to a 26-year-old G2, P1001 mother by vaginal delivery, which was complicated by placenta previa, as well as multiple malformations typical of AGOTC. Birth weight and gestational measurements were decreased for gestational age. Malformations included microcephaly; agnathia; astomia; aglossia; hypotelorism; downward slanting of fused palpebral fissures; microtia; nasal proboscis with 2 openings; choanal atresia; hypoplastic larynx; bilateral short limbs; bilateral syndactyly (third and fourth fingers); unilateral lungs; and agenesia of kidneys, ureters, adrenals and urinary bladder. Other viscera were within normal limits but small for gestational age. Microscopically, the placenta comprised dysplastic second-trimester edematous chorionic villi with intravillous hemorrhages. Examination of the brain was compromised by autolysis. Lung bacterial cultures were negative; karyotype was 46,XX. Etiologies have been linked to genetic, environmental, and teratogenic factors. Most cases appear to be sporadic; few cases were familial with heterozygous mutations in the PRRX1 and OTX2 genes, as well as unbalanced and balanced translocations. Nongenetic factors include teratogens (theophylline, salicylates, amidopyrine). Pathogenesis is considered to be a defect of blastogenesis, primarily involving the first branchial arch derivatives along with dysmorphogenesis of other midline craniofacial field structures. This case of AGOTC is unique in that it expands the associated malformations to include bilateral short lower limbs.

Mitragynine/Kratom as a Cause of Death in a Forensic Case

(Poster No. 84)
Busha Hika, BS (bhkbf@health.missouri.edu); Komal Ijaz, MD; Christopher C. Stacy, MD; Keith N. Norton, MD. Department of Pathology and Anatomical Sciences, University of Missouri Health, Columbia.

Mitragynine and 7-hydroxy mitragynine are psychoactive alkaloid components of the plant Mitragyna speciosa, also known as kratom. The use of mitragynine as a recreational drug and/or self-medication for opioid withdrawal has been increasing in the United States. Mitragynine exerts its central nervous system effect through modulation of monoamine and mu-opioid receptors. There are case reports of overdose of mitragynine causing respiratory depression, seizure, psychosis, and death. However, there is no consensus as to the lethal dose. Although postmortem mitragynine blood concentrations in fatalities have ranged from 20 to 600 ng/mL, there has been one report with a level of 4310 ng/mL. We present the case of a 49-year-old woman who was found by her husband struggling to breathe and later dying before she could receive medical attention. The deceased had a history of chronic pain and seizures treated with Protonix,
alprazolam, Depakote, hydrocodone, amitriptyline, and Latuda. Postmortem cardiac blood toxicology was significant for a mitragynine concentration of 4400 ng/mL and a hydrocodone concentration of 420 ng/mL. The high concentration of mitragynine, in addition to that of hydrocodone, indicates that the cause of death was intoxication by mitragynine and hydrocodone. With the increasing reports of death from an overdose of mitragynine (alone or in combination with other drugs), rapid screening methods should be developed in addition to the sophisticated gas chromatography. Our case also highlights the need for more studies regarding the toxicity of mitragynine, development of consensus as to the lethal dose, and treatment of overdose and withdrawal.

Ciliated Hepatic Foregut Cyst: An Unusual Presentation

Anita Arackal, MD (aarackal@montefiore.org); Kevin Kuan, MD; Nicole Panarelli, MD. Department of Pathology, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, New York.

A 64-year-old man with a history of hypertension and end-stage renal disease underwent deceased donor renal transplantation. On preoperative abdominal computed tomography, a 9-cm liver cyst in segment V of the right liver lobe was found. The patient succumbed to post-renal transplantation complication and passed away. During the authorized autopsy, a 9.5-cm smooth, thin-walled, tan cyst containing clear, serous fluid was found predominantly on the inferior aspect of the right lobe of the liver (Figure 3.85, A). Histologically, the cyst was lined with simple to pseudostratified columnar epithelium (Figure 3.85, B). A subepithelial connective tissue layer and irregular smooth muscle layer and an outer fibrous capsule were noted in certain areas (Figure 3.85, C and D). There were also focal areas of hemosiderin-laden macrophages. The above findings support the diagnosis of ciliated hepatic foregut cyst. Ciliated hepatic foregut cyst is a rare congenital cyst, usually found incidentally. It is a remnant of the embryonic foregut. The cyst is usually benign, but malignant transformation is reported. Most ciliated hepatic foregut cyst are approximately 3 to 4 cm and are commonly identified in segment IV of the left liver lobe. Patients are usually asymptomatic. They can be confused for simple biliary cyst or hydatid cyst.

A Summary of COVID-19 Autopsy Findings in Orange County, California: A Single-Institution Study

Joaquin Ponce Zepeda, MD (jponceze@hs.uci.edu); Jamie Nakagiri, MD; Jack Guccione, MD; Beverly Wang, MD; Cary Johnson, MD; Robert Edwards, MD. Department of Pathology and Laboratory Medicine, University of California Irvine, Orange.

Context: The COVID-19 pandemic has impacted every element of health care, including academic pathology practice. Postmortem examination has been a critical step in understanding the morbidity and mortality of SARS-CoV-2 infection. Epidemiologic data indicate that both biological risk factors and social determinants of health contribute to COVID-19 morbidity and mortality. In this single-institution study, we examine the common and uncommon findings in our exclusively Hispanic cohort of autopsy patients.

Design: Data were collected from autopsies in COVID-19–positive patients between May 2020 and March 2021, at the University of California Irvine.

Results: Twelve COVID-19–positive autopsies were performed during the 10-month period. The age range was 29 to 87 and included 2 women and 10 men, all of Hispanic descent. The immediate cause of death in 9 cases was respiratory failure secondary to COVID-19 pneumonia (Table). In the other 3 cases, COVID infection was incidental to the patient’s underlying cause of death, which included cases of septic peritonitis, alcoholic liver disease, and heart disease.

Conclusions: All patients had a history of multiple comorbidities, such as hypertension and diabetes, which contributed to the susceptibility and severity of illness. The median age of patients dying because of COVID 19 is 61 in our cohort (national median is 74 years of age). Despite the Hispanic population encompassing only approximately 34% of the population of Orange County, California, 100% of our autopsies were of Hispanic descent. This implicates that COVID-19 disproportionately affects the Hispanic population with a need for further education and focus on this population.
<table>
<thead>
<tr>
<th>Age, y</th>
<th>Sex</th>
<th>Cause of Death</th>
<th>Pertinent Clinical History</th>
<th>Major Autopsy Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>73</td>
<td>M</td>
<td>Respiratory failure, secondary to severe pulmonary SARS-CoV-2 infection due to existing comorbidities including type II diabetes and hypertension</td>
<td>Hypertension, type II diabetes</td>
<td>Severe hyaline membrane disease from acute to organizing with superimposed foci of acute bronchopneumonia, right pulmonary thromboembolus at the right lung hilum, advanced coronary artery disease, possible minimal myocarditis in the right ventricle, severe pass hepatic congestion, small vessel fibrin microthrombi in multiple organs</td>
</tr>
<tr>
<td>87</td>
<td>M</td>
<td>Respiratory failure due to COVID-19 pneumonia</td>
<td>Hypertension, type II diabetes</td>
<td>Severe hyaline membrane disease involving all 5 lobes of the lung, acute tracheobronchitis, severe triple-vessel coronary artery disease, chronic ischemic heart disease, diabetic glomerulosclerosis, renal cortical atrophy</td>
</tr>
<tr>
<td>72</td>
<td>M</td>
<td>Septic peritonitis</td>
<td>Multiple abdominal surgeries</td>
<td>Severe peritonitis secondary to jejunal perforation, status post surgical repair, anastomotic leak, and re-exploration, moderate coronary artery disease, acute tracheitis with mucosal ulceration, bilateral pleural effusions</td>
</tr>
<tr>
<td>29</td>
<td>M</td>
<td>Respiratory failure secondary to overwhelming COVID-19-associated pneumonia</td>
<td>Type I diabetes, poorly controlled</td>
<td>Pulmonary thromboembolus occluding the right main pulmonary artery, severe lobar pneumonia involving all 5 lobes of the lung, focal pulmonary aspergillosis</td>
</tr>
<tr>
<td>49</td>
<td>F</td>
<td>Respiratory failure secondary to severe COVID-19-associated pneumonia</td>
<td>Rheumatoid arthritis, hypertension, hyperlipidemia, type II diabetes, cardiac arrhythmia (treated with Eliquis)</td>
<td>Severe acute bronchopneumonia with pulmonary edema and intra-alevolar hemorrhage, chronic hypertensive heart disease, moderate to severe coronary artery disease, chronic renal insufficiency</td>
</tr>
<tr>
<td>84</td>
<td>M</td>
<td>Respiratory failure secondary to COVID-19 pneumonia, due by poorly controlled type II diabetes and advanced renal disease</td>
<td>Hypertension, type II diabetes</td>
<td>Foci of hyaline membrane disease and patchy acute bronchopneumonia, involving all 5 lobes of lung, acute tracheobronchitis, mild coronary artery disease, acute pyelonephritis superimposed upon advanced diabetic glomerulosclerosis and renal cortical atrophy</td>
</tr>
<tr>
<td>65</td>
<td>M</td>
<td>Multiorgan failure as a consequence of patient’s multiple medical comorbidities, complicated by his COVID-19 infection</td>
<td>Alcoholic cirrhosis status post liver and kidney transplant in 2011, hypertension, and type II diabetes</td>
<td>Generalized anasarca of the soft tissues, signs of severe passive congestion of all organs, advanced calcific coronary artery disease, chronic ischemic and hypertensive heart disease, end-stage renal disease, pulmonary edema and hemorrhage</td>
</tr>
<tr>
<td>69</td>
<td>M</td>
<td>Cardiac and respiratory failure due to coronary artery disease, complicated by a hospital acquired COVID-19 pneumonia</td>
<td>Non-ST elevation myocardial infarction (NSTEMI), coronary artery disease status post coronary artery bypass graft in 2002, pacemaker, hypertension, type II diabetes, benign prostatic hyperplasia, acute kidney injury, and chronic combined systolic and diastolic heart failure</td>
<td>Cardiomegaly, advanced coronary artery disease, pulmonary edema, mild cerebral atherosclerosis, moderate cerebral arteriolar sclerosis, multiple old infarcts in the right globus pallidus, left putamen, left thalamus, dorsal left basis pontis, and retro-olivary right medulla</td>
</tr>
<tr>
<td>46</td>
<td>M</td>
<td>Septic shock and acute respiratory distress syndrome secondary to COVID-19 pneumonia</td>
<td>Acute kidney injury, end-stage renal disease status post renal transplant in 2018, type II diabetes, and aspergillos pneumonia</td>
<td>Mild cardiomegaly, pulmonary edema, acute and chronic hyaline membrane disease, recanalized thrombus in lungs, globally sclerotic glomeruli consistent with end-stage renal disease, and coronary arteries show severe atherosclerosis and calcifications</td>
</tr>
<tr>
<td>43</td>
<td>M</td>
<td>Respiratory failure secondary to COVID-19 pneumonia, due to predisposing lung conditions such as pulmonary hypertension and pulmonary fibrosis</td>
<td>Type II diabetes, pulmonary hypertension, interstitial lung disease, and pulmonary fibrosis</td>
<td>Mild cardiomegaly, hyaline membrane disease, dense interstitial fibrosis, areas of pulmonary congestion, pulmonary edema, type 2 pneumocyte hyperplasia, and organizing phase of hyaline membrane disease. Small focus of acute bronchopneumonia. Moderate calcific atherosclerosis, 40%–50%. Centrilobular necrosis and hepatic congestion in the liver</td>
</tr>
</tbody>
</table>
Pulmonary Secondary Coinfection of *Pseudomonas aeruginosa* and Invasive Aspergillus Species in a Critically Ill COVID-19 Patient: Postmortem Findings to Support Clinical Management

((Poster No. 88)

Ying Sun, MD, PhD (sunny20@ecu.edu); Kotaro Takeda, MD, PhD; James Spears, PA; Ann Sutton, MD; Randall Falls, DO. Department of Pathology, East Carolina University/Vidant Health Center, Greenville, North Carolina.

The ongoing worldwide coronavirus disease 2019 (COVID-19) pandemic due to severe acute respiratory syndrome coronavirus 2 continues to be a focus of medical investigation. Recent studies report that acute respiratory distress syndrome due to evolution of viral infection is the predominant cause of mortality in critically ill COVID-19 patients. However, secondary bacterial and fungal coinfection in these patients may play a significant role in rapid respiratory collapse and mortality. To date, detailed investigations are rare. We present the autopsy findings of a critically ill 69-year-old female COVID-19 patient with hypertension. The patient died 2 months after admission despite aggressive management with antimicrobials, tracheostomy, anticoagulation, and vasopressor support. An autopsy was performed that adhered to Centers for Disease Control COVID-19 safety recommendations. Macroscopically, the lungs were hemorrhagic and edematous with significant growth of *Aspergillus*. Microscopically, sections exhibited extensive neutrophilic infiltrates, alveolar fibrin deposition, and focal abscess formation, consistent with acute bacterial infection. Respiratory cultures confirmed growth of pathogens of *Pseudomonas aeruginosa* and *Aspergillus flavus*. A dense radiating array of spores and septate hyphae with acute angle branching, extensive necrosis (Splendore-Hoeppli phenomenon), and vascular invasion was identified, consistent with invasive aspergillosis. Findings of hyaline membranes, interstitial fibrosis, and microvascular thrombosis suggested diffuse alveolar damage. These postmortem findings provide direct evidence of superimposed bacterial and fungal coinfection, which likely contributed to the patient’s hypoxia and subsequent demise. Although rare, coinfection should be considered in clinical practice in COVID-19 patients.

Adenopathy and Coagulopathy: An Unusual Presentation of Esophageal Signet Ring Cell Adenocarcinoma on Autopsy

(Poster No. 89)

Adeyinka O. Akinsanya, MBBS (aokinsan@iu.edu); Ashley S. Inman, MD. Department of Pathology and Laboratory Medicine, Indiana University, Indianapolis.

Esophageal signet ring cell adenocarcinoma is uncommon and characterized by discohesive malignant cells with intracellular mucin. Its infiltrative growth pattern, frequent lack of an identifiable mass lesion, and vague symptoms often delay the diagnosis and render a poor prognosis. We report an autopsy case of a 63-year-old man without a history of gastrointestinal reflux disease or Barrett esophagus who presented with abdominal pain, nausea, and vomiting. Radiologic imaging revealed splenic and bilateral renal infarctions, superior mesenteric and iliac artery occlusion, thickened distal esophagus, and intraabdominal lymphadenopathy. His condition deteriorated rapidly after hospitalization. Clinical suspicion for underlying lymphoma leading to hypercoagulability was high before his death. On autopsy, a transmural gastroesophageal junction lesion was discovered with para-aortic, periportal, and peripancreatic lymphadenopathy. Microthrombi were present systemically with infarctions in the heart, spleen, and kidneys. Histologic sections of the lesion and enlarged lymph nodes showed pleomorphic, infiltrative, discohesive tumor cells with minimal desmoplasia. Tumor cells were positive for cytokeratin (AE1/AE3) immunohistochemical stain and contained intracellular mucin with mucicarmine stain, confirming the diagnosis of signet ring cell adenocarcinoma. Hypercoagulability is a well-known paraneoplastic syndrome of gastrointestinal tumors but is uncommon with esophageal tumors. The signet ring cell histologic pattern is also uncommon in the esophagus. This unusual presentation serves as a reminder of the association and may help guide clinical decisions in future cases of widespread adenopathy and coagulopathy. It also highlights the key role of autopsy in enhancing medical knowledge.

Aggressive Classic Hodgkin Lymphoma Identified at Autopsy in a Patient With Extensive Cutaneous Warts: Possible Association With Immunodeficiency?

(Poster No. 90)

Mark Russell, MD (mark.a.russell@lumc.edu); Randall McGivney, DO, MBA; Ira Shetty, MD; Girish Venkataraman, MD; Kamran Mirza, MD, PhD; Carrie Fitzpatrick, PhD; Vijayalakshmi Ananthanarayanan, MD. 1Department of Pathology and Laboratory Medicine, Loyola University Medical Center, Maywood, Illinois; 2Department of Pathology and Laboratory Sciences, MacNeil Hospital, Berwyn, Illinois; 3Department of Adult Congenital Heart Disease, Electrophysiology, and Pediatric Cardiology, Advocate Children’s Hospital, Oak Lawn, Illinois; 4Department of Pathology, The University of Chicago Medicine, Chicago, Illinois; 5Department of Pathology and Laboratory Medicine, Loyola University Health System, Maywood, Illinois.

A 28-year-old man with a history of truncus arteriosus and cardiac arrhythmias presented with a productive, bloody cough and shortness of breath. Computed tomography scan of the chest revealed multiple lung nodules and mediastinal lymphadenopathy. The patient expired before an autopsy could be performed. At autopsy, gross examination showed bilateral exophytic warts on both palms (Figure 3.90, A) with multiple large nodular lesions in the lungs (Figure 3.90, B) and spleen as well as extensive lymphadenopathy. Histologically, the lesions in the lung were paucicellular with necrosis and scattered Hodgkin/Reed-Sternberg cells.
Sternberg (HRS) cells and few lymphocytes. The HRS cells stained positive for CD30 (Figure 3.90, C), CD15, PAX5 (dim), and negative for CD20 (rare weak), and Epstein–Barr virus (EBV) by in situ hybridization (Figure 3.90, D) supporting the diagnosis of lymphocyte-depleted EBV classic Hodgkin lymphoma. The cause of death was respiratory failure and pulmonary embolism. Clinical/immunologic workup 8 years prior to death indicated bilateral palmar verrucae with normal CBC but low absolute CD3 and CD4 T-cell counts with defective T-cell response on PHA test and normal serum immunoglobulin levels. There was positive EBV viremia with negative HIV and hepatitis C. With cardiac defects and primary T-cell defect, Di George syndrome was considered, and aCGH did not detect 22q11 microdeletion. Additional whole genome microarray analysis detected an approximately 3.9-Mb single copy gain of chromosome 6q13q14.1. Hodgkin lymphoma is rare in the setting of appropriate biosafety measures during autopsy. Given the known false-negative rates of nasopharyngeal swab testing for SARS-CoV-2 during the postmortem period, we hypothesized that postmortem tracheal swabs would provide more accurate information about SARS-CoV-2 infection status.

**Context:** In the spring of 2020, with the threat of a surge of potential SARS-CoV-2/COVID-19–related deaths, we aimed to develop a procedure for identifying SARS-CoV-2–positive decedents to use appropriate biosafety measures during autopsy. Given the known false-negative rates of nasopharyngeal swab testing for SARS-CoV-2 during the postmortem period, we hypothesized that postmortem tracheal swabs would provide more accurate information about SARS-CoV-2 infection status.

**Design:** From March to July 2020, postmortem nasopharyngeal (NPS) and tracheal (TS) swabs from decedents examined at University of Texas Medical Branch Hospital or Galveston County Medical Examiner Office were obtained and tested by ID NOW COVID-19 (Abbott) rapid molecular assay.

**Results:** Approximately 30% of cases tested positive for SARS-CoV-2, with either NPS, TS, or both positive. Among positive cases, about half were discordant between NPS and TS samples. The discordant results between NPS and TS were equally divided. Assuming no COVID-19 cases were missed by testing NPS and TS samples only, TS alone would have detected 75% (18 of 24) of cases and NPS alone would have detected 79% (19 of 24) (Table).

**Conclusions:** Compared with NPS, TS was not a more sensitive specimen type for postmortem SARS-CoV-2 detection.

<table>
<thead>
<tr>
<th>SARS-CoV-2 Test Results by Anatomic Site</th>
<th>NPS/TS, No. (%)</th>
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<tr>
<td>Total Cases</td>
<td>82</td>
<td>13 (15.9)</td>
<td>58 (70.7)</td>
<td>5 (6.1)</td>
</tr>
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Abbreviations: NPS/TS; Both NPS and TS from the same decedent tested positive for SARS-CoV-2; NPS/Ts; Both NPS and TS from the same decedent tested negative for SARS-CoV-2; NPS/TS; NPS tested negative and TS tested positive for SARS-CoV-2 from the same decedent; NPS/TS; NPS tested positive and TS tested negative for SARS-CoV-2 from the same decedent.

**Evaluating Nasopharyngeal Versus Tracheal Samples for Postmortem COVID-19 Testing**

(Poster No. 92)

**Jamie Kendrick, MD** (jckendri@utmb.edu); Ping Ren, PhD; Erin Barnhart, MD; Lu Chen, MS; Harshwardhan Thaker, MD; PhD; Judith Aronson, MD; Emma Henrie, MD. Department of Pathology, University of Texas Medical Branch at Galveston.

**Context:** In the spring of 2020, with the threat of a surge of potential SARS-CoV-2/COVID-19–related deaths, we aimed to develop a procedure for identifying SARS-CoV-2–positive decedents to use appropriate biosafety measures during autopsy. Given the known false-negative rates of nasopharyngeal swab testing for SARS-CoV-2 during the postmortem period, we hypothesized that postmortem tracheal swabs would provide more accurate information about SARS-CoV-2 infection status.

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**Interobserver Reproducibility and Diagnostic Accuracy for the Milan System Evaluation of Neoplasms Characterized by a Small Cell or Basaloid Morphology and Stromal Fragments**

(Poster No. 93)

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**Context:** The Milan System for Reporting Salivary Gland Cytopathology (MS) supplies uniform terminology, malignancy risk estimates and management recommendations. The system has fair interobserver reproducibility (κ = 0.42). Interobserver agreement varies with diagnostic category. Salivary gland neoplasms of undetermined malignant potential and suspicious for malignancy have poor interobserver agreement. Neoplasms characterized by cellular smears, stroma fragments, and small or basaloïd cells are difficult to classify. Little is known of the impact of the MS on interobserver agreement for these neoplasms.

**Design:** The first author's consultation files were searched for surgically confirmed cytology cases of cellular pleomorphic adenoma, monomorphic adenoma, adenoid cystic carcinoma, and polymorphous adenocarcinoma. Smear preparations were reviewed independently by 4 cytopathologists and assigned to the MS categories.

**Results:** Twenty-three specimens were categorized. Agreement was highest for categories benign neoplasm and malignant. Chance correct agreement was 0.28 with observed agreement of 56%. A consensus agreement was 0.28 with observed agreement of 56%. A consensus agreement was 0.28 with observed agreement of 56%.
**Conclusions:** Neoplasms characterized by cellular smears of basophilic or small cells and stromal fragments are associated with low interobserver agreement for categories of the MS. This group of neoplasms was associated with a lower k (0.28) than previously published agreement statistics for MS system (0.42). Neoplasms categorized as benign had a k score of 0.71 and malignancies a k of 0.72. Cytologic separation of monomorphic adenomas from adenoid cystic carcinomas and polymorphous adenocarcinomas has poor interobserver agreement.

**Repeat Thyroid Fine-Needle Aspiration Biopsies for Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance in the Era of Thyroid Molecular Testing**

(Plot No. 94)

Christopher J. O’Connor, MD, PhD (cocooner@gmail.com); Rajesh C. Dash, MD; Claudia K. Jones, MD; Sara X. Jiang, MD. Department of Pathology, Duke University, Durham, North Carolina.

**Context:** The American Thyroid Association recommends repeat fine-needle aspiration biopsy (FNAB) or molecular testing for atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS) nodules; however, the utility of repeat FNAB for AUS/FLUS when access to molecular testing is available is unclear.

**Design:** Thyroid nodule FNABs diagnosed as AUS/FLUS on initial biopsy and that underwent repeat FNAB were examined during a 12-month period. Eighty-two cases were included in this study (5 cases were excluded because of concurrent nodules with suspicious for follicular neoplasm/follicular lesion of undetermined significance (FN/SFN), suspicious for malignancy (SM), or malignant and 2 cases because of molecular testing of the initial biopsy).

**Results:** Of 82 repeat FNABs, 51.2% repeated as AUS/FLUS, with 34% reclassified to benign. Of all rebiopsies, 60% had subsequent molecular testing performed, including 1 of 28 benign (0.1%), 40 of 42 AUS/FLUS (95%), 6 of 6 FN/SFN (100%), and 1 of 2 SM (50%). Twenty-two of 82 nodules (27%) were excised, with 9 of 82 (11%) malignant on resection (Table).

**Conclusions:** For AUS/FLUS nodules that had repeat FNAB, approximately one-third (34%) reclassified to benign, and more than half (51%) did not change from AUS/FLUS (which in this scenario provided limited additional diagnostic value as the rate of malignancy of single AUS/FLUS nodules and repeat AUS/FLUS nodules does not differ). In addition, 3.7% (3 of 82) of rebiopsies were nondiagnostic, limiting the ability to further classify these nodules with molecular testing. The majority of repeat FNAB for AUS/FLUS ultimately underwent molecular testing. Our findings provide motivation to examine further the cost-benefit aspects of rebiopsy with reflex molecular testing for AUS/FLUS versus molecular testing on initial AUS/FLUS nodules (via either testing of direct smears or prospective molecular testing sample collection).

<table>
<thead>
<tr>
<th>Rebiopsy and Surgical Pathology Results of AUS/FLUS Thyroid Nodules</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Result on Repeat Biopsy</strong> for AUS/FLUS</td>
</tr>
<tr>
<td>Non-diagnostic</td>
</tr>
<tr>
<td>Benign</td>
</tr>
<tr>
<td>AUS/FLUS</td>
</tr>
<tr>
<td>Suspicious for follicular neoplasm</td>
</tr>
<tr>
<td>or follicular neoplasm</td>
</tr>
<tr>
<td>Suspicious for malignancy</td>
</tr>
<tr>
<td>Malignant</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

**The Importance of Detecting and Reporting the Presence of Mucin in Pancreatic Cysts**

(Plot No. 95)

Sherehan Zada, MD (sherehaz@uci.edu); Di Lu, MD; Min Han, MD, PhD; Beverly Wang, MD; Behdokht Nowroozizadeh, MD. Department of Pathology, University of California–Irvine, Orange.

**Context:** The diagnosis of mucinous cysts by cytology can significantly impact patient management; however, the diagnosis can be challenging when there is scant material. We aim to describe the cytomorphic characteristics and the influence of the cytologic findings on clinical management.

**Design:** We identified patients found to have mucin-containing cysts on cytology. The endoscopic ultrasound-guided, fine-needle aspiration (EUS/FNA) features, gross aspirate characteristics, ancillary tests, and cytomorphic features were described.

**Results:** Fourteen patients who underwent EUS/FNA of pancreatic cysts had mucin identified. Four cysts had scant mucin, 5 were moderate, and 5 were abundant (Table). Seven aspirates contained glandular cells that ranged from mildly to moderately atypical. In 13 cases, the clinical assessment was either intraductal papillary mucinous neoplasm (IPMN) or mucinous cystic neoplasm (MCN). In 5 cases, cytologic findings changed the clinical impression from pancreatic cyst not otherwise specified (NOS) to IPMN or MCN. In 6 cases, the clinical impression of IPMN was supported. In 1 case, the clinical impression of pseudocyst was changed to IPMN. In 1 case, the clinical impression of pancreatic cyst NOS was assessed as pseudocyst after FNA.

**Conclusions:** FNA can be useful in determining the nature of pancreatic cysts. Although it may yield scant material and cellularity, the cytomorphic features, with radiographic and chemical findings, can help determine if they are neoplastic. Although some aspirates in the case series were acellular, the presence of mucin raises the concern for mucinous neoplasm, warranting surveillance by EUS. This case series highlights the importance of detecting and reporting the presence of mucin by cytology.

**Patients With Pancreatic Cysts Containing Mucin**

<table>
<thead>
<tr>
<th>Case</th>
<th>Location</th>
<th>Amount of Mucin</th>
<th>String Sign, mm</th>
<th>Gross Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pancreatic tail</td>
<td>Scant</td>
<td></td>
<td>Thin, yellow, cloudy</td>
</tr>
<tr>
<td>2</td>
<td>Pancreatic uncinate process</td>
<td>Scant</td>
<td></td>
<td>Viscous</td>
</tr>
<tr>
<td>3</td>
<td>Pancreatic head</td>
<td>Scant</td>
<td></td>
<td>Viscous, brown</td>
</tr>
<tr>
<td>4</td>
<td>Pancreatic neck</td>
<td>Scant</td>
<td></td>
<td>Reddish, cloudy</td>
</tr>
<tr>
<td>5</td>
<td>Pancreatic neck</td>
<td>Moderate</td>
<td>12</td>
<td>Very viscous, clear</td>
</tr>
<tr>
<td>6</td>
<td>Pancreatic body</td>
<td>Abundant</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Poster No. 94*
It’s TEA Time: A Proof-of-Concept Study of a New Rapid Stain for Rapid On-Site Evaluation With Comparison With Toluidine Blue
(Poster No. 96)

Alejandro Mendoza, MD (asmendoza@yahoo.com); Kurt Schaberger, MD; Lydia Howell, MD; John Bishop, MD; Aurelia Lauderdale; Stanley Seko; Ronelson Hermosilla; Donald York; Alaa Afify, MD. Department of Pathology, University of California Davis Health, Sacramento.

Context: Adequacy assessment by rapid on-site evaluation (ROSE) improves the diagnostic yield of fine-needle aspiration (FNA) biopsies. Although advances have been made in the evaluation of ROSE, including telecytology, there have been no recent advances in the rapid stains used for ROSE. Diff-Quik and toluidine blue (TB), the 2 most common ROSE stains, each have unique limitations. In this proof-of-concept study, we compare performance of the new TEA stain, a unique mixture of TB, eosin, and alcohol, with TB as an alternative stain for ROSE.

Design: Fifty cases with adequate cellularity were selected from remnant body fluids in the cytology laboratory at the University of California Davis Medical Center during a 6-month period. Two slide smears were prepared from each case and stained with TB and TEA stains. Representative digital images of each slide were rated by 3 cytotechnologists and 2 cytopathologists using 5 criteria: presence of residual background staining, cytoplasmic detail, nuclear membrane clarity, chromatin texture, and staining of nucleoli. Each image quality criterion was given a score of 1 to 3. Overall image quality with TEA was rated significantly better than TB (Figure 3.96; A; $P < .05$). TEA provided a cleaner background with significantly better nuclear membrane definition, chromatin texture, and nucleoli details (Figure 3.96; B, TB; C, TEA). TEA performed similarly to TB for cellularity determination and cytoplasmic detail.

Conclusions: Rapid staining with TEA may be useful at ROSE as it is fast, easy, and provides excellent digital image quality. TEA merits further evaluation and could enhance telecytology for ROSE.

Comparison of Endoscopic Ultrasound-Guided, Fine-Needle Sampling Methods for Obtaining Adequate Material for Diagnosis and Mismatch Repair Protein Testing of Pancreatic Adenocarcinoma
(Poster No. 97)

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Context: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) and biopsy (EUS-FNB) are key sampling modalities for diagnosing pancreatic adenocarcinoma and obtaining material for mismatch repair protein (MMR) testing. At our institution, EUS-FNA is performed with rapid on-site evaluation (ROSE) whereas EUS-FNB is performed without ROSE with cell block (CB) creation only. This study aimed to compare these 2 methods regarding obtaining adequate material for diagnosis and for MMR testing.

Design: Performed retrospective review of sequential EUS-FNA and EUS-FNB cases from November 2018 to January 2021 that were collected by a single endoscopist. Inclusion criteria included pancreatic masses sampled by EUS-FNA or EUS-FNB with a final diagnosis of adenocarcinoma on either EUS material or resection. MMR adequacy was defined as the presence of 50 or more tumor cells on CB. Statistical comparisons were made using a $\chi^2$ test.

Results: Forty-one EUS-FNA and 41 EUS-FNB meeting inclusion criteria were identified. EUS-FNA obtained diagnostic material on 35 of 41 cases (85%), 24 of 37 CBs were adequate for MMR testing (65%). EUS-FNB obtained diagnostic material in 38 of 41 cases (93%); 35 of 41 CBs were adequate for MMR testing (85%). EUS-FNB was superior in obtaining material for MMR testing ($P = .03$).

Conclusions: There was no significant difference between EUS-FNA and EUS-FNB in obtaining adequate diagnostic material, but EUS-FNB was superior in obtaining adequate material for MMR testing. These data provide insight into how endoscopists can optimize obtaining EUS material for ancillary testing and how cytopathologists can optimize providing ROSE assessments.

Cytology Diagnosis of Intraductal Papillary Neoplasm of the Bile Duct
(Poster No. 98)

Sherehan Zada, MD (sherehaz@uci.edu). Department of Pathology, University of California–Irvine, Orange.

Intraductal papillary neoplasms of the bile duct (IPNBs) are characterized by a predominantly papillary growth pattern in dilated bile ducts. IPNBs are usually diagnosed after surgical excisions; however, rare cases in the literature reported IPNBs diagnosed on cytology prepared specimens. We report a 78-year-old man with an incidental liver mass. The diagnostic magnetic resonance imaging of the abdomen revealed left hepatic biliary dilation with a possible incidental liver hilum mass measuring approximately $5.4 \times 2.8$ cm. The patient subsequently underwent a diagnostic endoscopic ultrasound-guided, fine-needle aspiration of the liver mass. The smears showed cellular specimen with cuboidal to columnar epithelial cells forming papillary architecture. The neoplastic cells showed mostly low-grade dysplasia. A small subset of the tumor cells showed high nuclear to cytoplasmic ratio, hyperchromasia, and irregular nuclear membrane diagnostic of high-grade dysplasia (Figure 3.98, A through D). Based on these
findings, cytologic diagnosis of papillary neoplasm of the bile duct with focal high-grade dysplasia was rendered. The cytologic differential diagnosis included dysplastic ductal epithelium, cholangiocarcinoma, and metastatic carcinomas. Considering the cytology findings, the patient subsequently had a laparoscopic left hepatic lobectomy. Histology evaluation of the specimen confirmed the cytology diagnosis of papillary neoplasm of the bile duct with low-grade and high-grade dysplasia, and no evidence of invasive carcinoma was seen. In conclusion, cytologic evaluation is a viable method for diagnosing IPNBs, as it provides opportunities to further investigate the tumor grade the severity of dysplasia, and enable proper triage and treatment course of the patient.

Cytomorphologic Features of Newly Described cAMP Response Element Binding Protein–Related Neoplasms With Predilection for Mesothelial-Lined Cavities

(Poster No. 99)
Lindsey E. Kuschnerait, MD (lindsdavies@gmail.com); Devin R. Broadwater, MD; Melissa M. Van Dellen, MD; Samantha L. Butler, MD. Department of Pathology and Laboratory Services, Brooke Army Medical Center, San Antonio, Texas.

A novel malignant epithelioid neoplasm harboring fusions between Ewing sarcoma breakpoint region 1 (EWSR1) or fused in sarcoma (FUS) gene with members of the cAMP response element binding protein (CREB) family (EWSR1/FUS–CREB), with distinctive clinical, histologic, and immunophenotypic features, was recently reported in the literature. To date, only 13 cases of this neoplasm, which has a predilection for mesothelial-lined cavities, have been described. This is the first case to describe the cytologic features of this entity. An adolescent female with no significant past medical history presented with right flank pain. A computed tomography of the patient’s abdomen/pelvis showed bilateral pneumothoraces on the imaged lung bases and diffuse calcifications along the peritoneum with large-volume ascites. Further imaging revealed a 2.7-cm retroperitoneal mass deep to the pancreas and left renal vein. Computed tomography–guided biopsies with touch preparations were performed. Touch preparations revealed a highly cellular specimen with epithelioid cells presenting as loose clusters, sometimes as pseudopapillary arrangements, and single cells. The epithelioid cells had a moderate amount of cytoplasm with eccentrically located round monomorphic nuclei. Some myxoid fibrillary matrix was identified in the background (Figure 3.98, A and B). Histologic examination showed the reported characteristic findings of these CREB-related neoplasms to include epithelioid cells arranged predominantly in sheets with focal pseudopapillary growth. Conspicuous microcystic spaces and dystrophic calcifications were also seen (Figure 3.99, D and C). A panel of immunohistochemical stains showed that the lesional cells were positive for WT1 and AE1/AE3 but not calretinin or D-240. This case reports the cytomorphologic findings of this newly defined CREB-related malignant epithelioid neoplasm with predilection for mesothelial-lined cavities.
Littoral Cell Angioma of the Spleen With Extramedullary Hematopoiesis

(Poster No. 101)

Bhunesh Maheshwari, MD (bhunesh.maheshwari@roswellpark.org); Nakul A. Ravish, MBBS; Zhongbo Yang, MD. Department of Pathology, Roswell Park Comprehensive Cancer Center, Buffalo, New York.

Neoplastic lesions of the spleen are uncommon; among them littoral cell angioma (LCA) is a rare vascular tumor unique to the spleen. This tumor originates from the cells lining the venous sinuses of the splenic red pulp, showing dual endothelial and histiocytic differentiation. To date approximately 220 cases have been reported worldwide. We report a case of a 48-year-old woman with a history of breast carcinoma presenting with a 6.5-cm enlarging splenic mass, identified incidentally on computed tomography (CT) surveillance scan. A CT-guided core biopsy of the lesion was performed. Cytology of the tissue smears revealed a bloody sample with clusters of bland epithelioid foamy cells, few of which contain intracytoplasmic hemosiderin pigment. In addition, scattered atypical hyperchromatic large cells with multilobated nuclei were noted, morphologically resembling megakaryocytes (Figure 3.101, A). The corresponding core needle biopsy showed anastomosing vascular channels (Figure 3.101, B) lined by round plump neoplastic cells with occasional large atypical hyperchromatic cells in the vascular spaces (Figure 3.101, C). On immunohistochemistry the cells stained positive for CD31, CD68, and factor VIII (Figure 3.101, D), confirming a diagnosis of LCA. The large, atypical cells stained positive for CD61, consistent with megakaryocytes. A final diagnosis of LCA with extramedullary hematopoiesis was rendered. LCA when associated with extramedullary hematopoiesis can cause diagnostic challenges and be misdiagnosed as malignancy because of the atypical appearance of the megakaryocytes. Pathologists should be aware of this rare entity to avoid misdiagnosis, especially in a small biopsy or cytology sample.

Human Papillomavirus–Related Neuroendocrine Carcinoma of the Soft Palate

(Poster No. 102)

Nakul A. Ravish, MBBS (nakulrav@buffalo.edu); Bhunesh Maheshwari, MD; Zhongbo Yang, MD. Department of Pathology, Roswell Park Comprehensive Cancer Center, Buffalo, New York.

Neuroendocrine carcinomas affecting the oropharynx are extremely rare, with only 44 cases being reported since it was first identified. These tumors have a propensity to develop early regional lymphatic and systemic metastasis, increasing the necessity for early diagnosis. We report a case of a neuroendocrine carcinoma in the soft palate of a 60-year-old man presenting with persistent ear and neck pain while being treated for a sinus infection. A physical examination showed fullness in the soft palate; computerized tomography scan with contrast revealed a 2.2-cm mass centered in the soft palate. A fine-needle aspiration biopsy demonstrated a tumor composed of small to medium cells, arranged in loose cohesive clusters and as single cells (Figure 3.102, A). The neoplastic cells had scant cytoplasm with ovoid nuclei, showing fine stippled chromatin and inconspicuous nucleoli. An excisional biopsy of the mass demonstrates a 2-cell population. The predominant cells were large with abundant cytoplasm and nuclear pleomorphism (Figure 3.102, B); the minor population of cells were small to medium in size with scant cytoplasm (Figure 3.102, C). Both types of tumor cells reveal neuroendocrine nuclear features, staining positive for synaptophysin and chromogranin by immunohistochemistry. Furthermore, the tumor cells are positive for p16 and human papillomavirus 16/18 by in situ hybridization. A diagnosis of neuroendocrine carcinoma with mixed features of large and small cell was made. Human papillomavirus–related neuroendocrine carcinoma in the soft palate is extremely rare. Pathologists should be aware of this uncommon entity and know how to utilize ancillary studies to make an accurate diagnosis.
on chemotherapy and doing better. The purpose of this review is to highlight the importance of the clinical, radiologic, and cytologic correlation as well as the appropriate utilization of aspirate material for diagnosis, and expedited treatment because the prognosis of high-grade ESS is poor and complete resection should be performed as soon as possible.

Can Pheochromocytoma of the Adrenal Gland Scaled Score System Be Used in Cytologic Materials?
(Poster No. 104)

Abdullah Almajnooni, MD (almajnooni@hotmail.com); Subramanya Sakaleshpura Mallikarjunappa, MD; Ji-Weon Park, MD; Paolo Gattuso, MD; Lin Cheng, MD, Department of Pathology, Rush University Medical Center, Chicago, Illinois.

Context: Paraganglioma tends to follow a benign course; however, about 10% of cases can metastasize. The pheochromocytoma of the adrenal gland scaled score (PASS) system is sometimes used to predict paraganglioma’s aggressive behavior on histologic specimens where score $\geq 4$ is considered high risk. Here we evaluated whether the PASS system can be applied to cytologic material of paraganglioma.

Results: The 5 cytomorphologic features were sufficient to reach PASS score $\geq 4$ in all metastatic cases; therefore, the PASS system could be applied to predict the high-risk behavior of paraganglioma in cytologic specimens. The S100 heterogeneous immunostain pattern needs more investigation to determine the significance. Unlike previous publications, paraganglioma showed female predominance.

Summary of Cases of Paraganglioma With Cytologic Material

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Cellularity (Necrosis)</th>
<th>Mitosis ($&gt;3/10$ hpf)</th>
<th>Spindling</th>
<th>Nuclear Pleomorphism ($&gt;5$ Times)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (3)</td>
<td>2 (0)</td>
<td>0</td>
<td>0</td>
<td>1</td>
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<tr>
<td>2 (0)</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3 (1)</td>
<td>0 (0)</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>4 (3)</td>
<td>2 (0)</td>
<td>0</td>
<td>0</td>
<td>1</td>
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</tr>
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<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>7 (6)*</td>
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<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8 (2)</td>
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<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9 (5)*</td>
<td>2 (0)</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>10 (1)</td>
<td>1 (0)</td>
<td>0</td>
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</tr>
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<td>11 (0)</td>
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<td>0</td>
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</tr>
<tr>
<td>12 (5)b</td>
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<td>0</td>
<td>2</td>
<td>1</td>
</tr>
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</tr>
<tr>
<td>15 (5)*</td>
<td>2 (0)</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

Abbreviation: hpf, high-power fields.

a Metastasis.

b History of additional tumor.

Concurrent Plasma Cell Myeloma and Small Cell Carcinoma in the Iliac Bone
(Poster No. 105)

Joel Lanceta, MD (jlanceta@northwell.edu); Oana Rosca, MD; Wei Xue, MD, Department of Pathology, Northwell Health–Staten Island University Hospital, Staten Island, New York.

Collision tumors are defined as 2 histologically distinct neoplasms found in a single anatomic location. Because of their rarity, they may cause diagnostic challenges in small specimens. We report a case of a 73-year-old woman, current smoker, who presented with dizziness, dyspnea, and a left lower lung nodule. A subsequent positron emission tomography–computed tomography scan demonstrated a 2.5-cm FDG-avid peripheral lung nodule, as well as multiple FDG-avid bone metastases in bilateral ribs, vertebrae, sacrum, right ilium, and right pubic bone. Computed tomography–guided biopsy of the right iliac bone was performed with rapid on-site evaluation. Diff-Quik–stained imprints showed syncytial groups of neoplastic cells with scanty cytoplasm, hyperchromatic nuclei, and nuclear molding, and a smaller population of plasmacytoid cells. Fine-needle aspiration was performed, with specimen sent for flow cytometry. Immunostains on core biopsies supported small cell carcinoma: positive CK7, CAM5.2, CD56, synaptophysin, and chromogranin, and negative TTF-1, CD45, and p63/CK5/6. Ki-67 proliferative index was approximately 80%. Flow cytometry demonstrated a monocytic plasma cell population (>50%) positive for cytoplasmic λ, partial CD38, CD138, dimmer CD45, CD56, CD20, and CD19.

Undifferentiated Pancreatic Carcinoma With Osteoclast-like Giant Cells: Two Cases of Rare Variant From a Cytopathologist’s Eye
(Poster No. 106)

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We report 2 cases of a rare pancreatic malignancy, undifferentiated carcinoma (UC) of the pancreas with osteoclast-like giant cells, to enhance understanding of these rare tumors discovered by endoscopic ultrasound (EUS)–guided fine-needle aspiration (FNA) and report their morphologic, molecular, and clinical characteristics. The first case was that of an 83-year-old woman found to have a pancreatic mass on EUS-FNA of the right iliac bone. The second case was of a 73-year-old woman found to have a 9.5-cm left hepatic lobe mass and a concurrent 2.1-cm pancreatic tail mass. Both cases showed different presentations and morphologies but were found to have KRAS mutations (OGCs). The second case was of an 80-year-old man who was found to have a 9.5-cm left hepatic lobe mass and a concurrent 2.1-cm pancreatic tail mass. Both cases showed different presentations and morphologies but were found to have KRAS mutations (OGCs). The second case was of a 73-year-old woman found to have a 9.5-cm left hepatic lobe mass and a concurrent 2.1-cm pancreatic tail mass.
(G12D) mutation and CDKN2 copy number variations. Epithelial origin was supported both morphologically and immunohistochemically in the second case (CK7, AE1/3+), whereas the first case was negative for all epithelial markers (AE1/3, CK7, and EMA). In both cases the OGCs were positive for histiocytic (CD68) and negative for epithelial markers. The first patient is doing well on chemoradiotherapy with gemcitabine. In contrast, the second patient had progression of his pancreatic cancer with invasion into the stomach and possible peritoneal metastases precluding radiotherapy, and he was discharged on gemcitabine on local follow-up (Figure 3.106, A through D).

The Utility of Fine-Needle Aspiration Cytology in Assessment of Mesenchymal Neoplasms: A Study of 70 Cases

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Context: Fine-needle aspiration cytology (FNAC) of mesenchymal neoplasms (MNs) is a challenging area in cytopathology because of their morphologic heterogeneity. It represents a less invasive and cost-effective alternative to biopsies, and it is useful in distinguishing benign versus malignant lesions. The reported challenges regarding subtyping MNs have limited the use of FNAC.

Design: A retrospective search of our FNAC database of MNs from 2006 to 2020 with surgical follow-up was performed. We obtained the clinical data from available medical records, cytology, histology slides, and ancillary studies were reviewed.

Results: A total of 70 cases were included in our cohort (male to female ratio, 1:1). Of the cases, 51% of FNACs were performed for diagnostic purposes and 49% to assess metastatic disease. The involved sites are summarized in the Table. The study included 14 different subtypes of malignant MNs and 5 subtypes of benign MNs. Immunohistochemistry was performed in 33, and allowed the subtyping of 30. Ancillary studies improved our ability to provide a specific diagnosis, especially in MN of the gastrointestinal tract; 100% of benign gastrointestinal stromal tumors and schwannomas were correctly diagnosed. FNAC was 100% accurate for diagnosing benign versus malignant lesions. Fluorescence in situ hybridization performed in cell block confirmed 1 dedifferentiated liposarcoma and 1 synovial sarcoma. Cyto-histologic correlation had sensitivity, specificity, and positive and negative predictive values of 85.7%, 96.4%, 97.3%, and 81.8%, respectively.

Conclusions: FNAC, combined with clinical and radiologic data, provides important information in the evaluation of MNs and is a useful diagnostic tool with a high degree of accuracy. The limitations can be overcome with ancillary studies allowing definitive subtyping.

### Histologic Subtypes and Immunohistochemical Findings and Location of Mesenchymal Neoplasm

<table>
<thead>
<tr>
<th>Benign Mesenchymal Neoplasm</th>
<th>Total Cases, No. (%)</th>
<th>Immunocytochemistry (No. of Cases)</th>
<th>FNA Location (No. of Cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal stromal tumor</td>
<td>14 (20)</td>
<td>CD117+, DOG1+ (14)</td>
<td>Stomach (11) Esophagus (1) Duodenum (2)</td>
</tr>
<tr>
<td>Leiomyoma</td>
<td>7 (10)</td>
<td>Caldesmon+, desmin- (2)</td>
<td>Stomach (3) Esophagus (3) Skin (1) Neck (2) Supraclavicular area (1) Shoulder (1) Pelvis (1) Neck (1) Stomach (1) Parapharyngeal space (1) Scalp (1)</td>
</tr>
<tr>
<td>Lipoma</td>
<td>4 (5.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipoma</td>
<td>4 (5.7)</td>
<td>SOX10+ (1)</td>
<td></td>
</tr>
<tr>
<td>Schwannoma</td>
<td>4 (5.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiomyxoma</td>
<td>1 (1.42)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant mesenchymal neoplasm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chondrosarcoma</td>
<td>7 (10)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Medullary Thyroid Carcinoma Diagnosed on Endoscopic Ultrasound-Guided Fine-Needle Aspiration

(Poster No. 108)

Anoshia Afzal, MD (anoshia-afzal@ouhsc.edu); Evan Fowle, DO; Michael Magguilli, MD. Department of Pathology, University of Oklahoma Health Sciences Center, Oklahoma City.

Medullary thyroid carcinoma (MTC) is a relatively uncommon thyroid malignancy, and it accounts for about 4% of thyroid malignancies. MTC originates in the parafollicular or C cells, which are embryogenically neural crest–derived cells of the thyroid and are responsible for secreting calcitonin. MTC is sporadic in about 75% of cases and hereditary in about 25% of cases. The hereditary cases are a result of a germline mutation in RET proto-oncogene. We present a case of a 75-year-old man with extensive smoking history, who was found to have bilateral lung masses, a thyroid nodule, and mediastinal and hilar lymphadenopathy, along with lytic bone lesions. Given the history of smoking, a lung primary was favored, and he presented for endobronchial ultrasound-guided fine-needle aspiration (EBUS-FNA) and endobronchial biopsy of a hilar mass. On-site adequacy of lymph node aspirations revealed discohesive groups of cells with plump, spindled nuclei, granular chromatin, and abundant cytoplasm with amorphous acellular matrix material in the background (Figure 3.108, A through D). Endobronchial biopsy and immunoperoxidase stains confirmed the diagnosis of MTC. MTC has not been described in the literature as having been being diagnosed by EBUS-FNA or endobronchial biopsy. It is important to keep this differential in mind whenever a monotonous population with endocrine features is identified on an endobronchial biopsy. Our patient had extensive metastatic disease at the time of diagnosis and palliative treatment was opted for because of the extent and inoperable status of the disease.

Clinical Significance of HIV Detection in Women With Atypical Glandular Cells on Papanicolaou Testing

(Poster No. 109)

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Context: The significance of HIV testing in women with atypical glandular cells (AGC) on the Papanicolaou (Pap) test is undetermined.

Design: Pap tests with an AGC result from 2013 to 2019 with histologic follow-up within 1 year were included in this study.

Results: A total of 737 Pap tests were reported as AGC, including AGC not otherwise specified (PG1), AGC-atypical squamous cells of undetermined significance (AGC-LSIL), AGC-endocervical (AGC-EC), AGC-endometrial (AGC-EM), AGC-high-grade squamous intraepithelial lesions (AGC-HGSIL), and AGC–atypical glandular cells (AGC–AGC). The HIV-positive rate among patients with AGC was 12%, 6% of whom showed dysplastic squamous or glandular lesion on follow-up procedure. Of the HIV-negative patients, 38% showed neoplasia and 49% were associated with benign features. A χ² test was used to assess the correlation between HIV test results and neoplasia in the AGC Pap test. The HIV result is not useful

<table>
<thead>
<tr>
<th>Benign Mesenchymal Neoplasm</th>
<th>Total Cases, No. (%)</th>
<th>Immunocytochemistry (No. of Cases)</th>
<th>FNA Location (No. of Cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synovial sarcoma</td>
<td>5 (7.1)</td>
<td>TLE-1⁺, EMA⁺ (2)</td>
<td>Gluteus (1)</td>
</tr>
<tr>
<td>Pleomorphic fibroblastic sarcoma</td>
<td>5 (7.1)</td>
<td>EMA⁺, SATB2⁺, Keratin⁺, BFG1⁻ (1)</td>
<td>Lung (1)</td>
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<tr>
<td>Ewing sarcoma</td>
<td>4 (5.7)</td>
<td>Keratin⁻ (1)</td>
<td>Parotid (1)</td>
</tr>
<tr>
<td>Malignant gastrointestinal stromal tumor</td>
<td>4 (5.7)</td>
<td>CD117⁺ and DOG1⁻ (3)</td>
<td>Lung node (3)</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>3 (4.3)</td>
<td>Desmin⁻ (2)</td>
<td>Retroperitoneum (1)</td>
</tr>
<tr>
<td>Myxofibrosarcoma</td>
<td>3 (4.3)</td>
<td>Keratin⁻ (1)</td>
<td>Mediastinum (1)</td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td>2 (2.9)</td>
<td>Vimentin⁺, keratin⁻ (1)</td>
<td>Parotid (1)</td>
</tr>
<tr>
<td>Liposarcoma</td>
<td>2 (2.9)</td>
<td>Keratin⁻ and SATB2⁻ (1)</td>
<td>Parotid (1)</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>1 (1.42)</td>
<td>Desmin⁺, MyoD1⁺ (1)</td>
<td>Neck (1)</td>
</tr>
<tr>
<td>Angiosarcoma</td>
<td>1 (1.42)</td>
<td>ERG⁺, CD31⁺ (1)</td>
<td>Thyroid (1)</td>
</tr>
<tr>
<td>Chordoma</td>
<td>1 (1.42)</td>
<td>SOX10⁺ (1)</td>
<td>Ilium (1)</td>
</tr>
<tr>
<td>Malignant peripheral nerve sheath tumor</td>
<td>1 (1.42)</td>
<td>SOX10⁺ and CD68⁻ (1)</td>
<td>Lung node (1)</td>
</tr>
<tr>
<td>Malignant granular cell tumor</td>
<td>1 (1.42)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Neoplasm (PEComa) Diagnosed on Fine-Needle Aspiration
endocervical and endometrial sampling. The results should be followed up with a combination of cytology and endocervical and endometrial sampling.

HMB-45–Negative Malignant Perivascular Epithelioid Cell Neoplasm (PEComa) Diagnosed on Fine-Needle Aspiration and Core Biopsy

Anoshia Afzal, MD; Michael Quinton, MD; Michael Magguilli, MD; Evan Fowle, DO. Department of Pathology, University of Oklahoma Health Sciences Center, Oklahoma City.

Perivascular epithelioid cell tumors (PEComas) are a family of uncommon mesenchymal tumors that include multiple neoplasms in different organs such as sugar tumor of the lung, hepatic or renal angiomylipoma, and lymphangiomysyoma. Most are benign, but a small number of PEComas have an aggressive behavior with organ-specific high-risk features and are classified as malignant. We report a case of an 80-year-old woman with a known history of PEComa, status post radiation therapy in August 2018 followed by exploratory laparotomy with total hysterectomy and bilateral salpingo-oophorectomy in November 2018, who presented with a soft tissue pelvic mass (2.5 × 2.1 cm). Computed tomography–guided fine-needle aspiration of right pelvic wall mass was positive for malignant cells (Figure 3.110, A and B) and concurrent core biopsy revealed highly atypical epithelioid and spindle cells with areas of necrosis, readily visible mitoses, and striking nuclear pleomorphism (Figure 3.110, C). The malignant cells were positive for actin, desmin, p16, and Melan-A (Figure 3.110, D), and negative for HMB-45, SOX10, and S100. The morphology seen in the cell block material could easily be mistaken for a high-grade leiomyosarcoma, other mesenchymal tumors, or metastatic melanoma. The overall performance of immunohistochemistry on this case would have been quite suggestive of PEComa, but because of the uncommon nature may not have been diagnosed on cytology without the previous diagnosis. Given the differences in treatment and prognosis, the need to routinely perform myomelanocytic markers on primary cytology of high-grade mesenchymal gynecologic neoplasms is suggested, especially in cases where smooth muscle markers are positive.

Undifferentiated High-Grade Sarcoma With CIC Gene Rearrangement Diagnosed on Fine-Needle Aspiration and Core Needle Biopsy

Anoshia Afzal, MD; Michael Magguilli, MD; Evan Fowle, DO. Department of Pathology, University of Oklahoma Health Sciences Center, Oklahoma City.

Undifferentiated high-grade sarcomas are aggressive malignancies and include various entities with a broad range of morphologies and defining molecular findings. Diagnosing high-grade sarcomas on fine-needle aspirate or core biopsies is challenging because of several factors; however, as ever more entities are shown to harbor disease defining translocations and mutations, the efficacy of minimally invasive sampling is rapidly increasing in soft tissue neoplasms. We report a case of a 19-year-old woman with Marfan syndrome presenting with a large mediastinal mass causing significant airway compression. Fine-needle aspiration (FNA) of the mediastinal mass revealed a high-grade undifferentiated neoplasm with a round and spindle cell population (Figure 3.111, A through D) and focal myxoid stroma. The core biopsy showed similar findings along with necrosis. Immunohistochemistry was noncontributory and the biopsy material was exhausted in the initial workup. Eventually, she underwent core and FNA biopsies of a liver metastasis. The cytomorphology was similar to the previous sampling and FISH studies for a CIC break-apart probe revealed a CIC gene rearrangement. The final diagnosis was an undifferentiated high-grade sarcoma with CIC gene rearrangement. A partner gene was not targeted by this probe, but the most common partner gene is DUX4. Sarcomas with CIC gene rearrangement are classified as Ewing-like undifferentiated sarcomas and are usually associated with an aggressive clinical course and poor outcome. It is therefore important to keep CIC-rearranged sarcomas in mind when encountering a high-grade sarcoma on FNA and needle core biopsies, and to perform molecular genomic studies when appropriate.

Prevalence of Reactive Changes in Pregnancy and Its Association With Other Routine Pap Smear Findings

Shabnam Seydafkan, MD (Shabnam.seydafkan@downstate.edu); Dokpe Emechebe, MD; Kristina Loukeris, MD. Department of Pathology, SUNY Downstate Medical Center, Brooklyn, New York.

Context: Reactive cellular changes (RCC) and pregnancy-associated cervicovaginal smears are controversial issues. We reviewed prenatal cervicovaginal smears performed in our institution for a 1-year period to determine the prevalence of RCC and its association with other common cytologic findings.

Design: A retrospective review of the prenatal cervicovaginal smears between January 2020 and end of January 2021 was performed.

Results: A total of 177 cervicovaginal smears were retrieved. Three were unsatisfactory for evaluation and thus removed from study. The mean age of the patients was 30.54 years (range, 15–57 years; standard deviation, 6.012 years). Thirteen cases (7.47%) were diagnosed as low-grade squamous intraepithelial lesion, cannot be ruled out high-grade squamous intraepithelial lesion. RCC was found in 39 (22.41%) cases. In 18 of 39 cases (46.15% of total reactive changes and 13.43% of the total samples) RCC was the only diagnosis. High-risk HPV testing was done in 14 of 39 cases with RCC. Eleven of the 14 cases (78.57%) were negative for high-risk HPV. The nondysplastic diagnoses associated with RCC included inflammation (7 cases), fungal coinfection (11 cases), shift in vaginal flora (5 cases), and Trichomonas (4 cases).
cases). In statistical studies, there was no significant correlation between age and reactive or dysplastic changes. Reactive changes were significantly and negatively correlated to presence of low-grade dysplasia (correlation coefficient $r = -0.173, P = .02$).

**Conclusions:** RCC alone or in combination with other diagnoses is common during pregnancy. Further investigations on its associations with future dysplastic changes is warranted.

Reactive Atypical Cytologic Features Mimicking High-Grade Squamous Intraepithelial Lesions in Pap Smear

(Poster No. 113)

Shabnam Seydafkan, MD (Shabnam.seydafkan@downstate.edu); Dokpe Emchebe, MD; Navid Salahi, MD; Fatih Ozay, MD; Kristina Loukeris, MD. Department of Pathology, SUNY Downstate Medical Center, Brooklyn, New York.

High-grade squamous intraepithelial lesion (HGSIL) diagnosis is challenging because of various benign and malignant mimickers. Awareness of these mimickers will reduce the pitfalls when diagnosing HGSIL. A 79-year-old woman with history of total abdominal hysterectomy, unilateral oophorectomy, and chemotherapy secondary to low-grade uterine leiomyosarcoma 30 years prior presented with a 5-mm mass under the skin in midabdomen suspicious for metastasis. Imaging studies were negative for primary tumor elsewhere. Pap smear showed sheets and syncytical aggregates of cells with a high nuclear to cytoplasmic ratio and hyperchromatic nuclei suspicious for HGSIL (Figure 3.113, A and B); however, her cervical biopsy studies had been negative or reactive for the past 17 years (2003–2020) with regular yearly screening. P16 was negative. Vaginal cuff biopsy showed benign squamous mucosa with chronic inflammation (Figure 3.113, D). In reassessment, the atypical cells were diagnosed as reactive fibroblasts secondary to ulcerative process. The follow-up Pap at 6 months was benign and confirmed the presence of reactive process mimicking HGSIL (Figure 3.113, C). Cervicovaginal cytology specimens are challenging. Although Pap smear is a screening method for squamous lesions, mimickers of squamous lesions exist. The differential diagnosis in HGSIL may include not only glandular and adenosquamous cells but also poorly differentiated and benign spindle cell lesions. When reviewing cervicovaginal smears, the clinical correlation, and remote medical history, previous cytology studies as well as awareness about the less common entities can lead to the most precise diagnosis.

**BRD3–NUTM1–Expressing NUT Carcinoma of Lung on Cytology of Endobronchial Ultrasound-Guided Transbronchial Fine-Needle Aspiration: A Diagnostic Pitfall**

(Poster No. 115)

Sameer Chhetri Aryal, MD (schhetri1@hfhs.org); Shereen Zia, MD; Yulei Shen, MD; Kyle D. Perry, MD; Lisi Yuan, MD. Department of Pathology, Henry Ford Hospital, Detroit, Michigan.

NUT carcinoma is an aggressive type of poorly differentiated carcinoma with a variable degree of squamous differentiation characterized by the presence of BRD–NUT fusion oncogenes, the most common fusion form being BRD4–NUTM1 gene. Variant rearrangements involving the BRD3 and NSD3 gene occur in approximately one-third of the cases. A 36-year-old woman with shortness of breath was found to have a right-sided pleural effusion on chest x-ray. She was a never smoker without significant past medical illness. Computed tomography chest revealed an 8.5-cm heterogeneous mass in the right and mid upper lung (Figure 3.115, A). The cytopathologic findings of endobronchial ultrasound-guided transbronchial fine-needle aspiration showed syncytial sheets of atypical squamoid cells with variably prominent single or multiple nuclei, and rare individual cell keratinization (Figure 3.115, B). Monotonous-looking cells with high nuclear to cytoplasmic ratio and hyperchromasia were also present. The atypical squamoid cells showed abundant clear to eosinophilic cytoplasm on cell block preparation (Figure 3.115, C). The atypical cells were positive for CK7, p63, p40, and melanoma and lung cancer. He was found to have a lytic lesion in the left ilium on full-body computed tomography (CT) scan. A subsequent positron emission tomography–CT study demonstrated focal increased uptake, which prompted CT-guided core biopsy. Microscopic examination of the core showed hypercellular marrow with areas of multifocalized brown fat cells replacing the normal marrow elements (Figure 3.114, A and B). These cells showed positivity for S100 and were negative for CD68 and CD163 by immunohistochemical staining. In addition, an increased interstitial plasma cell population was highlighted by CD138, with no evidence of light-chain restriction by in situ hybridization for k and l. Cytokeratin (CAM5.2, AE1/3) and SOX10 were negative, which ruled out metastatic carcinoma and melanoma. Background trilineage hematopoiesis was present and unremarkable. These findings are consistent with intraosseous hibernoma with lytic changes. Although rare, recognition of this benign entity is critical, as its radiographic findings may suggest a malignant process.

Intraosseous Hibernoma With Osteolytic Change in the Appendicular Skeleton

(Poster No. 114)

Qiuhong Zhang, MD, PhD (qiuhong.zhang@ahn.org); Ariel Sandhu, MD; Yulin Liu, MD. Department of Pathology, Allegheny General Hospital, Pittsburgh, Pennsylvania.

Intraosseous hibernoma with osteolytic change is extremely rare and may mimic malignancy radiographically. Very few cases have been reported, and interestingly, none have been described in the appendicular skeleton. We report the case of an 84-year-old man with a history of
mCEA. The cytopathologic findings were consistent with squamous cell carcinoma with keratinization. However, the fusion panel–solid tumor revealed BRD3-NUTM1 fusion gene. The tumor was then reclassified as NUT carcinoma. Pulmonary NUT carcinoma should be suspected in all squamous cell carcinoma with unusual features, particularly in a nonsmoker and a young patient. We hereby report this case because the cytopathologic features of NUT carcinoma have been rarely documented and those of a primary NUT carcinoma of the lung with BRD3-NUTM1 fusion have never been reported.

Efficacy of Cytology in the Diagnosis of Malignant Pleural, Peritoneal, and Pericardial Serous Effusions by Tumor Type: One-Year Retrospective Institutional Study

(Poster No. 116)

Fatima Iqbal, MD (faiqbal@utmb.edu); Paul E. Young, MD; Luis A. Velasquez Zarate, MD; Cecilia Clement, MD. Department of Pathology, University of Texas Medical Branch, Galveston.

Context: Cytology examination of serous fluids is a minimally invasive and inexpensive procedure for malignancy diagnosis. Further, evaluation of serous fluid specimens can determine the primary site of origin. Cell blocks can be performed on serous fluids, which increase the diagnostic yield. This study aimed to assess the type of malignancy and frequency in pleural, pericardial, and peritoneal serous fluids.

Design: This is a retrospective study of all pleural, pericardial, and peritoneal fluids diagnosed as malignant retrieved from our electronic cytopathology database from June 2019 to June 2020. The cytology results were correlated with follow-up histologic (surgical pathology, autopsy) diagnoses. Also, radiologic findings obtained within 6 months of the cytology diagnosis were examined.

Results: A total of 573 serous fluids were received in the cytopathology laboratory, of which 70 were positive for malignancy (12%) (Table). Pleural effusions were the most common fluids received (53%), followed by peritoneal (43%) and pericardial (4%). The majority were ≥50 years old (88%), with female predominance (51%). Overall, adenocarcinoma of the lung was the most common malignancy in the study (27%) (see Table). All cytologic diagnoses were confirmed as malignant by histology and/or radiology. Cell block was prepared in 63 of 70 cases (90%), which helped to identify the origin of malignancy. The fluid was not a limitation to make the cell block.

Conclusions: Cytology of body cavity fluids is effective to identify malignancy type, providing an optimal source for cell block preparation. Our results showed a high concordance between cytologic and histologic diagnoses.

Frequency of Malignancies According to Serous Body Fluid Type

<table>
<thead>
<tr>
<th>Effusion Subtype</th>
<th>Cytologic Diagnosis</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleural, 53%</td>
<td>Adenocarcinoma, Lung origin</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Small cell carcinoma</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Breast carcinoma</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Adenocarcinoma, GI origin</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Consistent with mesothelioma</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Others (HCC, serous carcinoma, squamous cell carcinoma tongue)</td>
<td>6</td>
</tr>
<tr>
<td>Peritoneal, 43%</td>
<td>Adenocarcinoma, GI origin</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Adenocarcinoma, pancreatoctyliar origin</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Lymphoma</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Adenocarcinoma, Mullerian origin</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>High-grade ovarian serous carcinoma</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Others (breast carcinoma, HCC, vardenocarcinoma, lung origin)</td>
<td>7</td>
</tr>
<tr>
<td>Pericardial, 4%</td>
<td>Multiple myeloma</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Small cell carcinoma</td>
<td>2</td>
</tr>
</tbody>
</table>

Correlation of Fine-Needle Aspiration Diagnosis of Papillary Thyroid Carcinoma With Radiologic Findings

(Poster No. 117)

Paul E. Young, MD (paeyoung@utmb.edu); Fatima Iqbal, MD; Luis A. Velasquez Zarate, MD; Cecilia G. Clement, MD. Department of Pathology, University of Texas Medical Branch, Galveston.

Context: Papillary thyroid carcinoma (PTC) is the most common type of thyroid cancer. The American College of Radiology has developed the thyroid imaging reporting and data system (TI-RADS) for thyroid nodules, with scores ranging from 1 to 5. Recommendation for fine-needle aspiration (FNA) is provided based on TI-RADS score and nodule size, with TI-RADS 5 nodules ≥1 cm, TI-RADS 4 >1.5 cm, and TI-RADS 3 >2.5 cm recommended for FNA.

Design: This is a retrospective review of all thyroid FNAs performed at our institution during the past 2 years, identifying all cases of PTC and correlating them with their TI-RADS score.

Results: A total of 630 patient results were reviewed, revealing 25 diagnoses of PTC. Four patients with diagnosis of PTC had no in-house radiology and were excluded. Of the remaining 21 patients, 11 (52%) were TI-RADS 5, 9 (45%) TI-RADS 4, and 1 (5%) TI-RADS 3. Interestingly, 2 of the 9 patients with TI-RADS 4 nodules did not meet criteria for FNA (size ≥1.5 cm). These nodules were only aspirated for cytologic evaluation because of neck lymphadenopathy and clinical concern for metastatic thyroid cancer.

Conclusions: The majority of PTCs (90%) were detected following TI-RADS guidelines. Of nodules with PTC, 10% did not meet criteria for FNA and would have been missed in the absence of clinical suspicion. These nodules were all TI-RADS 4. This study underlines the importance of reviewing radiology and clinical findings prior to evaluating thyroid FNAs, with particular attention paid to TI-RADS 4 and 5 nodules.

Comparison of Endoscopic Ultrasound-Guided Fine-Needle Aspiration and Fine-Needle Biopsy in the Diagnosis of Solid Pancreatic Lesions

(Poster No. 118)

Luis Velasquez Zarate, MD (luchovz352@gmail.com); Fatima Iqbal, MD; Paul Young, MD; Ranjana Nawgiri, MD; Cecilia Clement, MD. Department of Pathology, University of Texas Medical Branch, Galveston.

Context: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is the standard method for sampling pancreatic lesions. This study compares the diagnostic accuracy of EUS-FNA with fine-needle biopsy (FNB) using core needles (Acquire or SharkCore).

Design: A retrospective review of 38 patients who underwent EUS-FNA either alone or combined with FNB (2017–2019) was conducted. Cytology diagnoses were categorized as benign, atypical, suspicious for malignancy, malignant, or nondiagnostic. Nondiagnostic or lost-to-follow-up cases were excluded (5 cases). Diagnostic accuracy was based on subsequent histologic and clinical evidence of malignancy with follow-up of at least 6 months.

Results: Seventeen of the 33 patients were evaluated by EUS-FNA alone. Twelve were called malignant/suspicious for malignancy, and all 12 confirmed as malignant. The other 16 patients were evaluated by combined EUS-FNA and FNB; 11 were called malignant/suspicious for malignancy, and all 11 were confirmed as malignant. Five were called benign/atypical, of which 4 were positive for malignancy and 3 confirmed as positive for malignancy. EUS-FNA was slightly more accurate (88% versus 81%), more sensitive (85% versus 78%), and with higher positive predictive value (60% versus 40%) than FNB. Specificity and positive predictive value were 100% with both techniques.

Conclusions: Although the sample size is limited, our findings suggest that the diagnostic performance of both methods is comparable, and perhaps slightly in favor of EUS-FNA alone. Additionally, FNB tends to be more expensive. Further studies with a larger sample size are warranted.

ThinPrep Blending: An Important Aid in Reducing the Unsatisfactory Papanicolaou Test Rate in Conjunction With Use of Carbomer-Free Lubricants

(Poster No. 119)

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1Department of Pathology, University of Texas Health San Antonio, San Antonio; 2Department of Pathology, University Health System, San Antonio, Texas.

Context: Specimen adequacy is a key component in the evaluation of Pap smears (Pap) and other gynecologic smears. At our hospital, the unsatisfactory Pap rates ranged from 4.1% to 8.1% in the period of January–December 2018. This is a retrospective study of the effect of appropriate carbomer-free lubricant use and repeat slide preparation after blending.
**Design:** During the period of June 2019–June 2020, 222 cases were identified as unsatisfactory. Eighteen were excluded because of inadequate specimen left over. A total of 204 cases were reprocessed with the blending protocol as follows: Contents were transferred into the blender cup and closed with the lid. The cup was placed on the base and blended on high for 10 seconds. The specimen was reprocessed in ThinPrep 2000 processor. The clinics were informed of appropriate lubricant use and most switched to carborner-free lubricant.

**Results:** Sixty initially unsatisfactory specimens remained unsatisfactory. A total of 144 Pap smears were satisfactory for evaluation as follows: 128 negative for intraepithelial lesion, 4 atypical glandular cells, 10 atypical squamous cells of undetermined significance, and 1 low-grade intraepithelial lesion. Of the unsatisfactory Pap smears, 71% were satisfactory for interpretation postblending.

**Conclusions:** Blending of Paps in conjunction with carborner-free lubricant use is a good method of reducing unsatisfactory rates and maintaining them within the appropriate benchmark level. This approach has resulted in an acceptable unsatisfactory rate (1.9% in July 2020, CAP benchmark median–50th percentile, as compared with 5.7% in January 2019, CAP benchmark 95th percentile).

**Assessment of Telecytology Rapid On-Site Evaluation on the Duration of Thyroid Fine-Needle Aspirations at a Multihospital Institution**

*(Poster No. 120)*

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**Context:** NorthShore pathologists perform rapid on-site evaluation (ROSE) at multiple hospitals. We recently implemented a telecytology system (intervention) for ROSE to enable pathologists physically located at one hospital to perform ROSE at a remote hospital location. The aim of this study was to evaluate the impact of our telecytology system on the duration of thyroid fine-needle aspiration (FNA) procedures.

**Design:** NorthShore’s telecytology system was built using a Zeiss Axiocam 208 (Carl Zeiss AG, Germany) digital camera and Zeiss ZEN 3.1 (Zen lite) acquisition software on an Elitebook (Hewlett-Packard Company, Palo Alto, California) laptop mounted to a mobile microscope cart connected to the hospital wireless network. VidyoConnect (Vidyo, Inc, Hackensack, New Jersey) screen sharing software is used to transmit live microscopic images to remote pathologists viewing the images on their desktop computers. Sixty FNAs before (in person) and after (telecytology) the intervention were analyzed using FNA procedure start and end times and number of thyroid nodules aspirated/1 evaluation episode. Unpaired t test was used to compare procedure durations.

**Results:** The difference in procedure time was significantly less for cases that involved only 1 nodule and 1 episode (52.5% of cases overall), which represented the cases that took the shortest time on average using both in-person and telecytology ROSE (Table). There was no statistically significant increase in procedure time after the intervention.

**Conclusions:** These findings suggest that telecytology reduced the duration of thyroid FNA procedures at NorthShore for short-duration cases without increasing duration for more complex cases.

**Comparison of Average Duration of Thyroid FNAs Using In-Person Versus Telecytology ROSE**

<table>
<thead>
<tr>
<th></th>
<th>Average Duration of In-Person ROSE, min</th>
<th>Average Duration of Telecytology ROSE, min</th>
<th>Average In-Person – Average Telecytology Difference, min</th>
<th>2-Tailed P Values (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>20.73 (n = 60)</td>
<td>19.03 (n = 60)</td>
<td>1.70</td>
<td>.31 (−1.58–4.98)</td>
</tr>
<tr>
<td>1 nodule, 1 episode</td>
<td>16.80 (n = 35)</td>
<td>12.61 (n = 28)</td>
<td>4.19</td>
<td>.01 (0.82–7.57)</td>
</tr>
<tr>
<td>2 nodules, 1 episode each</td>
<td>21.47 (n = 15)</td>
<td>23.71 (n = 8)</td>
<td>−2.25</td>
<td>.45 (−8.35–3.86)</td>
</tr>
<tr>
<td>3 nodules, 1 episode each</td>
<td>32.14 (n = 7)</td>
<td>27.14 (n = 7)</td>
<td>5.0</td>
<td>.27 (−4.45–14.45)</td>
</tr>
</tbody>
</table>

Abbreviation: ROSE: rapid on-site evaluation.

**Utilization of Molecular Identity Testing for Characterization of Tissue Origin in Gastrointestinal Specimens**

*(Poster No. 121)*

**Adam R. Davis, MD (Ardavis1024@gmail.com); Farah El-Sharkawy Navarro, MD; Rashmi Tondon, MD; Salvatore F. Priore, MD. Department of Pathology and Laboratory Medicine, Hospital of the University of Pennsylvania, Philadelphia.*

**Context:** Accurate diagnoses in anatomic pathology depend on specimen fidelity and histologic sections free of contamination. Any failure in the phases of specimen processing may result in safety and quality issues significantly impacting patient care. Herein we report the clinical utility of molecular pathology identity (MPID) testing for gastrointestinal specimens at our institution.

**Design:** All gastrointestinal pathology cases to date (n = 9) with MPID testing were identified. Clinical scenarios and diagnostic challenges were evaluated via individual case review. DNA was extracted from macrdissected formalin-fixed, paraffin-embedded tissue. Polymorphic noncoding short tandem repeat (STR) loci and a sex chromosome marker were amplified using the PowerPlex 16 System (Promega, Madison, Wisconsin). PCR products were separated by capillary electrophoresis and analyzed for the number of repeats of each STR allele. Alleles with matching repeat lengths at all STR loci and the sex chromosome marker proved shared identity of 2 specimens.

**Results:** Three clinical scenarios for MPID testing were identified: (1) contamination (ie, “floaters”), (2) specimen mislabeling, and (3) tumor origin in liver allograft recipients. MPID testing resolved specimen identification for 8 of 9 cases, with 1 equivocal result caused by technically challenging macrodissection of the specimen. Successful MPID testing prevented misdiagnoses, follow-up invasive procedures, and/or unnecessary therapy (37.5%); corrected specimen labeling errors (25%); and guided appropriate clinical management (ie, transplant revision versus chemotherapy) of tumors occurring in liver allograft recipients (37.5%; Figure 3.121).

**Conclusions:** MPID testing improved patient outcomes by confirming the origin of tissue in the event of contamination, specimen swaps, or tumors arising in solid organ allograft recipients.
Role of Automated Compressive Filtration in Improving Lymph Node Yield in Gastrointestinal Resections
(Poster No. 122)
Priscilla Quach, DO (pqquach@kumc.edu); Sydney Cooley, MS, PA; Maura O’Neil, MD; Rashna Madan, MBBS; Ameer Hamza, MD. Department of Pathology, University of Kansas Medical Center, Kansas City.
Context: Evaluating 12 lymph nodes (LNs) is considered the minimum target for accurate staging of colorectal cancer in colectomy specimens. Examining fewer than 12 LNs is considered a high-risk factor for recurrence per National Comprehensive Cancer Network guidelines. We aimed to assess the utility of automated compressive filtration (ACF) in improving LN yield.
Design: ACF was performed on 25 colorectal resections and 1 gastrectomy between November 2020 and February 2021. LNs were initially harvested by manual palpation. The remaining fibroadipose tissue was placed in acetone or dissect-aid solution for an average of 35 hours, after which ACF was used to identify additional LNs.
Results: Manual palpation yielded 19.8 ± 17.3 LNs per specimen. ACF yielded an additional 6.3 ± 5.5 LNs (24% increase compared with manual palpation alone). The mean number of blocks submitted for manual palpation was 8.5 ± 6.1, whereas for ACF an additional 11.4 ± 3.6 blocks were submitted. Pre- and post-ACF fibroadipe tissue weighed 66.6 ± 38.6 g and 20 ± 11.6 g, respectively (70% decrease). There was a single case (1 of 26; 3.8%) where additional positive LNs were found among ACF LNs; however, this did not result in an upstaging event. The cost of processing additional ACF blocks was estimated to be $111.50 per case (including materials, maintenance, and technician labor).
Conclusions: The likelihood of identifying LN metastases depends in part on the number of nodes examined, but at some level yields diminishing returns. Diligent manual palpation yields adequate number of LNs in most cases. ACF may be used in rare instances when manual efforts fail to yield adequate LN numbers.

A Conventional Polymerase Chain Reaction (PCR) and Endpoint Detection–Based SARS-CoV-2 Assay
(Poster No. 123)
Ranran Zhang, MD, PhD (ranran.zhang@aspirus.org); Donna J. Kincaid, CT, Hi Young Hong, MD. Department of Pathology, Aspirus Riverview Hospital, Wisconsin Rapids, Wisconsin.
Context: During the COVID-19 pandemic, testing availability at commercial laboratories was frequently limited with long turnaround time. Most sequence-based SARS-CoV-2 testing requires real-time PCR platform and similar reagents, limiting in-house testing development.
Design: An in-house SARS-CoV-2 test was developed based on existing instruments, including magnetic-bead–based RNA extraction system, conventional PCR cyclers, and fluorescent plate reader. The SARS-CoV-2 primer and probe sets for real-time PCR were used. Similar to real-time PCR, during the extension phase the reporter dye (FAM) was separated from the quencher dye (BHQ1), generating a fluorescent signal. However, the amplification was performed with a conventional PCR cycler, and endpoint detection was performed upon the completion of PCR amplification.
Results: The test was primarily validated using sputum/saliva specimen. The limit of detection was 125 viral genome equivalents/mL. The clinical performance was confirmed using sputum/saliva specimens from asymptomatic healthy volunteers and nasopharyngeal swabs from various viral transport media/buffer. The test joined and passed the API proficiency program. From June to November 2020, a total of 4439 tests were performed (3–92 tests/d), with turnaround time mostly within 48 hours. A preliminary retrospective review of results from 183 patients revealed 96% concordance among those who received concurrent/repeated testing using the same or different methodologies.
Conclusions: Conventional PCR amplification and endpoint detection is an alternative to real-time PCR-based SARS-CoV-2 testing. With its unique reagent requirement, our in-house medium-throughput test supported patient care and normalized hospital operation with minimal interruptions during testing and reagent shortages.

Utility and Yield of Stains for Microorganisms in Esophageal or Gastroesophageal Junction Biopsies
(Poster No. 125)
Aaron R. Huber, DO (aaron_huber@urmc.rochester.edu); Christa L. Whitney-Miller, MD. Department of Pathology and Laboratory Medicine, University of Rochester Medical Center, Rochester, New York.
Context: Pathologists frequently order stains to rule out infectious etiologies in cases of esophagitis, particularly those with active inflammation and/or ulceration/erosion. However, the utility and diagnostic yield of these stains have not been well studied.
Design: We retrospectively identified 261 separate esophageal and/or gastroesophageal junction specimens from 142 patients (79 males, 63 females; median age, 60 years) who had special stains ordered or had a diagnosis of candidal, herpetic, or cytomegalovirus esophagitis from 2016. Slides were reviewed to determine whether or not organisms or inclusions were present on hematoxylin and eosin (H&E) slides, ancillary stains, both, or neither.
Results: Active inflammation and/or ulceration/erosion was seen in 247 specimens (95%). There was a total of 327 stains ordered, including Gomori methenamine silver (100), periodic acid–Schiff (1), herpes simplex virus 1 and/or 2 (152) and cytomegalovirus (75) (all stains: Dako, Carpinteria, California). The staining results are summarized in the Table. There were 90 specimens with candidal esophagitis; in 83 (91%) the organisms were evident on H&E, and in 58 (64%) no stains were ordered. There were 2 cases of herpetic esophagitis, with both cases having inclusions on H&E, and in 58 (64%) no stains were ordered. There was a single case (1 of 26; 3.8%) where additional positive LNs were found among ACF LNs; however, this did not result in an upstaging event. The cost of processing additional ACF blocks was estimated to be $111.50 per case (including materials, maintenance, and technician labor).
Conclusions: The likelihood of identifying LN metastases depends in part on the number of nodes examined, but at some level yields diminishing returns. Diligent manual palpation yields adequate number of LNs in most cases. ACF may be used in rare instances when manual efforts fail to yield adequate LN numbers.

Anatomic Pathology Quality Assurance: Four-Year Trend of Continuous Improvement Utilizing Case Review as a Quality Metric
(Poster No. 124)
Mark L. Priebe, BS (mpriebe123@aol.com); Rodney Markin, MD, PhD. 1Department of Operations, QualityStar, Omaha, Nebraska; 2Department of Pathology and Microbiology, University of Nebraska Medical Center, Omaha.
Context: Peer review is the gold standard quality measurement tool. In surgical pathology, inspecting agencies recommend prospective or retrospective case review be performed on positive and negative cases using inter or intra laboratory pathologists. This study reviews longitudinal impact on quality of cancer cases utilizing external blinded quality assurance (QA) review by subspecialists.
Design: A total of 556 surgical pathology cases were secondarily reviewed during 4 years using a defined quality process from a single pathologist. Cases were sent to an appropriate subspecialist pathologist for the second QA review using whole slide digital imaging. QualityStar was utilized to standardize, collect, and report the data. The pathologist receiving the secondary QA review represented an average sampling of the regional institution’s anatomic pathology laboratory. During 4 years, double-blind images (digital images) and de-identified anatomic pathology reports were submitted electronically for review by NCI designated center–based subspecialists. Frequency of diagnostic and clerical learning comments (percentage of QA reviews receiving comments) were tracked with percentage QA review concordance. Results were shared with the reviewed pathologist.
Results: Learning comments generated a negative slope (8.0%–6.0%), a 25% reduction in 4 years, and a 2% improvement. A total of 122–128 cases per year were reviewed years 1–3, and the number increased to 184 in year 4. Tissue type case mix remained similar throughout the study.
Conclusions: Consistent QA case review and reporting by subspecialist offers improvement opportunity, discovery, and potential to positively influencing patient outcomes.
A Levey-Jennings–Like Chart for Anatomic Pathology Quality Control in General Community Practice

(Poster No. 126)

Albert Pedroza, BS; Nicholas Lintel, MD; Whitney Wedel, MD; Adam Horn, MD (ahorn@marylanning.org). Department of Pathology and Laboratory Medicine, Mary Lanning Healthcare, Hastings, Nebraska.

Context: Tracking diagnostic discrepancies is a common quality indicator in anatomic pathology, and cases are routinely overread as care is transferred to another facility. In community practice this frequently results in review by a subspecialist at a tertiary care center. Discrepancies are often viewed in isolation and are attributed to the original pathologist, without consideration for practice-wide trends or outside pathologists. We are a regional community hospital with well-established referral patterns to several neighboring systems and track details of all reviewed cases. Our goal was to evaluate overread cases for actionable trends.

Design: Between 2017 and 2020, cases with outside review were tracked, including facility sent, inside and outside pathologists, organ system, and nature of discrepancy (if any). A pivot table was created to manipulate the data based on all variables including trends over time.

Results: In 3 years, 521 cases (890 individual specimens) were sent to 16 facilities. There were 46 discrepancies, with a change in histologic grade being most common. Prostate specimens had the most upgrades, thyroid the most downgrades, and breast specimens were evenly split. When including only subspecialists, breast and prostate were exclusively upgraded. Over time there was an internal trend to be more aggressive. Of note, of 33 outside pathologists, 1 rendered 30% of all discrepancies, and 3 accounted for 67%.

Conclusions: We have demonstrated an easily implemented tool to allow community pathologists to trend the aggressiveness of their diagnoses based on outside review. It also calls attention to the possibility of external subjectivity.

Benefits of CAP15189 Accreditation in Managing the Coronavirus Disease 2019 (COVID-19) Crisis

(Poster No. 127)

Gaurav Sharma, MD, FACP; Caroline M. Maurer, MT(ASCP) (cmaurer@cap.org); Gerry D. Thomas, MT(ASCP); Wren Williams, BA; Department of Laboratory Medicine, Henry Ford Medical Center, Detroit, Michigan; Laboratory Improvement Programs, College of American Pathologists, Northfield, Illinois.

Context: International Organization for Standardization (ISO) 15189 medical laboratories requirements for quality and competence is an international standard that specifies the quality management system requirements for medical laboratories. The CAP15189 program provides accreditation to the ISO 15189 standard to more than 70 US and international laboratories. With special emphasis on systems readiness, process management, and risk management, CAP15189-accredited laboratories are expected to be prepared for systemic failures. The aim of this study was to gauge COVID-19’s impact on these laboratories and how they responded to the crisis.

Design: The CAP15189 Program leadership drafted a set of 16 questions covering different aspects of disaster response and nonperformance management. These questions were distributed to all CAP15189-accredited laboratories via an online survey.

Results: The survey had a 49% (37 of 76) response rate. Of responders, 95% were impacted by COVID-19. The largest segment of respondents was reference laboratories (59%), followed by academic medical centers (19%). The areas of disruption included personnel shortages (82%), operational gaps (79%), supply shortages (74%), and communication gaps (65%). A total of 94% stated that they had benefited from ISO 15189 management systems such as communication protocols (87%), standardization of practices (67%), culture of continual improvement (57%), transparency (54%), and risk monitoring (54%). Risk mitigation relied on management meetings (84%), staff huddles (68%), internal audits (36%), and risk registers (20%). Primary crisis leadership was equally shared by pathologists (39%) and administrators (39%).

Conclusions: Although a vast majority of CAP15189-accredited laboratories were impacted by COVID-19, they were able to effectively respond to the crisis by using ISO 15189–mandated management systems.

Clinical Laboratory: The Value of Patient Label Orientation

(Poster No. 128)

Ahmed Ahmed, MD (zahmed@health.southernalabama.edu); S. Shawn Liu, MD, PhD; Marta Gale, MS, MHSA; J. Eliott Carter, MD; Gary Camahan, MD, PhD; Guillermo A. Herrera, MD. Department of Pathology, University of South Alabama, Mobile.

Context: Laboratory turnaround time (TAT) is one of the most notable signs of laboratory service and is often used as a key performance indicator. Preanalytical indices for specimens entering the core chemistry laboratory should be regulated; if not, the TAT for samples is subject to delay with reportable information not reaching care teams effectively.

Design: To compare rates of incorrect label placement on collection tubes before and after focused training of nursing staff and hospital quality leaders as a quality improvement initiative. During a 14-day pretraining period, sample collection tubes submitted to the core chemistry laboratory were examined for incorrect label placement. After formal training sessions with nurse managers and hospital quality leaders, the same data were collected for a 10-day period.

Results: Our laboratory analyzed 8160 pretraining and 6480 posttraining collection tubes with focus on incorrect label placement. In the pretraining cohort, 945 collection tubes were identified as having incorrect label placement, with a daily average of 69.7 issues and error rate of 12%. In the posttraining period, a statistically significant decrease to 39.1 issues with an error rate of 5.2% (P < .002) was appreciated, demonstrating a quality improvement.

Conclusions: Our study demonstrated a comparative decrease rate of incorrect label placement for specimens submitted to the laboratory for an improved quality improvement initiative. Focused laboratory training to nurse managers and hospital quality leaders encourages communication improving error rates; an important quality improvement sign given the large proportion of body fluids undergoing evaluation in the laboratory. The information sheds light for laboratories to leverage training opportunities promoting growth.

Urinalysis With Reflex to Culture: Ordering Patterns and Impact of Different Reflex Criteria

(Poster No. 129)

Jessica Robertson-Patera, MD; Megan O. Nakashima, MD (nakashm@ccf.org). Robert J. Tomisch Pathology and Laboratory Medicine Institute, Cleveland Clinic, Cleveland, Ohio.

Context: Catheter-associated urinary tract infections are an important quality metric for hospitals. Thus, most strive to ensure that positive cultures reflect actual infections rather than catheter colonization. One potential strategy to reduce cultures is using a reflex mechanism where culture is only ordered based on abnormal urinalysis (UA) results. In our laboratory, leukocytes (WBC) >5 and/or positive leukocyte esterase (LE) trigger reflex cultures. We sought to examine use of this test and the potential impact of raising threshold to WBC >10.

Design: This is a single-institute retrospective analysis of ordering patterns and results of UA reflex to culture (UARFCX) between September 2020 and March 2021.

Results: A total of 3582 UARFCX were ordered, mostly on inpatients (IP; 2437; 68.0%), with 1071 (29.9%) outpatient (OP) and 74 (2.1%) emergency department (ED). UARFCX represented 5.1% of total UA during the study period (total 70 413 UA). Percentages of each that met reflex criteria are shown in the Table. IP and OP met criteria at a similar rate (43.3% versus 41.9%), the majority because of a positive LE (39.9% and 40.9%). A total of 214 (74%) samples with WBC>10 were...
LE; increasing WBC criteria to >10 would cause a decrease of 75 cultures: 67 IP (12 intensive care unit, 10 hematology/oncology), 7 OP, 1 ED.

**Conclusions:** UARFCX is relatively infrequently used in our institution. Raising the WBC threshold to >10 would have a small impact, as most samples reflex because of the positive LE. Additional studies will incorporate culture results.

<table>
<thead>
<tr>
<th>Location (No.)</th>
<th>Total % Reflexed</th>
<th>Reflexed for LE Only, %</th>
<th>Reflexed for WBC &gt;5 Only, %</th>
<th>Reflexed for WBC &gt;10 Only, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency room (74)</td>
<td>28.4</td>
<td>25.7</td>
<td>2.7</td>
<td>1.4</td>
</tr>
<tr>
<td>Inpatient (2437)</td>
<td>43.3</td>
<td>39.9</td>
<td>3.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Outpatient (1071)</td>
<td>41.9</td>
<td>40.9</td>
<td>1.0</td>
<td>0.7</td>
</tr>
</tbody>
</table>

**Improving Rapid On-Site Interpretation of Splenic Lesions: Our 24 Years of Experience**

Tiffany L. Alley, DO, PhD (Talley1@utmck.edu); Iris Zaretzki; Solomon Lee, DO; Laurentia Nodit, MD. Department of Pathology, University of Tennessee Graduate School of Medicine, Knoxville.

**Context:** Splenic biopsies are uncommon. Scant exposure makes rapid on-site evaluation (ROSE) challenging with sample limitations and interpretation pitfalls.

**Design:** Electronic database review identified 55 patients with splenic fine-needle aspiration and biopsy assessed by ROSE. Compared with final biopsy or splenectomy, ROSE interpretation was classified as true-negative, true-positive, false-negative, or false-positive. Discordant cases were critically evaluated to identify root cause of discrepancies.

**Results:** ROSE interpretation was true-negative in 25 cases, true-positive in 18 cases, and false-negative in 12 cases. No false-positive cases were noted. In 43 cases, there was correlation between ROSE and permanent biopsy when distinguishing between benign and malignant, without further characterization. The most common malignant process was lymphoma; 9 of 16 cases were recognized by ROSE. False-negative lymphoma cases had hypocellular smears with blood or necrosis. Metastatic malignancies were recognized in all cases. The overall sensitivity of ROSE to detect malignancy was 63%. The second most common diagnosis was granulomatous disease, correctly identified during ROSE in 54% of cases. Interpretative difficulties were created by admixture of benign splenic parenchyma/abnormal tissue, which hampered recognition, and abundant necrosis. Distinguishing hyperplasia from low-grade lymphoma was not possible by cytologic examination alone.

**Conclusions:** ROSE of splenic lesions allows for good correlation with the final diagnoses in 78% of cases and ensures appropriate triage of the specimens toward additional studies. Sampling and extensive necrosis were frequently responsible for discrepancies. Recommendations for error reduction address sampling, use of flow cytometry, and cultures to complement cytologic examination.

**Molecular Pathology Utilization Review Reveals Quality Improvement Opportunities and New Cases of Hereditary Cancer Syndromes**

Nupur Sharma, MD (sharmanu18@ecu.edu); Yaolin Zhou, MD. Department of Pathology, East Carolina University, Greenville, North Carolina.

**Context:** Pathologists can help address the complexity of molecular testing by assisting with tissue and test selection and interpretation. We developed a molecular pathology consultative service to review incoming and outgoing molecular tests.

**Design:** Beginning January 2021, we prospectively reviewed send-out molecular requests and incoming reference laboratory results and entered real-time updates as addenda to pathology reports. We additionally provided “mini consultations” by corresponding with clinicians directly on the front end (eg, deciding which test or specimen to send) and back end (eg, understanding results and potential caveats).

**Results:** From January 2021 to February 2021, we reviewed 210 cases (Table). Quantity insufficient (QNS, n = 25) or likely QNS specimens (n = 6) disproportionately involved lung (19 of 31, Fisher exact P < .001). We assisted with 23 MMR immunohistochemistry orders, clarified 10 (8 unspecified PD-L1), cancelled 7 (including 2 without tumor, 4 redundant), and recommended alternative blocks for 5, including a decalcified specimen. Changing MSI to MMR immunohistochemistry saved our institution $5060 and generated potentially $2888 billable professional interpretation charges. We alerted clinicians regarding 110 cases, including 5 probable germline mutation carriers who were offered genetics counseling. In a feedback survey, all 12 clinicians found our addenda useful, including updates on pending cases.

**Conclusions:** A robust molecular pathology consult service allows pathologists and clinicians to optimize the value of molecular testing. Our hands-on involvement helped identify more appropriate specimens for testing and ensure appropriate interpretation and patient management, such as targeted therapy and evaluation of inherited cancer syndromes. Further improvement opportunities include working to reduce QNS cases, which frequently affected lung aspirates.

**Summary Data of Molecular Pathology Cases Reviewed**

- Number of reviewed cases: 210
- Unique patients: 174
- Resulted cases: 139
- Cases with direct clinician communication: 110
- New inherited cancer mutations: 5
- QNS: 25
- Possible QNS: 6
- MMR IHC: 23
- PD-L1 clarified: 8
- Orders cancelled: 7
- Recommended better specimen: 5
- Frequently seen tumor types:
  - Colorectal cancer: 40
  - Lung adenocarcinoma: 30
  - Breast cancer: 25
  - Pancreatic cancer: 17
  - Endometrial cancer: 16
  - Lung squamous cell carcinoma: 15
  - Gastroesophageal cancer (including GIST): 11
  - Thyroid (including nonmalignant): 9

**Cell Line Control Mixtures for Calibration of Immunohistochemical Assays**

Alonso Castro, BS; Hannah Allison, BA; Andra Santos, BS; Yanique Sexton, BA; William S. Crawford, PhD; Regan S. Fulton, MD, PhD (fulton@arrayscience.com). Department of Research and Development, Array Science, LLC, Sausalito, California.

**Context:** Reliable standards to improve reproducibility among immunohistochemical assays are urgently needed, particularly for predictive biomarkers. We report the development of cell line–based controls to assess the ability of quantitative biomarker assays to detect specific concentrations of positive cells in a sample. We illustrate this concept in the context for 2 semiquantitative biomarkers.

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**Context:** Reliable standards to improve reproducibility among immunohistochemical assays are urgently needed, particularly for predictive biomarkers. We report the development of cell line–based controls to assess the ability of quantitative biomarker assays to detect specific concentrations of positive cells in a sample. We illustrate this concept in the context for 2 semiquantitative biomarkers.
Design: We constructed serial mixes of cell lines (T-47D, AU565, Jurkat, SP²; ATCC, Manassas, Virginia) progressively concentrating given target biomarkers, either estrogen receptor (ER) or Ki-67, to create a linear gradient presented as triplicate samples in a microarray format. Immunohistochemical staining was performed followed by scanning on a Grünium Ocus scanner with positive cell detection using QuPath software.

Results: Immunohistochemical staining for estrogen receptor (ER) showed significant differences in assay sensitivity between laboratories (Figure 3.132). Use of the control array by the lower-performing laboratory allowed precise comparison of antigen retrieval conditions to significantly improve ER sensitivity. An analogous Ki-67 array was used to assess interday assay repeatability in a single laboratory. Marked variation in sensitivity was observed when array slides were stained on different days.

Conclusions: Our goal is to utilize the concept of gradients of target cell positivity as calibration controls for biomarkers that have semiquantitative clinical thresholds. The results presented here demonstrate that such a tool can detect interlaboratory and interday assay variability. One laboratory was able to use the ER control to quantitatively reoptimize its assay. These tools have the potential for use in assay optimization, as well as routine quality control.

Crawford and Fulton are shareholders of Array Science, LLC.

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**Phakomatous Choristoma of the Eyelid and Orbit of a 26-Month-Old Male Infant: Lenscape of a Rare Pediatric Tumor**

(Poster No. 133)

Roselyne Choiniere, MD¹ (roselyne.choiniere@usherbrooke.ca); Philippe Echelard, MD²; Evan Kalin-Hajdu, MD²; Victor Kota, MD³

¹Department of Pathology, University of Sherbrooke, Québec, Canada; Departments of ²Pathology and ³Ophthalmology, University of Montreal, Québec, Canada.

Phakomatous choristoma (PC) of the eyelid and orbit is a rare pediatric tumor composed of epithelium of lenticular anlage, which may be underdiagnosed given its clinical and histopathologic diagnostic intricacies. We present the case of PC in the oldest patient reported, a 2-year-old male with a left inferonasal retroseptal orbit lesion. The 1.5-cm lesion consisted of a dense fibromatous nodule with numerous strands of epithelioid cells surrounded by a dense layer of PAS-positive basal membrane material. The tumor cells were positive for S100, D2-40, GLUT1, CD56, and CD68, synaptophysin, and chromogranin. Postoperative evolution was characterized by a significant degree of inflammation lasting a week that abated within 2 weeks. PCs are rarely suspected clinically, and most cases are misdiagnosed preoperatively as dermoid cysts with a male to female ratio of 19:7 (Table). Lesions uniformly behaved in a benign fashion without known recurrence, even in incompletely resected cases. In conclusion, this is the 28th reported case of PC since its first description in 1971. We performed extensive immunohistochemistry studies and are the first to describe positivity for D2-40, GLUT1, and CD56, findings that are concordant with native lens enolase; SMA, smooth muscle actin.

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<table>
<thead>
<tr>
<th>Patient Age</th>
<th>Sex, Laterality</th>
<th>Clinical Preoperative Diagnosis</th>
<th>IHC Staining</th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td>M, left</td>
<td>Dermoid cyst</td>
<td>+: S-100, D2-40, GLUT1, CD56; GFAP; -: keratin, EMA, SMA, CD31, CD34, CD68, synaptophysin, chromogranin</td>
</tr>
<tr>
<td>13</td>
<td>M, right</td>
<td>Dermoid cyst</td>
<td>+: S-100, vimentin, keratin</td>
</tr>
<tr>
<td>12</td>
<td>F, left</td>
<td>Dermoid cyst</td>
<td>+: S-100, vimentin, keratin</td>
</tr>
<tr>
<td>Infant</td>
<td>NR, NR</td>
<td>Neoplastic</td>
<td>+: S-100; -- keratin, EMA</td>
</tr>
<tr>
<td>10</td>
<td>F, left</td>
<td>Dacryocystocele</td>
<td>+: S-100, vimentin, keratin</td>
</tr>
<tr>
<td>10</td>
<td>M, right</td>
<td>Dermoid cyst, hemangioma</td>
<td>+: S-100, vimentin, keratin</td>
</tr>
<tr>
<td>7</td>
<td>NR, right</td>
<td>Dacryocystocele, dermoid cyst</td>
<td>+: S-100, GFAP, α, β crystalline; -- keratin, EMA, HMB45, actin, CD31, CD34, CD68</td>
</tr>
<tr>
<td>4</td>
<td>M, right</td>
<td>Neoplastic</td>
<td>+: S-100, vimentin, keratin, GFAP, EMA, SMA, synaptophysin, Melan-A</td>
</tr>
<tr>
<td>3</td>
<td>M, left</td>
<td>NR</td>
<td>+: S-100; -- vimentin</td>
</tr>
<tr>
<td>2.3</td>
<td>M, right</td>
<td>NR</td>
<td>+: S-100, vimentin, NSE; -- keratin</td>
</tr>
<tr>
<td>2</td>
<td>M, left</td>
<td>NR</td>
<td>+: vimentin, α, β, γ crystalline; -- keratin</td>
</tr>
<tr>
<td>2</td>
<td>M, right</td>
<td>NR</td>
<td>+: S-100, GFAP; -- keratin, desmin, HMB45, CD31, FLI1, synaptophysin, chromogranin</td>
</tr>
<tr>
<td>2</td>
<td>M, right</td>
<td>Dermoid cyst</td>
<td>+: S-100, vimentin, keratin, EMA, synaptophysin, chromogranin</td>
</tr>
<tr>
<td>2</td>
<td>M, left</td>
<td>Dermoid cyst</td>
<td>+: S-100, vimentin, NSE, α crystalline; -- keratin, GFAP, EMA</td>
</tr>
<tr>
<td>1</td>
<td>F, left</td>
<td>NR</td>
<td>+: S-100, vimentin, keratin</td>
</tr>
<tr>
<td>0.5</td>
<td>F, right</td>
<td>Lower lid skin tumor</td>
<td>+: S-100, vimentin, keratin, GFAP, EMA</td>
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</tbody>
</table>

Abbreviations: EMA, epithelial membrane antigen; FLI, friend leukemia integration site; GFAP, glial fibrillary acidic protein; GLUT1, glucose transporter 1; HMB, human melanoma black; IHC, immunohistochemistry; MSA, muscle-specific actin; NR, not reported; NSE, neuron-specific enolase; SMA, smooth muscle actin.

*a Selection of cases that reported IHC data only for abstract submission rules presented in order of age from oldest to youngest. The full table will be made available on the poster.*
Chondroid Syringoma of the Breast: An Unusual Location

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Cutaneous mixed tumors (Chondroid syringomas) are rare adnexal tumors with 80% incidence in head and neck. Their occurrence in other locations, such as breast skin, is quite rare and it mimics primary breast tumor; therefore, the exact diagnosis by histopathology is crucial. We report a 67-year-old woman, who for 5 years had a slow growing mass on the left breast with no other associated symptoms. Examination revealed a superficial round mobile subcutaneous mass, and a biopsy procedure was recommended. Microscopic evaluation showed biphasic tumor with epithelial and myoepithelial component and chondromyxoid stroma; favoring benign mixed tumor. Differential diagnosis was breast mass versus cutaneous mixed tumor. An excisional biopsy procedure was recommended. Microscopic evaluation showed biphasic tumor with epithelial and myoepithelial component and chondromyxoid stroma; favoring benign mixed tumor. Differential diagnosis was breast mass versus cutaneous mixed tumor. An excisional biopsy procedure was performed that revealed no breast tissue. Skin showed proliferated epithelial and myoepithelial cells in a hyalinized myxochondroid matrix (Figure 4.1, A and C). Immunohistochemistry stains were positive for AE1/AE3 (Figure 4.1, B), CK 5/6, CK-7, S-100, P63 (Figure 4.1, D), and P40. The above findings are most consistent with cutaneous mixed tumor. Because a mixed tumor of the breast is an uncommon tumor, it may be mistaken for a primary breast tumor clinically, radiologically, and even histopathologically. Therefore, it is important to differentiate the two to prevent unnecessary surgical intervention. Chondroid syringomas must be considered in any subcutaneous nodule. The tumor may exhibit atypical features and deep biopsy procedures are often required to assess features of malignancy. Late distant metastasis to lymph nodes, lungs, bone, and central nervous system or delayed malignant transformation is possible. With metastatic potential in mind, it is crucial to diagnose and treat these lesions in their early stage.

Acellular Dermal Filler Complications Mimicking Neoplastic Growth in Head and Neck Region

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Context: During the past decade, acellular dermal (alloderm) graft and dermal fillers (hyaluronic acid, polylactic acid, and facial cream) have been increasingly used for cosmetics and medical management reconstructive surgery. Rare complications of these procedures include localized facial and/or periorbital growths. We report 5 such cases with facial soft tissue reactions clinically mimicking tumors.

Design: A retrospective review of a 5-case series, acellular dermal graft, and filler injections at UC Irvine Medical Center was performed. Case 1 developed nasal mass, swelling, and drainage 3 years after Alloderm graft for empty nose syndrome, mimicking skin cancer. Case 2 developed a periorbital lipogranulomatous nodule, mimicking liposarcoma. Cases 3 and 4 manifested as facial/cheek masses after injection of dermal filler with nonhealing wound, mimicking skin cancer. Case 5, with history of facial cream use, presented with facial mass, mimicking lymphoma.

Results: Most reconstructive surgeries that use fillers generally heal rapidly without complications. Imaging findings correlated with foreign material. All cases demonstrated foreign body giant cell reaction and lipogranuloma formation. Infectious and malignant processes were excluded by special stains, immunomarkers, and molecular analysis (Table).

Conclusions: Although acellular dermal grafts are usually clinically inert, rare cases may present with abnormal tissue reactions. Recognition and careful evaluation of these lipomatous growths will aid in their appropriate management and treatment.

<table>
<thead>
<tr>
<th>Case Number</th>
<th>Age (Sex)</th>
<th>Surgical History</th>
<th>Presentation and Duration</th>
<th>Histopathology</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>69 (Female)</td>
<td>Rhinoplasty (2016 and 2017) drainage of swelling 2018</td>
<td>Clinically mimicking cutaneous cancer, 6 mo</td>
<td>Biopsy: synthetic material, fibrosis</td>
</tr>
<tr>
<td>2</td>
<td>55 (Female)</td>
<td>History of facial injections</td>
<td>Left orbital mass, 3 y</td>
<td>Biopsy: florid lipogranulomatous inflammation</td>
</tr>
<tr>
<td>3</td>
<td>66 (Female)</td>
<td>Rhinoplasty, hyaluronic acid injection complicated by nasal airway obstruction</td>
<td>Clinically mimicking cutaneous cancer, 2 y</td>
<td>Biopsy: varying in size and shape acellular material, hyaluronic acid</td>
</tr>
<tr>
<td>4</td>
<td>54 (Female)</td>
<td>Rhinoplasty, polylactic acid</td>
<td>Clinically mimicking cutaneous cancer, 21 mo</td>
<td>Excision: nasal implant showing fibrous tissue with acellular cystic spaces, containing acellular material (polylactic acid)</td>
</tr>
<tr>
<td>5</td>
<td>53 (Female)</td>
<td>Sinus surgery × 2 in 2012</td>
<td>Clinically mimicking cutaneous lymphoma, 1 y</td>
<td>Excision: lipogranulomatous formation, chronic inflammation</td>
</tr>
</tbody>
</table>
A Survey Study on Non-melanoma Skin Cancer Biopsies With Negative Margins: The Art of Reporting and Management

(Poster No. 3)

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Department of Pathology, University of Colorado, Aurora; Dermatology, Saint Louis University, Saint Louis, Missouri.

Context: Non-melanoma skin cancers (NMSC) are common malignancies. There is no consensus about whether to report margin status on biopsy specimens of NMSC. An important consideration is how margin status impacts patient management. Per our previously presented survey data, clinicians report divergent management for case scenarios of NMSC diagnosed on skin biopsy specimens with negative margins. Our aim was to elucidate factors contributing to clinicians’ management decisions to inform pathologists’ reporting practices and equip them for discussions with clinicians about management of these common malignancies.

Design: A survey was developed presenting case scenarios of a lesion on the arm clinically suspected to be NMSC with final pathology showing negative margins. Respondents were asked what they would do next. Options included perform an excision, perform electro-dessication and curettage, no further intervention, and “Other” with a free-text option. Our electronic survey was sent to professional groups and practices that included dermatologists, family practice physicians, and allied health professionals.

Results: Of 939 invited to participate, 126 (13.4%) completed our survey. The number of respondents who selected “Other” for the case scenarios ranged from 22–31 (17%–25%). Free-text responses centered on clinical monitoring (n = 18), discussing options with the patient (n = 9), and identifying specific factors that would influence management (Figure 4.3).

Conclusions: Reported management of NMSC diagnosed on a biopsy specimen with negative margins varies considerably and appears to depend on both clinician judgment and patient-specific and lesion-specific factors. Because clinicians appear to weigh multiple factors into their management decisions, pathologists should establish clear and specific factors. Because clinicians appear to weigh multiple factors into their management decisions, pathologists should establish clear and specific factors.

A Case of Pilomatrical Carcinoma, an Exceedingly Rare Cutaneous Carcinoma With Potential for Misdiagnosis

(Poster No. 4)

Aayushma Regmi, MBBS (aayushma.regmi@luhs.org); Aaron Muhlbaier, MD; Kumaram M. Mudalilar, MD; Jodi J. Speiser, MD. Department of Pathology and Laboratory Medicine, Loyola University Medical Center, Maywood, Illinois.

Abstracts

A 70-year-old man presented with a 0.5-cm nodule on the right auricle that involved the cartilage. A biopsy specimen taken at an outside institution was initially diagnosed as a sebaceous carcinoma. Subsequently, a wide local excision was performed. The excision showed a 1.4-cm ulcerated nodule. Histopathologic sections showed a poorly circumscribed invasive tumor with a nested and lobulated growth pattern composed of basaloid tumor cells (Figure 4.4, A) with marked pleomorphism and numerous atypical mitotic figures (Figure 4.4, B). Necrotic foci admixed with islands of “ghost cells” characteristic of pilomatrixal tumors were present (Figure 4.4, C). The tumor cells showed diffuse nuclear and cytoplasmic positivity for β-catenin (Figure 4.4, D) and were negative for androgen receptor and epithelial membrane antigen. These findings were consistent with pilomatrixal carcinoma (PC). PC is a rare neoplasm with approximately 130 cases reported. The tumor expresses differentiation toward the hair follicle matrix. CTNNB1 gene mutation that encodes β-catenin is involved in the molecular pathogenesis. PC is the malignant counterpart of benign pilomatrixoma, and distinction can be challenging. Features supporting malignancy in our case included an invasive growth pattern, abundant and atypical mitotic figures (>30/10 high-power fields), marked nuclear pleomorphism, and foci of necrosis. It is possible to miss this challenging diagnosis as it shares overlapping features of other cutaneous carcinomas, including basal cell carcinoma, adnexal neoplasms, and sebaceous carcinoma. It is crucial to consider PC in the differential diagnosis of basaloid tumors of the head and neck region as the local recurrence rate is high and lymph node/systemic metastasis have been reported.

Unexpected Immunostaining of Mycobacterium leprae With an Antibody Against Treponema pallidum

(Poster No. 5)

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We present the case of a 64-year-old South Asian woman with multiple enlarging, well-circumscribed erythematous plaques on her chest (Figure 4.5, A). The lesions extended to the trunk and had been present for 2 years. She was initially treated for dermatitis with topical steroids with no clinical improvement. A biopsy specimen from a lesion on the arm clinically suspected to be NMSC with final pathology showing negative margins. Respondents were asked what they would do next. Options included perform an excision, perform electro-dessication and curettage, no further intervention, and “Other” with a free-text option. Our electronic survey was sent to professional groups and practices that included dermatologists, family practice physicians, and allied health professionals.

Results: Of 939 invited to participate, 126 (13.4%) completed our survey. The number of respondents who selected “Other” for the case scenarios ranged from 22–31 (17%–25%). Free-text responses centered on clinical monitoring (n = 18), discussing options with the patient (n = 9), and identifying specific factors that would influence management (Figure 4.3).

Conclusions: Reported management of NMSC diagnosed on a biopsy specimen with negative margins varies considerably and appears to depend on both clinician judgment and patient-specific and lesion-specific factors. Because clinicians appear to weigh multiple factors into their management decisions, pathologists should establish clear and specific factors. Because clinicians appear to weigh multiple factors into their management decisions, pathologists should establish clear and specific factors.
staining structures with rod-shaped morphology (Figure 4.5, C; original magnification ×600). Fite acid-fast stain revealed abundant bacilli in the dermis inside macrophages forming clusters (globi) and extracellularly (Figure 4.5, D; original magnification ×600). Testing by polymerase chain reaction performed at a reference laboratory on formalin-fixed, paraffin-embedded tissue was positive for *Mycobacterium leprae*. Leprosy is an important global health concern. Approximately 75% of new cases detected annually in the United States are among immigrants. This case represents a potential pitfall with the use of *T. pallidum* IHC for identification of organisms. IHC has become increasingly popular because it is more sensitive than traditional silver stains in detection of *T. pallidum*. The cross-reactivity with mycobacteria has been reported in few cases. Awareness of staining of *Mycobacterium leprae* with antibodies against *T. pallidum* is important when interpreting results. Concurrent acid-fast stains should be performed when histopathologic or clinical suspicion exists.

Psoriasiform/Lichenoid Dermatitis After Receiving SARS-CoV-2 mRNA Moderna Vaccine

(Yahya Daneshbod, MD; Justin Kerstetter, MD. Department of Pathology, Loma Linda University, Loma Linda, California)

This is the first known report, to our knowledge, of a psoriasiform/lichenoid dermatitis post SARS-CoV-2 mRNA vaccine. A 65-year-old woman with Sjögren syndrome presented with psoriasiform/lichenoid dermatitis status after receiving the SARS-CoV-2 mRNA vaccine (Moderna). The rash showed up 5 days after the first immunization. The severity of the rash led her to visit her primary care physician. Physical examination showed erythematous/scaly rashes on her back and neck (Figure 4.6, A and B). A biopsy specimen showed mainly epidermal and superficial dermal involvement (Figure 4.6, C) by a psoriasiform hyperplasia with lichenoid inflammation and scattered necrotic keratinocytes (Figure 4.6, D). Rare eosinophils were seen in the superficial dermis. A diagnosis of a psoriasiform/lichenoid reaction was rendered. Two days later she presented with swollen and discolored, painful digits, and stiff sore neck. She was treated with systemic steroids for the rash that began to show improvement along with the neck and joint discomfort. To the best of our knowledge, this is one of the first reported cases of a post SARS-CoV-2 mRNA vaccine psoriasiform/lichenoid reaction. Post vaccine dermal events needing systemic corticosteroid therapy could affect the efficacy of the vaccine. Because this vaccine stimulates an immune response secondary to production of the spike protein (viral RNA integrates in the cells), the skin may be secondarily affected, and any underlying disease(s) may be exacerbated. The patient is being followed for recurrences of rash after second dose of vaccine. Follow up with more study may be of potential interest to determine the mechanism of these dermal manifestations.

Melanocytic Nevus With Inverted and Perineuriomatous Features

(John L. McAfee, MD (mcaveej@ccf.org); Jeffrey D. McBride, MD, PhD; Steven D. Billings, MD; Jennifer S. Ko, MD, PhD. Department of Anatomic Pathology, Cleveland Clinic, Cleveland, Ohio)

Melanocytic nevi with unusual maturation patterns may be difficult diagnostically and raise concern for melanoma. We present a case displaying both inverted type A and perineuriomatous features, a previously unreported pattern. The lesion was biphasic. In the superficial dermis, there was a population of spindled cells in a whorled arrangement in a myxocollagenous stroma (Figure 4.7, A, original magnification ×6, and B, original magnification ×100). The deep dermis and subcutaneous adipose tissue showed nested epithelioid melanocytes (Figure 4.7, A, original magnification ×6, and C, original magnification ×200). The epithelioid cells stained positively for SOX10, S100, and Melan-A. The epithelioid cells stained positively for SOX10, S100, and Melan-A. The spindled cells were positive for epithelial membrane antigen (EMA) (Figure 4.7, D, original magnification ×200) and CD34 and negative for SOX10, BRAF-V600E and PRAME stains were negative. Beta-catenin staining was cytoplasmic, p16 was retained, and the Ki-67 index was low. Fluorescence in situ hybridization studies were negative for gains at RREB1, CCND1, and...
MYC loci or losses at MYB or CDKN2A loci. These findings exclude a diagnosis of melanoma and confirm a combined inverted and perineuriomatous nevus. Inverted type A nevi may raise concern for melanoma because of the deep-seated epithelioid melanocytes that do not appear to mature. Nevi with perineuriomatous features may resemble desmoplastic melanoma due to the myxoid stroma and spindle cell morphology. Perineuriomatous nevi are also distinct from typical neuroidized nevi in their expression of EMA and lack of Melan-A, SOX10, and S100 expression. Awareness of these entities, and the fact that they may occur together, may help avoid misdiagnosis.

Pediatric Metastatic Melanoma Arising From a Congenital Melanocytic Nevus

(Poster No. 8)

Juanita Duran, MD1 (juanita.duran.r@gmail.com); Sarah K. Daley, MD1; Abdulah Alsowied, MD, PhD1; Cait N. Myrdal, BS2; Clara Curiel-Lewandrowski, MD3; Jose A. Plaza, MD4. Departments of 1Pathology, 2College of Medicine, and 3University of Arizona Cancer Center, University of Arizona, Tucson; 4Department of Pathology and Dermatology, The Ohio State University, Columbus.

Congenital melanocytic nevi (CMN), seen in 1%–3% of neonates, confers <1% risk of melanoma, which increases in larger lesions. Distinction between CMN proliferative nodules and melanoma may be challenging and understanding their genetic basis can help distinguish these entities. We report a case of metastatic melanoma in a 7-year-old boy, previously diagnosed with a proliferative nodule within a CMN. At 2-months-old, several left temporoparietal and occipital pigmented macules and patches ranging from 3–15 mm were noted. Initial biopsy specimen showed a dermal nevus with age-related epithelioid changes. A second biopsy was performed at 4-years-old, owing to the identification of a new palpable nodule within the nevus showed a markedly atypical nodular proliferation of melanocytes, arising in conjunction with a congenital nevus (Figure 4.8, A and B). Immunostaining with p16 was negative and phosphohistone-H3 showed a mitotic index of 5/mm². Array comparative genomic hybridization demonstrated gains in chromosomes 1q, 2, 6, 8, 13, 15, and 19 and losses involving chromosomes 3, 9, 10, 11, and 18 indicating significant genomic instability. Although melanoma was considered in the differential diagnosis, a proliferative nodule was favored, and wide local excision was performed without further findings. On molecular grounds this was plausible with genomic changes involving whole chromosomes, except for 1q gain. Two years later, left postauricular lymphadenopathy was noted revealing metastatic melanoma (Figure 4.8, C and D). A next-generation sequencing panel confirmed a high-allelic NRAS mutation. This case illustrates the challenges encountered in diagnosing pediatric melanocytic lesions as they are rare; however, incorporation of molecular techniques can help to accurately diagnose these lesions.

Multiple Myxoid Cellular Neurothekeomas in a Patient With Systemic Lupus Erythematosus

(Poster No. 9)

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Cellular neurothekeoma is a cutaneous tumor with a distinctive histologic appearance characterized by a dermal based multinodular proliferation of epithelioid to spindle cells. Although the tumor may show varying amounts of myxoid stroma, extensive myxoid change is uncommon. The tumor typically presents as a solitary nodule with a predilection for the head and neck and upper limbs; examples of multiple cellular neurothekeomas are decidedly rare. The present report describes a unique case of multiple myxoid cellular neurothekeomas arising in a 60-year-old woman with systemic lupus erythematosus. Two papular lesions were identified involving the skin inferior to the umbilicus and the left inguinal crease. Both lesions were histologically similar, forming a nodular mass composed of epithelioid cells in a prominent myxoid stroma. By immunohistochemistry the lesional cells expressed NKI/C3, microphthalmia transcription factor (MiTF), and CD68 with focal staining for PGP9.5, factor XIIIa, and CD10 also observed. The tumors were negative for S-100, SOX-10, epithelial membrane antigen, desmin, smooth muscle actin, glial fibrillary acidic protein, and CD34. The present case confirms that cellular neurothekeomas can present clinically as multiple lesions and can have a predominantly myxoid appearance, potentially mimicking other cutaneous myxoid lesions. The coexistence of multiple cellular neurothekeomas and systemic lupus erythematosus in this patient raises the possibility that systemic immune dysregulation could be a contributing factor to the development of multiple lesions.

T-Cell–Rich Angiomatoid Nonpolypoid Pseudolymphoma of the Skin

(Poster No. 10)

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Benign lymphohistiocytic infiltrates of the skin can mimic cutaneous lymphomas. T–cell-rich angiomatoid polypoid pseudolymphoma of the skin (TRAPP) was described as a benign, well circumscribed, nodular lymphohistiocytic infiltrate of the upper dermis with thickened capillaries (resembling high endothelial venules) similar to acral pseudolymphomatous angiookeratoma of children. This pseudolymphoma differs from acral pseudolymphomatous angiookeratoma of children as the infiltrate is less heterogeneous and occurs as a solitary polypoid papule/plaque in nonacral skin of adults. We report a case of nonpolypoid TRAPP. A 37-year-old woman presented with an “infected bump” for 8 months on the left upper chest that failed multiple topical treatments. A biopsy specimen
revealed a well-circumscribed nodular proliferation of capillary sized vessels surrounded by a brisk lymphohistiocytic infiltrate with plasma cells extending from the papillary dermis to the reticular dermis and embedded in a sclerotic stroma (Figure 4.10, A). Endothelial cells were plump without hobnailing (Figure 4.10, B). Lymphocytes extended into the thinned epidermis without an epidermal collar. The infiltrate stained with CD3, CD4, CD5, CD7, and CD8 (with equal staining of CD4 and CD8; Figure 4.10, C and D). CD68 stained admixed histiocytes. These findings were those of nonpolyloid TRAPP of the skin. TRAPP should be considered even in nonpolyloid lymphohistiocytic infiltrates of the skin.

**Atypical Hidradenoma With MUC4 Expression and CRTC1-MAML2 Rearrangement**

(Poster No. 11)

John L. McAfee, MD (mcabeej@ccf.org); Christopher C. Griffith, MD, PhD; Mobeen Rahman, MD; Steven D. Billings, MD; Shira Ronen, MD. Department of Anatomic Pathology, Cleveland Clinic, Cleveland, Ohio.

Adnexal neoplasms are notoriously difficult diagnostically. We report a challenging case of a 54-year-old man who presented with a nodule on the cheek for 6 months. Histopathologically, sections showed a multilobulated, partially cystic, and focally infiltrative dermal-based tumor arranged in solid and microcystic patterns (Figure 4.11, A). The cells had abundant granular and vacuolated eosinophilic cytoplasm and rounded nuclei with prominent nucleoli. There were rare mitotic figures, but marked pleomorphism or necrosis was not identified (Figure 4.11, B). The differential diagnosis included secretory carcinoma and atypical hidradenoma. Immunohistochemical studies showed diffuse staining for mammaglobin. p63 highlighted a subpopulation of cells with basal accentuation (Figure 4.11, C). SOX10 and S100 protein were negative. MUC4 was also positive in the lesional cells with an apparent luminal pattern (Figure 4.11, D). This immunophenotype did not fully resolve the morphologic differential diagnosis. Therefore next-generation sequencing was performed, which identified a CRTC1-MAML2 fusion. Based on these findings, a diagnosis of an atypical hidradenoma was rendered. To our knowledge, this is the first report to demonstrate MUC4 expression in hidradenoma. This finding underscores that MUC4 expression may be nonspecific, and that caution is required when using it to evaluate and differentiate adnexal neoplasms.

**CRTC1-MAML2 fusion has been found in approximately half of atypical hidradenomas in several studies. None of these studies specifically report findings with respect to atypical hidradenoma, and at least 1 study excluded any cases with atypical features. Further studies will be required to determine the overall frequency of MUC4 expression and CRTC1-MAML2 fusion in atypical hidradenomas.**

**Sacral Ulcers in Patients With Severe COVID-19**

(Poster No. 12)

John L. McAfee, MD (mcabeej@ccf.org); Anthony P. Fernandez, MD, PhD; Melissa Piliang, MD. Departments of 1Anatomic Pathology and Dermatology, Cleveland Clinic, Cleveland, Ohio.

Patients with severe, novel COVID-19 have numerous risk factors for ulcer development. These include prolonged bed rest as well as vasculopathy and coagulopathy, which affect a subset of patients. We present 2 cases of sacral ulcers in hospitalized COVID-19 patients with strikingly different histopathologic findings, illustrating different etiologies. Case 1 occurred in a 27-year-old woman with no significant medical history and an otherwise unremarkable skin exam. Disease complications included disseminated intravascular coagulation. A skin biopsy specimen showed a basket-weave stratum corneum with underlying epidermal necrosis. There was a mild dermal perivascular lymphocytic inflammatory infiltrate and no evidence of vasculopathy (Figure 4.12, A, original magnification ×40, and B, original magnification ×100). Case 2 occurred in a 65-year-old woman with a history of ulcerative colitis. She also displayed violaceous and retiform macules on the arms and legs. Coagulation studies were not performed. A biopsy specimen showed a basket-weave stratum corneum with underlying epidermal necrosis. The superficial dermis showed microscopic thrombi, eccrine gland necrosis, edema, and erythrocyte extravasation (Figure 4.12, C, original magnification ×100, and D, original magnification ×100). The findings in Case 1 were most consistent with a pressure ulcer, while the findings in Case 2 were consistent with vasculopathy, possibly related to COVID-19 retiform purpura. The findings did not correlate with known systemic coagulopathy in either case. Numerous cutaneous findings have been described in COVID-19 patients. Case 2 illustrates one of the rarer complications. These cases also highlight the value of ulcer biopsy specimen in COVID-19 patients, as these lesions may have multiple etiologies that are treatable.

**A Non-healing Perianal Wound in a Patient With HIV**

(Poster No. 13)

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A 52-year-old man presented for evaluation of a nonhealing perianal wound for 2 years. His medical history includes well-controlled HIV diagnosed in 2015, syphilis in 2015, and hypothyroidism. The perianal wound was tender, painful, and occasionally bleeding (Figure 4.13, A). The lesion was surgically excised and microscopic examination revealed granulation tissue with large numbers of plasma cells and scattered clusters of neutrophils (Figure 4.13, B). On the Warthin-Starry and Giemsa staining numerous intracellular round and elongated organisms were observed, consistent with chlamydia (Figure 4.13, C and D). The case was diagnosed as lymphogranuloma venereum (LVG). LVG is a sexually transmitted disease that is caused by *Chlamydia trachomatis* L1, L2, and L3 serotypes. *Chlamydia trachomatis* primarily infects lymphatics. There are 3 stages of the LGV. In the primary stage, a small, painless ulcer or proctitis can be observed. In the secondary stage painful lymph
node inflammation occurs. The third stage of the LGV is characterized by fibrosis and strictures, which develops in a minority of patients. The presentation in this case is unusual for LGV, while the timing of the lesion is most consistent with third stage. LGV is rarely diagnosed by histologic examination as most cases are diagnosed by serology and treated with antibiotics. In this atypical presentation, nonhealing, perianal wound over 2 years managed by surgical excision that led histologic diagnosis. Serological confirmation revealed IgA and IgG positivity for C. trachomatis.

**Sarcoïdosis-like Granulomatous Disease Manifestation in COVID-19**

(Poster No. 14)

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The spectrum of findings in COVID-19 continues to broaden with increasing cases. Cutaneous manifestations of COVID-19 are also polymorphous and different inflammatory patterns including lichenoid, perivascular, and chilblain-like changes have been reported. We report a case of a 52-year-old woman who presented with subcutaneous nodules on bilateral arms and hands with fatigue. Four weeks earlier, she tested positive for COVID-19 by polymerase chain reaction. On physical examination, these nodules were tender to palpation. Physical examination, these nodules were tender to palpation. Laboratory investigations revealed mildly elevated blood glucose and liver function tests. An excisional biopsy procedure of 1 nodule from the right elbow showed subcutaneous tissue with histiocytes, giant cells, and nonnecrotizing granulomas. Lymphocytes were the predominant inflammatory component seen both interstitially and at the periphery of granulomas. No evidence of foreign material was seen on light or polarized microscopy. Grocott’s methenamine silver and Fite stain were negative for fungal and acid-fast organisms, respectively. A final diagnosis of sarcoidosis-like granulomatous reaction was made. Subsequent laboratory test for angiotensin converting enzyme levels was normal. A chest computed tomography scan showed hilar lymphadenopathy with the largest node measuring 1.6 cm. A follow-up of 1 month since initial biopsy procedure shows persistent nodules. This is an interesting case of a sudden granulomatous reaction in the deep dermis and subcutaneous tissue that, in the absence of other causative factors, can be regarded as a sequel of COVID-19. Literature search shows 1 case of similar granulomatous eruption in a COVID-19 patient. Both clinicians and pathologists should be cognizant of such spontaneous presentation as a sign of COVID-19 (Figure 4.14).

**Cutaneous Plasmacytosis in Non-Asian Patients: A Clinicopathological Study of 2 Cases**

(Poster No. 15)

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Cutaneous plasmacytosis is a rare skin condition characterized by a mature, polyclonal plasma cell proliferation presenting as dark red to brown papules reported almost exclusively in Asian populations. We present plasmacytosis in 2 non-Asian patients. A 37-year-old African American woman presented with an 8-cm indurated plaque of red-brown discrete papules on the thigh (Figure 4.15, A) that developed after multiple arthropod bites. A 53-year-old White man with JAK-2 negative erythrocytosis and kidney disease presented with brown indurated plaques on the face and chest without lymphadenopathy. Biopsy specimens from both patients revealed a dense superficial and deep perivascular and interstitial lymphoplasmacytic infiltrate with occasional eosinophils, histiocytes, and germinal centers (Figure 4.15, B). The mature plasma cells outnumbered lymphocytes (Figure 4.15, C and D). CD38 and CD138 stained the plasma cells. In case 1, 80% of plasma cells were stained with IgG and 10% with IgG4. IgH gene rearrangement was not detected. In both cases, Kappa/Lambda immunostains and in situ hybridization showed no light chain restriction. Immunostains for treponemes were negative. Systemic disease was not detected in either patient. Both patients responded to local treatment with corticosteroids. The etiology of cutaneous plasmacytosis is unknown. Elevated levels of IL-6, which stimulates terminal B cells to differentiate into plasma cells, have been detected in some patients. The diagnosis of cutaneous plasmacytosis is made only after exclusion of monoclonal or systemic disease. Pathologists need to be aware of this rare entity when encountering mature plasmacytic infiltrates.

**Clinical, Histopathologic, and Molecular Profile of Malignant Melanoma With Rhabdomyosarcomatous Differentiation**

(Poster No. 16)

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Primary cutaneous malignant melanoma (MM) with rhabdomyosarcomatous differentiation is extremely rare and the underlying mechanisms remains largely unknown. We presented a case of MM with rhabdomyosarcomatous differentiation with molecular profile of MM to...
rhabdomyosarcomatous differentiation. The patient was a 72-year-old man who presented with a 1.5 cm partially pigmented lesion on the left lateral scalp. The excision revealed a superficial spreading MM (pT3aN0M0). Four months after surgery, the patient presented with an intensely pruritic rash overlying the surgical bed. A punch biopsy specimen revealed a proliferation of spindle-to-polygonal cells in the dermis. The lesions were negative for all the melanocytic markers and positive for vimentin and Myogenin, which indicated melanoma dedifferentiation at the time of recurrence. Re-examination of the wide-excision specimen revealed distinct small foci of rhabdomyosarcomatous differentiation concentrated at the advancing front of the infiltrating neoplastic melanoma cells. We performed genomic profiling of the original and relapsed tumor to further elucidate the mechanisms underlying this rare phenomenon. Both the original and recurrent tumor shared the NFI Q803 and CDKN2A p16fs*6 and p14ARF Q70fs*91 mutations. The recurrent tumor demonstrated a new telomerase reverse transcriptase (TERT) promoter 146C>T mutation. In melanoma, the TERT promoter mutations are associated with the markers of poor patient outcome. In combination with NFI and CDKN2A mutations, the noncoding TERT promoter mutations in recurrent tumors may extend cellular proliferation by stabilizing telomeres and critically in turn result in genomic instability, followed by acquisition of nonmelanocytic phenotypes.

Pseudomyoeneic Hemangioendothelioma Simulating Tropical Ulcer and Nodules

(Poster No. 17)

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Skin ulcers and nodules in a tropical country represent a diagnostic challenge with multiple etiologies, such as inflammatory conditions, infections, and tumors. We present a case of a 19-year-old man, with a 3-month violaceous, 2-cm nodular lesion on the thigh that appeared after an insect bite; satellite nodules and other distant ones within a linear distribution appeared 3 weeks later (Figure 4.17, A). A tropical ulcer and nodules syndrome and leishmaniasis was considered as initial diagnosis. Skin smear for leishmaniasis, culture for fungi, and mycobacteria were all negative. The ulcerated nodule was biopsied. Microscopic examination showed a dermal proliferation arranged in small sheets and foci of spindle and epithelioid cells within a background of mixed inflammatory infiltrate. The cells showed eosinophilic cytoplasm with eccentric oval bland nuclei and variably distinct nucleioli (Figure 4.17, B). The mitotic count was 3 per 10 hpf; no necrosis was seen. Immunohistochemical studies were diffusely positive for CK AE1/AE3, CK7, CD31, ERG (Figure 4.17, C and D), and focally for SMA, a diagnosis of pseudomyoeneic hemangioendothelioma (PH) was made. Magnetic resonance imaging showed 8 nodules of 5 to 15 mm in the subcutaneous cellular tissue and vastus lateralis. PH is an infrequent and rarely metastasizing endothelial tumor, frequently found in young adult males mimicking a myoid tumor or epithelioid sarcoma. This case reports a rare soft tissue tumor simulating tropical nodules. Recognition of PH is needed as it can mimic a variety of neoplasms; pose diagnostic challenges and emphasizes the importance of pathology studies when other diagnostic techniques fail.

Squamous Cell Carcinoma in the Adolescent and Young Adult: A Pediatric Cancer Center Experience

(Poster No. 18)

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Context: Squamous cell carcinoma (SqCC) is more common in older adults typically presenting in the fifth decade or later. In this study, we present our institutional experience with SqCC diagnosed in adolescents and young adults (AYA; 10–24 years).

Design: SqCC cases diagnosed at our institution over a period of 10 years (2010–2020) were identified from institutional archives. Nasopharyngeal carcinomas (Epstein-Barr virus associated) were excluded. Demographics, clinical presentation, and pathology were reviewed.

Results: Three cases of SqCC were diagnosed in AYA male patients 14–22 years (Table). Two tumors (Cases 1 and 2) demonstrated well-differentiated morphology, were localized at diagnosis, and completely resected with negative margins. One tumor demonstrated moderate differentiation, was locally invasive, and unresectable (Case 3). Two patients had known risk factors including prolonged immunosuppression and chronic tissue injury at a prior surgical site (Cases 1 and 3). In 2 patients, initial biopsy specimens were superficial and SqCC was diagnosed only on follow-up excisions (Cases 1 and 3). Two of 3 patients (Cases 1 and 2) are alive and well after resection (duration of follow-up: 3 years).

Conclusions: This study documents 3 AYA presentations of SqCC. Two of 3 presentations had predisposing risk factors. Localized presentations were completely resected with a favorable outcome.

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A Case of Mycosis Fungoides-like T-Cell Lymphoma With Anaplastic Lymphoma Kinase Expression
(Poster No. 19)

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Anaplastic lymphoma kinase (ALK) expression is exceptional in primary cutaneous T-cell lymphomas. Rare ALK positivity has been reported in primary cutaneous anaplastic large cell lymphoma. We report ALK expression seen in a primary cutaneous T-cell lymphoma with histologic and clinical features of mycosis fungoides. A 61-year-old man presented with erythematous scaly patches and plaques intermittently present since his teenage years and involving predominantly his trunk and proximal limbs. Approximately 7 years ago, he was diagnosed clinically with eczema, and 4 years later, he had a skin punch biopsy specimen that was read as psoriasis. The rash particularly worsened over the last year and progressed to involve more than 80% of his body surface area. Subsequent skin biopsy specimens showed an epidermotropic infiltrate featuring small-to-medium sized cytologically atypical lymphocytes (Figure 4.19, A) expressing CD2 (Figure 4.19, B), CD5, CD7, CD30 (Figure 4.19, C), and ALK (Figure 4.19, D). A positron emission tomography scan highlighted prominent, but not enlarged by size criteria, non-fluorodeoxyglucose avid bilateral inguinal and axillary lymph nodes. An inguinal lymphadenectomy showed dermatopathic lymphadenopathy with very rare scattered ALK-positive atypical lymphocytes without effacement of the nodal architecture. Flow cytometry of the lymph node showed 4% phenotypically abnormal lymphocytes without effacement of the nodal architecture. Subsequent skin biopsy specimens showed an epidermotropic infiltrate featuring small-to-medium sized cytologically atypical lymphocytes without effacement of the nodal architecture. Flow cytometry showed 4% phenotypically abnormal lymphocytes without effacement of the nodal architecture.

Analysis of Genetic Mutations in Benign and Malignant Adnexal Tumors
(Poster No. 20)

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Context: Skin adnexal neoplasms are a heterogeneous group of rare malignancies. In this study, we examined the frequency and type of gene mutations in different malignant adnexal tumors and compared with those observed in the benign tumors.

Objective: To assess the frequency and type of mutations in adnexal tumors.

Design: Gene mutation data were reported for 54 malignant adnexal tumors in the COSMIC database (https://cancer.sanger.ac.uk/cosmic) as of February 2021. Of 54 cases, only 43 contained histologic information. The histologic subtypes included eccrine adenocarcinoma (n = 18), apocrine carcinoma (n = 2), hidradenocarcinoma (n = 11), and pilomatrix carcinoma (n = 12).

Results: TP53 gene was found to be reported in approximately 25% of the malignant adnexal tumors. However, our histologic subtype-specific analysis showed TP53 mutations in approximately 78% (14 of 18) of eccrine adenocarcinoma samples (Figure 4.20). Of 4 TP53 mutation–negative samples, 3 samples showed the pathogenic exon 9 mutations in the PIK3CA gene (p.E542K and p.E545K) and 1 sample showed HRAS p.G12D gene mutation. All benign eccrine adenoma samples (5) showed only BRAF V600E mutation. In hidradenoma cases, PIK3CA is the frequently mutated gene with mutations observed in both exons 9 and 20. Of note, hidradenocarcinoma cases showed high frequency of TP53 mutations (45%) followed by the PIK3CA (27%). PIK3CA mutations were observed only in TP53 mutation–negative cases and all cases showed only exon 9 mutations. None of the malignant pilomatrix carcinoma and apocrine carcinoma showed TP53 gene mutations.

Conclusions: This study’s results provide evidence for the presence of distinct gene mutations in benign and malignant eccrine and hidradenocarcinoma. The data also provide a rationale for molecular screening of adnexal tumors for developing individualized therapeutic strategies.

Clinicopathologic Outcome of Surgical Excision for the Management of Cutaneous Squamous Cell Carcinoma In Situ
(Poster No. 21)

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Context: Squamous cell carcinoma in situ (SCCIS) is typically present as a well demarcated, erythematous hyperkeratotic plaque with an irregular border on sun exposed skin. There are different approaches for the management of SCCIS, such as topical Fluorouracil, topical Imiquimod, cryotherapy, radiotherapy, laser, curettage, or excision. In this study, we investigated recurrence rate of the SCCIS after surgical excision and the risk of developing invasive carcinoma from SCCIS.

Design: Surgical resection specimens of SCCIS (2018–2020) were retrieved. All cases were previously diagnosed with SCCIS and excised, subsequently represented for re-excision of the same site. Follow-up biopsy specimen results are classified in the following 3 groups as: cicatrix, recurrent SCCIS, and invasive squamous cell carcinoma.

Results: A total of 83 cases were included to the study. Among 83 cases, 46 cases (55.4%) were found to have cicatrix, 36 cases (43.5%) were found to have recurrent SCCIS, and 1 case (0.01%) was diagnosed as invasive squamous cell carcinoma, keratocanthoma type.

Conclusions: In conclusion, we found that the recurrence rate of SCCIS is unexpectedly high after surgical excision (43.4%), and progression to invasive squamous cell carcinoma was minute (0.01%) in contrary to current literature (3%–5%).

Pitfalls in Making the Distinction Between Desmoplastic Melanoma and Neurofibroma
(Poster No. 22)

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Desmoplastic melanoma (DM) and neurofibroma (NF) can be difficult to distinguish histologically. Both are spindle cell lesions and may be infiltrative with myxoid areas that may contain melanin pigment. There are histologic clues favoring one over the other, including mitoses, pleomorphism, mast cells, Wagner-Meissner, and Pacinian corpuscles; however, these are not always present complicating the task. Both demonstrate an immunophenotype with positive S-100, SOX-10, and negative Melan-A, HMB-45, and MART1. There have been reports that p53 staining can help differentiate, as DM demonstrates strong nuclear staining whereas NF stains negative. Neurofibromas can be differentiated based on their fingerprint pattern reactivity with CD34. Using molecular, DM lacks the classic mutations in BRAF, NRAS, and KIT but harbor loss of function mutations in NF1, TP53, and NFKBIE promoter mutations. We present a case of an 85-year-old woman who was diagnosed with DM of the left nasolabial fold. The initial biopsy specimen was diagnosed as DM and she underwent wide local excision. Histologically, it was composed of small bland cells with serpentine nuclei in a background of myxoid, delicate fibriillary stroma (Figure 4.22, A and B). It stained positive for S-100 and SOX-10, but the remaining melanocytic markers were negative. CD34 stained with the fingerprint pattern. P53 stained the nuclei of surrounding adnexa (Figure 4.22, C and D) but not the tumor. A final diagnosis of NF was made. This case demonstrates the challenge in differentiating DM from NF. We present this case as an important reminder that neurofibromas may histologically and immunophenotypically resemble DM.

Metastatic Dedifferentiated Melanoma: A Diagnostic Challenge and Therapeutic Implication

(Poster No. 23)

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Dedifferentiated melanoma (DDM) is defined by loss of diagnostic morphophenotypic features of melanoma, including immunohistochemical markers. This phenomenon has been reported, particularly in metastatic melanoma. The dedifferentiation is a reflection of phenotypic-genetic plasticity of melanoma and specifically the nonirreversibility of the multistep cancerogenesis. The recognition of DDM is of prime importance for the diagnostic challenges and therapeutic resistance. We report a case of 56-year-old man presenting for evaluation of spinal metastases. He was diagnosed with scalp lesion by a tumor mass (Figure 4.23, A). Histology of the vertebral lesion revealed solid sheets of poorly differentiated epithelioid tumor compatible with metastatic melanoma (Figure 4.23, B), but without melanin pigmentation. The tumor was negative for melanocytic differentiation markers (S-100, Melan-A, HMB-45, SOX10, Figure 4.23, C) or specific tumor lineage (negative for cytokeratin 7/20, MOC-31, CD45, p40) with patchy positivity for Pancytokeratin (AE1/AE3). Molecular study showed BRAF V600E (c.1799T>A) mutation (Figure 4.23, D). The diagnosis of DDM poses remarkable challenge due to a broad spectrum of differential diagnoses, including undifferentiated carcinoma and sarcomas, particularly if prior history is unknown and the tumor shows aberrant expression of nonmelanocytic differentiation markers of different lineages. Another important implication is that DDM emerges from genetic and epigenetic mechanisms resulting in resistance to immunotherapy and targeted therapy.

Diagnostic Dilemma of Primary Mucinous Carcinoma of the Skin With Metastasis

(Poster No. 24)

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Primary mucinous carcinoma of the skin (PMCS) is a rare adnexal tumor of sweat gland. It is a slow-growing tumor reported in peri-orbital region and scalp. We report a case of a 62-year-old man that presented with a subcutaneous nodule in right axilla in 2012. Imaging revealed a right axillary lesion, but no suspicious lesion was seen in other organs. Gross examination revealed a 4 × 3.5 × 2-cm dermal based nodule. Microscopic examination showed nests of uniform round to cuboidal epithelial cells in mucinous lakes. Immunohistochemical stains (IHC) showed positive CK7, ER, GATA-3, CEA, and negative TTF-1 and CK20. IHC profile excluded metastatic mucinous carcinoma of lung and colon. Differentiation from breast metastasis was difficult but in the absence of radiographic evidence of a breast mass, primary mucinous carcinoma of skin was diagnosed. In 2013, patient presented with lung nodules. A lung nodule biopsy specimen showed same histopathologic and IHC findings as from right axilla nodule favoring metastatic mucinous carcinoma. Recently, patient presented with left axillary nodule and excision revealed mucinous carcinoma likely metastasis from right axilla. Histopathologic distinction between primary and secondary mucinous tumors may be impossible. PMCS expresses AE1/AE3, CEA, ER, GATA-3, and variable positivity for GCDFP-15 and PR. Myoepithelial cells are present in the primary tumors. Therefore, positive staining for p63 and CK5/6 can be helpful. Distinguishing PMCS from metastatic mucinous carcinoma of breast can be challenging. Therefore, radiologic and clinical correlation is important (Figure 4.24).
Extramammary Paget Disease: An Unusual Presentation
(Poster No. 25)
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A 44-year-old woman presented with an asymptomatic well-defined brownish plaque (size 3 x 3 cm) on the pubic region from 7 years ago. It started during the third trimester of her pregnancy and gradually enlarged and showed a focal pink discoloration with white scales (Figure 4.25, A). There was no improvement using topical corticosteroid therapy. A skin biopsy specimen stained with hematoxylin-eosin showed lower epidermis containing solid nests of atypical pale cells and upward migration into upper epidermis (Figure 4.25, B). On immunohistochemistry, pale cells were positive for carcinoembryonic antigen (CEA), epithelial membrane antigen (EMA), cytokeratin 7 (CK7), gross cystic disease fluid protein-15 (GCDFP15), and negative for CK20 and S100 (Figure 4.25, C and D). Histology and immunohistochemistry findings were consistent with primary extramammary Paget disease (EMPD). We did not find any abnormality on genital and perianal examination. The lesion was excised with 1.5-cm safe margin and flapped. Apocrine-rich areas, such as genital or perianal areas, are common locations for EMPD but pubic region involvement is unusual. We should be mindful of EMPD for any long-standing scaly plaque located on milk lines (extended from axilla to groin). These lines contain Toker cells, which may be a precursor of Paget cells. EMPD usually presents with a reddish or whitish marginated plaque with scaling or ulceration. Primary EMPD is positive for GCDFP15 and negative for CK20. It is not associated with any underlying adenocarcinoma adjacent or distant to epidermal tumor, so early diagnosis is very helpful for complete treatment.

Misleading Dendritic Cells in Pigmented Bowen Disease on Reflectance Confocal Microscopy
(Poster No. 26)
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Bowen disease (BD) is an in situ variant of squamous cell carcinoma of the skin. Pigmented facial lesions (pigmented actinic keratosis, lentigo maligna, solar lentigo, lichenoid keratosis) can be challenging to diagnose due to the unique anatomic and histologic features of the facial skin and photoaging. In such lesions, reflectance confocal microscopy (RCM) can play an important role as an adjunct in vivo diagnostic technique. The presence of intraepidermal pagetoid bright cells is a suggestive feature of melanoma on RCM, though it must be kept in mind that the morphologic aspect of Langerhans cells with RCM can be similar to melanocytes. We present a case of pigmented BD (pBD) with misdiagnosed as lentigo maligna due to the presence of high-density of hyperreflective dendritic intraepithelial cells on RCM. A 73-year-old female patient was admitted for a pigmented lesion on the left cheek evolving from 1 year (Figure 4.26). RCM revealed an atypical honeycomb pattern in the epidermis and numerous stellate hyperreflective cells and multiple small circles with bright rims at the dermoepidermal junction. Histopathologic examination was typical for pBD. Typical RCM features of BD are cytologic atypia of keratinocytes and the architectural disorganization of the epidermis which presents as an atypical honeycomb pattern in the epidermis. Recently, reported studies highlighted that intraepidermal dendritic cells can be a confounding feature in pigmented AK and pBD. The exact nature of these hyperreflective cells remains to be clearly determined. Such misleading lesions need to be kept in mind to avoid worrying patients and excessive surgical treatment.

A Locally Aggressive Ameloblastic Fibro-Odontoma: A Case Report and Literature Review
(Poster No. 27)
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Ameloblastic fibro-odontoma (AFO) is a relatively rare, benign, noninvasive, mixed odontogenic neoplasm derived from epithelial and ectomesenchymal elements of the dental tissues. It usually presents with a mean age of 11.5 years and in the posterior segment of the mandible. It is extremely rare in the posterior maxilla. Although the latest World Health Organization edition classified AFO as developing odontoma, here we present a locally aggressive AFO in a 21-year-old man involving the posterior maxilla and sinus with bone destruction. The patient presents with a 2-year history of slowly progressive left facial swelling with malodorous drainage. The computed tomography scan revealed a 5.5 × 4.3-cm well-circumscribed expansile mass with mixed attenuation and peripheral calcification occupying the left maxilla and sinus with bone destruction of the hard palate and orbital rim.

According to the literature, most of the AFO cases were treated aggressively with left maxillectomy, palatectomy, and reconstruction surgery because of its radiologic findings, which suggested a locally invasive neoplasm. Histologically, the specimen showed a mixture of proliferative epithelial, mesenchymal tissue elements, and variable amounts of mineralized deposits consisting of enamel matrix and dentinoid deposits and the final diagnosis was AFO. In conclusion, we present a rare case of AFO with unusual aggressive presentation, age group, and site involved. The radiographic, histopathologic features, and therapeutic approaches of this unusual locally aggressive tumor are presented with the review of relevant literature.

Inflammatory Pseudotumor of the Head and Neck: Case Series
(Poster No. 28)

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Context: Inflammatory pseudotumor (IPT) is a fibroinflammatory process with aggressive behavior. It is uncommon in the head and neck (H&N) and has been reported infrequently in the pathology literature. IPT is a diagnosis of exclusion and is hallmarked by acute and chronic inflammatory infiltrates in a fibrous stroma. Clinical consideration is usually for primary malignancy due to presence of infiltrative masses with bone involvement. Biopsy specimens may only yield fibrotic tissue with nonspecific inflammation.

Design: Our surgical pathology files were searched for H&N IPT, and chart reviews were performed. All cases used clinical/pathologic correlation for diagnosis and excluded mimickers, including IgG4-related disease, malignancy, and infection.

Results: Five patients (3 men and 2 women; ages 61–79) were identified, all with rapid onset of cranial nerve neuropathy. Radiologically, lesions were large, infiltrative, and concerning for malignancy. There were nasopharyngeal, 1 in the maxillary sinus, and 1 in the orbit, all involving the skull base. Histologically, all biopsy specimens showed chronic, predominantly lymphocytic, inflammation with mild fibrosis (not storiform). One case had mild acute inflammation. Histology and immunohistochemistry features of IgG4-related disease were absent. Special stains and cultures for fungus and bacteria were negative. All received corticosteroid therapy at follow-up between 0 and 14 months; 1 patient showed clinical improvement, 2 progressed and underwent therapeutic radiation, 1 died of disease, and 1 had no follow-up.

Conclusions: These 5 cases, to our knowledge, are the largest IPT series in the H&N. IPT has diagnostic challenges and complex clinical presentation. Infiltrating malignant IgG4-related disease important, as the clinical courses and treatments vary.

FET-TFCP2-Rearranged Rhabdomyosarcoma: A Neoplasm Showing Frequent Head and Neck Location, Epithelioid and Spindled Morphology, and Diffuse Keratin Expression, Inviting Misdiagnosis as Sarcomatoid Carcinoma
(Poster No. 29)

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Recently, a novel subtype of rhabdomyosarcoma with FET-TFCP2 fusion was described that shows a predilection for bone, particularly craniofacial bones, exhibits spindled and epithelioid morphology, diffuse expression of cytokeratins, and ALK overexpression in the absence of ALK fusions. These cases may invite misinterpretation as sarcomatoid/spindle cell carcinoma with rhabdomyoblastic differentiation or even inflammatory myofibroblastic tumor. We present a case of a 54-year-old woman who presented with a 2.5-cm mass centered in the mandible bone with gingival extension. Biopsy and mandibulectomy specimens featured sheets of epithelioid cells with abundant eosinophilic cytoplasm as well as spindle cells (Figure 4.29, A and B) that focally showed rhabdomyoblastic differentiation. Based on differential expression of high and low molecular weight keratins (Figure 4.29, C, 34BetaE12 and CAM5.2, respectively) a diagnosis of sarcomatoid carcinoma was considered; however, no in situ carcinoma or squamous differentiation was identified, and Desmin and MYOD1 (Figure 4.29, D inset) showed multifocal positivity, with myogenin and p40 being negative. ALK was strongly expressed (Figure 4.29, D). Archer FusionPlex panel revealed a FUS-TFCP2 fusion transcript; thus, this case was confirmed as a FET-TFCP2-rearranged rhabdomyosarcoma. A tumor locally recurred 2 years later with no evidence of metastasis, so far. This case highlights the salient clinicopathologic features of FUS-TFCP2-rearranged rhabdomyosarcoma. Namely, an aggressive spindled and epithelioid rhabdomyosarcoma often of craniofacial bones with a propensity to diffusely express keratins. Awareness of this entity will help prevent misdiagnosis as sarcomatoid carcinoma and possibly allow for personalized therapy given their frequent ALK overexpression.

Mucinous Epithelium From the Nasal Sinuses: A Clinically Significant Differential Diagnosis
(Poster No. 30)

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Context: Mucinous epithelium and mucinous metaplasia of the nasal sinuses are rare. These lesions may contain mucin-producing cells, form masses, and yield abundant material on biopsy specimens.

Design: An electronic search of the surgical pathology files between June 2010 and June 2020 was performed for nasal sinus, curretage, papilloma, chronic sinusitis, adenocarcinoma, and nasal polyp. Cases identified by the search had clinical and imaging correlation.

Results: Two cases demonstrating fragments of pure mucin-producing columnar epithelium were identified from 234 reviewed cases. In 1 case, imaging and clinical evaluation disclosed mucosal thickening but no mass lesion. The second case revealed mucosal thickening and myeloidocytic metaplasia; neither showed infiltrative behavior.
nasal polyps. Microscopic examination of both cases revealed mucosal thickening of respiratory epithelium and thick basement membranes. There were small sheets of a papillary proliferation of columnar mucin-producing cells lacking nuclear atypia (Figure 4.30, A; hematoxylin-eosin, original magnification ×10). The cells were CK7 (Figure 4.30, B) and CK20 positive but negative for p63 and CDX2. The 6-month follow-up showed no evidence of recurrence in either case.

Conclusions: Fragments of pure mucinous epithelium are rare in sinonasal specimens and raise the differential diagnosis of the mucinous epithelium in respiratory adenomatoid hamartoma, intestinal-type sinonasal adenocarcinoma, and low-grade mucoepidermoid carcinoma. These lesions present as masses/polyps and are usually associated with abundant neoplastic epithelium with cytologic atypia. The reported cases appear to represent rare mucinous metaplasia with a benign course.

Middle Ear Adenoma, Vague Presentation, and an “Indispensable” Histopathologic Examination

(Doster No. 31)

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Middle ear adenoma, or neuroendocrine adenoma of the middle ear, accounts for less than 2% of all ear tumors. Hyams and Michael first described them in 1976, naming them middle ear adenomas. Later, they were characterized as a carcinoid tumor. The current consensus is that these represent the same tumor with different degrees of glandular and neuroendocrine differentiation. These benign tumors are seen in adults, with equal sex distribution. They present as ear fullness, tinnitus, ear pain, and facial weakness. On imaging, they appear as nonspecific, homogeneous, hypodense masses. Our case involves a 47-year-old woman presenting with right sided ear fullness and tinnitus. Computed tomography showed a soft tissue inflammatory mass within the middle ear. Definitive diagnosis could not be rendered but was consistent with a cholesteatoma, adenoma, or neurofibroma. Histopathologic examination of the excised mass demonstrated an infiltrative growth (Figure 4.31).

Synchronous Ipsilateral Lesions of the Parotid Gland: A Clinicopathologic Review

(Doster No. 32)

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Context: Salivary gland lesions represent 3% to 4% of all head and neck tumors. Synchronous ipsilateral lesions of the parotid gland have not been well reported. We report the clinical findings, pathologic characteristics, and incidence of synchronous ipsilateral lesions occurring in the parotid gland.

Design: The surgical pathology database at our institution was searched for parotid gland lesions diagnosed between 1995 and 2020. Those with synchronous lesions where evaluated, and the pertinent clinical and pathologic data were reviewed in detail.

Results: We identified 445 cases of parotid gland lesions. Of these 15 of 445 (3%), 10 men and 5 women, aged between 22 and 68 years, and a mean age of 52 years, were synchronous ipsilateral lesions (Table). Nine lesions were located on the right side and 6 on the left. Of 15 lesions, 8 (53%) underwent fine-needle aspiration prior to surgery; none assessed the 2 lesions.

Conclusions: Of ipsilateral synchronous lesions, 87% are benign, 62% share same histologic features. Half of the malignant cases had different histology that could impact patient’s management, while 67% occurred in males and on the right side is the most common. Coexistence of Warthin tumor with a lymphoepithelial cyst is rare, suggesting that both lesions may have a common embryologic pathway. Although most are benign, synchronous malignant lesions do occur, suggesting evaluation of all lesions prior to excision might be helpful in ensuring appropriate clinical management.

<table>
<thead>
<tr>
<th>Summary of Ipsilateral Synchronous Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both Benign (13)</td>
</tr>
<tr>
<td>3-Pleomorphic adenoma (PA), 4-warthin, 1-oncocytoma, 2-PA + Warthin, 1-PA + oncocytoma, 2-warthin + lymphoepithelial cyst</td>
</tr>
</tbody>
</table>

Combined Neuroendocrine and Squamous Cell Carcinoma of the Sinonasal Tract: A Morphologic and Immunohistochemical Analysis

(Doster No. 33)

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Context: Sinonasal malignancies constitute 3% of head and neck cancers, with squamous cell carcinoma (SCC) the most common histology. Neuroendocrine carcinomas (NEC) are rare, with a subset showing neuroendocrine carcinoma and a nonneuroendocrine component. Pathogenesis of these combined tumors is largely unknown. TP53 driver mutations may play a role.

Design: A database search for combined NEC was performed across 2 institutions (UNM and UCSF) spanning 15 years. Excluding NUT midline carcinoma, 3 cases qualified. All were morphologically NEC + SCC and were subjected to a comprehensive immunohistochemical evaluation.

Results: A comparative analysis of these cases is presented in the Table. Tumors demonstrated 2 components histologically, moderately to poorly differentiated SCC and high-grade NEC. Divergent differentiation was confirmed with lineage-specific markers. Only 1 patient received neoadjuvant chemotherapy before surgery with a remarkable response (marked decrease in the size of the primary lesion and resolution of liver metastases). Immunohistochemical staining for p53 was increased in 2 of 3 cases (both components), suggesting a role in carcinogenesis of these tumors. Ablation expression of beta catenin was not identified. One case tested positive for p16; the significance of which is unknown at this time. In addition, both cases with a small cell NEC component expressed PD-L1, suggesting a role for immunotherapy in treatment.

Conclusions: The findings of this study support the role of p53 mutation in a subset of combined NEC + SCC of the sinonasal tract. Recognition of this rare entity is important for optimal management of these aggressive neoplasms.

### Demographics and Immunohistochemical Analysis of Combined NEC + SCC

| Age, y | Sex | Location of tumor | Histology | Diagnosis on biopsy specimens versus resection | Treatment offered | Immunohistochemistry (Vendor) | p53 (% cells showing positive nuclear expression) | Beta catenin (Expression, localization), (BD transduction, San Jose, California) | p16 (Ventana Medical Systems, Oso Valley, Arizona) | Ki-67 (Ventana Medical Systems, Oso Valley, Arizona) | NUT protein (Cell signaling, Danvers, Massachusetts) | CD56 (Cell Marque, Rocklin, California) | Synaptophysin (Richard-Allen Scientific/Thermo Fisher Scientific, Kalamazoo, Michigan) | Chromogranin (Ventana Medical Systems, Oro Valley, Arizona) | P40 (Biocare Medical, Pacheco, California) | p63 (Biocare Medical, Pacheco, California) | CK 5/6 (Leica Biosystems, Buffalo Grove, Illinois) |
|--------|-----|------------------|-----------|-----------------------------------------------|-------------------|-----------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|
| 48     | Female | Maxillary sinus with liver metastasis | Squamous cell carcinoma + small cell carcinoma (intermixed) | Biopsy | Neoadjuvant chemotherapy (with marked response) followed by resection | Positive in squamous component | Positive in squamous component | Positive in neuroendocrine component | Positive, membranous | Positive, 40 (discrete nests) | Negative | Positive in neuroendocrine component | Positive in neuroendocrine component | Positive in neuroendocrine component | Not performed | Not performed | Positive in squamous component | Positive in squamous component | Positive in squamous component |

Ectopic Parathyroid Neoplasms in the Thymus: Parathyroid Adenoma and Parathyroid Neoplasm of Uncertain Malignant Potential With Diffuse Hyalinization

(Poster No. 34)

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Parathyroid neoplasms are uncommonly found in ectopic locations, including in thymus, retroesophageal region, thyroid, and pericardium, among others, with thymus relatively the most frequent. Most ectopic parathyroid neoplasms are parathyroid adenomas with rare case reports of atypical parathyroid adenoma (parathyroid neoplasm of uncertain malignant potential [PNUMP]) or carcinoma. We present 2 cases of ectopic parathyroid neoplasms in the thymus, 1 with adenoma and the other with atypical adenoma (PNUMP). A 72-year-old woman was found to have elevated serum calcium (10.4 mg/dL) and parathormone (PTH, 168 pg/mL) during evaluation of osteoporosis. A 28-year-old woman with past medical history of kidney stones had elevated serum calcium (11.1 mg/dL) and PTH (117 pg/mL). Parathyroid nuclear scan in both patients showed increased uptake in the anterior mediastinum. Thyrectomy was performed in both patients. The findings in the first case were those of an ectopic parathyroid adenoma (1.3 cm) (Figure 434, A). The second case was diagnosed as PNUMP (1.7 cm) based on partially encapsulated cellular parathyroid tissue composed mainly of chief cells. The lobules were separated by thick fibrous bands and...
showed diffuse hyalinization (Figure 4.34, B and C). Tumor cells focally infiltrated into the extracapsular adipose tissue and surrounding thymic tissue (Figure 4.34, D). No mitosis, necrosis, or vascular invasion were seen. These 2 cases illustrate the importance of recognizing the existence of ectopic parathyroid neoplasms in thymic tissue. Careful morphologic evaluation with adherence to diagnostic criteria of orthotopic parathyroid neoplasms is important in guiding clinical management.

Rheumatoid Laryngeal Nodules or Bamboo Nodes of the Vocal Folds
(Poster No. 35)

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The presence of rheumatoid nodules and bamboo nodes in the vocal cords represent a rare, but clinically well-recognized manifestation of an underlying autoimmune disorder. The lesions are thought to be the result of autoimmune complex deposition and phonotrauma. Bamboo nodes are bilateral cream-colored, transverse deposits in the middle third of the vocal cords. Because of their tendency to recur, treatment of the autoimmune disease is preferred over surgical removal. Consequently, the description of the histopathologic spectrum of these lesions is uncommon. We report a case of a 40-year-old woman smoker, with history of systemic lupus erythematosus, rheumatoid arthritis, and chronic obstructive pulmonary disease who presented with a 3-month history of dysphonia. Microdirect laryngoscopy demonstrated bilateral vocal cord nodules and excisional biopsies were performed. Histopathologic examination reveals fragmented hyperplastic squamous mucosa with poorly defined submucosal granulomas with transverse orientation with central eosinophilic amorphous nonpolarizable material and fibrinoid necrobiosis (Figure 4.35, A and B) surrounded by epithelioid and foamy histiocytes, scattered neutrophils and occasional giant cells (Figure 4.35, C). No vasculitis was observed. A Movat pentachrome stain demonstrates fragmented elastic fibers within the fibrinoid necrosis (Figure 4.35, D). Congo red and acid-fast bacilli stains were negative. The findings were consistent with autoimmune involvement of vocal cords categorized as rheumatoid laryngeal nodules or bamboo nodes. It is important for otolaryngologists and pathologists to be familiar with the clinical and histopathologic features of these lesions which could represent different stages of the same pathologic process. Autoimmune driven vocal fold lesions should be always suspected in young females complaining of dysphonia.

Gorlin Syndrome (Nevoid Basal Cell Carcinoma Syndrome): A Case Report and Literature Review
(Poster No. 36)

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Gorlin syndrome is a rare autosomal dominant disease caused by mutations in the sonic hedgehog signaling pathway, specifically the Drosophila patched gene (PTCH1). The disease is characterized by the development of multiple basal cell carcinomas at young ages. These tumors could present with other skin manifestations, such as palmpoplantar pits and extracutaneous manifestations such as odontogenic keratocysts and medulloblastoma. Gorlin syndrome has a prevalence ranging from 1 in 55 600 to 1 in 256 000. Our patient was a 30-year-old man who presented with cystic lesions involving the mandible and left maxilla. Computed tomography scan of the maxillofacial bones showed multiple maxillary and mandibular lesions, the largest being a lytic lesion involving the mandibular symphysis (1.3 × 4.3 × 2.3 cm) with maxillary hypoplasia. An excision was performed, which revealed classic features for an odontogenic keratocyst with a corrugated parakeratotic epithelium. Daughter cysts were identified, a finding that can be associated with recurrence. On review of the medical record, the patient also had a cranioptosis for premature closure of the frontal suture, basal cell carcinoma of the left eyelid, and nephrectomy for hydronephrosis. Of note, the patient’s parents did not have any history of tumors that are typically found in Gorlin syndrome. On further review, the patient had a deletion involving chromosome 9 (q22.1-q22.3), a location of the exact site of the PTCH1 gene. This case demonstrates the genetic heterogeneity in patients with Gorlin syndrome and how it can be a result of not only mutations in the PTCH1 gene, but also chromosomal losses.

Thyroid-like Low Grade Nasopharyngeal Papillary Adenocarcinoma Presenting as a Polyp in a Young Patient
(Poster No. 37)

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Primary nasopharyngeal papillary adenocarcinoma (NPPA) is a low-grade adenocarcinoma characterized by papillary configuration and exophytic growth. A subset of low-grade NPPAs can present with papillary thyroid carcinoma-like architecture and nuclear morphology. These tumors express immunoreactivity for TTF-1 but not for thyroglobulin and are referred to as thyroid-like low-grade NPPA (TL-LGNPPA). TL-LGNPPA are extremely rare tumors. Approximately 80% of cases were reported from East Asia. No etiologic agent including Epstein-Barr virus, human papillomavirus, or BRAF mutation has been linked to this neoplasia. It is unknown whether the prognosis of this neoplasia differs from other nasopharyngeal adenocarcinomas. We present a case of a 26-year-old White woman who was evaluated in an outside institution with a complaint of pharyngitis and left ear fullness sensation for several years. Initial imaging studies showed no masses or lesions. A nasopharyngeal endoscopy revealed a right nasal polypoid lesion. Biopsy of the lesion was performed and a diagnosis of a low-grade NPPA was rendered. The patient was referred to our institution for treatment. On review of the biopsy specimen, the lesion was reclassified as primary TL-LGNPPA (Figure 4.37, A through D). Immunohistochemistry revealed neoplastic cells to be positive for cytokeratin AE1/AE3, EMA, TTF-1 (Figure 4.37, B), while negative for...
Thyroglobulin (Figure 4.37, C) and PAX8 (Figure 4.37, D), supporting the diagnosis. Surgical excision of the residual tumor was performed with clear margins. The patient remains disease-free after 6 months. Understanding the histopathological features and clinical presentation of primary TL-LGNPPA is crucial for pathologists to avoid misdiagnosis and guide appropriate management of the patients.

**Terminal Deoxynucleotidyl Transferase Expression in Sebaceous Cells and Tumors With Sebaceous Differentiation**

*Poster No. 38*

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**Context:** Terminal deoxynucleotidyl transferase (TdT) is an intranuclear DNA polymerase that has been considered a characteristic feature of lymphoid precursor cells, functioning as a somatic mutagen, participating in the immunoglobulin and T-cell receptor gene rearrangements. The present study was conducted to investigate TdT expression in benign and neoplastic cells with sebaceous differentiation. Understanding the extent of TdT expression in nonhematopoietic cells is crucial as many pathologists rely on the expression of TdT to categorize the cells to be of hematopoietic origin.

**Design:** Twenty-six cases, including benign and neoplastic cells with sebaceous differentiation in various tumors, were stained for TdT using the anti-TdT mouse monoclonal primary antibody (EP266; Agilent-Dako, Santa Clara, California). A peroxidase-labeled secondary antibody (EnVision/HRP system; Agilent-Dako) was applied for antigen visualization. TdT expression was considered positive if expressed in the nucleus. The intensity of TdT expression was categorized from 0 to 3+.

**Results:** The selected cases yielded 15 benign and 14 malignant sebaceous proliferations. All 15 benign cases showed 1- to 2+ TdT nuclear staining (Figure 4.38, A and B). Furthermore, 6 of 14 cases (43%) of malignant neoplastic proliferations (sebaceous carcinoma and poorly differentiated carcinomas with variable sebaceous differentiation) showed 1- to 3+ TdT nuclear staining (Figure 4.38, C and D).

**Conclusions:** Our study confirms the expression of TdT in cells with sebaceous differentiation. Understanding the extent of TdT expression in nonhematopoietic tumors can prevent misinterpretation of rare lesions of epithelial origin expressing TdT.

**Identification of NTRK Fusion in Tumors From Various Organs by Immunohistochemical Assay With Pan-Trk (Epr17341) Monoclonal Antibody**

*Poster No. 39*

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**Context:** A recent study reported that immunohistochemical stain (IHC) for pan-TRK demonstrated the sensitivity of 96.2%, 100%, and 79.4% for the detection of NTRK1, NTRK2, and NTRK3, respectively, when compared with molecular testing (Solomon JP, et al. *Modern Pathology* 2020;33:38–46). After the US Food and Drug Administration approval of Larotrectinib, the detection of NTRK fusion in many late-stage cancers have become a standard part of management.

**Design:** IHC analysis was performed on 1363 cases of malignant tumors on tissue microarray sections from central nervous system/glioblastoma (n = 23), gynecologic (n = 244), lung (n = 228), mesothelioma (n = 17), thyroid (n = 85), gastrointestinal tract (n = 159), genitourinary tract (n = 440), head and neck (n = 49), salivary gland (n = 18), hepatobiliary (n = 49), melanoma (n = 32), neuroendocrine skin carcinoma (n = 28). The results were recorded as positive when more than 1% of tumor cells to be positively stained. Only 33 tumors demonstrated positivity. Three cases of secretory carcinoma of the parotid with molecular testing positive for ETV6-NTRK3 fusion on routine tissue sections were also included.

**Results:** Two cases of salivary secretory carcinoma from routine tissue sections showed diffuse nuclear positivity for pan-TRK. A small range of tumors (33 of 1363) demonstrated cytoplasmic positivity for pan-TRK as listed in the Table. The remaining tumors mentioned in the design were negative.

**Conclusions:** We expand the list of tumors that may be positive for NTRK fusion protein by IHC. The high diagnostic sensitivity, cost-effectiveness, and rapid turnaround time, the monoclonal antibody (EPR17341) may potentially be used as a screening marker to rule in NTRK positive tumors especially when DNA or RNA-based molecular testing is not available.

**Summary of Pan-TRK Positive Cases**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Total Positive Cases</th>
<th>0%–50% (1+/2+)</th>
<th>51%–75% (3+)</th>
<th>76%–100% (4+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phaeochromocytoma (n = 13)</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Glioblastoma (n = 23)</td>
<td>8</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Skin neuroendocrine Ca</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lung SCC (n = 99)</td>
<td>6</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Salivary gland Ca (n = 18)</td>
<td>9</td>
<td>2</td>
<td>0</td>
<td>7</td>
</tr>
</tbody>
</table>

**Small Round Blue Cell Tumors of the Sinonasal Tract: A Review of 29 Cases**

*Poster No. 40*

Shajia Rahman Ansari, MD (shajiarahman.ansari@bcm.edu); Ya Xu, MD. Department of Pathology, Baylor College of Medicine, Houston, Texas.

**Context:** The small round blue cell tumors (SRBCT) of the sinonasal tract are a heterogeneous group of tumors with diverse differentiation. Making an accurate diagnosis can be challenging due to overlapping histology of the SRBCT, especially in small biopsy specimens.
Design: We retrospectively reviewed our sinonasal tumors (including resections and biopsy procedures) from 2 large academic medical centers in the past 5 and 10 years, respectively. Clinical and demographic information was obtained from the electronic medical records.

Results: There were 29 cases of sinonasal SRBCT from 23 men (79%) and 6 women (21%), with ages ranging from 21 to 79 years. Of these, 9 extranodal NK/T-cell lymphomas were type (31%), 1 poorly differentiated carcinoma (3%), 1 sinonasal undifferentiated carcinoma (5%), and 1 extraskeletal Ewing sarcoma/primitive neuroectodermal tumor (3%). Based on these findings, we suggested an initial panel of immunostains for the workup of sinonasal SRBCT and provides a valuable starting panel of immunohistochemistry for workup, which preserves tissue for future ancillary and molecular testing. A high incidence of hematolymphoid malignancies might represent geographic–social determinants of the study population. A large-scale retrospective study is recommended to explore these determinants to narrow down the broad differential of sinonasal SRBCT.

Parapharyngeal Space Tumors: A Clinicopathologic Review
(Poster No. 41)

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Context: Parapharyngeal space neoplasms are rarely encountered during routine surgical pathology practice. They account for 0.5% of head/neck neoplasms. Owing to their rarity, we sought to assess the clinicopathologic characteristics of these neoplasms.

Design: The files at our institution from 1992 to 2020 were reviewed for parapharyngeal space lesions. All cases were included, and their clinical and pathologic data were collected.

Results: A total of 71 cases were identified, 42 females and 29 males. The mean age was 53 years, ranging from 21 to 79. Of these, 80% (57 of 71) were malignant—3 squamous cell carcinomas, 2 marginal zone lymphomas, 2 acinic cell carcinomas, and a case each of adenoid cystic carcinoma, chordoma, hemangiopericytoma, epithelial/mixed epithelial carcinoma, carcinoma in situ, adenoid cystic carcinoma, salivary duct carcinoma, and metastatic thyroid papillary carcinoma. Recurrence occurred in 21% (3 of 14) and 1.8% (1 of 57) of malignant and benign cases, respectively.

Conclusions: The most common lesions encountered in the parapharyngeal space were salivary gland tumors, consisting of 61% (43 of 71) of cases, with pleomorphic adenoma accounting for 81% (35 of 43) of them. Unusual tumors for this region such as meningioma and chordoma were also noted. A higher incidence of 59% (42 of 71) was observed in male patients. As our data suggest, most lesions in this region are benign, a watch-and-wait clinical approach might be considered rather than surgical intervention, especially in nonsymptomatic patients.

MAML2-Negative Oncocytic Mucoepidermoid Carcinoma of the Submandibular Gland: A Rare Neoplasm
(Poster No. 42)

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Mucoepidermoid carcinoma (MEC) is the most common salivary gland tumor. Oncocytic MEC is a rare variant. Only a few cases are reported involving mostly the parotid gland with only 4 cases reported in the submandibular gland. Mastermind-like 2 (MAML2) translocation is detected in approximately 66% of MEC and many oncocytic MEC. We present a rare case of MAML2-negative oncocytic MEC of the submandibular gland in a 73-year-old woman with an 11-month history of a left neck mass. Computed tomography revealed a large centrally necrotic left submandibular gland mass with a thick enhancing soft tissue rim. Fine-needle aspiration cytology confirmed malignancy. Left submandibular gland resection with marginal mandibulectomy and ipsilateral neck dissection was performed. Grossly, a circumscribed, solid-cystic tumor arising from the submandibular gland was identified. Microscopic examination revealed an infiltrative proliferation of oncocyes forming cords, nests, and sheets. Focally, a conventional mucoepidermoid carcinoma morphology with squamoid and intermediate cells (Figure 4.42, A) along with cysts lined by squamoid, intermediate, columnar, and rare vacuolated cells was present. Two ipsilateral cervical lymph nodes and mandible (Figure 4.42, B) were involved. Immunohistochemical stains demonstrated positivity for p63 (Figure 4.42, C), P40, mucicarmine (weak) (Figure 4.42, D), and weak and rare GATA 3 and CD56 positivity and negativity for CK7, TTF-1, thyroglobulin, calponin, S-100, and Pax-8 supporting our diagnosis. No rearrangement of the MAML2 gene on fluorescence in situ hybridization testing was identified, tested at 2 different centers. An awareness that MAML2 negative MEC exists will prevent misdiagnosis and incorrect treatment as many of its differentials are benign.
Pigmented Lesions in the Mucosa of the Head and Neck: A Clinical/Pathologic Review
(Poster No. 44)

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Context: Mucosal pigmented lesions in the head and neck region vary in their etiology and clinical significance. We present a retrospective study of these lesions with emphasis on their clinical and pathologic characteristics.

Design: The electronic medical system at our institution was reviewed for clinical/pathologic findings of mucosal pigmented lesions between January 1996 and July 2020.

Results: A total of 56 cases were identified. Of these, 30.4% were malignant melanomas, and 69.6% were benign pigmented lesions consisting of melanosis (36%), amalgam tattoo (41%), nevi (12.8%), and lentigo (10.2%). For melanoma, the age range was 28 to 100 years, the mean was 68.3 years and the female to male ratio was 2.4:1. Locations were as follows: sinonasal tract (47.1%), gingiva (17.6%), tongue (11.8%), tonsils (11.8%), palate (5.9%), and larynx (5.9%).

Benign pigmented lesions, the age range was 25 to 89 years, the mean was 68.3 years and the female to male ratio was 2.4:1. Locations were as follows: sinonasal tract (47.1%), gingiva (17.6%), tongue (11.8%), tonsils (11.8%), palate (5.9%), and larynx (5.9%).

Conclusions: Mucosal pigmented lesions of the head and neck have a broad differential diagnosis. In this study, most of these lesions (69.6%) were benign. The female to male ratio was 2.4:1 for malignant lesions and 1.05:1 for benign lesions. The most common location for mucosal melanomas was the sinonasal tract (47.1%) and for benign pigmented lesions was the oral mucosa (43.6%).

Oncocytic Lipoadenoma of the Parotid Gland: A Case Report and Focus on the Differential Diagnoses
(Poster No. 45)

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Biphasic lipomatous neoplasms of the salivary glands are extremely rare and most of them arise in the parotid gland. Oncocytic lipoadenomas are considered a histologic variant of these lesions, still to be included by the World Health Organization classification. The mean age is 58 years and usually presents with a slowly growing mass. Information to date support a benign nature with no risk of recurrence or metastasis. We present a 66-year-old woman with a history of multiple myeloma, when seen during follow-up a parotid nodule was palpated. An ultrasound-guided core biopsy specimen of the lesion showed a proliferation of cytologically bland oncocytic cells intermingled with adipose tissue. A superficial parotidectomy was performed and revealed a 2.7 x 2 x 1.6-cm well-circumscribed homogeneous white-yellow nodule. Histologically, the lesion was encapsulated (Figure 4.45, A and C) and composed by oncocytic cells with minimal atypia mixed with mature fat cells (Figure 4.45, B and D). No necrosis, vascular invasion, or mitosis were identified. The oncocyes expressed AE1/AE3, EMA and p63 in a basal cell distribution. Tumor cells were negative for smooth muscle actin and PAX8. A diagnosis of oncocytic lipoadenoma was made. No recurrence has been reported after 6 months. Diagnosis, particularly in core biopsy specimens, may be challenging because malignant oncocytic neoplasms invading the fat are in the differential diagnosis. However, lack of atypia and mitotic activity, as well as noninfiltrative growth (usually confirmed in the surgical excision) help to confirm the diagnosis. Other primary differential diagnoses include oncocytoma, Whartin tumor, and nodular oncocytic hyperplasia.
Fabry Disease of the Lacrimal Gland and Orbit
(Poster No. 47)

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Fabry Disease is a lysosomal storage disorder, classically owing to an X-linked deficiency in ceramide trihexosidase also called a-galactosidase A (a-Gal A). This deficiency leads to accumulation of glycosphingolipids in vascular endothelial lysosomes of the skin, kidneys, heart, brain, and other organs. World-wide incidence of Fabry disease estimated in the range of 1 in 40 000 to 117 000. Ophthalmologic manifestations have been described in the anterior segment and retina but rarely in the lacrimal gland. We present the case of a 26-year-old man presented with bilateral upper eyelid fullness from steatoblepharon, enlarged, prolapsed lacrimal glands, and dermatochalasis. He underwent bilateral blepharoplasties with lacrimal gland biopsy procedure and anchoring of the lacrimal gland to the superotemporal orbital rim. The lacrimal gland specimens were sent for electron microscopy, which consisted of acinar epithelial cells with glycosphingolipid intracytoplasmic inclusions (Figure 4.47). The patient had a history of Fabry disease with classical ophthalmic findings. Recent studies have demonstrated elimination of GB3 deposits from cells of blood vessels of conjunctiva after 6 months of treatment with enzyme replacement therapy (ERT). Our patient had ERT for the 7 years leading up to his presentation. It is unclear if these kinds of treatments would address or improve those with symptomatic lacrimal gland involvement. We believe this is the first report of histopathologic evidence of Fabry disease affecting the lacrimal gland.

Florid Myofibroblastic Proliferation Induced by Ruptured Ectopic Craniopharyngioma of the Sinonasal Region: Cause of Diagnosis Pitfall
(Poster No. 48)

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Primary ectopic craniopharyngiomas are very rare. We report a case occurring in the sinonasal region along with its potential major diagnostic pitfalls. A previously healthy 46-year-old man presented with 3-weeks history of severe right sided epistaxis. Imaging studies revealed a 4.2-cm heterogeneous enhancing mass centered and in the right ethmoid and superior/middle nasal passages. The mass eroded into adjacent structures and invaded through the cribiform plate resulting in thickened dura. The sellar region and pituitary gland were normal. A biopsy specimen of the mass revealed a spindle cell proliferation embedded within a mostly hyalinized stroma with focal myxoid change. The spindle cells were atypical with prominent nucleoli, high nucleocytoplasmic ratio, and occasional mitoses. No atypical mitoses were noted. The immunostains, the spindle cells were positive for smooth muscle actin and negative for keratins, neural, melanocytic, and muscle markers. The diagnosis of sarcoma not otherwise classified was made. The patient later underwent resection of the mass. Histologic examination revealed a ruptured adamantinomatous craniopharyngioma with spillage of keratin into adjacent soft tissue triggering a florid and atypical myofibroblastic proliferation. Awareness of the possibility of ectopic craniopharyngioma resulting in florid atypical myofibroblastic proliferation is crucial to avoid erroneous diagnosis (Figure 4.48).

Epithelial Myoepithelial Carcinoma: An Unusual Histologic Presentation With Oncocytic Low Grade Features
(Poster No. 49)

Recep Nigdelioglu, MD (rcpnig@gmail.com); Hans Magne Hamm vag, MD; Alessa P. Aragao, MD; Swati Mehrotra, MD; Vijayalakshmi Ananthanarayanan, MD. Department of Pathology, Loyola University, Maywood, Illinois.

Salivary gland tumors are diverse with heterogenous histologic features and multiphenotypic differentiation. However, the classification of salivary gland tumors can be challenging without the utilization of appropriate immunohistochemical stains. We present the case of a 73-year-old man presenting with a right parotid mass. His cytology specimen showed salivary gland neoplasm of uncertain potential. The histologic sections of the tumor showed a nodular, well-circumscribed
oncocytic mass without significant nuclear atypia, no perineural invasion, or infiltrative pattern (Figure 4.49, A, H&E). Areas of tubulo-trabecular proliferation and biphenotypic differentiation were present, best appreciated with the use of immunostains. Myoepithelial component is highlighted by keratins, S100 (Figure 4.49, B), SMA (Figure 4.49, C), p63 (Figure 4.49, D), and calponin. Oncocytic luminal cells are positive for SOX10 and cytokeratins. P53 shows wild-type staining pattern. Overall, these findings support a final diagnosis of oncocytic epithelial myoepithelial carcinoma (EMCA) with low-grade features. Oncocytic EMCA is an extremely rare variant of salivary gland neoplasm and should be considered in the differential diagnosis of oncocytic salivary gland neoplasms. The use of myoepithelial/basal cell markers are often helpful in reaching the correct diagnosis in challenging cases, as demonstrated in this case. In addition, the concentric perinodular pattern of sclerosis seen in EMCA is somewhat distinct from the central scar in oncocytomas.

Social Media With Cytopathology Highlights
(Poster No. 50)

Swati Satturwar, MD1 (spalikondawar@gmail.com); Xiaoyin “Sara” Jiang, MD2; Maren Fuller, MD; Samer Khader, MD; Liron Pantanowitz, MD, MHA.1,4 Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; 2Department of Pathology, University of Michigan, Ann Arbor; 3Department of Pathology, Texas Children’s Hospital, Houston; 4Department of Pathology, University of Michigan, Ann Arbor.

Context: Social media makes it possible to easily reach millions of people. These platforms have become a popular way for medical professionals to network, market, educate, and share challenging cases. Not surprisingly, there are many social media posts about cytopathology. Our aim was to evaluate such cytology social media posts to determine the quality of this online content.

Design: A retrospective review of 400 cytology posts on different social media platforms (Facebook n = 133, Instagram n = 134, Twitter n = 134) was undertaken. The hashtags #cytopathology, #cytology, #cytopath, #FNA, #FNAFriday, and #Pap were used to search for cytology-related posts. Data collected included account information (individual versus institutional, country, followers), post details (patient identifiers, case type, cytology preparations, images, reason for post, diagnosis), and reactions (likes, retweets/shares, comments).

Results: These data are summarized in the Table. Nongynecologic cytology comprised the most common case type, followed by exfoliative, and gynecologic cases. The most frequent posts overall were thyroid fine-needle aspirations. Most popular posts were interactive cases (questions followed by answers/mystery cases) and those with histopathology correlation. While patient-protected health information was not revealed in these posts, 2 cases on Facebook did partially reveal a patient’s face.

Conclusions: Social media has become a popular global platform for cytopathology education and seeking informal consultation for challenging cytology cases. Facebook was used primarily for consults, whereas Twitter and Instagram included mostly educational posts. The educational content posted contained many informative images and was of excellent quality. The high number of followers, likes, and post comments indicates the extensive reach social media can have in cytopathology.

<table>
<thead>
<tr>
<th>Evaluated Parameter</th>
<th>Facebook</th>
<th>Instagram</th>
<th>Twitter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of posts</td>
<td>133</td>
<td>133</td>
<td>134</td>
</tr>
<tr>
<td>Average days since post</td>
<td>85 (range, 1–428)</td>
<td>141 (range, 1–485)</td>
<td>156 (range, 1–481)</td>
</tr>
<tr>
<td>USA versus International</td>
<td>International &gt; USA</td>
<td>Not reported &gt; USA</td>
<td>USA &gt; international</td>
</tr>
<tr>
<td>Person posting</td>
<td>Pathologist</td>
<td>Pathologist + others</td>
<td>Pathologist + others</td>
</tr>
<tr>
<td>Reason for post</td>
<td>Consult &gt; education</td>
<td>Education &gt; consult</td>
<td>Education &gt; consult</td>
</tr>
<tr>
<td>Number of followers</td>
<td>Range, 0–1121</td>
<td>Range, 0–1548</td>
<td>Range, 15–11300</td>
</tr>
<tr>
<td>Likes per post</td>
<td>42/post (range, 2–608)</td>
<td>109/post (range, 2–616)</td>
<td>51/post (range, 0–226)</td>
</tr>
<tr>
<td>Retweets/shares</td>
<td>20/post (range, 1–150)</td>
<td>2/post (range, 0–22)</td>
<td>4/post (range, 0–70)</td>
</tr>
<tr>
<td>Post comments</td>
<td>0</td>
<td>0</td>
<td>21/post (0–102)</td>
</tr>
<tr>
<td>Image number per post</td>
<td>12/post (range, 1–104)</td>
<td>3/post (range, 1–10)</td>
<td>3/post (range, 1–22)</td>
</tr>
<tr>
<td>Image quality</td>
<td>Poor &gt; good</td>
<td>Good &gt; poor</td>
<td>Good &gt; poor</td>
</tr>
<tr>
<td>Concurrent histology</td>
<td>1.5%</td>
<td>15.0%</td>
<td>15.6%</td>
</tr>
<tr>
<td>Final diagnosis provided</td>
<td>13%</td>
<td>100%</td>
<td>87%</td>
</tr>
</tbody>
</table>

Medical Student Crash Course to Neoplastic Hematology: Video and Knowledge Assessment
(Poster No. 51)

Bradley Drumheller, MD (brdc5063@gmail.com); Dale Frank, MD. Department of Pathology and Laboratory Medicine, University of the Hospital of Pennsylvania, Philadelphia.

Context: The diagnosis of hematologic neoplasms is inherently challenging. Clinical features and morphologic terms are often vague and overlapping. Medical students struggle to understand overarching classification themes during their traditional introduction to these topics. The aim of this study was to mitigate these problems by developing an effective multimedia resource (“Crash Course”) for the self-directed learner.

Design: A quasiexperimental design was structured modeling Kern’s 6-step approach to medical education curriculum development. The
The Pathology Club of UWI (Poster No. 53)

Ann-Marie Ming Hon, BMedSc (annemariejmehon@gmail.com); Chalapathi Rao Adidam Venkata, MBBS, MD, DCP; Catherine Morris, MD; Alfredo Walker, MBBS, DM(Path).1 Departments of 1Clinical Medical Sciences, Faculty of Medical Sciences and 2Paracultural Sciences, Faculty of Medical Sciences, The University of the West Indies, St. Augustine, Trinidad and Tobago; 3Department of Pathology, Port of Spain General Hospital, Port of Spain, Trinidad and Tobago; 4Department of Pathology and Laboratory Medicine, Faculty of Medicine, University of Ottawa, Ontario, Canada.

Context: The Pathology Club of UWI (University of the West Indies) was established to foster Caribbean medical student interest in pathology and laboratory medicine (PALM) and provide support to those aspiring to specialize in PALM through mentorship, shadowing, and research opportunities across the Medical Faculties of the St. Augustine, Mona, and Cave Hill campuses.

Design: A constitution was prepared and submitted with supporting documents to The UWI Guild of Students. Official registration of the club was received on July 31, 2020 and the club was launched via an inaugural virtual event on August 6, 2020. Virtual activities and events highlighting various pathologies and fields of pathology are held weekly and monthly, respectively, and members participate in activities via WhatsApp, Instagram, and Facebook.

Results: The club has been a massive success and positive feedback has been received from club members and guests at virtual events. There are 265 members from the 3 campuses of The UWI with 241 students from St. Augustine, 22 from Mona, and 2 from Cave Hill. The club has 3 social media platforms with a total of 516 followers/subscribers. Instagram has 408 followers, Facebook 54 followers, and YouTube 54 subscribers.

Conclusions: The club has served to spark the interest of undergraduate medical students in PALM across the 3 campuses of the UWI. Many students have expressed interest in pursuing pathology and the activities, initiatives, and events have effectively served to highlight the scope of PALM and inspire students to pursue careers in PALM.

A Unique “Platoon” System Utilizing Digital Pathology to Continue Surgical Pathology Trainee Education During the COVID-19 Pandemic (Poster No. 54)

Sayak Ghatak, MD, PhD (ghatak003@umn.edu); Daudo Arif, MD; Mahmoud Kahlifa, MD, PhD; Michelle Dolan, MD. Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis.

Context: The COVID-19 pandemic has impacted every aspect of the healthcare sector in the United States. This abstract was aimed at assessing the impact on pathology residency education at an academic center in the state of Minnesota during the governor’s stay-home-order (executive orders 20-20, 20-33) in March 2020.

Design: With the restriction on elective surgeries (executive order 20-09), the surgical pathology leadership decided to convert to a “platoon”-based rotation system due to increased COVID-19 burden and decreasing surgical case volume. Fifteen pathology residents were divided into 3 equal groups, and each group rotated through surgical pathology every 3 weeks. During each “platoon week,” the surgical
Coping With the COVID-19 Pandemic: How a Master’s in Clinical Laboratory Sciences Program Adapted Through Modification of Existing Resources

(Poster No. 55)

Debbie Isabella; Carol A. Carbonaro, PhD; Faisal M. Huq Ronny, MD, PhD (faisal@nymc.edu). Department of Pathology, Master’s in Clinical Laboratory Sciences Program, New York Medical College, Valhalla.

Context: In March 2020, the governor of New York issued an executive order requiring nonessential businesses closed and limiting any concentration of individuals outside their home, to prevent the spread of SARS-CoV-2. Closure and social distancing requirements resulted in suspension of classroom instruction and laboratory training at hospitals for this Master’s in Clinical Laboratory Sciences program. Adaptation through modification of available teaching modalities allowed uninterrupted learning and may serve as a model for future crises.

Design: Teaching modalities included remote instruction, laboratory simulations, self-directed learning, and on-site training in clinical and academic laboratories emphasizing maintenance of social distancing.

Results: In Spring 2020, lectures switched to the Zoom platform and exams to an online learning platform. Students could not continue at hospital laboratories to conserve personal protective equipment (PPE). With temporary New York State Department of Education approval, self-directed learning, Medialab courses, Medialab Simulator slide review, and YouTube videos substituted for hands-on activities. Assessments were similar to those given students before the executive order. In Fall 2020, lectures remained remote. Clinical internship training resumed after a delay; supplementation continued, as described. As each hospital accepted students, the school supplied each with PPE. Introduction to clinical laboratory science, including a wet lab, was held in a lab for 25 students and 2 instructors, limited to 9 students and 2 instructors with face masks. Students acclimated to modifications described.

Conclusions: The real-time need to deliver laboratory science education during a time of statewide closure using available teaching modalities resulted in uninterrupted academic and clinical training. This novel form of modified education may be considered in new curricula development.

Health Law During COVID-19: An Introductory Course for Medical Students and Pathology Residents

(Poster No. 56)

Robert J. Christian, MD, MS (chrisrob@ohsu.edu); Ken M. Gatter, JD, MD. Department of Pathology, Oregon Health & Science University, Portland.

Context: COVID-19 has brought local, state, and federal public health responses to our attention. This abstract describes a seminar, Health Law during COVID-19, for medical students and pathology residents at a major academic teaching hospital and assesses its effect on participants’ knowledge of various aspects of public health law in the United States, including how law can impact Social Determinants of Health.

Design: Health Law during COVID-19 encompassed 5 sessions, each consisting of a prerecorded lecture viewed at a convenient time, followed by a small group discussion. Topics covered included state and federal legislative and judicial power, constitutional law, administrative law, relevant appellate decisions, and Social Determinants of Health (Table). Federalism and the balance between government authority and individual rights were common threads throughout the course. Course evaluations were sent to medical student participants, and pre- and postcourse questionnaires sent to resident participants to assess their knowledge of health law both before and after the course.

Results: A total of 17 medical students and 4 residents attended 1 of 3 Health Law during COVID-19 courses. Medical student reactions to the class were positive and outperformed the undergraduate medical education department average, though not significantly (mean 5.48 versus 5.16, SD 0.68). Residents performed better on postcourse questionnaires (mean 100%) compared to precourse questionnaires (mean 78%).

Conclusions: Our data show the Health Law and COVID-19 course to be both engaging and effective for teaching trainees, including pathology residents, public health law while helping them identify potential avenues to address upstream Social Determinants of Health as physicians.

Abbreviated Course Syllabus, Including Weekly Course Topic and Correlating Discussion Points

<table>
<thead>
<tr>
<th>Weekly Course Topic</th>
<th>Abbreviated Health Law During COVID-19 Course Syllabus</th>
</tr>
</thead>
<tbody>
<tr>
<td>State of emergency</td>
<td>COVID-19 around the world: lock-downs, military-enforced curfew, mass surveillance</td>
</tr>
<tr>
<td>Jacobson v Massachusetts, 1905</td>
<td>Constitutional protections</td>
</tr>
<tr>
<td>COVID-19 and social determinants of health</td>
<td>Disparate impact on particular groups, within and outside healthcare settings</td>
</tr>
<tr>
<td></td>
<td>Possible approaches to solutions including personal, professional, and institutional strategies</td>
</tr>
<tr>
<td></td>
<td>Discussion about legal issues for an explicitly race cognizant vaccine rollout plan</td>
</tr>
<tr>
<td></td>
<td>(Message: How broadly SDOH expand outside the hospital, clinic and laboratory doors, and law’s impact on SDOH)</td>
</tr>
</tbody>
</table>
A Comprehensive Audiovisual Specimen Grossing Tool for Pathology Education
(Poster No. 57)
Tahmina Sultana, MD (tahmina.sultana@mail.mcgill.ca); Jonathan K. Lai, MD, MSc; Ayesha Baig, MD; Oluymii Ajise, MD; Zu-hua Gao, MD. Department of Anatomical Pathology, McGill University, Montreal, Quebec, Canada.

Context: Specimen handling and grossing are critical steps for achieving accurate diagnosis. Despite the existence of published specimen grossing manuals, the standardized operating procedures for grossing surgical specimens still vary among institutions. Our goal was to develop specimen grossing videos for commonly encountered surgical specimens to educate our residents and pathologist assistants, which will eventually benefit our patients.

Design: Based on service volume and specimen complexity, we selected commonly encountered surgical specimens in each pathology subspecialty at McGill University Health Centre. For every specimen, the script for the video was edited by a staff pathologist and the grossing procedure was performed by an experienced resident. We used high-definition cameras, appropriate lighting, and voice-over technology to make fine adjustments of the films.

Results: We produced 9 high-quality grossing videos. Each video was followed by a quiz style discussion on the differential diagnoses and associated syndromes of the entities, including renal cell carcinoma, gastrointestinal adenocarcinoma, germ cell tumors, hepatic tumors, and dermatologic neoplasm. These videos were made available to all our residents and pathologist assistants within our department.

Conclusions: Based on the comprehensive outcome of this project, these videos have proven to be a great teaching tool and expand resident learning rather than traditional lecture formats and aims to increase student engagement and comprehension. Cytopathology and surgical pathology at our institution has followed a traditional model in which classroom time is focused on active engagement and education by allowing residents to independently problem solve, actively learn, and present cases to their faculty. The ability to support the treatment of severely ill COVID-19 patients.

Flipped Sign Out in Anatomic Pathology Education
(Poster No. 59)
Byron Barksdale, MD (barks20@gmail.com); Ayseun Keske, MD; Kaillin Sundling, MD, PhD; Megan Fitzpatrick, MD. Department of Pathology and Laboratory Medicine, University of Wisconsin Hospitals and Clinics, Madison.

Context: A flipped classroom is an evidence-based pedagogic approach to learning in which classroom time is focused on active learning rather than traditional lecture formats and aims to increase student engagement and comprehension. Cytopathology and surgical pathology at our institution has followed a traditional model in which residents preview cases followed by a faculty-led sign out. A flipped sign out approach was introduced to enhance resident engagement while facilitating physical distancing during the COVID-19 pandemic, and a short survey was given to residents to assess their experience.

Design: Flipped sign out for the purposes of our survey is defined by the trainee driving the microscope and presenting the case information, diagnostic areas, and questions to the attending, after the resident has their experience. 19 pandemic, and a short survey was given to residents to assess their experience.

Conclusions: Having in-house plasma collection allowed Nuvance Health to effectively collect convalescent plasma and distribute it to patients as necessary. We were prepared to meet future uncertain needs early in the pandemic.
Implementing a Virtual Cytology Rotation During the COVID-19 Pandemic
(Poster No. 60)
Byron Barksdale, MD1 (bbarks20@gmail.com); Aysenur Keske, MD2; Kaityl Sundling, MD, PhD2; Megan Fitzpatrick, MD1; Joshua Faulkes2; Marie Daleo, MD, PhD1; Kaitlin Sundling, MD, PhD1; Megan Fitzpatrick, MD1; Joshua Faulkes2; Marie Daleo, MD, PhD1; Mary Kate Krause.1 Department of Hygiene, Madison. and Clinics, Madison;2Department of Cytology, Wisconsin State Lab of Pathology and Laboratory Medicine, University of Wisconsin Hospitals and Clinics, Madison.

Context: The COVID-19 pandemic brought many challenges for teaching pathology residents, as traditional sign out at a multihheaded microscope did not adequately allow for optimal physical distancing. Balancing the risks of potential COVID-19 exposure with the benefits of in-person clinical experiences required innovative practices. To enhance resident and faculty/staff education and safety, a virtual cytology rotation was developed for postgraduate year 1 residents. This teaching approach was not only fill this gap but also serve as the nidus for a formalized pathology education program.

Results: Resident performance in the virtual rotation was comparable to that of the in-person rotation and had clear benefits. A narrative experience of our coauthor, a resident who completed the rotation, is described. Benefits of the virtual experience included greater independence with case interpretation, as well as more opportunities for self-reflection.

Conclusions: Implementation of a virtual cytology rotation was successful and comparable to in-person rotations. Independence was enhanced in this decentralized learning environment. In the future, virtual pathology rotations may offer a suitable, and even enhanced, alternative to in-person sign-out.

Virtual Teaching for International Pathology Trainees: A Silver Lining During the Pandemic
(Poster No. 61)
Sherrisse Sandy, MBBS; Aamy Roopnarine, MBBS; Chezaph Charles, MBBS; Melanie Johncilla, MD (mjohnci1@gmail.com). Department of Pathology, Port of Spain General Hospital, Port of Spain, Trinidad and Tobago.

Context: Pathology trainees from resource-restricted countries often lack a structured educational program. They rely primarily on learning at the microscope with pathologists. The COVID pandemic compromised education among trainees in 1 institution in Trinidad as pathologists worked from home. We hypothesized that virtual teaching would not only fill this gap but also serve as the nidus for a formalized pathology education program.

Design: One subspecialty trained pathologist was asked by trainees to prepare weekly 1-hour lectures for their group of 5 in April 2020. Teaching sessions were organ-system based. Using a constructivist teaching approach, the 4-week cycle began with an overview of features of the organ system, followed by pattern-based approaches of evaluation, to ancillary testing. For the fourth week, the students were sent web-based scanned unknown slides or images and presented on assigned entities. This teaching approach contained redundancies to allow for cumulative learning.

Results: Most lectures were delivered by 1 pathologist during the 10-month period with occasional guest lectureships from subspecialty trained pathologists. There was full trainee participation throughout the sessions. Accuracy among unknown cases began at 60%. There was an increase to 80% over the last 4 cycles. Three of the 5 trainees also participated in research projects. Virtual teaching will continue with added participation from invited US, Canada, and in-country pathologists.

Conclusions: These sessions led to the development of a structured educational program in this resource-restricted institution. This trainee-driven, constructivist theory–based initiative can be used as a model to fill knowledge gaps among trainees at similar institutions.

Trainee Wellness During the COVID-19 Pandemic: An Institutional Experience
(Poster No. 62)
Alice Dobi, MD1 (dobi.alice@gmail.com); Christopher Julien, MD1; Rifat Mannan, MD.1 2Department of Pathology, Pennsylvania Hospital, Philadelphia; 2Department of Pathology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia.

Context: The COVID-19 pandemic has put an increased strain on the physical and mental well-being of residents. We sought to share our experience during this difficult period.

Design: Our residency program has undertaken several wellness initiatives to support trainees. A questionnaire was distributed to the residents to evaluate their experience.
**Resident Wellness Survey**

<table>
<thead>
<tr>
<th>Questions</th>
<th>Response (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. In which of the following areas did you feel adequately supported by the program? (Check all that apply)</td>
<td>Personal physical health (75). Personal mental health (50). Access to PPE (100). Access to testing if needed (75). Protection from getting infected with COVID-19 (88). rotations for every student were canceled; the pathology rotation was identified as a requirement if a virtual online pathology rotation were created. Owing to the COVID-19 pandemic, all in-person</td>
</tr>
<tr>
<td>3. How satisfied are you with your program’s safety measures concerning COVID-19? Very satisfied (75). Satisfied (25). Neutral (0). Dissatisfied (0). Very dissatisfied (0)</td>
<td></td>
</tr>
<tr>
<td>4. How did the quality of training and education at your program change during the pandemic compared with the prepandemic period? Improved (57). Same as before (43). Worsened (0)</td>
<td></td>
</tr>
<tr>
<td>5. Which of the following sign out methods have been applied in your program during the pandemic? (Check all that apply)</td>
<td>In person “double-scoped” sign out wearing masks (38). In person “double-scoped” sign out wearing masks and across plexiglass barrier (88). Remote sign out using video conferencing software (such as Microsoft Teams) (100). In person sign out on a multiheaded microscope with social distancing and wearing masks (38). No in person/remote sign out with attending; preview and feedback only (38)</td>
</tr>
<tr>
<td>6. How safe do you feel with the sign out measures employed during the pandemic? Very safe (62). Safe (38). Neutral (0). Unsafe (0). Very unsafe (0)</td>
<td></td>
</tr>
<tr>
<td>7. Do you think adequate resources (on-line/in person) are available to help the trainees deal with stress or related issues (eg, counseling, therapy, etc.)? Strongly agree (25). Agree (50). Neutral (25). Disagree (0). Strongly disagree (0)</td>
<td></td>
</tr>
<tr>
<td>8. What are your sources of wellness and support during the pandemic? (Check all that apply) Family (100). Friends (75). The residency program and the department (62.5). Pets (38). Spirituality (25)</td>
<td></td>
</tr>
<tr>
<td>9. How satisfied are you with the residency program’s support during this crisis? Very satisfied (75). Satisfied (25). Neutral (0). Dissatisfied (0). Very dissatisfied (0)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: PPE, personal protection equipment.

**Results:** The wellness measures adopted by our program were as follows: (1) safety measures to protect from infection, including “platooning” of services during peak of pandemic (creating an “active” batch and a “reserve” batch, safe sign out methods, “online” didactics and conferences, and early vaccination for COVID-19; (2) monthly meeting with residents and program director to address concerns; (3) 2 mentorship programs, including resident–faculty mentorship and resident–peer mentorship; (4) financial assistance, including resident book award, meal coupon, and free monthly lunch; (5) lectures on importance of mental health and career planning; and (6) access to online/person professional counseling to deal with stress. Based on survey results (Table), the risk of acquiring COVID-19 infection and personal physical health were major concerns of our trainees. Nobody acquired COVID-19 infection and all felt satisfied with the safety measures. The quality of training and education during the pandemic either improved (57%) or stayed the same (43%). The majority of residents felt that adequate resources have been provided to optimize their wellness and expressed overall satisfaction with the support from residency program.

**Conclusions:** The pathology residency program was able to create a satisfying environment for the residents prioritizing the safety and well-being of the trainees during the pandemic.

**Converting Pathology Elective to Virtual Rotation on a Short Notice** (Poster No. 63)

Niti Manglik, MD; Ellen F. Dudrey, MD (ellen.dudrey@ttuhsc.edu). Department of Medical Education and Pathology, Paul L. Foster School of Medicine, Texas Tech Health Science Center El Paso.

**Context:** Pathology electives at our institution consist of rotations through the following anatomic and clinical pathology sections: histology/surgical pathology, blood bank, clinical chemistry, and microbiology. Students are expected to present a case during the elective. Owing to the COVID-19 pandemic, all in-person rotations for every student were canceled; the pathology rotation was identified as a requirement if a virtual online pathology rotation were created.

**Design:** Fourth year students needing electives were identified and online resources covering anatomic and clinical pathology were selected. Rotations were composed of a core group of resources used by all students and smaller portions were tailored to the students’ intended residency. Core resources included training in genomics, blood bank website (https://www.bbguy.org/), Wheater’s Functional Histology, https://www.webpathology.com, https://neuropathology-web.org/, and microscopic photos taken by pathology faculty. Faculty and students met at regular intervals using the Webex platform to discuss material and answer questions. Students were graded using questions/quizzes pertinent to the course materials. Each student gave a virtual case presentation tailored to their area of interest.

**Results:** Verbal feedback from the students at the end of the rotation was very positive. Students indicated that they thought the information provided during the rotation would benefit them in their training programs.

**Conclusions:** An online pathology elective was created on short notice. The elective included elements from both anatomic and clinical pathology and was tailored to students’ interests.

**A Rare Case of Intraventricular Myxoid Mesenchymal Tumor With EWSR1-ATF1 Fusion** (Poster No. 64)

Harsihata Mehrotra, MD (hmehrota1@fhhs.org); Abhir Mukherjee, MD; Laura Favazza, DO. Department of Pathology, Henry Ford Health System, Detroit, Michigan.

A 37-year-old woman presented with history of dizziness, blurry vision, and headaches for 7 months. Brain magnetic resonance imaging revealed a well-circumscribed, lobulated, enhancing 2.9-cm mass in the upper atrium of left lateral ventricle with vasogenic edema and mild rightward midline shift. Four additional areas of enhancement were noted suspicious for leptomeningeal dissemination. She underwent a left parietal craniotomy with near gross total resection. The tumor was very positive. Students indicated that they thought the information provided during the rotation would benefit them in their training programs.

**Conclusions:** An online pathology elective was created on short notice. The elective included elements from both anatomic and clinical pathology and was tailored to students’ interests.

**A Rare Case of Intraventricular Myxoid Mesenchymal Tumor With EWSR1-ATF1 Fusion**

Ellen F. Dudrey, MD

Tumor With EWSR1-ATF1 Fusion

Abstracts
Laboratory Medicine and Pathology, Mayo Clinic Florida, Jacksonville; Arch Pathol Lab Med

Abstracts

DO1; Jorge Torres-Mora, MD2; Mark E. Jentoft, MD. 11 Department of brain radiotherapy. now clinically stable 6 months postoperation and undergoing whole brain radiotherapy.

Intradural Schwannoma of Lumbar Spine With Abundant Psammomatous Calcifications

(Poster No. 65)

Justin T. Snow, MD1 (snow.justin@mayo.edu); Tracy R. Schachner, DO1; Jorge Torres-Mora, MD2; Mark E. Jentoft, MD.1 1Department of Laboratory Medicine and Pathology, Mayo Clinic Florida, Jacksonville; 2Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota.

Schwannomas are benign nerve sheath tumors that develop from differentiated Schwann cells that myeline peripheral nerves, cranial nerves, and spinal cord nerve roots. Degenerative changes in schwannomas are common and can include cystic degeneration, hemorrhage, ancient change, dystrophic calcifications, and, rarely, ossification. Psammomatous calcifications are rare in schwannomas and may raise concern for melanotic schwannoma (malignant melanotic nerve sheath tumor). We report a case of a 19-year-old woman who was found to have an incidental 2.4-cm intradural lumbar lesion on imaging. Surgery was performed that revealed a grossly lobulated, pink-tan soft tissue mass that microscopically showed classical schwannoma morphology (Figure 4.65, A, original magnification ×100), hyalinized vessels, cystic degeneration, hemorrhage, and ancient change; however, scattered throughout tumor were numerous psammomatous calcifications (Figure 4.65, B, original magnification ×100). No melanin pigment, epithelioid cytomorphology, lacy or granular dystrophic calcifications, or ossification were seen. An immunohistochemical stain for S100 was diffusely positive (Figure 4.65, C, original magnification ×100) while HMB-45, Melan-A, epithelial membrane antigen, and PR were negative. A PRKAR1A immunostain (which can be lost in melanotic schwannoma) showed retained expression (Figure 4.65, D, original magnification ×100). These findings supported the diagnosis of schwannoma with psammomatous calcifications. While calcifications can often be seen in schwannomas, they are very rarely psammomatous calcifications; a finding that may raise suspicions for meningioma or melanotic schwannoma. Evaluation for melanin pigment and epithelioid cytomorphology, in addition to application of immunostains to assess for meningotheelial and melanocytic differentiation, can be useful to arrive at the correct diagnosis.

A Rare Case of Polymorphous Low-Grade Neuroepithelial Tumor of the Young With Focal High Grade Features

(Poster No. 66)

Isma Perveze, MD1 (pervezei@health.missouri.edu); Sahibu Sultan Habeebu, MD2; Melissa Gener, MD. 2 1Department of Pathology, University of Missouri, Columbia; 2Department of Pathology, University of Missouri, Kansas City.

Polymorphous low grade neuroepithelial tumor of the young (PLNTY) is a morphologically and molecularly distinct tumor that has been described in recent literature. We describe a rare case of PLNTY with focal high-grade features, which is the first such case reported in the literature to our knowledge. A 14-year-old adolescent boy presented with treatment resistant epilepsy. Imaging revealed a 3-cm temporal lobe lesion with calcifications. The patient underwent surgical resection of the lesion and interestingly varied tumor morphologies were seen in different areas of the neoplasm. Specifically, there were areas with oligodendroglioma-like features along with areas showing ganglioglioma-like, diffuse astrocytoma-like, and pleomorphic xanthoastrocytoma-like morphologies within the same tumor. Immunohistochemical staining was significant for intense positivity for CD34 in tumor cells. While the Ki-67 positivity was low (1%) in majority of the tumor cells, there were foci with pleomorphic cells, higher mitotic count, and proliferation index of up to 20%. Molecular studies revealed BRAF V600E mutation along with CDKN2A and CDKN2B deletions. IDH-1 mutation and 1p/19q co-deletion were not identified, thus establishing a diagnosis of PLNTY. PLNTY is a newly described entity and the few cases reported so far in literature categorize it as a low-grade tumor. The novel finding of focal high-grade features described in this case raises the possibility of it being a more aggressive tumor. Given the extremely limited literature available about PLNTY, this case with its unusual high-grade features should help in better characterization and appropriate management of this rare entity.

Intramusosal Schwannoma of the Distal Ulna

(Poster No. 67)

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A 27-year-old man with no known past medical history presented to Los Angeles County + USC Medical Center with left hand pain for more than 10 months. Magnetic resonance imaging demonstrated a 3.2 × 1.3 × 3.8-cm contrast enhancing mass involving the ulnar distal diaphysis with extension through the cortex and into the surrounding soft tissue. The differential diagnosis included benign and malignant entities, such as an aneurysmal bone cyst and telangiectatic osteosarcoma. Multiple biopsies using rapid on-site cytologic evaluation were performed. Touch preparations revealed bland spindled cells and scattered degenerating cells (Figure 4.67, A). Histologic examination of the formalin-fixed, paraffin-embedded tissue cores revealed a benign spindle cell proliferation with predominantly Antoni A pattern morphology and Verocay bodies (Figure 4.67, B). There were focal areas of papillary endothelial hyperplasia. Increased mitotic activity and tumor necrosis were not identified. Tumor cells were strongly positive for S-100, CD34 highlighted endothelial cells, and Ki-67 was less than 3% (Figure 4.67, C and D). This is a unique case of an intramusosal schwannoma, adding to the limited number of reported cases in the
literature, and the first case report of a schwannoma involving the distal ulna. Most schwannomas do not involve bone. Those that do, however, can be easily mistaken for other types of bone tumors due to the rare nature of this entity. The purpose of this case report was to increase awareness of a specific type of destructive lesion within the distal forearm to help guide diagnosis and improve future patient outcomes.

Central Nervous System-Type Neuroepithelial Tumor Arising From an Immature Teratoma in a Pediatric Patient: A Rare Case Presentation

(Poster No. 68)

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Immature ovarian teratomas (IOTs) are a relatively common subset of ovarian tumors, comprising 10% to 20% of ovarian malignancies within the first 2 decades of life. When immature neural tissue is found within the IOT, it may display various amounts of maturation; but development of central nervous system tumors arising from immature neural elements is exceedingly rare. We describe a case of a central nervous system (CNS)-type neuroepithelial tumor arising in association with IOT. The patient is a previously healthy 8-year-old girl who presented with abdominal pain of 3-days duration. Computed tomography demonstrated a 15-cm left ovarian cystic mass favored to represent an ovarian teratoma. The patient underwent unilateral oophorectomy. Histologic examination of the specimen showed tissue types of all three germ layers, including retinal, adipose, chondroid, and squamous type tissues (Figure 4.68, A). The majority of the sections displayed immature cerebellar tissue with areas of hypercellular, mitotically active glial tissue with foci of palisading necrosis concerning for an adult-type CNS tumor (Figure 4.68, B and C). Immunohistochemical staining for glial fibrillary acidic protein was negative, while synaptophysin and NeuN showed diffuse positivity (Figure 4.68, D), suggesting a neurocytoma-like tumor. Few reports have described these adult-type CNS tumors in association with IOTs, and we believe this is of the youngest patients to be reported. In the handful of cases reported with follow-up, patients were alive with no evidence of disease at 33 months. This case highlights a rare entity presenting in a young patient with good surgical outcomes.

Intradural Extramedullary Hemangiopericytoma of the Thoracic Spinal Cord: Report of a Rare Case

(Poster No. 69)

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Meningeal solitary fibrous tumor (SFT)/hemangiopericytoma (HPC) is a rare and typically dural-based neoplasm that represents <1% of primary central nervous system tumors. Since SFT and HPC share the same genetic alteration, fusion of the NAB2 and STAT6 genes at the 12q13 locus, they are classified as 2 distinct histologic phenotypes within the same entity. Nuclear expression of STAT6 by immunohistochemistry is highly sensitive and specific for SFT/HPC. Unlike SFT (grade I), HPC is a malignant neoplasm and behaves more aggressively. It is graded based on the mitotic count per 10 hpf as grade II (<5 mitoses) and grade III (>5 mitoses). Adjuvant radiotherapy improves survival in patients with HPC. The majority of cases are supratentorial, with spinal SFT/HPC comprising approximately 10% of cases. We present a rare case of intradural extramedullary hemangiopericytoma (grade III) of the thoracic spinal cord. An 81-year-old woman presented with progressive weakness and loss of sensation in both legs. Magnetic resonance imaging of the spine showed a 3.1-cm lobular, homogeneously enhancing intradural extramedullary mass at T11/T12 with cord compression. The patient underwent surgery to remove the mass. Grossly, the mass was composed of white-pink rubbery tissue. Histology revealed a cellular tumor with marked nuclear pleomorphism and up to 8 mitoses per 10 hpf (Figure 4.69, A). On immunohistochemistry, tumor cells were positive for CD34 (Figure 4.69, B), CD99 (Figure 4.69, C), and STAT6 (Figure 4.69, D). Meningeal hemangiopericytoma of the spinal cord is rarely encountered. Correct diagnosis of HPC is crucial because patients benefit from adjuvant radiotherapy.
**Multifocal Epstein-Barr Virus–Associated Smooth Muscle Tumor of the Brain: An Unusual Presentation**

*(Poster No. 70)*

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Epstein-Barr virus (EBV) is known for its oncogenic potential in a wide variety of cell types. Believed to arise from EBV-infected myogenous cells of the blood vessel walls, EBV-associated smooth muscle tumor (EBV-SMT) is an exceedingly rare tumor that occurs in severely immunocompromised patients. While most cases present with a solitary mass, multifocal, synchronous lesions have been documented. We present an unusual case of multifocal EBV-SMT in the central nervous system in a HIV+ patient as the primary clinical manifestation.

The patient is a 30-year-old woman, with a history of congenital HIV infection and uterine fibroid, who presented to the emergency department due to rapidly progressive right-sided weakness. Imaging studies demonstrated a 2.6-cm, well-circumscribed intradural extramedullary mass compressing the upper cervical spinal cord as well as a 1.8-cm dural-based mass in the right frontal lobe (Figure 4.70, A). Both masses were resected and showed very similar histopathology. Microscopic examination showed highly cellular, monotonous spindle cell proliferations with variable vascularity. The cells exhibited eosinophilic cytoplasm, ovoid to elongated nuclei, and inconspicuous nucleoli (Figure 4.70, B). Mitotic figures were easily identified. Immunohistochemical staining showed the tumor to be positive for smooth muscle actin (Figure 4.70, C). Additional stains were negative for S100, glial fibrillary acidic protein, epithelial membrane antigen, STAT-6, and CD99, ruling out the more common spindle cell neoplasms in the central nervous system. The Epstein-Barr encoding RNA in situ hybridization stain was diffusely positive (Figure 4.70, D). As such, the diagnosis of multifocal EBV-SMT was made.

**Chordoid Meningioma of the Clivus: A Great Mimicker and Diagnostic Pitfall**

*(Poster No. 71)*

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Meningioma is the most common neoplasm occur in the central nervous system. It typically appears as a distinct, well-circumscribed dural-based mass that occurs on the surface of the brain or spinal cord. Imaging study are highly accurate in diagnosing meningioma. When tumors occur at uncommon anatomic sites; however, histopathologic characterization plays an important role in determining definitive diagnosis and prognosis. We present a case of chordoid meningioma of clivus that can be mistakened confused with other clival tumors, such as chondrosarcoma and chordoma. The patient is a 51-year-old woman with a remote history of nasopharyngeal carcinoma, status post resection and radiotherapy. She presented to emergency department for slurred speech and tongue deviation. Magnetic resonance imaging of the brain revealed a 2.4-cm mass originating from the clivus and extending downward through the foramen magnum (Figure 4.71). The mass was resected, and microscopic examination revealed the tumor was composed of cells forming clusters and cords within abundant mucinous background. The tumor cells are spindled to epithelioid in shape, with moderate amount eosinophilic cytoplasm and bland nuclei. While focal areas of the tumor were reminiscent of meningioma, this was not a typical location nor histologic feature. Immunohistochemical stains showed the tumor cells to be positive for epithelial membrane antigen, progesterone receptor, and somatostatin receptor 2A, while negative for S100, cytokeratin, and brachyury. An Alcian blue histochemical stain strongly highlighted the background mucin. Consequently, the case was signed out as chordoid meningioma, World Health Organization grade II.

**Glioblastoma With Rhabdoid Features: A Rare and Most Aggressive Variant of Glioblastoma**

*(Poster No. 72)*

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Glioblastoma, the most aggressive malignant primary brain tumor, has poor prognosis despite advances in multimodality treatment. Glioblastoma with rhabdoid features is rare and even more aggressive. Generally, not all glioblastoma with rhabdoid features is associated with mutation or deletion of the INI1 gene. We present an example of 57-year-old man, with prior excision of right temporal subtotally necrotic astrocytoma (2 months ago; glial fibrillary acidic protein and p53 positive, IDH1 negative) without follow-up, presented with new onset of right-hand numbness and tingling. Neuroimaging showed multiloculated cystic mass (6.6 × 4.3 × 4.9 cm) with vasogenic edema.
surrounding previous resection cavity in the right temporal lobe with midline shift and herniation. Histology of resection showed extensive diffuse necrosis with small areas of viable tumor showing high-grade, pleomorphic astrocytic cellularity, vascular endothelial proliferation (Figure 4.72, A) and several mitosis. Several areas in the viable tumor showed rhabdoid morphology characterized by large eccentric nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm (Figure 4.72, B). The viable tumor tissue was diffusely and strongly positive for glial fibrillary acidic protein (Figure 4.72, C). Ki-67 proliferation marker focally labelling up to 40%, epithelial membrane antigen was focally positive, synaptophysin/chromogranin were negative. Nuclear INI-1 stain was preserved (Figure 4.72, D). MGMT gene promoter methyl-ation was not detected. He received postoperative hyperfractionated radiotherapy with concurrent temozolomide. Unfortunately, within 2 months of surgery the patient died. In summary, glioblastoma with rhabdoid feature is a rare and very aggressive astrocytic tumor which may not show INI-1 loss as in our presented case.

**Dysplastic Cerebellar Gangliocytoma, Lhermitte-Duclos Disease, in Previously Undiagnosed Cowden Syndrome: Case Report and Review of the Literature**

(Poster No. 73)

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Dysplastic cerebellar gangliocytoma, also known as Lhermitte-Duclos disease (LDD), is a rare, unilateral hamartomatosus tumor most commonly occurring in the left posterior fossa. In adults, LDD presents almost exclusively in the setting of germline PTEN mutations (PTEN hamartoma tumor syndrome). We report the case of a 24-year-old man with no significant medical history who presented with headaches, “whooshing” sensation in his ears, and intermittent loss of vision in the right eye. Magnetic resonance imaging of the brain demonstrated hydrocephalus and a large, right posterior fossa mass concerning for LDD. Given his visual disturbance and degree of hydrocephalus the decision was made to surgically excise the right cerebellar mass. Microscopic evaluation revealed enlarged cerebellar folia (Figure 4.73, A) with a proliferation of atypical ganglion cells (Figure 4.73, B), consistent with dysplastic cerebellar gangliocytoma (LDD). Based on this diagnosis, he was referred for genetic testing, which identified a pathologic variant in the **PTEN** gene consistent with Cowden syndrome (CS). Screening for CS-associated malignancies identified a suspicious thyroid nodule, which was biopsied. This was consistent with multinodular goiter, a finding seen in up to 75% of CS patients. Despite this benign biopsy specimen, he will require close follow-up for thyroid and various other malignancies that patients with CS are at increased risk for developing. Our case demonstrates that although rare, LDD can be the initial manifestation of CS, a diagnosis that carries long-term clinical management and genetic counseling implications.

**Left, Middle Cerebral Artery Infarct in a Child With COVID-19 Infection and Multisystem Inflammatory Syndrome in Children**

(Poster No. 74)

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There are few reports of neurologic complications of SARS-CoV-2 infection in children. While the pathophysiology of acute stroke in children infected with COVID-19 remains unclear, some hypothesize a causal role for a hyperactive immune response in the development of neurologic injury. We present the case of a 3-year-old boy who was admitted with a 4-day history of acute gastrointestinal symptoms, fever, and rash, and who, at presentation, had a hypotensive shock, with mild left ventricular myocardial dysfunction. Laboratory assays documented elevated inflammatory markers. He was also SARS-CoV-2 positive. These results satisfied the criteria for the multisystem inflammatory syndrome (MIS-C). He was admitted and treatments included methylprednisolone, intravenous immunoglobulin, aspirin, and heparin. The next day, he developed right hemiparesis and aphasia; the Pediatric National Institutes Stroke Scale score was 26 points. Magnetic resonance imaging showed focal areas of restricted diffusion involving the left temporal and parietal cortex and subcortical white matter, indicative of a left, middle cerebral artery infarct. An endovascular thrombectomy was performed at 8 hours after the onset of his neurologic deficits. He regained spontaneous movement of his right extremities less than 24 hours after thrombectomy. Histopathologically, the removed thrombus was a laminated clot with an early organization by fibroblasts and myxoid debris, suggesting it was likely an embolus. This case suggests that the hyperactive cytokine response characteristic of MIS-C was responsible for a hypercoagulable state leading to the embolic occlusion and highlights the need for further study of the pathophysiology of neurologic complications of SARS-CoV-2 infection in children.

**A Rare Case of Primary Central Nervous System Melanoma**

(Poster No. 75)

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We report a 66-year-old man without a history of cutaneous or mucosal melanoma who presented with altered mental status. Magnetic resonance imaging showed a 2.7-cm diffusely enhancing intradural, extramedullary mass centered at the T1-T2 level with subsequent surgical resection of the tumor performed. The histology showed tumor comprised of heavily pigmented spindle to epithelioid tumor cells growing in nests with moderate cytologic and low mitotic count (2/10 hpf). Differential diagnoses included metastatic versus primary malignant melanoma and malignant melanotic nerve sheath tumor (so-called melanotic schwannoma). Immunohistochemical studies showed diffuse positivity for S-100, HMB45, SOX-10, and Melan A in the tumor cells. MIB-1 showed a low proliferative index. There was a loss of BAP-1; however, PPKARIA expression was retained. Further molecular studies detected GNAQ Q209L mutation. BRFV 600E mutation was not detected. Primary malignant melanoma of the central nervous system (CNS) is an uncommon tumor with an annual incidence of 0.3 cases per 10 million. They arise from leptomeningeal melanocytes. These tumors show strong association with GNAQ mutation (especially codon 61) unlike melanotic nerve sheath tumors that show PPKARIA mutation. Malignant melanoma of CNS is a highly aggressive tumor with poor prognosis and metastatic potential. However, it has a better prognosis than metastatic melanoma. Mutations in codon 209 (within the RAS-like domain) transform GNAQ into a dominant-acting oncogene that contributes to developing a subset of melanocytic neoplasms that do not harbor the more common melanoma-associated somatic mutations in BRF and NRAS. Loss of BAP-1 is an adverse prognostic marker in these tumors.

**Nocardial Brain Abscess: A Rare Cause of Cerebral Abscess With Fatal Outcome**

(Poster No. 76)

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Brain abscesses (BA) in the United States are rare (0.3–1.3 cases/100,000 per year). They most frequently occur from *Staphylococcus* and *Streptococcus* infection either by direct spread from head/neck or hematogenous spread, particularly from lung. Less commonly, in immunocompromised patients, BA can be caused by such other organisms as fungi and parasites. Nocardia accounts for only 2% of all BA and is associated with high mortality rate. We present a case of an 81-year-old man who was under treatment for splenic marginal zone lymphoma (ibrutinib), developed neurological deficits. Brain and chest imaging showed multiple ring-enhancing lesions in bilateral
frontal and left parietal lobes (Figure 4.76, A) and right, middle lung lobe nodular opacity with pleural effusion. Imaging differential was BA versus tumor. Chemotherapy was withheld and started intravenous vancomycin, meropenem, and voriconazole. Cultures from blood, brain, and lung lesions failed to reveal the causing organism. Brain lesion histology revealed necrotizing acute and chronic granulomatous inflammation (Figure 4.76, B and C). Immunostains and special stains did not show evidence of lymphoma (PAX-5/CD3/CD20), fungus, acid-fast bacilli, viral inclusions, toxoplasma, or spirochetes organisms. Focal thin beaded Gram-positive filamentous branching bacteria were present (Figure 4.76, D), also positive with Gomori methenamine silver and fite stains compatible with Nocardia. Voriconazole was discontinued and continued on meropenem and Bactrim. Unfortunately, the patient died 11 days after brain biopsy diagnosis. Nocardial BA carries the highest mortality rate (60%) among all bacterial BA, particularly in immunocompromised patients and those with multiple lesions. Early diagnosis and aggressive treatment are essential to avoid a fatal outcome.

Unusual BRAF PRKAR2B-BRAF Fusion Ganglioglioma: A Review of 2 Cases
(Poster No. 77)

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Ganglioglioma is a well-differentiated glioneuronal neoplasm composed of dysplastic ganglion cells and neoplastic glial cells. BRAF V600E mutation occurs in 20% to 60% of gangliogliomas and is associated with a good prognosis. A 12-year-old boy presented with right-sided weakness. Magnetic resonance imaging showed a frontal cystic mass extending to vertex from corona radiata (6.5 × 5.4 cm). Tumor was well circumscribed and showed disorganized ganglion-like cells, intervening small-glial cells, eosinophilic-granular bodies, and prominent perivascular lymphoplasmacytic cell infiltrates (Figure 4.77, A). Peripheral tissue showed scattered calcifications. In the second case, a 21-year-old-woman presented with headaches and tinnitus. Magnetic resonance imaging showed a large heterogeneous enhancing cystic-solid mass in right parietal region (4.5 × 4 cm) with vasogenic edema. Lesion was low grade with glial component and scattered atypical ganglion cells. Occasional eosinophilic-granular bodies and perivascular lymphoplasmacytic cell infiltrates (Figure 4.77, B). Both cases showed synaptophysin and chromogranin expression in dysplastic ganglion cells, low Ki-67 proliferation index, and BRAF PRKAR2B-BRAF fusion. BRAF mutations lead to constitutive MEK-ERK signaling, promoting oncogenic transformation. BRAF mutations have been reported in 20% of cancers with the majority of mutations occurring at the V600 position. The rearrangement in this tumor is predicted to result in a chimeric protein that includes the BRAF kinase domain but lacks the N-terminal auto-inhibitory domain. Fusions with similar breakpoints in BRAF have been reported as constitutively active and oncogenic, hyperactivating the MAPK pathway and exhibiting transformation activity similar to the V600 position. BRAF mutations lead to constitutive MEK-ERK signaling, promoting oncogenic transformation, and predicted to be activating. Patients with BRAF fusions have been reported to benefit from MEK inhibitors.

Redox Imbalance in the Pathogenesis and Progression of Neuropsychiatric Disorders: Proposing a New Model of Classification
(Poster No. 78)

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Context: Redox balance within the human body is maintained by a finely calibrated system consisting of oxidative mechanisms responsible for the burst release of reactive oxygen species and antioxidant defense mechanisms that use glutathione, thiol containing protein side chains, and lipids to control and tune the reactive oxygen species as needed. Redox imbalance has been implicated in the pathogenesis and progression of multiple neuropsychiatric disorders; however, these investigations are usually limited to either reactive oxygen species generation, or the antioxidant defense mechanism aspect of the redox imbalance.

Design: We present an extensive review of the literature concerning the role of redox imbalance within neuropsychiatric disorders, and propose a new method of classification of neuropsychiatric disorders, namely redox spectrum disorders. We use the proposed model to assess multiple disorders and allocate them as belonging to pro/antioxidant branch of the spectrum based on the findings in our literature review. We specifically focus on schizophrenia that associates predominantly with the loss/failure of antioxidant defense
Not All SMARCA4 (BRG1) Deficient Brain Tumors are Atypical Teratoid Rhabdoid Tumors
(Poster No. 79)

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A 63-year-old man with a 40-year history of smoking presented with a tremor in his left lower leg. Magnetic resonance imaging of the brain showed a peripherally enhancing round mass (2.2 cm) in the right superior parietal lobe. Computed tomography scan of the chest reported perihilar and mediastinal lymphadenopathy. Hemoxylins–eosin–stained sections revealed a high-grade tumor with multiple foci of necrosis and numerous mitoses. Tumor cells were medium to large, with irregular nuclear membranes and prominent eosinophilic nuclei. Scattered large pleomorphic cells were present with dense eosinophilic cytoplasm and occasional eccentrically placed nuclei. Differential diagnosis included a primary central nervous system malignancy, metastatic carcinoma, germinoma, and metastatic melanoma. An extensive immunohistochemical (IHC) panel performed was inconclusive (Table). Concurrent fine-needle aspiration (perihilar lymph node) revealed similar morphology and IHC staining profile. Next-generation sequencing (brain mass) revealed a hypercellular tumor with multiple foci of necrosis and numerous mitoses. Tumor cells were small with granular chromatin (Figure 4.81, B), positive for PR, −α-inhibin, and calcitriol. There was loss of SMARCA2 and SMARCA4. Next-generation sequencing showed somatic mutations in SMARCA4 and TGBR1 with a tumor mutation burden of 2.6 Mb. Here, we describe a case of SMARCA2, SMARCA4-deficient small cell carcinoma of the ovary. Of note, our tumor had abundant tumor infiltrating lymphocytes. Recent evidence suggests these tumors respond to checkpoint inhibition. Small cell carcinoma of the ovary is a monogenic, nonhypermutated disease, which contributes to the low tumor mutation burden. This can inappropriately steer clinicians away from using checkpoint inhibitors. However, the abundance of tumor infiltrating lymphocytes suggests an immunogenic tumor microenvironment, which may be a result of the transcriptional program regulated by SMARCA4. We seek to raise awareness of this highly aggressive entity with potential therapeutic implications.

<table>
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<th>Summary of Immunohistochemistry Panel</th>
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<td><strong>Immunohistochemical Stain</strong></td>
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<td>Napsin A, NUT, Pax-8, CDX2, CD45</td>
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Small Cell Carcinoma of the Ovary, Hypercalcemic Type With Tumor Infiltrating Lymphocytes
(Poster No. 81)

Jordan M. Steinberg, MD* (jsteinberg3@northwell.edu); Hossein Hosseini, MD; Robert Soslow, MD; Xiaojing O’Leary, MF. 1Department of Pathology and Laboratory Medicine, Lenox Hill Hospital, New York, New York; 2Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, New York.

Ovarian small cell carcinoma is a rare, aggressive entity subclassified into pulmonary and hypercalcemic subtypes. The hypercalcemic type can have more rhabdoid differentiation and usually accompany hypercalcemia. As a rule, these tumors harbor mutations in SWI/SNF chromatin remodeling complex specifically the 2 helicases/ATPases (BRM/SMARCA2 and BRG1/SMARCA4). We present a 42-year-old woman who complained of early satiety and bloating. Ultrasonography demonstrated a 12.5-cm abdominal mass. She underwent salpingo-oophorectomy. Grossly the mass was solid, cystic, and focally hemorrhagic. Microscopically the tumor cells were arranged in solid nests with rosettes containing areas of necrosis (Figure 4.81, A) and abundant tumor infiltrating lymphocytes around the tumor (Figure 4.81, A and B). The tumor cells were small with granular chromatin (Figure 4.81, B), positive for WT1 (Figure 4.81, D) synaptophysin (Figure 4.81, C) negative for ER/PR, −α-inhibin, and calcitriol. There was loss of SMARCA2 and SMARCA4. Next-generation sequencing showed somatic mutations in SMARCA4 and TGBR1 with a tumor mutation burden of 2.6 Mb. Here, we describe a case of SMARCA2, SMARCA4-deficient small cell carcinoma of the ovary. Of note, our tumor had abundant tumor infiltrating lymphocytes. Recent evidence suggests these tumors respond to checkpoint inhibition. Small cell carcinoma of the ovary is a monogenic, nonhypermutated disease, which contributes to the low tumor mutation burden. This can inappropriately steer clinicians away from using checkpoint inhibitors. However, the abundance of tumor infiltrating lymphocytes suggests an immunogenic tumor microenvironment, which may be a result of the transcriptional program regulated by SMARCA4. We seek to raise awareness of this highly aggressive entity with potential therapeutic implications.
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**Context:** The College of American Pathologists/American Society of Clinical Oncology (CAP/ASCO) recommends HER2 testing before initiation of targeted therapy for patients with advanced gastrointestinal adenocarcinoma (GÉA), using immunohistochemistry (IHC) followed by fluorescence in situ hybridization (FISH) in cases with an IHC result of 2+.

**Results:** During the study period, 475 GEAs had HER2 testing performed in our lab; of these, 100 (21.1%) had prior 2+ IHC result, 156 (33%) were amplified, 239 (50%) were nonamplified, and 80 (27%) were indeterminate. Following RAI1 testing, 60 (75%) of 80 indeterminate cases were reclassified as nonamplified and 20 (25%) were reclassified as amplified, increasing total amplified cases to 176 (37%). The correlation between the average CEP17 and RAI1 copy number for all cases was weak ($R^2 = 0.044$).

**Conclusions:** Using the alternate probe RAI1 reclassifies 25% of original HER2 IHC indeterminate gastrointestinal cancers as amplified, which become eligible for targeted therapies.

### Liver Transplantation-Induced Bone Marrow Transplantation and Graft-Versus-Host Disease as Identified by Short Tandem Repeat Chimerism Analysis: Coincidental Rare Case Presentations

(Poster No. 83)

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#### Characteristics of Patients With Hematopoietic Engraftment and GVHD After Liver Transplant

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patient A</th>
<th>Patient B</th>
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<tr>
<td><strong>Patient A</strong></td>
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<tr>
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<td>Buccal swab</td>
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</tr>
<tr>
<td>Donor tissue for allele ID</td>
<td>Pre-perfusion donor liver</td>
<td>Pre-perfusion donor liver</td>
</tr>
<tr>
<td><strong>Peripheral Blood</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD3+ enriched population</td>
<td>100% donor</td>
<td>74% donor</td>
</tr>
<tr>
<td>CD3+3- enriched population</td>
<td>75% donor</td>
<td>100% donor</td>
</tr>
<tr>
<td>Total</td>
<td>95% donor</td>
<td>100% donor</td>
</tr>
<tr>
<td>Survival, d</td>
<td>58</td>
<td>81</td>
</tr>
</tbody>
</table>

Abbreviations: GVHD, graft-versus-host disease; HCC, hepatocellular carcinoma; ID, identification; NASH: nonalcoholic steatohepatitis.

### A KMT2A-AFF3 Fusion Resulting From a Complex Three-Way Chromosomal Rearrangement in Pediatric Acute Lymphoblastic Leukemia

(Poster No. 84)

Lauren J. Miller, MJ (laejmiller@mcw.edu); Vasiliki Leventakid, MD; Holli M. Drendel, PhD; Kathleen M. Bone, PhD. Department of Pathology, Medical College of Wisconsin, Milwaukee.

The KMT2A-AFF3 fusion [(t(12;21)(q11.2;q23.2))] is a rare mutation occurring in pediatric B-cell acute lymphoblastic leukemia (B-ALL). We report a case of B-ALL with this fusion further complicated by the presence of a FLT3 mutation (p.Ile836Del), an NFI mutation, and an additional rearrangement of chromosomes 8 and 17 in a subset of cells. Our patient was a 2-year-old boy who presented with 3 weeks of intermittent fevers and was found to be anemic and neutropenic. Bone marrow biopsy specimen showed 82% blasts with a corresponding 36.7% blast population detected by flow cytometry, a diagnosis of B-ALL. Karyotype analysis on cultured bone marrow cells demonstrated a complex 3-way rearrangement involving KMT2A and an unknown fusion partner, with translocations involving chromosomes 1, 2, and 11, as well as a rearrangement involving chromosomes 8 and 17, resulting in the fusion partner as AFF3 and also identified the FLT3 mutation, which can be found in infant B-ALL with KMT2A rearrangements, confirmed the presence of the rearrangement of chromosomes 8 and 17, and determined the NFI mutation occurred from loss of heterozygosity in only tumor cells. The KMT2A-AFF3 fusion resulted from a highly complex series of events at the chromosomal level and indicate a poor prognosis. This case demonstrates a highly complex presentation of a rare gene rearrangement with only a few cases previously being described in the literature.

### Immunohistochemistry and FISH Correlation of Amplified Areas in Breast Carcinoma Cases With Genomic Heterogeneity

(Poster No. 85)

Diane M. Wilcock, MS1; Joshua F. Coleman, MD2; Deepika Sirohi, MD3; Evin Gulbahce, MD, MSCF (evin.gulbahce@path.utah.edu). Department of Pathology, ARUP Labs, Salt Lake City, Utah; 2Department of Pathology, University of Utah, Salt Lake City.

**Context:** The College of American Pathologists/American Society of Clinical Oncology (CAP/ASCO) defines genetic heterogeneity (GH) in HER2 fluorescence in situ hybridization (FISH) testing of breast cancers as subpopulation of amplified cells in $\geq 10\%$ to $<50\%$ of tumor cells. The purpose of this study was to investigate the correlation of amplified cells on immunohistochemistry (IHC) and FISH in cases with GH.
Design: Our national reference laboratory database was searched for HER2 GH by keyword “subpopulation” on breast tissues between January 2016 and December 4, 2020. Our lab receives requests for both FISH testing only, and IHC followed by FISH if IHC is equivocal. Cases without accompanying IHC slide were excluded. In old cases where the original FISH slides were discarded, the test was repeated to localize areas of amplification and match to IHC slides. At the time of this abstract, 12 eligible cases were analyzed. Hemoxylin-eosin, IHC, and FISH slides were reviewed manually and scanned with GenASIs system. Areas of FISH-amplified subpopulation were matched to IHC slide on scanned slides.

Results: In 9 of 12 (75%) cases with subpopulation of amplified cells (<50% amplified cells), these areas matched to small areas (<10%) of intense circumferential staining on the 2+ IHC slides (“Mini 3+”). In 1 additional case, it matched to focal area of micropapillary morphology on a 1+ IHC case (Table).

Conclusions: Majority of cases with subpopulation of amplified tumor cells on FISH corresponds to areas of <10% circumferential intense protein expression on 2+ IHC (“Mini 3+”). It is uncommon to identify FISH amplified subpopulations in areas without intense protein expression or micropapillary phenotype.

**Immunohistochemistry Staining, FISH-Amplified Areas in Breast Carcinoma Cases**

<table>
<thead>
<tr>
<th>FISH-Amplified Subpopulation (n)</th>
<th>Yes/No (Number/Total, % Matching)</th>
<th>FISH-Amplified Area Matching, % Matching</th>
</tr>
</thead>
<tbody>
<tr>
<td>IHC Staining</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2+ with &lt;10% intense circumferential membrane staining</td>
<td>4/5 (9/9, 100)</td>
<td></td>
</tr>
<tr>
<td>“Mini” 3+ (n = 9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1+ with micropapillary area (n = 1)</td>
<td>0/1 (1/1, 100)</td>
<td></td>
</tr>
<tr>
<td>1+ (n = 2)</td>
<td>1* 1 (0/2, 0)</td>
<td></td>
</tr>
<tr>
<td>Total (n = 12)</td>
<td>5/7 (9/12, 75 to 100%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a On retrospective review, a minute area of amplified cells appears to represent intermixed DCIS.

**Prevalence and Clinical Correlates of HPV (by p16 Immunohistochemistry) in a Large Patient Cohort With Oral Squamous Cell Carcinoma From a Tertiary Care Hospital in India**

(Poster No. 86)

Garima Rawat, MDS1 (garima3103@gmail.com); Hema M. Aiyer, MD2; Gaurav Sharma, MD2; Anshuman Kumar, MCh3 Departments of 1Oral and Maxillofacial Pathology, Pathology and 3Surgical Oncology, Dharmsala Narayana Superspeciality Hospital, Delhi, India.

Context: Human papillomavirus (HPV) infection plays an important role in the etiopathogenesis of oropharyngeal squamous cell carcinomas as a positive prognostic marker. The p16 protein expression detection immunohistochemically, is a robust surrogate marker of active high-risk HPV infection. Unlike oropharyngeal carcinoma, in oral squamous cell carcinoma (OSCC), prognostic significance of p16 positivity is unclear. This study aimed to investigate the significance of p16 protein expression in relation to clinicopathologic parameters and prognosis in patients with OSCC.

Design: Two hundred fifty patients surgically treated for OSCC were enrolled in the study. The most common anatomic sites of oral carcinoma were the tongue lateral border and buccal mucosa followed by other sites. All tumors were analyzed immunohistochemically for p16 protein expression (Ventana Medical Systems Inc., Oro Valley, Arizona). The results were correlated with the clinicopathological parameters, analyzed statistically, and all cases have been followed up for minimum of 3 months.

**Clinicopathologic Parameters**

<table>
<thead>
<tr>
<th></th>
<th>Total Cases 250, n (%)</th>
<th>p16-Negative Cases 229, n (%)</th>
<th>p16-Positive Cases 21, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>195 (78)</td>
<td>180 (78.60)</td>
<td>15 (71.43)</td>
</tr>
<tr>
<td>Female</td>
<td>55 (22)</td>
<td>49 (21.40)</td>
<td>6 (28.57)</td>
</tr>
<tr>
<td><strong>Age, y</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤58</td>
<td>156 (62.40)</td>
<td>143 (62.45)</td>
<td>13 (61.90)</td>
</tr>
<tr>
<td>&gt;58</td>
<td>94 (37.60)</td>
<td>86 (37.55)</td>
<td>8 (38.10)</td>
</tr>
<tr>
<td><strong>Site</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tongue</td>
<td>90 (36.00)</td>
<td>79 (34.50)</td>
<td>11 (52.38)</td>
</tr>
<tr>
<td>Buccal mucosa</td>
<td>73 (29.20)</td>
<td>69 (30.13)</td>
<td>4 (19.05)</td>
</tr>
<tr>
<td>Lower alveusos</td>
<td>48 (19.20)</td>
<td>44 (19.21)</td>
<td>4 (19.05)</td>
</tr>
<tr>
<td>Lip</td>
<td>6 (2.40)</td>
<td>4 (16.17)</td>
<td>2 (9.52)</td>
</tr>
<tr>
<td>Other sites (GBS, RMT, SP, FOM, upper alveolus)</td>
<td>25 (13.20)</td>
<td>25 (14.41)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Grade</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WD SCC</td>
<td>149 (59.60)</td>
<td>138 (60.26)</td>
<td>11 (52.38)</td>
</tr>
<tr>
<td>MD SCC</td>
<td>88 (35.20)</td>
<td>80 (34.93)</td>
<td>8 (38.10)</td>
</tr>
<tr>
<td>PD SCC</td>
<td>10 (4.00)</td>
<td>8 (3.49)</td>
<td>2 (9.52)</td>
</tr>
<tr>
<td>Spindle cell SCC</td>
<td>3 (1.20)</td>
<td>3 (1.31)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Tumor size (pT)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pT1</td>
<td>39 (15.60)</td>
<td>38 (16.59)</td>
<td>1 (4.76)</td>
</tr>
<tr>
<td>pT2</td>
<td>70 (28.00)</td>
<td>63 (27.51)</td>
<td>7 (33.33)</td>
</tr>
<tr>
<td>pT3</td>
<td>47 (18.80)</td>
<td>44 (19.21)</td>
<td>3 (14.29)</td>
</tr>
<tr>
<td>pT4a</td>
<td>94 (37.60)</td>
<td>84 (36.68)</td>
<td>10 (47.62)</td>
</tr>
<tr>
<td><strong>Nodal status (pN)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pN0</td>
<td>142 (56.80)</td>
<td>129 (56.33)</td>
<td>13 (61.90)</td>
</tr>
<tr>
<td>pN1</td>
<td>233 (9.20)</td>
<td>22 (9.61)</td>
<td>1 (4.76)</td>
</tr>
<tr>
<td>pN2a,b,c</td>
<td>32 (12.80)</td>
<td>29 (12.66)</td>
<td>3 (14.29)</td>
</tr>
<tr>
<td>pN3b</td>
<td>45 (18.00)</td>
<td>41 (17.90)</td>
<td>4 (19.05)</td>
</tr>
<tr>
<td>pNx</td>
<td>8 (3.20)</td>
<td>8 (3.49)</td>
<td>-</td>
</tr>
<tr>
<td><strong>PNI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PNI present</td>
<td>71 (28.40)</td>
<td>65 (28.38)</td>
<td>6 (28.57)</td>
</tr>
<tr>
<td>PNI absent</td>
<td>179 (71.60)</td>
<td>164 (71.62)</td>
<td>15 (71.43)</td>
</tr>
<tr>
<td><strong>ENE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ENE present</td>
<td>50 (20)</td>
<td>46 (20.09)</td>
<td>4 (19.05)</td>
</tr>
<tr>
<td>ENE absent</td>
<td>200 (80)</td>
<td>183 (79.91)</td>
<td>17 (80.95)</td>
</tr>
</tbody>
</table>

Abbreviations: ENE, extranodal extension; FOM, floor of mouth; GBS, gingivobuccal sulcus; MD, moderately differentiated; PD, poorly differentiated; PNI, perineural invasion; RMT, retromolar area; SCC, squamous cell carcinoma; SP, soft palate; WD, well differentiated.


(Poster No. 87)

Alaaeddin Alrohaibani, MD; Alyssa Penning, MD; Terry Morgan, MD, PhD (morgante@ohsu.edu). Department of Pathology, Oregon Health and Science University, Portland.

Context: Extracellular vesicles (EVs) contain plasma membrane surface markers that provide insights into their cell source. We developed and validated a multiplex nanoscale flow cytometry approach to image and count cell-specific EV populations using a novel human “EV-Lyoplate” with 3 differently colored monoclonal antibodies per
Functional PTEN Mutations in Progestin-Resistant De Novo Endometrial Intraepithelial Neoplasia

(Poster No. 88)

Maeed Mohen nasab, MD (mohenasab@ohsu.edu); Cigdem Ak, PhD; Todd Williams, MD; Chris Corless, MD, PhD; Terry Morgan, MD, Department of Pathology, Oregon Health and Science University, Portland.

Context: Endometrial adenocarcinoma is the most common gynecologic malignancy with 10% of cases arising in reproductive age women. Endometrial intraepithelial neoplasia (EIN), including simple hyperplasia and complex hyperplasia with atypia (CAH), is a precursor lesion. Depending on the classification of EIN and concomitant obesity, 25% to 50% of cases fail to respond to progestin therapy. We hypothesize that non-responders may have mutations in PTEN that affect function but not expression.

Design: Retrospective case-control study of 49 de novo endometrial biopsy specimens diagnosed with EIN (41 CAH and 8 simple hyperplasia). Included cases required diagnoses confirmed by 2 pathologists and a history of progestin therapy combined with at most 3 to 6 months of hysteroscopic evaluation and biopsy procedures. Regions of interest containing EIN were sampled for DNA analysis using histologic sections and the commercially available GeneTrails solid tumor panel. Protein expression was measured in serial sections by Nanostring immunolabeling and GeoMx spatial profiling. Data were analyzed by X and unsupervised clustering with adjusted P values.

Results: Clinical follow-up revealed 24 responders (8 simple hyperplasia and 16 CAH) and 25 progestin nonresponders (CAH) with either progression to adenocarcinoma by 3 months, or no response by 6 months. PTEN mutations above the variable allele frequency were identified in 19 of 25 nonresponders and 2 of 16 responders with CAH yielding a likelihood ratio of 6 (2–23) (P < .001). Nanostring revealed no difference in PTEN expression between groups.

Conclusions: Although there are no significant differences in PTEN expression in progestin nonresponders compared with responders, there is a significantly increased frequency of PTEN functional mutations.

Genomic Profiling-Based Survival Rate of Glioblastoma Multiforme

(Poster No. 89)

Hetal Gujaria, MD (gujaria@ohsu.edu); Preeti Malik, MD, MPHF; Urvish Patel, MD, MPH; Richa Jaiswal, MD, MSCR; Nkechinyere Unachukwu, MD; Bibimariyam Nasyroleafa, MD; Nikhilsek Anand, MD; Raghavendra Tirupathi, MD; Ashish Patel, MD, PhD. 1Department of Pathology, Oregon Health and Science University, Portland; 2Department of Neurology and Public Health, Icahn School of Medicine at Mount Sinai, New York, New York; 3Department of Pathology, Medical University of South Carolina, Charleston; 4Department of Pathology, Interfaith Medical Center, New York, New York; 5Department of Pathology, siParadigm Diagnostic Informatics, Pine Brook, New Jersey; 6Department of Pathology, American University of Antigua College of Medicine, Osbourn, Antigua and Barbuda; 7Department of Internal Medicine, Keystone Health, Chambersburg, Pennsylvania; 8Department of Pathology and Translational Pathobiology, Louisiana State University Health, Shreveport.

Context: Glioblastoma multiforme (GBM) is the most aggressive brain tumor with overall dismal survival of 2.2% over 3 years. There are limited data in the literature highlighting whole genome sequencing and overall survival for GBM patients. We aimed to evaluate whole genomic profile, epidemiologic characteristics, and survival at 12 and 24 months with common mutations.

Design: We used cibioPortal cancer genomic (The Cancer Genome Atlas (TCGA) PanCancer Atlas and Firehose Legacy) to study the epigenetic characteristics and genomic profile of GBM patients. Log-rank test and Kaplan-Meier estimator were used to analyze 12-month and 24-month survival rates with common mutations. Patients with 2 or more overlapping mutations were excluded.

Results: We identified 2041 GBM patients, the majority of whom were aged between 50 and 70 years with 51.1% males and 32.5% females. A total of 37.6% were white and 4.1% were black; 78.8% were deceased and 18.4% were alive; and 95.1% had primary and 3.0% had recurrent cancer. Most common mutations associated with reduced survival were as follows: TP53: 362 (17.7%), PTEN: 341 (16.7%), EGFR: 3056 (19.4%), TTN: 156 (7.6%), NFI: 156 (7.6%), MUC16: 117 (5.7%), PIK3R1: 97 (4.7%), and IDH1: 59 (2.8%). Overall survival after initial diagnosis was 59% and 24% following 12 and 24 months, respectively, with the lowest among TTN (30%;0%), TP53 (36.4%;9%), CDKN2A (42.3%;15.4%), MDM2 (53.6%;24.7%), EGFR (56.1%;22.4%), MDM4 (71.4%;0%), and TP53 (84.2%;45.3%, P < .001) (Figure 4.89).

Conclusions: TP53 was the most commonly dysregulated gene followed by PTEN and EGFR. TTN and PTEN (lowest survival at 12 months) and TTN and MDM4 (lowest survival at 24 months) mutations were associated with the worst prognosis. These new insights may provide the foundation for developing new future therapies for these patients.

Machine Learning Model PD-L1 22c3 Scoring of a Multiscanner: Real-World Reference Laboratory Non-small Cell Lung Carcinoma Dataset Generates Scores Comparable With Manual Pathologist Scoring

(Poster No. 90)

Sergine Brutus, PhD (sergine.brutus@pathai.com); Michael Griffin, MS; Cyrus Hedvat, MD, PhD; Benjamin Glass, MS; Nishant Agrawal, MS; Sara Hoffman, BSc; Raquelle Ellis, BSc; Murray Resnick, MD; Victoria Mountain, PhD; Ian Wapinski, PhD; Michael Montalto, PhD; Andrew Beck, MD, PhD; Ronald Paler, MD. 1Department of Scientific Programs, PathAI, Boston, Massachusetts; 2Department of Integrated Oncology, Labcorp, Burlington, North Carolina.

Context: PD-L1 scoring by manual pathology in nonsmall cell lung carcinoma (NSCLC) can predict drug response. Prior machine learning (ML) assessment of pathology images was able to identify and quantify cell types, tissue regions, and PD-L1 immunohistochemistry within NSCLC samples with high resolution. Here, pretrained ML-based PD-L1 scoring models were applied to a real-world NSCLC clinical dataset.

Design: Pretrained ML algorithms (PathAI, Boston, Massachusetts) were deployed on 150 diverse NSCLC samples collected from local tumor and metastatic sites from subjects. Samples were stained for PD-L1 (22C3 pharmDx, Agilent Technologies, Santa Clara) and digitized...
into whole slide images (WSIs) using 2 scanners (Philips UF5, Ventana iScan Coreos) for each case. Using WSIs from both scanners, ML algorithms counted the proportion of all PD-L1 positive cancer cells with respect to total cancer cells within tumor regions to generate 2 sets of slide-level PD-L1 22C3 scores. Manual PD-L1 scores, calculated by an expert pathologist on glass slides, were compared with both sets of algorithm-derived PD-L1 scores using Pearson correlation statistics.

Results: Algorithm-derived PD-L1 22C3 scores generated from WSIs from both scanners were highly correlated with the continuous manual scores (Ventana: Pearson 0.87, P < .05, Philips: Pearson 0.86, P < .05).

Conclusions: PathAI pretrained algorithms generated PD-L1 22C3 scores for WSI scanned on 2 separate platforms that were highly correlated to manual scores. This study demonstrates the feasibility of generalization, automated derivation of accurate scores from a diverse dataset of clinical images. Application of ML-based approaches has the potential to improve efficiency in pathology workflows and clinical decision-making.

Brutis, Griffin, Hedvat, Glass, Agrawal, Hoffman, Resnick, Mountain, Wapinik, Montalto, and Beck are shareholders in PathAI. Paler is a shareholder with Labcorp.

Performance Evaluation of Automated SARS-CoV-2 on the BD Max System (Poster No. 91)

Rita H. Khoury, MD (rhkhoury@acalubs.com); Peter Gudaitis, BA; Prital Patel, BA; Asha Gandhi, BS; Jasmin Kheir, AA; Dauna Gudaitis, BA. Acalubs, Inc., East Brunswick, New Jersey.

Context: COVID-19 is pandemic infection caused by SARS-CoV-2 virus, which has claimed more than 500,000 deaths in the United States. The first step to fight the disease is identifying the infected patient to stop the spread of the disease; however, since no testing was available for the virus several manufacturers have developed tests under Emergency Use Authorization from the FDA.

Design: The BioGX SARS-CoV-2 Reagents for BD MAX System is a real-time reverse transcriptase–polymerase chain reaction test targeting N1 and N2 regions of the SARS-CoV-2 virus. Internal control included in every sample, external positive and negative controls are run daily. The assay time is about 3 hours for 24 samples with the option to add another run after 90 minutes. The assay was evaluated for precision, reproducibility, limit of detection, and accuracy; the percentage agreement for the evaluation steps were calculated. Statistical analyses were done using Analyse-it.

Results: The percentage agreement for precision, reproducibility, and accuracy were 100%. The limit of detection was verified at 1000 copies. The patients’ correlation was 100%. The instrument has the capability of running over 200 samples/day.

Conclusions: The BioGX SARS-CoV-2 Reagents for BD MAX gave the benefit of a fully automated, high precision, accurate, and acceptable sensitivity assay. Although the assay is available, there is a limited supply of reagents and more work is needed to increase the production to be able to make the test available to more patients. In addition, more validation is needed to explore the possibility of using the test for asymptomatic patients.

Clinical Presentations and Laboratory Findings in Patients With COVID-19 Infection: Correlation of Laboratory Findings at Initial Presentation With Severity and Outcome (Poster No. 92)

Jwan A. Alallaf, MD (jwan.al-allaf@tmcmed.org); Ethan Al-Husseinawi, MBChB, PhD; Claire Louise Young, MD; Musaab H. Al Ansari, PhD; Abdelmoreim Elfagir, MPH, MSHI; An-Lin Cheng, PhD; Emanthia Omoscharka, MD; Hana Hamdan, MD; Valericia Mateescu, MD; Soheila Hamidpour, MD; Kamani Lankachandra, MD. 1Department of Pathology, University of Missouri, Kansas City, Kansas City; 2Department of Pathology, University of Kansas Medical Center, Kansas City.

Context: COVID-19 is a new emerging pandemic. This research seeks understanding of the clinical and laboratory changes in COVID-19 patients to predict the outcome.

Design: COVID-19 patients enrolled retrospectively from March through April 2020. Patients were divided into the following 3 groups: severe (inpatient), moderate emergency room (ER), and mild (outpatient), and their data collected.

Results: A total of 130 patients were enrolled, including (42.3%) outpatient, (30%) inpatient, and (27.7%) ER. African Americans comprised most of all groups (50%). Inpatient were significantly older (P = .01), mostly males (58.97%) with significant difference in presentation (P < .05). The majority of inpatient and ER were nonsmokers, and both groups had high mean body mass index. Lymphopenia was found in (71.79%) of inpatient compared with ER (P = .01). Inpatient had higher absolute neutrophil count (ANC) compared with ER (P = .04). Monocytosis, eosinopenia, and normal platelet count were noted in both groups. Higher monocyte distribution width in inpatient (90.48%) (< .001). Higher mean D-dimer, PT time, fibrinogen, and ferritin levels were noted in inpatient. All patients were negative for influenza A, B, and respiratory syncytial virus. The case fatality rate was 12.82% in inpatient compared with 3.85% in all groups. Older age, higher white blood cell count, ANC, and platelet count were associated with longer hospital stay and increased mortality (P < .05).

Conclusions: The current study demonstrates a unique pattern of demographic, clinical, and laboratory data that could predict morbidity and mortality, including older age, African American, male, comorbidities, higher white blood cell count, ANC, platelet count, and high monocyte distribution width. This could potentially guide resource utilization.

Non-toxicigenic Clostridioides difficile Sepsis in a Patient With Colonic Perforation as a Complication of Systemic Amyloidosis (Poster No. 93)

John E. Markantonis, DO1 (john.markantonis@phhs.org); Andrew Clark, PhD1; Ithiel J. Frame, MD, PhD2; Purva Gopal, MD1; Dominick Cavuoti, DO1; Clare McCormick-Baw, MD, PhD1. 1Department of Pathology, UT Southwestern Medical Center, Dallas, Texas; 2Department of Pathology, University of Mississippi Medical Center, Jackson.

Amyloidosis is caused by a heterogeneous group of disorders ranging from genetic syndromes to byproducts of hematologic malignancy. Gastrointestinal amyloidosis is an uncommon presentation of systemic amyloidosis. We present a 63-year-old woman with abdominal pain who had a past medical history of rheumatoid arthritis, gastroesophageal reflux disease, and stage-stage renal disease requiring hemodialysis. She was previously hospitalized at a different institution with colitis and underwent endoscopy there for evaluation of reflux disease. Histopathology revealed amyloid deposits in the esophagus, stomach, and duodenum. On admission she complained of nausea, vomiting, and profuse watery diarrhea, with physical examination revealing an acute abdomen. Blood cultures and stool for Clostridioides difficile testing were obtained. Abdominal imaging revealed colonic perforation (Figure 4.93, A). She emergently underwent extensive bowel resection where histopathology revealed extensive amyloid deposits in the lamina propria and vessel walls (Figure 4.93, B). Despite multiple negative C. difficile toxin assays, anaerobic blood bottles flagged positive with Gram-positive, spore-forming rods within 24 hours (Figure 4.93, C), colonies of which fluoresced green under ultraviolet light (Figure 4.93, D). Nontoxicigenic strains of C. difficile identified as the sole isolate of

Abdominal Imaging
blood cultures are a rare occurrence. Bowel perforation as a complication of amyloidosis is uncommon, and the authors hypothesize that the patient’s newly diagnosed amyloidosis with gastrointestinal involvement was the predisposing factor to perforation. The patient’s aggressive treatment for colitis is likely what selected for and precipitated the non-toxicogenic C. difficile that entered the bloodstream after perforation.

Successful Validation of Anterior Nasal “Dry Swab” for Collection and Transport of Specimens to the Testing Laboratory for SARS-CoV-2 Real-time Reverse Transcriptase PCR Assay

(Poster No. 94)

Peter Reinhardt, PhD; Ravi Ranjan, PhD; Ashley Moineau, MS; Erin Poulin; Pa Tamba Ngorn, PhD; Amy Burnsise, PhD; Alivia Rinaldi, BS; Vendita Joltari, MD (vijothari@umass.edu). Institute for Applied Life Sciences: Clinical Testing Center, University of Massachusetts, Amherst.

Context: The IALS Clinical Testing Center (ICTC) at UMass Amherst performs a laboratory developed SARS-CoV-2 real-time reverse transcriptase–polymerase chain reaction assay (ICTC SARS-CoV-2-RT-PCR) to determine COVID-19 status. The assay is a nucleic acid amplification test intended for qualitative detection of RNA from SARS-CoV-2 isolated and purified from anterior nasal swab (ANS) specimens in transport media. This validation study was performed to include the use of ANS stored in dry specimen tubes (DST) or “dry swabs” to facilitate self-collection and transportation of large numbers of ANS collected on university campuses and state community-based testing sites.

Design: Three ANS in DST and one ANS in media (VTM/saline/other) were obtained from 46 subjects. The result obtained from the ICTC SARS-CoV-2-RT-PCR using ANS in DST was compared with results obtained from in-house ANS in media assay and reference laboratory assay for ANS in DST and media. The stability of ANS in DST was evaluated at room temperature after 24 hours, 48 hours, 72 hours, and after reconstitution with transport medium at similar time intervals.

Results: There was 100% concordance between results of ANS in DST when compared with reference laboratory results. The results were also concordant when compared with ANS in media using ICTC SARS-CoV-2-RT-PCR and remained concordant at 24, 48, and 72 hours and until 48 hours after reconstitution.

Conclusions: Results using ANS in DST or “dry swabs” are comparable to ANS specimens collected in media for up to 72 hours. In addition, the results are also reproducible when “dry swabs” are reconstituted with media within 48 hours.

Comparison of Sofia SARS Antigen FIA Test With Reverse Transcriptase Polymerase Chain Reaction Test for Detecting SARS-CoV-2 in Nasopharyngeal Samples

(Poster No. 95)

Anna S. Bouck, BS1 (Anna.s.bouck.med.dartmouth.edu); Michael Lambert, BS2; Dorothy A. Martin, BS1; Heather B. Steinmetz, BS1; Samantha F. Allen, BS1; Joel A. Lefferts, PhD1; Bing Ren, MD, PhD, 1Department of Pathology and Laboratory Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire; 2Department of Laboratory Services, Springfield Hospital, Springfield, Vermont.

Context: COVID-19, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), resulted in a global pandemic and changed the way we think about testing methods. While many diagnostic techniques are available to detect this virus, the benefits and limitations of each method influence their utility and availability. Reverse transcriptase–polymerase chain reaction (RT-PCR) demonstrates high sensitivity but requires the availability of a molecular laboratory and highly skilled technicians. Rapid antigen testing is a point-of-care method that provides results within minutes but is limited by the possibility of false-negative results and the requirement of testing within 5 days of symptom onset.

Design: A total of 435 nasopharyngeal samples were collected from 435 individuals at Springfield Hospital and Dartmouth-Hitchcock Medical Center between July 2020 and October 2021. The study population consisted of 13 symptomatic patients, 16 postexposure patients, 3 healthcare workers for surveillance, and 402 patients for screening. Samples were examined using both Sofia SARS antigen FIA test and RT-PCR test. Comparing Sofia with RT-PCR with RT-PCR as the criteria standard, positive percent agreement and negative percent agreement were calculated.

Results: Compared with RT-PCR, Sofia rapid antigen test has a positive percent agreement of 87.5% (14 of 16) and a negative percent agreement of 100% (419 of 419). Two RT-PCR–positive samples were determined to be negative by Sofia (Table).

Conclusions: Compared with RT-PCR, Sofia rapid antigen testing shows high negative percent agreement and reasonable positive percent agreement. While further validation studies are needed, Sofia rapid antigen testing provides a relatively reliable diagnostic approach for COVID-19.

Comparing RT-PCR and Sofia Antigen Test Results

<table>
<thead>
<tr>
<th></th>
<th>RT-PCR Positive</th>
<th>RT-PCR Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofia Positive</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Sofia Negative</td>
<td>2</td>
<td>419</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>419</td>
</tr>
<tr>
<td></td>
<td>435</td>
<td></td>
</tr>
</tbody>
</table>

T2SARS-CoV-2 Panel is Able to Detect All SARS-CoV-2 Variants as Confirmed by Genomic Surveillance

(Poster No. 96)

M. Nabuan Naufer, PhD (mnaufer@t2biosystems.com); Christopher A. Steele, BS; Jessica L. Snyder, PhD. Department of R&D, T2 Biosystems, Lexington, Massachusetts.

Context: The SARS-CoV-2 virus, the causative agent of the COVID-19 pandemic, can result in severe respiratory infection and death. Over the course of the pandemic, mutated variants of the virus have been documented globally. As the virus continues to evolve, it is critical that diagnostics be able to still detect the virus. We analyzed SARS-CoV-2 sequences to confirm that the T2SARS-CoV-2 Panel detects the currently documented variants and developed a routine screening methodology to confirm detection of emerging novel variants.

Design: Near full-length, high-coverage (>29,000 bp, Ns < 5%) records were downloaded from GISAID. A Python script was used to evaluate sequences associated with most recent submissions from the US as well as of the variants, B.1.1.7, B.1.351, and P.1, against T2SARS-CoV-2 primers/probes. Highly prevalent (>5%) and thermodynamically unfavorable mutations in primer/probe regions would be flagged for additional testing. New sequence data are monitored biweekly.

Results: Of 5097 most recent sequence submissions (as of March 4, 2021) from the US, 34 unique mismatched records were identified. A total of 8190, 2181, and 479 records were analyzed for variants B.1.1.7, B.1.351, and P.1 respectively. Analysis of variants B.1.1.7, B.1.351, and P.1 identified 17, 6, and 3 unique mismatched records, respectively. No mutations were deemed thermodynamically unfavorable or had a prevalence of greater than 5%.

Conclusions: Based on in silico analysis of the GISAID database, the T2SARS-CoV-2 panel detects all identified variants and recent SARS-CoV-2 viruses. Continued routine surveillance of new sequence data will ensure early confirmation that T2SARS-CoV-2 will detect any emerging variants.

All authors own stock in T2 Biosystems.

Disseminated Nontuberculous Mycobacterial Infection in a 3-Year-Old Juvenile Idiopathic Arthritis Patient

(Poster No. 97)

Dennis Drehner, DO1 (ddrehner@nemours.org); Mary Toth, MD2; Dorothea Douglas, MD2; Kenneth Alexander, MD2; Adriana Cadilla, MD2. Departments of 1Pediatrics, Nemours Children’s Hospital, Orlando, Florida; and 2Pediatrics, Nemours Children’s Hospital, Orlando, Florida.

Nontuberculous mycobacteria infections are increasing in incidence and prevalence. The organisms are ubiquitous and infections difficult to treat. Juvenile idiopathic arthritis (JIA) affects nearly 300,000 individuals in the United States. Biologic disease-modifying medications, such as infliximab, are frequently used. There are multiple reports of mycobacterial infections complicating treatment with biologics in adults. Pediatric cases are rare. We report disseminated nontuberculous mycobacterial infection in a 3-year-old girl with JIA. The patient was diagnosed with JIA at age 4 years and presented with 6 months of bilateral hip pain. Laboratory studies showed erythrocyte sedimentation rate 38 (0–32) mm/hr, C-reactive protein 8.3 (0.0–4.9) mg/L, and antinuclear antibody negative. She was initially treated with oral corticosteroids and weekly methotrexate. Later infliximab treatment controlled the arthritis.

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and normalized inflammatory markers. Sixteen months after diagnosis she developed neck pain, low-grade fever, and cervical adenopathy. An excisional biopsy specimen of a right cervical node showed necrotizing granulomatous inflammation with positive acid-fast staining organisms. Two organisms grew in culture and were identified by MALDI-TOF mass spectrometry (Bruker, Billerica, Mass) as *Mycobacterium abscessus* and *Mycobacterium tuberculosis*. A positron-emission tomography scan found extensive abdominal pelvic adenopathy, a posterior scalp lesion, and a lytic lesion in the L1 vertebral body consistent with disseminated disease. Additional studies at another institution showed interferon gamma receptor-1 deficiency. The cellular responses initiated by interferon gamma are central to control of mycobacterial infections. Tumor necrosis factor alpha is part of that response. Infliximab blocks tumor necrosis factor from interacting with its receptors (Figure 4.97).

Rapid Screening for Meningitis/Encephalitis Panel Testing Appropriateness When Panel Supplies are Limited
(Poster No. 98)

Ayush C. Srivastava, MBBS (asrivastava1@umc.edu); Ithiel J. Frame, MD, PhD. Department of Pathology, University of Mississippi Medical Center, Jackson.

Context: Throughout the COVID-19 pandemic, our institution experienced shortages of the BioFire FilmArray meningitis/encephalitis (ME) panel, a multiplex molecular assay for rapid identification of common microbial pathogens in cerebrospinal fluid (CSF). The hypothesis of our study was that traditional laboratory CSF parameters can be used to screen for appropriate use of the ME panel.

Design: A retrospective review of adult and pediatric patients who underwent ME panel testing was conducted from January 2018 through February 2021.

Results: A total of 1952 ME panels were reviewed from 1853 unique patients. A total of 181 targets were detected on 169 panels (8.7% positivity). Of positive panels, 162 of 169 panels (95.9%) had at least 1 abnormality among the 4 CSF indices (glucose, protein, white blood cell count, red blood cell count); 7 of 169 panels (4.1%) did not have abnormal CSF indices. The top ordering locations included pediatric emergency department, pediatric intensive care unit, and adult neurology/neurosurgery.

Conclusions: Our review of more than 3 years showed positivity of <10%, suggesting the test is overused in our diverse patient population. Of samples with at least 1 microbial target detected, 96% had an abnormality in CSF indices. In the setting of limited panel availability, applying simple screening rules before running the test, such as requiring at least 1 abnormal CSF index abnormality, may reduce unnecessary testing. Knowing where the specimens are most frequently ordered allows for targeting physician engagement in such screening methods.

Utilization of a Novel Diagnostic Assay to Improve Turnaround Time and Accurate Diagnosis and Treatment of Secondary Candidemia in a Critically Ill Immunosuppressed COVID-19 Patient
(Poster No. 99)

Ashley L. Cubillos, PharmD; Elisabeth Chandler, PharmD; Fran Cioffi, MT(ASCP). Departments of Pharmacy and Microbiology, Lee Health, Fort Myers, Florida.

T2Candida Panel (T2C) (T2 Biosystems, Lexington, Massachusetts) is a nonculture-based diagnostic test providing direct molecular detection of Candida species from whole blood in 5 to 5 hours. We report a case of a critically ill COVID-19 patient with secondary candidemia who received immune suppressing pharmacotherapy, where usage of T2C enabled rapid diagnosis leading to initiation of appropriate antifungal therapy in 8 hours. Our patient was an elderly male admitted with COVID-19 initially requiring low-flow oxygen. During his hospitalization he received azithromycin, methylprednisolone, and tocilizumab therapy in addition to supportive therapy. His oxygen requirements increased, and he was intubated on hospital day 3. On day 14, he developed new fever (100.4°F) and chest X-ray showed increased opacities. A suctioned sputum culture grew *Klebsiella aerogenes* and *Proteus mirabilis*, and he was treated with cefepime on day 15. Fever continued to escalate on hospital days 15 and 16 (101.9°F and 103°F respectively), prompting additional blood cultures along with T2C on Day 16. The T2C in 4 hours resulted positive for *Candida albicans*/*Candida tropicalis*; anidulafungin was initiated and fever resolved within 24 hours. The blood culture was positive for yeast, 29 hours after T2C result, and after an additional 17 hours *C. albicans* was identified on culture. The patient stabilized and was transitioned to a long-term acute care facility. Utilization of novel T2C enabled timely and accurate diagnosis of candidemia, rapid initiation of targeted antifungal therapy, and positive outcome in a COVID-19 patient.

Cutaneous Protothecosis in a Patient Using Topical Steroids: Unique Presentation of a Rare Pathogen
(Poster No. 100)

Karamatullah Danyal, MD, PhD (karamatullah.danyal@outlook.com); Jessica Crothers, MD; Dinehart Matthew, MD; Anne Stowman, MD; Sean Bullis, MD. Department of Pathology and Laboratory Medicine, UVM Medical Center, Burlington, Vermont.

Though ubiquitously present in the environment, *Prototheca* spp are otherwise uncommon human pathogens. A recent rise in incidence likely reflects changes in both environmental and host factors (eg, global climate change and increased prevalence of immunocompromised individuals). Extremely rare in immunocompetent individuals, protothecosis is often not considered in the differential diagnosis unless significant immunosuppression exists. We present a case of a cutaneous protothecosis in a 75-year-old man with a progressively worsening skin wound despite his immunocompetent host status. A punch biopsy specimen revealed superficial ulceration with a mixed inflammatory infiltrate and numerous sporangia, many with characteristic morula morphology consistent with *Prototheca* spp. Further investigation revealed ongoing use of topical betamethasone to the region (~180 days) for a prior diagnosis of cutaneous sarcoidosis. Additional tissue was submitted for culture and grew dry, white colonies at 5 days. Genus-level identification was confirmed by VITEK2 using yeast identification card. Whole genome sequencing was performed on isolated colonies, revealing a genome length of 17.0 Mb with 92.79% sequence identity to *Prototheca wickerhamii*. Two megabase did not align to any publicly available reference genomes, raising the possibility that this isolate has acquired additional genes, some of which may be associated with increased pathogenicity, though likely reflects the general paucity of publicly available *P. wickerhamii* reference genomes. In the constantly changing climate of our planet, this case highlights the need to broaden differential diagnoses to include novel and emergent pathogens in minimally immune-suppressed patients and the ability of genomic sequencing to enhance our understanding of these organisms (Figure 4.100).

Mycobacterium Abscessus: A Looming, Unrecognized Threat
(Poster No. 101)

Ariel Sandhu, MD (ariel.sandhu2@ahn.org); Quihong Zhang, MD. Department of Pathology, Allegheny Health Network, Pittsburgh, Pennsylvania.

Abstracts
Infections caused by rapidly growing mycobacteria are increasing worldwide and are notoriously difficult to treat because of innate antibiotic and disinfectant resistances. *Mycobacterium abscessus* is one of the most antibiotic-resistant mycobacteria, yet it is ubiquitous in the environment, capable of causing serious, often opportunistic respiratory, skin and mucosal infections, especially in hospital settings. Despite increasing incidence of infection, in-house methods of detection and further characterization of them have not caught up. We report the first detected instance of *Mycobacterium abscessus* at our facility in a 67-year-old woman. The patient had a history of acute myeloid leukemia status after allogeneic peripheral blood stem cell transplant. She presented to our institution for blood transfusion with intermittent fevers and profound neutropenia. Imaging revealed new lung nodules and a 3.5-cm subcutaneous firm mass over her humerus. Positive blood cultures detected by Bactec FX showed beaded gram-positive rods at 3 days, 10 hours after collection in aerobic tubes. A Kinyoun stain was performed showing acid fast organisms, and it was subbed to a slant Lowenstein Jensen Media for growth. The media was then sent to LabCorp for DNA sequencing and susceptibility testing, which revealed *M. abscessus* Complex without further specification. Unfortunately, the patient withdrew from active care and passed away shortly without initiating antibiotic therapy. Disseminated *M. abscessus* has a dismal prognosis, and severe disease is associated with underlying malignancy, particularly with hematologic disease.

**Granulomatous-Lymphocytic Interstitial Lung Disease as the First Manifestation of an Underlying Immune Deficiency and Its Possible Relationship With Malignancies**  
(Ph.D. No. 102)  
Andrii Puzyrenko, MD, PhD (apuzyrenko@mcw.edu); Yuri Sheinin, MD, PhD. Department of Pathology, Medical College of Wisconsin, Milwaukee.

Patients with granulomatous-lymphocytic interstitial lung disease (GLILD) are almost always associated with common variable immune deficiency (CVID); however, GLILD is reported in other primary immune deficiency. We report on GLILD as the first manifestation of an underlying 22q11.2 deletion syndrome and possibly related to malignancies. A 53-year-old woman was diagnosed with dermatofibrosarcoma protuberans (DFSP) in 2018 (immunohistochemical stain showed that the tumor cells are positive for CD34; fluorescence in situ hybridization indicated a t(17;22)). The tumor was surgically removed without additional therapy. Further workup demonstrated abnormalities in her chest computed tomography scan, including numerous lung pulmonary nodules. The left lower lobe wedge demonstrated nodular lymphoid hyperplasia, follicular bronchiolitis, also areas of noncaseating granulomas. A computed tomography chest scan in 2020 demonstrated multiple solid pulmonary nodules in the right lower lobe. The right lower lobe wedge showed features of GLILD, including lymphoplasmacytic infiltrates, follicular bronchiolitis, organizing pneumonia, and nonnecrotizing granulomas (Figure 4.102). The previous tissue from 2018 was also rereviewed and demonstrated similar features. To this end, she displayed no symptoms of CVID, such as no history of recurrent infections or diffuse adenopathy and no evidence of splenomegaly or lymphoma. Rearrangements of the chromosome 22q11.2 region can be associated with GLILD. The distal deletion breakpoint occurs in the LCR22 of chromosome 22, and most of those in LCR22-3a. DFSP is characterized by the presence of t(17;22) that also can involve LCR22-3a and may activate platelet-derived growth factor beta polypeptide that drives tissue proliferation. It is possible, particularly given the facts that there is evidence that GLILD might be associated with DFSP.

**Epstein-Barr Virus–Associated Smooth Muscle Tumors of the Lung and Adrenal: Incidental Findings in a Kidney Transplant Patient**  
(Ph.D. No. 103)  
Chinelo P. Onyenekwu, MD (onyenekwu@mcw.edu); Yuri Sheinin, MD, PhD. Department of Pathology, Medical College of Wisconsin, Milwaukee.

Epstein-Barr virus (EBV)-associated smooth muscle tumors occur less frequently in posttransplant patients than EBV-associated lymphoproliferative disorders. We present a 39-year-old woman with multifocal lung nodules and a left adrenal mass, 16 years after kidney transplant for systemic lupus erythematosus nephropathy. The patient had received high-dose corticosteroids, tacrolimus, mycophenolate, and valacyclovir therapies, and had no lupus flares. During evaluation for a repeat kidney transplant for chronic kidney disease due to allograft nephropathy, computerized tomography imaging showed a left adrenal mass and multiple lung nodules ranging from 0.3 to 0.7 cm, which increased in size over 4 months. She underwent a left adrenalectomy and biopsy procedure of 2 of the lung lesions. Pathology examination showed a 4.3-cm firm, well-circumscribed nodule within the adrenal medulla, with scattered hard yellow areas. Histologically, there was a bland proliferation of spindle cells with elongated nuclei and abundant eosinophilic cytoplasm as well as some scattered foci of dystrophic calcification. The lung biopsy specimens showed similar proliferation, without evidence of mitotic activity, nuclear pleomorphism, or invasion (Figure 4.103, A and D). The tumor cells were positive for smooth muscle actin, desmin, and SMMS and negative for S100 and SOX10. Epstein-Barr encoding region in situ hybridization showed diffuse positive nuclear staining in the adrenal and lung tumors (Figure 4.103, B and C). These findings are consistent with EBV-associated smooth muscle tumors. EBV-associated smooth muscle tumors although rare, may occur with diffuse pattern of pulmonary involvement and should be considered in patients with solid organ transplant and incidental findings of multiple organ lesions on imaging.
Challenging Diagnosis of TTF-1–Negative, GATA-3–Positive Lung Adenocarcinoma: Case Report and Review of the Literature
(Poster No. 104)

Jason Sinclair, MD (jsdscfd@umsystem.edu); Magda Esebua, MD; Carla Caruso, MD. Department of Pathology, University of Missouri, Columbia.

Pulmonary adenocarcinoma is the most common nonsmall cell carcinoma in the lung and is typically TTF-1 positive and p40/p63 negative. Here, we present a case of pulmonary adenocarcinoma in a 59-year-old woman with an aberrant immunohistochemical profile. The patient presented with a painful posterior lower neck/upper back soft tissue mass increasing in size over the course of 2 to 3 months, a 43 pack-year smoking history, a nonproductive cough, and a 20-lb weight loss over the course of several months. Thoracic computed tomography and magnetic resonance imaging demonstrated a centrally necrotic posterior neck mass and a right upper lobe lung mass with extension to the right hilum, carina, and the left hilum. Fine-needle aspiration (FNA) of the neck mass demonstrated poorly differentiated malignant cells positive for CK7 and GATA-3, and negative for CK5/6, CK 20, GCDFP-15, TTF-1, Napsin, p40, PAX8, and synaptophysin. These cells showed 30% to 40% ER positivity but were PR and HER2 negative. Endobronchial FNA of the left mediastinum demonstrated GATA-3 positive, TTF-1 negative adenocarcinoma morphologically similar to the neck mass. Computed tomography–positron emission tomography scan showed normal breast activity. Mammography and breast magnetic resonance imaging were both benign. Thus, the case was diagnosed as poorly differentiated metastatic pulmonary adenocarcinoma. Likewise, absence of TTF-1 expression alone also occurs in a minority of cases. However, GATA-3 positivity concurrently with TTF-1 negativity is rather uncommon. Therefore, our case emphasizes the importance of considering TTF-1-negative, GATA-3-positive lung adenocarcinoma for pulmonary masses with diagnostically challenging immunohistochemistry profiles.

Glomus Tumor of the Lung: Incidental Rare Tumor
(Poster No. 105)

Samreen Fathima, MD (samreen1608@gmail.com); Haifying Zhang, MD. Department of Pathology, Baylor University Medical Center, Dallas, Texas.

Glomus tumors of lung are rare indolent neoplasms. Typically, these benign neoplasms, which originate from neuroarterial structure called glomus body, are seen in deep dermis, subungal regions of extremities. We present a case of 62-year-old man with incidental glomus tumor of lung. Patient presented with incidental lung nodules in the right lobe of lung. Chest X-ray showed a largest pulmonary nodule of 1.2 cm in the right upper lobe and one smaller 0.5-mm lesion in right middle lobe. Transthoracic biopsy was performed on the larger nodule. Histopathologic examination revealed cohesive sheet of cells with monotonous bland appearing round nuclei and moderate amount of eosinophilic cytoplasm. Rare mitoses were present. No prominent nucleoli or tumor necrosis was identified. Immunohistochemistry played a pivotal role in diagnosis, revealing strong and diffuse positivity for smooth muscle actin, caldesmon, calponin, and collagen IV. Ki-67 proliferation index was 3% to 5%. Negative staining included markers CK cam 5.2, CK AE 1/3, synaptophysin, chromogranin, TTF-1, CDX-2, PAX8, NKX3.1, calretinin, p63, CD45, CD138, SOX10, S100, MART-1, HMB45, HepPar1, tryptase. No cytologic atypia was noted and diagnosis of Glomus tumor was made. Patient received right wedge resection of middle lobe and right upper lobectomy. The rarity glomus tumors in lung makes this a challenging diagnosis, immunohistochemistry with histologic correlation can aid in accurate diagnosis (Figure 4.105).

B3 Thymoma With Clear Cell Features Masquerading as Metastatic Clear Cell Carcinoma of the Kidney
(Poster No. 106)

Chinelo P. Onyenekwu, MD (oneyenekwu@mcw.edu); Kenneth A. Iczkowski, MD; Yuri Sheinin, MD, PhD. Department of Pathology, Medical College of Wisconsin, Milwaukee.

Thymomas are predominantly low-grade malignant neoplasms of the anterior mediastinum. The B3 thymoma is associated with aggressive behavior and rarely displays clear cell morphology. The diagnosis of thymoma with clear cell features is especially challenging in the settings of secondary clear cell malignancy. A 54-year-old man underwent radical nephrectomy due to a large clear cell renal cell carcinoma, grade 3 (Figure 4.106, D), involving renal vein. During surveillance, computed tomography imaging of the chest showed a 3-cm mediastinal mass that was assumed to be a metastasis. Ten months after nephrectomy the mediastinal mass was resected. Microscopic examination demonstrated sheets and lobules of large polygonal cells with irregular, focally raisinoid nuclei, granular chromatin, occasional small nucleoli, prominent eosinophilic to clear cytoplasm, and distinct cell borders. Fibrous septa, perivascular spaces, and scant small lymphocytes were present. The tumor was encapsulated, with microscopic transcapsular invasion of the adjacent adipose tissue. There were 2 mitoses per 10 hpf and no necrosis. Tumor cells showed diffuse positivity for wide-spectrum CK, p40, and PAX-8 and patchy positivity for CAIX (Figure 4.106, A through C); CK7, CD5, CD117, and Epstein-Barr encoding region in situ hybridization were negative. Based on histologic appearance and p40 expression the tumor was diagnosed as thymoma, World Health Organization type B3. This presentation emphasizes the role of judicious use of immunohistochemistry in arriving at a definitive diagnosis in the context of malignancy with clear cell and ambiguous histopathologic features, despite a high index of suspicion for metastatic cancer.

COVID-19 Impact on Lung Nodule Management in an Inner-City Hospital
(Poster No. 107)

Gabriela M. Oprea-Ilie, MD (goprea@emory.edu); Anurag Khanna, MD; Geoffrey Smith, MD; Eric L. Flenaugh, MD. Department of Pathology, Emory University, Atlanta, Georgia; Department of Pulmonary & Critical Care Medicine, Morehouse School of Medicine, Atlanta, Georgia.
A Rare Case of Mixed Squamous Cell and Glandular Papilloma in Peripheral Bronchus With Extensive Growth Into Lung Parenchyma

(Ying Sun, MD, PhD; Areeba H. Rizvi, MD; Kotaro Takeda, MD, PhD; Ann Sutton, MD; Thomas Sporn, MD. Department of Pathology, East Carolina University/Vidant Health Center, Greenville, North Carolina.)

Solitary endobronchial papilloma is a rare benign pulmonary neoplasm. Among the 3 subtypes, squamous cell papilloma, glandular papilloma, and mixed-squamous cell and glandular papilloma (MSCGP), MSCGP is the rarest with a predilection for older male smokers. MSCGP usually exhibits focal endobronchial growth in the trachea and bronchi and is rarely located peripherally. Here, we report a case of peripheral MSCGP with alveolar infiltration. A 54-year-old female nonsmoker presented with chronic cough and hemoptysis. Computed tomography found a 5.6-cm left peripheral mass. Bronchoscopy revealed a peripheral endobronchial exophytic mass. Biopsy specimen showed papillary architecture with marked squamous metaplasia. Left upper lobectomy was performed. Grossly, 1 peripheral ill-defined 5.6 × 2.1 × 1.1-cm solid mass was identified with pucked pleura. Microscopically, the tumor was composed of papillary architectures with thick fibrovascular cores. The linings were admixtures of nonkeratinizing squamous and pseudostratified ciliated glandular epithelium showing bland cytomorphology with focal reactive changes. Mitotic activity and necrosis were absent. Adjacent parenchyma showed extensive inflammatory and reactive changes, consistent with post-obstructive pneumonia. Immunohistochemically, tumor cells were CK5/6 diffuse strong positive and TTF-1 weak positive with CK7 positive luminal layer and p40 positive basal layer. Mediastinal lymph nodes were negative for metastasis by pan-cytokeratin staining. In contrast to usual MSCGP, this tumor was peripherally located and directly extended into the adjacent alveolar spaces. Future studies are necessary to explore the pathogenesis of these lesions.

Ground Glass Opacity: What’s in a Name?

(James W. Roberts, MD (james.wesley.roberts@emory.edu); Geoffrey Smith, MD; Frank Schneider, MD; Gabriela M. Opres-Ilie, MD; Eric L. Flenzaugh, MD. 1Department of Pathology, Emory University, Atlanta, Georgia; 2Department of Pulmonary & Critical Care Medicine, Morehouse School of Medicine, Atlanta, Georgia.)

Context: Ground glass opacity (GGO), a nonspecific finding on X-ray and computed tomography imaging, consists of a hazy opacity not obscuring the underlying bronchial structure. The underlying pathology varies from benign conditions (pulmonary edema, infections including COVID-19, and Pneumocystis pneumonia), to malignancies such as adenocarcinoma, most frequently lepidic spread type.

Design: An electronic search for GGO lesions in comparison with other types (single or multiple nodules, spiculated masses, etc.) diagnosed in our lung nodule clinic was performed for the last 7 months. Tissue was collected for histopathologic examination using tip-tracked-guided fine-needle aspiration, biopsy procedure, and/or bronchial brushing. We compared association of GGO with adenocarcinoma of the lung with lepidic spread (Figure 4.109, A and B).

Results: We identified 122 patients (64 male). We diagnosed 82 malignancies, mostly primary lung carcinomas. Average age at presentation was 62.5 years, similar between men and women. We found a statistically significant association of GGO with adenocarcinoma with lepidic spread (ADCC-L): The Fisher exact test statistic value is 0.0014 (P < .05). When calculating by sex, this significance was lost in men (P = .06).

Conclusions: GGO showed statically significant association with lung ADCC-L in our patient population. Combined cytologic/histologic and imaging data are important for an optimal classification of carcinoma with lepidic spread. Tip-tracked-guided procedures obtain diagnostic tissue from these challenging to sample lesion.
Long-Term Survival of Patients With Micropapillary Lung Adenocarcinoma: Morphology and Molecular Features With Exemplary Case Report

(Poster No. 110)

Shannon Rodgers, DO (sroder5@hfhs.org); Sameer Chhetri Aryal, MD; Joseph Montecalvo, MD; Laura Favazza, DO; Zhiqiang Wang, MD. Department of Pathology and Laboratory Medicine, Henry Ford Health System, Detroit, Michigan.

Context: Micropapillary (MP) lung adenocarcinoma is known for its aggressive behavior. Some studies, however, showed variable outcomes depending on certain elements, including proportions of MP components. We report a cohort with more than 5-year follow-up and molecular profiling of 1 exemplary case.

Design: We reviewed surgical resections during 2014 to 2015 and divided the cohort into the following 3 categories: good (no recurrence), intermediate (recurrence), poor (deceased) (Table). One 2005 case (Case 1, category 2) was included for molecular characterization because of the MP predominant morphology, 7.2-cm size and 3.5-cm size of the primary and recurrent tumors. Using a 52-gene next-generation sequencing (NGS) panel, we tested the primary tumor (papillary, MP portions) and the recurrent tumor by hybrid capture method using Illumina MiSeq instrument and data analysis by SOPHiA DDM platform.

Results: We identified 19 cases with overall 74% 5-year survival. NGS detected 2 TP53 Tier 1/2 variants; MET exon 14 skipping mutation, and 1 Tier 3 KMT2D variant on the MP portion. In contrast, the recurrent tumor exhibited 101 variants with 23 Tier 1/2 variants, including EGFR p.Gly719Cys and 1 same variant TP53 p.Arg213* with documented 1% occurrence in all tumors.

Conclusions: MP and non-MP portions can have similar genetic alterations and such tumors may pursue a nonaggressive clinical course. Prolonged tumor growth accumulates genetic damage, and the extent can be striking. Findings of our cohort support literature and the molecular data obtained with a 13-year interval offered a rare chance to gain insights on tumor evolution.

Summary of Clinical and Major Histologic Information

<table>
<thead>
<tr>
<th>Categories</th>
<th>Cases</th>
<th>Age/Sex (Years to Follow-Up)</th>
<th>Predominant Histologic type, Location</th>
<th>Tumor size (cm)/% of Micropapillary Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - Good</td>
<td>11 Cases</td>
<td>62–89/4 males:7 females</td>
<td>Lepidic, acinar, papillary</td>
<td>0.9–4.2 cm (highest &gt;50%)</td>
</tr>
<tr>
<td>2 - Intermediate Case 1</td>
<td>65/male</td>
<td>Papillary, micropapillary</td>
<td>7.2 cm</td>
<td></td>
</tr>
<tr>
<td>2 - Intermediate Case 1 follow-up</td>
<td>78/male (3 years later)</td>
<td>Left lower lobe</td>
<td>&gt;50%</td>
<td></td>
</tr>
<tr>
<td>2 - Intermediate Case 2</td>
<td>58/male</td>
<td>Papillary, micropapillary</td>
<td>3.5 cm</td>
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<tr>
<td>2 - Intermediate Case 2</td>
<td>58/male</td>
<td>Right upper lobe</td>
<td>&gt;50%</td>
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<tr>
<td>2 - Intermediate Case 2 follow-up</td>
<td>62/male (4 years later)</td>
<td>Acinar, solid, papillary, MP</td>
<td>2.2 cm</td>
<td></td>
</tr>
<tr>
<td>2 - Intermediate Case 3</td>
<td>66/male</td>
<td>Right lower lobe</td>
<td>&lt;5%</td>
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</tr>
<tr>
<td>2 - Intermediate Case 3</td>
<td>66/male</td>
<td>Acinar</td>
<td>3.5 cm</td>
<td></td>
</tr>
<tr>
<td>2 - Intermediate Case 3</td>
<td>70/male (4 years later)</td>
<td>Left lower lobe</td>
<td>&lt;5%</td>
<td></td>
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<tr>
<td>3 - Poor Case 1</td>
<td>57/Female (deceased)</td>
<td>Lepidic, acinar, cribriform, solid, MP</td>
<td>2.3 cm</td>
<td></td>
</tr>
<tr>
<td>3 - Poor Case 2</td>
<td>86/Male (deceased)</td>
<td>Acinar, papillary, solid, MP</td>
<td>3.0 cm</td>
<td></td>
</tr>
<tr>
<td>3 - Poor Case 3</td>
<td>80F (deceased)</td>
<td>Right lower lobe</td>
<td>15%</td>
<td></td>
</tr>
<tr>
<td>3 - Poor Case 4</td>
<td>64/female (deceased)</td>
<td>Solid</td>
<td>&gt;50%</td>
<td></td>
</tr>
<tr>
<td>3 - Poor Case 5</td>
<td>77/female (deceased)</td>
<td>Right upper lobe</td>
<td>&lt;5%</td>
<td></td>
</tr>
</tbody>
</table>

Improving Anatomic Pathology Staff Schedules With Epic

Beaker: Data Science Use Case in a Dermatopathology Practice Group

(Poster No. 111)

Martin C. Chang, MD, PhD (martin.chang@uvmhealth.org); Valerie Cortright; Anne M. Stowman, MD. Department of Pathology & Laboratory Medicine, University of Vermont Medical Center, Burlington.

Context: Epic is a widely used electronic medical record. An increasing number of pathology departments are adopting the Epic Beaker Anatomic Pathology (Beaker AP) module. Our dermatopathology slide volume is high, subject to batch histology processing, and covered by 3 pathologists (2.4 full-time employment) with complex academic schedules. Adoption of Beaker AP facilitated near-real-time tracking of slide volumes. Our objective was to use data science to align slide volumes to staff schedules and improve satisfaction.

Design: Using Beaker AP’s workbench reporting, all dermatopathology slide volumes for 5 consecutive months were tracked and analyzed as time-series using Python 3 scripts (http://www.python.org). We created pivot tables and data-plots to visualize the time-course of slide volumes. We redistributed pathologists and histology staff to match more busy time periods. Changes in workload, slide distribution, and satisfaction (by survey) were calculated.

Results: For 5 months, 15,156 slides were distributed to our dermatopathologists, and 63.5% (mean) of slides were ready before 11 AM. Postadjustment, 1 month data (3150 slides) showed 71.5% of slides ready before 11 AM, improving mean turnaround time from 48.8 to 40.5 hours. Percentage of slides distributed to pathologists A (0.9 FTE), B (0.8 FTE), and C (0.7 FTE) changed from 34%, 36%, 29%, to 44%, 29%, 26%,
respectively, more closely approximating rank order. The changes resulted in higher satisfaction among all pathologists.

**Conclusions:** Beaker AP has inbuilt case tracking and reporting functions, but not turnkey solutions for workflow management. Data science can augment the usefulness of Beaker AP reporting. Simple data-driven adjustments to staff scheduling can increase satisfaction.

**Digital Immunohistochemistry in Northern Alberta**  
(Poster No. 112)

Anna M. Piskorski, MD (anna.piskorski@gmail.com); Mary Melnyk, MLT. Department of Pathology, Dynalife Medical Labs, Edmonton, Alberta, Canada.

**Context:** Owing to the remote locations of the hospitals affiliated with our laboratory, Dynalife, immunohistochemistry slides have a turnaround time (TAT) of 48 to 72 hours. Digitalizing the immunohistochemistry slides would provide quicker TAT and better patient care.

**Design:** The following criteria was used to select immunohistochemical slides: staining platform, retrieval, detection system, chromosome, and staining pattern. There were 20 different stains included in the validation study (Table). This yielded 382 slides. All slides were scanned by the Aperio GT450 scanner at ×40 magnification. We recruited 8 pathologists for the study. Six pathologists were in the laboratory in Edmonton while 2 were from remote sites, Grand Prairie and Fort McMurray, respectively. Each pathologist underwent a training session with a review of the viewing software, Aperio eSlide Manager, before the study. The pathologists were asked to interpret the glass slide and record the findings on a worksheet. After a washout period of 1 month, the pathologist interpreted the corresponding digital images and reported the findings. All results were collated in an excel spreadsheet for interpretation.

**Results:** One case was excluded due to a scanning error that resulted in an uninterpretable image. There was 100% concordance between the remaining 381 glass and digital slides. Digitalizing immunohistochemistry slides for remote hospitals resulted in a decreased TAT (<24 hours) from the time the case was assembled.

**Conclusions:** The ordering pathologist can view the immunohistochemistry slide on the same day as it is assembled. This enables the case to be finalized or further immunohistochemistry slides to be ordered promptly.

<table>
<thead>
<tr>
<th>Immunohistochemistry Stains</th>
<th>DAKO</th>
<th>Low pH</th>
<th>High pH</th>
<th>High pH cocktail</th>
<th>Low pH cocktail</th>
<th>Extended high retrieval</th>
<th>Red</th>
<th>Ventana</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenotypic markers</td>
<td>PIN</td>
<td>MIB1</td>
<td>ERG</td>
<td>p40/D240/p40</td>
<td>p16</td>
<td>p53</td>
<td>CD20</td>
<td>Kappa</td>
</tr>
<tr>
<td>Staining markers</td>
<td>p16</td>
<td>p53</td>
<td>p53</td>
<td>p40/D240/p40</td>
<td>p53</td>
<td>p100</td>
<td>GATA3</td>
<td>Lambda</td>
</tr>
<tr>
<td></td>
<td>PIN</td>
<td>MIB1</td>
<td>ERG</td>
<td>p40/D240/p40</td>
<td>p16</td>
<td>p53</td>
<td>CD20</td>
<td>Kappa</td>
</tr>
</tbody>
</table>

**Discordant Cases Summary**

<table>
<thead>
<tr>
<th>Glass Diagnosis</th>
<th>WHI Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-grade squamous intraepithelial lesion</td>
<td>Low-grade intraepithelial lesion</td>
</tr>
<tr>
<td>Sessile serrated adenoma</td>
<td>Hyperplastic polyp</td>
</tr>
<tr>
<td>Focal intestinal metaplasia of the antrum</td>
<td>Normal</td>
</tr>
<tr>
<td>Actinic keratosis</td>
<td>Lichen simplex chronicus</td>
</tr>
<tr>
<td>Tubular adenoma with focal high-grade dysplasia</td>
<td>Tubular adenoma negative for dysplasia</td>
</tr>
<tr>
<td>Chronic antral gastritis with intestinal metaplasia</td>
<td>Chronic antral gastritis</td>
</tr>
</tbody>
</table>

**Digital Pathology Validation for Primary Sign Out**  
(Poster No. 113)

Anna M. Piskorski, MD (anna.piskorski@gmail.com); Mary Melnyk, MLT. Department of Pathology, Dynalife, Edmonton, Alberta, Canada.

**Context:** Advances in technology have revolutionized pathology pushing whole slide imaging to the mainstream. We undertook a study to validate digital pathology for primary diagnosis sign out.

**Design:** Four pathologists were recruited for the study. Each pathologist viewed a training video in addition to 1-on-1 training sessions on the image viewer software, Aperio eSlide Manager. Retrospective case review of the 4 reporting pathologists’ worklists from at least 2 months prior was conducted. Case selection included cases routinely seen by the department. Cases included biopsy specimens and resections with accompanying extra levels, immunohistochemistry, or special stains. A separate search was conducted for cases with frozen sections and/or touch prep slides to enhance the variety of the cases. All slides were scanned by the Aperio GT450 and reviewed on the Aperio Viewing Station. The reporting pathologist interpreted the digital slide and recorded the diagnosis in the image viewer software. All diagnoses were collated in an excel spreadsheet and compared to the original diagnosis rendered on glass slides.

**Results:** There were 108 cases initially included in the study. Two cases were excluded from the analysis as the reporting pathologist did not enter a final diagnosis. This yielded 106 cases, 194 parts or reads, or 728 slides. The concordance rate was 95% for 106 cases and 96% for 194 parts/reads. The discordance rate was 5% and 4%, respectively (Table).

**Conclusions:** This study demonstrated a high rate of concordance. In addition, it highlighted the pitfalls encountered in digital pathology seen on a closer examination of the discordant cases.

![Immunohistochemistry Stains](image_url)

**Assessment of Tumor-Infiltrating Lymphocytes in Head and Neck Squamous Cell Carcinoma and Invasive Breast Carcinoma H&E-Stained Slides: Inter-observer Agreement and Visual Versus Computer-Assisted Evaluation**  
(Poster No. 114)

Javier A. Baena-Del Valle, MD1 (javier.baena@fsfb.org.co); Mauricio A. Palau-Lázaro, MD2; Margarita Baldión-Elorza, MD3; Catalina Buritica-Cifuentes, MD4; Patricia Bernal-Trujillo, MD5; Gonzalo Ucrós-Rodríguez, MD6; Alvaro Muñoz-Pérez, MD7; Vanessa Osorio-Serrano, MD8; Javier Segovia-Gómez, MD9; Alberto Escallon-Cubillos, MD10; José A. Hakim-Tawil, MD11; Paula A. Rodríguez-Urrego, MD12; Departments of 1Pathology and Laboratory Medicine, 2Diagnostic Imaging, Section of Nuclear Medicine, 3Institute of Oncology Carlos Ardila Lulle and 4Surgery, Section of Head and Neck Surgery, Fundacion Santa Fe de Bogota University Hospital, Bogota, Colombia.

**Context:** Characterizing the tumor microenvironment has emerged as a new line of study in solid tumors, because quantification of tumor infiltrating lymphocytes (TILs) reflects the immune response in the tumor microenvironment and helps determine patient outcome and response to certain therapies. Although some working group guidelines aimed to standardize visual TILs assessment have been published, there are still many limitations to its use in daily practice. The aim of this study was to evaluate the interobserver agreement of visually assessed TILs and a visual versus computer-assisted evaluation comparison.

**Design:** A total of 47 samples from head and neck squamous cell carcinoma (n = 37) and invasive breast carcinoma (n = 10) patients were included. Low-density TMAs were constructed, and slides were stained with H&E. Digital quantitation of TILs was performed by separating the intratumor stroma using an object classifier (Figure 4.114, A and B), followed by a cell classification based on nuclear/cytoplasmic ratio (Figure 4.114, C) and smoothed features (Figure 4.114, D) by using QuPath v0.2.3. Visual quantification of TILs was performed by 4 pathologists.
Sharing is Caring: Solutions for Managing Specimens Processed in Multiple Specialty Laboratories

Michelle Stoffel, MD, PhD (michellestoffelmpdphd@gmail.com); Rodney A. Schmidt, MD, PhD; Andrew Bryan, MD, PhD; David C. Chhieng, MD; Patrick C. Mathias, MD, PhD; Noah G. Hoffman, MD, PhD. Department of Laboratory Medicine and Pathology, University of Washington, Seattle.

Context: Specimens collected in a single container that need to be divided and processed among multiple specialty labs require careful management of complex logistics and communication challenges. If a specimen is initially routed to the wrong lab, it may be incorrectly processed (e.g., placed in formalin before culture is performed). Examples of “shared specimens” with multiple orders include body fluids (e.g., cerebrospinal fluid) with cytology, flow cytometry, cytogenetics, or microbiology orders, and tissue samples with molecular testing, microbiology, or surgical pathology orders. Our institution is changing electronic health record (EHR) vendors, destabilizing our existing management solution. The new workflow faced multiple barriers to success, including 2 distinct laboratory information systems (LIS) managing the same specimens (Table).

Design: Laboratorians, clinicians, and EHR consultants conducted a multifactorial process redesign. We mapped current workflow faced multiple barriers to success, including 2 distinct laboratory information systems (LIS) managing the same specimens (Table). The main limitation is dependency on clinicians understanding specimen requirements adequately to flag them, which is an anticipated challenge.

Conclusions: Managing shared specimens among specialty labs is complex, even more so when there are multiple LIS systems involved. Deep understanding of workflow and technical limitations are critical to management. Human factors must be anticipated and addressed with collaboration and communication.

<table>
<thead>
<tr>
<th>Shared Specimen Challenges and Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Challenge</td>
</tr>
<tr>
<td>Tracking shared specimens among specialty labs in the context of 2 distinct LIS software systems for anatomic and clinical pathology specimens</td>
</tr>
<tr>
<td>Determining knowledge and communication gaps among specialty labs</td>
</tr>
<tr>
<td>Engaging clinician stakeholders in mutual specimen stewardship</td>
</tr>
</tbody>
</table>

Automation of Ordering Levels on Routine Colonic Biopsies With a Deep Learning Algorithm

Anna M. Piskorski, MD (anna.piskorski@gmail.com); Mary Melnyk; Vinoth Babu, MBA; Navaneeth Kamballur K. Kottayil, PhD; Tyler Verdun, MD. 1 Department of Pathology, Dynalife Medical Labs, Edmonton, Alberta, Canada; Departments of 1Project Development and 1Machine Learning Development, AltaML, Edmonton, Alberta, Canada.

Context: Dynalife is a high-volume laboratory in Alberta with a high volume of colonic biopsy specimens. To look for polyps in benign colonic mucosa 2% of all blocks in the laboratory are submitted for levels. This is approximately 24,000 blocks. We looked at a machine learning algorithm to automate the process.

Design: Benign colon biopsy slides and colon biopsy slides with polyps were selected for the study. Colonic biopsy specimens with colitis were excluded from the normal colon biopsy set. All colon polyps routinely seen by the department were included in the study. This yielded 734 abnormal slides and 375 normal slides. All slides were scanned by Aperio GT450 and underwent a pre- and postscan quality check. The slides were divided into two data sets and subdivided into train, validate and test categories (Table). A convolutional neural network (CNN)–based model was used for image classification into normal and abnormal biopsy slides. The model was trained, best
parameters were selected with the validation set, and verified with the test set of images. The algorithm generated a heat map on the whole slide image and generated a slide level label of abnormal or normal (needs levels).

**Results:** The performance report on the combined test dataset showed an accuracy, precision, and sensitivity of 91%.

**Conclusions:** This study demonstrates a novel machine learning tool that can accurately and precisely identify polyps in colonic mucosa. Integration into a digital pathology workflow would enable automation of ordering levels on normal colonic mucosa biopsy specimens.

Transfusion Medicine Informatics: Clinical Decision Support Tools in Promoting Appropriate Blood Utilization: A Focus on the User Experience

(Poster No. 117)

Riley A. O’Hara, MD (rohara2@uw.edu); Monica B. Pagano, MD; Patrick C. Mathias, MD, PhD; Hamilton C. Tsang, MD. Department of Laboratory Medicine and Pathology, University of Washington, Seattle.

**Context:** Clinical decision support (CDS) tools increase efficiency of blood product ordering, delivery processes, and improve the appropriateness of orders. CDS alerts were implemented in the electronic medical record at this institution. This study investigated whether implementation of CDS tools led to measurable change in ordering practices and to quantify the user burden of CDS tools.

**Design:** CDS alerts triggered for consensus-derived thresholds in hemoglobin/hematocrit, platelet count, international normalized ratio, and fibrinogen established for red blood cell, platelet, plasma, and cryoprecipitate, respectively. Pertinent data were analyzed from the 16-month period after implementation.

**Results:** Refer to the Table for a summary of alerts fired during the analysis period. Comparing the first 8 months to the second 8 months of data, there was a statistically significant decrease in the overall number of alerts fired in the later 8 months ($P = .02$). A significant decrease in alerts fired for red blood cell products drove this change ($P = .01$); the change in number of alerts fired was not significant for platelets, plasma, or cryoprecipitate. Of all alerts fired, 892 ended in a cancellation (7.59% of alerts total). The average time it took for a user to respond was 9.624 seconds. The total amount of time alerts displayed was 104 4000 seconds (~29 hours), compared with 75 126 blood products transfused.

**Conclusions:** CDS alerts can guide ordering providers with minimal user burden while increasing safety and quality of ordering. User behavior changed over 16 months, with less alerts firing over time. A significant change in overall blood utilization was not observed.

<table>
<thead>
<tr>
<th>Summary of Alerts Fired During the 16-Month Analysis Period</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product Type</strong></td>
</tr>
<tr>
<td>Total number of alerts fired</td>
</tr>
<tr>
<td>Total number of products ordered</td>
</tr>
<tr>
<td>Percent of orders that triggered an alert</td>
</tr>
<tr>
<td>Percent of alerts fired</td>
</tr>
<tr>
<td>Percent of total canceled orders</td>
</tr>
<tr>
<td>Potential cost savings by cancelation (acquisition cost only) ($)</td>
</tr>
</tbody>
</table>

Error-Free Body Fluid Interpretation in the Laboratory: A Quality Improvement Study

(Poster No. 118)

Oluwatobi O. Ozoya, MD, MPH (oluwatobi@usf.edu); Philip R. Foulis, MD, MPH; George T. Carlton; Loveleen C. Kang, MD; Steven J. Agosti, MD. 1Department of Pathology and Cell Biology, University of South Florida, Tampa; 2Department of Pathology & Laboratory Medicine, University of Washington, Seattle.

**Context:** Body fluids submitted to the laboratory require the coordination of chemistry, hematology, microbiology, and cytopathology departments. Clinicians, without guidance, may inadvertently not order tests critical for proper interpretation of the fluid. Because fluid samples are often shared between departments, they may not be forwarded to the appropriate department for analysis. Furthermore, a hematologist technologist is usually not trained in the interpretation of body fluid cellular morphology. These common challenges result in errors, which can be minimized with a machine learning approach.

**Design:** Specific clinician order sets were created in the electronic medical record to assist in placing critical fluid analysis orders. Samples are tracked and a department is notified if a sample is missing. All fluids are reviewed by pathologists and they perform critical steps that include full interpretation of associated chemistry reports, correlation of fluid results across other departments, and saving interesting cases for trainees. To enhance the quality of reporting, our department implemented a few improvement policies.

**Results:** Seventy percent reduction in wrong orders on fluids from body fluid cellular morphology. These common challenges result in errors, which can be minimized with a machine learning approach.

**Conclusions:** Our center has been able to minimize errors in reporting and enhanced the detection rate of malignancies. The pathologist’s review provides an inclusive interpretation of fluids and error-free diagnosis. This approach provides a robust environment for teaching pathology residents and fellows.

Patterns and Utility of Fecal Calprotectin in Patients With Microscopic Colitis

(Poster No. 119)

Ibrahim Abukhilar, MBBS (ibrahim-abukhilar@uiowa.edu); Matthew Kraskowski, MD, PhD; Andrew Bellizzi, MD; Sarag Boukhar, MBChB; Anna Merrill, PhD. Department of Pathology, University of Iowa Hospitals and Clinics, Iowa City.

**Context:** Calprotectin is a cytoplasmic protein that is released upon neutrophilic activation. Measuring fecal calprotectin (FC) is used for monitoring inflammatory bowel disease activity and distinguishing it from irritable bowel syndrome; however, its utility in other types of colitis has not been well investigated.

**Design:** Cases of collagenous colitis (CC) and lymphocytic colitis (LC) between 2015 and 2020 were retrieved from our database. Endoscopy and histopathologic findings were reviewed to confirm the diagnosis. Fifteen CC and 13 LC cases were included as FC was done at the time of diagnosis (pretreatment). Sixty-two cases of normal endoscopy and microscopy were selected as a control group. One-way analysis of variance (ANOVA) and receiver operating curve (ROC) analysis of FC were performed.

**Results:** Abnormally elevated FC (>50 μg/g) was identified in 77% and 64% of CC and LC cases, respectively. Only 1.6% of control cases had mildly elevated FC of 54 μg/g. The mean FC of CC and LC groups (246 and 214, respectively) were significantly higher than the control group (mean = 22.4); $P \leq .05$ (Figure 4.119). LC and CC groups had no...
statistically significant difference in the mean FC ($P = .8$). The area under the curve was 0.93 with ROC analysis. At the suggested cutoff of 50 µg/g, the sensitivity was 78.6%, specificity was 98.4% with a likelihood ratio of 48.7.

### High Serum Free Light Chain Levels Portend Renal Damage and Poorer Survival in Patients With Light Chain Multiple Myeloma

**Yulan Jin, MD, PhD**

(Yjin@augusta.edu); Natasha M. Savage, MD; Roni J. Bollag, MD, PhD; Anand P. Jillella, MD; Hongyan Xu, PhD; Gurmukh Singh, MD, PhD, MBA. 1 Departments of Pathology, Hematology/Oncology, and Biostatistics & Data Sciences, Augusta University, Augusta, Georgia.

**Context:** Monoclonal immunoglobulins provide an indication of the tumor burden in a given patient with plasma cell neoplasm. Previous studies have revealed an association between high levels of serum free light chains and poorer outcome in patients with light chain predominant multiple myeloma. In the current study, we examined the correlation of serum free light chain concentration with survival in patients with light chain myeloma and further explored the underlying mechanisms.

**Design:** We studied 65 light chain myeloma cases (26 lambda and 39 kappa). The correlations of serum free light chain concentration with survival, estimated glomerular filtration rate, urin protein concentration, serum albumin, alanine aminotransferase, bilirubin, and other clinical parameters were examined. The data were analyzed by t-test, X² test, and using the R software package for change point analysis.

**Results:** Change point analysis identified an inflection point of 455 mg/L of light chain concentration that separated the high group of 26 patients (from the low group of 39. More severe renal damage (eGFR: 34.3 ± 33.2 versus 62.7 ± 52.3, $P < .01$) and a poorer survival (30.1 ± 24.9 versus 58.3 ± 52.9 months, $P < .01$) were identified in the high-level subgroup compared with low level subgroup.

**Conclusions:** Excess serum free light chains in light chain myelomas appear to add to the disease burden by inflicting renal damage and reducing survival. Monitoring of serum free light chain levels and customizing treatments to address this laboratory parameter are warranted.

Singh is a consultant with Diazyme Inc and HealthTap.

### A Patient Without Glycated Hemoglobin A1C

**Azin Mashayekhi, MD**

(AMashayekhi@uams.edu); Hoda Hagrass, MD, PhD; Justin Bean, MLS. Department of Pathology and Laboratory Services, University of Arkansas for Medical Sciences, Little Rock.

The glycated hemoglobin (HbA1C) is a gold standard benchmark for long-term glycemic control. Various factors may influence HbA1C measurements and interpretation accuracy, including hemoglobin (Hb) variants. The most common Hb variants are HbS, HbE, HbC, and HbD. We describe patient laboratory results with no HbA1C peak and large peak in the E window on ion-exchange high-performance liquid chromatography, and normal fructosamine level. Complete medical history in this patient includes left foot cellulitis, microcytic anemia, hypertension, and Type 2 diabetes. The D-10 Hb profile was reran to show a peak of 85.6% in the A2 area. The specimen was sent to a reference laboratory for confirmation by electrophoresis cascade. The patient was confirmed to have HbE (93.0%; Table). HbE is abnormal hemoglobin with a single-point mutation in the β chain. HbE diseases may be found in heterozygotes, homozygotes, and compound heterozygous states (eg, HbE/R-thalassemia). Both heterozygotes and homozygotes are asymptomatic and have microcytic hypochromic anemia. Considering the history, clinical findings, and laboratory test results, our case is most likely diagnosed as homozygous HbE disease, which carries 2 mutant β genes and, therefore, no HbA1c. Typically, HbE is only mildly increased to less than 15% in this disorder. Doubly heterozygous HbE/β-thalassemia is the main alternative diagnostic consideration in this case. Both HbE disease and HbE/β-thalassemia are characterized by anemia, presence of HbE by Hb electrophoresis. Individuals with HbE/β-thalassemia can have a more devastating clinical course and have a greater HbF degree of elevation ranging from 13% to 40%.

<table>
<thead>
<tr>
<th>Reference Laboratory Result</th>
<th>Parameter</th>
<th>Results</th>
<th>Reference Intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin A quantitation</td>
<td>0.0</td>
<td>95.0%–98%</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin A2</td>
<td>4.5</td>
<td>1.5%–3.3%</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin F</td>
<td>2.5</td>
<td>0.0%–0.9%</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin S</td>
<td>0.0</td>
<td>&lt;0.0%</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin E</td>
<td>93.0%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### SARS-CoV-2 Antibody Testing in Long-Term Care Facilities

**Rita H. Khoury, MD**

(Rkhoury@aculabs.com); Peter Guidaitis, BA; Asha Gandhi, BS; Dauna Guadaitis, BA. Aculabs, Inc., East Brunswick, New Jersey.

**Context:** COVID-19 is the pandemic infection caused by a new strain of coronavirus, SARS-CoV-2, with more than 98 million confirmed cases and more than 500,000 deaths; the number might be higher because some cases are mild or with no symptoms. Although we do not have enough knowledge about the immunity nor the body response to the infection, serology tests are very important to understand the past exposure and immunity toward SARS-CoV-2 and the seroprevalence in the population.

**Design:** We collected 2166 samples from residents in long-term care facilities for SARS-CoV-2 antibody testing. The Roche Elecsys Anti-SARS-CoV-2 (Roche, Basel, Switzerland), a qualitative assay that uses a recombinant protein representing the nucleocapsid antigen for the determination of antibodies against SARS-CoV-2, was used on all samples tested. Data were separated into sex and age. Statistical analyses were done using Analyse-it.

**Results:** A total of 1259 (58.1%) samples were from women and 907 (41.9%) were from men; median age for women was 70.9 years and 68.1 years for men (Table). Overall positive rate was 74.1%; however, men had a higher positive rate with 80.5% and women had a positive rate 68.5%. Some of the patients tested had neither positive molecular test nor COVID-19 symptoms.

**Conclusions:** Our data showed that the majority of the long-term care facilities resident and employees had positive results even without confirmed cases, which could be due to a higher exposure among them.
and the presence of asymptomatic cases. The higher positivity rate in men could be due to combination of physiological difference, different behaviors (smoking, alcohol consumption), and higher prevalence of predisposing factors that make them more susceptible to get COVID-19.

| Summary of Anti–SARS-CoV-2 Testing |
|-------------------------------|---|
| Women | Men |
| Median age | 74.1 | 68.2 |
| Total sample | 1259 | 907 |
| % positive | 69.5 | 80.5 |

**Conflicting SS-A/Ro Test Results: A Novel Test Artifact**

*(Poster No. 123)*

Stephanie Conrad, MD (sconrad@tuftsmedicalcenter.org); Steven Bogen, MD. Department of Pathology, Tufts Medical Center, Boston, Massachusetts.

A 28-year-old woman with an undifferentiated connective tissue disease was seen for routine follow-up. In past years, her anti-nuclear antibody (ANA) and SS-A/Ro antibody test results were either negative or weakly positive. A repeat SS-A/Ro antibody level was extremely high, beyond the reportable range. This test was repeated and confirmed. The laboratory had adopted a new vendor for autoimmune testing. When the test was repeated using the previous vendor’s kit, there was no detectable SS-A/Ro antibody. This case highlights SS-A/Ro antibody levels that are either beyond the reportable range or negative, depending on the test vendor. To resolve this discrepancy, we performed an ANA test. The ANA test result was negative; the Hep-2 cells showed cytoplasmic but not nuclear staining (Figure 4.123). This patient has extremely high levels of monospecific SS-A/Ro-52 antibodies. SS-A/Ro52 localizes to the cytoplasm of Hep-2 cells, accounting for the cytoplasmic staining. The laboratory's new SS-A/Ro immunoassay incorporates both SS-A/Ro-60 and recombinant SS-A/Ro52. The previous test used purified SS-A/Ro without any quality check to ensure SS-A/Ro52 is present. The previous test only detected SS-A/Ro and failed to detect SS-A/Ro52. This deficiency can miss relevant patients because the Ro52+/Ro60- antibody phenotype is described in association with undifferentiated connective tissue disease.

**The Impact of End-of-Life Transfusions on Blood Utilization at an Academic Medical Center**

*(Poster No. 125)*

Ashley D. Ellis, MD(aellis@bloodworksnw.org); Daniela Hermelin, MD; Nicole Neeley, BS; Douglas Blackall, MD, MPH.1 Department of Medical Services, Bloodworks Northwest, Seattle, Washington; Department of Pathology, Saint Louis University School of Medicine, Saint Louis, Missouri; 2Department of Laboratory Services, Providence Health and Services, Portland, Oregon.

**Context:** Healthcare resource utilization increases at the end of life; however, blood product utilization is not well studied. A retrospective cohort study was conducted at an academic tertiary care hospital to review blood product utilization in patients who expired. A total of 866 patients expired during the study period (Table). Of these patients, 387 (44.7%) were transfused in the final 30 days of life. The cohort used 22.2% of all blood products. Of 11,087 red blood cell (RBC) units, 19.5% were transfused to the cohort. Trauma patients received 27.5% of units. Patients with liver disease received 33% of all plasma and 45.3% of all cryoprecipitate. Oncology patients received 40.8% of all platelets. Most patients received RBCs (85.3%). The proportion of platelet and plasma transfusions among these patients was similar at 41.9% and 38.7%, respectively. Only 17.3% of patients received cryoprecipitate. Most patients (75%) expired in intensive care units. Of the remainder, 18% expired on medical/surgical floors, 6% expired in the emergency department, and 1% expired peripartum.

**Cohort Characteristics**

<table>
<thead>
<tr>
<th>Sample size (n)</th>
<th>387</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males % (n)</td>
<td>57.9 (224)</td>
</tr>
<tr>
<td>Females % (n)</td>
<td>42.1 (163)</td>
</tr>
<tr>
<td>Age: mean/median/range</td>
<td>58.7/61/17–95</td>
</tr>
<tr>
<td>Cause of death, n (%)</td>
<td></td>
</tr>
<tr>
<td>Hepatic</td>
<td>67 (17.3)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>61 (15.8)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>59 (15.3)</td>
</tr>
<tr>
<td>Intracranial hemorrhage/stroke</td>
<td>52 (13.4)</td>
</tr>
<tr>
<td>Trauma</td>
<td>43 (11.1)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>39 (10.1)</td>
</tr>
<tr>
<td>Other</td>
<td>66 (17.0)</td>
</tr>
</tbody>
</table>

**Retrospective Pilot of the Utility of SARS-CoV-2 Serology in Decision Making When Molecular Testing Was Delayed**

*(Poster No. 124)*

Shikha Malhotra, MBBS (malhotras8@upmc.edu); Sarah E. Wheeler, PhD. Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh.

**Context:** Nucleic acid amplification tests (NAAT) are the diagnostic gold standard for COVID-19; however, difficulties with sampling, turnaround times, and test shortages created gaps in testing in many hospitals in spring 2020. Reliable serologic testing was fast, widely available, and did not require the technical expertise of many NAAT platforms. In the above situation, we undertook a retrospective pilot study to ascertain the clinical value of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibody testing in patients presenting to our hospital for medical care and having SARS-CoV-2 molecular testing ordered.

**Design:** Our goal was to correlate NAAT and serology from within 24 hours of presentation. All cases (n = 81) with adequate residual specimen for serologic testing were included. NAAT was performed using the Cepheid GeneXpert platform (Sunnyvale, CA) or a Laboratory Developed Test based on the Centers for Disease Control and Prevention protocol. Serologic total SARS-CoV-2 antibody testing was performed on the Siemens ADVIA Centaur XP system (Erlangen, Germany).

**Results:** A total of 16 of 81 cases had reactive serology of which 14 had molecularly detectable infection. The correlation between reactive serology and molecular detection was seen in both symptomatic and asymptomatic individuals. Nonreactive serology (n = 65) correlated with negative NAAT results in asymptomatic individuals (13 of 15) but not in symptomatic individuals (24 of 50).

**Conclusions:** This study indicated that reactive serologic testing could be another clinically useful tool for triaging suspected COVID-19 patients when molecular testing was not immediately available. Prior history of SARS-CoV-2 infection and population prevalence should also be considered.

Malhotra is a shareholder of Siemens. Wheeler has received grant or research support from Siemens Healthineers.

**Conclusions:** The final 30 days of life account for significant blood product utilization. To assess resource stewardship, further study is being undertaken to determine the appropriateness of transfusion in this cohort in comparison to patients who did not expire in close proximity to transfusion.
Outcomes in Coronavirus Disease 2019 Patients on Extracorporeal Membrane Oxygenation Requiring Massive Transfusion
(Poster No. 126)

Stephanie Conrad, MD (sconrad@tuftsmedicalcenter.org); Raymond Comenzo, MD; Judy Forbes; Shauna Mazzola; Nuong Phan; Leslie Lussier; Jensyn Cone Sullivan, MD. Department of Pathology, Tufts Medical Center, Boston, Massachusetts.

Context: Extracorporeal membrane oxygenation (ECMO), an invasive form of cardiac and respiratory support, has provided a survival benefit in patients with severe acute respiratory distress but is associated with a heightened risk of massive bleeding. Severe COVID-19 has been associated with coagulopathic derangement and respiratory distress requiring ECMO. We compared outcomes in ECMO patients with and without COVID-19 requiring massive transfusion (MT).

Design: We performed a retrospective chart review of patients on ECMO requiring MT from January 2020 to 2021, and collected data regarding number and type of blood products transfused, red blood cell to plasma transfusion ratio, COVID-19 status, 24-hour and 30-day mortality, and time from MT to death (Table).

Results: During this period 10 of 80 patients on ECMO required MT, 3 with COVID-19 and 7 without. Median numbers of red blood cell, plasma, and platelet units and cryoprecipitate pools transfused were 8, 4, 2 and 0, respectively, in patients with COVID-19 and 6, 6, 1, and 2 in patients without COVID-19. There were no significant differences in products used between the 2 groups. Within 24 hours of MT 0 of 3 and 4, 2 and 0, respectively, in patients with COVID-19 and 6, 6, 1, and 2 in patients without COVID-19 died and within 30 days of MT 2 of 3 and 3 of 7 in these 2 groups died.

Conclusions: In this small patient series, we found no significant differences in product requirements or outcomes between patients with COVID-19 and those without on ECMO requiring MT.

### Summary of Blood Product Transfusions in Trauma

<table>
<thead>
<tr>
<th>Transfused</th>
<th>pRBC</th>
<th>FFP</th>
<th>PLT</th>
<th>Cryo</th>
</tr>
</thead>
<tbody>
<tr>
<td>All major traumas</td>
<td>Issued</td>
<td>431</td>
<td>82</td>
<td>26</td>
</tr>
<tr>
<td>Transfused</td>
<td>118</td>
<td>35</td>
<td>12</td>
<td>26</td>
</tr>
<tr>
<td>% transfused</td>
<td>27.4</td>
<td>42.7</td>
<td>46.1</td>
<td>66.7</td>
</tr>
<tr>
<td>% transfused in ED</td>
<td>88.1</td>
<td>77.1</td>
<td>75.0</td>
<td>88.4</td>
</tr>
<tr>
<td>MTP Patients</td>
<td>Issued</td>
<td>151</td>
<td>74</td>
<td>22</td>
</tr>
<tr>
<td>Transfused</td>
<td>87</td>
<td>33</td>
<td>12</td>
<td>25</td>
</tr>
<tr>
<td>% transfused</td>
<td>57.6</td>
<td>44.6</td>
<td>54.5</td>
<td>69.4</td>
</tr>
<tr>
<td>Mean issued</td>
<td>6.6</td>
<td>3.1</td>
<td>0.8</td>
<td>0.7</td>
</tr>
<tr>
<td>Mean transfused</td>
<td>3.1</td>
<td>0.9</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>% transfused in ED</td>
<td>87.3</td>
<td>75.8</td>
<td>75.0</td>
<td>88.0</td>
</tr>
</tbody>
</table>

Abbreviations: IQR, interquartile range; pRBC, packed red blood cells; FFP, fresh frozen plasma; PLT, platelets; Cryo, cryoprecipitate.

<table>
<thead>
<tr>
<th>Patients on ECMO Requiring Massive Transfusion</th>
<th>Negative</th>
<th>Positive</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (n)</td>
<td>7</td>
<td>3</td>
<td>0.03</td>
</tr>
<tr>
<td>Male, Female</td>
<td>4, 3</td>
<td>2, 1</td>
<td></td>
</tr>
<tr>
<td>Age, years, median (IQR)</td>
<td>52 (27–64)</td>
<td>43 (26–55)</td>
<td></td>
</tr>
<tr>
<td>ECMO indication, n (%)</td>
<td>Respiratory failure</td>
<td>3 (44)</td>
<td>3 (100)</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>4 (58)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Blood products received, n, median (IQR)</td>
<td>RBC units</td>
<td>6 (2–21)</td>
<td>8 (7–16)</td>
</tr>
<tr>
<td></td>
<td>Plasma units</td>
<td>6 (3–16)</td>
<td>4 (1–16)</td>
</tr>
<tr>
<td></td>
<td>Platelet units</td>
<td>1 (1–9)</td>
<td>2 (0–7)</td>
</tr>
<tr>
<td></td>
<td>Cryoprecipitate pool</td>
<td>2 (0–6)</td>
<td>0 (0–4)</td>
</tr>
<tr>
<td></td>
<td>Total products received, n, median (IQR)</td>
<td>14 (6–52)</td>
<td>12 (10–43)</td>
</tr>
<tr>
<td>Ratio RBC units:plasma units, median (IQR)</td>
<td>1.2 (0.58–1.6)</td>
<td>2.0 (1.0–7.0)</td>
<td></td>
</tr>
<tr>
<td>Mortality, n (%)</td>
<td>24 hr</td>
<td>2 (29)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>30 d</td>
<td>3 (43)</td>
<td>2 (67)</td>
<td></td>
</tr>
<tr>
<td>Time to death, hours, median (IQR)</td>
<td>52 (27–64)</td>
<td>43 (26–55)</td>
<td></td>
</tr>
</tbody>
</table>

Cost Analysis of Switching From Massive Transfusion Pack to Whole Blood at Level 1 Trauma Center
(Poster No. 128)

Behnam Rafiee, MD (behnam2776@gmail.com); Bebu Ram, MD; Mark Friedman, DO. Department of Pathology, New York University Winthrop Hospital, Mineola.

Context: Massive transfusion protocols (MTP) to trauma patients with massive bleeding improves their survival. Administration of 1:1:1 ratio of red blood cells (RBCs):plasma:platelets has become the standard of care in terms of MTP. However, while the (1:1:1) approximates whole blood (WB), some centers have switched to the use of WB for trauma, because this provides for balanced resuscitation as all the components are transfused simultaneously with less dilution from anticoagulant/ preservative compared to (1:1:1). In addition, using (1:1:1) carries unavoidable risk for waste of components.

Design: We retrospectively collected trauma cases with MTP during second half of 2020 from HCLL/WELLSKY. Then based on the current fees we evaluated the potential cost saving using the WB instead of (1:1:1).

Results: During the second half of 2020, 27 cases of trauma patients received MTP at NYU Hospital–Long Island. Given the $266, $210, $510, and $40 cost for each unit of WB, RBCs, platelet, and plasma, respectively, using WB instead of (1:1:1) in trauma patients could have potentially decreased the cost by approximately $26 000 during a 6-month period that can be annualized to about $52 000. If we figure in technologist and nursing costs ($2200/unit transfused), administration of WB instead of (1:1:1) will have decreased the total cost by approximately $900 000/year. In addition, using WB for trauma patients can potentially prevent the waste of blood products that usually happens in administration of (1:1:1).

Conclusions: WB transfusion instead of (1:1:1) in trauma patients will have decreased the cost of patient management by more than $900 000/year and helps save precious blood components for other patients.

How Do We Determine Adequate Blood Product Inventory to Maintain Remote Refrigeration at a Pediatric Level 1 Trauma Center?
(Poster No. 127)

Christopher J. Dilli, BS (christopher.dilli@health.slu.edu); Daniela Hermelin, MD. Department of Pathology, Saint Louis University School of Medicine, Saint Louis, Missouri.

Context: The implementation of remote refrigeration in the emergency department setting provides immediate access to blood products, reducing delays when every second matters. Through a retrospective review of all emergency-release blood bank forms, we determined the par universal blood product inventory to sustain a pediatric Level 1 Trauma Center.

Design: All 2020 emergency release forms of a Level 1 Pediatric Trauma Center were retrospectively reviewed for patient demographics (age, sex, and weight), medical justification, blood units issued and transfused, and transfusion location.

Results: Of 166 emergency release forms investigated, 106 patients were considered Level 1 traumas and were issued a total of 431 units of packed red blood cells (pRBCs), 82 fresh-frozen plasma (FFP), 26 platelet (PLT) and 39 cryoprecipitate. Of pRBCs, 27.4% were transfused (118 of 431 transfuse/issue ratio). In 17% of this cohort, a massive transfusion protocol (MTP) was activated after receiving the first trauma pack of 2 pRBCs (mean age = 15 years, weight = 57.2 kg). The average number of units transfused in initial trauma pack were 0.49 pRBCs and the average number of MTP units transfused were 1.55 pRBCs, 0.88 FFP, 0.35 PLT. Of these units, 85.3% were transfused in the emergency department.

Conclusions: Performing a 1-year retrospective review of emergency released blood products can help determine blood product inventory levels needed to sustain remote refrigeration services for a Level 1 Pediatric Trauma center. In our case, it was determined that a par level of 2 units of whole blood and a single MTP bundle (4 pRBCs/4 FFP) would suffice.

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</tr>
</tbody>
</table>
Trends in Pathology Biobanking Operations: Experience From the Midwestern Division of The Cooperative Human Tissue Network, 2016–2020
(Poster No. 129)

Anil V. Parwani, MD, PhD, MBA1 (anil.parwani@osumc.edu); David Nohle, MS1; Randy Mandt, BA1; Marta Crouce, MD, PhD2; Rajiv Dhir, MBBS, MD, MBA3; Leona Ayers, MD, MD1; Leona Ayers, MD. MD1; Leona Ayers, MD, MD1; 1Department of Pathology, The Ohio State University, Columbus; 2Department of Pathology, Case Western Reserve University, Cleveland, Ohio; 3Department of Pathology, University of Pittsburgh, Pittsburgh.

Context: The Cooperative Human Tissue Network (CHTN) Midwestern Division (MWD) is 1 of 6 funded by the National Cancer Institute to procure and ship high-quality human tissue samples to qualified investigators in the United States and Canada. “Streaming” samples procured and processed at each investigator’s directions is emphasized rather than banking tissues based on a single protocol. Some canned samples are also used and more difficult to serve requests are “networked” to other CHTN divisions to satisfy requests more quickly. The mix of requested anatomic sites and preparations (fresh, frozen, and fixed) offers a window into evolving human tissue research trends.

Design: The Research Tissue Procurement Information System, developed and used by the Ohio State University Department of Pathology, was queried for numbers of samples shipped during a 5-year period (2016–2020). Counts of various anatomic sites and preparations were analyzed and graphed.

Results: Numbers of fresh samples requested have surpassed both frozen and fixed over the 5-year period (Figure 4.129) illustrating number of samples shipped by CHTN MWD by preparation type. The trends of numbers of samples requested and shipped by CHTN MWD from some anatomic sites are increasing as follows: kidney (291–796) and liver (167–321). Others have decreasing trends as follows: lung and bronchus (996–491), skin (413–184), and prostate (255–141).

Conclusions: Fresh samples are increasingly more requested than either frozen or fixed. The numbers of samples requested and shipped by CHTN MWD from some anatomic sites have increasing trends (kidney, liver) or decreasing trends (lung and bronchus, skin, prostate).

Integrating the Laboratory: House Staff Patient Safety and Quality Improvement Council
(Poster No. 130)

Zan Ahmed, MD1 (zahmed@healthsouthAlabama.edu); J. Elliot Carter, MD1; Michael Chang, MD, 2Departments of 1Pathology and 2Health Administration, University of South Alabama, Mobile.

Context: Preanalytical analysis is an area well recognized as a source of delay in the turnaround time of a clinical laboratory. Residents are involved in front-end work and perform clinical duties at all levels of the workflow. They are suited to triage, identify, and pinpoint constricted points in quality and patient safety issues. As hospitals systems are reimbursed in the modern era through quality, preventive health, and healthcare outcomes keen resident integration is required in improving patient safety. The clinical laboratory is a unique realm in this world and proper resident integration through house-staff councils can serve as unique vessels for improvements in health systems.

Design: Residents interested in quality improvement and patient safety were recruited to join a council through submission of a letter of interest. A minimum of 1 resident was selected to represent their respective department with program director approval. The council members then elected a chair and vice chair through a voting process.

Results: In a 6-month interval, our house staff patient safety and quality improvement council was able to successfully complete one clinical laboratory quality-improvement initiative relating to preanalytical laboratory collection tube labeling. An additional 4 projects are in the pipeline.

Conclusions: Academic health systems are uniquely positioned to leverage opportunities for growth. Through initiation of a resident-led patient safety quality improvement council laboratories are able to prosper in the area of quality. The implementation of such a council can serve as a vessel to undertake projects disseminating outside of the laboratory, especially in view of preanalytical processes.

An Uncommon Case of Candida metapsilosis Aortic Valve Endocarditis
(Poster No. 131)

Alok K. Sinha, MD1 (sinhaa@etsu.edu); Patrick N. Costello, MD, 2Department of Pathology, East Tennessee State University, Johnson City; 2Department of Pathology, Johnson City Medical Center/Watauga Pathology Associates, Johnson City, Tennessee.

Fungal endocarditis (FE) is an uncommon, frequently fatal type of endocarditis representing only 1.3% to 6% of infectious endocarditis cases. Candida albicans is the most common pathogen causing FE followed by Candida parapsilosis complex. This complex consists of 3 closely related species, namely C. parapsilosis, C. orthopsilosis, and C. metapsilosis. We report the case of a 54-year-old man with no significant medical history who initially presented with a 3-month history of abdominal pain. Radiologic studies showed intraabdominal abscesses and pleural effusion. Blood cultures grew Candida species for which he received intravenous antibiotics. The patient presented again with worsening chest pain and dyspnea. Transthoracic echocardiogram revealed an aortic valve vegetation consistent with FE, for which he required valve replacement. Histopathologic examination of the valve showed acute endocarditis with vegetations containing abundant fungal spores consistent with candida species. Croccot methanamine silver stains showed ovoid spores (2-3 μm) with broad-based budding. Repeat blood cultures were positive for Candida metapsilosis, which is the least prevalent species of the complex. This case demonstrates Candida metapsilosis aortic valve endocarditis, which has not been often reported in the literature, in a patient with no significant risk factors for fungal endocarditis. C. metapsilosis is now being increasingly recognized as a bloodstream pathogen. Treatment is the combination of surgery and antymycotic agents.

A Case of IgG4-Related Disease Resulting in Constrictive Pericarditis?
(Poster No. 132)

Shaun T. Webb, DO (shaunwebb1989@live.com); Pouyan Kheirkhah, MD; Steven Garzon, MD. Department of Pathology, University of Illinois at Chicago.

Immunoglobulin G4 (IgG4)-related disease, first recognized in 2003 as a systemic disease in association with autoimmune pancreatitis, has been shown to affect nearly every organ system in the body. The most commonly affected organs are the biliary tree and salivary glands, but rarely the cardiovascular system, including the pericardium, can be involved. A 63-year-old man with a medical history of benign essential hypertension and gastroesophageal reflux disease presented to our institution with new-onset lower extremity edema and quickly progressing dyspnea on exertion. He was diagnosed with fluid overload and was admitted for aggressive diuresis and workup, which raised suspicion for cardiac etiology. Right heart catheterization showed hemodynamic changes suggestive of constrictive pericarditis. A pericardectomy was performed, and intraoperatively the pericardium

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was noted to be inflamed and thickened. Samples were sent to pathology and microbiology. Histologic examination revealed extensive fibrosis and chronic inflammation. Microbiological workup was negative, as was a Congo red stain for amyloid. Further workup revealed 25% of the plasma cells to be IgG4 positive. In our opinion these findings, including the marked fibrosis, tumefactive enlargement/thickening of the pericardium, increased IgG4-positive plasma cells, and negative microbiological workup, indicate a possible diagnosis of IgG4-related disease of the pericardium, although not all criteria have been met and other entities on the differential such as postviral pericarditis must be considered. To date, no definitive diagnosis has been reached after extensive workup, and this case highlights the difficulty in rendering a diagnosis in cases of constrictive pericarditis of unknown etiology.

IgG4-Related Disease Presenting as or With Isolated Giant Cell Temporal Arteritis

(Vasudevan D. Mahalingam, DO (vasudevan.mahalingam@beaumont.org); Ping L. Zhang, MD, PhD; Zhenhong Qu, MD, PhD. Department of Pathology and Laboratory Medicine, Beaumont Health and Oakland University William Beaumont School of Medicine, Royal Oak, Michigan.

Immunoglobulin G4 (IgG4)-related diseases are a group of disorders that can afflict multiple organs and have well-defined diagnostic characteristics. Its presentation as giant cell temporal arteritis (GCTA) is largely unrecognized. We report a single case here of an 81-year-old woman with no significant medical history. The patient presented with progressive right-sided vision loss. Concurrent laboratory workup showed elevated C-reactive protein (CRP) 53 mg/L and erythrocyte sedimentation rate (ESR) 42 mm/hr. A 3.2-cm segment of temporal artery was biopsied for pathologic examination. Histologically, severe active arteritis with lymphohistiocytic infiltrates, mural thickening, severe (>90%) luminal stenosis, and giant cells were noted (Figure 4.133, A and B)—typical findings of conventional GCTA. However, the inflammatory infiltrates also included many peripheral plasma cells confirmed by positive MUM1 immunostain, of which >90% were strongly positive for IgG4 by immunohistochemistry (Figure 4.133, C and D). The diagnosis of “giant cell temporal arteritis with features of IgG4-related disease” was rendered. Other types of arteritis including microscopic polyangiitis, Buerger disease, and granulomatosis with polyangiitis were excluded. She received high-dose intravenous methylprednisolone therapy for 3 days and was switched to oral prednisone therapy with taper. The vision in her right eye stabilized on day 4 of treatment and her ESR and CRP returned to normal. She was discharged home with ongoing rheumatologic follow-up. Serum immunoglobulin testing performed shortly after discharge showed decreased IgG-1 and IgG-2 levels with normal IgG-3 and IgG-4, consistent with posttreatment effects. Evaluation of the findings thus far are suggestive of IgG4-related disease presenting as isolated giant cell temporal arteritis.