Abstracts and Case Studies From the College of American Pathologists 2018 Annual Meeting (CAP18)

Abstract and case study poster sessions will be conducted during the 2018 College of American Pathologists Annual Meeting (CAP18), which is scheduled for October 20 to 24, 2018. The meeting will take place at the Hyatt Regency, Chicago, Illinois. The poster sessions will occur in the CAP18 Exhibit Hall. Specific dates and times for each poster session are listed below; “poster focus” times are dedicated poster viewing periods. Also shown before each poster session are the subject areas that will be presented.

POSTER SESSION 100: SUNDAY, OCTOBER 21, 2018
1:00 PM–4:30 PM; Poster Focus, 1 PM–2 PM
Gastrointestinal and Liver Pathology; Breast Pathology; Cardiovascular Pathology

Hepatobiliary Cystadenoma With Malignant Transformation to Hepatobiliary Cystadenocarcinoma: A Case Report With Literature Review

(Poster No. 1)
Ding Dai, MD, PhD (daid14@ecu.edu); F. Zahra Aly, MD, PhD. Department of Pathology and Laboratory Medicine, East Carolina University, Greenville, North Carolina.

Hepatobiliary cystadenocarcinoma is an uncommon neoplasm. We report on an unusual hepatobiliary cystadenoma with cystadenocarcinoma transformation. To the best of our knowledge, this is the first case to illustrate the transformation process from benign to malignant within the single mass lesion in liver. A 72-year-old asymptomatic man presented with a liver mass on November 9, 2017, which was 4.5 × 4.5 cm on computed tomography. Fine-needle aspiration was performed on January 9, 2018, and showed no overtly malignant cells; however, the specimen was of limited cellularity. Positron emission tomography scan on September 9, 2015, displayed no significant difference in hypermetabolic activity. Follow-up examination on October 4, 2017, showed increase in mass size to 7.3 × 6.5 cm. The patient underwent hepatic segmentectomy on November 9, 2017, for definitive diagnosis. The resection specimen showed a single pale-tan, firm mass with focally irregular borders. Microscopic examination showed a single mass composed of benign hepatobiliary serous cystadenoma with a transitional zone and small area of carcinoma. Histologically, the tumor showed the typical features of a hepatocystadenoma, which consists of multilocular cysts with a single layer of flattened or cuboidal epithelial cells without underlying ovarian stroma. The malignant area displayed more solid architecture with nests and trabecular or organoid well-differentiated tumor cells. Immunohistochemical studies were supportive of the biliary origin with positive immunohistochemical stains for CK7, CK19, and CEA. Synaptophysin, chromogranin, CD56, and mucicarmine were negative, which excluded neuroendocrine and mucinous neoplasm. Molecular profile analysis showed ARID1A positivity. Follow-up data during 3-month duration showed no evidence of recurrence or metastases (Figure 1).

Ménétrié Disease With Associated Early Gastric Cancer

(Poster No. 2)
Jing Du, MD (jingdu0713@gmail.com); Eun Young Lee, MD. Department of Pathology, University of Kentucky, Lexington.

Ménétrié disease (MD) is a rare hypertrophic gastropathy characterized by thickening of the gastric mucosa in the form of giant rugal folds, hypochlorhydria, and protein loss. It occurs in 2 forms, depending on the patient’s age: (1) adults have progressive disease with insidious onset and significant morbidity and mortality; (2) children usually have sudden onset and the disease is often self-limited. The etiology of MD is still unknown, but the association with cytomegalovirus infection in children has been well documented in previous studies. The risk of malignancy in MD is not yet entirely elucidated. Clinical evidence supports that MD is a disorder involving excess EGFR signaling. Cetuximab, an epidermal growth factor receptor inhibitor, became the first-line therapy for MD and it has been successful in some patients. Our patient was a 48-year-old woman with progressive gastrointestinal symptoms related to MD and transfusion-dependent iron-deficiency anemia for 8 years. Total gastrectomy was performed because she did not have good response to cetuximab and was found to have a 3-cm mass endoscopically. Total gastrectomy specimen showed large tortuous gastric folds in gastric fundus and body (Figure 2, doi: 10.5858/arpa.2018-0293-AB
Reprints not available.
SMAD4 Expression in Pancreatic Ductal Adenocarcinomas With the New AJCC 8th Edition Staging

(Poster No. 3)

Ari Kassardjian, MD, PhD (akassardjian@mednet.ucla.edu); Nick Stanzione, MD; Hanlin Wang, MD, PhD. Department of Pathology, UCLA, Los Angeles, California.

Context: An important genetic change in pancreatic cancer is the SMAD4 mutation, which leads to the loss of SMAD4 protein expression. Many studies have shown that the loss of SMAD4 expression is associated with poor prognosis. However, other studies have found no correlation between the loss of SMAD4 expression and poor outcome. The goal of the current study was to evaluate SMAD4 expression in the different T, N, and overall tumor stages with the new AJCC 8th edition staging.

Design: Pathology and clinical follow-up database was retrospectively queried for patients who had undergone surgical resection for pancreatic ductal adenocarcinoma between 2014 and 2017. Tumors were restaged according to the new definitions described in the 8th edition AJCC manual.

Comparison of SMAD4 Expression in Different Stages of Pancreatic Ductal Adenocarcinomas (N = 110)

<table>
<thead>
<tr>
<th>SMAD4 Expression</th>
<th>Positive, No. (%)</th>
<th>Negative, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T stage (8th edition)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1 (a, b, c)</td>
<td>12 (60)</td>
<td>8 (40)</td>
</tr>
<tr>
<td>T2</td>
<td>25 (36.8)</td>
<td>43 (63.2)</td>
</tr>
<tr>
<td>T3</td>
<td>14 (18.2)</td>
<td>18 (24.3)</td>
</tr>
<tr>
<td>N stage (8th edition)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>16 (53.3)</td>
<td>14 (46.7)</td>
</tr>
<tr>
<td>N1</td>
<td>17 (29.8)</td>
<td>38 (70.2)</td>
</tr>
<tr>
<td>N2</td>
<td>8 (32)</td>
<td>17 (68)</td>
</tr>
<tr>
<td>Stage group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IA</td>
<td>7 (63.6)</td>
<td>4 (36.4)</td>
</tr>
<tr>
<td>IB</td>
<td>7 (53.8)</td>
<td>6 (46.2)</td>
</tr>
<tr>
<td>IIA</td>
<td>2 (33.3)</td>
<td>4 (66.7)</td>
</tr>
<tr>
<td>IIIB</td>
<td>17 (30.4)</td>
<td>39 (69.6)</td>
</tr>
<tr>
<td>III</td>
<td>18 (33.3)</td>
<td>16 (66.7)</td>
</tr>
<tr>
<td>Tumor size, cm</td>
<td>2.7</td>
<td>3.4</td>
</tr>
<tr>
<td>Survival, mo</td>
<td>21.5</td>
<td>6.3</td>
</tr>
</tbody>
</table>

Results: A total of 110 patients with resected pancreatic ductal adenocarcinomas were included in this study. Overall, 37.3% of cases were positive for SMAD4 expression (Table). Lower-staged tumors had a greater proportion of SMAD4 expression. Among the T1-, T2-, and T3-staged tumors, 60%, 36.8%, and 18.2% of cases showed positive SMAD4 expression, respectively. A higher proportion of tumors with no lymph node metastasis was positive for SMAD4 expression (53.3%); however, there did not appear to be a significant SMAD4 expression difference between cases with N1 and N2 diseases. On average, SMAD4-negative tumors were 0.7 cm larger than SMAD4-positive tumors and were associated with an overall shorter patient survival.

Conclusions: In the present study, preserved SMAD4 expression is associated with lower-staged tumors, smaller tumor size, and higher survival rates compared with tumors showing loss of SMAD4 expression.

A Mouse Monoclonal Antibody to Islet 1 Reacts With Liver Tissue and Tumors in a Similar Pattern as Glutamine Synthetase

(Poster No. 4)

Daniel J. Pelletier, MD (daniel-pelletier@uiowa.edu); Chana R. Sachs, MA; Ume Salma Shaik Amjad, PhD; Dawn E. Quelle, PhD; Andrew M. Bellizzi, MD. Department of Pathology, University of Iowa Hospitals and Clinics, Iowa City.

Context: We perform immunohistochemistry (IHC) on metastatic neuroendocrine tumors of occult origin to assign primary site, including the pancreas–specific transcription factor islet 1 (ISL1). ISL1-stained liver metastases demonstrate pericentrivascular cytoplasmic hepatocyte staining (Figure 3, A), reminiscent of that seen with glutamine synthetase (GS). GS is diffusely expressed by β-catenin–activated hepatic adenomas (HAs) and some hepatocellular carcinomas (HCCs) and demonstrates maplike/anastomosing staining in focal nodular hyperplasia (FNH).

Design: ISL1 (clone 40.3A4; 1:200) and GS (clone 6/GS; 1:500) IHC were performed on tissue microarrays: 159 HCCs, 45 HAs, 31 FNHs. Staining was diffuse, maplike/anastomosing, or negative (pericentrivascular or absent). For diffuse staining, intensity (0–3+) and extent (0–100%) were evaluated with an H-score (intensity × extent) calculated. Western blots were performed on mouse liver tissue lysates; GS should react as a 42-kDa band.

Results: Diffuse staining was noted in 77% (mean H-score 126) and 29% (mean H-score 142) of HCCs and 7% (mean H-score 157) and 2% (mean H-score 270) of HAs with GS and ISL1, respectively. Maplike/anastomosing staining was seen in 97% (with GS) and 90% (with ISL1) of FNHs. All ISL1-positive HCCs were GS positive, and ISL1 positivity predominated in tumors with stronger GS positivity. Western blots revealed a prominent 42-kDa band with the GS but not the ISL1 antibody. A less prominent 50-kDa band was detected with both (Figure 3, B).

Conclusions: ISL1 IHC reacts with liver tissue/tumors similarly to GS, though ISL1 is less sensitive. Although ISL1 did not react with the major 42-kDa protein in a Western blot of liver tissue, both GS and ISL1 reacted with a minor 50-kDa protein.

CDX-2–Positive Yolk Sac Tumor Presenting as a Colon Mass in a Patient With Ulcerative Colitis: A Potential Diagnostic Pitfall

(Poster No. 5)

Khaled Alkhateeb, MBBS (kjalkhateb@louisville.edu); Houda Alattassi, MD; Nemencio Konquillo, MD. Department of Pathology, University of Louisville, Kentucky.

Yolk sac tumor (YST) initially presenting as an extragonadal mass is a diagnostic challenge because of histologic variability and tendency to mimic somatic tumors. We present a case of a 27-year-old woman who presented with phelegmon at the ileocecum with a history of ulcerative colitis for more than 10 years. Gross examination showed a large mass in the cecum extending to the ileocecal valve. Histologically, the tumor...
Assessing Novel Mutations in Colorectal Carcinoma Using Next-Generation Sequencing

(Poster No. 8)

Craig Cousineau, DO1 (craig.cousineau@beaumont.edu); Wei Li, MD2; Jason Douglas, MD, PhD2; Harry Wasyvary, MD; Bryan Thibodeau, PhD2; Claire Peeples, MD2. 1Departments of 1Pathology, 2Colorectal Surgery, and 3BioBank, Beaumont Health, Royal Oak, Michigan.

Context: In the United States there are more than 130 000 new cases of colorectal cancer annually. Characterizing mutations involved in the pathogenesis of colorectal adenocarcinoma is an important step toward developing gene-based therapies. Next-generation sequencing (NGS) enables screening for variants in large panels of genes in tissues.

Design: We collected formalin-fixed, paraffin-embedded tissue from rectal adenocarcinoma cases, including biopsy and surgical resection specimens. Patients came from 2 groups: those with a complete response (CR) to preoperative therapy (n = 8), and those who

Clinical and Histologic Characteristics

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>10 mo</td>
<td>15 mo</td>
<td>23 mo</td>
</tr>
<tr>
<td>Age at Kasai</td>
<td>10 wk</td>
<td>10 wk</td>
<td>9 wk</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Size of nodule, cm</td>
<td>0.7</td>
<td>0.5 x 2</td>
<td>1.0</td>
</tr>
<tr>
<td>Background liver</td>
<td>Biliary cirrhosis</td>
<td>Cirrhosis, adenomatous to dysplastic nodules</td>
<td>Biliary cirrhosis, 2nd incipient microscopically HCC</td>
</tr>
<tr>
<td>Histology</td>
<td>Early HCC</td>
<td>Well-differentiated HCC and HB fetal and blastic</td>
<td>Moderately differentiated HCC and incipient HCC</td>
</tr>
<tr>
<td>AFP</td>
<td>Normal</td>
<td>Elevated (303.1)</td>
<td>Normal</td>
</tr>
<tr>
<td>β-Catenin</td>
<td>Membranous and cytoplasmic</td>
<td>HCC: membranous; HB: membranous, cytoplasmic, and nuclear</td>
<td>Membranous</td>
</tr>
<tr>
<td>Glutamine synthetase</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Glypican 3</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>MO31</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>SALL4</td>
<td>Not done</td>
<td>Negative in both</td>
<td>2+ patchy nuclear</td>
</tr>
<tr>
<td>Prox 1</td>
<td>Not done</td>
<td>HB: 2–3+; HCC: weak +</td>
<td>2+ patchy nuclear</td>
</tr>
</tbody>
</table>

Conclusions: CMV infection poses serious risks in immunocompromised patients. The yield for testing lower gastrointestinal (GI) specimens from this group is consistently low. We evaluate features increasing the yield of immunohistochemistry (IHC) and its effect on clinical outcome.

Design: We reviewed all positive lower GI cases during 10 years. Data collected included primary disease, biopsy indication, serologic results, clinical suspicion, treatment, and outcome. We also recorded endoscopic and histologic inflammation grade, virocytes (H&E and IHC), unique histology, and biopsy site and number. Control cases included 51 IHC-negative cases and IHC-negative internal controls from the study group.

Results: Fifty patients were eligible for study. The distribution of underlying disease was similar between study and control patients. Clinical features predicting CMV IHC positivity included positive serology and clinical concern (both P < .001). Uninfamed or mildly inflamed mucosa was more common in CMV-negative biopsies (P = .04). Amongst patients with proven CMV infection, positive biopsy sites tended to have higher levels of eosinophils and more severe inflammation than negative sites. Sixteen of 34 treated patients had adverse outcomes in the test group compared with 8 out of 51 in the control group. Patients with greater than 5 positive cells on CMV IHC were more likely to require colonic resection or suffer mortality compared with those with fewer inclusions.

Conclusions: CMV colitis in immunocompromised patients carries an increased risk of adverse outcomes, which varies by virocyte count. Clinical concern, positive serology, and severe histologic activity help predict which biopsies are most likely to have positive IHC results.
responded poorly (NR, n = 8). NGS using the Human Comprehensive Cancer GeneRead DNAnexus Targeted Panel, which screens for variants in 160 genes, was performed.

**Results:** In both groups we found mutations in genes previously implicated in colorectal cancer, including PTEN and NF1. Mutations in genes that have not been described in colorectal cancer, such as GNAQ (3 of 8 CR and 5 of 8 NR) and ATM (5 of 8 CR and 5 of 8 NR), were also identified.

**Conclusions:** GNAQ codes for a guanine nucleotide-binding protein that couples transmembrane receptors to intracellular pathways. Mutations have been reported in melanoma and ocular neoplasms. ATM is involved in cell division and repairing damaged DNA. ATM mutations have been described in several cancers, including breast and pancreatic. GNAQ and ATM mutations are novel findings in rectal carcinoma, present in 50% and 62.5% of specimens, respectively. Interestingly, all patients with the GNAQ mutation harbored the same variant. Going forward, we will confirm these mutations in additional specimens, and compare the mutation profile between NR and CR to identify mutations that predict response to therapy.

**Epithelioid Angiomyolipoma of the Liver**
(Poster No. 9)

Mohammed Abdalla, MBBS (abosseed85@gmail.com); Yasmin Yusuf, MD; Sarwat Gilani, MD. Department of Pathology, Westchester Medical Center, Valhalla, New York.

Epithelioid angiomyolipoma (EAML) of the liver is a rare neoplasm and is often misdiagnosed as a malignant neoplasm, such as hepatocellular carcinoma, because of nonspecific clinical and radiologic features. The histomorphology and immunohistochemical staining profile are important in the diagnosis of EAML. We report a case of a 46-year-old woman with a 6-month history of abdominal pain who was found to have a 2.4-cm liver mass on CT scan corresponding to a LI-RADS (Liver Reporting and Data System) category LR5 lesion (ie, highly suspicious for hepatocellular carcinoma). Liver biopsy was performed and a diagnosis of EAML was made. Later, the patient underwent liver segmentectomy (Figure 4, A). Microscopically (Figure 4, B) the tumor was composed of epithelioid cells in nests and sheets with vacuolated and pink granular cytoplasm. Nuclei were oval to round with a few prominent nucleoli. No cytologic atypia, necrosis, or mitosis was present. The tumor showed focal fatty component and few abnormal thick-walled blood vessels. Immunohistochemically, the neoplastic cells were positive for Melan-A, HMB-45 (Figure 4, C), and SMA (Figure 4, D), and negative for S100, HEPAR1 arginase, CAM 5.2, and AE1/AE3. The final diagnosis was EAML. This uncommon tumor with clinical and radiologic features that mimic hepatocellular carcinoma presents a diagnostic challenge to clinicians and radiologists. Moreover, the epithelioid variant of angiomyolipoma usually lacks or shows minimal fatty component and abnormal thick-walled blood vessels, which further presents a diagnostic challenge to pathologists. Careful histologic examination and appropriate immunohistochemical staining are essential to reach the correct diagnosis.

**Drug and Herbal/Dietary Supplement–Induced Liver Injury: A 5-Year Experience in a Tertiary Care Center**
(Poster No. 10)

Ayesha S. Siddique, MD (ayesha.siddique@hhchealth.org); Saverio Ligato, MD. Department of Pathology and Laboratory Medicine, Hartford Hospital, Hartford, Connecticut.

**Context:** Drug-induced liver injury (DILI) and herbal/dietary supplement (HDS)–related liver injury is a rare idiosyncratic reaction with potentially devastating clinical outcomes. It may present unique diagnostic challenges and require a close collaboration between the clinician and the pathologist for an accurate diagnosis.

**Design:** A retrospective review of all clinically proven patients with DILI/HDS who presented to our institution from January 2013 through December 2017 was performed. In each case, slides were reviewed for assessment of the histopathologic pattern of injury and correlated with the causative agent.

<table>
<thead>
<tr>
<th>Histopathologic Pattern</th>
<th>Total, No. (%)</th>
<th>Drugs/HDSs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis</td>
<td>17 (48.6)</td>
<td>Nitrofurantoin Black cohosh¹ Ceftriaxone Methimazole Total parenteral nutrition</td>
</tr>
<tr>
<td>Acute</td>
<td>5 (14.3)</td>
<td>Black cohosh¹ Ceftriaxone Methimazole Total parenteral nutrition</td>
</tr>
<tr>
<td>Acute with extensive necrosis</td>
<td>8 (22.9)</td>
<td>Diclofenac Acetaminophen Black cohosh¹ Infliximab Isoniazid</td>
</tr>
<tr>
<td>Autoimmune-like</td>
<td>3 (8.6)</td>
<td>Triagealom and statin Ezetimibe Hydroxycut⁶ Rizatriptan¹ Methyldrostanolone Trimethobenzamide Hydrochloride⁵</td>
</tr>
<tr>
<td>Chronic</td>
<td>1 (2.9)</td>
<td>Triazolam and statin Ezetimibe Hydroxycut⁶ Rizatriptan¹ Methyldrostanolone Trimethobenzamide Hydrochloride⁵</td>
</tr>
<tr>
<td>Cholestatic hepatitis</td>
<td>6 (17.1)</td>
<td>Triazolam and statin Ezetimibe Hydroxycut⁶ Rizatriptan¹ Methyldrostanolone Trimethobenzamide Hydrochloride⁵</td>
</tr>
<tr>
<td>Macroversicular and microvesicular steatohepatitis</td>
<td>5 (14.3)</td>
<td>Trimeprstin-sulfamethoxazole⁶ L-asparaginase Valproic acid HAART Amiodarone Hydroxycut⁶</td>
</tr>
<tr>
<td>Mixed cholestatic hepatitis with steatosis and biliary duct injury</td>
<td>2 (5.7)</td>
<td>Dronedarone⁴ Hydroxycut⁶</td>
</tr>
<tr>
<td>Nonnecrotizing granulomatous hepatitis</td>
<td>1 (2.9)</td>
<td>BCG</td>
</tr>
</tbody>
</table>

Abbreviations: BCG, bacillus Calmette-Guérin; HAART, highly active antiretroviral therapy; HDS, herbal/dietary supplements.

¹ Actaea racemosa or Cimicifuga racemosa.
² Contains caffeine, lady’s mantle extract (Alchemilla vulgaris), wild olive extract (Olea europea), cumin extract (Cuminum cyminum), wild mint extract (Mentha longifolia), and, in some products, green coffee bean extract (Coffea canephora).
³ Not previously reported.
⁴ Unusual patterns for this drug/HDS.
⁵ contains caffeine, lady’s mantle extract (Alchemilla vulgaris), wild olive extract (Olea europea), cumin extract (Cuminum cyminum), wild mint extract (Mentha longifolia), and, in some products, green coffee bean extract (Coffea canephora).
⁶ Not previously reported.

**Results:** Thirty-five cases of DILI/HDS were identified (male to female ratio = 1:1.7; age range, 18–79 years; median age, 52 years. Histopathologic patterns of injury and corresponding causative drugs/
HDs are summarized in the Table. Acute hepatitis (45.7%) was the most common histopathologic pattern of injury and nonneutrophilic granulomatous hepatitis (2.9%) was the least common. The majority of the histopathologic patterns of injury were consistent with those previously reported in the literature; however, 2 unusual cases of cholestatic hepatitis with bile duct injury and steatosis due to dimeredarone and hydroxyacet and 1 case of steatohepatitis due to trimethoprim-sulfamethoxazole were identified. Furthermore, we report 2 cases of cholestatic hepatitis due to the use of trimethobenzamide hydrochloride and rizatriptan that have not been previously reported.

Conclusions: In our study, most cases displayed “typical” histopathologic patterns of DILI/HDs. However, some new patterns of hepatic injury were also observed, reaffirming the pivotal role of the clinician and hepatopathologist in the care of patients with DILI/HDs.

Assessment of the Diagnostic Rate of Gastric Intestinal Metaplasia Following Cessation of Reflex Alcian Blue Histochemical Staining

(Poster No. 11)

Jennifer Reppucci, DO
(jreppucci@ufl.edu); Greg Olsen, MD; Maira Gaffar, MD; Danielle Harrell, DO; Zhourong Jin, MD; Ashwinis Lankalaka, MD; David H. Gonzalo, MD; Jesse L. Kresak, MD; Xiuli Liu, MD, PhD; Michael Feely, DO. Department of Pathology, University of Florida, Gainesville.

Context: Practices have used reflexive ancillary testing to aid in the detection of intestinal metaplasia (IM) in gastric biopsies; however, this system has been increasingly questioned. We assessed the impact of gastric IM detection and correlated these findings with the background gastric histologic findings.

Design: Gastric biopsy reports for 6 months preceding (reflex period) and 6 months immediately following the cessation of upfront AB staining (selective period) were reviewed. Reports were assessed for the presence or absence of IM, if AB was performed, and the existence of background mucosal disease.

Results: A total of 2411 reports were reviewed, with 1145 during the reflex period and 1266 during the selective period. IM was diagnosed in 191 (7.9%), with 109 of 1145 (9.5%) in the reflex period and 82 of 1266 (6.5%) in the selective period, a difference that proved significant ($P = .006$). There was no statistical difference between the rates of IM detection between the periods in chronic inactive gastritis (10.3% versus 9.9%, $P = .91$) or reactive gastropathy (5.7% versus 4.1%, $P = .50$). However, examination of the rates of IM diagnoses in cases of active gastritis revealed a decrease of approximately 45% in the selective period during the reflex period (21.8% versus 11.9%, $P = .01$).

Conclusions: Cessation of upfront AB staining may be associated with an overall decrease of IM detection in gastric biopsy material, however, it is largely isolated to cases of active gastritis. Attention must be given when evaluating cases with this finding as robust inflammation may mask subtle IM.

Hepatocyte Nuclear Factor 1B as a Diagnostic Marker for Pancreaticobiliary Carcinoma

(Poster No. 12)

Michelle X. Yang, MD, PhD1; Ryan Coates, MD1 (ryan.coates@uvmhealth.org); Abyi Ambaye, MD1; Juli-Anne Gardner, MD1; Richard S. Zubani, MD1; Joan Skelly, MS1; Yuan Gao, MD1; Mari Mino-Kenudson, MD1; Departments of 1Pathology, 2Hematology/Oncology, and 3Medical Biostatistics, University of Vermont Medical Center, Burlington; 4Department of Urology and Pathology, University of Rochester, Rochester, New York; 5Department of Pathology, Massachusetts General Hospital, Boston.

Context: Diagnosing pancreatic ductal adenocarcinoma (PDAC) in the setting of metastasis with an unknown primary remains very challenging because of the lack of specific biomarkers.

Design: Using tissue microarray and immunohistochemistry, we investigated the protein expression pattern of transcriptional factor HNF-1B in 127 primary PDACs, 17 metastatic PDACs, and 278 nonpancreatic carcinomas.

Results: HNF-1B was expressed in all nonneoplastic pancreaticobiliary epithelium of the primary pancreaticobiliary carcinomas. HNF-1B was immunoreactive less frequently in clear cell carcinomas of the kidney and Mullerian origin. Gastroesophageal, lung, and prostate adenocarcinomas occasionally expressed HNF-1B in up to 37% of cases. HNF-1B was completely negative in hepatocellular, colorectal, breast, and lung squamous cell carcinomas. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of HNF-1B for primary pancreaticobiliary carcinoma are 84%, 75%, 66%, 85%, and 78%. The expression of HNF-1B was significantly associated with tumor size $\geq$ 2 cm and high tumor grade by multivariable analysis.

Conclusions: The association of increased expression of p27 with a higher risk of mortality suggests that p27 may have prognostic value in PDAC. A larger cohort should be useful in confirming this association.

A Case Report of Azathioprine-Induced Liver Injury Leading to Liver Transplantation

(Poster No. 14)

Aaron Sohn, MD (aaron.j.sohn@gmail.com); James Mitchell, MD; Attin Agarwal, MD. Department of Pathology, Baylor University Medical Center at Dallas, Texas.

Azathioprine is an immunosuppressant commonly prescribed to patients who underwent organ transplant to prevent transplant rejection. Patients on this medication can potentially experience different types of adverse effects, including myelosuppression, malignancy, and hepatitis. Acute cholestatic injury, one of the forms of hepatotoxicity, is often a self-limiting disease that occurs at a rate of 1 in 1000 patients taking this medication. We present a rare case of acute cholestatic injury in a patient taking azathioprine that eventually led to failed transplanted liver. Our patient is a 60-year-old man with a history of orthotopic liver transplant several years prior to presentation because of cirrhosis from hepatitis C Virus. The patient had been doing well until he started looking “yellow” while asymptomatic otherwise. A complete metabolic panel ordered by his primary care physician showed significant transaminitis, and his liver biopsy at admission showed moderate to severe acute cellular rejection. Throughout his hospital...
course, the patient kept deteriorating despite clinical care from multiple specialties and eventually had to undergo a repeat liver transplant. Examination of the transplanted liver showed marked zone 2 and 3 ischemic changes, mild periportal inflammation, and an extensive, marked panlobular cholestasis. Review of the literature confirms that such findings are consistent with findings of azathioprine-induced liver injury. We present this rare case of drug-induced liver injury to highlight the importance of keeping azathioprine as a differential diagnosis when encountering liver specimens with the aforementioned histomorphology, as early detection is a key to successful patient care.

**Adenocarcinoma Confined to a Polyp: Pathologic Factors Determining Nodal Status**

*(Poster No. 15)*

Zahra Alipour, MD (alipourz@wustl.edu); Christopher Hartley, MD; Deyali Chatterjee, MD. Department of Pathology, Washington University in St Louis, Missouri.

**Context:** Not infrequently, an incidental pT1 adenocarcinoma is completely removed by polypectomy. Despite considerable literature on the subject, the parameters that determine whether or not subsequent surgery is indicated are still uncertain. Our aim was to address this issue by comprehensively analyzing various histologic factors in these tumors that could indicate a risk for nodal disease.

**Design:** Our study included a retrospective cohort of all polypectomies harboring an incidental adenocarcinoma that had subsequent segmental resection for nodal staging and no residual primary tumor. Various histologic parameters were assessed, namely, size of polyp, size of invasive focus, distance from deep margin, deep margin positivity, tumor differentiation, tumor budding, lymphovascular invasion, peritumoral chronic inflammation, and type of desmoplastic reaction. These features were compared with the binary outcome variable of lymph node positivity at resection using Excel 2013 (Microsoft, Redmond, Washington).

**Results:** There were a total of 57 cases identified in this cohort, with all slides available for review. Although polyp size correlated with size of invasive tumor (P < .001), none of the histopathologic factors examined (Table) showed any correlation with lymph node status other than the presence of myxoid, immature desmoplastic stroma (as opposed to collagenous, mature desmoplastic stroma) with a 12.75 odds ratio (95% CI, 1.41–115).

**Conclusions:** Recent studies have shown the prognostic significance of the type of stromal response in colorectal adenocarcinomas, but this is the first study to show the significance in pT1 adenocarcinomas arising in a polyp. This is an interesting and unexpected finding, and needs studies on larger cohorts for further validity.

### Correlation of Polypectomy Variables With Lymph Node Positivity at Resection: Univariate Logistic

<table>
<thead>
<tr>
<th>Polypectomy Variable</th>
<th>P Value</th>
<th>Odds Ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size of entire polyp, cm</td>
<td>.91</td>
<td>0.94</td>
<td>0.33</td>
<td>2.67</td>
</tr>
<tr>
<td>Largest size of invasion, mm</td>
<td>.11</td>
<td>1.23</td>
<td>0.95</td>
<td>1.58</td>
</tr>
<tr>
<td>Deep margin positive</td>
<td>.74</td>
<td>0.69</td>
<td>0.07</td>
<td>6.43</td>
</tr>
<tr>
<td>Distance from deep margin, mm</td>
<td>.91</td>
<td>0.98</td>
<td>0.71</td>
<td>1.35</td>
</tr>
<tr>
<td>Tumor differentiation</td>
<td>.41</td>
<td>2.12</td>
<td>0.36</td>
<td>12.55</td>
</tr>
<tr>
<td>Tumor budding</td>
<td>.11</td>
<td>4.08</td>
<td>0.72</td>
<td>23.16</td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td>.25</td>
<td>2.93</td>
<td>0.46</td>
<td>18.63</td>
</tr>
<tr>
<td>Chronic inflammation</td>
<td>.8</td>
<td>1.23</td>
<td>0.25</td>
<td>6.07</td>
</tr>
<tr>
<td>Immature desmoplastic response</td>
<td>.02</td>
<td>12.75</td>
<td>1.41</td>
<td>114.93</td>
</tr>
</tbody>
</table>

**Esophageal Granular Cell Tumor and Eosinophils:**

*A Referral Center Experience of 22 Cases*

*(Poster No. 16)*

Christopher M. Chandler, MD (chandld@uw.edu); Paul E. Swan son, MD; Deepi M. Reddi, MD. Department of Pathology, University of Washington, Seattle.

**Context:** Gastrointestinal granular cell tumors (GCTs) are rare; the most common site is esophagus (eGCT). Recent literature suggests a link between eosinophilic esophagitis (EOE) and eGCT. The aim of our study was to determine if EOE or other disorders associated with eosinophilia are consistently associated with eGCT.

### Cytomegalovirus Colitis:

*A Clinicopathologic Study of 117 Cases*

*(Poster No. 17)*

Katrina Krogh, MD (katrina.krogh@northwestern.edu); Andrew Bandy, MD; Audrey Deeken-Draisy, MD; Ryan Jones, MD, PhD; Guang-Yu Yang, MD, PhD; Maryam Kherad Pezhouh, MD. Department of Pathology, Northwestern Memorial Hospital Feinberg School of Medicine, Chicago, Illinois.

**Context:** Cytomegalovirus (CMV) is a globally prevalent virus that infects immunocompromised and immunocompetent patients. CMV colitis is a common manifestation in immunocompromised patients and mimics other diseases. This leads to delayed diagnosis and adverse outcomes. This study aims to assess clinicopathologic predictors of CMV colitis including associated diseases, gastrointestinal symptoms, endoscopic findings, and histologic findings.

**Design:** We searched our electronic pathology database for patients diagnosed with CMV colitis and identified 117 cases between 2003 and 2017. Clinical features, endoscopic findings, and histologic findings were reviewed.

**Results:** Patients ranged from 17 to 80 years old (median, 53 years) with a male to female ratio of 1.3:1. At diagnosis, 115 patients (98%) were immunocompromised and 2 (2%) were immunocompetent. Immunocompromised patients’ histories included solid organ transplant (57%), bone marrow transplant (20%), IBD (9%), HIV (9%), recent chemotherapy (3%), and concurrent autoimmune disease (2%). These patients presented with diarrhea (87%), bloody diarrhea (8%), hematochezia (3%), severe anemia (1%), and rectal pain (1%). Endoscopic findings included erythema, edema, ulceration, friability, exudate, and mass formation. CMV viral inclusions were present on H&E in 72 patients (61%), and 45 (39%) required immunohistochemistry. Characteristic histologic findings included minimal to severe active colitis with cryptitis, crypt abscesses, and increased crypt epithelial apoptosis. Four patients showed evidence of concurrent graft-versus-host disease. Immunocompetent patients’ histories included end-stage renal disease and a history of unprotected anal sex.

**Conclusions:** To predict CMV colitis risk, assessment of associated diseases and clinical symptoms is crucial. The pathologist should be vigilant about CMV colitis in immunocompromised patients with diarrhea and a history of solid organ/bone marrow transplant.

**Clinically Aggressive Microsatellite Unstable Adenocarcinomas:**

*Strong Indication for Identifying the Underlying Culprit(s) to Precisely Guide Clinical Management*

*(Poster No. 18)*

Fengming Chen, MD, PhD (chenf@pennstatehealth.psu.edu); Lei Lou, MD; Mingjun Dun, MD; Wei Jiang, MD; Lei Jiang, MD; Department of Pathology, the 2nd Hospital of Hebei Medical University, Shijiazhuang, China; Department of Pathology, H. Lee Moffitt Cancer Center, Tampa, Florida.

**Context:** Clinically aggressive microsatellite unstable (CMA) adenocarcinomas are a distinct entity that is characterized by high levels of microsatellite instability (MSI) and is associated with poor outcomes. In the current era, targeted therapies could play a critical role in the management of CMA adenocarcinomas. However, the predictive factors associated with MSI in adenocarcinomas are not yet well established.

**Design:** We retrospectively searched our pathology database from 1999 to 2018 for eGCTs. Archived slides and medical records were reviewed.

**Results:** Twenty-two patients (12 men and 10 women; age range, 33–66 years; median age, 48 years) had eGCT (size range, 0.04–2.0 cm; median, 0.6 cm). Thirteen had a history of gastroesophageal reflux disease, 4 had Barrett esophagus, and 1 had EOE. Fifteen eGCTs had intraluminal eosinophils (6 with peak >10 eosinophils/μl, 200 high-power field [hpf]); of these, 12 also had eosinophils in lamina propria (5 with peak >10 eosinophils/hpf). eGCTs with atypical features (including nuclear enlargement and prominent nucleoli) were more likely to have increased eosinophils in nonneoplastic compartments than those without atypia. Pleomorphism and spindled cells were seen in 5 eGCTs (mean peak intraluminal eosinophils, 27.2 per hpf); 2 of these had Barrett esophagus. The single eGCT in EOE had only 2 intraluminal eosinophils/hpf.

**Conclusions:** We found no association between EOE and eGCT. Instead, most patients had gastroesophageal reflux disease or Barrett esophagus. eGCT patients with significant eosinophilic infiltrates (peak >10/hpf) in eosophageal lamina propria also had significant intraluminal eosinophils. Eosinophilia, common in eGCT and adjacent stroma, likely drives atypical/reactive histologic features, but a pathogenetic relationship between eosinophil-rich inflammatory conditions and eGCT has not yet been established.

**Clinically Aggressive Microsatellite Unstable Adenocarcinomas:**

*Strong Indication for Identifying the Underlying Culprit(s) to Precisely Guide Clinical Management*
Microsatellite instability (MSI) contributes to carcinogenesis, tumor behavior, therapeutic efficacy, and prognosis. Sporadic MSI and Lynch syndrome cancers are histologically indistinguishable. Generally, MSI tumors are less aggressive, associated with earlier stages and devoid of lymphovascular invasion. However, we have encountered MSI tumors demonstrating highly invasive behavior, lymphovascular involvement, and distant metastasis. It is pivotal to recognize these ominous features and uncover the molecular alteration when investigating MSI; such information would significantly impact clinical decision making and patient outcome. Two resected MSI tumors were analyzed. The histomorphology, immunoprofile, and next-generation sequencing (NGS) findings were investigated and discussed. The first case was a hepatic flexure colonic adenocarcinoma in a 69-year-old woman; the tumor perforated the colon and stomach and metastasized to the liver. Immunostains showed loss of MLH1 and PMS2 (Figure 5, A through D); NGS identified KRAS V600E mutation. The second case was a left colon adenocarcinoma in a 76-year-old man. The tumor perforated the colon and invaded into duodenum and omentum despite concurrent FOLFOX chemotherapy. Further tests revealed that MLH1 and PMS2 were absent in tumor, whereas NGS identified BRAF V600E mutation. The second case was a left colon adenocarcinoma in a 76-year-old man. The tumor perforated the colon and stomach and metastasized to the liver. Immunostains showed loss of MLH1 and PMS2 (Figure 5, A through D); NGS identified KRAS and TP53 mutations. Based on these findings, the patients received modified post-surgery chemotherapy, with no evidence of recurrence 1.5 years later. MSI does not necessarily mean a less-aggressive clinical course. Comprehensive approaches should be taken to identify the culprit(s) underlying/in addition to MSI. Such testing should be uniformly performed to best guide effective and targeted therapeutic strategies. These efforts will fine-tune and improve the treatment regimens and influence the genetic counseling of patients’ families.

Gastrointestinal Pathology in Pediatric Hematopoietic Stem Cell Transplant Recipients: A Single Institution Experience of 3 Decades

(Poster No. 20)

Zahra Alipour, MD (alipourz@wustl.edu); Elizabeth Utterson, MD; Robert Rothbaum, MD; Louis Dehner, MD; Mai He, MD. Department of Pathology, Washington University in St Louis, Missouri.

Context: In transplant patients, the gastrointestinal (GI) tract is affected by the immunocompromised state, therapies, and underlying diseases. We studied the spectrum of GI pathologies in hematopoietic stem cell transplant recipients.

Design: In a retrospective chart review, 27 years of departmental archives in pathology were searched for pediatric GI biopsies with clinical history of hematopoietic stem cell transplants.

Results: Of 82 patients, comprising 70 (85.4%) bone marrow and 12 stem cell transplants, 38 biopsies (46.3%) were performed within 100 days of transplant. Among 43 esophageal biopsies, 13 (30.1%) showed esophagitis, including 1 herpetic infection, and 9 (20.9%) represented gralt-versus-host disease (GVHD). Of 64 gastric biopsies, 28 (43.8%) showed GVHD (mostly grade I), 1 (1.5%) had EBV+ posttransplant lymphoproliferative disorder, and 1 expressed recurrent Hodgkin lymphoma. Among 69 duodenal and 22 terminal ileum biopsies, 29 (42.0%, mostly grade II) and 8 (36.3%) represented GVHD, respectively. Eighty-two colon biopsies were examined; 43 with GVHD (52.4%): of 8 right colon biopsies, 4 (50%) had cryptitis and 1 (12.5%) had GVHD, and 5 (41.1%) GVHD, 3 (25%) cryptitis, and 1 EBV+ posttransplant lymphoproliferative disorder were appreciated in 12 left-colon biopsies. Also, 6 (35.2%) GVHD including 1 CMV+ subject and 5 (29.4%) cryptitis were identified in rectosigmoid colon (n = 17). There were 45 nonspecific colon biopsies, representing most frequently 28 GVHD (62.2%) and 5 (11.1%) active colitis with cryptitis. Posttransplant lymphoproliferative disorder was seen in the same patient.

Conclusions: A broad variety of GI pathology has been observed. The incidence of GVHD was from 20.9% to 52.4% at different locations, with more severity in duodenum. Posttransplant lymphoproliferative disorder was seen in 1 patient (1.2%) at 2 different sites.

Primary Rectal Synovial Sarcoma: A Rare Case Report

(Poster No. 21)

Sarah Findeis, MD (sarah findeis@bswhealth.org); Atin Agarwal, MD. Department of Pathology, Baylor University Medical Center, Dallas, Texas.

Primary synovial sarcomas of the gastrointestinal tract are extremely rare, and within that group, a majority are reported in the upper gastrointestinal tract (eg, esophagus and stomach). We present the second reported case (to our knowledge) of primary synovial sarcoma of the rectum. A 48-year-old woman presented with hematochezia and was found on initial colonoscopy to have an exophytic rectal tumor. Biopsy showed a high-grade, poorly differentiated tumor that was positive for CKA1E-3 (focal), EMA (focal), vimentin (diffuse, strong), CD99 (diffuse, strong cytoplasmic with membrane accentuation), and BCL-2 (diffuse, strong). The tumor was negative for CAM5.2, neuron-specific enolase, CD34, CD10, CD117, muscle-specific actin, smooth muscle actin, and desmin. The Mit-1 value was 15%. Molecular studies for the SYT-SSX1 and SYT-SSX2 fusion transcripts via reverse transcription polymerase chain reaction were done and were positive for the SYT-SSX1 fusion transcript. The patient underwent a low anterior resection and there was a 6.3 × 4.1 × 4.0-cm mass that extended through the muscular layer into the perirectal adipose tissue with 4 of 18 lymph nodes positive for malignancy. Recurrence occurred approximately 1.5 years after resection and despite systemic chemotherapy, the patient died 46 months after her first tissue diagnosis.
Drug-induced liver injury (DILI) occurs frequently and accounts for more than 40% of all fulminant hepatic failure (FHF) patients in the United States. Most of the DILI cases that result in FHF are secondary to acetaminophen. Here we present a case of FHF in a female patient who was started on levetiracetam for 2 weeks (500 mg/6 h) to manage seizure following an ischemic stroke. The patient presented to the emergency room with hypotension, delirium, and markedly elevated liver enzymes (baseline: ALK, 106 U/L; ALT, 51 U/L; and AST, 91 U/L; presentation: ALK, 217 U/L; ALT, 692 U/L; AST, 1532 U/L). All other laboratory study results, including viral hepatitis panel, CMV, EBV, HIV, HSV, acetaminophen level, 3,4-antitrypsin, anti-smooth-muscle antibody, ceruloplasmin, and immunoglobulin level, were unremarkable. The patient’s serum levetiracetam level was notably elevated at 80 µg/mL (normal range, 12–46 µg/mL). Levetiracetam and atorvastatin were stopped upon consideration of drug-induced liver injury. However, within 48 hours of admission, the patient’s condition deteriorated and she passed away. At autopsy, findings consistent with a toxic liver injury were identified. Histologic findings include the diffuse centriflobular pattern of necrosis, cholestasis, and mild lymphocytic inflammation in a background of steatosis (Figure 6, A and B). No histologic findings of portal vein obliteration or advanced fibrosis were identified, confirming acute medication injury as the cause of her liver injury. The few previously published case reports describing this association are reviewed, and the importance of liver function test in patients on levetiracetam should be kept in mind.

A Case of Metastatic Solid Pseudopapillary Tumor in an Elderly Male Patient

(Paper No. 24)

George Mao, MD (george.r.mao@gmail.com); Taha Sachak, MD; Ming Jin, MD, PhD. Department of Pathology, Ohio State University, Columbus.

Solid pseudopapillary neoplasm (SPN) is a rare low-grade neoplasm that accounts for 1% to 2% of all pancreatic exocrine neoplasms. More than 90% of reported cases have occurred in young women, with a higher prevalence in black and Asian populations. Herein we report an unusual case of a 78-year-old white man who presented with SPN metastasis in the liver. The patient was diagnosed with an SPN 15 years ago, for which he underwent distal pancreatectomy. He was found to have adrenal metastases 11 years later, and underwent adrenalectomy. The patient underwent partial hepatectomy without neoadjuvant therapy. Grossly, the 4.5 × 4.5 × 2.3-cm resected mass was well circumscribed with tan-yellow cut surfaces. The majority of the mass was necrotic, but it did demonstrate a focal area of viable tumor cells at the periphery. Microscopically, the tumor exhibited pseudopapillary architecture due to cuffing of the small blood vessels by neoplastic cells, which had moderate amounts of eosinophilic cytoplasm. The nuclei were small, round, and uniform, with some demonstrating focal longitudinal grooving. Immunostaining demonstrated absence of AE1/AE3, chromogranin, and synaptophysin expression. Staining for β-catenin revealed aberrant nuclear localization, confirming the diagnosis of SPN (Figure 7, A through D). Although SPN often follows an indolent clinical course with low malignant potential, metastases can present even a decade after complete resection. Furthermore, prior case series have suggested SPNs in males behave more aggressively than the traditional indolent course that is seen in females with SPNs. Therefore, SPN should continue to be entertained as a possibility even years after definitive surgery, especially in male patients.
Mixed acinar-neuroendocrine tumors (ACCNETs) of pancreas are extremely rare and introduce a diagnostic challenge because of heterogeneous chymotrypsin immunoreactivity and overlapping morphologic features. We report a 64-year-old woman who initially presented with abdominal pain and was found to have a pancreatic body/tail mass measuring 11 x 10.6 cm. Fine-needle aspiration showed a neuroendocrine carcinoma with a high proliferative index (Ki67 = 90%) (Figure 8, A and B). Subsequently, she underwent distal pancreatectomy and splenectomy, which revealed metastatic pancreatic neuroendocrine carcinoma positive for chromogranin, synaptophysin, and CD56 (Figure 8, C) and negative for chymotrypsin. Resection was followed by chemoradiation; however, disease recurred. Microsatellite instability (MSI) testing showed an MSI-high tumor. Whole-exome sequencing revealed multiple alterations with no approved targeted therapy, including somatic mutations in MLH1, MEN1, and NF1. These variants were not seen in germline DNA. Interestingly, transcriptome analysis showed high expression of trypsinogen and chromogranin A and moderate expression of pancreatic lipase, synaptophysin, and chymotrypsin, raising the possibility of an ACCNET. Repeat chymotrypsin stain (Figure 8, D) on several tumor blocks showed focal positivity, supporting the diagnosis of ACCNET. The patient’s disease progressed despite chemotherapy and immunotherapy. She died with widespread metastatic disease 18 months after diagnosis. ACCNET is a malignant tumor with an incidence of 1 per million. Awareness of this disease is important as transplantation may allow long-term survival even in metastatic disease.

Recurrent Hepatic Epithelioid Hemangioendothelioma Confirmed at 10 Years Post–Liver Transplantation

(Poster No. 26)

Allison Cooper, MD (allison.cooper@bswhealth.org); Meghan Koch, DO. Department of Pathology, Baylor University Medical Center, Dallas, Texas.

Hepatic epithelioid hemangioendothelioma (HEHE) is a rare vascular neoplasm with uncertain risk factors. HEHE may be multifocal and bilobar, necessitating transplantation. Extraneoplastic disease is often present and not a contraindication to transplant. We report a case of HEHE with recurrence 10 years post-transplant. A 42-year-old woman with pruritus and right upper quadrant pain presented for liver transplantation. Medical history included primary biliary cirrhosis treated with ursodiol. Ascites and hepatosplenomegaly were present. Laboratory findings included elevated alkaline phosphatase (281 U/L), total bilirubin (2.3 mg/dL), AST (49 U/L), and ALT (39 U/L). Antinuclear antibodies were present (titer 1:1280; homogenous pattern). Imaging demonstrated liver and lung masses with epithelioid hemangioendothelioma confirmed on biopsy. Histologic examination of the explanted liver demonstrated CD34-positive epithelioid cells in fibromyxoid stroma with intracytoplasmic lumina, some containing erythrocytes (Figure 9, A and B). A cirrhotic background was present. Features of primary biliary cirrhosis were not identified. Post-transplant imaging demonstrated liver masses in the first 2 years after transplant, which subsequently resolved. Fibrosis was identified on imaging after 1 year. At 9 years, the liver appeared to be macronodular with bandlike fibrosis. Histologic examination of core biopsies did not demonstrate recurrence. Ten years after transplant, the patient developed ascites, abdominal pain, and fever. Biopsy demonstrated recurrent HEHE with bands of CD31-positive and CD34-positive elongate cells and intracytoplasmic lumina in fibrous stroma (Figure 9, C and D). HEHE is a malignant tumor with an incidence of 1 per million. Awareness of this disease is important as transplantation may allow long-term survival even in metastatic disease.

Carbonic Anhydrase IX Immunohistochemical Expression in Mismatch Repair–Deficient Colorectal Adenocarcinomas

(Poster No. 27)

Karina Hiroshima, BS1 (khiroshi@u.rochester.edu); Meenal Sharma, MBBS2; Raul S. Gonzalez, MD3; Rebecca Amorese, BS4; Elena Gupta, BS4; Caitlin Foor-Pessin, MD2; Laura Frado, MD2; Danielle Marino, MD2; Arthur J. DeCross, MD; Qi Yang, AAS1; Jennifer J. Findeis-Hosey, MD1; Aaron R. Huber, DO.1 Departments of 1Pathology and Laboratory Medicine and 2Gastroenterology and Hepatology, University of Rochester Medical Center, Rochester, New York.

Context: Colorectal adenocarcinoma (CRA) is the fourth most common cancer in the United States. Immunohistochemical (IHC) assessment of mismatch repair (MMR) status can identify CRAs that are MMR deficient (dMMR), which may impact prognosis and treatment. Carbonic anhydrase IX (CAIX) is a transmembrane glycoprotein that is expressed with tumor hypoxia. CAIX expression has been associated with adverse prognostic factors in other cancers. In our study, we examined CAIX expression in dMMR CRAs, which is not well documented in the literature.

Design: Sixty-three CRAs were included in a tissue microarray. CAIX IHC was performed and graded based on staining intensity (0–3+) and percentage of epithelial tumor staining.

Results: CAIX IHC expression was identified in 50 of 61 cases (82.0%), without statistically significant difference among tumor grades. There was increased expression of CAIX in the deep leading edge of the tumor in 44% of cases, whereas 56% of cases demonstrated decreased or no difference in CAIX expression. Necrotic tumors demonstrated CAIX expression in 18 of 23 cases (78.26%) versus 25 of 36 nonnecrotic tumors (69.4%, P = .46). CAIX expression was present in 61.9% of lymph nodes/tumor deposits.

Conclusions: Although high CAIX expression was not associated with morphologic features or nodal status, it was identified in a majority of the dMMR CRAs in this study. Prior studies have demonstrated high CAIX expression in tumors from patients with Lynch syndrome. The tumor hypoxia and acidic tumor environment may contribute to genomic instability in these tumors. More studies are needed, but high CAIX expression may have future therapeutic implications.
**Gastrointestinal Submucosal Microscopic Ganglioneuromatosis as the Initial Presenting Pathologic Finding for Multiple Endocrine Neoplasia Type 2B in a Child With Chronic Constipation**

(Poster No. 28)

**Juan Rong, MD, PhD** (jruong@ucsd.edu); Wen Jiang, MD; Robert Newbury, MD; Suzanne Tucker, MD. 1Department of Pathology, University of California San Diego; Departments of 2Surgery and 3Pathology, Rady Children’s Hospital, University of California San Diego.

Multiple endocrine neoplasia type 2B (MEN2B) is a rare, aggressive autosomal dominant hereditary syndrome characterized by medullary thyroid carcinoma, pheochromocytoma, mucosal neuroma, intestinal ganglioneuroma, and marfanoid habitus. Patients may variably present with nonspecific symptoms, including deceased muscle tone and constipation. MEN2B is caused by RET mutation located on chromosome 10q11.2. The majority of the patients carry a de novo mutation. All patients with MEN2B will develop early-onset medullary thyroid carcinoma, which determines overall clinical prognosis. The American Thyroid Association recommends prophylactic thyroidectomy before the age of 1 year. Given the typical delay in diagnosis because of high rate of de novo RET mutation and lack of family history, improved knowledge of the nonendocrine manifestation is crucial in early diagnosis and optimizing clinical management. We report a case where an 8-year-old boy with a history of severe constipation was hospitalized for abdominal distension, fecal impaction, and sepsis. Endoscopic biopsy revealed gastrointestinal submucosal microscopic ganglioneuromatosis without mass-forming lesions. Together with his marfanoid appearance and “blubbery lips” with multiple mucosal neuromas on clinical examination, suspicion for MEN2B was raised. Workup revealed moderately elevated serum calcitonin and bilateral small thyroid nodules on ultrasound. Subsequent genetic testing confirmed RET codon M918T mutation and the diagnosis of MEN2B was established. Total thyroidectomy and pretracheal lymph node excision were performed. Pathology demonstrated bilateral multifocal medullary thyroid carcinoma and metastasis to the pretracheal lymph node. This case demonstrates that gastrointestinal submucosal microscopic ganglioneuromatosis is an important pathologic finding that should raise the suspicion for MEN2B.

**Focal Nodular Hyperplasia in a 16-Month-Old Male Child**

(Poster No. 29)

**Damodaran Narayan, MBBS, PhD** (dnarayan@uwhealth.org); Shelly M. Cook, MD. Department of Pathology and Laboratory Medicine, University of Wisconsin Hospital and Clinics, Madison.

Focal nodular hyperplasia (FNH) is the most common benign hepatic mass lesion in children. Elevated AFP and normal β-hCG were found on laboratory studies. Abdominal MRI showed a large left hepatic lobe mass (7.3 × 5.9 × 4.9 cm). An IR-guided biopsy revealed hyperplastic hepatocyte nodules separated by thick fibrous septa with embedded bile ductules and thick-walled blood vessels, reminiscent of cirrhosis (Figure 10, A). Nonclonal deletion of the long arm of chromosome 1 was detected by chromosomal analysis. Immunohistochemistry studies revealed geographic staining for Glutamine synthetase and cytoplasmic staining of β-catenin (Figure 10, B and C). These histomorphologic features and immunohistochemistry staining results were consistent with FNH. A lateral segmentectomy (segments 2, 3) was performed. Grossly, a bulging subcapsular mass with patchy tan-white areas on cross section was observed (Figure 10, D through F). The patient’s postoperative course and follow-up has remained uneventful. The pathogenesis of FNH is presumed to involve a congenital vascular anomaly with localized interruption of blood flow, which results in hyperplasia of the remaining hepatic parenchyma.

**Loss of HOXB13 Expression in Rectum/Sigmoid Adenocarcinoma**

(Poster No. 30)

**Faisal Saeed, MD** (faisal.saeed@wmchealth.org); Minghao Zhong, MD. Department of Pathology, New York Medical College at Westchester Medical Center, Valhalla, New York.

**Context:** Recent studies identified HOXB13 (G84E) mutation is the most common germline mutation associated with prostate cancer. Men with this mutation have a 10- to 20-fold increased risk of prostate cancer. HOXB13 maintains a high expression level into adulthood in normal prostate and distal colon. We recently found that HOXB13 is down-regulated in ductal adenocarcinoma of prostate. Thus, we would like to investigate the expression of HOXB13 in rectum/sigmoid adenocarcinoma.

**Design:** We collected 53 cases of colon adenocarcinoma: 5 from cecum and 48 from rectum/sigmoid. The blocks containing both normal mucosa and carcinoma were subjected to HOXB13 immunostaining. Immunostaining was carefully examined to determine presence or absence of nuclear staining of HOXB13.

**Results:** For all 5 cases of cecum adenocarcinoma, both normal mucosa and carcinoma were negative for HOXB13. For rectum/sigmoid adenocarcinoma cases, all 48 (100%) normal mucosa was positive for HOXB13. However, only 6 of 48 (12.5%) cases of rectum/sigmoid adenocarcinoma were positive for HOXB13. A majority of them (42 of 48 cases; 87.5%) showed loss of HOXB13 expression (Figure 11, A through D).

**Conclusions:** This is the first study of HOXB13 expression in colonic adenocarcinoma. Compared with benign colonic glands, a majority of rectum/sigmoid adenocarcinoma showed loss or decrease of HOXB13 expression. Our data suggest that down-regulation of HOXB13 is important for rectum/sigmoid adenocarcinoma carcinogenesis. Further studies including sequencing of HOXB13 in rectum/sigmoid adenocarcinoma are warranted.
SOX-10 and Calretinin Expression in Schwann Cell Hamartoma Gastrointestinal Polyps Support Their Schwann Cell Origin

(Poster No. 31)

Amir Samani, MD1; Ali R. Samani2; Maryam Samani, BSc3; Samieh Khosravinia, MD1,21. Department of Pathology, William Osler Health System, Brampton, Ontario, Canada; 2Department of Research, Amir Samani Medicine Professional Corporation, Richmond Hill, Ontario, Canada.

Context: Schwann cell hamartoma, formerly known as mucosal neuromatoma, is frequently found in the form of small polyps in the large intestine. These lesions are positive for S100, perhaps with more intensity than neurofibroma.

Design: To investigate the expression of SOX-10 and calretinin in Schwann cell hamartoma, 3 lesions from appendix and ascending and sigmoid colon were identified. Immunohistochemistry with antibodies for SOX-10, calretinin, S-100, Mart-1, and HMB-45 was performed.

Results: All lesions were strongly and diffusely positive for S-100 (cytoplasmic and nuclear), SOX-10 (nuclear), and calretinin (mainly dotlike cytoplasmic and in some cells, especially the lesion of appendix, both cytoplasmic and nuclear) (Figure 12). No staining with Mart-1 and HMB-45 was identified.

Conclusions: SOX-10 is a transcription factor playing a role in the development and maintenance of Schwann cells and melanocytes. In soft tissue tumors, Schwann cells can be detected with SOX-10 in schwannoma and neurofibroma. Granular cell tumors also express SOX-10, supporting their possible Schwann cell origin. The expression of SOX-10 by Schwann cell hamartoma is a strong proof for the Schwann cell origin of those lesions. Calretinin is a vitamin D–dependent calcium-binding protein structurally related to S100 and inhibin. That S100 protein–positive cells ensheathed calretinin–positive axons is an indication of Schwann cell origin (Human Pathol. 2009;40[8]:1159–1167). Accordingly, calretinin is expressed in schwannomas and granular cell tumors, whereas it is not expressed in neurofibromas or has weak and focal expression. The expression of SOX-10 and calretinin in Schwann cell hamartomas is strong proof for the Schwann cell origin of those lesions.

All Lymph Nodes With Metastatic Adenocarcinoma in Colorectal Resections Are Not the Same

(Poster No. 32)

Sonia Kamanda, MD1; James Sullivan, MD2; Oksana Yaskiv, MD3; Rebecca M. Thomas, MD4 (rthomas22@nshs.edu). Departments of 1Pathology and 2Surgery, Northshore LIJ Health System, New Hyde Park, New York.

A 75-year-old man underwent a low anterior resection for a moderately differentiated sigmoid adenocarcinoma, with 2 of 17 positive lymph nodes. An umbilical hernia repair performed simultaneously also showed microscopic adenocarcinoma. The morphology of the adenocarcinoma in the umbilical hernia and 1 lymph node (Figure 13, A) was similar, and different from the sigmoid adenocarcinoma and a second lymph node (Figure 13, B). The glands were without necrosis and more rounded with vesicular nuclei. On immunohistochemistry, this was CK20+, PSA+ (Figure 13, C), and CDX2+ (Figure 13, D). The other positive lymph node was morphologically similar to the sigmoid adenocarcinoma, which was CK20+, CDX2+, and PSA+. The patient was diagnosed with metastatic prostate carcinoma in the umbilical hernia and in 1 lymph node. The sigmoid tumor was pT2 N1a M1 instead of pT2 N1b M1c. At the time of surgery, the existence of prostate cancer was not known. Subsequent investigations revealed prostate cancer 17 years earlier, treated with brachytherapy; the patient had been lost to follow-up. After surgery, the serum PSA level was 18.5 and 19.75 the following month. Metastatic adenocarcinoma in lymph nodes of colorectal resections may arise from different primary malignancies, affecting stage and management; a remote malignancy may be brought to light or a new malignancy discovered. Genitourinary carcinomas in particular may metastasize to the same lymph nodes as distal colorectal carcinomas; the morphology of the tumors may be more similar than different. A low threshold for immunohistochemical workup is recommended and CDX2 positivity may be misleading.

Reticulin Stain Is a Highly Specific Complementary Stain for Diagnosing Collagenous Colitis Histopathologically

(Poster No. 33)

Neeelima Valluru, MD (neeelimavalluru@outlook.com); Xianzhong Ding, MD, PhD; Yihong Ruby Ma, MD, PhD. Department of Pathology, Loyola University Medical Center, Maywood, Illinois.

Context: Collagenous colitis (CC) is a type of microscopic colitis without distinct endoscopic changes. Microscopically, CC is characterized by preservation of crypt architecture and an increase in inflammatory cells within the lamina propria. The pathognomonic finding is the presence of a thickened subepithelial collagen layer, thicker than 10 μm. The collagen band in CC is composed of type VI collagen, tenascin, and a minor amount of types I and III collagen. Trichrome stains highlight collagen type I and IV whereas reticulin stain stains collagen type III. We sought to apply reticulin stain in diagnosing CC.

Design: Thirty-nine cases of CC diagnosed by H&E staining from 2009 to 2014 at our institute were retrieved and 40 cases of lymphocytic colitis (LC) from the same time period served as negative control. Reticulin and trichrome stains were performed and the results were compared.

Results: Both trichrome and reticulin stains show irregular and ragged collagen layer with entrapment of inflammatory cells, stromal cells, and small capillaries in all CCs; therefore, the sensitivity is 100% for both stains. Surprisingly, reticulin stain displays a better basketweave pattern than trichrome stain that is diagnostic for CC. In comparison with LC, 7 of them showed false positivity by trichrome stain (specificity = 82.5%) whereas only 1 of them was focally positive by reticulin stain (specificity = 97.5%).

Conclusions: Compared with trichrome stain when diagnosing CC, reticulin stain has equal sensitivity but better specificity and the staining pattern is easier to interpret. When H&E features are not convincing, reticulin stain can function as a complementary diagnostic tool.
CD8-Predominant Lymphocytic Esophagitis Is Associated With Gastroesophageal Reflux Disease

(Poster No. 34)

Robin Moiseff, MD1 (robin.moiseff@hitchcock.org); Nicholas Olson, MD1; Richard Rothstein, MD2; Elizabeth Brickley, PhD3; Mikhail Lisovsky, MD, PhD1; Departments of 1Pathology and 2Medicine, Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire; 3Department of Epidemiology, Dartmouth College Geisel School of Medicine, Hanover, New Hampshire.

Context: An association between lymphocytic esophagitis (LyE) and gastroesophageal reflux disease (GERD) has not been established. GERD frequently overlaps with primary esophageal motility abnormalities. Considering that motility abnormalities have a known association with LyE, the goal of this study was to elucidate whether LyE is associated with GERD in patients with normal esophageal motility.

Design: The study group was derived from 246 patients with severe GERD evaluated for Nissen fundoplication. One hundred sixty-two patients had adequate biopsies and no evidence of motility abnormalities by manometry. A control group consisted of 142 cases of Candida esophagitis. LyE was defined as increased peripapillary intraepithelial lymphocytes (IELs) with absent or rare granulocytes and no other features of esophagitis. The cutoffs for normal IEL were based on previously reported values. IELs were counted in the most affected field of view (×400). IELs were typed using CD4/CD8 immunohistochemistry.

Results: Twenty-four patients (14.8%) had biopsies with increased IEL. Two major patterns of lymphocytic inflammation emerged: LyE in 11 patients (6.8%) (mean ± SD age 49 ± 12 years, M:F = 5:6), and haphazardly dispersed IEL within an area of reflux esophagitis in 11 patients (6.8%) (age 47 ± 11 years, M:F = 8:3). All LyE cases showed CD8 T-cell predominance (CD4:CD8 = 0.27 ± 0.25). In contrast, only 2 Candida esophagitis cases (1.6%) had LyE with CD8 T-cell predominance (P < .02). The odds of having CD8-predominant LyE were significantly elevated in GERD as compared with the Candida group (odds ratio, 5.13; CI, 1.12–23.6).

Conclusions: The data suggest that LyE with CD8 T-cell predominance is associated with GERD.

In Situ Hybridization for Albumin Is Helpful in the Diagnosis of Challenging Hepatobiliary Tumors

(Poster No. 35)

Mary Wong, MD, MBA (mary.wong@cshs.org); Brent Larson, DO; Mariza Venturina, MD, Deepti Dhall, MD. Department of Pathology and Laboratory Medicine, Cedars-Sinai Medical Center, Los Angeles, California.

Context: In situ hybridization (ISH) for albumin is reportedly highly sensitive and specific for primary hepatobiliary (pHB) tumors. This study evaluated clinical utility of albumin ISH in diagnosing poorly differentiated pHB tumors. This study evaluated the clinical utility of albumin ISH in diagnosing poorly differentiated pHB tumors. This study evaluated the clinical utility of albumin ISH in diagnosing poorly differentiated pHB tumors. This study evaluated the clinical utility of albumin ISH in diagnosing poorly differentiated pHB tumors.

Design: Albumin ISH was positive in 18 of 21 HCCs, specifically 5 of 6 hilar/extrahepatic, 10 intrahepatic CCs (ICCs); 4 combined pHB tumors difficult to classify; 16 cholangiocarcinomas (CCs), including 21 hepatocellular carcinomas (HCCs); 4 poorly differentiated pHB tumors, particularly poorly differentiated HCCs that are negative or only focally positive for other hepatocellular markers. ISH for albumin may be helpful in differentiating ICC from extracellular CC and metastatic adenocarcinoma if metastatic hepatoid adenocarcinoma is not in the differential diagnosis. ISH for albumin is a useful marker for identifying poorly differentiated pHB tumors, particularly poorly differentiated HCCs that are negative or only focally positive for other hepatocellular markers.

Conclusions: ISH for albumin is a useful marker for identifying poorly differentiated pHB tumors, particularly poorly differentiated HCCs that are negative or only focally positive for other hepatocellular markers. ISH for albumin may be helpful in differentiating ICC from extracellular CC and metastatic adenocarcinoma if metastatic hepatoid adenocarcinoma is not in the differential diagnosis.

Primary Squamous Cell Carcinoma of the Pancreas: A Rare Case Report

(Poster No. 36)

Kai Wang, MD (kaiwang@uab.edu); Rongjun Guo, MD. Department of Pathology, University of Alabama at Birmingham.

Primary squamous cell carcinoma (SCC) of the pancreas is a very rare entity. It accounts for up to 0.7% of pancreatic carcinomas. The tumor is associated with extremely poor survival, with a median survival period of 6 months. It has been suggested that it originates from the pancreatic ductal cells. Because native pancreatic tissue lacks squamous epithelium, diagnosis of a primary pancreatic SCC is made only after metastatic disease and adenocarcinoma carcinoma, another rare primary tumor of the pancreas, have been excluded. Here, we report a case of squamous cell carcinoma of the pancreas with a distinct origin. The patient was a 61-year-old woman with a history of pancreatic cystic mass since 2006. An EUS in October 2014 showed a perigastric/pancreatic 9.3 × 6.8-cm anechoic lesion with irregular, hyperechoic walls. Cytology from the procedure demonstrated abundant anucleate squamous cells and keratinous debris, and sheets of hypercellular squamous epithelium with atypia that were suspicious for squamous cell carcinoma. Distal pancreatectomy and splenectomy were then performed. Grossly, a large and ruptured 6.5 × 4.0 × 2.5-cm cystic lesion was identified. Inside the cyst, there were tan-white firm tan-white nodules. Histologically, some areas showed benign lymphoepithelial (squamous epithelia) cysts from which in situ and invasive squamous cell carcinoma arose. To our knowledge, this is the first report that a squamous carcinoma originated from a benign lymphoepithelial lesion in the pancreas.

G Cells Can Be Identified in the Gastric Body of Autoimmune Gastritis

(Poster No. 37)

Daniel Dresser, MD (danieldresserca@gmail.com); Xianzhong Ding, MD, PhD; Yihong Ma, MD, PhD. Department of Pathology, Loyola University Medical Center, Maywood, Illinois.

Context: Autoimmune gastritis (AG) is a body-predominant gastritis characterized by presence of anti-parietal cell and/or anti-intrinsic factor antibodies and destruction of oxyntic glands. It is difficult to distinguish atrophic body mucosa from antral mucosa on H&E stains, especially with pseudopyloric gland metaplasia. Gastrin immunostains identifying G cells are useful for this purpose because G cells are normally present only in the antrum. However, it is not uncommon to encounter positive gastric staining in the body. This study aimed to interpret the results of gastrin immunostains in AG.

Design: Fifty-seven cases of AG diagnosed between 2015 and 2017 in our institute were retrieved, including 55 biopsies and 2 sleeve gastrectomies. Slides were reviewed and gastrin immunostains were analyzed for G-cell number, distribution, and their association with intestinal metaplasia.

Results: G cells were identified in the body of 38 cases (67%). Intestinal metaplasia was noted in 45 (79%) of the gastric bodies. All 38 cases had G cells in rare single-cell pattern at the areas with intestinal metaplasia. Fourteen cases had randomly scattered distribution, 15 cases had crypt distribution, and 9 cases had both a random and a crypt pattern. In contrast, G cells in the antrum demonstrated an evenly glandular pattern at neck areas.

Conclusions: It is not uncommon to encounter G cells in the gastric body of AG, particularly with intestinal metaplasia. However, the number and pattern of these cells are different from those in the antrum. This observation can potentially aid the pathologist in avoiding the misinterpretation of body-type mucosa as antrum.

Squamous Cell Carcinoma of the Pancreas: A Rare Case Report

(Poster No. 38)

Neha Gupta, MBBS (ngupta@northwell.edu); Morris Edelman, MD. Department of Anatomic Pathology and Laboratory Medicine, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, New Hyde Park, New York.

A 6-year-old boy with POLD mutation and history of global developmental delay, temperature disregulation, epilepsy, and cardiac arrest presented with reduced bowel movements, abdominal distension, and severe constipation. He had multiple admissions since birth...
Comparison of Hepatocellular Carcinomas in Cirrhotic and Noncirrhotic Livers

(Boster No. 39)

Benjamin L. Mazer, MD, MBA1 (benjamin.mazer@yale.edu); Anisha Jain1; Yanhong Deng, MPH; Qinxin Wang, MPH; Mark Benedict, DO; Charles Cha, MD; Romulo Celli, MD; Dhanpat Jain, MD; Tamar Taddei, MD; Xuchen Zhang, MD, PhD. Departments of 1Pathology, 2Public Health, 3Surgical Oncology, and 4Internal Medicine, Yale University School of Medicine, New Haven, Connecticut.

Context: Cirrhosis remains the strongest risk factor for hepatocellular carcinoma (HCC); however, incidence of HCC in noncirrhotic livers is increasing. Differences between cirrhotic and noncirrhotic HCC have not been recently studied in light of changing disease etiologies in the developed world.

Design: HCC biopsies and resections (2010–2014) were studied. History and slides were reviewed to assess background liver disease, including fibrosis and etiology. Histologic features of HCC were assessed, including grade, subtype, histologic patterns, steatosis, and cytoplasmic and nuclear features. Histologic pattern, clear cell change, and steatosis were scored at 10% intervals. Other histologic features were recorded dichotomously. Comparisons in pathologic features were made between noncirrhotic (stages 0–3) versus cirrhotic liver (stage 4).

Results: A total of 431 HCC cases (300 cirrhotic, 171 noncirrhotic) were identified. Noncirrhotic patients were more likely to have hepatitis B or liver disease of unknown etiology, whereas hepatitis C was more common in cirrhotic patients. HCCs in noncirrhotic livers were larger (mean, 5.7 cm) compared with cirrhotic livers (mean, 3.1 cm) (P < .001). HCCs in noncirrhotic livers were more likely to have macrovascular, perisinusoidal, or extracanalicular and clear cell HCC patterns were more common in noncirrhotic livers. Most other features did not differ in noncirrhotic HCCs. Contrary to common belief, there was no difference in steatosis in HCC or background liver between the 2 groups.

Multiple Hepatic Myelolipomas in a Posttransplant Liver

(Boster No. 40)

Hamza Tariq, MD (TariqH@uthscsa.edu); Brian Klazynski, MD. Department of Pathology and Laboratory Medicine, University of Texas Health Science Center at San Antonio.

Myelolipomas are rare benign tumors of mature hematopoietic tissue and fat that most commonly arise in the adrenal glands. Extra-adrenal myelolipomas are exceedingly rare and have been reported in the presacral region, liver, mediastinum, perirenal region, stomach, and spleen. The etiology is unknown; however, it is hypothesized that they arise because of embolization of bone marrow tissue and/or reactivation of peritoneal embryonic connective tissue in response to a triggered stimulus. To date, no cases of multiple myelolipomas in a posttransplant liver have been reported in the literature. We report the case of a 58-year-old white man who had an orthotopic liver transplant in 1998 secondary to chronic hepatitis C infection. He presented in February 2018 with nausea, vomiting, and body aches. His laboratory results showed elevated bilirubin, alkaline phosphatase, aspartate aminotransferase, and alanine aminotransferase levels. Ultrasound of the liver showed multiple echogenic liver lesions. Magnetic resonance cholangiopancreatography was performed and revealed multiple variably sized lesions in the liver with the largest measuring 6.0 cm. These lesions demonstrated a fat signature on the MRI. A liver biopsy was performed. Diff-Quik–stained touch imprints showed myeloid and erythroid hematopoietic cells as well as scattered benign hepatocytes. The H&E stained sections of the liver biopsy revealed trilaminate bone marrow hematopoietic elements mixed with mature adipose tissue diagnostic of a myelolipoma. No atypia, bone, or cartilaginous tissue was identified. The radiologic differential diagnosis of this rare hepatic lesion includes angiomylipoma, lipoma, and liposarcoma. Therefore, a biopsy is required for accurate diagnosis and subsequent management (Figure 14).
Angiolipofibromas represent rare mesenchymal polyps that have been described in the gastrointestinal tract. Reported sites include the colon, small bowel, and esophagus. These polyps are usually small (7–12 mm) aside from one case that had a 3- to 4-cm mass in the stomach wall lesion. This was subsequently considered to have grown from an existing smaller lesion. Both the abdominal and liver masses were subsequently biopsied and showed a proliferation of monomorphic epithelioid cells with distinct cell membranes, fine chromatin, and clear to finely vacuolated pale eosinophilic cytoplasm arranged in nests and solid sheets. The tumor cells were immunoreactive for calretinin, D2-40, HBME, CK5/6, CK19, CK7, and WT-1. PAS and PAS-D highlighted the intracytoplasmic glycogen deposits. The tumor cells were negative for GATA-3, CK20, inhibin, arginase, HMGB5, p63, glycogen-3, CD117, DOG1, CDX2, Pax8, TTF-1, chromogranin, synaptophysin, and albumin in situ. Based on the immunophenotype and morphology, the tumor was diagnosed as epithelioid mesothelioma, clear cell variant. Clear cell variant of peritoneal epithelioid mesothelioma should always be considered in patients with an abdominal or pelvic mass with clear cell features regardless of the clinical course. Given the rarity of such an entity, its clinical course and prognosis remains unclear.

**Conclusion:** Angiolipofibromas are benign mesenchymal gastrointestinal polyps that are most likely hamartomatous in etiology and are seen in middle-aged adults. There is no apparent predilection with respect to sex or anatomic site within the colon. Importantly, this lesion may mimic malignancy clinically, as seen in one of our cases, although they are completely benign. Pathologists should be aware of this entity when approached with a mesenchymal polyp in the colon.

Perforated Appendiceal Mass During Pregnancy

(Michael H. Schild, DO (michael.schild@duke.edu); Bruce D. Leckey, DO; Cynthia D. Guy, MD. Department of Pathology, Duke University, Durham, North Carolina)

A 30-year-old woman at 28 weeks’ gestation presented to the emergency department with acute right lower abdominal pain and vomiting. Physical examination revealed abdominal rigidity and rebound tenderness. Laboratory values were significant for leukocytosis. Magnetic resonance imaging demonstrated a 5-cm inflammatory mass medial to the cecum, concerning for appendicitis. During an exploratory laparotomy, a large phlegmon was identified in the right lower abdomen, and the appendix was adherent to the terminal ileum and cecum. An appendectomy was performed. Gross examination revealed a diffusely hemorrhagic, edematous appendix with purulent exudate on the mucosal and serosal surfaces. A perforation was identified, communicating with a peri-appendiceal abscess. Histopathology confirmed gangrenous appendicitis; however, in addition a masslike formation of stromal and glandular elements was identified (Figure 16, A and B). The mass was embedded within the appendiceal wall and protruded into the lumen. The stromal component was characterized by large, polygonal cells with eosinophilic cytoplasm, well-defined cell borders, and round nuclei. The glandular element exhibited intraglandular tufting, hobnailing, cytoplasmic vacuolation, and clear nuclei. Our diagnosis was decidualized appendiceal endometriosis with perforation. Although endometriosis is common in women of childbearing age, appendiceal endometriosis is uncommon and affects less than 1% of the general population. Perforated appendicitis secondary to endometriosis during pregnancy is extremely rare, with only 5 reported cases. Our patient did not have a known history or symptoms of endometriosis. Currently, no consensus exists on whether elective appendectomy is indicated for suspected appendiceal endometriosis. In women, the differential diagnosis for an appendiceal mass should include endometriosis.

**Primary Intestinal Leiomyosarcoma: An Uncommon Cause of Gastrointestinal Bleeding**

(Benjamin Lang, MD (Benjamin.Lang@BSWHealth.org); Atin Agarwal, MD. Department of Pathology, Baylor University Medical Center, Dallas, Texas)

Primary intestinal leiomyosarcoma is a rare gastrointestinal malignancy with only 27 reported cases in the literature. These malignant smooth muscle tumors pose diagnostic difficulties secondary to their location, nonspecific symptoms, and relative infrequency. A 78-year-old man was referred to our institution by his primary care physician for anemia workup. Initial endoscopy and colonoscopy were negative. Subsequent evaluation by video capsule endoscopy showed bleeding in the distal jejunum. An upper balloon-assisted endoscopy was performed, showing an ulcerated proximal jejunal mass. Biopsies were difficult to obtain secondary to poor visualization and were ultimately superficial and unrevealing. Computed tomography scan of the abdomen and pelvis showed a 4-cm mass with no evidence of metastatic disease. An exploratory laparotomy was performed with extensive small bowel and terminal ileum resection.
Histopathologic Features of Pembrolizumab-Associated Hepatitis

(Paper No. 47)

David Escobar, MD, PhD (david-escobar@northwestern.edu); Andrew Bandy, MD; Amanda Cheung, MD; Josh Levitsky, MD; Mary Kinella, MD; Sambasiva Rao, MD; Guang-Yu Yang, MD; Maryam K. Pezhouh, MD; Departments of 1Pathology and 2Gastroenterology and Hepatology, Northwestern University, Chicago, Illinois.

Pembrolizumab is an immune checkpoint inhibitor offering improved outcomes for patients with advanced malignancies. Despite the successful therapeutic responses, many patients will develop immune-related adverse events involving any organ. Pembrolizumab-associated hepatitis has been described clinically; however, to our knowledge, there is scant literature describing the histopathologic features associated with this entity. A 60-year-old woman with metastatic thymoma status post 2 cycles of pembrolizumab presented with dyspnea, weakness, and elevated liver chemistries (AST 198, ALT 112, ALK-P 648, and total bilirubin 9.1). A liver biopsy was performed. The portal tracts were expanded by marked dense inflammatory cells consisting mostly of lymphocytes and histiocytes. Severe bile duct injury with bile duct loss was highlighted by cytokeratin 7 immunolabeling. Focal mild central venulitis, mild cholestasis, and macrovesicular steatosis were also present. The lobules showed mild chronic inflammation with focal parenchymal granuloma along with rare single-cell hepatocyte and confluent necrosis. CD3 and CD20 immunostains highlighted the dense portal inflammation to be predominantly of T lymphocytes. Trichrome and reticulin stains confirmed mild portal fibrosis. No stainable iron and inflammation were noted. CD3 and CD20 immunostains highlighted the dense portal inflammation to be predominantly of T lymphocytes. Trichrome and reticulin stains confirmed mild portal fibrosis. No stainable iron and inflammation were noted. CD3 and CD20 immunostains highlighted the dense portal inflammation to be predominantly of T lymphocytes. Trichrome and reticulin stains confirmed mild portal fibrosis. No stainable iron and inflammation were noted.

Clinicopathologic Overview of Infarcted Epiploic Appendages

(Paper No. 48)

Caroline Dignan, MD (Caroline_Dignan@URMC.Rochester.edu); Adya Senior; Saul S. Gonzalez, MD. Department of Pathology and Laboratory Medicine, University of Rochester Medical Center, Rochester, New York.

Context: Epiploic appendages are fatty peritoneal structures on the external surface of the colon. If infarcted, they either become necrotic in situ or auto-amputate and float freely in the abdomen. They often show an “egglike” appearance, with a smooth, glistening, ovoid outer shell and central fat necrosis. Infarcted epiploic appendages (IEAs) have received little pathologic scrutiny.

Design: We reviewed 52 IEAs from 49 patients, recording patient age, sex, and body mass index (BMI); indication for surgery; surgical impression of the IEA; and lesion size, gross appearance, central fibrosis, rind thickness, necrosis, hemorrhage, inflammation, calcification, and ossification. Characteristics were compared across attached and loose IEAs using Fisher exact text and the unpaired t test.

Results: Average age was 54 years, male to female ratio was 13:36, and average BMI was 31.4. Twenty-eight IEAs were attached and 22 were loose; location was unclear in 2. Most were incidental; 3 attached cases caused “appendagitis.” Most (31; 60%) had the classic egglike appearance. Rind thickness averaged 0.84 mm. Common histologic findings included fat necrosis (84%), calcification (67%), and fibrosis (58%). Attached cases had a larger mean size (1.8 versus 1.3 cm, P = 0.048), but the rinds were similar in thickness. Loose cases were more often necrotic (100% versus 75%, P = .01); attached cases were more often hemorrhagic (36% versus 5%, P = .01) and inflamed (64% versus 14%, P < .001).

Conclusions: IEAs have different morphology whether they remain attached to peritoneum (where they increase in size and cause local hemorrhage/inflammation) or become necrotic and detached. Loose cases are usually incidental; attached cases may cause symptoms.

Extragastrointestinal Stromal Tumor With Ultrastructural Features of Neuronal Differentiation

(Poster No. 49)

Hongjie Li, MD, PhD (hongjie.li01@downstate.edu); Nicholas D. Cassai, BS; Rosemary L. Wieczorok, MD. 1Department of Pathology, SUNY Downstate Medical Center, Brooklyn, New York; 2Department of Pathology, Veterans Affairs New York Harbor Healthcare System, New York, New York.

Extragastrointestinal stromal tumors (EGISTs) are very uncommon and account for less than 5% in a large series of stromal tumors. Although EGISTs seem to have morphologic and immunohistochemical similarities with GISTs, their pathogenesis, incidence, genetic background, and prognosis are not completely known. Here we report an interesting case of EGISTs with ultrastructural features of neuronal differentiation that have been characterized in gastrointestinal autonomic nerve tumors. A 71-year-old man was incidentally found to have a mesenteric mass in 2013 on CT. Recently, the patient presented for evaluation of progression of mesentry mass and CT revealed one 4.3 × 4.1-cm rounded mass within the upper abdominal mesentery. Histologic examination revealed spindle cells arranged in small fascicles, low mitotic rate, and focal necrosis. Immunohistochemically, the tumor cells showed strong positivity for c-kit, DOG-1, and CD34; focal positivity for S100; occasional positivity for synaptophysin; and negativity for CD56 and chromogranin. Electronic microscopy showed elongated cytoplasmic processes devoid of basement membrane material (asterisks), rare neurosecretory granules (arrow), immature junction (circle), and skeniod fibers (S) (Figure 18). C-Kit mutation analysis revealed a duplication of Ala502-Tyr503 in exon 9 associated with intermediate response to imatinib. Thus, double dosing of imatinib 800 mg was suggested to clinicians. EGISTs tend to have a more aggressive biological behavior than their gastrointestinal counterparts. Complete surgical resection is the most effective treatment associated with the use of imatinib in the presence of adverse prognostic factors. In any case, a strict follow-up is necessary because of high recurrence rates.

Abstracts
Gastrointestinal Symptoms With Common Variable Immunodeficiency–Like Pathologic Features Leading to Diagnosis of Good Syndrome

(Poster No. 50)

Oluwotobi Odetola, MD (oluwotobi.odetola@lumc.edu); Reza Ebrahghi, MD; Vijayalakshmi Ananthanarayan, MD; Xianzhong Ding, MD, PhD; Yihong Ma, MD, PhD. Department of Pathology and Laboratory Medicine, Loyola University Medical Center, Maywood, Illinois.

Good syndrome (GS), combined thymoma and hypogammaglobulinemia, was first reported in 1954. It is a rare adult-onset immunodeficiency, predisposing to various infections. We report the case of a 61-year-old woman who was diagnosed with GS 4 years after the first serious clinical manifestations (colon perforation and sepsis) in 2013. She underwent partial left hemicolectomy and subsequently developed multiple episodes of Clostridium difficile infection. She presented to our center on 3 occasions with significant diarrhea. Initially in 2015, sigmoidoscopy revealed erythematous mucosa and pathology reported active colitis with ulceration, negative for CMV and HSV. Subsequently in 2016, colonoscopy was normal. However, biopsies showed paucity of plasma cells, so common variable immunodeficiency was considered. Follow-up tests revealed extremely low levels of immunoglobulins and she was put on intravenous immunoglobulin. In 2017, a thymoma was resected, leading to the diagnosis of GS. In 2017, colonoscopy and pathology were similar to those of 2016 and further workup did not identify B lymphocytes by CD20 immunostain. T-cell ratio and distribution appeared normal. Considering immune dysfunction and infection as possible etiologies of diarrhea, budesonide was added and symptoms improved. The slides of 2015 were reviewed and no plasma cells were noted. This case alerts pathologists to keep immunodeficiency diseases in mind because lack of plasma cells can be easily missed. Imaging studies looking for thymoma are suggested in patients lacking plasma cells to differentiate GS from common variable immunodeficiency. On the other hand, the finding of a thymoma should prompt immunodeficiency-related tests for possible GS.

Positive Nodular Metastasis in an Intraductal Oncocytic Papillary Neoplasm With Microinvasion

(Poster No. 51)

Sundis Mahmood, DO (sundis.mahmood@hitchcock.org); Bing Ren, MD. Department of Pathology, Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire.

Intraductal oncocytic papillary neoplasm, the rarest of the 4 histologic subtypes of intraductal papillae mucinous neoplasms, is characterized by complex arborizing papillae, oncocytic cells, and intraepithelial lumina formation. Because there are limited reports on pathologic characteristics and management of the intraductal oncocytic papillary neoplasm, we present a case of microinvasive intraductal oncocytic papillary neoplasm with positive nodal metastasis and its management. A 57-year-old man presented with acute pancreatitis and was found to have a necrotic cystic lesion in pancreatic tail on CT imaging (Figure 19, A). Magnetic resonance cholangiopancreatography was suggestive of a mixed-type (main and branch ducts) intraductal papillar mucinous neoplasm with a 4-cm cystic lesion in the tail of the pancreas and dilatation of the proximal pancreatic duct. Upper endoscopic ultrasound showed longitudilke projections in the cystic cavity and pancreatic duct with nodular formation. Histologic examination of biopsy material demonstrated a 4.5-cm high-grade intraductal oncocytic papillary neoplasm with microscopic invasion involving the main duct (Figure 19, B). In addition, 2 of 19 lymph nodes were involved by metastatic carcinoma. The immunostaining results showed the neoplastic cells were positive for Hep Par 1 (Figure 19, C) and MUC5A (Figure 19, D), focally positive for MUC1, and negative for MUC2 and CDX2, which supports the diagnosis. The patient received chemotherapy with gemcitabine and Abraxane and adjuvant radiation therapy. Seventeen months postresection there is no clinical evidence of recurrence and metastasis.

Does Invasive Colorectal Micropapillary Adenocarcinoma Harbor a Distinct Molecular Alteration?

(Poster No. 52)

David Escobar, MD, PhD (david-escobar@northwestern.edu); Andrew Bandy, MD; Katrina Krogh, MD; Guang-Yu Yang, MD; Maryam K. Pezhouh, MD. Department of Pathology, Northwestern University, Chicago, Illinois.

Context: Invasive micropapillary adenocarcinoma is a rare variant of colonic adenocarcinomas with poor prognosis. Categorization of molecular alterations in micropapillary predominant colorectal tumors may help further characterize signaling pathway alterations seen in these lesions and predict response to treatment.

Design: We reviewed colon resections with colonic adenocarcinoma at our institution for the last 2 years and identified 9 cases that were micropapillary predominant (9 of 108 cases; 7%). The expression of hMLH1, hMSH2, hMSH6, and hPM2S mismatch repair proteins was reported. Ion AmpliSeq second generation sequencing was performed on the 9 tumors for analysis of mutations in KRAS, EGF, BRAF, PIK3CA, AKT1, ERBB2, PTEN, NRAS, STK11, MAP2K1, ALK, DDR2, CTNNB1, MET, TP53, SMAD4, FBX7, FGFR2, NOTCH1, ERBB4, FGFR1, and FGFR2.

Results: Patient demographics included median age of 50 years (range, 34–61 years), with female to male ratio of 2:1. In this cohort of micropapillary adenocarcinomas, all cases (9 of 9; 100%) occurred in the sigmoid or rectum and were lymph node positive. All cases (9 of 9; 100%) had intact expression mismatch repair proteins. However, 8 cases (8 of 9; 89%) were found to harbor a mutation involving TP53, and 1 of those 8 cases additionally harbored a mutation involving KRAS.

Conclusions: This study suggests that micropapillary colonic adenocarcinomas are characterized by classic chromosomal instability with TP53 mutation. Research concerning the spectrum of TP53 mutations, some of which may be amenable to targeted drug therapy, is still ongoing. Meanwhile, categorization of tumor types that show repeated alterations in TP53 may help guide continued research in the field of targeted drug therapy.

Utility of Histologic Findings in Cirrhosis

(Poster No. 53)

Mushal Noor, MB, BS (Mushal_noor@urmc.rochester.edu); Roula Katerji, MD; Raul S. Gonzalez, MD. Department of Pathology and Laboratory Medicine, University of Rochester Medical Center, Rochester, New York.

Context: Once a liver is cirrhotic, it can be difficult to establish the cause based on histology. This study assessed pathologic findings in cirrhotic livers and correlated them with established clinical diagnoses.

Design: For 258 cirrhotic liver biopsy/section specimens, we searched medical records for clinical diagnosis and disease-associated laboratory values (including iron studies, serologic testing, and genotyping) and evaluated slides for >5% macrovesicular steatosis, Mallory hyaline, more than rare plasma cells or eosinophils, ductular/lobular cholestasis, glycogenated nuclei, iron, and PAS-D–positive globules within hepatocytes. Histologic findings suggestive of a diagnosis were compared between patients with and without that diagnosis using Fisher’s exact test.

Results: Across all cases, 56% had macrovesicular steatosis, 27% had Mallory hyaline, 18% had plasma cells, 10% had eosinophils, 38% had lobular cholestasis, 29% had ductular cholestasis, 37% had glycogenated nuclei, 24% had iron (2-grade 2), and 13% had PAS-D–positive
globules. Most findings were not significantly related to a commonly associated diagnosis (steatosis and alcoholic/nonalcoholic steatohepatitis \(P = 0.09\)); plasma cells and autoimmune hepatitis \(P = 0.40\); lobular cholestasis and primary sclerosing cholangitis/primary biliary cirrhosis \(P = 0.06\); iron and hemochromatosis \(P = 0.24\); PAS-D–positive globules and \(\alpha_1\)-antitrypsin \(\alpha 1\) deficiency \(P = 0.13\); glycogenated nuclei and Wilson disease \(P = 0.65\)). However, Mallory hyaline was more often seen in patients with than without clinical steatohepatitis (35% versus 20%, respectively; \(P = 0.08\)).

**Conclusions:** Macrovesicular steatosis, plasma cells, lobular cholestasis, iron, and glycogenated nuclei should not be relied upon in isolation to establish a causative diagnosis in cirrhosis. PAS-D–positive globules are not definitive evidence of \(\alpha 1\) deficiency, and ductular cholestasis doesn’t necessarily imply sepsis. Only Mallory hyaline appears to have utility in suggesting a diagnosis in cirrhosis.

### Undifferentiated Colon Cancer Presenting With Paraneoplastic Leukemoid Reaction: Case Report and Literature Review

*(Poster No. 54)*

Ibrahim M. Abukhiran, MBBS (ibrahim-abukhiran@uiowa.edu); Daniel J. Pelletier, MD; Andrew M. Bellizzi, MD; Sarag A. Boukhar; MBChB. Department of Pathology, University of Iowa Hospitals and Clinics, Iowa City.

Paraneoplastic leukemoid reaction (PLR) is an extremely rare presentation of solid tumors. To our knowledge, this is the first English-literature report of isolated primary colon cancer presenting with PLR. A 70-year-old presenting with watery diarrhea was found to have a white blood cell count (WBCC) of 105.4 K/mm\(^3\). Results of extensive infectious and hematologic investigations, including bone marrow examination with flow cytometric, cytogenetic, and molecular analysis, were negative. Five weeks after initial presentation, CT scan of the abdomen showed a large ascending colon mass. Surgical resection demonstrated an undifferentiated, MLH-1–deficient colon cancer, which was notable for a marked intratumoral neutrophilic infiltration (Figure 20). Resection, without additional intervention, led to a dramatic decrease of WBCC from 162.5 K/mm\(^3\) (day of the surgery) to 42.2 K/mm\(^3\) (following day) to 11.7 K/mm\(^3\) (1 week later). Systematic English-literature review revealed 53 patients presenting with PLR from 1976 to 2017: mean age 61 years, 2.5:1 male to female ratio, mean peak WBCC 67.6 K/mm\(^3\) (predominantly neutrophilic). The most common primary site was lung (\(n = 13\), 25%). In the digestive system (\(n = 20\)), the following primary sites were encountered in descending order: liver (35%), gallbladder (25%), pancreas (15%), stomach (15%), esophagus (5%), and concurrent liver/colon (5%). Most of the liver tumors were poorly differentiated hepatocellular carcinoma with a sarcomatous element. Intratumoral neutrophilic infiltration was reported in 7 cases. Eighty-five percent (26 cases tested) showed elevated serum and/or body fluid granulocyte colony-stimulating factor (G-CSF) or granulocyte/macrophage colony-stimulating factor and all 15 tumors tested showed G-CSF immunopositivity, making tumor secretion of G-CSF a plausible mechanism for PLR.

### A Novel Approach for Hyaluronic Acid Detection and Interpretation Across Multiple Tumor Types

*(Poster No. 55)*

Carrie Aldrich, PhD (carrie.aldrich@ROCHE.COM); Erika Walker, BS; Genevieve LaBahn, BA; Tyler Foutch, MS; James Hinton, MS; Xuemin Liu, PhD; Janine Feng, MD; Bryce Portier, MD, PhD; Jeff Pearson, MBA; Paco Delgado, MBA, BS.1 Departments of 1CDx, 2Assays-CDx, 3CDx-Discovery, and 4Medical Affairs, Roche Tissue Diagnostics, Tucson, Arizona.

**Context:** Hyaluronic acid (HA) is a linear glycosaminoglycan composed of repeating disaccharide units of glucuronate and N-acetylglucosamine. Recent literature has shown that the extracellular matrix or stroma of tumors contains highly expressed noncellular elements such as HA, which creates an environment favoring tumor invasiveness and persistence. As such, HA is considered a potential diagnostic target. However, HA detection has been challenging because it is highly conserved across species and ubiquitously present in nearly all the tissues. A sensitive and specific assay is needed.

**Design:** Recombinant protein technology can overcome limitations of the traditional methods that rely on an endogenous HA binding protein (HABP). A novel recombinant HABP was generated, consisting of TSG-6 (a member of the HA binding protein family) bound to a rabbit Fc receptor, known as rec-HABP, with its intended use being detection of HA in tissues. Ten percent NBF–fixed gastric, breast, pancreatic, and cholangiocarcinoma tumor tissues stained by the rec-HABP were used to evaluate the overall performance of this novel assay.

**Results:** It was observed that the Ventana assay using rec-HABP shows high specificity and sensitivity compared with the existing immunohistochemistry assays. An automated procedure using OptiView DAB immunohistochemistry detection on BenchMark advanced staining instruments provides reproducible staining results using several tumor indications. A practical interpretation method is proposed and presented.

**Conclusions:** It was demonstrated that this novel HA assay is highly specific for HA in a clinical setting. An ease-of-use automated staining procedure for human FFPE tissues can also reduce the entry barriers in clinical practice.

All authors are employees of Roche/Ventana. Dr Liu is a shareholder of Illumina stock. Drs Portier and Delgado are shareholders of Roche stock.

### Colloid Carcinoma of the Gallbladder: An Incidental Rare Tumor With Debatable Prognosis

*(Poster No. 56)*

Annie Garcia, MD (annie.garcia@bcm.edu); Jason Chen, MD; Shilpa Jain, MD. Department of Pathology and Immunology Department, Baylor College of Medicine, Houston, Texas.

Mucinous adenocarcinoma of gallbladder is defined as tumor with >50% extracellular mucin component. It constitutes 25% of gallbladder carcinomas. Pure mucinous (colloid) carcinoma is a distinct subtype with mucin component comprising >90% and it is exceedingly rare. An 88-year-old Asian man presented with a 1-week history of right upper quadrant pain with fever. Ultrasound showed gallstones with thickened wall, with findings suggestive of emphymatous cholecystitis. CT scan further showed possible fistulization to small bowel. The patient underwent urgent open cholecystectomy for complicated acute perforated cholecystitis. Grossly, the gallbladder wall was disrupted, tan-white, thickened up to 2 cm, and >90% granular and girty on sectioning. Microscopic examination showed a mucinous adenocarcinoma predominantly composed of pools of extracellular mucin containing clusters of tumor cells forming glandular architecture with surface dysplasia. The tumor cells were positive for CK7, CDX-2, and (patchy) CK20. Mismatch repair proteins were intact. Cystic duct and liver bed margins were involved by carcinoma. The patient decided not to pursue any medical treatment. Five-month follow-up CT scan showed partially calcified nodule in the cholecys-tectomy bed, with calcified porta hepatitis and portacaval lymph nodes suggestive of locally advancing disease without distant metastasis. Pure mucinous carcinoma is discussed because of its extreme rarity, acute presentation, nonspecific clinical and radiologic features altered by excessive mucin, advanced stage of presentation, and uncertain prognosis. A meticulous gross examination of the gallbladder wall in older patients is crucial for appropriate diagnosis and staging.
Rectal Mucinous Adenocarcinoma With Features Reminiscent of Adenocarcinoma Ex–Goblet Cell Carcinoid: An Unusual Morphology

(Poster No. 57)

Tiffani M. Mathew, MBBS (tmmath03@exchange.louisville.edu); Julie Anne Bishop, MD; Houda Alattassi, MD; Nenencia Ronquillo Jr, MD. Department of Pathology and Laboratory Medicine, University of Louisville, Kentucky.

Goblet cell carcinoid (GCC) tumors account for less than 5% of primary appendiceal tumors. Here we report a case of rectal tumor in a 65-year-old man with morphologic features reminiscent of adenocarcinoma ex–goblet cell carcinoid. The low-content resection, and the specimen showed a large, fungating, friable mass in the rectum straddling the peritoneal reflection. Microscopy showed mucinous adenocarcinoma with features of signet ring cells. Fifteen percent of the tumor also showed areas reminiscent of GCC, appearing as tubules and cryptlike structures composed of goblet-like cells distended with mucin and occasional granular eosinophilic cytoplasm. Synaptophysin immunostain was predominantly positive in areas with signet ring cell and GCC-like morphology. Additionally, the conventional and mucinous components of the tumor demonstrated patchy positivity for synaptophysin. Nine lymph nodes contained metastatic tumor with morphologic features of mucinous adenocarcinoma, conventional adenocarcinoma, signet ring cells, and GCC-like cells. There is no high-grade neuroendocrine component morphologically. On imaging, the appendix appeared unremarkable. However, diagnosis of GCC of the appendix is seldom made preoperatively because most appendiceal tumors are not mass-forming lesions. Pathologists should be aware of this and raise a consideration of a metastasis from an appendiceal primary. Primary GCC outside the appendix is extremely rare, and the literature is conflicting if it does occur outside of the appendix.

Congenital Epidermoid Cysts of the Cecum: Case Presentation and Suggested Histogenesis

(Poster No. 58)

Paulyann I. Maclayton, MD1 (pimaclayton@houstonmethodist.org); Eric M. Haas, MD2; Patricia Chévez-Barrios, MD3. Departments of 1Pathology and Genomic Medicine and 2Colon and Rectal Surgery, Houston Methodist Hospital, Houston, Texas; 3Department of Pathology and Genomic Medicine, Houston Methodist Hospital and Weill Cornell Medical College of Cornell University, Houston, Texas.

Congenital epidermoid cysts of the cecum are extremely rare. They are typically cutaneous lesions with limited reports of internal organ involvement. There are only 9 cases reporting epidermoid cysts of the cecum. The etiology is classified as either acquired or congenital. Acquired lesions are considered a result of implantation of epidermal fragments during abdominal trauma or surgery. Congenital lesions lack history of intraabdominal trauma/surgery and are thought to be a result of aberrant embryogenic ectodermal implantation into the gut. We report a case of a cecal epidermoid cyst in a 74-year-old man with no history of lower abdominal surgery or trauma and explore the possible histogenesis of this lesion in abdominal viscera. Our patient underwent a laparoscopic resection of a 10-cm intramuscular cystic mass of the right lower abdomen. The lesion was adherent to the muscularis propria that includes the basal lamina. The lower abdominal quadrants were explored, and the cecum was found to be adherent to the lateral abdominal wall. The cyst was resected en bloc, with the cecum separate from the abdominal wall. The lesion was sent for pathology examination. The histology showed an inclusion cyst with a lamina propria and subepithelial collagen with superficial bandlike areas that frequently merged with irregular deeper patches, few foci of increased intraepithelial lymphocytes, capillaries, and moderate infiltrates of mixed inflammatory cells. Helicobacter pylori infection was not detected by Diff-Quik stain or urease test. No other clinical explanation was identified and the endoscopic and histopathologic findings were deemed diagnostic of congenital gastrointestinal cysts. Follow-up endoscopy 3–4 months showed similar findings after symptomatic treatment. Congenital gastrointestinal cysts are diagnostically challenging and recognition requires awareness of its existence and histologic pattern. The cause of congenital gastrointestinal cysts is unknown and no effective treatment has been established. Better understanding of the disease will require study of a larger number of patients to establish diagnostic criteria and therapeutic strategies.

Loss of β2-Microglobulin Expression Is Associated With Favorable Clinical Outcome in MMR-Deficient Colorectal Cancers

(Poster No. 60)

Xin Zhang, BMed1 (xin_zhang@urmc.rochester.edu); Karina Hiroshige, BS2; Umesh Sharma, MBBS2; Richard S. Gonzalez, MD2; Rebecca Allen, BS3; Elena Gupta, BS3; Caitlin Foor-Peressin, MD1; Laura Framo, MD2; Daniello Marino, MD2; Arthur J. DeCross, MD2; Qi Yang, AAS1; Jennifer J. Findes-Hosey, MD2; Aaron R. Huber, DO3. Departments of 1Pathology and Laboratory Medicine and 2Gastroenterology and Hepatology, University of Rochester Medical Center, Rochester, New York.

Context: β2-Microglobulin (B2M) is a component of major histocompatibility complex class I molecules that is present on all nucleated human cells. Loss of B2M expression is frequently seen in MMR-deficient (dMMR) tumors, leading to the development of immune escape variants and more aggressive tumors. We evaluated the clinicopathologic effect of loss of expression of B2M on dMMR colorectal adenocarcinomas (CRAs).

Design: Sixty-four dMMR CRAs were included in a tissue microarray. Based on their B2M immunohistochemical staining, they were classified as positive (any positive staining, >0%) or negative (complete loss, 0%). B2M status was correlated with clinicopathologic features.

Results: Loss of B2M expression by immunohistochemistry was identified in 19 cases (29.7%). Of these, 13 (68.4%) were well to moderately differentiated, 7 (36.8%) demonstrated lymphovascular invasion, and 8 (42.1%) had lymph node metastases. Positive B2M expression was identified in 45 cases (70.3%). Of these, 26 (57.8%) were poorly differentiated, 26 (57.8%) showed lymphovascular invasion, 23 (51.1%) lymph node metastases, 9 (20%) had perineural invasion, and 40 (88.9%) were AJCC pathologic stage T3 or greater (Table).

Conclusions: Loss of B2M expression, by immunohistochemistry, in dMMR CRAs is associated with lower-grade tumors, lower rates of lymphovascular invasion, perineural invasion, lymph node metastases, and lower tumor stage. This is in contrast to what is expected based on the mechanism of B2M in regard to antigen presentation and warrants additional investigation.

Summary of Results: MMR-Deficient Colorectal Adenocarcinomas

<table>
<thead>
<tr>
<th>B2-Microglobulin</th>
<th>Negative, No. (%)</th>
<th>Positive, No. (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>19 (29.7)</td>
<td>45 (70.3)</td>
<td>&lt;.05 (0)</td>
</tr>
<tr>
<td>Well to moderately differentiated</td>
<td>13 (68.4)</td>
<td>19 (42.2)</td>
<td>.06</td>
</tr>
<tr>
<td>Poorly differentiated</td>
<td>6 (31.6)</td>
<td>26 (57.8)</td>
<td>.06</td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td>7 (36.8)</td>
<td>26 (57.8)</td>
<td>.13</td>
</tr>
<tr>
<td>Perineural invasion</td>
<td>0 (0)</td>
<td>9 (20)</td>
<td>.04*</td>
</tr>
<tr>
<td>Lymph node metastasis</td>
<td>8 (42.1)</td>
<td>23 (51.1)</td>
<td>.51</td>
</tr>
<tr>
<td>AJCC, grade T3 and above</td>
<td>13 (68.4)</td>
<td>40 (88.9)</td>
<td>.048*</td>
</tr>
</tbody>
</table>

*Statistically significant.

Arch Pathol Lab Med—Vol 142, September 2018

Abstracts e19
A Rare Case of Synchronous Gastric Diffuse Large B-Cell Lymphoma and Gastric Adenoma in a Background of Helicobacter pylori–Associated Gastritis

(Poster No. 61)

Vamsi Parimi, MD, MPH (vamsi.parimi@nyumc.org); Nicholas Ward, MD; Cynthia Liu, MD, PhD; Suparna A. Sarkar, MD, PhD. Department of Pathology, NYU, Secaucus, New Jersey.

Gastric colonization with Helicobacter pylori is a known risk factor for peptic ulcers (10%), gastric carcinoma (1%–3%), and mucosa-associated lymphoid tissue (<0.1%). We report a unique case of a 70-year-old woman with a remote history of bleeding gastric ulcers found to have an incidental large gastric diffuse large B-cell lymphoma, non-geminal center (nGC) phenotype. Upper gastrointestinal endoscopy and ultrasound demonstrated a large, infiltrative and ulcerative submucosal mass (10.3 cm) at the lesser curvature of the stomach. CT and PET scans were discordant with a hypermetabolic mass without additional disease. Separate additional biopsies were remarkable for a gastric adenoma, in a background of H pylori gastritis and intestinal metaplasia. A diffuse infiltration of large atypical lymphocytes with irregular nuclei, vesicular chromatin, distinct nucleoli, and numerous apoptotic figures was noted. Flow cytometry analysis highlighted the aberrant B lymphocytes coexpressing CD45, CD20, CD79a, and negative for CD5, CD19, CD10, CD23, CD38, and restricted for surface κ immunoglobulin. Immunohistochemically the neoplastic cells were positive for CD20, CD79a and co expressed MUM-1 (40%) and were negative for CD3, CD10, BCL2 and BCL6 (10%) with brisk mitotic activity (60%–80%), compatible with non–GC-immune–phenotype DLBCL (Han algorithm). Molecular studies were positive for clonal immunoglobulin gene rearrangement. FISH studies were negative for BCL6, BCL2, and MYC. The patient was scheduled to be treated with 6 cycles of R-CHOP followed by radiotherapy with substitution of etoposide for vincristine to avoid peripheral neuropathy for occupational reasons.

Poorly Differentiated Biliary Adenocarcinoma Leading to a Boerhaave Syndrome

(Poster No. 62)

Albina Murzabdillaeva, MD (albina.murzabdillaeva@uth.tmc.edu); Tahiana Bolosuova, MD; Nfn Aakash, MD; Yasir Ali, MD; Jacob Armstrong, MD; Bihong Zhao, MD. Department of Pathology and Laboratory Medicine, the University of Texas Health Science Center McGovern Medical School, Houston.

Boerhaave syndrome is a longitudinal transmural disruption of the esophagus due to an acute increase in esophageal pressure after forceful vomiting and blunt abdominal trauma. There are cases reported secondary to bowel obstructions such as incarcerated hernias and gallstone ileus. Here we describe an unusual case of Boerhaave syndrome due to biliary cancer. The patient was an 87-year-old man without known history of cancer who presented with nausea, vomiting, and severe epigastric pain. X-ray revealed left pneumothorax and bowel obstruction pattern. Computed tomography showed pneumobilia and gallbladder mass, fluid-filled esophagus, gastric distention, and ill-defined mass within the liver. The patient underwent chest tube insertion and flexible esophagogastroduodenoscopy, which revealed esophageal rupture at the left esophagogastric junction. The patient became too unstable for surgery and expired within 20 hours of admission. On autopsy, the decedent was found to have a 6-cm esophageal perforation, with spillage of gastric content into pleural and mediastinal cavities, and an inferior hepatic mass adhering to the duodenum and hepatic flexure of the colon. Grossly, the liver lesion was a 3.5-cm tan-white, fibrous masses completely encasing the gallbladder. Microscopic examination revealed poorly differentiated adenocarcinoma involving the liver, duodenum, and pericolonic adipose tissue, which was immunohistochemically positive for CK7, CK19, and CK20 and negative for CDX2, supporting a diagnosis of poorly differentiated biliary adenocarcinoma. Boerhaave syndrome accounts for 15% of esophageal perforations and is associated with high morbidity and mortality, and is fatal in the absence of prompt treatment. We report this case to increase awareness of this entity.

Transition From Narrative to Synoptic Reporting: A Single Institution’s 10-Year Experience

(Poster No. 63)

Bebu Ram, MD (bram@nywinthrop.org); Behnam Rafiee, MD; Mala Gupta, MD; Iman Hanna, MD. Department of Pathology, NYU Winthrop Hospital, Mineola, New York.

Context: Gastrointestinal stromal tumors (GISTs) constitute up to 90% of mesenchymal neoplasms of the gastrointestinal tract that are managed surgically. Endoscopic submucosal dissection (ESD) is an effective modality to resect mucosal and submucosal lesions of the gastrointestinal tract including GISTs. In January 2014, we implemented pathology synoptic reporting for GISTS removed by ESD. We evaluated the impact of standardization on the completeness of pathology reports.

Design: After obtaining internal review board approval, electronic medical records were searched for cases of GIST treated by ESD from January 1, 2008, to December 31, 2017. Fifty-two cases were found and allocated into 2 groups: prestandardization (24 cases) and poststandardization (28 cases). Pathology reports from both groups were reviewed to compare prestandardization and poststandardization completeness of reports for essential variables, including size of lesion, histologic type, mucosal involvement, depth of invasion, margins, ulcer, mitotic rate, immunohistochemistry for CD117, Miettinen risk of progression, and pT staging. The collected data were analyzed using x² test to evaluate difference for reporting of each variable. P < .05 represented a statistically significant difference in this study.

Results: We noted improvement in reporting of 5 variables: size of lesion, mucosal involvement, depth of invasion, Miettinen risk of progression, and pT staging. Three of those variables showed statistically significant improvement: mucosal involvement (57.1% versus 92.9%, P = .01); pT (42.9% versus 12.5%, P = .03); and Miettinen risk of progression (85.7% versus 56.5%; P = .02).

Conclusions: Our study supports that a standardized synoptic summary can improve the quality and completeness of pathology reports.

Evaluation of a Novel Histologic Scoring System for Gastrointestinal Graft-Versus-Host Disease

(Poster No. 64)

Ayesha Farooq, MD (afarooq@mcw.edu); Daniel Rowan, MD; Luis Carillo, MD; Christopher Hartley, MD; Catherine Hagen, MD. 1 Department of Pathology, Medical College of Wisconsin, Milwaukee; 2 Department of Pathology, Washington University in St Louis, Missouri.

Context: The Lerner system is the most commonly used histologic grading system for gastrointestinal (GI) graft-versus-host disease (GVHD), but fails to provide prognostic stratification. The aim of this study was to develop a histologic grading system for GI GVHD that incorporates apoptotic counts and assess its prognostic significance.

Design: Colon biopsies taken to assess for GVHD from 2008 to 2014 were retrospectively reviewed for the maximum number of apoptotic bodies per 10 contiguous crypts (ap/10), crypt dropout, and ulceration. A novel histologic scoring system was developed combining scoring of stool apoptotic bodies per 10 contiguous crypts (ap/10), crypt dropout, and ulceration. Clinical information was collected from chart review.

Results: The study group consisted of 122 colon biopsies from 84 patients and 97 endoscopy procedures (M:F 1:1.3; mean age 53.6 years). Patients with Lerner grade 4 (ulceration) had significantly worse GVHD-specific survival compared with patients with GVHD Lerner grades 1–3 (HR 2.7; 95% CI, 1.1–14.6; P = .03). Patients with >6 ap/10
also had significantly worse GVHD-specific survival compared with patients with 1–6 ap/10 (HR 4.6; 95% CI, 2.0–13.3; P = .004). Using our newly proposed scoring system, patients with an overall histologic score of 3–4 had significantly worse GVHD-specific survival compared with patients with a score of 0–2 (HR 6.2; 95% CI, 4.4–36.1; P < .001) (Figure 21, A through D).

Conclusions: Our proposed histologic scoring system using apoptotic count and mucosal irregularities provides prognostic stratification. Further studies are necessary to validate this scoring system.

A Rare Case of Hepatoblastoma With Cholangioblastic Features

(Poster No. 65)

Jia Qin, MD, PhD (jia.qin@mountsinai.org); Swan Thung, MD; Fumiko Dekio, MD; Stephen Ward, MD. Department of Pathology, Icahn School of Medicine at Mount Sinai Medical Center, New York, New York.

Hepatoblastoma is a rare malignant tumor accounting for less than 1% of all pediatric cancers. The morphology is varied, with numerous histologic subtypes. Some hepatoblastomas demonstrate cholangiocytic differentiation and have been termed cholangioblastic hepatoblastoma. We present a case of hepatoblastoma with a cholangioblastic pattern. A 12-month-old girl with no significant medical history presented with increased crankiness and abdominal distension for 2–3 weeks. Laboratory test results were remarkable for marked elevated AFP (17 280 ng/mL). Abdominal CT showed a 13.7-cm well-circumscribed heterogenous mass with central necrosis and calcifications in the right hepatic lobe. Biopsy was performed showing a mixed epithelial-mesenchymal hepatoblastoma with fetal and teratoid features, including pigmented melanocytes, squamous epithelium, and ganglion cells. Within the fetal epithelial component, foci of glandular structures with complete or incomplete lumina were identified. These structures resembled biliary ducts, but were clearly distinct from preexisting small bile ducts entrapped in the tumor. Immunohistochemically, the glandular component was diffusely positive for CK19, focally positive for CK7 and BCL-2, and negative for glypican-3. Interestingly, CK19 also stained single cells within fetal epithelial components, which might represent its multifocal differentiation pathway. The morphology and immunohistochemical findings are consistent with cholangioblastic pattern of hepatoblastoma. The patient underwent right extended hepatectomy followed by 6 cycles of chemotherapy. She is free of disease 6 months postsurgery. As more cases of cholangioblastic hepatoblastoma are identified, future studies can better characterize the clinical behavior of this rare tumor (Figure 22).

We report a 25-year-old woman presenting with right-sided abdominal pain who was found to have an appendiceal mass on imaging. Appendectomy showed involvement by diffuse ganglioneuromatosis (DG) with a transmural proliferation of loose spindled neural cells with interspersed ganglion cell clusters. Immunohistochemical stains for S100 protein, synaptophysin, and neurofilament highlighted the neural and ganglion cell hyperplasia in various layers of the appendix. DG is a benign hamartomatous proliferation of neural tissue and appendiceal involvement has been reported in <5 cases in the English literature. Knowledge of DG and its syndromic association could help detect patients with a variety of germ-line mutations including neurofibromatosis type 1 and multiple endocrine neoplasia 2b. No genetic testing guidelines exist for DG. However, given the high correlation of DG with hereditary cancer syndromes, genetic testing was recommended and pursued. Our patient was found to have a pathogenic variant, c.1541_1542delAG (p.Gln514Argfs*43), in NF1 gene. This sequence change deletes 2 nucleotides from exon 14 of the NF1 mRNA (c.1541_1542delAG), causing a frame shift at codon 51, creating a premature translational stop signal (p.Gln514Argfs*43), and resulting in an absent or disrupted protein product. Loss-of-function variants in NF1 are pathogenic and particular variant has been reported in many individuals affected with neurofibromatosis type 1. Half of neurofibromatosis type 1 cases are inherited and the remainder are the result of de novo mutations. In view of clinical outcomes and associated risk of developing malignancy, pathologic recognition with ancillary genetic testing is warranted in cases with DG lesions (Figure 23).

Concurrent Distinct Mucosal Lesions in the Gastrointestinal Tract of an Immunocompromised Patient

(Poster No. 67)

Domenika A. Ortiz, MD; Rochelle Freire, MD; Claudia P. Rojas, MD (C.Rojas@med.miami.edu); Clara Milikowski, MD; Monica Garcia-Buitrago, MD. 1Department of Pathology, University of Miami, Florida; 2Department of Pathology, Jackson Memorial Hospital, Miami, Florida.

Immunocompromised patients are at higher risk to develop concomitant opportunistic infections or neoplasms. Their assessment can be challenging because of the number of pathologies that can arise from the gastrointestinal tract. Kaposi sarcoma and malakoplakia are 2 distinct entities commonly reported in patients receiving immunosuppressive protocols, reflecting a dependence of host immune system. We report a case of a 64-year-old man status post kidney transplant because of diabetes mellitus and hypertension who presented with diffuse ganglioneuromatosis of appendix: A harbinger for neurofibromatosis-1

(Poster No. 66)

Siavash Azadmanesh Samimi, MD1 (sazadmaneshsamimi@houstonmethodist.org); Mukul Divatia, MD1; Jae Ro, MD1; Jean-Paul Lefave, MD. 1Departments of 1Pathology and 1Surgery, Houston Methodist Hospital, Houston, Texas.
recurrent epigastric pain, nausea, and vomiting and was on treatment with tacrolimus and prednisone. During hospitalization, he was found to have cytomegalovirus viremia. An upper endoscopy and colonoscopy procedures were performed. The findings included an 8-mm raised gastric lesion with umbilicated center and three 5-mm cecal nodules. Biopsies were taken from both lesions. The histologic evaluation of the gastric lesion biopsy revealed a neoplastic spindle cell nodule with mild to moderate atypia arranged in fascicles and separated by slitlike vessels, consistent with Kaposi sarcoma (Figure 24, A). HHV-8 immunostain was positive in the spindle cells (Figure 24, B). The biopsy of cecal nodules revealed a collection of enlarged histiocytes with abundant, granular pale cytoplasm and small basophilic calcified inclusions, and neutrophilic infiltrate, consistent with malakoplasia (Figure 24, C). Von Kossa stain highlighted the Michaelis-Gutmann bodies. None of the biopsies showed cytomegalovirus infection (Figure 24, D). Immunocompromised hosts are prone to develop different concurrent neoplastic and infectious lesions, which usually have no specific clinical presentation. The pathologist should have a high index of suspicion for opportunistic infections and virus-related neoplasms.

Foreign-Body Appendicitis: A Case Series

(Master No. 68)

Maren Y. Fuller, MD1 (marenfullermd@gmail.com); Daniel Leino, MD2; Miguel Reyes-Mugica, MD3; Alexandra Kovach, MD1; Jose Velazquez Vega, MD4; Shelley Caltharp, MD5; Tricia Bhatti, MD6; Raul Gonzalez, MD7.1 Department of Pathology, Children’s Hospital of Pittsburgh of UPMC, Pittsburgh, Pennsylvania; 2Department of Pathology and Laboratory Medicine, Cincinnati Children’s Hospital, Cincinnati, Ohio; 3Departments of Pathology, Microbiology, and Immunology, Vanderbilt University Medical Center, Nashville, Tennessee; 4Department of Pathology & Laboratory Medicine, Emory University, Atlanta, Georgia; 5Department of Pathology, Children’s Healthcare of Atlanta, Georgia; 6Department of Pathology, Children’s Hospital of Philadelphia, Pennsylvania; 7Department of Pathology and Laboratory Medicine, University of Rochester Medical Center, Rochester, New York.

Context: Appendicular foreign bodies are a rare cause of appendicitis. We performed this study to determine the varied causes and consequences of foreign-body appendicitis.

Design: On retrospective review of the pathology archives of 6 institutions, we identified 49 appendix specimens containing a foreign body (defined as ingested, nondigestible material). We recorded the type of foreign body, patient age and sex, symptoms, imaging findings, and surgical findings, gross findings, and microscopic findings, as available.

Results: Median patient age was 8 years (range, 1 day–18 years). The foreign bodies included hair (23), plant material (9), BB pellets (2), magnets (2), foreign material not otherwise specified (8), and 1 each of the following: bead, bone, metal necklace, pencil lead, and splinter. Of 43 cases with available clinical information, 31 patients presented with abdominal pain and 18 were preoperatively diagnosed as having appendicitis or appendicular inflammation. Imaging identified only the 5 metallic objects. Five cases had clinical or gross appendiceal perforation, and 3 with plant material. The plant material was grossly identified in 27 of 40 cases with available gross descriptions. Of the 27 cases with an identifiable foreign body macroscopically, 10 were associated with foreign-body giant cell reaction.

Conclusions: Hair and plant material appear to be the most common foreign objects found in the appendix; they can cause mucosal damage and a foreign-body giant cell reaction. Metallic objects were uncommon. Although appendicular foreign bodies in children are rare and sometimes asymptomatic, they may lead to perforation, which occurred in 10% of cases in this series.

Loss of 5-Hydroxymethylcytosine Expression Is Frequent in Colorectal Carcinoma and Is Not Associated With the CpG Island Methylator Phenotype

(Paper No. 69)

Hiba Ibrahim, MD (hiba.ibrahim@umassmemorial.org); Karen Dresser, BS; Jacob Bledsoe, MD. Department of Pathology, University of Massachusetts, Worcester.

Context: 5-hydroxymethylcytosine (5hmC) is a marker of active demethylation and has been shown to be reduced in a variety of cancers. The aim of our study was to investigate 5hmC protein expression in colorectal carcinoma and to explore its relation to the CpG island methylator phenotype including MSI and BRAF mutations.

Design: 5hmC immunohistochemistry (IHC) was performed on 19 cases of colorectal carcinoma. MSI and BRAF mutation status had been determined previously by IHC. 5hmC staining was scored by intensity (0, negative; 1, weak; 2, moderate; 3, strong) and percentage of tumor cells staining (0, negative; 1, 1%-10%; 2, 11%-50%; 3, >50%). A combined score (0–9) was calculated from multiplying intensity by percentage scores. Loss of 5hmC staining was considered combined score <4. Stromal cells were used as a positive control. P values were estimated by Fisher exact test.

Results: Loss of 5hmC staining was present in 10 of 19 cases (53%), including 6 of 10 cases with MSI and 4 of 9 cases without MSI (P = .66). Loss of 5hmC expression was observed in 4 of 5 cases with BRAF mutation and 3 of 6 BRAF wild-type cases (P = .55).

Conclusions: Our study demonstrates that 5hmC expression is decreased in a significant proportion of colorectal carcinomas, with no association to MSI or BRAF mutation. These findings suggest that aberrant DNA methylation is a common event contributing to the pathogenesis of colorectal carcinoma. Loss of 5hmC does not appear to be more frequent in colorectal cancers of the CpG island methylator phenotype.

Development of Multifocal Hepatocellular Carcinoma in a Noncirrhotic Patient With Short Bowel Syndrome During Teduglutide Therapy

(Paper No. 70)

Jia Qin, MD, PhD1 (jia.qin@mountsinai.org); Thomas Schiano, MD2; Marialisabel Fiel, MD1. Departments of 1Pathology and 2Medicine, Icahn School of Medicine at Mount Sinai Medical Center, New York, New York.

Teduglutide is approved for the treatment of parenteral nutrition–dependent adult patients with short bowel syndrome. Its use has been theorized to lead to the development of certain cancers. De novo development of hepatocellular carcinoma in a patient during teduglutide treatment has never been documented in the literature. A 48-year-old man with long-standing Crohn disease had short bowel syndrome due to partial enterectomy and colectomy. Because of his parenteral nutrition dependency, teduglutide was given and had enabled him to achieve nutritional autonomy off parenteral nutrition and his liver enzymes had normalized. But 3 years later, he presented with upper abdominal pain and elevated liver enzymes. Abdominal PET/CT revealed a noncirrhotic liver with 2 large hypermetabolic masses in bilateral lobes. Radiologic findings were suspicious for bilobar hepatic malignancy with lymph node metastasis. Biopsies demonstrated poorly differentiated hepatocellular carcinoma with extensive tumor necrosis in the right hepatic lobe and well-differentiated hepatocellular carcinoma, steatohepatitic subtype, in the left hepatic lobe. Immunostains were performed and confirmed the diagnosis of hepatocellular carcinoma. The background liver showed stage II nonalcoholic steatohepatitis. The patient underwent locoregional therapy and teduglutide had been discontinued. This is the first documented case of long-term teduglutide use leading to the development of hepatocellular carcinoma from noncirrhotic liver in a patient during teduglutide therapy. There is no current recommendation for the surveillance of hepatic malignancies in patients on teduglutide therapy. Regular medical and radiologic examinations are recommended based on this case report (Figure 25).

Teduglutide is approved for the treatment of parenteral nutrition–dependent adult patients with short bowel syndrome. Its use has been theorized to lead to the development of certain cancers. De novo development of hepatocellular carcinoma in a patient during teduglutide treatment has never been documented in the literature. A 48-year-old man with long-standing Crohn disease had short bowel syndrome due to partial enterectomy and colectomy. Because of his parenteral nutrition dependency, teduglutide was given and had enabled him to achieve nutritional autonomy off parenteral nutrition and his liver enzymes had normalized. But 3 years later, he presented with upper abdominal pain and elevated liver enzymes. Abdominal PET/CT revealed a noncirrhotic liver with 2 large hypermetabolic masses in bilateral lobes. Radiologic findings were suspicious for bilobar hepatic malignancy with lymph node metastasis. Biopsies demonstrated poorly differentiated hepatocellular carcinoma with extensive tumor necrosis in the right hepatic lobe and well-differentiated hepatocellular carcinoma, steatohepatitic subtype, in the left hepatic lobe. Immunostains were performed and confirmed the diagnosis of hepatocellular carcinoma. The background liver showed stage II nonalcoholic steatohepatitis. The patient underwent locoregional therapy and teduglutide had been discontinued. This is the first documented case of long-term teduglutide use leading to the development of hepatocellular carcinoma from noncirrhotic liver in a patient during teduglutide therapy. There is no current recommendation for the surveillance of hepatic malignancies in patients on teduglutide therapy. Regular medical and radiologic examinations are recommended based on this case report (Figure 25).

Teduglutide is approved for the treatment of parenteral nutrition–dependent adult patients with short bowel syndrome. Its use has been theorized to lead to the development of certain cancers. De novo development of hepatocellular carcinoma in a patient during teduglutide treatment has never been documented in the literature. A 48-year-old man with long-standing Crohn disease had short bowel syndrome due to partial enterectomy and colectomy. Because of his parenteral nutrition dependency, teduglutide was given and had enabled him to achieve nutritional autonomy off parenteral nutrition and his liver enzymes had normalized. But 3 years later, he presented with upper abdominal pain and elevated liver enzymes. Abdominal PET/CT revealed a noncirrhotic liver with 2 large hypermetabolic masses in bilateral lobes. Radiologic findings were suspicious for bilobar hepatic malignancy with lymph node metastasis. Biopsies demonstrated poorly differentiated hepatocellular carcinoma with extensive tumor necrosis in the right hepatic lobe and well-differentiated hepatocellular carcinoma, steatohepatitic subtype, in the left hepatic lobe. Immunostains were performed and confirmed the diagnosis of hepatocellular carcinoma. The background liver showed stage II nonalcoholic steatohepatitis. The patient underwent locoregional therapy and teduglutide had been discontinued. This is the first documented case of long-term teduglutide use leading to the development of hepatocellular carcinoma from noncirrhotic liver in a patient during teduglutide therapy. There is no current recommendation for the surveillance of hepatic malignancies in patients on teduglutide therapy. Regular medical and radiologic examinations are recommended based on this case report (Figure 25).
Melanoma of the Rectum: A Rare Mimic of Poorly Differentiated Carcinoma and Sarcoma

Poster No. 72

Gaofei Fan, MD (gffan@yahoo.com). Department of Pathology and Laboratory Medicine Services, Huntington VA Medical Center, Huntington, West Virginia.

Primary anorectal melanoma is a rare and aggressive malignancy. Patients commonly present with advanced, even metastatic, disease. Unlike cutaneous melanoma, anorectal melanoma has no known risk factors. A 74-year-old man with history of prostate cancer presented with rectal bleeding. Colonoscopy revealed a rectal mass. The mass itself was about 4 cm in size, located in the anterior left lateral wall. The tumor started from about 2 cm from anorectum and extended to 5 cm toward the proximal rectum. The low portion of the tumor involved internal sphincter. Biopsy of the rectal mass was performed and submitted for intraoperative consultation. The sections showed a high-grade malignant neoplasm of spindled and epithelioid cells with numerous mitoses and apoptosis infiltrating among benign colorectal mcosa, undermining benign squamous epithelium, and extending into muscle fibers. By immunohistochemistry, the tumor cells were positive for S100, Melan-A, HMB45, and MITF and were negative for AE1/AE3, CK7, CK20, CD56, CD117, P63, PSA, and LCA. No BRAF V600E or V600K mutations were detected. No c-KIT mutation was identified. Radiologic studies did not show any metastases. He underwent an abdomino-perineal resection (APR). He is still alive 2 years after APR with a metastatic to left groin lymph node. This entity can be easily misdiagnosed as poorly differentiated carcinoma and sarcoma. We should always perform a S-100 stain when colorectal poorly differentiated carcinoma and sarcoma are suspected. A positive S-100 stain suggests the tumor to most likely be a melanoma.

Myxoma in a Cecal Polyp: The First Case Report

Poster No. 74

Caroline Bsirini, MD (caroline.bsirini@urmc.rochester.edu); Aaron R. Huber, DO; Jennifer J. Findeis-Hosey, MD. Department of Pathology and Laboratory Medicine, University of Rochester, Rochester, New York.

Myxomas are benign mesenchymal neoplasms with unknown etiology. The most common location for these lesions is the atrium. However, they can also occur in the skin, joints, muscles, mandible, maxilla, and sinonasal tract. There are very few published reports of myxoma in the gastrointestinal (GI) tract, and these are limited to the stomach and small intestines. We are presenting to our knowledge, the first case report of a myxoma in the colon presenting as a polyp. A 49-year-old woman with a family history of colon cancer underwent a screening colonoscopy and was found to have a 0.2-cm sessile polyp in the cecum. Microscopically the polyp was hypocellular, was well demarcated from the surrounding mucosa, and consisted exclusively of myxoid stroma and bland spindle cells in the lamina propria without cytologic atypia. The overlying colonic epithelium showed no dysplasia. V600K mutations were not found. By immunohistochemistry, the tumor cells were positive for S100, Melan-A, HMB-45, and MITF and were negative for AE1/AE3, CK7, CK20, CD56, CD117, P63, PSA, and LCA. No BRAF V600E or V600K mutations were detected. Myxomas in the GI tract are very rare, with this being the first reported case of a polypoid colonic myxoma. Previous reports of GI myxomas are limited, with only 1 case report of a gastric myxoma and limited reports of small intestinal myxoma, all of which were submucosal lesions.
Synchronous presence of a cardiac myxoma was reported in some of these cases. This represents a newly identified mesenchymal polyp of the colon and pathologists should be aware of this diagnostic entity to avoid misinterpretation.

**Aberrant Expression of PAX8 in Metastatic Colorectal Carcinoma**

(No. 75)

Sharon J. Song, MS, MD (sharon.song@uphs.upenn.edu); M. Carolina Reyes, MD; Stuti Shroff, MD. Department of Pathology, Hospital of University of Pennsylvania, Philadelphia.

Paired box 8 (PAX8) is a transcription factor critical in the development of the thyroid, Müllerian system, and renal/upper urinary tracts, and thus is a highly sensitive marker for carcinomas originating from these sites. Although weak/focal PAX8 expression has been described in tumors from other sites, many, including lung adenocarcinomas, colon cancers, and breast and adrenal neoplasms, are consistently negative for PAX8. Here we describe a case of metastatic colorectal adenocarcinoma with aberrant positive nuclear staining for PAX8, the first such case to be reported in the literature. The patient, a 47-year-old woman, had a 10-cm obstructing rectal mass, a biopsy of which showed invasive moderately differentiated adenocarcinoma. Concurrently, the patient was also noted to have liver and lung metastases and a 15-cm ovarian mass. Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed to exclude an ovarian primary. Histology of the large ovarian mass showed variably sized cribriform glands composed of pseudostratified columnar cells with moderate cytologic atypia (Figure 27, A). The tumor also involved the contralateral ovary and uterine serosa. Immunohistochemically, the tumor was positive for CK20 (Figure 27, B) and CDX2 (Figure 27, C) and negative for CK7. The majority of tumor cells showed PAX8 positivity (Figure 27, D). A diagnosis of metastatic colorectal adenocarcinoma with aberrant PAX8 expression was rendered. Although PAX8 is a sensitive and relatively specific immunomarker, its expression in adenocarcinomas, colon cancers, and breast and adrenal neoplasms, should be interpreted with caution. It should be used in conjunction with clinical history, histomorphology, and other immunostains to determine the tumor site of origin.

**Correlation of E-Cadherin Expression With Histologic Type and Grade of Gastric Adenocarcinoma**

(No. 76)

Nosheen Nabi, MBBS (n.nabir@yahoo.com). Department of Pathology, Pakistan Institute of Medical Sciences, Islamabad, Pakistan.

**Context:** Gastric adenocarcinoma has poor prognosis and is diagnosed at advanced stage when the treatment is usually proven ineffective. Therefore, it is very important to search for novel immunohistochemical markers that help in both early detection and effective treatment of this disease. The loss of E-cadherin, a cell adhesion protein in gastric epithelium, leads to cell invasion and distant metastasis. There is a significant correlation of its loss with histologic type and grade of gastric adenocarcinoma. The objective of this study is to determine the expression of E-cadherin in histologic types and grades of gastric adenocarcinomas that has both prognostic and therapeutic roles in gastric adenocarcinoma.

**Results:** Of the selected 81 cases, 53 (65%) had intestinal-type adenocarcinoma and 28 (35%) were patients with diffuse type of adenocarcinoma. There was a significant statistical correlation of loss of E-cadherin with histologic type of adenocarcinoma. Of the 28 cases of diffuse-type gastric adenocarcinoma, 10 cases, along with 4 cases out of 53 cases of intestinal adenocarcinoma (all of which were poorly differentiated adenocarcinoma), showed complete loss of E-cadherin. All well-differentiated cases showed high expression of E-cadherin.

**Conclusions:** There is correlation of E-cadherin expression with the histologic type and grade of gastric adenocarcinoma. It was observed that as the grade of the adenocarcinoma gets higher there is more loss of E-cadherin expression, which proves its prognostic significance.

**Institutional Experience With Tumor Deposits in Colorectal Cancer Highlights Their Frequency and Adverse Biologic Significance**

(No. 77)

Chana R. Sachs, MA (chana-sache@uiowa.edu); Woodlyne Roquiz, DO; Daniel J. Pelletier, MD; Eric M. Destrampe, DO; Sarag Boukhar, MBChB; Anthony N. Snow, MD; Andrew M. Bellizzi, MD. Department of Pathology, University of Iowa Hospitals and Clinics, Iowa City.

**Context:** The AJCC 7 staging system defined tumor deposits (TDs) as discrete tumor nodules separate from the main tumor mass within the lymph drainage area of the tumor without identifiable lymph node (LN) tissue. It elevated TDs to “LN metastasis equivalency” (constituting stage III disease). The 2010 SEER data (cited in AJCC 8 system) reported TD and N1c frequencies of 10% and 3%, respectively, which seemed lower than our clinical impression.

**Design:** We performed chart review of all in-house colon cancer resections from January 1, 2010, to July 20, 2017, recording age; sex; tumor site, size, and grade; presence of lymph-vascular invasion (LVI), perineural invasion (PNI), TDs, and LNs; AJCC 7 T, N, M; vital status; and general versus gastrointestinal (GI) pathologist. Fisher exact test was used with P < .05 considered significant.

**Results:** TD status was reported in 86% of 515 resections, with TDs present in 28% (124 of 441). Completeness of reporting and TD frequency did not differ between general and GI pathologists (P = .52 and .74, respectively). Seventy-five percent occurred with and 25% without LN metastasis, for an N1c rate of 7%. TDs were associated with greater risk of death and more frequent LVI, PNI, T3/4, LN positivity (N1c), and metastatic disease (M+) (all P < .001) (Table). Patients with TDs were less likely to be alive (57%) than those with LVI (68%; P = .06), PNI (66%; P = .19), T3/4 (71%; P = .007), and N+ disease (65%; P = .23).

**Conclusions:** TDs were 3 times more frequent than previously reported, though the proportion with/without concurrent LN metastasis was the same. Completeness of reporting and frequency did not differ between general and GI pathologists. TDs correlated with adverse histologic features and reduced survival.

**Relationship of TDs to Clinicopathologic Parameters**

<table>
<thead>
<tr>
<th>Relationship of TDs to Clinicopathologic Parameters</th>
<th>TD Present, ( n = 124 )</th>
<th>TD Absent, ( n = 317 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive</td>
<td>57</td>
<td>81</td>
</tr>
<tr>
<td>LVI</td>
<td>82</td>
<td>36</td>
</tr>
<tr>
<td>PNI</td>
<td>55</td>
<td>16</td>
</tr>
<tr>
<td>T3/4</td>
<td>94</td>
<td>69</td>
</tr>
<tr>
<td>N+</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>M+</td>
<td>15</td>
<td>3</td>
</tr>
</tbody>
</table>

**The Histopathologic Features of Clear Cell, Steatotic, and Steatohepatitic Hepatocellular Carcinoma Subtypes**

(No. 78)

Mary Wong, MD, MBA (mary.wong@cshs.org); Brent Larson, DO. Department of Pathology and Laboratory Medicine, Cedars-Sinai Medical Center, Los Angeles, California.

**Abstracts**
**Context:** Historically, clear cell hepatocellular carcinoma (ccHCC) has been vaguely defined, leading to conflicting reports on its clinicopathologic features. However, more precise definitions have been proposed in recent literature. We sought to apply these new criteria to a series of ccHCC, identifying 68 cases. Applying these criteria, tumors were divided into early HCC (n = 4; E-HCC), steatotic HCC (n = 11; S-HCC), steatohepatitic HCC (n = 34; SH-HCC), chromophobe HCC (n = 2; C-HCC), and ccHCC, not otherwise specified (n = 15; ccHCC-NOS). Tumor, background liver, and clinical features were obtained from reviewed slides and clinical records.

**Results:** Although cytoplasmic macrovesicular steatosis was common in E-HCC/S-HCC/SH-HCC (n = 49 of 66, 74.2%), many had an admixture of steatotic and flocculent cytoplasm (n = 44 of 49; 89.7%). C-HCC and ccHCC-NOS had variably flocculent and/or optically clear cytoplasm without steatosis (n = 17). Although ccHCC-NOS exhibited the highest lymphovascular invasion rate (66.7% versus 43.1%), this trend did not reach statistical significance (P = .1). Steatohepatitis in background liver was significantly more common in S-HCC and SH-HCC than in ccHCC-NOS (P = .006). Other significant differences were noted in clinicopathologic features of tumor or background liver.

**Conclusion:** New definitions left only 22.7% of ccHCC as ccHCC-NOS, which did have macrovesicular steatosis in tumor cell cytoplasm like the other subtypes. S-HCC, SH-HCC, and E-HCC frequently arose in the background of steatohepatitis, suggesting an etiologic difference like the other subtypes. S-HCC, SH-HCC, and E-HCC frequently arose in the background of steatohepatitis, suggesting an etiologic difference like the other subtypes.

---

**Traditional Serrated Adenoma With High-Grade Dysplasia Involving the Esophagus and the Associated High-Grade Adenocarcinoma: A Novel and Challenging Entity**

(Poster No. 79)

Melinda Fang, MD1; Brian J, Martens, DO2; Let Lou, MD2; Lynh Nguyen, MD; Kun Jiang, MD, PhD3; Department of Pathology, University of South Florida, Tampa; Department of Pathology, the 2nd Hospital of Hebei Medical University, Shijiazhuang City, China; Department of Pathology, H. Lee Moffitt Cancer Center, Tampa, Florida.

Traditional serrated adenomas (TSAs) pose challenges both in diagnosis and management. The histomorphology and molecular underpinnings resulting in TSAs have not been fully defined. TSAs have been identified predominantly within the left colon and described to have slitlike serrations and ectopic crypts. A diagnosis of TSA in the upper gastrointestinal tract is exceedingly rare, especially in the esophagus; further association with invasive adenocarcinoma is even rarer. A 49-year-old woman presented for a second opinion regarding worsening dysphagia, anorexia, and a midesophageal mass. Two prior biopsies of the mass were diagnosed as “prolapse polyp with no dysplasia.” A diagnosis of TSA in the upper gastrointestinal tract is exceedingly rare, especially in the esophagus; further association with invasive adenocarcinoma is even rarer. A 49-year-old woman presented for a second opinion regarding worsening dysphagia, anorexia, and a midesophageal mass. Two prior biopsies of the mass were diagnosed as “prolapse polyp with no dysplasia.” A diagnosis of TSA in the upper gastrointestinal tract is exceedingly rare, especially in the esophagus; further association with invasive adenocarcinoma is even rarer. A 49-year-old woman presented for a second opinion regarding worsening dysphagia, anorexia, and a midesophageal mass. Two prior biopsies of the mass were diagnosed as “prolapse polyp with no dysplasia.” A diagnosis of TSA in the upper gastrointestinal tract is exceedingly rare, especially in the esophagus; further association with invasive adenocarcinoma is even rarer. A 49-year-old woman presented for a second opinion regarding worsening dysphagia, anorexia, and a midesophageal mass. Two prior biopsies of the mass were diagnosed as “prolapse polyp with no dysplasia.” A diagnosis of TSA in the upper gastrointestinal tract is exceedingly rare, especially in the esophagus; further association with invasive adenocarcinoma is even rarer. A 49-year-old woman presented for a second opinion regarding worsening dysphagia, anorexia, and a midesophageal mass. Two prior biopsies of the mass were diagnosed as “prolapse polyp with no dysplasia.” A diagnosis of TSA in the upper gastrointestinal tract is exceedingly rare, especially in the esophagus; further association with invasive adenocarcinoma is even rarer. A 49-year-old woman presented for a second opinion regarding worsening dysphagia, anorexia, and a midesophageal mass. Two prior biopsies of the mass were diagnosed as “prolapse polyp with no dysplasia.” A diagnosis of TSA in the upper gastrointestinal tract is exceedingly rare, especially in the esophagus; further association with invasive adenocarcinoma is even rarer. A 49-year-old woman presented for a second opinion regarding worsening dysphagia, anorexia, and a midesophageal mass. Two prior biopsies of the mass were diagnosed as “prolapse polyp with no dysplasia.” A diagnosis of TSA in the upper gastrointestinal tract is exceedingly rare, especially in the esophagus; further association with invasive adenocarcinoma is even rarer. A 49-year-old woman presented for a second opinion regarding worsening dysphagia, anorexia, and a midesophageal mass. Two prior biopsies of the mass were diagnosed as “prolapse polyp with no dysplasia.” A diagnosis of TSA in the upper gastrointestinal tract is exceedingly rare, especially in the esophagus; further association with invasive adenocarcinoma is even rarer. A 49-year-old woman presented for a second opinion regarding worsening dysphagia, anorexia, and a midesophageal mass. Two prior biopsies of the mass were diagnosed as “prolapse polyp with no dysplasia.” A diagnosis of TSA in the upper gastrointestinal tract is exceedingly rare, especially in the esophagus; further association with invasive adenocarcinoma is even rarer. A 49-year-old woman presented for a second opinion regarding worsening dysphagia, anorexia, and a midesophageal mass. Two prior biopsies of the mass were diagnosed as “prolapse polyp with no dysplasia.” A diagnosis of TSA in the upper gastrointestinal tract is exceedingly rare, especially in the esophagus; further association with invasive adenocarcinoma is even rarer. A 49-year-old woman presented for a second opinion regarding worsening dysphagia, anorexia, and a midesophageal mass. Two prior biopsies of the mass were diagnosed as “prolapse polyp with no dysplasia.” A diagnosis of TSA in the upper gastrointestinal tract is exceedingly rare, especially in the esophagus; further association with invasive adenocarcinoma is even rarer. A 49-year-old woman presented for a second opinion regarding worsening dysphagia, anorexia, and a midesophageal mass. Two prior biopsies of the mass were diagnosed as “prolapse polyp with no dysplasia.”

**Chemoprevention Effect of Withaferin A, a Natural Compound, on Mouse Models of Colorectal Carcinogenesis**

(Poster No. 80)

Andrea Breaux, MD1; Renjitha Vohra, PhD2; Chendil Damodaran, PhD2, Houda Alatassi, MD1; Departments of Pathology and Urology, University of Louisville, Kentucky.

**Context:** Colorectal cancer is the most common cancer and a leading cause of cancer-related deaths. Development of sporadic disease takes an average of 15–20 years, so establishing preventive measures is possible. We are interested in a dietary compound, withaferin A (WA), which possesses chemotherapeutic and chemopreventive properties.

**Design:** We used 2 animal models to study the chemopreventive effect of WA. In intestinal tumorigenesis model C57BL/6-Apc<sup>min</sup>, mice at 6 weeks of age were fed with the vehicle or WA (4 mg/kg body weight of mice) for 5 d/wk for 12–14 weeks. The other model was azoxymethane/dextran sulfate sodium, which induces gut inflammation and tumorigenesis. Intrapertoneal injection of azoxymethane (8 mg/kg) was followed by 3 cycles of dextran sulfate sodium. WA (3 mg/kg body weight of mice) was administered 5 times/wk for 8–10 weeks. After necropsy, the tumor tissues underwent histopathologic and molecular analysis. An unpaired Student t test was used for statistical analysis.

**Results:** Oral administration of WA to Apc<sup>min</sup>-mice lead to a significant decrease in the number of polyps and colon tumors (colon: 42%, P = .02; proximal: 53%, P = .006; middle: 27.84%, P = .28; distal: 32.8, P = .001) when compared with vehicle-treated mice. Similarly, in azoxymethane/dextran sulfate sodium, oral administration of WA reduced polyp multiplicity by 40% (P = .02) compared with controls. The treatment group of both models showed inhibition of prosurvival signaling markers (Notch1, PAKT, and NFKB) and a decrease in proliferative markers.

**Conclusions:** Our results suggest that WA effectively suppresses intestinal polyp development and colitis-mediated colon carcinogene sis, suggesting a preventive and therapeutic role in colon cancer models.

**Mass-Forming Ischemic Colitis: A Clinicopathologic Conundrum**

(Poster No. 81)

Alexandra M. Danakas, DO1 (alexandra_danakas@urmc.rochester.edu); Bushra G. Fazili, MD2; Aaron R. Huber, DO.1 1Department of Pathology and Laboratory Medicine, University of Rochester Medical Center, Rochester, New York; 2Department of Medicine, Division of Gastroenterology/Hepatology, Gastroenterology Group of Rochester, New York.

Ischemic colitis (IC) results from reduced vascular perfusion causing mucosal injury. Although there are occlusive and nonocclusive etiologies, all show similar histologic features. In rare instances, IC may form a masslike lesion, mimicking malignancy. A 55-year-old woman presented with hematochezia and diarrhea and underwent colonoscopy. Three months prior she was treated with steroids for autoimmune hepatitis following an admission for jaundice. On colonoscopy, a masslike lesion was identified at the ileocecal valve (Figure 28, A). Notably, on previous imaging studies, no mass was detected within the abdomen. The biopsies demonstrated hyperplastic lamina propria, atrophic crypts, ulceration, and active inflammation, indicative of IC (Figure 28, B and C). A repeat colonoscopy in 2 months revealed complete resolution of the masslike lesion at the ileocecal valve.
Medication-Induced Morphologic Mimic of Whipple Disease in Patient With End-Stage Renal Disease
(Poster No. 83)

Deepika Savant, MD (dsavant@northwell.edu); Arvind Rishi, MD; Margaret Cho, MD; Rebecca Thomas, MD. Department of Pathology, Zucker School of Medicine at Hofstra/Northwell, Lake Success, New York.

A 75-year-old man with end-stage renal disease (ESRD), hemodialysis, and administration of phosphate-binding agent calcium acetate (PhosLo) presented with anemia and weakness. Upper endoscopy showed an erythematous duodenal mucosa; a biopsy revealed prominent aggregates of macrophages in the lamina propria with granular cytoplasm (Figure 30, A and B) and PAS/D positivity (Figure 30, C). No organisms were identified on the AFB stain. The findings were suggestive of Whipple disease. However, the confirmatory polymerase chain reaction (PCR) assay for Tropheryma whippelii was negative. On closer examination, several macrophages were noted to have intracytoplasmic, refractile, crystalline material that was faintly positive on the iron stain (Figure 30, D). Our case report aims to alert pathologists of a medication-induced histologic mimic of Whipple disease in the duodenum that was observed in the clinical setting of ESRD, hemodialysis, and administration of phosphate-binding agents. Although the aggregates of PAS/D–positive macrophages in the duodenum were suggestive of Whipple disease by light microscopy, the confirmatory PCR assay was negative. The refractile material is likely medication associated, given the clinical setting of ESRD and dialysis. Phosphate-binding agents such as lanthanum have been reported to elicit a histiocytic response with macrophages containing finely granular basophilic foreign material. This patient was not on lanthanum, but had been prescribed a different phosphate-binding agent, calcium acetate (PhosLo). We suggest that there are other drugs used in ESRD that may produce changes similar to lanthanum, and may be a mimic for Whipple disease.

Low-Grade Follicular Lymphoma Underlying a Colonic Tubular Adenoma
(Poster No. 84)

Charles K. Childers, MD (charles.k.childers4.mil@mail.mil); Jared M. Andrews, MD. Department of Pathology and Laboratory Services, Madigan Army Medical Center, Tacoma, Washington.

Follicular lymphoma is a relatively indolent lymphoma of germinal center B cells characterized by overexpression of BCL-2. We present a case of follicular lymphoma that accompanied a colonic tubular adenoma found during routine colonoscopy in a 59-year-old woman. A 1.0-cm polyp was identified and excised at colonoscopy via hot snare. Low-power histologic examination demonstrated a typical follicular lymphoma with low-grade dysplasia (including loss of mucin, pencillate hyperchromatic nuclei, and loss of maturity) as well as apparent underlying chronic inflammation that expanded the lamina propria (Figure 31, A). However, further investigation of the lamina propria revealed a vaguely nodular proliferation of lympho-
cytes that lacked polarization found in typical reactive germinal centers. High-power views showed poorly formed nodules of a monotonous proliferation of centrocyte-like cells that lacked tingible body macrophages and mitotic activity (Figure 31, B). Immunohistochemical analysis revealed the nodules, as well as diffuse areas, strongly expressed BCL2 (Figure 31, C) and coexpressed CD20, CD10, and BCL6 (Figure 31, D), supporting a diagnosis of a low-grade follicular lymphoma. A follow-up bone marrow biopsy was consistent with follicular lymphoma involvement. Tubular adenomas are often associated with increased lamina propria inflammation, including reactive lymphoid aggregates. Our case highlights that an underlying lymphoma may be easily missed if typical features of reactive germinal centers, to include polarization, cellular polymorphism, and the presence of tingible body macrophages, are not routinely evaluated. A brief inspection of underlying inflammation in a tubular adenoma should be performed to rule out an occult lymphomatous process.

Pancreatic Sharkcore Biopsies as First-Line Procedures: Diagnostic Success and Histologic Barriers

(Poster No. 85)

Kevin Anderson, MD, PhD; Robert Najarian, MD (rnajaria@bidmc.harvard.edu). Department of Pathology, Beth Israel Deaconess Medical Center, Boston, Massachusetts.

Context: Pancreatic endoscopic ultrasound fine-needle biopsy (EUS-FNB) is an emerging technology for the diagnosis of solid pancreatic lesions. At our institution, EUS-FNB has become the first-line procedure for rendering such a diagnosis. In this study, we examined the diagnostic yield of the first FNB obtained in our patients, as well as explored histologic barriers to definitive diagnoses.

Design: Following a search of our pathology laboratory information system, 450 first-time FNBs were identified during the period between 2013 and 2017. Reports were evaluated for the presence of definitive neoplastic diagnoses versus those yielding categorical diagnoses of atypical, negative, or benign. All cases with available slides lacking definitive diagnoses (n = 133) or with a benign diagnosis (n = 20) were re-reviewed. These cases were graded with respect to tissue integrity, measurement of the largest intact tissue fragment, and a semiquantitative assessment of blood contamination.

Results: A total of 301 cases (66.9%) yielded definitive neoplastic diagnoses. In nondiagnostic samples, the average and median intact sizes of tissue were 0.10 and 0.06 cm (0.00–0.15 cm), respectively, compared with 0.20 and 0.20 (0.05–0.40) cm for benign diagnoses. In nondiagnostic samples, the tissue was considered satisfactory, suboptimal, and unsatisfactory in 36%, 5%, and 59% of the cases, respectively. Blood contamination was mild in 16% of cases, moderate in 7% of cases, and significant in 77% of cases.

Conclusions: Our results show that EUS-FNB has a high rate of diagnostic success as the first-line procedure for diagnosis. In cases that do not yield a definitive diagnosis on the initial biopsy, blood contamination is a significant hindrance in obtaining diagnostic FNB samples.

Eosinophilic Esophagitis: Does IgG4 Play a Role in Diagnosis?

(Poster No. 86)

Nicholas Stanzione, MD (nicholasstanzione@mednet.ucla.edu); Amanda Pope, MD; Bita Naini, MD; Laura Wozniak, MD. Departments of Pathology & Laboratory Medicine and Pediatric Gastroenterology, University of California, Los Angeles.

Context: The pathogenesis of eosinophilic esophagitis (EoE), although known to be allergy driven, is poorly understood. Studies have shown that EoE is associated with increased IgG4 deposits, increased epithelial IgG4 deposits, and subepithelial IgG4-positive plasma cells. This suggests that IgG4 may be an IgG4-mediated process and that IgG4 staining may be useful in differentiating EoE from gastroesophageal reflux disease.

Design: We performed a retrospective study of 31 patients with EoE (clinical and endoscopic findings suspicious for EoE, confirmed diagnosis based on the presence of >15 eosinophils/high-power field in distal and proximal biopsies). Exclusion criteria included preexisting diagnosis of EoE or treatment prior to endoscopy. Four cases of gastroesophageal reflux disease and 4 normal controls were included for comparison. Histopathologic review and IgG4 immunohistochemical staining were performed.

Results: EoE patients were significantly more likely to have positive IgG4 staining compared with controls (15 of 29 EoE cases versus 0 of 8 control cases; P = .01). Of the 15 positive cases, 6 cases had IgG4-positive plasma cells within the lamina propria, 2 of the cases had epithelial staining only, and 7 cases had positive staining in both. Twelve of 15 positive cases showed positivity in both distal and proximal biopsies. No significant clinical, endoscopic, or histologic differences were identified.

Conclusions: EoE patients were significantly more likely to stain for IgG4 compared with controls. Although positive IgG4 staining was specific for EoE (100%), it had a poor sensitivity (48%). Our study suggests that although IgG4 may play a role in the pathogenesis of EoE, it is not a reliable marker of disease diagnosis.

α-Fetoprotein–Secreting Esophageal Adenocarcinoma: A Case Report and Review of Literature

(Poster No. 87)

Debasmita Das, MD (debasmita.das@wchn.org). Department of Pathology and Laboratory Medicine, Danbury Hospital, Danbury, Connecticut.

α-Fetoprotein (AFP)–secreting adenocarcinoma of the esophagus arising de novo from the esophageal mucosa is a rare entity. This report describes a patient with AFP-producing adenocarcinoma with no previous history of dysplasia or adenoma. The patient is a 64-year-old man who presented with increased α-fetoprotein levels with a previous history of treated chronic hepatitis C. Computed tomography scan of the abdomen showed circumferential wall thickening of the distal esophagus/gastroesophageal junction. There were streak artifacts through the liver without cirrhosis or focal hepatic mass identified. Endoscopy and biopsy of the gastroesophageal junctional mass revealed invasive poorly differentiated adenocarcinoma. AFP immunohistochemical stain was performed, which was negative. For staging, an upper endoscopic ultrasound was performed that revealed the lesion extending endoscopically to the proximal stomach on the lesser curvature. Biopsy of the proximal stomach mass showed invasive poorly differentiated adenocarcinoma, histologically similar to the previously biopsied GE junction mass. The exact origin of the tumor (distal esophagus versus gastric) could not be determined on a histologic basis. There were no findings of a malignant precursor-like adenoma or dysplasia. The serum AFP levels responded extremely well to chemotherapy and radiotherapy and dropped from 593.3 ng/mL to 2.2 ng/mL posttreatment. Although the AFP-secreting esophageal adenocarcinoma had a negative AFP immunohistochemical stain, the drop in the AFP level after treatment supports our diagnosis. Thus, careful monitoring of the serum AFP levels at regular intervals could be a useful marker to indicate recurrence of esophageal carcinoma despite negative immunohistochemical staining for AFP.
Hepatocellular Carcinomas With 4 Differentiations Including Conventional Hepatocellular, Clear Cell Hepatocellular, Neuroendocrine Carcinoma, and Cholangiocarcinomatous All Arising in Cirrhosis: A Case Report and Literature Review

(Poster No. 88)

Chelsea Styles, MD (cstyles@med.umich.edu); Henry Appelman, MD, Department of Pathology, University of Michigan, Ann Arbor.

Hepatocellular carcinomas (HCCs) with uncommon differentiations have been reported in the literature. However, HCCs with multiple differentiations are rare. We report a case of a 65-year-old man with cirrhosis secondary to nonalcoholic fatty liver disease, chronic lymphocytic leukemia (CLL), and clear cell renal cell carcinoma. During routine HCC screening, a slowly enlarging liver lesion (1.9 cm) was detected by imaging and ablated. Several enlarged lymph nodes, attributed to CLL, were also detected. During the next year, 2 additional suspicious liver lesions (0.6–2.0 cm) were found on imaging, but no intervention was performed until liver transplantation. The patient’s explanted liver contained multiple masses (0.8–3.5 cm) within background cirrhosis. All of the masses had areas of traditional HCC, which were Hep-Par 1 and Arginase 1 positive. One mass had areas of cholangiocarcinomatous differentiation that were CK7 positive. A second mass had a focus of neuroendocrine carcinoma that was synaptophysin-, chromogranin A–, and CD56-positive. A third mass had clear cell differentiation. The patient’s liver function improved after transplant, but a few months later, several enlarging lymph nodes were identified on imaging. Cytology of a peripancreatic node and biopsy of a supraclavicular node showed metastatic neuroendocrine carcinoma. Given the nodal metastases, he was treated conservatively. Despite treatment, his disease progressed with new metastases to his spine and pelvis. At this point, he began hospice care and died 2 months later. To our knowledge, this is the first case report of multiple HCCs with 4 differentiations simultaneously occurring in a patient with cirrhosis.

An Unusual Huge Cystic Tumor of Liver: Intrahepatic Biliary Cystadenoma

(Poster No. 89)

Ghulam Ilyas, MBBS1 (ghulam.ilyas@downstate.edu); Agba Wajdan Baqir, MBBS2; Muhammad Atiq, MBBS2 1Department of Pathology, SUNY Downstate Medical Center, Brooklyn, New York; 2Department of Liver Transplantation and Hepatobiliary Pancreatic Surgery, Shifa International Hospital, Islamabad, Pakistan.

Intrahepatic bile duct cystadenoma is an uncommon neoplasm of the biliary duct and accounts for less than 5% of nonparasitic cysts of liver. The average age of presentation is 45 years and 85% occur in women. It may occur in association with polycystic liver disease, abnormal hepatobiliary anatomy. Grossly, the cystadenoma usually presents as an encapsulated, solitary, usually mucinous, multilocular cyst. The inner surface is smooth with few trabeculations. Complications include intracystic hemorrhage, bacterial infection, spontaneous rupture, recurrence, and malignant transformation. Treatment is complete excision with clear margins. We present a case of a 33-year-old woman who presented with abdominal distension and difficulty breathing for the past 6 months. She had nausea, vomiting, and unintentional 10-pound weight loss during the past few months. Physical examination showed moderate abdominal distension and mild tenderness in right hypochondrium. Laboratory studies showed a mildly elevated γ-glutamyl transferase at 72 U/L (normal, 9–36 U/L). Abdominal CT scans revealed hepatomegaly (35 cm) with a huge multiloculated, multiseptated, predominantly fluid attenuating lesion occupying all the right lobe of liver with few internal calcifications and a small associated nodular component (Figure 32, A). The resected specimen weighed 7.25 kg and serial sectioning revealed multiloculated cystic mass with tan-green color and gelatinous cystic material. Microscopic sections showed cyst wall lined by columnar to cuboidal mucinous epithelium overlying the fibrocollagenous stroma (Figure 32, B). Adipose tissue and smooth muscles were also seen in the wall (Figure 32, C).

Collision of Autoimmune Pancreatitis and Solid Pseudopapillary Tumor Producing a Large, Locally Aggressive Mass

(Poster No. 90)

Lucy Jager, MD (lucy.jager@ucdenver.edu); Kalpana M. Devaraj, MD, MHS. Department of Pathology, University of Colorado Anschutz Medical Campus, Aurora.

Solid pseudopapillary tumor of the pancreas is a rare neoplasm of low malignant potential and excellent prognosis after complete surgical resection. IgG4-related pancreatitis (type 1 autoimmune pancreatitis) is a mass-forming lesion that can radiographically mimic pancreatic cancer but is treated with steroid therapy. Coexisting pancreatic neoplasm with autoimmune pancreatitis is exceedingly rare. We report a case of a 47-year-old woman who presented with acute pancreatitis and worsening abdominal pain. Imaging showed a large cystic and solid mass involving the pancreatic body and tail with progressive mass enlargement and splenic vein occlusion with development of collateral circulation. The mass was diagnosed as a solid pseudopapillary tumor by fine-needle aspiration. En bloc resection included distal pancreas, spleen, distal stomach, distal duodenum, and superior mesenteric vein. On gross examination, the 9-cm mass involved the pancreas and invaded peripancreatic soft tissue and stomach wall. Histologic examination demonstrated small discontinuous foci of classical solid pseudopapillary tumor characterized by pseudopapillae formed by delicate blood vessels lined by monotonous cells (Figure 33, A). The tumor was positive for β-catenin (Figure 33, A, inset). The majority of
the 9-cm mass was composed of lymphoplasmacytic inflammation and spindle cell proliferation (Figure 33, B) with associated destruction of pancreatic ducts and obliterative phlebitis (Figure 33, C), consistent with autoimmune pancreatitis. Immunohistochemical stain for IgG4 showed more than 50 plasma cells per high-power field (Figure 33, B, inset). The autoimmune pancreatitis invaded the gastric wall (Figure 33, D) and peripancreatic soft tissues, giving the clinical impression of a locally aggressive solid pseudopapillary tumor.

A Mysterious and Exceedingly Rare Case of a Cecal Mass
(Poster No. 91)

Mohamed Alhamar, MD (dr.alhamar@gmail.com); Beena Umar, MD; Mohammad Raoufi, MD. Department of Pathology, Henry Ford Hospital, Detroit, Michigan.

Appendiceal intussusception is an extremely rare condition with a reported incidence of 0.01% and was first described by McKidd in 1858. Clinical presentation varies with different cases, with some patients being completely asymptomatic and some presenting with acute appendicitis or chronic nonspecific abdominal pain. We report a case of a 37-year-old woman with a history of recurrent hospitalizations for intractable nausea, vomiting, and right lower quadrant abdominal pain. She presented again with the aforementioned symptoms. Physical examination showed right lower quadrant tenderness with no rebound tenderness or guarding. CT scan revealed an indefinite cecal mass and subcecal colonoscopy showed a soft and mobile polypoidal lesion in the cecum wall with an intact overlying mucosa. She underwent robotic ileocecectomy. Intraoperative consultation showed a 2.0 cm mass composed of lymphoplasmacytic inflammation and scattered ganglion cells. The lesion was lined by normal-looking colonic mucosa with prominent lymphoid follicles (Figure 34). The overall findings were compatible with those of an inverted appendix. Appendiceal intussusception is classified into 5 types based on the site and degree of intussusception. Our case represents an example of complete invagination/inversion of the appendix into the cecum (Type V). In conclusion, we present this case because of its rarity. Appendiceal intussusception often constitutes a diagnostic challenge and increasing the awareness of this condition will facilitate earlier diagnosis and appropriate management.

Early Prediction of Neoplastic Progression in Barrett Esophagus by a Panel of Biomarker Testing: A 14-Year Experience
(Poster No. 92)

Young Choi, MD (ychokim@gmail.com); Ruth Haynes, MD; Andrew Bedford, MD. Department of Pathology, Bridgeport Hospital, Bridgeport, Connecticut.

Context: The stepwise progression from gastroesophageal reflux disease (GERD) to Barrett esophagus (NDBE) and dysplasia/esophageal adenocarcinoma (EAC) is a multistep neoplastic process associated with several genetic abnormalities. Limitation of histologic diagnoses demands reliable objective indispensable biomarker testing.

Design: This study consisted of (1) review of 303 histology biopsies from 97 patients undergoing endoscopic surveillance up to 14 years’ duration; (2) biomarker testing of p16, p53, cyclin D1, MCM2, Ki-67, and MUC2 by immunohistochemistry on FFPEs; and (3) fluorescence in situ hybridization (FISH) testing on CytoBrush samples using 4 probes (8q24 [MYC], 9p21 [CDKN2A], 7q12 [ERBB2], and 20q13.2 [JNZF2]).

Results: Most of the NDBE showed stepwise morphologic changes, ultimately to dysplasia/EAC in long-term follow-up, with progression rate ranging from 2 to 10 years, and coexistence of multigrade dysplasia. Aberrant P53+ P16+ expression was detectable in NDBE (6.2%), NDBE with indefinite dysplasia (NDBE-IND; 11.1%), and GERD. P16 expression was an early event in neoplastic progression. P53 alteration in NDBE/NDBE-IND was greater among patients who progressed to low-grade dysplasia (LGD)/high-grade dysplasia (HGD). Strong Ki-67, cyclin D1, and MCM2 expression was seen in LGD and HGD. FISH testing with homogenous loss of p16 (43%–67%) in NDBE-IND and tetrasomy in LGD was associated with aberrant p53 expression.

Conclusions: Homozygous loss of p16 and tetrasomy on FISH, aberrant p53 and P16 expression, and overexpression of Ki-67, MCM2, and cyclin D1 in NDBE and NDBE-IND are predictable to neoplastic progression. Thus, the combination of protein biomarkers and FISH testing could improve early risk stratification and foster a cost-effective surveillance program.

A Novel Sarcomatoid, MSH6-Lost, Microsatellite Instable Ampullary Adenocarcinoma With Unexpected “Sarcomatous” Histomorphology
(Poster No. 93)

Brian J. Martens, DO1 (brianmartens@health.usf.edu); Melinda Fang, MD2; Lei Lou, MD; Kun Jiang, MD.1 Department of Pathology, University of South Florida, Tampa; 2Department of Pathology, the 2nd Hospital of Hebei Medical University, Shijiazhuang City, China; 3Department of Pathology, H. Lee Moffitt Cancer Center, Tampa, Florida.

Patients with mutated mismatch repair genes face an increased risk of developing a spectrum of malignancies. Pathologists need to be aware that these patients are prone to develop gastrointestinal carcinomas with unusual “noncarcinomatous” histomorphology that does not resemble the recognized Lynch syndrome spectrum. One should keep microsatellite instability in mind when classifying a tumor biopsy for the first time, as this is the key step in initiating the clinical course. Here we introduce an initially missed microsatellite instable carcinoma from our consultation service. The patient was a 51-year-old woman without any cancer history who presented to an outside institution because of jaundice and fever. Endoscopy identified a 4-cm ampulla mass. A diagnosis of sarcomatous malignancy with rhindob features was originally rendered. The patient presented to our institution for a second opinion and to initiate chemoradiation targeting the “sarcoma.” Ancillary tests were performed on the acquired outside material. The tumor cells were labeled by CAM5.2 and CDX2 despite the “sarcomatous” and focally solid/nested histomorphology. A mucicar-
Mesenchymal Hamartoma of the Liver

(Poster No. 94)

Phoenix D. Bell, MD (phoenix_bell@urmc.rochester.edu); Michael G. Drage, MD, PhD. Department of Pathology and Laboratory Medicine, University of Rochester Medical Center, Rochester, New York.

A 3-year-old girl with a past medical history of autism spectrum disorder and global developmental delay presented with a several-month history of decreased appetite, fatigue, and abdominal distension. An abdominal X-ray showed striking hepatomegaly. Ultrasound demonstrated a large multicystic mass in the right upper quadrant with thick septations and internal debris. MRI revealed mass effect on the stomach and small bowel, with rolled cobblestoned borders and fibrinous granulation tissue at the ulcer base. Results of a complete blood count with differential analysis, basic metabolic panel, and rapid plasma reagin were unremarkable. On histopathology, both skin and colon biopsies showed a dense proliferation of histiocytes and lymphocytes. Immunostaining was positive for CD1a, CD4, and weakly positive for CD45 and CD68. CD20 and CD3 were negative. Electron microscopy of the skin biopsy showed Birbeck granules within the cytoplasm of a Langerhans cell. The skin lesion was negative for BRAF.V600 mutation. A bone marrow biopsy was negative for CD1a and S100. We report an unusual case of Langerhans cell histiocytosis occurring in an adult male with gastrointestinal involvement showing negative BRAF mutation.

Pathology Reporting Practices in Gastric Biopsies With Intestinal Metaplasia: A Single Institution Experience and a Call for Change

(Poster No. 96)

Grace L. Malvar, MD (gmalvar@bidmc.harvard.edu); Shweta Shinagare, MD; Katharine Germansky, MD; Robert Najarian, MD. Departments of 1Pathology and 2Internal Medicine, Beth Israel Deaconess Medical Center/ Harvard Medical School, Boston, Massachusetts; 3Department of Pathology, Hallmark Healthcare Systems, Melrose, Massachusetts.

Context: Gastric intestinal metaplasia (GIM) and associated atrophic gastritis are considered preneoplastic conditions that confer an up to 6-fold increase for gastric cancer, the second leading cause of cancer death worldwide. Multifocality of GIM and an incomplete type of intestinal metaplasia have also been linked to increased gastric cancer risk. Proposed algorithms for optimal endoscopic surveillance in GIM patients based on such risk factors and histologic findings on initial biopsies exist, yet uniform pathologic reporting criteria are not well established.

Design: A review of 150 cases of GIM from 2013 to 2015 in a single institution was performed to investigate the reporting of this finding. Histopathologic assessment included identification of GIM type (complete, incomplete), presence and grade of dysplasia, and associated gastritides, including H pylori gastritis. Pathology reports were reviewed for biopsy indication, mention of GIM type, presence and type of dysplasia, and presence and type of associated gastritis.

Results: Complete-type and incomplete-type GIM were seen in 126 (84%) and 19 (12.7%) cases, respectively. The antrum was the predominant site (84%), with multifocal GIM seen in 11.3% of cases. Nearly 25% (24.8%) of patients had associated histologic H pylori infection. Atrophic gastritis was demonstrated in 8.7% of patients. Surprisingly, in the presence of GIM, 23% of patient reports failed to mention the presence/absence of dysplasia, and none mentioned GIM type.

Conclusions: There is considerable variability and lack of standardization in GIM pathology reporting. Mandatory inclusion of GIM type and dysplasia status may aid in clinical decision making to establishing appropriate surveillance in GIM patients, especially those at increased risk for gastric cancer.

Thyroid Transcription Factor 1 (TTF-1) Positivity in Colorectal Carcinoma: A Pitfall in Diagnosis of Metastatic Carcinoma of Unknown Origin

(Poster No. 97)

Anas Bernieh, MBBS (abernieh@umc.edu); Frank Torres, MD; Varsha Manucha, MD. Department of Pathology, UMMC, Jackson, Mississippi.

Primary lung adenocarcinomas are classically thyroid transcription factor 1 (TTF-1) positive, whereas secondary carcinomas are negative for TTF-1. Nevertheless, it has been described that metastatic colorectal...
OR51E1 Expression Correlates With Perineural Invasion in Pancreatic Neuroendocrine Tumors

(Paper No. 98)

Margaret Black, MD (margaret.black@nymc.org); Rami Imam, MD; Rulian Xu, MD; Wenqing Cao, MD. Department of Pathology, New York University, New York City, New York.

Context: Pancreatic neuroendocrine tumors (PanNETs) constitute 3%–5% of pancreatic malignancies and have increasing incidence. Although worse prognosis is associated with larger size, high mitotic rate, and vascular and perineural invasion, little is known about tumor growth and metastasis in PanNETs. OR51E1 is an olfactory receptor protein that plays a role in transducing odorant signals through neurotransmitter pathways. OR51E1 is normally expressed in cells with neuroendocrine functions. It is also a potential marker for prostate carcinoma and small intestinal neuroendocrine carcinomas (SI-NETs). We examine expression of OR51E1 in PanNETs and SI-NETs and its correlation with prognostic indicators.

Design: Thirty-nine PanNET (12 females, 27 males) and 11 SI-NET (3 females, 8 males) specimens were analyzed for OR51E1 expression. H-scoring was used to evaluate staining intensity (0–3+) and percentage of positive cells. One-way analysis of variance or Student t test correlated mean H-score with clinical and histopathologic parameters.

Results: Nonneoplastic acinar, duct, and islet cells displayed OR51E1 staining. Seven of 11 SI-NETs (63.6%) and 26 of 39 PanNETs (66.7%) displayed cytoplasmatic staining. Seven of 38 (18.4%) PanNETs had stronger staining than PanNETs. Of PanNETs, 35% of OR51E1 staining did not correlate with tumor size, Ki-67, mitotic rate, or stage. Interestingly, decreased OR51E1 expression correlates with perineural invasion (H-score 113.7 ± 9.9 versus 67.0 ± 15.1; P = .01).

Conclusions: This is the first demonstration of OR51E1 expression in normal and neoplastic tissue. The association between OR51E1 expression and perineural invasion in PanNETs implicates the role of OR51E1 in tumor spread. OR51E1 has potential use as a prognostic indicator for PanNETs.

Concomitant Presentation of New Onset of Microscopic Collits in a Patient With Active Inflammatory Bowel Disease

(Paper No. 99)

Christopher Chandler, MD (cchandl@uw.edu); Deepti Reddi, MD. Department of Pathology, University of Washington, Seattle.

The association between microscopic colitis and inflammatory bowel disease is unclear. There are case reports of symptomatic microscopic colitis in patients with quiescent inflammatory bowel disease. Here we present a case of concomitant presentation of new-onset microscopic colitis in a patient with active inflammatory bowel disease. The patient was a 75-year-old man with history of hypertension, myocardial infarction, Type II diabetes mellitus, psoriasis on adalimumab, and distal ulcerative colitis. Despite mesalamine treatment, he had chronic diarrhea for years and weight loss. The patient underwent esophagogastroduodenoscopy and colonoscopy for persistent nonbloody diarrhea. On endoscopy, the esophagus and duodenum were normal and the stomach showed patchy mucosal erythema. There was moderate to severe inflammation with granular ground-glass appearance of the mucosa, involving the rectum up to 25 cm from the anus, and the remaining bowel was normal. The microscopic examination of the second and third portion of the duodenum showed no pathologic diagnosis. The colon biopsy was transverse, and descending colon showed increased intraepithelial lymphocytes, consistent with lymphocytic colitis. The biopsy from the rectosigmoid area showed moderate chronic active colitis with architectural distortion, basal lymphoplasmacytosis, cryptitis, and crypt abscess, consistent with chronic active colitis and the patient’s history of inflammatory bowel disease. There was no evidence of infection by histology and microbiology culture studies. This case highlights the recognition of microscopic colitis in inflammatory bowel disease patients and the clinical significance of performing biopsies from all anatomical segments of colon to increase the diagnostic yield.

Intra-Abdominal Lymphatic Malformation in an Elderly Patient

(Paper No. 100)

Tayler A. Van Denakker, MD1 (tayler.vandenaakker@mountsinai.org); Adnan Mubasher, MD; Muhammad Qazi, MD; Lawrence Kiss, MD.1 Department of Pathology, Mount Sinai, New York, New York; 2Department of Pathology, Maimonides Medical Center, New York, New York.

Lymphangiomas are benign lymphatic malformations with a poorly understood pathogenesis. Lymphangiomas are most commonly a disease of children, with nearly 50% presenting at birth and up to 90% presenting before 2 years of age. These lymphatic malformations are subdivided into 3 classes: microcystic, macrocystic (including cystic hygroma), and combined, with all 3 subtypes showing a predilection for the head and neck. According to Sunnem B et al, lymphangiomas in 61 patients were examined, revealing the head to be the most common site (n = 35), followed by the neck (n = 25), then trunk and extremities (n = 43), and finally 6 cases of the internal organs (n = 1 of abdomen). Of note, 14 cases of intra-abdominal lymphangiomas occurred in the age of 5 years in 60% of cases. We describe an interesting case of an 82-year-old woman who presented with multiple episodes of abdominal pain requiring 2 hospitalizations during 6 months. She ultimately presented with signs and symptoms of small bowel obstruction. Partial small bowel excision with mesentery revealed a segment of bowel, with a tan, vascularized, fluctuating, lobulated mass measuring 6.1 × 4.2 × 3.9 cm attached within the mesentery of the specimen. Sectioning of the mass revealed milky-white contents admixed with thickened gelatinous contents contained within the thin, tan septate mucosa of the mass. Immunohistochemistry analysis revealed CD31, CD34, and D2-40 positive contents within the cells of the mass. Tumor cells had a typical, macroscopic, and microscopic findings supports the diagnosis of macrocystic lymphangioma.

Gastric Heterotopia Presenting as a Rectal Mass: A Case Report Illustrating the Confusion With Specimen Mix-Up

(Paper No. 101)

Rehan Rais, MBBS (rais@wustl.edu); Deyali Chatterjee, MD. Department of Pathology, Washington University in St Louis, Missouri.

Gastric heterotopia has been described at various locations including rectum. In the gastrointestinal tract, it commonly presents as a polyp, but the presentation as a mass lesion is very rare. Here we report a 54-year-old man who underwent his first screening colonoscopy, which showed a nonobstructing, noncircumferential, and nonbleeding 2.5-cm mass in the upper rectum. Histologic examination of the biopsy material, however, showed almost unremarkable gastric oxyntic mucosa. There was no colorectal mucosa. Although the histologic identification was not challenging, the pathologic interpretation was difficult. It led to the confusion of specimen mix-up, and the patient had to undergo another procedure in a different hospital, with the same outcome. The consideration of gastric heterotopia did not occur, especially because there was no normal tissue native to the biopsy site, compounded by the confusing endoscopic presentation. He was finally referred to our institution, and the outside pathology material was submitted in-house consultation. In retrospect, with 2 similar biopsy findings, a diagnosis of gastric heterotopia was rendered. The patient then underwent an endoscopic mucosal resection (representative image in Figure 37) with clear margins. It is important to be aware that specimen mix-up may occur at any level of specimen processing, from
collection to preparation of slides; however, this case report illustrates the caveat that a wrong assumption in this regard may lead to unnecessary invasive procedures for the patient. A conscious awareness of heterotopias in general is important to avoid this pitfall.

Sessile Serrated Adenoma/Polyp With Cytologic Dysplasia: Evaluation of Pathologists’ and Gastrointestinal Specialists’ Compliance With Recommendations

(Poster No. 102)

Amir Samani, MD (amirsamani@hotmail.com); Maryam Samani, BSc; Ali Reza; Samieh Khosravinia, MD. Department of Research, Amir Samani Medicine Professional Corporation, Richmond Hill, Ontario, Canada.

Context: Conventional dysplasia can develop in sessile serrated adenoma (SSA). The 4th edition of the World Health Organization Tumours of the Digestive System recommends the term “SSA/P with cytologic dysplasia.” Grading of dysplasia and diagnosis of “mixed SSA/P-tubular adenoma” are discouraged. Accordingly, guidelines for postpolypectomy surveillance have recommendations for SSA/P with or without dysplasia, regardless of grading of dysplasia. We designed a survey to determine how effectively this terminology is being implemented by pathologists and gastrointestinal (GI) specialists.

**Question for pathologists**

- Do you grade dysplasia in SSA/P?
  - Yes: 69%
  - No: 31%

**Question for Gastroenterologists**

- Does grading of dysplasia in SSA/P play a role in postpolypectomy follow-up?
  - Yes: 59%
  - No: 41%

**Fair or Different Follow-up Plans for Mixed Polyp vs. SSA with Dysplasia**

- Same Follow-up: 20%
- Different Follow-up: 80%

**Design:** Two separate questionnaires were sent to pathologists and GI specialists. Pathologists were asked the following questions: (1) Do you grade dysplasia in SSA/P?; (2) If a polyp has SSA and tubular adenoma components, do you call it “mixed polyp with SSA and TA” or “SSA with cytologic dysplasia”? GI specialists were asked the following questions: (1) Does grading of dysplasia in SSA/P play any role in postpolypectomy follow-up? (2) Do you have different follow-up plans for “mixed polyp with SSA and TA” versus “SSA with cytologic dysplasia”?

**Results:** Sixty-five pathologists from North America and Asia completed the survey. Of those, 69% do grade dysplasia in SSA/P, and 61.5% still use the term “mixed polyps.” Eighteen GI specialists from North America, Europe, Asia, and Australia completed the survey. Of those, 56% have different follow-up plans based on grading of dysplasia in SSA/P. Twenty-two percent have different follow-up plans for SSA/P with cytologic dysplasia versus “mixed polyps” (Figure 38).

**Conclusions:** Grading of dysplasia is still being applied for SSA/P by more than half of pathologists, which affects postpolypectomy follow-ups.

Recurrent Nested Stromal Epithelial Tumor in a 26-Year-Old Man—A Rare Presentation of a Rare Malignancy: A Case Report and Literature Review

(Poster No. 103)

Benjamin A. Cook, MD (benjamin.a.cook10.mil@mail.mil); George T. Leonard, MD, PhD. Department of Pathology, Madigan Army Medical Center, Tacoma, Washington.

Nested stromal epithelial tumor (NSET) is a rare epithelial/mesenchymal tumor most common in young female patients. We present a case of a recurrent and metastatic NSET of the liver. A 26-year-old man presented with right upper quadrant pain and intermittent constipation. MRI demonstrated a 13.1-cm multilobated mass. The resection specimen showed a circumscribed tumor comprising distinct nests and trabeculae of uniform, cytologically bland spindled to epithelioid cells in a myofibrolastic stroma. The cells were positive for epithelial markers and negative for neuroendocrine markers, c-kit, DOG-1, desmin, and S-100. WT-1 staining was nonspecific and β-catenin demonstrated nuclear accumulation. Results of cytogenetic studies and FISH were unremarkable. Initial descriptions of NSET describe a nonhepatocytic, nonbiliary tumor with nests of spindled and epithelioid cells surrounded by a myofibrolastic stroma. The differential diagnosis of this tumor includes synovial sarcoma, desmoplastic small round cell tumor, spindle cell sarcomatoid carcinoma, metastatic tumors, and carcinoid tumor. A literature search reveals a mean age range of 2–34 years at presentation with a female to male ratio of 2:1. Seven cases had associated cushingoid symptoms. One study showed increased β-catenin staining (as in our case) and a deletion of exon 3. The course for these tumors is variable. One death has been reported due to disease, and 2 additional deaths due to complications of transplant. Three cases of metastatic disease and 3 cases of recurrence have been identified. Our patient is unique in the respect that he is male, has recurrent disease, and local metastasis to the abdominal wall and peritoneum (Figure 39, A through D).
Peritumoral amyloid deposition is a rare feature of MALT lymphomas. It is typically localized and does not affect prognosis, but can confound pathologic interpretation and imaging-based follow-up studies. Despite that the stomach is the most common site of MALT lymphoma, amyloid deposition has been described almost exclusively in extraintestinal sites and, to our knowledge, not in the stomach. We hypothesized that the amyloid deposition could be due to the presence of MALT lymphomatous infiltration of the stomach. The goal of this study was to elucidate this phenomenon and to confirm the hypothesis that MALT lymphoma infiltration of the stomach could result in peritumoral amyloid deposition.

**Methodology:**

A 64-year-old woman with upper abdominal pain, morbid obesity, and chronic nausea and esophageal reflux underwent an exploratory laparotomy. A small bowel obstruction was found to be due to a migrated Angelchik prosthesis that was found adjacent to the spleen. The patient recently underwent laparoscopic removal of the foreign body and Roux-en-Y gastric bypass. A biopsy of the small bowel showed a diffuse infiltrate of plasmacytoid lymphocytes intermingled with amorphous hyaline material. The cells were negative for CD45, CD19, BCL-2, CD79a, and light chain but were negative for CD20, CD43, CD30, BCL-1, CD3, CD5, and light chain. H. pylori was not detected immunohistochemically. MALT1 gene rearrangement was absent by fluorescent in situ hybridization. Peritumoral AL-λ kappa amyloid was identified by Congo red stain and in situ hybridization. Serum IgG and k levels were elevated (3810 and 158.2 mg/dL, respectively). A PET scan was negative for extragastric involvement. The tumor persisted endoscopically and histologically despite anti- H. pylori therapy and multiple administrations of rituximab. Amyloid deposition and absent CD20 expression are associated with plasmacytoid morphotype. These are important considerations in optimizing chemotherapy and monitoring responses because persistent amyloid reportedly can mask tumor regression.

**Results:**

- Both EZH2 and H3K27me3 are expressed in a significant portion of pancreatobiliary carcinomas, more frequently in GBA and ICC, respectively. Targeted EZH2 inhibitors therapy may be useful in those cancers. Because there is no correlation between positive expression of EZH2 and H3K27me3 positivity, other enzymes may also be involved in H3K27 trimethylation.

**Conclusion:**

The results suggest that EZH2 and H3K27me3 may be potential targets for drug therapy in pancreatobiliary carcinomas. Further studies are needed to confirm these findings and to investigate the role of EZH2 and H3K27me3 in the pathogenesis of these tumors.
surveillance and risk of developing cancer in these adenomas are related to number, size, and presence of high-grade dysplasia. Patient surveillance varies from 10 years if no polyp is detected to 3 years if there is high-grade dysplasia. Generally, a polyp is removed with various amount of nonneoplastic mucosa; sometimes, it becomes fragmented after polypectomy. In both conditions, more than one piece of tissue is present. If the focus is mainly on finding a polyp, only one fragment (which may not be neoplastic but reactive epithelium with features of hyperplastic polypl) may be evaluated and an adenoma may be missed. We reviewed 77 cases (32 women and 45 men) with diagnosis of tubular adenoma in the last 2 months of 2017 to see how many had reactive changes similar to that of hyperplastic polypl. The patients ranged in age from 25 to 92 years. Each case had between 1 and 11 polyps with a total of 179 tubular adenomas. The number of pieces on each slide ranged between 1 and 15. Hyperplastic change was found on 14 slides (7.82%). Although this number is not large, it may be considered a pitfall in accurate evaluation of adenomatous change in a polyp. Careful evaluation of the slide with attention to the number of fragments should be pursued to avoid misdiagnosis of tubular adenoma.

**IMP3 Expression in Mismatch Repair–Deficient Colorectal Adenocarcinomas**

*(Poster No. 108)*

Karina Hiroshige, BS1 (khiroshig@ur.rochester.edu); Meenal Sharma, MBBS1; Raul S. Gonzalez, MD, MD1; Rebecca Amorese, BS2; Elena Gupta, BS1; Caitlin Foor-Pessin, MD2; Laura Frado, MD, MD1; Danielle Marino, MD, MD1; Arthur J. DeCross, MD, MD2; Qi Yang, AAS1; Aaron Huber, DO1; Jennifer J. Findeis-Hosey, MD1; Departments of 1Pathology & Laboratory Medicine and 2Medicine, University of Rochester Medical Center, Rochester, New York.

**Context:** Insulin-like growth factor II (IGF-II) messenger RNA binding protein 3 (IMP3) is an oncofetal RNA binding protein encoded by the IGF2BP3 gene. IMP3 has been demonstrated to be overexpressed in multiple human malignancies and has been associated with poor prognosis in colorectal carcinomas, including the presence of lymph node metastases. Here we examine the expression of IMP3 among mismatch repair (MMR)-deficient colorectal carcinomas.

**Design:** Sixty-two MMR-deficient colorectal adenocarcinomas were included in a tissue microarray, including tumor and nodal disease/tumor deposits (n = 27), when applicable. IMP3 immunohistochemistry was performed and classified as positive (greater than 1% of tumor cells with cytoplasmic positivity) or negative.

**Results:** IMP3 immunohistochemical expression was identified in 35 (56.5%) of examined primary tumors and 9 (39.1%) of examined lymph node metastases. The majority (18; 51.4%) of IMP3-positive tumors were well to moderately differentiated, with lymphovascular invasion (18; 51.4%), and a pathologic stage of pT3 or greater (24; 68.6%). There was no statistically significant difference between IMP3-positive and IMP3-negative tumors in terms of tumor grade, lymphovascular invasion, perineural invasion, or presence of lymph node metastases/tumor deposits (Table).

**Conclusions:** IMP3 expression has been previously demonstrated to be associated with poor prognosis in colorectal carcinomas. Here we examine IMP3 expression in MMR-deficient colorectal carcinomas and find no statistically significant difference in examined clinicopathologic characteristics between IMP3-positive and IMP3-negative tumors. This suggests that those tumors where IMP3 expression is prognostically significant are not MMR deficient.

**IMP3 Immunohistochemical Expression in MMR-Deficient Colorectal Adenocarcinomas**

<table>
<thead>
<tr>
<th>IMP3 Positive, No. (%)</th>
<th>IMP3 Negative, No. (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 35</td>
<td>n = 27</td>
<td></td>
</tr>
<tr>
<td>Well to moderately differentiated</td>
<td>18 (51.4)</td>
<td>17 (63.0)</td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td>18 (51.4)</td>
<td>13 (48.1)</td>
</tr>
<tr>
<td>Perineural invasion</td>
<td>5 (14.3)</td>
<td>4 (14.8)</td>
</tr>
<tr>
<td>pT3 or greater</td>
<td>24 (68.6)</td>
<td>18 (66.7)</td>
</tr>
</tbody>
</table>

**Sessile Serrated Adenoma of the Appendix: A Retrospective Review of 115 Cases**

*(Poster No. 110)*

Philip M. Barber, MBBS (barber.philip@hotmail.com); Rodrigo Murillo Alvarez, MD; Li Ge, MD. Department of Pathology, Orlando Health, Orlando, Florida.

**Context:** The sessile serrated adenoma (SSA) of the colon is a well-known polyoid colonic lesion with low potential to develop dysplasia. The counterpart of this lesion in the appendix shares architectural and histologic features, but its association with dysplasia, appendiceal cancer, and clinical significance is not yet fully understood.

**Design:** We conducted a retrospective observational study, which included a review of the electronic medical records of a community-based practice to identify all patients who were diagnosed with appendiceal SSA between August 2010 and September 2017. Patient demographics and concurrent diagnoses with SSA were noted.

**Results:** During the study period, 115 patients were diagnosed with an appendiceal SSA. Analysis of the demographic data revealed a 1.67:1 female to male ratio. The age range was 15–93 years old, with a median age of 55 years.
Large Ulcerated Mass Mimicking Anal Carcinoma Caused by Herpes Simplex Virus Infection

(Poster No. 112)

Jiemin Zhou, MD (jzhou@uhosp.org); Tammey Naab, MD. Department of Pathology, Howard University Hospital, Washington, DC.

Anusitis is described as inflammation of the anal canal. The most common cause of anusitis is related to diet and use of laxatives. Other causes include ulcerative colitis, Crohn disease, ischemia, vasculitis, and bacterial and viral infectious causes. We report the case of a 55-year-old man who initially presented to the emergency department for a cough and then incidentally mentioned he had a purulent anal ulcer for 2 weeks that had worsened. He was prescribed oral antibiotics and referred to a general surgery clinic. He had a history of HIV positivity with an undetectable viral load at this time. Despite antibiotic therapy, the patient complained of the mass becoming larger, chronic fatigue, bloating, and an unexpected weight loss of 15 pounds during 3 months. The colorectal surgeon scheduled a frozen section to confirm that the 6.5 x 3-cm ulcerated mass was malignant. The frozen section revealed atypical cells, some of which appeared multinucleated, with ground-glass appearance suggestive of herpes simplex. Additional biopsies were taken that revealed ulcerated herpetic anusitis with granulation tissue, florid plasma cell proliferation, and no evidence of malignancy. HSV immunostain was positive whereas Treponema immunostain was negative. κ and λ by in situ hybridization stains were performed and were consistent with reactive polyclonal plasma cell proliferation. This case highlights that ulcerating anal masses do not always represent malignancy or abscesses from bacterial causes but can also be due to viruses such as HSV.

Withdrawn.

Diffuse Schwann Cell Hamartomatosis: An Important Diagnostic Consideration in Limited Biopsy Specimens

(Poster No. 111)

Timothy D. Law, MD (timothylaw123@gmail.com); Ganna Shesta-kova, MD, PhD; Wamda Goreal, MD. Department of Pathology, University of California, Irvine, Orange.

Diffuse Schwann cell hamartomatosis is a rare, benign mucosal lesion of the colon and rectum that consists of an unencapsulated Schwann cell proliferation confined to the lamina propria. The differential diagnosis for diffuse Schwann cell hamartomatosis includes schwannoma, and it is of clinical importance to differentiate these 2 diagnostic entities because of significant differences in management. Because of its superficial location, a Schwann cell hamartoma is not an indication for bowel resection; however, a schwannoma will commonly involve the muscularis propria and necessitate bowel resection. We report the case of a 54-year-old woman with family history significant for colon cancer before age 50 who underwent sigmoidoscopy with the finding of rectal ulceration. A biopsy of the lesion revealed a low-grade spindle cell lesion suggestive of a schwannoma. A low-anterior resection was performed for further evaluation, and the specimen was grossly examined to reveal a 0.2-cm tan-white scar at the previous biopsy site. No masses or ulcerations were identified. Histologic examination of tissue sections revealed a diffuse, ill-defined, spindle cell proliferation in the lamina propria with bland nuclei, dense eosinophilic cytoplasm, and indistinct cellular borders (Figure 43, A). Immunohistochemical staining showed the neoplastic cells to be positive for S100 (Figure 43, B) and negative for EMA, CD34, and CD117. These histologic findings and immunohistochemical staining patterns are diagnostic for diffuse Schwann cell hamartomatosis. It is imperative to exercise caution when diagnosing schwannoma on a limited biopsy specimen in order to reduce the rate of unnecessary procedures.

High-Grade Glandular Dysplasia Can Be Confirmed by Positive Staining With Progenitor Cell Marker CD133

(Poster No. 115)

Craig Cousineau, DO (craig.cousineau@beaumont.edu); Zhen-ghong Qu, MD; Ping Zhang, MD. Department of Pathology, Beaumont Health, Royal Oak, Michigan.

Context: Our group and others have previously shown that colonic adenocarcinoma overexpresses CD133. High-grade glandular dysplasia (HGGD) is a well-recognized precursor of invasive colonic adenocarcinoma, defined by architectural changes (cribriform pattern) and cytologic atypia (rounding of nuclei in dysplastic cells). The aim of our current study was to investigate whether CD133 can be used to distinguish HGGD with or without significant cytologic atypia from low-grade dysplasia.

Design: We collected 20 nonneoplastic cases with reactive bowel tissue (10 ischemic and 10 inflammatory bowel disease), 12 cases with......
HGGD (8 with and 4 without significant cytologic atypia), 8 cases with only low-grade glandular dysplasia, and 10 cases of invasive adenocarcinoma. All cases were stained with CD133 (AC 133 monoclonal antibody); surface membranous staining was evaluated and graded from 0 to 3+.

Results: CD133 staining was negative in all reactive bowel cases, whereas all colonic adenocarcinomas showed 2–3+ positivity. All cases of HGGD displayed 2–3+ surface membranous staining, both with and without cytologic atypia. CD133 staining was almost entirely negative in cases with only low-grade dysplasia, aside from 1 case with focal positive surface membranous staining.

Conclusions: Although HGGD with cytologic atypia can be easily identified morphologically, HGGD without significant cytologic atypia can be further supported by evidence of positive surface membranous staining for CD133. Meanwhile, low-grade dysplasia, either as individual cases or between areas of HGGD, stains almost exclusively negative for CD133. In summary, our study indicates that CD133 surface expression closely correlates with HGGD.

Does Monosomy of Chromosome 17 Impact Interpretation of HER2 Fluorescence In Situ Hybridization Results in Breast Carcinoma Patients: A Study in a Large Cohort of Patients From a Tertiary Referral Laboratory in India

(Submitted by Aditi Dewan, MD; Lata Kini, MD; Shivani Sharma, DCP, DNB; Ajay Pandita, PhD; Sankar Mohan, PhD; Beklashwar Salona, DMLT, BSc, MLT; Arjun S. Rana, BMLT. 1Department of Pathology and Lab Medicine, Core Diagnostics, Gurugram, Haryana, India; 2Department of Pathology and Lab Medicine, Core Diagnostics, Hayward, California.

Context: Monosomy of chromosome 17 is well documented, with overall HER2 gene testing, overall prognosis, and responsiveness to targeted therapy. We evaluated the impact of chromosome 17 monosomy on HER2 gene testing along with clinicopathologic correlation and treatment outcomes.

Design: We retrospectively analyzed our data of HER2 fluorescence in situ hybridization (FISH) testing during 1 year and identified cases with monosomy of chromosome 17 in breast carcinoma patients. Monosomy was defined as reduction of CEP17 signals with or without reduction of HER2 signals to less than 1.4 per cell. HER2 FISH results were reported in accordance with 2013 ASCO/CAP guidelines. Patient demographics, histopathology findings, and results of immunohistochemistry testing were also retrieved.

Results: Overall 800 patients underwent HER2 FISH testing, of which 30 cases (3.75%), all invasive ductal carcinoma, not otherwise specified (Figure 44, A and C), had chromosome 17 monosomy. Three of the 30 cases were HER2 amplified (Figure 44, B), by ratio as well as by average number of signals per cell, whereas 27 cases were nonamplified (Figure 44, D). Eleven of the 30 cases exhibited loss of both HER2 and CEP 17 signals, whereas 19 cases had a loss of CEP 17 signals without loss of HER2 signals. All 3 amplified cases were histologically grade 3 with negativity for estrogen and progesterone receptors on immuno-

Malignant Mesothelioma Misdiaqnsed as Metastatic Breast Carcinoma: A Cautionary Tale of the Reliance on GATA3 Immunostain

(Submitted by Maria Zayko, DO; Don Asberry, MD. 1Department of Pathology, East Tennessee State University Quillen

Adenoid Cystic Carcinoma of the Breast With Aggressive Clinical Behavior and a Novel Cytogenetic Feature

(Submitted by Lames Hamoodi, MD; Rachel Stewart, DO; Sainain Wei, PhD; Hayder Saeed, MD; Edward Romond, MD; Kurt Hodges, MD. 1Departments of 1Pathology and Laboratory Medicine, 2Hematology, and 3Oncology, University of Kentucky, Lexington; 4Department of Pathology and Laboratory Medicine, University of Utah, Salt Lake.

Adenoid cystic carcinoma (ACC) of the breast is a rare triple-negative malignancy that characteristically has an excellent prognosis and rarely metastasizes. However, the solid variant may have a higher incidence of lymph node involvement and recurrence compared with other subtypes. The MYB-NFIB translocation has been linked to salivary and mammary gland ACC. We report 2 cases of solid variant ACC of the breast with aggressive clinical behavior, both diagnosed in young women. Histologic sections showed solid nests of cells with basoloid features and c-kit positivity (Figure 45, A through D). Our first patient (age 36) was diagnosed with a pT1bN0 tumor and underwent mastectomy but developed liver metastases within 6 months, after which she received chemotherapy but died of her disease. Our second patient (age 35) had pT2N1a ACC and underwent mastectomy but developed liver metastases within 3 months was found to have early evidence of liver metastases. She received aggressive chemotherapy and is in remission more than 5 years after her diagnosis of metastatic disease. Because of the atypical behavior of these tumors, we performed fluorescence in situ hybridization testing for the MYB-NFIB gene rearrangement, which was negative in both cases. However, MYB (6q23.3) break-apart probes showed trisomy or tetrasyoun (or copy number gain) for the MYB gene locus in approximately 50% of cells in both cases. A point of unknown significance is that both patients were within 6 months postpartum at the time of diagnosis of ACC. These findings may indicate a novel cytogenetic feature associated with aggressive clinical behavior in this rare and usually indolent primary tumor of the breast.
Primary Epithelioid Angiosarcoma of the Breast: A Rare and Challenging Biopsy Diagnosis

(Roster No. 119)

Rachelle P. Mendoza, MD (Rachelle.Mendoza@downstate.edu); Kristina Loukeris, MD. Department of Pathology, SUNY Downstate Medical Center, Brooklyn, New York.

Breast epithelioid angiosarcoma is almost exclusively secondary to previous radiation or chronic lymphedema. Primary epithelioid angiosarcoma is rare in breast and may mimic malignancies such as carcinoma or benign endothelial lesions on limited biopsy material. A 70-year-old woman presented with a slowly enlarging, firm, fungating mass. A 2-year history of right radical mastectomy 11 years earlier for invasive ductal carcinoma, presented with a contralateral lesion and underwent a left simple mastectomy that showed ER/PR–positive invasive ductal carcinoma. A PET scan revealed a left pleural effusion with lobulated pleural thickening concerning for malignant effusion and pleural studding. Pleural biopsy showed sheets of high-grade epithelioid cells similar to the left breast carcinoma. Although ER negative, in the context of ipsilateral histologically similar tumor and positivity for GATA3 and CK7, metastatic breast carcinoma was diagnosed, and the patient underwent systemic chemotherapy. A follow-up PET scan showed improvement in chest disease, but detected a hypermetabolic left axillary lymph node. Lymph node biopsy revealed infiltration by small epithelioid cells and tubular structures lined by hobnail cells suspicious for mesothelioma. The tumor cells were positive for GATA-3 (weak), calretinin, cytokeratin 5/6, and WT-1, confirming a diagnosis of epithelioid mesothelioma. The patient received palliative chemotherapy and died several months later. She had no known asbestos exposure. GATA3 is a well-known marker of breast and urothelial carcinoma, but is expressed in many other tissues, including normal and neoplastic mesothelium. Pathologists must use GATA3 cautiously and expand the panel when other stain results are discordant in order to avoid a serious misdiagnosis.

Clinicopathologic Analysis of BRCA-Positive and BRCA-Negative Filipino Patients

(Poster No. 120)

Francis P. Tria, IV, MD; Jose Jasper Andal, MD; Frances Victoria Que, MD; Loraine Kay D. Cabral, MSC; Rosil Dimalibot, RMT; Ruby K. Li, MD; Manueltto A. Madrid, MD; Raymundo W. Lo, MD; Luisa D. Enriquez, PhD; Marcelo Imasa, MD; Daphne C. Ang, MD (daphnecnhuaang@yahoo.com). Departments of 1Pathology, 2Internal Medicine–Medical Oncology, and 3Research and Biotechnology Division, St Luke's Medical Center, Quezon City, Philippines.

Context: The Philippines has a reported annual breast cancer (BC) incidence of 47.7 per 100 000. We recently reported a 6.25% BRCA mutation rate among Filipinos who fulfill the NCCN criteria for BRCA genetic assessment. Here, we compared clinicopathologic characteristics of BRCA mutation carriers and noncarriers in patients with BC and gynecologic malignancies (GC).

Design: Various clinicopathologic characteristics (age, sex, tumor histopathology, hormone status) were collected from 115 patients with BC or GC.

Results: The median age of patients at diagnosis was 45 years (range, 18–72 years). The majority of patients were diagnosed with BC (85%), followed by ovarian cancer (15%). The predominant BC histology was invasive ductal carcinoma (84%). On the other hand, clear cell carcinoma was the predominant ovarian cancer histology (33%). The age at diagnosis of BRCA1-mutant patients tended to be younger than that of patients without the mutation (P = .36). The BRCA1-mutant patients had significantly more ER-negative BC than the group without BRCA1 mutation (P = .007). BRCA1-mutant patients showed more HER2-negative BC and higher stage of BC at diagnosis compared with BRCA1-negative patients (P = .29). The BRCA2-mutant patients showed more ER-negative BC than the BRCA2-negative group (P = .29). In contrast to BRCA1 mutation, there were no differences in age at diagnosis, stage of disease, and HER2 status of BRCA2 mutant and negative patients.

Conclusions: This is the first study comparing clinicopathologic characteristics of BRCA mutation carriers and noncarriers in a Filipino cohort. BRCA1 and BRCA2 mutant Filipino patients have distinct clinicopathologic features. BRCA2-mutant patients have more similar clinicopathologic features with sporadic BC.

Two Cases of Pleomorphic Hyalinizing Angiectatic Tumor Involving the Breast

(Poster No. 121)

Cynthia Reyes Barron, MD (cynthia_reyes-barron@urmc.rochester.edu); Charles Sturgis, MD; David Hicks, MD; Erin Downs-Kelly, DO. 1Department of Pathology, University of Rochester Medical Center, Rochester, New York; 2Department of Pathology, Cleveland Clinic, Cleveland, Ohio.

Pleomorphic hyalinizing angiectatic tumor (PHAT) is a rare, slow-growing, locally aggressive subcutaneous mesenchymal neoplasm typically occurring in the lower extremities. We present 2 cases of PHAT occurring in breasts. The first case involves an 86-year-old man presenting with a painless breast mass with no previous history of malignancy. The second case involves a 56-year-old woman presenting with a new breast mass 10 years after lumpectomy, chemotherapy, and radiation for invasive ductal carcinoma. Biopsies and subsequent resection specimens of both cases had very similar morphology consisting of prominent thin-walled ectatic vessels lined by fibrin with perivascular hyalinization within a variably cellular spindle stroma with inflammatory cells and hemosiderin (Figure 47, A through C, case 1; D, case 2). The spindle cells varied from bland to pleomorphic with intranuclear inclusions and were negative for desmin and low-molecular-weight cytokeratin, but positive for CD34 in case 1 and
negative in case 2. The histologic differential diagnosis included other spindle cell neoplasms such as myofibroblastoma, spindle cell carcinoma, spindle cell lipoma, solitary fibrous tumor, schwannoma, undifferentiated pleomorphic sarcoma, and hemispheric fibrolipomatous tumor. Both the histologic and immunohistochemical findings were consistent with PHAT, although the location was highly unusual. Treatment is complete surgical excision; local recurrence is seen in 30%–50% of cases without metastases reported to date. After successful complete surgical excision with negative margins, both patients were lost to follow-up. Awareness of the possibility that PHAT may occur in the breast will aid recognition and avoid unnecessary radical surgery and other therapeutic modalities.

**Amyloid Tumor of the Breast in Primary Sjögren Syndrome: The Third Reported Case**

(Poster No. 122)

Kristen Ruby, DO (kristen.n.ruby@hitchcock.org); Nolan Maloney, MD; Kristen E. Muller, DO. Department of Pathology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire.

Since its original description in 1973, amyloid deposition in the breast has been reported only rarely. It can present as a localized amyloid tumor, secondary to invasive breast carcinoma or hematologic malignancy, or as a sequela of systemic amyloidosis. Although associations between amyloid deposition and autoimmune diseases are recognized, there are, to our knowledge, only 2 reported cases of the coexistence of primary Sjögren syndrome and breast amyloid deposition. We report a case of a 41-year-old woman with a strong family history of breast cancer who presented with a 1.2-cm lobulated breast mass with calcifications on routine screening mammography (Figure 48, A). Her past medical history was significant for primary Sjögren syndrome diagnosed 10 years prior. A core needle biopsy revealed extensive stromal deposition of amorphous eosinophilic material that was strongly Congo red positive and showed apple-green birefringence under polarized light, consistent with amyloid (Figure 48, B and C). Dystrophic calcifications and small polytypic lymphoplasmacytic infiltrates were also present. Liquid chromatography tandem mass spectrometry detected a peptide profile consistent with AL (λ)-type amyloid deposition. Subsequent surgical excision was negative for underlying breast and hematologic malignancy. She had no other clinical or laboratory evidence of systemic amyloidosis. This represents the third reported case of a breast amyloid tumor in a patient with primary Sjögren syndrome. Amyloid deposition in the breast may be the first clinical manifestation of systemic amyloidosis or secondary to a breast or hematologic malignancy, and awareness of this entity is essential for appropriate postoperative management.

**Atypical Microglandular Adenosis With Associated Triple-Negative Breast Carcinoma With Metaplastic Features: A Case Report With Molecular Findings**

(Poster No. 123)

Sundis Mahmood, DO1 (sundis.mahmood@hitchcock.org); Jonathan Marotti, MD2; Hugo Arias-Pulido, PhD2; Kristen Muller, DO.1 Departments of 1Pathology and 2Microbiology and Immunology, Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire.

Microglandular adenosis (MGA) is a rare lesion of the breast composed of infiltrative small glands that characteristically lack myoepithelium, strongly express S100, and are triple negative (estrogen receptor, progesterone receptor, and HER2 negative). MGA is associated with invasive carcinoma in about a third of cases, and it is suggested that MGA represents a nonobligate precursor in a subset of triple-negative breast carcinomas. This is supported by recent molecular studies demonstrating shared mutations in MGA and associated breast carcinomas, with the majority of cases harboring identical TP53 mutations. We report a case of a 54-year-old woman who presented with a 2.5-cm left breast mass. Core needle biopsy revealed a high-grade, triple-negative invasive ductal carcinoma with metaplastic features. Next-generation sequencing using the 50-gene Cancer Hotspot Panel v2 (IonTorrent) revealed mutations in FGF2 and TP53. The patient was started on neoadjuvant chemotherapy; however, because of side effects, she underwent mastectomy and axillary dissection before chemotherapy was completed. The mastectomy revealed a 3.0-cm invasive ductal carcinoma with metaplastic features (Figure 49, A). A 1.5-cm focus of MGA (Figure 49, B) was present immediately adjacent to the invasive carcinoma, which lacked myoepithelium (Figure 49, C, p63). The MGA demonstrated atypical features including gland complexity, cell stratification, increased mitotic figures, and loss of luminal secretions. Both MGA and the invasive carcinoma were triple negative and showed strong expression of S100 (Figure 49, D). Somatic mutation analysis is currently in progress on the MGA component to assess the relationship of MGA to the invasive carcinoma in this case.
Pleomorphic Invasive Lobular Carcinoma of the Male Breast: Report of 2 Cases
(Poster No. 124)
Albina Muzrabdillaeva, MD (albina.muzrabdillaeva@uth.tmc.edu); Yi Tat Tong, DO; Jacob Armstrong, MD; Peisha Yan, MD; Songlin Zhang, MD, PhD. Department of Pathology and Laboratory Medicine, the University of Texas Health Science Center McGovern Medical School, Houston.

Male breast cancer represents <1% of all breast cancers, among which lobular type accounts for 1%. There are 4 reported cases of male breast pleomorphic invasive lobular carcinoma (ILC) in the literature, and we report 2 cases from our institution. The first case concerns a 63-year-old man who presented with a left neck mass, progressive facial numbness, and bilateral cervical lymphadenopathy. Neck mass biopsy revealed infiltrative carcinoma with highly pleomorphic nuclei, suggesting possible metastatic carcinoma. After a month, a left breast induration was found, and ultrasound displayed a 1.7-cm retro-areolar lesion. Magnetic resonance imaging of the brain identified cerebellar lesions. The neck and breast mass biopsies identified similar tumor morphology with lympho-vascular invasion. The immunohistochemistry was ER+/PR−, Her2−, E-cadherin+, GATA3+, and p120 cytoplasmic+, confirming metastatic pleomorphic ILC. After 4 months of chemother-apy and irradiation, the patient developed another brain metastasis. The second case involves a 79-year-old man with a left breast mass and skin induration was found, and ultrasound displayed a 1.7-cm retro-areolar lesion. Magnetic resonance imaging of the brain identified cerebellar lesions. The neck and breast mass biopsies identified similar tumor morphology with lympho-vascular invasion. The immunohistochemistry was ER+/PR−, Her2−, and E-cadherin+, supporting invasive lobular carcinoma. Breast ultrasound and mastectomy specimen proved pleomorphic ILC. Nottingham grade 3, with negative axillary lymph nodes. Twelve-month follow-up showed no evidence of metastasis or recurrence. Pleomorphic ILC is an extremely uncommon entity among male patients. High alert and awareness of male breast pleomorphic ILC are key factors for rendering an accurate diagnosis, especially in metastatic disease.

FOXP3 Expression in T Cells as a Prognostic Biomarker in Triple-Negative Breast Cancers
(Poster No. 125)
Padmini A. Manrai, MD (padmini.manrai@yale.edu); Tao Zuo, MD; Benjamin L. Mazer, MD, MBA; Parker Wilson, MD, PhD; Malini Harigopal, MD. Department of Pathology, Yale New Haven Hospital, New Haven, Connecticut.

Context: T cells are associated with disease-free survival and overall survival in triple-negative breast cancer. Forkhead box protein 3 (FOXP3), a marker for CD4+ and CD25+ regulatory T cells, has been studied in other cancers such as prostate and ovarian cancers; however, FOXP3 expression in T cells and its prognostic significance in patients with triple-negative breast cancer have not been extensively studied.

Design: Tissue microarrays were used to analyze 179 triple-negative breast cancers with immunohistochemical staining of FOXP3. Absence or presence of FOXP3 staining was assessed and matched to known survival data.

Results: Univariate analysis showed a statistically significant positive correlation between FOXP3 positivity in T cells and a better prognosis of patients (P < .001, Fisher exact test). Out of 179 tissue microarrays analyzed, 98 expressed FOXP3 in T cells whereas 81 did not. Of the 98 tissues with FOXP3-positive T cells, approximately two-thirds of the patients were alive at the time of survival data collection, and one-third were deceased. Of the 81 tissues with FOXP3-negative T cell status, there was an equal distribution between living and deceased patients (Figure 50).

Conclusions: These results demonstrate the potential for FOXP3 as a prognostic biomarker in triple-negative breast cancers. FOXP3 positivity in T cells correlates with a better prognosis for patients with triple-negative breast cancer. Multivariate analysis is currently being conducted to determine if FOXP3 is an independent predictor of prognosis. A logistic regression model comparing FOXP3 positivity with established tumor prognostic factors will be included.

Fibroepithelial Lesions: The Utility of Using a Template of Histologic Criteria on Core Needle Biopsy
(Poster No. 126)
Patricia Zot, MD (patricia.zot@vcuhealth.org); Lorraine Colon Cartagena, MD; Bryce Hatfield, MD; Michael Idowu, MD, MPH; Valentina Robia, MD, PhD. Department of Pathology, Virginia Commonwealth University, Richmond.

Context: A diagnosis of fibroepithelial lesion (FEL) is used when overlapping features of phyllodes tumor (PT) and fibroadenoma (FA) are identified on core needle biopsy (CNB) and often triggers a surgical excision. The purpose of this study was to evaluate the utility of a template consisting of a set of histologic criteria to better refine the interpretation of these lesions.

Design: A retrospective cohort of cases diagnosed as FEL on CNB between 2008 and 2017 was re-reviewed using a set of histologic criteria to render a diagnosis of either FA or PT based on the predominant histologic features. The reviewers were blinded to the diagnosis on excisional specimens. We compared the diagnosis made using the template with the original CNB and surgical excision diagnoses. The template used the following criteria: stromal and glandular heterogeneity, mitotic activity, and cytologic atypia, among others.

Results: With the use of the template, there was improved corroboration of diagnosis on CNB with excisional diagnosis, 73.5% and 41.7% for FA and PT, respectively (see Table). However, 6 of 34 cases (17.6%) diagnosed as PT on CNB were diagnosed as FA on excision and 5 of 12 cases (41.7%) diagnosed as PT on CNB were diagnosed as FA on excision.

Conclusions: This study showed that although the use of the template reduced the use of FEL on CNB, some discrepancies in the diagnosis remain between CNB and excision. Continued revision and prioritization of certain criteria within the template may help in refining the diagnosis on CNB.

Correlation Between Diagnoses Using the Proposed Criteria

<table>
<thead>
<tr>
<th>CNB Diagnosis (Original Diagnosis Not Using the Template), No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNB Diagnosis (With Use of the Template)</td>
</tr>
<tr>
<td>FA (n = 34)</td>
</tr>
<tr>
<td>PT (n = 12)</td>
</tr>
<tr>
<td>Total (N = 46)</td>
</tr>
</tbody>
</table>

Excision Diagnosis (Original Diagnosis Not Using the Template), No. (%)

<table>
<thead>
<tr>
<th>CNB Diagnosis (With Use of the Template)</th>
<th>FA</th>
<th>PT</th>
<th>FEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>FA (n = 34)</td>
<td>25 (73.5)</td>
<td>6 (17.6)</td>
<td>3 (8.8)</td>
</tr>
<tr>
<td>PT (n = 12)</td>
<td>5 (41.7)</td>
<td>5 (41.7)</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td>Total (N = 46)</td>
<td>30 (65.2)</td>
<td>11 (23.9)</td>
<td>5 (10.9)</td>
</tr>
</tbody>
</table>

Diagnosis of Breast Fibromatosis on Core Needle Biopsy
(Poster No. 127)
Shenon Sethi, MBBS (Shenon_Sethi@rush.edu); Fatima Mir, MBBS; Ritu Ghai, MD; Vijaya B. Reddy, MD; Paolo Gattuso, MD. Department of Pathology, Rush University Medical Center, Chicago, Illinois.

Context: Fibromatosis is an uncommon benign breast mesenchymal neoplasm that can be managed conservatively. It can pose a diagnostic challenge, with a key factor being accuracy of diagnosis, which is often prioritized on CNB. The correlation between diagnoses using the template showed significant correlation between the template diagnosis and the excision diagnosis with a p-value of 0.0006.
challenge on core needle biopsy (CNB) as it can mimic spindle cell carcinoma, pseudoangiomatous stromal hyperplasia, nodular fasciitis, myofibroblastoma, and phyllodes tumor, among others.

**Design:** We identified a total of 21 cases (2002–2017) that either were diagnosed as fibromatosis or included fibromatosis as a differential diagnosis on CNB. We reviewed the pertinent clinical, morphologic, and immunohistochemical findings.

**Results:** Most of the cases involved women (95.2%) with an average age of 49 years. Two women had a history of prior breast surgery. A total of 90.4% of cases favored or included fibromatosis as a differential diagnosis on CNB. Nearly 86% (85.7%) of cases underwent excision, of which 3 were diagnosed as fibroadenomas and 1 as low-grade fibromyxoid sarcoma; the remainder were fibromatosis. The average size of fibromatosis was 2.2 cm. Seven cases had 1 or more margins that were involved at excision. Of these, only 1 underwent re-excision, but the remaining 6 cases did not have a reportable recurrence on last follow-up. Up to 60% of the CNBs were evaluated by immunohistochemistry, of which 75% showed nuclear expression of β-catenin and cytoplasmic expression of SMA, and all (100%) were negative for CD34, S100, and high-molecular-weight cytokeratin.

**Conclusions:** Fibromatosis in breast has a favorable outcome and extremely low risk of local recurrence. A panel of immunohistochemical stains that includes β-catenin, CD34, SMA, S100, and high-molecular-weight cytokeratin would aid in correct diagnosis on CNB and thus can help manage this neoplasm in a more conservative approach.

**Ki-67 and Oncotype DX Recurrence Score Concordance in Invasive Breast Carcinoma**

(Poster No. 128)

Amanda L. Meindl, MD (amanda.meindl@northwestern.edu); Brian S. Finkelman, MD, PhD; Carissa LaBoy, MD; Brannan Griffin, MD; Kalliopi P. Siziopikou, MD, PhD; Jennifer Pincus, MD; Suguna Narayan, MD, PhD; Ryan Brancamp, MD; Luis Z. Blanco, MD, Department of Pathology, Northwestern University and Feinberg School of Medicine, Chicago, Illinois.

**Context:** Ki-67 immunohistochemistry is a widely used cancer proliferation assay; however, it has poor reproducibility and could potentially be improved with automated algorithms. Additionally, Oncotype DX recurrence score (ORS), which evaluates cancer proliferation pathway genes, has become a popular prognostic indicator; however, it is more expensive and has slower turnaround. Determining the concordance between these assays could help pathologists focus on those that are most efficient without sacrificing accuracy.

**Design:** One hundred patients with invasive carcinoma (104 total specimens) were evaluated for manual (m) semiquantitative Ki-67 score, ORS at diagnosis, and automated (a) quantitative Ki-67 score obtained using software. Ki-67 was reported as a percentage and as a semiquantitative category. Concordance was assessed between mKi-67 and aKi-67 categories and between Ki-67 and ORS categories via Cohen κ.

**Results:** mKi-67 and aKi-67 categories were concordant in 58 of 104 cases (55.7%). aKi-67 underestimated mKi-67 in 39 of 104 cases (37.5%). Actual reported percentages were significantly higher for mKi-67 than for aKi-67 (P < .001); the median absolute difference between the 2 indices was 4.9% (IQR 2.5%-13%). During a median follow-up time of 4.8 years (IQR 3.6-5.1 years), local recurrence and/or distant metastases occurred in 7 of 100 patients.

**Conclusions:** aKi-67 scores consistently underestimated manual scores and showed no significant concordance with ORS, suggesting that automated algorithms likely need substantial manual training to improve accuracy. Additionally, mKi-67 showed moderate to poor concordance with ORS, suggesting that these 2 assays, despite both assessing cancer proliferation, likely provide independent information on breast cancer recurrence risk and prognosis.

**Localized Breast Amyloidosis: A Rare Presentation of λ Light Chain AL Amyloidosis**

(Poster No. 129)

Debbie R. Walley, MD1 (darigney@umc.edu); Harpreet Talwar, MD2; Sarika Jain, MD3; Varsha Manuch, MD, PhD, Departments of 1Pathology and 2Radiology, University of Mississippi Medical Center, Jackson.

Primary amyloidosis of the breast is a rare entity reported in postmenopausal women that presents as a breast mass suspicious for malignancy. It is reported to be most often associated with systemic amyloidosis or with hematologic malignancy. We present a case of a 66-year-old woman with a medical history significant for stage IA grade 2 mixed endometrioid adenocarcinoma and mucinous adenocarcinoma of the uterus. A screening mammogram showed a 3.6-cm right upper outer breast mass (Figure 51, A). The patient underwent a stereotactic biopsy of the lesion. Microscopic examination demonstrated extracellular deposits of eosinophilic amorphous material associated with focal clusters of mature plasma cells in the breast tissue (Figure 51, B). The material showed apple-green birefringence under polarized light (Figure 51, C) with Congo red stain. In situ hybridization revealed λ light-chain excess (Figure 51, D). Amyloid typing by liquid chromatography tandem mass spectrometry demonstrated immunoglobulin light chain (AL) amyloidosis (λ)-type. Further clinical evaluation showed no evidence of renal, liver, heart, or nerve damage. No osteolytic or osteoblastic lesions were identified on an osseous survey. Serum protein electrophoresis was negative for a monoclonal protein and the κ:λ ratio was within normal limits. Localized amyloidosis is rare, comprising only 12% of immunoglobulin light chain (AL) amyloidosis cases, and is usually κ type in breast. This is an unusual case of localized immunoglobulin light chain (AL) amyloidosis (λ)-type with extracellular amyloid deposition in the breast.

**Rare Variant of Solid Papillary Carcinoma With IDH2 Alteration**

(Poster No. 130)

Koorosh Haghayeghi, MD (koorosh.haghayeghi@lifespan.org); Nimesh R. Patel, MD; Ece Uzun, MD; Cynthia L. Jackson, MD; Yihong Wang, MD; Shamal Mangray, MD; Sonja Chen, MD, Department of Pathology and Laboratory Medicine, Rhode Island Hospital, Providence.

Solid papillary carcinoma with reverse polarity, also known as breast tumor resembling tall cell variant of papillary thyroid carcinoma, is an uncommon variant of solid papillary carcinoma with distinct clinicopathologic features and IDH2 p.R172 hotspot mutations reported in 13 of 26 cases in the literature to date. Metastatic disease to an intramammary lymph node and to bone was reported in 2 cases in which IDH2 molecular analysis was not performed. Because of limited data, we draw further attention to this entity with an additional case report. A 61-year-old woman was found to have a subcentimeter area of asymmetry on mammographic screening. Histologic sections from the biopsy of the lesion showed a mass characterized by solid, circumscribed nodules in a jigsawlike growth pattern. The epithelial nests had a fibrovascular core with foamy histiocytes and a double-layered columnar epithelium without a lumen. The cells appeared back to back with apical nuclei (reverse polarization). There was loss of CK5/6 expression, and p63 and myosin demonstrated lack of a myoepithelial layer. E-cadherin stain showed only lateral membrane expression, with MUC1 apical staining pattern and strong positive nuclear reactivity in 10% of cells with estrogen receptor antibody. Next-generation sequencing of the tumor revealed an IDH2 p.R172M hotspot mutation. The patient went on to
receive radiation therapy and is free of disease at 1-month follow-up. Recognition of this entity and further investigation are warranted to determine whether there is any difference in prognosis compared with typical solid papillary carcinoma.

Clinical Relevance of HER2-HER3 Heterodimer (H23D) Expression in HER2-Positive and HER2-Negative Breast Cancer

(Poster No. 131)

Renata Duchnowska, MD, PhD; Weidong Huang, MD, PhD; (huangw29@labcorp.com); Jeffrey Sperinde, PhD; Gerald Wallweber, PhD; Tomasz Trojanowski, MD, PhD; Tomasz Mandat, MD, PhD; Anna Kowalczysz, MD, PhD; Bogumiła Czartoryska-Arlukowicz, MD; Barbara Radecka, MD, PhD; Bożena Jarosz, MD, PhD; Wojciech Biernat, MD, PhD; Jacek Jassem, MD, PhD; Department of Oncology, Military Institute of Medicine, Warsaw, Poland; Departments of "Clinical Research and "Oncology Research and Development," Monogram Biosciences—LabCorp Specialty Testing Group, South San Francisco, California; Departments of "Neurosurgery and "Neurosurgery and Children’s Neurosurgery Clinic, Medical University of Lublin, Poland; "Department of "Neurosurgery, Institute of Oncology, Warsaw, Poland; "Department of Oncology and Radiotherapy, Medical University of Gdañsk, Poland; "Department of Clinical Oncology, Białystok Oncology Center, Białystok, Poland; "Department of Clinical Oncology, Opole Oncology Center, Opole, Poland.

Context: H23D is the most potent signaling dimer of HER2. However, the lack of reliable methods to measure H23D has hampered establishing the clinical relevance of this biomarker. We have previously reported a quantitative H23D assay in matched primary tumors and brain metastases in breast cancer patients. Here, H23D levels in formalin-fixed, paraffin-embedded primary breast tumors were examined for correlations with clinical outcomes.

Design: The study included 52 advanced breast cancer patients administered chemotherapy, endocrine therapy, and/or trastuzumab. The bilateral breast specimens were accessioned, or (2) another breast case or a case fragment accidentally placed in the cassette, (3) misidentification of the whole specimen during accessioning, or (4) incidental malignancy. The correlation of H23D levels trended toward significance with shorter RFS (HR = 1.9; P = .06), and was significant with shorter OS (HR = 3.2; P = .007). Correlations were strongest in the HER2-negative subset (N = 41) for both RFS (HR = 2.9; P = .03) and OS (HR = 5.6; P = .003), independent of quantitative HER2 expression level. In a multivariate model containing H23D, HER2, and hormone receptor status, H23D was an independent correlate of both RFS (HR = 3.5; P = .02) and OS (HR = 6.5; P = .009) in the HER2-negative subset. HER2 in this subset did not correlate with RFS (P = .51) but did correlate with OS (HR = 4.4; P = .01).

Conclusions: Increased H23D levels correlated with shorter RFS and OS in the HER2-negative patients, independent of quantitative HER2 expression level. Further study is warranted to determine whether patients with HER2-negative tumors that express elevated H23D may benefit from HER2-targeted therapy.

Rosai-Dorfman Disease of the Breast: A Possible Mimic of Malignancy

(Poster No. 133)

Kunwar Singh, MD (kunwar.singh@mountsinai.org); Zachary Grimes, DO; Malary Mani, MD; Alexander Filatov, MD; Wen Fan, MD. Department of Pathology, Mount Sinai Health System, New York, New York.

Sinus histiocytosis with massive lymphadenopathy, also known as Rosai-Dorfman disease, is a rare benign clinical entity that is characterized by the proliferation of histiocytes within lymph nodes or, less frequently, extranodal sites. Along with fevers and chills, patients typically present with massive painless cervical lymphadenopathy. Rosai-Dorfman disease that is confined to the breast is an uncommon presentation. Here we present a 71-year-old woman with right breast asymmetry and no personal or family history of breast cancer. A mammogram was performed that revealed a 0.6 × 0.5 × 0.4-cm oval isoechoic mass located at 12:30N2 axis. Further evaluation with ultrasound-guided core biopsy was obtained. Histologic examination of the core biopsy revealed clusters of mature lymphocytes and plasma cells with proliferative areas of large histiocytic cells featuring abundant pale eosinophilic cytoplasm and atypical round vesicular nuclei. These proliferative areas separated the lymphoplasmacytic clusters forming a nodular infiltrate surrounded by fibroadipose tissue (Figure 52, A and B). Within these proliferative areas, lymphophagocytosis (emperipolesis) by the histiocytes was appreciated (Figure 52, C). An S100 immunohistochemical stain highlighted the phenomenon (Figure 52, D). Given the morphologic and immunohistochemical features, a diagnosis of Rosai-Dorfman disease was established. Our report aims to highlight the importance of considering Rosai-Dorfman disease as a...
**Lymphocytic Mastitis: A Clinical Pathologic Review**

*(Poster No. 135)*

Anam Naumaan, MBBS (anam_naumaan@rush.edu); Fatima Mir, MBBS; Shenon Sethi, MBBS; Ritu Ghai, MD; Paolo Gattuso, MD. Department of Pathology, Rush University Medical Center, Chicago, Illinois.

**Context:** Lymphocytic mastitis is a benign disease, characterized by dense intralobular, perilobular, and perivascular lymphocytic infiltrate, lobular atrophy, and fibrosis, which may clinically and radiographically mimic a primary breast malignancy. We report the clinical, radiographic, and histologic features of lymphocytic mastitis.

**Design:** The pathology files at our institution were reviewed from 1993 to 2017 for a diagnosis of mastitis, along with other systemic diseases in these patients, corresponding imaging, and the type of specimen sent for pathologic examination.

**Results:** A total of 61 cases were identified: 34 (55.7%) cases of granulomatous, 20 (32.8%) lymphocytic, 5 (8.2%) plasma cell, and 2 (3.3%) lupus mastitis. All cases of lymphocytic mastitis were in the age range of 27–70 years (mean: 44.5 years). Clinical information was available in 7 cases, of which 5 had a history of diabetes mellitus (2 also had hypothyroidism). Imaging was available in 11 cases, 10 (91%) of which were ill-defined hypoechogenic masses requiring biopsy, and 1 case showed an ill-defined area with a dilated duct, mimicking a primary breast malignancy on gross examination, and lymphoma histologically. Eleven cases were diagnosed on core biopsy (3 needed to be followed by a lumpectomy), 8 on lumpectomy, and 1 on mastectomy. Ancillary studies were necessary in 3 cases, confirming the diagnosis of lymphocytic mastitis and ruling out a lymphoma.

**Conclusions:** Lymphocytic mastitis occurs in patients with concomitant diabetes mellitus or other autoimmune diseases, which points toward an autoimmune cause. Lymphocytic mastitis also may mimic a primary breast neoplasm clinically and radiographically. Histologically, the main differential diagnosis is MALoma/marginal zone lymphoma, and can sometimes be difficult to differentiate.

**Upgrade Rate of Intraductal Papilloma Versus Atypical Papillary Lesions Diagnosed on Breast Needle Core Biopsy**

*(Poster No. 136)*

Ari Kassardjian, MD, PhD (akassardjian@mednet.ucla.edu); Cherish Meyerson, MD; Neda Moatamed, MD. Department of Pathology, UCLA, Los Angeles, California.

**Context:** Papillary breast lesions diagnosed on core biopsy pose a management predicament because these lesions are neither malignant nor premalignant; however, they require excision. This study compared the results of needle core biopsy with excision of pure intraductal papillomas (IPs) and atypical papillary lesions.

**Results:** A total of 61 cases were identified: 34 (55.7%) cases of granulomatous, 20 (32.8%) lymphocytic, 5 (8.2%) plasma cell, and 2 (3.3%) lupus mastitis. All cases of lymphocytic mastitis were in the age range of 27–70 years (mean: 44.5 years). Clinical information was available in 7 cases, of which 5 had a history of diabetes mellitus (2 also had hypothyroidism). Imaging was available in 11 cases, 10 (91%) of which were ill-defined hypoechogenic masses requiring biopsy, and 1 case showed an ill-defined area with a dilated duct, mimicking a primary breast malignancy on gross examination, and lymphoma histologically. Eleven cases were diagnosed on core biopsy (3 needed to be followed by a lumpectomy), 8 on lumpectomy, and 1 on mastectomy. Ancillary studies were necessary in 3 cases, confirming the diagnosis of lymphocytic mastitis and ruling out a lymphoma.

**Conclusions:** Lymphocytic mastitis occurs in patients with concomitant diabetes mellitus or other autoimmune diseases, which points toward an autoimmune cause. Lymphocytic mastitis also may mimic a primary breast neoplasm clinically and radiographically. Histologically, the main differential diagnosis is MALoma/marginal zone lymphoma, and can sometimes be difficult to differentiate.

**Atypical papillary lesion (n = 23)**

Invasive ductal carcinoma 4 (17.4)

Atypical papillary lesion (n = 23)

Invasive ductal carcinoma 3 (13)

**Phenotype From Surgical Resection**

<table>
<thead>
<tr>
<th>Diagnosis at Biopsy</th>
<th>Mean Age, y</th>
<th>Diagnosis at Resection</th>
<th>No. (%) of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraductal papilloma (n = 64)</td>
<td>51.6</td>
<td>Intraductal papilloma 44 (68.7)</td>
<td></td>
</tr>
<tr>
<td>Sclerosing adenosis 5 (7.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign breast, no residual papilloma 4 (6.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibroadenoma 1 (1.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADH/FEA + papilloma 6 (9.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DCIS 1 (1.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LCIS 1 (1.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Invasive ductal carcinoma 2 (3)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Phenotype From Core Biopsy and Subsequent Pathology From Surgical Resection**

<table>
<thead>
<tr>
<th>Diagnosis at Biopsy</th>
<th>Mean Age, y</th>
<th>Diagnosis at Resection</th>
<th>No. (%) of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign breast, no residual papilloma 2 (8.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sclerosing adenosis 1 (4.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraductal papilloma 1 (4.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADH/FEA + papilloma 5 (21.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DCIS 1 (4.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LCIS 6 (26.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Encapsulated papillary carcinoma 4 (17.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Invasive ductal carcinoma 3 (13)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Design:** Our internal database was retrospectively queried for patients who underwent needle core biopsy and a subsequent excision between 2013 and 2017. Patients without excisions were excluded.

**Results:** A total of 87 patients with needle core biopsies and subsequent excision were included in this study (Table). Sixty-four patients (mean age 51.6) were diagnosed with pure IP on core biopsy and 23 patients (mean age 68.6) were diagnosed with “atypical papillary lesion.” The diagnosis on excision for IP was as follows: IP = 44 cases
Significance of Lobular Neoplasm (Lobular Carcinoma In Situ and Atypical Lobular Neoplasm) as the Sole Finding on Breast Needle Core Biopsies

(Poster No. 137)

Monica Aldulescu, DO (Monica.Aldulescu@lumc.edu); Ayse Irem Kilic, MD; Bogdan Isaila, MD; Xiuzhen Duan, MD; Stefan Pambuccian, MD. Department of Pathology, Loyola University Medical Center, Maywood, Illinois.

Context: Lobular neoplasm (LN) as the sole finding on needle core biopsies is relatively uncommon and its significance is unclear/controversial. Furthermore, studies frequently lump these 2 findings (lobular carcinoma in situ [LCIS] and atypical lobular neoplasia [ALH]) together, making it even more difficult to understand their significance. The aim of this study was to determine the short- and long-term follow-up of patients with LN as the sole finding on their breast needle core biopsy (BNCB).

Design: We searched our department's electronic database in a 10-year interval. Cases diagnosed with LCIS and/or ALH were further studied and any follow-up within the study period was recorded. The results were compared with the follow-up results of patients diagnosed with atypical ductal hyperplasia (ADH) as the sole finding on BNCB during the same period.

Results: We identified 3886 BNCB sets. Thirty-one cases of LCIS and 26 cases of ALH served as the sole finding. A total of 128 cases showing ADH as the sole finding served as the control group. Same-site follow-up of patients diagnosed with atypical ductal hyperplasia (ADH) as the sole finding on BNCB during the same period showed an upgrade rate of pure IP to atypical low-grade malignancy was 6%. The upgrade rate for “atypical papillary lesions” diagnosed on core biopsy was 10 times higher (60.8%) compared with IP. Given an upstage rate of 15.4% for pure intraductal papillomas diagnosed on core biopsy, surgical excision is a reasonable course of action.

Conclusions: In the present study, the upgrade rate of pure IP to atypical low-grade malignancy was 6%. The upgrade rate for “atypical papillary lesions” diagnosed on core biopsy was 10 times higher (60.8%) compared with IP. Given an upstage rate of 15.4% for pure intraductal papillomas diagnosed on core biopsy, surgical excision is a reasonable course of action.

Immunohistochemical Microsatellite Instability Testing of Breast Biopsies as a Tool for Ruling Out Lynch Syndrome: A Case Report and Literature Review

(Poster No. 138)

Brian S. Finkelman, MD, PhD (brian.finkelman@northwestern.edu); Jennifer L. Pincus, MD; Luis Z. Blanco Jr, MD; Kalliopi P. Sziopikou, MD, PhD. Department of Pathology, Northwestern University Feinberg School of Medicine, Chicago, Illinois.

Lynch syndrome, a well-known familial cancer syndrome caused by mutations in DNA mismatch repair genes (MLH1, MSH2, MSH6, and PMS2), increases the lifetime risk of multiple malignancies, classically including colorectal, endometrial, and ovarian cancers. Recent research suggests that these patients may also have an increased risk for breast cancer, particularly with mutations in MSH6 and PMS2. We present a case of a 26-year-old woman with a breast mass at high risk for having Lynch syndrome (ie, a history of neuroblastoma at age 2 months and a mother with Lynch syndrome). Biopsy demonstrated invasive ductal carcinoma with mucinous features. A 1.6-cm, grade 2, ER/PR+, and HER2- invasive mucinous carcinoma was present in her subsequent mastectomy. One of 6 sentinel lymph nodes showed micrometastatic carcinoma without extranodal extension. Low axillary dissection showed 8 additional negative lymph nodes. Immunohistochemical microsatellite instability testing of the mastectomy specimen, performed because of the high suspicion of a Lynch syndrome association, demonstrated intact DNA mismatch repair proteins (Figure 54, A through D). This case illustrates the importance of identifying and testing breast cancer patients at high risk for Lynch syndrome because breast cancer may be an initial presentation. Testing can allow patients to start appropriate screening regimens for other Lynch syndrome–associated malignancies or, as in this case, to avoid unnecessary screening and monitoring. In summary, this case demonstrates the potential utility of microsatellite instability immunohistochemical testing in breast cancer patients with a personal and/or family history of Lynch syndrome–associated malignancy and should be considered in relevant clinical cases.

Encapsulated and Solid Papillary Carcinomas of the Breast: In Situ or Invasive?

(Poster No. 139)

Malvika H. Solanki, MD, MPH, PhD (malvikas03@gmail.com); Amanda F. Derylo, MD; Alexis M. Visitecky, MS; Julie M. Jorns, MD. Departments of 1Pathology and Laboratory Medicine, 2Radiology, and 3Biostatistics, Medical College of Wisconsin, Milwaukee.

Context: Classification of encapsulated papillary carcinoma (EPC) and solid papillary carcinoma (SPC) as in situ or invasive carcinoma has been debated. Recent studies have looked at the role of collagen IV (Col IV) and matrix metalloproteinases (MMPs) to help make this differentiation, but with variable results. We investigated the differential staining patterns of Col IV, MMP1, and MMP13 in cases of EPC and SPC with and without invasion.

Design: A retrospective database search (2007–2017) identified EPC/SPC cases (n = 49). Slides and reports were reviewed. Immunohistochemistry for myoepithelial cell (MEC) markers, Col IV, MMP1, and MMP13 were interpreted. EPC, SPC, and EPC/SPC with and without invasion were compared.

Results: Tumors comprised 41 (83.7%) EPC and 8 (16.3%) SPC. All EPC/SPC were estrogen receptor (ER) positive and most (46; 93.9%) were low/intermediate grade. Twenty-five (51%) had associated invasive carcinoma and 24 (49%) did not. EPC/SPC with invasion (17 of 25; 68%) was significantly associated with absence of MEC staining in EPC/SPC when compared with noninvasive (8 of 24; 32%) (P = .01). MMP1 and MMP13 showed differential staining in EPC/SPC without statistical significance. EPC/SPC with invasion had larger EPC/SPC (mean, 1.4 versus 1 cm) compared with noninvasive, without statistical significance. Col IV was absent or discontinuous in all cases.

Conclusions: Only absence of MEC in EPC/SPC was associated with invasion, supporting that MEC loss is an important step in EPC/SPC progression and that EPC/SPC may represent a lesion in transition from in situ to invasive carcinoma.

Breast Carcinoma Metastases to Thyroid Neoplasm: A Rare Tumor-to-Tumor Lymphovascular Metastasis

(Poster No. 140)

Xing Zhao, MD (xingzhao@creighton.edu); Ly Luu, MD; Dali Huang, MBBS; Seounghyug Kwon, MD; Guiyuan Li, MD, PhD. Department of Pathology, Creighton University, Omaha, Nebraska.

A 58-year-old postmenopausal white woman presented with an abnormal mammogram showing a mass in the left breast and...
lymphadenopathy in the right axillar. A CT scan also showed a left thyroid nodule and a left adrenal mass. She had a double mastectomy with bilateral axillary lymph node dissection and a bilateral salpingo-ooophorectomy, followed by chemoradiation therapy and Herceptin. After a thyroid fine-needle aspiration showed metastatic breast carcinoma (Figure 55, A and B), a partial thyroidectomy was also performed. The left breast mass was diagnosed as an invasive lobular carcinoma with metastasis to 11 of the left axillary lymph nodes. Five of the 9 right axillary lymph nodes, on the other hand, had metastatic ductal carcinoma with no known primary tumor in the right breast. The final pathologic staging was pT3 N3a and pT0 N2a for the left and right breast, respectively. Whereas the left adrenal mass was a paraovarian serous cystadenoma, the thyroid was diagnosed as a follicular adenoma (Figure 55, C) with no overt metastatic focus on routine histology. However, ER- and PR-positive tumor cells were found in the lymphovascular spaces of the adenoma (Figure 55, D) but not in the thyroid tissue. The woman’s recent genetic study showed CHEK2 gene mutation. Metastasis to a primary thyroid neoplasm is extremely rare. Cytology can sometimes offer advantages over resection specimens in identifying lymphovascular invasion or rare tumor cells. Clinically complicated multi-organ neoplasms should prompt genetic studies of the patient to guide future patient care.

Impact of the 2018 Revision to the American Society of Clinical Oncology/College of American Pathologists HER2 Recommendation Guideline

(Poster No. 141)

Gary Tozbikian, MD1 (gary.tozbikian@osumc.edu); Adlin Gordion-Arroyo, MS1; Debra Zynger, MD.1 Departments of 1Pathology and 2College of Medicine, the Ohio State University, Columbus.

Context: The proposed 2018 revision to the ASCO/CAP HER2 guideline raises the thresholds for categorizing a patient as HER2 positive. We evaluated how the proposed 2018 guideline will change HER2 rates in breast carcinoma diagnosed at our center.

Design: We reviewed a retrospective series of breast core biopsies with invasive carcinoma from 2014 to 2017, scored under the 2013 ASCO/CAP guideline (n = 1002). At our institution, HER2 immunohistochemistry (IHC) and fluorescent in situ hybridization (FISH) are simultaneously performed. In cases of intratumoral heterogeneity or an IHC equivocal result, FISH is routinely read in conjunction with the IHC. FISH is conducted counting a minimum of 50 nuclei. All cases were rescoring according to the proposed 2018 guideline. Concordance was reported by percentage and agreement by κ coefficient.

Results: Overall 10% of HER2 FISH cases were reclassified (κ = 0.79). HER2 FISH equivocal results were eliminated (9.6% to 0%; P < .001), with all becoming negative. The HER2 FISH rate decreased (12.5% to 12.1%; P = .79), with 0.4% reclassified as negative. For FISH reclassified cases, the HER2 IHC results were equivocal (67%), IHC− (32%), and IHC+ (1%). All IHC/FISH double-equivocal cases (6.6%) were reclassified as negative.

Conclusions: Our institution’s approach to HER2 testing with dual IHC/FISH testing, IHC mapping to guide FISH analysis, and FISH counting of >20 nuclei allows for an assessment of the impact of the proposed 2018 guideline on HER2 rates. Overall 6.8% of patients will be reclassified as HER2. The numbers of patients who will become ineligible for anti-HER2 therapy will increase by at least 0.3%, and will likely exceed that because of reduced repeat HER2 testing.

Dr Tozbikian is a member of the Genentech Speaker’s Bureau.

Gene Expression Analysis of Tumor-Associated Neutrophils and Macrophages in Triple-Negative Breast Carcinomas Among Different Ethnic Groups

(Poster No. 142)

Deborah Jebakumar, MD1 (Deborah.Jebakumar@BSWHhealth.org); Jian He, MD2; Kimberly Walker, MHA, MLS, MP (ASCP)CM; Arundhati Rao, MD; PhD1 1Department of Pathology, Baylor Scott & White Health, Temple, Texas; 2Department of Hematopathology, the University of Texas MD Anderson Cancer Center, Houston.

Context: Triple-negative breast cancers (TNBCs) are associated with robust immune response, including tumor-associated neutrophils (TANs) and macrophages (TAMs), which are associated with an increase in metastatic potential. We hypothesize that a differential gene expression will be evident among Caucasian (CA) and African American (AA) ethnic groups.

Design: The database was searched and 84 patients (42 AA and 42 CA) with TNBC were identified. Total mRNA was extracted (Qiagen) and the mRNA expressions of 770 breast cancer–related genes were quantitated and analyzed using nSolver Analysis software (V2.5), of which 30 were studied. CD68 immunohistochemistry was performed on tissue microarrays.

Results: IFITM1, IFN-γ, FOX-p3, CSF1, CSF2RB, CSF3R, SYK, and CD 40 LG showed statistically significant differences in expression between the 2 ethnic groups with P < .05 (Figure 56, A and B). CD68 immunohistochemistry showed increased TAMs as a component of tumor-infiltrating immune cells (P = .002) in the AA subset. The
differential expression of these genes correlated with an increase in metastasis \( P = .04 \) and recurrences \( P = .003 \) in the AA subset.

**Conclusions:** Our study identified statistically significant differential expression of immune cell infiltration markers that correlates with unfavorable outcomes. Notably, the increased expression of CTSS and CSF genes and the inverse correlation of IFN-\( \gamma \) and VEGF-C expression with outcome in the AA subset of TNBCs are possibly linked to increased angiogenesis and higher rates of metastasis. These genes could serve as useful biomarkers of outcome as well as therapeutic targets in the AA subset of TNBCs.

**Acinic Cell Carcinoma of the Breast: Report of a Rare Primary Breast Cancer Subtype**

(Poster No. 143)

Hilde G. Vardeh, MD; Eleanor R. Levin, MD; James L. Connolly, MD; Liza M. Quintana, MD (lmuquinta@bidmc.harvard.edu); Department of Pathology, Beth Israel Deaconess Medical Center, Boston, Massachusetts.

Primary acinic cell carcinoma of the breast is an exceedingly rare triple-negative subtype of breast cancer. Since the first case was reported in 1996, only 47 cases have been reported in the literature. Although the prognosis has generally been reported as favorable with an indolent course, reports of lymph node metastases, local recurrences, and distant metastases have been reported. We report a case of a primary acinic cell carcinoma in a 49-year-old woman with a history of contralateral lobular neoplasia. The patient presented with a new palpable mass. Clinical examination revealed a 3-4 cm fullness that was mobile to the chest wall. Mammography demonstrated tissue densities as well as grouped amorphous calcifications at middle depth within her breast. An ultrasound showed a conglomerate of 2 masses that measured 1.9 cm in greatest dimension with indistinct margins. Two core needle biopsies revealed an acinic cell carcinoma in a background of flat epithelial atypia with associated calcifications and lobular neoplasia. Microscopic examination demonstrated an infiltration of haphazardly distributed small, round glands with clear to amphophilic and granular cytoplasm (Figure 57, A). Occasional lumina contained eosinophilic secretions. The tumor cells demonstrated expression of lysozyme, S100 (Figure 57, B), and \( \alpha \)-antichymotrypsin (Figure 57, C). The cytoplasmic granules were PAS positive and diastase resistant. Additionally, p53 stain showed strong, diffuse staining, consistent with a mutant pattern (Figure 57, D). Stains for ER, PR, and HER2 were negative.

**Application of “Established” Criteria to 102 LG-CISAD Lesions**

<table>
<thead>
<tr>
<th>Dyscohesion( ^a )</th>
<th>Monotony( ^a )</th>
<th>Vacuoles( ^a )</th>
<th>Nucleoli( ^a )</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-LCIS, No. ( (% \text{ (n = 64)} )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 (23)</td>
<td>63 (98)</td>
<td>56 (88)</td>
<td>49 (77)</td>
</tr>
<tr>
<td>S-DCIS, No. ( (% \text{ (n = 38)} )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 (10)</td>
<td>36 (95)</td>
<td>28 (74)</td>
<td>30 (79)</td>
</tr>
<tr>
<td><em>P</em> value</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>.19</td>
<td>.55</td>
<td>.11</td>
<td>.1</td>
</tr>
</tbody>
</table>

\( ^a \geq 50\% \text{ of cells.} \)

**Synchronous Metastatic Pleomorphic Invasive Lobular Carcinoma of the Breast and Primary FIGO Grade 1 Endometrioid Adenocarcinoma of the Uterus: A Potential Mimicker of Dedifferentiation**

(Poster No. 145)

Qishi Yu, MBBS, MS (QYi@uwhealth.org); Paul Weisman, MD. Department of Pathology, University of Wisconsin, Madison.

Pleomorphic lobular carcinoma (PLC) is an aggressive form of invasive lobular carcinoma that, like conventional invasive lobular carcinoma, may metastasize to unusual sites including the endometrium. Furthermore, metastasis may occur decades after the primary diagnosis. As the cells of PLC typically lack intracytoplasmic lumina, exhibit rhabdoid morphology, and are characteristically negative for both E-cadherin and PAX8, metastatic PLC to the endometrium may mimic an undifferentiated endometrial carcinoma. The unusual scenario of PLC metastatic to a synchronous FIGO grade 1 endometrioid adenocarcinoma (mimicking a “dedifferentiated” endometrial carcinoma) would only compound this diagnostic problem. Here, we present such a case. A 65-year-old woman with a remote (17 years prior) history of breast cancer and 5 years of tamoxifen therapy presented with heavy vaginal bleeding. Endometrial biopsy revealed a FIGO grade 1 endometrioid adenocarcinoma. A subsequent polypectomy again revealed the FIGO grade 1 endometrioid adenocarcinoma, but also showed an adjacent dyshesive, E-cadherin-negative rhabdoid cell population (PLC). Based on immunohistochemistry, the PLC was negative for E-cadherin and PAX8, much like the undifferentiated component of a dedifferentiated endometrial carcinoma (Figure 58, A through C); however, the PLC was diffusely positive for GATA-3 (Figure 58, D). ER, and AE1/AE3—features that would be highly unusual for a dedifferentiated endometrial carcinoma. Additionally, mismatch repair proteins showed loss of MLH1 and PMS2 expression in the endometrioid adenocarcinoma, but retained expression in the PLC. The use of GATA-3, ER, cytokeratins, and mismatch repair protein immunohistochemistry may aid in the recognition of
metastatic PLC and avoid misdiagnosis of undifferentiated or dedifferentiated endometrial carcinoma.

Endosalpingiosis in an Axillary Sentinel Lymph Node Mimicking Metastatic Breast Cancer

(Douglas Allison, MD; Fei Chen, MD, PhD; Michael Bannan, MD; Pratibha S. Shukla, MD. Department of Pathology, NYUniversity Langone Health, New York, New York.

Axillary lymph node dissection can cause chronic pain, numbness, limitation of movement, and a risk for infection in approximately one-third of patients. Sentinel lymph node biopsy is associated with significantly reduced morbidity. Identification of carcinoma in sentinel lymph nodes may lead to axillary lymph node dissection. False-positive result can lead to unnecessary axillary node dissection associated with increased morbidity. Immunostain for cytokeratin is routinely used for highlighting micrometastasis in sentinel nodes. Endosalpingiosis, commonly seen in pelvic lymph nodes, is defined as heterotopic glands lined by benign fallopian tube–type epithelium with ciliated, nonciliated, and intercalated peg cells. It rarely involves supradiaphragmatic lymph nodes. We report the case of a 59-year-old woman with core biopsy–proven right breast invasive mammary carcinoma (NST) who underwent wire-guided lumpectomy and sentinel node biopsy. A few epithelial glands (Figure 60, A) lined by low-cuboidal columnar epithelial cells with absence of ciliation or intercalated peg cells are present in the capsule and parenchyma of the sentinel node. There is no cytologic atypia or mitoses identified. There are no myoepithelial cells surrounding the glands. The morphologic features of the glands are completely distinct from those of the invasive mammary carcinoma (Figure 60, B). Immunostaining was performed, and the glands were strongly positive for WT1 (Figure 60, C) and PAX8 (Figure 60, D) and negative for GATA3, CD10, calponin, and p63/SMM. The morphologic features and immunostaining pattern support benign Müllerian glandular inclusions rather than a metastatic carcinoma. Although a rare finding, it is important to be aware of the possibility of benign Müllerian glandular inclusions in axillary lymph nodes to avoid overdagnosis of metastatic carcinoma. The location and histologic features of the epithelial inclusions should be carefully examined, and immunostaining can be very helpful in differentiating Müllerian glandular inclusions from metastatic carcinoma.

Don't Belong Here:

Metastatic Colonic Adenocarcinoma in Breast

(Binny Khandakar, MBBS, MD; Roshan Mahabir, MD; Sharmila Ghosh, MD; Ammar Matloob, MD; Kunwar Singh, MD; Wen Fan, MD; Abdelsalam Sharabi, MD. Department of Pathology, Mount Sinai Health System, New York, New York.

Most breast malignancies are primary; metastasis to breast from extramammary site is extremely uncommon. Extramammary metastasis represents approximately up to 2%, whereas the incidence is about 6% in autopsy series; the variability represents inclusion and exclusion of hematologic malignancies. The majority of extramammary metastases arise from melanomas, rhabdomyosarcomas, lung, ovary, and prostate in males, excluding hematolymphoid malignancies. Metastasis to breast is usually seen in younger individuals (age range, 30–45 years),
The Micropapillary Subtype of Invasive Ductal Carcinoma of the Breast Is Underreported: A National Reference Laboratory Experience

(Paper No. 149)

Michael Balatico, MD

Context: The micropapillary subtype of invasive ductal carcinoma (IDC) has implications for both prognosis and fluorescence in situ hybridization (FISH) testing, and this special type of carcinoma has received attention from the College of American Pathologists (guideline, 2013). ARUP is a national reference laboratory that receives cases from across the nation for laboratory testing. Breast pathologists from the University of Utah report cases for appropriate testing in addition to evaluating internal cases and conducting research.

Design: We conducted a study of in-house breast cancer cases, overreads, and cases sent for FISH testing. Most cases were compiled by a single pathologist during prospective review, and some were retrospective. All cases demonstrated micropapillary features upon review. We recorded whether the original report included a mention of this subtype in the diagnosis.

Results: Seventy-six cases from 2015 to 2018 were found to have invasive ductal carcinoma with micropapillary features upon review by an experienced breast pathologist (REP). Two cases were excluded because the outside hospital diagnostic reports were not available. Cases were received from 27 institutions (large academic and community hospitals) from 19 states within the United States (New York, Pennsylvania, Virginia, Texas, Illinois, Indiana, Colorado, Utah, Wyoming, Wisconsin, Arizona, Michigan, California, Ohio, Florida, Maryland, Kentucky, New Hampshire, and Maine). Most cases were biopsies, but some were excisions or metastases, and one was a cytology case. Twenty-three outside reports (30%) diagnosed IDC with micropapillary features; the remainder did not.

Conclusions: Even when present, the micropapillary subtype of invasive ductal carcinoma is underreported up to 70% of the time from institutions across the country.
A Fine-Tuned Inception V3 Convolutional Neural Network Architecture Accurately Distinguishes Between Benign and Malignant Breast Histology

(Poster No. 152)

Devin R. Broadwater, MD (broadwaterdevin@gmail.com); Nathaniel E. Smith, MD. Department of Pathology, SAUSHEC, San Antonio, Texas.

Context: Convolutional neural networks (CNNs) have revolutionized the field of computer vision with impressive gains in accuracy on image recognition tasks within the past several years. Application of CNNs to diagnostic pathology has been minimal, however. Here, we demonstrate fine-tuning an Inception V3 CNN model with relatively few training images accurately and confidently distinguishes between various benign and malignant lesions of the breast.

Design: A total of 354 images of 4 classes of breast pathology, including benign lobules (154), duct ectasia (38), ductal carcinoma in situ (84), and invasive ductal carcinoma (78), were acquired. Images were randomly partitioned into training (80%) and validation sets (20%). The training set was used to fine-tune a customized fully connected layer on top of the Inception V3 CNN architecture using pretrained ImageNet convolutional layer weights. The customized FC layer contained a single 256-unit hidden layer and 4 final output units with softmax activation to output a probability distribution.

Results: The CNN showed 100% accuracy. Accurate prediction was defined as the model outputting its maximum probability prediction on the true class. Mean predicted probability of the true class over the entire validation set was 0.959 with a standard deviation of 0.105. Eighty-eight percent of validation images showed a predicted true class probability of ≥0.90. A single validation image showed a true class probability of less than 0.5 (0.486).

Conclusions: Fine-tuning the Inception V3 architecture provides a remarkably accurate and confident CNN model to distinguish between malignant and benign classes in breast pathology.

Oncotype DX Is a Laboratory Test

(Poster No. 153)

Nena C. Wendzel, DO, MS (nena.c.wendzel.mil@email.mil); Justin M. Wells, MD. Department of Pathology, Walter Reed National Military Medical Center, Bethesda, Maryland.

Context: Oncotype DX recurrence score (RS) is prognostic of recurrence and is predictive of benefit with chemotherapy in breast cancer. Clinicians often perceive this score as infallible, but it does not receive the intense scrutiny of other tests such as HER2 immunohistochemistry. We initiated a pilot project using the Magee score (MS) as a quality check before using RS for decisions.

Design: Patients with an RS had an MS calculated, compared, and presented at tumor board. Clinically significant mismatches were defined as a discrepancy of risk group that would result in different therapy recommendations. These triggered review of histology to ensure appropriate grading, IHC results, and that a representative section was submitted for testing.

Results: Sixteen specimens (62%) had matching MS and RS risk groups. Of 10 risk mismatches, 9 resulted in no change in treatment plan. One (4%) was considered significant (RS = 22 and MS = 11) as the patient would have been at least offered chemotherapy with a RS of 22 but not 11. Review confirmed low-grade morphology and ER and PgR H-scores of 300. Sections submitted for testing had limited tumor around biopsy change centrally, a known cause of falsely elevated RS. Upon discussion with Genomic Health, testing of the core biopsy was offered, which returned a RS of 9.

Conclusions: Our pilot study highlights that Oncotype DX testing without a quality plan may have inappropriately changed a patient’s care. As RS increases in importance with the AJCC 8th edition, we must educate our clinicians on possible risks and design ways to mitigate them.

Proper Immunohistochemistry Panel for Correct Diagnosis of Cytokeratin-Negative but P63- and GATA3-Positive Breast Malignancies

(Poster No. 154)

Amir Samani, MD (amirsamani@hotmail.com); Brian Olsen, MD; Manisha Lamba, MD; Nikolina Curcin, MD; Ginette Lajoie-Starkell, MD; Said Ismail, MD. Department of Pathology, William Osler Health System, Brampton, Ontario, Canada.

Context: Breast carcinomas are infrequently negative for low-molecular cytokeratins. Alternatively, high-molecular-weight cytokeratins, p63, and GATA3 may be helpful in proving the epithelial origin of these malignancies, including metaplastic carcinomas. Some carcinomas may be reactive only to p63 or GATA-3. Study of small core biopsies may be particularly challenging in this setting.

Design: Three cases of breast core biopsy with malignant infiltrating cells were identified. Cores showed round to spindle tumor cells with foci of pseudoglandular formation. By immunohistochemistry, tumor cells were negative for cytokeratins but positive for p63 and GATA3. Cytokeratin expression was seen in <1% of tumor cells with moderate intensity. All cases were negative for p40 (ΔNp63). Although it has been shown that p40 may be less sensitive than p63 in metaplastic carcinomas, the complete lack of staining for p40 is unusual. A second panel of immunostains including B- and T-cell markers (including PAX-5 and CD2/CD4) was used to investigate the possibility of lymphoma (Figure 64).
**Results:** Two breast lesions were ABC-type (CD10; Bcl6; MUM1) and germinal center-type B-cell lymphoma. One breast lesion was CD30-positive (T-cell) anaplastic large cell lymphoma.

**Conclusions:** GATA3 is normally expressed by a subset of T cells. In addition, lymphomas may express p63, whereas p40 is not known to be expressed. Expression of estrogen receptor has been shown in lymphoid cells. As breast carcinoma may be negative for cytokeratins and only express GATA-3 and/or p63, including lymphocyte markers in the immunohistochemistry panel is essential to reach a correct diagnosis.

**Fibroepithelial Lesions: Still a Diagnostic Conundrum in Breast Cord Needle Biopsies**

*(Poster No. 155)*

Lorraine Colon-Cartagena, MD (lorraine.coloncartagena@vcuhealth.org); Patricia Zot, MD; Bryce Hatfield, MD; Michael Idowu, MD, MPH; Valentina Robila, MD, PhD. Department of Pathology, Virginia Commonwealth University, Richmond.

**Context:** The diagnosis of fibroadenoma (FA) and phyllodes tumor (PT) can be rendered on core needle biopsy (CNB) when the classic features are present. However, a diagnosis of fibroepithelial lesion (FEL) is used when overlapping features are identified, often triggering surgical excision. The purpose of this study was to determine the positive predictive value of FEL on CNB, refine the evaluation of these lesions, and possibly reduce the rate of unnecessary surgical procedures and costs.

**Design:** We studied a retrospective cohort of 59 cases diagnosed as FELs on CNB between 2001 and 2017. We correlated the CNB and the surgical excision diagnoses and determined the proportion of cases diagnosed as FA, PT, or FEL.

**Results:** Altogether, 64.4% of FELs on CNBs were diagnosed as FA on surgical excision, and 27.1% were diagnosed as PT. A diagnosis favoring FA on CNB was corroborated on excision, with a positive predictive value of 88% (see Table). Our findings were independent of age, size, and radiologic contour of the lesions.

**Conclusions:** This study highlights that FEL lesions with predominant histologic features of FA have a high positive predictive value; therefore, they may be amenable to clinical follow-up, rather than surgical excision. However, lesions with no predominant histologic features of FA/PT warrant an excision.

<table>
<thead>
<tr>
<th>Correlation Between Core Needle Biopsy and Surgical Excision Diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis on Biopsy</td>
</tr>
<tr>
<td>Fibroadenoma</td>
</tr>
<tr>
<td>Fibroepithelial lesion (n = 36)</td>
</tr>
<tr>
<td>FEL, favor fibroadenoma (n = 16)</td>
</tr>
<tr>
<td>FEL, favor phyllodes (n = 7)</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

**Sentinel Lymph Node Biopsy for Patients With Ductal Carcinoma In Situ: Just in Case Versus Choosing Wisely**

*(Poster No. 156)*

Lindsey Flaker, BS; Ashley Holloman, MD* (ashley.holloman@bcm.edu); Jayne Paulson, MD; Jennifer Stumph, MD.* 1Department of Pathology, Michigan State University College of Human Medicine, Grand Rapids; 2Department of Pathology & Immunology, Baylor College of Medicine, Houston, Texas; Departments of 3Surgery and 4Pathology, Spectrum Health, Grand Rapids, Michigan.

**Context:** Surgical treatment following a diagnosis of ductal carcinoma in situ (DCIS) on breast biopsy often includes the choice to have a sentinel lymph node biopsy (SLNB) performed. SLNB involves increased costs and risks to the patient and requires careful consideration. The aim of this study is to compare the rate of positive SLNB with the lymphedema risk and added costs.

**Design:** A retrospective case review was performed on patients treated in the Spectrum Health Hospital System who had a breast core biopsy showing DCIS performed from January 1, 2011, to June 30, 2015, excluding patients with prior or concurrent invasive breast cancer. Risk analysis of SLNB procedure was obtained from the literature. Cost analysis was estimated using personal communication and CPT coding.

**Results:** Of the 449 patients meeting inclusion criteria, 131 had an SLNB performed at the time of surgical excision. Only 5 patients had a positive sentinel node (3.8%). The risk of lymphedema from an SLNB is reported to be 5.6%. The number needed to treat to find 1 positive sentinel lymph node is 26 patients, with an estimated cost of $65 000.

**Conclusions:** The low risk of a positive SLNB at 3.8% stands in contrast to the significant lymphedema risk for this procedure. Although performing a sentinel lymph node biopsy in patients with DCIS may provide benefit in a select few, the vast majority will be burdened with added cost and risk. Without a strong clinical suspicion for invasive carcinoma, routine performance of SLNB in patients with DCIS should be discouraged.

**Phyllodes Tumors of the Breast: Difficulties in Classification Utilizing the World Health Organization Criteria**

*(Poster No. 157)*

Liza M. Quintana, MD1 (lmquinta@bidmc.harvard.edu); Gabrielle E. Cervoni, MD; Dayna Neo, MPH; Michele Hacker, ScD, MSPH; Abram Recht, MD; Ranjna Sharma, MD; Stuart J. Schnitt, MD. 2Department of “Pathology, Surgery, Obstetrics, and Gynecology, and Radiation Oncology, Beth Israel Deaconess Medical Center, Boston, Massachusetts; 3Department of Pathology, Brigham and Women’s Hospital, Boston, Massachusetts.

**Context:** Phyllodes tumors (PTs) are uncommon fibroepithelial neoplasms, accounting for <1% of breast tumors. PTs are classified according to the World Health Organization criteria as benign, borderline, or malignant based on a combination of histologic features. However, some lesions are difficult to classify because they demonstrate features associated with more than one category. How often this is problematic has not been previously studied.

**Design:** We reviewed H&E sections of 69 PTs from 69 patients treated by breast-conserving therapy at a single institution from January 1, 2000, to June 30, 2015. Features used to classify PT as benign, borderline, or malignant were recorded individually for each case: tumor border, stromal cellularity, stromal atypia, mitotic activity, stromal overgrowth, and malignant heterologous elements.

**Results:** Of the 69 PTs evaluated, 37 (54%) had features from one category (30 benign, 7 borderline, 0 malignant). Three cases had malignant heterologous elements (liposarcoma), so were classified as malignant despite not meeting all criteria. Two cases met all criteria for malignant PT except well-circumscribed and focally permeative borders, respectively. Twenty-seven cases had features of benign and borderline PT and rare cases had features of malignant PT.

**Conclusions:** In a consecutive series of PTs from a single institution, nearly half of the cases (46%) had histologic features from more than one category (benign, borderline, malignant), thereby creating difficulties in classification. How best to classify PT with features that overlap 2 or more categories is problematic because it is unclear which feature(s) is the strongest driver of clinical behavior and should, therefore, be given more weight.

**Importance of Diagnosing Solid Papillary Carcinoma of the Breast for Surgical Management**

*(Poster No. 158)*

Dali Huang, MBBS (dalihuang@creighton.edu); Teddi Tubre, MD; Susan Ngung Kwon, MD, MPH; Wayne E. Fenka, MD; Agnes B. Colanta, MD; Nicholas E. Dietz, MD. Department of Pathology, CHI Health Creighton University Medical Center Bergan Mercy, Omaha, Nebraska.

**Context:** Solid papillary carcinoma (SPC) is rare, accounting for <1% of all breast carcinomas. It is classified into in situ and invasive carcinoma (World Health Organization 2012) but the precise distinction between these 2 remains difficult, especially on biopsies. However, it usually has an indolent course even if invasive, and patients with SPC may not require sentinel lymph node evaluation with an invasive component.

**Design:** We identified 4 patients with excision and sentinel lymph node biopsy for invasive SPC from our pathology database between 2016 and 2018, including 1 with bilateral disease. Histopathologic features from 5 excision specimens were reviewed.
**Results:** One specimen presented with nodular well-circumscribed mass grossly (Figure 65, A) whereas the other 4 were irregular masses or cystic. All specimens demonstrated solid nodules with cohesive, monotonous cells in “geographic jigsaw pattern” and intratumoral networks of fibrovascular cores, with 1 specimen showing extracellular mucin production (Figure 65, B). All specimens showed areas with absence of peripheral myoepithelial component on p63 and smooth muscle myosin (Figure 65, C). Four of 5 specimens were positive for synaptophysin and/or chromogranin (Figure 65, D). Sentinel lymph nodes biopsy was negative for all 5 specimens. The sections were stained with H&E and von Kossa stains. In a 15 minute scan, which guided the subsequent sectioning and cross-sectional images of paraffin-embedded samples at 15 µm resolution.

**Conclusions:** SPC rarely involves the lymph nodes, even in tumors with an invasive component, and sentinel lymph node biopsy may not be indicated for these patients. Our series showed no metastasis in 5 specimens, consistent with the indolent nature of the process. It is important to identify SPC on biopsy specimens, as it may prevent unnecessary sentinel lymph node evaluation.

**A Rare Case of Primary Leiomyosarcoma Arising in the Right Atrium**

(Poster No. 159)

Nadia Hameed, MD1,2 (nnameed@health.southalabama.edu); Krutika Patel, MD1; Monira Haque, MD2; John J. Lazarchick, MD.1

1Department of Pathology, University of South Alabama, USA Medical Center, Mobile; 2Department of Pathology, Mobile Infirmary Medical Center, Mobile, Alabama.

Primary cardiac leiomyosarcoma is an extremely rare tumor with an incidence rate less than 0.25% of all primary cardiac tumors. Leiomyosarcomas are highly aggressive tumors, with mean survival of 6 months after diagnosis. The most common site is the left atrium, followed by right atrium and ventricles. Although controversy exists regarding the optimal management, because of its rarity use of multimodal therapy has showed better outcomes. We present a case of an 81-year-old woman with abdominal pain and weakness, with past history of myocardial infarction, pulmonary embolus, syncopal episodes, and hypertension. Imaging studies revealed a heterogeneous mass occupying the right atrium with inferior vena cava obstruction, multiple pulmonary nodules, and liver lesions. Gross examination of the resection specimen showed a 7-cm tan-gray mucinous mass. Histologic examination showed neoplastic spindle-shaped cells, arranged in an interdigitating/fascicular configuration with areas of background myxoid change, with high-grade nuclear atypia. Mitotic activity was estimated at 24/10 high-power fields, with atypical forms. Focal apoptotic cells were present; broad bands of necrosis were not identified. The neoplastic cells were positive for vimentin, desmin, and smooth muscle actin and negative for S-100. Based on the histomorphology and immunohistochemical pattern, the tumor was diagnosed to be a high-grade cardiac leiomyosarcoma. Our case exhibits multiple unique presentations: a large primary leiomyosarcoma in an elderly woman in a rare location of right atrium, underlined by the presenting cardiac and respiratory symptoms. This case highlights the need for a definitive diagnosis in a rare entity to establish standardized management guidelines.

**Correlative Detection of Isolated Single and Multicellular Calcifications in the Internal Elastic Lamina of Human Coronary Artery Samples**

(Poster No. 160)

Han Wen, PhD1 (han.wen@nih.gov); Alejandro Morales-Martinez, BS2; Huoxun Xiao, PhD1; Thomas C. Larsen, BS3; Catherine P. Nguyen, BS1; Eric E. Bennett, MS2; Zu X. Yu, MD, PhD1; Alan T. Remaley, MD, PhD1; Boehm Manfred, MD, PhD1; Ahmed M. Gharib, MD1.1 National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland; 2Department of Bioengineering, University of California, Berkeley.

**Context:** Histopathology protocols often require sectioning and processing of numerous microscopy slides to survey a sample. Trade-offs between workload and sampling density means that small features can be missed. We identified a solution to this problem in the histology of coronary artery samples of a deceased HIV patient.

**Design:** We developed a prototype X-ray tomographic scanner dedicated to scouting for histopathology. It obtained depth-resolved cross-sectional images of paraffin-embedded samples at 15 µm resolution in a 15 minute scan, which guided the subsequent sectioning and microscopy. The sections were stained with H&E and von Kossa stains.

**Results:** Correlative tomographic and histologic images revealed 2 types of microcalcifications: scattered loose calcifications typically found in atherosclerotic lesions, and isolated focal calcifications in one or several cells in the internal elastic lamina and occasionally in the tunica media. Figure 66 is an example of the latter, showing level-matched tomography and histologic images (A and B), and magnified views where the calcification (arrows) is seen as an X-ray dense dot in C, and a dark spot by the von Kossa stain in D.

**Conclusions:** We speculate that the focal calcifications were the initiation of medial calcification linked to kidney disease, but rarely detected at this early stage because of their similarity to particle contaminants introduced during histologic processing. The dedicated tomographic scanner provided several-fold contrast to noise ratio in 1/11th the scan time of a commercial tabletop micro-CT. It is a step toward a dedicated scouting tool for routine use in pathology laboratories.

**Mucinous Adenocarcinoma of the Colon With Right Ventricle Metastasis in Lynch Syndrome**

(Poster No. 161)

Weimei Shi, MD, PhD (weimei.shi@bmc.org); Josefa Tan, MD; Carmen D. Sarita-Reyes, MD. Department of Pathology, Boston Medical Center, Boston, Massachusetts.
Primary cardiac tumors are rare, with metastasis being more common. Cardiac metastasis with right ventricular involvement by colorectal cancer is barely reported. We report a case involving a 75-year-old woman who presented with an ascending colon mass. The biopsy showed invasive moderately differentiated adenocarcinoma. Molecular studies showed loss of MLH1 and PMS2 and BRAF V600E mutation, suggesting Lynch syndrome. Subsequently, the patient underwent hemicolecotomy and Whipple procedure with resection of the duodenum. Histopathology showed mucinous adenocarcinoma, stage pT4b, pN0. After 10 months, the patient presented with shortness of breath and heart failure. A transthoracic echocardiogram revealed a large mass in the right ventricle almost completely filling the right ventricular outflow tract up to the level of the pulmonary valve, and a large pericardial effusion. The patient underwent an emergency open heart surgery with removal of tumor from the right ventricle and right ventricular outflow tract and drainage of large pericardial effusion. The right ventricle was full of tumor arising from the septum and extending into the right ventricular outflow tract. Histologic examination of the mass revealed metastatic adenocarcinoma consistent with primary colon cancer (Figure 67, A). Immunohistochemical studies demonstrated positive staining of tumor cells for CD20 and CDX2, and no staining for CK7 (Figure 67, B through D). No tumor cells were identified in the pericardial fluid. This case profiles mucinous adenocarcinoma of the colon with right ventricle metastasis, and should serve to broaden the differential diagnosis of cardiac tumors.

Fatal Lymphocytic Myocarditis Associated With Pembrolizumab Therapy: Emerging Cardiac Complications of Tumor Immunotherapy

David Carr, MD (dacarr@ucsd.edu); Jeenal Gordhandas, MD; Jonathan Lin, MD, PhD; Grace Lin, MD, PhD. Department of Pathology, UC San Diego, La Jolla, California.

Immune checkpoint inhibitors have shown promising results in the treatment of various tumors but have also been associated with a new class of adverse events termed immune-related adverse events (IRAEs). IRAEs can affect any organ system and range in severity from minor to life-threatening. We present a case of a 76-year-old man who experienced sudden cardiac arrest while undergoing pembrolizumab. Lymphocytic myocarditis is a rare side effect of immune checkpoint inhibitor therapy and the precise pathophysiology is uncertain. As such, identifying patients at increased risk is not yet feasible. It is crucial to maintain a high index of suspicion for IRAEs such as lymphocytic myocarditis, especially as immune checkpoint inhibitor therapy becomes more widespread.

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma With Scattered Hodgkin/Reed-Sternberg–Like Cells: A Clinically Important Differential Diagnosis From Overt Hodgkin Lymphoma Transformation

Debbie R. Walley, MD (darin@umc.edu); John Lam, MD; Sanka Jain, MD. Department of Pathology, University of Mississippi Medical Center, Jackson.

We present a rare case of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) with admixed Hodgkin/Reed-Sternberg (HRS)–like cells in a 63-year-old woman with known history of CLL/SLL. She presented with gradual worsening of right cervical lymphadenopathy and 60-pound weight loss. Computed tomography demonstrated adenopathy of right parotid and neck regions measuring 14.7 × 5.8 × 12.3 cm and extensive lymphadenopathy in the chest, abdomen, and pelvis. An excisional biopsy of the neck mass showed complete effacement of the lymph node architecture by a proliferation of small lymphoid cells, scattered proliferation centers (PCs), many
well-formed granulomas composed of histiocytes and giant cells, and scattered HRS-type cells (Figure 68, A and B). Flow cytometry showed a CD5+, CD19+, CD23+ B-cell population. Immunohistochemical stains with adequate controls were performed. The small lymphoid cells were LEF1 positive (Figure 68, C) and cyclin D1 negative. The HRS-type cells were positive for CD30, CD15, MUM1, and EBV-LMP-1 (Figure 68, D). Special stains for acid-fast bacilli and fungal organisms were negative. Two variants of CLL/SLL in the presence of HRS-like cells were recognized: isolated HRS cells in a background of CLL/SLL (Type I) and HRS cells in an inflammatory background typical of classical Hodgkin lymphoma (Type II). Type II variant is rare (0.4%–0.7%) and requires chemotherapy. Type I is rarer than type II and its significance is controversial. In a recent study, few type I cases progressed to type II. Overall, it is clinically important to differentiate type I variant from type II. Until further studies clarify the prognosis, type I variant necessitates close follow-up; however, chemotherapy is not currently warranted.

**Pseudo-Gaucher Cells in Association With Pediatric Hodgkin Lymphoma**

(Poster No. 3)

Okechukwu V. Nwogbo, MBBS1 (onwogbo@augusta.edu); Rebecca L. Larsen, DO1; Natasha M. Savage, MD1; Ashin Ameri, MD.2

1Department of Pathology and 2Department of Pediatrics, Hematology/Oncology Section, Medical College of Georgia at Augusta University, Augusta.

Gaucher disease is an autosomal recessive defect of the β-glucocerebrosidase enzyme resulting in an accumulation of β-glucocerebroside in macrophages, leading to increased blue cytoplasm with a “folded tissue paper” appearance (Figure 69, D). These cells are difficult to distinguish from pseudo-Gaucher cells by morphology alone, which are macrophages that have ingested cellular products because of rapid cell turnover (Figure 69, C). These cells are frequently seen in bone marrow aspirates of patients with chronic myeloid leukemia, but can also be seen, albeit more rarely, in association with plasma cell myeloma, acute lymphoblastic leukemia, and hemoglobinopathies. Herein, we present a case of pseudo-Gaucher cells in the staging bone marrow aspirate of a 15-year-old with classical Hodgkin lymphoma.

The patient presented with a 2-month history of right cervical lymphadenopathy. A lymph node biopsy revealed classical Hodgkin lymphoma; there was expansion of the interfollicular areas of the lymph node with numerous Reed-Sternberg cells (Figure 69, A) that expressed PAX-5 (dim), CD30, and CD15. A staging bone marrow evaluation revealed mild eosinophilia without evidence of lymphoma (Figure 69, B). Aspirate smears also revealed numerous Gaucher-like cells. Leukocyte β-glucosidase test revealed normal enzyme activity (14.7 nmol/h/mg), thereby ruling out Gaucher disease and confirming that these cells were pseudo-Gaucher cells. Treatment with adriamycin, bleomycin, vincristine, etoposide, prednisone, and cyclophosphamide (ABVE-PC) was started. This case represents an uncommon presentation of pseudo-Gaucher cells in the bone marrow aspirate of a pediatric patient with Hodgkin lymphoma, which has only been reported twice in the literature to our knowledge.
Familial Platelet Disorder and \textit{RUNX1} Mutation With Development of B-Lymphoblastic Leukemia

\textbf{(Poster No. 5)}

\textbf{Mara Banks, MD} (mbanks1@augusta.edu); \textbf{Diana Metry, MBCHB}; \textbf{Imran Ahmad, MD}; \textbf{Jeremy Pantin, MD}; \textbf{Natasha M. Savage, MD}. \textsuperscript{1} Departments of 1Pathology and 2Medicine (Hematology/Oncology), Medical College of Georgia, Augusta.

\textit{RUNX1} is a gene on chromosome 21q22 that encodes 1 subunit of a core binding factor that regulates expression of several genes that are critical for hematopoiesis. Familial platelet disorder with predisposition to acute myeloid leukemia (AML) and/or myelodysplastic syndrome (MDS) is an autosomal dominant disorder with unknown frequency. The clinical presentation is variable, but most patients have mild to moderate bleeding diathesis and increased risk of myeloid neoplasms. Herein, we report a case of familial \textit{RUNX1} mutation and associated bleeding diathesis with development of B-lymphoblastic leukemia (B-ALL). The patient is a 47-year-old white woman with history of bleeding diathesis (menorrhagia and excessive postsurgical bleeding) with normal platelet count and morphology. Platelet aggregation studies revealed absent aggregation with epinephrine and arachidonic acid and decreased secondary aggregation with adenosine diphosphate and collagen. Aggregation with ristocetin was normal. Platelet glycoprotein expression (GPIb and GPIlb/IIa) was normal. \textit{RUNX1} mutational analysis revealed c.159del c (p.S53Rfs* 19). After several years of follow-up, the patient presented with fatigue and pancytopenia. A bone marrow biopsy was performed (Figure 71, A and B), which revealed acute leukemia most consistent with B-ALL. The blasts expressed CD34 and TdT with very dim CD19, CD20 (subset; Figure 71, C), CD79a (subset), and PAX5 (subset; Figure 71, D) without MPO or CD3. Karyotype revealed 46,XX,der(7)t(1;7)(q12;q31); \textit{FLT3}-ITD mutation, which has been reported only once in the current literature. The patient was treated with hyper-CVAD followed by allogenic transplant from an unrelated donor. This case represents development of B-ALL in a patient with germline \textit{RUNX1} mutation, which has been reported only once in the current literature.

Liver Myeloid Sarcoma

\textbf{(Poster No. 6)}

\textbf{Sadia Sultana, MD} (ssultana2@houstonmethodist.org); \textbf{Josh A. Bowdler, MD}; \textbf{April Ewton, MD}; \textbf{Arthur W. Zieske, MD}. Department of Pathology, Houston Methodist Hospital, Houston, Texas.

Myeloid sarcoma (MS) is an extramedullary solid tumor mass consisting of myeloid blasts and is considered equivalent to acute myelogenous leukemia. MS involving liver typically demonstrates mass with predominant parenchymal and periportal infiltration. Here we present an interesting case of MS in a patient with history of glioblastoma who presented with hepatosplennomaligey and lymphadenopathy mimicking lymphoma. The pattern of hepatic involvement and clinical impression also was unusual for MS. Bone marrow biopsy and aspirate with cytogenetic and FISH studies were performed for pancytopenia. Subsequent liver biopsy was also performed because of hepatosplenomaligey and lymphadenopathy. Imaging showed lymphadenopathy; therefore, initial clinical impression was lymphoma, possibly hepatosplenomaligey. Bone marrow biopsy was hypercellular and diagnosed as MDS with 20q12, and \textit{RUNX1}IT1 copy gains were detected. Liver biopsy revealed normal hepatic architecture. However, the sinusoids were infiltrated with mononuclear cells. The majority of the cells showed open chromatin, prominent nucleoli, and abundant eosinophilic cytoplasm. The neoplastic cells were positive for CD45, CD43, CD56, and CD68. According to recent World Health Organization classification, infiltration of any site of the body by myeloid blasts in a patient with leukemia is not classified as MS unless it presents with tumor masses. Our case is diagnostically challenging because of atypical clinical presentation with unusual histomorphologic features without any mass lesion. Abnormal FISH study shows \textit{RUNX1}IT1, a gene that encodes a protein usually blocks hematopoietic differentiation. This protein is observed in many nonhematologic malignancies. Our patient had high-grade glioma and MS, which can be potentially related with \textit{RUNX1}IT1 mutation (Figure 72).

Anterior Mediastinal Collision Tumor Composed of Classical Hodgkin Lymphoma and Atypical Mantle Cell Lymphoma

\textbf{(Poster No. 7)}

\textbf{Alireza Salem, MD} (alireza.salem@bswhealth.org); \textbf{Mhair Dekmejian, MD}; \textbf{Tuan Tran, MD}; \textbf{John Krause, MD}. Department of Pathology, Baylor University Medical Center, Dallas, Texas.

A 60-year-old woman with an anterior mediastinal mass underwent incisional biopsy showing a lymphocytic infiltrate associated with compartmentalizing fibrosis and background histiocytes without significant eosinophils, neutrophils, or plasma cells. Evaluation was more challenging because of crush/cautery artifact and the fragmented nature of the biopsy. Occasional residual lymphoid follicles with expanded mantle zones were present. There were patchy loose collections of large atypical cells with prominent nuclei, some with binucleation and multinucleation reminiscent of Reed-Sternberg cells. Immunohistochemical stains showed these large atypical cells to be positive for CD30 and MUM1 and negative for CD3, CD5, CD15, CD20, PAX5, OCT2, BOB1, ALK1, TdT, BCL6, EBER in situ hybridization, and pancytokeratin. Although these findings were consistent with classical Hodgkin lymphoma, flow cytometry unexpectedly identified a distinct population of monotypic B cells with nonspecific immunophenotype (positive for CD19, CD20, and \lambda light chain and negative for CD5, CD10, CD11b, CD22, and CD23). Further immunohistochemical evaluation showed the expanded mantle zones and interfollicular small B-cell areas to be positive for BCL1 and SOX-11. A staging bone marrow biopsy during this workup showed similar monotypic B-cell infiltrates, and fluorescence in situ hybridization confirmed presence of \textit{IGH}/\textit{CCND1} t(11;14) gene rearrangement. The overall morphologic,
immunophenotypic, and cytogenetic features were diagnostic of a collision tumor composed of classical Hodgkin lymphoma and atypical CD5-negative mantle cell lymphoma, an unusual and unexpected combination. Although flow cytometry unsurprisingly missed the Hodgkin lymphoma component, it was instrumental in initially detecting the atypical mantle cell lymphoma component that may have otherwise been overlooked.

**Evaluating PTEN Expression Level in Relation to PI3K Inhibitor Response in Primary Diffuse Large B-Cell Lymphoma**

Hani Katerji, MD (hani_katerji@urmc.rochester.edu); Annalynn Williams, MS; Paul M. Barr, MD; Andrew G. Evans, MD, PhD. Department of Pathology, University of Rochester, New York.

**Context:** B-cell receptor signaling and downstream PI3K activation are critical to B-cell lymphoma survival. PI3K inhibitors are effective therapies, but response rates are variable. The tumor suppressor PTEN is a primary negative regulator of PI3K, and is variably expressed in lymphoma. We sought to determine if PTEN expression patterns in primary diffuse large B-cell lymphoma (DLBCL) correlate with clinical response to PI3K inhibitors.

**Design:** We identified 22 DLBCL patients treated with PI3K. Fifteen had FFPE tumor biopsies available for PTEN evaluation by immunohistochemistry (IHC). Intensity of cytoplasmic PTEN staining was scored semiquantitatively: 0 = negative; 1 = weak; 2 = moderate; 3 = strong. Correlations between PTEN expression and overall response rate, progression-free survival (PFS), and overall survival (OS) were examined by Fisher exact test and Kaplan-Meier analyses, respectively.

**Results:** IHC for PTEN demonstrated 6 negative (40%), 6 weakly positive (40%), 1 moderately positive (7%), and 2 strongly positive cases (13%). Comparing low expressers (score = 0–1) versus high expressers (score = 2–3), no correlation was observed with overall response rate (Table). PFS and OS were also not statistically different. Comparing high versus low expressers, median PFS was 65 days (95% CI, 44–241) versus 54 days (95% CI, 21–211; P = .78) and median OS was 289 days (95% CI, 230–289) versus 177 days (95% CI, 59–335; P = .51).

**Conclusions:** The lack of a significant correlation between PTEN expression and measured clinical outcome suggests decreased levels of PTEN in primary DLBCL may not be primarily responsible for the partial efficacy of PI3K inhibitors. Small sample size, however, limits these analyses, and larger group study is planned to corroborate these results.

<table>
<thead>
<tr>
<th>PTEN Expression</th>
<th>No Response, No. (%)</th>
<th>Response, No. (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>8 (66.7)</td>
<td>4 (33.3)</td>
<td>.51</td>
</tr>
<tr>
<td>High</td>
<td>3 (100.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
</tbody>
</table>

**Composite Lymphoma: Unusual Case Report**

Asha Sagee, MD1 (sagee@etsu.edu); Emily Patterson, MD, 2 Department of Pathology, East Tennessee State University, Johnson City, Tennessee; 3 Department of Pathology, Watauga Pathology Associates PC, Johnson City Medical Center, Johnson City, Tennessee.

Composite nodal Hodgkin lymphoma (HL) and marginal zone lymphoma (MZL) is uncommon, and when it does occur, it most frequently involves mucosal organs including the small intestine, thyroid gland, stomach, and lungs. Such composite HL and MZL cases are very rare as nodal primaries, with only very few cases reported. We report a case of a 67-year-old man who presented with left inguinal lymphadenopathy prompting excisional biopsy. Histologically, sections demonstrated nodal effacement by 2 abnormal lymphoid populations. The first population was characterized by small to intermediate-sized lymphocytes with a monocytoid appearance and expression of CD20, CD79a, Pax5, and CD15. The second population was characterized by large, transformed cells with morphologic features of Reed-Sternberg (RS) cells. The large cells expressed Pax5 (dim) and CD30 with negative or variable expression of CD45, CD20, CD79a, and CD15. These RS-like cells showed some association with the B-cell infiltrates, although they were more associated with a T-cell–predominant background. CD3 highlighted the small T cells that focally formed rosettes around the large neoplastic cells in keeping with a Hodgkin-like milieu. In summary, composite lymphomas are rare and can be diagnostically challenging to recognize and classify. They should be considered when 2 morphologically and phenotypically distinct malignant lymphoid populations are present. Because of the rarity of composite lymphomas, there is currently no standardized treatment, with therapeutic approaches dependent solely on the individual lymphoma subtypes.

**A Rare Case of Acute Myeloblastic Lymphoma With Deletion of 16q11.1 in an HIV Patient Treated With Highly Active Antiretroviral Therapy**

Faisal M. Huq Ronny, MD1 (fmhronny@hotmail.com); Mary Lynn Nierodzik, MD2; Mary Ann Perle, PhD, 3 Departments of 1Pathology and 2Medicine, New York University School of Medicine, New York, New York.

Abnormalities of chromosome 16q are commonly seen in myeloid neoplasms and usually involve a CBFB gene rearrangement. Cases with deletion of the long arm of chromosome 16 as a sole abnormality are rare. Reported breakpoints are variable and can include the entire long arm from 16q11.1 to the terminal end, or loss of smaller regions. We report here a case of de novo acute myeloblastic leukemia (AML) with del(16)(q11.1) as a sole abnormality in an HIV+ male on HAART. This 48-year-old HIV-positive man well controlled on Genvoya (CD4 600, undetectable viral load) presented to his primary care physician with continuous unexplained fatigue, cough, and red spots (petechiae) on lower extremities. CBC results were WBC 5.1/mL, Hgb, 8.1 g/dL; and platelets, 371/mL, with 33% blasts with Auer rods on peripheral smear.

Flow cytometry of the bone marrow aspirate revealed a large population of myeloblasts (75% of total events) that were positive for CD34, CD117, CD38, HLA-DR, CD33, CD13 (partial), CD64 (partial), and CMPO. Chromosome analysis of the bone marrow showed 46,X,Y,-del(16)(q11.1) in 16 of 20 metaphase cells; no additional abnormalities were detected. Metaphase and interphase FISH with a CBFB breakapart probe demonstrated absence of a CBFB gene rearrangement and confirmed a deletion. To our knowledge there are only a few reports of del(16)(q11.1) as a sole abnormality in myeloid neoplasms, including AML. Our case and the rare other reported cases suggest that this may be a recurrent aberration associated with AML. Additional cases are needed to further characterize this abnormality and provide prognostic information.

**Acute Monocytic Leukemia and Myeloid Sarcoma in a Patient With Usher Syndrome**

Cynthia Reyes Barron, MD (cynthia_reyes-barron@urmc.rochester.edu); Genevieve Crane, MD, PhD. Department of Pathology, University of Rochester Medical Center, Rochester, New York.

A 45-year-old woman with Usher syndrome and associated congenital deafness, progressive blindness due to retinitis pigmentosa, and latent autoimmune diabetes presented to the emergency department with generalized malaise, dizziness, and lower pelvic pain. A firm, friable posterior vaginal wall mass was found on examination. She was hyperglycemic and admitted to critical care for acute diabetic ketoacidosis. She developed progressive anemia and thrombocytopenia and her white blood cell count was elevated at 30.4 K/µL, initially attributed to infection after recent intrauterine device removal. The CBC prompted a peripheral blood smear review that showed 60% monocyctic blasts (Figure 74, A, ×100). Flow cytometry and bone marrow biopsy showed increased atypical monocytic cells (Figure 74, B, ×600) comprising 40% of total leukocytes with 24% immature forms and was diagnostic of acute monocytic leukemia (AML). Subsequent biopsy of the vaginal mass showed a myeloid sarcoma with a phenotype similar to that of the AML (Figure 74, C, ×20X; D, CD56 immunostain, ×600). Infiltration of the buccal mucosa/other sites was not well appreciated. Mutations in several genes including MYO7A, CDH23, USH2A, and CLRN1 are associated with Usher syndrome and are linked to function of auditory and visual systems. Although Usher syndrome is not known to be associated with increased risk of AML, mutations have been associated with AML arising out of MDS, and both CDH23 and USH2A have been associated with lymphoblastic lymphoma. This case includes an unusual presentation of myeloid
sarcoma involving the vaginal wall and a potential previously undescribed link between Usher syndrome and genetic predisposition to leukemia.

Flow Cytometric Detection of Recurrent Follicular Lymphoma With Leptomeningeal Involvement in a Cerebrospinal Fluid Sample With an Exceedingly Low White Blood Cell Count
(Poster No. 12)

Safina Hafeez, MD (safina.hafeez@hhchealth.org); Woo Cheal Cho, MD; Peter Shen, MD. Department of Pathology and Laboratory Medicine, Hartford Hospital, Hartford, Connecticut.

Follicular lymphoma is usually an indolent non-Hodgkin lymphoma that rarely involves the central nervous system (CNS). Flow cytometric detection of such lymphoma in cerebrospinal fluid (CSF), however, is often challenging because of the low cellularity and viability of CSF samples. Here, we report our experience in a 52-year-old man whose relapsed follicular lymphoma with leptomeningeal involvement was confirmed by flow cytometric analysis of CSF despite an exceedingly low white blood cell count. The patient had been in remission for 10 years following the initial diagnosis and subsequent therapy with rituximab. On recent restaging evaluation, however, the patient was found to have diffuse lymphadenopathies. Subsequent excisional lymph node biopsy showed involvement by recurrent follicular lymphoma (World Health Organization grade 2–3A, CD10+/A-restricted) for which chemotherapy was initiated. Following the fifth cycle of chemotherapy, he was found to have diplopia and left ptosis consistent with left third nerve palsy. Flow cytometric analysis of CSF (white blood cell count of 3/mm³) showed an abnormal B-cell population comprising 60% of total cells, which displayed CD10, CD19 (dim partial), CD45, and A restriction without definitive CD20 or CD5 (Figure 75, A and B). The findings were most consistent with CNS involvement by recurrent follicular lymphoma. To our knowledge, flow cytometric detection of follicular lymphoma cells in a CSF sample with such a low cellularity has not been previously described in the literature.

Acute Promyelocytic Leukemia With Cryptic PML-RARA Rearrangement
(Poster No. 13)

Christine A. Liang, MD (christine.a.liang@uth.tmc.edu); Jeff Conyers, MD; Lei Chen, MD. Department of Pathology, University of Texas Health Science Center at Houston.

Acute promyelocytic leukemia (APL) is an acute myeloid leukemia subtype with characteristic morphology and immunophenotypic features, as well as a unique chromosomal rearrangement. The PML/RARA (retinoic acid receptor α) fusion gene can be detected by cytogenetics, fluorescence in situ hybridization (FISH), or polymerase chain reaction. Remarkably, there are rare patients with undetectable PML/RARA by cytogenetic and/or FISH studies. We report a case of a 17-year-old male who presented with nausea and bloody vomiting. Head CT scan showed hemorrhage with concern for herniation requiring an emergent decompressive craniotomy. Laboratory results showed anemia, thrombocytopenia, and leukocytosis. Coagulopathy was illustrated by a positive DIC panel. Blast features (irregular nuclear contours and Auer rods) on peripheral blood smear were suggestive of APL, consistent with flow cytometric findings. The patient was immediately treated with all-trans retinoic acid and showed a good response. Cytogenetics and FISH studies on peripheral blood and bone marrow were negative for PML/RARA and variants. However, polymerase chain reaction detected PML/RARA fusion gene, making it a FISH-negative cryptic PML-RARA rearrangement. FISH studies can miss small cryptic insertions because of weak fluorescent signals. Reverse transcriptase polymerase chain reaction, Southern blotting, or direct sequencing can detect this hidden translocation. This case encourages clinicians to consider cryptic APL with “APL blast morphology and flow features,” despite negative preliminary cytogenetics and FISH studies. Furthermore, many APL patients present with life-threatening coagulopathy as the first clinical manifestation. A prompt diagnosis of APL and immediate treatment with all-trans retinoic acid are crucial to save a patient’s life.

Clinical Significance of MDS-Related Mutations in 114 Consecutive Cases of Unexplained Cytopenia
(Poster No. 14)

Kai Zhang, MD (kzhang1@geisinger.edu). Geisinger Medical Laboratory, Geisinger.edu, Danville, Pennsylvania.

Context: The diagnostic value of somatic mutations in myelodysplastic syndrome (MDS) is unclear.

Design: Next-generation sequencing profiling (56 genes) was performed and reviewed from 114 patients with unexplained cytopenia. The patients included those with nonclonal idiopathic cytopenia of unknown significance (n = 36), clonal cytopenia of undetermined significance (CCUS) (n = 23), and MDS (n = 52). MDS patients included MDSSLD and MLD (n = 23), RS (n = 9), MDSEB (n = 18) and del(5q) (n = 2) by 2016 World Health Organization classification.

Results: The Table shows comparison of frequency and the variant allele frequency (VAF) of various mutations between CCUS and MDS patients. One hundred percent of CCUS patients had mutations per definition (61% with 1 mutation, 26% with 2 mutations, and 13% with 3 or more mutations). Ninety-two percent of MDS patients had mutations (40% with 1 mutation, 23% with 2 mutations, and 37% with 3 or more mutations). Forty-four percent of MDSEB patients had p53 mutation versus only 12% of other subtypes of MDS patients. Eighty-nine percent of MDS-58 had SF3B1 mutation versus 2.3% in other subtypes of MDS and 22% in CCUS.

Conclusions: (1) More than 20 mutated genes are found in MDS and CCUS, and commonly mutated genes are TET2, ASXL1, DNMT3A, SF3B1, TP53, and U2AF1, with VAF for each one greater than 15%. (2) CCUS and MDS share similar clinical and molecular features suggesting a spectrum of diseases. (3) p53 mutation found in much higher frequency in MDSEB suggests its association with disease progression. (4) The finding of SF3B1 mutation helps diagnosis of MDS-58.
Increased pSTAT3 Expression in Classical Hodgkin Lymphoma Is Associated With Advanced Disease

(Poster No. 15)

Farhan Khan, MD (farhan.khan@wustl.edu); Friederike Kreisel, MD; Eric J. Duncavage, MD; Marianna B. Ruzinova, MD. Department of Pathology, Washington University, St. Louis, Missouri.

Context: Recent studies have shown that amplification of 9p24, containing Janus kinase 2 (JAK-2) locus, is associated with poor clinical outcome in classic Hodgkin lymphoma (CHL). JAK-2 recruits and phosphorylates signal transducers and activators of transcription (STATs). Relationship between expression levels of molecules affected by 9p24 amplification, such as pSTAT3, and clinical outcomes in CHL cases has not been established. We investigated the expression and prognostic significance of pSTAT3 expression in a cohort of CHL cases.

Design: We identified 70 cases of CHL seen in our institution between 2001 and 2011. Immunohistochemistry (IHC) for pSTAT3 (clone D3A7, Cell Signaling) was performed, with intensity and percentage of positive Reed-Sternberg cells scored independently by 2 pathologists. Staining intensity was scored as 0 (negative), 1 (weak), 2 (moderate), and 3 (strong). Averaged IHC results were correlated with survival using the Kaplan-Meier method, and statistical analysis was performed using the log-rank and Z score tests.

Results: Of 70 cases, 63 showed increased intensity ≥2. Increased pSTAT3 staining intensity was associated with advanced disease (stage III or IV) at presentation (P = .009). There was no significant association between increased pSTAT3 expression and progression-free survival.

Conclusions: Our study shows that increased intensity of pSTAT3 staining is associated with advanced stages of CHL. Additional studies involving larger cohorts of CHL patients are needed to fully evaluate the association between pSTAT3 expression and clinical outcome. Increased expression of pSTAT3 represents a potential therapeutic target in CHL patients presenting with advanced disease.

Abstracts
or solid organ transplant because of the differences in management and follow-up versus other B-cell non-Hodgkin lymphomas.

Mixed-Phenotype Acute Leukemia, T/Myeloid, With Variable Immunophenotype in Peripheral Blood and Bone Marrow

(Poster No. 18)

Natalya Hakim, MD (natalya.hakim@uky.edu); Melissa Kesler, MD; Amy Gewirtz, MD; Gerhard C. Hildebrandt, MD; Dava West Piecoro, MD. Department of Pathology and Laboratory Medicine, University of Kentucky, Lexington.

T/myeloid mixed-phenotype acute leukemia (MPAL) is a rare leukemia showing evidence of both T-cell and myeloid differentiation. Our case is that of a previously healthy adult presenting with pancytopenia and 40% circulating blasts morphologically resembling myeloblasts without Auer rods. At our institution, immunophenotyping of new acute leukemias is deferred to a forthcoming definitive bone marrow biopsy specimen. However, this patient presented on a weekend, so flow cytometry was performed on peripheral blood. This demonstrated blast expression of myeloid antigens (CD117, CD13, CD33, CD15, partial MPO) as well as cytoplasmic CD3. A bone marrow sample collected several days later showed no convincing blast cCD3 expression by either flow cytometry or immunohistochemistry. Peripheral blood was sent to a second flow cytometry laboratory where blast cCD3 expression was confirmed. A diagnosis of T/myeloid MPAL was rendered. Cytogenetic studies on marrow aspirate demonstrated 5q and 7q deletions and complex karyotype, including gain of multiple chromosomes. Next-generation sequencing on bone marrow and peripheral blood both showed TP53 mutation and 2 variants of unknown significance in TET2 and CREBBP. This case demonstrates how leukemias can show variable antigen expression in different sites (blood, bone marrow, lymph node/tissue). Although these variations are often trivial, sometimes there can be variable expression of a lineage defining antigen. In our example, the patient’s leukemia would have been subtyped as a straightforward acute myeloid leukemia had only bone marrow blasts been immunophenotyped. This allows for discussion regarding optimal blast immunophenotyping strategies; should more than one involved compartment be examined?

The Plague: More Than a Decade of Hematologic Data From the New Mexico Area

(Poster No. 19)

Sierra Musick, MD1 (sierra.r.musick.mil@mail.mil); David Lynch, MD2; Tracy L. George, MD3; Karissa Culbreath, PhD, D(ABMM). 3

1Department of Pathology, Brooke Army Medical Center, San Antonio, Texas; 2Department of Pathology, University of Utah, Salt Lake City; 3Department of Pathology, The University of New Mexico, Albuquerque.

Context: Since 1970, human infections with Yersinia pestis have been identified in 13 states in the United States, with the highest density in California, Colorado, Arizona, and New Mexico. In this series, we report the hematologic abnormalities associated with Y pestis infection in an endemic region of the Southwestern United States.

Design: This analysis included hematologic data on 9 patients with culture-confirmed Y pestis infection in the New Mexico area of the United States from January 2000 to November 2015. Three of the 9 patients had blood smears performed. Data was collected retrospectively in association with Tricore Reference Laboratories (Albuquerque, New Mexico).

Results: The 9 patients ranged in age from 10 to 78 years old (median, 57 years). Leukocyte counts were overall elevated with a median of 11.9 × 10^9/L (range, 5.5–56.5 × 10^9/L). The absolute neutrophil count was elevated in 7 of 9 patients with a median of 11.3 × 10^9/L (1.3–36.7 × 10^9/L) and platelet counts were overall decreased with a median of 100 × 10^9/L (40–269 × 10^9/L). The median hemoglobin was 15.6 g/dL (10.6–18.1 g/dL). On blood smear, neutrophils showed toxic changes. The characteristic bipolar staining pattern of the bacilli was observed on one smear (Figure 78).

Conclusions: Neutrophilia and mild thrombocytopenia without anemia were consistently seen, but this finding was not uniform. Although the hematologic aspects of Y pestis infection are often nonspecific, identifying the characteristic bacteria by microscopy can provide an early clue to the diagnosis. This case series serves to enhance knowledge of plague epidemiology in the United States and highlight the hematologic aspects of infection.

Acute Promyelocytic Leukemia With Unusual Morphologic Features and Cytogenetic Findings

(Poster No. 20)

Michael Moravek, MD (michael.moravek@lumc.edu); Moiz Vora, MD; Ameet R. Kini, MD, PhD. Department of Pathology, Loyola University Medical Center, Maywood, Illinois.

Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia associated with poor prognosis in the absence of therapy.
However, treatment with all-trans retinoic acid (ATRA) leads to a favorable prognosis. We present the case of a 55-year-old man who was admitted with pneumonia and was treated with antibiotics. He was also found to have significant leukopenia, leading to a bone marrow biopsy. The biopsy demonstrated a marked increase in cells with dispersed chromatin, coarse cytoplasmic granules, and absence of perinuclear halos suggestive of abnormal promyelocytes. However, these cells had round to oval nuclei and did not have the bilobed or coin-on-coin nuclear features typically seen in APL promyelocytes (Figure 79). APL is characterized by the presence of a specific t(15;17)(q24.1;q21.2) chromosomal translocation leading to the production of a PML-RARA fusion protein that arrests myeloid cells at the promyelocyte stage of development. However, cytogenetic studies of the bone marrow aspirate on our patient demonstrated an isochromosome derivative chromosome 17 designated as ider(17)(15;17). FISH studies showed presence of 3 PML-RARA fusion signals, instead of the typically seen 2 PML-RARA fusion signals. Because of the rarity of this entity, the response to ATRA therapy of ider(17)(15;17) APL compared with that of traditional APL has not been fully established. Although our patient has shown a good initial response to ATRA therapy, the long-term prognosis is unknown. Awareness of these unusual morphologic and cytogenetic features will facilitate an accurate diagnosis of these APL cases and clarify the optimal therapeutic regimen.

FLT3-ITD Mutated Acute Promyelocytic Leukemia With Isolated Central Nervous System Relapse

(Poster No. 21)

Vinita Kukkar, MD (vinita_asija@yahoo.co.in); Katalin Banki, MD; Robert Hutchison, MD. Department of Pathology, SUNY Upstate Medical University, Syracuse, New York.

Internal tandem duplication of the fms-like tyrosine kinase 3 (FLT3-ITD) correlates with poor-prognosis acute promyelocytic leukemia (APL). Isolated central nervous system (CNS) relapse is a rare event in APL. We describe a rare occurrence of FLT3-ITD APL with isolated CNS relapse. A 14-year-old adolescent male presented with bleeding, leukocytosis (107.5 K/μL) with 95% microgranular promyelocytes, and blasts in peripheral blood and bone marrow (Figure 80, A and B). Cyto genetic and molecular studies showed t(15;17). PML-RARA Bcr3 isoform with FLT3-ITD. Spinal fluid examination was not performed initially because of coagulopathy risk. Induction with ATRA and idarubicin resulted in morphologic and molecular remission. At the end of induction, lumbar puncture revealed CNS disease with karyotypic evolution and disease progression (Figure 80, C through E). Four months of ATRA and intrathecal chemotherapy failed to achieve CSF remission; however, systemic remission continued. CSF morphologic remission was later achieved with craniospinal irradiation. Soon after, he presented with CNS hemorrhage and treatment discontinued. The presence of leukemic cells in the CSF after induction suggests CNS involvement at the time of diagnosis. Persistence of leukemia in the CNS after several months of treatment, despite complete systemic remission, suggests that the CNS served as a sanctuary for the leukemic cells. Eradication of leukemic cells from the CNS is challenging with ATRA-based treatment alone. Preliminary studies suggest ATRA and FLT3 inhibitors synergize to eliminate FLT3-mutated leukemic cells. Patients meeting certain high-risk criteria including the presence of FLT3-ITD could benefit from FLT3 inhibitors as well as CNS prophylaxis.

CD25 in B-Lymphoblastic Leukemia

(Poster No. 22)

Intisar Ghleilib, MD1 (ighleilib@augusta.edu); Kristine Badin, MD; Jessica Hambrick, BS; Anand Jillella, MD; Natasha M. Savage, MD. Departments of 1Pathology and 2Medicine (Hematology/Oncology), Medical College of Georgia, Augusta.

CD25, also known as interleukin-2 receptor α chain, is encoded by the IL2RA gene. Along with the β (IL2RB) and the common γ (IL2RG) chain, it constitutes the high-affinity IL2 receptor. It is a transmembrane protein present on activated T cells, activated B cells, some thymocytes, myeloid precursors, and oligodendrocytes. Expression of CD25 is noted on numerous hematopoietic neoplasms including adult T-cell lymphoma/leukemia, as it is the receptor for HTLV-1, and numerous B-cell neoplasms. Moreover, aberrant expression of CD25 is part of the minor diagnostic criteria for systemic mastocytosis. Per the 2016 World Health Organization, expression of CD25 by B-lymphoblastic leukemia (B-ALL) in adults is “highly associated” with BCR-ABL1. Herein we report a case of CD25 positive B-ALL without BCR-ABL1. A 65-year-old man presented with leukocytosis and an absolute neutrophilia without eosinophilia. Many circulating blasts were seen. A bone marrow was performed. Flow cytometric immunophenotyping revealed a blast population expressing CD19, CD10, CD34, CD33, CD13 (dim), and CD25. CD20 was predominately negative. The marrow was hypercellular with predominance of blasts and adequate megakaryocytes with some clustering. Eosinophilia was not present. Cytogenetic studies did not identify BCR-ABL1, but rather t(8;22), consistent with BCR-FGFR1. The patient was treated with hyper-CVAD, but remission was not achieved. Less than 2 months after initial diagnosis, he succumbed to disease. CD25 expression is commonly associated with BCR-ABL1 in adult B-ALL. However, if not detected, another BCR fusion partner may be present, such as FGFR1 (Figure 81).

Mixed Phenotype Acute Leukemia Associated With t(8;12): Report of a Rare Case

(Poster No. 23)

Monira Haque, MD (mhaque@health.southalabama.edu); Nadia Hameed, MD; Jacek M. Polski, MD. Department of Pathology, University of South Alabama, Mobile.

Mixed phenotype acute leukemia (MPAL) is a rare form of acute leukemia comprising 2%–5% of all acute leukemias. B/myeloid MPAL is the most common form (about 59%), followed by T/myeloid MPAL. Herein we present a very unusual case of MPAL (T/myeloid) in a 5-year-old girl presenting with recent onset of low-grade fever, gingivostomatitis, and cervical lymphadenopathy. Blood smear showed
leukocytosis (WBC 3.15 x 10^9/L), anemia (hemoglobin 5.9 g/dL), and thrombocytopenia (platelets 36K/μL). Peripheral smear showed about 50% blasts. Bone marrow aspiration and biopsy revealed hypercellular marrow with 46% blasts. The blasts were medium-sized to large with fine to coarse chromatin and prominent nuclei, and few showed irregular nuclear contours. Few blasts demonstrated faint cytoplasmic granules. On flow cytometry, the blasts demonstrated strong and diffuse expression of CD13, CD33, MPO, CD2, cytoplasmic CD3, CD5, and CD7. The immunoprofile was consistent with MPAL (T/myeloid). Cytogenetic testing revealed an interesting finding: t(8;12)(q13:p13) ETV6/NCOA2. This translocation is very rare and has been reported in just 11 cases in the literature to date. It most often appears in childhood leukemia, particularly in T-cell acute lymphoblastic leukemia. Only 3 cases of MPAL with this rare genetic profile have been reported in literature. A prognostic significance of this rare translocation cannot be ascertained because of the rarity of its reported incidence. MPAL is a diagnostic and therapeutic challenge owing to its rarity and heterogeneity. The association of t(8;12)(q13:p13) in this case makes it interestingly unique and hence merits recognition.

An Anaplastic Thyroid Carcinoma With Associated Well-Differentiated Follicular Neoplasm or a Collision Tumor of Hematologic Neoplasm With Follicular Thyroid Neoplasm Component?

(Poster No. 24)

Xi Zhang, MD, PhD (xizhang1@montefiore.org); Yinhua Wang, MD, PhD; Xuejun Tian, MD, PhD. Department of Pathology, Montefiore Medical Center, Bronx, New York.

Collision tumor refers to the coexistence of 2 adjacent but histologically distinct tumor components at the same anatomic site. Collision tumor could pose a diagnostic challenge. We report a case of a 65-year-old woman who presented with a complex thyroid nodule by ultrasound studies and underwent thyroid lobectomy. Grossly, the nodule was capsulated, measuring 2.6 cm in greatest dimension. Microscopically, there were 2 distinct populations of atypical cells. One population was composed of pleomorphic, discohesive cells with prominent nuclei, irregular nuclear contours, some with multinucleation, with admixed mature plasmacytoid cells (Figure 82, A). The second population showed a microfollicular pattern with focal cytologic features of enlarged clear nuclei, some with nuclear grooves and occasional pseudoinclusions. (Figure 82, C). Immunoperoxidase study demonstrated that the first population was positive for p53 but negative for AE1/3. Further immunoperoxidase study showed a clonal plasma cell population that was positive for CD3, CD56, λ, CD43, CD45 (subset and weak), and MUM1 and negative for CD3, CD20, PAX5, CD30, BCL-1, PAX8, TTF1, thyroglobulin, synaptophysin, calcitonin, chromogranin, EBV, and S100. MUM1 was positive in the first population but negative in the second population of cells (Figure 82, B and D). The findings were consistent with a plasma cell neoplasm. The second population showed features consistent with noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP). Based on our knowledge, this is the first reported case for the thyroid involvement by a collision tumor of a plasma cell neoplasm with an NIFTP.

Myeloid Sarcoma of Small Intestine With Unusual Clinical Presentation and Presence of CBFβ (16q22) Rearrangement

(Poster No. 25)

Recep Nigdelioglu, MD (rcpnig@gmail.com); Ameet R. Kini, MD, PhD. Department of Pathology, Loyola University, Maywood, Illinois.

Myeloid sarcoma (MS) is characterized by proliferation of myeloid blasts outside the bone marrow. MS can involve any site of the body with various cytogenetic abnormalities. We report a case of a myeloid sarcoma in a 58-year-old woman with intestinal involvement and rearrangement of the 16q22 locus. The patient presented with 1 week of upper abdominal pain, nausea, and vomiting with no improvement. She had no recent travel or sick contact and past medical history noted hyperlipidemia and hysterectomy. Her complete blood counts were within normal limits. CT of her abdomen showed diffuse mural wall thickening of multiple proximal and mid jejunal small bowel loops and adjacent mesenteric hyperemia, suggesting acute infectious or inflammatory enteritis. A definitive mass was not seen. She underwent exploratory laparotomy and a segmental bowel resection was performed. Microscopic examination of the lesion revealed a heterogenous population of cells ranging from round to spindle shaped and possessing nuclei with dispersed chromatin. Immunohistochemical studies showed positivity for CD34, CD45, CD68, MPO, and lysozyme and negativity for keratin AE1/AE3, S100, desmin, and ALK-1. FISH with a dual-color break-apart probe specific for the CBFβ gene was consistent with rearrangement of the CBFβ (16q22) locus. Her bone marrow biopsy showed a normal bone marrow with no evidence of leukemia. The patient was given induction chemotherapy, which resulted in resolution of symptoms. This study demonstrates that MS can involve small intestine, and differential diagnosis should be considered in patients even when imaging analysis does not show presence of a mass (Figure 83).

Acquired Pure Red Cell Aplasia in an Infant Following Bone Marrow Transplant

(Poster No. 26)

Yonah C. Ziemba, MD (yonah.ziemba@gmail.com); Judith P. Brody, MD; Silvat Sheikh-Fayyaz, MD; Kalpana S. Reddy, MD. Department of Pathology and Laboratory Medicine, Hofstra Northwell School of Medicine, Lake Success, New York.

Pure red cell aplasia (PRCA) is an entity defined by normocytic anemia, severe reticulocytopenia, and marked decrease/absence of bone marrow erythroid precursors with preservation of other hematopoietic lines. Congenital PRCA presents in infancy as Diamond-Blackfan anemia, caused by ribosomal protein gene mutations. Acquired PRCA typically presents in adulthood and is idiopathic or caused by autoimmune diseases, viral infections, or thymomas. We present a 9-month-old male infant diagnosed with N-RAS mutated juvenile myelomonocytic leukemia who received a haploidentical bone marrow transplant (BMT). The donor and recipient were both O+. He received tacrolimus as prophylaxis for graft-versus-host disease and was
discharged after donor chimerism studies by FISH showed 98.5% donor cells. Two months later he was hospitalized for vomiting, CBC data showed only anemia (reticulocyte count 0.2%). FISH showed 69% donor cells. Bone marrow biopsy displayed trilineage hematopoiesis but markedly decreased nonmature erythroid precursors, consistent with PRCA. No evidence of parvovirus or increased blasts/monocytes was noted. The patient was successfully treated with red blood cell support and prednisolone. This is a rare case of noncongenital acquired PRCA in an infant, and also possibly the first reported case of PRCA secondary to ABO-mismatched BMT. Earlier PRCA cases due to ABO-mismatched BMT were attributed to antigen mismatch. Our case, with fully matched ABO-type BMT, implies a different mechanism for acquired PRCA, possibly tacrolimus related. This hypothesis is supported by reports of PRCA induced by tacrolimus in solid transplant patients. Thus, tacrolimus should be considered when PRCA follows any type of BMT.

**CD8**+ Breast Implant–Associated Anaplastic Large Cell Lymphoma: Immunophenotypic Characterization by Flow Cytometry

(Poster No. 27)

Katrina M. Collins, MD (katrina.collins@hhchealth.org); Joseph A. DiGiuseppe, MD, PhD. Department of Pathology, Hartford Hospital, Hartford, Connecticut.

According to the 2018 National Comprehensive Cancer Network Guidelines, flow cytometry of aspirated peri-prosthetic fluid is an essential component of the diagnostic workup of breast implant–associated anaplastic large cell lymphoma. However, few reports of breast implant–associated anaplastic large cell lymphoma characterize its immunophenotype by flow cytometry. We acquired flow cytometric data describing CD8+ cases are lacking. Here we report a case of CD8+ breast implant–associated anaplastic large cell lymphoma and describe its immunophenotype as determined by flow cytometry. A 50-year-old woman with a history of left breast cancer, treated with mastectomy and radiation therapy followed by breast reconstruction with silicone gel implants, presented with left breast swelling. Aspirated periprosthetic fluid contained large, pleomorphic cells with prominent nucleoli and cytoplasmic vacuoles, singly, in pairs, and in clusters, raising a differential diagnosis of recurrent carcinoma and lymphoma. Flow cytometry revealed a population of abnormal CD45−/CD8+ lymphocytes with high SSC, which were positive for CD30 and expressed several T-cell antigens (CD2, CD5, CD7, and CD8), but lacked CD3. Polymerase chain reaction demonstrated clonal T-cell receptor γ-chain rearrangement. By contrast, among 4 published cases of CD4− and CD4−/CD8+ breast implant–associated anaplastic large cell lymphoma characterized by flow cytometry, CD2, CD5, and CD7 were negative in 3, 4, and 4 cases, respectively. These results highlight a potential immunophenotypic differences between CD8+ breast implant–associated anaplastic large cell lymphoma and the more common CD4+ and CD4−/CD8+ examples of this disorder.

Automated Diagnosis of Lymphoma With Digital Pathology Images Using Deep Learning

(Poster No. 28)

Hanadi El Achi, MD (hanadi.s.elachi@uth.tmc.edu); Lei Chen, MD; Amer Wahed, MD; Nghia Nguyen, MD. Department of Pathology, University of Texas Health Science Center at Houston.

**Context:** Because of subtle differences in histologic findings between various types of lymphoma, initial microscopic assessment often presents a challenge to pathologists. Automated diagnosis applying machine learning algorithms to digital images would be helpful to assist pathologists. Recent studies showed promising results using machine learning to detect malignancy in whole slide imaging for breast, pulmonary, gastrointestinal tract, and prostate specimens. In our study, we applied deep learning to study 4 diagnostic categories in lymph node specimens and predicted the clinical outcome. We used a modified convolutional neural network algorithm as the machine-learning method to build a lymphoma diagnostic model for 4 categories: benign lymph node, diffuse large B-cell lymphoma, Burkitt lymphoma, and small lymphocytic lymphoma. Our software was written in R language and runs on Microsoft Windows 10 64-bit edition. We obtained digital whole slide images of hematoxylin and eosin–stained slides from 128 previously diagnosed cases (32 for each diagnostic category). Five representative images, 40 × 40 pixels in dimension, were taken for each case. A total of 640 images were obtained, of which 580 were used for training and 60 for testing.

**Results:** At the beginning, testing was performed for one image selected randomly at a time; accuracy was only 82%. However, combining 5 images to test every category showed excellent diagnostic accuracy of 100%.

**Conclusions:** We developed a novel digital pathology diagnostic model for 4 histology types of lymph nodes with excellent results. Our study provided a proof of concept for incorporating automated lymphoma diagnosis using digital microscopic images into pathology workflow to augment pathologists’ productivity.

**An Unusual Presentation of Diffuse Large B-Cell Lymphoma Arising in Primary Skeletal Muscle**

(Poster No. 29)

Krutika S. Patel, MD (kspatel@health.southalabama.edu); Jacek M. Polski, MD. Department of Pathology, University of South Alabama, Mobile.

Primary skeletal muscle lymphomas are exceedingly rare, with an incidence rate of less than 0.1% in lymphomas of the extremities. Diffuse large B-cell lymphoma (DLBCL) may present with extranodal disease in up to 40% of cases. DLBCLs are aggressive tumors, with heterogeneous presentation and variable therapeutic response and prognosis. Our case is a rare example of DLBCL arising in primary skeletal muscle without associated immunodeficiency. A 38-year-old man presented with a fixed, throbbing swelling of 6 months extending from the anterior upper thigh to knee. Staging PET scan revealed an FDG-avid 19.5-cm well-circumscribed isodense lesion, with central hypermetabolism, raising concerns for soft tissue sarcoma. Histology revealed diffuse dense proliferation of small to large lymphoid cells intermingled within skeletal muscle. Immunostaining of these tumoral cells demonstrated positivity for CD20, BCL2, and partly BCL6. Fifty percent of the tumor cells were strongly positive for Ki-67. Based on these histo-immunophenotypic features, the tumor was diagnosed as DLBCL, with non–germinal center type with relatively low proliferation index. Despite advances in imaging modalities, accurate diagnosis of soft tissue tumors remains a challenge. The therapeutic options for lymphomas are different from those for soft tissue sarcomas. An accurate International Prognostic Index is necessary for determining treatment and predicting outcomes of patients with aggressive lymphomas. Our case highlights the need for recognition of such rare clinical presentation and unusual localization of DLBCL for an early accurate diagnosis of such rare tumors.

**Coexistence of JAK2 V617F Mutation and BCR/ABL1 P190 Fusion in a Patient With a Remote History of Polycythemia Vera and Subsequent Development of Chronic Myeloid Leukemia: A Possible Acquisition of BCR/ABL1 Fusion on a JAK2 V617F Mutant Clone With Switched Phenotype**

(Poster No. 30)

Jenna McCracken, MD, PhD (jenna.mccracken@duke.edu); Endi Wang, MD, PhD. Department of Pathology, Duke University, Durham, North Carolina.

JAK2 V617F mutation and BCR/ABL1 fusion are 2 common oncogenic events resulting in myeloproliferative neoplasms. The 2 mutations are often mutually exclusive, with JAK2 V617F seen most frequently in polycythemia vera and BCR/ABL1 defining chronic myeloid leukemia. Although rare cases have been reported to possess both JAK2 V617F and BCR/ABL1, the clonal relationship of the 2 genetic events and their dynamic evolution has not yet been clarified. Herein, we report a case of JAK2 V617F-positive polycythemia vera that was stably treated for 13 years before acquiring the e1a2 BCR/ABL1 fusion resulting in phenotypic switch to chronic myeloid leukemia. Our female patient began treatment for polycythemia vera at age 52 with phlebotomy for 4 years before requiring hydroxyurea to control her increasing leukocytosis, then switched to ruxolitinib 7 years later because of splenomegaly. Thirteen years after initial diagnosis, she began to experience constitutional symptoms, with laboratory evidence of marked leukocytosis (31.5 × 10^9/L), mild anemia, and thrombocytopenia. Blood smear review demonstrated left-shifted neutrophilia, monocytosis (15%), and absolute basophilia. Quantitative RT-PCR for BCR/ABL1 detected the e1a2 fusion transcript (57% in reference to the control gene product). The (JAK2 V617F) mutant clone was detected in greater than 90% of cells. Together, these data suggest that the 2 mutations occur on the same clone. This case illustrates the acquisition of e1a2 BCR/ABL1 on a JAK2 mutant clone with phenotypic switch to a myelomonocytic variant of chronic myeloid leukemia. It remains to be investigated whether
preexisting JAK2 mutation drives neoplastic differentiation toward myeloid instead of B-lymphoblastic lineage.

**An Unusual Clinical Presentation of Burkitt Lymphoma as Interstitial Lung Disease**  
*(Poster No. 31)*

Ashley K. Volarić, MD (aek4@virginia.edu); Alejandro Gru, MD. Department of Pathology, University of Virginia, Charlottesville.

A 64-year-old man was referred by his pulmonologist for a lung biopsy in the setting of a 2-year history of interstitial lung disease and recent 3-month history of worsening shortness of breath, 10-pound weight loss, diffuse body aches, and night sweats. Chest computed tomography showed bilateral ground-glass and reticular opacities consistent with interstitial lung disease (Figure 84, A). Lung wedge biopsies demonstrated lymphomatous cells within the alveolar septi (Figure 84, A) composed of medium-sized lymphocytes with vesicular nuclei, prominent nucleoli, admixed tingible body macrophages, and several mitotic figures and apoptotic debris in a starry-sky pattern (Figure 84, C). Immunohistochemical workup revealed tumor cell positivity for CD20, CD10, Pax5, Bcl-6, C-myc, and Ki-67 with a high proliferation index (>95% of cells). Fluorescent in situ hybridization studies demonstrated C-myc rearrangement, supporting the diagnosis of Burkitt lymphoma with initial interstitial pulmonary involvement. Laboratory studies were significant for tumor lysis syndrome with a uric acid level of 13.9 mg/dL (reference range, 3.5–7.3 mg/dL), lactate dehydrogenase of 9535 units per liter (reference range, 125–250 U/L), and calcium of 14.2 mg/dL (reference range, 8.5–10.5 mg/dL). One round of aggressive R-CODOX chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, cyclophosphamide, and prednisone) was successfully administered, but in a week after hospital discharge, the patient became septic in the setting of neutropenia and died shortly thereafter. Burkitt lymphoma is an aggressive B-cell non-Hodgkin lymphoma that can rarely involve the lung parenchyma on initial clinical presentation, mimicking an interstitial lung disease.

**A Rare Case of Hodgkin Lymphoma Variant of Richter Transformation**  
*(Poster No. 32)*

Ly T. Luu, MD (lyluu@creighton.edu); Minh Mays, MD; Xing Zhao, MD; Guiyuan Li, MD, PhD. Department of Pathology, Creighton University, Omaha, Nebraska.

A 75-year-old man was diagnosed with small lymphocytic lymphoma/chronic lymphocytic leukemia (SLL/CLL) in September 2012. In January 2016, he had multiple new hypermetabolic nodes in the left supraclavicular lymph nodes involving the mediastinum, right hilum, and right supraclavicular region were seen on PET scan. Biopsy in the setting of a 2-year history of interstitial lung disease and recent 3-month history of worsening shortness of breath, 10-pound weight loss, diffuse body aches, and night sweats. Chest computed tomography showed bilateral ground-glass and reticular opacities consistent with interstitial lung disease (Figure 84, A). Lung wedge biopsies demonstrated lymphomatous cells within the alveolar septi (Figure 84, A) composed of medium-sized lymphocytes with vesicular nuclei, prominent nucleoli, admixed tingible body macrophages, and several mitotic figures and apoptotic debris in a starry-sky pattern (Figure 84, C). Immunohistochemical workup revealed tumor cell positivity for CD20, CD10, Pax5, Bcl-6, C-myc, and Ki-67 with a high proliferation index (>95% of cells). Fluorescent in situ hybridization studies demonstrated C-myc rearrangement, supporting the diagnosis of Burkitt lymphoma with initial interstitial pulmonary involvement. Laboratory studies were significant for tumor lysis syndrome with a uric acid level of 13.9 mg/dL (reference range, 3.5–7.3 mg/dL), lactate dehydrogenase of 9535 units per liter (reference range, 125–250 U/L), and calcium of 14.2 mg/dL (reference range, 8.5–10.5 mg/dL). One round of aggressive R-CODOX chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, cyclophosphamide, and prednisone) was successfully administered, but in a week after hospital discharge, the patient became septic in the setting of neutropenia and died shortly thereafter. Burkitt lymphoma is an aggressive B-cell non-Hodgkin lymphoma that can rarely involve the lung parenchyma on initial clinical presentation, mimicking an interstitial lung disease.

**A Rare Case of Coexistent JAK2 and CALR Mutations in a Young Patient With Essential Thrombocytopenia**  
*(Poster No. 33)*

Faisal M. Huq Ronny, MD, PhD (fmrhronny@hotmail.com); Naima Ismaii, PhD; Matija Snuderl, MD. 1Department of Blood Bank and Transfusion Medicine, Thomas Jefferson University Hospital Pathology, Philadelphia, Pennsylvania; 2Division of Molecular Pathology, New York University Langone Medical Center, New York, New York.

Essential thrombocytopenia (ET) is a rare clonal myeloproliferative neoplasm characterized by a persistent increase in the platelet count with hyperplasia of bone marrow megakaryocytes. Janus kinase 2 (JAK2) and calreticulin (CALR) are the most frequent mutations in ET. Although originally considered mutually exclusive, recent studies showed that JAK2 and CALR mutations can coexist in 4% of ET cases in 29- to 77-year-old patients. Interestingly, CALR mutations detected in these cases are mostly deletions. Only one case with a CALR 5 bp insertion was described in a 57-year-old man. We present a novel case of a younger patient, a 35-year-old man with no significant history and a newly diagnosed ET that had concurrent CALR 5 bp insertion and JAK2 V617F mutation. The peripheral blood showed marked thrombocytosis (1928 K/μL) with mild leukocytosis (13.4 K/μL). Karyotyping and FISH were negative. t(9;22) BCR-ABL1 fusion product was not detected by RT-PCR. Further molecular testing revealed the presence of JAK2 V617F point mutation and CALR 5-bp insertion with an approximate allele burden of 45/46%, consistent with the case described above. It is unclear if these mutations were present early in the disease, or if one or both were acquired at a later time point. Based on the allele burden, it is conceivable that 2 populations coexist and points to the possibility of 2 clinically coexisting disorders. Further studies are needed to establish the prevalence, characteristics, treatment response, and significance of this rare finding.

**Primary Vaginal T-Cell Lymphoma in a Patient With a History of Chronic Lymphocytic Leukemia:**  
*A Rare Case Report*  
*(Poster No. 34)*

Monira Haque, MD (mhaque@health.southalabama.edu); Leonel Maldonado, MD; Nadia Hameed, MD; Javier A. Laurini, MD; Jacek Maldonado, MD (mhaque@health.southalabama.edu); Leonel Maldonado, MD; Nadia Hameed, MD; Javier A. Laurini, MD; Jacek
Primary manifestation of non-Hodgkin lymphoma (NHL) in the female genital tract is extremely rare, accounting for less than 1% of all extranodal NHL. Among these, vagina is the most unusual location. Most vaginal NHLs are B-cell type, with less than 5 cases of primary vaginal peripheral T-cell lymphoma not otherwise specified (NOS) reported to date. We present a rare case of primary vaginal T-cell lymphoma diagnosed in an 84-year-old woman who was referred to our hospital with perineal pain and a 5.2-cm ulcerated lower vaginal mass. The patient had a history of chronic lymphocytic leukemia that was stable and being followed up. Peripheral smear revealed lymphocytosis with small mature lymphocytes (42,000/μL). Lymphadenopathy was not detected on CT scan. The clinical impression was that of a vaginal carcinoma, and a transvaginal biopsy was performed. Microscopic examination showed diffuse infiltration of lamina propria by medium-sized neoplastic cells with scant cytoplasm, irregular nuclear contours, vesicular chromatin, and prominent nucleoli. Immunohistochemically, the neoplastic cells displayed positive CD3, CD5, CD4, and CD30, focal positivity for CD15, and loss of CD8. The neoplastic cells were negative for CD20, ALK-1, PAX5, CD43, Bel-2, Bel-6, CD56, cytokeratin, and EBV-LMP1. Clinically, a diagnosis of primary extranodal peripheral T-cell lymphoma, NOS of the vagina, stage IE was established. The rarity of this diagnosis in a vagina, along with its occurrence in a patient with a history of preexisting chronic lymphocytic leukemia likely as a second, completely independent event, makes this case highly interesting and worth reporting.}

ExTRANODAL NONCUtANEOUS MATURE T-CELL LYMPHOMA: Common Laboratory Findings and Clinical Follow-up

(Mohamed Masoud, MD; Robin Williams, MT; Hongwei Ma, MD; Ming Xie, MD) Department of Pathology, Beaumont Health System, Troy, Michigan.

Context: Mature T-cell lymphomas (TCLs) are relatively uncommon and may involve lymph nodes, skin, and extranodal noncutaneous organs. Nodal TCLs often present as late-stage disease with unfavorable outcomes. Extranodal noncutaneous TCLs, however, may remain as localized disease with different treatment strategy and improved prognosis.

Design: This study is focused on the common laboratory findings in patients with extranodal noncutaneous mature TCL with clinical follow-up and compared with nodal TCLs.

Results: There were 9 patients, 5 men and 4 women (median age, 52 years; range, 33–96 years), including 1 extranodal T/NK-cell lymphoma, 1 ALCI, ALK-1 type; 1 enteropathy associated T-cell lymphoma (EATL); and 6 peripheral TCLs, not otherwise specified. All patients showed masslike lesions by clinical evaluations. Seven patients had abnormal CBC findings, including 6 anemia, 2 thrombocytopenia, and 2 leukopenia. TCR gene rearrangement studies were performed in 5 patients and all were positive for monoclonal TCR-γ. No patients showed concurrent bone marrow or lymph node involvement by either pathology and/or clinical studies. Four patients received chemotherapy. Five patients had no chemotherapy; 3 had a surgical procedure and 2 had conservative management only. Two patients died of disease and 7 patients were in remission or alive with disease.

Conclusions: Extranodal noncutaneous TCLs are more likely to be localized disease without systemic involvement. Anemia was the most common abnormal CBC finding, followed by thrombocytopenia and leukopenia. Clinical management is more variable with fewer patients receiving chemotherapy. Surgical treatment alone and conservative management were the treatment of choice in more patients with relatively favorable clinical outcome.

NONSECRETORY PLASMA CELL MYELOMA LACKING IMMUNOGLOBULIN LIGHT-CHAIN EXPRESSION

(Mohamed Mustafa, MD (mmanusfa@iuui.edu); Jiehao Zhou, MD, PhD. Department of Pathology, Indiana University School of Medicine, Indianapolis. A 70-year-old man presented with fatigue and shortness of breath. Physical and imaging study results were within normal limits. Complete blood count showed pancytopenia. Serum/urine protein electrophoresis and/or immunofixation demonstrated extensive myeloma involvement. Bone marrow biopsy showed numerous plasmacytoid cells replacing normal hematopoiesis.

Acute Myeloid Leukemia Without Maturation Demonstrates a Lineage Switch to Acute Megakaryoblastic Leukemia 16 Days After Induction Chemotherapy

(Comby A. Cantu, MD (comby.cantu@duke.edu); Lian-He Yang, MD, PhD; Endi Wang, MD, PhD. Department of Pathology, Duke University Health System, Durham, North Carolina.

Lineage switch is rare, with literature limited to case reports or small series. The majority of reported cases switch between B-lymphoblastic leukemia and acute myeloid leukemia (AML) involving MLL gene rearrangements in pediatric patients. Herein, we report an unusual case of AML without maturation (AML-M7) that converted to acute megakaryoblastic leukemia (AML-M7) by morphology and immunophenotypic profiling during induction chemotherapy. The patient was a 62-year-old man who presented with anemia, thrombocytopenia, and marked leukocytosis with 15% circulating blasts. Subsequent bone marrow biopsy showed 67% blasts (Figure 87, A) that were positive for CD13, CD33, CD117, and myeloperoxidase and negative for CD41, CD61, and Von Willebrand factor antigen (Figure 87, B). Cytochemistry revealed a normal male karyotype. The diagnosis of AML was made, and the patient received standard induction chemotherapy. Sixteen days after the induction, bone marrow biopsy demonstrated 35% blasts and proliferation of small, hypolobate megakaryocytes (Figure 87, C). The blasts were positive for CD41, CD61, and Von Willebrand factor antigen (Figure 87, D). The lineage was apparently converted to megakaryoblast (AML-M7). Cytochemistry detected a tetraploid clone, in addition to normal karyotype. Despite aggressive management, the patient expired 30 days after the induction. This case underwent an intramyeloid infiltration.
lineage switch that may suggest an existence of neoplastic common progenitor, probably at stage of committed myeloid progenitor or pluripotent stem cell, which generates a repertoire of heterogeneous subclones with various differentiation potentials. Certain subclones may resist the ongoing chemotherapy, and thus be selected. Lineage switch predicts insensitivity to conventional chemotherapy and heralds a dismal clinical outcome.

**Waxing and Waning Brain Lesions: A Case of Central Nervous System Involvement in a Patient With Mycosis Fungoides**

(Poster No. 38)

Bushra Nazir, MD\(^1\) (Bushra.Nazir@tuhs.temple.edu); Nadia Ali, MD\(^2\); Abir Mukherjee, MD\(^3\); Ashish Bains, MD. \(^1\) Departments of \(^1\)Pathology and \(^2\)Hematology/Oncology, Temple University Hospital, Philadelphia, Pennsylvania.

Mycosis fungoides (MF) is the most common cutaneous T-cell lymphoma. It has a protracted course and is generally confined to the skin. Central nervous system (CNS) involvement is exceedingly rare and almost always associated with an advanced stage or other sites of extracutaneous involvement. We report a case of a 70-year-old man with a diagnosis of MF established 4 years prior who presented with CNS lesions in the absence of peripheral blood or any other extracutaneous site of involvement. The patient was treated with topical steroids, nitrogen mustard preparations, phototherapy, and interferon. He presented with seizure disorder subsequent to the MF diagnosis (plaque stage) and imaging studies identified multiple scattered enhancing lesions in the brain, which on initial biopsy were nondiagnostic and thought to be inflammatory in nature. The lesions waxed and waned by MRI studies, but persisted. A repeat brain biopsy was nondiagnostic and thought to be inflammatory in nature. The lesions eventually resolved by concurrent radiation therapy and chemotherapy with temozolomide. A brief course of lomustine was initiated upon disease progression 1 year after diagnosis, but proved ineffective and was discontinued. Upon recovery of her peripheral blood counts, the patient began therapy with interferon. Following her second nivolumab therapy, she was admitted with persistent fever and worsening pancytopenia. Bone marrow examination revealed a markedly hypocellular marrow with a virtual absence of hematopoietic elements, consistent with acquired aplastic anemia. Comfort care measures were initiated, and the patient expired shortly thereafter. The present case expands the spectrum of immune-related adverse effects associated with immune checkpoint inhibitor therapy to include acquired aplastic anemia.

**Immune Checkpoint Inhibitor–Associated Acquired Aplastic Anemia**

(Poster No. 39)

Katrina M. Collins, MD (katrina.collins@hhchealth.org); Joseph A. DiGiuseppe, MD, PhD. Department of Pathology, Hartford Hospital, Hartford, Connecticut.

Despite the remarkable progress resulting from the incorporation of immune checkpoint inhibitors into the treatment of patients with cancer, the use of these agents has also led to the development of autoimmune disorders (termed immune-related adverse effects) involving virtually all organ systems. In the hematopoietic system, autoimmune hemolytic anemia, neutropenia, and thrombocytopenia have all been described. However, acquired aplastic anemia, which is thought to result from immune-mediated destruction of hematopoietic stem and progenitor cells, has not been documented pathologically in association with immune checkpoint inhibitor therapy. We present here a case of acquired aplastic anemia, which arose following treatment of recurrent glioblastoma multiforme with the PD-1 inhibitor nivolumab.

The patient was a 57-year-old woman who underwent surgical resection of a right temporoparietal glioblastoma multiforme (GBM) after being diagnosed by concurrent radiation therapy and chemotherapy with temozolomide. A brief course of lomustine was initiated upon disease progression 1 year after diagnosis, but proved ineffective and was discontinued. Upon recovery of her peripheral blood counts, the patient began therapy with interferon. Following her second nivolumab therapy, she was admitted with persistent fever and worsening pancytopenia. Bone marrow examination revealed a markedly hypocellular marrow with a virtual absence of hematopoietic elements, consistent with acquired aplastic anemia. Comfort care measures were initiated, and the patient expired shortly thereafter. The present case expands the spectrum of immune-related adverse effects associated with immune checkpoint inhibitor therapy to include acquired aplastic anemia.

**Unique Finding of 12q24.3 in Nodular Sclerosing Classical Hodgkin Lymphoma, Syncytial Variant**

(Poster No. 40)

Rebecca Levy, MD (ralevy@uams.edu); Jeanette Ramos, MD, Department of Pathology, University of Arkansas for Medical Sciences, Little Rock.

The nodular sclerosing subtype (NS) of classical Hodgkin lymphoma (CHL) is the most common; the syncytial variant (SV) of CHL-NS is an easily recognized morphologic finding. It has been suggested that SV patients may have a more aggressive disease. Recent larger studies have shown that the SV subgroup has a decreased complete response and shorter progression-free survival rates in comparison with the standard CHL-NS group. Prior cytogenetic studies focused on comparing CHL and Epstein-Barr virus (EBV) expression and showed EB-negative CHL had more complex karyotypes than EBV-positive CHL. The cytogenetic findings of SV have not been well established. We diagnosed 2 adolescent males with CHL-NS, SV with complex karyotypes. One patient presented with right neck lymphadenopathy and night sweats. The other presented with a left axillary mass and denied B symptoms. Both patients’ lymph node nodules showed classic morphologic features of CHL-NS, SV and were EBV negative. Their cytogenetic analysis showed complex karyotypes with hyperdiploidy, multiple aneuploidies, and independent chromosomal breakpoints (Table). The cases showed an unusual similarity of an aberrant 12q24.3 focus, which is most commonly seen in adenocarcinoma of the pancreas, ovary, breast, prostate, and lung. It has been identified in hematopoietic entities including acute myeloid leukemia, acute lymphoblastic leukemia, and inflammatory myeloid disorders. This is compelling evidence for further in-depth studies to analyze the cytogenetic findings of a large series of CHL-NS, SV and correlate the specific 12q24.3 cytogenetic findings with clinical outcomes.
Evaluation of HLA-DR Expression in Chronic Lymphocytic Leukemia

(Poster No. 41)

Sahar Nozad, MD1 (sehreno@yahoo.com); Justin Rueckert, DO2; John H. Lunde, MD.1 Departments of 1Hematopathology and 2Pathology, University of Vermont Medical Center, Burlington.

Context: Genetic abnormalities convey important prognostic information in chronic lymphocytic leukemia (CLL). HLA-DR, a widely used marker in the diagnosis of lymphohematopoietic disorders, is consistently positive in CLL. We studied the prognostic significance of the strength of HLA-DR expression by flow cytometry in CLL by comparing the results with the cytogenetic analysis of the same cases.

Design: A total of 159 cases of CLL from 7 consecutive years that had both flow cytometric and cytogenetic analysis performed were evaluated. The diagnostic sample types included peripheral blood, tissue, and bone marrow. For each case, the mean intensity of HLA-DR fluorescence by flow cytometry was recorded as a quantitative measure of expression strength. The cases were classified into 4 prognostic groups (good, good-intermediate, intermediate, and high risk) based on their cytogenetic findings. A Kruskal-Wallis test was used to compare the distribution of HLA-DR among these 4 prognostic groups.

Results: The Kruskal-Wallis test indicated a significant difference in the distributions of HLA-DR expression among the 4 prognostic groups (χ² = 12.0, P = .007). The good prognostic group had significantly higher levels of HLA-DR expression compared with the other 3 groups (median of 8.1 compared with median of 6.0, 5.7, and 4.6 in the other 3 groups).

Conclusions: This study shows that higher levels of HLA-DR expression in CLL is associated with a better prognosis, as defined by the cytogenetic findings. HLA-DR may potentially be applied as a prognostic marker to predict disease progression and overall survival.

Immunophenotypic and Hematologic Profile of Pediatric Acute Lymphoblastic Leukemia in the Philippines

(Poster No. 42)

Qareem Pido, MD; Evelyn Verana, RMT; Symonette Sandoval, MD; Raymundo Lo, MD; Daphne C. Ang, MD (daphnechuaang@yahoo.com). Department of Pathology, Philippine Children’s Medical Center, Quezon City, Philippines.

Context: Acute leukemia in the Philippines has a reported incidence of 109 per 100 000 and accounts for 47.8% of pediatric malignancies in the country. There is paucity of published reports on the incidence of pediatric acute lymphoblastic leukemia (ALL) subtypes and no previously published reports on pediatric ALL immunophenotyping in the Philippines.

Design: Hematologic parameters (complete blood count), bone marrow studies, and immunophenotyping by flow cytometry analysis were retrieved from 98 consecutive native ALL cases at Philippine Children’s Medical Center between January and December 2017.

Results: Of the 98 subjects, 87 (89%) had B-ALL and 11 (11%) had T-ALL. There were 63 (64%) males and 35 (36%) females, with a median age of 6 years (10 months–18 years). Among the B-ALL patients, the median hemoglobin, white blood cell count, platelet count, and bone marrow blasts percentage were 77.5 g/L, 17 × 10⁹/L, 37 × 10⁹/L, and 70%, respectively. Blasts were present in the peripheral smears in 54% of cases. Among the B-ALL cases, CD19, CD10, CD79a, and CD34 expression were seen in 86 (99%), 85 (98%), 82 (94%), and 74 (85%) of cases, respectively. The most common aberrant myeloid marker expressed was CD15 (47%). Among the T-ALL cases, CD10, CD5, CD25, CD34, and CD4 expression were seen in 10 (91%), 10 (91%), 8 (73%), 4 (36%), 6 (55%), and 2 (18%), respectively. Aberrant CD13 myeloid antigen expression was seen in 27% of T-ALL cases. No statically significant associations were found between aberrant myeloid expression and clinical and hematologic parameters.

Conclusions: The clinical, hematologic, and immunophenotypic profile of Filipino pediatric ALL patients predominantly conforms with the published data in Asia.
Diagnosis of hematolymphoid malignancies.

Emphasizing the importance of performing a comprehensive panel for keratin positivity in our case could be misleading in isolation, account for approximately 20% of primary effusion lymphomas. The expression support the diagnosis of PEL. EBV-negative PELs tend to markers (CD20, PAX5), the HHV8 positivity and lack of light-chain approximately 80%. Although plasmablastic lymphoma and anaplastic

expr

HHV8 by in situ hybridization. Ki-67 showed a proliferative index of 80%.

Expression of CD79a, AE1/AE3, calretinin, CK7, Napsin A, D2-40, MOC-31, TTF-1, CK-20, and cyclin D1, and also negative for κ and λ light chains and EBV by in situ hybridization. Ki-67 showed a proliferative index of approximately 80%. Although plasmablastic lymphoma and anaplastic meloma may also have expression of CD138 and lack other B cell markers (CD20, PAX5), the HHV8 positivity and lack of light-chain expression support the diagnosis of PEL. EBV-negative PELs tend to occur in older HIV-negative patients from HHV8-endemic areas and account for approximately 20% of primary effusion lymphomas. The keratin positivity in our case could be misleading in isolation, emphasizing the importance of performing a comprehensive panel for diagnosis of hemato lymphoid malignancies.

Central Nervous System Myelomatosis With Extended Survival in Relapsed Multiple Myeloma: A Case Report and Review of the Literature

(Poster No. 45)

Neda Wick, MD (neda.wick@phhs.org); Mingyi Chen, MD, PhD.
Department of Pathology, University of Texas Southwestern Medical Center, Dallas.

We report a case of a 51-year-old Hispanic man who was initially diagnosed with IgA λ monoclonal gammopathy. Four years later, he developed symptomatic lytic bone lesions and compression fractures. Bone marrow biopsy revealed plasma cell myeloma (70% of marrow cellularity) with multiple high-risk genetic abnormalities (1q rearrangement, monosomy 13, and t(4;14)). After radiation and chemotherapy with bortezomib/lenalidomide/dexamethasone, a bone marrow biopsy showed complete remission. Three years later, he was referred to the oncoology service because of concerns for recurrence and persistent neck pain. Magnetic resonance imaging revealed multiple enhancing intraxial lesions, with the largest measuring 19 × 16 mm (Figure 90, A and B). Additionally, multiple enhancing lesions were identified within the spinal cord at C6-7, T-11, and S1 levels. Cerebrospinal fluid cytology and flow cytometry confirmed myeloma involvement of the central nervous system, evidenced by numerous pleomorphic plasma cells (Figure 90, C). Thirteen months later, after receiving aggressive treatment with whole brain/craniospinal radiation and intrathecal cytarabine, he passed away because of systemic involvement and multi-organ failure. Central nervous system involvement is a rare (1-1%) complication of myeloma with a poor clinical outcome. The spectrum of presentation includes localized intraparenchymal lesions, solitary cerebral plasmacytoma, or central nervous system myelomatosis. High-risk genetic abnormalities, λ monoclonal myeloma, multi-organ involvement, plasma cell leukemia, and prior therapy are associated with increased risk of central nervous system involvement and poor prognosis.

HIV-Associated Epstein-Barr Virus–Positive Polymorphic Lymphoproliferative Disorder Resembling Posttransplant Immunodeficiency States

(Poster No. 46)

Mohammed Alghamdi, MD (Maalgh02@louisville.edu); Barina Aqil, MD. Department of Pathology and Laboratory Medicine, University of Louisville, Kentucky.

Polymorphic lymphoproliferative disorders associated with immunodeficiency or posttransplant have been a well-recognized entity. Very few reports of similar disorders have been described in association with HIV infection. We report a case of a 31-year-old HIV+ man who presented with generalized lymphadenopathy. Biopsy of the lymph node showed effacement of the architecture with numerous confluent clusters of transformed lymphoid cells of medium and large size admixed with plasmacytoid forms. There were also transition forms among the transformed cells and the plasma cells. Thus, there was a full range of plasmacytic differentiation. The κ and λ stains showed that all of the plasmacytoid forms in varying stages of differentiation were polyclonal and were strongly positive for CD79a, CD138, and MUM1. The CD30 stain was positive in the transformed lymphoid cells, some of which were EBV-positive. No clonal B-cell population was detected by flow cytometry. IGH rearrangement was negative by FISH. In conclusion, polymorphic B-cell lymphoproliferative disorders in association with HIV infection are comparable morphologically and molecularly to those arising after solid organ transplantation. As in the case of their polymorphic PT-LPD counterparts, their malignant status and relationship to monomorphic B-cell lymphomas remains uncertain.

Transient Stress Lymphocytosis Reveals the Underlying Monoclonal B-Cell Lymphocytosis

(Poster No. 47)

Abubaker Elshaik, MD (elshaik@bcm.edu); Reka Szigeti, MD.
Department of Pathology & Immunology, Baylor College of Medicine, Houston, Texas.

Transient stress lymphocytosis is a relatively uncommon reactive process. It typically associates with emergency medical conditions, such as cardiac emergencies, trauma, and life-threatening bleeding. Here we present a rare case of transient stress lymphocytosis in a patient with cardiac emergency revealing the underlying monoclonal B-cell lymphocytosis. A 66-year-old man was admitted with severe chest pain. A complete blood count showed lymphocytosis (WBC 18.02 × 10^9/L with 11.9 × 10^9/L [66.2%] lymphocytes). Because of the significant absolute lymphocytosis, the peripheral blood smear was reviewed, which showed small lymphocytes with clumped chromatin, along with the presence of smudge cells, suspicious for chronic lymphocytic leukemia/ small lymphocytic lymphoma. To further characterize these atypical lymphocytes, flow cytometric immunophenotyping was performed. A κ and λ double-negative small B cell population was identified coexpressing CD5 and CD23 (58% of total events = 4.8 × 10^9/L lymphocytes), consistent with monoclonal B-cell lymphocytosis with a chronic lymphocytic leukemia phenotype. Transient stress lymphocytosis usually presents with an absolute lymphocyte counts range of 4 to 13 × 10^9/L. It typically resolves within 24 to 48 hours after its onset without specific treatment for the lymphocytosis. In our case, the transient stress lymphocytosis triggered the morphologic review of the peripheral blood smear, which eventually resulted in the discovery of the underlying monoclonal B-cell lymphocytosis. This case highlights the importance of morphologic examination of peripheral blood smears with significant absolute lymphocytosis in the elderly population and the importance of flow cytometric immunophenotyping of suspicious cases for flow cytometric studies.

Novel Emergence of JAK2 V617F Mutation in a Patient With a Long History of Myelodysplastic Syndrome

(Poster No. 48)

Nicole Girard, MD (nicole.girard@hsc.utah.edu); Kristin H. Karner, MD. Department of Pathology, University of Utah, Salt Lake City.

JAK2 V617F mutations are classically associated with myeloproliferative neoplasms and less commonly with overlap syndromes with both
Mixed-phenotype acute leukemias (MPAL) with myelodysplasia-defining cytogenetic abnormalities represent a rare diagnostic subgroup that current World Health Organization guidelines recommend categorizing primarily as AML with myelodysplasia-related changes (AML-MRC), though it has recently been argued that because of the frequent response of MPAL to ALL-type induction regimens, these patients may be more appropriately categorized as a unique subset of AML with myelodysplasia-related changes. Here, we report the first documented case of MPAL with t(v;11q23.3) and a minor subclonal population harboring i(17q10), which is consistent with AML-MRC. The collection of additional data is warranted to better characterize the cytogenetic progression, clinical behavior, and treatment outcomes of these uncommon entities.

**A Rare Case of CD38-Negative Plasmablastic Lymphoma**

(Poster No. 51)

Aziv Azar, MD (avakaziv@yahoo.com); Sarika Jain, MD; John Lam, MD. Department of Pathology, University of Mississippi Medical Center, Jackson.

An 83-year-old man, positive for human immunodeficiency virus (HIV), presented with a 6-week history of an exophytic mass in the gingivobuccal sulcus tethered to the maxillary gingiva. Histologic sections of the biopsy showed squamous mucosa with a dense band of connective tissue. On closer inspection, there was a focus of diffuse infiltration of atypical cells with plasmacytoid features. These cells were negative for CD38 and expressed CD138, CD45, and CD79a. The Ki67 index was elevated at 70% (Figure 92, D). ALK and EBV stains were performed to rule out ALK-positive diffuse large B-cell lymphoma and plasmablastic lymphoma, respectively, and were negative. This case demonstrates an unusual clinical presentation of extramedullary plasmacytoma. Although most cases are considered cured after local therapy, the presence of an increased mitotic index in this case may portend aggressive disease.
Histioytic Sarcoma With Primitive Hematopoietic Differentiation: An Unusual Presentation

(Poster No. 52)

Fahad N. Khan, MD (fahad.khan1@mountsinai.org); Muhammad Qazi, MD; Adnan Mubashar, MD; Abdelsalam Sharabi, MD; Muhammad Sheraz, MD. Department of Pathology and Laboratory Medicine, Icahn School of Medicine at St Luke’s West Hospital Center, New York, New York.

Histioytic sarcoma (HS) is a rare neoplasm with a devastating prognosis. The diagnostic challenge is to effectively characterize such malignancies. Currently, the diagnosis strongly relies on immunohistochemistry. A limited, bonafide case series on HS has been reported and there are no standard therapy guidelines because of limited molecular and clinically actionable data in the literature. A 63-year-old white man presented with a history of chronic cough, night sweats, weight loss, intermittent fevers, and diffuse maculopapular rash. Initial workup revealed pancytopenia, teardrop RBCs on the smear, and elevated lactate dehydrogenase. Imaging revealed hepatosplenomegaly with multiple hypodense foci in the spleen and dense lesions at the Iliac crest. Bone marrow biopsy showed interstitial infiltration by large atypical cells with ovoid, irregular, indented, convoluted nuclei, vesicular chromatin, and prominent eosinophilic nucleoli, ample eosinophilic cytoplasm, giant cells, frequent mitosis, and apoptosis (Figure 93, A and B). Immunohistochemistry positivity for CD68 (Figure 93, D), CD163, CD14, CXCL13, CD43, BCL6, CD25, and focal punctate MPO staining (Figure 93, C) is consistent with marrow involvement by a primitive hematopoietic neoplasm of histioytic/myeloid derivation. Next-generation sequencing detects TP53 and MYD88 mutations with a variant of SF3B1. Further evaluation of the splenic densities has been advised for the ultimate tumor characterization. The patient, however, is currently undergoing curative intent chemotherapy with EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin), and showing relief of primary symptoms. This case highlights the challenging characterization of neoplasm(s) with no standard therapy and to our knowledge is the only case to be reported with bilineage differentiation.

Modified Surface-Fitting Algorithm for Whole Slide Imaging in Hematology

(Poster No. 53)

Yuefeng Yin, MS1 (13115109108@163.com); Minxin Chen, PhD2; Yimin Zhu, PhD3.1 Department of WS1, Bionovation Biotech Inc, San Diego, California; 2Department of Mathematics, Soochow University, Suzhou, China; 3Department of Nano-Biomedicine, Suzhou Institute of Nano-Tech and Nano-Bionics, Chinese Academy Sciences, Suzhou, China.

Context: Whole slide imaging (WSI), which needs to convert conventional glass slides to digital slides, is the most recent imaging modality being used by pathology departments. Currently, it takes a long time to get the satisfying digital images of blood smear, bone marrow, and other cytologic slides under a high-magnification lens for WSI because of the curved surface of the slide, which somehow limits the wide application of WSI. The precise estimation of the heights of random sites on slides could provide a powerful tool to improve the scanning speed without compromising the quality of images, especially under a high-magnification lens.

Design: The height of the standard measuring point of the curved-surface object to be measured is measured and calculated through the mathematical expression according to the measured coordinates of the standard measuring point of the standard curved-surface object as a template.

Results: The heights of random sites within the area (20 × 50 mm) restricted by 9 sites were calculated and the accuracy was within 0.2 μm. In the premise of ensuring the quality of images, it takes 90 seconds or less to finish one piece of ×100 oil-immersion WSI and its optical resolution was 0.1 μm, which is the fastest speed with the current rapid scanning technique under microscope.

Conclusions: The algorithm for measuring the height on the curved surface is well applied to an automatic microscopic scanning, particularly under a high-magnification lens, which makes the advantages of high imaging definition, high scanning speed, and automation of the system more outstanding.

Author Yin is an employee of and shareholder of Bionovation Biotech, Inc. Drs Chen and Zhu are consultants for Bionovation Biotech, Inc.
neoplasm or leukemia on a 2-year follow-up since stem cell transplant. This is a very rare case that presented with nodal deposits. Cytogenetic analysis is crucial in the identification of these cases. The case is presented in view of its rarity.

An Unusual Case of CD30-Positive Malignant Neoplasm Presenting as a Nasal Mass: A Challenge in Classification

(Poster No. 55)
Xi Zhang, MD, PhD (xzhang1@montefiore.org); Yanhua Wang, MD, PhD; Xuejun Tian, MD, PhD, Department of Pathology, Montefiore Medical Center, Bronx, New York.

CD30-positive hematologic neoplasm could be very challenging in diagnosis and further classification. Here we report a case of a 64-year-old woman presenting with a rapidly enlarging nasal mass. The sections showed diffuse infiltration of discohesive, small, intermediate- to large-sized atypical cells with irregular nuclear contours, some with eccentric nuclei, vesicular to fine chromatin, variable nucleoli, and moderate amounts of cytoplasm (Figure 95, A). Large areas of necrosis were seen. Initial immunoperoxidase study showed that the atypical cells were strongly and uniformly positive for CD30 (Figure 95, B). Subsequent immunoperoxidase study showed that the neoplastic cells were also positive for CD4, CD25, CD43 (Figure 95, C), CD99, and granzyme B (Figure 95, D) and negative for CD2, CD3, CD5, CD7, CD8, TIA1, ALK1, EMA, LMP1, CD34, TdT, CD56, CD57, MPO, CD20, PAX5, and CD79a. CD4, CD30, CD43, CD99, and CD25 could be positive in myeloid sarcoma and mature T-cell lymphoma. Lack of expression of myeloperoxidase and CD34 did not support the diagnosis of myeloid sarcoma and mature T-cell lymphoma. Absence of the common pan-T-cell antigens also could not render a diagnosis of T-cell lymphoma. Molecular study showed clonal gene rearrangement in the T-cell receptor T-β A, C and T-γ V9, V10, V11 regions. EBER in situ hybridization study and Western blot for human T-cell lymphotropic virus (HTLV) I/II were both negative. The major differential diagnoses included ALK-negative anaplastic large cell lymphoma (ALCL) and peripheral T-cell lymphoma, not otherwise specified. The strong CD30 positivity and the overall immunoprofile favored the diagnosis of ALK-negative ALCL.

Large B-Cell Lymphoma With IRF4 Rearrangement Involving the Orbit: An Unusual Presentation

(Poster No. 57)
Neha Gupta, MBBS (ngupta4@northwell.edu); Morris Edelman, MD; Peihong Hsu, MD; Xinmin Zhang, MD; Silvat Sheikh-Fayyaz, MD, Department of Anatomic Pathology and Laboratory Medicine, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, New Hyde Park, New York.

A 13-year-old adolescent boy presented with bruising and swelling of the left eye for 3 months. Imaging study revealed a left orbital lesion measuring 1.5 × 1.8 × 1.5 cm, with extension to the left nasolacrimal duct, which was suspicious for rhombomycosarcoma. The biopsy showed diffuse lymphoid proliferation of intermediate- to large-sized cells with irregular nuclei. There was no ‘starry-sky’ appearance or necrosis. Immunohistochemical staining revealed that the neoplastic cells were positive for CD20, CD79a, PAX5, BCL2, BCL6, CD10, MUM1, and CD43 and were negative for TdT (terminal deoxynucleotidyl transferase), cyclin D1, and CD5. Proliferative index was 90%. Fluorescence in situ hybridization study was negative for MYC-immunoglobulin H (IgH), BCL6, or BCL2-IgH gene rearrangement but was positive for IgH rearrangement and gain of BCL2. Further study with next-generation sequencing identified an IgH-IRF4 rearrangement. Based on these findings, a diagnosis of large B-cell lymphoma with IRF4 rearrangement was rendered. The patient received induction chemotherapy, followed
by a maintenance phase. Follow-up imaging study of the neck revealed no lymphadenopathy. Pediatric diffuse large B-cell lymphoma is more often of the germinal-center, B-cell-like type, with a high incidence of c-MYC translocation and rare t(14;18). Large B-cell lymphoma with IRF4 rearrangement is a new provisional entity occurring in children and young adults with good prognosis. It commonly involves the head and neck area with the Waldeyer ring being the most common site. The growth pattern may resemble follicular lymphoma or diffuse large B-cell lymphoma. Strong IRF4/MUM1 expression is seen in association with BCL6 and a high proliferative index, but patients lack MYC and BCL2 rearrangements. Our case is unusual for its clinical presentation.

**A Case of Rare Composite Lymphoma: Diagnostic Challenges**

(Poster No. 58)

Sandyharani Dasaraju, MD (sdasaraju@health.southalabama.edu); Roshanak Derakhshandeh, MD; Jacek Polski, MD. Department of Pathology, University of South Alabama, Mobile.

Composite lymphoma (CL) refers to the presence of 2 morphologically and immunophenotypically separate lymphoma components in the same tissue at the time of clinical presentation. There are few reports about composite follicular lymphoma (FL) and mantle cell lymphoma (MCL) in the literature. Here, we report a 70-year-old man who presented with sudden lower-extremity numbness and urinary retention. Imaging studies showed generalized lymphadenopathy. The patient underwent bilateral cervical lymph node biopsy. Microscopic sections of right and left cervical lymph nodes revealed the presence of abnormal follicles with irregularities and indistinct germinal center with more than 16 centroblasts in a high-power field. Abnormal follicles were positive for BCL2, BCL6, and Ki-67. Flow cytometry demonstrated more than 16 centroblasts in a high-power field. Abnormal follicles and neoplastic B cells coexisted in small lymphoma cells with both diffuse and nodular pattern. Moreover, FISH cytogenetic study revealed rearrangement of BCL-2, BCL-6, and trisomy 12. While cyclin D1 immunostain confirms the presence of mantle cell lymphoma, the cytogenetic study confirms the presence of follicular lymphoma. In conclusion, CL is not common and it needs meticulous examination of the lymph node to avoid missing this diagnosis. Our case emphasizes the importance of employing immunohistochemistry, cytogenetics, and molecular genetics with different techniques in making this specific diagnostic entity.

**Therapy-Related Early T-Cell Precursor Acute Lymphoblastic Leukemia**

(Poster No. 59)

Kirstin Bier, BS; Richard Hammer, MD; Katsiaryna Laziuk, MD (laziukk@health.missouri.edu). Department of Pathology and Anatomical Sciences, University of Missouri School of Medicine, Columbia.

The World Health Organization recognizes therapy-related myeloid neoplasms as a unique entity distinguished by prior iatrogenic exposure to various cytotoxic agents. Here we present the first case of early T-cell precursor acute lymphoblastic leukemia occurring post therapy for breast cancer. The patient was a 65-year-old woman with triple negative invasive ductal carcinoma treated with docetaxel and cytoxan with complete remission 10 years prior. She presented with generalized fatigue, weakness, right lower extremity swelling, and pain. CBC showed thrombocytopenia and 28% blasts while a bone marrow showed subtotal replacement by blasts. Flow cytometric analysis performed on blood and bone marrow revealed blasts with expressing bright CD34, CD56, CD7, moderate CD5, CD13, and CD33, heterogeneous CD11b, CD10, dim CD45, and dim to negative CD117, CD36, and CD61. The blasts were negative for CD15, CD16, CD33, HLA-DR, CD64, CD14, cMPO, TdT, CD22, and other related B-cell and T-cell antigens. This pattern is consistent with early T-cell precursor acute lymphoblastic leukemia. Chromosome analysis revealed 1q duplication, 7q deletion, and trisomy 8. Trisomy 8 and 7q deletion are often associated with therapy-related neoplasms. Next-generation sequencing showed mutations of NOTCH1, IDH2, and DNMT3A. Mutations of NOTCH1, IDH2, and DNMT3A have been related in early T-cell precursor acute lymphoblastic leukemia. Additionally, IDH2 and DNMT3A mutations are reported at a high frequency while NOTCH1 mutations are at a low frequency. To our knowledge, this is the first reported case of therapy-related early T-cell precursor acute lymphoblastic leukemia in a patient with a history of antitubulin and alkylating agent treatment.

**Incidental Diagnosis of Intravascular Large B-Cell Lymphoma in a Transplant Recipient**

(Poster No. 60)

Byron Barksdale, MD (bbarksdale@uwhealth.org); Daniel Fosythe, DO; Erin Brooks, MD; David Yang, MD. Department of Pathology and Laboratory Medicine, University of Wisconsin Hospitals and Clinics, Madison.

A 58-year-old woman received an allotopic liver transplant for nonalcoholic steatohepatitis-induced cirrhosis. Intravascular large B-cell lymphoma (IVLBCl) was subsequently identified within her explanted liver in a thrombus with immunohistochemical staining positive for CD20 (Figure 97, A through C). A hepatic biopsy one week later demonstrated involvement with IVLBCl and a cholestatic pattern of injury. Systemic therapy with rituximab and prednisone was initiated 2 weeks post-transplant, but more-aggressive chemotherapeutic regimens were not tolerated as she had severe leukopenia, infections, and worsening liver function. She developed anastomotic strictures and her condition steadily declined until she presented with ascending cholangitis and died 8 weeks after her transplantation. At autopsy, IVLBCl was identified only in her transplanted liver and was extravascular (Figure 97, D), in an area of extramedullary hematopoeisis. IVLBCl is a rare form of systemic non-Hodgkin lymphoma that proliferates within small vessels and often remains undiagnosed until autopsy. Its clinical course frequently leads to a rapid decline and demise. It may present with a myriad of symptoms and can mimic many other diseases. There are 2 common patterns of presentation in IVLBCl, a classical variant with neurological symptoms and a so-called Asian variant that presents with a hemophagocytic syndrome. Two other cases have been reported in liver transplant recipients, and one was successfully treated and survived disease free for at least one year after tolerating a more aggressive chemotherapeutic regimen. pathologists and transplant teams alike are advised to keep this diagnosis in mind when encountering atypical intravascular hepatic cellular infiltrates.

Subcutaneous Panniculitis-Like T-Cell Lymphoma

(Poster No. 61)

Hebin Song, MD (hebin.song@ahn.org); Yulin Liu, MD; Alok Mohanty, MD; Anna Balog, MD; Jan Silverman, MD. Department of Pathology and Laboratory Medicine, Allegheny General Hospital, Allegheny Health Network, Pittsburgh, Pennsylvania.

Subcutaneous panniculitis-like T cell lymphoma (SPTCL) is a rare cytotoxic T cell lymphoma accounting for less than 1% of non-Hodgkin lymphoma. The manifestations of this rare lymphoma may be variable at onset and mimic an infectious or autoimmune process, which potentially could cause a delay in diagnosis and treatment. A 56-year-old woman presented with a purple, painful plaque measuring 2 cm in diameter on the right lower back. There was no history of trauma or any other generalized symptoms and she was initially treated for cellulitis.
With increasing pain, erythema, and enlargement, and negative cultures over 2 months, she was referred to our tertiary/quaternary hospital. CT scan was performed and interpreted as showing cellulitis, and she was started on IV antibiotics and subsequently taken for surgical debri-
dement. The lesion grossly measured 11 cm × 5 cm, and histologic examination demonstrated a subcutaneous infiltration by atypical lymphoid cells. The histologic aspect was characterized by dispersed, hyperchromatic nuclei surrounded by pale, scant cytoplasm. The cells infiltrated the fat lobules with adipocyte rimming and granulomatous reaction, resembling a panniculitis. On immunohistochemistry stains, the cells were positive for CD3, CD8, CD43, and TIA and negative for CD4, CD30, CD56, and EBV, diagnostic for SPTCL. SPTCL is a rare cytotoxic T-cell lymphoma representing less than 1% of all non-Hodgkin lymphomas that could be potentially misdiagnosed as a benign process. Therefore, early diagnosis of this rare malignancy is crucial in expediting appropriate treatment and better survival.

**The Important Role of Pathology in the Diagnosis of Hemophagocytic Lymphohistiocytosis**

*(Poster No. 62)*

Hongzhi Xu, MD, PhD (hxu@lsuhsc.edu); Guillermo Herrera, MD; Eric Wei, MD, PhD. Department of Pathology and Translational Pathobiology, Louisiana State University Health Science Center, Shreveport.

**Context:** Hemophagocytic lymphohistiocytosis (HLH) is a syndrome characterized by excessive activation of the immune system. The diagnostic criteria, originally studied in the pediatric population, are yet to be validated in the adult population, especially in acquired HLH.

**Design:** In this retrospective study, we analyzed 11 cases in our institution during the last 10 years. Clinical presentations and laboratory results, histopathology, immunohistochemistry, flow cytometry, and cytogenetics of each case were studied.

**Results:** Male to female ratio was 1.7:1 with median age of 31 years. Six cases were associated with autoimmune diseases, 3 cases were associated with malignancies, and 2 cases were associated with viral infection. Average time from the onset of symptoms to diagnosis was 3.5 days. Clinical and laboratory findings included fever (90%), skin rashes (30%), lymphadenopathy (35%), hepatomegaly (60%), neurologic symptoms (20%), cytopenia (75%), hypertriglyceridemia (40%), elevated serum ferritin (40%), elevated CD25 (10%), and low NK cell activities (35%). All cases have hemophagocytosis (in bone marrow, lymph node, skin, and liver). Only 10% of patients meet the diagnostic criteria suggested by HLH-2004 trial. In our study, using criteria of 2 clinical symptoms combined with positive hemophagocytosis, 100% of cases were detected.

**Conclusions:** We found the diagnostic criteria suggested by HLH-2004 trial are neither sensitive nor specific. However, if 2 clinical symptoms combined with hemophagocytosis, it yields a better result. Because of a high mortality rate for HLH, a prompt, accurate diagnosis is required. For those with clinical suspicion, an early biopsy for pathological study is highly indicated.

**Surprise Finding After Workup of IgM Monoclonal Gammapathy**

*(Poster No. 63)*

Bhunesh Maheshwari, MD (bhunesh.maheshwari@uhospitals.org); Satyapal Chahar, MD; Rose Beck, MD, PhD. Department of Pathology, University Hospitals Cleveland Medical Center, Cleveland, Ohio.

Large granular lymphocyte (LGL) leukemia is a chronic lymphoproliferative disorder (LPD) of T or NK cells, characterized by a monoclonal LGL population, most often of CD8+ T cells, in blood, bone marrow (BM), and spleen. We describe a 63-year-old man evaluated for immunoglobulin (Ig) M–K monoclonal gammapathy, who, surprisingly, had 2 different atypical lymphoid entities: CD8+ T-LGL and B-cell LPD. At presentation, a complete blood cell count showed white blood cell (WBC) counts of 9.1 × 10^9 cells/L (46.4% lymphocytes, 40% neutrophils, 10.8% monocytes, 2.6% eosinophils, and 0.2% basophils), hemoglobin was 12.6 g/dL, mean corpuscular volume was 96 fL, and platelets were 204 × 10^9/L. The LGLs comprised 30% of circulating WBCs (Figure 98, A). Serum protein electrophoresis showed monoclonal bands of 0.5 g/dL. The BM biopsy revealed a hypercellular marrow with 2 atypical lymphoid populations detected by flow cytometry: a CD4+CD56+/T-cell receptor VB-restricted T cell population (12% of cells), consistent with T-LGL leukemia, and a CD5+/CD10+/k-restricted B-cell population (<1% of cells). Correspondingly, the core biopsy showed CD20-rich lymphoid aggregates (Figure 98, B and C), as well as an interstitial increase in CD3+ cells (Figure 98, D). STAT3 and STAT5B mutations are found in approximately 30% and approximately 2% of all T-LGL cases, respectively, with STAT5B mutations present in about 50% of CD4+ T-LGL, whereas the MYD88 mutation is present in about 90% of lymphoplasmacytic lymphoma. Lymphoid next-generation sequencing panel performed to evaluate those genes was negative, although the presence of low-level (<10%) or rare variants could not be excluded. The T-LGL leukemia is typically associated with autoimmune disease and cytopenias. The less-frequent CD4+ type T-LGL leukemia is also associated with a second malignancy in about 30% of cases, as illustrated in this case.

**Plasmablastic Lymphoma in an HIV-Negative Adult After Liver Transplantation**

*(Poster No. 64)*

Khalida Ibrahim, MD (kiba0@louisville.edu); Samer Al-Quran, MD. Department of Pathology and Laboratory Medicine, University of Louisville, Louisville, Kentucky.

We present a case of plasmablastic lymphoma (PBL), an uncommon subtype of monoclonal posttransplantation lymphoproliferative disorder (PTLD), in an HIV-negative 62-year-old man. The patient underwent orthotopic liver transplantation for cirrhosis from nonalco-
holic steatohepatitis. Seven months later, he developed polymorphic PTLD diffusely involving the entire colon. He presented 3 years later with a right-sided pleural effusion for which he underwent thoraco-
scopic decortication. Histologic sections from the pleural tissue showed a diffuse infiltrate of plasmablastic cells with brisk mitotic activity and frequent apoptosis. Immunohistochemistry showed these cells to be CD38+, CD138+, MUM1+, CD10+, CD79a+, and PAX5+ with high Ki-67 labeling of the tumor nuclei (>95%). In situ hybridization for Epstein-Barr virus (EBER) was diffusely positive. Fluorescence in situ hybridization studies demonstrated gains of MYC and IGH with loss of BCL2; the results were negative for rearrangements of ALK, BCL6, MYC, and IGH-BCL2. These findings supported a diagnosis of EBV+PBL-PTLD. Plasmablastic lymphoma-PTLD has a very aggressive disease course with a median overall survival of 11 months. Approximately 60% of cases are EBER+; those tend to present earlier after transplantation. Tumor cells generally show immunoreactivity for CD38 and CD138 but lack mature B-cell markers. Although cases of PTLD comprise approximately 25% of de novo malignancies after liver transplantation, PBL-PTLD after liver transplantation has only rarely been reported in adult liver-transplant recipients (Figure 99).
**Breast Implant–Associated Anaplastic Large Cell Lymphoma in a BRCA2+ Woman**

(Poster No. 65)

**Tiffany C. Levine, MD**1 (tiffany.c.levine.mil@mail.mil); Elizabeth M. Fowler, MD.2 1Department of Pathology, Madigan Army Medical, Puyallup, Washington; 2Department of Pathology, Naval Hospital, Bremerton, Washington.

Breast implant–associated anaplastic large cell lymphoma is a provisional entity in the latest update of the World Health Organization classification, which is defined as a T-cell lymphoma with features of ALK–anaplastic large cell lymphoma arising in association with breast implants. As of 2015, 173 cases were reported in the literature. We present the case of a 56-year-old woman with a BRCA2 germline mutation 3 years after bilateral prophylactic mastectomy with textured implants who presented with a right breast seroma. Fluid aspiration demonstrated a predominance of large cells with abundant cytoplasm and irregular nuclear contours with scattered, multilobated nuclei (Figure 100, A). By immunohistochemistry, the large cells were positive for CD45, CD30 (Figure 100, B), CD3, CD4, CD43, and CD5 (partial) and were negative for ALK, CD8, CD20, and PAX5. Flow cytometric analysis showed an aberrant T-cell population with high side scatter and surface CD45, CD3, CD4, and CD7; moderate CD56; and CD5 in a subset, which was negative for CD8, B-cell markers, and CD10. Those features were diagnostic of anaplastic large cell lymphoma and, given the clinical history, breast implant–associated, anaplastic large cell lymphoma was favored. Subsequent bilateral explant and capsulectomy revealed a minute focus of adherent, atypical CD30+ cells along the edge of the right capsule (Figure 100, C and D). This case further supports the association between breast implants and anaplastic large cell lymphoma and brings up the question as to the significance, if any, of a BRCA germline mutation in the development of this entity, a question to be explored.

**Composite, Diffuse Large B-Cell Lymphoma and Classic Hodgkin Lymphoma**

(Poster No. 66)

**Brian Pahn, DO** (bpahn@tu.edu); Jiehao Zhou, MD, PhD. Department of Pathology, Indiana University School of Medicine, Indianapolis.

Composite lymphoma is uncommon and is defined as 2 or more distinct lymphomas that occur within the same anatomic location. Most composite lymphomas have been recognized as bimorphic processes derived from a common precursor clone. We present a 29-year-old woman with no significant medical history who presented with B symptoms. Imaging studies showed mediastinal and bilateral cervical lymphadenopathy. A biopsy of the left cervical node demonstrated 2 distinct lymphomatous processes with a sharp and distinct transition border (Figure 101). One process consisted of a sheet of large, atypical lymphoid cells that were positive for CD20, PAX5, CD45, BCL–6, and MUM1 and were negative for CD30, CD15, and CD10. The second process consisted of few scattered Reed-Sternberg (R-S) and R-S–like cells in a background of mixed inflammatory cells, including small lymphocytes, histiocytes, and eosinophils. The neoplastic cells were positive for CD30, CD15, and PAX5 and were negative for CD20 and CD45. EBER in situ hybridization was negative in both components. A diagnosis of composite lymphoma consisting of diffuse large B-cell lymphoma, not otherwise specified, ABC type, and classic Hodgkin lymphoma was rendered. Diagnosis of composite lymphoma can be very challenging because one lymphoma component often overshadows the other component. This case illustrates the crucial role of careful morphology evaluation and appropriate immunohistochemistry study in diagnostic workup of composite lymphoma.

![Composite, Diffuse Large B-Cell Lymphoma and Classic Hodgkin Lymphoma](image)
Rosai-Dorfman Disease of the Breast: A Case Report and Review of Literature

(Poster No. 68)

Xiaofeng Zhao, MD, PhD (xiaofeng.zhao@tuhs.temple.edu); Congli Wang, MD, PhD; Ashish Bains, MD. Department of Pathology and Laboratory Medicine, Temple University Hospital, Philadelphia, Pennsylvania.

Rosai-Dorfman disease (RDD) is an uncommon and idiopathic proliferative disorder of histiocytes, which usually involves the cervical lymph nodes and, less commonly, extranodal sites. However, RDD confined to the breast is rare, with fewer than 30 cases reported. Recognition of this entity is important because it can mimic malignancy in both clinical presentation and radiographic appearance. We report on a 44-year-old woman with a medical history significant for hypertension and obesity who presented with a palpable right breast mass. Mammogram and ultrasound of the right breast showed a 3.0 × 1.9 × 1.7-cm irregular, indistinct, hyperdense mass with hypoechoic areas 12 to 13 cm from the nipple, which was concerning for malignancy with BI-RADS (Breast Imaging Reporting and Data System) category 4. A core needle biopsy showed a polymorphic, atypical lymphoplasmacytic infiltrate of breast tissue. A following lumpectomy showed an ill-defined, yellow to pink-tan, firm lesion measuring 3.6 × 3.0 × 2.0 cm, with histopathology confirming an atypical lymphoplasmacytic infiltrate with the presence of S100+ histiocytes, demonstrating emperipolesis (Figure 103). Findings were consistent with Rosai-Dorfman disease. On follow-up, the patient developed a left abdominal wall mass with similar histopathology and an S100+ CD1a+ histiocytic infiltrate. Although RDD usually involves lymph nodes, the disease can have extranodal manifestations, usually involving skin, soft tissue, bone, upper respiratory tract, and orbital adnexa. Moreover, RDD that is confined to the breast is very rare. Microscopically, RDD should be differentiated from other benign or malignant histiocytic lesions. Clinically, it also frequently mimics invasive breast carcinoma. Awareness and appropriate diagnosis of this entity are essential for proper management.

Co-occurrence of Hairy Cell Leukemia and T-Cell Large Granular Lymphocytic Leukemia: Report of 2 Cases

(Poster No. 69)

Kavitha Juvvala, MBBS (kavitajjj@gmail.com); Jagmohan Sidhu, MD. Department of Pathology and Laboratory Medicine, United Health Services Hospitals, Johnson City, New York.

Our first case involved a 75-year-old woman who presented with mild anemia (hemoglobin [Hgb], 11.4 g/dL) and thrombocytopenia (platelets, 120,000/mL), and a low to normal white blood cell count (43,000/mL). We found 17% hairy cells in her peripheral blood (PB). Bone marrow (BM) biopsy showed 40% cellularity with 95% hairy cell component. Immunohistochemical stain results were CD20+/CD79a+/annexin A1+/CD2/CD3/CD5+/CD7+/CD8+/CD55+/CD56−/CD79b−/CD8−. FISH/V600E mutation was positive. Follow-up complete blood cell counts (CBCs) have been within reference range. Our second case involved a 75-year-old man who presented with pneumonia and absolute lymphocytosis (415,000/μL) and about 44% hairy cells in the PB. An FCM analysis showed about 38% hairy cells, and about 4% to 5% were immunophenotypically abnormal (dim CD2+/CD3+/CD5+/CD7+/CD8+/CD55+/CD56−) γ/δ large granular lymphocytes. Polymerase chain reaction (PCR) for B&F V600 mutation was positive. Follow-up complete blood cell counts (CBCs) have been within reference range. Both cases involved 75-year-old patients, who went into remission with cladribine therapy. Those patients have persistent LGLL in their blood. It appears that LGLL is more likely to coexist with HCL when the patient is his or her eighth decade. An understanding of the association of HCL and LGLL in older patients suggests the presence of LGLL should be investigated when cytopenias do not go away after HCL remission (Figure 104).

Unusual Progression of Follicular Lymphoma After Acquisition of MYC Rearrangement

(Poster No. 70)

Nathan Ryan, MD1 (nryan@augusta.edu); M. S. Nawaz, MD2; Ravi Kolhe, MD3; Locke Bryan, MD2; Natasha M. Savage, MD.1 Departments of 1Pathology and 2Medicine (Hematology/Oncology), Medical College of Georgia, Augusta.

A 63-year-old woman with follicular lymphoma was followed closely on active surveillance for approximately 6 years without treatment. During surveillance, she noted symptomatic lymphadenopathy; disease progression was confirmed via imaging. Multiple treatment modalities were attempted, including high-dose steroids, chlorambucil, rituximab monotherapy, bendamustine with rituximab, and ultimately R-CHOP because of the lack of treatment response. She subsequently presented...
with a popular rash. A biopsy revealed cutaneous involvement by her lymphoma, which showed blastoid morphology (Figure 105, A) expressing CD79a and PAX5 without expression of TdT or CD34. Fluorescence in situ hybridization revealed a MYC rearrangement. The patient then developed weakness; a lumbar puncture revealed cerebrospinal fluid involvement (Figure 105, B) with leptomeningeal enhancement noted on imaging. Following 3 cycles of MATROX regimen, she developed leukocytosis with many circulating blastoid cells. Peripheral blood-flow cytometry revealed a CD7+/HLA-DR- population without expression of pan–B–cell markers. A bone marrow biopsy was performed to determine whether that was an unusual progression of her lymphoma versus a therapy-related myeloid neoplasm. The bone marrow was extensively involved by blastoid cells (Figure 105, C) without expression of all pan–B–cell markers. Cytogenetic studies revealed a complex karyotype, including MYC translocation and t(14;18), which was consistent with cytogenetic evolution of her known lymphoma. She subsequently received R-ICE and later miniBEAM, but ultimately succumbed to her disease. This represents an unusual progression of lymphoma with loss of pan–B–cell markers and acquisition of CD7 (Figure 105, D) after cytogenetic evolution. Disease progression such as this may be missed via routine immunohistochemistry and cytogenetic studies must be relied on for accurate diagnosis.

**Metastatic Merkel Cell Carcinoma to the Bone Marrow**
(Poster No. 71)
Roula Katerji, MD (roula_katerji@urmc.rochester.edu); Genevieve Marie Crane, MD, PhD. Department of Pathology, University of Rochester, Rochester, New York.

Merkel cell carcinoma (MCC) is a rare but aggressive neuroendocrine carcinoma of the skin. It frequently metastasizes to lymph nodes but is only rarely reported in the bone marrow. We report a case of a 55-year-old man with a history of testicular seminoma in 2008 followed by orchectomy and radiation and chronic lymphocytic leukemia (CLL) in 2010 with cytogenetics within reference range, TP53 mutation, and 80% bone marrow involvement. In 2017, he had a 6.7 × 3.5-cm buttock lesion; biopsy proved MCC, with lymph node metastasis. After 4 cycles of anti-PD1 immunotherapy, he developed normocytic anemia, thrombocytopenia, and lymphocytosis. Positron emission tomography scan showed avid bone marrow lesions. Bone marrow aspirate showed atypical cells arranged individually and in clusters, with a high N/C ratio and pale-blue cytoplasm reminiscent of blasts but in clusters (Figure 106, A). The bone marrow was extensively replaced by small blue cells, apoptotic debris, and sheets of necrosis (Figure 106, B), with minimal evidence of residual hematopoiesis. The tumor cells showed cytokeratin-20 staining in a dotlike, perinuclear pattern (Figure 106, C) and were strongly positive for CD56 (Figure 106, D). Flow cytometry showed a population of CD45+; CD56+ cells lacking other markers. CD56+ B-cells with a phenotype characteristic of CLL were also identified. The clinical history of 3 malignancies (MCC, CLL, and seminoma) raised concern for a possible genetic predisposition. In addition, approximately 80% of MCCs have been associated with Merkel cell polyomavirus. Patients with CLL have an increased risk of developing MCC, and it may create a permissive immunologic environment for its development. This remains an important area for further study.

**Retroperitoneal Marginal Zone Lymphoma in a Patient With Rheumatoid Arthritis**
(Poster No. 72)
Kristina Gvozdjan, MD (kgvozdjan@pennstatehealth.psu.edu); Michael G. Bayerl, MD. Department of Pathology, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania.

Patients with rheumatoid arthritis (RA) have an increased risk of developing lymphoma. Although disease regression may be achieved solely by discontinuation of methotrexate, most patients require chemotherapy. Herein, we describe the case of a 69-year-old man with RA on methotrexate with an incidentally found retroperitoneal mass on computed tomography measuring 12.6 × 10.6 × 11.1 cm. Core biopsy demonstrated monocytophagic lymphocytes positive for CD20 and BCL2, focally positive for CD34, and negative for CD10, CD23, cyclin D1, BCL6, and EBER, consistent with marginal zone lymphoma (MZL). The decision was made to discontinue methotrexate. After 5 months of observation, the tumor increased in size to 16.8 × 11.7 × 15.0 cm, prompting initiation of rituximab. However, the patient soon developed cervical lymphadenopathy and parotid gland enlargement, with core biopsies demonstrating extranodal MZL of mucosa-associated lymphoid tissue. The O-CHOP regimen was then instituted; however, only 1.5 years since the original diagnosis, the abdominal mass grew to the point of ulceration through the abdominal wall. Punch biopsy of the skin demonstrated sheets of large neoplastic cells immunoreactive for PAX5, CD79a, BCL6, BCL2, and c-MYC (40%–50%), and negative for MUM1, CD10, cyclin D1, and EBER, consistent with diffuse large B-cell lymphoma (DLBCL) with double expression. MYC gene rearrangement was not detected. Therefore, this is a rare case of retroperitoneal MZL in a patient with RA that rapidly progressed to DLBCL. The importance of generous sampling of similar lesions is emphasized because it may facilitate early detection of a more aggressive tumor component.

**Histopathologic Characterization of Rosai-Dorfman Disease**
(Poster No. 73)
Aishwarya Ravindran, MMBS1 (ravindran.aishwarya@mayo.edu); Gaurav Goyal, MMBS2; Ronald S. Go, MD; Karen L. Rech, MD.3 Department of 1Pathology and Laboratory Medicine and 2Division of Hematology, Mayo Clinic, Rochester, Minnesota.

**Context:** Rosai-Dorfman disease (RDD) can show nodal and extranodal manifestations. Fairly nonspecific histology makes the diagnosis challenging. We aimed to characterize the histologic and immunohistochemical features in patients with RDD.

**Design:** In our institutional database (1997–2017), 18 patients with RDD had formalin-fixed, paraffin-embedded tissue for immunohistochemical (IHC) studies. The IHC was graded as negative, weak (1+), intermediate (2+), or strong (3+) in at least 30% of RDD histiocytes. Arch Pathol Lab Med

**Abstracts e73**
Results: Patients included 13 women and 5 men; median age at diagnosis was 54 years (range, 21–87). Nine patients had multifocal disease affecting lymph nodes, paraspinal soft tissue, dura, liver, heart, orbit, testis, parotid, and nasal septum; others were limited to lacrimal gland (n = 1) or skin (n = 8). Two patients also had autoimmune disease. Histologically, the lesions showed numerous plasma cells, frequent lymphoid aggregates, and fibrosis. In all cases, RDD histiocytes showed emperipolesis and were positive for CD163 (2–3%; 83%), CD68 (2–3%; 39%), S100 (2–3%; 94%), and cyclin D1 (3%; 100%). Most cases were positive for OCT2 (3%; 95%), EZH2 (2–3%; 74%), and p16 (2–3%; 63%), with subset positivity for p53 (2%; 47%), BCL2 (2%; 21%), factor XIIa (2–3%; 31%), and PD-L1 (2%; 11%). Three patients with multifocal disease showed distinctly strong staining for factor XIIa and p16. GRAP2, V600E, ALK, CD1a, PD-1, and Langerin were uniformly negative.

Conclusions: Rosai-Dorfman disease represents a heterogeneous clinical group that can involve a variety of anatomic sites. Moreover, RDD histiocytes are best identified by staining for CD163, S100, and cyclin D1. Strong coexpression of factor XIIa and p16 may be associated with multifocal disease.

Myeloid Sarcoma Causing Small Bowel Obstruction in a Young Patient

(Hong-guang Gao, MD) (Poster No. 74)

Hong-guang Gao, MD1 (ghg01@gmail.com); Daniel Riess, BS2; Jun Liu, MD, PhD1; Janusz Godzn, MD, MD1;1 Department of Pathology, Jefferson Health/New Jersey, Cherry Hill; 2Montclair State University, Montclair, New Jersey.

A myeloid sarcoma (chloroma) is an extramedullary manifestation of acute myeloid leukemia (AML). We report a case of this entity with unusual clinical presentation. This 29-year-old patient presented with 2 weeks of progressive abdominal pain, associated nausea, and vomiting. A computed tomography scan revealed a soft tissue mass encasing and obstructing the small bowel. A resection of the obstructed bowel with the tumor was performed. Gross examination found 2 separate mesentry nodules (4.8 and 4.5 cm) infiltrating into the bowel wall. Hematoyxlin–eosin–stained sections showed a monotonous population of discohesive, medium to large cells diffusely infiltrating the full thickness of the bowel. Immunohistochemical stains demonstrated the tumor cells were positive for CD45, CD43, CD34, CD117, myeloperoxidase, and lysozyme and were negative for CD20, CD79a, CD5, CD5, CD10, CD30, and CD57. The morphology and immune profile were diagnostic for myeloid sarcoma. Myeloid sarcoma is a rare tumor and usually presents as a manifestation of relapse after treated acute myeloid leukemia. The most common anatomic sites of this tumor are the skin and the gums. This patient had complete blood cell count data within reference range at the time of surgery. A follow-up bone marrow study after the surgery was negative for myeloid neoplasm. Primary myeloid sarcoma (without a known preexisting or concomitant diagnosis of leukemia), as in our case, is particularly rare. In almost all reported cases of primary myeloid sarcoma, acute leukemia develops in the median time of 7 months. Molecular and fluorescence in situ hybridization testing on this tumor is important in guiding treatment and predicting prognosis.

A Very Unusual Case of Composite Lymphoma With a High-Grade B-Cell Lymphoma Component With MYC and BCL2 Rearrangements and a Small Lymphocytic Lymphoma Component

(Rashmi Manur, MD, MPH1 (rashmi.manur@uphs.upenn.edu); Gabriel C. Caponetti, MD1;1 Department of Pathology and Laboratory Medicine, Pennsylvania Hospital, Philadelphia; 2Department of Pathology and Laboratory Medicine, Hospital of the University of Pennsylvania, Philadelphia.

Composite lymphomas (CLs) are rare neoplasms in which 2 or more lymphomas involve the same anatomic site. The lymphomatous components described in literature include Hodgkin, follicular, mantle cell, diffuse large B-cell, and small lymphocytic. We report the case of a 64-year-old man with no significant medical history who presented with cervical lymphadenopathy and B symptoms. Hematoyxlin–eosin–stained sections of cervical lymph node biopsy showed areas with a “starry sky” appearance containing sheets of large centroblastic cells, tingible body macrophages, frequent apoptotic cells and mitoses, and admixed areas with sheets of small lymphocytes with clumped chromatin, without mitoses or apoptosis (Figure 107, A and B). The high-grade component (HGC) was CD10+, BCL6+/+, MYC+, and Ki67 (50%). The low-grade component was CD5+, CD25+, CD10+, BCL6+, MYC+, and Ki67 (20%). Flow cytometry showed light chain restriction and low forward light scatter (FSC) in one B-cell clone and light chain restriction and low FSC in a second clone (Figure 107, C). Fluorescence in situ hybridization identified MYC and BCL2 rearrangements (Figure 107, D). Overall findings were diagnostic of CL with a high-grade B-cell lymphoma component with MYC and BCL2 rearrangements and a small lymphocytic lymphoma (SLL) component. It is possible that this CL is an extremely rare case of Richter transformation at presentation with “double hit” cytogenetics, which is clonally unrelated to the SLL component. To our knowledge, this type of CL has not been previously reported. The diagnosis of CL can be challenging, and the identification of an HGC with “double hit” cytogenetics is vital for appropriate treatment and prognostic stratification.

Intraocular Implant-Associated Cutaneous Anaplastic Large Cell Lymphoma

(Mugahed Hamza, MD) (Poster No. 76)

Mugahed Hamza, MD1 (mhamza@bcm.edu); Barrett Lawson, MD1; Liye Suo, MD, PhD; Daniel Rosen, MD, Med1;1 Department of Pathology and Immunology, Baylor College of Medicine, Houston, Texas; 2Department of Pathology and Immunology, Michael E. DeBakey VA Medical Center, Houston, Texas.

Anaplastic large cell lymphoma is an aggressive non-Hodgkin lymphoma characterized by anaplastic cytology and CD30 membrane expression. Although many cases are sporadic, a correlation with prosthesis, in particular with breast implants, has been described. We describe the clinicopathologic presentation of 2 cases of anaplastic large cell lymphoma associated with intraocular implants. Patients presented at the Michael E. DeBakey VA Medical Center (Houston, Texas). Immunohistochemical stains were performed using a Leica (Wetzlar, Germany) Bond III Immunostainer according to manufacturer specifications. Fluorescence in situ hybridization (FISH) studies for DUSP22 and TP63 were performed at Neogenomics Labs (Aliso Viejo, California). A 51-year-old man and a 66-year-old man presented with slowly progressing suprorbital red, patchy skin lesions after intraocular implant placement (Medpor high-density polyethylene) 8 years and 2 years earlier, respectively. Microscopic examination of both cases showed similar findings corresponding to a large lymphoid cell population confined to the dermis. Immunohistochemical stains showed atypical lymphoid cells positive for CD30, CD3, CD5, and MUM1 but negative for ALK1, CD8, CD4, CD15, CD20, CD56, BCL6, PAX5, and cyclin D1. The Ki-67 proliferation index was more than 70%. The FISH studies for DUSP22 (IRF4), (6p25.3), and TP63 (3q28) rearrangement were negative. Both patients are alive with disease after 4 years and 2 years since diagnosis, respectively. CD30+ cutaneous lymphoproliferative disorders require a multidisciplinary approach and clinical and pathologic correlation for appropriate diagnosis and treatment. Anaplastic large cell lymphoma has been reported to be associated with implants, and the cases presented raise the possibility of an association with intraocular implants. Further investigation is warranted.
Hematogones: Canaries in the Bone Marrow (Poster No. 77)
Alisha D. Ware, MD (agordy26@jhmi.edu); Amy S. Duffield, MD, PhD. Department of Pathology, Johns Hopkins Hospital, Baltimore, Maryland.

Context: Hematogones are B-cell precursors present at low levels in healthy bone marrow, detectable by flow cytometry. Loss of hematogones is associated with primary marrow disorders, including myelodysplastic syndrome. Here, we examine the relationship between hematogones and recurrent acute myeloid leukemia (AML).

Design: The pathology database was searched for cases of recurrent/relapsed AML from January 2011 to August 2017. Seventy-nine of those patients had a normal surveillance marrow with flow cytometric evaluation in the 6 months prior to relapse.

Results: The average patient age was 56 years. There were 53 de novo and 26 secondary AMLs. Thirty-eight percent of surveillance biopsies lacked hematogones. The average age was similar in patients with (54 years) and without (61 years) hematogones. The median time between surveillance and relapse was shorter in patients without (62 days) versus with hematogones (100 days). There was no significant difference in the number of patients with no hematogones in de novo (40%) versus secondary AML (35%; P = .81). Patients with no hematogones at surveillance (70%) were more likely to lack hematogones at recurrence (30%; P = .001). Thirty-nine patients had a bone marrow transplant prior to relapse, 77% of whom had hematogones at surveillance (versus 48% of those without transplant; P = .01).

Conclusions: These findings suggest that absence of hematogones in otherwise healthy marrow biopsy from a patient with a history of AML may act as a “canary in the coal mine” for recurrence even in the absence of immunophenotypic or molecular evidence of relapse. Quantification and reporting of the hematogones may be of value in patients with a history of AML.

A Case Report of Acute Myelomonocytic Leukemia With Concurrent inv(16) and t(9;22) Chromosomal Abnormalities (Poster No. 78)
Jing Lu, MD, PhD (jilu@wakehealth.edu); Mark J. Pettenati, PhD; Stacey S. O’Neill, MD, PhD; Michael W. Beaty, MD. Department of Pathology, Wake Forest School of Medicine, Winston-Salem, North Carolina.

Acute myeloid leukemia (AML) is classified into subtypes defined by lineage differentiation and specific chromosomal abnormalities. The AML with CBFB-MYH11 (core binding factor β- myosin heavy chain 11) rearrangement resulting from inv(16)(p13.1q22), or t(16;16)(p13.1q22) accounts for about 5% of AML cases. The Philadelphia chromosome resulting from t(9;22) is a hallmark for chronic myeloid leukemia but is also rarely seen in de novo AML. Concurrent inv(16) and t(9;22) is rare. Here, we report on an 81-year-old white man with history of recurrent, benign, fibrous tumors who presented with dyspnea on exertion. Further workup revealed monocytosis with circulating blasts (17%) in the peripheral blood (Figure 108, A). The bone marrow touch preparation showed increased blasts (11%). Atypical eosinophil precursors with immature basophilic granules and hyposegmentation were present (Figure 108, B). Bone marrow core biopsy exhibited increased blasts and eosinophil precursors (Figure 108, C). Flow cytometry showed the leukemic blasts were positive for CD34, CD38, CD45, and CD117 and were negative for CD14. Metaphase fluorescent in situ hybridization with a CBFB break-apart probe showed an inv(16) in 90% of cells and a BCR/ABL translocation of (9;22) in 40% of cells (Figure 108, D). A p210 BCR/ABL fusion product was detected in the peripheral blood sample by quantitative real-time polymerase chain reaction. The patient responded well with chemotherapy. Repeat bone marrow study at day 35 showed no increase in blasts, was negative for split in the CBFB gene, and was negative for BCR/ABL fusion. These findings represent a very rare de novo AML with coexisting inv(16) and t(9;22) chromosomal abnormalities.

Tryptase Positivity in a Chronic Myeloid Leukemia Case With Marked Basophilia (Poster No. 79)
Youssef Khafateh, MD (y0khaf01@louisville.edu); Ashley Mathew, MMBS; Barina Ajil, MD. Department of Pathology and Laboratory Medicine, University of Louisville, Louisville, Kentucky.

Chronic myeloid leukemia is the most common myeloproliferative disorder that can occur at any age, with peak incidence between 50 and 60 years. Basophilia is seen in a variety of reactive and neoplastic conditions. It is commonly associated with chronic myeloid leukemia, notably in accelerated phase or during blast crisis. We report a case of a 41-year-old man who presented for consultation at our institution and was diagnosed initially with chronic myeloid leukemia in the chronic phase, with polymerase chain reaction results that were positive for BCR/ABL1 p210 fusion. He was then placed on treatment, but his medication was changed twice because of recurrent pancytopenia. His most recent biopsy demonstrated chronic myeloid leukemia with marked basophilia of more than 80%, indicating an accelerated phase (Figure 109, A and B). Interestingly, tryptase stain showed increased positivity (Figure 109, C) with a similar pattern as CD123 (Figure 109, D). Similar findings were noted in the splenectomy specimen. No increase in mast cells was seen by morphology or immunophenotype. Tryptase is a protease that is mainly expressed in mast cells and, so far, had been used widely as a specific marker for mast cells. Basophils do not contain a significant amount of tryptase. However, studies in recent years have demonstrated that immature neoplastic basophils can express a detectable amount of tryptase, and our case supports that finding. Therefore, tryptase should not be regarded as a specific marker for mast cells when approaching various myeloid neoplasms, including chronic myeloid leukemia.

Acute Leukemia of Ambiguous Lineage Presenting With Retroperitoneal Lymphadenopathy (Poster No. 80)
Albina Murzabdillaeva, MD1 (albina.murzabdillaeva@uth.tmc.edu); Chen Chen, MD, PhD2; Manju Ambell, MD3; Lei Chen, MD, MD1.
1Department of Pathology and Laboratory Medicine, The University of Texas Health Science Center, McGovern Medical School, Houston; 2Department of Pathology and Laboratory Medicine, Baylor College of Medicine, Houston.

Acute leukemia of ambiguous lineage (ALAL) is a rare and aggressive disease (about 4% of acute leukemia). It lacks clear lineage differen-
tion and mostly presents with heterogeneous morphologic or clinical features and molecular profile; worse prognosis is seen with higher incidence of complex cytogenetic aberrancies. We describe a case with a cervical mass having a unique 21q- and 12p- aberrancy, which has not, to our knowledge, been previously reported. Our patient is a 41-year-old woman who presented to an outside hospital with lower abdominal pain, enlarged uterus, and retroperitoneal lymphadenopathy, concerning for malignancy. She was transferred to our hospital for further management. Cervical biopsy and endometrium curettage showed sheets of medium-sized blasts with finely dispersed chromatin, inconspicuous nucleoli, and frequent mitotic figures. Bone marrow biopsy and peripheral blood smear showed many blasts with scant blue cytoplasm with few cytoplasmic vacuoles and inconspicuous nucleoli; no Auer rods were seen. Immunophenotype on cervical biopsy, peripheral blood, and bone marrow was similar, with no clear lineage markers (positive for CD2, CD7, CD38, CD79A [subset], CD117, Tdt [subset], and MPO [subset]). Cytogenetic results showed 2 abnormal clones with complex karyotype. Fluorescence in situ hybridization was abnormal with 12p- and 21q-. However, no mutation was detected by an acute myeloid leukemia molecular profile with a 24-gene panel. Polymerase chain reaction was negative for FLT3-ITD and FLT3-TKD mutations. A diagnosis of ALAL was made, and patient was started on hyper-CVAD chemotherapy. She initially responded to therapy and achieved complete remission after approximately 7 weeks of chemotherapy. However, our patient relapsed shortly thereafter, which was confirmed with pelvic lymph node and bone marrow biopsy.

B-Lymphoblastic Leukemia With t(5;14)(Q31;Q32) With Severe Hypereosinophilia Presenting With Minimum Peripheral Blasts

(Poster No. 81)

Kuixing Zhang, MD1 (kzhang@uci.edu); Milton Drachenberg, MD2 Department of Pathology, University of California, Irvine, Medical Center, Orange; 2Department of Pathology, Long Beach Memorial Medical Center, Long Beach, California.

B-lymphoblastic leukemia with t(5;14)(q31;q32) is a rare neoplasm of lymphoblasts, in which the blasts harbor a translocation between an IL3 and an IGH gene, resulting in variable, reactive eosinophilia. It is very rare, accounting for less than 1% of all acute lymphocytic leukemias. The blasts contain more than > 10% blasts in the bone marrow aspirate. Cytogenetic and FISH studies of the peripheral blood and bone marrow failed to identify any genomic abnormalities, including myeloid/lymphoid neoplasms with eosinophilia gene arrangements, such as 4q12 (FIP1LI/CHIC2/ PDGFRα), 5q31.3 (PDGFRβ), or 8p11 (FGFR1). Moreover, bone marrow FISH failed to detect t(12;19) (IGH-VH) rearrangement. However, next-generation sequencing specifically targeting IGH-IL3 revealed that gene rearrangement. The eosinophilia of B-lymphoblastic leukemia with t(5;14)(q31;q32) because of constitutional overexpression of IL3 is generally considered reactive. The nuclear dysplastic feature of this case is rare and a confounding factor in reaching the correct diagnosis. To make it worse, FISH and cytogenetic studies were negative for IGH rearrangement or any other genetic abnormalities. The diagnosis was established by a further study using more sensitive next-generation sequencing with this specific panel of IGH-IL3. This interesting case provides an example of the importance of morphology to direct target next-generation sequencing to establish a diagnosis.

Atypical CD8+ T-Cell Lymphocytosis in a Patient With HIV

(Poster No. 82)

Etan Marks, DO1; Zeina Khairy, MD1 (zkhairy@montefiore.org); Yanhua Wang, MD, PhD2; Yang Shi, MD, PhD Department of Pathology, Montefiore Medical Center, Bronx, New York.

A 41-year-old woman with uncontrolled HIV infection presented with sepsis. HAART (highly active antiretroviral therapy) was initiated. She developed acute leukocytosis. A peripheral blood smear showed markedly increased, atypical lymphocytes. On flow cytometry, these cells comprised 84.5% of the total population and expressed CD2, CD3, CD4, CD5, CD8, CD10, CD11a, CD11b, CD20, CD34, CD45, CD71 (erythroid), TIA1, and TCRγδ. They did not express CD4, CD5, CD7, CD10, CD19, CD25, CD33, CD34, CD64, CD117, or TCRγδ. A monoclonal peak was detected by T-cell receptor gene rearrangement. The atypical lymphocytosis was thought to be related to the HAART. Subsequently, HAART was held, and the patient’s leukocytosis partially resolved. A flow cytometry of the peripheral blood 2 weeks later showed persistence of the atypical population with additional loss of CD3 and expression of CD33. Next-generation sequencing for the peripheral blood showed STAT3 and TET2 mutations. A cytogenetic analysis of the bone marrow showed a complex karyotype. The patient succumbed to her disease and died 6 months later. The HIV-associated CD8+ lymphocyte population was clonal in the peripheral blood and can even be monoclonal; however, it is typically benign. In this case, the complicated cytogenetic changes and the gene mutations favored a malignant process. The temporal relationship of this disease with HAART suggests that it might be part of the immunologic response to HIV infection or HAART. Further investigation of the underlying mechanism poses a possible new type of atypical lymphocytosis and HIV infection/HAART is warranted.

Acute Megakaryoblastic Leukemia With RAM Phenotype and CBF-GLIS2 Fusion

(Poster No. 83)

Satyapal Chahar, MBBS (satyapal.chahar@uhhospitals.org); Bhuvan Maheshwari, MBBS; Yanchun Li, MD. Department of Pathology, University Hospitals Cleveland Medical Center, Case Western Reserve University, Cleveland, Ohio.

Acute megakaryoblastic leukemia (AMKL) is a rare subtype of acute myeloid leukemia (AML) in the pediatric population, accounting for 10% of pediatric AML. There are 2 types of AMKL in the pediatric population: Down syndrome–related AMKL is associated with a GATA1 mutation and good prognosis, whereas non–Down syndrome-related AMKL, except t(11;22), has a poor prognosis, and little is known about the underlying molecular/cytogenetic changes. We report a case of non–Down syndrome–related AMKL with a special immunophenotype (RAM phenotype) and CBF-GLIS2 fusion. Our case involves an 18-month-old, previously healthy girl who presented with fever for 3 weeks and right leg pain. Laboratory tests revealed anemia (hemoglobin 7.2g/dl) and increased erythrocyte sedimentation rate and C-reactive protein. A bone marrow biopsy was performed that showed AMKL. Of note, the blasts had the RAM phenotype: CD45 negative, HLA-DR negative, CD38 dim to negative, and CD56 bright. Chromosomal analysis results were within reference range, and myeloid next-generation sequencing panel was negative for tested pathogenic mutations. The AML fluorescence in situ hybridization study was negative. Molecular test showed CBF-GLIS2 fusion. Our patient received a donor bone marrow transplant, and the 100th day posttransplant bone marrow biopsy was within reference range. Based on the regular molecular/cytogenetic studies, this patient should be stratified as standard risk. However, it has been reported that RAM immunophenotype identifies otherwise standard-risk pediatric patients with high induction failure rate and extremely poor outcomes. Meanwhile, the CBF-GLIS2 mutation has also been implicated in inferior outcomes in pediatric patients with AMKL. This patient has 2 unfavorable features, suggestive of a possible relationship between RAM immunophenotype and CBF-GLIS2 fusion.

Development of Chronic Myeloid Leukemia (CML) in a Patient With a Long History of Plasma Cell Myeloma: A Possible Therapy-Related CML

(Poster No. 84)

Siddhartha Sen, MD, PhD (siddhartha.sen@duke.edu); Endi Wang, MD, PhD Department of Pathology, Duke University, Durham, North Carolina.

Therapy-related myeloid neoplasms are a group of heterogeneous neoplasms occurring as complications of chemotherapy and/or radiotherapy. Herein, we describe a rare case of therapy-related chronic myelogenous leukemia (CML) in a 79-year-old woman with plasma cell myeloma. The patient was diagnosed with a plasmaacytoma/myeloma 14 years earlier. She was treated with lenalidomide, dexamethasone, porterus, surgery, and radiotherapy for lytic bone lesions. Posttreatment bone marrow biopsies were negative for myeloma. Thirteen years after the initial diagnosis, she developed a new lytic bone lesion along with elevation of free k light chains, and systemic therapy for myeloma was restarted. She tolerated the treatment well, but experienced progressive leukocytosis with neutrophilia, basophilia, and thrombocytosis. A bone marrow biopsy was, therefore, performed, which showed myeloid hyperplasia and atypical megakaryocyte hyperplasia (bone marrow aspirate and core biopsy; Figure 110, A and B), along with a small population of phenotypically abnormal...
plasma cells (CD56 and CD138 immunostains; Figure 110, C and D). These morphologic features were consistent with a diagnosis of CML, in addition to the plasma cell neoplasm. The diagnosis of CML was confirmed by fluorescence in situ hybridization for BCR/ABL1 fusion. Therapy-related myeloid neoplasms mainly comprise acute myeloid leukemia and myelodysplastic syndrome, but few cases of therapy-related CML have been reported. Plasma cell neoplasm as a primary malignancy in therapy-related myeloid neoplasms is rare and is extremely rare in therapy-related CML. In this case, ionizing radiation-induced double-stranded breaks are likely implicated in the development of reciprocal translocation between BCR and ABL1, thereby leading to CML.

**Persistent Concentric Perifollicular Granulomas in a Case of Isolated IgG4-Related Lymphadenopathy**

*(Poster No. 85)*

Anu Peter, MD (anu.peter@tuhs.temple.edu); Nikolina Dioufa, MD, PhD; Michael Bromberg, MD, PhD; Ashish Bains, MD. Department of Pathology, Temple University Hospital, Philadelphia, Pennsylvania.

Immunoglobulin G4-related lymphadenopathy (IgG4-LAD) may occur in a setting of extranodal IgG4-related disease (IgG4-RD), which is considered an immune-mediated fibroinflammatory condition characterized by several histologic features: a dense lymphoplasmacytic infiltrate, storiform fibrosis, and obliterator phlebitis. When lymph node involvement occurs, it can show various histomorphologic patterns, none being specific to IgG4-LAD. We report a case of a 54-year-old woman with a history of diabetes mellitus who presented with persistent, isolated submandibular LAD that showed peculiar perifollicular granulomas on excisional biopsies 2 years apart from each other. Targeted additional workup identified markedly increased IgG4 plasma cells in tissue sections (Figure 111) and an elevated serum IgG4 level of 364 mg/dL. Clinical and radiologic workup did not identify any other specific abnormalities associated with IgG4-RD. Autoimmune and infectious workup results were also negative. Patient was not considered to be a candidate for prednisone because of her uncontrolled diabetes and received rituximab with near-complete resolution of the submandibular lymphadenopathy. In this case, the diagnosis of IgG4-LAD was solely suggested by the presence of perifollicular granulomas in the absence of other findings of IgG4-RD. The diagnosis was confirmed on the second lymph node biopsy 2 years after the initial biopsy. Although not unique to IgG4-LAD, perifollicular granulomas, when present in a concentric arrangement, in the absence of other definable etiologies, may suggest an etiologic association with IgG4-expressing plasma cell infiltrate and should prompt additional workup for IgG4-LAD/RD.

**Concurrent Extravcitary Primary Effusion Lymphoma and Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Occurring in One Lymph Node**

*(Poster No. 86)*

Neha Gupta, MBBS (ngupta4@northwell.edu); Peihong Hsu, MD; Judith Brody, MD; Xinmin Zhang, MD; Silvat Sheikh-Fayyaz, MD. Department of Anatomic Pathology and Laboratory Medicine, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, New Hyde Park, New York.

A 66-year-old man with persistent leukocytosis was recently diagnosed with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) on a neck lymph node biopsy. His lymphadenopathy rapidly progressed after the initial biopsy, which raised a concern of Richter transformation. A rebiopsy showed that the nodal architecture was completely effaced by both small lymphocytic and large lymphoid proliferation. The large, atypical cells exhibited abundant cytoplasm and prominent nucleoli arranged in a diffuse pattern with partial necrosis and numerous mitotic figures. Immunohistochemical studies revealed that the large cells were positive for CD43, CD138, MUM1, human herpesvirus-8, and Ki-67 (95%–100%) and were negative for CD20, CD79a, Pax5, CD5, CD30, EBER (in situ hybridization), and ALK-1, whereas the small cell component demonstrated a CLL/SLL immunophenotype. Based on these findings, the patient was diagnosed with concurrent extracavitary primary effusion lymphoma (E-PAL) and CLL/SLL. He received standard chemotherapy, and his clinical course was complicated by neutropenia, tumor lysis syndrome, pneumonia, and recurrence at 1.5 years. He developed chronic pleural effusion 2.5 years later, and a pleural biopsy revealed sarcomatoid mesothelioma. Despite further treatment with chemotherapy, he died of multiple organ failure 4.5 years after the initial diagnosis. Extracavitary primary effusion lymphoma is a rare manifestation of primary effusion lymphoma associated with human herpesvirus-8 and presenting as an isolated, solid mass in extracavitary sites. Primary effusion lymphoma and E-PAL commonly occur in HIV-positive patients. This is the first reported case, to our knowledge, of concurrent E-PAL with CLL/SLL in HIV-negative patient, which might represent transformation of CLL/SLL to E-PAL.

**Report of One Case of Juvenile Myelomonocytic Leukemia With N-RAS Mutation in an Infant**

*(Poster No. 87)*

Neha Gupta, MBBS (ngupta4@northwell.edu); Xinmin Zhang, MD; Judith Brody, MD; Kalpana Reddy, MD; Silvat Sheikh-Fayyaz, MD. Department of Anatomic Pathology and Laboratory Medicine, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, New Hyde Park, New York.

A 6-month-old boy presented with 2 days of fever, 3 weeks of cough, congestion, anorexia, rash, and fatigue. He was found to have a diffuse petechial rash and a distended abdomen. Ultrasound revealed hepatosplenomegaly. Complete blood cell count revealed leukocytosis (78 000/µL), mild thrombocytopenia (93 000/µL), and mild anemia (9.4 g/dL), with striking monocytosis (28 000/µL). Serum lactate dehydrogenase, liver function test results, and uric acid were mildly elevated with coagulopathy. A bone marrow aspirate revealed hypercellular marrow with myeloid and erythroid maturation; increased monocytic cells, including both mature and atypical forms (20%); 10% blasts, with coagulopathy. A bone marrow aspirate revealed hypercellular marrow with myeloid and erythroid maturation; increased monocytic cells, including both mature and atypical forms (20%); 10% blasts, including promonocytes; and markedly decreased megakaryocytes. There was mild dyserythropoiesis. Flow cytometry demonstrated 20% monocytic cells positive for HLA-DR (partial), CD11b, CD13 (partial), CD14 (partial), CD64, CD15 (partial), CD33 (dim) and CD2 and
negative for CD34, CD56, and CD117. Cyto genetic and fluorescent in situ hybridization studies were negative for monosomy 7 and BCR/ABL1 fusion. A diagnosis of juvenile myelomonocytic leukemia (JMML) was suspected and then confirmed by the detection of an NRAS mutation. The child received haploidentical stem cell transplant from her mother. Follow-up 2 months later with a bone marrow biopsy revealed trilineage hematopoiesis with no increase in blasts and aberrant monocytes. The JMML is a rare hematopoietic disorder accounting for 2% to 3% of all childhood hematologic malignancies. Moreover, JMML displays an aggressive and rapidly progressive course requiring stem cell transplantation for cure. Thus, mutational analysis of patients with JMML should be performed quickly. More than 80% of patients with JMML have mutations in the RAS signaling pathway genes, with 20% to 25% of patients having NRAS or KRAS mutations.

**Nonsecretory Nonproducer Plasma Cell Myeloma: Rare Entity and Common Findings**

(Poster No. 89)

Eric X. Wei, MD, PhD1 (ericxwei@yahoo.com); Jie-gen liang, MD, PhD; Hong L. Drum, MD. 1Department of Pathology, LSU Health, Shreveport, Louisiana; 2Department of Pathology, University of Medicine and Dentistry of New Jersey, Newark; 3Department of Pathology, NeoGenomics Laboratories, Irvine, California.

**Context:** Nonsecretory nonproducer plasma cell myeloma (NSNPPCM) comprises about 15% of nonsecretory multiple myelomas with no cytoplasmic immunoglobulin synthesis. Its clinicalopathologic features are rarely reported.

**Design:** We analyzed 32 cases of NSNPPCM by clinical, histopathologic, immunophenotypic, cytogenetics/fluorescence in situ hybridization, and molecular studies.

**Results:** The male to female ratio was 1.5, with a median age of 71 years. Twenty-nine patients presented with anemia and/or other cytopenia. Seven had lytic bone lesions. Fifteen had no monoclonal protein in serum or urine. The rest (n = 17) did not have a history of M proteins. Nineteen showed more than 50% plasma cells. In 11 cases, the plasma cells were significantly larger, with abundant cytoplasm and low N/C ratio. The cells were mostly negative for CD19 and CD20 and were positive for CD56. The expression of immunoglobulin lambda chain was different, with immunoglobulin (lg) A most common. There were no heavy chain diseases with polyclonal B cells and absent lymphadenopathy. IgH translocation was found in 12 cases with chromosome 11 (CCND1) being the translocation partner in 8 cases, and an unknown chromosome partner in 4 cases. Within the group with IgH rearrangement, the frequency of del(13q) or monosomy 13 was 60%, which is significantly higher than that in the group without IgH rearrangement (13.3%; P < .01). One case of NSNPPCM evolved from previous k-restricted PCM. After 1 year being absent for light chains, the patient regained k clones in plasma cells.

**Conclusions:** This may be the largest reported series of NSNPPCM. These findings suggest that NSNPPCM shares very similar genetic events with conventional myeloma, with IgH rearrangement, t(11;14) translocation, and del(13q) as common genetic abnormalities.

**Neutrophilic-Chronic Myeloid Leukemia With Extreme Thrombocytosis (N-CML WET) Is Not Always Associated With p230 BCR-ABL1 Fusion Protein**

(Poster No. 90)

Kavitha Juvala, MBBS (kavijj@gmail.com); Jagmohan Sidhu, MD, Department of Pathology and Laboratory Medicine, United Health Services Hospitals, Johnson City, New York.

A 32-year-old man presented with mild neutrophilia (10 500/μL), extreme thrombocytosis (3.3 million/μL) (Figure 113), and no splenomegaly. Bone marrow showed marked hypercellularity with reactive myelodysplasia with many micromegakaryocytes and 2% myeloblasts. Cytogenetic analysis found 46,XY,t(9;22)(q34;q11.2) and fluorescence in situ hybridization revealed BCR-ABL1 fusion. Upon reverse transcription-polymerase chain reaction (RT-PCR) p210 transcript (69.0813%) was detected. An ASXL1 gene mutation was detected by next-generation sequencing. The patient's complete blood cell count normalized, and p210 transcript reduced to 0.20% after dasatinib therapy. After 18 months, he presented with marked neutrophilia (48 700/μL), extreme thrombocytosis (3.5 million/μL), 2% myeloblasts, and absolute basophilia because he had stopped dasatinib. Most cases of chronic myeloid leukemia (CML) have p210 BCR-ABL1 fusion protein. In rare cases it is p230 or p190. Variant proteins can influence the phenotype/clinical manifestations; for example, p190 CML can look like chronic myelomonocytic leukemia, and p230 CML can look like chronic neutrophilic leukemia or essential thrombocytemia, depending on the marked neutrophilia or extreme thrombocytosis, and have less-severe or absent cytogenetic abnormalities. Nonsecretory nonproducer plasma cell myeloma may rarely be present.
FLT3-Tyrosine Kinase Domain (FLT3-TKD) Mutation Profile Across Cytogenetic Risk Groups in Acute Myeloid Leukemia

(Poster No. 91)

Sharif Adwan, MD1 (shareefadwan@gmail.com); Juan Ma, MD2; Lisong Shen, MD, PhD2; Zhuang Feng, MD, PhD2; Phil Raess, MD, PhD2; Elie Traer, MD, PhD4; Richard Press, MD, PhD1; Jennifer Dunlap, MD1; Guang Fan, MD, PhD2. 1Departments of 1Pathology and 2Hematology-Oncology, Oregon Health & Science University, Portland, Oregon.

Context: FLT3 receptor tyrosine kinase mutations are found in approximately 30% of patients with acute myeloid leukemia (AML), either as internal tandem duplications (FLT3-ITD) or, less commonly, as point mutations in the tyrosine kinase domain (FLT3-TKD). Midostaurin, an FLT3 inhibitor, was recently approved by the US Food and Drug Administration for treatment of FLT3-mutated AML, including FLT3-ITD and FLT3-TKD mutations occurring at codons 835 (FLT3-TKD835).

This study investigated the occurrence of FLT3-TKD mutations at 835 and other than 835 (FLT3-TKD non-835) in patients with AML and correlated FLT3-TKD mutation status with cytogenetic risk groups.

Design: The study included 242 patients with AML from Oregon Health & Science University (March 2013–November 2017). FLT3-ITD was evaluated by size-discrimination polymerase chain reaction (PCR) and FLT3-TKD mutations were evaluated by next-generation sequencing. Conventional cytogenetics was also performed. Overall survival for different FLT3 mutations was evaluated by the Kaplan-Meier method.

Results: Among 242 patients with AML, 4 FLT3 mutation groups were included: FLT3-ITD (n = 63); FLT3-ITD&ITD (n = 14); FLT3-ITD (n = 60); and FLT3 wild type (n = 97). FLT-ITD mutations were seen in 85% (214/253) of cases, of which 61% were FLT3-TKD835. FLT3-TKD non-835 mutations were seen in 15% (38/253) of cases, while 14% (36/253) of cases had FLT3 wild type. FLT3-ITD had the highest risk of adverse survival, while FLT3 wild type had the lowest risk. FLT3-TKD835 mutations had a higher risk of adverse survival compared to FLT3-TKD non-835 and FLT3 wild type, with a hazard ratio of 1.96 (95% CI: 1.08-3.57) and 5.68 (95% CI: 1.75-18.47), respectively.

Conclusions: FLT3-TKD mutations are independently associated with adverse survival in AML. This study highlights the importance of comprehensive mutational analysis in AML to guide personalized therapy and improve patient outcomes.

Distributions of FLT3 Mutations in Cytogenetic Risk Groups of AML

<table>
<thead>
<tr>
<th>Group</th>
<th>Intermediate</th>
<th>Favorable</th>
<th>Adverse</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLT3-TKDb835</td>
<td>19</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>FLT3-TKD non-835</td>
<td>19</td>
<td>2</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>FLT3-TKD&amp;ITD</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>

Spectrum of Hematologic Malignancies in a Pediatric Center in the Philippines

(Poster No. 92)

Joana Paula S. Artaiz, MD; Qareem Pido, MD; Evelyn Verana, RMT; Symonette A. Sandoval, MD; Raymundo W. Lo, MD; Daphne C. Ang, MD; and Ma. Cecilia Chuaang, MD. Department of Pathology, Philippine Children’s Medical Center, Quezon City, Philippines.

Context: Pediatric malignancies in the Philippines have a reported incidence of approximately 3500 new cases per year, and approximately 50% to 60% of cases are hematologic malignancies (HMs). Information on the spectrum of pediatric HM is sparse.

Design: This was a retrospective, descriptive study of patients diagnosed with HM at a single tertiary institution in the Philippines from January 2013 to December 2017. We reviewed the clinical and histologic parameters of 214 consecutive patients diagnosed with HM.

Results: Of the 214 patients diagnosed with HMs, 127 (65%) were males and 67 (35%) were females. The overall median age (MA) at diagnosis was 7 years (range 7 months to 18 years). The MA for myeloid and lymphoid malignancies were 5 and 9 years, respectively. Acute lymphoblastic leukemia was the most frequent HM (53.3%; MA, 6 years) in our pediatric population, followed, respectively, by non-Hodgkin lymphoma (NHL; 14.5%; MA, 9.8 years), acute myeloid leukemia (10.3%; MA, 8.5 years), Langerhans cell histiocytosis (8.4%; MA, 1 year), classic Hodgkin lymphoma (7.9%; MA, 14 years), and myeloid sarcoma (1%; MA, 7.5 years). Myeloproliferative neoplasm, myelodysplastic neoplasm, and multiple myeloma accounted for 0.5% each. Seven (3.3%) cases of HM had no immunologic workup. Among the cases of NHL, Burkitt lymphoma was the most common (32.3%), followed, respectively, by diffuse large B-cell lymphoma (16.3%), anaplastic large cell lymphoma (16.1%), acute B lymphoblastic lymphoma (12.9%), acute T lymphoblastic lymphoma (12.9%), subcutaneous panniculitis-like T cell lymphoma (6.5%), and extranodal marginal zone lymphoma (3.2%).

Conclusions: This single-institution study of the HM spectrum in the pediatric population parallels that of the national cancer registry of the Department of Health of the Philippines.

Myelodysplastic Syndrome With Ring Sideroblasts, SF3B1 Mutation, and β-Thalassemia Trait: Report of Rare Case

(Poster No. 93)

Seyed Amin Hojat, MD1 (ahojat@tuftsmedicalcenter.org); Grace Shih–Hui Kao, MD2; Monika Pilchowska, MD, PhD.1 Departments of 1Pathology and Laboratory Medicine and 2Hematology/Oncology, Pathology, Tufts Medical Center, Boston, Massachusetts.

Establishing etiology of anemia can be difficult, and multiple causes need to be considered. Herein, we report on a 60-year-old man of Asian ethnicity who presented to the hospital for evaluation of anemia. Patient had a longstanding history of normocytic anemia (hemoglobin, 7.5–9.1 g/dL), diabetes, and elevated ferritin (>1000 ng/mL). On presentation, laboratory results showed moderate to severe anemia (hemoglobin, 7.8 g/dL), with total bilirubin level (1.0 mg/dL) and reticulocyte count (1.7%) within reference range. Peripheral blood smear showed target cells and tear drop cells as well as schistocytes. Hemoglobin electrophoresis identified an A2 pattern with 10.4% F and 2.8% A2. Further analysis revealed mutation in hemoglobin β globin chain gene (IVS II-654 C>T), consistent with severe β-thalassemia; however, β-thalassemia did not sufficiently account for his presentation. Bone marrow biopsy revealed erythroid hyperplasia, dyspoiesis, and numerous ringed sideroblasts. Cytogenetic studies identified only loss of chromosome Y, and next-generation sequencing analysis detected SF3B1 mutation. Based on the clinical and pathologic workup, a diagnosis of myelodysplastic syndrome with ring sideroblasts was made in addition to the diagnosis of β-thalassemia. Abdominal magnetic resonance imaging scan showed increased iron deposit in the liver that was confirmatory for secondary hemochromatosis. At this time, he continues to require transfusion support and iron chelation. The next step will be an evaluation for bone marrow transplant. This case demonstrates the diagnostic complexity of anemia, and the necessity of considering multiple causes before arriving at final diagnosis.
A Rare Case of Myeloid Sarcoma in a Patient With Relapsed T-Lymphoblastic Lymphoma and Primary Myelofibrosis

(Poster No. 94)

Jessica Tomsula, MD (jatomsula@houstonmethodist.org); Arthur Zieske, MD; Suyang Hao, MD; Youli Zu, MD, PhD. Department of Pathology, Houston Methodist Hospital, Houston, Texas.

Myeloid sarcoma is a rare myeloid neoplasm occurring outside of the bone marrow. It frequently develops in patients with an underlying myeloid leukemia. It has also been described in patients with a history of myelodysplasia or a myeloproliferative neoplasm, including primary myelofibrosis. In addition, a few cases are reported in the literature of myelodysplasia or a myeloproliferative neoplasm, including primary myelofibrosis, and myeloid sarcoma. The patient is a 61-year-old African American man who presented with relapsed T-lymphoblastic lymphoma of the supraclavicular nodes in November 2017. Lymph node biopsy demonstrated cells positive for Tdt, CD1a, CD2, CD4 (partial), CD8 (partial), and CD3 and negative for CD10 and CD34, consistent with his previous immunophenotype. A bone marrow biopsy performed at relapse showed megakaryocytic hyperplasia with atypical forms, hypercellular marrow, and erythroid hypoplasia with moderate myelofibrosis (MF-2). A focal Tdt population of small cells was also present. Two months later, the patient presented with neutropenic fever and a papular rash of the right extremity, upper back, and abdomen concerning for Aspergillus infection or T-cell acute lymphoblastic leukemia. Biopsy of the lesions showed infiltration of large, atypical myeloid cells that were positive for CD45 (faint), MPO, CD43, and CD68 but were negative for CD3, CD5, Tdt, CD20, CD34, CD117, and CD1a. These findings led to the diagnosis of myeloid sarcoma. The myeloid sarcoma in this case may be the result of leukemic transformation of the patient’s primary myelofibrosis.

An Unusual Cause of Diverticulitis

(Poster No. 95)

Saleh Heneidi, MD1 (sheheneidi@augusta.edu); Rebecca Larsen, DO; Imran Ahmad, MD2; Locke Bryan, MD; Natasha M. Savage, MD.1 Departments of 1Pathology and 2Medicine (Hematology/Oncology), Medical College of Georgia, Augusta.

There is a spectrum of B-cell proliferations, both clonal and nonclonal, of varied malignant potential that display similarities across immunodeficiency backgrounds. Knowledge of the patient’s immunodeficiency status, Epstein-Barr virus (EBV) serologic studies, EBV titers, and evaluation for EBER within lesional cells is essential for accurate diagnosis. A 59-year-old woman presented with a 2-month history of fevers and lower abdominal pain. Computed tomography scan demonstrated sigmoid diverticulitis, which failed to improve with bowel rest and antibiotics. Resection of the involved bowel was performed. Histologic evaluation of the colon revealed multiple diverticula and a well-circumscribed mucosal ulcer (Figure 114, A) associated with a significant inflammatory infiltrate. This infiltrate was heterogeneous in appearance, consisting of small lymphocytes, numerous plasma cells (Figure 114, B), and plasmablasts (Figure 114, C). In addition, the diverticula showed a marked morphologically heterogeneous mucosal plasmacytosis with associated plasmablasts. Immunohistochemical analysis demonstrated a mixture of both κ- and λ-positive plasma cells and plasmablasts expressing CD138, MUM1, and EBER (Figure 114, D). An EBV+ lymphoproliferative disorder was diagnosed. The diagnosis triggered additional workup. HIV testing was positive (HIV-1 RNA of 572 552 copies/mL), and EBV polymerase chain reaction titers were positive (5 670 786 copies/mL). The patient rapidly deteriorated with worsening abdominal pain and confusion. Imaging revealed rapid advancement of soft tissue infiltrative disease throughout the abdomen. Cerebrospinal fluid revealed few large lymphoid cells with deep blue cytoplasm and prominent nucleoli; these were also seen circulating in the peripheral blood. The patient expired soon after. To our knowledge, this is the first reported case of HIV-associated EBV+ lymphoproliferative disorder presenting as diverticulitis.

Leiomyoadenomatoid Tumor: A Collision Tumor or a Variant of Adenomatoid Tumor?

(Poster No. 96)

Ghadah Al Sannaa, MD1 (galasanna@houstonmethodist.org); Ziad M. El-Zaateri, MD2; Lizmarie Andino, MD2; Daniel Schmolze, MD3; Darren Chapman, MD4; Alberto Ayala, MD; Jae Y. Ro, MD, PhD.1 1Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Texas; 2Department of Pathology, Mangini Lakhia Delahoussaye & Associates, Houston; 3Department of Pathology, City of Hope National Medical Center, Duarte, California; 4Department of Urology, Pearland Urology, Pearland, Texas.

Adenomatoid tumor is the most common neoplasm of epididymis. The term leiomyoadenomatoid tumor was proposed by Epstein in 1992 to describe an adenomatoid tumor/leiomyoma hybrid tumor. Epididymal leiomyoadenomatoid tumor is exceedingly rare. To our knowledge, only 2 such cases have been reported in the literature. Here, we report 2 additional cases. The first case involves a 28-year-old man who presented with an intrascrotal swelling, which on ultrasound (US) consisted of a 1-cm hypoechoic, intratesticular mass suspicious for germ cell tumor. The second case involves a 50-year-old man who had a slowly growing, right scrotal swelling for 5 years and developed acute pain. Ultrasound revealed a 3-cm, heterogeneous intratesticular mass. Both patients had negative serum tumor markers and underwent radical orchiectomy. Both neoplasms demonstrated similar histomorphology. The neoplasms involved the epididymis and were composed of mesothelial-lined tubules embedded in a fibromuscular stroma (Figure 115, A and B). The stroma displayed myofibroblastic differentiation evident by expression of smooth muscle actin (Figure 115, C), muscle-specific antigen, minimal/focal desmin (Figure 115, D), and caldesmon staining. Those findings prompted the diagnosis of leiomyoadenomatoid tumor. The histogenesis of leiomyoadenomatoid tumor remains uncertain. It may represent a collision of adenomatoid tumor and leiomyoma or a variant of adenomatoid tumor associated with smooth
muscle proliferation. We think that our 2 cases represent a variant of adenomyomatoid tumor that exhibits myofibroblastic, rather than smooth muscle differentiation of the stroma. We propose the use of the term *adenomyomatoid tumor* to describe this entity.

**An Unusual Case of Coccidioidomycosis posadasii Presenting as Epididymitis**  
(Poster No. 97)  
Kevin Cao, BS1 (kecao@utmb.edu); Jennifer C. Espinales, BS1; Adam L. Booth, MD2; William Eng, MD2; Joseph Sonstein, MD3; Eduardo J. Eyzaguirre, MD.2 1School of Medicine, 2Department of Pathology, and 3Division of Urology, University of Texas Medical Branch, Galveston.

*Coccidioides immitis* and *Coccidioides posadasii* are spore-forming soil fungi found in the southwest United States. Inhaled spores lead to “Valley fever,” a rare pulmonary illness. Of those with Valley fever, 0.6% of patients will develop systemic disease. A 27-year-old man presented with right-sided testicular pain and swelling. Two 1.5-cm masses were identified in the right epididymal tail by ultrasound. At that time, the patient chose to pursue pain management without further intervention. Two years later, the patient returned with worsening symptoms. A detailed history revealed the patient had emigrated from Mexico and spent time working in central Texas at a plant nursery. He denied any history of tuberculosis, fungal infection, or associated symptoms. Surgical excision was performed, and the mass was successfully separated from the right testis. Grossly, the mass had a thick, fibrous capsule containing tan, pasty, purulent material, which was sent to microbiology for bacterial and fungal culture. Microscopy revealed a necrotizing, granulomatous reaction with yeasts and giant cells (Figure 116, A and B). Gomori methenamine silver (Figure 116, C) and periodic acid–Schiff diastase (Figure 116, D) further highlighted the yeasts. Fungal culture confirmed *Coccidioides posadasii* by next-generation sequencing, and serology subsequently returned positive for *Coccidioides* antibodies. Fluconazole therapy was initiated after pathologic diagnosis. *Coccidioides posadasii* are slow-growing infections in the epididymis that should be considered in a healthy patient who resided or transited through an endemic area. A comprehensive medical and travel history should be obtained to broaden the differential diagnosis of epididymal cysts.

---

**MiT Family Translocation Renal Cell Carcinoma: A Case With Unusual Morphology and Clinical Presentation in an 11-Year-Old Girl**  
(Poster No. 98)  
Shahbaz A. Khan, MD (Shahbaz-Khan@ouhsc.edu); Zhongxin Yu, MD; Charles A. Lawrence, MD. 1Departments of 1Pathology and 2Radiology, The University of Oklahoma Health Sciences Center, Oklahoma City.

*Mt* family translocation renal cell carcinoma (RCC) occurs predominantly in children and young adults, with a mean and median age of around 25 and 20 years, respectively. It is associated with fusion of the *TFE3* or *TFEB* gene to a number of other genes. Histologically, it is associated with pleomorphic and polymorphic growth patterns, including papillary, alveolar, and nested patterns. We report on a case of a metastatic translocation RCC in an 11-year-old girl diagnosed on a cervical lymph node biopsy. She presented with a left-sided neck mass, fatigue, and weight loss for several weeks. Imaging studies showed a large mass appearing to be centered at the left adrenal gland and infiltrating into her left kidney and through retroperitoneum as well as widespread metastatic lesions in lungs, entire bony skeleton, liver, and lymph nodes in the mediastinum and neck, clinically suspicious for neuroblastoma despite patient’s age. Cervical lymph node biopsy showed a neoplasm with pseudopapillary morphology with clusters of small cells centered on hyaline cores and rare psammoma bodies (Figure 117, A through D). The neoplastic cells strongly expressed PAX8, CD10, and AMACR and produced diffuse, weakly positive staining for pancytokeratin and HMB–45. Fluorescence in situ hybridization was positive for *TFE3* gene rearrangement, consistent with diagnosis of translocation RCC. Additional immunohistochemical stains ruled out neuroblastoma, adrenocortical carcinoma, and solid pseudopapillary neoplasm of pancreas. This unusual clinical presentation, as well as pseudopapillary morphology, of RCC should be considered as a diagnostic possibility among extensive differential diagnoses for a neck mass with pseudopapillary morphology in the pediatric population.

---

**Malignant Solitary Fibrous Tumor of the Prostate: Report of 2 Cases**  
(Poster No. 99)  
Ahmed Bakshswin, MD (Bakshswin@ccf.org); Ryan Berry, MD; Brian P. Rubin, MD, PhD; Jesse K. McKenney, MD. Department of Pathology, Cleveland Clinic Foundation, Cleveland, Ohio.

Solitary fibrous tumor (SFT) is a rare mesenchymal neoplasm originally described involving the pleura, but it has been reported in virtually all anatomic locations. Biologically, it is classified by the World Health Organization as having an intermediate biologic potential (rarely metastasizing); however, clearly malignant SFTs do occur, and they are aggressive tumors with a poor prognosis. Malignant SFT is seldom described in the prostate, with only 5 cases reported to date, to our knowledge. We present 2 additional cases in 73-year-old and 55-year-old men who initially presented with classic symptomatology of benign prostatic hyperplasia and mildly elevated prostate-specific antigen levels. Both underwent transurethral resection of the prostate. Microscopic examination revealed tumors that were mainly composed of ovoid to spindle cells with evenly distributed chromatin and inconspicuous nuclei, arranged haphazardly or in short fascicles with associated staghornlike vessels, which had variable amounts of...
collagen. Both cases exhibited areas of marked high-grade cytomorphologic atypia. Case 1 had a mitotic index of 3 per 10 high-power fields, and no necrosis was noted. In case 2, mitotic activity was brisk and exceeded 20 per 10-high power fields. Tumor necrosis was also identified in case 2. The differential diagnosis for both cases included prostatic stromal sarcoma and SFT. STAT6 immunohistochemistry was performed and showed strong, diffuse nuclear reactivity in both cases (in both the low-grade and high-grade foci), confirming the diagnosis as SFT. In summary, we describe 2 new cases of malignant SFT of the prostate that clinically mimicked benign prostatic hyperplasia (Figure 118).

Endometriosis With Cystic Degeneration in Men: A Report of 2 Cases

Khalife Al-Obaidy, MD (dr.khaleel.alobaidy@gmail.com); Muhammad Idrees, MD. Department of Pathology, Indiana University, Indianapolis.

Endometriosis in men is extremely rare, with only few cases reported in the English literature. Different theories have been proposed regarding its origin. We performed a retrospective search of our institutional records between 1985 and 2017, and 2 cases of testicular and epididymal endometriosis were found. Hematoxylin-eosin slides were reviewed, and the morphologic features were described. Clinical and follow-up information was obtained from physicians’ notes. The ages were 50 and 43 years, and sizes were 2 and 4.2 cm, respectively. No significant chemical or hormonal exposure was identified. One patient had the mass for 5 years, which had lately started to grow significantly. Both lesions were cystic and contained hemorrhagic fluid. Microscopy revealed cysts and occasional glands lined by low-columnar to cuboidal epithelium, reminiscent of endometrium. The spindle cell stroma resembled endometrial stroma and contained abundant hemosiderin-laden macrophages. One case was predominantly intratesticular, with a minute focus of endometrial-type glands and stroma within the tunica vaginalis. Focal chronic inflammation and epithelial denudation were present in both cases as well. The surrounding testicular and epididymal structures adjacent to the cystic mass were histologically unremarkable. Endometriosis with cystic degeneration is an extremely rare lesion in men. The location of the 2 tumors in our series, along the route of the Müllerian duct, supports the theory that these lesions arise from embryonic remnants that lead to the development of endometriosis.

Substaging of T1 Urothelial Bladder Neoplasms Based on Extent of Lamina Propria Invasion

Kanika Taneja, MD (ktaneja1@hfhs.org); Zhichun Lu, MD; Sean R. Williamson, MD; Nilesh S. Gupta, MD. Department of Pathology, Henry Ford Health System, Detroit, Michigan.

Context: Urothelial carcinoma can progress in subsequent transurethral resections for some patients. Patients with lamina propria invasion (pT1) pose a clinical challenge. We hypothesized that this stage of progression may be affected by the extent of lamina propria invasion.

Design: Retrospective review of pathologic material on 180 patients with pT1 between 2011 and 2014 was undertaken. Specimens with no muscle identified (n = 39), those with no follow-up biopsies/cytology (n = 17), and those with noninvasive initial biopsies (carcinoma in situ/pTis or pTa; n = 9) were excluded, leaving 115 assessable patients with initial pT1 diagnosis. Extent of lamina propria invasion was divided into focal (single microscopic focus of invasion within a papillary tumor stalk or within the lamina propria at the tumor base), multifocal (>1 invasive tumor focus), or extensive (extensive tumor burden within the lamina propria). Progression was defined as higher stage on subsequent specimens. Nonprogression was defined as tumor of the same or lower stage, or no tumor on subsequent biopsy.

Results: Of 115 patients, 26 (24%) had progression, whereas 87 (76%) did not. Extent of invasion was greater in patients who progressed (multifocal/extensive, 16 of 28; 57%), in contrast to those who did not progress (27 of 87; 31%; P = .007) (Table). Extent of invasion into the lamina propria is significantly associated with subsequent progression of bladder urothelial carcinoma after transurethral resection (P = .007) in univariate analysis. Substaging T1 lesions in the context of extent of invasion permits the identification of distinctive risk groups that may be helpful in designing therapeutic and monitoring strategies.

### Descriptive Characteristics of 115 Patients With pT1 Bladder Cancer on Transurethral Resection

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Stage Progression (n = 28)</th>
<th>No Stage Progression (n = 87)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up, mo, median (IQR)</td>
<td>14.5 (4.5–29.0)</td>
<td>21.0 (7.0–39.0)</td>
<td>.15</td>
</tr>
<tr>
<td>Age, y, median (IQR)</td>
<td>66.0 (53.5–82.5)</td>
<td>71.0 (64.0–82.0)</td>
<td>.26</td>
</tr>
<tr>
<td>Sex, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>4 (14)</td>
<td>18 (21)</td>
<td>.59</td>
</tr>
<tr>
<td>Male</td>
<td>24 (86)</td>
<td>69 (79)</td>
<td></td>
</tr>
<tr>
<td>Extent of invasion, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Focal (n = 72)</td>
<td>12 (43)</td>
<td>60 (69)</td>
<td>.007</td>
</tr>
<tr>
<td>Multifocal (n = 33)</td>
<td>10 (36)</td>
<td>23 (26)</td>
<td></td>
</tr>
<tr>
<td>Extensive (n = 10)</td>
<td>6 (21)</td>
<td>4 (5)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: IRQ, interquartile range.

The Role of Plasma Cell Infiltration in Polyomavirus Allograft Nephropathy: A Retrospective Study

Nasima K. Majeed, MD (nasima.k.majeed@gmail.com); Osama Elfituri, MD; David M. Loeffler, DO; Nathan Aardsma, DO; Suman Setty, MBBS, PhD. Department of Pathology, University of Illinois at Chicago.

Context: Polyomavirus infection is a common cause of renal allograft loss. The diagnosis of polyomavirus allograft nephropathy by light microscopy alone, in the allograft biopsy, can be a challenge because of patchy involvement by the infection and shared diagnostic criteria with acute rejection. However, the distinction is important for therapeutic decision making.

Design: We performed a retrospective review of 37 transplant kidney biopsies with polyomavirus allograft nephropathy performed between 2012 and 2018. Clinical criteria, including age, gender, time after transplant, and serum creatinine levels, and morphologic characteristics, including lymphocytic and plasma cell inflammation, tubular atrophy, and interstitial fibrosis scoring, were studied.

Results: In our study, the median age of the patients at transplantation was 59 years, the interval to the index biopsy was 13.1 months, and serum creatinine level was 1.86 mg/dL. The biopsies had a median of 35% inflammation, of which, 37% were plasma cells with a maximum of 35 plasma cells in one high-power field (Figure 119, A). In all 37 cases, SV-40 large T antigen was...
detected mainly in the cortex (Figure 119, B). Significant plasma cell inflammation was noted in 24 of 37 biopsies (mainly stage B).

Conclusions: This study shows that the presence of plasma-rich cellular infiltrate could be an indicator of polyomavirus infection with two-thirds of cases having more than 10% plasma cells. This is particularly true in cases of negative C4d and other signs of rejection; however, negative immunohistochemistry for SV-40 large T antigen may possibly be due to the patchy involvement of the virus or in “burnt-out” cases.

**SMAD4 as a Potential Marker for Renal Tumors**

*Poster No. 103*

Sina Zomorrodian, DO (Sina.Zomorrodian@wmchealth.org); Min-ghao Zhong, MD; Christian Salib, MD; Alexandra Budhai, MD. Department of Pathology, New York Medical College at Westchester Medical Center, Valhalla.

**Context:** The tumor suppressor gene SMAD4 is mutated in roughly 55% of pancreatic and 20% of colorectal carcinomas. Recent studies have implicated SMAD4 in the progression of renal cell carcinoma (RCC). It is, therefore, of interest to examine the immunohistochemical expression of SMAD4 in various RCCs and their adjacent benign parenchyma to deduce a potential role for SMAD4 in RCC carcinogenesis.

**Design:** The SoftPath database was used to collect renal tumor specimens. Tissue microarray was performed on 35 clear cell, 22 papillary, 11 chromophobe, 13 oncocytes, 6 clear cell papillary, 2 mucinous tubular and spindle cell carcinomas, 1 collecting duct carcinoma, and 1 acquired cystic disease–associated RCC. Each sample (tumor and adjacent benign tissue) was stained with hematoxylin-eosin and SMAD4. Samples that did not stain were assigned a 0, weak staining was assigned a 1, and staining with moderate intensity was assigned a 2 (Figure 120, A through D). Average staining scores were calculated for each tumor subtype.

**Results:** Healthy parenchyma exhibited generally weak staining, whereas staining was generally absent across tumor variants, with the exception of oncocytoma. A statistically significant difference in staining between tumor and healthy parenchyma from clear cell, papillary RCC, and chromophobe samples and their benign counterparts was observed.

**Conclusions:** Although there was a statistically significant difference in tumor and healthy parenchyma staining across some groups, the subjectivity of scoring a negative from a weak positive and overall weak staining across samples renders SMAD4 of low utility in distinguishing between tumor and benign tissue, as well as distinguishing between RCC subtypes.

**Invasion of Rete Testis, Hilar Fat, and Epididymis by Testicular Malignant Germ Cell Tumors Does Not Justify Upstaging to pT2**

*Poster No. 104*

Ayeshia Farooq, MD, MBBS1 (afarooq@mcw.edu); Tegan Miller, MD2; Ondrej Hes, MD, PhD3; Nicola Pavan, MD4; Beth Braunhut, MD3; Samarpit Rai, MD4; Joy Liu, MD5; Aniko Szabo, PhD4; Oleksandr N. Kryvenko, MD4; Merce Jorda, MD, PhD4; Kenneth A. Iczkowski, MD.1

1Department of Pathology, Medical College of Wisconsin, Milwaukee; 2Department of Pathology, Christie Hospital, Manchester, United Kingdom; 3Department of Pathology, Charles University, Plzeň, Czech Republic; 4Department of Pathology, University of Miami/Jackson Memorial Hospital, Miami, Florida.

**Context:** The significance of rete testis, hilar fat, or epididymis involvement by malignant germ cell tumors is controversial. AJCC cancer staging (8th edition) classifies involvement of any of these structures as pT2; however, disagreement persists as to whether these findings, in the absence of lymphovascular vascular invasion (LVI), warrants a pT1 stage. A cohort of testicular malignant germ cell tumors (MGCTs) were studied to clarify the significance of involvement of these structures in pathologic staging.

**Design:** We reviewed consecutive pT1 and pT2 orchiectomies with MGCTs performed between 2000 and 2013 from 4 academic institutions. The cases were divided into 3 groups: group 1, no invasion; group 2, rete testis pagetoid, rete testis direct invasion, hilar fat, and epididymis; and group 3, LVI, spermatic cord, and tunica vaginalis invasion. Follow-up was 1–18 years in all but 37 patients. Analysis of variance F test and chi² tests were used to compare the 3 groups.

**Results:** For nonseminomas in group 2, pagetoid spread to rete and epididymis invasion were the most common. For seminoma, pagetoid spread to the rete was by far the most common (Table). For nonseminoma, no significant difference was detected in risk of recurrence among the 3 groups, although infrequent recurrence in group 2 was a limitation. For seminoma, however, risk of recurrence in group 2 was commensurate with group 1.
Conclusions: pT1 testicular MGCT with or without involvement of rete testis, hilar fat, and/or epididymis do not have a rate of recurrence significantly different from pT1 for seminoma. For nonseminoma, those 4 types of invasion were significantly different that differences among groups were not detected, and a larger study sample is warranted.

Nonepithelial Neoplasms of the Urinary Bladder: A Clinical/Pathologic Review

(Poster No. 105)

Fatima Mij, MBBS (fatima_mij@rush.edu); Hussein Alnajar, MD; Prih Rohra, MD; Jayjay Blanco, MD; Sara Javidiparsijani, MD; Vijaya Reddy, MD; Ritu Ghai, MD; Pincas Bitterman, MD; PaoloGattuso, MD. Department of Pathology, Rush University Medical Center, Chicago, Illinois.

Context: Nonepithelial neoplasms of the urinary bladder are rare (2% of all urinary tract tumors) and present a diagnostic/therapeutic challenge. We present a retrospective study of the clinicopathologic characteristics of the nonepithelial neoplasms involving the urinary tract.

Design: All nonepithelial urinary bladder neoplasms seen at our institute from 1994 to 2017 were studied retrospectively. Clinicopathologic data were reviewed.

Results: Data from 39 patients with nonepithelial bladder tumors were analyzed: 20 women (51%) and 19 men (49%), with mean age of 57 years (range, 32–80 years). There were 26 malignant (67%), 5 low-malignant potential lesions (13%), and 8 benign tumors (20%). Eighteen of 26 malignant tumors (69%) were hematologic malignancies; 5 of 18 were primary lymphomas (3 large cell lymphomas, 1 marginal zone, 1 blastoid B-cell lymphoma), and 13 of 18 were secondary hematologic malignancies. Eight of 26 cases (31%) were malignant sarcomas; 4 of 8 were primary sarcomas (leiomyosarcoma, fibroblastic sarcoma, fibrosarcoma, and high-grade sarcoma, not otherwise specified), and 4 of 8 were metastatic sarcomas. Three of 5 low-malignant potential lesions (60%) were inflammatory myofibroblastic tumors, 1 solitary fibrous tumor (20%), and 1 parangangioma (20%). Seven of 8 benign tumors (87.5%) were hemangiomas, and 1 (12.5%) was a leiomyoma.

Conclusions: Seventeen of 26 malignant nonepithelial tumors of urinary bladder (65%) were not primary. Lymphoma was the most common nonepithelial malignant tumor encountered in the urinary bladder. Diagnosing high-grade lymphoma can be challenging, especially in a small biopsy because the tumor can mimic other primary or metastatic tumors of the urinary bladder. Hemangiomas are frequent in the urinary bladder. A variety of sarcomas and low-malignant potential spindle-cell tumors may be confused with sarcomatoid carcinoma/carcinosarcoma, which may cause diagnostic difficulties. Despite the rarity, it is important to be aware of these neoplasms to avoid a misdiagnosis because clinical characteristics do not differentiate them from other bladder tumors, and histopathologic diagnosis may be challenging.

Carcinoma of the Rete Testis: A Rare Testicular Malignancy

(Poster No. 106)

David A. Suarez-Zamora, MD1 (da.suarez33@uniandes.edu.co); Karen T. Galvis-Castro, MD2; Mauricio Cifuentes-Barreto, MD2; Mauricio A. Palau-Lazaro, MD1; Paula A. Rodriguez-Urrego, MD.1 Departments of 1Pathology and Laboratories and 2Urology, Fundación Santa Fe de Bogotá, Bogotá DC, Colombia.

Carcinoma of the rete testis is a rare testicular neoplasm, with approximately 60 cases reported in the literature. It usually occurs in men older than 60 years and has an aggressive biological behavior. We present a case of a 56-year-old man who consulted for a 1-month history of a testicular mass. Scrotal ultrasound revealed a poorly vascularized, ill-defined, solid lesion in the middle portion of the right testicle, measuring 12 mm in diameter. The patient underwent radical orchiectomy and retroperitoneal lymph node dissection. Microscopic examination of the white testicular nodule showed a tumor displaying complex papillary-cystic architecture (Figure 121, A). Some cells had a clear cytoplasm with prominent nuclei and open chromatin (Figure 121, B). At the periphery, there was an in situ component composed of cells with nuclear stratification and scanty cytoplasm, growing in a papillary pattern (Figure 121, C). The tumor infiltrated the tunica albuginea focally. The differential diagnosis included the possibility of a testicular adenocarcinoma, Müllerian-rest carcinoma, mesothelioma, and metastatic carcinoma. Immunohistochemical stains were positive for CK AE1/AE3, CK7, CK34βE12, D2-40, and PAX8 (Figure 121, D) but were negative for calretinin, TTF-1, GATA3, glypican, OCT3/4, hCG, CD30, p63, RCC, PSA, and inhibin. Computed tomography scan of thorax, abdomen, and pelvis presented no evidence of metastatic disease. These findings were those of a primary rete testis carcinoma. Pathologists should be aware of this rare condition, and metastatic carcinomas from several sites should always be excluded. The presence of an in situ component and the intratesticular location is against Mullerian-rest carcinomas.

Does Nuclear Grade and Nuclear Morphology Predict Outcomes in Primary Localized Prostate Cancer?

(Poster No. 107)

Kseniya Shin, MS1 (deksentia@uw.edu); Lawrence True, MD2; Maria Tretiakova, MD, PhD2. Departments of 1Chemistry and 2Pathology, University of Washington, Seattle.

Context: Prostate cancer nuclear grading (NG), which was part of the World Health Organization system, was abandoned because of conflicting studies and lack of prognostic significance. However, some recent studies have reclaimed NG importance as an independent prognostic factor in predicting biochemical recurrence (BCR) after radical prostatectomy (RP). We aimed at studying NG and multiple nuclear features in an RP cohort enriched for cases of grade groups 1 and 2 with long follow-ups.

Design: Study included 127 RP’s with the following Gleason scores: ≤6 (37%), 3 + 4 (46%), 4 + 3 (15%), ≥8 (2%). A BCR was present in 63
patients (50%; mean time to recurrence, 39 months) whereas 64 patients (50%) were without BCR (mean, 86 months of follow-up). Tissue microarrays were constructed with 1-mm duplicate cores. We analyzed NG based on nucleolar prominence at ≥×10, nuclear size, pleomorphism, nuclear shape, nuclear membrane thickening, chromatin texture, and presence of mitoses. Study pathologists were blinded to outcome.

Results: We found a weak association between BCR and larger nuclear size (odds ratio [OR], 1.5), irregular nuclear shape (OR, 1.63), and chromatin texture (OR, 1.73). The tumors with a coarse chromatin pattern correlated with BCR (OR, 5.92; \( P = .07 \)), but did not reach statistical significance. Moreover, no significant association between nuclear features and BCR was found on Cox regression analysis or between NG and grade groups (\( R^2 = 0.02 \); Figure 122).

Conclusions: Our study did not reveal significant value in assessing NG, mitoses, and other nuclear features in predicting BCR of primary localized prostate cancer, except for chromatin coarseness. A follow-up study with a larger sample is ongoing.

**Diagnostic Utility of 5-Hydroxymethylcytosine (5-hmC) Immunohistochemistry in Distinguishing Urothelial Carcinoma In Situ From Benign or Reactive Urothelial Mucosa**

(Poster No. 108)

Fedaa Najdawi, MBBS (fedanaajdawi@gmail.com); Karen Dresser, BS; Kristine Cornejo, MD. Department of Pathology, University of Massachusetts Medical School, Worcester.

Context: Dysregulated DNA methylation, followed by abnormal gene expression, is an epigenetic hallmark of many malignancies. Studies confirmed that 5-hydroxymethylcytosine (5-hmC), an intermediate in the demethylation process, is depleted in malignancies, including urothelial carcinoma. We examined expression of 5-hmC as a diagnostic tool in differentiating urothelial carcinoma in situ (CIS) from nonneoplastic urothelium.

### Immunohistochemical Results of 5-hmC and Ki-67 in CIS and Nonneoplastic Urothelium

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>5-hmC Loss, No. (%)</th>
<th>5-hmC Retained, No. (%)</th>
<th>High Ki-67 Index, No. (%)</th>
<th>Low Ki-67 Index, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urothelial CIS (n = 28)</td>
<td>18 (64.3)</td>
<td>10 (35.7)</td>
<td>21 (75)</td>
<td>7 (25)</td>
</tr>
<tr>
<td>Nonneoplastic urothelium (n = 36)</td>
<td>0 (0)</td>
<td>36 (100)</td>
<td>4 (11.1)</td>
<td>32 (88.9)</td>
</tr>
<tr>
<td>Benign urothelial mucosa (n = 20)</td>
<td>0 (0)</td>
<td>20 (100)</td>
<td>1 (5)</td>
<td>19 (95)</td>
</tr>
<tr>
<td>Reactive urothelial mucosa (n = 16)</td>
<td>0 (0)</td>
<td>16 (100)</td>
<td>3 (18.8)</td>
<td>13 (81.2)</td>
</tr>
<tr>
<td>Urothelial CIS (n = 28)</td>
<td></td>
<td></td>
<td>26 (93)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Nonneoplastic urothelium (n = 36)</td>
<td></td>
<td></td>
<td>4 (11)</td>
<td>32 (89)</td>
</tr>
<tr>
<td>Benign urothelial mucosa (n = 20)</td>
<td></td>
<td></td>
<td>1 (5)</td>
<td>19 (95)</td>
</tr>
<tr>
<td>Reactive urothelial mucosa (n = 16)</td>
<td></td>
<td></td>
<td>3 (19)</td>
<td>13 (81)</td>
</tr>
</tbody>
</table>

**Design:** We examined expression of 5-hmC and the Ki-67 proliferative index by immunohistochemistry in a series of CIS (n = 28) and nonneoplastic urothelium (n = 36; benign, n = 20; reactive, n = 16). 5-hmC nuclear staining was assessed as follows: percentage of cells staining (0; no staining; 1; 1%–10%; 2; 11%–50%; 3; 51%–100%) and staining intensity (0; 1; 2; and 3). Scores were calculated by multiplying the percentage and intensity (range, 0–9; loss ≤ 3). Ki-67 was classified into a low (0%–5%) and high (>5%) index. Statistical analysis was performed with the Fisher exact test.

Results: Among the 28 CIS cases, 18 (64.3%) demonstrated a loss of 5-hmC, whereas expression was retained in all 36 nonneoplastic urothelium (Table) (\( P < .001 \)). Most CIS cases (75%; n = 21) showed a high Ki-67 index with diffuse/stratified staining, compared with only 4 nonneoplastic cases (11%), with staining limited to the basal/lower one-third of the epithelium (\( P < .001 \)). Loss of 5-hmC or high Ki-67 index has a 93% sensitivity and 89% specificity in distinguishing CIS from nonneoplastic urothelium (\( P < .001 \)).

Conclusions: We demonstrate that loss of 5-hmC expression and a high Ki-67 index can be of diagnostic utility in distinguishing CIS from nonneoplastic urothelium. These findings also suggest that the loss of 5-hmC is an epigenetic event in CIS.

**A Unique Case of a Large (19.3 cm by Imaging) Cystic Prostatic Adenocarcinoma Ductal Type**

(Poster No. 109)

Paige A. Peterson, MD (paige.peterson@ucdenver.edu); Lian Zhang, MD; Francisco G. La Rosa, MD. Department of Pathology, University of Colorado Anschutz Medical Campus, Aurora.

Cystic prostatic adenocarcinoma (CyPCa) is relatively rare, and mostly secondary to tumor hemorrhage or necrosis. Most CyPCa are small, with only 5 cases reported larger than 10 cm. The case presented here is the largest CyPCa ever described, to our knowledge, found in a 62-year-old man with history of asymptomatic hematuria and negative cancer family history. Initial imaging examination 3 years earlier revealed a 3.9-cm, left seminal vesicle cyst; prostate-specific antigen (PSA) was 13.5 ng/mL, and a month after that, to 30 ng/mL; recent imaging showed a 19.3-cm, complex cystic mass in the pelvis arising posteriorly to the prostate in the area of the left seminal vesicles (Figure 123, A). A fine-needle aspirate of the cyst showed no malignancy. The patient underwent a radical prostatectomy with complete excision of the cyst. Gross examination (Figure 123, B) revealed a 324-g, 20.0 × 8.0 × 5.0-cm specimen, including a 6.0 × 5.2 × 3.5-cm prostate gland firmly attached at its base to a large (18.5 × 8.0 × 5.0 cm) previously emptied fibromembranous cyst, arising at the left seminal vesicles. Sections of the prostate showed a tan-white prostatic parenchyma with multiple small mucinous cysts. Dissection of the largest cyst showed an internal surface with brown folds lined by micropapillary lesions. Histopathology revealed a CyPCa ductal type (Gleason score, 8) (Figure 123, C) arising at the base of the prostate, invading the left seminal vesicle and urinary bladder neck and widely spreading through the internal surface of the cyst (Figure 123, D). Bone scan results were negative, and follow-up at 3 months showed no evidence of biochemical recurrence. This uncommon CyPCa presentation was a diagnostic challenge before pathologic examination.

**Pleomorphic Giant Cell Carcinoma of Prostate: Report of 2 Cases With Detection of PIK3CA Mutation**

(Poster No. 110)

Ziad M. El-Zaatari, MD (zmel-Zaatari@houstonmethodist.org); Mukul K. Divatia, MD; Steven S. Shen, MD, PhD; Alberto G. Ayala,
Müllerianosis of the Urinary Bladder: A Clinicopathologic Study

(Poster No. 112)

Khaele Al-Obaidey, MD (dr.khaled.alobaidy@gmail.com); Muhammad Idrees, MD. Department of Pathology, Indiana University, Indianapolis.

Context: Müllerianosis of the urinary bladder (MUB) is a rare entity that occurs in women during their reproductive period. It consists of cervical, tubal, or endometrial epithelium within the wall of the urinary bladder. The pathogenesis is still unclear; however, a metaplastic derivation of Mullerian tissue is one of the preferred theories. Herein, we describe the clinicopathologic features of this entity.

Design: Seven cases were found in a retrospective search of our institutional records between 1985 and 2017. Hematoxylin–eosin slides were reviewed, and the morphologic features were described. Clinical and follow-up information was obtained from physicians’ notes.

Results: All patients were women. The mean age at time of diagnosis was 39 years (range, 35–55 years). Three patients presented with urinary bladder mass, and 4 cases were incidental. The lesions were diagnosed after cystectomy (n = 4), after transurethral resection of bladder tumor (n = 2), and on a ureteric-polyp biopsy (1). Adenomyosis (n = 1) and endometriosis (n = 2) were noticed in clinical notes. Two patients had a history of abdominal surgeries. Microscopically, it displayed clusters of benign glands, lined predominantly by a single layer of cuboidal epithelium and endocervical-type mucinous epithelium. Cysts lined by flattened-to-cuboidal ciliated epithelium resembling fallopian tube epithelium were also observed (n = 2). Endometrial glands and stroma were present (n = 1). No cytologic atypia or mitosis was identified.

Conclusions: The MUB is a rare nonneoplastic lesion that may present as a mass. It accounted for 0.5% of bladder specimens at our institution. It may develop as a consequence of prior surgery and is often associated with endometriosis elsewhere. Awareness of the entity is crucial, because it may be mistaken for a neoplasm.

Difference in Sensitivity of ERG-Expressing Prostate Cancer to Radiation and Androgen Ablation

(Poster No. 113)

Le L. Aye, DO (Le.Aye@med.usc.edu); Kyle Hurth, MD, PhD; Manju Aron, MD; Andy Sherrod, MD; Guang-Qian Xiao, MD, PhD.
Abbreviation: IHC, immunohistochemistry.

Omar Jaber, MD. 21 Department of Pathology, University of Iowa

**Abstracts**

May contribute to such difference in responses. The association of ERG expression with the androgen signaling pathway has been performed regarding the different morphologic response and sensitivity of ERG-expressing PCa to these 2 treatments.

**Design:** Two tissue microarrays were generated from salvage prostatectomies for recurrent PCa after radiotherapy and androgen ablation. ERG immunohistochemistry was used to detect the expression of ERG in recurrent PCa. Nuclear immunoreactivity with monoclonal ERG antibody (Abcam, Cambridge, Massachusetts) was considered positive.

**Results:** Of a total of 50 recurrent PCa cases after radiotherapy, 40 displayed no treatment effect with 50% ERG expression, whereas 10 demonstrated treatment effect with no ERG expression. Of a total of 52 recurrent PCa after androgen ablation, 41 exhibited treatment effect with 32% ERG expression, and 11 without treatment effect with 9% ERG expression (Table).

**Conclusions:** The treatment effect versus no treatment effect in recurrent PCa represent the morphologic manifestation of different responses to the treatment. Our results indicate that ERG+ PCa is more resistant to radiation, but more sensitive to hormonal therapy than ERG- PCa. The results imply a potential predictive value of ERG expression in recurrent PCa responses to radiation versus androgen ablation therapy. TMPRSS2:ERG gene translocation and its known close association of ERG expression with the androgen signaling pathway may contribute to such difference in responses.

### Expression of ERG in Recurrent Prostate Cancer (PCa) With Treatment Effect and Without Treatment Effect After Radiotherapy and Androgen Ablation

<table>
<thead>
<tr>
<th></th>
<th>Postradiation Recurrent PCa</th>
<th>Postandrogen Ablation Recurrent PCa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No treatment effect</td>
<td>With treatment effect</td>
</tr>
<tr>
<td>ERG-IHC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive cases</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Negative cases</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Total cases</td>
<td>40</td>
<td>10</td>
</tr>
<tr>
<td>Positive cases, %</td>
<td>50</td>
<td>0</td>
</tr>
<tr>
<td>P value</td>
<td>P &lt; .05</td>
<td>P &lt; .05</td>
</tr>
</tbody>
</table>

**The Role of Immunohistochemistry in Distinguishing Primary Adenocarcinoma of the Bladder From Secondary Involvement by Colorectal Adenocarcinoma**

(Poster No. 114)

Renee Eigsti, MD1 (renee-eigsti@uiowa.edu); Andrew Bellizzi, MD1; Omar Jaber, MD, MSc2. 1Department of Pathology, University of Iowa Hospitals and Clinics, Iowa City; 2Department of Pathology, King Hussein Cancer Center, Amman, Jordan.

**Context:** Distinguishing primary adenocarcinoma of the bladder (PACB) from secondary involvement by colorectal adenocarcinoma (SCRAC) is challenging. We studied the role of immunohistochemistry (IHC) in differentiating these 2 tumors using CK7, CK20, CDX2, cadherin 17 (CDH17), SATB2, β-catenin, GATA3, and P40 immunohistochemical stains.

**Design:** Eight PACBs, including 2 urachal adenocarcinomas, and 5 SCRACs were studied. The best paraffin-embedded tissue block was selected for IHC. The percentage of expression and intensity of staining by calculating the mean H score for each stain was performed, and the results were compared between PACB and SCRAC (Table).

**Results:** Both PACB and SCRAC showed variable expression of CK20, CDX2, SATB2, and CDH17. CDH17 showed strong and diffuse staining in both tumors (7 of the 8 PBACs and all 5 SCRACs). The PACB showed membranous, but not nuclear, expression of β-catenin. The SCRAC showed no expression of CK7, GATA3, or P40. SATB2 results were often positive in PACB (5 of 8), whereas GATA3 (2 of 8; H score, 100 and 5; weak to moderate staining intensity) and P40 (1 of 8; H score, 2; weak staining intensity) was mostly expressed rarely and focally. No single stain showed a statistically significant P value.

**Conclusions:** Used alone, no stain was statistically significant in distinguishing these 2 tumors, possibly because of small sample size. However, a pattern of combined staining can favor one tumor over the other. Expression of CK7, GATA3, and P40 (up to any extent), along with membranous β-catenin staining and lack of SATB2 expression, favors PACB. Nuclear β-catenin favors SCRAC. CK20, CDH17, and CDX2 are not helpful in this setting.

### Immunostain Parameters of Adenocarcinoma of Bladder Compared With Secondary Colorectal Adenocarcinoma

<table>
<thead>
<tr>
<th></th>
<th>Bladder (n = 8)</th>
<th>Colon (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Staining, %</td>
<td>Mean H Score if Positive Staining</td>
</tr>
<tr>
<td>CK7</td>
<td>50</td>
<td>41.25</td>
</tr>
<tr>
<td>CK20</td>
<td>88</td>
<td>224</td>
</tr>
<tr>
<td>CDX2</td>
<td>88</td>
<td>211</td>
</tr>
<tr>
<td>SATB2</td>
<td>63</td>
<td>131</td>
</tr>
<tr>
<td>CDH17</td>
<td>88</td>
<td>287</td>
</tr>
<tr>
<td>β-catenin</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>GATA3</td>
<td>25</td>
<td>53</td>
</tr>
<tr>
<td>P40</td>
<td>13</td>
<td>2</td>
</tr>
</tbody>
</table>

**Abbreviation:** IHC, immunohistochemistry.

### An Incidental Finding of Paratesticular Malignant Mesothelioma During Operation for Hydrocelectomy

(Poster No. 115)

Karah D. Odegaard, MD (karah.odegaard@usd.edu); Kimberlee C. Tams, MD; DesiKae M. Muirhead, MD; Amy M. Kerkvliet, MD. Department of Pathology, University of South Dakota Sanford School of Medicine, Sioux Falls.

Paratesticular malignant mesothelioma is a rare and aggressive malignancy, accounting for approximately 0.5% to 1.4% of all malignant mesotheliomas. Fewer than 500 cases have been described in the literature. The tumor typically presents as a painless scrotal mass and is associated with a history of asbestos exposure, long-standing hydrocele, trauma, or radiation. Treatment consists of radical orchietomy, although approximately 60% of cases will recur. We report a case of an incidental paratesticular malignant mesothelioma in a 73-year-old...
A Rare Presentation of Endometriosis Mimicking a Ureteral Tumor

(Akisha Glasgow, MD (akisha.glasgow@uhhospitals.org); Gregory MacLennan, MD, Department of Pathology, University Hospitals Cleveland Medical Center, Cleveland, Ohio.)

Endometriosis is defined as endometrial glandular and stromal tissue found outside of the uterus. The most common site for endometriosis is the ovary, but rarely, it can involve the urinary tract, with a prevalence of <0.1% to 0.4% of endometriosis cases. Of the cases identified within the urinary tract, the bladder is the most common site of involvement being affected 8 times more than the ureter. Endometriosis is estrogen-dependent and, therefore, is usually identified in females of reproductive age with a peak age of 44 years. We present a case of a 57-year-old woman with no known medical history, who presented acutely with left abdominal pain, with a computed tomography scan that revealed a 7.1-cm, partially multicystic mass in the lower pole of the right kidney. She underwent laparotomy and bilateral pelvic and peritoneal exploration, with removal of a 7.0-cm, partially multicystic mass on the left side, consistent with endometriosis. Microscopic examination revealed a mass in the distal ureter measuring 3.5 × 3.0 × 1.5 cm. On microscopic examination, endometriosis was identified within the muscularis propria (Figure 127, A and B) as well as the periureteral tissue (Figure 127, C and D). Although endometriosis is a common condition, this case illustrates the rare and unusual presentation of endometriosis in a postmenopausal woman as a ureteral mass.
the omentum. Microscopic examination showed solid tumor growth pattern separated by thin septa. Tumor cells were composed with eosinophilic cytoplasm, hyperchromatic nuclei, and perinuclear halos. Immunohistochemically, tumor cells were positive for CD10, CK7, PAX8, patchy RCC, and CAIX and were negative for ER and vimentin. Ovary with metastatic ccRCC is a rare entity, and ovarian ChRCC metastasis has not, to our knowledge, been reported in the literature. Metastatic ccRCC in ovary can cause diagnostic challenges for ovarian clear cell carcinoma. The biologic behavior in our case remained indolent, like most ChRCCs, but was resistant to treatment, and debulking surgery is a treatment option (Figure 128).

Immunohistochemical Detection of PD-L1 Expression on Bladder Small Cell Carcinomas Using Ventana SP263 Clone

(Poster No. 119)
Haiyan Liu, MD (hliu1@geisinger.edu); Angie Biting, HT(ASCP), QIHC; Dustin Lin; Fan Lin, MD, PhD. Department of Laboratory Medicine, Geisinger Health System, Danville, Pennsylvania.

Context: Small cell carcinoma of the bladder (SCCB) is an uncommon, but clinically aggressive, tumor. Patients often present with locally advanced or metastatic disease. PD-1 blockage therapies have demonstrated some efficacy in the treatment of urothelial carcinoma. Expression of PD-L1 in SCCB has not been well reported. We investigated the expression of PD-L1 in SCCB, which can potentially be useful in determining the role of PD-1/PD-L1 blockage treatment.

Design: A total of 31 SCCBs were retrieved from the pathology archives, and a tissue microarray block was constructed with 2 punched cores for each case. Immunohistochemical stain for PD-L1 (SP263 clone, prediluted, Ventana Medical Systems, Oro Valley, Arizona) was performed with the Ventana Ultra platform. Complete or partial membranous staining was regarded as positive. The positive results were recorded as a percentage with a 5% incremental increase. Less than 1% staining was considered negative.

Results: Seven of 31 cases (22.6%) were positive for PD-L1. Two cases demonstrated diffuse staining (>50% of tumor cells stained). The detailed results of positively stained cases are listed in the Table.

Conclusions: Our preliminary result demonstrates that a significant percentage of small cell carcinomas of the bladder were positive for PD-L1 when using the Ventana SP263 clone, which may potentially offer a treatment option for using PD-1/PD-L1 blockages in targeting this highly aggressive tumor.

Summary of Positive Staining Results

<table>
<thead>
<tr>
<th>Case No.</th>
<th>PD-L1, % Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>7</td>
<td>5</td>
</tr>
</tbody>
</table>

Profiles of Monoclonal Gammopathy With Renal Significance Versus Heavy-Burden Cases of Monoclonal Nephropathy

(Poster No. 120)
Zongshen Lai, MD (Zongshen.Lai@Beaumont.org); Hassan D. Kanaan, MD; Wei Li, MD; Ping L. Zhang, MD. Department of Pathology, Beaumont Health, Royal Oak, Michigan.

Context: In cases of either myeloma or MCN, renal diseases affected by monoclonal immunoglobulin and/or light chains are usually severe, which is considered a “heavy burden” (HB), and such cases are overqualified for monoclonal gammopathy with renal significance (MGRS). The remaining types of monoclonal nephropathy with renal injury/significant proteinuria can be classified as MGRS. Our study goal was to retrospectively review a feasibility of MGRS concept in our monoclonal nephropathy cases.

Design: Based on our current information, we evaluated our 2262 renal biopsies and identified 59 cases with monoclonal nephropathy, representing only 2.6% of all biopsies. We divided the monoclonal nephropathy cases into MGRS and HB groups for further analysis.

Results: Among them, 31 of 59 cases (53%) were qualified as MGRS currently, including 13 AH/AAL amyloidosis and other monoclonal nephropathies. The remaining 28 of 59 cases (47%) were classified into the HB group. The mean ages of patients in MGRS and HB groups were similar (>60 years old). The MGRS group had mean serum creatinine levels of 2.55 mg/dL, which was twice the reference range, but was significantly lower than that in the HB group (6.57 mg/dL).

Conclusions: Our data indicate that the HB group had a significantly higher level of serum creatinine than the MGRS group had, supporting the view that HB renal disease may carry a worse prognosis.

Vasitis Nodosa–Like Reaction Mimicking Prostatic Carcinoma: A Near Miss Caused by Immunoconfusion and Prevented by Second Review

(Poster No. 121)
Baidarbi Chakraborty, MD (baidarbi.chakraborty@tuhs.temple.edu); Tunde Farkas, MD; Mahul Amin, MD; Rachana Choksi, MD; Daniel Eun, MD; Niraj Jhala, MD; Suad Tarafi, MD. 1Department of Pathology, Temple University Hospital, Philadelphia, Pennsylvania; 2Department of Pathology, University of Tennessee Health Science Center, Memphis.

Vasitis nodosa is a relatively uncommon, benign proliferation of vas deferens epithelium in response to mechanical obstruction or traumatic injury following vasectomy. Morphologic diagnosis is often challenging for an unsuspecting pathologist. We present here a case of this uncommon lesion that mimicked prostate cancer. A 60-year-old man with history of prostate cancer (radical prostatectomy 5 years earlier) presented with flank pain radiating to the groin. His recent prostate-specific antigen (PSA) levels were <0.02 ng/mL. Computed tomographic scan revealed a multilocular mass in the right pelvis abutting the rectum. At surgery, a pelvic side wall mass was noted encasing the external iliac vessels. Microscopy of the mass revealed fibroconnective and fatty tissue with scattered glands composed of a single layer of cuboidal cells with vesicular nuclei and occasional, small nucleoli. These glands stained for PSA and PSAP. A diagnosis of prostatic adenocarcinoma, Gleason score 6 (3+3), was rendered. As part of a continuous quality-assurance process, a second focused review was conducted, which discovered luminal and extravasated spermatids inducing an inflammatory reaction in the surrounding stroma. The diagnosis was revised to vasitis nodosa–like reaction with sperm granuloma, which was confirmed by additional expert opinion. Awareness of this uncommon entity mimicking prostate carcinoma is important. Immunohistochemical stains should be interpreted in the context of morphologic evidence. Second opinions and quality assurance protocols are important to avoid pitfalls, especially for such uncommon entities.

A Rare Case of Embryonal Rhabdomyosarcoma of the Testis in an Adult Male

(Poster No. 122)
Julian J. Samuel, MD (Julian.Samuel@mountsinai.org); Ippolito Modica, MD. Department of Pathology and Laboratory Medicine, Mount Sinai St. Luke’s, Mount Sinai West, New York, New York.

Embryonal rhabdomyosarcoma is a malignant, primitive mesenchymal neoplasm that shows variable differentiation toward embryonic skeletal muscle. Embryonal rhabdomyosarcoma is the most common sarcoma in the pediatric population and is seen frequently in the genitilia but rarely presents at this site in adulthood. We present the case of a 20-year-old man with a 6-month history of an enlarging, painless lump in the left testis. A scrotal ultrasound revealed an irregular, solid, exophytic mass arising from the testicle. He underwent a radical orchietomy. Gross evaluation showed a 9-cm-long, white-tan, encapsulated, focally lobulated, gelatinous firm to hard, testicular mass invaded which was twice the reference range. The resected testis and spermatic cord, and tunica vaginalis. Histopathologic examination demonstrated malignant rhabdomyoblastic cells. The tumor extended to the rete testis, hilar fat, spermatic cord, epididymis, and tunica vaginalis. Lymphovascular invasion was identified. Immunohistochemical studies showed the tumor cells were positive for desmin and myogenin and were negative for germ cell and epithelial markers (PLAP, CD117, OCT4, SALL4, CD30, and pankeratin). A diagnosis of embryonal rhabdomyosarcoma of the left testis was made. Postoperative staging computed tomographic scans identified retroperitoneal...
lymph nodes suspicious for metastases. He underwent lymphadenectomy of the regional retroperitoneal lymph nodes. Histopathologic evaluation revealed metastatic embryonal rhabdomyosarcoma to the para-aortic, left renal hilar, and left adrenal hilar lymph nodes. To date, the patient has received adjuvant chemoradiotherapy with no relapse of disease. The accurate diagnosis of this entity at an extremely unusual age and site was paramount to initiating his further therapeutic management.

**Primary Presentation of Myeloid Sarcoma Involving the Testis and Kidney Without Peripheral Blood or Bone Marrow Involvement: A Rare Case Presentation**

(Poster No. 123)

Archi Patel, MD\(^1\) (patella4@etsu.edu); Emily Patterson, MD.\(^2\)

\(^1\)Department of Pathology, East Tennessee State University, Johnson City; \(^2\)Department of Pathology, Watuga Pathology Associates, Johnson City Medical Center, Johnson City.

Myeloid sarcoma is a neoplasm of immature granulocytes, monocytes, or both involving any extramedullary site. Myeloid sarcoma involving the testis and kidney is uncommon and very rarely occurs as an isolated mass independent of bone marrow involvement. We report on a unique presentation of myeloid sarcoma involving right testis and kidney without bone marrow involvement. The patient was a 71-year-old man with an incidentally discovered 4.1-cm, right renal mass and 1.6-cm testicular mass. Right orchietomy and kidney biopsy were performed and demonstrated diffuse sheets of immature neoplastic cells with enlarged nuclei, prominent nucleoli and vesicular chromatin. The neoplastic cells were positive for CD117 and myeloperoxidase and showed an elevated proliferation index of 50% to 60% with Ki-67, consistent with the diagnosis of myeloid sarcoma. No bone marrow involvement by leukemic cells was identified. The patient began treatment with a hypomethylating chemotherapy agent (azacitidine [Vidaza, Celgene, Summit, New Jersey] and is continuing medical care at a local facility. Most myeloid sarcomas are reported in patients with associated acute myeloid leukemia. Myeloid sarcoma is rarely recognized as an isolated tumor without evidence of peripheral blood or bone marrow leukemia. In such cases, the initial diagnosis of myeloid sarcoma can be difficult and increases the risk for misdiagnosis. Myeloid sarcoma should be considered in the differential diagnosis of morphologically immature or poorly differentiated neoplasms, which often require a panel of immunohistochemical stains for definitive diagnosis. The differential diagnoses in these cases include melanomas, high-grade lymphomas, and other small round cell tumors, such as Ewing sarcoma.

**Massive Scrotal Fibrosis in Association With Retroperitoneal Fibrosis**

(Poster No. 124)

Hamza N. Gokozan, MD (hamza.gokozan@uhhospitals.org); Wisam Dahoud, MD; Robin Elliott, MD. Department of Pathology, University Hospitals Cleveland Medical Center, Cleveland, Ohio.

A 55-year-old man with a history of idiopathic retroperitoneal fibrosis presented with a slowly growing, painless scrotal mass. Imaging revealed an 11 cm fibrotic unilocular cystic mass (Figure 129, A). Radical orchiectomy was performed because of concern for malignancy. Gross pathologic examination of the mass revealed a thick, fibrous capsule containing fluid and an atrophic testis and epididymis. Microscopic examination showed a dense lymphoplasmacytic infiltrate with germinal center formation in a background of storiform fibrosis (Figure 129, B; ×200). By immunohistochemistry, IgG4+ plasma cells (Figure 129, C; ×200) and total IgG+ cells (Figure 129, D; ×200) were increased, with a ratio of 60%. Obliterative thrombophlebitis was not identified. The approach to scrotal masses should start with the exclusion of testicular and paratesticular primary malignancies. Nonneoplastic conditions to be considered include various cysts, mass-forming lymphedema, and the sequelae of chronic epididymo-orchitis. IgG4-related disease is a new entity characterized with at least 2 of the following major histopathologic findings: dense lymphoplasmacytic infiltrate containing increased IgG4+ plasma cells, fibrosis arranged at least focally in a storiform pattern, and obliterative phlebitis. Studies show that nearly one-half of the idiopathic retroperitoneal fibrosis cases are IgG4 related. Scrotal involvement of IgG4-related disease and diagnostic criteria are not well established. Although IgG4-related disease of the para-testicular region is extremely rare, it should be considered in patients with a history of a sclerosing disease, such as retroperitoneal fibrosis.

The New Morphologic Features of Intraductal Carcinoma of Prostate

(Poster No. 125)

Faisal Saeed, MD\(^1\) (faisal.saeed@wmchealth.org); Jonathan I. Epstein, MD\(^2\); Minghao Zhong, MD, PhD.\(^3\) \(^1\)Department of Pathology, New York Medical College, Westchester Medical Center, Valhalla; \(^2\)Department of Pathology, Johns Hopkins Medical Institutions, Baltimore, Maryland.

**Context:** Intraductal carcinoma of prostate (IDC-P) is characterized by prostatic carcinoma involving ducts and/or acini. The presence of IDC-P is usually associated with a high-grade Gleason score and adverse prognostic parameters. Recording the intraductal component has been made part of the recent College of American Pathologists cancer protocol template for prostate cancer. Previous studies and publications emphasized that IDC-P is usually prostatic acinar carcinoma involving medium to large ducts. Here, we identified new morphologic features that are different from classic IDC-P.

Design: We screened all prostatic carcinoma cases (both biopsy and resection) from 2012 to 2017 in our institution. We also included 13 cases of ductal adenocarcinoma of prostate. We first identified IDC-P
(by morphology and PIN4 triple stain, if necessary), then we focused on cases of IDC-P with nonclassic morphology.

**Results:** Approximately 1000 prostate cancer cases were reviewed. The IDC-P was identified in approximately 10% of the cases. Two nonclassic IDC-P morphologic types were identified: (1) in contrast to medium to large duct involvement, 3 cases demonstrated small ducts/acini involvement by IDC-P, with the small size due to either absence of small ducts/acini or compressed larger ducts (Figure 130, A and B); and (2) ducts with ductal carcinoma, instead of acinar carcinoma, as in classic IDC-P. Ten of the 13 cases (77%) had intraductal carcinoma at the periphery of the ductal adenocarcinoma (Figure 130, C and D).

**Conclusions:** Our study demonstrates examples of nonclassic IDC-P morphology: (1) small-sized ducts/acini can be involved by IDC-P, and (2) ductal carcinoma is often associated with IDC-P. Herein, we are expanding the morphologic spectrum of IDC-P. Pathologists should be aware of these new morphologic types of IDC-P.

**PD-L1 andMismatch Repair Protein Expression in Upper Tract Urothelial Carcinoma**

(Poster No. 126)

Aida L. Valencia-Guerrero, MD (aida.valencia12@gmail.com); Ediz F. Cosar, MD; Karen Dresser, BS; Kristine M. Cornejo, MD. Department of Pathology, UMass Memorial Medical Center, Worcester, Massachusetts.

**Context:** Patients with Lynch syndrome are at increased risk of developing upper tract urothelial carcinoma (UTUC). PD-L1 expression has been associated with BRAF mutations and identified in a subset of microsatellite-unstable colorectal carcinomas correlated with worse outcomes. We assessed UTUCs for mismatch repair proteins, PD-L1, and BRAF V600E expression by immunohistochemistry and possible correlations with outcome.

**Design:** A total of 49 UTUCs were obtained from the surgical pathology files and analyzed by immunohistochemistry for mismatch repair proteins (MLH1, PMS2, MSH2, and MSH6), PD-L1, and BRAF V600E expression. Membranous/cytoplasmic PD-L1 expression of more than 5% of tumor cells was considered positive. A retained/positive or loss/negative result was given for the remaining stains. Results were correlated with patient outcomes.

**Results:** Of the 49 UTUCs, there was retained expression of mismatch repair proteins in 48 cases (98%). There was loss of expression of MSH2/MSH6 in 1 case (2%) that showed concurrent PD-L1 expression. Four cases showed PD-L1 expression (8%), and all cases were negative for BRAF V600E staining. Two of 10 patients who died of disease had PD-L1 expression with a mean follow-up interval of 42 months (range, 2.5–116 months). The patient with concurrent MSH2/MSH6 loss and PD-L1 expression was alive with disease at 42 months. A patient with PD-L1 expression died of postoperative complications. Three of the 14 patients who developed metastases contained PD-L1 expression.

**Conclusions:** Although we could not demonstrate a strong correlation between microsatellite instability, PD-L1 expression, and clinical outcomes because of the small cohort, this study suggests PD-L1 expression may be associated with poor outcome in UTUCs.

**Antibody-Mediated Renal Allograft Rejection: Association of Complement Split Product C4d Deposition With Peritubular Capillary Basement Membrane Lamellation**

(Poster No. 127)

Zeinab Moussa, MD1 (zeinab.moussa2@utoledo.edu); Daniel Rospert, BS2; Jorge Ortiz, MD2; William Gunning, PhD1; Amira Gohara, MD1. Departments of 1Pathology and 2Surgery and the 3College of Medicine, University of Toledo Medical Center, Toledo, Ohio.

**Context:** The complement split product C4d is a useful marker of antibody-mediated rejection (AMR) when deposited on capillaries' endothelium of renal allografts (RA) early after transplantation. The purpose of this study was to examine the correlation between peritubular capillaries basement membrane (PTCBM) of RA with AMR and the deposition of C4d. We hypothesize that there was a correlation between PTCBM multilayering and C4d deposition in AMR of RA.

**Design:** This was a retrospective study evaluating all C4d+ and negative RA biopsies taken at the University of Toledo Medical Center between January 1, 2013, and July 31, 2017 that used an electron microscope tool. Biopsies of patients diagnosed with systemic lupus erythematosus and diabetes mellitus, in which renal inflammation was present, were evaluated as additional controls. We examined 30 peritubular capillaries per biopsy by electron microscope, and the average number of layers of basement membrane per capillary was calculated. A biopsy was considered to have PTCBM lamellation if that average had more than 2.5 layers of PTCBM. C4d positivity was evaluated in all RA biopsies with immunofluorescence or immunohistochemistry.

**Results:** The results of our study are shown in the Table.

**Conclusions:** There is a statistically significant association between PTCBM multilayering and peritubular capillary C4d deposition in RA with AMR when compared with C4d-negative biopsies (P = 0.048). These findings might be helpful as early diagnostic and prognostic markers to optimize treatment and contribute to the development of future targeted therapy.

<table>
<thead>
<tr>
<th>Peritubular Capillary Basement Membrane Multilayering in C4d-Positive and C4d-Negative Renal Allografts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Layers</td>
</tr>
<tr>
<td>Multilayering (≥2.5 layers)</td>
</tr>
<tr>
<td>No multilayering (&lt;2.5 layers)</td>
</tr>
</tbody>
</table>

**Plasmacytoid Variant of Urothelial Carcinoma: A Series of Three Cases of This Rare Entity**

(Poster No. 128)

Aditi Dewan, MD (aditi.dewan@corediagnostics.in); Lata Kini, MD; Ekta Jain, MD, DNBB; Shivani Sharma, DCP; DNB; Kunal Sharma, DNB; Vandana Sharma, MSC; Munmun Bhattacharya, MSC; Brijpal S. Yadav, BSc, MLT. Department of Pathology and Laboratory Medicine, Core Diagnostics, Gunugram, Haryana, India.

**Context:** Plasmacytoid urothelial carcinoma is a rare histologic variant of bladder carcinoma with poor clinical outcomes. Herein, we discuss the pathologic and immunohistochemical features of 3 cases of this uncommon entity.

**Design:** We retrospectively identified 3 cases of plasmacytoid urothelial carcinoma diagnosed at our institute during 1 year. Pathologic and immunohistochemical findings were recorded. Additionally, demographic data, clinical findings, and treatment data were retrieved.

**Results:** Patient age ranged from 40 to 65 years, with 1 woman and 2 men. Two patients presented with complaints of lower abdominal pain whereas one patient presented with a large pelvic mass. Cystoscopy revealed ulceration and thickening of the bladder wall in 2 of the 3 cases. Histopathologically, all cases showed a tumor infiltrating the bladder wall arranged in diffuse sheets and cords composed of discohesive cells with polygonal cell outlines, eccentric hyperchromatic nuclei, and moderate to abundant eosinophilic cytoplasm (Figure 131, A). A differential diagnosis of urothelial carcinoma, plasmacytoma,
signet-ring cell carcinoma, and rhabdomyosarcoma was considered. All cases were immunopositive for CK7, CK20, GATA3 (Figure 131, B), and CD138 (Figure 131, C) with polyclonal light chain expression and loss of E-cadherin (Figure 131, D), which helped in determining the diagnosis of plasmacytoid urothelial carcinoma.

**Conclusions:** Plasmacytoid variant of urothelial carcinoma is a rare entity with defined histologic and immunohistochemical features and needs to be identified and differentiated from other entities with a plasmacytoid morphology because of its aggressive behavior, poor prognosis, and differences in therapeutic approach.

**Can We Hit the Target? One Institution’s Comparison of MRI/US Fusion-Targeted Prostate Biopsies With Systematic Ultrasound-Guided Prostate Biopsies**

(Poster No. 129)

Christopher A. Febres Aldana, MD¹ (christopher.febres@msmc.com); Sarah Alghamdi, MD⁴; Pukhraz Basra, MD⁴; Thomas A. Weppelmann, PhD, MPH⁴; Yumma Omarzai, MD¹; Robert J. Poppiti, MD.¹ Arkadi M. Rywlin MD Department of Pathology and Laboratory Medicine, Mount Sinai Medical Center, Miami Beach, Florida; ²Arkadi M. Rywlin MD Department of Pathology and Laboratory Medicine, Herbert Wertheim College of Medicine, Florida International University, Miami Beach.

**Context:** Prostate cancer has traditionally been detected by random sampling. Advances in magnetic resonance imaging (MRI), along with systematic cores were collected.

**Results:** The overall cancer detection rates were 43.5% and 50.6% for the FTB and SUB, respectively. A total of 127 targeted lesions were identified on MRI, and subsequent FTB detected cancer in only 30% of those cases. An MRI failed to identify 24% (11 of 45) of the cases with cancer proven by SUB. The FTB missed 42% (19 of 45) of the cancer detected by SUB in commonly sampled zones. The FTB cancer-detection rate for lesions located in areas not sampled by SUB was 33% (12 of 36). For carcinomas detected by both methods, the agreement on Gleason score was 0.756 (95% CI, 0.462–0.889). The cancer detection rates adjusted by PI-RADS scores are shown in Figure 132. Acute inflammation was detected in 26% and 50.5% of FTB and SUB specimens, respectively.

**Conclusions:** In this study, SUB outperformed FTB. A significant number of prostate cores with undetectable lesions by MRI revealed cancer by SUB, showing that some cancers are MRI invisible. Moreover, negative FTB in the presence of SUB-proven cancer could be attributed to operator technique.

**Unusual Renal Findings in Klippel-Trenaunay Syndrome**

(Poster No. 130)

Alex Clavijo, MD (aclavijo@augusta.edu); Matthew Powell, MD; Nikhil Patel, MBBS; Daniel Kleven, MD. Department of Pathology, Augusta University, Augusta, Georgia.

Klippel-Trenaunay syndrome (KTS) typically presents at birth with a port-wine stain and progresses through infancy with hypertrophy of bone and soft tissues and malformation of veins. Clinically, vascular complications often present as varicose veins, cellulitis, lymphedema, and venous thromboembolism. Mutations are often sporadic, and the incidence of KTS is approximately 1 in 100 000 worldwide. Reported cases have identified rare extravascular manifestations, such as ocular and gastrointestinal. We present a patient with KTS and an unusual renal manifestation. A 44-year-old woman with a history of metastatic breast cancer underwent imaging for staging. This identified systemic vascular complications of KTS, such as an absent left femoral vein as well as an atrophic right kidney with hemorrhagic cystic lesions. Subsequent imaging showed a lesion in the lateral aspect of the right renal pole, which was concerning for renal cell carcinoma, in addition to multiple cystic lesions. After nephrectomy, gross examination revealed diffuse cortical atrophy with multiple cystic lesions filled with bloody, serous, or thick colloidlike fluid and no definite tumor. Microscopic examination showed an atrophic kidney with severe arteriosclerosis and vascular proliferation. There was unusual cystic dilation of the Bowman capsule with atrophy and crowning of glomeruli. To date, literature on KTS with renal manifestations has involved hemangiomatous changes but has not, to our knowledge, reported glomerular changes. These changes may have led to an abnormal appearance on imaging that could be mistaken for a vascular neoplasm histologically (Figure 133).

**Effect of Androgen Deprivation on NKX3.1 Expression in Metastatic Prostatic Adenocarcinoma**

(Poster No. 131)

Adebowale J. Adeniran, MD (adebowale.adeniran@yale.edu); Kevin Pelland, MD; Peter A. Humphrey, MD; PhD; Guoping Cai, MD. Department of Pathology, Yale University School of Medicine, New Haven, Connecticut.

**Context:** Androgen-deprivation therapy has become a standard treatment for patients with metastatic prostate cancer. The histology of both the healthy and neoplastic tissue may be significantly altered with this therapy, making the assessment of specimens difficult. Because of its highly restricted expression in epithelial cells, NKX3.1 can be used as a diagnostic biomarker for prostate cancer, and it shows better sensitivity than prostate-specific antigen (PSA) for identifying prostatic adenocarcinoma. The aim of this study was to determine whether there was any effect of androgen-deprivation therapy on the expression of NKX3.1 in metastatic prostatic adenocarcinoma.

**Design:** A retrospective search of our database was conducted for patients with metastatic prostate cancer who had been on androgen-deprivation therapy before the biopsy of the metastatic lesions. The hematoxylin-eosin slides were reviewed for confirmation of the original diagnoses, and immunohistochemical stains for PSA, NKX3.1, and
androgen receptor (AR) were performed. The histologic diagnoses were stratified as usual prostatic adenocarcinoma and poorly differentiated carcinoma, with or without morphologic evidence of neuroendocrine differentiation.

Results: A total of 31 patients were identified: 16 cases of usual prostatic adenocarcinoma, 5 cases of poorly differentiated carcinoma without evidence of neuroendocrine differentiation, 5 cases of poorly differentiated carcinoma with neuroendocrine differentiation, and 5 cases of pure small cell carcinoma. The immunohistochemical profile for each of the diagnostic categories is summarized in the Table.

Conclusions: Androgen-deprivation therapy results in loss of expression of NKX3.1, and the loss of expression is more pronounced with transformation into less-differentiated tumors.

<table>
<thead>
<tr>
<th>Immunohistochemical Profile</th>
<th>NKX3.1</th>
<th>PSA</th>
<th>AR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual prostatic adenocarcinoma (n = 16)</td>
<td>1/4/14</td>
<td>9/11</td>
<td>9/11</td>
</tr>
<tr>
<td>Small cell carcinoma (n = 5)</td>
<td>0/5</td>
<td>0/3</td>
<td>0/4</td>
</tr>
<tr>
<td>Poorly differentiated carcinoma with neuroendocrine differentiation (n = 5)</td>
<td>0/5</td>
<td>0/4</td>
<td>0/3</td>
</tr>
<tr>
<td>Poorly differentiated carcinoma (n = 5)</td>
<td>4/5</td>
<td>2/4</td>
<td>4/5</td>
</tr>
</tbody>
</table>

Rosai-Dorfman Disease, a Rare Mimicker of Testicular Malignancy, Associated With Marginal Zone Lymphoma
(Poster No. 132)

Victoria C. Vaughan, MD (victoria.vaughan@ucdenver.edu); Lian Zhang, MD, PhD; Zenggang Pan, MD, PhD; Francisco G. La Rosa, MD, Department of Pathology, University of Colorado Denver, Aurora.

Vascular tumors of the genitourinary system are uncommon and typically include arteriovenous malformations, capillary hemangiomas, and lymphangiomatisos. Anastomosing hemangiomas, a variant of capillary hemangioma, is a benign vascular lesion that can involve the kidney, perinephric adipose tissue, and testis. Anastomosing hemangiomas consist of thin-walled vascular channels showing a complex anastomosing growth pattern with hobnailing, but lack endothelial atypia. Because of the vascular nature of this lesion, the main differential diagnosis is a primary renal angiosarcoma. Renal angiosarcomas are rare, highly aggressive, malignant tumors that react with vascular immunohistochemical markers. Here, we report 2 cases, an anastomosing hemangioma and a primary renal angiosarcoma from a single institution, focusing on the microscopic distinctions and difficulties in making the correct diagnosis. In the first case, a 48-year-old woman presented with end-stage renal disease presented with pyelonephritis and was found to have a 1.5-cm renal mass that was assumed to be renal cell carcinoma. Because of the vascular immunoreactivity, bland appearance of the endothelial cells, and low proliferation index, a diagnosis of anastomosing hemangioma was made. In contrast, a 64-year-old man presented with right flank pain and was found to have a 12.5-cm, hemorrhagic renal mass. The size, cytologic atypia, invasive architecture, and high mitotic activity led to the diagnosis of a primary renal angiosarcoma. Anastomosing hemangioma and primary renal angiosarcoma are uncommon tumors that may have similar clinical presentations and share immunoreactivity with vascular markers. Careful histologic examination is essential to make an accurate diagnosis of these tumors with markedly different prognoses.

Immunohistochemical Differentiation of Renal Oncocytomas and Renal Cell Carcinoma, Chromophobe Type, Using Cyclin D1
(Poster No. 134)

Oluwatobi Odetola, MD (oluwatobi.odetola@lumc.edu); Guliz Barkan, MD; Stefan Pambuccian, MD, Department of Pathology and Laboratory Medicine, Loyola University Medical Center, Maywood, Illinois.

Context: Renal oncocytomas (ROs) and renal cell carcinoma, chromophobe type (RCC-Ch), are thought of as 2 entities within a spectrum. The morphologic differentiation of the 2 lesions is sometimes difficult, necessitating the use of immunohistochemical (IHC) stains. To date, there is no acceptable immunostain that is positive in RO and negative in RCC-Ch. Therefore, this study set out to use the IHC panel cyclin D1 and CK7 to differentiate between RO and RCC-Ch.

<table>
<thead>
<tr>
<th>Interpretation of CK7 and Cyclin D1 Results</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclin D1</td>
<td>Positive</td>
</tr>
<tr>
<td>RO</td>
<td>13 (TP)</td>
</tr>
<tr>
<td>RCC-Ch</td>
<td>6 (FP)</td>
</tr>
<tr>
<td>CK7</td>
<td></td>
</tr>
<tr>
<td>RO</td>
<td>24 (TP)</td>
</tr>
<tr>
<td>RCC-Ch</td>
<td>0 (FP)</td>
</tr>
</tbody>
</table>

Abbreviations: FN, false-negative; FP, false-positive; RCC-Ch, renal cell carcinoma, chromophobe type; RO, renal oncocytoma; TN, true-negative; TP, true-positive.

Design: A review of the electronic medical record for 10 years was performed, yielding 18 cases of RO and 27 cases of RCC-Ch. After confirmation of the diagnoses, appropriate paraffin tissue blocks were selected for IHC studies. CK7 and cyclin D1 immunostains were
Cassie Xu, MD1 (cassie.xu@ucdenver.edu); Sammie J. Roberts, MD2; Eric P. Wartchow, BSc; Gary Mierau, PhD; Kevin D. Muelken, MD3; Francisco G. La Rosa, MD.

A Case of C4 Glomerulopathy Evolving From Membranous Glomerulonephritis to Dense-Deposit Disease

(Poster No. 135)

Cassie Xu, MD1 (cassie.xu@ucdenver.edu); Sammie J. Roberts, MD2; Eric P. Wartchow, BSc; Gary Mierau, PhD; Kevin D. Muelken, MD3; Francisco G. La Rosa, MD.1 Department of Pathology, University of Colorado, Anschutz Medical Campus, Aurora; 2Department of Pathology, Children’s Hospital of Colorado, Aurora; 3Department of Nephrology, UCHealth Northern Colorado, Fort Collins.

C4-mediated glomerulopathy (C4-MG) is characterized by single deposition of C4 in the absence of other immune deposits; it includes C4–dense-deposit disease and C4-glomerulonephritis. We present a unique case of C4-MG in a 24-year-old woman who 4 years earlier presented with nephrotic-range proteinuria, hypertension, and marked decrease of C4 in the context of negative autoimmune and infectious tests. Her first renal biopsy showed membranous glomerulonephritis with deposition of immunoglobulins, C3, and C1q and multiple intramembranous electron-dense deposits (Figure 135, A). She showed some improvement after immunosuppressive therapy, but during the next years, she developed decreasing renal function and proteinuria. A current renal biopsy demonstrated severe nephroclerosis; the viable glomeruli showed moderate mesangial matrix expansion and thickening of basement membranes (Figure 135, B) with coarse granularities and spikes. This time, all immunofluorescent stains were negative, but electron-dense subepithelial humps were observed (Figure 135, C). Additional staining for C4d revealed multiple granular deposits (Figure 135, D) and a retrospective C4d staining of the first biopsy showed very similar reactivity. The evolution of membranous glomerulonephritis into C4-MG is a very rare event, only described, to our knowledge, in a case with initial postinfectious glomerulonephritis. Three other cases of C4-MG have been described with C4–dense-deposit disease; all cases showed C4 deposits by immunostainings and electron-dense deposits on electron microscopy. The proposed pathophysiology of C4-MG is dysregulation of the lectin pathway of the complement cascade. Awareness of this entity is crucial for diagnosis, mainly when only serum C4 levels are low, standard immunostains are negative, and electron-dense deposits are present, requiring additional C4-specific studies.

Spontaneous Renal Artery Dissection: A Disease That Masquerades as Renal Artery Stenosis

(Poster No. 136)

Jian-Hua Qiao, MD; Sean Villaflor, MD (seanvillaflor@gmail.com). Department of Pathology, California Hospital Medical Center, Los Angeles.

Spontaneous renal artery dissection (SRAD) is a rare occurrence that poses a difficult diagnostic challenge for physicians because of the nonspecific presentation of flank pain and elevated blood pressure. We present a case of SRAD in a 48-year-old man who presented with episodic, radiating, left flank pain and elevated blood pressure refractory to antihypertensive medications. Computer tomography (CT) of the abdomen revealed hypoattenuation of the left kidney, which prompted further imaging with CT angiogram. The CT angiogram failed to detect the intimal flap defect in the renal artery and misled the diagnosis toward renal artery stenosis. Because of failure of conservative treatment, nephrectomy was elected. Gross and microscopic findings shed more light into the final diagnosis of SRAD because microscopic investigation revealed dissection along the entire renal artery (Figure 136, A and B). The dissection itself had created the luminal stenosis of the renal artery (Figure 136, C). This case provides insight into the pathophysiology of renal artery stenosis as a result of renal artery dissection. The distinct, yet subtle, morphology in dissection can be missed because the initial diagnosis of renal artery stenosis is more common. Renal artery stenosis is far more prevalent, yet that association with SRAD provides an important link that changes the course of treatment and outcomes for the patient.

Mixed Epithelial and Stromal Tumor of the Kidney

(Poster No. 137)

Sharmila Ghosh, MD (sharmila.ghosh@mountsinai.org); Roshan Mahabir, MD, PhD, MPH; Sonyang Yuan, MD. Department of Pathology, Mount Sinai West, Icahn School of Medicine, New York, New York.

Mixed epithelial and stromal tumor of the kidney (MESTK) is a rare and recently defined renal neoplasm. Microscopically, the tumor is composed of biphasic epithelial and stromal components. These tumors have a benign behavior. Malignant transformation has been reported in extremely rare cases. We report a case of a 43-year-old woman with a history of hypertension. She had an incidentally detected, 4.6-cm, heterogeneous enhancing renal upper pole mass and smaller hypodensities, probable cysts, in the kidney; for which, she underwent a left radical nephrectomy. Grossly, a 6.0 × 3.5 × 2.0-cm upper pole, multiloculated mass with solid morules and containing clear serous fluid was identified. Multiple cysts were present in the kidney, the largest measuring 2 cm was noted at the lower pole. Microscopically, the tumor was composed of biphasic components, including variable amounts of epithelial and stromal components. The stroma was lined by a single layer of cuboidal cells with a hobnail appearance surrounded by ovarian-like stroma. Focal spindle cells (20%–30% of tumor) revealed marked nuclear atypia and frequent mitoses (up to 2 high-power fields), consistent with sarcomatous transformation. The tumor stroma was
immunopositive for desmin, CD10, WT1, ER, PR, and CD99 and was negative for S100, HMB-45, TLE1, MYOD1, and myogenin. The EMA stain was positive for cystic lining cells. Ki-67 stain showed increased proliferative activity in sarcomatous area. Fewer than 10 cases of MESTK have been reported in the literature. The histogenesis and clinical behavior of this unique tumor remains to be further clarified. Close follow-up is recommended.

Urothelial Carcinoma of the Graft Kidney: A Rare Case Report
(Poster No. 138)

Muhan Joyce Chen, MD, PhD1 (joyce.chen@moutnsinai.org); Diane Wang, MD2; G. Kenneth Haines III, MD2; Jane Houldsworth, PhD3; Alan Benvenisty, MD, FACS2; Qiusheng Si, MD, PhD.1 Departments of Pathology and Surgery, Mount Sinai Hospital, New York, New York.

Malignancy after transplantation is a leading cause of death in renal transplant recipients. However, the donor-derived malignancy is rarely reported. We herein report a case of a 62-year-old woman who presented with hydronephrosis and acute renal failure 34 years after renal transplantation. Radiologic findings showed a mass in the graft kidney and multiple bladder masses. Bladder biopsies revealed a high-grade papillary urothelial cell carcinoma (UCC) and she underwent a nephro-uretero cystectomy. Grossly, the surgical specimen contained a well-circumscribed, flesh-colored mass in the lower pole of the graft kidney (Figure 137, A and B) and more than 50 tan, small polypoid nodules in the bladder (Figure 137, C). Histology demonstrated a high-grade papillary UCC involving the graft kidney, ureter, and the native bladder, with metastasis to 1 of 13 obturator lymph nodes, sparing the 2 native kidneys and ureters. To determine the origin of the tumor, molecular analysis of 16 short tandem repeats (mapped to different chromosomes) was performed on renal bladder tumors and the native kidney, and revealed the UCC was of donor origin. It is known that transplant recipients have an increased risk of UCC compared with the general population, but this case lacks the well-documented risk factors, and revealed the UCC was of donor origin. It is known that transplant recipients have an increased risk of UCC compared with the general population, but this case lacks the well-documented risk factors.
Captagon-Induced Renal Tubulopathy

(Poster No. 142)

Rawan Aljaras, MD; Hisham Abu Farsak, MD; Hussam Abu-Farsah, MD (filab@yahoo.com). 1Department of Internal Medicine, Jordan University, Amman, Jordan; 2Department of Internal Medicine, Jordan University of Science and Technology, Amman, Jordan; 3Department of Pathology, First Medical Laboratory, Amman, Jordan.

Acute renal failure can be a complication of drugs. Captagon (also known as fenethylline) contains amphetamine and theophylline. The drug is used as a psychostimulant. It has been increasingly used by teenagers as an illegal drug. We report on a 21-year-old man who presented with abdominal pain, hematuria, mild proteinuria, and severe oliguria. His creatinine rapidly progressed from 1.1 to 16 mg/dL in 1 week. The nephrologist started him on renal dialysis. Kidney size by ultrasound was within reference range. A renal biopsy was performed.

The preliminary clinical diagnosis was rapidly progressive glomerulonephritis. The renal biopsy showed severe vacuolization of the proximal tubules (Figure 140, A and B), hematoxylin-eosin (C), trichrome. The glomeruli were almost normal. No interstitial inflammation was seen, and no tubular necrosis was seen. Red blood cell casts were seen in the tubules. Immunofluorescence studies showed negative staining in the glomeruli for immunoglobulin (Ig) G, IgM, IgA, C3, C4, and C1q. Immunoperoxidase for CD68 was strongly positive in the tubules (Figure 140, D). The histopathologic diagnosis was severe toxic tubulopathy. Inquiry about illegal drug intake revealed Captagon intake 2 weeks prior to his presentation. The patient abstained from Captagon intake, and his creatinine dropped in 1 week to 3.5 mg/dL and, at the end of the third week, to 1.14 mg/dL. This represents the first report, to our knowledge, of Captagon-related renal tubular injury. Recognizing this type of renal tubular injury is important in preventing end-stage renal disease in drug addicts.

Into the Nerves: Sarcomatoid Urothelial Carcinoma With Extensive Perineural Invasion

(Poster No. 143)

Binny Khandakar, MBBS, MD (binny.khandakar@moutnsinai.org); Roshan Mahabir, MD; Malary Mani, MD; Wenjing Shi, MD; Jihong Sun, MD. Department of Pathology, Mount Sinai Health System, New York, New York.

Primary sarcomatoid urothelial carcinoma (UC) of urinary bladder is very uncommon, representing only 0.1% to 0.3% of all UCs. It is regarded as an aggressive neoplasm with distinct prognostic and therapeutic implications. Incidence of perineural invasion (PNI) in UC is reported to be as low as 6.8% in cystectomy specimens. Moreover, PNI is associated with adverse prognosis. Extensive PNI is an extremely uncommon finding in UCs. Here, we describe a rare case of sarcomatoid UC, showing extensive PNI in a radical cystectomy specimen. A 73-year-old man complaining of hematuria was found to have a bladder mass on imaging. Initial ultrasound was within reference range. A renal biopsy was performed. The preliminary clinical diagnosis was rapidly progressive glomerulonephritis. The renal biopsy showed severe vacuolization of the proximal tubules (Figure 140, A and B), hematoxylin-eosin (C), trichrome. The glomeruli were almost normal. No interstitial inflammation was seen, and no tubular necrosis was seen. Red blood cell casts were seen in the tubules. Immunofluorescence studies showed negative staining in the glomeruli for immunoglobulin (Ig) G, IgM, IgA, C3, C4, and C1q. Immunoperoxidase for CD68 was strongly positive in the tubules (Figure 140, D). The histopathologic diagnosis was severe toxic tubulopathy. Inquiry about illegal drug intake revealed Captagon intake 2 weeks prior to his presentation. The patient abstained from Captagon intake, and his creatinine dropped in 1 week to 3.5 mg/dL and, at the end of the third week, to 1.14 mg/dL. This represents the first report, to our knowledge, of Captagon-related renal tubular injury. Recognizing this type of renal tubular injury is important in preventing end-stage renal disease in drug addicts.
focally for AE1/AE3, p63, and uroplakin, suggesting that the sarcomatoid component was possibly a dedifferentiation of the carcinomatous component. A final diagnosis of sarcomatoid carcinoma was made. We present this case for its rarity and uncommon aggressive feature in the form of extensive PNI.

**PTEN at the Crossroads of Metabolic Syndrome and Clear Cell Renal Cell Carcinoma**

(Poster No. 144)

Snehal Sonawane, MBBS, DNB (snehal@uic.edu); Zhengdong Lei, PhD; Mark Maienschein-Cline, PhD; Suman Setty, MBBS, PhD. Department of Pathology, University of Illinois at Chicago, Illinois.

**Context:** Metabolic syndrome has recently been associated with increased risk and high morbidity and mortality for certain types of cancer. *PTEN* (phosphoinositide phosphatase) is a tumor-suppressor gene that functions by antagonizing PI3K/AKT/mTOR signaling. This pathway has been implicated in tumor genesis of clear cell renal cell carcinoma (ccRCC) and also serves as a main mechanistic link between metabolic syndrome and cancer by increasing growth factor signaling. Our aim was to elucidate the role of *PTEN* immunohistochemistry (IHC) and its relationship with components of metabolic syndrome (diabetes, hypertension, obesity) and other clinicopathologic features that include nuclear grade, tumor stage, and overall survival of patients with ccRCC.

**Design:** A tissue microarray of 103 ccRCCs was constructed and characterized using light microscopy and PTEN IHC. The IHC results were analyzed comparing patients’ clinicopathologic characteristics and survival.

**Results:** Higher tumor grade and tumor stage showed poor outcome in our study, which is a well-established finding in the literature. Nuclear PTEN loss strongly correlated with higher tumor grade (*P* = .03) but failed to show correlation with tumor stage (*P* = .06). There was no significant correlation between reduced nuclear PTEN IHC expression and age, sex, hypertension, body mass index, diabetic status, and tumor stage. PTEN loss also showed a trend toward reduced survival, but it failed to achieve statistical significance (*P* = .4).

**Conclusions:** PTEN IHC can serve as a method to identify a subset of tumors with poor outcome. Although analysis of higher grade did not detect a role for metabolic status, further investigation of the large subset of grade 2 tumors may shed light on the role of metabolic status on tumor behavior.

**Two Cases of Unclassified Renal Cell Carcinoma With Unique Mucinous Tubulopapillary Architecture, Background Dense Fibrotic Stromal, and Psammomatosus Calcification: Still Unclassified or a New Subtype of Renal Cell Carcinoma?**

(Poster No. 145)

Woo Cheal Cho, MD (woocheel.cho@hhhealth.org); Jonathan Earle, MD. Department of Pathology and Laboratory Medicine, Hartford Hospital, Hartford, Connecticut.

A small subset of renal cell carcinomas (RCCs) falls into the diagnostic category of unclassified RCC, despite its unique morphologic patterns. We report 2 cases of “unclassified” RCCs with distinct but identical morphologic and immunophenotypic patterns in adult men (age range, 52–66 years). By gross examination, the tumors were well circumscribed and predominantly solid with a tan, homogenous cut surface with focal spongy areas. Microscopically, the tumors showed a tubulopapillary growth pattern with markedly dilated papillae/tubules filled with mucin in a densely fibrotic stroma (Figure 142, A and B). The neoplastic cells lining the papillae/tubules were monotonous with round-to-ovoid nuclei without high nucleolar grade features. Scattered psammoma bodies (Figure 142, C) and mast cells within the mucin-filled papillae/tubules (Figure 142, D) were frequently seen. No definitive hobnail epithelium or spindle cell areas were identified. Immunohistochemically, the tumor cells were positive for AMACR, CK7, FAX8, cyclin D1 (patchy), CAIX (local), CD10 (local), and SDHB (retained). CD117 only highlighted the mast cells within the papillae/tubules, and CK20 and TFE3 were negative. Alcian blue (pH 2.5) highlighted abundant mucin within the papillae/tubules. The findings did not fit into any of the currently recognized subtypes of RCC, including papillary RCC, tubulocystic RCC, mucinous tubular and spindle cell carcinoma, or even the recently described biphasic squamoid alveolar RCC. However, these unique morphologic patterns with distinct immunoprofiles in 2 different patients raise the possibility that these tumors may represent a new variant of RCC. Further studies, including cytogenetic analyses, are needed to better characterize these tumors.
positive for p40 and negative for OCT34 and D2-40 (Figure 143, C and D). The single layer of germ cell neoplasia in situ at the periphery of the intratubular teratoma was negative for p40 and positive for OCT34 and D2-40. Although teratoma is a common component in an adult germ cell tumor, an intratubular manifestation is exceptional. The present case illustrates this rare finding.

**Sarcomatoid Carcinoma of the Prostate With Osteosarcomatous Differentiation**

(Poster No. 147)

Ali M. Ali, MD1 (ali.ali@bcm.edu); Abubaker Elshaikh, MD2; Michael Iltmann, MD, PhD2; Department of Pathology & Immunology, Baylor College of Medicine, Houston, Texas; 2Department of Pathology, Michael E. DeBakey VA Medical Center, Houston.

Sarcomatoid carcinoma (SC) with osteosarcomatous differentiation of the prostate is an exceedingly rare tumor of the prostate, representing less than 1% of all prostate tumors. Many of the reported cases exist in the background of a previous or existing diagnosis of acinar adenocarcinoma. It has been proven that the sarcomatous component is a dedifferentiation of the carcinoma component because they both share the same epithelial origin. The mean time of progression from acinar adenocarcinoma is 3 years. The presence of heterologous elements has been shown in one case series to make no difference in the overall prognosis of the disease. We report a case of prostate SC with osteosarcomatous differentiation in a 69-year-old man. The patient was first diagnosed with prostatic adenocarcinoma, Gleason score 4 + 4, on a biopsy. A transurethral resection of the prostate was then performed. He was started on hormone ablation therapy and remained free of disease. Sixteen years later, magnetic resonance imaging of the prostate showed an abnormal, enhancing mass completely replacing the normal architecture of the prostate, with extension into the bladder, prostatic urethra, and the rectum. A transurethral resection of the bladder neck tumor was consistent with high-grade prostatic SC with heterologous bone. The carcinoma and the sarcomatous components closely blend into each other and pancytokeratin and vimentin staining reflects that differentiation pattern. The SC of the prostate is a rare tumor that could arise de novo or in the background of a previous acinar adenocarcinoma and is associated with a poor overall prognosis.

**Morphologic Analysis of Unclassified Renal Cell Carcinoma: A 10-Year, Single Institutional Experience and Future Strategic Approaches to Reclassification**

(Poster No. 148)

Woo Cheal Cho, MD (woochal.cho@hhchealth.org); Katrina Collins, MD; Jonathan Earle, MD. Department of Pathology and Laboratory Medicine, Hartford Hospital, Hartford, Connecticut.

**Context:** Unclassified renal cell carcinoma (uRCC) is a diagnostic category for renal carcinomas that do not fit into any of the recognized subtypes of RCC. It constitutes a significant portion of RCCs and currently has no standard therapy. Thus, accurate subtyping of RCCs is clinically significant for therapy and prognostication. Here, we aim to characterize the morphologic features of RCCs leading to this diagnostic category and discuss potential strategic approaches to reclassification of uRCCs.

**Design:** Our electronic database was queried for cases signed out as renal cell carcinoma, unclassified during a 10-year period (2007-2017), and morphologic features of identified cases were reevaluated.

**Results:** A total of 38 cases of uRCC meeting the 2016 World Health Organization diagnostic criteria were identified (median age, 60 years; male to female ratio, 1:9; 23 total and 15 partial nephrectomies; Table). Tumors (median size, 7.25 cm) predominantly showed either an unrecognized epithelial cell subtype (47%) or a combination of features of more than 1 recognized subtype (42%). A rare subset of tumors was assigned to this category because of low- or high-grade unclassified oncocytic features (8%). Overall, necrosis, mucin production, sarcomatoid features, and rhabdoid features were seen in 37%, 11%, 8%, and 5% of cases, respectively.

**Conclusions:** Proper assignment to a known subtype of RCC is important practically because it can influence therapy and/or clinical trial eligibility. We believe our proposed strategies, including detection of copy number alterations via molecular karyotyping, may help eliminate some of these morphologically ambiguous cases and ultimately provide clinicians with more-accurate prognostication.

**Morphologic Features of Unclassified Renal Cell Carcinoma (2007–2017), n = 38**

<table>
<thead>
<tr>
<th>Morphologic Features</th>
<th>Frequency, No. (%)</th>
<th>Strategic Approach to Reclassification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unrecognized epithelial cell subtype</td>
<td>18 (47)</td>
<td>IHC for TFE3, TFEB, HMB-45, and Melan-A or FISH with TFE3 or TFB break-apart probe (MIT family translocation RCC)</td>
</tr>
<tr>
<td>Combination of recognized subtypes</td>
<td>16 (42)</td>
<td>SNP microarray platform (OncoScan) for −3p or +5q (ccRCC)</td>
</tr>
<tr>
<td>Low- or high-grade unclassified oncocytic features</td>
<td>3 (8)</td>
<td>IHC for SDH, FH, and CK20 (SDH-deficient RCC, FH-deficient RCC, and ESCRTCC, respectively)</td>
</tr>
</tbody>
</table>

**Detection of BK Polyomavirus in Allograft Renal Biopsies: Comparison of Diagnostic Sensitivity and Specificity of RNA In Situ Hybridization Versus Immunohistochemistry**

(Poster No. 149)

Fan Lin, MD, PhD (flin1@geisinger.edu). Department of Laboratory Medicine, Geisinger Health System, Danville, Pennsylvania.

**Context:** The distinction between polyomavirus nephropathy and acute T-cell-mediated cellular rejection in an allograft renal biopsy is crucial because the treatment options are different. Because SV-40 is 70% homologous to the JC and BK virus, the antibody against SV-40 large T antigen has been widely used to detect them; however, it does not distinguish BK from JC. We investigated the diagnostic sensitivity and specificity of polyomavirus detection in allograft renal biopsies by comparing RNA in situ hybridization (RNA ISH) and immunohistochemistry (IHC) using the Leica (Wetzlar, Germany) Bond III platform.

**Design:** Seventeen cases of BK+ and 17 cases of BK+ renal transplant biopsies were retrieved from the pathology archives. Then, IHC and RNA ISH were performed on those 34 cases, using anti-SV-40 T-antigen mouse monoclonal antibody (DP02/PAB416, 1:100, EMD Chemicals Inc) and the specific RNAscope probe to BK polyomavirus (V-BKPyV–large T, Advanced Cell Diagnostics Inc, Newark, California),
Conclusions: Our preliminary data suggest that (1) the diagnostic sensitivity of RNA ISH with the RNAscope technology is similar to that of IHC in detecting BK polyomavirus in allograft renal biopsies; and (2) RNA ISH is entirely specific in detecting BK virus because it can distinguish BK from SV-40 and JC virus.

Urothelial Undifferentiated Pleomorphic Sarcoma Metastatic to the Brain

(Poster No. 150)

Leonel Maldonado, MD1 (lmaldonado@health.southalabama.edu); Monira Haque, MD2; Thomas Boudreau, MD3; John J. Lazarchick, MD.2
1Department of Anatomic and Clinical Pathology, University of South Alabama Medical Center, Mobile; 2Department of Anatomic and Clinical Pathology, Mobile Infirmary Medical Center, Mobile.

We report on the case of a 50-year-old woman with a remote history of a spinal cord oligodendroglioma who presented to the Mobile Infirmary Medical Center because of neurologic symptoms. A brain magnetic resonance imaging scan was performed revealing a 4-cm, hyperenhancing mass within the right frontal and parietal lobes, abutting the meninges and with surrounding vasogenic edema. Hematoxylin-eosin (H&E) sections from the brain mass showed a moderately cellular infiltrative neoplastic process in a sheetlike pattern composed of cells with oval-elongate nuclei with moderate nuclear pleomorphism, occasional distinct nucleoli, uneven chromatin patterns, and relatively abundant clear/eosinophilic cytoplasm. Up to 7 mitoses per high-power field, as well as necrosis, were identified. The neoplastic cells were positive for vimentin and CD68 and negative for GFAP, EMA, pankeratin, CAM 5.2, S100, vimentin, actin, and desmin. Olig2 (highlighted brain parenchyma), mutant IDH1 (negative), and ATRX (retained) were performed at the Mayo Clinic (sent for consultation; Rochester, Minnesota). The tumor was considered a high-grade malignant neoplasm with sarcomatous features. Systemic evaluation to exclude the possibility of a metastatic lesion was recommended. Subsequently, the patient underwent a computed tomography scan of the abdomen/pelvis, which revealed a 10-cm bladder mass extending beyond the left wall toward the dome. Representative H&E sections of the bladder mass showed a high-grade sarcoma consistent with undifferentiated pleomorphic sarcoma (UPS) with identical histomorphology and immunophenotype with the previous intracranial mass, undifferentiated pleomorphic sarcoma (UPS) with identical histomorphology.

Results: The previous intracranial mass was considered a high-grade malignant neoplasm with sarcomatous features. Systemic evaluation to exclude the possibility of a metastatic lesion was recommended. Subsequently, the patient underwent a computed tomography scan of the abdomen/pelvis, which revealed a 10-cm bladder mass extending beyond the left wall toward the dome. Representative H&E sections of the bladder mass showed a high-grade sarcoma consistent with undifferentiated pleomorphic sarcoma (UPS) with identical histomorphology and immunophenotype with the previous intracranial mass, undifferentiated pleomorphic sarcoma (UPS) with identical histomorphology.

Conclusions: The previous intracranial mass was considered a high-grade malignant neoplasm with sarcomatous features. Systemic evaluation to exclude the possibility of a metastatic lesion was recommended. Subsequently, the patient underwent a computed tomography scan of the abdomen/pelvis, which revealed a 10-cm bladder mass extending beyond the left wall toward the dome. Representative H&E sections of the bladder mass showed a high-grade sarcoma consistent with undifferentiated pleomorphic sarcoma (UPS) with identical histomorphology and immunophenotype with the previous intracranial mass, undifferentiated pleomorphic sarcoma (UPS) with identical histomorphology.

Are Diagnostic Comments Included in Pathology Reports Readable by Patients?

(Poster No. 151)

Ayse Irem Kilic, MD1 (ayse.kilic@lumc.edu); Razvan Lapadat, MD1; Eva M. Wojck, MD2; Alexander Truskinovsky, MD2; Stefan Pambuccian, MD.1
1Department of Pathology, Loyola University Medical Center, Maywood, Illinois; 2Department of Pathology, Roswell Park Cancer Institute, Roswell Park, New York.

Context: Initially designed to be read by clinicians, pathology reports are currently also read by patients with variable and sometimes limited literacy skills. The aim of this study was to measure the readability of the nontemplated, free-text diagnostic comments (DC) section of pathology reports issued in surgical pathology, hematopathology, dermatopathology, neuropathology, medical liver/kidney pathology, and fine-needle aspiration cytology.

Design: We searched our department’s electronic database (CoPath vs, Sunquest, Tucson, Arizona) for reports containing DCs issued in

Results: We searched our department’s electronic database (CoPath vs, Sunquest, Tucson, Arizona) for reports containing DCs issued in

An Electronic Strategy to Eliminate Duplicate Genetic Testing Using Clinical Decision Support

(Poster No. 152)

Jacquelyn D. Riley, MS1; Glenn Stanley, BS2; Robert Wylie, MD1; Holly Burt, BS1; Sandi Horwitz, BS3; Gary W. Procop, MD4 (procopg@yahoo.com). Departments of 1Laboratory Medicine, 2Hospital Informatics, 3Medical Operations and Laboratory Medicine, and 4Pathology and Laboratory Medicine, Cleveland Clinic, Cleveland, Ohio.

Context: Constitutional molecular genetic tests (CMGTs) for inherited traits and diseases generally should not be repeated. Duplicate CMGT orders, however, occur. We designed an electronic intervention to stop duplicate CMGT orders.

Design: We created an once-in-a-lifetime (OIAL) clinical decision-support tool (CDST) that created block repeat CMGT orders but allowed providers to override the intervention by calling the laboratory to request repeat testing. All override requests were reviewed, but we retrospectively assessed repeat test requests for validity. We monitored repeat-test cancelations and override requests and calculated the costs avoided by not performing duplicate CMGTs during 3 consecutive years. We also determined which tests were repeated with the greatest frequency.

Results: The OIAL CDST blocked 793 individual test orders from 42 unique CMGTs. There were 83 (10.5%) override requests, of which 68 (81.9%) were deemed justified; justified repeat requests were primarily due to the previous test not being performed or inconclusive test results. Factor V Leiden polymerease chain reaction, x2X2-antitrypsin genotyping, and hemochromatosis genotyping were the top 3 most commonly duplicated CMGT orders, respectively. The OIAL intervention, during 3 years, stopped 710 unnecessary repeat CMGTs, for a cost avoidance of $98,597 without impeding care delivery.

Conclusions: A CDST for CMGT is a reliable means to stop unnecessary duplicate orders and to alerting clinicians to existing test results. Employing exclusion codes could facilitate the placement of appropriate repeat orders, when “results” indicate that the test could not be performed or the results were inconclusive. These improvements are currently being implemented for the optimization of this CDST at our institution.

International Second-Opinion Consultation Via Whole Slide Digital Imaging: Seven Years of Experience at the UCLA Center for Telepathology and Digital Pathology

(Poster No. 153)

Justin Caron, MD (jcaron@mednet.ucla.edu); Jianyu Rao, MD. Department of Pathology and Laboratory Medicine, University of California, Los Angeles, Los Angeles.

Context: Despite robust interest and the potential to improve patient care, few studies to date have published describing the use of whole slide digital imaging (WSI) in the setting of an international academic telepathology consultation service.

Design: Consultations were submitted during a 7-year period to the University of California, Los Angeles (UCLA), Center for Telepathology and Digital Pathology, in partnership with Second Affiliated Hospital of Zhejiang University (Hangzhou, China). Glass slides were converted to
WSI in China with the Aperio ScanScope XT slide scanner (Leica Biosystems, Wexler, Germany) and uploaded to a Web-based interface for reviewing digital slides. Cases were assigned to pathologists at UCLA based on expertise. Approximately 20 to 30 cases per year were selected randomly for quality control (QC). Comparisons between glass and digital diagnosis were made by the pathologist who made the initial digital diagnosis. The washout period was 3 months.

**Results:** During a 7-year period, a total of 2197 surgical and cytopathology cases were submitted to UCLA for teleconsultation. Neopathology samples were most frequent (487 cases), followed by bone/soft tissue (316 cases), and gastrointestinal (210 cases). Cytologic specimens included 180 fine-needle aspiration and 54 Papanicolaou/nongynecology cases. Intraobserver agreement (concordance) was 91% overall. There were 5 major and 14 minor discordances. Causes included incorrect slides submitted for QC and sample selection.

**Conclusions:** Few reports detailing the use of telepathology for international consultation have been published to date. Here, we show that WSI can be used for second-opinion diagnoses with excellent intraobserver concordance between glass and digital slides. A strong QC program is essential to ensure concordance between digital and glass slide diagnosis.

**The 20-Year Saga of Structured Tumor Pathology Reporting: The Advantages and Value of Technology Tools**

**Poster No. 154**

Zongshan Lai, MD (Zongshan.Lai@beaumont.Org); Colin Appleford, DO; Kimberly Pieters, MS; Zhenhong Qu, MD. Department of Pathology, Beaumont Health, Royal Oak, Michigan.

**Context:** It has taken 20 years for standardization of tumor reports to prevail. Retrospectively, a lack of effective technologic tools has contributed to the slow progress. The dominant rudimentary dictation-transcription method is inefficient. Increasing report standards (elements and formats) without comparable effective tools renders the update ineffective and costly. We assess the efficiency of 2 reporting methods to highlight the need to improve reporting by a simple technology.

<table>
<thead>
<tr>
<th>Cancer Checklist (Organ/Site)</th>
<th>Data Points* (Lines in Checklist), No.</th>
<th>Dictation Time, s (by Pathologist)</th>
<th>Web-form Time, s (by Pathologist)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast (DCIS)</td>
<td>24–27</td>
<td>172.7 ± 45.9 (n = 20)</td>
<td>102.3 ± 8.2 (n = 15)</td>
</tr>
<tr>
<td>Breast (IDC, lymph nodes)</td>
<td>35–39</td>
<td>225.8 ± 34.3 (n = 28)</td>
<td>142.1 ± 5.2 (n = 24)</td>
</tr>
<tr>
<td>Breast (DCIS, IDC, lymph nodes)</td>
<td>42–44</td>
<td>302.4 ± 58.9 (n = 22)</td>
<td>174.5 ± 3.2 (n = 15)</td>
</tr>
<tr>
<td>Colon</td>
<td>23–24</td>
<td>167 ± 28.8 (n = 28)</td>
<td>92 ± 0.87 (n = 19)</td>
</tr>
<tr>
<td>Kidney</td>
<td>19–21</td>
<td>138.6 ± 14.6 (n = 7)</td>
<td>80.67 ± 1.5 (n = 5)</td>
</tr>
<tr>
<td>Lung</td>
<td>19–22</td>
<td>192 ± 35.15 (n = 9)</td>
<td>21.33 ± 4.42 (n = 5)</td>
</tr>
<tr>
<td>Prostate</td>
<td>24–26</td>
<td>157.5 ± 23.44 (n = 20)</td>
<td>96.24 ± 24.13 (n = 16)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>15–17</td>
<td>121.22 ± 28.0 (n = 26)</td>
<td>64 ± 5.24 (n = 20)</td>
</tr>
<tr>
<td>Endometrium</td>
<td>22–24</td>
<td>151.9 ± 22.7 (n = 11)</td>
<td>88.36 ± 1.15 (n = 11)</td>
</tr>
</tbody>
</table>

Abbreviations: DCIS, ductal carcinoma in situ; IDC, in situ ductal carcinoma.

* The number of data points (ie, lines in a checklist) to dictate varies with the complexity of some specimens.

**Design:** A Web-based reporting tool with a cascade drop-down list was compared with the prevailing dictation-transcription method for efficiency, which was measured by time and workflow. Operational models to update reporting content were also examined to assess the advantage of using a correct technologic tool or tools.

**Results:** The Web tool reduced the time it took a pathologist to generate a final tumor report compared with the use of the dictation-transcription method (Table) because filling out a Web form is much easier than operating a dictaphone. The Web method also simplified the workflow by eliminating the need for routine transcription. An operational model using a Web-reporting system as top content control greatly simplified the process of reporting and drastically reduced the cost associated with the continuous demand to update tumor checklists.

**Conclusions:** The correct technology tool can greatly promote standardization of tumor reporting by enhancing efficiency, increasing user compliance, and cutting institutional costs. It may serve as an innovative operational model that can potentially reduce cost by millions nationwide.

**Patient Flag—A Safe Blood Transfusion Strategy**

**Poster No. 155**

Asha Sigei, MD1 (sigeia@etsu.edu); Deanna Gray,2; Talat Parveen, MD,2 1Department of Pathology, East Tennessee State University, Johnson City; 2Department of Pathology, Mountain Home VA Center, Johnson City.

With the recent rapid expansion of electronic health record systems (EHRs) throughout medical practice, health care institutions have taken advantage of various technologic tools to reduce unnecessary transfusion and improve the overall practice of transfusion medicine. Various technologies used by Veterans Health Administration (VHA) to promote safe blood-transfusion practices include blood bank software package; bar code–assisted, positive patient identification; and transfusion verification software application. We report one of the technologic strategies at Mountain Home VA Hospital to reduce transfusion complications. With the burgeoning increase in the amount of data in EHRs, locating the correct data for the correct patient at the correct time can be challenging. Previously, data on prior transfusion encounters would be buried deep in the VHA electronic medical record (computerized patient record system [CPRS]). Trying to look for transfusion-related data was difficult and increased the chances of missing prior transfusion recommendations, further increasing the risk of transfusion-related complications. The transfusion committee approved the use of an electronic patient flag, which aims to more easily identify patients with previous transfusion-related complications. The approved category 2 patient flag represents a change in data presentation and is visible when initially signing into the patient’s chart in the CPRS. The flag has detailed information concerning transfusion history, any special needs that the patient may have, and recommendations for subsequent transfusions. This represents a simple, yet
How Often and Why Are Pathologists Including Diagnostic Comments in Pathology Reports?

Ayse Irem Kilic, MD1 (ayise.kilic@lumc.edu); Razvan Lapadat, MD; Alexander Truskinovsky, MD; Stefan Pambuccian, MD.1 Department of Pathology, Loyola University, Maywood, Illinois; 2Department of Pathology, Roswell Park Cancer Institute, Roswell Park, New York.

Context: The pathology report is the main communication tool between pathologists and clinicians. However, no previous study, to our knowledge, has focused on diagnostic comments (DCs). The aim of this study was to determine the frequency of DCs and their purpose in pathology reports issued in surgical pathology, hematopathology, dermatopathology, neuropathology, medical liver/kidney pathology, and fine-needle aspiration cytopathology.

Design: Our departmental electronic database was queried for reports issued in 2016 containing DCs. A natural language processing library (koRpus/R Package) was used to analyze the reason or reasons for including a comment and the frequencies of DCs were calculated for each service.

Results: Comments were included in 8765 of 35 937 (24.4%) of reports. The highest rate of DCs was in hematopathology and medical liver/kidney and the lowest in surgical pathology (χ², P < .001 for both comparisons). Within surgical pathology, head and neck/lung pathology had the highest rate of reports with comments, whereas soft tissue and bone pathology had the lowest. Dermatopathology was most likely to use a comment for microscopic description and differential diagnostic considerations, whereas hematopathology, medical liver/kidney, and neuropathology used comments principally to describe the results of ancillary studies.

Conclusions: The use of diagnostic comments varies widely according to the intended audience of the pathology report; they are more frequent in medical liver/kidney and hematopathology and hematology reports. The reasons for providing DCs also varied according to the service, but DCs were mostly used to document the results of clinical information, ancillary studies, microscopic findings, and differential diagnostic considerations.

Predicting Prognosis of Acute Myeloid Leukemia With Deep-Learning Analysis

Mei Lin, MD (Mei.Lin@uth.tmc.edu); Lei Chen, MD; Amer Wahed, MD; Andy N. Nguyen, MD. Department of Pathology and Laboratory Medicine, University of Texas Health Science Center, Houston.

Context: Deep learning has a crucial role in big data analysis in cancer genomics. Deep-learning algorithms can extract conclusive information from complex data with multiple layers through a hierarchical learning process. In this study, we explored how deep learning was used to predict prognosis of acute myeloid leukemia (AML) using knowledge from various aspects as input that included age, common cytogenetics abnormalities, and mutations.

Design: Data for 94 AML cases from The Cancer Genome Atlas database were used in this study. Data included 10 common cytogenetics abnormalities, age, 23 of the most-common mutations, and prognosis (days to death [DTD]). We implemented a deep-learning network consisting of autoencoders that were stacked to form a network consisting of autoencoders that were stacked to form a hierarchical deep models; from which, high-level features are compressed, organized, and extracted. The network is written in R language and is trained to predict prognosis (poor for DTD <730 days, good for DTD >730 days) given data in a case (cytogenetics, age, and mutations).

Results: Our deep-learning network predicted prognosis of AML at a successful rate of 83%.

Conclusions: Deep learning, a revolutionary technology, is anticipated to be an integrated part of the future practice of molecular diagnosis and prognosis prediction using next-generation sequencing data. As a proof-of-concept study, our preliminary results demonstrate a practical application in this area. It is expected that more-accurate approaches in dealing with big data in cancer genomics will be developed in the near future.

Concordance of Remote Real-Time Frozen Section Slide Image Diagnosis in Surgical Pathology

Shaun Boyes, MD1 (shaun.boyes@lumc.edu); Razvan Lapadat, MD; Ewa Borys, MD; Maria Picken, MD; Swati Mehrotra, MD; Vijayalakshmi Anantharanayanan, MD; Stefan Pambuccian, MD; Vamsi Parimi, MD; Dariusz Borys, MD.1 Department of Pathology, Loyola University Medical Center, Maywood, Illinois; 2Department of Pathology, New York University, New York.

Context: Digital pathology slide scanners can save a permanent digital slide image, and some scanning systems have the ability to allow real-time viewing (RTV) of slides. Although RTV does not create a permanent digital image, it enables quick viewing of slides from pathologists in remote sites. This can be useful during frozen sections because time to diagnosis is critical. The objective of our study was to determine interobserver variability in diagnosing frozen section slides digitally in real time compared with the original frozen section glass slide (FS-G) diagnosis.

Design: A total of 27 frozen section patient cases (32 specimens) from random anatomic sites from 2014 and 2015 were selected for RTV. An offsite pathologist loaded slides into an Aperio LV1 slide scanner for real-time viewing. Six surgical pathologists from varying subspecialties evaluated the frozen section slides (in real time) having remote control over the slides, rendering a diagnosis of positive or negative for malignancy. Clinical information (age, sex, and specimen location) were available to the pathologists.

Results: Twenty-five cases had positive results for squamous cell carcinoma, 1 case was positive for serous carcinoma, and 1 case was positive for adenocarcinoma. The concordance between FS-G and RTV interpretation among all pathologists ranged from 93.8% to 96.9% (Table). The concordance between FS-G and RTV diagnosis was high (93.8% and 96.9%). This study was performed to evaluate concordance of frozen section diagnoses between FS-G and digital RTV and showed that real-time frozen section evaluation from remote sites have similar quality and reliability as on-site light microscope evaluation.

<table>
<thead>
<tr>
<th>Pathologists</th>
<th>Positive for Malignancy, No./N (%)</th>
<th>Negative for Malignancy, No./N (%)</th>
<th>Overall Concordance, No./N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FS-G</td>
<td>27/32 (87.5%)</td>
<td>5/5 (100)</td>
<td>32/32 (100)</td>
</tr>
<tr>
<td>1</td>
<td>26/27 (96.3%)</td>
<td>5/5 (100)</td>
<td>31/32 (96.9)</td>
</tr>
<tr>
<td>2</td>
<td>26/27 (96.3%)</td>
<td>5/5 (100)</td>
<td>31/32 (96.9)</td>
</tr>
<tr>
<td>3</td>
<td>26/27 (96.3%)</td>
<td>4/5 (80)</td>
<td>30/32 (93.8)</td>
</tr>
<tr>
<td>4</td>
<td>20/21 (95.2%)</td>
<td>5/5 (100)</td>
<td>25/26 (96.2)</td>
</tr>
<tr>
<td>5</td>
<td>26/27 (96.3%)</td>
<td>5/5 (100)</td>
<td>31/32 (96.9)</td>
</tr>
<tr>
<td>6</td>
<td>25/26 (96.2%)</td>
<td>5/5 (100)</td>
<td>30/31 (96.8)</td>
</tr>
<tr>
<td>Offsite</td>
<td>26/26 (100)</td>
<td>4/5 (80)</td>
<td>30/31 (96.8)</td>
</tr>
</tbody>
</table>

Optimizing Delta Checks in a Large Hospital System

Paul Christensen, MD1 (pachristensen@houstonmethodist.org); Melanie Kwan, BS; Joseph Noffsinger, MT; Xin Yi, PhD; Roger L. Bertholf, PhD.1 Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Texas; 2Department of Pathology, Texas A&M College of Medicine, Bryan-College Station.

Context: Delta checks are a quality-control tool for identifying mislabeled patient samples, sample-quality problems, and analytic random errors. The adequacy of our configured delta check rules was unknown.

Design: We retrospectively queried 5 weeks of data from our laboratory information system for all results on analytes with configured delta checks. We compared orders with positive delta checks to the calculated absolute and percentage of delta values in all sequential patient orders.

Results: Our currently configured phosphorous delta check of 50%/26/26 (96.3%) 5/5 (100) 31/32 (96.9) 25/26 (96.2) 30/31 (96.8) 30/31 (96.8)
skeewed, with 18% of all flagged tests falling left of the threshold (<50%) and 82% falling right of the threshold (>150%). No percentage of delta configuration exists that would reduce the phosphorus delta check rate to 1% and also identify cases below and above the 50% to 150% thresholds. In contrast, the calculated absolute delta curve was normally distributed with a mean (SD) of 0 (1) mg/dL (Figure 145). An absolute threshold of ±3 mg/dL resulted in a positive delta check rate of 1%.

Conclusions: Our configured phosphorus rule initiated a disproportionate number of positive delta checks. Switching to an absolute delta check allowed us to reduce the positive rate and still capture outliers at both ends of the curve. Optimizing all delta check rules may refine or explain the diagnosis, or to document the results of additional tests or consultations. Little is known about the use of equivocal or ambiguous terminology (EAT) in pathology reports. The aim of this study was to determine the frequency of EAT in the DCs of pathology reports issued in surgical pathology, hematopathology, dermatopathology, neuropathology, medical liver/kidney pathology, and fine-needle aspiration cytopathology.

Design: We searched our department’s electronic database (Sunquest CoPath version 6) for reports containing DCs issued in 2016. A natural language processing library (koRpus/R Package) was used to analyze the frequency of use of EAT with terms such as consistent with, indicative of, suggestive of, and suspicious for.

Results: The frequency of EAT words that could be misinterpreted or used as hedges that were identified in 8765 DCs of the 35 937 tests or consultations. Little is known about the use of equivocal or ambiguous terminology (EAT) in pathology reports. The aim of this study was to determine the frequency of EAT in the DCs of pathology reports issued in surgical pathology, hematopathology, dermatopathology, neuropathology, medical liver/kidney pathology, and fine-needle aspiration cytopathology.

Design: We searched our department’s electronic database (Sunquest CoPath version 6) for reports containing DCs issued in 2016. A natural language processing library (koRpus/R Package) was used to analyze the frequency of use of EAT with terms such as consistent with, indicative of, suggestive of, and suspicious for.

Results: The frequency of EAT words that could be misinterpreted or used as hedges that were identified in 8765 DCs of the 35 937 reports was analyzed. The most common was consistent with, which was used in 25% of DCs overall and the most frequently by hematopathology (27%, P < .001 for both comparisons). Clinical correlation recommended was used in 4.4% of all DCs and was most frequent in hematopathology and medical liver/kidney pathology. The lowest frequency of EAT was in surgical pathology.

Conclusions: Although DCs are meant to improve communication with clinicians, they frequently include EAT, which can decrease the clinician’s comprehension of the pathology report. Further studies are needed to determine the acceptable level of EAT in pathology reports.

Integration of Laboratory Information System With University Hospital Electronic Medical Record System With HL7 Interfaces

(Poster No. 161)
Eric X. Wei, MD, PhD (ericxwei@yahoo.com), Department of Pathology, Louisiana State University Health Science Center, Shreveport.

Context: Epic is a common electronic medical record (EMR). Our medical center with several hospitals has been using Epic since 2011. Laboratory information systems (LIS) Sunquest and CoPath were long used before Epic implementation. Here, we provide an account of integration and upgrades of the clinical and anatomic pathology LIS with Epic using health level 7 (HL7) interface engines.

Design: Our analysis covers approximately 8 years of data collected from before and after implementations of interface specification documents. The underlying rationale includes accurate, faster, and secure data exchange; positive patient identification; and minimal numbers of systems and interfaces.

Results: Orders for Sunquest and CoPath placed in Epic are sent to Sunquest via interface engine Cloverleaf and Sunquest Application Manager (SAM). CoPath orders received in Sunquest are sent back to SAM and CoPath. Order status updates, laboratory-generated orders, laboratory, and CoPath results are sent back to SAM. The SAM then sends them back to Epic via Cloverleaf. Epic files the updates and results. CoPath runs billing extracts for technical and professional billings. Sunquest then runs billing extracts and generates billing transactions from clinical laboratories and incorporates charges from CoPath. Cloverleaf sends technical charges to Epic and creates a separate file for the professional billings. Turnaround time improved significantly compared with historic baselines after integration, along with fewer mislabeled specimens.

Conclusions: The LIS integration with Epic provides effective and adequate functionality for our medical center, immediate access to patient clinical information for laboratory staff, and monitoring of specimen workflow and add-on tests by clinicians and nurses.

Bone Marrow Cellularity: A Comparison of Traditional Visual Estimation Versus Digital Image Analysis

(Poster No. 162)
Angela M. Theiss, MD1 (Angela.Theiss@uvmhealth.org); Sahar Nozad, MD;2 Nicole A. Boufard, BS;2 Juli-Anne Gardner, MD;2 Douglas J. Taatjes, PhD;2 Katherine A. Devitt, MD.1 1Department of Pathology & Laboratory Medicine, University of Vermont Medical Center, Burlington; 2Department of Pathology & Laboratory Medicine, University of Vermont College of Medicine, Burlington.

Context: Bone marrow cellularity (BMC), as a percentage or a fat-to-cell ratio, gives crucial information about the state of hematopoietic tissue and is a recommended parameter for inclusion in bone marrow reports per 2016 College of American Pathologists guidelines. Its estimation is subjective, relying on a visual “best guess.” Relevant studies are decades old and use labor-intensive, time-consuming methods. This study evaluates digital imaging as a method of assessing BMC.

Design: Twenty bone marrow biopsies with a range of reported cellularities were selected for the study. Systematic random sampling was used to identify and photograph 10 random fields within each biopsy. Cellular areas of the resulting 200 images were analyzed with MetaMorph Imaging 7.0 software using the color-threshold technique. Digital results were compared with reported visual estimations using simple statistics and paired t tests.

Results: Reported cellularities from bone marrow reports of 20 cases ranged from <5% to 100%, and were reported by 5 hematopathologists. Digital cellularities ranged from 9.5% to 90.2%. The methods of visual estimation and digital analysis were very highly correlated (r = 0.97, P < .001). There was a significant difference in cellularity determined by visual estimation (mean [SD] = 48.25 [31.13]) and digital (52.68 [25.4]); t(19) = -4.425, P < .05). Within each biopsy, BMC varied substantially, up to 48% within the same case.

Conclusions: Visual estimation of BMC produces consistently lower results than those obtained via digital image analysis, and BMC varies substantially within each sample. The very high correlation between digital image analysis and visual estimation of BMC suggests digital analysis could have a role in standardization of this subjective parameter.

Bone marrow cellularity (BMC), as a percentage or a fat-to-cell ratio, gives crucial information about the state of hematopoietic tissue and is a recommended parameter for inclusion in bone marrow reports per 2016 College of American Pathologists guidelines. Its estimation is subjective, relying on a visual “best guess.” Relevant studies are decades old and use labor-intensive, time-consuming methods. This study evaluates digital imaging as a method of assessing BMC.

Design: Twenty bone marrow biopsies with a range of reported cellularities were selected for the study. Systematic random sampling was used to identify and photograph 10 random fields within each biopsy. Cellular areas of the resulting 200 images were analyzed with MetaMorph Imaging 7.0 software using the color-threshold technique. Digital results were compared with reported visual estimations using simple statistics and paired t tests.

Results: Reported cellularities from bone marrow reports of 20 cases ranged from <5% to 100%, and were reported by 5 hematopathologists. Digital cellularities ranged from 9.5% to 90.2%. The methods of visual estimation and digital analysis were very highly correlated (r = 0.97, P < .001). There was a significant difference in cellularity determined by visual estimation (mean [SD] = 48.25 [31.13]) and digital (52.68 [25.4]); t(19) = -4.425, P < .05). Within each biopsy, BMC varied substantially, up to 48% within the same case.

Conclusions: Visual estimation of BMC produces consistently lower results than those obtained via digital image analysis, and BMC varies substantially within each sample. The very high correlation between digital image analysis and visual estimation of BMC suggests digital analysis could have a role in standardization of this subjective parameter.
Androgen Receptor Expression in Granulosa Cell Tumors: Implications for Antiandrogen Therapy

(Poster No. 1)

Rachel Whitehair, MD1 (rwhitehair@virginia.edu); Linda Duska, MD2; Anne Mills, MD1. Departments of 1Pathology and 2Obstetrics and Gynecology, University of Virginia, Charlottesville.

Context: Most ovarian granulosa cell tumors (GCTs) can be managed with resection, but approximately 25% recur. Advanced cases are typically managed with platinum-based chemotherapy, but efficacy is limited. Hormonal approaches have shown promise but have focused on gonadotropin-releasing hormone agonists/antagonists, estrogen antagonists, and synthetic progestins. Androgen antagonism has historically been limited to prostate cancer but has recently expanded to include other androgen receptor (AR)-positive tumors, such as breast and endometrial carcinoma. We herein assess AR expression in ovarian GCT to determine whether these tumors may be candidates for antiandrogen therapy.

Design: Twenty-nine ovarian GCTs (25 adult-type and 4 juvenile-type cases) were stained on whole sections for AR (Dako, clone M3562, 1:200). Expression was scored for intensity (0, negative; 1, weak; 2, moderate; and 3, strong) and extent (percentage of positive cells).

Results: Of all GCTs, 58.6% (17 of 29) were AR+, including 52% (13 of 25) of adult-type and 100% (4 of 4) of juvenile-type tumors. Most expressed AR only weakly and focally, with only 4 cases showing staining greater than the 25% threshold and no cases exceeding 50% staining. A single juvenile-type case showed ≥3 staining involving 15% of the tumor cells.

Conclusions: AR expression is common among ovarian GCTs, with roughly half of cases showing at least focal expression. Strong, diffuse expression is, however, rare. These data suggest that antiandrogen therapy may be of some utility for a subset of advanced GCTs, particularly juvenile-type tumors.

Phenotypic Switch of Extravillous Trophoblasts in Maternal Spiral Artery Remodeling With Implication for Preeclampsia

(Poster No. 2)

Pelin Zhang, MD, PhD (pzmllc@gmail.com). Department of Pathology, New York Presbyterian-Brooklyn Methodist Hospital, Brooklyn.

Context: Maternal spiral artery remodeling is a critical step of implantation. Abnormal spiral artery remodeling likely results in early pregnancy loss and preeclampsia.

Design: The implantation sites of 60 cases of routine abortion specimens were reviewed for maternal vascular remodeling by the maternal vascular remodeling group. TOPBP1 was not expressed in any of the cases. RAD6, RAD18, RAD70, TOPBP1 (Abcam, Cambridge, United Kingdom), PCNA, and RAD51 (Epitomics, Burlingame, California), was performed on 26 cases of cervix that were negative for intraepithelial lesion or malignancy (NILM), 20 cases of low-grade squamous intraepithelial lesion (LSIL), and 21 cases of high-grade squamous intraepithelial lesion (HSIL), and lesional tissue was compared with controls. Digital image analysis was performed on whole slide images (Aperio, Leica Biosystems, Wetzlar, Germany) and results were recorded as an expression score that incorporated the percentage of positivity and the staining intensity.

Results: For 7 antigens, differences in expression score were seen among diagnostic groups. TOPBP1 was not expressed in any of the cases. RAD6, RAD18, RAD70, BRC2 were statistically significant between NILM and HSIL, with lower expression levels in LSIL. Differences in expression scores for RAD1, RAD70, BRC1A1, and BRC2 were statistically significant between NILM and HSIL cases (.01 < p < .02) but not between NILM and LSI or LSIL and HSIL.

Conclusions: Evaluation of several HPV oncogenes by immunohistochemistry with image analysis is promising as a sensitive method of detecting high-risk HPV-associated cervical squamous lesions.

Coexistence of Minimal Deviation Adenocarcinoma of Endometrium and Endometrioidadenocarcinoma of Endometrium

(Poster No. 4)

Zhonghua Liu, MD, PhD (zliu35@buffalo.edu); David Crossland, MD. Department of Pathology, University at Buffalo, New York.

Minimal deviation adenocarcinoma, also known as adenoma malignum, is a rare endocervical malignancy. It is easily missed because of its benign-looking histologic features. Unlike most endocervical adenocarcinomas, minimal deviation adenocarcinoma appears unrelated to human papillomavirus (HPV) infection. Herein, we report on a case of synchronous endometrioid adenocarcinoma of the endometrium and minimal deviation adenocarcinoma of the endocervix. The patient is a 59-year-old woman who presented with postmenopausal bleeding. Previous Papanicolaou smears were negative for malignancy; HPV testing had been consistently negative. Endometrial curettage revealed endometrial intraepithelial neoplasia. The patient subsequently underwent laparoscopic hysterectomy and bilateral salpingo-oophorectomy. Gross examination showed a 3.4-cm endometrial polyp; the specimen was otherwise grossly unremarkable. Microscopically, 2 spatially and morphologically distinct glandular neoplasms were identified. The first neoplasm was primary endometrial showing very superficially invasive, back-to-back, and fused glands having little intervening stroma, consistent with a well-differentiated endometrioid adenocarcinoma. Incidentally, the endocervix was found to contain an infiltrative proliferation of well-formed glands, many of which were lined by a single layer of deceptively bland, mucinous columnar cells. This second glandular proliferation was extensive; it invaded deeply into endocervical stroma. Mitotic figures and apoptotic bodies were infrequent; host stromal desmoplastic response was minimal. These features support a diagnosis of minimal deviation endocervical...
An Uncommon Case of Clear Cell Carcinoma Arising From Abdominal Wall Endometriosis

(Poster No. 5)

Cao Jin, MD, PhD (Cjin2@Northwell.Edu); Shweta Chaudhary, MD. Department of Pathology and Laboratory Medicine, Northwell Health, Lake Success, New York.

Abdominal wall endometriosis represents 1% to 2% of all endometriosis lesions. Malignant transformation of abdominal wall endometriosis is an even rarer event. The malignant transformation of endometriosis in the abdominal wall is a rare event, and fewer than 30 cases have been reported in the literature. Among them, clear cell carcinoma is the more common histologic subtype. Here, we present a case of a 56-year-old woman with a surgical history of 2 caesarean sections, who had an increasing painless mass for the past 3 decades. In 2016, cytology showed metastatic carcinoma of Müllerian origin. The patient was treated with chemotherapy for 6 sessions. In 2017, patient reported that the tumor has extended to the surface of the abdominal wall. Surgical excision was performed. Gross examination demonstrated a 9.0 × 8.5 × 3.0-cm, necrotizing, fungated, nodular lesion. The mass involved subcutaneous tissue and dermis and was ulcerating through the epidermis. Microscopic examination revealed a solid and tubulocystic growth pattern (Figure 146, A and B) with scant focus of endometriosis identified adjacent to invasive carcinoma focal areas (Figure 146, C). High-power microscopy showed hofnailing and clear cell changes (Figure 146, D). The tumor cells were positive for CK7, PAX8, vimentin, and napsin. Uterus, cervix, bilateral tubes, and ovaries were negative for carcinoma. The overall findings of morphology and immunohistochemistry are consistent with diagnosis of endometriosis-associated clear cell carcinoma. We suggest that increasing attention to the transformation of endometriosis into clear cell carcinoma in the abdominal wall may shed additional light on the pathogenesis of the lesions.

Neurocytoma Arising From an Ovarian Mature Teratoma in a Pediatric Patient

(Poster No. 6)

Rochelle Freire, MD; Domenika A. Ortiz, MD; Claudia P. Rojas, MD (Crojas@med.miami.edu). Department of Pathology, University of Miami, Miami, Florida.

Mature cystic teratoma (MCT) is a tumor composed of mature tissues originating from the 3 germ cell layers. Additional neoplasms may uncommonly arise within MCT; those of central nervous system origin are unusual. Central neurocytoma is a rare intraventricular brain tumor, found in young middle-aged adults. We report a case of a 16-year-old girl who consulted for abdominal pain, and a large, nontender pelvic mass. Ultrasound and computed tomography revealed a left ovarian mass with solid and cystic components. The patient underwent laparoscopic left ovarian cystectomy. Gross examination revealed a 16 × 13 × 10-cm mass. The cyst was filled with sebaceous material, hair, and a tooth. Microscopic examination was consistent with MCT, including brain tissue. Within the brain tissue, a 0.5-cm, uniform, round, oligodendroglioma-like cells embedded in neuropil islands mass was identified (Figure 147, A). The lesion was positive for synaptophysin (Figure 147, B) and neurofilament (Figure 147, C) and negative for OLG2 and GFAP (Figure 147, D) by immunohistochemistry. The diagnosis rendered was neurocytoma arising within a MCT. To our knowledge, this is the first pediatric case to be reported and the third known case of a peripheral neurocytoma originating from a MCT. When looking at this type of tumor, the pathologist must be aware that tumors may develop from any component of the mature teratoma. Careful inspection and proper sampling are always encouraged.

Malignant Brenner Tumor: A Rare Case Report

(Poster No. 7)

Valarie McMurtry, MD, PhD (valarie.mcmurtry@hsc.utah.edu); Ting Liu, MD. Department of Pathology, University of Utah, Salt Lake City.

Brenner tumors are a subset of rare ovarian neoplasms representing 1% to 2% of ovarian tumors; the malignant form of Brenner tumors represents less than 1% of all Brenner tumors. Although malignant Brenner tumors are well described histologically, there is limited research on the malignant transformation of those tumors because of their scarcity. The cell of origin for Brenner tumors is currently unknown. It has been postulated to originate from ovarian surface epithelium through transitional cell metaplasia, although recently, Walthard cell rests have been indicated. Immunohistochemical studies are needed elucidate the origin of these rare tumors. In this case study, a 51-year-old woman was found to have a multicystic, 15-cm, right
ovarian mass. The tumor was composed of both invasive transitional-type epithelium, benign and borderline Brenner components, and Walthard cell nests leading to a diagnosis of malignant Brenner tumor (Figure 148, A). Malignant and benign components were stained with PAX8, p53, p63, cyclin D1, and estrogen receptor. PAX8 and estrogen receptor were negative in both the malignant and benign Brenner tumor components. p53 (Figure 148, C) had patchy positivity in the basal layer of the transitional cell epithelium and in the benign Brenner tumor components. Cyclin D1 (Figure 148, B) and p63 (Figure 148, D) were diffusely positive in the malignant and benign Brenner tumor components. Interestingly, p53 staining was stronger and more diffuse in the benign Brenner tumor components than it was in the transitional cell epithelium. This staining pattern suggests that malignant Brenner tumor does not arise from Mullerian origin, supporting the hypothesis of Walthard cell rest as the cell of origin for malignant Brenner tumor.

Fluorescent In Situ Hybridization for the X and Y Chromosome Centromeres Helps Differentiate Between Gestational Choriocarcinoma and Nongestational Trophoblastic Neoplasms

(Paper No. 8)
Rumeal D. Whaley, MD (rdwhaley@iu.edu); Liang Cheng, MD; Thomas M. Ulbright, MD. Department of Pathology and Laboratory Medicine, Indiana University School of Medicine, Indianapolis.

Context: Gestational choriocarcinoma usually presents during the reproductive years, typically within 1 year of pregnancy. Other tumors that mimic it include choriocarcinoma of germ cell origin and somatic carcinomas with trophoblastic differentiation. It is important to separate these tumors for treatment and prognostic reasons. We, therefore, performed fluorescent in situ hybridization (FISH) for the X and Y chromosome centromeres to determine its utility in identifying gestational origin of clinically ambiguous metastatic trophoblastic neoplasms in women.

Design: A review of female patients with metastatic trophoblastic neoplasms who had no evidence of prior gestational trophoblastic disease was performed. Samples were forwarded for FISH analysis for the X and Y chromosome centromeres.

Results: Four cases met the criteria (see Table); all displayed trophoblast cells and necrosis. Three had classic biphasic proliferations of mononucleated trophoblasts admixed with syncytiotrophoblast cells and abundant hemorrhage, whereas case 3 showed solid nests of large trophoblast cells and smaller epithelioid cells in a sparsely hemorrhagic background. Cases 2 and 4 (50%) contained Y chromosomes, confirming its mediastinal origin. Cases 1 and 3 would ordinarily require molecular genotyping to rule out paternal genetic material, although case 1 subsequently recurred with yolk sac tumor, confirming its mediastinal origin.

<table>
<thead>
<tr>
<th>Initial Pathologic Diagnosis and FISH Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
</tbody>
</table>

Abbreviation: FISH, fluorescent in situ hybridization; PD, poorly differentiated.

Conclusions: Fluorescent in situ hybridization for detection of the X and Y chromosome centromeres is a good screening test for gestational choriocarcinoma. It provided a definitive diagnosis of metastatic gestational choriocarcinoma in 2 of 4 potential cases that lacked a clinical history of gestational trophoblastic disease. An additional benefit is that more laboratories have the capability to perform FISH than can perform molecular genotyping for definitive diagnosis.

PD-L1 Expression in Serous and Endometrioid Cancers in Ovary and Uterus: A Comparative Analysis

(Paper No. 9)
Dana Razzano, MD (Dana.Razzano@gmail.com); Minghao Zhong, MD, PhD; Liying Han, MD. Department of Pathology, New York Medical College at Westchester Medical Center, Valhalla.

Context: There is a wealth of resources about the prognostic indication of ovarian tumors and PD-L1 staining pattern, but there is a paucity of information about how the ovarian staining pattern compares with endometrium. In addition, there are no studies, to our knowledge, that also compare the staining pattern of immune infiltrate as a comparison measure.

Design: Our study consisted of 20 cases, including 5 cases of each of the following tumors: serous carcinoma of the ovary and of endometrium and endometrioid adenocarcinoma of the ovary and of endometrium. All cases were subjected to PD-L1 immunochemistry staining, and expression was analyzed in the tumor cells and the tumor microenvironment.

Results: Of the tumor cells 70% (14 of 20) showed positive staining for PD-L1 and 55% (11 of 20) showed positive staining in the tumor microenvironment. High-grade serous carcinoma of the ovary stained the strongest and most consistently with 80% (4 of 5) of cases staining tumor cells positive. All tumor types showed some PD-L1 positivity in the tumor cells (Figure 149). There is variable expression of tumor cell infiltrate in all tumor types. There was no difference in staining pattern between uterine and ovarian endometrioid tumor cells.

Conclusions: PD-L1 positivity was found in all types of malignancies, regardless of histology. Further analysis with a larger sample size is needed to establish a definite correlation with prognosis. Endometrioid endometrial carcinoma was noticeably different from high-grade serous ovarian carcinoma, and it tested in a larger sample size, might yield statistically significant differences to aid in distinguishing these entities.

An Unusual Case of Late-Recurred Dedifferentiated Ovarian Pure Sertoli Cell Tumor

(Paper No. 10)
Mohamed Alshah, MBBCh (Mohamed.alshah@downstate.edu); Kajeswari Jayakumar, MD; Jianying Zeng, MD. Department of Pathology, State University of New York Downstate Medical Center, Brooklyn.

Ovarian Sertoli cell tumors are rare (<0.5% of ovarian neoplasms) pure sex cord tumors composed of Sertoli cells with rare, if any, Leydig cells. Sertoli cell tumors can present with a variety of histologic patterns, which may complicate diagnosis and treatment. Tubular pattern is the most common histologic pattern of pure Sertoli cell tumors. Here, we present a case of an 80-year-old woman referred for a large multicystic abdominal mass causing an abdominal incisional hernia. Computed tomography of the abdomen and pelvis with contrast shows a 20 × 17 × 10.5-cm, large intra-abdominal cystic mass with complex internal septations and enhancing nodules. Thirteen years earlier, in 2004, she had a total abdominal hysterectomy and bilateral salpingo-oophorectomy for a left ovarian mass and a stage IA, Federation International de Gynecologie et Obstetrique grade I endometrioid carcinoma. The left ovarian mass was diagnosed as pure Sertoli cell tumor showing a predominantly well-differentiated tubular pattern with intermediated differentiated tubules and uncommon sarcomatoid spindle cell areas. In comparison, the current recurrent/metastatic abdominal tumor presented as a uniform sarcomatoid diffuse pattern with barely perceptible tubular differentiation. A small focus of Leydig cells was also identified. Inhibin and calretinin immunohistochemistry were positive, and epithelial membrane antigen was negative to support the diagnosis. Pure Sertoli cell tumor with late recurrence (13 years after original presentation) is an unusual presentation because most Sertoli cell tumors recur within 2 to 3 years of the original presentation. In
addition, the absence of well-formed tubules in the recurrent tumor demonstrates a dedifferentiated histologic pattern.

**Risk Assessment of Endometrial Cancer Based on European Society for Medical Oncology Guidelines: The Value of Second Review**  
(Poster No. 11)

Lin Zhang, MD (Lin.Zhang.1@uth.tmc.edu); Xiaohong Wang, MD; Hui Zhu, MD; Jing Liu, MD; Bihong Zhao, MD; Jamie Buryanek, MD; Peisha Yan, MD; Songlin Zhang, MD. Department of Pathology and Laboratory Medicine, University of Texas Health Science Center, Houston.

Context: Endometrial cancer can be classified into 3 risk categories using European Society for Medical Oncology (ESMO) guidelines (low, intermediate, and high risk) based on key pathologic features, such as tumor type, grade, and depth of myometrial invasion. The goal is to assess the value of second review on the risk category assessment of endometrial cancer.

Design: Five pathologists independently evaluated one representative section on each case for Federation International de Gynecologie et Obstetrique (FIGO) grade, myometrial invasion, and tumor subtypes. The majority opinion was used as the second opinion, and the tie-breaker on FIGO grade was resolved by a sixth pathologist review.

Results: The study included 15 biopsies and 75 hysterectomies. For FIGO grade, 25 (25/90, 27.8%) cases had discrepancies with 19 minor (G1 versus G2) and 6 major (G1/2 versus G3). For myometrial invasion, 11 of 75, (14.7%) cases had discrepancies (>50% versus <50%). For tumor types, there was no discrepancy regarding type I or type II endometrial cancer. Eleven of 90 cases (12.2%) would have risk category changes with the second review opinion. After being adjusted by tumor stage, 3 of 90 cases (3.3%) still had risk category discrepancies compared with the original reports.

Conclusions: Our study is consistent with literature showing there is significant discrepancy (27.8%) among pathologists on the FIGO grading, but most changes are minor and have no effect on the risk assessment. The discrepancy of myometrial invasion has a greater effect on the risk assessment, and the discrepancy is significant (14.7%). A second review of endometrial cancer may be necessary to optimize patient care, especially in stage I, type I endometrial cancer.

**Endometrioid Type Adenomyoma, Rare Location in the Cervix**  
(Poster No. 12)

Raafat Makary, MD, PhD; Brett Baskovich, MD; Jaime Morel, MD; Sandra A. Siller, MD (sandra.siller@jax.ufl.edu). Department of Pathology, University of Florida, Jacksonville.

Minimal deviation adenocarcinoma (MDA), adenoma malignum, is a rare variant of cervical adenocarcinoma. It is characterized by diffusely infiltrative, well-differentiated glands with minimal cytologic atypia and no desmoplastic reaction. It is not related to human papillomavirus and characteristically has an immunophenotype typical for gastric-type adenocarcinoma. Herein, we describe a case of MDA arising from the uterine corpus. To our knowledge, this is the fourth case described in the English-language literature. The patient is a 56-year-old, postmenopausal woman who presented to emergency department with vaginal bleeding. Imaging showed heterogeneous thickening of the myometrium and a complex ovarian cyst. CA19-9 level was 6410 U/mL. Gross examination of the uterus showed a rounded, well-circumscribed, partially cystic, tan mass that measured 9 cm at greatest dimension and occupied the entire anterior myometrium. It was located directly beneath a smooth, grossly unremarkable endometrial lining. Microscopically, malignant glands with abundant intracellular mucin and minimal cytologic atypia (Figure 151, A) were dissecting through the myometrium (Figure 151, B). The endometrial lining showed foci of mucinous metaplasia and tumor involvement. Focal extension into the lower uterine segment/upper endocervix was seen. Immunopheno-
MSH6 Mismatch Repair Protein Immunohistochemical Expression in Endometrial Cancer and Lynch Syndrome: An Academic Institution 5 Year Experience

(Poster No. 15)

Ashley N. Scheiderer, MD* (ascheiderer@utmck.edu); Kristopher J. Kimball, MD; Larry C. Kilgore, MD; Daniel H. Snyder, DO; Amila Orucuevic, MD, PhD. Departments of Pathology and *Obstetrics and Gynecology, University of Tennessee Medical Center, Knoxville.

Context: Mismatch repair protein (MMRP) status by immunohistochemistry (IHC) testing guides the evaluation of Lynch syndrome (LS) in patients with endometrial cancer. The loss of nuclear expression warrants clinical correlation with genetic counseling and assessment for germline testing. Per College of American Pathologists guidelines, only complete loss of nuclear MMRP expression is considered an abnormal test result. Loss of expression of PMS2 only, MSH2 and MSH6, or MSH6 only indicates a high probability of LS, with the latter reportedly significantly associated with LS in patients with endometrial cancer. Results on rarely observed heterogenous MMRP staining are emerging and require validation.

Design: We investigated the significance of patterns of loss of MSH6 protein staining and its correlation to genetic test results in all patients with endometrial cancer who underwent hysterectomy in our institution from January 2012 through December 2017.

Results: Twenty of 483 patients (4.1%) had a loss of MSH6 protein staining, either alone or in combination with other MMRP (see Table). Heterogenous MSH6 staining was observed in 2 cases. Three-fourths of patients with MSH6 IHC loss underwent genetic testing; 57% tested positive for LS. The IHC loss of MSH6 alone corresponded to MSH6 gene mutation in 62.5% of tested patients. Interestingly, MSH6 gene mutation was never seen when MSH6 IHC loss was combined with other MMRP loss.

Conclusions: Results show that complete IHC loss of MSH6/MMRP alone or in combination with others has 62.5% and 60% positive-predictive value for LS, respectively. Development of an algorithm to increase the positive-predictive value of this test, perhaps by including clinicopathologic tumor characteristics and family history to MMRP IHC, is warranted.

Data:

<table>
<thead>
<tr>
<th>Pattern of MSH6 Loss by IHC, No./n</th>
<th>Genetic Testing Performed, No.</th>
<th>Genetic Testing Declined, No.</th>
<th>Gene Mutation and No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSH6 alone (n = 11)</td>
<td>3</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>MSH6/MSH2 (n = 6)</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>MSH6/PMS2 (n = 1)</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>MSH6 alone</td>
<td>0</td>
<td>Genetic results</td>
<td>pending; MSI unstable by PCR</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>MSH2 = 1/2; MSH2 = 1/2</td>
</tr>
<tr>
<td>MSH6 heterogenous staining</td>
<td>0</td>
<td>*Genetics not performed;</td>
<td></td>
</tr>
<tr>
<td>(n = 1)</td>
<td></td>
<td>positive MLH1 promoter</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>methylation</td>
<td></td>
</tr>
<tr>
<td>MSH6 heterogenous staining/MLH1 +</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>PMS2 complete loss (n = 1)</td>
<td></td>
<td></td>
<td>PMS2 = 1/1</td>
</tr>
<tr>
<td>Total number of cases (n = 20 of 483)</td>
<td>5/20</td>
<td>8/20</td>
<td>5/20</td>
</tr>
</tbody>
</table>

Abbreviations: EPCAM, epithelial cell adhesion molecule; IHC, immunohistochemistry; MLH, MutL homolog; MSH, MutS homolog; MSI, microsatellite instability; MLH1, microsatellite instability–low; PCR, polymerase chain reaction; VUS, variants of uncertain significance.

Uterine Angiomyoma (Vascular Leiomyoma): A Rare Subtype of Uterine Leiomyoma

(Poster No. 16)

Noor Marji, BMS (noormarji87@yahoo.com); Raafat Makary, MD, PhD. Department of Pathology, University of Florida, Jacksonville.

Uterine angiomyoma (vascular leiomyoma or angioleiomyoma) is an extremely rare variant of uterine leiomyoma with only 15 cases being reported until 2015. Women with uterine angiomyoma present with pelvic pain and vaginal bleeding, similar to other variants of uterine leiomyoma. We present a case of a 44-year-old woman complaining of abnormal uterine bleeding for 12 months with no response to hormonal
therapy. The patient underwent total hysterectomy with bilateral salpingo-oophorectomy. Gross examination showed a circumscribed, intramural, grey-tan, whorled mass (6 x 5 x 5 cm) with spotty hemorrhage. Histology of the mass revealed a leiomyoma, predominantly formed of numerous aggregates of thick wall arterial blood vessels. The muscle fibers appeared to be stemming from and swirling around the thick wall of the blood vessels with no defined interface between the 2 components (Figure 153, A and B). Adequate tumor sampling revealed no necrosis or conspicuous mitoses. HMB-45 immunostain was performed and it was negative. HM-B45 negativity helps to exclude the diagnosis of uterine perivascular epithelioid cell tumor, which was considered in the differential diagnosis. Angioleiomyoma or vascular leiomyoma is a unique rare variant of uterine leiomyoma. It is different from other variants of uterine leiomyoma in that it arises from the smooth muscles of the blood vessels that characterize this lesion, rather than the smooth muscle fibers of the myometrium, which is the case of the other subtypes of leiomyoma. Angioleiomyoma is a benign tumor. Complete excision remains the mainstay of the treatment for thorough sampling to exclude malignancy in the lesion.

Adult granulosa cell tumors (AGCT) constitute 1% to 2% of all ovarian tumors and are associated with FOXL2 gene mutation. Sex cord tumors with annular tubules (SCTAT) are very rare tumors associated with Peutz-Jeghers syndrome (PJS). In one-third of cases, the PJS-associated SCTATs tend to be bilateral, microscopic, and harbor STK11 mutation. Non-PJS SCTAT may show small foci resembling microfollicles of AGCT, although typical areas of AGCT are not seen. We report the first case, to our knowledge, of mixed SCTAT and AGCT. A 64-year-old woman presented with postmenopausal bleeding for which she underwent hysterectomy and bilateral salpingo-oophorectomy. An incidental 7-cm left adnexal mass with intact outer surface and a solid yellow-tan cut surface was noted. Microscopically, the tumor was predominantly composed of AGCT with solid sheets of monotonous cells with grooved nuclei and Call-Exner bodies. A minor component of SCTAT with tumor cell nests surrounded by basement membrane-like material, simple and complex annular tubules enclosing eosinophilic hyaline material, was present. Both components were distinct yet admixed and were diffusely positive for inhibin. No adjuvant therapy was provided because the tumor was stage IA. The patient has no evidence of disease after 5 years of follow-up. This unique case is the first reported case, to our knowledge, of a nonsyndromic SCTAT with concurrent AGCT. Because both components are associated with distinct mutations, molecular testing will provide insights into these mutations that may have had a role in the tumorigenesis of this unusual neoplasm.

**Diagnosis by Morphology Alone? A Morphologic and Immunophenotypic Concordance Study of Ovarian High-Grade Serous Carcinoma**

(Poster No. 19)

Sadia Sayeed, MD (sadia.sayeed@vcuhealth.org); Woon Chow, MD PhD; Bryce Hatfield, MD; Steven Smith, MD, PhD; Cora Uram-Tuculescu, MD. Department of Pathology, Virginia Commonwealth University Health System, Richmond.

**Context:** In the current era of neoadjuvant chemotherapy for metastatic ovarian high-grade serous carcinoma (OHGSC), diagnosis is often made on omental/peritoneal biopsies. Correlation between metastatic disease and primary tumor is often presumed and has implications for patient care. In this single institutional study, we compared primary and concurrent metastatic OHGSC cases morphologically and immunophenotypically to assess the reliability of diagnosis based on the metastatic specimen.

**Design:** Available consecutive cases of OHGSC, or mixed OHGSC, with primary and concurrent metastatic tumor, from 2002 to 2016, were retrieved. Slides were reviewed by 3 pathologists and tumors were evaluated for the following features: architectural pattern, cytologic atypia, mitoses, and necrosis. Tissue microarrays of the primary and matched metastatic tumors were constructed, and immunohistochemical (IHC) stains were performed and interpreted.

**Results:** Of the 66 primary OHGSC cases retrieved, matched primary and metastatic tissues were available for 41 cases. Two cases were classified as high-grade endometrioid carcinomas upon review and were excluded. Overall, there was a high concordance (92%) between the morphology of primary and metastasis and sufficient material for adequate IHC staining. The results demonstrate high concordance between OHGSC primary and metastatic specimens in both morphologic and immunophenotypic features. Our experience confirms the concept that the characteristics of the metastatic tumors sufficiently mirror the primary.

### Concordance of IHC Expression

<table>
<thead>
<tr>
<th>Immunohistochemical Marker</th>
<th>Concordance, n = 39, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>p53</td>
<td>35 (90)</td>
</tr>
<tr>
<td>p16</td>
<td>38 (97)</td>
</tr>
<tr>
<td>WT1</td>
<td>35 (90)</td>
</tr>
<tr>
<td>ER</td>
<td>38 (97)</td>
</tr>
<tr>
<td>PR</td>
<td>39 (100)</td>
</tr>
<tr>
<td>Napsin A</td>
<td>39 (100)</td>
</tr>
<tr>
<td>PAX8</td>
<td>38 (97)</td>
</tr>
</tbody>
</table>

Conclusions: The results demonstrate high concordance between OHGSC primary and metastatic specimens in both morphologic and immunophenotypic features. Our experience confirms the concept that the characteristics of the metastatic tumors sufficiently mirror the primary.

---

**Ovarian Sex Cord Tumor With Annular Tubules With Adult Granulosa Cell Tumor: The First Report of a Co-occurrence**

(Poster No. 18)

Ruby J. Chang, MD; Ramya Masand, MD. 1Department of Pathology, Baylor College of Medicine, Houston, Texas; 2Department of Pathology, Ben Taub General Hospital, Houston, Texas.

Spectrum of Pediatric Uterine Pathology: The Dallas Perspective

(Poster No. 17)

Amanda L. Strickland, MD (amanda.l.strickland@gmail.com); Charles Timmons, MD, PhD; Dinesh Rakheja, MD. Department of Pathology, University of Texas Southwestern Medical Center, Dallas.

**Context:** Pediatric uterine diseases encompass a wide range of pathologic processes with different behaviors and prognoses. A prompt and accurate diagnosis is essential for appropriate management. The purpose of this study is to describe the spectrum and incidence of uterine pathology at our institution during the past 20 years.

**Design:** After approval by the institutional review board, a review of all pathology reports from a large, metropolitan, pediatric hospital, from January 1, 1996, to April 1, 2017, was conducted. Inclusion criteria were uterine pathology at our institution during the past 20 years.

**Results:** Cases were retrieved for 32 female patients with 32 specimens and 35 diagnoses. The age ranged from 4 months to 17 years (mean, 11.5; median, 13). Miscellaneous benign lesions, the most common being decidualized endometrium (n = 7; 20%), comprised most of the diagnoses (n = 14; 40%). This was followed by congenital malformations (n = 11; 31.4%), such as didelphic, hypoplastic, and unicornuate uterus. There were 4 cases with inflammation (11.4%) and one with neoplasia (teratoma; 2.86%). Five cases (14.3%) had no histopathologic abnormality.

**Conclusions:** Uterine lesions are uncommon in children, and although benign, usually require special attention because of the relatively wide differential diagnoses and the potential significant consequences later in adulthood. Similar studies from other pediatric institutions from across the world may illustrate any geographic or ethnic variations in pediatric uterine pathology.

**Ovarian Sex Cord Tumor With Annular Tubules With Adult Granulosa Cell Tumor: The First Report of a Co-occurrence**

(Poster No. 18)
findings of the primary tumor to be reliably used for pathologic diagnosis and treatment decisions.

A Rare Case of Langerhans Cell Histiocytosis of the Vulva
(Poster No. 20)
Ashly Cordero Rivera, MD (ashly.corderorivera@osumc.edu); Wei Chen, MD, PhD. Department of Pathology, Ohio State University Wexner Medical Center, Columbus.

Primary Langerhans cell histiocytosis (LCH) of the vulva is extremely rare. An English literature search revealed fewer than 40 reported cases of LCH limited to the female genital tract. We present a case of a 56-year-old woman with burning, chronic vulvodynia and dyspareunia and persistent posterior Fourchette splitting despite estrogen therapy. Vestibulectomy with vaginal advancement was performed. Microscopic examination revealed a small, nodular, dermal proliferation of epithelioid cells with occasional nuclear grooves, admixed with eosinophils, in a background of mild, chronic inflammation (Figure 154, A and B). Immunohistochemistry results showed the epithelioid cells to be positive for S100, CD1a (Figures 154, C and D), and CD68 (weak, not shown), but negative for Melan-A. Therefore, the diagnosis of LCH was rendered. Morphologic differential diagnosis include lymphoma, macrophage activation syndromes, as well as other histiocytic and dendritic cell disorders. Primary genital LCH is very rare; nevertheless, it should be included in the differential diagnosis when a patient presents with a chronic vulvar lesion recalcitrant to therapy. The symptoms and gross appearance of LCH are nonspecific, ranging from rash, nodule, or ulcer, with or without pruritus. A tissue biopsy is the gold standard to demonstrate a proliferation of S100, CD1a, and Langerin-positive Langerhans cells. Vulvar involvement by a systemic LCH should always be excluded before rendering a diagnosis of primary LCH of the vulva. Fortunately, prognosis of LCH limited to the genital tract appears to be favorable.

Mesonephric Adenocarcinoma of the Uterine Corpus: Report of 2 Cases
(Poster No. 21)
Arti Easwar, MD (arti.easwar@hhchealth.org); Ayesha S. Siddique, MD; Srinivas Mandavilli, MD. Department of Pathology and Laboratory Medicine, Hartford Hospital, Hartford, Connecticut.

Mesonephric adenocarcinoma is well described as a tumor in the cervix and, rarely, in other sites, including vagina and broad ligament. However, this form of adenocarcinoma rarely occurs in the uterine corpus. We present 2 cases of mesonephric adenocarcinoma of the uterine corpus, along with a review of important immunohistochemical studies. One patient presented with a large pelvic mass causing rectal fullness. Upon hysterectomy, a 14.5-cm, nodular, and friable mass, extending from the fundus into the endometrial cavity, was identified. The mass had focal gelatinous areas along with hemorrhage and calcifications. Histologically, it had glandular or acinar features, with slitlike spaces, and papillary architecture in a hyalinized background. The cells were mostly columnar with moderate nuclear atypia and scattered mitosis. Eosinophilic secretions/debris was identified in the lumen. The other patient underwent a hysterectomy for uterine prolapse and was found to have a 5-cm, intramural nodule with gelatinous cut surface. Histologically, this tumor had multiple patterns—tubular, endometrioid, retiform, and serouslike cell buds, and it displayed intraluminal eosinophilic secretions. Immunohistochemically, both tumors were positive for the expression of GATA3, CK7, and PAX8. CD10 showed patchy positivity in the intraluminal debris. Estrogen and progesterone receptors were negative. This immunohistochemical profile confirmed a mesonephric adenocarcinoma of the uterine corpus. This report adds to the very limited literature on mesonephric adenocarcinoma presenting in the uterine corpus, including its immunohistochemical features (Figure 155).

Endometrial Carcinoma With Mixed Small Cell Carcinoma and Endometrioid Carcinoma
(Poster No. 22)
Jeptha T. Johnson, MD (jeptha.johnson@gmail.com); Kristen E. Natale, DO. Department of Pathology, Walter Reed National Military Medical Center, Bethesda, Maryland.

Small cell carcinoma of the endometrium represents less than 1% of all endometrial carcinomas. We report a mixed small cell neuroendocrine carcinoma that was diagnosed as endometrioid carcinoma on initial biopsy. A 59-year-old, postmenopausal woman was evaluated for vaginal bleeding by dilation and curettage with biopsy. The patient was diagnosed with endometrioid carcinoma and was referred to our institution for a hysterectomy and staging procedure. Microscopically, the specimen contained atypical, back-to-back, endometrial-type glands consistent with endometrioid carcinoma as well as a second population of intermediate-sized cells with scanty cytoplasm that resembled lymphocytes, intermixed and surrounding the endometrial-type glands. These cells had a high mitotic activity and immunostaining for CD56 and synaptophysin confirmed neuroendocrine differentiation. Atypical cells with similar morphology were identified within pelvic lymph nodes and had the same immunoprofile. A diagnosis of endometrial carcinoma with mixed small cell neuroendocrine carcinoma and endometrioid carcinoma was rendered. Immunohistochemical testing for mismatch repair suggested a defect in MLH1 protein. Most of the small cell carcinomas of the endometrium will present with a mixed component, and the case reported here demonstrates the difficulty in initial diagnosis of these tumors. Currently, their pathogenesis and whether they represent synchronous malignancies or transformation of a primary tumor, is poorly understood. Treatment of these aggressive tumors is rarely standardized, and patients have a very poor prognosis. With this case report, we hope to draw attention to this uncommon entity as well as stimulate interest in further research of its pathogenesis and treatment options.
Granulosa cell tumors (GCTs) account for 2% of ovarian tumors. The GCTs present with numerous morphologic variation. The appearance of bizarre nuclei in GCTs was first characterized by R. H. Young (1983). We present a case of a 50-year-old, nulliparous woman who presented with vomiting, abdominal pain, and increase in abdominal girth. Computed tomography scan showed heterogeneously enhancing, left adrenal mass measuring up to 12.7 cm. Exploratory laparotomy was performed, excising a tan-red, hemorrhagic, irregular mass measuring 10 × 6.5 × 4.5 cm. Cut sections revealed a multiloculated cystic and friable mass containing hemorrhagic fluid. A frozen section of the representative sample showed numerous sheets of cells with bizarre and enlarged hyperchromatic nuclei with multinucleated cells. Additional sampling showed similar cells with interspersed cells forming microfollicles with grooved nuclei. Granulosa cell tumor was favored. Permanent sections showed numerous sheets of cells with bizarre and enlarged hyperchromatic nuclei with multinucleated cells. There were interspersed areas showing diffuse microfollicular pattern of cells with pale grooved nuclei, typical of adult-type GCT. Mitotic figures were seen, locally up to 3/10 high-power fields. Immunostains for inhibin, calretinin, and vimentin were diffusely positive in both typical GCT cells and cells with bizarre nuclei. Tumor cells were negative for CAM 5.2 and pancytokeratin. Next-generation sequencing revealed missense mutations in FOXL2, ATM, PIK3CA, and p53 genes. FOXL2 mutation, being specific for adult GCT, helps rule out mimics. The GCT with predominantly bizarre nuclei required thorough sampling to reveal areas of typical morphology. Focused immunohistochemistry and molecular studies were crucial to diagnosis.

**Perivascular Epithelioid Cell Tumor of the Uterus With a Concurrent Submucosal Uterine Leiomyoma: A Case Report and Literature Review**

(Poster No. 26)

Christian Salib, MD (christian.salib@wmchealth.org); Minghao Zhong, MD, PhD; Fouzia Shakil, MD, PhD. Department of Pathology, Westchester Medical Center, Valhalla, New York.

Perivascular epithelioid cell tumors (PEComas) are mesenchymal tumors of perivascular epithelial cells that demonstrate myomelanocytic differentiation, coexpressing melanocytic and muscle markers. PEComas typically present in middle-aged women (80%–90%), with a median age of 46 years, and are associated with tuberous sclerosis complex (TSC). Here, we report on a rare case of uterine PEComa with concurrent submucosal uterine leiomyoma in a 35-year-old, premenopausal woman who presented with abdominal pain. Pelvic magnetic resonance imaging revealed a narrowly pedunculated subserosal uterine fundal, heterogeneously enhancing mass with internal blood product. A second 1.0-cm submucosal intrauterine fibroid was also identified. Both ovaries and fallopian tubes appeared unremarkable. Uterine myometrium was performed. Grossly, the specimen measured 10 × 5.0 × 2.0 cm and displayed a tan-pink and brown, partially disrupted serosal surface. Sectioning revealed a red-brown and tan, partially variegated and congested soft tissue appearance, with areas of both solid and cystic degeneration. Microscopically, the lesion revealed nests and sheets of epithelioid cells within a hyalinized stroma displaying abundant cytoplasm, fine nuclear chromatin, prominent nuclei, and occasional
Differentiating DCE from high-grade EC can be diagnostically positive cells. The data were exported for scoring and statistical analysis. Clones, 22c3 and SP142. The slides were then digitally scanned. Computer morphometric analysis was used to determine the percentage of PD-L1–study. There are 4 immunohistochemical (IHC) assays registered with the US Food and Drug Administration, which raises the possibility of variation malignancies. Uterine cervical cancer is also being evaluated for targeted immunotherapy with PD-L1, with 34% shown to express PD-L1 in one grade EC, which is a helpful diagnostic clue.

MMR expression is more frequently seen in DCE than it is in high-grade EC, which is uncommon in high-grade EC; and (3) abnormal undifferentiated component of DCE usually expresses neuroendocrine a transition from well-differentiated carcinoma to undifferentiated distinction: (1) thorough sampling of the specimen is the key to identify confirmed the patient has a germline mutation of the tumor showed loss of MSH2 and MSH6 proteins; genetic testing confirmed the presence of this entity among general surgical pathologists.

Dedifferentiated Carcinoma of the Endometrium in Lynch Syndrome: A Case Report and Literature Review

Hao Chen, MD, PhD (hao.chen@utsouthwestern.edu); Yan Peng, MD. Department of Pathology, UT Southwestern Medical Center, Dallas, Texas.

Dedifferentiated carcinoma of the endometrium (DCE) is a rare type of endometrial carcinoma and composed of undifferentiated carcinoma and well-differentiated endometrioid carcinoma components. The DCE has more-aggressive behavior than high-grade endometrioid carcinoma (EC). A possible association between DCE and Lynch syndrome has been reported. We present a case of DCE in a 54-year-old woman. This 3.5-cm tumor was exophytic and consisted mainly of solid sheets of high-grade malignant cells with brisk mitotic activity. After extensive sampling, a small focus (0.2 cm) of well-differentiated EC was identified. A sharp transition between the 2 components was evident. The well-differentiated component was strongly and diffusely positive for ER, PR, vimentin, and pancytokeratin (AE1/AE3), whereas the high-grade, solid component showed only weak, patchy positivity for those makers. Interestingly, the high-grade component was positive for chromogranin A; the well-differentiated component was negative. The tumor showed loss of MSH2 and MSH6 proteins; genetic testing confirmed the presence of a germline mutation of the MSH2 gene. Differentiating DCE from high-grade EC can be diagnostically challenging. The following points may be helpful in making this distinction: (1) thorough sampling of the specimen is the key to identify a transition from well-differentiated carcinoma to undifferentiated carcinoma that is characteristic of DCE; (2) immunophenotypically, the undifferentiated component of DCE usually expresses neuroendocrine markers, which is uncommon in high-grade EC; and (3) abnormal MMR expression is more frequently seen in DCE than it is in high-grade EC, which is a helpful diagnostic clue.

A Rare Case of Endometrial Adenocarcinoma With Adenoma Malignum Pattern of Invasion: An Encounter With a Deceptive Nemesis

Mohammad I. Barouqa, MD (mbarouqa@montefiore.org); Angela Baldwin, MD, MPH; Xi Zhang, PhD, MD; Sonali Lanjewar, MD; Tiffany Hebert, MD. Department of Pathology, Montefiore Medical Center, Bronx, New York.

Diffusely infiltrative adenocarcinoma with adenoma malignum pattern is a deceptive myometrial-invasive tumor with rare case reports in the literature. The peculiar morphology of this entity can be misinterpreted as benign adenomyosis, mesonephric hyperplasia, mesonephric adenocarcinoma, and tuboendometrioid hyperplasia. We are reporting this unusual and incidental finding in a 65-year-old patient who underwent vaginal hysterectomy for stage III pelvic organ prolapse. Endomyometrial sections showed diffusely infiltrating, round, regularly shaped, crowded glands, with minimal stromal reaction, invading haphazardly 50% of the examined myometrium. The lining epithelium was cuboidal with minimal nuclear atypia and clear-to-pale eosinophilic cytoplasm with eosinophilic luminal secretions (Figure 157). This particular morphology raised the differential diagnosis of mesonephric hyperplasia/mesonephric adenocarcinoma, clear cell carcinoma, and cervical adenocarcinoma. However, the tumor cells were negative for mesonephric markers, which included CD10, GATA3, PAX5, and calretinin. The tumor cells were also negative for mCEA and napsin-A, ruling out cervical adenocarcinoma and clear cell carcinoma, respectively, whereas the positivity for PAX8 and ER confirmed the diagnosis of endometrioid adenocarcinoma with adenoma malignum pattern of invasion. Involvement of cervix by endometrial carcinoma upgrades from the pT stage to pT2. However, when found in cervix, this lesion can be missed because of “benign” morphology and may lead to incorrect cancer staging. This case demonstrates the diagnostic challenges in detecting an adenoma malignum pattern of invasion in endometrioid adenocarcinomas of the uterus. Additionally, it is unique for its rarity and the lack of awareness of this entity among general surgical pathologists.

Comparison of 2 Different Clones of Anti–PD-L1 Antibodies on Uterine Cervical Tissue Microarray by Digital Image Analysis

Brian Cone, DO (bcone@mednet.ucla.edu); Neda Moatamed, MD. Department of Pathology and Lab Medicine, University of California, Los Angeles.

Context: The programmed death-ligand 1 (PD-L1) immunologic regulatory axis is an important target for cancer immunotherapy in multiple malignancies. Uterine cervical cancer is also being evaluated for targeted immunotherapy with PD-L1, with 34% shown to express PD-L1 in one study. There are 4 immunohistochemical (IHC) assays registered with the US Food and Drug Administration, which raises the possibility of variation in staining across platforms. One study found that 3 of the 4 assays were interchangeable in evaluating non–small cell lung cancers, whereas the fourth missed 50% of the tumors. This discordance among testing platforms and cancer types highlights one of several major challenges in testing.

Design: The aim of this study was to determine whether 2 common PD-L1 IHC clones equally assess cervical cancer expression. The IHC was used to assess PD-L1 expression using a tissue microarray of cervical tissues, composed of 94 carcinomas and 6 benign cores using 2 commonly used clones, 22c3 and SP142. The slides were then digitally scanned. Computer morphometric analysis was used to determine the percentage of PD-L1–positive cells. The data were exported for scoring and statistical analysis.

Results: Overall, the SP142 assay was associated with statistically significant greater levels of PD-L1 staining than the 22c3 in cervical malignancies (37% and 8%, respectively, P < .001; Table).

Conclusions: The staining discrepancy might be related to the epitope specificity of the 2 clones in cervical carcinomas or related to the staining methodologies. Future studies are needed for normalization and standardization of the antibody clones to aim for a uniform PD-L1 reaction across the platforms.
Table 2: Comparison of PD-L1 reactions by digital image analysis in All Cores of Cervix TMA

<table>
<thead>
<tr>
<th></th>
<th>n = 100</th>
<th>1a</th>
<th>1b</th>
<th>2a</th>
<th>2b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clone 22c3 (Dako) (n)</td>
<td>58</td>
<td>33</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Clone 22c3 (Dako) (%)</td>
<td>58%</td>
<td>33%</td>
<td>1%</td>
<td>1%</td>
<td>7%</td>
</tr>
<tr>
<td>Clone SP142 (Ventana) (n)</td>
<td>24</td>
<td>23</td>
<td>16</td>
<td>1</td>
<td>36</td>
</tr>
<tr>
<td>Clone SP142 (Ventana) (%)</td>
<td>24%</td>
<td>23%</td>
<td>16%</td>
<td>1%</td>
<td>36%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fisher Exact p-Value</th>
<th>Negative</th>
<th>Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clone 22c3 (Dako) (n)</td>
<td>92</td>
<td>8</td>
</tr>
<tr>
<td>Clone SP142 (Ventana) (n)</td>
<td>63</td>
<td>37</td>
</tr>
</tbody>
</table>

### Characterization of the Immune Microenvironment of Granulosa Cell Tumors

(Poster No. 30)

Anna C. Dusenbery, MD (acd4y@virginia.edu); Zachary Chinn, MD; Linda Duska, MD; Anne Mills, MD. Department of Pathology, University of Virginia, Charlottesville.

**Context:** Granulosa cell tumors (GCTs) can typically be managed surgically but have the capacity for extraovarian extension, local recurrence, and occasional metastasis. In these advanced settings, existing treatment options have limited efficacy. Given the successes of immunotherapy in other tumor types, immune modulatory treatments have been considered for recurrent/metastatic GCTs. However, the immune microenvironment of GCTs has not been well-established.

**Design:** Immunohistochemical staining was performed with PD-L1, indolamine dioxygenase-2,3 (IDO), and CD8 on archival GCT cases. PD-L1 and IDO were scored in both the tumor cell and associated immune-cell compartments at various staining thresholds. Intratumoral vascular staining with IDO was also noted. CD8+ cytotoxic T cells were quantitated per high-power field, averaged across 10 fields.

**Results:** A total of 25 adult GCTs and 4 juvenile GCTs were analyzed. CD8 highlighted the relative lack of cytotoxic T lymphocytes. PD-L1 tumor staining was negative in all cases. PD-L1 immune cell staining was focally positive in 5 of 25 adult GCTs and highlighted peripheral macrophages or within areas of cystic degeneration and hemorrhage. The IDO tumor staining was positive in only one GCT (adult). The IDO immune cell staining was negative in all cases. The IDO was positive in the endothelium of small tumor vessels in 4 adult GCTs.

**Conclusions:** Most GCTs are immunologically quiescent for IDO and PD-L1 and are unlikely to respond to corresponding immunotherapy. Occasional tumor-associated immune cells show focal PD-L1 positivity, restricted to tumor-associated macrophages. A small subset of adult GCTs demonstrate strong IDO+ intratumoral vessels. Both features are of unclear clinical significance.

### Ovarian Carcinosarcoma and Concurrent Serous Tubal Intraepithelial Carcinoma With Next-Generation Sequencing Suggesting an Origin From the Fallopian Tube

(Poster No. 31)

Sharlene Helene C. See, MD (sharlene.see@northwestern.edu); Amir Behdad, MD; Kruti P. Maniar, MD; Luis Z. Blanco Jr, MD. Department of Pathology, McGaw Medical Center of Northwestern University, Chicago, Illinois.

There has been a recent paradigm shift in the concept of ovarian serous carcinoma carcinogenesis. Studies have shown that ovarian high-grade serous carcinomas originate, at least in a significant subset, from the fallopian tube. Serous tubal intraepithelial carcinoma (STIC) is now generally accepted as the earliest form of pelvic high-grade serous carcinoma. Pelvic carcinosarcomas or malignant, mixed, Müllerian tumors are rare, highly aggressive, biphasic tumors that usually arise in the ovary, fallopian tube, or peritoneum. Evidence suggests that these tumors are monoclonal and that the sarcoma component is derived from the carcinoma or from a stem cell undergoing divergent differentiation. Currently, there remains little data regarding its origin, with rare case reports and series suggesting an association with STIC by immunohistochemistry and genetics. We report on a case of a 74-year-old woman presenting with a 16.0-cm, predominantly solid, enhancing pelvic mass. The patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy. Histologically, the ovarian tumor was composed of a high-grade serous carcinoma component and a chondrosarcoma component. In addition, one fallopian tube had STIC.
The STIC (Figure 158, A), high-grade serous carcinoma component, and chondrosarcoma component (Figure 158, B) were all diffusely positive for p53 (Figure 158, C and D) and p16 by immunohistochemistry. Next-generation sequencing was performed separately on each component, demonstrating an identical TP53 gene c.376-1G>A 5’ splice site pathogenic mutation in all 3 components. Our findings confirm the relationship between the carcinoma and sarcoma components and suggest that carcinosarcomas may also originate from the fallopian tube.

Programmed Death Ligand-1 (PD-L1) Expression Is Up-Regulated and Related to the Pattern of Invasion in FIGO Stage I Vulvar Squamous Cell Carcinomas

(Poster No. 32)

Hermann Brustmann, MD, PhD (ddrbrustmann@hotmail.com). Department of Pathology, Landesklinnikum Baden-Neuendoing, Baden, Austria.

Context: The immune checkpoint protein PD-L1 is expressed in different types of cancer and is a potential prognostic factor as well as therapeutic target. This study investigated whether PD-L1 expression is related to neoplastic progression in vulvar epithelia.

Design: The PD-L1 immunoexpression was evaluated in normal squamous vulvar epithelia (n=20), usual type vulvar intraepithelial neoplasia (uVIN, n=23), differentiated VIN (dVIN, n=21), and Federation Internationale de Gynecologie et Obstetrique (FIGO) stage I vulvar invasive keratinizing squamous cell carcinoma (ISCC, n=35), regarding the pattern of invasion in ISCC. Cohesive growth with well-delineated borders was considered pushing, whereas dissociative growth in small groups or single cells was defined as diffuse pattern. Immunostaining was done with a monoclonal anti–PD-L1 antibody (clone SP263, Ventana Medical Systems, Oro Valley, Arizona) and scored for membranous and cytoplasmic reactivity to determine upregulation and overexpression (score 0/1, 0%–5% immunoreactive cells; score 2+, >5% to 50% immunoreactive cells; score 3+, >50% immunoreactive cells).

Results: PD-L1 immunoexpression was comparable and low in normal epithelia and VINs (score 0/1, n=59; score 2+, n=5, in VINs only; score 3+, n=0), was significantly increased (P<.001) in ISCC (score 0/1, n=13; score 2+, n=16; score 3+, n=6), and was significantly related to a diffuse pattern of infiltration (P<.001). Staining was frequently accentuated at the invasive margins of ISCC. PD-L1 expression of epithelial cells and tumor infiltrating lymphocytes was not correlated.

Conclusions: PD-L1 expression is upregulated in vulvar low-stage ISCC, related to the development of an invasive phenotype reflecting the initiation of cancer immunoediting, and to an aggressive diffuse type of stromal invasion.

A Case of Intraplacental Choriocarcinoma in a Monochorionic Diamniotic Pregnancy

(Poster No. 33)

Vimal Krishnan, MD1 (vimal.krishnan@umontreal.ca); Audrey-Ann Labrecque, MD2; Sandrine Wavrant, MD2; Dorothée Dal-Soglio, MD. Department of Pathology and Obstetrics and Gynecology, University of Montreal, Québec, Canada.

Intraplacental choriocarcinoma, defined as a focus of choriocarcinoma located within the placenta, is a rare variant that accounts for 0.04% of gestational trophoblastic diseases. Sixty-two cases have been described in the literature, with prior history of gestational trophoblastic disease and primigravida being possible etiologies. Here, we describe a case of a 31-year-old woman (gravida 3 para 1 [healthy term delivery], aborta 1), who was treated during her pregnancy for stage IV twin-to-twin transfusion syndrome by laser ablation of fetal anastomoses and transabdominal amnioreduction. She delivered monochorionic diamniotic twins by elective caesarean section at 36 weeks and 4 days. Both infants had an APGAR (American Pediatric Gross Assessment Record) family screen- ing of 9–9–10. Macroscopic examination of the placenta did not reveal any lesions. On microscopic examination, a small focus of atypical trophoblastic proliferation limited to the surface of the chorionic villi was present (Figure 159, A). There was marked pleomorphism, eosinophilic nucleoli, and <10 mitoses/high-power field. No stromal or vascular invasion was noted. Upon immunohistochemical staining, the tumor cells were strongly positive for β-human chorionic gonadotropin (β-HCG; Figure 159, B), negative for inhibin (Figure 159, C), and exhibited a strong Ki-67 proliferation index (Figure 159, D). Additional sampling and sectioning did not reveal other foci. A diagnosis of localized intraplacental choriocarcinoma was made. The patient was asymptomatic, had serial serum B-HCG values within reference range, and had a metastatic workup with no abnormal findings. Our knowledge, this is the first report of intraplacental choriocarcinoma in a twin pregnancy. Appropriate sampling and examination of the placenta is essential for the diagnosis and management of gestational trophoblastic diseases.
Abnormal vaginal bleeding is a common symptom with uterine leiomyomata being a common cause. We present a patient with abnormal vaginal bleeding and uterine leiomyomata by imaging with unusual findings on endometrial biopsy. The patient is a 52-year-old, postmenopausal woman with a known history of chronic myeloid leukemia, BCR-ABL1-positive for 2.5 years with progression to blast phase 4 months before presentation. Although she was taking tyrosine kinase inhibitors (most recently bosutinib), this was done intermittently, and she refused induction chemotherapy with bone marrow transplantation after diagnosis of blast phase. She then presented with heavy vaginal bleeding for 3 months. Imaging revealed uterine leiomyomata, both submucosal and subserosal. An endometrial biopsy was performed before uterine artery embolization. The endometrium showed partial effacement by large mononuclear cells with a high nuclear to cytoplasmic ratio, dispersed chromatin, and prominent nucleoli. Mitoses were frequent. Immunohistochemistry was performed revealing diffuse positivity in these cells for myeloperoxidase and positivity in a subset for apocrine change. Immunohistochemistry was performed revealing diffuse positivity in these cells for myeloperoxidase and positivity in a subset for apocrine change—two characteristics that can occur in mammary and extramammary fibroadenomas. Apical and extramammary fibroadenomas are an important rare diagnostic entity to be aware of. We discuss the relevant literature on apical fibroadenomas, etiology of these tumors arising in the anogenital region, and significance of apocrine change.

**An Unusual Cause of Vaginal Bleeding**

(Matthew Powell, MD (matpowell@augusta.edu); Chadburn Ray, MD; Jeremy Pantin, MD; Natasha Savage, MD; Nikhil Patel, MD. Departments of Pathology, Obstetrics and Gynecology and Medicine-Hematology/Oncology, Augusta University, Augusta, Georgia.

Human Papillomavirus–Negative, Poorly Differentiated Carcinoma of Cervical Origin in a 14-Year-Old Female: A Rare Entity With a Novel KAT6A-NCOA2 Translocation

(Poster No. 37)

Sharon J. Song, MS, MD1 (sharon.song@uphs.upenn.edu); Kay J. Park, MD; Kamarasan Cooper, MBChB, DPhil; Lea Surrey, MD; M. Carolina Reyes, MD.1 Department of Pathology, Hospital of University of Pennsylvania, Philadelphia; 2Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, New York; 3Department of Pathology & Laboratory Medicine, Children’s Hospital of Philadelphia, Pennsylvania.

Cervical malignancies are extremely uncommon in the pediatric and adolescent population, accounting for less than 3% of cancers. Tumors in this age group are either carcinomas, sarcomas, or germ cell tumors. Carcinomas of the lower female genital tract, although common in adults, are rarely seen in pediatric patients. Here, we describe a case of a 14-year-old girl who presented with menorrhagia and pain 1 year after menarche. Imaging showed a 9-cm mass centered in the cervix. She underwent a radical abdominal hysterectomy, which revealed an exophytic, fleshy, ulcerated, necrotic, and hemorrhagic mass entirely replacing the cervix (Figure 162, A). On histology, a high-grade epithelial neoplasm with solid/papillary components (Figure 162, B) and diskoheisic, plasmacytoid morphology was seen (Figure 162, C). The neoplastic cells were positive for AE1/3 and PAX8 and focally weakly positive for EMA, CK7, CD10, CD99 (Mic-2), WT1, glypican-3, and p63. Most tumor cells showed patchy positivity for p16 with focal areas showing diffuse and strong staining, whereas human papillomavirus (HPV) mRNA in situ hybridization confirmed HPV negativity. p53 showed wild-type staining. A targeted RNA-sequencing panel (ArcherDx) revealed a novel KAT6A-NCOA2 fusion gene. This translocation has been reported in patients with acute mixed-lineage...
leukemia but has not yet been identified in solid tumors, whereas NCOA2-associated fusions with different partners have been reported in a variety of solid tumors, such as colorectal carcinomas. Despite receiving adjuvant chemoradiation therapy, the patient developed widespread metastatic disease. This case highlights an extremely rare pediatric presentation of HPV-negative cervical carcinoma with a novel translocation and poor prognosis.

Uterine liposarcoma is rare. The presence of adipocytes in the uterine corpus and their neoplastic transformation has been a focus of speculation. A search within institutional archives identified only 2 cases of primary uterine liposarcoma in the past 20 years (1997–2017). Clinical, gross, and microscopic features were reviewed. The patients were 71 and 70 years old. They presented with abdominal pain, weight loss, and uterine mass on imaging. Both underwent hysterectomy and bilateral salpingo-oophorectomy. Grossly, the tumors originated from the myometrium, measuring 8 and 11-cm. Cut surfaces were tan and solid, with areas of mucoid change and necrosis. Microscopic evaluation of one case showed sheets of epithelioid cells with hyperchromatic nuclei and eosinophilic cytoplasm. Necrotic areas demonstrated adipocytes with spindle cells suggestive of an infarcted lipoleiomyoma. The second case primarily consisted of spindle cells arranged in a fascicular pattern. The mucoid change showed alternating hypocellular myxoid with hypercellular spindled areas. Both cases revealed small foci of lipogenic areas with pleomorphic lipoblasts. Immunohistochemical stains showed CD10 positivity, whereas they were negative to focally reactive for MDM2, cyclin D1, h-caldesmon, and smooth muscle actin. Fluorescence in situ hybridization results for MDM2 amplification was negative in both cases. Primary pleomorphic liposarcoma of the uterus is extremely rare. In a CD10+ high-grade uterine sarcoma, extensive tumor sampling is the key to establishing the diagnosis because the diagnostic features of liposarcoma may be focal. Evaluating for MDM2 amplification by fluorescence in situ hybridization is important to exclude the more common entity of a dedifferentiated liposarcoma of the retroperitoneum.

**FIGO Grade 1 Endometrioid Endometrial Carcinoma With Microcystic, Elongated, and Fragmented Pattern**

(No. 40)

Sushma Ravirala, MBBS (sushmaravirala@moundsinai.org); Mallary Mani, MD; Julian Samuel, MD; Poojaben Dhorajiya, MBBS; Ippolito Modica, MD. Department of Pathology, Mount Sinai St Luke’s Roosevelt Hospital, New York, New York.

Endometrioid endometrial carcinoma (EEC) represents 80% of all endometrial carcinomas. Federation International de Gynecologie et Obstetrique (FIGO) grade 1 EEC typically is associated with excellent prognosis. However, a specific pattern of myometrial invasion characterized by microcystic, elongated and fragmented (MELF) glands are associated with increased risk for lymphovascular invasion and lymph node (LN) metastasis in a few of these low-grade neoplasms. We present a unique case of FIGO grade 1 EEC in a 59-year-old woman who underwent total hysterectomy, bilateral salpingo-oophorectomy, and pelvic and right sentinel node lymphadenectomy. Histologic examination of the hysterectomy specimen revealed well-differentiated neoplastic glands, showing less than 5% solid growth pattern, with uniform, mildly enlarged nuclei, consistent with FIGO grade 1 (Figure 163, A). Further microscopic evaluation revealed less than 50% myometrial invasion; however, the invasive component showed microcystic and fragmented, neoplastic cells with abundant eosinophilic cytoplasm (Figure 163, B). This specific infiltrative pattern in inflammatory stroma rendered the diagnosis of FIGO grade 1 EEC with MELF pattern. Increased suspicion for lymphovascular invasion led to careful microscopic and immunohistochemical studies in evaluation of the pelvic and retroperitoneal lymph nodes.

**The Incidence of Plasma Cells in Women With Recurrent Pregnancy Loss**

(Poster No. 38)

Suzanne Iwaz, MD (suzanneiwaz@yahoo.com); John Groth, MD. Department of Pathology, University of Illinois, Chicago.

**Context:** The incidence of chronic endometritis, has been variably reported in 7% to 57% of patients with recurrent pregnancy loss, supporting the use of antibiotics. Chronic endometritis, is a disease well known clinically, although definitive pathologic criteria remains elusive. This has resulted in the variable incidence of chronic endometritis in recurrent pregnancy loss. Therefore, we investigated the presence of plasma cells and chronic endometritis in patients with recurrent pregnancy loss.

**Design:** Endometrial biopsies from 139 patients with recurrent pregnancy loss, defined as 2 or more unexplained pregnancy losses, with at least one loss of 10-weeks or more size, were analyzed. We defined chronic endometritis, as the presence of 3 or more plasma cells with at least one loss of 10-weeks or more size, were analyzed. The incidence of chronic endometritis was 30.2%. The incidence of chronic endometritis in this patient was 30.2%. The average plasma cell count was 9.96 per case, with a range from 0 to 250. The average plasma cell count in women subsequently pregnant, versus women unable to conceive, was 9.25.

**Conclusions:** The incidence of chronic endometritis in this patient cohort with recurrent pregnancy loss was 30.2%, supportive of a potential role of chronic endometritis in recurrent pregnancy loss. However, the absolute plasma cell count may not be predictive of future pregnancy status.

**Uterine Pleomorphic Liposarcoma: A Rare Primary Uterine Sarcoma**

(Poster No. 39)

Luke Blower, MD (luke.blower@osumc.edu); Adrian Suarez, MD; Hans Iwenofu, MD; Wei Chen, MD, PhD. Department of Pathology, Ohio State University Wexner Medical Center, Columbus.
Paraganglioma Arising From Mature Cystic Teratoma: Presentation of a Case and Review of the Literature
(Poster No. 41)
Dooa Y. Alqaidy, MD1 (dalqaidy@gwu.edu); Gaby Moawad, MD2; Rochelle Simon, MD1; Stephanie Barak, MD1. 1Departments of Pathology and 2Gynecology and Obstetrics, George Washington University, Washington, DC.

Paragangliomas are neuroendocrine tumors that develop from the neural crest cells. The presence of paraganglioma in the female reproductive system has been occasionally reported in the literature; cases have been reported involving the vagina, ovaries, or uterus. The occurrence of paraganglioma in cystic teratoma is extremely rare, and only 4 cases have been previously reported. We present a case of a 32-year-old, nulligravid woman with a history of chronic right pelvic pain for several months. Pelvic magnetic resonance imaging demonstrated 2 pelvic masses with complex cystic and solid components, arising from the left and right ovaries and occupying much of the anterior true pelvis. Consequently, the patient underwent diagnostic laparoscopy and bilateral ovarian cystectomy. Microscopic examination of the left ovarian mass revealed a mature teratoma with a large amount of glial and neural tissue. Adjacent to the glial tissue was a proliferation of cells with round nuclei, fine chromatin, and scant cytoplasm in a vague nesting pattern. Neither atypia nor mitosis was detected. Immunohistochemical studies were performed and revealed the cells to be strongly immunoreactive for synaptophysin and CD56, consistent with neuroendocrine differentiation. S100 highlighted the spindle (sustentacular) cells between the neoplastic cells. Overall, the histologic features and immunohistochemical profile were consistent with a paraganglioma arising from mature ovarian teratoma. This site of presentation is unusual for paraganglioma. Pathologists should be aware that this entity may also occur within otherwise typical mature teratoma and, therefore, entertain the diagnosis when microscopic findings are suggestive of a neuroendocrine tumor.

Two Rare Cases of Fallopian Tube Teratomas
(Poster No. 42)
Ariane Robison, MD (arobiso2@hfhs.org); Beena Umar, MD; Arthur Gaba, MD; Ghassan Allo, MD, MSc, FRCP. Department of Pathology, Henry Ford Hospital, Detroit, Michigan.

Teratomas are not infrequently found in ovaries. They are only rarely described within other genital organs, and only about 70 cases of fallopian tube teratomas have been reported in the English literature. We present 2 cases of fallopian tube teratomas, in 2 different clinical contexts. The first patient is a 32-year-old (gravida 2, para 2) [2GP2] woman who underwent bilateral partial salpingectomy for sterilization at the time of cesarean section. No tumor was identified clinically. At gross examination, the left fallopian tube was distorted with luminal tan-yellow grumous material and hair. On microscopic evaluation, the intraluminal tumor measured 0.4 cm. The second case was an incidental finding of a fallopian tube tumor in a 43-year-old G2P2 woman who presented for left salpingectomy following a diagnosis of a right fallopian tube teratoma discovered on right salpingo-oophorectomy at an outside institution. No tumor was identified grossly within the left fallopian tube, but a 0.5-cm tumor was discovered on microscopy. Histologically, the fallopian tube luminal masses of both patients demonstrated similar morphology, being composed of a solid nodule with mature tissue of ectodermal (epidermis, sebaceous glands, and hair follicles), mesodermal (fat and cartilage), and endodermal (gastrointestinal glands and thyroid follicles) embryonic origin (Figure 163, D), and CAM 5.2-positive cells in one right pelvic LN. The right sentinel LN revealed similar, cytokeratin-positive cells. We present this case to raise awareness of low-grade ECC with MELF pattern and its association with lymphovascular invasion, as demonstrated in this unique case with both pelvic and sentinel LN metastasis. Accurate diagnosis may aid clinicians in long-term monitoring of these patients.

Highly Cellular Leiomyoma With Seedling Leiomyomas: A Rare Mimic of Low-Grade Endometrial Stroma Sarcoma
(Poster No. 44)
Hao Chen, MD PhD; Katja Gwin, MD (Katja.gwin@utsouthwestern.edu). Department of Pathology, University of Texas Southwestern Medical Center, Dallas.

Highly cellular leiomyoma (HCL), as an uncommon variant of leiomyoma, may represent a diagnostic challenge for pathologists to distinguish from low-grade endometrial stromal sarcoma (ESS). Especially in the rare scenario of HCL being associated with highly cellular seeding leiomyomas in the adjacent myometrium, the low-power appearance can easily lead to misinterpretation as low-grade ESS.

Inflammatory Myofibroblastic Tumor Associated With the Placenta
(Poster No. 43)
Jeptha T. Johnson, MD1 (jeptha.johnson@gmail.com); Rubina H. Mattu, MD; Qi Liang, PhD; Justin M. Wells, MD; Alejandro Luñá Contreras, MD. 1Department of Pathology, Walter Reed National Military Medical Center, Bethesda, Maryland; Departments of Gynecologic Pathology, Molecular Diagnostics Laboratory and Bone and Soft Tissue Pathology, Joint Pathology Center, Silver Spring, Maryland.

Inflammatory myofibroblastic tumors (IMTs) are tumors of low malignant potential, most commonly involving lung, retroperitoneum, and peritoneum. The IMTs are rare in the gynecologic tract, with case reports of tumors involving the placenta. Our case documents an IMT in association with pregnancy and the placenta, highlighting an extremely rare presentation of an uncommon neoplasm. Our patient is a 32-year-old, multiparous woman with no significant pregnancy complications, normal-appearing placenta, and fetal anatomy by ultrasound, who underwent cesarean section. The placenta was submitted along with a 2.9 × 2.4 × 0.9-cm detached nodule. On histologic examination, the nodule comprised a proliferation of cells of myofibroblastic origin, which were immunoreactive for ALK1, CD10, and WTI, along with scattered inflammatory cells. Fluorescence in situ hybridization revealed an ALK rearrangement, metacentric abnormality, which were confirmed by next-generation sequencing detected an in-frame TIMP3-ALKex18 fusion. This rearrangement has only been rarely reported in uterine IMT. The IMT is a mesenchymal tumor of myofibroblastic origin that has potential for local recurrence but low metastatic risk. In association with the placenta, IMT has previously been reported in 5 cases, and to our knowledge, this is the first IMT associated with the placenta with a confirmed TIMP3-ALK fusion transcript. Recent techniques have demonstrated that at least a subset of placental IMTs are of uterine origin, with short tandem repeat genotyping demonstrating maternal origin of placental IMTs. With this case report, we hope to raise awareness of this rare lesion and encourage further research into its pathogenesis.
Distinction between these 2 entities is, however, prudent because biologic behavior and patient management vary significantly. Here, we present a case of HCL that possessed features raising concerns for low-grade ESS, including a highly cellular mass with irregular borders (Figure 165, A), small vessel clusters (Figure 165, B), seeding nodules mimicking invasion reminiscent of an ESS pattern (Figure 165, C), and subendothelial nodules mimicking lymphovascular invasion (Figure 165, D). Morphologic features of the tumor were, however, compatible with smooth muscle differentiation, including (1) spindle cells forming a fascicular architecture; (2) presence of large, thick-walled vessels; (3) focal hyalinized stroma; and (4) cleftlike spaces. Immunohistochemistry revealed positivity for the smooth markers desmin, SMA, and h-caldesmon, and negativity for CD10. As an extremely rare variant of leiomyoma, HCL with seeding leiomyomas possess features raising concern for low-grade ESS. Helpful morphologic features, such as fascicular architecture; large, thick-walled vessels; hyalinized stroma; and cleftlike spaces are suggestive of HCL. Histologic features and an appropriate immunostaining panel can be extremely helpful in the differential diagnosis.

Metastasis to Fallopian Tube Mucosa From Mucinous Appendiceal Carcinoma: A Report of 2 Cases
(Poster No. 45)
Sarah Al-Awami, MD (sarah.al-awami@bcm.edu); Ramya Masand, MD. Department of Pathology, Baylor College of Medicine, Houston, Texas.

Metastasis to the fallopian tube (FT) is rare. Recent literature suggests that mucosal alterations of the FT are primary tubal lesions. This had led to a paradigm shift in the classification of ovarian tumors with studies proposing a tubal origin for these tumors, and clinicians advocating distal salpingectomy to decrease rates of ovarian cancer. This is based on the theory that metastatic carcinoma cannot involve FT mucosa alone. We present 2 cases of isolated mucosal metastases to the FT from appendiceal tumors. Two women, 36-years-old and 72-years-old, presented with adnexal masses. Both had a history of appendectomy. The tubes in both cases were distended with mucin, and the ovary had surface mucin. Microscopic examination showed multifocal, low-grade, mucinous epithelium with focal papillations and tufting, interspersed by normal tubal epithelium. The mucinous tumors were diffusely positive for CK20 and CDX2, focally positive for CK7, and negative for ER and PAX8. Ovaries had mucin pools with no epithelium. Based on morphology and immunohistochemical features, it is likely the current practice would be to assign primary origin of a tumor to the FT, whereas these tumors were of appendiceal origin metastatic to FT mucosa. These cases are unique in that no other organs were involved. It is important not to dismiss these mucosal alterations as benign tubal mucinous metaplasia. In addition, these cases prove that mucosal metastasis can occur and reappraisal of them in the presence of “intraperitoneal” tumor is necessary.

Perivascular Epithelioid Cell Tumor of the Uterine Cervix: An Unusual Location of a Rare Neoplasm With a Unique Genetic Alteration
(Poster No. 46)
Paulynn I. Maclayton, MD1; Ekeke O. Okoye, MD1; Koen, MD; Ekeke I. Okoye, MD1; Talent Theparee, MD2; Scott H. Rich, MD1; Jennifer A. Hipp, MD, PhD. Department of Pathology, University of Toledo Medical Center, Toledo, Ohio.

Perivascular epithelioid cell tumors (PEComas), also known as myomelanocytic tumors because of their variable coexpression of melanocytic and smooth muscle markers, are rare distinctive mesenchymal neoplasms. Although not common, most PEComas of the gynecologic tract have been reported in the uterine corpus. PEComas of the uterine cervix are extremely rare, with fewer than 12 cases reported in the literature. We report the case of a 51-year-old woman who presented with menorrhagia and anemia. Radiographic imaging showed uterine leiomyomata. After failure of medical management, she underwent a total hysterectomy. Gross examination of the specimen confirmed leiomyomata, as well as an incidental, red-brown, 0.8-1.0-cm cervical nodal. On microscopy, the tumor was composed of infiltrating epithelioid cells with abundant eosinophilic cytoplasm and nuclear pleomorphism. No necrosis, vascular invasion, or mitotic activity was identified. Immunostaining of the tumor showed positivity for HMB-45, Melan-A (focal), pancytokeratin, desmin (focal), and estrogen receptor. The morphology and immunoprofile were compatible with a PEComa. Multiple gene sequencing was performed detecting genomic loss of TSC2 and STK11. The loss of TSC2 supports the diagnosis of PEComa because many of these tumors have loss-of-function TSC1/2 mutations. To our knowledge, STK11 mutations have not previously been described in PEComas; however, STK11 and TSC2/1 are both involved in the mTOR pathway. In conclusion, when evaluating epithelioid neoplasms of the cervix, PEComas should be included in the broad differential diagnosis.

Stratified, Mucin-Producing Intraepithelial Lesion: An Easily Missed and Challenging Glandular Lesion of the Cervix
(Poster No. 47)
Jenna L. Purdy, MD (jenna.purdy@utoledo.edu); Jennifer A. Hipp, MD, PhD. Department of Pathology, University of Toledo Medical Center, Toledo, Ohio.

Context: Stratified, mucin-producing intraepithelial lesion (SMILE) of the cervix is a poorly recognized, high-grade lesion displaying hybrid features of high-grade squamous intraepithelial lesion (HSIL) and adenocarcinoma in situ (AIS). The lesion is characterized by a multilayering, dysplastic, mucin-producing epithelium rather than a single layer of dysplastic glandular epithelium (as in AIS) or a multilayering, dysplastic, purely squamous epithelium (as in HSIL). Despite being classified as a high-grade lesion, histologic features are more subtle than HSIL and AIS and are easily missed.

Results: Of the 17 cases reviewed, 1 showed definitive features of SMILE, which was previously diagnosed as HSIL. Another case, previously called negative, showed atypical glands suspicious for SMILE. The total incidence of SMILE in our study was 11% (2 of 17).

Conclusions: SMILEs should be considered when diagnosing dysplastic glandular lesions of the cervix. SMILEs are often associated with HSIL, so extreme caution should be used to determine margin status when resected. In addition, the prognostic significance of SMILEs is not known; however, recent studies suggest that SMILEs should be regarded as variants of AIS for patient management purposes, underscoring the significance of accurately identifying this entity.

Granulomatous Metritis and Cervicitis Associated With Common Variable Immunodeficiency Presenting With Vaginal Bleeding
(Poster No. 48)
Toni Theparee, MD (ttetheparee@northshore.org); Crystal Bockoven, MD; Elisheva Shanes, MD; Lin Liu, MD. Department of Pathology and Laboratory Medicine, NorthShore University Health System, Evanston, Illinois.

Diffuse granulomas within the uterine corpus and cervix are an uncommon finding usually associated with instrumentation or surgical manipulation. Up to 22% of patients with common variable immunodeficiency (CVID) have granulomatous diseases, commonly occurring
in the skin, lung, lymph nodes, spleen, and liver. We report a case of a 51-year-old woman who presented with increasingly heavy and irregular vaginal bleeding for the past 2 years. Gynecologic ultrasound demonstrated an enlarged uterus with features of adenomyosis. A prior endometrial biopsy revealed scant atrophic endometrial glands. The patient was previously diagnosed 4 years earlier with CVID after presenting with an erythematous rash on her face. Skin biopsies demonstrated granulomatous inflammation negative for fungal or mycobacterial organisms. An axillary lymph node biopsy demonstrated nonnecrotizing granulomatous lymphadenopathy and decreased serum immunoglobulin (Ig) G and IgA levels were noted. A hysterectomy was electively performed. Grossly, no endometrial or myometrial mass was present. Histology demonstrated poorly formed, noncaseating granulomas surrounded by a cuff of T lymphocytes diffusely extending throughout the myometrium and cervix and involving the endometrium (Figure 166, A through D). The lymphocytes demonstrated mild CD8+ T-cell predominance. Stains for fungi and mycobacteria are negative. These findings were similar to the prior skin biopsies and strongly suggested uterine involvement by a systemic granulomatous process consistent with CVID. A literature search did not reveal any prior case reports of granulomatous metritis and cervicitis associated with common variable immunodeficiency. This case highlights that granulomatous inflammation occurring in CVID may involve the endometrium and cervix and present with vaginal bleeding.

Primary Ovarian Leiomyosarcoma: A Rare Ovarian Tumor

(Poster No. 49)

Arch Patel, MD

Department of Pathology, ETSU, Johnson City, Tennessee; Department of Pathology, Wake Forest Baptist Medical Center, Winston-Salem, North Carolina

Primary sarcomas of the ovary are rare gynecologic tumors, which represent about 4% of all ovarian tumors. Chondrosarcomas, fibrosarcomas, endometrial stromal sarcomas, angiosarcomas, rhabdomyosarcomas, and leiomyosarcomas have been reported. Primary leiomyosarcoma of the ovary represents only 1% of ovarian tumors; about 60 cases have been reported in the literature. We report a case of a 62-year-old woman with the 5-cm, left ovarian mass with pelvic adhesions. A bilateral salpingo-oophorectomy procedure was performed, and we received 5-cm, tan-white, firm ovarian mass with attached 4.1-cm, dilated fallopian tube. Histologically, the mass showed atypical hyperchromatic, pleomorphic spindle cells arranged in fascicular/random pattern with marked mitotic activity (>30 mitotic/10 high-power fields), focal hyaline degeneration and coagulative necrosis. The atypical spindle cells showed immunoreactivity with desmin and actin. The histology and immunophenotypic features of the tumor supported the diagnosis of leiomyosarcoma. There was no evidence of malignancy in other organs. After treatment, patient’s condition was stable. Unfortunately, these tumors are aggressive and have a poor prognosis. It is important to recognize this entity at early stage for better patient survival. Surgery is the cornerstone of treatment, whereas the role of chemotherapy and radiotherapy is still not clear because substantial data are lacking for the treatment of this aggressive tumor.

Endometrioid Endometrial Adenocarcinoma in Patients Younger Than 50 Years: Mismatch Repair Protein Expression and Correlation With Clinicopathologic Features

(Poster No. 50)

Zainab A. Almatar, MBBS (zainab.almatar@bcm.edu); Jasmeet Assi, MD; Ramya Masand, MD. Department of Pathology and Immunology, Baylor College of Medicine, Houston, Texas

Context: Despite recommendations for universal screening of endometrial adenocarcinoma (EAC), expense of immunohistochemistry (IHC) for mismatch repair proteins (MMRP), and molecular genetic testing are cost prohibitive in resource-limited environments. An EAC is a disease of hyperestrogenism, with a small proportion related to microsatellite instability (MSI). We assessed incidence of MSI in medically underserved women diagnosed with endometrioid EAC (EEAC) younger than 50 years to determine whether specific factors help streamline IHC and molecular profiling.

Design: Patients younger than 50 years with EEAC from 2012 to present were identified. Patient age, race, body mass index (BMI), family history, follow-up data, and tumor grade and stage were noted. Moreover, MMRP IHC was performed.

Results: Ninety-three women younger than 50 years had MMRP IHC (median age, 42 years; BMI, 37.7 kg/m2; loss of MMRP by IHC, 9 of 93 patients; 7 had MLH1 and PMS2 loss, 1 had MSH2 and MSH6 loss, and 1 had MSH6 loss only). Of the 7 patients with MLH1 and PMS2 loss, 4 were grade 2 and 3 were grade 3 tumors with stage I (n = 1), II (n = 2), III (n = 3), and IV (n = 1). Patients with MLH2 and MSH6 loss and isolated MSH6 loss had grade 2, stage 1 tumors.

Conclusions: Incidence of MMRP loss is lower than reported in our population. No difference in BMI existed between patients with or without loss. Compared with MSS carcinomas, women with MSI (MSH1 and PMS2 loss) have higher grade and higher likelihood of extrauterine disease. In resource-limited environments, clinicopathologic features can help triage women to MSI testing.

More Than Just a Fat Embolus Seen in a Patient With Sickle Cell Crisis and an Anatomic Deviation

(Poster No. 51)

Rachel Jug, MB, BCh, BAO (rachel.mattson@duke.edu); Grant Harrison, MD; Alan D. Proia, MD, PhD. Department of Pathology, Duke Health, Durham, North Carolina

A 31-year-old, African American woman presented to the emergency department with lower back and extremity pain and weakness after spending extended periods of time in the sun, which stimulated a recurrence of her frequent sickle cell pain crisis symptoms. Laboratory investigations revealed hyperbilirubinemia and leukocytosis. Seven days later, she developed worsening hypoxia and was admitted to the medical intensive care unit with acute chest syndrome. An echocardiogram of her heart revealed an ejection fraction of 35%; she was treated with heparin and an exchange transfusion. She became acutely hypotensive and developed refractory metabolic acidosis. She had cardiac arrest, and despite aggressive resuscitation attempts, death was pronounced. Typical histologic findings of patients with sickle cell disease and end-organ damage were seen on postmortem, including an autoinfarcted spleen, diffuse global glomerulosclerosis, pulmonary hypertension, bowel infarction, acute myocardial infarction, and bone marrow infarction leading to fat emboli, highlighted by special staining with osmium tetroxide (Figure 167, A through D). A distinct and unusual finding was an obstructing right coronary artery embolus composed of infarcted bone marrow, possibly because of the concurrent probe-patent atrial septal defect found at autopsy. This case highlights the morbidity and mortality of pain crises and acute chest syndrome, and despite aggressive resuscitation attempts, death was pronounced. Typical histologic findings of patients with sickle cell disease and end-organ damage were seen on postmortem, including an autoinfarcted spleen, diffuse global glomerulosclerosis, pulmonary hypertension, bowel infarction, acute myocardial infarction, and bone marrow infarction leading to fat emboli, highlighted by special staining with osmium tetroxide (Figure 167, A through D). A distinct and unusual finding was an obstructing right coronary artery embolus composed of infarcted bone marrow, possibly because of the concurrent probe-patent atrial septal defect found at autopsy. This case highlights the morbidity and mortality of pain crises and acute chest syndrome, and despite aggressive resuscitation attempts, death was pronounced. Typical histologic findings of patients with sickle cell disease and end-organ damage were seen on postmortem, including an autoinfarcted spleen, diffuse global glomerulosclerosis, pulmonary hypertension, bowel infarction, acute myocardial infarction, and bone marrow infarction leading to fat emboli, highlighted by special staining with osmium tetroxide (Figure 167, A through D). A distinct and unusual finding was an obstructing right coronary artery embolus composed of infarcted bone marrow, possibly because of the concurrent probe-patent atrial septal defect found at autopsy. This case highlights the morbidity and mortality of pain crises and acute chest syndrome, and despite aggressive resuscitation attempts, death was pronounced.

More Than Just a Fat Embolus Seen in a Patient With Sickle Cell Crisis and an Anatomic Deviation

(Poster No. 51)

Rachel Jug, MB, BCh, BAO (rachel.mattson@duke.edu); Grant Harrison, MD; Alan D. Proia, MD, PhD. Department of Pathology, Duke Health, Durham, North Carolina

A 31-year-old, African American woman presented to the emergency department with lower back and extremity pain and weakness after spending extended periods of time in the sun, which stimulated a recurrence of her frequent sickle cell pain crisis symptoms. Laboratory investigations revealed hyperbilirubinemia and leukocytosis. Seven days later, she developed worsening hypoxia and was admitted to the medical intensive care unit with acute chest syndrome. An echocardiogram of her heart revealed an ejection fraction of 35%; she was treated with heparin and an exchange transfusion. She became acutely hypotensive and developed refractory metabolic acidosis. She had cardiac arrest, and despite aggressive resuscitation attempts, death was pronounced. Typical histologic findings of patients with sickle cell disease and end-organ damage were seen on postmortem, including an autoinfarcted spleen, diffuse global glomerulosclerosis, pulmonary hypertension, bowel infarction, acute myocardial infarction, and bone marrow infarction leading to fat emboli, highlighted by special staining with osmium tetroxide (Figure 167, A through D). A distinct and unusual finding was an obstructing right coronary artery embolus composed of infarcted bone marrow, possibly because of the concurrent probe-patent atrial septal defect found at autopsy. This case highlights the morbidity and mortality of pain crises and acute chest syndrome, and despite aggressive resuscitation attempts, death was pronounced.
Alveolar capillary dysplasia and renal tubular dysgenesis are known fatal entities in pediatric pathology; however, they can easily escape the untrained eye. At first glance, the organs can look completely healthy, but with careful perlustration and review of the clinical scenario, the meticulous pathologist can identify the necessary diagnostic clues. We present a case of a 6-day-old boy born at 30 weeks gestation. The infant suffered from respiratory distress at birth and was noted to have minor dysmorphic features. His respiratory status continuously deteriorated, suffered from respiratory distress at birth and was noted to have minor dysmorphic features. His respiratory status continuously deteriorated, and he expired on day 6. The lungs showed thickened alveolar septae, congested capillaries, and medial hypertrophy of small pulmonary arteries. Also noted was a decrease in capillaries away from the alveolar epithelium and malposition of branches of the pulmonary vein next to pulmonary arteries (Figure 168, A and B). Veins are not normally located adjacent to the arteries in the lungs making this a case of alveolar capillary dysplasia with misalignment of the veins. The second case is a 1-day-old twin boy born at 32 weeks gestation. There was a twin-twin transfusion syndrome with prenatal selective laser photocoagulation. At birth, the infant suffered respiratory distress because of lung hypoplasia. Initially, the kidneys were enlarged and looked congested. Closer inspection revealed a decrease in the number and poorly developed proximal tubules (EMA stain) with a diagnosis of renal tubular dysgenesis (Figure 168, C and D). A good grasp of developmental pathology and a keen eye are vital for the diagnosis because of the fatality of these disorders.

**Mortalities Associated With Clostridium Difficile Colitis: A 14-Year Retrospective Review of 928 Autopsy Cases**

*(Poster No. 53)*

**Design:** A 14-year retrospective review (2003–2017) of all adult autopsies was performed at our institution. Comprehensive medical reports and autopsy findings were analyzed to define whether the terminal events of hospitalized patients were attributable primarily to *C difficile* colitis.

**Results:** Eight of 928 autopsy cases (0.86%) were diagnosed with *C difficile* colitis. Patients with *C difficile* colitis had a mean age of 57.5 years. Three patients were admitted for viral pneumonia, bronchopneumonia, and pulmonary emboli. One patient presented after craniectomy for multiple strokes, and another had received chemoradiation for breast cancer. The remaining patients had advanced autoimmune disease. All patients were treated with antibiotics, and their clinical courses were complicated by septic shock and pancolitis. In 4 cases (0.43%), direct consequences of *C difficile* colitis were the immediate cause of death.

**Conclusions:** Although reported case-fatality rates of *C difficile* colitis in hospitalized patients is roughly 6% in large series, the prevalence of fulminant *C difficile* colitis as the immediate cause of death in large autopsy series is not widely reported. We find a prevalence of 0.43%, establishing a baseline for future surveillance and prevention.

**Easily Overlooked Cases in Pediatric Pathology: Reading Between the Lines in Alveolar Capillary Dysplasia and Renal Tubular Dysgenesis**

*(Poster No. 52)*

Alicia Hirzel, MD, MPH; Maria Goiburú, MD (Maria.goiburu@jhsmiami.org); Claudia P. Rojas, MD, Department of Pathology, University of Miami Miller School of Medicine/Jackson Health System, Miami, Florida.

**Immune-Related Adverse Effects in a Patient With Melanoma Treated With Checkpoint Inhibitors: An Autopsy Case Study and Review of the Literature**

*(Poster No. 54)*

Miguel A. Salinas, BS (misalain@UTMB.EDU); Maria del Mar Rivera Rolon, MD; Benjamin B. Gelman, MD, PhD. Department of Pathology, University of Texas Medical Branch, Galveston.

Novel antineoplastic therapies that target cytotoxic T-lymphocyte-associated antigen 4 and programmed death cell receptor-1 are considered first-line therapy for the treatment of metastatic melanoma. They are immune checkpoint inhibitors because they function to boost the humoral immune T-lymphocyte response against malignant cells. Within the past decade, these therapies have accrued immune-related adverse events, which have ranged from benign gastrointestinal effects to fatal endocrinopathies, such as hypophysitis. The decedent in this case study was a 65-year-old man who suffered from metastatic melanoma and was treated with 3 cycles of combined ipilimumab and nivolumab. Despite 4 months of therapy, the patient died. Autopsy findings confirmed metastatic melanoma in the liver, lungs, and spine. The investigation also revealed extensive T-lymphocyte infiltration of the adenohypophysis, adrenal glands, skin, liver, and spleen. The pathology described indicated the presence of immune-mediated, organ-specific damage. This highlights the vast potential for autoimmune-like changes in several organ systems that can occur in patients given checkpoint inhibitors. Ipilimumab-driven autoimmune hypophysitis is of particular concern because it can lead to serious comorbidity, as observed in this patient (Figure 169). Cytotoxic T-lymphocyte-associated antigen inhibitors produce a high incidence of endocrine side effects as compared with other classes of immune checkpoint inhibitors. Clinicians must be increasingly aware of potentially catastrophic side effects associated with these agents.
Pigment Nephropathy in Hereditary Hemorrhagic Telangiectasia With Liver Involvement

(Poster No. 55)

Haris Mirza, MBBS, PhD (haris.mirza@yale.edu); Brian West, MD. Department of Pathology, Yale School of Medicine, New Haven, Connecticut.

Hereditary hemorrhagic telangiectasia (HHT) is an autosomal-dominant disorder that affects 1 per 10,000 people. The patients develop multiple arteriovenous malformations (AVMs). The AVMs form in one or more large organs, including brain, liver, lungs, and kidneys. Here, we present a case of HHT. The patient had negative results for common HHT mutations (ACVRL1 and ENG) and developed multiple gross and microscopic liver AVMs. Liver also showed periductal fibrosis, bile duct necrosis, sinusoidal fibrosis, and alternating groups of atrophic and regenerating hepatocytes resulting in nodular hyperplasia, consistent with previously described features of HHT liver disease. The patient developed a pseudoaneurysm, which is not a feature of the disease. The pseudoaneurysm progressed to formation of an aortopulmonary artery fistula. The fistula was repaired surgically, but on autopsy, we noted small defects at the repair site. Interestingly, the patient developed pigment nephropathy. Although AVMs in kidneys have been reported, pigment nephropathy has not, to our knowledge, been described in HHT. In healthy individuals, blood flows from high-pressure, thick-walled arteries to arterioles, low-pressure capillaries, and into the thin-walled veins. In HHT, blood bypasses the capillaries and high-pressure arterial blood transfers directly to veins, which are ill-equipped to handle high pressures. This leads to vascular enlargements that compress and irritate adjacent tissues and cause hemorrhage and hemolysis because of turbulent blood flow and finally high-output heart failure. The current patient had transfusion-dependent hemolytic anemia. Pigment nephropathy likely resulted from hemolytic anemia caused by AVMs and concomitant aortopulmonary artery fistula. Patient died from high-output cardiac failure (Figure 170).

Miliary Tuberculosis and Schistosomiasis Leading to Fatal Hemophagocytic Lymphohistiocytosis

(Poster No. 56)

Edwin Partovi, MD (edwin.partovi@yale.edu); Benjamin L. Mazer, MD, MBA; Jon S. Morrow, MD, PhD. Department of Pathology, Yale University School of Medicine, New Haven, Connecticut.

Tuberculosis in nonendemic countries can present nonspecifically and is associated with significant morbidity and mortality. We report an autopsy case of miliary tuberculosis complicated by schistosomiasis and hemophagocytic lymphohistiocytosis. The patient was a 48-year-old man who had immigrated to the United States from Ghana more than 25 years earlier. He presented with 3 weeks of diffuse abdominal pain, weight loss, icterus, and intermittent fevers. Cytopenias were present on admission. The patient met clinical criteria for hemophagocytic lymphohistiocytosis. Despite an extensive workup for the underlying infectious or malignant etiology, an underlying cause was not identified, and he died on the 11th day after admission. At autopsy, the patient was found to have necrotizing granulomas in the lungs, bone marrow, lymph nodes, liver, spleen, and kidneys (Figure 171, A). Acid–fast bacilli stain revealed mycobacterial organisms (Figure 171, B), and molecular studies confirmed the presence of M. tuberculosis IS6110 transposon. Hemophagocytic histiocytes were identified in the bone marrow and lymph nodes (Figure 171, C). Microscopic examination also revealed Schistosoma eggs in the urinary bladder, prostate, colon, and small intestine (Figure 171, D). Eggs showed extensive calcification and an absent inflammatory response, suggestive of chronic infection. Tuberculosis has a rare but documented association with hemophagocytic syndromes. Predisposition to active tuberculosis in those with chronic helminth infections, such as schistosomiasis, has been reported. In conclusion, tuberculosis should be considered in patients with nonspecific presentation, who have a hemophagocytic syndrome, and the immunomodulatory effects of helminth coinfection are an important association to account for in those with advanced tuberculosis.

Coexistence of 15q24 Microdeletion With Single Umbilical Artery and Genitourinary Anomalies in One Woman’s Fetus

(Poster No. 57)

Yaobin Liu, MD, PhD (yaobin.liu@tenethealth.com); Ashley Lentini, MD; Beth Mapow, DO. Department of Pathology, Drexel University College of Medicine, Philadelphia, Pennsylvania.

An intrauterine fetal demise was diagnosed in a 28-year-old G3P0020 woman at 37 weeks of pregnancy. The mother has a significant history of 2 prior miscarriages. The prenatal course for this pregnancy was complicated by 20-week ultrasound findings of polyhydramnios, absent left kidney, and intrauterine growth restriction. Major fetal findings at autopsy included cytogenetic analysis showing 15q24 microdeletion,
Correlation of Premortem Clinical Diagnosis Versus Postmortem Microscopic Findings of Dementia: A Retrospective Autopsy Study

Amy C. Custer, BS (amy.custer@rockets.utoledo.edu); Neha Varshney, MD; Amira Gohara, MD. Department of Pathology, University of Toledo College of Medicine and Life Sciences, Toledo, Ohio.

Context: Dementia is a group of symptoms associated with a decline in mental function because of pathologic disorders affecting the brain, such as Alzheimer disease (AD), Parkinson disease, frontotemporal lobe degeneration, mixed dementia, or age-related senile changes. Of US cases of dementia, 60% to 80% are caused by AD, 6% to 8% by Parkinson disease, and 50% are attributed to mixed dementia. Because of clinical and neuropathologic overlap seen in these disorders, many patients are incorrectly diagnosed. The type of dementia diagnosed determines downstream factors, such as subsequent treatment, prognostic outcomes, and future family planning for disorders having genetic implications. This study aimed to emphasize the value of postmortem microscopic evaluation in individuals with a history of dementia.

Design: A retrospective review was performed using the University of Toledo’s PowerPath database. Autopsy cases performed between 2005 and 2017 were reviewed, and cases having a clinical history of dementia were selected for evaluation. Seventy-four such cases were identified, and comparisons between their premortem and postmortem diagnosis of dementia were made.

Results: Forty-nine of 74 cases (66%) were identified to have inconsistencies between their premortem and postmortem diagnosis. Of those, 10% of cases clinically diagnosed as AD showed no signs of AD microscopically, and 8% of cases clinically diagnosed as Parkinson disease were microscopically found to be AD.

Conclusions: The overlapping forms of dementing disease present a great challenge for clinicians and researchers. Autopsies are required to gain a better understanding of disease processes and a definitive diagnosis. Moreover, further correlations between microscopic findings and clinical presentations should be made to reach reliable clinical diagnoses.

Disseminated Scedosporiosis Presenting With Ischemic and Hemorrhagic Strokes During Therapy for Acute Leukemia

Nada Al Qaysi, MD (nalqaysi@ufl.edu); Jason Gregory, MD; Wendy Stroh, DO; Anthony Yachnis, MD. Department of Pathology, Immunology and Laboratory Medicine, University of Florida College of Medicine, Gainesville.

Scedosporium sp. is a ubiquitous fungus that may cause infections in immunocompromised patients. Central nervous system involvement is unusual and may include meningitis, encephalitis, and abscesses. We report on a 46-year-old man with history of relapsed, B-cell, acute lymphocytic leukemia, after a bone marrow transplant and donor lymphocyte infusion, who developed fever and neurologic deficits during induction chemotherapy. Cerebrospinal fluid analysis showed no leukemic involvement. Brain imaging demonstrated multifocal acute infarcts followed later by hemorrhagic transformation. Blood cultures were positive for fungal organisms and further speciation yielded Scedosporium sp. Despite prophylactic treatment with voriconazole and addition of micafungin, the patient continued to be febrile and clinically deteriorated with seizures and multorgan failure. Autopsy revealed purulent nodules in multiple organs, consistent with disseminated disease. Histopathologic study including GMS stains revealed tissue invasion by fungal organisms having septeal hyphae with 45° angle branching, and associated inflammation and necrosis. The brain was swollen with bilateral uncil herniations and contained multilocal subarachnoid and parenchymal hemorrhages. Areas of angioinvasive...
fungal involvement were accompanied by ischemic changes in adjacent brain tissue. Fungus was also identified in hemorrhagic fibrinopurulent material in areas of vascular rupture, including the subarachnoid space. Infections caused by *Scedosporium* spp are life threatening and resistant to multiple antifungal agents. This case illustrates an unusual nervous system, opportunistic fungal infection, which should be considered in patients with hematologic malignancies and immunosuppression.

**Tuberculous Meningitis: An Elusive Diagnosis and the Role of Autopsy and Molecular Diagnostics**

(Poster No. 62)

Marie E. Perrone, MD (perronem@uw.edu); Caitlin Latimer, MD; Luis F. Gonzalez-Cuyar, MD; Corinne L. Fligner, MD; Florencia Jalkis, MD; Luis Chu, MD; Andrew Reichenbach, MD; David S. Priemer, MD. Department of Pathology, Yale School of Medicine, New Haven, Connecticut.

We lack sufficiently sensitive serologic tests to reliably make a premortem diagnosis of active tuberculosis or tuberculous meningitis. A 38-year-old, otherwise healthy, woman was admitted with signs and symptoms of subacute meningitis. Analysis of the cerebrospinal fluid (CSF) showed a lymphocytosis, and broad-spectrum antibiotics and antivirals were initiated. Imaging studies showed ventriculomegaly and basal meningeal enhancement. No bacterial or viral etiology to her meningitis could be identified, and she progressed to a comatose state. A diagnosis of tuberculous meningitis was considered; however, cultures and polymerase chain reaction (PCR)—based assays performed on multiple samples of CSF were repeatedly negative. A QuantIFERON Gold (Cellestis, Hilden, Germany) study was indeterminate because of a failing mitogen control. A temporal-lobe biopsy showed necrotizing granulomatous inflammation without organisms being identified in the biopsy via histochemical stains, culture, or PCR. Despite initiation of an antituberculosis regimen, the patient died 2 months after presentation. At autopsy, histologic sections of the brain again demonstrated granulomatous inflammation. Although other etiologies, such as autoimmune disease, were considered, the histology was most consistent with an infectious etiology. At the time of autopsy, fresh tissue from the basal meninges—radiographically and pathologically the most severely affected region—had been frozen. The PCR performed on the fresh-frozen basal meninges sample by the University of Washington Clinical Microbiology Laboratory was positive for *Mycobacterium tuberculosis* DNA. We demonstrate the difficulty in making a diagnosis of tuberculous meningitis, the value of reserving fresh tissue for molecular diagnostics at autopsy, and the value of autopsy to provide answers for families and clinicians.

**Retrospective Postmortem Study of Lungs From Patients With Pulmonary Sarcoidosis**

(Poster No. 63)

Hatem Kaseb, MD, PhD, MPH (hatem.kaseb@yale.edu); Ahmad Charifa, MD; Xuchen Zhang, MD, PhD. Department of Pathology, Yale School of Medicine, New Haven, Connecticut.

**Context:** Sarcoidosis is an autoimmune disease that results in multiorgan dysfunction. Sarcoid pulmonary disease may progress to end-stage pulmonary disease and lead to severe, restrictive lung failure, necessitating lung transplant. Pathologic features of end-stage pulmonary sarcoidosis are not well defined. Here, we reviewed histologic features of early and end-stage pulmonary sarcoidosis and tried to assess the contributing role of pulmonary sarcoidosis to the death of the patients.

**Design:** We reviewed the autopsy cases from the archives of Yale Pathology Department between January 2000 and January 2018. Our inclusion criteria included patients who had a confirmed prior biopsy diagnosis of pulmonary sarcoidosis. Twelve cases met our inclusion criteria.

**Results:** The patient ages ranged between 29 and 66 years. Most were African American (83%). The mean disease duration was 5.6 (5.7) years (mean [SD]). Interestingly, only 50% of the patients were females. Of the patients, 50% had marked lung involvement, and 58% of the patients had extrathoracic involvement. Of the patients, 25% had honeycombing and were staged as end-stage pulmonary sarcoidosis. Half of the patients presented with numerous granulomas that were predominantly in the peripheral peribronchioral and lung parenchymal areas. Pulmonary sarcoidosis led to pulmonary hypertension in 33% of the patients. Sarcoidosis was a contributing factor in 24% of the patients. Conclusion: Pulmonary sarcoidosis is a distinct disease entity that can be categorized pathologically as early and end stage. Less than half of the patients with pulmonary sarcoidosis have died of pulmonary-related causes.

**Acute Esophageal Necrosis (Black Esophagus): A Rare Finding in 2 Autopsies**

(Poster No. 64)

Rumeal D. Whaley, MD (rdwhaley@ut.edu); Carrie L. Phillips, MD; David S. Priemer, MD. Department of Pathology and Laboratory Medicine, Indiana University School of Medicine, Indianapolis.

Acute esophageal necrosis (black esophagus) has a reported prevalence of 0.2%. The condition gets its name because of the striking black discoloration of the esophagus that begins at the gastroesophageal junction. Although an exact etiology for black esophagus is not well defined, the leading causes appear to be ischemia and gastric outlet obstruction. Reported associations include infections, glucose derangements, malignancy, and alcoholism. Clinical features commonly include dysphagia, epigastric pain, and septic complications. Hematemesis occurs in 70% of cases. Esophageal perforation is an uncommon, but frequently lethal, complication. These nonspecific features often contribute to a delayed clinical diagnosis or a diagnosis that is only established at autopsy. We present 2 autopsy patients with clinically undiagnosed black esophagus. Patient 1 was a 62-year-old woman with a medical history of diabetes, hypertension, hyperlipidemia, and Zollinger-Ellison syndrome. She presented with nausea, vomiting, cough, decreased appetite, and weight loss. Patient 2 was a 51-year-old man with a medical history of alcoholism, diabetes, hyperlipidemia, and hypertension. He presented after 2 days of abstinence from alcohol with nausea, vomiting, and hematemesis. At autopsy, both esophageal mucosae displayed a deep-black, circumferential discoloration that sharply originated at the gastroesophageal junction (Figure 172, A). Esophageal perforation was identified in patient 1 but not patient 2. Microscopic examination confirmed extensive mucosal necrosis in both cases (Figure 172, B). Because of frequently nonspecific clinical presentations, increased awareness and a high degree of clinical suspicion is required for early recognition and proper treatment of black esophagus. Additionally, an association with Zollinger-Ellison syndrome has not, to our knowledge, been previously reported.

**Corroboration of Clinical Acute Kidney Injury With Postmortem Acute Tubular Necrosis**

(Poster No. 65)

Scott Wolfe, DO (swolfe@northwell.edu); Alex Williamson, MD. Department of Pathology, Northwell Health, Lake Success, New York.

**Context:** Acute kidney injury (AKI) is a common clinical diagnosis with a myriad of etiologies, including acute tubular necrosis (ATN). There is debate in the available literature regarding the ability to histologically diagnose ATN in a background of variable postmortem autolysis at autopsy. This study sought to evaluate one histologic parameter—detached strips and/or whorls of proximal tubular epithelium—that has been proposed in the literature as allowing differentiation of ATN from autolysis in postmortem kidney tissue (Figure 173). The study included control cases of postmortem autolysis in the background of an acute clinical AKI. The study sought to evaluate one histologic parameter—detached strips and/or whorls of proximal tubular epithelium—that has been proposed in the literature as allowing differentiation of ATN from autolysis in postmortem kidney tissue (Figure 173). The study and control cases included postmortem kidney tissue from 30 patients; fifteen who did and 15 who did not have a clinical diagnosis of AKI at the time of death. Subjective assessment of autolysis (slight, moderate, marked) and the presence of detached strips and/or whorls of proximal tubular epithelium were assessed at ×200 in hematoxylin–eosin–stained slides from the 30 cases. A χ² test with Yates correction was used to compare results.

**Results:** Nearly one-half of the study cases with clinical AKI demonstrated detached strips and/or whorls of proximal tubular epithelium, whereas none of the control cases with a clinical AKI demonstrated such histologic changes (0 of 15). This difference was statistically significant using a χ² analysis with Yates correction (P = .01). Moreover, the histologic finding was appreciated in kidneys regardless of their degree of autolysis.
In conclusion, lung involvement in HLH is rare and may be fatal. The main histologic feature is diffuse alveolar histiocytic infiltration with intra-alveolar infiltrate of histiocytes exhibiting hemophagocytosis. However, lung findings have not been widely described in the literature, although lung involvement portends a higher mortality. Autopsy study of 27 children with familial HLH found evidence of hemophagocytosis in the lungs; however, the incidence of lung involvement is unclear. Specific histopathologic lung findings in older patients or those with infectious triggers of the disease are even less well known. We present a case of a previously healthy 18-year-old man who was diagnosed with Epstein-Barr virus and adenovirus infection. The patient remained febrile, despite treatment, and became acutely hypovolemic and hypotensive, requiring intubation and pressor support. An HLH diagnosis was made by bone marrow biopsy, based on HLH-2004 criteria. Treatment was started. The patient required extracorporeal membrane oxygenation and multiple blood products, eventually developing multisystem organ failure and passing away 34 days after admission. Autopsy findings were notable for heavy, firm, and diffusely hemorrhagic lungs; hepatosplenomegaly; and lymphadenopathy. Histologic examination of the lungs revealed diffuse intra-alveolar infiltrate of histiocytes exhibiting hemophagocytosis. Histiocytes were highlighted by CD68 stain. There was also diffuse alveolar damage. Spleen and lymph nodes showed hemophagocytosis. In conclusion, lung involvement in HLH is rare and may be fatal. The main histologic feature is diffuse alveolar histiocytic infiltration with hemophagocytosis.

**Gross Injury Patterns in Overdose Cases: An Interesting Observation at the Medical Examiner’s Office**

(Poster No. 68)

Reema Khan, MD1 (reema.khan@lumc.edu); Daniel Dresser, MD; Adrienne Segovia, MD2; Ponni Arunkumar, MD3; Vijayakalshimi Ananthanarayanan, MD4. 1Department of Pathology, Loyola University Medical Center, Maywood, Illinois; Departments of 2Medical Examiner and 3Chief Medical Examiner, Office of the Medical Examiner, County of Cook, Chicago, Illinois.

**Context:** Overdose has been a major cause of death in forensic autopsies. However, gross injury patterns in single-drug overdose (OD) cases have not been analyzed. Our aim in this study was to determine a gross morphologic patterns of injury in lungs, hearts, and brains in cases of overdose.

**Design:** We searched the medical examiner’s office database for single-drug OD cases from January 1, 2014, to September 15, 2017. We recorded the age (18 years or older), race, gender, lung weight, heart weight, and brain weight. A control group (CG 1) for the brain weight was determined by analyzing those with gunshot wounds (GSWs) to the chest/back cases. Another control group (CG 2) for the lungs weights and heart weights was determined by analyzing cases of GSWs to the head.

**Results:** We found 199 single-drug OD cases in our database, of which, 167 cases fit our criteria. Of those cases, 63% of deaths were due to an opiate OD (Table). Of the 167 cases, 70% displayed pulmonary edema, whereas only 4% of cases showed no significant gross lung injury pattern. Specifically, for the cocaine and fentanyl OD, pulmonary edema was observed in 63% and 81% of cases, respectively.

**Conclusions:** Most OD cases show pulmonary edema as a gross lung injury pattern. Our study set shows that pulmonary edema is also
Dissociated Herpes Simplex Type 1 Viremia and Fulminant Herpes Hepatitis With Associated Herpetic Gastroesophageal Junction Lesion Following Oropharyngeal Surgery for Squamous Cell Carcinoma

Ian Dryden, MD (drydenj@ucmail.uc.edu); Kristina Brannock, MD.

Department of Pathology, University of Cincinnati Medical Center, Cincinnati, Ohio.

Herpes simplex virus type 1 (HSV-1) is a common cause of mucocutaneous lesions in children and adults. In addition, HSV-1 can involve the peripheral and central nervous system, as well as the trachea, esophagus, lungs, and liver. Disseminated herpetic viremia is rarely seen in immunocompetent adults and typically only seen in immunocompromised patients. Here, we present a case of a 68-year-old white man who underwent oropharyngeal surgery 3 weeks after diagnosis of squamous cell carcinoma (SCC) involving the base of tongue. After discharge, he presented on postoperative day 6 (POD 6) with fever, cough, tachycardia, hypoxia, and dysphagia. His initial workup was concerning for aspiration-related complications, and endoscopy demonstrated findings suggestive of severe esophagitis, tracheitis, acute bronchitis, and pneumonia. On POD 12, he developed acute respiratory distress syndrome, which subsequently progressed into a culture-negative, sepsislike syndrome with associated lymphopenia and transaminitis. The infectious disease workup was remarkable for abnormal histoplasma, cytomegalovirus, and HSV-1 serologies. After death, on POD 16, his bone marrow biopsy results demonstrated hemophagocytic lymphohistiocytosis and other findings suggestive of viremia; furthermore, his bronchial vascular viral culture demonstrated growth of HSV-1. The postmortem examination demonstrated findings consistent with HSV-1-mediated esophagitis, hepatitis, and pneumonitis. In this case, the immediate cause of death was disseminated HSV-1 viremia with diffuse alveolar damage and fulminant hepatitis. The underlying cause of death was likely secondary to the physiologic stress induced by surgical intervention and an occult herpetic gastroesophageal junction lesion.
REPORTED TICK EXPOSURE. SEROLOGY WAS POSITIVE FOR EHRlichia IMMUNO- GLOBULIN G (1:1024). HOWEVER, MORULAe WERE NOT SEEN ON PERIPHERAL BLOOD SMears OR BUFFY COAT, AND POLYMERASE CHAIN REACTION STUDY FOR EHRlichia DNA was negative. SHE FAILED TO RESPOND TO A COURSE OF DOXYCYCLINE AND DEVELOPED ADDITIONAL SYMPTOMS, WHICH INCLUDED ARTHRAlGia, PLEURITIC CHEST PAIN, AND A LOCALIZED RASH OVER THE EYEBROWS. SHE LATER PRESENTED WITH AN EPISODE OF CONFUSION AND WAS ADMITTED TO THE HOSPITAL. LABORATORY STUDIES WERE POSITIVE FOR ANTINUCLEAR ANTIBODIES AND ANTI–DOUBLE-STRANDED DNA. SHE was TREATED WITH STEROIDS AND MYCO Phenolate MOFEtti. HER COURSE WAs COMPLICATED BY DETERIORATING RENAl FUNCTION, AND CLINICAL EVIDENCE OF HEMOPHAGOCYTIC Lymphohistiocytosis (ferritin, >40 000 ng/mL; tri- GLYCERIDES, 604 mg/dL; IL2 receptor, 2810 pg/mL; AND LOW NK CELL ACTIVITY), IN CONJUNCTION WITH PANCYTOPENIA. RESPIRATORY CULTURE GREW ASPERGILLUS FUMIGATUS. SHE DEVELOPED Worsening acidemia, BECAME HYPO TENSION, AND EXPIRED. POSTMORTEM EXAMINATION CONFIRMED GLOMERULAR CHANGES CONSISTENT WITH LUPUS NEPHRITIS AND THE PRESENCE OF HEMOPHAGOCYTOSIS AND ALSO REVEALED INVASIVE ASPERGILOsis INVOLVING THE HEART, LUNGS, KIDNEYS, AND GASTROINTESTINAL TRACT. EHRLICHIOSIS HAS OVERLAPPING CLINICAL FEATURES WITH SYSTEMIC LUPUS ERYTHEMATOSUS, AND FALSE-POSITIVE SEROLOGIC STUDIES FOR EHRlichia MAY, RARELY, OCCUR IN THE SETTING OF THIS DISEASE. IT IS IMPORTANT FOR CLINICIANS AND LABORATORIANS TO BE AWARE OF THIS ASSOCIATION TO ENSURE TIMELY DIAGNOSIS (Figure 175).

A CASE OF PEDIATRIC CAROLI SYNDROME

(POSTER No. 73)

Ghulam Ilyas, MBBS1 (ghulam.ilyas@downstate.edu); Agha Waj- dan Baqir, MBBS2; Charles Shao, MD, PhD.2 1Department of Pathology,
2Department of Pathology, Kings County Hospital, Brooklyn.

CAROLI SYNDROME IS A GENETICALLY LINKED DISEASE THAT LIES WITHIN THE DISEASE SPECTRUM OF CONGENITAL HEPATIC FIBROSIS AND AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE (ARPKD). THE DISEASE IS CHARACTERIZED BY DILATATION OF THE INTRAHEPATIC BILARY DUCT. THE ARPKD, THE MAIN CULPIT, IS CAUSED BY MUTATIONS IN THE PKHD1 GENE, WHICH ENCODES THE PROTEIN FIBROCYSTIN. FIBROCYSTIN HAS BEEN LOCALIZED TO CIAA ON CHOLANGIOTYES AND THE RENAL COLLECTING DUCT EPITHELIAL CELLS. THIS RECEPTOR PROTEIN IS IMPORTANT IN BILARY AND COLLECTING DUCT DIFFERENTIATION. THE PREDOMINANT COMPLICATIONS OF CAROLI SYNDROME CONSIST OF PORTAL HYPERTENSION AND ITS CONSEQUENCES, RECURRENT CHOLANGITIS REQUIRING PROPHYLACTIC ANTIBIOTICS, AND END-STAGE RENAL DISEASE. TREATMENT CAN INCLUDE PERCUTANEOUS DRAINAGE, ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAHy, AND LIVER RESECTION. UNFORTUNATELY, FOR PATIENTS WITH CAROLI SYNDROME, A LIVER TRANSPLANT MAY BE THE MOST APPROPRIATE TREATMENT OPTION. WE ARE PRESENTING A CASE OF A 3-DAY-OLD GIRL WITH CONGENITAL AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE AND PULMONARY HYPOPLASIA IN HYPOXIC RESPIRATORY FAILURE AND Oliguric WITH SEVERE METABOLIC ACIDOSIS. THE BABY DIED, AND AN AUTOPIsY WAS PERFORMED. INTERNAL ORGANS REVEALED HYPOLASTIC LUNGS (COMBINED, 31.1 g; REFERENCE RANGE, 45.1 g ± 12.2 g) AND NEPHROMEGALY (COMBINED, 193 g; REFERENCE RANGE 21.3 g ± 6.0 g). THE CUT SURFACE OF KIDNEYS SHOWED SMALL CYSTIC SPACES IN THE CORTEX AND MEDULLA, AND THE LIVER SHOwED MULTIPLE WHITE AREAS OF FIBROSIS (Figure 176, A). Renal histologic examination revealed subcapsular cysts, tubular dilation, and duct ectasia with severe vascular congestion. Poor corticomedullary differentiation was seen (Figure 176, B). MICROSCOPY showed diffuse, abnormal bile duct proliferation and periporal fibrosis. Lobular architecture was distorted by bile duct proliferation and fibrosis (Figure 176, C).

UTILITY OF POSTMORTEM DIAGNOsis IN MUCORMYcosis

(POSTER No. 74)

Alain Cagaanan, DO (Acagaanan@uwhealth.org); Erin Brooks, MD. Department of Pathology & Laboratory Medicine, University of Wisconsin Hospital and Clinics, Madison.

Context: Mucormycosis (previously designated zygomycosis) predominantly affects immunocompromised and diabetic patients. Diagnosis can be challenging because of its varied presentations, rapidly progressive clinical course, and lack of reliable serum testing options. Because our institution has the fourth largest US transplant program and is associated with a comprehensive cancer center, many immunocompromised patients at risk of contracting fungal infections are seen annually. Given the high cost of transplanting an organ, our team encourages autopsy in cases of organ transplant recipient death to advance knowledge of disease pathogenesis. Because many gaps remain in understanding the epidemiology of this often-lethal infection, autopsy can provide valuable information regarding trends seen in such fatalities.

Design: Autopsy reports within our electronic database from the years 2003–2018 were searched using terms zygomycosis, mucormycosis, and Rhizopus. Autopsy reports and records from cases in which cause of death was attributed to the fungal infection were reviewed.

Results: Eight patients (male/female = 1:1) were identified, with an average age of 58 years (range, 39–72 years). Comorbidities, infection extent, and test results are summarized in the Table. 

Conclusions: Our autopsy study suggests that fatal mucormycosis overwhelmingly occurs in immunocompromised patients and invariably involves the lungs (8 of 8; 100%). Most decedents have multiorgan involvement at the time of death (6 of 8; 75%). Mucormycosis usually presents in a background of polymicrobial infection (7 of 8; 87.5%). Galactomannan and β-1,3-glucan results are not useful. In most cases, mucormycosis was diagnosed at postmortem examination (5 of 8; 62.5%), although that may represent selection bias. Histologic sections are useful because fungal morphology corresponding to Mucorales is generally seen (8 of 8; 100%).
A Case of Primary Prostatic High-Grade B-Cell Lymphoma With MYC and BCL6 Rearrangements and the Subsequent Autopsy Findings

(Poster No. 75)

Zhiwei Yin, MD, PhD1 (zhiwei1@njms.rutgers.edu); Khalid Algarrahi, MD2; Donghong Cai, MD, PhD2; Ozlem Fidan-Ozbilgin, MD2

1Department of Pathology, New Jersey Medical School-Rutgers, Newark; 2Department of Pathology and Laboratory Medicine Services, VA New Jersey Medical Center, East Orange.

Primary prostate lymphoma is extremely rare. Here, we report on a case of primary prostatic high-grade B-cell lymphoma with MYC and BCL6 rearrangements and the subsequent autopsy findings. The patient was an 81-year-old, white man who presented with urinary outlet obstruction. He was diagnosed as having benign prostate hyperplasia, followed with transurethral resection of prostate. We performed hematoxylin-eosin immunohistochemistry stains and a subsequent autopsy, whereas the chromosomal rearrangement fluorescence in situ hybridization (FISH) studies were performed in a commercial laboratory. Histology and ancillary studies revealed diffuse infiltration of large, atypical lymphocytes mixed with tingible body macrophages forming a “starry sky” pattern, with a phenotype of CD20+ , Bcl2+ , MUM1- , CD10- , and a Ki-67 proliferative index around 75%. The related FISH study detected MYC and BCL6 gene rearrangement (double hit). A high-grade B-cell lymphoma with MYC and BCL6 rearrangements was established (World Health Organization, revised 4th edition, 2017). Patient did not respond to REPOCH chemotherapy and succumbed to the disease 6 months later. Autopsy revealed a giant pelvic lymphoma mass—encased rectum, prostate, and urinary bladder. In addition, the lymphoma cells extensively invaded the endocardium, myocardium, epicardium, peri-cardial fat, and coronary arteries. All other organs were free of lymphoma involvement (Figure 177). A thorough review of the autopsy revealed extensive invasion of the heart and exempted all other organs, including bone marrow. This finding is rather perplexing and deserves further studies.

Anomalous Origin of the Left Pulmonary Artery From the Aorta: A Rare Form of Congenital Heart Disease

(Poster No. 76)

Maira Gaffar, MD (mgaffar@ufl.edu); Jennifer Reppucci, DO; Archana Shenoy, MD; Wendy Stroh, DO; Diane Spicer, BS, PA(ASCP). Department of Pathology, University of Florida, Gainesville.

Anomalous origin of the pulmonary artery (PA) is an exceedingly rare cardiac malformation and accounts for approximately 0.12% of congenital heart disease (CHD). Very few cases of a left PA arising from the ascending aorta have been reported in the literature because an anomalous origin of the right PA is 4 to 5 times more common than the left. The pathophysiology is thought to be due to abnormalities in the aortic arch. We present a case of the left PA originating from the ascending aorta (Figure 178) in a 6 day-old girl (34 week, 2 day gestational age), which was discovered on echocardiogram and confirmed at autopsy. On gross examination, the pulmonary trunk gave rise to the right PA; however, the left PA originated from the ascending aorta as an intrapericardial structure. The left PA crossed over the anterior aspect of the pulmonary trunk–right PA bifurcation, giving a crossed appearance. The infant had additional cardiac abnormalities, including a large perimembranous ventricular septal defect, patent ductus arteriosus, patent foramen ovale, dysplastic aortic valve, and mild-to-moderate pulmonary valvular stenosis. Timely surgical intervention is critical because the corresponding lung is exposed to systemic blood pressure and volume, leading to irreversible pulmonary vascular damage. If untreated, the risk of mortality is 70% in the first year. In this case, the clinical course was complicated by severe necrotizing enterocolitis, and she decompensated before surgical correction was attempted. This case documents an extremely rare cardiac malformation and the gross anatomic findings before surgical correction.
Metastatic Germ Cell Tumor: A Rare Case of Extragonadal Pure Choriocarcinoma in a Young Man

(Poster No. 77)

Jeff Wang, MD (jeff.wang@yale.edu); Demetrios Braddock, MD, PhD. Department of Pathology, Yale, New Haven, Connecticut.

Choriocarcinoma in males is a rare and highly malignant germ cell neoplasm that exhibits trophoblastic differentiation. These tumors consist as a component of a mixed germ cell tumor or a pure choriocarcinoma, with the latter having a poorer prognosis. Although the primary site is usually the testes, rare cases have been reported arising from the midline from displaced primordial germ cells. We present a case of a 29-year-old man who died of a metastatic pure choriocarcinoma with no identifiable testicular tumor or fibrotic area suggestive of regressed primary. The patient’s initial presentation was shortness of breath with elevated serum β-hCG. The biopsies on the metastatic lesions revealed choriocarcinoma with immunohistochemical stains positive for β-hCG, pan-CK, and CAM 5.2 and negative for OCT4, CD117, and CD30. Because of the immense tumor burden, the patient subsequently died from multiorgan-system failure and cerebral hemorrhages. On autopsy, metastases were discovered in the lung, liver (Figure 179, A), brain, rectum, right adrenal gland, and omentum. Grossly, the tumor was highly infiltrative and hemorrhagic. Histologic analysis revealed necrotic and hemorrhagic tumor beds with large, atypical, and pleomorphic cells with prominent nucleoli (Figure 179, B). These tumor cells stained for β-hCG (Figure 179, C) and were negative for OCT4 (Figure 179, D), CD117, and CD30, characterizing this as a pure choriocarcinoma. No evidence of testicular primary was identified on gross and microscopic analysis making this case an extragonadal choriocarcinoma.

Disseminated Histoplasmosis and Bilateral Pheochromocytomas in a Patient With Type 1 Neurofibromatosis: An Autopsy Case With Rare Pulmonary and Other Clinical Manifestations

(Poster No. 79)

Brannon G. Broadfoot, MD (bbroadfoot@uams.edu); Asangi R. Kumarapeli, MD, PhD. Department of Pathology, University of Arkansas for Medical Sciences, Little Rock.

Neurofibromatosis type 1 (NF1) is a dominantly inherited genetic disorder with highly variable clinical manifestations. We present the autopsy findings of a 37-year-old African American woman with a history of NF1, hypertension, and seizures who presented with severe dyspnea, chills, myalgia, enesis, and abdominal pain and who died within 10 hours of hospital admission. She had experienced worsening myalgia and upper respiratory symptoms for 2 weeks preceding her death. Postmortem examination revealed numerous cutaneous nodules, a cavitary lesion in the left lower lung, pulmonary edema, apical subpleural emphysematous blebbing, hilar adenopathy, and tricuspid regurgitation (Figure 181, A). Multiple right orbital soft tissue tumors (Figure 181, B); diffuse granulomatous disease of the lungs, hilar nodes, spleen, and liver (Figure 181, B); pulmonary arterial hypertension and interstitial fibrosis; myocardial hypertrophy, diffuse myocarditis (Figure 181, C); and multiple remote microinfarcts in the cerebellum. Silver staining highlighted abundant fungal yeast forms consistent with histoplasmosis in the necrotizing granulomas of the hilar nodes, liver, and lung, including the cavitary lesion (Figure 181, D). Pulmonary hypertension and interstitial fibrosis are known rare complications of NF1. Myocarditis in NF1 is not well described. Here, we report, for the first time, to our knowledge, on disseminated histoplasmosis and chronic cavitary pulmonary histoplasmosis in a patient with NF1, who was otherwise immunocompetent.
is unknown whether chronically elevated catecholamines from pheochromocytomas and the NF1-induced lung injury predisposed this patient to severe disseminated fungal infection.

Pontocerebellar Hypoplasia Type 3 Maps to Chromosome Band 7q11.23: An Autopsy Case Report of a Novel Genetic Variant

(Kritika Krishnamurthy, MD1 (Kritika.Krishnamurthy@msmc.com); Amilcar A. Castellano-Sanchez, MD3; Christopher A. Fébres-Aldana, MD1; Jyotsna Kochiyil, MD2; Carole Brathwaite, MD4; Robert J. Poppiti, MD5 Departments of 1Pathology and 2Radiology, Mount Sinai Medical Center, Miami Beach, Florida; 3Department of Pathology, Mount Sinai Medical Center and Florida International University Herbert Wertheim College of Medicine, Miami Beach; 4Department of Pathology, Nicklaus Children’s Hospital and Florida International University Herbert Wertheim College of Medicine, Miami; 5Department of Pathology, Mount Sinai Medical Center and Florida International University Herbert Wertheim College of Medicine, Miami Beach.

Pontocerebellar hypoplasia type-3 (PCH3) is an autosomal-recessive disorder characterized by a small cerebellar vermis, hyperreflexia, and seizures. PCH3 has been described in Middle Eastern families in association with a homozygous truncating mutation of the PCLO gene in locus 7q11.21. This is the first case, to our knowledge, of PCH 3 reported in the United States. The patient is a 1-week-old girl, born at term, to a 26-year-old G4A3P0 woman. At birth, the baby was depressed and hypertonic. Magnetic resonance imaging revealed cerebellar and brainstem hypoplasia (Figure 182, A). Her parents accepted natural death. Postmortem examination revealed palmar simian crease. The cerebellum measured 2.5 cm from side to side and 1 cm rostral to caudal. The vermis was rudimentary. Sectioning revealed a flattened, linear fourth ventricle, scant abortive cerebellar folia, and a markedly small cerebellum when compared with the cerebrum and with age-matched size (Figure 182, B). Hematoxylin-eosin-stained sections of cerebellum revealed scant rudimentary folia. A rudimentary unilobal emboliform nucleus was identified (Figure 182, C). The remaining cerebellar nuclei were absent. Chromosomal microarray showed an interstitial duplication of 841 kb on chromosome band 7q11.23. Heterozygous interstitial 7q11.23 duplication is associated with hypoplasia of cerebellum, corpus callosum, and temporal lobes in children with cognitive impairment meeting criteria for autism spectrum disorders. This is the first case, to our knowledge, of 7q11.23–associated PCH3. Locus 7q11.23 contains FGL2 and GSAP genes and is 5 MB upstream of the 7q11–21 region, suggesting a possible linkage. This novel genomic finding represents a new familial variant of PCH3 and further strengthens its association with the 7q11 locus.

Invasive Fungal Infections in Recipients of Hematopoietic Stem Cell Transplants: Ongoing Diagnostic Challenges

(Yanping Wang, MD, PhD (ywang4@uwhealth.org); Erin G. Brooks, MD. Department of Pathology and Laboratory Medicine, University of Wisconsin Hospital and Clinics, Madison.

Despite advances in fungal therapeutic and biomarker testing options, invasive fungal infections remain a major cause of morbidity and mortality in recipients of hematopoietic stem cell transplants (HSCTs). We report on the case of a 52-year-old man with Waldenström macroglobulinemia, which was refractory to chemotherapy, who underwent autologous HSCT. He was initially prescribed oral fluconazole but transitioned to intravenous therapy 10 days after HSCT because of a small bowel obstruction attributed to chemotherapy-related mucositis. Chest x-ray revealed multifocal pulmonary opacities. Bronchoalveolar lavage was performed; lavage fluid cultures were negative for bacterial, fungal, or viral organisms other than rhinovirus. A lavage galactomannan antigen immunoassay was indeterminate. The patient expired 15 days after HSCT. At autopsy, disseminated fungal infection involved the trachea (Figure 183, A), lungs (Figure 183, B), and gastrointestinal tract (Figure 183, C and D). Lung tissue cultures grew Aspergillus fumigatus. This case suggests that invasive fungal infections after HSCT remain a significant risk, even in patients who have received antifungal prophylactic therapy and aggressive monitoring. Despite overwhelming systemic infection, fungal diagnostic testing may be negative. Microscopic examination and cultures are frequently insensitive; additionally, as Aspergillus is a common contaminant,
even cases that are culture positive may be misinterpreted. Although fungal biomarkers, such as galactomannan and 1,3-β-D-glucan, can prove to be helpful adjunctive tests, sensitivity and specificity may be suboptimal. Pathologists are encouraged to maintain a high level of suspicion, despite negative antemortem testing results, and should be aware that flucanazole is not effective therapy against Scedosporium spp. Postmortem examination remains a valuable surveillance tool and can provide critical epidemiologic information in such cases.

Speaking From Among the Kidneys: End-Stage Renal Disease Is Overlooked as a Cause of Death at Autopsy

(Meredith A. Reynolds, MD (meredith.reynolds@uchospitals.edu); Kammi J. Henriksen, MD; Anthony Chang, MD. Department of Pathology, University of Chicago, Illinois.)

Context: There is an underappreciation of the importance of renal function among both physicians and the public. Patients with end-stage renal disease (ESRD) who require dialysis have a 1-year mortality rate of 20%. Furthermore, kidney disease is reported as the ninth leading cause of death in the United States.

Design: We searched our autopsy database (2007–2017) using clinical history search queries end-stage renal disease, end-stage kidney disease, ESRD, chronic renal disease, and chronic kidney disease. Gross and microscopic descriptions were reviewed to assess disease severity. The final diagnosis and autopsy summaries were reviewed to determine whether renal failure was appropriately correlated with the cause of death. Cases in which the cause of death was unrelated to kidney function were excluded.

Results: Ninety-three patients with a history of ESRD and gross and microscopic confirmation at autopsy were identified. Of those, the causes of death were reported as cardiovascular (37%), infection/sepsis (40%), pulmonary disease (acute respiratory distress syndrome, pulmonary embolism, interstitial lung disease; 4%), hemorragh (6%), liver disease (nonalcoholic steatohepatitis cirrhosis; 1%), renal disease (Lupus nephritis; 1%), and systemic disease, including amyloidosis, multiple myeloma, and systemic lupus erythematosus in 5 cases (5%). The cause of death was unknown in 5 cases (5%). In 24 cases (26%), ESRD was identified as a contributing cause of death.

Conclusions: In summary, ESRD is often overlooked at autopsy, particularly in patients with cardiovascular disease and/or sepsis. Accurate assessment and documentation of ESRD contributing to mortality is important for educating physicians, counseling surviving kin, maintaining accurate records, and directing future research efforts.

Scimitar Syndrome With Tetralogy of Fallot and Pulmonary Atesia in a Newborn: A Lethal Association

(Odille P. Mejia, MD (mejiaodille@gmail.com); Vathany Sriganian-shan, MD. Department of Pathology, Mount Sinai Medical Center, Miami Beach, Florida.)

Scimitar syndrome is an anomalous pulmonary venous return to the inferior vena cava, usually from the right lung. It is extremely rare, with a prevalence of 1 to 3 per 100,000 births. It is thought to be a primary developmental anomaly of lung with secondary anomalous venous drainage as a result of which one or more pulmonary veins will drain to a location other than the left atrium. This results in a left to right shunt, which is usually hemodynamically insignificant; however, an association with tetralogy of Fallot can lead to severe pulmonary hypertension, heart failure and death. Our case is that of a 4-month-old girl born with a prenatal diagnosis of tetralogy of Fallot, pulmonary atresia with major aortopulmonary collateral arteries, DiGeorge syndrome, and pulmonary hypertension. She was born with an APGAR (appearance, pulse, grimmace, activity, respiration) family screening of 8 of 8 and required oxygen shortly after birth because of desaturation. A computed tomography angiogram showed scimitar vein to the right lung, collateral to the left lung, and partial anomalous vein. She developed episodes of hypotension with cyanosis and decreased perfusion. Despite medical effort, the baby died. Timely suspicion and diagnosis with prompt initiation of treatment is important in these cases. Therapeutic angiography combined with surgery helps eliminate the collateral flow, correcting the venous drainage and the intracardiac abnormality, preventing the development of pulmonary hypertension (Figure 184).

Bilateral Pulmonary Aplasia Accompanied With Calvarial Ossification Defects

(Manando Nakasaki, MD, PhD (mnakasaki@uci.edu); Robert Edwards, MD, PhD. Department of Pathology & Laboratory Medicine, University of California, Irvine Health, Orange.)

Bilateral pulmonary aplasia is a rare, congenital malformation in which no lung parenchyma forms despite the presence of bronchial buds and is, therefore, incompatible with extrauterine life. We report a rare autopsy case of pulmonary aplasia in a newborn accompanied with prominent calvarial ossification failure. The decedent was a 38-week, 1-day estimated gestational age boy born to a 28-year-old G1P0 mother. Prenatal magnetic resonance imaging studies showed polyhydramnios, normal cardiac and gastrointestinal anatomy, and mild left-sided pefiectasia. Flexible bronchoscopy after delivery noted a normal larynx but a collapsed airway without visualized tracheal cartilages. Autopsy revealed a tracheal tube and main bronchial bifurcation 3 cm below the larynx, ending in asymmetric blind-ended pouches. Microscopically, the tracheal wall was lined with respiratory epithelium and contained discontinuous cartilage islands and abundant submucosal bronchial glands. The calvarium was poorly calcified with 6-cm circular regions of ossification over the lateral temporoparietal hemispheres, but was otherwise unmineralized. Although unilateral pulmonary aplasia occurs with an incidence of roughly 1 per 100,000 live births, the etiology and incidence of bilateral pulmonary aplasia remains poorly understood because of its rarity. Multiple mechanisms have been suggested, including genetic, syndromic, environmental, and traumatic factors. Although VANCRERL (vertebral, anal, cardiac, tracheal, renal, limb) association and Mardini-Nyhan association are known to exhibit lung aplasia accompanied with skeletal defects, the calvarial abnormality seen in our case has not, to our knowledge, been reported in combination with pulmonary aplasia.

Disseminated Scedosporium apiospermum Infection With Cardiac Abscess Resulting in a Complete Heart Block in a Posttransplant Patient

(David Wells, MD (wellsd89@uw.edu); Desiree Marshall, MD; Florencia Jalkitis, MD. Department of Anatomic Pathology, University of Washington Medical Center, Seattle.)

Scedosporium apiospermum/Pseudallescheria boydii is a ubiquitous environmental hyaline mold with clinical relevance in causing disease in solid organ transplant patients with associated high-mortality rates ranging from 50% to 80%. We report the case of a 66-year-old man with a history of hepatitis C cirrhosis, who had previously undergone orthotopic liver transplant 15 years earlier, who presented to the hospital in decompensated liver failure resulting in a second liver transplant. His postoperative course was complicated by sepsis of multiple possible sources with cultures and molecular studies demonstrating Candida glabrata fungemia and Aspergillus sp within the lung.
Tissue culture and molecular studies of a small ulcer along the dorsum of the right foot demonstrated *Scedosporium apiospermum*. Despite treatment with appropriate antifungals, his condition worsened, and he developed progressive heart block with echocardiogram demonstrating a septal mass. In this setting, he was transitioned to comfort care on postoperative day 29. Autopsy showed a widely disseminated fungal infection with abscesses at multiple sites, including kidneys, lungs, thyroid, and brain. Additionally, there was evidence of ascending lymphangitic spread from the right foot and periaortic abscesses. The heart demonstrated a large abscess replacing the interventricular septum (Figure 185, A) with hyphae identified on histology (Figure 185, B). Postmortem cultures grew *Pseudallescheria boydii* complex. Posttransplant patients are at increased risk for opportunistic infections because of immunosuppression. This case serves as a dramatic example of this risk and highlights the role of autopsy in clinical-pathologic correlation and clarification of infectious agent when cultures reveal multiple organisms.

Calciphylaxis, delineated by Selye in 1961, is a rare, potentially fatal entity that has continued to pose a major diagnostic and therapeutic challenge. Calciphylaxis is predominantly seen in patients with end-stage renal disease on dialysis. A 35-year-old female patient with severe end-stage renal disease secondary to focal segmental glomerulosclerosis on long-term dialysis presented with 6 weeks of painful erythematous to violaceous plaques over the right breast, buttocks, and thighs. A punch biopsy of right thigh skin showed calcification in subcutaneous fat, confirmed with Von Kossa stain, and consistent with calciphylaxis that subsequently involved other visceral organs, and with cutaneous manifestations in the advanced stages. Calciphylaxis is a systemic illness that may trigger a vicious cascade of unusual forms of calcifications in a variety of organs. The presence of skin lesions should trigger systemic evaluation for calcifications to reduce mortality and morbidity rates in these patients.

Acute esophageal necrosis, also known as black esophagus, is a rare physical finding seen during postmortem examination. It is caused by a combination of poor perfusion and increased irritation of the esophagus, resulting in blackened discoloration of the esophageal mucosa. Although rare, the presence of black esophagus should direct forensic pathologists to focus the investigation into potential underlying causes of death, including both alcoholic and diabetic ketoacidosis. Two autopsies conducted at the University of Wisconsin between 2002 and 2017 showed gross evidence of acute esophageal necrosis. Case 1 was that of a 59-year-old woman found deceased at home with known chronic alcohol abuse. Her blood alcohol level was 0.207% g/dL. Case 2 was that of 47-year-old man found deceased in a hotel room with a history of insulin-dependent diabetes and polysubstance abuse. He was found to have hyperglycemia by vitreous glucose testing and ketosis in both blood and vitreous analysis. Both cases showed diffusely blackened esophageal mucosa, which on histologic sections, showed epithelial loss with dense submucosal neutrophilic infiltration and overlying hemorrhage/hemosiderin deposition. Mortality rates in patients with black esophagus are reported to be as high as 36%, depending on etiology. Black esophagus is a relatively striking feature, easily seen during routine opening or inversion of the esophagus. Because it may be one of the few physical manifestations of a fatal metabolic derangement, the presence of acute esophageal necrosis at the time of postmortem examination should prompt a deeper and more exhaustive investigation to uncover possible fatal underlying conditions.
Association of Alagille Syndrome With Advanced Cardiac, Cranial, and Peripheral Vascular Disease

(Poster No. 88)

Azadeh Esmaeil, MD (azadehesmaeil@ouhsuc.edu); Sepideh Asadbeigi, MD; Carlos Dominguez Rangel, MD; Henry Tran, MD. Department of Pathology, University of Oklahoma Health Science Center, Oklahoma City.

Alagille syndrome (ALGS) is an autosomal-dominant genetic disorder caused by mutations in genes JAG1 or NOTCH2. The liver, heart, eyes, face, and skeleton are classically affected and constitute the main criteria for clinical diagnosis, but clinical features may be highly variable. The precise pathophysiological etiology of ALGS is unclear, but multiple case reports of vascular anomalies/events have led some authors to speculate a mechanism related to impaired JAG1 or NOTCH2 involvement in vascular development and/or remodeling. We, thus, present an autopsy case of a 15-year-old girl and ALGS patient with a documented mutation in JAG1. The patient had died from massive, multifocal, acute cerebral infarction and subarachnoid hemorrhage, and her history was significant for remote cerebrovascular accidents, moyamoya disease, Takayasu arteritis, and aortic coarctation. In addition, autopsy examination revealed a descending aortic arch aneurysm, an abdominal aorta stenosis, a superior vena cava stenosis, left pulmonary artery stenosis, pulmonary and aortic valve stenosis, and bilateral renal artery stenosis. By histology, arteries demonstrated variable atherosclerosis, with some coronary arteries even showing complete occlusion. Of note, her lipid profile contained elevated levels of low-density lipoprotein (LDL), total cholesterol, and LDH/HDL ratio at 170/44 mg/dl, 246 mg/dl, and 4.5, respectively. With the overall cardiac, cerebral, and peripheral vascular findings, this case represents perhaps the most advanced degree of vascular involvement documented in a patient with ALGS. Given these findings, it is plausible that a combination of impaired vascular remodeling and liver impairment (with abnormal lipid profile) may lead to progressive vascular anomalies in ALGS through an atherosclerotic process.

Arterial Thrombosis in a Patient With Breast Cancer Causing Rectal Necrosis and Septic Shock

(Poster No. 89)

Clay Jarrell, MD (clayjarrell@creighton.edu); Teddii Tubre, MD; Gyujuan Li, MD, PhD. Department of Pathology, Creighton University, Omaha, Nebraska.

The association between cancer and thromboembolism has been known for many years. In breast cancer, thrombosis appears to be less common compared with other cancers, but patients are still at higher risk than the general population, and thrombosis can contribute to morbidity and mortality. Currently, the literature reports risks are highest shortly after diagnosis and when receiving chemotherapy or hormone treatment. Most reports show the risks are higher for venous thrombosis, with relatively few reports of arterial thrombosis. To our knowledge, arterial thrombosis has only been reported in the extremities, the heart, and the central nervous system. We, therefore, present a case of rectal arterial thrombosis found on autopsy in a patient with breast cancer. A 75-year-old woman with a medical history of breast cancer, with smoking history and hypertension, presented to the emergency department with complaints of weakness, fatigue, and abdominal pain. Esophagogastroduodenoscopy showed a large, friable mass involving the distal stomach and duodenal bulb. Endoscopic ultrasound revealed a suspicious, 2.4-cm perigastric lymph node. Fine-needle aspiration of the lymph node, without passing through the primary tumor, showed squamous epithelium lined cyst with chronic inflammation and calcification, the surgery was avoided and a drain was placed within the cyst, instead. After surgery, patient’s hospital course was uneventful. In conclusion, recognizing these benign entities and making the correct diagnosis in cytology is crucial to avoid a major surgery, which can be detrimental to the patient.

Lymphoepithelial Cysts of the Pancreas: A Case Report of a Benign, Diagnostically Challenging Lesion

(Poster No. 90)

Katherine C. Tuminello, MD (ktuminello@umc.edu); Anas Bernihe, MBBS; Hillary B. Sims, MD; Rim Alkawas, MD; Israh Akhtar, MD. Department of Pathology, University of Mississippi Medical Center, Jackson.

Lymphoepithelial cyst of the pancreas is a rare, benign cyst, first described by Lüchtrath and Schriever in 1985. The mean age of occurrence is 55 years, with men being more commonly affected than women. These are well circumscribed and can be multinocular or unicocular. Microscopically, the cyst is lined by squamous epithelium with subepithelial lymphoid tissue containing lymphoid follicles and is separated from the pancreatic parenchyma by a thin fibrotic capsule. These are discovered incidentally and are difficult to differentiate preoperatively from other cystic pancreatic lesions. In the endoscopic ultrasound, they appear solid, heterogeneous, and well circumscribed. We present a case of a 49-year-old woman with complicated medical history referred to our institute for a 3.5-cm pancreatic mass that showed nonaggressive features. Endoscopic ultrasound-guided fine-needle aspiration revealed keratinous debris, including anucleated squames and benign squamous epithelial cells with numerous lymphocytes and ductal epithelial cells in the background. Based on the cytomorphologic features a diagnosis of lymphoepithelial cyst was suggested. A Whipple surgery was planned, but after an intraoperative consult of the cyst, which showed squamous epithelium lined cyst with chronic inflammation and calcification, the surgery was avoided and a drain was placed within the cyst, instead. After surgery, patient’s hospital course was uneventful. In conclusion, recognizing these benign entities and making the correct diagnosis in cytology is crucial to avoid a major surgery, which can be detrimental to the patient.

Fine-Needle Aspiration of a Perigastric Lymph Node: A Potential Pitfall in the Diagnosis of Gastric Medullary Carcinoma

(Poster No. 91)

Iris Martin, MD, MPH (martinir@musc.edu); Daniel Skipper, DO; Jack Yang, MD; David Lewin, MD. Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston.

Gastric medullary carcinoma is rare, representing approximately 8% of gastric carcinomas with more than 80% associated with Epstein-Barr virus. We report the case of a 63-year-old man who presented with several months of abdominal pain. Esophagogastroduodenoscopy showed a large, friable mass involving the distal stomach and duodenal bulb. Endoscopic ultrasound revealed a suspicious, 2.4-cm perigastric lymph node. Fine-needle aspiration of the lymph node, without passing through the primary tumor, showed malignant cells singly and in loosely cohesive clusters with eccentric, enlarged, and round nuclei; vesicular chromatin; prominent nucleoli; and delicate cytoplasm in a background of lymphocytes (Figure 187, A). Subsequent biopsies of the stomach showed malignant cells with identical cytologic features in a prominent lymphohistiocytic background (Figure 187, B). By immunohistochemistry, the tumor cells were positive for AE1/AE3, CAM 5.2, villin, and Epstein-Barr virus by in situ hybridization. The findings were consistent with gastric medullary carcinoma. Following chemotherapy, a subtotal gastrectomy revealed a 3.5-cm mucosal ulcer in the pylorus. Microscopic examination showed residual tumor within the muscularis propria without residual tumor cells in the perigastric lymph nodes (Figure 187, C). Few cases have reported the cytologic findings of this carcinoma. Given our aspirate was from a lymph node, the lymphoid component of the tumor was not considered until the surgical biopsies of the stomach were reviewed. It is prudent to recognize subtle
Thymoma in Pleural Fluid

Abeer M. Salama, MD1 (abeer.salama@mountsinai.org); Jian J. Jing, MD, PhD2; Maria Habib, MD3; Maureen Zakowski, MD. 1 Departments of 1Pathology and 2Radiology, Icahn School of Medicine at Mount Sinai, New York, New York.

Thymomas account for less than 1% of neoplasms. The thymoma incidence in the United States is 0.15 per 100 000 person-years. Usually in the anterior mediastinum, pleural seeding is rare. Mediastinoscopy is seldom useful because it does not often reach the anterior mediastinum. Fine-needle aspiration is an effective but underused tool. We report a case of locally advanced thymoma, complicated by pleural effusion in a young woman. Pleural fluid cytology was successfully used for diagnosis. Patient presented with chest pain, dyspnea and a mass involving the mediastinum, diaphragm, and lung parenchyma. Fine-needle aspiration was performed, and resection confirmed type B2 thymoma. Three years later, computed tomography showed a new chest wall mass. Pleural fluid cytology showed keratin-positive neoplastic epithelial cells in a background of small lymphocytes. Thymoma was diagnosed. Pleural effusion cytology can identify many types of tumors, but thymomas are rare and can be misdiagnosed as lung cancer or other epithelial tumors. The cytologic diagnosis of thymoma in pleural fluid is extremely challenging, and because of its infrequent presentation and failure to recognize epithelial cells, immunohistochemical stains are often needed. Thymomas constitute a problem in diagnosing pleural fluids. Cytology is an effective tool, but thymomas may be underdiagnosed because of their rarity. Attention must be paid to the epithelial cells present, and they must be distinguished from mesothelial cells. Immunohistochemistry is very useful and a broad-spectrum keratin marker should be used (Figure 188).

Utility of Whole Genome Single-Nucleotide Polymorphism Microarray (SNPM) and Targeted Somatic Mutations in an Evaluation of a Cytologically Challenging Case of Mesothelioma

Nwogbo Okechukwu, MD (ONWOGBO@augusta.edu); Sravan Kururi, MD; Sunish Sharma, MD; George Wang, MD; Benjamin Johnson, BS; Ashis Mondal, PhD; Chetan Pundkar, PhD; Alka Chaube, PhD; Ravindra B. Kolhe, MD, PhD. Department of Pathology, Medical College of Georgia, Augusta University, Augusta.

We present a case of a 76-year-old woman who came for evaluation of a left lung nodule and left pleural effusion. Chest x-ray was performed, which showed left pleural effusion. A chest computed tomography was performed that showed left pulmonary nodules, a moderate pleural effusion, and mediastinal and hilar adenopathy. Positron emission tomography/computed tomography showed significant involvement of the paratracheal and subcarinal lymph node area (multilatination N2 disease). ThinPrep smear and cell block of the pleural fluid demonstrated predominance of clustered, atypical mesothelial cells and background inflammatory cells. The whole genome single-nucleotide polymorphism microarray (SNPM) was performed on the DNA isolated from formalin-fixed, paraffin-embedded (FFPE) cell block, following the manufacturer’s protocol (OncoScan assay, Affymetrix, Inc). The raw data were analyzed in Chromosome Analysis Suite 3.0 software and were matched to in silico FFPE reference sets. This platform consists of 274 000 probes, including 74 somatic mutations from 9 genes (BRAF, KRAS, EGFR, IDH1, IDH2, PTEN, PIK3CA, NRAS, and TP53). The SNPM showed massive genomic instability and 3p21.1 deletion, including the BAP1 gene. Genes associated with malignant mesothelioma (MM) were interrogated, and multiple abnormalities (TNFRSF14, DVL1, UBE4B, SETD2, CDKN2A, among others) were identified. Later, the patient underwent video-assisted thoracic surgery pleural biopsy and mediastinal lymph node dissection. Histology confirmed an epithelioid-type mesothelioma. We describe a powerful technology for investigating cytologically difficult cases. This report emphasizes the value of decisive molecular alterations in arriving at the critical threshold of establishing a diagnosis on cytology cases (Figure 189).

Pulmonary Carcinosarcoma: A Diagnostic Challenge

Malary M. Mani, MD (malary.mani@mountsinai.org); Zachary Grimes, MD; Binny Khandakar, MBBS, MD; Roshan Mahabir, MD, PhD, MPH; Diane D. Du, MD. Department of Pathology, Mount Sinai St Luke’s/Mount Sinai West Hospital Center, New York, New York.

Pulmonary carcinosarcoma is a rare neoplasm representing less than 1% of lung cancers. It is characterized by a biphasic histopathologic pattern consisting of both epithelial and sarcomatous components. Often, diagnosis of these heterogenic tumors can be challenging because biopsy may only represent one component. We report a case of pulmonary carcinosarcoma in a 61-year-old woman, smoker, presenting with a chronic cough. Chest computed tomography scan revealed multiple bilateral pulmonary masses, up to 6.1 cm, with associated mediastinal and hilar adenopathy. Bronchoscopy revealed a lobulated endobronchial lesion occluding the left lower lobe. Transbronchial fine-needle aspiration of level 7, R10, R4 lymph nodes, and biopsy of the mass was obtained. Histologically, the biopsy revealed predominantly necrotic tissue showing only few highly atypical epithelial cells. Cytologic evaluation, however, revealed 2 populations of tumor cells, a solid component composed of poorly differentiated, glandular, epithelioid cells (Figure 190, A) and a predominant sarcomatous component composed of mixed spindle (Figure 190, B) and giant cells. Immunohistochemistry revealed the epithelioid component strongly positive for TTF1, napsin A (Figure 190, C), MOC31, CK5, and CK AE1/AE3. The sarcomatous component stained strongly positive for vimentin (Figure 190, D). CD31, Fli1, and negative for TTF1, napsin A, and MOC31. Both components were negative for p@, Melan-A, S100, CD30, CD117, caldesmon, myogenin, WT1, and D2-40. Cytogenetics was negative for EGFR and KRAS mutations. The cytology and immunophenotypic findings were consistent with a diagnosis of pulmonary carcinosarcoma. We present this rare case to highlight this diagnostically challenging entity and the significance of thorough cytologic evaluation to achieve an accurate diagnosis.
Fine-Needle Aspiration Cytology on Salivary Gland Benign and Malignant Lesions: Results of 285 Cases From a Single Academic Institution

(Poster No. 95)

Ali Al-Habib, MD (ali.n.alhabib@uth.tmc.edu); Suhair Al Salhi, MD; Manju Ambellil, MD; Christine Liang, MD; Hui Zhu, MD; Jing Liu, MD, PhD; Peisha Yan, MD; Jaiyeola Thomas-Ogunniyi, MBBS; Songlin Zhang, MD, PhD. Department of Pathology, University of Texas Health Science Center, Houston.

Context: Fine-needle aspiration (FNA) cytology guided by ultrasound is widely used to evaluate lesions of salivary glands (SGs). Currently, the debate focuses on the reliability of FNA as a diagnostic tool and its usefulness in treatment planning. The aim of this investigation was to test the diagnostic accuracy of FNA on SG lesions.

Design: A retrospective FNA cytology report review from January 2011 to March 2017 was performed. The results were classified as unsatisfactory/nondiagnostic, benign/nonneoplastic, atypical/neoplastic, suspicious, and malignant. The sensitivity, specificity, accuracy, positive-predictive value (PPV), and negative-predictive value (NPV) were calculated using follow-up histologic diagnosis.

Results: During the study period, 285 FNAs were performed. The sites included parotid (257; 90.2%), submandibular (22; 7.7%), and other sites (6; 2.1%). The diagnosis was 18 nondiagnostic (6.3%), 63 benign (22.1%), 14 atypical (4.9%), 142 neoplastic (49.8%), 7 suspicious (2.5%), and 41 malignant (14.4%). There were 120 follow-up surgical specimens (42.1%). For diagnosing malignant lesions, FNA had a sensitivity 76.3%, a specificity of 93.5%, an accuracy of 87.8%, a PPV of 85.3%, and an NPV of 88.9%. For diagnosing neoplastic lesions (benign and malignant), FNA had a sensitivity 89.7%, a specificity of 100%, an accuracy of 90.4%, a PPV of 100%, and an NPV of 42.1%.

Conclusions: Our results support FNA cytology as a useful tool for diagnosis and presurgical planning of SG lesions. The sensitivity, specificity, accuracy, and PPV are higher when diagnosing neoplastic lesions as compared with malignant lesions, indicating the challenge of differentiating some low-grade malignancies from benign lesions based on cytomorphology. The low NPV for neoplastic lesions is largely due to the limited cytology material. Correlation with imaging and clinical findings is essential to make a negative/nonneoplastic diagnosis with a limited sample.

The Risk of Malignancy Associated With the Milan System Salivary Gland Fine-Needle Aspiration Diagnostic Categories: A Single Institution Experience

(Poster No. 96)

Recep Nigdelioglu, MD (rcpnig@gmail.com); Grazina U. Chatt, CT (ASCP); Shaun Boyes, MD; Razvan C. Lapadat, MD; Razan Massarani-Wafai, MD; Guliz A. Barkan, MD, FIAC, FACP; Eva M. Wojcik, MD; Stefan Pambuccian, MD, FACP; Swati Mehrotra, MD, FIAC. Department of Pathology, Loyola University, Maywood, Illinois.

Context: Fine-needle aspiration (FNA) diagnosis of salivary gland (SG) is limited by a lack of defined diagnostic categories. Variability in the use of diagnostic categories and use of descriptive reports further reduce the utility of SG FNA in patient management. The Milan System (TMS) proposes a unified classification scheme, wherein the diagnostic categories are coupled with a risk of malignancy (ROM) and management algorithm. This study attempted to calculate the malignancy risk associated with the diagnostic categories proposed by TMS at our institution and compare that with the literature.

Design: A retrospective cohort of FNA of SG with subsequent histologic correlate was retrieved from our files (2008–2017). Using TMS guidelines, aspirates were reclassified as nondiagnostic (I), nonneoplastic (II), or atypical cells of undetermined significance (III), neoplasms benign (IVA), neoplasms malignant (IVB), suspicious for malignancy (V), or malignant (VI). Sensitivity, specificity, and accuracy of cytologic diagnosis and ROM for all categories were calculated based on histologic correlation.

Results: The sensitivity, specificity, and diagnostic accuracy were calculated as 74.4%, 81.8%, and 85.6% (Table).

Conclusions: Our sensitivity, specificity, and diagnostic accuracy parallel that described in the literature. The ROMs in our data set parallel those proposed by The Milan System. Moreover, TMS provides a common language for pathologists, clinicians, and surgeons, which will optimize the use of salivary gland cytology in patient management.

<table>
<thead>
<tr>
<th>Risk of Malignancy (ROM)</th>
<th>Case No.</th>
<th>Diagnostic Categories</th>
<th>Cases (n = 167), No.</th>
<th>ROM, %</th>
<th>Expected ROM (TMS), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Nondiagnostic</td>
<td>24</td>
<td></td>
<td>20.83</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>2 Nonneoplastic</td>
<td>15</td>
<td></td>
<td>6.67</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>3 AUS</td>
<td>19</td>
<td></td>
<td>26.32</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>4 Benign</td>
<td>66</td>
<td></td>
<td>7.58</td>
<td>&lt;5</td>
<td></td>
</tr>
<tr>
<td>5 SUMP</td>
<td>11</td>
<td></td>
<td>18.18</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>6 Suspicious</td>
<td>4</td>
<td></td>
<td>50.00</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>7 Malignant</td>
<td>28</td>
<td></td>
<td>96.43</td>
<td>90</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AUS, atypia of undetermined significance; SUMP, salivary gland neoplasm of uncertain malignant potential; TMS, The Milan System.

Undifferentiated Pleomorphic Sarcoma Involving the Pleura and Presenting as Malignant Effusion

(Poster No. 97)

Ronald Araneta, MD (ronaldaraneta@jax.ufl.edu); Heba Saad, MD; Megan Brown, MD; Jinous Saremian, MD. Department of Pathology, University of Florida College of Medicine, Jacksonville.

Sarcomas account for approximately 5% of malignant effusions and usually occur in the setting of limb or pleural involvement. The diagnosis is usually made with knowledge of history and review of prior material from the primary tumor. However, radiation and chemotherapy may effect cellular changes that differ from the original neoplasm, precluding a correct diagnosis. Knowledge of the features of sarcoma in body fluids and awareness of the therapeutic changes are helpful in the diagnosis. This is a case of a previously diagnosed, undifferentiated pleomorphic sarcoma of the thigh in a 47-year-old man presenting with dyspnea 4 months after resection of the soft tissue primary. Initial imaging revealed pleural effusion. Pleural fluid cytology revealed single round/oval cells with cytoplasmic vacuolization, irregular nuclear contours, nuclear membrane in-folding, prominent nucleoli (Figure 191, A and B), and atypical mitoses in a myxoid background, which were positive for vimentin and CD10, similar to the thigh primary (Figure 191, C and D). Upon fluid drainage, the pleural thickening and nodularity became evident and, on excision, revealed involvement by undifferentiated pleomorphic sarcoma, morphologically similar to the thigh tumor. Unlike fine-needle aspirates, sarcomas in fluid lack the stromal and vascular pattern/tissue arrangement and are often dispersed, tend to round up with indistinct cellular borders, and exhibit nuclear pleomorphism and multinucleation. Radiation changes may bring about cell ballooning, cytoplasmic vacuolization, and nuclear enlargement. Recognition of cellular features of sarcomas in body fluids and therapeutic changes may aid, and in this instance, even precede diagnosis of pleural involvement by sarcomas.
Metastatic Spindle Cell Melanoma to the Thyroid Gland: A Rare Case With a Potential Diagnostic Pitfall on Cytology (Poster No. 98)

John M. Gross, MD (jmg144@gmail.com); Agnes Colanta, MD; Thomas Ruma, MD. Department of Pathology, Creighton University School of Medicine, Omaha, Nebraska.

Spindle cell melanoma accounts for less than 4% of all melanomas and often creates diagnostic dilemmas because it is often negative for traditional melanocyte-specific immunostains (HMB-45, MITF, Melan-A), is typically nonpigmented, and like traditional melanomas, can present as distant metastasis long after a primary diagnosis. We present the case of a 68-year-old man with an enlarged lymph node in the deep neck tissues, adjacent to the thyroid gland. Fine-needle aspiration cytology revealed bland spindle cells arranged in a vague papillary architecture (Figure 192, A and B). Papillary thyroid carcinoma was the initial diagnostic impression, until a review of the medical record revealed the patient’s history of melanoma of the distal extremity in 2001. Without the convenience of a cell block for immunohistochemical staining, the diagnosis was clenched by reprocessing the original cytology sample and performing a SOX10 IHC on unstained smears. A few remaining tumor cells were present and stained strongly positive for SOX10 (Figure 192, C). Papillary thyroid carcinoma was diagnosed. Subsequently, the patient had an excisional biopsy revealing a high-grade spindle cell neoplasm (Figure 192, D). This case demonstrates several important points, including the diagnostic pitfalls in spindle cell melanoma, its long duration of metastatic potential, the utility of performing immunohistochemistry on unstained cytologic smears, and the unusual presentation of metastases to the perithyroidal lymphatic basin.

The Value of Cell Block in the Diagnosis of Body Fluids (Poster No. 99)

Faisal Mrair, MD (fhmrair@gmail.com); Quoc Nguyen, MD; Kamapriya Vidhun, MD; Lynn O’Donnell, CT, MHA; Mary S. Chacho, MD. Department of Pathology and Laboratory Medicine, Danbury Hospital, Danbury, Connecticut.

Context: Our laboratory routinely makes ThinPrep slides on body fluids and cell blocks from the remaining sediment. This study examines when adding the cell blocks contributed to the final diagnosis.

Design: Body fluids that had a ThinPrep and a cell block prepared in 2015 were reviewed by blinded pathologists with knowledge of only the clinical information provided at the time of initial evaluation. For this study, cases were diagnosed based on ThinPrep findings alone, then assessed whether or not a cell block could aid in diagnosis (either to help characterize the cells seen on the ThinPrep slide or for the purposes of special stains/immunohistochemistry).

Results: We studied 285 body-fluid samples. Diagnosis on ThinPrep alone was 194 negative cases, 29 atypical/indeterminate/lymphoid processes, 14 suspicious for malignancy cases, 45 malignant/neoplasia cases, and 3 nondiagnostic cases. Diagnosis on cellblock alone was 199 negative cases, 25 atypical/indeterminate/lymphoid processes, 8 suspicious cases, 52 malignant/neoplastic cases, and 1 nondiagnostic case. Addition of cell blocks led to change in diagnosis with a reduction in suspicious cases from 14 to 8 and an increase of malignant/neoplastic cases from 45 to 56. Of the 142 cases received with a history, or suspicion, of malignancy, a final diagnosis of malignancy/neoplasia was made in 49 cases, with cell block adding value in 11 cases. Of all 285 cases, 56 had a final diagnosis of malignancy/neoplasia.

Conclusions: Adding cell blocks had a little value in cases in which the ThinPrep was benign. The cell block was beneficial in cases in which the ThinPrep by itself was suspicious of, or positive for, malignancy/neoplasia or with a clinical suspicion or history of malignancy/neoplasia.

Synchronous Pancreatic Tumors in a Patient With a History of Wilms Tumor: A Case of Pancreatic Adenocarcinoma and Lipid-Rich Neuroendocrine Tumor (Poster No. 100)

Huiya Huang, MD, PhD (hhuang@mcw.edu); Tamara Giorgadze, MD, PhD. Department of Pathology, Medical College of Wisconsin, Milwaukee.

Synchronous tumors are defined as 2 or more primary tumors identified in the same patient at the same time. Synchronous tumors represent a very small portion of pancreatic tumors. Although there is a higher incidence of secondary malignant neoplasms in patients with a history of Wilms tumor, pancreatic tumors are very infrequently secondary malignant neoplasms in that population. We report a case of synchronous pancreatic tumors in a 48-year-old man with a history of Wilms tumor. Two pancreatic lesions were identified by imaging study in the pancreatic head and body, respectively, Fine-needle
To our knowledge, this is the first case of synchronous pancreatic cancer. The neuroendocrine tumor had the characteristic vacuolated, lipid-rich cytoplasm (Figure 193, C and D), which reportedly is mostly found in von Hippel-Lindau syndrome or multiple endocrine neoplasia type 1 syndrome, but no common cancer-associated mutation was identified. The neuroendocrine tumor cells were positive for synaptophysin, chromogranin, and adipophilin and were negative for CD56, CD10, PAX8, and WT1 immunostains. Further molecular testing was performed on both tumors in our case using next-generation sequencing with a 50-gene panel (Ion AmpliSeq Cancer Hotspot Panel, version 2, Life Technologies, Carlsbad, California), but no common cancer-associated mutation was identified. To our knowledge, this is the first case of synchronous pancreatic tumors in a patient with history of Wilms tumor.

**Metastatic Pulmonary Adenocarcinoma to the Ovaries: A Carcinoma of Unknown Primary Diagnostic Conundrum**

*Ronald Araneta, MD (ronaldaraneta@jax.ufl.edu); Heba Saad, MD; Arun Gopinath, MD; Jaime Morel Ruiz, MD; Jinous Saremian, MD.* Department of Pathology, University of Florida College of Medicine, Jacksonville.

Metastatic neoplasms to the ovary often cause diagnostic problems. Ovarian metastases account for 5% to 10% of all ovarian tumors. Most of these tumors arise from the gastrointestinal tract (stomach/colon), breast, and endometrium. Of the few metastatic tumors to the ovary, lung carcinomas account for 2% to 4% of cases. Ovarian metastases often occur in women with a prior history of extracranial cancer with a median detection interval of 2 years. Possible metastatic pathways include retrograde lymphatic spread, transperitoneal dissemination, and hematogenous metastasis. The usual presentation is that of a pelvic tumor, such as abdominal or pelvic pain, gastrointestinal or urinary disturbances, abdominal distension, or abnormal uterine bleeding. We present a 29-year-old woman who initially presented with bilateral pulmonary thromboembolism and a prominent right submandibular lymph node. Further imaging revealed bilateral ovarian masses. The initial clinical impression was ovarian carcinoma metastatic to the submandibular lymph node. Fine-needle aspiration biopsy of the submandibular lymph node and subsequent pathology of the left oophorectomy specimen revealed metastatic adenocarcinoma (Figure 194, A) that was positive for cytokeratin 7 (CK7) (Figure 194, B), napsin A (Figure 194, C), and thyroid transcription factor 1 (TTF1) (Figure 194, D) and was negative PAX8 staining, confirming the diagnosis of an ovarian metastasis from a primary lung adenocarcinoma. Further workup also revealed the tumor to harbor an ALK (D5F3) mutation. Cranial imaging also revealed metastatic disease to the brain. The patient has undergone stereotactic brain radiosurgery and is currently on ALK-inhibitor therapy.
Granular Cell Tumor Arising in the Thyroid Gland: Report of an Unusual Case and Review of the Literature

(Poster No. 104)

Alisa M. Caudell, MD (tykal@musc.edu); Kathryn G. Lindsey, MD. Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Mount Pleasant.

Granular cell tumors (GCTs) are soft tissue tumors of neural origin that most commonly arise in the tongue and subcutaneous tissue. The GCTs that arise in the thyroid gland appear to be exceptionally rare because only 12 cases have been reported in the literature. We present a case of a 24-year-old woman who presented with an enlarging right thyroid nodule and dyspnea. Fine-needle aspiration was performed and showed a pure population of large cells with abundant eosinophilic, granular cytoplasm, and indistinct cell borders. The nuclei were round to spindled with inconspicuous nucleoli (Figure 195, A and B). The cytologic findings were suggestive of GCT. Subsequently, a right hemithyroidectomy was performed. Histologic examination of this resection specimen confirmed the diagnosis of GCT arising within the thyroid gland (Figure 195, C and D). This case adds to the few reports that describe the clinical presentation and pathologic features of GCT arising in the thyroid gland. Moreover, GCT should be differentiated from cytologically similar entities that are more commonly seen in the thyroid, such as Hurthle cell neoplasm and medullary carcinoma. Immunohistochemistry can aid in the differentiation of these lesions. Although primary GCT of the thyroid is rare, it should be considered in the differential diagnosis of a thyroid lesion in a young woman patient with fine-needle aspiration findings of large cells with abundant granular, eosinophilic cytoplasm and indistinct cell borders.

Clear Cell Sarcoma Versus Malignant Melanoma on Cytology: A Diagnostic Challenge

(Poster No. 105)

Sachica C. Cheris, MD, MBA1 (sachica.cheris@duke.edu); Mary Ann B. Rutkowski, CT(ASCP)2; Amanda Martin Kelley, MD3; Ellen Giampoli, MD.2 1Department of Pathology, Duke University Medical Center, Durham, North Carolina; 2Department of Pathology, University of Rochester Medical Center, Rochester, New York; 3Department of Pathology, Rochester Regional Hospitals, Rochester.

We describe a case of metastatic clear cell sarcoma in a 35-year-old woman. She is among the longest surviving patients with clear cell sarcoma (CCS) and originally presented with the disease in her left foot. Four years after an initial recurrence involving the left distal femur, a scan revealed masses in the ovary, pancreas, and lungs, as well as hemorrhagic ascites. Her ascitic fluid was examined, and the cells were cytologically identical to metastatic melanoma. Diff-Quick tests showed single tumor cells and cells in clusters with frequent pseudoglandular architecture (Figure 196, A). Papanicolaou-stained smears revealed cells in clusters with granular cytoplasm, oval nuclei with prominent macronucleoli, and mitosis (Figure 196, B). The cell block showed monotonous, clear to eosinophilic, ovoid to plasmacytoid cells with prominent nucleoli and occasional multinucleated, wreathlike giant cells (Figure 196, C). Similar cells were seen in the ovarian masses within nests of ovoid to spindled cells with melanin pigment within their cytoplasm (Figure 196, D). The cells were positive for S100, Melan-A, and HMB-45. Although CCS is exceedingly rare, it has many overlapping cytomorphic features with melanoma. It is important to distinguish these 2 aggressive and often pigmented lesions. Melanocytic markers applied in cases of CCS, along with its cytologic similarities to melanoma, make calling CCS a melanoma a potential pitfall. Distinctive features of CCS not commonly seen in melanoma include the presence of wreathlike giant cells, pseudoglandular structures, minimal pleomorphisms, and the presence of intracytoplasmic glycogen (detected by PAS-D). Identifying the EWSR1-ATF gene fusion from t(12;22)(q13;q12) is also immensely useful in confirming the diagnosis of CCS.

Suspicous for Hurthle Cell Neoplasm in Bethesda Category IV Thyroid Cytopathology: A Clinical and Histologic Correlation

(Poster No. 106)

Cameron C. Felty, DO (Cameron.C.Felty@hitchcock.org); Christopher R. Jackson, MD; Louis J. Vaikus, MD, PhD; Xiaoying Liu, MD. Department of Pathology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire.

Context: Thyroid fine-needle aspirations (FNA) meeting criteria for Bethesda category IV, suspicious for Hurthle cell neoplasm, can be seen in a wide range of benign and malignant pathologic entities. We investigated the clinicopathologic correlation among thyroid FNAs with cytology suspicious for Hurthle cell neoplasm.

Design: The departmental database was searched for all Bethesda category IV thyroid FNAs with a diagnosis of suspicious for Hurthle cell neoplasm. Patients’ demographics, ultrasonographic features, and corresponding surgical pathology reports from cases meeting inclusion criteria were reviewed. Analysis of variance and χ2 tests were performed to detect statistically significant differences in patient demographics and ultrasonographic features between benign and malignant lesions.

Results: During a 5.5-year period, 3539 thyroid FNAs were performed, 73 (2%) of which were diagnosed as suspicious for Hurthle cell neoplasm. Of those 73 patients, 54 (74%) underwent thyroidectomy, 6 (8%) were followed clinically, whereas the remaining 13 patients (18%) were lost to follow-up. In patients who underwent thyroidectomy and had available surgical pathology reports, 44 of 52 (85%) had a Hurthle cell predominant process at the site corresponding to their previous FNA. A malignant neoplasm was present in 17 of 52 (33%) of cases, whereas the remaining 35 of 52 cases (67%) were benign. Statistically significant differences were present in size (P = .005) and vascularity (P = .01) between neoplasic and nonneoplastic processes.

Conclusions: The risk of malignancy in patients with Bethesda category IV aspirates, suspicious for a Hurthle cell neoplasm, at our institution was 33%, consistent with the implied risk of malignancy in category IV FNA thyroid aspirates published in the 2017 Bethesda System.
Desmoplastic Small Round Cell Tumor by Fine-Needle Aspiration Biopsy: Report of 2 Cases and Review of Literature

(Poster No. 107)

Doan Lai, MD (doan-lai@ouhsc.edu); Kwok-ling Kam, MD; Laura Adhikari, MD. Department of Pathology, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma.

Desmoplastic small, round-cell tumor (DSRCT) is a rare, aggressive mesenchymal tumor most frequently seen in young adults and children with predominance in men, characterized by a specific t(11;22)(q13;q12) translocation. Cytologic features of only about 50 cases have been reported. We reviewed fine-needle aspiration biopsy (FNA) features on 2 cases, a 27-year-old man and 25 year-old pregnant woman, at Oklahoma University Medical Center in 2016. The FNAs were performed, and a definitive diagnosis was made in both cases. The smear preparations were hypercellular and showed loose cohesive clusters and dispersed primitive appearing cells possessing fine chromatin and high nuclear to cytoplasmic ratio, with occasional papillary-like stromal fragments. Apoptotic bodies and mitotic figures were easily identified. Desmoplastic stroma was noted in one case. The differential diagnoses included Wilms tumor, rhabdomyosarcoma, mesothelioma, Ewing sarcoma, small cell carcinoma, and lymphoma. On cell block, the tumor cells strongly stained for pancytokeratin and displayed perinuclear, dotlike staining for desmin. The translocation t(11;22)(q13;q12) was confirmed with aspirate smears for reverse transcriptase-polymerase chain reaction in both cases. Both patients were treated for disease based on the FNAs diagnosis. DSRCT is a rare soft tissue tumor which is not widely reported based on cytology/FNA alone. Awareness of the cytologic features and adequate specimen to demonstrate presence of t(11;22)(q13;q12) translocation is essential for making a definitive diagnosis.

Vertebral Body Fine-Needle Aspiration: A Retrospective Analysis

(Poster No. 108)

Brittany Cody, MD (brittany_cody@rush.edu); Yahya A. Al-Ghamdi, MBBS; Paolo Gattuso, MD. Department of Pathology, Rush University Medical Center, Chicago, Illinois.

Context: Fine-needle aspiration (FNA) is a minimally invasive procedure used for cytologic examination and diagnosis. The aim of this study was to evaluate the utility of FNA for diagnosis of vertebral body lesions.

Design: Departmental archives from 1982 to 2016 were searched for vertebral body FNA. The cases were then evaluated for concurrent biopsy and further for concordance of FNA and biopsy findings.

Results: Eighty-four cases were retrieved, including 48 women, 35 men, and one unknown. The mean age was 53.79 years (range, 10–84). Cytologic diagnoses included benign (n = 28; 33.3%), adenocarcinoma including breast carcinoma (n = 23; 27.4%), squamous cell carcinoma (n = 8; 9.5%), other carcinomas (n = 11; 13.1%), hematolymphoid neoplasms (n = 9; 10.7%), sarcoma (n = 2; 2.4%), other malignancy (n = 2; 2.2%), and one case was nondiagnostic (n = 1; 1.2%). Among 58 cases whose charts were available for review, 23 had concurrent biopsies. Of those 23 cases, 21 (91.3%) were in agreement with the fine-needle biopsy, one case was with discrepancy, and one case was nondiagnostic by both FNA and biopsy. The single discrepant case was negative for malignant cells by FNA, whereas the biopsy showed metastatic adenocarcinoma consistent with known breast primary. Of the 27 cases that were benign by FNA and biopsy, 7 (25.9%) had a history of malignancy.

Conclusions: In summary, FNA is a sensitive methodology for detection of vertebral body malignancies, with results similar to that of biopsy. Of 83 aspirates, 27 (32.5%) were benign, alleviating the need for more invasive interventions.

Evaluation of Transformation Zone Adequacy in Cervical Papanicolaou Smears of Biopsy-Proven Squamous Cell Carcinoma Cases: A Pilot Study

(Poster No. 109)

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

Context: Studies have shown contradictory evidence regarding the importance of sampling the endocervical/transformation zone (EC/TZ). The goal of this study was to identify demographic and clinical factors that may predict the absence of EC/TZ components in cervical Papanicolaou (Pap) smears, and its effect on the cytologic diagnosis, on cases in which a follow-up cervical biopsy showed squamous cell carcinoma (SCC).

Design: An electronic record search of biopsy-proven SCC cases at the University of Texas Medical Branch from 2015–2017 was performed. Biopsies were correlated with the previous Pap results. EC/TZ adequacy was investigated, along with demographic and clinical variables that could affect the EC/TZ sampling. Variables of interest included age, body mass index, ethnicity, smoking history, alcohol and drug use, exogenous hormone therapy, parity, and high risk-human papillomavirus status.

<table>
<thead>
<tr>
<th>Previous Pap Diagnosis in Biopsy-Proven SCC Cases</th>
<th>Total No. per Pap Diagnosis (%) (n = 69)</th>
<th>No. per Pap Diagnosis Performed at University of Texas Medical Branch (n = 37)</th>
<th>Inadequate EC/TZ (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>3 (4.3)</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Atypical squamous cells of undetermined significance</td>
<td>1 (1.5)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Atypical squamous cells of undetermined significance, cannot exclude high grade</td>
<td>8 (11.6)</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Low-grade squamous intraepithelial lesion</td>
<td>2 (2.9)</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>High-grade squamous intraepithelial lesion</td>
<td>28 (40.6)</td>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td>High-grade squamous intraepithelial lesion, cannot rule out invasion</td>
<td>6 (8.6)</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>12 (17.4)</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Atypical glandular cells of undetermined significance</td>
<td>1 (1.5)</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Unknown</td>
<td>8 (11.6)</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>

Abbreviation: SCC, squamous cell carcinoma.

Results: Sixty-nine cases of biopsy-proven cervical SCC were identified, of which 37 had a previous Pap smear performed at our institution. Average age of the patients was 42.6 years. Seven of 37 Pap smears showed inadequate EC/TZ, with no impact on the Pap diagnosis (Table). Among all variables examined, older age appears to correlate with inadequate EC/TZ. The remaining variables of interest did not affect EC/TZ sampling.

Conclusions: Absence of EC/TZ on Pap smears did not impact the cytologic diagnosis in this studied case. Our preliminary data might suggest that these cases could be managed without early repeat of the Pap test. The methodology developed in this project will be applied in a larger study with the aim of contributing to patient care and management.
Sarcomatoid Carcinoma in Cytology: Case of a Rare Entity Presenting in Pleural and Pericardial Fluid Preparations

Atreyee Basu, MD (Atreyee.Basu@nyumc.org); Anthony Simms, MD; Tanam C. Brandler, MD, MS. Department of Pathology, NYU Langone Medical Center, New York, New York.

Sarcomatoid carcinoma is a rare finding in pleural and pericardial fluid. To date, very few cases have been reported. We present a case of a 59-year-old woman who presented with coughing for 5 months. Chest computed tomography scan revealed a 6.0-cm cavity mass in the left lung base, bulky mediastinal and left hilar lymphadenopathy with a 1.8-cm right hilar lymph node. An additional 1.2-cm right adrenal mass was also seen, suggestive of metastatic disease. During a period of several months, the patient developed breathlessness, tachycardia, pleuritic chest pain, and generalized weakness and was admitted to the hospital. She was found to have pleural and pericardial effusions, which were drained and sent to cytology. The cytology fluid revealed enlarged and highly pleomorphic malignant cells, some displaying multinucleation, with irregular nuclear borders, coarse chromatin, and prominent nucleoli. Tumor cells were positive for CK7 and Vimentin and negative for MOC-31, Ber-EP4, B72.3, Sox10, Melan-A, TFF-1, Napsin-A, and CK20. A concurrent surgical biopsy of the tumor mass displayed immunopositivity for AE1/AE3 and CAM 5.2. The tumor was negative for p40, TTF-1, calretinin, D2-40, and STAT6. A diagnosis of sarcomatoid carcinoma with giant cells and spindle cells was rendered. Sarcomatoid carcinomas of the lung are very uncommon and comprise 1% of non–small cell lung carcinomas (NSCLCs) and are not often identified in cytology specimens. Despite its rarity, it is important to keep this entity in the differential diagnosis of a fluid specimen with bizarre nuclear atypia and the above staining pattern.

Metastatic Malignant Melanoma to the Esophagus: First Case Demonstrated by Endoscopic Ultrasound-Guided Fine-Needle Aspiration

Beena Umar, MD1; Robert L. Pompa, MD; Mohamed Alhamar, MD; Nicholas J. Horton, MD; Thomas Marshall, MD; Ziyong Zhang, MD. 1Departments of Pathology & Laboratory Medicine and 2Gastroenterology, Henry Ford Health System, Detroit, Michigan; 3Department of Family Medicine, Alcona Health Center, Alpena, Michigan.

Metastatic malignant melanoma to the esophagus is extremely rare. Extensive literature search has revealed only 15 cases so far (1895–2017). All were diagnosed on surgical specimens. We report a case of metastatic malignant melanoma to the esophagus, the first case diagnosed by endoscopic ultrasound (EUS)–guided fine-needle aspiration (FNA). A 91-year-old man had developed cough for 8 months. Past medical history included asbestos exposure and resection of melanoma of left neck 21 years ago. He underwent computed tomography of the chest, which revealed a 4.3-cm middle mediastinal mass that appeared to be contiguous to the esophagus. Further PET scan suggested the mass was of esophageal origin. Subsequent EUS examination showed an intraluminal lesion likely originating from the submucosa of the esophageal wall between 29 and 33 cm from incisors. The lesion appeared solid, hypoechoic, and heterogenous with well-defined sonographic borders (Figure 197, A). FNA was performed and a very cellular sample was obtained, which contained many large epithelioid malignant tumor cells with high-grade bizarre nuclei, prominent mitotic activity, and occasional large nucleoli. Intracytoplasmic brown pigment was noted focally (Figure 197, B and C). Immunohistochemistry showed positive staining for S100, SOX-10, Melan-A, and C-kit. Combined morphology and immunoprofile were consistent with malignant melanoma. The diagnosis of melanoma involving the esophagus may not be considered in routine cytopathology practice; although extremely rare, in any patient who has a history of melanoma (including those with a very remote history such as our patient), melanoma should always be considered in the differential diagnosis of a new mass at any anatomic location.

See, Test, & Treat: 3 Years’ Experience

Jing Liu, MD, PhD; Mei Lin, MD (mei.lin@uth.tmc.edu); Sadia Sultana, MD; Laura C. Nwogu, MD; Annelisse Veloz-Perez, MD; Elizabeth M. Jacobi, MD; Manuel D. Arana Rosainz, MD PhD; Diadel M. Saulino, DO; Josh A. Showalter, MD; Yumi A. Kojima, DO; Angelic Padilla, MD; Hui Zhu, MD, PhD; Songlin Zhang, MD, PhD; Yu Bai, MD, PhD; Robert L. Hunter, MD, PhD. Department of Pathology and Laboratory Medicine, University of Texas McGovern Medical School, Houston.

Context: Cervical cancer is a highly prevalent disease; however, thousands of women die from this cancer each year. See, Test, & Treat is the College of American Pathologists (CAP) Foundation’s flagship program. It delivers pathologist-led free cervical and breast cancer screenings and same-day results to women who are uninsured or underinsured. We hosted this event by providing cervical cancer screenings between 2015 and 2017.

Design: Our pathology participants included 5 pathologists, 12 pathology residents, cytotecnologists, and technicians. We served 311 women aged 20 to 64 years and performed 291 Papanicolaou (Pap) tests, 232 HR-HPV tests, 24 cervical biopsies, and 14 loop electrocautery excision procedures (LEEPs). The HR-HPV test was performed on women ≥30 years old or with a diagnosis of ASCUS. The pathology residents were involved in patient education sessions at Bayshore Clinic.

Results: Pap tests were 16 (6.2%) with epithelial abnormalities. HR-HPV tests were positive in 20 cases (8.6%). Cervical biopsies/LEEPs discovered 14 low-grade squamous intraepithelial lesions and 5 high-grade squamous intraepithelial lesions. We reviewed 23 Pap smears with concurrent HPV testing and explained HPV testing and the importance and the frequency of these screening tests. Educational sessions were conducted in English and Spanish to facilitate optimal communication with the patients and their families.

Conclusions: Pathologists, together with a team of health care professionals, donated their time and expertise to deliver same-day screening, results, and connection to follow-up care. We identified the patients with precancerous cervical lesions. The role of patient education is particularly important and influential to the underserved community by establishing habits of preventive care. Cervical cancer will be prevented if we work together.

Low-Grade Squamous Intraepithelial Lesions and HPV Results: A Study of Quantitative Correlation With Follow-up Histopathology

Christine R. Rupcich, MD (christine_r_rupcich@rush.edu); Ji-Weon Park, MD. Department of Pathology, Rush University Medical Center, Chicago, Illinois.

Context: Studies show high-risk HPV is detected in 85% of low-grade squamous intraepithelial lesions (LSILs). Possible causes for false-negative HPV testing results include interfering substances, low copy number of HPV, inadequate cellularity, among others. This study aims to determine if a quantitative relationship exists between HPV results and number of koliocyes present.

Design: We reviewed the pathology database year 2016 for LSIL Pap smears with concurrent HPV testing. There were 178 total cases: 48 (27%) were negative for HPV and 130 (73%) were positive. The slides were reviewed to count the number of koliocyes present (1 case excluded for missing slide). They were divided into 3 categories: low (0–
Fifty-two specimens (58%) had some degree of atypia/dysplasia. Of these, 67 patients had follow-up with 90 total specimens. (20.2%) intermediate, and 40 (31.0%) high (28 Pap smears with LSIL with positive HPV results, 63 (48.8%) were categorized as low, 26 (20.2%) intermediate, and 40 (31.0%) high (28 Pap smears with >200 koilocytes). Of these, 67 patients had follow-up with 90 total specimens. Fifty-two specimens (58%) had some degree of atypia/dysplasia. Of these, 67 patients had follow-up with 90 total specimens.

Conclusions: This study shows that LSILs with negative HPV results are more likely to have a lower number of koilocytic cells present. However, the HPV results were a better predictor of dysplasia in subsequent follow-up. To our knowledge, this is the first study examining the quantitative correlation of koilocytes in a Pap smear to the HPV test results.

**Amylase Crystalloids in Fine-Needle Aspiration of a Parotid Lesion**

(***Poster No. 114***)

Tanvi Verma, MD (vermatanvi@gmail.com); Erin Langford, MD; Yulin Liu, MD; Jan Silverman, MD. Department of Pathology, Allegheny General Hospital, Allegheny Health Network, Pittsburgh, Pennsylvania.

There are many types of crystalline structures such as amylase, tyrosine, collagenous crystalloids, oxalate, and intraluminal crystals seen in fine-needle aspiration (FNA) smears of salivary gland lesions. Amylase crystalloids are polygonal, platelike, or needle shaped and are most often seen in benign, nonneoplastic conditions, especially infections and cysts. A 78-year-old woman presented with left neck pain and swelling for 10 days, aggravated by meals. Antibiotics provided no relief. On examination, a 3-cm firm, tender left parotid mass was palpated. Contrast CT scan demonstrated a heterogeneous solid and cystic mass along the posterior margin of the left parotid gland. FNA was performed by using a 25-gauge needle, and 12 mL of cloudy pink fluid was obtained. The smears revealed acute and chronic inflammatory cells, histiocytes, and acellular structures with rhomboid, polygonal, and needle-like shapes. These structures were nonbirefringent on polarized microscopy and stained bright orange with Papanicolaou and deep blue with Diff-Quik stains. These morphologic features were consistent with amylase crystalloids. No malignant cells were detected. At follow-up 10 days later, neck swelling had improved. Amylase crystalloids occur infrequently in FNA smears. Their lack of association with malignant conditions in literature favors a diagnosis of a benign lesion when seen on FNA smears of the salivary gland. However, well-established cytologic criteria are a must to rule out malignancy. It is also important to differentiate other types of crystalloids from amylase crystalloids, as the former can be seen in malignant salivary gland tumors.

**Not All Thoracic Neuroendocrine Tumors Are From the Lung: Presentation of Interesting Effusion Findings**

(***Poster No. 115***)

Andrea Hernandez, DO (andrea.hernandez@nyumc.org); Tamar C. Brandler, MS, MD; Andre Moreira, MD, PhD; Aylin Simsr, MD. Department of Pathology, New York University, New York.

Metastatic neuroendocrine tumors may pose a diagnostic challenge, particularly when the site of primary origin is unknown. Given that >50% of neuroendocrine tumors occur in the lung or gastrointestinal tract, other origins are often overlooked. We present the case of a 63-year-old man referred to us after ultrasonography performed for liver transaminase elevation showed scattered splenic lesions. A PET scan revealed an FDG-avid supraclavicular lymph node. We aperformed a pericardial fluid drainage and found an amylase crystalloid deposit. Histologic examination showed amylase crystalloids and synaptophysin (Figure 198, B), and PAX-8 (Figure 198, C), and were negative for TTF-1 (Figure 198, D). Ki-67 stain performed on the concurrent pericardial resection showed 40% to 70% proliferation.

Type B2 thymomas are lymphocyte-rich tumors consisting of neoplastic polygonal epithelial cells with round to slightly ovoid nuclei, vesicular chromatin with small, prominent nucleoli set in a background of numerous immature T cells. Most patients (54%) present with myasthenia gravis, while others experience local symptoms (chest pain, cough, dyspnea, and superior vena cava syndrome). Rarely, these tumors present with pure red cell aplasia, hypogammaglobulinemia, and/or other autoimmune disorders. B2 thymomas occur in the anterior mediastinum but commonly show infiltration into the surrounding and adjacent structures as well as pleural dissemination. We present a case of a 51-year-old woman with a history of myasthenia gravis and a B2 thymoma who underwent thymectomy in 2010 presenting with myasthenia exacerbation characterized by weakness of all extremities,
bilateral eyelid closure weakness, mild ptosis, mild speech difficulties, and difficulty of breathing. Imaging showed a left lower lobe lung mass involving the pleura. Core imprint and biopsy showed epithelial tumor cells admixed with proliferating immature T lymphocytes (Figure 199, A and B). The epithelial cells are highlighted by cytokeratin (Figure 199, C) CK5/6 and FAX-b, while most T lymphocytes are terminal deoxynucleotidyl transferase (TdT) positive (Figure 199, D). The prognostic significance of various hematopoietic cells available in thymomas (stage III and IV) have poor prognosis, resulting in death. Currently, the patient is undergoing plasma exchanges and has survived 2 recent episodes of cardiac arrest due to severe bradycardia. Possible treatment options are currently being discussed with the patient.

Intrathyroidal Lymphoepithelial Cyst Mimicking a Colloid Nodule on Fine-Needle Aspiration

(Poster No. 117)

Hasanain Hasan, MD; Reese Randle, MD; Zeinab Hasan, MD; Julie Dueber, MD (jcdueber@gmail.com). Departments of Pathology and Surgery, University of Kentucky, Lexington.

Intrathyroidal lymphoepithelial cysts are part of the spectrum of changes associated with chronic lymphocytic thyroiditis. A 42-year-old woman presented with a 4.5-cm dominant left thyroid nodule. She had a history of Hashimoto disease that was diagnosed at age 9 years. Ultrasound examination showed a heterogenous, isoechogenic nodule without calcifications consistent with a colloid cyst. The background thyroid was diffusely heterogeneous. Fine-needle aspiration showed abundant thick blue-violet material with craking on Diff-Quik-stained slides and light blue to pink material on Papanicolaou-stained slides. Few groups of follicular cells and macrophages were within the material. The findings were consistent with a benign colloid nodule (Bethesda category II). Owing to the size of the nodule, a lobectomy was performed. Gross examination showed a 3.0-cm hemorrhagic cavity with surrounding pale thyroid tissue. Microscopic examination showed a predominantly denuded cyst lining with foci of squamous epithelium consistent with an intrathyroidal lymphoepithelial cyst. The background thyroid had smaller lymphoepithelial cysts, solid cell nests, and marked chronic lymphocytic thyroiditis. Scant colloid was present. The lymphoepithelial cyst was marked, which may indicate that the abnormal glycogenated cells in 26 cases (52%) and only 19 atypical cells with features diagnostic of ASCUS (38%). We found 33 atypical glyco
genated cells in review of 50 LSIL Pap test slides (66%) and 28 had features diagnostic of LSIL (56%). In the latter study, only 6 of these abnormal cells were marked in the screening process (12%).

Conclusions: During the screening process a low percentage of cells were marked, which may indicate that the abnormal glycogenated cells are not viewed with scrutiny. We recommend more attentiveness to the glycogenated cells when evaluating Pap test slides.

Papillary Thyroid Carcinoma With Hobnail Features Arising in a Background of Langerhans Cell Histiocytosis in Thyroid Gland

(Poster No. 120)

Yan Liu, MD, PhD; (yanliu@llu.edu); Mai Gu, MD, PhD; Pedro De Andrade Filho, MD; Camilla Cobb, MD; Anwar Raza, MD; Pamela Wat, MD. Departments of Pathology and Surgery, Loma Linda University Health, Loma Linda, California; Department of Pathology, PathCare Diagnostics Inc, Corona, California.

Papillary thyroid carcinoma (PTC) associated with thyroid Langerhans cell histiocytosis (LCH) is extremely rare. Here, we describe a case of PTC arising in a background of LCH as demonstrated in fine-needle aspiration, core needle biopsy, and surgical resection specimens. A 44-year-old woman diagnosed with LCH in the lung and scalp skin 6 years ago presented with an anterior neck mass. A computed tomography scan revealed heterogeneous enhancement of the thyroid gland with an 8.3×3.2-cm infiltrative mass involving its anterior aspect. Fine-needle aspiration showed a highly cellular yield composed of sheellite-like and occasional papillary arrangements of cells displaying enlarged nuclei with irregular nuclear contours, occasional intranuclear pseudoinclusions and grooves, pale finely granular chromatin, multiple micro
nucleoli, and dense squamous cytoplasm (Figure 200, A). A second population of single and loosely cohesive large cells with similar longitudinal nuclear grooves but abundant lacey cytoplasm and inconspicuous nucleoli was also present (Figure 200, B). Rare cosinophilcs were noted in the background. Core biopsy and surgical resection specimens showed a similar dual cell population. The morphologic and immunophenotypic features support the presence of extensive Langerhans cell infiltration within the fibrovascular cores of PTC (Figure 200, C and D) and cobbling surrounding benign thyroid follicles. Interestingly, characteristic “comet-like cells” and hobnail appearance were noted focally within the PTC component in cytologic and histologic preparations, respectively. In conclusion, although LCH displays cytomorphicologic overlap with PTC, careful microscopic
Gastrointestinal stromal tumor (GIST) is the most common KIT-positive soft tissue sarcoma arising in the GI tract. Although KIT immunostaining is a sensitive marker for GISTs, KIT can be expressed in other tumors including melanoma and high-grade sarcomas. We report the case of a 64-year-old woman presenting with abdominal pain, noted on abdominal computed tomography to have a 14-cm solid, heterogeneous mass involving the hepatic flexure. Colonoscopy showed a submucosal mass circumferentially involving the colon above the ileocecal valve. Needle biopsies demonstrated a highly cellular neoplasm containing oval to spindle cells (Figure 201, A) with high mitotic activity (Ki-67 > 75%). The tumor was diffusely positive for KIT (Figure 201, B) and SMA and negative for CD34, Desmin, S100, and DOG1 (Figure 201, C). Initial results were suggestive of GIST and the patient underwent consultation for initiation of neoadjuvant imatinib therapy. MDM2 gene amplification was confirmed by FISH (Figure 201, D) and raised the possibility of a dedifferentiated liposarcoma. No KIT or PDGFRα mutations were detected. Resection revealed a solid, heterogeneous mass invading the muscular wall of the colon. Microscopy demonstrated a predominantly spindle cell lesion arranged in fascicles with transition to a well-differentiated liposarcoma (both components exhibited MDM2 amplification). Interestingly, KIT positivity was limited to the minor component of high-grade oval cells with scant cytoplasm. KIT positivity traditionally associated with GISTs is not specific for GIST. Since therapy is radically different for GIST and dedifferentiated liposarcoma, it is important to be aware of this diagnostic pitfall, especially for tumors involving the GI tract.

We present a case of a 68-year-old man recently diagnosed with Gleason 7 prostatic adenocarcinoma who was noted to have inguinal lymphadenopathy and a mass near the base of the penis on staging imaging. Microscopically, biopsies demonstrated proliferation of atypical, round cells with dense, globular eosinophilic cytoplasm in a myxohyaline background (Figure 202, A; ×100). Immunohistochemical stains were positive for CAM 5.2 (focal; Figure 202, B), ERG (Figure 202, C), CD34, and GATA-3, and were negative for PSA, PSMA, TTF-1, CDX-2, chromogranin, synaptophysin, AE1/AE3, NKX3.1, and S100, and showed loss of INI1 expression (Figure 202, D). Given the patient’s age and diagnosis of prostate cancer, metastatic disease was a diagnostic consideration. Epithelioid morphology, conspicuous nucleoli, and staining for ERG may be misleading. However, the remaining immunohistochemical and microscopic features were quite atypical for prostate cancer. Thus, given the positive staining with CD34 and loss of INI1, a diagnosis of epithelioid sarcoma, proximal type was rendered. Epithelioid sarcoma is a rare soft tissue sarcoma that occurs most commonly in young adults and is twice as common in males. Although it has a relatively distinct morphology, it may be confused with a variety of conditions, particularly carcinomas. It is categorized into classical and proximal types, of which the proximal type is less common and more aggressive. Treatment requires early radical excision combined with radiochemotherapy. There is high risk for local recurrence and metastasis, requiring long-term follow-up. In addition to its rarity, we feel that this case of proximal-type epithelioid sarcoma occurring in the penis illustrates potential diagnostic confusion with metastatic prostate cancer.

Pleomorphic Hyalinizing Angiectatic Tumor: A Rare and Challenging Case
(Poster No. 123)
Ashley Holloman, MD1 (ashley.holloman@bcm.edu); Komal Arora, MD2; Ya Xu, MD, PhD.2 1Department of Pathology & Immunology, 2Department of Pathology and Laboratory Medicine, Baylor College of Medicine, Houston, Texas.

We present a case of a 68-year-old man recently diagnosed with Gleason 7 prostatic adenocarcinoma who was noted to have inguinal lymphadenopathy and a mass near the base of the penis on staging imaging. Microscopically, biopsies demonstrated proliferation of atypical, round cells with dense, globular eosinophilic cytoplasm in a myxohyaline background (Figure 202, A; ×100). Immunohistochemical stains were positive for CAM 5.2 (focal; Figure 202, B), ERG (Figure 202, C), CD34, and GATA-3, and were negative for PSA, PSMA, TTF-1, CDX-2, chromogranin, synaptophysin, AE1/AE3, NKX3.1, and S100, and showed loss of INI1 expression (Figure 202, D). Given the patient’s age and diagnosis of prostate cancer, metastatic disease was a diagnostic consideration. Epithelioid morphology, conspicuous nucleoli, and staining for ERG may be misleading. However, the remaining immunohistochemical and microscopic features were quite atypical for prostate cancer. Thus, given the positive staining with CD34 and loss of INI1, a diagnosis of epithelioid sarcoma, proximal type was rendered. Epithelioid sarcoma is a rare soft tissue sarcoma that occurs most commonly in young adults and is twice as common in males. Although it has a relatively distinct morphology, it may be confused with a variety of conditions, particularly carcinomas. It is categorized into classical and proximal types, of which the proximal type is less common and more aggressive. Treatment requires early radical excision combined with radiochemotherapy. There is high risk for local recurrence and metastasis, requiring long-term follow-up. In addition to its rarity, we feel that this case of proximal-type epithelioid sarcoma occurring in the penis illustrates potential diagnostic confusion with metastatic prostate cancer.

Pleomorphic Hyalinizing Angiectatic Tumor: A Rare and Challenging Case
(Poster No. 123)
Ashley Holloman, MD1 (ashley.holloman@bcm.edu); Komal Arora, MD2; Ya Xu, MD, PhD. 1Department of Pathology & Immunology, 2Department of Pathology and Laboratory Medicine, Baylor College of Medicine, Houston, Texas.

We present a case of a 68-year-old man recently diagnosed with Gleason 7 prostatic adenocarcinoma who was noted to have inguinal lymphadenopathy and a mass near the base of the penis on staging imaging. Microscopically, biopsies demonstrated proliferation of atypical, round cells with dense, globular eosinophilic cytoplasm in a myxohyaline background (Figure 202, A; ×100). Immunohistochemical stains were positive for CAM 5.2 (focal; Figure 202, B), ERG (Figure 202, C), CD34, and GATA-3, and were negative for PSA, PSMA, TTF-1, CDX-2, chromogranin, synaptophysin, AE1/AE3, NKX3.1, and S100, and showed loss of INI1 expression (Figure 202, D). Given the patient’s age and diagnosis of prostate cancer, metastatic disease was a diagnostic consideration. Epithelioid morphology, conspicuous nucleoli, and staining for ERG may be misleading. However, the remaining immunohistochemical and microscopic features were quite atypical for prostate cancer. Thus, given the positive staining with CD34 and loss of INI1, a diagnosis of epithelioid sarcoma, proximal type was rendered. Epithelioid sarcoma is a rare soft tissue sarcoma that occurs most commonly in young adults and is twice as common in males. Although it has a relatively distinct morphology, it may be confused with a variety of conditions, particularly carcinomas. It is categorized into classical and proximal types, of which the proximal type is less common and more aggressive. Treatment requires early radical excision combined with radiochemotherapy. There is high risk for local recurrence and metastasis, requiring long-term follow-up. In addition to its rarity, we feel that this case of proximal-type epithelioid sarcoma occurring in the penis illustrates potential diagnostic confusion with metastatic prostate cancer.

Pleomorphic Hyalinizing Angiectatic Tumor: A Rare and Challenging Case
(Poster No. 123)
Ashley Holloman, MD1 (ashley.holloman@bcm.edu); Komal Arora, MD2; Ya Xu, MD, PhD. 1Department of Pathology & Immunology, 2Department of Pathology and Laboratory Medicine, Baylor College of Medicine, Houston, Texas.
Low-grade fibromyxoid sarcoma (LGFMS) is a relatively rare soft tissue tumor. It typically occurs in the proximal extremities or trunk but is rarely described as a primary neoplasm within the thoracic cavity. We report a case of an LGFMS of the pleura with confirmatory workup. A 50-year-old man presented with recurrent right pleural effusions for 2 months and was found to have multiple pleural nodules. Grossly, the tumor consisted of a firm, white, irregularly shaped, glistening mass with a white cut surface. Sections showed a fairly circumscribed spindle cell neoplasm with moderate cellularity and alternating myxoid and fibrous areas (Figure 203, A). Tumor cells exhibited mild to moderate atypia but no necrosis or significantly increased mitosis. Immunostains for CK, SMA, Desmin, EMA, CD34, and calretinin were all negative. AMUC4 stain was positive (Figure 203, B). Findings were consistent with a low-grade fibromyxoid sarcoma. Fluorescence in situ hybridization (FISH) study, using dual-color break-apart probes flanking the common breakpoint site in the FLIS gene (16p11) (CytoCell, Inc), indicated possible FLIS rearrangement, and clonal evolution with gain of an additional copy of FLIS gene and loss of 3 telomeric repeats to the FLIS gene. Further studies will be attempted to elucidate the exact nature of the rearrangement. Although rare, LGFMS should be considered as a possibility for a spindle cell intrathoracic tumor. MUC4 staining and FISH studies are most helpful in the diagnostic workup.

Intracortical Chondroma Arising in Femur: Presentation of a Rare Case

(Donghai Wang, MD, PhD (donghai.wang@downstate.edu); Vicent Vigorita, MD; Amir Momeni, MD; Joshua Kagan, MD; Anthony Nicastri, MD; Jianying Zeng, MD. Department of Pathology, SUNY Downstate Medical Center, Brooklyn, New York.

Intracortical chondroma is an exceedingly rare variant of chondroma, with only 11 cases reported in the English literature. The current case was that of a 27-year-old woman who presented with left knee pain for several months. There was no swelling, erythema, or tenderness and the motion of the knee joint was not limited. Radiographs and computed tomography (CT) scan revealed a 1.5-cm cortically based lytic lesion in the distal metaphysis of left femur. The lesion was well circumscribed with a rim of sclerotic bone (Figure 205, A). MRI showed the lesion was low to intermediate signal on T1- and high signal on T2-weighted images (Figure 205, B). No cortical permeation or soft tissue
extension was identified. CT-guided biopsy was performed. Histologically, the tumor was composed of hypocellular hyaline cartilage with focal increased cellularity and moderate nuclear atypia. No mitotic figures were identified and proliferation rate by Ki-67 immunostaining was low (<2%) (Figure 205, C and D). Based on clinicoradiologic correlation, a pathologic diagnosis of intracortical chondroma was entertained. The patient underwent curettage and bone grafting. The surgical specimen showed similar pathologic finding as biopsy. Atypical features, such as atypia or increased cellularity, were considered in the differential diagnosis. Clinical, radiologic, and pathologic correlation is key to the correct diagnosis.

**Ewing Sarcoma With Epithelial Differentiation, Including “Adamantinoma-like” Features: Clinicopathologic, Immunohistochemical, and Molecular Cytogenetic Profile of 20 Cases Diagnosed at a Single Institution in India**

(Paper No. 128)
Bhарат Rekhi, MD, DNB, MCAP (rekhi.bharat@gmail.com); Omshree Shetty, PhD; Tushar Vora, MD; Jyoti Bajpai, MD, DM; Departments of 1Surgical Pathology, Division of Molecular Pathology and Translational Medicine, 2Division of Molecular Pathology and Translational Medicine, and 3Medical Oncology, Bone and Soft Tissues, Disease Management Group, Tata Memorial Hospital, Mumbai, India.

**Context:** Ewing sarcomas (ESs) with epithelial differentiation, including “adamantinoma-like” features, are rare tumors.

**Design:** Twenty cases of ESs with epithelial differentiation, diagnosed during 2011–2017, were included after review. Immunohistochemistry was performed on formalin-fixed, paraffin-embedded tissue sections by immunoperoxidase method using a MACH2 Universal HRP-Polymer detection kit. EWSR1 rearrangement was tested by fluorescence in situ hybridization.

**Results:** Twenty cases occurred involving 10 males and 10 females, with age ranging from 8 to 36 years (average, 21 years), commonly in upper extremities (n = 6), followed by pelvis (n = 4), paravertebral tissues (n = 4), lower extremities (n = 3), calcaneum (n = 1), supraclavicular region (n = 1), and lung (n = 1). Seventeen tumors were either diagnosed as ESs (n = 15; Figure 206, A), or favored as ESs over synovial sarcomas (SSs, n = 2). Two cases were diagnosed as “preferably” SSs and as a single case as a poorly differentiated carcinoma (PDCA). The most common histopathologic pattern was nesting type, comprising basaoid round to oval malignant cells (Figure 206, B). Immunohistochemically, tumor cells showed membranous positivity for MIC2 (20/20); diffuse positivity for Fli1 (17/17); focal positivity for synaptophysin (4/12), and variable positivity for pancytokeratin (AE1/AE3) (Figure 206, C) (17/18) and EMA (3/3). Seventeen tumors (85%) displayed EWSR1 rearrangement (Figure 206, D). Treatment and follow-up (11 months–17 years) details were available in 14 cases (70%). Most patients (7/14) were treated with specific neoadjuvant chemotherapy, followed by resection. Six patients (42.8%) were offered chemotherapy and 9 (64.2%), adjuvant radiotherapy. Three cases developed recurrences and 4 developed metastasis. Finally, 6 patients were alive with disease, 2 were free of disease, and 6 were receiving treatment.

**Conclusions:** This study constitutes as one of the largest in documentation of these rare tumors. Diagnosis of ESs with epithelial differentiation requires molecular confirmation. Exact diagnosis has significant treatment implications, as these tumors are treated differently from their mimics, including SSs, PDCA, and myoepithelial carcinomas.

**Nodal and Extranodal Myeloid Sarcoma: A Clinical Pathologic Review**

(Paper No. 129)
Prith Rohra, MD (prith.rohra@rush.edu); Waqas Mahmud, MD; Fatima Mir, MD; Jayjay Blanco, MD; Karina Furlan, MD; David Lucero, Departments of 1Surgical Pathology, Division of Molecular Pathology and Translational Medicine, and 2Medical Oncology, Bone and Soft Tissues, Disease Management Group, Tata Memorial Hospital, Mumbai, India.

**Purpose:** Myeloid sarcoma is a rare extramedullary tumor characterized by the proliferation of myeloid cells. It is primarily a nodal disease, and extranodal involvement is rare.
MD; Paolo Gattuso, MD. Department of Pathology, Rush Medical Center, Chicago, Illinois.

Context: Myeloid sarcoma is an extramedullary presentation of leukemia, composed of mature or immature myeloid blasts. It can occur de novo or in association with AML, MPNs, or MDS. We reviewed the clinicopathologic features of myeloid sarcomas diagnosed in our institution in view of the literature.

Design: Myeloid sarcomas diagnosed from 1997–2016 at Rush Medical Center were reviewed. Clinicopathologic findings including age, sex, accompanying hematologic diseases, anatomic site of involvement at time of diagnosis and relapse were noted along with cytogenetic features.

Results: Fifty-five myeloid sarcoma patients were identified (40 men and 15 women) with age ranging from 21 to 79 years. The most common location at the time of relapse was lymph node (17/55 [31%]) followed by skin (6/55 [11%]), brain (6/55 [11%]), bone (6/55 [11%]), soft tissue (4/55 [7%]), intranasal (2/55 [3%]), breast (2/55 [3%]), orbit (2/55 [3%]), retroperitoneum (2/55 [3%]), and 1 each in bladder, skeletal muscle, pelvis, abdomen, lung, paravertebral, mediastinum, and ovary. Twenty-two of 55 (40%) had an abnormal karyotype. Twenty-five of 55 (45%) had bone marrow involvement at the time of diagnosis. Nineteen of 55 (34%) died ofthe disease.

Conclusions: Myeloid sarcoma is more common in males (40/55 [72%]). Any site of the body may be involved, lymph nodes being the most common (17/55 [31%]). Mean survival after the diagnosis of myeloid sarcoma was 3.5 years. Myeloid sarcoma is a neoplasm with variable morphologic and phenotypic features that may create a challenging diagnosis for a pathologist especially when a diagnosis of AML is not established.

Massive Localized Lymphedema of Thigh, a Complication of Morbid Obesity, Clinically Mimicking Liposarcoma

(Raafat F. Makary, MD, PhD; Sarah Fernandez, MD; Daren Brow, MD. Department of Pathology, Shands Hospital, UF, Jacksonville, Florida.)

Massive localized lymphedema (MLL) is a rare condition that typically complicates morbid obesity usually in middle-aged female patients. The lesion has predilection for lower abdomen and inner side of the thigh. The lesion may become extremely large, infected, ulcerated, or necrotic, raising clinical concern for malignancy. We present a case involving a large, painless right inner thigh mass (Figure 207, A) in a 46-year-old morbidly obese woman (469 pounds). The mass was very heavy, limiting her ability to walk, and caused her to lose balance and fall. Grossly, the resected lesion (60 x 40 cm) weighed 28 pounds and was covered by “peau d’orange”–appearing skin. Serial sectioning showed lobulated fibrous tissue separated by white fibrous septa (Figure 207, B and C). Histology showed subcutis expansion by edema, fibrotic septa with dilated lymphatics (Figure 207, D), and focal fat necrosis. The postoperative course was uneventful and the patient regained her ability to walk. MLL is a benign reactive pseudotumor, mostly associated with morbid obesity. Pathogenesis of MLL is multifactorial including lymphatic/vascular obstruction by large folds of adipose tissue. MLL may be complicated by infection, ulceration, or tissue necrosis. MLL may become extremely large, concerning for malignancy, and may be histologically confused with sclerosing well-differentiated liposarcoma. However, the preserved lobulated architecture of subcutaneous fat and lack of significant cytoatypia or lipoblasts are distinctive for MLL. Angiosarcoma complicating chronic lymphedema has been reported in MLL. No evidence for sarcomatous change was identified in our case. The treatment of choice is surgical excision. However, recurrence may be expected with persistent underlying morbid obesity.

High-Grade Extraskeletal Myxoid Chondrosarcoma: A Case Report of an Uncommon Entity

(Fatimah Alruwaii, MBBS; Zhaoxiong Chen, MD, PhD. Department of Pathology, Indiana University School of Medicine, Indianapolis.)

Extraskeletal myxoid chondrosarcoma (EMC) is a soft tissue malignant tumor characterized by specific chromosomal abnormalities. This disease has historically been considered indolent both histologically and clinically. A rarer subset of EMC exists that demonstrates higher morphologic grade and worse prognosis. The subset has been sometimes referred to as high-grade EMC. Herein we present a case of this entity that underwent rapid clinical progression. The patient is a 69-year-old man with a 22-cm right lateral thigh mass. Resection specimen showed vaguely nodular mass with a pink-tan cut surface with focal hemorrhage and necrosis. Histologic examination showed cytologically malignant neoplasm composed of nests and trabeculae of epithelioid cells with quite conspicuous amphophilic cytoplasm and plump vesicular nuclei with variably prominent nucleoli. These cells were associated with a myxoid matrix. Other parts of the tumor showed solid nests and sheets of high-grade epithelioid cells. The differential diagnosis considered for the case included myoepithelial carcinoma and high-grade EMC. Immunohistochemical stains were performed and showed that the malignant cells were negative for S100 protein, GFAP, EMA, and pan-keratin, thus ruling out myoepithelial carcinoma. FISH analysis was positive for NR4A3 gene rearrangement. The case was signed out as a high-grade EMC. High-grade EMC is a rare type of EMC that often displays epithelioid morphology. Tumors of this type are strongly associated with aggressive clinical behavior, and may resemble conventional EMC and may present a diagnostic challenge because of the unusual higher-grade morphology.

Malignant Ossifying Fibromyxoid Tumor

(Ayesha S. Siddique, MD (ayesha.siddique@hhchealth.org); Srini vas Mandavilli, MD. Department of Pathology and Laboratory Medicine, Hartford Hospital, Hartford, Connecticut.)

Ossifying fibromyxoid tumor (OFMT) is a rare soft tissue tumor, described in 1989 and currently classified as a neoplasm of uncertain origin with intermediate biologic potential. Limited studies have been reported and malignant variants are even rarer. Molecular testing has further refined the classification of this entity. We present a case of a 61-year-old woman with past excision of a subcutaneous thigh mass, clinically diagnosed as a sebaceous cyst or lipoma. Excision demonstrated a 4-cm mass that on histologic examination revealed a well-circumscribed tumor with moderate cellularularity composed mainly of epithelioid cells with variable atypia (Figure 208, A). The epithelioid areas had focal of hyalinization reminiscent of sclerosing epithelioid fibrosarcoma (Figure 208, B) and other hypocellular areas with myxoid changes (Figure 208, C). There were foci of severe atypia with spindle cells, mitoses (12/10 high-power fields; Figure 208, D), and rare necrosis. Rare spicules of mature bone were present in the periphery of the tumor. Immunohistochemical studies displayed focal positivity for S100, while SOX-10, EMA, desmin, caldesmon, myogenin, TLE-1, STAT6, and MUC4 were negative. H3K27 showed no loss of expression. Molecular testing by FISH analysis was positive for Ph1 gene.
Primary Subcutaneous Ewing Sarcoma in an Older Adult

(Poster No. 133)

Yan Chen Wongworawat, MD, PhD (ychenwongworawat@llu.edu); Laura Denham, MD. Department of Pathology, Loma Linda University, Loma Linda, California.

Primary subcutaneous Ewing sarcoma is a rare, superficially located lesion primarily seen in younger patients, typically younger than 50 years. We describe a very unusual case of primary subcutaneous Ewing sarcoma in an older male. A 53-year-old man with past medical history of coronary artery disease presented with a large left shoulder mass, bilateral lower extremities numbness and slight weakness, and incontinence. MRI showed a 20-cm large left posterolateral shoulder subcutaneous mass with mildly prominent left axillary lymph nodes, as well as a 13-× 6 extraluminal mass with associated severe canal stenosis. Resection of the left shoulder mass revealed monotonous population of round, medium-sized cells with mildly irregular borders, coarse to vesicular chromatin, and small nucleoli. Bands of sclerotic fibrous tissue focally separated areas of sheetlike growth into nests. Immunohistochemically, the tumor cells were positive for S100 (weak), CD99 (membranous), and keratin (focally). A biopsy of the left shoulder mass showed similar histology. Cytogenetic studies revealed a translocation involving the EWSR1 (22q12) gene. The overall morphologic, immunophenotypic, and cytogenetic features supported a Ewing sarcoma. To our best knowledge, this is the first report of primary subcutaneous Ewing sarcoma in a patient older than 50 years. Our case highlights the need to consider Ewing sarcoma as a differential diagnosis of a subcutaneous small round blue cells lesion, even if the patient is older than is typical for Ewing sarcoma. Our case is of older age than is typical for Ewing sarcoma.

The Challenge in the Diagnosis of Atypical Giant Cell Tumor of Bone by Computed Tomography–Guided Core Biopsy

(Poster No. 135)

Heba Saad, MD (heba.saad@jax.ufl.edu); Ronald Araneta, MD; Jinous Saremian, MD; Anwer Siddiqui, MD; Raafat Makary, MD, PhD. Department of Pathology, University of Florida College of Medicine, Jacksonville.

Giant cell tumor of bone is benign, but locally destructive, typically arising in the meta-epiphysis of long bones with predilection for the knee. It is characterized by presence of mononuclear cells and abundant multinucleated giant cells. Atypical behavior and metastatic potential in giant cell tumors are uncommon (2% of cases). We report a case of atypical giant cell tumor from a 28-year-old man with sickle cell disease presenting with worsening left knee pain for 3 months. MRI of knee showed bone infarction with lytic lesion (4.7 × 5.4 × 6.9 cm) of medial femoral condyle, endostal scalloping, cortical disruption, and internal enhancement (Figure 209, A), concerning for infarction-induced sarcoma. Computed tomography–guided core biopsy revealed extensive necrosis; spindle/oval mononuclear tumor cells with eosinophilic, finely vacuolated cytoplasm; focal prominent nuclear pleomorphism; occasional mitoses (Figure 210 B through D); rare multinucleated giant cells; and hemosiderin pigment admixed with woven bone. The histology did not support the diagnosis of infarct-induced sarcoma but was consistent with an atypical bone tumor with rare giant cells. The tumor was treated by curettage in an outside institution. Pathology consultation at Memorial Sloan Kettering Cancer Center described the findings similar to the previous biopsy as cellular atypia with rare giant cells and tumor positivity for H3K27M consistent with giant cell tumor of bone with atypical features concerning for high recurrence risk and malignancy, even though frank sarcomatous features were not present. Making a diagnosis of atypical giant cell tumor of bone could be challenging on a core biopsy and requires careful cytomorphologic evaluation.
The patient is a 26-year-old man with obesity and hypertension, who initially presented with right lower extremity weakness, numbness, and pain. Physical examination showed right foot drop and ankle clonus. MRI of the thoracic spine found an epidural mass from T6 to T8 with narrowing of the spinal canal and causing cord compression. A follow-up computed tomography scan was suggestive of erosive spondyloarthropathy. Surgical resection was performed and showed a white "cheeselike" lesion compressing the dura. An intraoperative smear of the tissue showed abundant amorphous material (Figure 211, A), suggestive of crystalloids. Frozen and permanent sections (Figure 211, B) showed whitish aggregates of strandlike material, surrounded by inflammatory cells, including many foreign body giant cells. Under polarized light this material revealed strongly negatively birefringent needle-shaped crystals (Figure 211, C and D), consistent with monosodium urate crystals. In the literature that describes spinal/axial gout, the patient usually has a known and prolonged history of gout affecting the appendicular skeleton, typically with a history of gouty tophi, whereas this was our patient’s initial presentation, making the diagnosis difficult, since the index of suspicion was low. Also, axial gout usually presents with spinal cord compression on imaging; however, in this case, the radiologic impression was that of a mass lesion, mimicking a neoplasm or hematoma, further clouding the diagnosis.

In conclusion, primary presentation of gout as an epidural mass is exceedingly rare. A cheeselike consistency grossly and amorphous material microscopically should prompt the pathologist to examine the slide under polarized light to arrive at the correct diagnosis.

---

Calcium pyrophosphate dihydrate (CPPD) crystal deposition disease generally occurs in articular and para-articular structures. Rarely, extraarticular structures are involved. We present the uncommon case of an 81-year-old man with past medical history of coronary artery disease and type 2 diabetes mellitus who reported approximately 5 years of progressive dysphagia limited to solids, and dyspnea. A tender, immobile mass surrounding the left sternoclavicular joint (SCJ) was found on physical examination without palpable lymphadenopathy in the cervical, supraclavicular, or axillary chains. MRI with contrast revealed a left sternoclavicular noncalcified mass with joint effusion extending along the undersurface of the left proximal clavicle, measuring 2.9 cm in diameter, suggestive of a primary soft tissue neoplastic lesion. Left sternoclavicular synovectomy with medial clavicle excision was performed (Figure 212, A). On microscopic examination (Figure 212, B and C), the synovium was composed of numerous foci of dystrophic calcifications with mild cellular response consisting mostly of histiocytes. Many rhomboid crystals with positive birefringence were identified in these areas consistent with CPPD crystal deposition disease. To our knowledge, this case represents the fourth described instance of SCJ tophaceous CPPD. Adding this report to the body of literature contributes to the expansion of proper identification of a rare condition that could potentially jeopardize adjacent vascular, respiratory, or digestive structures. Performing diagnostic imaging and biopsy could avoid misdiagnosis of malignancy and more aggressive surgical resection.
in undifferentiated pleomorphic sarcoma (UPS). We report a case of a 68-year-old woman with soft tissue tumor in the right anterior calf with the histopathologic examination showing large rounded to polygonal pleomorphic cells with irregular hyperchromatic nuclei and prominent nucleoli with intact neutrophils in their eosinophilic cytoplasm (Figure 213, A and B). Immunohistochemistry studies showed diffuse positivity of these cells for vimentin (Figure 213, C) with negative expression of cytokeratin CAM 5.2 epithelial marker; CD45, CD43, and CD30 lymphocytic markers; CD21, a dendritic cell marker; CD20 for B lymphocytes; CD3 for T lymphocytes; S100 to rule out neural crest-derived tumors; CD1A for Langerhans histiocytes; and Myogenin and Desmin for myogenic neoplasms. CD68 and CD163 were used to highlight intratrabecular histiocytes, which are common findings in UPS. Lysozyme was used to highlight the neutrophils within the neoplastic cells (Figure 213, D). These findings were consistent with high-grade UPS. This is a novel report of an UPS with emperipolisis. Further studies of its medical significance in other soft tissue tumors, in combination with other malignancies at the molecular level, or in correlation with treatment, would be helpful in achieving targeted therapy for UPS.

Periosteal Osteosarcoma of the Frontal Bone: First Ever Reported Case
(Poster No. 139)

Christina Ombres, MD1 (ombres@health.usf.edu); Nicole D. Riddle, MD,2 1Department of Pathology, University of South Florida, Tampa; 2Department of Pathology, Ruffolo, Hooper, and Associates/ Tampa General Hospital, Tampa, Florida.

Periosteal osteosarcoma is an uncommon variant of osteosarcoma that typically develops in the second to third decades of life on the surface of long bones—femur (~45%) and tibia (~40%)—in the region of the diaphysis (65%) followed by the metaphysis. Treatment is optimally limb-salvage complete surgical resection with adjuvant chemotherapy being of controversial utility. To date there is 1 case in the literature of a periosteal osteosarcoma on the occipital bone and mandible, but to the best of the authors’ knowledge, this is the first case reported of the frontal bone. A 67-year-old man with a clinical history significant for head trauma 12 years earlier, resulting in subdural hematoma and seizures, presented to plastic surgery with a 1.5-year history of a growing forehead mass. The lesion was 4.5 cm, grossly calcified and was believed by the surgeon to be an osteoma. No radiologic studies were performed before surgery. At procedure, the lesion was present encompassing a large part of the surface of the frontal bone and was removed in 1 piece. Pathology received a lesion with a “roughened” concave surface of thick dense cortical bone with variable cartilaginous component towards the convex surface. Histologic slides demonstrated classic features of periosteal osteosarcoma with atypical bone and cartilage. Periosteal osteosarcoma is a relatively uncommon variant of osteosarcoma and exceedingly rare in the cranium/head and neck (Figure 214).

Predominant Osteosarcomatous Differentiation in a Dedifferentiated Liposarcoma
(Poster No. 140)

Laura Baugh, DO, PhD (Laura.Baugh@BSWhealth.org); David Watkins, MD; Atin Agarwal, MD, Department of Pathology, Baylor University Medical Center, Dallas, Texas.

Well-differentiated liposarcomas may undergo dedifferentiation in approximately 10% of cases, but divergent differentiation with osteosarcomatous components is rare. Osteogenesis in well-differentiated/dedifferentiated liposarcoma has been debated in the literature regarding its metastatic/neoplastic nature. Molecular research suggests that low-grade osteosarcoma and well-differentiated liposarcoma might share a portion of their genetic background, since amplification of the MDM2 and CDK4 genes is present in both sarcomas. We present a case of an 80-year-old man with history of hypertension, arthritis, hyperlipidemia, and atypical lipoma (remote history in left posterior thigh), with an enlarging left posterior thigh mass. The diagnosis on biopsy was intermediate-grade sarcoma, suggestive of dedifferentiated liposarcoma (MDM2 and CDK4 positive). Imaging by computed tomography revealed no evidence of metastatic disease in the chest, abdomen, or pelvis. Following resection of the mass, a diagnosis of dedifferentiated liposarcoma (MDM2 and CDK4 positive) with predominant osteosarcoma (80%) was rendered from the remote history of atypical lipoma. Twenty-eight mitotic figures/10 high-power fields were identified. Well-differentiated liposarcoma areas were not seen. Several reports have documented similar findings with various grades of osteosarcomatous differentiation in well-differentiated/dedifferentiated liposarcoma, predominantly in retroperitoneal and intramuscular locations. The morphology of dedifferentiated areas can vary widely and create interpretive difficulties. Our case exhibited a large proportion (>80%) of osteosarcomatous differentiation. Currently, the biologic potential of osteosarcomatous growth pattern in well-differentiated/dedifferentiated liposarcoma is not entirely clear owing to the rarity of the tumor. Additional case studies and clinical results will hopefully clarify its nature and potential.

Lack of Evidence of Adverse Histologic Findings in Joint Tissue After a 1- to 3-Year Interval of Viscosupplementation Injections
(Poster No. 141)

Marriam Aalai, MD1 (maalai@nyuwinthrop.org); Daniel Shapiro, MD2; Saman Vojdani, MD3; Vincent Vigorita, MD.1 1Department of Pathology, NY University Winthrop Hospital, Mineola, New York; 2Department of Surgery, Stony Brook University Hospital, Stony Brook, New York; 3Department of Pathology, New York Downtown Orthopedic Associates, New York.

Context: Viscosupplementation injections have been used in the therapy of osteoarthritis of the knee; however, their efficacy and risk of adverse reaction remains controversial. This retrospective study evaluated the presence or absence of adverse histologic effects in the synovium and articular cartilage at the time of total knee replacement within 3 years of viscosupplementation with Euflexxa.

Design: Forty total knee replacements during a 4-year period from NYU Winthrop Hospital’s pathology department with a diagnosis of end-stage osteoarthritis were selected for microscopic analysis. Twenty involved Euflexxa injections of the knee 1 to 3 years before surgery. Twenty that did not receive viscosupplementation were used as controls. The cases, read in a blinded fashion, focused on the synovium, most likely to demonstrate an adverse reaction, and residual articular cartilage, most likely to benefit from viscosupplementation. Synovium was categorized by degree of hyperplasia and inflammation. Residual articular cartilage was categorized by staining intensity, graded on a scale of 0 to 3.

Results: The control group showed 9% minimal to moderate synovial hyperplasia, and 55% minimal chronic inflammation. The
injection group showed 38% minimal to moderate synovial hyperplasia, and 31% minimal chronic inflammation. Articular cartilage findings were not appreciably different in both groups.

Conclusions: The analysis of synovium and residual cartilage demonstrated no significant identifiable differences between the 2 groups. Therefore, in our cases, there were no discernible adverse effects of prearthroplasty viscosupplementation, in either synovial tissue or articular cartilage at the time of total knee replacement for degenerative joint disease after a period of 1 to 3 years.

Chondroblastic Osteosarcoma With Pulmonary Metastasis in an Adolescent With Rothmund-Thomson Syndrome

(Poster No. 142)

Kevin Cao, BS1 (kecao@utmb.edu); Adam L. Booth, MD2; Suimin Qiu, MD, PhD2; School of Medicine and 1Department of Pathology, University of Texas Medical Branch, Galveston.

Rothmund-Thomson syndrome is a rare autosomal recessive genodermatosis due to deletions in the RECQL4 gene. Affected individuals present with characteristic growth deficiency, skeletal abnormalities, and poikilodermia. A 13-year-old boy with a history of poikiloderma, bilateral radioulnar synostosis, and congenital absence of the right thumb and its metacarpal presented with a red, papular, perioral rash accompanied by right knee and left elbow pain. Imaging revealed a soft tissue mass surrounding the right distal femoral metaphysis. Frozen section biopsy of the mass revealed a high-grade sarcoma with hyperchromatic spindle cells producing osteoid and anaplastic lacunar cells in malignant cartilage. Permanent sections confirmed the diagnosis of chondroblastic osteosarcoma (Figure 215, A and B). No signs of metastasis were present and the patient underwent chemotherapy. Two years later, routine follow-up imaging demonstrated bilateral inguinal lymphadenopathy and nodules in the middle lobe of the right lung. A lung wedge resection revealed multiple well-stained bilateral inguinal lymphadenopathy and nodules in the middle lobe of the right lung. A lung wedge resection revealed multiple well-circumscribed white-tan, hard nodules. Histology showed malignant bone formation, osteoid production, and vascular invasion consistent with metastatic chondroblastic osteosarcoma (Figure 215, C and D). Rothmund-Thomson syndrome was suspected clinically. Molecular studies failed to detect mutations in the RECQL4 gene. Rothmund-Thomson syndrome is a unique disease presenting in early childhood with poikiloderma, unusual musculoskeletal pain, and a greater risk for development of osteosarcoma. Deletions in RECQL4 on chromosome 8 result in impaired splicing processes. Genetic testing may be ordered when the syndrome is suspected to confirm clinical findings. However, as in our case, deletions in RECQL4 gene are not detected in approximately 33% of affected individuals.

1Department of Pathology, Yale-New Haven Hospital, New Haven, Connecticut; 2Department of Clinical Histopathology, Guy’s, King’s and St Thomas’ School of Medicine, St Thomas’ Hospital, London, United Kingdom; 3Department of Pathology, University of Arkansas, Little Rock; 4Department of Pathology, Kantonsspital Baselland, Liestal, Switzerland.

Context: Inflammatory pseudotumor is an umbrella term used to describe rare, benign proliferations of fibrohistiocytic and/or myofibroblastic spindle cells arising in the setting of chronic inflammation. There have been recent efforts to classify pseudotumors into etiologic and histiogenic subtypes, ranging from inflammatory myofibroblastic tumors to IgG4-related inflammatory pseudotumors. We have reviewed the literature for cases of inflammatory pseudotumor arising owing to infection, which is rare.

Design: We searched the PubMed database for the terms “infectious pseudotumor,” “inflammatory pseudotumor infection,” “mycobacterial spindle cell,” “plasma cell granuloma,” and “pseudotumor” combined with the terms “bacteria,” “bacterial,” “virus,” “viral,” “fungus,” “fungi,” “fungal,” “amoeba,” “amoebic,” “parasite,” or “parasitic.” We selected only those cases that met the following 3 criteria: (1) histology of the mass is described, (2) the mass is composed of a benign spindle cell proliferation in an inflammatory background, and (3) a specific infectious agent was identified by culture, serology, polymerase chain reaction (PCR), immunohistochemistry, or special stains.

Results: We identified 101 cases of infectious pseudotumor, of which 52 occurred in immunosuppressed patients. These pseudotumors were associated with a variety of organisms, including bacteria (73%), viruses (17%), fungi (8%), and parasites (2%). The most common sites were lymph node (23%) and lung (18%). The tumors commonly stained for CD68, and/or SMA (Table).

Conclusions: Infectious pseudotumors are a unique subset of inflammatory pseudotumors that may be treated conservatively with antibiotics. Correct diagnosis may obviate the need for surgical excision and steroid therapy. To identify infectious cases, special stains and culture are recommended.

Locations of Infectious Pseudotumors

<table>
<thead>
<tr>
<th>Location</th>
<th>Cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymph nodes</td>
<td>23 (23)</td>
</tr>
<tr>
<td>Lung/pleura</td>
<td>18 (18)</td>
</tr>
<tr>
<td>Skin</td>
<td>13 (13)</td>
</tr>
<tr>
<td>Spleen</td>
<td>10 (10)</td>
</tr>
<tr>
<td>Soft tissue</td>
<td>10 (10)</td>
</tr>
<tr>
<td>Brain/dura</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Liver</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Luminal gastrointestinal tract</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Intranasal</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Kidney</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Heart</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Middle ear</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Pelvis (multiple organs)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Urachal remnant</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

* Two patients had simultaneous lung and liver pseudotumors.

A Rare Case of Tenosynovial Giant Cell Tumor With Chondroid Metaplasia Involving the Temporomandibular Joint

(Poster No. 144)

Shaun Boyes, MD1 (shaun.boyes@lumc.edu); Albert Song, MD2; Dariusz Borys, MD.1 Departments of 1Pathology and 2Radiology, Loyola University Medical Center, Maywood, Illinois.

We present the case of a 58-year-old man who presented with a right parotid mass that he had noticed 4 to 6 months prior. His past medical history consisted of hypertension and hyperlipidemia, with no history of malignancy. On physical examination, a 4-cm firm, fixed mass was identified in the right preauricular region. There was no skin involvement. Computed tomography scan of the neck showed an intensely enhancing lesion measuring 2.3 × 2.1 × 2.0 cm in the right parotid gland, which was well defined with no invasion of adjacent structures. Histologic sections showed a proliferation of rounded to anaplastic lacunar cells in malignant cartilage. Permanent sections confirmed the diagnosis of chondroblastic osteosarcoma (Figure 215, A and B). No signs of metastasis were present and the patient underwent chemotherapy. Two years later, routine follow-up imaging demonstrated multiple well-stained bilateral inguinal lymphadenopathy and nodules in the middle lobe of the right lung. A lung wedge resection revealed multiple well-circumscribed white-tan, hard nodules. Histology showed malignant bone formation, osteoid production, and vascular invasion consistent with metastatic chondroblastic osteosarcoma (Figure 215, C and D). Rothmund-Thomson syndrome was suspected clinically. Molecular studies failed to detect mutations in the RECQL4 gene. Rothmund-Thomson syndrome is a unique disease presenting in early childhood with poikiloderma, unusual musculoskeletal pain, and a greater risk for development of osteosarcoma. Deletions in RECQL4 on chromosome 8 result in impaired splicing processes. Genetic testing may be ordered when the syndrome is suspected to confirm clinical findings. However, as in our case, deletions in RECQL4 gene are not detected in approximately 33% of affected individuals.

1Department of Pathology, Yale-New Haven Hospital, New Haven, Connecticut; 2Department of Clinical Histopathology, Guy’s, King’s and St Thomas’ School of Medicine, St Thomas’ Hospital, London, United Kingdom; 3Department of Pathology, University of Arkansas, Little Rock; 4Department of Pathology, Kantonsspital Baselland, Liestal, Switzerland.

Context: Inflammatory pseudotumor is an umbrella term used to describe rare, benign proliferations of fibrohistiocytic and/or myofibroblastic spindle cells arising in the setting of chronic inflammation. There have been recent efforts to classify pseudotumors into etiologic and histiogenic subtypes, ranging from inflammatory myofibroblastic tumors to IgG4-related inflammatory pseudotumors. We have reviewed the literature for cases of inflammatory pseudotumor arising owing to infection, which is rare.

Design: We searched the PubMed database for the terms “infectious pseudotumor,” “inflammatory pseudotumor infection,” “mycobacterial spindle cell,” “plasma cell granuloma,” and “pseudotumor” combined with the terms “bacteria,” “bacterial,” “virus,” “viral,” “fungus,” “fungi,” “fungal,” “amoeba,” “amoebic,” “parasite,” or “parasitic.” We selected only those cases that met the following 3 criteria: (1) histology of the mass is described, (2) the mass is composed of a benign spindle cell proliferation in an inflammatory background, and (3) a specific infectious agent was identified by culture, serology, polymerase chain reaction (PCR), immunohistochemistry, or special stains.

Results: We identified 101 cases of infectious pseudotumor, of which 52 occurred in immunosuppressed patients. These pseudotumors were associated with a variety of organisms, including bacteria (73%), viruses (17%), fungi (8%), and parasites (2%). The most common sites were lymph node (23%) and lung (18%). The tumors commonly stained for CD68, and/or SMA (Table).

Conclusions: Infectious pseudotumors are a unique subset of inflammatory pseudotumors that may be treated conservatively with antibiotics. Correct diagnosis may obviate the need for surgical excision and steroid therapy. To identify infectious cases, special stains and culture are recommended.

Locations of Infectious Pseudotumors

<table>
<thead>
<tr>
<th>Location</th>
<th>Cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymph nodes</td>
<td>23 (23)</td>
</tr>
<tr>
<td>Lung/pleura</td>
<td>18 (18)</td>
</tr>
<tr>
<td>Skin</td>
<td>13 (13)</td>
</tr>
<tr>
<td>Spleen</td>
<td>10 (10)</td>
</tr>
<tr>
<td>Soft tissue</td>
<td>10 (10)</td>
</tr>
<tr>
<td>Brain/dura</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Liver</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Luminal gastrointestinal tract</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Intranasal</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Kidney</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Heart</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Middle ear</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Pelvis (multiple organs)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Urachal remnant</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

* Two patients had simultaneous lung and liver pseudotumors.
multinucleated giant cells and hemosiderin deposition were also present (Figure 216). Immunohistochemistry stains revealed CD68 positivity in the giant cells. S100 and p63 were negative. The morphologic features and immunohistochemistry staining patterns were consistent with tenosynovial giant cell tumor with chondroid metaplasia. Tenosynovial giant cell tumor with chondroid metaplasia is a rare proliferative disorder that has a predilection for the temporomandibular joint. The differential diagnosis includes chondroblastoma and dedifferentiated chondrosarcoma. This unusual case shows that chondroid metaplasia can occur in tenosynovial giant cell tumors involving the temporomandibular joint, and thus should be considered in the differential diagnosis of temporomandibular joint masses.

Case Report of Adult Spindle Cell Rhabdomyosarcoma
(Poster No. 145)
Mohamed Kahila, MD (mohamed.kahila@downstate.edu); Donghai Wang, MD; Mary Grace Centeno, MD; Amir Momeni Boroujeni, MD; Jianying Zeng, MD. Department of Pathology, SUNY Downstate Medical Center, Brooklyn, New York.

Spindle cell rhabdomyosarcoma (SCR) is a rare subtype of rhabdomyosarcoma that can impose diagnostic challenges. The 2013 World Health Organization Classification of Tumors of Soft Tissue and Bone classifies SCR as a separate entity, rather than as a rare variant of embryonal rhabdomyosarcoma. SCR is considered to be linked with sclerosing rhabdomyosarcoma, with a predilection for the paratesticular location, especially in boys. Interestingly, several studies have described SCR occurring in adults, with a unique penchant for head and neck, and extremities. Compared to the pediatric type, adult-SCR has a worse prognosis. We report the case of a 38-year-old woman with a 15.5 × 4.2 × 6.9-cm mass arising from the peroneal compartment of the right leg, with significant nuclear atypia, which requires careful cytomorphic evaluation. In view of the limited sampling nature of core biopsy, which may not reflect the histologic spectrum of the lesion, ancillary studies such as S100, SATB2 (for solitary fibrous tumor), MDM2 amplification, and CDk4 (for well-differentiated liposarcoma) may be helpful in excluding other histologically overlapping lesions.

Facial Spindle Cell Lipoma:
A Challenging Diagnosis in Core Needle Biopsy
(Poster No. 146)
Heba Saad, MD (heba.saad@jax.ufl.edu); Ronald Araneta, MD; Jinous Saremian, MD; Anwer Siddiqi, MD; Raafat Makary, MD, PhD. Department of Pathology, University of Florida College of Medicine, Jacksonville.

Most spindle cell lipomas (SCLs) occur in adult males. Almost all of the tumors are solitary, asymptomatic (if small), located in the subcutaneous tissue of the posterior neck, upper back, and shoulder girdle. Rarely maxillofacial regions are affected. We report a case of spindle cell lipoma diagnosed by an ultrasound-guided core biopsy from a 49-year-old man with complaints of a postauricular mass (5.9 cm) for 2 years fluctuating in size and becoming painful. The biopsy showed mature adipocytes and fibroblast-like spindle cells (Figure 217, A through C), strongly positive for CD34 (Figure 217, D), admixed with collagen fibers. Diagnosis of SCL can be challenging in small biopsies because of the histologic overlap with other lesions including dermatofibrosarcoma protuberans, nerve sheath tumors, well-differentiated liposarcoma, and lipomatous hemangioepithelioma/solitary fibrous tumor. Dermatofibrosarcoma is similarly CD34+ with fat contents; however, the characteristic storiform growth pattern of dermatofibrosarcoma is not seen in SCL. Spindle cell lipoma can be confused with benign nerve sheath tumors (neurofibroma and schwannoma) but the spindle cells in nerve sheath tumors are S100 protein positive and CD34–: The distinction of SCL from well-differentiated liposarcoma mainly relies on the absence of multivacuolated lipoblasts and significant nuclear atypia, which requires careful cytomorphic evaluation. In view of the limited sampling nature of core biopsy, which may not reflect the histologic spectrum of the lesion, ancillary studies such as S100, SATB2 (for solitary fibrous tumor), MDM2 amplification, and CDk4 (for well-differentiated liposarcoma) may be helpful in excluding other histologically overlapping lesions.

A Rare Case of Myelolipoma Causing Cholecystitis
(Poster No. 147)
Roshan Mahabir, MD, PhD, MPH (roshan.mahabir@mountsinai.org); Binny Khandakar, MBBS; Malary Mani, MD; Alexander Filatov, MD. 1 Department of Pathology, Mount Sinai St. Luke Roosevelt, New York, New York; 2 Department of Pathology, Mount Sinai Beth Israel, New York, New York.

Myelolipomas are rare benign neoplasms composed of both mature adipose and hematopoietic elements. The adrenal gland is the most common site and extra-adrenal myelolipomas are exceedingly rare with only a few case reports. Here we report myelolipoma as a potential cause of cholecystitis that has never previously been reported. A 57-year-old woman presented with multiple episodes of right upper quadrant pain; imaging showed no stones or lesions and a mildly thickened gallbladder wall consistent with cholecystitis. The patient underwent a laparoscopic cholecystectomy with a removal of a 5.3 × 2.5 × 2.1-cm gallbladder with pink-green smooth serosa and a brown shaggy hepatic resection margin. The specimen was opened to show thin-green bile and no stones, with the gallbladder wall averaging 0.1 to 0.2 cm in thickness. There was a 0.6-cm-diameter firm lymph node located at the cystic duct with a fleshy cut surface. Microscopically, the gallbladder showed mild chronic cholecystitis and the lymph node was benign, with mature adipose tissue, nucleated red cells, myeloid...
elements, and megakaryocytes. Immunohistochemistry was done and the following findings were noted: Factor VIII highlighting megakaryocytes, E-cadherin expressed in nucleated red cells, and myeloperoxidase positivity in myeloid elements. Myelolipoma within the lymph node was diagnosed. In this case, there were no stones or strictures and no other causes except the mass effect of the enlarged lymph node to account for cholecystitis. We present this case to highlight a rare cause of cholecystitis that presented a diagnostic dilemma (Figure 218).

A Rare Case of Translocation-Negative Extraskeletal Myxoid Chondrosarcoma

John M. Gross, MD (jmg144@gmail.com); Nick Dietz, MD. Department of Pathology, Creighton University School of Medicine, Omaha, Nebraska.

Extraskeletal myxoid chondrosarcoma (ESMC) is a malignant mesenchymal neoplasm of uncertain differentiation characterized by an abundant myxoid matrix, multilobular architecture, and uniform cells arranged in cords, clusters, and fine networks. These tumors are characterized by most commonly a t(9;22)(q22;q12) translocation or less frequently, t(9;17)(q22;q11) or t(9;15)(q22;q21) translocation. Molecular characterization of the t(9;22) and t(9;17) variants results in $\text{NR4A3}$ fusions in 90% of cases. NR4A3 fusions are considered the hallmark of ESMC. Herein, we describe the case of a 68-year old woman with a 9.7-cm mass within the subcutaneous tissue of the right gluteus. Surgical resection revealed a multilobulated, myxoid and gelatinous mass in the subcutis focally involving the gluteus muscle (Figure 219, B). Histologic evaluation revealed bland spindle cells arranged in interconnecting cords, small clusters, and complex trabeculae with uniform oval nuclei and inconspicuous nucleoli. Minimal mitotic activity was present. Tumor cells stained negatively for pancytokeratin, S100, Desmin, SMA, and CD34 by immunohistochemistry. Fresh tissue was submitted for cytogenetics, revealing a normal karyotype. Furthermore, FISH analysis was negative for EWSR1 break-apart and NR4A3 fusion genes. Despite the negative molecular studies, we believed this tumor was an example of a translocation-negative ESMC. Owing to the rarity of this occurrence, expert consultation was obtained and agreed with our diagnosis. After this case was processed, some NR4A3-negative ESMCs were found to harbor loss of SMARCB1 (INI1) by either loss of function or gene deletion. From a clinical viewpoint, further studies are necessary in discovering novel molecular targets, as this could potentially be a promising therapeutic strategy.

Metastatic Pseudomyogenic Hemangioendothelioma: An Unexpected Biological Behavior

(Poster No. 149)

Karen T. Galvis-Castro, MD1; David A. Suarez-Zamora, MD1 (da.suarez33@uniandes.edu.co); Paula A. Rodriguez-Urrego, MD1; Adriana A. Florez-Vargas, MD2; Luis E. Pino-Villarreal, MD2; Christian D. Castro-Gomez2; Mauricio A. Palau-Lazaro, MD.1 Departments of 1Pathology and Laboratories and 2Carlos Ardila Lüelle Oncology Institute, Fundación Santa Fe de Bogotá, Bogotá D.C., Colombia.

Pseudomyogenic hemangioendothelioma (PHE), also known as epithelioid sarcoma-like hemangioendothelioma, is a rare soft tissue tumor with approximately 130 cases reported in the literature that usually arises in the lower extremities of young males. Although it typically displays an indolent behavior, less than 8% of reported cases have developed metastasis. We present the case of a 34-year-old woman who consulted for a 1-month history of headache associated with right-sided temporal hemianopsia and a 10-mm painful subcutaneous nodule in the right shoulder. Brain computed tomography and MRI scan showed multiple supratentorial white matter lesions with hemorrhagic component, measuring 4 to 15 mm in diameter. CT-PET scans also showed multiple metabolically active bone lesions suggestive of malignancy. Biopsy specimens from the brain, right iliac bone, and right shoulder skin were taken. Skin sections showed a deep dermal spindle cell proliferation with vesicular nuclei and eosinophilic cytoplasm, growing in an infiltrative pattern without significant atypia or pleomorphism (Figure 220, A). Iliac bone sections showed the same findings as the skin, but with a subset of tumor cells with atypical epithelioid morphology and bizarre vesicular nuclei (Figure 220, B). The brain biopsy showed greater cytologic pleomorphism with bizarre polygonal or epithelioid cells and atypical vesicular nuclei (Figure 220, C). The immunohistochemistry stains were positive for CD31, ERG, cytokeratin AE1/AE3, and FOSB (Figure 220, D), but negative for CD34, S100, desmin, and EMA. These findings were consistent with those of a disseminated PHE. This case report is a reminder that, although extremely rare, PHE may show an aggressive biological behavior and can present with brain metastases.
Primary intrathoracic liposarcomas are rare and most of the reported cases arise from mediastinum and pleura. Extremely rare cases of primary intrapulmonary liposarcoma are reported. We report a case of primary intrapulmonary well-differentiated liposarcoma (WDLs) infiltrating the left atrial wall after multiple recurrences despite surgical and adjuvant radiotherapy/chemotherapy. The patient, a 39-year-old man, previously underwent right lower lobectomy for a primary lung WDLs 11 years ago. He developed recurrence 9 years later and went for a second incomplete resection. The tumor recurred within 2 years despite proton beam therapy and chemotherapy. Recent computed tomography of the chest showed a marginalized hypodense mass within the right lung base (13.7 × 8.5 × 9.8 cm) invading the right hilum, left atrium, and possibly the esophagus (Figure 221, A). During the current resection, the tumor was removed en bloc with a portion of left atrial wall infiltrated by tumor. Pathologic examination showed a soft pale yellow tumor. The neoplasm was closely associated with lymph nodes. IHC aspiration biopsy (FNAB) showed a malignant neoplasm negative for epithelial and lymphoid markers by immunohistochemistry (IHC). The patient received radiation and chemotherapy for presumed metastatic squamous cell carcinoma with reduction in size of the mass. Six months later, the residual lesion was resected. The neoplasm consisted of pleomorphic polygonal cells and prominent nucleoli with scattered multinucleated tumor cells. Resection margins were uninvolved by tumor. The neoplasm was closely associated with lymph nodes. IHC showed that the tumor cells were positive for vimentin, equivocal for CD68, and negative for cytokeratin AE1/AE3, OSCAR, CK5/6, CAM 5.2, p63, CD34, smooth muscle actin, desmin, S100, CD30, chromogranin, synaptophysin, HMB-45, MART-1, OCT3/4, CD3, CD20, GFAP, FLI-1, and INI-1. EBER by situ hybridization was negative. With the presence of adjacent lymph nodes, the neoplasm was thought to represent a metastatic carcinoma in lymph nodes with extracapsular extension. On subsequent reevaluation of the tumor, pleomorphic lipoblasts were identified, and the diagnosis was revised to PLS. Follow-up 2 years later showed no clinical evidence of recurrence. The tumors such as PLS can be encountered in unusual sites such as the head and neck region, and may clinically mimic commonly encountered neoplasms such as metastatic carcinomas.

**A Dedifferentiated Liposarcoma With Peculiar Neural-like Histology and Metaplastic Ossification**

(Poster No. 153)

Juan Ding, MD, PhD (bettyding77@gmail.com); Jocelyn Villanueva, MD; Qing Chang, MD, PhD. Department of Pathology, SIUH, Staten Island, New York.

Dedifferentiated liposarcoma is a biphasic malignant neoplasm composed of a well-differentiated liposarcoma and a cellular non-lipogenic sarcoma. We report a case of dedifferentiated liposarcoma arising from the right retroperitoneum, adjacent to the upper pole of the kidney. A 61-year-old woman was found to have a right exophytic renal mass upon MRI. She underwent right nephrectomy. Three isolated nodular masses were identified in the perirenal fat of the right kidney. The largest nodule (No. 1) was 2.5 cm in the greatest dimension adjacent to the kidney; the cut surface was white (45%), oval (6%), firm and bulging with focal calcification. The medium (No. 2) and smallest nodule (No. 3) were 2 cm and 1 cm in the greatest dimension, respectively. The cut surface showed yellow lobulated fatty tissue. Histopathology examination revealed 2 distinct appearances. In the No. 1 nodule, it showed a
cellular cytologic atypical spindle cell proliferation in a discrete whorled structure (neural-like) with scattered mitosis (Figure 222, A and B). Multifocal metastatic ossification was present (Figure 222, C). No necrosis was seen. The No. 2 and No. 3 nodules consisted of mature adipose tissue showing variation in size along with scattered atypical hyperchromatic stromal cells (Figure 222, D). Immunohistochemistry showed diffuse nuclear positivity for MDM2 and CDK4. In summary, dedifferentiated liposarcoma is the most common liposarcoma in the deep peritoneal area; extensive sampling and MDM2 and CDK4 stains are crucial to render the correct diagnosis. Additional follow-up is needed to preclude a more aggressive behavior.

Utility of Whole-Genome Single Nucleotide Polymorphism Microarray and Targeted Somatic Mutations in Evaluation of Cytologically Bland but Clinically Worrisome Lipomatous Lesion on a Core Biopsy

((Poster No. 154)

Nwogbo Okechukwu, MD (onwogbo@augusta.edu); Sravan Kavuri, MD; George Wang, MD; Benjamin Johnson, BS; Ashis Mondal, PhD; Alka Chaubey, PhD; Chetan Pundkar, PhD; Ravindra B. Kolhe, MD, PhD. Department of Pathology, Medical College of Georgia at Augusta University, Augusta.

We present a case of an 81-year-old woman with history of right thigh mass. Magnetic resonance imaging showed a 13.3 × 13 × 7.6-cm lipomatous-appearing mass in the medial compartment of the proximal thigh within adductor magnus. It mostly followed fat-signaling characteristics on all sequences, mild internal stranding and vascularity, without areas concerning for dedifferentiation, but did show some signal differences (more hypointense) on T2 and enhanced images. Radiologic differential diagnosis included lipoma versus well-differentiated liposarcoma versus myxoid liposarcoma in areas that are more T2 hyperintense. H&E staining of the 16-gauge core biopsy specimen showed mostly mature adipocytes with uniform nuclei resembling normal adipose tissue. There were focal areas within the adipocytes with atypical nuclei. The whole-genome single nucleotide polymorphism microarray (SNPM) was performed on the DNA isolated from an area with atypical adipocytes following manufacturer’s protocol (OncoScan assay, Affymetrix, Inc.). The raw data were analyzed in Chromosome Analysis Suite 3.0 software and were matched to in silico FFPE reference sets. This platform consists of 274,000 probes including 74 somatic mutations from 9 genes (BRAF, KRAS, EGFR, IDH1, IDH2, PTEN, PIK3CA, NRAS, and TP53). The SNPM demonstrated amplification in MDM2 gene (4–5 copies) along with gains in AT16, DUSP12, CPM, YEATS4, and FFRS2. Based on the SNPM data, a diagnosis of atypical lipomatous tumor/well-differentiated liposarcoma was made on the biopsy specimen. We describe a powerful technology for investigating histologically difficult cases with limited sampling (core biopsy). This report emphasizes the value of decisive molecular alterations in arriving at the critical threshold of establishing a definite diagnosis (Figure 223).

Dr Kolhe has served as a consultant to Illumina and Qiagen.

Extramedullary Hematopoiesis in a Spindle Cell Lipoma

(Poster No. 155)

Phoebe Hammer, BA (hammerp@ohsu.edu); Peter Stenzel, MD. Department of Pathology, Oregon Health & Science University, Portland.

Spindle cell lipoma (SCL) is a benign tumor composed of fibrous tissue and fat that occurs most commonly on the neck and back of adult males. Instances with variations on histologic appearance or occurrence in unusual sites may pose difficulties in diagnosis, most notably if features suggest liposarcoma. We encountered an SCL in a 79-year-old man who presented with an enlarging back mass at the site of a previous lipoma excision 30 years previously. Examination of the surgical specimen revealed a 6.2-cm well-circumscribed tan-yellow lesion. Microscopically, classic features of spindle cell lipoma were identified, including mature adipocytes, bland spindled cells, collagen bundles, and myxoid stroma as well as rare lipoblasts. Giemsa and CD117 immunostains highlighted numerous mast cells. The spindle cells stained strongly for CD34. Scattered throughout the lesion were small groups of hematopoietic cells of 3 lineages. No abnormality was identified by fluorescence in situ hybridization with a probe for CREST, SPP1, CPM, YEATS4, and FFRS2. Based on the SNPM data, a diagnosis of extramedullary hematopoiesis was observed in a solitary fibrous tumor, a lesion sometimes considered to be related to SCL. SCL with hematopoietic elements. Notably, extramedullary hematopoiesis was observed in a solitary fibrous tumor, a lesion sometimes considered to be related to SCL. SCL with extramedullary hematopoiesis should be distinguished from sclerotic extramedullary hematopoietic disorders.

Soft Tissue Chondroma of the Palm: Case Report and Literature Review

(Poster No. 156)

Graham Dixon, BA; Peter Kragel, MD (kragelp@ecu.edu). Department of Pathology, ECU, Greenville, North Carolina.

Soft tissue chondroma (STC) is a rare benign cartilaginous tumor. We report the clinical, radiographic, and pathologic findings of STC in a 42-
A Rare Case of Congenital Factor X Deficiency Diagnosed in a 12-Year-Old Girl (Poster No. 157)

Hani Katerji, MD (hani_katerji@urmc.rochester.edu); Hannah L. McRae, BA; Majed A. Refaai, MD. Department of Pathology, University of Rochester, New York.

Coagulation factors are important plasma proteins for normal hemostasis. Factor X (FX), which is a vitamin K-dependent serine protease, is a key factor in thrombus formation. FX deficiency is an extremely rare bleeding disorder that may be either acquired or congenital. A 12-year-old girl presented to the hospital after sustaining 2 unusual episodes of epistaxis within 1 week. The first episode lasted 15 minutes, while the second episode persisted for 1 hour despite applying continuous pressure. The patient reported occasional gingival bleeding while brushing her teeth and prolonged bleeding after minor cuts. Her menstrual cycles were regular, with occasional gingival bleeding while brushing her teeth and prolonged bleeding after minor cuts. Her menstrual cycles were regular, with occasional gingival bleeding while brushing her teeth and prolonged bleeding after minor cuts.

Clinical symptoms, and family history, a diagnosis of congenital FX deficiency was rendered. In summary, congenital FX deficiency is a lifelong disorder, which is extremely rare, but if not diagnosed at younger ages or if proper precautions are not taken during invasive or surgical procedures, serious complications may evolve. Patients with FX deficiency should be prophylactically managed as needed, with the consideration of using the recently approved human plasma-derived FX concentrate, which allows for better management.

SESSION 300

Correlation Between Titers and Hemolysin Testing to Prevent Out-of-Group Platelet Hemolytic Transfusion Reactions: Is the Titer Enough Information? (Poster No. 158)

Walter Linz, MD (walter.linz@bswhealth.org); Sean Trevathan, MD; Yasmine King, MT(ASCP)SBBcsm, MPH. Department of Pathology, Baylor Scott & White, Temple, Texas.

Context: ABO group matching for single donor platelet (SDP) products is a challenge for most transfusion services as SDP supply is limited, the shelf-life is short, and demand is often urgent/emergent. Consequently, many SDP transfusions are ABO-group incompatible. These minor incompatible transfusions constitute a hemolytic risk. To mitigate this risk, our medical center uses serologic titers from O SDP products and results of an ex vivo hemolysin test to exclude potential risky SDP units. Our research question: To what extent do titers and hemolysin testing correlate?

Design: We conducted a retrospective 2-year single center review of hemolysin test results and saline serologic titers of anti-A and anti-B in O SDP donors.

Results: Serologic titration studies (anti-A and anti-B) and hemolysin testing were performed on group O SDP donors collected at our blood center. SDP products from donors with an anti-A or anti-B titer $\geq$ 64 were excluded from use in minor incompatible transfusions. Of 68 donors, anti-A titers ranged from 2 to $>512$ and anti-B titer ranged from 8 to 512. Thirty-nine percent of donors had anti-A titer 64 or less. Three donors had a positive hemolysin test result. Two of the 3 hemolysin positive donors had anti-A titers of 512; the third had an anti-A titer of 128.

Conclusions: Positive hemolysin test result and high donor titer generally correlate. Use of the cutoff alone appears effective at titer 64 or less though 61% of potential group O units are excluded. Either the titer cutoff levels must be low or both tests must be used.

An Audit on Appropriateness of Transfusion Orders by Physicians: A Single Center Experience (Poster No. 159)

Faisal Huq Ronny, MD, PhD (faisal.huq.ronny@jefferson.edu); Mary Harach, BS, MT(ASCP), CQA(ASQ), SSGB. Department of Blood Bank and Transfusion Medicine, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania.

Context: Ongoing performance improvement efforts known as blood utilization review include review for appropriateness of transfusion orders. Evidence-based transfusion guidelines and strategies for improved blood utilization have been shown to be cost-effective and safe.

Design: Data were collected retrospectively during a 3-year period (January 1, 2015–December 31, 2017). A total of 1606 blood product orders using indications other than recommended transfusion indications were reviewed post transfusion by transfusion medicine physicians for appropriateness and categorized as “Indicated,” “Not indicated,” or “Clinical judgement” as per blood bank transfusion guidelines.

Results: Of the total blood products ordered using “Other Indications,” 391/1606 (24%) were found to be indicated for patient transfusion, 723/1606 (45%) were not indicated, and 492/1606 (31%) were deferred to clinical judgment. For RBC orders, 160/506 (32%) were indicated, 174/506 (54%) not indicated, and 172/506 (34%) clinical judgement. For platelet orders, 155/732 (21%) were indicated, 329/732 (45%) not indicated, and 248/732 (34%) clinical judgement. For plasma orders, 60/319 (19%) were indicated, 200/319 (63%) not indicated, and 59/319 (18%) clinical judgement. For cryoprecipitate orders, 16/49 (33%) were indicated, 20/49 (41%) not indicated, and 13/49 (26%) clinical judgement.

Conclusions: The study aimed to audit appropriateness of transfusion ordering as a tool for physician education. By providing physicians access to guidelines and data on their usage, this may help to modify physician-ordering practices for transfusion.

Effect of Positive Patient Identification on Wrong Blood in Tube Errors: A Single Center Experience (Poster No. 160)

Faisal Huq Ronny, MD, PhD (fmlronny@hotmail.com); Mary Harach, BS, MT; Jay H. Herman, MD. Departments of Pathology and Blood Bank and Transfusion Medicine, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania.

Design: Data were collected retrospectively during a 3-year period (January 1, 2015–December 31, 2017). A total of 1606 blood product orders using indications other than recommended transfusion indications were reviewed post transfusion by transfusion medicine physicians for appropriateness and categorized as “Indicated,” “Not indicated,” or “Clinical judgement” as per blood bank transfusion guidelines.

Results: Of the total blood products ordered using “Other Indications,” 391/1606 (24%) were found to be indicated for patient transfusion, 723/1606 (45%) were not indicated, and 492/1606 (31%) were deferred to clinical judgment. For RBC orders, 160/506 (32%) were indicated, 174/506 (54%) not indicated, and 172/506 (34%) clinical judgement. For platelet orders, 155/732 (21%) were indicated, 329/732 (45%) not indicated, and 248/732 (34%) clinical judgement. For plasma orders, 60/319 (19%) were indicated, 200/319 (63%) not indicated, and 59/319 (18%) clinical judgement. For cryoprecipitate orders, 16/49 (33%) were indicated, 20/49 (41%) not indicated, and 13/49 (26%) clinical judgement.

Conclusions: The study aimed to audit appropriateness of transfusion ordering as a tool for physician education. By providing physicians access to guidelines and data on their usage, this may help to modify physician-ordering practices for transfusion.
Context: “Wrong blood in tube” (WBIT) errors where the blood in the tube is not from the actual patient may lead to often catastrophic outcomes from incompatible transfusion. This retrospective study of WBIT errors was performed after our institution adopted a new patient EMS (Electronic Matching System) in the second quarter of 2017 that requires barcode of patient and sample identification through EPIC (Epic Systems Corporation) to determine and compare the incidence of WBIT. Previously, patient and specimen identification was performed manually.

Design: Our blood bank Quality Plan (QP) mandates that all reports of mislabeled and miscollected specimens be continuously monitored and analyzed. Three years of data (2015–2017) were reviewed. WBIT errors are categorized as suspected (with no discrepant blood typing history and/or second draw specimen) and confirmed (discrepant typing).

Results: In that study period, type and screen testing was performed on 126,487 specimens before EPIC went live on March 31, 2017. As per QP reports a total of 41 confirmed and 98 suspected WBIT errors were identified. The estimated WBIT rate was 1 in 3085 samples, comparable to 1 in 2262 for confirmed cases in the WBIT literature. Since April 2017, type and screens were performed on 41,808 specimens. Only 1 confirmed and 25 suspected WBIT errors were identified. The estimated WBIT rate was 1:41,808 for confirmed cases.

Conclusions: We conclude that implementing positive patient/sample identification through barcode labeling at the bedside reduced WBIT errors, especially of the confirmed category (Figure 225).
of a TERT promoter mutation. In situ hybridization identified codelletion of 1p and 19q in each of the cases. Aggregate findings were consistent with the diagnosis of glioblastoma, IDH-wild type, using WHO 2016 classification criteria. Literature review revealed several studies where 1p/19q codelletion was present in up to 6% of glioblastoma cases.

**Conclusions:** A small but distinct subset of glial neoplasms with combined histologic, immunohistochemical, and molecular features other than glioblastoma may present a diagnostic challenge. Using the 2016 WHO criteria, manifest 1p and 19q codelletion.

**Acanthamoeba Granulomatous Encephalitis in a Patient on Bruton Tyrosine Kinase Inhibitor Therapy**

(PSoter No. 2)

Amelia Nakamishi, MD (amelia.nakanishi@ubhospitals.org); Mark Cohen, MD. Department of Pathology, Case Western Reserve University, Cleveland, Ohio.

Case reports of ibrutinib-related invasive fungal infections are emerging in patients with lymphoproliferative disorders after treatment with the Bruton tyrosine kinase inhibitor ibrutinib. The spectrum and severity of invasive fungal infections in this patient population suggests a synergy between certain diseases and small molecule tyrosine kinase inhibitors producing a profound level of immunodeficiency. Before the advent of ibrutinib these patients were considered low risk for invasive fungal infections, but are now seen with atypical presentations with substantially increased mortality rates. Acanthamoeba granulomatous encephalitis is a rare opportunistic infection, which has not previously been reported in this clinical scenario. We present a case of a 64-year-old man with a past medical history of ibrutinib-treated chronic lymphocytic leukemia who presented with altered mental status. A temporal lesion was seen on magnetic resonance imaging, but flow cytometry and infectious workup of cerebrospinal fluid for varicella zoster virus, herpes virus, Strept antigen, N meningitidis antigen, and cryptococal antigen were negative. After unsuccessful stereotactic biopsy, open biopsy demonstrated necrotizing granulomatous inflammation containing 20- to 40-µm trophozoites with central karyosomes, as well as similarly sized cysts, consistent with either Acanthamoeba or Balanamuthia species. Subsequent immunohistochemical and polymerase chain reaction analyses, performed by the Center for Disease Control and Prevention, confirmed the presence of Acanthamoeba species. The patient was started on miltefosine, sulfadizine, flucytosine, fluconazole, and azithromycin, but experienced multiple complications and expired 3 months after admission. Acanthamoeba granulomatous encephalitis should be within the differential diagnosis of enhancing brain lesions in patients treated with Bruton tyrosine kinase inhibitors.

**Glioblastoma With a Cluster of Genomic Alterations (CDK4, IDH1, ATRX, CDKN2A, CREBBP, CSFIR, MLH1, MSH6, NOTCH1, PRDM1, RAD50, TP53): Clinical Significance and Future Therapeutics**

(PSoter No. 3)

Sean M. Hacking, MB, BCh, BAO (shacking@northwell.edu); Deepika Savant, MB, BS; Michael Schulder, MD; Mansoor Nasim, MD, PhD.1 Departments of Pathology and Neurosurgery, Northwell Health, Lake Success, New York.

A 48-year-old woman with an enlarging right brain mass on CT/MRI (previously diagnosed as astrocytoma) underwent surgical resection. Histology showed a glioma with nuclear atypia, increased mitotic activity, microvascular proliferation, and focal necrosis (glioblastoma). IDH1-R132H showed positive staining in tumor cells, findings suggestive of anaplastic glioblastoma. Next-generation sequencing identified a cluster of genomic alterations including CDK4 amplification with mutations in IDH1, ATRX, CDKN2A, CREBBP, CSFIR, MLH1, MSH6, NOTCH1, PRDM1, RAD50, and TP53 with a high tumor burden. There was no epidermal growth factor receptor mutation seen. The patient exhibited a profound level of immunodeficiency. Before the advent of ibrutinib these patients were considered low risk for invasive fungal infections, but are now seen with atypical presentations with substantially increased mortality rates. Acanthamoeba granulomatous encephalitis is a rare opportunistic infection, which has not previously been reported in this clinical scenario. We present a case of a 64-year-old man with a past medical history of ibrutinib-treated chronic lymphocytic leukemia who presented with altered mental status. A temporal lesion was seen on magnetic resonance imaging, but flow cytometry and infectious workup of cerebrospinal fluid for varicella zoster virus, herpes virus, Strept antigen, N meningitidis antigen, and cryptococal antigen were negative. After unsuccessful stereotactic biopsy, open biopsy demonstrated necrotizing granulomatous inflammation containing 20- to 40-µm trophozoites with central karyosomes, as well as similarly sized cysts, consistent with either Acanthamoeba or Balanamuthia species. Subsequent immunohistochemical and polymerase chain reaction analyses, performed by the Center for Disease Control and Prevention, confirmed the presence of Acanthamoeba species. The patient was started on miltefosine, sulfadizine, flucytosine, fluconazole, and azithromycin, but experienced multiple complications and expired 3 months after admission. Acanthamoeba granulomatous encephalitis should be within the differential diagnosis of enhancing brain lesions in patients treated with Bruton tyrosine kinase inhibitors.

**Corticoadenoma Adenoma With Infiltrating Lymphoid Follicles: A Diagnostic Anomaly**

(PSoter No. 5)

Roshan Mahabir, MD, PhD, MPH (roshan.mahabir@mounainai.org); Amir Banahhashi, MD; Melissa Umphlett, MD; Julian Samuel, MD; Abir Salama, MD; Mary Foster, MD, PhD.1 Department of Pathology and Laboratory Medicine, Mount Sinai St. Luke Roosevelt, New York, New York; 2Department of Pathology, The Mount Sinai Hospital, New York, New York; 3Department of Pathology, Icahn School of Medicine at Mount Sinai, New York, New York.

Lymphocytic hypophysitis (LYH) in association with pituitary adenoma is a rare entity and is usually associated with prolactinomas. The presence of lymphoid follicles within a pituitary adenoma has only been reported in 1 previous case. Here we present a case of a 75-year-old woman with an LYH-like infiltrate of a corticoadenoma pituitary adenoma. The patient initially presented with bitemporal hemianopic field defect consistent with an enlarging 4- to 5-cm pituitary mass distorting the optic chiasm on radiology. She underwent primary transsphenoidal resection of the mass and 7 months later had a repeat resection of a component of the tumor owing to increasing adrenocorticotropic hormone levels. Both resections showed moderately to focally densely cellular tumor composed of a monomorphic population of basophilic tumor cells with moderate nuclear pleomorphism and effacement of the normal trabecular architecture. Scattered throughout the tumor were large lymphoid aggregates, including lymphoid follicle-like formations with definitive germinal centers and without associated destruction of pituitary parenchyma. The inflammatory infiltrate was composed of polyclonal B- and T-cell lymphocytes and plasma cells. The tumor cells were reactive for ACTH and showed an elevated Ki-67 (18%). The tumor had up to 4 mitotic figures per 10 high-power fields and up to 4% of tumor cell nuclei were positive for p53. The patient had an elevated cortisol level with no associated destruction of pituitary parenchyma. The lymphocytic infiltrate was composed of polyclonal B- and T-cell lymphocytes and plasma cells. The tumor cells were reactive for ACTH and showed an elevated Ki-67 (18%). The tumor had up to 4 mitotic figures per 10 high-power fields and up to 4% of tumor cell nuclei were positive for p53. The patient had an elevated cortisol level with no associated destruction of pituitary parenchyma. The inflammatory infiltrate was composed of polyclonal B- and T-cell lymphocytes and plasma cells. The tumor cells were reactive for ACTH and showed an elevated Ki-67 (18%). The tumor had up to 4 mitotic figures per 10 high-power fields and up to 4% of tumor cell nuclei were positive for p53. The patient had an elevated cortisol level with no associated destruction of pituitary parenchyma.
A Case of Constitutional Mismatch Repair Deficiency Syndrome Resulting From a Germline PMS2 Mutation

(Catherine K. Gestrich, DO; Marta Couce, MD, PhD; Mark Cohen, MD. Department of Pathology, University Hospitals Cleveland Medical Center/Case Western University, Cleveland, Ohio.)

Constitutional mismatch repair deficiency (CMMRD) is a rare childhood syndrome resulting from a biallelic germline mutation in one of the mismatch repair genes (MLH1, MSH2, MSH6, PMS2). The inheritance pattern is autosomal recessive, although de novo mutations have been reported. These patients often present with café au lait macules, resulting in a misdiagnosis of neurofibromatosis type I. However, patients with CMMRD develop a broad spectrum of malignant tumors. These include hematologic, brain, and intestinal tract malignancies. Most of these patients do not reach adulthood. We present a case of a 3-year-old boy with café au lait macules, microcephaly, and a right posterior parietal brain mass. Resection of the lesion showed a high-grade diffuse astrocytic tumor. Neoplastic cells were immunoreactive with GFAP, vimentin, and p53. CMMRD was suspected and mismatch repair immunohistochemistry was performed. Loss of PMS2 staining was identified, consistent with a biallelic mutation of the PMS2 gene. Next-generation sequencing was performed to confirm this diagnosis. Unfortunately, the patient expired 16 months after undergoing resection and radiation therapy. Autopsy findings demonstrated residual high-grade astrocytic tumor, extensively involving the right and left cerebral and cerebellar hemispheres. CMMRD is a devastating cancer predisposition syndrome. It should be considered in the differential diagnosis of pediatric patients presenting with café au lait macules who develop malignant tumors. Currently, multiple treatment modalities are being investigated, including checkpoint inhibitors.

Metastatic Carcinoma Involving Meningioma: Report of 2 Cases

(Natalya Hakim, MD; Janna Neltner, MD. Department of Pathology, University of Kentucky Chandler Medical Center, Lexington, Kentucky, Lexington.)

A 36-year-old man with no significant history presented with an intractable left side headache. Imaging showed a mass and cranial nerve palsy confirmed a glioblastoma multiforme. After months of treatment, he returned with a left scalp lesion and bitemporal hemianopsia, which was diagnosed as gliosarcoma. Afterwards, he entered hospice care until his death. At autopsy, an ulcerated lesion was seen on the left occipitoparietal lobe with tumor extending into the scalp (Figure 227, A and B). The dural surfaces showed multiple masses spreading from the left temporal lobe to the parietal lobe while enveloping the occipital lobe bilaterally. The brain was asymmetrical with the left parieto-occipital lobe removed and filled with necrotic material. A well-circumscribed lesion in the right frontal lobe was also noted and showed tumor microscopically (Figure 227, C and D). While no gross tumor was seen on the optic chiasm, it was present microscopically. Gliosarcoma is a rare variant of IDH-wild-type glioblastoma containing distinct gliomatous and sarcomatous components. Gliosarcomas comprise 0.59% to 0.76% of all adult brain tumors affecting adults in their 40s to 60s with a higher proportion in males. The cell of origin is now thought to result from advanced glioma dedifferentiation with subsequent loss of GFAP expression and acquisition of a sarcomatous phenotype. Metastasis to extracranial sites is rare; however, tumor extension within the brain is common. Clinical treatment reported in the literature is limited, thus treatment, and unsurprisingly the poor prognosis, is like glioblastoma multiforme. Our case is unique for the patient’s young age and extensive tumor spread to the dura mater.

Metastatic Atypical Meningioma: A Rare Phenomenon With Profound Clinical Impact

(Al Smith, BS; Emily Bachert, MD; Dana Richards, MD. Department of Pathology and Laboratory Medicine, University of Kentucky Chandler Medical Center, Lexington.)

A 66-year-old woman with history of carcinoma of unknown origin with neuroendocrine features involving a meningioma. Case 2 involves a 66-year-old woman with history of invasive lobular carcinoma, presenting with acute vision loss. An MRI showed regular enhancing mass in the left anterior fossa radiologically consistent with meningioma. The corresponding resection revealed a small portion of psammomatous meningioma with infiltrating carcinoma similar morphologically to the patient’s known lobular breast carcinoma. Immunohistochemically, the carcinoma component was strongly positive for EMA, ER, CK AE1/AE3, which was similar to the staining profile of her original lobular breast carcinoma. The meningioma component was weakly positive for EMA and negative for cytokeratin. These findings confirmed the diagnosis of metastatic lobular carcinoma involving a meningioma.

A Case of Gliosarcoma Extension into Dermis in a Young Adult

(Seunghyug Kwon, MD, MPH; Nicholas E. Dietz, MD. Department of Pathology, Creighton University, Omaha, Nebraska.)

A 36-year-old man with no significant history presented with an intractable left side headache. Imaging showed a mass and cranial nerve palsy confirmed a glioblastoma multiforme. After months of treatment, he returned with a left scalp lesion and bitemporal hemianopsia, which was diagnosed as gliosarcoma. Afterwards, he entered hospice care until his death. At autopsy, an ulcerated lesion was seen on the left occipitoparietal lobe with tumor extending into the scalp (Figure 227, A and B). The dural surfaces showed multiple masses spreading from the left temporal lobe to the parietal lobe while enveloping the occipital lobe bilaterally. The brain was asymmetrical with the left parieto-occipital lobe removed and filled with necrotic material. A well-circumscribed lesion in the right frontal lobe was also noted and showed tumor microscopically (Figure 227, C and D). While no gross tumor was seen on the optic chiasm, it was present microscopically. Gliosarcoma is a rare variant of IDH-wild-type glioblastoma containing distinct gliomatous and sarcomatous components. Gliosarcomas comprise 0.59% to 0.76% of all adult brain tumors affecting adults in their 40s to 60s with a higher proportion in males. The cell of origin is now thought to result from advanced glioma dedifferentiation with subsequent loss of GFAP expression and acquisition of a sarcomatous phenotype. Metastasis to extracranial sites is rare; however, tumor extension within the brain is common. Clinical treatment reported in the literature is limited, thus treatment, and unsurprisingly the poor prognosis, is like glioblastoma multiforme. Our case is unique for the patient’s young age and extensive tumor spread to the dura mater.
Meningiomas are relatively common neoplasms, accounting for up to 26% of all primary intracranial tumors. These tumors are generally benign in their course, and the prognosis is often very positive. Metastasis from meningioma is an exceedingly rare phenomenon that has only been described in occasional case reports. We present the case of a 62-year-old woman who initially was diagnosed with an atypical meningioma on a left temporal biopsy that was performed during the first recurrence of the tumor (World Health Organization grade II). The biopsy demonstrated a hypercellular tumor with sheeting architecture, an average of 7 mitoses per 10 high-power fields, and prominent nucleoli. The patient underwent resection; however, she experienced recurrence shortly thereafter and underwent multiple subsequent gamma knife radiosurgery procedures. Six years after this resection, she began to experience low back pain with difficulty ambulating due to a large paraspinal mass. Imaging studies revealed a neoplastic process involving the liver, right iliac crest, and multiple vertebral. A biopsy and subsequent resection of the right iliac bone lesion revealed a hypercellular tumor of spindled to epithelioid cells in a whirling pattern with areas of necrosis. These cells demonstrated a similar morphology to the primary tumor and stained positively for EMA, PR, and CD99, consistent with metastatic meningioma. Furthermore, a biopsy of the liver lesion was also compatible with metastatic meningioma. This case demonstrates an atypical meningioma with an incredibly rare and aggressive clinical course, and it emphasizes the need for close clinical follow-up in these patients.

Primary Diffuse Large B-Cell Lymphoma of Dura, Clinically Presenting as a Meningioma

(Poster No. 10)

Pathavkumar J. Patel, MD (papelat@utwcn.edu); James Vaughan, MD; Christopher Clark, MD. Department of Pathology, University of Tennessee Medical Center Knoxville, Knoxville.

Primary dural lymphoma (PDL) is a subentity of primary leptomeningeal lymphoma and originates from the dura mater without systemic disease. PDL is a rare, typically low-grade lymphoma, which accounts for less than 1% of central nervous system lymphomas. We present an unusual case of high-grade diffuse large B-cell lymphoma as a PDL with radiographic features mimicking a meningioma. A 26-year-old woman presented in the emergency room following a motor vehicle accident related to new-onset seizure while driving. She had history of anxiety, depression, panic attacks, and headache for a few months. CT scan and MRI of the head revealed a 2.4-cm left frontal convexity mass with features of an atypical meningioma. As a treatment option, the patient elected to proceed with surgery. Histologic sections of mass showed small round blue cell tumor and necrosis. To evaluate the origin of tumor cells, a panel of immunohistochemical stains (Pancytokeratin, S100, GFAP, CD99, CD34, EMA, CD3, CD10, CD20, CD45, BCL2, BCL6, MUM1, Cyclin D1, PAX5, EBV) and flow cytometry were performed. Overall features were compatible with high-grade diffuse large B-cell lymphoma with germinal center type. Fluorescence in situ hybridization results (BCL2, MYC, BCL6 break-apart) were negative. Bone marrow biopsy was negative for involvement. She received 6 cycles of chemotherapy, consolidative radiation, and intrathecal chemotherapy. Radiation therapy is being done with the hope of tumor head and neck metastases, with the surgical site that appears to be chronic and improving. Early diagnosis is important because this is a rare disease with favorable clinical outcome as compared to other primary central nervous system lymphomas.

A Challenging Diagnosis: Myxoid Variant of Metaplastic Meningioma

(Poster No. 11)

Zaynab Al-Duwal, MD (zalduwal@metrohealth.org); Dan Cai, MD, PhD. Department of Pathology, MetroHealth Medical Center/Case Western Reserve University, Cleveland, Ohio.

Myxoid variant of metaplastic meningioma is a rare variant of meningioma that arises from the meningothelial cells. We report the case of a patient with metaplastic meningioma, myxoid variant, and discuss the histopathologic and immunohistochemical challenges. The patient is a 43-year-old woman who presented to the emergency department with fatigue, headache, and altered mental status. Her past medical history included type-1 diabetes mellitus and sleep apnea. Head computed tomography (CT) scan and MRI were obtained. Head CT without contrast demonstrated a ring-enhancing lesion, occupying right cerebral tempo-occipital lobe. The patient underwent surgery and we received the specimen in multiple fragments. Hematoxylin-eosin sections of tumors were extensively hemorrhagic and necrotic. There was extensive circlization with fibrillary bands dividing the tumor into lobules of varying size and shape. In some of the bands, there was florid endothelial hyperplasia, but the low cellularity density and absence of pleomorphism argued against gliosarcoma. There were broad areas of necrosis in which there were multiple thrombosed blood vessels. Approximately 90% of the tumor cells are GFAP immunopositive, but small foci of glial fibrillary acidic protein–immunonegative cells were present. The Ki-67 labeling index was approximately 90% and about 40% of the tumor cells were p53 immunopositive. In some lobules the tumor cells were RMDO-20 immunopositive, raising the possibility that the tumor may be a “neural” subtype of gliosarcoma. Immunopositivity for IDH was problematic: there were areas of immunonegativity and immunopositivity, IDH1–wild-type, and IDH2 mutation, and MGMT-promoter methylation by polymerase chain reaction were not detected; epidermal growth factor receptor (EGFR) gene amplification by FISH revealed positivity for EGFR amplification with average EGFR signal number per cell of >15.2.

Glioblastoma With Widespread Metastases

(Poster No. 12)

Stephanie Shea, MD (stephanie.shea@mountsinai.org); Melissa Umphlett, MD; Nadejda Tsankova, MD, PhD. Department of Pathology, Icahn School of Medicine at Mount Sinai, New York, New York.

Glioblastoma is the most common malignant brain tumor in adults, with an incidence of approximately 3.2 per 100,000 per year. Despite this neoplasm’s aggressively and rapidly invasive nature, metastases, especially distant metastases, are rarely reported. With a 5-year survival rate of about 5.1%, most patients with glioblastoma may not survive long enough to develop diagnosable metastatic lesions. As treatment regimens are optimized and overall survival rates improve, the prevalence of metastasis in glioblastoma may increase. This report presents the case of a woman who was diagnosed with glioblastoma, IDH1–wild-type, at age 73 years. Around the time of diagnosis, a computed tomography scan of the chest and abdomen demonstrated a nonspecific, 1.6-cm nodule in the left breast and a subcentimeter pulmonary nodule. She underwent surgical resection and chemoradiotherapy with temozolomide. About 6 months later, she received radiosurgery for local recurrence. Almost a year after primary diagnosis, computed tomography chest and abdomen scan demonstrated a 3.9-cm mass in the left breast, a smaller breast nodule, and multiple masses of the lungs, liver, and bones (lytic). While clinical suspicion was for metastatic breast cancer, biopsy of both breast and bone lesions confirmed glioblastoma. Immunohistochemistry on the confirmed glioblastoma had metastasized to all of the sites identified by computed tomography, as well as to multiple additional sites. This rare case of widespread glioblastoma metastases demonstrates the potential for distant and diffuse spread in this aggressive tumor. In addition to presenting this unique case in greater detail, we will present a brief review of the literature regarding glioblastoma with metastases.

Differential Diagnosis of Small Cell Glioblastoma and Gliosarcoma

(Poster No. 13)

Shamima Sultana, MD (Shamima.Sultana@wmchealth.org); George Kleinman, MD. Department of Pathology, Westchester Medical Center, Valhalla, New York.

Small cell glioblastoma is a histologic subtype of glioblastoma with characteristic features of highly proliferative, monotonous small glial cells with high nuclear–cytoplasmic ratio. Morphologically, malignant lymphoma or small cell metastatic carcinoma should be carefully discriminated. Some cases are difficult to differentiate from gliosarcoma. In this report, we present a case of small cell glioblastoma of a 62-year-old man who presented with a right-sided intracranial mass. Neuroimaging studies showed ring-enhancing lesion, occupying right cerebral tempo-occipital lobe. The patient underwent surgery and we received the specimen in multiple fragments. Hematoxylin–eosin sections of tumors were extensively hemorrhagic and necrotic. There was extensive circlization with fibrillary bands dividing the tumor into lobules of varying size and shape. In some of the bands, there was florid endothelial hyperplasia, but the low cellularity density and absence of pleomorphism argued against gliosarcoma. There were broad areas of necrosis in which there were multiple thrombosed blood vessels. Approximately 90% of the tumor cells are GFAP immunopositive, but small foci of glial fibrillary acidic protein–immunonegative cells were present. The Ki-67 labeling index was approximately 90% and about 40% of the tumor cells were p53 immunopositive. In some lobules the tumor cells were RMDO-20 immunopositive, raising the possibility that the tumor may be a “neural” subtype of gliosarcoma. Immunopositivity for IDH was problematic: there were areas of immunonegativity and immunopositivity, IDH1–wild-type, and IDH2 mutation, and MGMT-promoter methylation by polymerase chain reaction were not detected; epidermal growth factor receptor (EGFR) gene amplification by FISH revealed positivity for EGFR amplification with average EGFR signal number per cell of >15.2.
Unusual Presentation of Sarcoïdosis With Deadly Neurological Manifestations

(Poster No. 14)

Haider Mejbel, MD (mejbel@etsu.edu); Emilie Cook, DO; Robert Schmadeka, MD; John Schweitzer, MD. Department of Pathology, East Tennessee State University, Johnson City.

We report an unusual presentation of neurosarcoidosis in a 33-year-old African American man. He was found collapsed at home following an episode of severe headache and a seizure-like attack. At the hospital, the patient was comatose with Glasgow coma scale 3 and no brainstem reflexes. Head computed tomography scan revealed diffuse cerebral edema with hydrocephalus and cerebellar tonsillar herniation. Placement of a fourth ventricular drain failed to improve his clinical status. Multiple mediastinal and hilar lymph nodes were enlarged on chest computed tomography. A brain flow study confirmed brain death and the patient was taken off the ventilator and pronounced dead. Sections of the brain revealed nonnecrotizing granulomas with giant cell formation and multiple calcifications centered in the subarachnoid space with an extensive involvement of the optic chiasm and extension along the Virchow-Robin space into brain elsewhere. The periaqueductal gray of the midbrain had a hemorrhagic area with complete aqueudal disruption and obliteration of the lumen in addition to pan-necrosis of the surrounding neuropil. The left middle cerebellar peduncle showed similar changes. Special stains on multiple sections failed to reveal microorganisms. A similar granulomatous process was demonstrated in the mediastinal and hilar lymph nodes. Sarcoidosis is a multisystem chronic granulomatous disease with 5% to 10% of cases demonstrating in the mediastinal and hilar lymph nodes. The pericentral necrosis and hemorrhage. Microscopic examination revealed a tumor composed of sheets of monomorphic epithelioid to rhabdoid cells showing focal discohesion. Individual cells had moderate eosinophilic cytoplasm and eccentric, pleomorphic nuclei (Figure 229, A). Extensive areas of necrosis (Figure 229, B), atypical mitosis, and microvascular proliferation were noted. The neoplastic cells expressed S100 and GFAP (Figure 229, C). INI1 was retained (Figure 229, D) and staining for IDH1 was negative. Ki-67 proliferative index was up to 40% in the maximum proliferating area. Based on the morphology and immunostaining pattern, diagnosis of an epithelioid glioblastoma was rendered, with recommendation for further testing for BRAF V600E mutation. It is important to distinguish this rare variant from other glioblastomas, since it has a particularly poor prognosis and demonstrates early progression with dismal median survival.

Papillary Tumor of Pineal Region: A Diagnostic Dilemma

(Poster No. 15)

Shivani Sharma, DCP, DNB (shivani.sharma@corediagnostics.in); Lata Kini, MD; Aditi Dewan, MD; Ekta Jain, MD. Department of Pathology and Laboratory Medicine, Core Diagnostics, Gurugram, Haryana, India.

Papillary tumor of pineal region is a rare entity and detailed histomorphological and immunohistochemical analysis is necessary for an authentic diagnosis. We present the case of a 55-year-old man who presented with vomiting, loss of appetite, and difficulty in walking. Computed tomography scan revealed a well-defined isodense solid mass lesion along the posterior aspect of the third ventricle and the pineal gland region that measured 2.1 x 1.9 x 1.8 cm. A differential diagnosis of germinoma or pineocytoma was kept. We received paraffin blocks for review and immunohistochemistry. H&E-stained section showed a cellular neoplasm arranged in the form of papillae and solid areas. The nuclei were round to oval with stippled chromatin. Mitotic index was 1 to 3 per 10 high-power fields. No necrosis or microvascular proliferation was seen. The differential diagnosis included papillary tumor of pineal region (PTPR), pineocytoma, choroid plexus papilloma, metastatic carcinoma, and papillary ependymoma. The tumor cells were diffusely positive for PanCK and EMA (focally), synaptophysin, and NSE. GFAP, vimentin, CK7, CK20, CD56, and Oct3/4 were negative. The Ki-67 proliferation index was 5%. In view of the papillary architecture on morphology and characteristic immunopositivity for PanCK, a diagnosis of papillary tumor of pineal region, World Health Organization grade II, was proposed. The index case highlights the importance of identifying a papillary morphology and PanCK positivity in a neuroepithelial tumor. The panel should include PanCK, CK18, synaptophysin, GFAP, and Kir7.1. More information is required through larger series to determine the prognosis and standard treatment protocol of this rare entity (Figure 228).

Epithelioid Glioblastoma: A Rare Histologic Subtype With a Specific Molecular Signature

(Poster No. 16)

Kunal Sharma, DNB1 (drkunalsharma@yahoo.com); Aditi Dewan, MD2; Udita Dewan, MD2; D. K. Vatsal, MS, MCh3; Lata Kini, MD.1 1Department of Onco-Pathology and Laboratory Medicine, Core Diagnostics, Gurugram, Haryana, India; 2Department of Pathology and Laboratory Medicine, Dewan Histopathology & Diagnostic Centre, Lucknow, India; 3Department of Neurosurgery, ICON Hospital, Lucknow, India.

Epithelioid glioblastoma is a rare histologic type of World Health Organization grade IV astrocytic tumors with epithelioid to rhabdoid cells along with atypical mitosis, microvascular proliferation, and necrosis. The tumor typically shows BRAF V600E mutation in up to 50% of cases and is negative for IDH1 and IDH2 mutations. A 35-year-old man presented with chief complaints of headache, diplopia, diminution of vision, and difficulty in walking. Computed tomography scan of the brain showed a right parieto-occipital space-occupying lesion. The patient underwent a right parieto-occipital craniectomy with complete removal of the lesion. Gross examination showed multiple irregular tumor fragments aggregated to a size of 4 x 4 x 2.5 cm. Cut section was tan-white with areas of necrosis and hemorrhage. Microscopic examination revealed a tumor composed of sheets of monomorphic epithelioid to rhabdoid cells showing focal discohesion. Individual cells had moderate eosinophilic cytoplasm and eccentric, pleomorphic nuclei (Figure 229, A). Extensive areas of necrosis (Figure 229, B), atypical mitosis, and microvascular proliferation were noted. The neoplastic cells expressed S100 and GFAP (Figure 229, C). INI1 was retained (Figure 229, D) and staining for IDH1 was negative. Ki-67 proliferative index was up to 40% in the maximum proliferating area. Based on the morphology and immunostaining pattern, diagnosis of an epithelioid glioblastoma was rendered, with recommendation for further testing for BRAF V600E mutation. It is important to distinguish this rare variant from other glioblastomas, since it has a particularly poor prognosis and demonstrates early progression with dismal median survival.
Relapsed Salivary Gland Acinic Cell Carcinoma With Brain Metastasis Presenting as Intracranial Hemorrhage

(Poster No. 17)
Shamima Sultana, MD, PhD (Shamima.Sultana@wmchealth.org); George Kleinman, MD. Department of Pathology, Westchester Medical Center, Valhalla, New York.

Acinic cell carcinoma is an uncommon low-grade malignant tumor of the salivary glands, in which some cells resemble normal acinic cells. Most of these tumors occur in the parotid gland. Women are affected more often than men, and the age at occurrence is earlier than in other salivary gland cancers. Most cases are unilateral, and bilateral involvement has rarely been reported. Acinic cell carcinomas rarely metastasize, but they have a high tendency to recur locally if they are incompletely excised. We describe a case with metastatic acinic cell tumor to the brain. A 54-year-old woman was diagnosed with right parotid gland acinic cell carcinoma and underwent repeated excision (twice) in 2013 and she was in remission. In 2016, she came to our emergency department with aphasia and right hemiparesis. A radiographic head magnetic resonance imaging revealed a left parietal lobe mass suggestive of intracranial mass versus intracranial hemorrhage. A left parietal craniotomy was carried out and tissue was submitted for pathology. The lesion consists almost entirely of unorganized blood clot. Microscopically, the lesion displayed blood clots admixed with small fragments of cortex and white matter and clusters of tumor cells with strikingly basophilic cytoplasm. Immunostains reveal tumor cells are positive for CK8/18, α1-antitrypsin and are focally positive for S100.

Giant Lateral Ventricle Central Neurocytoma Without Preceding Symptoms From Increased Intracranial Pressure

(Poster No. 18)
Shamima Sultana, MD, PhD (Shamima.Sultana@wmchealth.org); George Kleinman, MD. Department of Pathology, Westchester Medical Center, Valhalla, New York.

Central neurocytoma (CNC) is an extremely rare tumor comprising <1% of all central nervous system tumors, ordinarily a benign intraventricular brain tumor that typically forms from the neuronal cells of the septum pellucidum. Most central neurocytomas grow inwards into the ventricular system, forming interventricular neurocytomas. This leads to 2 primary symptoms of central neurocytoma: blurred vision and increased intracranial pressure. We present a rare case of central neurocytoma in a 35-year-old man who had occipital headache that was relieved with ibuprofen for 1 year and had an episode of generalized tonic clonic seizure. Computed tomography scan revealed a 6.0 × 6.0 × 4.8-cm mass at the level of the body of the lateral ventricles, resulting in severe obstructive hydrocephalus. Right craniotomy was performed and we received fragments of grayish tissue, resembling the gray matter that was admixed with areas of hemorrhage. Microscopically, the tumor was composed of uniform, small to medium-sized cells with rounded nuclei, finely stippled chromatin, and inconspicuous nucleoli, along with scant cytoplasm, and were embedded in eosinophilic fibrillar matrix-forming rosettes. Immunohistochemistry revealed immunopositivity for synaptophysin (≈100%), RMDo-20 (10%), and Neu N (60%–70%); and immunonegativity for GFAP and P53. GFAP immunostain highlighted reactive gliosis at the periphery and occasional trapped astrocytes. Ki-67 labeling index was variable from 1% to 10%.

Denture Cream–Associated Hypocupreemic Myeloneuropathy Secondary to Hyperzincuria: Case Report, Comparison With Gastrectomy-Associated Copper Deficiency, and Literature Review

(Poster No. 19)
Deepak Donthi, MD, MPH (donthi17@ecu.edu); Richard Jordan, BS; Philip Boyer, MD, PhD. Department of Pathology, Vidant Medical Center and East Carolina University, Greenville, North Carolina.

Both chronic reduction in copper absorption in the duodenum and chronic, excess zinc intake lead to reduced serum and organ system copper levels and can manifest with myeloneuropathy and hematologic disease, either anemia or pancytopenia. Clinical muscle and nerve biopsy histopathologic findings in 2 individuals presenting with severe myeloneuropathy due to hypocupremia were reviewed. PubMed and Google Scholar literature searches were performed by using relevant search criteria. A 52-year-old woman status post gastric antrectomy for peptic ulcer disease (control) and a 58-year-old woman with chronic denture cream use presented with progressive sensorimotor neuropathy. In both, muscle biopsy revealed denervation, and nerve biopsy revealed active and chronic axonopathy. Both had severe hypocupremia and the latter had hyperzincuria. Copper supplementation and discontinuation of denture cream use, in the latter, led to some neurologic improvement. Thirty-eight patients presenting with anemia or/and myeloneuropathy symptoms and with reduced copper stores due to denture cream ingestion have been reported in the literature. Most patients had increased serum zinc and 24-hour urinary zinc excretion, when measured. With discontinuation of zinc-based denture cream use and copper supplementation, serum copper levels normalized and anemia corrected. However, while some improvement in myeloneuropathy symptoms occurred in most patients, significant residual deficits persisted in all patients. Dissemination of information about the risk of excess zinc ingestion due to the use of zinc-based denture cream or prolonged zinc supplement use is important. Use of non–zinc-based denture creams and elimination or minimization of the use of zinc-based denture cream can prevent adverse neurologic outcomes.

Dr Boyer has served as a paid expert witness for patient lawsuits against denture cream manufacturers.

Clinical Impact of Mastocytosis in Meningioma

(Poster No. 20)
Raafat Makary, MD, PhD; Daryoush Tavanaiepour, MD; Aysha Mubeen, MD (aysha.mubeen@jax.ufl.edu). Departments of Pathology and Neurosurgery, UF College of Medicine, Jacksonville, Florida.

Meningiomas can be infiltrated by cells from the immune system, including mast cells (MCs). MCs, usually in small numbers, were mainly perivascular and disseminated in the tumor. However, MC-rich meningiomas are relatively rare. MCs secrete an abundance of MC mediators may be an underlying mechanism in some of these tumors. MC mediators may disrupt the integrity of the blood-brain barrier and impact the clinical presentation. We present a case of a 41-year-old woman with history of seizures and diffuse headaches worsened by bright lights. MRI revealed a 2.4-cm left temporoparietal enhancing extraxial dural-based mass without vasogenic edema (Figure 230, A). Histology showed World Health Organization grade 1 fibroblastic meningioma infiltrating skull bone. Numerous perivascular and stromal granulated mast cells were present with associated edema (Figure 230, B through D). MCs are reported in all types and grades of meningiomas; however, higher MC number was reported in secretory, chordoid, cystic/microcystic meningiomas. Mastocytosis in meningioma has been implicated in the pathogenesis of migraines, headaches, and seizures independent of the tumor size/grade. This may explain the symptoms in the presented case. Vasogenic edema is common in intracranial meningiomas (even low-grade) from vascular endothelial growth factor secreted by meningioma cells or in large quantities from MCs and other MC mediators as shown in different studies. MC mediators may be an underlying mechanism in some meningiomas.
case of meningioma-related subdural hematomas. MC-induced perivascular edema and disruption of the blood-brain barrier may facilitate brain metastases or colonization of meningioma by metastases, multiple sclerosis, autism, and brain “fog.” In conclusion, variable clinical presentations may be associated with mastocytosis in meningioma.

Cholesterol-Reducing Agent Myopathy: Spectrum of Histopathologic Features

(Poster No. 21)

Wen Zhong, MD1 (zhongw16@ecu.edu); Mike A. Singer, MD, PhD2; Ebene C. Evans, BS1; Philip J. Boyer, MD, PhD1. 1Department of Pathology and Brody School of Medicine, East Carolina University, Greenville, North Carolina; 2Department of General Medicine Branch 2, Division of Clinical Evaluation and Pharmacology/Toxicology, Center for Biologies Evaluation and Research, US Food and Drug Administration, Silver Spring, Maryland.

While clinical features of statin myopathy and, less commonly, monotherapy fibrate myopathy, have been reported in the literature, histopathologic features have been documented in only a relatively small number of cases. As atins are increasingly prescribed, a clear understanding of possible myopathic effects is important. Case reports are presented representing cholesterol-reducing agent myopathy in the setting of statin (75-year-old man) and fibrate (62-year-old man) monotherapy. A PubMed literature review was conducted by using the key words statin, fibrate, and myopathy. A consensus descriptive definition is compiled. Literature review identified muscle biopsy findings in 116 cases associated with statin monotherapy, 20 with statin and fibrate combination therapy, and 16 with fibrate monotherapy. Findings on muscle biopsy in the 2 case reports were typical of changes described in the literature. Characteristic histopathologic features of active statin and fibrate myopathy are indistinguishable and include (1) immaculate necrosis of individual myofibers with associated macrophage infiltrates along with regenerative changes and (2) absence of an associated lymphocytic inflammatory infiltrate. Subacute and chronic myopathic features may also be seen depending on the time elapsed after onset of myopathic symptoms. Immune- mediated myopathies are rare causes of monotherapy fibrate myopathies. In rare cases, the medication appears to unmask a previously asymptomatic metabolic myopathy. Cholesterol-reducing agent myopathy most commonly manifests with toxic myopathic features. If biopsy is performed weeks to months after discontinuation of statin and/or fibrate therapy, the active phase and associated active myopathic changes of statin- or fibrate-induced myopathy may have resolved, thus posing difficulties for histopathologic interpretation.

Dura-Based Primary Central Nervous System Marginal Zone Lymphoma, Mucosa-Associated Lymphoid Tissue—Type Mimicking Meningioma: Diagnosis and Treatment Choices in Youngest Case to Date

(Poster No. 22)

Renuka Malenie, MD1 (malenie15@ecu.edu); Philip J. Boyer, MD, PhD2; Bethany D. Vallangeon, MD1; Patrick J. Moore, MD1; Darla K. Liles, MD1; Weil Andrew, MD2; Hyder J. Arastu, MD1. Departments of 1Pathology and Laboratory Medicine, 2Internal Medicine, Division of Hematology/Oncology, and 3Radiation Oncology, Vandivert Medical Center, East Carolina University, Greenville, North Carolina.

Extranasal marginal zone mucosa-associated lymphoid tissue (MALT) lymphomas affecting the central nervous system are infrequent, with only occasional case reports in the literature, most commonly seen in middle-aged to older individuals. This lymphoma is associated with involvement of the dura rather than neureparchyma. There are currently no defined treatment protocols/guidelines. We describe the case of a 22-year-old woman diagnosed with a MALT lymphoma of the dura. A literature review was performed. The patient presented with headaches dissimilar from previous migraine headaches she had experienced. Imaging identified a dural-based mass associated with the right petrous ridge causing moderate mass effect, favoring meningioma. Gross total resection was undertaken via a right suboccipital craniotomy. Histologically revealed an atypical lymphoid infiltrate consisting of small, round, mature-appearing lymphocytes with a B-cell phenotype (CD45/CD20+) without discernible coexpression of CD5, CD23, BCL1, or BCL6. Immunoglobulin heavy chain gene rearrangement was detected by polymerase chain reaction. She was treated with 6 cycles of rituximab, cyclophosphamide, vincristine, and prednisone. Imaging at 6- and 12-month intervals post resection was negative. An involved-field radiation therapy is scheduled. To date 42 cases of dura-based MALT lymphoma have been reported; 29 involve women 33 to 77 years of age, 2 of which presented in an infratentorial location. To our knowledge, this case reports the youngest patient with dura-based primary central nervous system MALT lymphoma and is among the young monomorphy of cases presenting infratentorially. MALT lymphomas may present as a dural-based mass mimicking meningioma. Patients’ outcome will add to the limited therapy options currently available.

Atypical Neutrophilic Papulopanniculitis Tumor of the Peculiar Type Mimicking Meningioma: Diagnosis and Treatment

(Poster No. 23)

Yan Chen Wongworawat, MD, PhD1 (ychenwongworawat@llu.edu); Yin A. Liu, MD, PhD2; Robin Dietz, MD1; Charles L. White III, MD, Jefferson Rosenfeld, MD1; Ravi Raghavan, MBBS, MD, MKpath,1 Departments of 1Pathology, 2Pediatrics and Neurology, and 3Neurol- ogy, Loma Linda University Medical Center, Loma Linda, California; 4Department of Pathology, University of Texas Southwestern Medical Center, Dallas.

A 29-year-old man presented with rapidly progressive severe neck weakness, asymmetrical bilateral upper extremity weakness, profound muscle wasting, bulbar dysfunction, and weight loss. During the course of 1 year, his speech became unintelligible, he became gastrostomy and tracheostomy/ventilator dependent, and wheelchair bound. He had mild intellectual disability and was a candidate for cranial radiosurgery for a surgically refractory mass. A PubMed literature review was conducted by using the key words “malignant lymphoma” in tumors of the cranial compartment. No clear evidence exists to indicate whether this case presents a unique entity or represents atypical meningioma. The patient was treated with 6 cycles of rituximab, cyclophosphamide, vincristine, and prednisone. Imaging at 6- and 12-month intervals post resection was negative. An involved-field radiation therapy is scheduled. To date 42 cases of dura-based MALT lymphoma have been reported; 29 involve women 33 to 77 years of age, 2 of which presented in an infratentorial location. To our knowledge, this case reports the youngest patient with dura-based primary central nervous system MALT lymphoma and is among the minority of cases presenting infratentorially. MALT lymphomas may present as a dural-based mass mimicking meningioma. Patients’ outcome will add to the limited therapy options currently available.

Carcinoma ex Pleomorphic Adenoma Metastatic to the Peculiar Lymph Node

(Poster No. 24)

Roshan Mahabir, MD, PhD, MPH1 (roshan.mahabir@mountsinai.org); Amir Banhashemi, MD, MD; Mary D. Umphlett, MD; Mary Fowkes, MD, PhD1. 1Department of Pathology, Mount Sinai St. Luke Roosevelt, New York, New York; 2Department of Pathology, Mount Sinai Hospital, New York, New York; 3Department of Pathology, Mount Sinai Icahn School of Medicine, New York, New York.

Carcinoma ex pleomorphic adenoma (CEPA) is an aggressive malignancy with a high rate of recurrence and metastasis. Most cases metastasize to lungs, bone, spleen, and liver. Here we report a rare case of metastatic CEPA to the pineal gland and brain in a 59-year-old man with a history of parotid pleomorphic adenoma 30 years prior and CEPA with metastasis to multiple ipsilateral lymph nodes 4 years prior. The patient presented with increasing dizziness and decreased visual acuity and was found to have hydrocephalus on imaging. MRI showed multiple lesions within the brain parenchyma and an enhancing midline lesion with obstruction of the cerebral spinal fluid outflow tract. The patient had therapeutic shunt placement and underwent resection of tumors in the pineal gland and cerebrum, both of which microscopically showed a similar pattern of moderately cellular nests of epithelioid cells with small round uniform mitotic figures and pleomorphic nuclei with prominent nucleoli. The tumor had focal gland formation and invaded surrounding parenchyma. There were areas of extensive comedo-type necrosis in the cerebellum. Immunohistochemical analysis showed tumor cells were strongly positive for CAM 5.2, CK7, and...
androgen receptor. The tumor cells showed patchy positivity for CEA and were negative for CK20 and calponin. Neurofilament and synaptophysin stains highlighted only the surrounding pineal gland. This case represents the second documented case of an aggressive CEPA tumor metastatic to the brain and pineal gland requiring early recognition and appropriate management.

Unexpected FAT1 (D2258fs*2) Genomic Alterations Identified in Glioblastoma: Deep Gene Sequencing Showing More Data?  
(Poster No. 25)

Sean M. Hacking, MB, BCh, BAO (shacking@northwell.edu); Deepika Savant, MB, BS; Mansoor Nasim, MD, PhD. Department of Pathology, Northwell Health, Lake Success, New York.

A 50-year-old man presented with amnesia and ataxia during a short time period. Computed tomography of the head showed a 6.4x4.3-cm lesion with mass effect on left lateral ventricle, as well as left-right shift. Histology showed high-grade glioma with nuclear atypia (gemistocytic), increased mitotic activity, microvascular proliferation, and focal necrosis. Immunostains were positive for GFAP, p53 (100% strong nuclear staining), EGF receptor (positive), and Ki-67 (up to 60%); as per World Health Organization 2016 classification, the tumor was classified as glioblastoma. Next-generation sequencing showed amplification of CDK4 and PIK3CA (not uncommon) and an uncertain variant in FAT1 (D2258fs*2). Significant therapies targeting CDK4 and PIK3CA amplification status have been FDA approved for other tumors, but have not been approved for glioblastoma. These therapies include Palbociclib for CDK4 and Everolimus for PIK3CA. The tumor board at our institution was not sure what to do with the data. More research needs to be done regarding the possible use of therapeutics for glioblastoma; therapies targeting the same genomic alterations have been used in other tumor types. Regarding the unclear variant in FAT1 (D2258fs*2), to the best of our knowledge this has not been reported in glioblastoma. Although possibly disease associated, with paucity of clinical and functional evidence regarding this variant, it makes its clinical significance currently unclear. We strongly believe that unknown mutations need to be reported and followed up to define their clinical significance.

Diffuse Midline Glioma H3 K27-Mutant in an Adult and a Child  
(Poster No. 26)

Sepideh N. Asadbeigi, MD1 (sepideh-asadbeigi@ouhs.uc.edu); Jo Elle G. Peterson, MD; Naina L. Gross, MD; Bradley N. Bohnstedt, MD; Rene Y. McNall-Knapp, MD; James D. Battiste, MD, PhD; Kar-Ming Fung, MD, PhD.1 Departments of 1Pathology, 2Neurosurgery, 3Pediatrics (Hematology and Oncology), and 4Neurology (Oncology), University of Oklahoma Health Sciences Center, Oklahoma City.

Diffuse midline glioma, H3 K27M-mutant, World Health Organization grade IV (DMGM), is a newly recognized entity in the 2016 World Health Organization classification. They are uncommon and the median age of diagnosis is 5 to 11 years. Owing to their rarity in adults, their recognition can be challenging, albeit the histopathology and phenotypes of adult and pediatric cases are similar. We are presenting 2 cases to illustrate this. The first patient was a 41-year-old woman who presented with seizure. MRI showed an enhancing suprasellar mass involving the hypothalamic region. The resected tumor was a neoplastic glial proliferation with endothelial proliferations. The tumor cells were focally positive for synaptophysin and largely negative for glial fibrillary acidic protein (GFAP), positive for H3 K27M, and negative for H3 K27Me3. The second case involved a 6-year-old girl who presented with lethargy. MRI showed a thalamic hemorrhage followed by an enhancing mass in the right thalamus. The resected mass showed a high-grade, cellular glial proliferation with focal endothelial proliferation. The tumor cells were diffusely positive for GFAP, positive for H3 K27M, and negative for H3 K27Me3. Some necrosis was present in both of the DMGM cases but there were no pseudopalisading necrosis. The presence of endothelial proliferation, variable negative expression of GFPA, variable positive expression of synaptophysin, and 50% mutation rate of p53 in DMGM can easily suggest other diagnoses including glioblastoma, neurocytoma, glioneuronal tumors, and embryonal tumor of the central nervous system tumors in DMGM with particularly high cellularity. Owing to their rarity, the diagnosis of DMGM is more challenging in adults and should be recognized.

Primary Synovial Sarcoma of the Anterior Mediastinum: A Rare Twist on the “4 Terrible Ts” of Anterior Mediastinal Masses  
(Poster No. 27)

John M. Gross, MD1 (jm1444@gmail.com); Peter Abosolo, MD2; Deborah Perry, MD; Jeri Bedniecek, MD; Julia A. Bridge, MD.1 Departments of Pathology, Creighton University School of Medicine, Omaha, Nebraska; 2Department of Pathology, Children’s Hospital, Omaha, Nebraska; 3Department of Pathology, University of Nebraska Medical Center, Omaha.

Synovial sarcoma is a mesenchymal tumor that displays a variable degree of epithelial differentiation, including gland formation, and has a specific chromosomal translocation t(X;18)(p11;q11) leading to the formation of an SS18-SSX fusion gene. Primary synovial sarcomas of the anterior mediastinum are exceedingly rare. The most common tumors in the anterior mediastinum are often referred to as “the 4 terrible Ts”: thymoma, teratoma/germ cell, (terrible) lymphoma, or thyroid tissue. We present a case of a 15-year-old boy presenting with chest pain for several months. A chest computed tomography revealed a 10.0 × 8.0-cm, lobular, mixed solid and cystic mass of the anterior mediastinum with resultant mass effect on the heart and great vessels (Figure 231, A). A biopsy contained dense sheets of monotonous ovoid to spindled cells with vesicular chromatin, dotlike nucleoli, ampie mitotic figures, and necrosis (Figure 231, B). Immunohistochemistry showed focal pancytokeratin expression (Figure 231, C) as well as strong, diffuse, membranous CD99 expression (Figure 231, D). Additionally, molecular diagnostics detected the SS18-SSX2 fusion transcript by RT-DNA amplification. The primary occurrence of an anterior mediastinal synovial sarcoma is very rare with only a few reported cases in the world literature. A diagnosis of synovial sarcoma should be entertained with any spindled to biphasic tumor in this location. Finally, this case highlights the importance of prompt clinical suspicion and accurate histopathologic diagnosis, including immuno- histochemical and molecular studies, in the diagnosis of an unusual tumor in an unusual site.

Primary Lung Intravascular Large B-Cell Lymphoma Clinically Mimicking Sarcoidosis: A Rare Case Report and Review of Literature  
(Poster No. 28)

Sara Masood, MD1 (masood@etsu.edu); Sarah Kassaby, MD; Karthik Vijayan, MD2; John C. King, MD; Yurong Wheeler, MD, PhD.1 Departments of 1Pathology and 2Pulmonology, East Tennessee State University, Johnson City.
Intravascular large B-cell lymphoma (IVLBCL) is a rare distinct subtype of systemic extranodal non-Hodgkin lymphoma, where mature B-cell lymphoma cells proliferate exclusively in the lumina of small vessels. A primary pulmonary presentation is very uncommon, and a diagnosis can be difficult owing to the lack of detectable tumor masses or specific radiographic findings, which may lead to a delayed diagnosis and poor prognosis. We report a case of a 73-year-old man who initially presented with night sweats, intermittent fever, worsening dry cough, and shortness of breath. Computed tomography scans revealed atelectasis and calcified mediastinal lymphadenopathy, raising a suspicion for sarcoidosis. Multiple lung biopsies were performed. Microscopically, atypical lymphocytes were identified within capillaries, small arteries, and veins. These lymphocytes were large with prominent nuclei (Figure 232). Immunohistochemical staining showed the tumor cells were positive for CD20, CD79a, Pax-5, CD10, and Mum-1, while negative for CD3, cytokeratin, S100, and CD34. LDH serum level was increased (480 IU/L). Extrapulmonary lymphoma was not detected elsewhere in the patient. These findings support the diagnosis of primary lung IVLBCL. The patient is currently undergoing chemotherapy with R-CHOP regimen. Literature review of 41 cases demonstrated occurrence of primary lung IVBCL in patients 35 to 85 years of age with a slight male predominance (1.4:1). The most common clinical presentation was fever associated with dyspnea. Awareness of this wide spectrum of clinical presentation in IVBCL is important for a timely diagnosis and consequently a proper treatment.

Evaluation of Programmed Death Ligand 1 (PD-L1) Expression and Its Association With Clinicopathologic Features in Filipino Patients With Lung Cancer

(Poster No. 29)

Flora Mae G. Sta. Ines, MD; Jose Jasper Andal, MD; Daphne C. Ang, MD (daphnehchuang@yahoo.com). Department of Pathology, St. Luke’s Medical Center, Global City, Philippines.

Context: Lung cancer (LC) treatment involves immune checkpoint mechanisms involving programmed cell death (PD-1)–programmed cell death ligand (PD-L1) axis. PD-L1 expression on tumor cells (TCs) has been previously reported to predict response to PD-1/PD-L1 inhibitors. There are currently no data regarding pattern of PD-L1 expression in TCs and immune cells (ICs) in LC of Filipino patients.

Design: Clinicopathologic characteristics of 77 consecutive naive LC samples with PD-L1 testing using the clone 22C3 pharmDX kit were retrieved. PD-L1 expression on TCs and immune cells (ICs) were evaluated.

Results: Of the 77 cases, 56 were males and 21 were females. The median age at diagnosis was 67 years (32–88 years). The cases include 53 cases of adenocarcinoma; 8 of squamous cell carcinoma; 5 of adenosquamous carcinoma; 10 of non–small cell LC, not otherwise specified; and 1 case of small cell LC. Specimen types included 8 pleural effusion cell block samples, 33 tumor cell block samples, and 36 tissue biopsies. Of the 36 tissue biopsies, tumor-infiltrating lymphocytes were identified in 67% of cases. PD-L1 expression in TCs and ICs was not significantly different (52% and 68%, respectively, P = .64). PD-L1 tumor proportion scores (TPS) were as follows: TPS >50, TPS = 1–49, and TPS < 1% were observed in 21%, 31%, and 48% in our lung cancer cohort, respectively. PD-L1 expression in TCs did not correlate with age, sex, or histology.

Conclusions: PD-L1 expression was seen in more than half (52%) of LC patients in our cohort. The prognostic value of PD-L1 and clinical response to checkpoint inhibitors in the Filipino population need to be further investigated.

Lung Adenocarcinoma With Predominantly Rhabdoid Morphology Presenting as a Lower Gastrointestinal Bleed

(Poster No. 30)

Sierra Musick, MD (sierra.r.musick.mil@mail.mil); Brent Huddleston, MD. Department of Pathology, Brooke Army Medical Center, San Antonio, Texas.

Tumors with predominantly rhabdoid morphology are rare and pose a diagnostic challenge when presenting as metastases from an unknown primary location. A good clinical history and strategic immunohistochemistry panel are paramount, as most malignancies with predominantly rhabdoid morphology are extremely aggressive and swift implementation of treatment maximizes the patient’s chances of success. We present the case of a 57-year-old man with a history of HIV who presented with several weeks of fatigue and a lower gastrointestinal bleed. On imaging, he was found to have a small intestinal mass and a right upper lung cavitary lesion with mediastinal lymphadenopathy; infectious diseases were ruled out. Upon small-bowel resection due to uncontrollable bleeding, a hemorrhagic cavitary mass involving the mucosa and suberosal fat was identified. The neoplasms showed sheets of pleomorphic cells with abundant, finely vacuolated granular eosinophilic cytoplasm and eccentrically placed, irregularly shaped nuclei with vesicular chromatin. Subsequent mediastinal lymph node fine-needle aspiration showed similar morphology and both specimens demonstrated positivity for TTF-1, FLI1, and CK7. The tumor cells from both sites were negative for desmin, Myo-D1, CD45, and S100. No other masses were found on further imaging, leading to the diagnosis of a primary lung adenocarcinoma with metastasis to the small bowel. This case highlights the diagnostic difficulty in assigning metastatic tumors with predominantly rhabdoid morphology to a primary location and serves to enhance knowledge of the clinical and histologic spectrum of lung adenocarcinomas.

Utility of a Comprehensive Cost-Effective Targeted DNA/RNA Panel (170 Genes) on a Next-Generation Sequencing Platform in Evaluation of Lung Cancers for Prognosis and Therapeutics

(Poster No. 31)

Ravindra B. Kolhe, MD, PhD (rkolhe@augusta.edu); Ashis Mondal, Ph.D; Chetan Pandkar, Ph.D; Benjamin Johnson, BS; Alka Chauhey, PhD. Department of Pathology, Medical College of Georgia at Augusta University, Augusta.

Context: Currently, next-generation sequencing techniques are being widely used as a tool in routine oncology workflows. Most laboratories use either DNA-based panels or 2 separate DNA and RNA panels. The objective of our project was to evaluate the utility of a comprehensive 170-gene enrichment–based targeted panel that simultaneously analyzes DNA and RNA in lung non–small cell carcinoma (NSCLC). The panel targets all coding exons in 170 genes, 55 genes for protein kinases, 74 for mRNA transcripts, and 41 for small RNAs. H&E slides were examined and the diagnoses were confirmed. Subsequently, sequencing was performed on DNA/RNA isolated from formalin fixed, paraffin-embedded tissue on a NGS platform (NextSeq, Illumina). The variant and fusion calls were read and interpreted on the software provided by the manufacturer (Illumina, San Diego, California).

Results: All the calls with high confidence on the NGS platform matched 100% with the PCR and FISH findings in all the 22 cases (Figure 233).

Utility of a Comprehensive Cost-Effective Targeted DNA/RNA Panel (170 Genes) on a Next-Generation Sequencing Platform in Evaluation of Lung Cancers for Prognosis and Therapeutics

(Poster No. 31)
Conclusions: In this study, we present an NGS panel in which tumor-specific information on genes that are considered highly important in lung tumors can be investigated in a single panel, thus providing sample efficiency and cost reduction.

Dr Kolhe has served as a consultant to Illumina and Qiagen. Thoracic Solitary Fibrous Tumor With Dedifferentiation: Appropriate Differential Diagnosis (Poster No. 32) Ganna Shestakova, MD, PhD; Zada Sherehan Zada, MD; Wamda Goreal, MD. 'Department of Pathology, University of California, Irvine, Orange; 'Department of Medicine, University of Aleppo, Syrian Arab Republic.

Solitary fibrous tumors (SFTs) are mesenchymal neoplasms that occur ubiquitously in the body. Thirty percent of SFTs occur in association with the thoracic cavity. Dedifferentiation or malignant transformation occurs in less than 1% of cases with 30 cases reported worldwide. Dedifferentiated SFT warrants an adverse prognosis and its recognition is paramount for appropriate diagnosis, treatment, and patient follow-up. We report a case of a large thoracic solitary fibrous tumor (18 × 13 × 9 cm, 1485 g) with an area of dedifferentiation or sarcomatoid component arising in the mediastinum of a 59-year-old man. Morphology and immunohistochemistry supported SFT with a juxtaposed high-grade dedifferentiated area separated from the conventional SFT by the thin fibrous septae. Cytophenetic and immunohistochemical studies were implemented to arrive at the correct diagnosis. H&E routine staining showed spindle cell neoplasm with a sharply demarcated high-grade sarcomatoid area consistent with the dedifferentiated component. By immunohistochemistry, the well-differentiated SFT area was immunoreactive with CD34, Bcl-2, and Stat-6, but not with S100 protein, WT-1, desmin, calretinin, SMA, or AE1/3. Importantly, Stat-6 immunoreactivity was preserved in a sarcomatoid high-grade area, consistent with a dedifferentiated SFT.

Focal immunoreactivity with Tle-1 prompted further workup for SSY18 (SYD) rearrangement to rule out synovial sarcoma. The Ki-67 labeling index in the dedifferentiated area was approximately 10%. Stat-6 is instrumental in indicating correct origin in mesenchymal tumors showing high-grade sarcomatoid area. This case is diagnosed as a dedifferentiated SFT from its Stat-6 expression in conventional and high-grade dedifferentiated areas (Figure 234).

A Case Report Study of a Rare Pulmonary Sarcomatoid Carcinoma Diagnosis (Poster No. 33) Yasir Ali, MD (yasir.d.ali@uth.tmc.edu); Manju Ambelil, MD; Albina Muzabaddilova, MD; Peisha Yan, MD. Department of Pathology and Laboratory Medicine, The University of Texas Health Science Center McGovern Medical School, Houston.

Sarcomatoid carcinoma is a rare cancer that can occur in multiple organs, such as skin, bone, thyroid, adrenals, pancreas, and urinary tract. Pulmonary sarcomatoid carcinoma (PSC) is highly aggressive and constitutes less than 1% of all lung cancers. The World Health Organization subclassifies it into 5 main variants including pleomorphic, giant cell, spindle cell, carcinosarcoma, and pulmonary blastoma. This is a case report of 60-year-old African American woman smoker who presented with chronic left-sided upper back, shoulder, and chest pain. Imaging revealed a large mass in the left upper lobe with mediastinal and chest wall invasion for which a fine-needle core biopsy was performed for pathologic diagnosis. Microscopic examination of the core biopsy reveals poorly differentiated atypical cells with spindle cell morphology. Immunohistochemical stains with appropriate controls demonstrate tumor cells that are positive for pancytokeratin and vimentin. The tumor cells are negative for CK7, CK20, CK5/6, EMA, P40, PAX8, D2-40, calretinin, and TTF1. Ki-67 shows high proliferative index. This staining pattern supports the diagnosis of poorly differentiated carcinoma with sarcomatoid carcinoma features. Because of the poor prognosis of the patient’s condition and her complicated clinical course, pulmonary sarcomatoid carcinoma is an aggressive rare lung malignancy that has been associated with a significantly worse prognosis than other types of non–small cell lung carcinomas. We report the case to enrich the literature with more cases, which help us in early recognition and appropriate treatment of this uncommon entity.

Intraoperative Assessment of Disease Extent in a Patient Who Presented With Pneumonia-like Mucinous Lung Adenocarcinoma (Poster No. 34) Abbye E. McEwen, MD, PhD (amcewen@uw.edu); Haodong Xu, MD, PhD. Department of Pathology, University of Washington, Seattle.

Primary pulmonary adenocarcinoma has numerous different radiographic presentations. Many cases present with a consolidation pattern that can mimic diffuse pulmonary parenchymal processes like infectious pneumonia. This is the case of an 84-year-old man, a former sheet metal worker with significant asbestos exposure and a remote history of smoking, who presented with a right lower lobe consolidation that did not resolve with antimicrobial therapy. Computed tomography and PET imaging studies showed a hypermetabolic area in the right lower lobe with extensive surrounding consolidation of all 3 lobes. This prompted a biopsy of the lower lobe mass, which demonstrated adenocarcinoma. A biopsy of the right upper lobe performed intraoperatively demonstrated mucinous adenocarcinoma, percutaneously obtained at the time of the operative diagnosis. The presence of right upper lobe involvement was confirmed in the final resection specimen. Grossly, a firm white mass was found in the posterior right lower lobe. The mass was surrounded by consolidated, myxoid-appearing lung parenchyma with extensive involvement of the lower, middle, and upper lobes. Histologically, the main mass (hypermetabolic on PET) consisted of invasive adenocarcinoma with mucinous and nonmucinous features including papillary and micropapillary patterns. Mucinous adenocarcinoma was identified in the consolidated areas of all 3 right lung lobes. This case underscores the importance of intraoperative consultation in patients with pulmonary consolidation in the context of known adenocarcinoma, as radiology alone cannot distinguish between pneumonic-like adenocarcinoma and nonneoplastic processes.
The diagnosis of small cell lung cancer (SCLC) is based on morphology and a characteristic immunophenotype that includes cytokeratin positivity, TTF-1 positivity in many cases, and evidence of neuroendocrine differentiation with markers such as CD56, synaptophysin, and chromogranin. We report a case of SCLC expressing desmin, positive for pancytokeratin, CK7, CD56, TTF1, desmin. A 34-year-old man with a history of smoking presented with 3 months of progressive cough and wheezing. Computed tomography scan demonstrated a 7-cm mediastinal and tracheal mass. Bronchoscopy revealed a fungating mass in the mid to distal trachea that was biopsied and debulked. Hematoxylin-eosin–stained sections (Figure 235, A and B) showed tumor cells with a high nuclear to cytoplasmic ratio and hyperchromatic nuclei forming sheets and nests. Nuclear molding, increased mitoses, extensive necrosis, and apoptotic cells were also present. Given the patient’s young age and tumor location, a broad differential diagnosis was considered. The tumor cells were strongly positive for pancytokeratin, CK7, CD56, TTF1 (Figure 235, C), desmin, and synaptophysin, and chromogranin. Interestingly, desmin (Figure 235, D) was focally positive, although negative for myogenin and WT-1. FISH was negative for EWSR1. The morphologic appearance and the ancillary studies supported the diagnosis of a high-grade neuroendocrine tumor best classified as SCLC. Given the radiographic and bronchoscopic findings, a lung primary and a thymic primary were both suggested. An extensive review of literature did not show any prior reports of desmin positivity in small cell carcinoma originating in a thoracic site. Such aberrant expression should be kept in mind when cases are histologically atypical or when the clinical presentation is unusual, as in this case.

### Lipoid Pneumonia-like Reaction Associated With THC Use and Vaping (Electronic Cigarette Use)

**(Poster No. 37)**

Sandra White, MD (swhite@cellnetix.com); Timothy Wade, MD; Daniel Olsen, MD. Department of Pathology, CellNetix Pathology and Laboratories, Seattle, Washington.

The legalization of marijuana in Washington State in 2012 has coincided with an increase in the use of electronic cigarettes (e-cigarettes/vaping). We report 2 cases of lipogenic foreign material in patients with a positive history of marijuana use. The patients, ages 26 and 31 years, both presented with chest pain and shortness of breath. The 26-year-old patient presented with worsening right lower lobe and right middle lobe cavitory lesions and associated pulmonary infiltrates that progressed to persistent patchy airspace opacities and interlobal septal thickening by imaging. This patient reported regular use of marijuana via vaping. The 31-year-old patient presented with pleural blebs and spontaneous pneumothorax after smoking marijuana. This patient reported using 2 g of marijuana per day via smoking; however, the specific method of marijuana smoking is unknown. Lung biopsies from both patients demonstrated lipid material with associated foreign body reaction consistent with lipid pneumonia. Exogenous lipid pneumonia is essentially a foreign body giant cell reaction to fat. Cases of exogenous lipid pneumonia have previously been described in association with inhalation of fat-containing substances such as petroleum jelly, mineral oil, some laxatives, sesame oil pulling, and other fat-containing substances. The active cannabinoids within marijuana are lipid soluble and therefore, a hydrophobic solution is required for vaping that may contribute to a lipid pneumonia. Owing to recent changes in state laws, use of marijuana via vaping could be an emerging cause of pulmonary disease associated with an exogenous lipid pneumonia-like reaction.

### Rare Case of a Centrally Located Pulmonary Sclerosing Pneumocytoma Mimicking Carcinoma on Frozen Section

**(Poster No. 38)**

Morgan Blakely, MD (morgan.blakely@mountsinai.org); Mary Beth Beasley, MD. Department of Pathology, Mount Sinai Hospital, Icahn School of Medicine, New York, New York.

Pulmonary sclerosing pneumocytomas (SCs) are rare benign neoplasms thought to arise from primitive respiratory epithelium and are characterized by 2 cell types: surface and round cells. SCs most commonly present in women aged 40 to 50 years and almost exclusively (94.6% in the largest series of 100 cases) in the periphery of the lung. SCs are known to be a challenge on cytology, frozen section, and biopsy, particularly with limited material. We present a diagnostically challenging case of a 49-year-old Asian woman with an SC arising in a central hilar location and mimicking adenocarcinoma on cytology, biopsy, and frozen section. On fine-needle aspiration cytology, a diagnosis of atypical cells cannot rule out adenocarcinoma was rendered. Bronchial mini-forceps biopsy showed atypical cells, suggestive of adenocarcinoma (Figure 236, A). On frozen section, the mass displayed glandular-like spaces with significant nuclear atypia and was diagnosed as favor adenocarcinoma (Figure 236, B). Grossly, the tumor was 3.8 × 3.2 cm within the left upper lobe and centrally located next to the main stem bronchus (Figure 236, C). On permanent sections, the tumor displayed all 4 characteristic morphologic patterns of SC: papillary, sclerotic, solid, and hemorrhagic (Figure 236, D). Immunohistochemically, the surface cells were positive with CK7, while the round cells were positive for progesterone receptor. Both cell types
were positive with TTF-1 as expected. This case demonstrates that the pathologist must be vigilant for the potential morphologic pitfalls of SC on biopsies and frozen section, even in centrally located tumors.

Characterizing the Microbiologic Milieu in the Posttransplant Lungs of Cystic Fibrosis Patients: A Single Institution Study
(Poster No. 39)

Austin McHenry, BS; Vijayalakshmi Anantharanayanan, MD; Erin Lowery, MD; Daniel Dilling, MD. Departments of Pathology and Pulmonary & Critical Care Medicine, Loyola University Chicago, Maywood, Illinois.

Context: Patients with cystic fibrosis (CF) often require lung transplant owing to chronic tissue damage from persistent infection and airway inflammation. Acute cellular rejection (ACR) in this population is often complicated by posttransplant microbial colonization. However, the role of specific microbiologic infection on ACR in this population remains incompletely understood.

Design: We correlated microbiologic agents isolated from posttransplant bronchoalveolar lavage in patients with CF collected at the time of routine rejection surveillance with transbronchial biopsy rejection status. ACR statuses were collected from final diagnosis reporting, based on the 2007 revised International Society for Heart and Lung Transplantation grading scheme. We examined 18 posttransplant lungs at Loyola University Medical Center, correlating to 173 biopsies. Microbiologic isolates were categorized as bacterial, fungal, or community-acquired respiratory viruses (CARVs). Herpesviridae were excluded. Results were analyzed by paired 1-way ANOVA.

Results: Of the biopsies, 120 (69.3%) had correlating BAL studies positive for microbiologic isolation, of which 80.0% (96) were bacterial, 25% (30) fungal, and 10.8% (13) CARVs. There was no significant correlation between microbiologic isolation and ACR status for bacterial isolation (P = 0.21), fungal isolation (P = 0.10), or CARV isolation (P = 0.17).

Conclusions: The systematic evaluation of airway microbiologic isolation in this study shows that the presence of clinical infection alone may not be a predictor of higher-grade rejection in CF patients. Ongoing studies include correlation with histopathologic neutrophil and eosinophil infiltration, presence of airway fibrosis, bronchiolitis obliterans, chronic lung allograft dysfunction, and survival data.

Uncommon Presentation of Lymphoma as a Pleural-Based Cavitary Lesion
(Poster No. 40)

Garth W. Strohbehn, MD, MPH; Vasuki Anandan, MD. Department of Internal Medicine, University of Michigan, Ann Arbor; Department of Pathology, Veterans Administration Ann Arbor Medical Center, Ann Arbor, Michigan.

A 72-year-old man with rheumatoid arthritis treated with abatacept, methotrexate, and prednisone presented with 3 weeks of fatigue, shortness of breath, and dry cough, unresponsive to antibiotics. Computed tomography of the chest showed bilateral pleural-based cavitary masses with areas of central necrosis (Figure 237, A). Positron emission tomography subsequently revealed hypermetabolic bilateral lung masses and left cervical lymphadenopathy of similar standardized uptake values (Figure 237, B). Core needle biopsy of the right pleura showed the infiltrates were composed of large, malignant-appearing cells with irregular nuclear contours, and scant cytoplasm admixed with areas of necrosis. The presence of extensive necrosis made epithelial malignancy the primary suspect. Initial panel of immunostains targeted against different types of carcinomas, including CK7, CK20, Napsin, TTF-1, p63, and CK5/6, was negative. Following this, a broad-based lymphoma and melanoma panel was attempted. Negative S100 and MART-1 did not support a melanoma diagnosis. However, positive LCA, CD20, and BCL6 costaining (Figure 237, C) and MUM1 (Figure 237, D) confirmed a nongerminall center-type diffuse large B-cell lymphoma (DLBCL). DLBCL is the most common subtype of non-Hodgkin lymphoma occurring in the lung, and there is a known association with rheumatoid arthritis. The unique presentation of this case as a pleural-based cavitation lesion has not been reported and deserves increased awareness to aid in better diagnosis.

A Novel DICER1 Mutation Associated With Pleuropulmonary Blastoma: A Report of 2 Cases in Siblings
(Poster No. 41)

Bruce D. Leckey, DO; John M. Carney, MD; Elizabeth N. Pavlisko, MD. Department of Pathology, Duke University Medical Center, Durham, North Carolina.

Pleuropulmonary blastomas are rare aggressive pediatric lung malignancies associated with DICER1 (14q32.13, encoded protein is a ribonuclease) mutations. We present 2 cases, that of a 2-year-old girl with several months of upper respiratory tract symptoms as well as that of a 6-month-old girl, a sibling, undergoing screening owing to a strong family history of malignancy. Computed tomography of the 2-year-old girl revealed a heterogeneous, cystic and solid, septated mass occupying the right hemithorax. A lobectomy was performed. Gross examination revealed a multicystic and solid mass containing grapelike protrusions. Histopathological demonstration cystic spaces and solid areas of rhabdomyosarcoma (Figure 238, A), chondrosarcoma (Figure 238, B), and undifferentiated spindle cell sarcoma. Immunohistochemistry demonstrated positive immunoreactivity for myoD1, myogenin, and desmin (Figure 238, C) with negative immunoreactivity for pancytokeratin. Electron microscopy demonstrated immature spindle cells with intracytoplasmic glycogen, variable amounts of actin and myosin.
filaments, as well as prominent sarcomere formation with distinct Z-bands (Figure 238, D). This tumor was classified as a type II pleuropulmonary blastoma. Metastasis to the diaphragm was present at the time of initial diagnosis. Screening computed tomography of the 6-month-old girl demonstrated a 6 × 7-mm cystic lesion with a single septation in the posterior basal segment of the right lower lobe. A lobectomy was performed and gross examination showed a multi-septate cystic lesion. Histopathology revealed cystic spaces lacking malignant cells consistent with type I r pleuropulmonary blastoma. Sequence analysis in both cases confirmed the same DICER1 mutation, intron 15 c.2437-2A>G, which has not been previously described in the literature and likely represents a pathogenic mutation.

A Rare Case of Pleuroparenchymal Fibroelastosis in a Patient With Bilateral Pneumothoraces

(Poster No. 42)

Aaron Muhlbaier, MD1 (aaron.muhlbaier@lumc.edu); Katie Young, MD2; Kevin P. Simpson, MD2; Vijayalakshmi Ananthanarayanan, MD.1 Departments of 1Pathology and 2Pulmonary and Critical Care Medicine, Loyola University Medical Center, Maywood, Illinois.

In 1992, Amitani et al described an idiopathic interstitial lung disease characterized by dense fibrosis of the visceral pleura and subjacent lung parenchyma with a predilection for the upper lobes. Two decades later, pleuroparenchymal fibroelastosis (PPFE) became the widely adopted terminology. To date, there have been an estimated 120 cases reported. We present the case of a 65-year-old woman with a history of interstitial lung disease complicated by multiple pneumothoraces, who was admitted to our hospital for worsening dyspnea. Recently retired, the patient worked at a factory for 30 years, with exposure to dust and paint/paint thinners. Otherwise, the patient had no other known history of environmental exposure and denied any history of smoking. Chest imaging revealed bilateral apical pneumothoraces, septal thickening, bronchiectasis, and a bilateral subpleural distribution of ground glass opacities. For definitive diagnosis, wedge biopsies of the left lung were performed, showing pleural and subpleural parenchymal fibrosis, most prominent in the upper lobe. Trichrome and EVG stains highlighted the fibroelastosis centered on the pleura and subpleural parenchyma. No granulomas were identified. The main differential diagnosis was apical caps. Based on the overall morphology of our case, a final diagnosis of idiopathic pleuroparenchymal fibroelastosis was made. A distinct clinicopathologic entity, pleuroparenchymal fibroelastosis should be considered in the differential diagnosis of interfstitial lung diseases, notably in cases of subpleural fibrosis with upper lobe predominance or in patients with spontaneous pneumothoraces. Early diagnosis and prompt referral for lung transplant is crucial, as this disease is associated with a poor prognosis.

Immune Microenvironment in Large Cell Neuroendocrine Carcinoma of the Lung

(Poster No. 43)

Marina K. Baine, MD, PhD (marina.baine@yale.edu); Nikita L. Mani, PhD; David L. Rimm, MD, PhD; Robert J. Homer, MD, PhD. Department of Pathology, Yale University, New Haven, Connecticut.

Context: Examination of the tumor immune microenvironment by assessing tumor-infiltrating lymphocytes (TILs) and tumor PD-L1 expression has become a valuable tool in determining prognosis and response to therapy. Currently these data are not available for pulmonary large cell neuroendocrine carcinoma (LCNEC), likely owing to its extremely low incidence.

Design: Using multiplexed quantitative immunofluorescence (QIF), we measured levels of TIL subsets in 3 distinct tumor areas in 21 cases of LCNEC. Tumor immune status (cold versus hot-dormant versus hot-active) was determined from the number of CD3 TILs, and Granzyme B and Ki-67 expression. Tumor and TIL expression of PD-L1 (22C3) was quantified by brown stain immunohistochemistry using established criteria for non–small cell lung cancer.

Results: The predominant TILs were CD3 and CD8 T cells, with moderate intratumor heterogeneity for all TIL subsets. Only 14% of LCNECs demonstrated tumor PD-L1 expression (>1%), with marked intratumor heterogeneity. PD-L1 on TILs was similarly heterogeneous but more frequently positive (77%), and had no correlation with tumor PD-L1. LCNECs were approximately evenly split between immunologically hot (52%; 38% active, 14% dormant) and cold (48%). Hot-active tumors had the highest TIL PD-L1 expression (P < .001, Figure 239). LCNECs with high TILs irrespective of T-cell subset had higher TIL PD-L1 expression (P = .005, P = .02, Figure). No correlation between tumor PD-L1 expression and tumor immune status or TIL subsets was identified.

Conclusions: Very few LCNECs were PD-L1-positive, with marked intratumor heterogeneity. PD-L1 expression on TILs was higher in immunologically “hot-active” and T-cell–rich tumors, irrespective of T-cell subset. Evaluation of the clinical significance of our findings is underway.

Necrotizing Granulomas With Fungal Hyphae Manifesting as Solid Lung Nodules Mimicking Lung Cancer

(Poster No. 44)

Josephine Dermawan, MD, PhD (dermawe@ccf.org); Sanjay Mukhopadhyay, MD. Cleveland Clinic, Cleveland, Ohio.

Context: In lung nodules resected to rule out malignancy, we have encountered necrotizing granulomas with fungal hyphae that do not fulfill criteria for mycetoma, invasive aspergillosis, allergic bronchopulmonary aspergillosis (ABPA), or chronic necrotizing aspergillosis. This study aims to delineate the clinicopathologic features and significance of such cases.

Design: We retrieved all lung biopsies/resections in which fungal hyphae were identified histologically (2000–2017). After classifying cases into the well-recognized forms of pulmonary aspergillosis, a distinctive subset was identified within the remaining cases. The clinical, radiologic, and pathologic features of this group were reviewed.

Results: Of 126 cases containing fungal hyphae, 76 met criteria for invasive fungal disease (32), mycetoma (25), allergic bronchopulmonary aspergillosis (3), or chronic necrotizing aspergillosis (16). Within the remainder, 13 manifested as solid (noncavitary) lung nodules on imaging (12) or pathologic examination (1). All patients (10 men and 3 women, 55–74 years old) were smokers with emphysema, and were
immunocompetent or mildly immunocompromised. Radiologically, most nodules were solitary and subpleural, and all occurred in an emphysematous background. PET scans (available in 8) were positive in 7. Malignancy was suspected clinically in 10. Histologically, all cases showed necrotizing granulomas containing septate fungal hyphae with narrow-angle branching without vascular invasion, fungus balls, or eosinophilia. Six patients received antifungal therapy. On follow-up, nodules did not recur or progress to invasive fungal disease.

**Conclusions:** Aspergillosis can manifest as solid lung nodules mimicking malignancy. Although this variant is histologically similar to chronic necrotizing aspergillosis, radiologically the nodules are not cavitary, and most patients do not have clinical features of progressive chronic infection.

**Epithelioid Angiosarcoma Involving the Pleura**

*(Poster No. 45)*

Oluwatobi Odetola, MD (oluwatobi.odetola@lumc.edu); Swati Mehrotra, MD; Stefan Pambuccian, MD. Department of Pathology and Laboratory Medicine, Loyola University Medical Center, Maywood, Illinois.

We present the case of a 49-year-old woman with a history of latent tuberculosis (treated in 2012) and right ovarian mass who was transferred to our center for further management of recurrent ascites and pleural effusions. Computed tomography scan of the thorax and abdomen showed moderate ascites with no adnexal mass, multiple hypodense liver lesions, right-sided pleural effusion, and atelectasis. Investigations for infectious, metabolic, and heavy metal toxicity etiologies returned negative findings. Right lung wedge biopsies and pleural fluid cytology were done. Histologic sections showed diffuse pleural thickening that consisted of bland epithelioid cells with moderate to abundant eosinophilic cytoplasm, centrally placed nuclei with irregular borders, vesicular chromatin, binucleation, and prominent nucleoli (Figure 240, A and B). Two main growth patterns were seen: vasoformative (vascular lakes, poorly formed vascular spaces lined by tumor cells and RBC-containing intracytoplasmic lumen) and solid (strandlike and infiltrative). Abundant mitotic figures were also identified (Figure 240, C and D). The adjacent lung showed no involvement by the lesion. Differential diagnoses considered included benign mesothelial hyperplasia, mesothelioma and adenocarcinoma, primary “pseudomesotheliomatous” or metastatic. Immunohistochemical studies performed showed that the tumor cells were negative for epithelial and mesothelial markers. The tumor cells were positive for CD31, FLI-1, D2-40, and factor VIII–related antigen. Pleural fluid cytology was negative for malignancy. Based on the above, a diagnosis of epithelioid angiosarcoma involving the pleura was made. Malignant pleural vascular tumors are very rare. Primary pleural angiosarcoma is very aggressive and rapidly fatal with about 70% of patients dead of the disease within 7 months. Therefore, prompt diagnosis is very important.

**Immunohistochemical Detection of EGFR L858R Mutation in Lung Adenocarcinomas Using a Point Mutation–Specific Monoclonal Antibody**

*(Poster No. 47)*

Fan Lin, MD, PhD (flin1@geisinger.edu). Department of Laboratory Medicine, Geisinger Health System, Danville, Pennsylvania.

**Context:** Molecular testing for epidermal growth factor receptor (EGFR) mutations and deletions in lung adenocarcinomas (LADCs) is performed when a sufficient tumor sample is available. When a sample is limited, such as fine-needle aspiration (FNA) sample, application of IHC with these mutation-specific antibodies may be useful. We investigated the usefulness of anti-EGFR L858R antibody in identifying EGFR L858R point mutation in LADC on FNA and surgical samples.

**Design:** Thirty-six LADC cases with confirmed molecular testing results for EGFR on FNA/biopsy samples were retrieved from the pathology archives, including L858R point mutation (N = 12, 5 FNA and 7 surgical samples), exon 19 deletion (N = 12), and wild type (N = 12). Immunohistochemical staining using anti-EGFR L858R point mutation monoclonal antibody (AC-0317A/EP344; 1:100 dilution; Epitomics, Inc) was performed on these 36 cases. Only membranous or membranous and cytoplasmic staining was regarded as positive. The results were

---

**Crystal-Storing Histiocytosis Involving the Lung**

*(Poster No. 46)*

Melanie Lang-Orsini, MB, BCh, BAO (mlangorsini@tuftsmedicalcenter.org); Masha Bilic, MD; Sucharita Kher, MD; Monika Roychowdhury, MD. Departments of 1Pathology and 1Pulmonary Clinic Division of Pulmonary Critical Care and Sleep Medicine, Tufts Medical Center, Boston, Massachusetts.

Crystal-storing histiocytosis is a rare disorder characterized by accumulation of crystalline immunoglobulins in the cytoplasm of histiocytes. It may affect any organ and present in localized or generalized form. Approximately 90% of patients have an associated lymphoproliferative disorder. Lung is a rare site of involvement. We report the case of a 66-year-old woman who presented with shortness of breath and multiple bilateral ground glass opacities on computed tomography of the chest. Gross examination of a lung wedge resection specimen showed multiple ill-defined gray-white nodules. Microscopic examination revealed sheets of spindled to epithelioid cells with abundant, densely eosinophilic cytoplasm with occasional linear striations, bland ovoid nuclei, and scattered nucleoli (Figure 241, A). Intermixed lymphoplasmacytic aggregates were seen. Lesional cells were positive for CD68 (Figure 241, B), λ, IgA (Figure 241, C), IgG, and IgM. Stains for smooth muscle actin, caldesmon, HMB-45, Melan-A, and various cytokeratins were negative. Electron microscopy demonstrated numerous elongated and rhomboid intracytoplasmic inclusions (Figure 241, D). Serum protein electrophoresis showed a monoclonal IgM κ in a polyclonal background. A diagnosis of pulmonary crystal-storing histiocytosis was made; however, an overt lymphoproliferative disorder was not identified. Follow-up imaging at 6 months showed disease progression in the lungs with involvement of lymph nodes and spleen. Flow cytometry of a bone marrow aspirate showed a small population of abnormal B cells. The patient is scheduled for excisional lymph node biopsy. This case emphasizes the importance of close follow-up for this rare seemingly benign entity, as it may antedate a lymphoproliferative disorder.
recorded: 0 (no stain), 1+ (<25% of tumor cells stained), 2+ (26%–50% of tumor cells stained), 3+ (51%–75% of tumor cells stained), and 4+ (>75%).

Results: Of the 12 L858R point mutation cases, 7 (58%, 2 FNA and 5 surgical samples) were diffusely 3+ or 4+ positive with a membranous or membranous/cytoplasmic staining pattern; 3 showed cytoplasmic staining only; and 1 case was negative. In contrast, all cases with exon 19 deletion or wild type were negative or only weakly positive with a cytoplasmic staining pattern.

Conclusions: Our preliminary data suggest that this anti-EGFR L858R mutation–specific antibody has moderate sensitivity and high specificity in identifying L858R point mutation in lung adenocarcinomas even on FNA/small tissue samples.

**Biomarker Testing Survey for Non–Small Cell Lung Carcinoma**

(Poster No. 48)

Manoj Gadar, MD (manoj.gadar@yahoo.com); Carolina Strosberg, MD; Masoumeh Ghayour, MD; Farah Khalil, MD; Kun Jiang, MD; Samer Saleem, MD; Ardeshr Hakami, MD. Department of Pathology, Moffitt Cancer Center, Tampa, Florida.

**Context:** Biomarkers like epidermal growth factor receptor (EGFR), ALK, PD-L1, KRAS, ROS-1, BRAF, MET/RET, and PTEN are performed for non–small cell lung carcinoma (NSCLC) for clinical decision-making. The objectives of this study were to analyze the molecular biomarkers’ practice in NSCLC, and determine potential process improvement.

**Design:** An online survey was sent that included 10 questions regarding the biomarkers’ testing for NSCLC. About 80 oncologists/medical professionals responded to the questions.

**Results:** Most clinicians (75%–96%) typically performed EGFR, ALK, PD-L1, KRAS, ROS-1, BRAF, MET/RET, and PTEN in metastatic NSCLC (mNSCLC) by 45% and 69% of clinicians, respectively. Most clinicians (94%) requested tissue core biopsy in patients with mNSCLC. One year earlier, PD-L1 was 65% useful and currently it is 80% useful. Thirty-four percent of patients asked for PD-L1 testing in mNSCLC.

**Conclusions:** Testing of EGFR, ALK, PD-L1, and ROS-1 biomarkers is most commonly (75%–96%) performed in NSCLC, typically at the time of diagnosis. Testing of MET/RET and PD-L1 biomarkers is less commonly performed. It typically takes 1 to 2 weeks to get PD-L1 result on biopsy. Tissue core biopsy is most commonly requested currently for mNSCLC. Lack of tissue is the most common barrier that prevents ordering of PD-L1 testing. One year earlier, PD-L1 testing was 65% useful and currently it is 80% useful; 34% of patients ask for PD-L1 testing in mNSCLC.

**Solitary Fibrous Tumor of the Parotid Gland**

(Poster No. 49)

Nafiseh Janaki, MD (nafiseh.janaki@uhhospitals.org); Mahmut Akgul, MD; Satyapal Chahar, MBBS; Marta Couce, MD, PhD. Department of Pathology, University Hospitals Cleveland Medical Center, Case Western Reserve University, Cleveland, Ohio.

Solitary fibrous tumor (SFT) arising from the salivary gland is rare. We describe the case of a patient with SFT of the parotid gland. An 18-year-old man presented with a painless, slow-growth mass overlying the right temporomandibular joint and impeding right ear hearing. Imaging showed a well-circumscribed, heterogeneous, and vascular mass. Upon parotidectomy, the tumor was confined to the gland with no facial nerve involvement. Histologically, the tumor was hypercellular consisting of atypical spindle cells arranged in short fascicles and medium-sized branching vessels (Figure 242, A and B). Neoplastic cells exhibited 8 mitoses/10 high-power fields, positive immunostaining for Bcl-2, CD34 (Figure 242, C and D), STAT6, and vimentin, and no immunoreactivity for CD10 and SMA, favoring the SFT diagnosis. The patient underwent radiotherapy and showed no recurrence in a 2-year clinical and radiologic findings that can mimic common parotid tumors. Although most cases are benign, the behavior of tumor can be unpredictable with reports of recurrence and rare metastasis. Malignant SFTs usually are hypercellular with atypia, necrosis, and most importantly, increased mitoses (>4/10 high-power fields). Parotid SFTs with aggressive behavior and bone destruction have been reported. Regardless of the site, tumor cells are often positive for vimentin, CD34, Bcl-2, STAT6, and CD99, but negative for CK, EMA, and S100. NAB2-STAT6 gene fusion has been recently linked to SFT, which drives STAT6 nuclear expression. SFT should be suspected in the context of a slow-growing parotid mass. Pathologic evaluations are essential for the definitive diagnosis.

**HPV in Cytology Specimen From Head and Neck Cancers: A Mount Sinai Hospital Review**

(Poster No. 50)

Roshan Raza, MD (roshan.raza@mountsinai.org); Adnan Mushabber, MD; Roshan Mahabir, MD; Muhammad Qazi, MD. Department of Pathology, Mount Sinai St. Luke’s Roosevelt Hospital, New York, New York.

**Context:** In recent times, an increasing incidence of oropharyngeal cancers has been observed, which is now attributed to human papillomavirus (HPV). In this review, we present the incidence of head and neck cancers diagnosed from cytology specimens from a single health center in urban New York.

**Design:** Cytology specimens from head and neck sites (neck, pharynx, oral cavity, tongue, and tonsil) were retrospectively reviewed (January 2011–October 2015).

**Results:** Thirty-one cytology specimens fitting the inclusion criteria were identified. The predominant histologic diagnoses for the cytology specimens were NKSCC (nonkeratinizing squamous cell carcinoma, 9/31) and conventional SCC (squamous cell carcinoma, 18/31). The most prevalent site of origin for cytology specimens was the neck (26/31; 83.67%). Most of these specimens (90.32%) were positive for HPV Wide Spectrum. Similarly, most (64.52%) were positive by p16 staining. All NKSCC specimens were positive for both the HPV Wide Spectrum and HPV16. About half (55.56%) of NKSCCs were p16 positive, with some negative (22.22%) and focal staining pattern (22.22%) interspersed. Most SCC specimens (85.71%) were positive for the HPV Wide Spectrum and HPV16. Most of these specimens (64.29%) were p16 positive, with the remaining (35.71%) displaying focal staining. A positive result for HPV Wide Spectrum and HPV16 correlated well with a positive p16 staining result (19/28; 67.86%). All 31 specimens were HPV18 negative.

**Conclusions:** In our review, SCC conventional type was the most common malignancy identified, occurring mostly in men and associated with high-risk HPV16 strain; these facts correspond with the available literature.

**Congo Red–Positive Nonamyloid Deposit in External Auditory Canal**

(Poster No. 51)

Atreyee Basu, MD (Atreyee.Basu@nyumc.org); Nicole J. Boczek, PhD; Surendra Dasari, PhD; W. Edward Highsmith, PhD; Ellen D.
McPhail, MD; Paul J. Kurtin, MD; Daniel Jethanamest, MD; Fang Zhou, MD

Departments of Pathology and Otolaryngology-Head and Neck Surgery, NYU Langone Medical Center, New York, New York; Department of Pathology, Mayo Clinic, Rochester, Minnesota; Departments of Health Sciences Research and Pathology, Mayo Clinic, Rochester, Minnesota.

A 54-year-old woman presented with progressive sensorineural hearing loss since childhood and progressive bilateral ear canal stenosis that has required increasingly frequent debridements. Her father and brother also had early-onset hearing loss. Otoscopy revealed bilateral external auditory canal (EAC) narrowing, left greater than right. She underwent left meatoplasty and canaloplasty with excision of subcutaneous soft tissue (Figure 243, A). Histologic evaluation of the subcutaneous soft tissue showed amorphous eosinophilic material (Figure 243, B; H&E) that was Congo red positive (Figure 243, C) with green birefringence under crossed polarization light microscopy (Figure 243, D). Liquid chromatography tandem mass spectrometry (LC-MS/MS) did not identify a peptide profile indicative of amyloidosis, nor was a specific amyloid precursor protein detected. However, abundant cochlin protein spectra were present, and there was a possible amino acid substitution in exon 9. However, Sanger sequencing of exon 9 did not identify any variations. Sequencing of the remainder of the COCH gene is underway. Cochlin deposits have been reported in the inner and middle ear. Ours is the first reported case of EAC cochlin deposition. While our investigations have thus far not found an etiology, possible explanations include genetic variation outside of exon 9, altered mRNA splicing, dysregulated cochlin expression or trafficking, mutated cochlin-interacting proteins, or disordered posttranslational modification. Surgical pathologists who encounter specimens from the inner, middle, or external ear canal should be aware of the possibility that cochlin deposition may mimic amyloid as homogeneous eosinophilic material under crossed polarization light microscopy.

Secretory Carcinoma of the Salivary Glands: A Case Series and Literature Review

(Poster No. 52)

Mark H. Kavesh, MD (mkavesh@ufl.edu); Yanel De Los Santos, MD; Peter A. Drew, MD; Jingyang Feng, MD (eat8m@virginia.edu); Edward Stelow, MD. Department of Pathology, University of Virginia, Charlottesville.

Squamous Cell Carcinoma of the Eustachian Tube Is Not Associated With Human Papillomavirus and Epstein-Barr Virus Infection: A Case Report and Literature Review

(Poster No. 54)

Jingyang Feng, MD (jfang@cookcountyhhs.org). Department of Pathology, John H. Stroger Hospital of Cook County, Chicago, Illinois.
Two common human oncogenic viruses, human papillomavirus (HPV) and Epstein-Barr virus (EBV), are known to cause certain types of squamous cell carcinoma (SCC) of the head and neck. The viruses’ status has emerged as a prognostic marker that significantly impacts clinical management. Primary SCC of the eustachian tube (ET) is a rare tumor. To the best of our knowledge, there is no study investigating the role of HPV and EBV in this tumor. We report a case of SCC of the ET and explore if there is any association between these 2 viruses and the tumor by literature review. A 47-year-old man who presented with gradual hearing loss was found to have a 17-mm mass in the cartilaginous right ET. An endoscopic biopsy of the mass revealed an invasive, nonkeratinizing squamous cell carcinoma. Immunohistochemical stain for P16 is negative within the tumor and there is no evidence of active EBV infection with EBV-encoded RNA (EBER) in situ hybridization. A review of literature shows that in addition to HPV and EBV, there are other factors that can lead to the development of head and neck SCC, such as exposure to ultraviolet light and chronic inflammatory processes. In our case, there is prominent chronic inflammation and squamous metaplasia noted in the pseudostratified columnar epithelium of the ET. This case indicated that the chronic inflammation and metaplastic process might play an important role in pathogenesis of SCC of the ET instead of HPV and EBV infection.

A Challenging Case of Salivary Duct Carcinoma of the Parotid Gland Metastatic to the Lung: A Case Report With Cytology and Histology Correlation

(Paper No. 55)

David Henriquez Ticas, MD (David.HenriquezTicas@bcm.edu); Jasmeet Assi, MD; Deborah Citron, MD; Christie Finch, MD; Ya Xu, MD, PhD. Department of Pathology & Immunology, Baylor College of Medicine, Houston, Texas.

Salivary duct carcinoma is a rare and highly aggressive parotid malignancy that morphologically resembles that of ductal carcinoma of the breast. We report a case of a 64-year-old man with right parotid enlargement, cough, and hoarseness for 1 month. Computed tomography imaging of the neck showed a 1.8-cm mass in the right parotid, and a spiculated 3.6-cm mass in the right upper lobe. A fine-needle aspiration (FNA) and biopsy of this lung mass showed an adenocarcinoma. Immunohistochemistry demonstrated the tumor was immunoreactive for CK7 (diffuse), CDX-2 (weak, focal), CK20, TTF-1, Napsin-A, and p40. An FNA of the right parotid mass showed similar morphology and immunohistophenotype as that seen in the lung mass. However, further workup was limited owing to the scant amount of material obtained from parotid FNA. This prompted a reevaluation of the previous lung mass specimen. Additional immunostains showed the tumor was positive for GATA-3 and androgen receptor (AR). These findings were suggestive of a diagnosis of metastatic salivary duct carcinoma of parotid origin. The subsequent right parotidectomy specimen revealed a salivary duct carcinoma, with metastasis to 1 periparotid lymph node. Malignant salivary gland tumors are rare entities and exhibit considerable diagnostic difficulty owing to their heterogeneous and overlapping histologic features in individual tumors. The ability to recognize the features of cytology and histology, and immunostaining pattern of salivary duct carcinoma, particularly AR positivity, is important to render the correct diagnosis, especially in metastatic tumors.

Pediatric Warthin-like Variant of Salivary Mucoepidermoid Carcinoma: An Uncommon Mimicker of Warthuin Tumor

(Paper No. 56)

Elena V. Daoud, MD, PhD (elena.daoud@phhs.org); Justin Bishop, MD; Bahram R. Ollai, MD; Eric Berg, MD; Charles F. Timmons, MD, PhD. *Department of Pathology, UT Southwestern Medical Center, Dallas, Texas; †Department of Pathology, ProPath Laboratory, Dallas, Texas; ‡Department of Pediatric Surgery, Childrens Medical Center, Dallas, Texas; §Department of Pathology, UT Southwestern Medical Center/Childrens Medical Center, Dallas, Texas.

Mucoepidermoid carcinoma (MEC) is the most commonly diagnosed malignancy of the salivary gland. One of its recently reported morphologic variants, a Warthin-like variant, can have a striking histologic resemblance to benign Warthin tumor but can be a diagnostic pitfall. While both tumors can look similar, close examination of epithelial lining at high power will help in the final determination. We report a case of parotid gland Warthin-like MEC in a 13 year-old girl. While the neoplasm was composed of cystically dilated glands with prominent lymphoid stroma (Figure 245, A) with multilayered eosinophilic epithelium (Figure 245, B), it did not exhibit the classic, bilayered oncocytic epithelium that defines benign Warthin tumor. The lining included occasional mucus cells and squamoid plaque-like epithelial thickening (Figure 245, C). Because MEC, while uncommon in children, is much more likely than Warthin tumor, observation of Warthin-like features should prompt diagnostic consideration of the Warthin-like variant of MEC. Fluorescence in situ hybridization for the MEC-specific MAML2/CRTC1 rearrangement can confirm the diagnosis. Several cases of Warthin-like variant of MEC in adults and a single case in a 17-year-old have been described. The present case reports the youngest known patient and illustrates that the Warthin-like variant, like other forms of MEC, can occur in the pediatric population, and pediatric pathologists must be aware of its existence and diagnostic features to avoid misdiagnosis as the more familiar Warthin tumor.

A Rare Case of Primary Pleomorphic Liposarcoma of the Parotid Gland: Cytologic and Histologic Findings

(Paper No. 57)

Kara L. Chan, MD (kara.chan@phhs.org); Justin A. Bishop, MD; Elizabeth M. Kurian, MD. Department of Pathology, University of Texas Southwestern Medical Center, Dallas.

Pleomorphic liposarcoma is the least common subtype of liposarcoma and only rarely occurs in the head and neck. Only 2 cases have been reported in the parotid; to our knowledge, the cytopathologic features of pleomorphic liposarcoma in this location have not been described. We report the third known case of primary pleomorphic liposarcoma of the parotid gland and include fine-needle aspiration findings. A 36-year-old woman presented with a 4-month history of a rapidly enlarging left preauricular mass. Fine-needle aspiration cytology demonstrated abundant fibrillary matrix-like material containing round to spindled cells (Figure 246, A) with scattered larger cells, occasional nuclear inclusions, and a rare multivacuolated cell (Figure 246, B). The subsequent core biopsy revealed highly pleomorphic spindle cells, some with prominent nuclear inclusions, and fplet-like giant cells within a myxoid stroma. Rare pleomorphic lipoblasts were present (Figure 246, C). The parotidectomy specimen contained a 6.5-cm, encapsulated, tan-yellow tumor with focal necrosis. Microscopic examination showed similar morphology and immunohistophenotype as that seen in the lung mass. However, further workup was limited owing to the scant amount of material obtained from parotid FNA. This prompted a reevaluation of the previous lung mass specimen. Additional immunostains showed the tumor was positive for GATA-3 and androgen receptor (AR). These findings were suggestive of a diagnosis of metastatic salivary duct carcinoma of parotid origin. The subsequent right parotidectomy specimen revealed a salivary duct carcinoma, with metastasis to 1 periparotid lymph node. Malignant salivary gland tumors are rare entities and exhibit considerable diagnostic difficulty owing to their heterogeneous and overlapping histologic features in individual tumors. The ability to recognize the features of cytology and histology, and immunostaining pattern of salivary duct carcinoma, particularly AR positivity, is important to render the correct diagnosis, especially in metastatic tumors.
SOX10 Stains a Subset of Basaloid Squamous Cell Carcinomas: A Diagnostic Pitfall

(Poster No. 58)

Austin McCuiston, MD (amccuis1@jhmi.edu); Lisa Rooper, MD. Department of Pathology, Johns Hopkins Hospital, Baltimore, Maryland.

Context: SOX10 has recently emerged as a useful marker of myoepithelial, acinar, and intercalated duct differentiation in salivary tumors, with expression in acinic cell carcinoma, adenoid cystic carcinoma, basal cell neoplasms, and myoepithelial neoplasms. Basaloid squamous cell carcinoma (SCC) is a subtype of head and neck SCC that mimics several of these salivary tumors through its characteristic adenoidal architecture and basement membrane material production. The staining profile of SOX10 has not yet been evaluated in basaloid SCC.

Design: All cases of head and neck basaloid SCC between 2000 and 2017 were identified from the surgical pathology archives of a large academic hospital. A tissue microarray was constructed to include 34 cases; 2 were evaluated on whole-slide sections. SOX10 immunohistochemistry was performed.

Results: SOX10 was positive in 9 of 36 basaloid SCCs (25%), with diffuse staining (>70%) in 4 cases, moderate staining (10%–70%) in 3 cases, and focal staining (<10%) in 2 cases. All cases lacked a clear biphasic staining pattern.

Conclusions: Although SOX10 can highlight myoepithelial, acinar, and intercalated duct differentiation in salivary tumors, it cannot be considered a specific marker of salivary origin in head and neck carcinomas. Positivity for SOX10 in 25% of basaloid SCC presents a diagnostic pitfall that compounds morphologic overlap between these tumor types. The lack of biphasic SOX10 reactivity may help differentiate basaloid SCC from adenoid cystic carcinoma and basal cell adenocarcinoma, 2 of its closest mimics; however, SOX10 should be used with caution within this differential diagnosis.

Classical Hodgkin Lymphoma in the Sphenoid Sinus: A Most Unexpected Site of Origin

(Poster No. 59)

Olumide Odeyemi, MD (olumide.odeyemi@ucdenver.edu); Julie Rosser, DO. Department of Pathology, University of Colorado, Aurora.

Primary sinonasal lymphoma is a relatively rare disease, particularly in Western societies, and the vast majority of these are non-Hodgkin lymphoma (NHL). Classical Hodgkin lymphoma (CHL) characteristically originates in lymph nodes. Extranodal involvement of CHL is known to occur, albeit rarely, and often during the disease course or upon relapse. We report a case of a 63-year-old woman with primary CHL of the sphenoid sinus. The patient presented to the emergency department with complaints of flashing light in both eyes, right greater than left. Magnetic resonance imaging studies revealed a 4.2-cm enhancing mass filling the sphenoid and left posterior ethmoid sinuses. Positron emission tomography–computed tomography showed no evidence of disease elsewhere in the body. Histologic examination of the mass revealed a diffuse mixed inflammatory infiltrate with intercalating thin fibrous bands. Scattered large atypical cells with moderate amounts of cytoplasm, enlarged nuclei with irregular nuclear contours, and prominent eosinophilic nucleoli were noted within the inflammatory infiltrate. Immunohistochemical studies showed the large atypical cells to be positive for CD15 and CD30 (Figure 247), and negative for CD20 and CD45. An in situ hybridization study for small EBV-encoded RNA (EBER) was also positive in the large atypical cells. Together, the histomorphologic and immunophenotypic findings support the diagnosis of Epstein-Barr virus–positive CHL. Primary CHL of the nasal sinus is an extremely rare phenomenon. Given that NHL or reactive conditions are more likely to manifest in the sinonasal area, careful histologic examination and judicious use of immunohistochemical studies are essential.

Cervical and Anal Mycobacterium avium Complex Presenting as Malignancy

(Poster No. 60)

Roshan Mahabir, MD, PhD, MPH1 (roshan.mahabir@mountsinai.org); Sushma Ravirala, MBBS1; Alexander LaFortune, MD2; Jose Fefer, MD2; Nebras Zeizafoun, MD,3 Departments of 1Pathology and 2Medicine, Infectious Disease, Mount Sinai St. Luke Roosevelt, New York, New York.

The incidence of Mycobacterium avium complex (MAC) has decreased dramatically owing to the widespread use of antiretroviral therapy (ART), yet opportunistic infection continues to present in HIV-positive patients. Owing to its relative rarity, diagnosis can be overlooked. We present the case of a 43-year-old man with poorly controlled HIV/AIDS, history of opportunistic infections, hepatitis C virus, hypertension, depression, and treated syphilis with a 2-year history of painful ulcerated anal masses, inguinal and bilateral cervical lymphadenopathy along with right cervical skin ulceration, fevers, chills, and night sweats. Computed tomography (CT) scan of the abdomen and pelvis showed a perirectal mass, regional lymphadenopathy, and enhancement along
the jejunum; CT neck scan showed diffuse adenopathy with a large conglomerate right-sided mass involving the overlying skin. Clinically, this was suspected to be an advanced malignant neoplasm and biopsy of both cervical and anal lesions revealed similar findings; presence of benign ulcerated fibroconnective tissue with granulation tissue; special staining for GMS was negative, and acid-fast staining was positive for intracellular bacilli along with positive cultures for Mycobacterium avium. Owing to the strong clinical impression of malignancy, repeated biopsy was performed and similar findings revealed no evidence of malignancy. With a more stringent regimen of ART and antymycobacterials, the patient had a decreased viral load as well as an increase in CD4 count, but with associated expansion and drainage of the cervical masses (compatible with MAC immune reconstitution inflammatory syndrome) that ultimately resolved with further therapy. This case demonstrates a treatable and preventable infectious disease that can be associated with a poor prognosis if not readily recognized (Figure 248).

Mammary Analogue Secretory Carcinoma of Salivary Gland Presented With Extensive Large Nerve Invasion

(Poster No. 61)

Ethar Al-Husseinawi, MD, PhD (Ethar.Al-Husseinawi@tmcmed.org); Soheila Hamidpour, MD; Evanthia Omoscharka, MD. Department of Pathology, Truman Medical Center-UMKC, Kansas City, Missouri.

Mammary analogue secretory carcinoma (MASC) is a rare new entity of salivary gland neoplasm that is characterized by its outstanding morphologic and molecular similarities to secretory carcinoma of the breast. It harbors ETV6-NTRK3 fusion gene that has not been found in any other salivary gland tumor. Our patient, a 46-year-old woman, presented with a right submandibular gland mass. Fine-needle aspiration was performed in our pathology department and showed cellular specimen composed predominantly of groups of oncocytic cells. Tumor cells show bubbly cytoplasm on H&E. Given histologic features, the differential diagnosis included oncocytosis, oncocytoma, acinic cell carcinoma, and MASC. Immunohistochemical stains showed the tumor cells were positive for mammaglobin (strong diffuse positivity), S100 (diffuse positivity), while DOG1 stain was patchy. Periodic acid–Schiff cells were positive for mammaglobin (strong diffuse positivity), S100 carcinoma, and MASC. Immunohistochemical stains showed the tumor cells show extensive involvement of the submandibular and sublingual salivary glands. Microscopically it showed an unencapsulated lobulated mass with fibrous septa in between. Tumor cells showed extensive involvement of the submandibular and sublingual glands, with extensive large nerve invasion, with extension to surrounding fat tissue. The diagnosis of MASC was rendered on the basis of histopathologic picture and of immunohistochemical and special stain patterns. The diagnosis was solidified by detecting ETV6 (12p13.2) gene rearrangement by using FISH analysis. A diagnosis of MASC may be feasible when it exhibits the classic histology along with strong staining for mammaglobin and S100, and a characteristic ETV6-NTRK3 gene fusion.

A Rare Presentation of Rosai-Dorfman Disease

(Poster No. 62)

Vijay Patel, MD (vpatel493@gmail.com); J. Michael McCoy, DDS. Department of Pathology, University of Tennessee Medical Center, Knoxville.

This case represents an unusual presentation of a relatively uncommon disease. A 70-year-old woman presented to her physician with a 3-week history of nasal obstruction and congestion. A contrast computed tomography scan revealed an ill-defined 2.2-cm soft tissue mass appearing to arise in the left posterior nasal cavity. This soft-tissue mass occluded the nasal passages and involved the turbinates. The patient was referred to an otolaryngologist, who in turn performed nasal endoscopy and confirmed the presence of an obstructing mass. A biopsy of the mass demonstrated chronic inflammation with no other definitive findings. After considering the presentation, imaging studies, and biopsy findings, the decision was to surgically remove as much of the abnormal tissue as possible. Routine hematoxylin-eosin–stained tissue sections of the excised surgical material demonstrated a diffuse collection of histiocytes with large nuclei and single, prominent nucleoli. The histiocytes appeared to contain intact lymphocytes within their cytoplasm (emperipolesis) and were surrounded by reactive lymphocytes. Immunohistochemical staining for S100 and CD68 confirmed that the lesional cells were indeed histiocytes, and negative reactivity to CD1a and S100 staining ruled out Langerhans cell histiocytosis. Nonreactive microbial stains also ruled out the presence of bacteria, fungi, and mycobacteria. Given these histologic features, the diagnosis of extranodal sinus histiocytosis with massive lymphadenopathy (extranodal Rosai-Dorfman disease) was offered. A rare and biologically benign entity, Rosai-Dorfman disease most commonly presents in lymph nodes. Presentation in the nasal cavity and paranasal sinuses is exceedingly rare; a current literature review demonstrated very few reported cases (Figure 249).

Morphologic Characterization and Molecular Correlates of (Mammary Analogue) Secretory Carcinoma of Salivary Gland Origin

(Poster No. 63)

Aditi Vidholia, MBBS1; Ava Bhattarai, MBBS1; Deqing Ma, MD1; James McDermott, MD2; Robert A. Robinson, MD1; Anand Rajan KD, MBBS1 (anand-rajan@uiowa.edu). 1Department of Pathology, University of Iowa Hospitals and Clinics, Iowa City; 2Cytopathology Laboratory, Carolinas Laboratory Network, Charlotte, North Carolina.

Context: Secretory carcinoma (also known as mammary analogue secretory carcinoma, or MASC) is a predominantly low-grade salivary gland neoplasm with distinctive histologic and immunohistochemical features. MASC exhibits several patterns including solid, tubular, microcystic, papillary, and cribriform with varying levels of infiltration. MASC harbors a characteristic ETV6-NTRK3 gene fusion resulting from a balanced chromosomal translocation, t(12;15)(p13;q25). This results in the fusion of ETV6, a transcription regulator, to NTRK3, a membrane receptor kinase. Recently, MASCs have been shown to harbor fusions involving exons other than 5 and 15 in ETV6 and NTRK3, respectively, or noncanonical fusions that involve genes other than NTRK3 (ETV6-X). It has been suggested that these cases may exhibit more invasive growth, as compared to those with classical ETV6-NTRK3.

Design: We retrieved 5 cases of MASC diagnosed between 2008 and 2017 from the files. A novel RNA fusion panel was devised and used to obtain both confirmation of diagnosis and full characterization of the fusion product, that is, both partner gene nucleotide sequences.
**Results:** All 5 MASCs had varied morphologic features, including tubulocystic and papillary patterns. One case exhibited widespread single cell infiltration. On molecular analysis, all cases exhibited ETV6-NTRK3 gene fusion.

**Conclusions:** We conclude that the more infiltrative phenotype is not exclusively associated with atypical exon fusion or unknown ETV6 partners. The classical ETV6-NTRK3 fusion, though more commonly associated with low-grade behavior, can have a single cell infiltrative pattern with a potentially more aggressive course and a younger age at presentation.

**Primary Thyroid INI1-Deficient Carcinoma: Is It Truly Anaplastic?**

(Mathieu Merzianu, Zhifei Zhang, MD, PhD1 (zhifeizhangzzf@gmail.com); Ameer Hamza, MD; Basim Al-Khafaji, MD. Department of Pathology, St. John Hospital and Medical Center, Detroit, Michigan.

INI1-deficient carcinoma has been recently reported in various sites including head and neck. We present an INI1-deficient carcinoma of the thyroid gland and report on the INI1 protein expression (BAF47, 1:25; Bio SB) in benign (n = 89) and malignant (n = 96; 10 follicular, 66 papillary, 8 medullary, 3 poorly differentiated, and 7 anaplastic thyroid carcinomas) samples in a thyroid tissue microarray. Nuclear reaction was considered positive regardless of intensity. A 67-year-old woman presented with dysphagia due to a 6-cm, well-delineated thyroid mass with mucoid cut surface. Histologically, the tumor exhibited solid, alveolar, and pseudopapillary architecture with markedly dyscohesive, monomorphic epithelioid and focally rhabdoid/plasmacytoid neoplastic cells in an abundant myxoid stroma. No ductal or follicular formation or differentiated thyroid carcinoma was present (Figure 250). Extensive extrathyroid, lymphovascular, and perithyroid nodal involvement was present. Tumor was interpreted elsewhere as epithelioid sarcoma and anaplastic thyroid carcinoma. Tumor cells expressed AE1/AE3, EMA, CK18, and vimentin, and were negative for TTF-1, thyroglobulin, PAX-8, calcitonin, CD34, EBER, and other neuroendocrine, myoepithelial, and melanocytic markers. Proliferation index by Ki-67 was 15% (range, 5%–30%). INI1 expression was lost in tumor cells (Figure 250).

**Extranodal Metastatic Tumors to the Head and Neck Region: A Clinical Pathologic Review**

(Mathieu Merzianu, Zhifei Zhang, MD, PhD1 (zhifeizhangzzf@gmail.com); Ameer Hamza, MD; Basim Al-Khafaji, MD. Department of Pathology, St. John Hospital and Medical Center, Detroit, Michigan.

Context: Extranodal metastatic tumors to the head/neck region are infrequent in clinical practice and may be confused with a primary head/neck neoplasm. This study aimed to characterize the clinical and pathologic features of these neoplasms.

**Design:** Surgical pathology files at our institution were reviewed for cases of extranodal metastases to the head/neck region.

**Results:** Ninety-two cases (48 women and 44 men) of extranodal metastatic tumors to the head/neck region were recorded. Age ranged from 29 to 94 years (mean, 62 years). The most common sites were as follows. Twenty-eight (30.4%) were scalp: 8 breast, 6 renal, 5 melanoma, 4 lung, 3 prostate, 1 cervix, and 1 T-cell leukemia. Twenty-four (26.1%) were thyroid: 11 renal, 8 breast, 3 lung, 1 follicular lymphoma, and 1 osteosarcoma. Eleven (12%) were nasal cavity: 6 renal and 1 case each of breast, prostate, myeloid sarcoma, ALL B-cell, and melanoma. Nine (9.8%) were oral mucosal metastases: 3 lung and 1 case each of colon, prostate, hepatoma, breast, liposarcoma, and 1 unknown primary. Eight were eye: 2 breast, 2 lung, and 1 case each of ALL B-cell type, prostate, C, and carcinoma. Six (6.5%) were skull: 3 breast, 1 renal, 1 carcinoma, and 1 endometrial stromal sarcoma. Four (4.3%) were sellar metastases: 3 breast and 1 lung. Two were parotid gland: 1 lung and 1 melanoma.

**Conclusions:** The most common tumors encountered were breast carcinoma (28.2%) and renal (26.1%). The most common metastatic sites were scalp (30.4%) and thyroid (26.1%). Awareness of these groups of extranodal metastatic tumors may avoid incorrect interpretation, which can compromise clinical or surgical management.

**Solitary Extranodal Rosai-Dorfman Disease of the Jaw Bone: An Exceedingly Rare Presentation**

(Mathieu Merzianu, Zhifei Zhang, MD, PhD1 (zhifeizhangzzf@gmail.com); Ameer Hamza, MD; Basim Al-Khafaji, MD. Department of Pathology, St. John Hospital and Medical Center, Detroit, Michigan.

Rosai-Dorfman disease, also known as sinus histiocytosis with massive lymphadenopathy, is a nonneoplastic lesion principally affecting lymph nodes. Concurrent extranodal disease occurs frequently; however, solitary extranodal disease involving the jawbone is exceedingly rare with fewer these patients may benefit from aggressive surgical and possible targeted therapeutic options.
Small Cell Neuroendocrine Carcinoma of the Nasal Cavity
With Coexisting Invasive Adenocarcinoma, In Situ Adenocarcinoma, and In Situ Squamous Cell Carcinoma
(Poster No. 68)
Saeed Asiry, MBBS
(Tsaeed_asiry@hotmail.com); Susan Jormak, MD; Todd Anderson, MD; Jessica Lim, MD; Gady Har-El, MD; Pamela Unger, MD. Departments of Pathology and Head and Neck Surgery, Northwell Health - Lenox Hill Hospital, New York City, New York.

Small cell neuroendocrine carcinoma of the nasal cavity and paranasal sinuses is a rare tumor and morphologically identical to its counterparts in the lungs and other head and neck sites. It has a rare association with high-risk HPV infection and previous radiation but no strong smoking association. In some rare examples, small cell neuroendocrine carcinoma is combined with either squamous cell carcinoma or adenocarcinoma. We report the case of a 45-year-old man with a history of nasal stuffiness and bleeding for 6 months. Imaging studies showed an extensive mass in the left nasal cavity extending into the ethmoids and skull base with involvement of the orbital contents of the left eye. A biopsy of the mass showed small cell neuroendocrine carcinoma (>50% of tumor in the biopsy) combined with invasive adenocarcinoma, in situ adenocarcinoma, and an in situ squamous cell carcinoma. Immunohistochemistry supported the diagnosis of the small cell neuroendocrine carcinoma component showing positivity for neuroendocrine markers and high Ki-67 proliferative index (>90%). Subsequent resection of the tumor showed small cell neuroendocrine carcinoma with no adenocarcinoma or squamous cell carcinoma identified. In summary, we present a rare case of combined small cell neuroendocrine carcinoma with adenocarcinoma and in situ squamous cell carcinoma. It is well documented that adenocarcinoma with mutated EGFR can transform into small cell carcinoma in the lung when resistance to EGFR tyrosine kinase inhibitors develops. Our case may represent a morphologic spectrum of a single clonal neoplastic process dominated by a dedifferentiated small cell neuroendocrine component.

Sclerosing Polycystic Adenoma With Concurrent Warthin Tumor
(Poster No. 69)
Michael Greas, MBChB (mrgeas@llu.edu); Mia Perez, MD. Department of Pathology, Loma Linda University Medical Center, Loma Linda, California.

Sclerosing polycystic adenoma (SPA) is a rare tumor of salivary glands with features reminiscent of fibrocystic disease, sclerosing adenosis, and/or adenosis tumor of breast. The most common site is the parotid (80% of cases) followed by the submandibular gland. SPA occurs over a wide age range (9–84 years) and has no sex predilection. First described by Smith et al under the name sclerosing polycystic adenosis, it was thought to be an inflammatory or reactive process. We report a case of sclerosing polycystic adenoma with concurrent Warthin tumor of the parotid. A 70-year-old man had a right parotid lesion for which fine-needle aspiration was performed with diagnosis of Warthin tumor. Excision specimen revealed an incidental 3-mm SPA. Histologically, the tumor is an unencapsulated lobular and mildly cystic ductal proliferation with a central radial scar, dense collagenous stroma, and mild chronic lymphoplasmacytic inflammation. On high power, a dual cell population of bland luminal and inconspicuous luminal myoepithelial cells is seen (Figure 251, A and B). Although not essential for diagnosis, the preserved lobular architecture can be highlighted by positive staining for p63 and SMA in the myoepithelial cells. Proliferation indices are very low (1%–2%) on Ki-67 stains. It has been proven a clonal process by HUMARA assay with a reported 10% risk of local recurrence. It is important to recognize this entity as a benign neoplasm and adopt the recent proposed nomenclature of SPA.

<table>
<thead>
<tr>
<th>Differential Diagnosis of Rosai-Dorfman Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosai-Dorfman Disease</td>
</tr>
<tr>
<td>Morphology</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Immunohistochemical profile</td>
</tr>
</tbody>
</table>

Small Cell Neuroendocrine Carcinoma of the Nasal Cavity
With Coexisting Invasive Adenocarcinoma, In Situ Adenocarcinoma, and In Situ Squamous Cell Carcinoma
(Poster No. 68)
Saeed Asiry, MBBS
Tsaeed_asiry@hotmail.com); Susan Jormak, MD; Todd Anderson, MD; Jessica Lim, MD; Gady Har-El, MD; Pamela Unger, MD. Departments of Pathology and Head and Neck Surgery, Northwell Health - Lenox Hill Hospital, New York City, New York.

Small cell neuroendocrine carcinoma of the nasal cavity and paranasal sinuses is a rare tumor and morphologically identical to its counterparts in the lungs and other head and neck sites. It has a rare association with high-risk HPV infection and previous radiation but no strong smoking association. In some rare examples, small cell neuroendocrine carcinoma is combined with either squamous cell carcinoma or adenocarcinoma. We report the case of a 45-year-old man with a history of nasal stuffiness and bleeding for 6 months. Imaging studies showed an extensive mass in the left nasal cavity extending into the ethmoids and skull base with involvement of the orbital contents of the left eye. A biopsy of the mass showed small cell neuroendocrine carcinoma (>50% of tumor in the biopsy) combined with invasive adenocarcinoma, in situ adenocarcinoma, and an in situ squamous cell carcinoma. Immunohistochemistry supported the diagnosis of the small cell neuroendocrine carcinoma component showing positivity for neuroendocrine markers and high Ki-67 proliferative index (>90%). Subsequent resection of the tumor showed small cell neuroendocrine carcinoma with no adenocarcinoma or squamous cell carcinoma identified. In summary, we present a rare case of combined small cell neuroendocrine carcinoma with adenocarcinoma and in situ squamous cell carcinoma. It is well documented that adenocarcinoma with mutated EGFR can transform into small cell carcinoma in the lung when resistance to EGFR tyrosine kinase inhibitors develops. Our case may represent a morphologic spectrum of a single clonal neoplastic process dominated by a dedifferentiated small cell neuroendocrine component.
Papillary Carcinoma of Stensen Duct With Intestinal Differentiation

(Poster No. 70)

Mohamed E. Mostafa, MD1 (mmostafa@mwc.edu); Amrou Abdelkader, MD2; Bryan Hunt, MD; Michael E. Stadler, MD3; Tamara Giordadze, MD1. Departments of 1Pathology and 2Otolaryngology, Medical College of Wisconsin Affiliated Hospital, Milwaukee.

Stensen duct (SD) carcinomas (SDCs) are exceedingly rare with <40 reported cases. We present a unique case of a primary SDC with papillary features and intestinal differentiation. A 74-year-old man presented with fullness on the right buccal mucosa for 1 year. Physical examination revealed a 2.0-cm papillae lesion centered in the SD with mobile tumor bulk deep to the mucosa. MRI revealed a T2 enhancement in the right buccal mucosa at the SD opening with abnormal enlargement and thickening up to 0.55-cm diameter of the distal right SD. A transoral excision of the entire SD with right lymphnode dissection was performed. Spillage of tumor from the SD opening was noted during the surgical dissection of the duct. Gross examination revealed a 2.2 × 1.1 × 0.8-cm tan–red superficial parotid continuous with 1.0-cm-long × 0.6-cm-diameter SD. Sections of the duct revealed a tan-gray mass obliterating its distal portion with dilatation of the duct proximally. Tumor was composed of fibrovascular cores lined by atypical oval to columnar cells with nuclear pseudo-dilatation of the duct proximally. Tumor cells were positive for p40, focally positive for p63, and negative for HPV 18. Eight of 10 cases were positive for p16. All cases were positive for HPV Wide Spectrum and of these 6 cases, 4 were positive for HPV 16, 18 and for p16, were retrospectively reviewed (January 2011–October 2015).

Results: A total of 412 surgical pathology specimens with malignancies from head and neck sites (neck, pharynx, oral cavity, tongue, and tonsil) were identified. Only 10 of 412 specimens (2.4%) were diagnosed as SCC and most patients were men (70%). Most diagnoses were made on the basis of histology and immunohistochemistry (p40, p63) and/or with available prior diagnosis in cases of recurrent/metastatic disease. Where required, additional immunostaining (for vimentin, EMA, CAM 5.2, CK7, CEA, S100, GFAP, CK20, chromogranin, synaptophysin, BCL2, and Ber-EP4) was assessed to rule out other differential diagnoses. Of these 10 SCC cases, 6 were positive for HPV Wide Spectrum and of these 6 cases, 4 were positive for HPV 16. Eight of 10 cases were positive for p16. All cases were negative for HPV 18.

Conclusions: Our review shows an incidence of 2.4% of BSCC (2% in reported literature) with a male predominance. The histopathologic differential diagnosis for BSCC is broad and we observed a relatively higher number (6 of 10) of cases positive for HPV.

Sclerosing Mucoepidermoid Carcinoma With Eosinophilia of the Thyroid Arising in a Patient With Parotid Basal Cell Adenoma

(Poster No. 73)

Mushal Noor, MB, BS1 (Mushal_noor@urmc.rochester.edu); Jacob Moalem, MD; Abberly Lott-Limbach, MD.1 Departments of Pathology and Laboratory Medicine and 2Surgery, Division of Endocrine Surgical Oncology, University of Rochester Medical Center, Rochester, New York.

Sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) is a rare malignancy in the thyroid, with approximately 50 cases reported in the literature. Thyroid SMECE is considered distinct from salivary gland SMECE; however, its rarity, data on the clinicopathologic and molecular features are limited. We report a case of a 53-year-old woman, a smoker with Hashimoto thyroiditis, with no family history of thyroid cancer or of radiation exposure. A 5-cm left thyroid nodule was discovered on physical examination. Fine-needle aspiration revealed atypia of undetermined significance and pathology of left thyroid lobectomy specimen showed nests of tumor cells (Figure 253, A and B). After surgery, the patient commented on a small and sometimes painful left preauricular lump for nearly 20 years. Fine-needle aspiration of the lesion was characterized as epithelial neoplasm. Left superficial parotidectomy and subsequent pathology revealed lesional cells...
positive for β-catenin, CK7, S100, SMA, p63, with focal luminal EMA and CAM 5.2 staining. A diagnosis of low-grade basaloid neoplasm, favoring basal cell adenoma, was made, thus establishing the thyroid SMECE as a primary lesion (Figure 253, C and D). Completion thyroidectomy was deemed unnecessary. Even though it is a rare entity, awareness of SMECE of the thyroid is important, especially in the setting of a concomitant salivary gland lesion, to rule out metastasis.

Recognition of CD30+ Benign Tongue Lesion and Avoidance of Excision

(Poster No. 74)

Adnan Mubasher, MD (adnan.mubasher@mountsinai.org); Kunwar Singh, MD; Tayler Van Denakker, MD; Muhammad Qazi, MD; Margaret Brandwein, MD. Department of Pathology, Mount Sinai Health System, New York, New York.

Ulcers are a common occurrence in the oral cavity including tongue. Traumatic ulcerative granuloma with stromal eosinophilia (TUGSE) presents as a large ulcer on tongue with heaped up margins resembling squamous cell carcinoma. This rare entity is a benign disorder histologically characterized by reactive ulceration with diffuse polymorphic inflammatory infiltrate extending from superficial mucosa into the deep connective tissue. TUGSE likely symbolizes a cluster of related disorders with overlapping clinicopathologic features and has an association with repetitive trauma, although the exact pathogenesis is not well established. We present a case of a 74-year-old woman with slow-healing recurrent ulcer of the left lateral border of tongue. Biopsy of the lesion revealed marked inflammation with increased eosinophils and diagnosis of TUGSE was rendered. Partial glossectomy was performed to exclude any underlying carcinoma and the lesion was circumferentially excised down to the muscular plane with frozen section analysis revealing a benign process. Examination of surgical specimen

SMARCB1 (INI-1) Unstable Sinonasal Carcinoma

(Poster No. 75)

Adnan Mubasher, MD (adnan.mubasher@mountsinai.org); Muhammad Qazi, MD; Fahad Khan, MD; Tayler Van Denakker, MD; Shiraz Qazi, MD. Department of Pathology, Icahn School of Medicine at Mount Sinai St. Luke’s-West Hospital, New York, New York.

SMARCB1 (INI-1) is a tumor suppressor gene, loss of which has been shown to lead to rhabdoid morphology. Multiple tumors including renal medullary carcinomas, epithelioid sarcomas, and rhabdoid tumor of infancy, to name a few, have been associated with this gene. However, loss of this gene is a rare occurrence in sinonasal carcinomas. We describe a case of INI-1 unstable sinonasal carcinoma with varied morphology showing areas of basaloid, rhabdoid, and plasmacytoid differentiation. A 56-year-old man presented with buccal swelling, gum bleeding, and soreness. Upon examination and radiology, an exophytic mass involving second molar tooth, extending medially along the left hard palate and maxillary sinus was identified (Figure 255, D). Histology revealed admixture of basaloid cell with necrosis and areas of rhabdoid morphology (Figure 255, A and B). In certain areas, the tumor shows discohesive round blue cell with basophilic cytoplasm, focal pleomorphism, and conspicuous to prominent cherry red nucleoli, while in other areas plasmacytoid and rhabdoid morphology with eccentric nuclei were noted. Immunohistochemistry was negative for CD34, Chromogranin, Desmin, p16, S100, Synaptophysin (-/+), AE1/AE3, AR, CD56, CK5/6, and ps10 and positive for EMA, VIM, and CAM 5.2 (negative in spindle cell area and strongly positive in areas with rhabdoid morphology). The tumor was negative for INI-1 (SMARCB1) (Figure 255, C). Only 9 cases of this variant of sinonasal carcinoma have been reported in the English literature. Diffuse loss of INI-1 on immunohistochemistry and varied morphology make this a unique case and emphasize the utility of SMARCB1 immunohistochemistry in differential diagnosis of these cases.

Arch Pathol Lab Med

Abstracts
Adnexal Carcinoma With Eccrine Differentiation of the Foot: A Rare Cutaneous Neoplasm

(Poster No. 76)

David A. Suarez-Zamora, MD1 (da.suarez33@uniandes.edu.co); Paula A. Rodriguez-Urrego, MD2; Mariam C. Rolon-Cadena, MD3; Karen T. Galvis-Castro, MD; Camilo Soto-Montoya, MD; Mauricio A. Palau-Lazaro, MD.1 Departments of 1Pathology and Laboratory Medicine, 2Dermatology, and 3Orthopaedic Surgery, Fundación Santa Fe de Bogotá, Bogotá D.C., Colombia.

Adnexal carcinomas are rare cutaneous tumors considered a diagnostic challenge. These tumors may derive from structures that have a common origin such as the apocrine and eccrine sweat glands, sebaceous glands, and hair follicles. We present the case of a 21-year-old woman with an unremarkable medical record, who consulted for a 1-year history of a painful mass with progressive growth in the dorsum of the left foot. MRI demonstrated a heterogeneous, encapsulated mass in the soft tissues of the third intermetatarsal space at the diaphysis of the third and fourth metatarsal bone, without involvement of periosteum. The patient underwent partial surgical resection, and an extranodal diagnosis of malignant giant cell tumor versus adnexal carcinoma was required for extrainstitutional diagnosis of malignant giant cell tumor versus adnexal carcinoma was made. The surgical specimen was referred to our institution for a second opinion. Microscopic examination showed an invasive epithelial neoplasm (Figure 256, A), displaying some areas with squamoid morphology and keratin pearl formation (Figure 256, B) and another one with small ductal structures (Figure 256, C). Focus of necrosis were appreciated (Figure 256, D). Immunostains were positive for cytokeratin AE1/AE3, cytokeratin 5/6, P63, EMA, and CEA, but negative for desmin, SMA, and S100 protein. These findings suggested an adnexal carcinoma with eccrine differentiation. This case report is a reminder that adnexal carcinomas are a diagnostic challenge even for experienced pathologists and can affect the deep soft tissues of the foot in young women, without cutaneous manifestation. Recognition of adnexal carcinomas is essential for early treatment and to prevent aggressive behavior.

A “Berti-like” Lymphoma: Transformation of a Case of Lymphomatoid Papulosis to an Aggressive CD8+ Epidermotropic T-Cell Lymphoma

(Poster No. 77)

Pavandeep Gill, MD1 (pavandeep.gill@albertahealthservices.ca); Justin Chia, MD5; Lesley Street, MD4; Étienne Mahe, MD.1 Departments of 1Pathology and Laboratory Medicine, 2Dermatology, and 3Hematology, University of Calgary, Alberta, Canada.

Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma, often referred to as “Berti” lymphoma, is a rare entity with a rapid and typically fatal clinical course. While the clinicopathologic features are typically aggressive, this entity shares some histomorphologic overlap with lymphomatoid papulosis type D, a much more indolent disease. We report an intriguing case of presumed transformation of indolent lymphomatoid papulosis into Berti lymphoma. A 51-year-old man presented with 2 left wrist papules. Histology revealed an epidermotropic T-cell lymphoproliferative process with prominent CD30+ anaplastic-appearing cells, consistent with lymphomatoid papulosis type D (Figure 257, A and B). These lesions resolved within months. During the subsequent years, the patient presented with several other papulonodules of increasing size and number, with associated ulceration and crusting and a lack of spontaneous resolution. Repeated biopsies demonstrated an atypical epidermotropic infiltrate of CDB8+ lymphocytes, now CD30+ (Figure 257, C and D). T-cell receptor β and γ rearrangement studies, with initial and follow-up lesions compared, demonstrated identical electropherographic profiles in the T-cell receptor β locus, but dissimilar T-cell receptor γ patterns: 1 peak common to both lesions, with 1 peak lost to the follow-up CD30+ lesions. The patient died from complications of lymphoma 6 years after the appearance of the first lesions, and 3 years after the development of the CD30+ lesions, despite multiple lines of therapy including high-dose chemotherapy and autologous stem cell transplant. This unusual case highlights the potential extremes of disease transformation in cutaneous lymphomas and the utility of T-cell clonality studies in suggesting clonal evolution.

Sarcomatoid Dedifferentiation in Malignant Melanoma: An Immunohistochemical and Molecular Analysis of a Series

(Poster No. 78)

Kaila Buckley, MD1 (kaila.buckley@osumc.edu); Michael Arnold, MD, PhD2; Christina Arnold, MD3; O. Hans Iwenotu, MD.1 Department of Pathology, The Ohio State University, Columbus; 2Department of Pathology, Nationwide Children’s Hospital, Columbus, Ohio.

Context: The broad morphologic spectrum and inherent immunophenotypic heterogeneity in malignant melanoma (MM) may lead to misclassification and suboptimal therapies. There have been few precedent reports of undifferentiated pleomorphic sarcoma (UPS) and rhabdomyosarcoma (RMS) arising in MM, an entity with a considerably poor outcome. We present 3 cases of MM with high-grade sarcomatoid dedifferentiation (DD) comprising RMS and UPS phenotypes, initially felt to represent primary sarcomas.

Design: The clinical, gross, microscopic, immunohistochemical, and molecular features of 3 cases of DD MM were reviewed.

Results: The tumors were located in the breast, left forearm, and left lower back, and ranged from 3.2 to 4.6 cm. Histologically, all cases show a distinct biphenotypic high-grade malignant neoplasm composed of a melanocytic component (exhibiting abundant eosinophilic cytoplasm and prominent nuclei) and a spindled sarcomatoid component. By IHC, the sarcomatoid area was positive for muscle markers, and negative for melanocytic markers, vascular markers, and epithelial markers, whilst the melanocytic areas were positive for melanocytic markers and negative for epithelial, vascular, and muscle markers (Figure 258). A diagnosis of MM with UPS DD (patients No. 1 and 3) and MM with RMS DD (patient No. 2) was made. BRAF V600E mutation analysis was positive in patient No. 1. NRAS mutation analysis was positive in patient No. 3. Patients No. 1 and 3 were treated with...
dabrafenib/trametinib and pembrolizumab with partial and stable responses.

**Conclusions:** MM with sarcomatoid DD is highly aggressive and the melanocytic component can be focal, thus suggesting a primary sarcoma. Accurate diagnosis is imperative, as these tumors respond better to targeted immunotherapy over conventional chemotherapy.

---

**Dermatofibrosarcoma Protubersans Presenting as a Gluteal Abscess**

(Poster No. 80)

Ali Afsari, MD (alafs@huhosp.org); Sara Mustafa, MD; Tammy Naab, MD. Department of Pathology, Howard University Hospital, Washington, District of Columbia.

Dermatofibrosarcoma protubersans (DFSP), a low-grade superficial sarcoma, has a tendency to recur locally when incompletely excised and rarely metastasizes unless fibrosarcomatous transformation occurs. It usually presents as a slow-growing plaque or nodule arising on the trunk of a young adult between the ages of 20 and 40 years and is more common in African Americans. Usual locations are chest, back, shoulder, abdominal wall, and proximal extremity. This uncommon tumor is characterized by latency in initial detection. We report a case of a 38-year-old African American woman who presented with a nonhealing left gluteal abscess with granulation tissue measuring 4 × 2.4 × 2.3 cm. She first noticed the painful mass 8 months before she sought medical attention. Initial presentation was to the emergency department where the abscess was lanced and an antibiotic was prescribed. The abscess partially healed but recurred. Three weeks later, the abscess was excised with inking of the tissue margins. Examination revealed abscess, necrotic spindle cells, and monomorphous spindle cell proliferation displaying a storiform pattern. Diffuse strong CD34 expression confirmed the diagnosis of DFSP, which involved the inked tissue margin. This case illustrates an unusual presentation of DFSP as a nonhealing abscess and highlights the utility of carefully examining tissue submitted as an abscess and inking tissue margins. Re-excision with a wide tissue margin has been scheduled to prevent recurrence.

---

**Melanocytic Nests in Association With Regression of Basal Cell Carcinoma**

(Poster No. 81)

Christopher Jackson, MD1 (christopher.r.jackson@hitchcock.org); Gregory D. Seidel, MD2; Shabnam Montalb, MD3; Cameron Felly, DO4; Kristen N. Ruby, DO5; ShaoFeng Yan, MD, PhD.1 1Department of Pathology, Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire; 2Department of Dermatopathology, North East Dermatology Associates Skin Solutions, Portsmouth, New Hampshire.

**Context:** Basal cell carcinomas (BCCs) are known to be populated by melanocytes. Intraepidermal and dermal melanocytic nests associated with BCC regression have been observed but are not well described in literature. We postulate that these nests are derived from BCC regression, leaving melanocytes to “collapse” into nest formation. The purpose of this study is to document this histologic phenomenon and evaluate its associated clinical presentations and outcomes.

**Design:** A pathology database search at our institution yielded 14 cases of BCC, which displayed regressive changes and coexisting melanocytic nests. Slides and medical records were reviewed and the histologic features were evaluated. Immunohistochemistry study with antibody to Melan-A was used to evaluate melanocytes.

**Results:** Eleven of 14 lesions were clinically consistent with BCC, while 3 were described as pigmented lesions. All cases showed BCC at various stages of regression as demonstrated by the presence of fibroplasia, increased vascularity, and lichenoid lymphoplasmacytic infiltrate with numerous colloid bodies. Melan-A–immunopositive junctional and dermal basoloid melanocytic nests were associated with lichenoid inflammation and colloid bodies in all cases. Nestled melanocytes were bland with small nuclei and minimal cytoplasm. Adjacent nonregressed foci of BCC were heavily colonized by melanocytes. Although 4 patients were lost to follow-up, none of the remaining patients experienced recurrence or a subsequent melanocytic neoplasm (mean follow-up = 3.7 years).

**Conclusions:** Cytologically bland melanocytic nests associated with BCC exhibiting lichenoid inflammation, fibroplasia and increased vascularity, and clinically indolent behavior support the hypothesis that these melanocytic nests are derived from regression of BCC.
An Interesting Case of Biphenotypic Acute Leukemia Presenting as Cutaneous Eruptions
(Poster No. 82)
Neha Varshney, MD1 (nehabarshn6@gmail.com); Hayder Abdulwahid, MD2; Abdelrouf I Al Agha, PA, MBA, MPH3; Mohammad Saud Khan, MD4; Lorie Gottwald, MD2; Cherian Verghese, MD5; Robert Booth, MD1. Departments of 1Pathology, 2Medicine, and 3Dermatology, University of Toledo Medical Center, Toledo, Ohio.

Acute leukemia (AL) is classified as myeloid or lymphoid on the basis of morphologic characteristics and the expression of CD markers. Rarely, leukemia cells express markers of more than 1 lineage known as hybrid, mixed-lineage, or biphenotypic AL, which have poor prognosis as compared to either acute myeloid leukemia or acute lymphoblastic leukemia. We present a case of a 53-year-old, Middle-Eastern man with a history of non-M3 acute myeloid leukemia in remission. He presented to dermatologist with a fever and maculo-nodular eruptions on his chest, abdomen, and back. A skin biopsy was performed, which showed perivascular infiltrates of atypical cells in the dermis with several mitotic figures. On further workup, palpable cervical, axillary, and inguinal lymphadenopathies were noted. A biopsy from enlarged cervical lymph node was obtained, a portion of which was sent for flow cytometry. Lymph node revealed a mixed population of cells with blasts suggestive of myeloid origin; however, flow cytometry revealed both myeloblast (positive for CD13, CD15, CD33, CD34, CD45, and CD117) and lymphoid (positive for CD10 and CD5) populations. This case was considered discordant and a repeated biopsy revealed DFSP (Figure 260, A and B). The patient underwent a wide local excision and the tumor extensively involved all margins. Repeated resection of margins was done, followed by adjuvant radiotherapy. The patient is currently doing well, but with cosmetic facial changes. Histologically, DFSP is characterized by uniform spindle cells in a storiform pattern often infiltrating the subcutaneous tissue. CD34 is used as an adjunct to diagnosis mainly to differentiate from dermatofibroma. However, many other spindle cell lesions including spindle cell lipoma, solitary fibrous tumor, cellular digital fibroma, among others, can be positive for CD34. Misdiagnosis leads to delay in treatment with potential of further local extension and destruction by the tumor. DFSP is a locally aggressive tumor and an accurate diagnosis is vital for proper management. Small biopsy samples have a potential for misinterpretation. Immunohistochemical stains like CD34 should be interpreted with caution in the differential diagnosis of spindle cell lesions.

Secondary Anetoderma Due to Molluscum contagiosum Infection
(Poster No. 84)
Alessandar Krbanjievic, MD, PhD1 (akrbarn2@uic.edu); Regina O’Brien, MD2; Michelle Bain, MD3; Marylee Braniecki, MD1. Departments of 1Pathology and 2Dermatology, University of Illinois at Chicago.

Anetoderma is a rare benign cutaneous disorder characterized by a progressive loss of elastic dermal fibers. A discrete defect clinically manifests as flaccid macular, papular, or depressed lesion. Secondary anetoderma (SA) usually occurs at skin sites that have been previously affected by an infectious, autoimmune, or a neoplastic process. We herein report an uncommon case of anetoderma secondary to a Molluscum contagiosum infection in a prepubertal boy involving his lower extremities. A 10-year-old boy had a history of developing puritic, small bumpy lesions on his leg in the past year. Physical examination revealed a flesh-colored papule with hyperkeratotic center (<0.3 cm in diameter) located on the upper part of his leg, plus 3 additional erythematous papules located within a depressed scar on his left medial knee. A skin punch biopsy revealed the presence of Molluscum bodies associated with perifollicular acute and chronic inflammation. The elastic stain demonstrated fragmentation and perifollicular loss of elastic fibers. This finding of secondary anetoderma in the setting of M contagiosum infection strongly implicates the virus causing the anetoderma. We share this case demonstrating M contagiosum is a relatively common pediatric viral infection, yet the occurrence of secondary anetoderma to this viral infection is uncommon.

Pilomatricoma: An Entity to Consider in the Differential Diagnosis of Multiple and Recurrent Skin Nodules in Syndromatic and Nonsyndromatic Patients
(Poster No. 85)
Ahmed Shehabeldin, MD1 (anshehabeldin@houstonmethodist.org); Megan S. Ketcham, MD2; Seema Mullick, MD3; Parul Shah, DO4; Jae Ro, MD, PhD1. Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Texas; Departments of 1Pathology and 2Genomic Medicine and 3Internal Medicine, Houston Methodist Sugar Land Hospital, Sugar Land, Texas.

Pilomatricoma is a relatively common benign skin tumor with follicular differentiation that typically occurs as a solitary lesion; however, multiple pilomatricomas rarely occur. Few cases of multiple pilomatricomas have been reported to arise in association with other disease conditions, such as myotonic dystrophy, Rubinstein-Taybi syndrome, familial adenomatous polyposis syndrome, Turner syndrome, Kabuki syndrome, and childhood cancer syndrome constitutio nal mismatch repair syndrome. In particular, myotonic dystrophy is an inherited muscular dystrophy that is clinically and genetically heterogeneous. Patients with myotonic dystrophy are at an increased risk for developing benign and malignant neoplasms. Herein, we report 2 cases of multiple pilomatricomas that were clinically misdiagnosed. Both cases involved women and were clinically diagnosed with either sebaceous cysts or epidermal cysts, with subsequent pathologic examination confirming the diagnosis of pilomatricomas. In case 1, a 62-year-old patient had multiple pilomatricomas (>30) as well as myotonic dystrophy and invasive ductal carcinoma of the breast. In addition, the patient had a family history of myotonic dystrophy and different cancers in several family members. In case 2, a 49-year-old patient had multiple pilomatricomas (>13) as well as phyllodes tumor of borderline malignancy, and low-grade squamous intraepithelial lesion of the uterine cervix. We aim to highlight pilomatricoma as a differential diagnosis of multiple skin tumors.
nodules and its association with myotonic dystrophy and other syndromes. Moreover, since the association with malignancy is frequent, diligent search for possible concurrent malignancy in other organs should be performed when multiple pilomatricomas are diagnosed in a patient.

**Distinct SRY-Related HMG-Box Gene-10 (SOX-10) Immunopatterns in Cutaneous Scars: A Potential Pitfall in the Diagnosis of Desmoplastic Malignant Melanoma**

(Poster No. 86)

Christopher A. Febres Aldana, MD (christopher.febres@msmc.com); John Alexis, MB, ChB. Department of Pathology and Laboratory Medicine, Mount Sinai Medical Center, Miami Beach, Florida.

**Context:** Desmoplastic malignant melanoma (DMM) presents as an amelanotic spindle cell proliferation resembling a cutaneous scar. Pathologic distinction can be difficult in re-excision specimens because DMM is negative for conventional melanoma markers such as HMB-45 and Melan-A, and scars may be positive for S100 protein and SOX-10.

**Design:** Hematoxylin-eosin stains and SOX-10 immunohistochemical stains (Biocare Medical) were evaluated in 12 cases of DMM and compared to 35 old cutaneous scars from women with prior cesarean section, and 8 re-excision scars. Cellular densities were calculated on captured images using ImageJ 1.51t (National Institutes of Health).

**Results:** SOX-10 was expressed in DMM (100%), old scars (91%), and re-excision (75%) scars. The density was higher in DMM than scars (822.9 ± 116.9 cells/mm² versus 188.37 ± 20.40 cells/mm², P < .001). Hypercellular scars can show SOX-10-positive-rich areas that may be mistaken for DMM. In scars, SOX-10-positive cells are small, round to spindled, and located within perivascular spaces or entrapped in fibrous tissue with linear arrangement (Figure 261, A and B; scale bar: 100 μm). In DMM, the malignant cells show enlarged atypical nuclei with a haphazard distribution and tendency to invade as single cells or clusters (Figure 261, C and D). Neutrophilic (67%), angiotropism (42%), and periadnexal spread (58%) were unique to DMM.

**Conclusions:** Cutaneous scars commonly contain SOX-10-positive cells. Identification of melanoma cells while evaluating DMM specimens requires not only immunoreactivity for SOX-10 but also assessment of tissue architecture, cellular distribution, and nuclear features.

---

**Squamous Differentiation in Eccrine Poroma of the Vulva**

(Poster No. 88)

Shira Ronen, MD (sronen@mcw.edu); Amanda Hopp, MD; Behnaz Behmaram, MD. Department of Pathology, Medical College of Wisconsin, Milwaukee.

Eccrine poromas are cutaneous neoplasms derived from the acrosyringium. They most often present on plantar and palmar skin, but they may also occur at any site containing sweat glands. Though rare cases of vulvar porocarcinomas are reported in the literature, to our knowledge, benign eccrine poromas has only been documented 4 times in the vulva. We present a rare case of vulvar poroma in an 82-year-old woman with a painless 4-cm lesion that had been present for the past several months and was bleeding intermittently. The clinical impression was of a verrucous lesion, most likely a large condyloma. No other significant medical history was noted. Histologic examination revealed a plaque-like, endophytic lesion growing into the papillary dermis with pushing borders and composed of monotonous cuboidal cells with ample pink cytoplasm and bland nuclei (Figure 263, A through D). Atypia and mitoses were rare. Duct formation was identified. Extensive areas of squamous differentiation, including keratohyalin granules, squamous eddies, and the formation of keratin whorls, were seen resembling seborrheic keratosis. The presence of squamous differentiation in eccrine poromas is an unusual phenomenon. As far as we know, eccrine poromas of the vulva with squamous differentiation has not been previously reported. However, the dual potential for ductal differentiation and keratinization is a well-known characteristic of eccrine cells in porocarcinoma of the vulva. Awareness of this phenomenon prevents misdiagnosis with seborrheic keratosis or possibly a well-differentiated squamous cell carcinoma.
The patient presented with a 12-year-old girl who developed a palpable mass of her left upper arm several weeks following routine vaccination injection. The mass persisted during the ensuing weeks and within months became increasingly tender and worrisome to the patient and family. Upon examination and radiographic studies, the mass reached a size of approximately 3 cm in greatest dimension. Ultrasonography showed a tubular structure in the subcutaneous tissue, and MRI showed a bilobed tubular structure with a differential diagnosis of a fluid collection or 2 adjacent lymph nodes. After a period of watchful waiting without resolution, the mass was surgical excised. A well-defined central cystlike region of granulomatous, focally necrotizing histiocytic inflammation was identified, coursing the entire length of the specimen. To our knowledge, necrotizing granulomas have not been previously reported as a tissue reaction at a vaccination site. It is important to recognize these unusual reaction patterns in order to appropriately counsel the patient and family, and to provide adequate treatment and counseling for the potential of similar recurrence with subsequent vaccination.

**DExH-Box Helicase 34 as a Novel Prognostic Biomarker in Melanoma**

(Poster No. 91)

Lijun Xue, MD, PhD1 (lxue@llu.edu); Xiyong Liu, MD, PhD2; Justin Kerstetter, MD.1 1Department of Pathology, Loma Linda University Medical Center, Loma Linda, California; 2Department of Biomarker Development, California Cancer Institute, Temple City.

**Context:** DHX34 gene encodes DExH-box Helicase 34, which plays critical roles in cellular metabolism, cellular proliferation, and/or neoplastic transformation. However, the clinical significance of DHX34 remains unknown.

**Design:** We conducted Kaplan-Meier and multivariate survival analysis, gene set enrichment analysis (GSEA), and correlation study for DHX34 and microRNA 393 in 4 published gene array data sets (GSE53118, GSE69904, E-MTAB-4725, and TCGA) with a total of 595 cases of melanoma. TargetScan Human v7.1 was performed to analyze the possible binding sites of microRNA 393 on DHX34.

**Results:** The survival analysis revealed that DHX34 mRNA expression levels were significantly related to poor overall survival (log-rank P = .003) and progression-free survival (log-rank P = .009) linked to melanoma. As with increase of mRNA expression levels, the survivability of patients decreased in a dose-dependent manner. The GSEA showed that expression of DHX34 could significantly enrich gene signatures including undifferentiation, cancer invasiveness, and metastasis. DHX34 expression was significantly increased in melanoma compared to normal skin and benign melanocytic skin nevus. miR-939 might be potentially binding the DHX34 transcript at position from 49 to 56. A correlation test showed that DHX34 mRNA expression was significantly and inversely correlated with miR-939 expression in melanoma tissue samples. Multivariate analysis further validated this opposite significance of DHX34 and miR-939. The same phenomenon was observed in other tissue organs, such as liver and kidney.

**Conclusions:** High DHX34 mRNA expression level is significantly related to poor survival, which might be modulated by miR-939 in melanoma tumor cells. This result indicates that DHX34 has a potential to serve as a prognostic biomarker.
Westward Expansion of Blastomycosis
(Poster No. 92)

Victoria C. Vaughan, MD (victoria.vaughan@ucdenver.edu); Sarah Donnell, MD; Paige Peterson, MD; Whitney High, MD, JD, MEng. Department of Pathology, University of Colorado at Denver, Aurora.

Blastomycosis is an infection caused by the dimorphic fungus *Blastomyces dermatitidis*, which causes pulmonary infection with subsequent hematogenous spread to skin and bone, and rarely the central nervous system. Less commonly, it may be primarily cutaneous following traumatic injury. The current endemic map for *B. dermatitidis* spans from Manitoba to Louisiana, extending to the East Coast. We present a case of blastomycosis occurring in a patient living outside the accepted endemic area. A 70-year-old man from South Dakota presented a year and a half ago to an outside institution with septic shock and stroke of unknown etiology and a papulovesicular rash over the left leg. He recently presented to our dermatology clinic with a pink, shiny plaque on a yellow base with a brown serpiginous border extending from the left knee to the ankle (Figure 265, A). It was biopsied and cultured. A similar lesion covered the lower abdomen. Light microscopy revealed dermal acute and chronic inflammation and yeast forms with broad-based budding highlighted by Grocott methenamine silver (Figure 265, B) and periodic acid-Schiff–diastase stains. On inhibitory mold agar, the culture grew a buff-colored mold with delicate silver (Figure 265, C) and periodic acid-Schiff–diastase stains. On microscopic examination of the culture, using lactophenol cotton blue stain, revealed septate hyphae and conidio-phores, each of which attaches a single conidium (Figure 265, D). Finally, DNA probe confirmed fungal identification. In addition to Midwestern, South-central, and Southeastern states, we present a case of blastomy-cosis from South Dakota, suggesting an expansion of the endemic area, and highlighting the significance of reassessing the paradigm.

A Patient With Concurrent Metastatic Merkel Cell Carcinoma, Chronic Lymphocytic Leukemia, and Profound Axillary Lymph Node Enlargement
(Poster No. 94)

Veronika Kholodovych, BSPS (veronika.kholodovych@rockets.utoledo.edu); Amy Custer, BS; Thomas Blomquist, MD, PhD; Nicole R. Dominik, MD; Honglui Sun, MD, PhD. Department of Pathology, University of Toledo Medical Center, Toledo, Ohio.

Merkel cell carcinoma (MCC) is a rare aggressive neuroendocrine neoplasm of the skin commonly found in sun-exposed areas of older patients with immune dysfunction. The association between MCC and lymphoproliferative neoplasms, such as chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), has been documented in literature. Both tumors are composed of round blue cells with high nuclear to cytoplasmic ratios and increased mitotic indices. Owing to the clinical and histologic overlap between the 2 entities, coexistence of both can obscure accurate diagnosis. We report a case of a 68-year-old man with CLL/SLL who presented with a left elbow mass, clinically suspected to be a lipoma. Excision revealed MCC with positive peripheral margins. Five months later, the patient returned with multiple palpable nodules on the left elbow/forearm and profound axillary lymphadenopathy. Re-excision confirmed recurrent MCC and lymph node dissection revealed 25 lymph nodes, some demonstrating massive enlargement, the largest measuring 9.5 cm in length (Figure 266, A). Three lymph nodes were found to contain histologically proven metastatic MCC juxtaposed with CLL/SLL on H&E (Figure 266, B), proven with CK20 and CD20 immunostaining (Figure 266, C and D, respectively). This case demonstrates the difficulty in clinical, gross, and microscopic identification of metastatic lesions in lymph nodes of CLL/SLL patients. This

Linear Porokeratosis With Eccrine Involvement: An Uncommon Clinical Presentation and Histopathology
(Poster No. 93)

Kristina Wakeman, MD1 (kwakeman@uic.edu); Ariel Leifer, MD2; Marylee Braniecki, MD.1 Departments of 1Pathology and 2Family Medicine, UIC, Chicago, Illinois.

Porokeratosis is a benign epithelial tumor characterized histologically by abnormal keratinization and cornoid lamellae. It typically presents as atrophic-appearing patches that have a distinct raised annular border. Variants of porokeratosis include classic, localized, linear, punctuate, disseminated superficial, and porokeratotic adnexal ostial nevus. Linear porokeratosis and porokeratotic adnexal ostial nevus are rare variants and both typically present in childhood. We share this unusual case of a 66-year-old African American woman who presented with a violaceous papular rash that had spread linearly from the right wrist to the forearm during the course of a year. Skin biopsy revealed cornoid lamellae with involvement of eccrine glands. Solely based on histology, the differential diagnosis included linear porokeratosis involving acrosyringium and a porokeratotic adnexal ostial nevus. Porokeratotic adnexal ostial nevus seemed a less likely diagnosis based on the clinical appearance of the rash. Therefore, the clinical and histologic features were overall most consistent with a linear porokeratosis involving eccrine glands. Cornoid lamellae are pathognomonic for porokeratosis but can be found in other entities, including both inflammatory and neoplastic processes. We present this case to elucidate the spectrum of clinical and histopathologic findings in porokeratosis. Furthermore, as porokeratosis has a risk of malignant transformation, the recognition of the histologic spectrum of findings and their clinical settings becomes essential for correct diagnosis and appropriate treatment.

Abstracts
quandary warrants further investigation into lymph node gross and histologic assessment in situations of integrated neoplasms. Additionally, this case reaffirms the necessity to evaluate new cutaneous lesions in CLL/SLL patients for the possibility of new primary neoplasms and ensure appropriate treatment and improve outcomes.

Trichoadenoma: A Histopathologic Diagnosis—An Uncommon Lesion Presenting on the Buttock

(Sara Masood, MD; Thomas M. Soike, MD. Department of Pathology, ETSU, Johnson City, Tennessee.)

Trichoadenoma is an uncommon, benign follicular tumor. A misnomer, trichoadenoma does not demonstrate glandular differentiation; instead, Nikolowski initially described this entity as a well-differentiated tumor with adenomatous level of organization, which lies between a true hair nevus or a trichoepithelioma. Trichoadenomas arise from the infundibular portion of the pilosebaceous unit and have a predilection for the face and buttock. Our case is that of a 44-year-old man presenting with multiple slowly enlarging skin lesions. The clinical impression was skin tags. Postoperative histopathologic examination revealed multiple horn cysts lined by keratinized granular cell layer surrounded by squamous epithelial proliferation. This was consistent with the diagnosis of a trichoadenoma, which is a well-defined intradermal lesion demonstrating areas of cystic and solid components (Figure 267). There was no evidence of a basaloid/germ cell proliferation of epithelium, which would suggest a trichoepithelioma, a similar lesion included in the differential diagnosis. Literature review demonstrated 7 cases presenting on this site, with a male predominance (2:5:1). Trichoadenoma is a histopathologic diagnosis that warrants differentiation from other benign follicular tumors such as trichofolliculoma and trichoepithelioma. The latter may undergo malignant transformation. It is also essential to differentiate these lesions from an infundibular cystic variant of squamous cell carcinoma, considered a malignant counterpart of a trichoadenoma. In conclusion, trichoadenoma is a benign entity with no evidence of recurrence or malignant transformation.

A Program for Competency Assessment and Quality Control of Provider-Performed Microscopy Testing in a Regional Health Care System

(Harold H. Harrison, MD, PhD; Elzabeth M. Amarose, BS, MLS(ASCP); Elsie H. Yu, PhD. Department of Laboratory Medicine, Geisinger Medical Center, Danville, Pennsylvania.)

Context: Provider-performed microscopy (PPM) procedures are a Clinical Laboratory Improvement Amendments (CLIA)–defined group of nonwaived, moderate complexity tests that are performed by physicians and midlevel providers in conjunction with examination of a patient. When performed under the CLIA license of the main clinical laboratory, the CLIA laboratory director and laboratory operations leaders are responsible for its quality assurance and assessing PPM provider competency. In 2014, a College of American Pathologists (CAP) requirement for direct competency assessment replaced the old clinical credentialing approach. To adapt to the challenges of this change we developed the program reported here for wet mounts, KOH preparations, and fern testing.

Design: We developed a compliant PPM competency and quality program for 200 providers and 43 sites in 4 clinical disciplines, consisting of (1) annual online training module; (2) annual assessment of technical consultant and provider competency; (3) development of daily QC materials; (4) development of supplemental PT materials; and (5) creation of forms to document 1 through 4.

Results: Competency assessment necessitated building a hierarchy of laboratory directors and technical consultants who trained and assessed the competency of progressive levels of subsidiary providers. New and abnormal QC specimens were photomicrographed and e-mailed to PPM providers (with permission) reviewed each day of testing by the provider performing the testing. Documentation was kept at each site and centrally in the system POCT office. One year was spent in preparation and 1 year in implementation.

Conclusions: Working with the clinical departments, we achieved a scalable, centralized management system for multisite PPM competency assessment, daily QC, alternative and supplemental PT, and EHR documentation.

Prevalence of Single α Hemoglobin Mutation in Eastern North Carolina: Series of 7 Cases of Hemoglobin G–Philadelphia in the Past 49 Years With Literature Review

(Ding Dai, MD, PhD; Aparna Thombare, MD, MPH; Richard J. Baltaro, MD, PhD. Department of Pathology and Laboratory Medicine, East Carolina University, Greenville, North Carolina.)

Context: Of more than 6000 different patients with a hemoglobinopathy since 1969, only 7 cases of homozygous or heterozygous hemoglobin (Hb) G–Philadelphia instead of the expected 140 (based on 1/5000 frequency) have been diagnosed at the East Carolina University and its hospital system serving 1.4 million people in 29 counties in Eastern North Carolina.

Design: Retrospective review of 49 years of hospital, medical school, and all clinics’ archives.

Results: Two cases of homozygous HbG and 5 cases of heterozygous HbG were identified by using high-performance liquid chromatography (HPLC) and gel electrophoresis. The 2 cases of homozygous HbG–Philadelphia associated with biallelic α genes deleted concern 2 healthy adult African American women with mild microcytic anemia. HPLC profiles showed similar pattern with HbG constituting about 100% of total Hb. Acid gel and alkaline gel electrophoresis confirmed the diagnosis. The homozygous HbG–Philadelphia associated with homozygous α-thalassemia by DNA sequence analysis of α-globin gene was confirmed. Clinically, the heterozygous HbG–Philadelphia patients were 6 to 58 years old. All subjects exhibited mild to moderate normocytic and normochromic anemia.

Conclusions: Our records show 7 cases instead of the expected 140 cases. HbG–Philadelphia is the most common α chain hemoglobinopathy found. The African American population in East Carolina is greater than 700,000 and the expected frequency of HbG–Philadelphia is about 1 in 5000 (Hoyer J; 2003). We postulate that the African American population of Eastern North Carolina is genetically different from that reported in other geographic areas of the United States, possibly owing to consanguinity or origination from a different part of Africa.

Utilization of Aldolase Testing

(Diane-Ngan Trang, MD; Wieslaw Furmaga, MD. Department of Pathology, University of Texas Health Science Center, San Antonio.)

Context: Aldolase is an enzyme of the glucose metabolic pathway abundantly present in the skeletal muscle. Plasma concentration of aldolase has been used as a nonspecific marker for muscle and liver damage. Despite availability of more specific tests for diagnosis of the muscle and liver damage, aldolase is still ordered for this purpose. The aim of our study is an evaluation of how aldolase testing has been used in respect to the appropriate indications such as dermatomyositis and rhabdomyolysis.

Design: Clinical orders for aldolase testing from October to January 2017 were reviewed and compared to the patients chart for their
appropriateness. The number of correctly ordered tests was compared to the total number of orders.

**Results:** A total of 140 cases were ordered throughout October to January 2017. Of those 140 cases, 30 cases were clinically appropriate when using our criteria. Ninety-three cases of the 140 were ordered before aldolase was removed from the order set and 47 cases were ordered afterward. Of the 93 orders, 17% were clinically appropriate, while 30% of the 47 orders were clinically appropriate.

**Conclusions:** There was a drastic change in the number of total orders after aldolase was removed from the order sets along with the percentage of clinically appropriate orders. This is likely indicative that most aldolase orders were in fact a side effect of aldolase being included in specific order sets.

**Correlation of Lactate Values and Severity of Sepsis**  
(Poster No. 99)

Lisa Duncan, MD  
(ldduncan@utmck.edu). Department of Pathology, University of Tennessee Graduate School of Medicine, Knoxville.

**Context:** Lactate levels have become a standard measurement for determining the severity of a septic patient. The criteria for sepsis have been classified as a combination of an infection with a systemic inflammatory response syndrome (SIRS). The Centers for Medicare and Medicaid Services has deemed that patients with a lactate concentration \( \geq 4.0 \text{ mmol/L} \) be classified as having septic shock.

**Design:** We retrospectively reviewed 1066 patients previously diagnosed with sepsis during a 3-month period. Lactate levels and blood culture results were recorded. Record charts were reviewed and determined if the patient met the criteria for sepsis. The patient data were then statistically analyzed to compare septic patients to nonseptic patients.

**Results:** This study included 814 patients; of these, 281 (34.5%) had positive blood cultures, while 38 (3.6%) of the positive cultures had a lactate concentration \( \geq 4.0 \text{ mmol/L} \). Lactate values ranged from 0.2 to 14.3 mmol/L. Additionally, 533 (65.5%) of these patients had negative blood cultures, including 72 patients (13.5%) with a lactate concentration \( \geq 4.0 \text{ mmol/L} \). Negative blood culture lactate results ranged from 0.4 to 26.6 mmol/L. Both sets of lactate levels were compared to secondary lactate levels. The \( P \) value when comparing patients with positive and negative blood cultures was 0.26, thus there is no significant difference between the groups.

**Conclusions:** Comparing the results from patients with positive and negative blood cultures showed that lactate levels have no significant difference between the 2 groups. Following the trend in both cases, lactate levels appear to be very similar throughout differing severities. Thus, correlating sepsis to lactate levels can lead to misdiagnoses.

**A Case of Pseudohypertriglyceridemia in a Patient Admitted for Pancreatitis**  
(Poster No. 100)

Ayesha Farooq, MD, MBBS  
(afarooq@mcw.edu); Angela Treml, MD; Jessica Colon, PhD, DABCC. Department of Pathology, Medical College of Wisconsin, Milwaukee.

A 37-year-old woman with history of diabetes mellitus type 1, end-stage renal disease, liver disease, chronic obstructive pulmonary disease, and congestive heart failure presented to the emergency department with abdominal pain, nausea, and vomiting. Labs have test results showed elevated lipase of 680 units/L (reference range, 13–4500 units/L). The patient reported no family history of enzyme deficiency or elevated triglycerides. Follow-up to rule out enzyme deficiency is pending. Triglyceride levels decreased to 1315 mg/dL (reference range, 4500 mg/dL after 4500 mg/dL) after 4500 mg/dL after 4500 mg/dL. These results along with clinical and radiologic findings suggested a diagnosis of hypertriglyceridemia-mediated pancreatitis. The patient was discharged and continued lipid-lowering therapy.

**Conclusions:** These results along with clinical and radiologic findings suggested a diagnosis of hypertriglyceridemia-mediated pancreatitis. The patient was discharged and continued lipid-lowering therapy.

**Efficacy of Stopping the 100-Gram Oral Glucose Tolerance Test When Criteria Are Established Before 3 Hours**  
(Poster No. 101)

Ali Rashidbaigi, MD  
(alirashidbaigi@gmail.com); Alyeesha B. Wilhelm, BS;2 Christopher Caroway, MD; Selwyn Baptist, MD.1  
1Department of Pathology, Robert Wood Johnson–Barnabas Health Medical Center, Livingston, New Jersey; 2Department of Anatomy and Pathology, St. George’s University School of Medicine, St. George’s, Grenada.

**Context:** To diagnose gestational diabetes mellitus (GDM), screen-positive patients undergo the oral glucose tolerance test (OGTT). At St. Barnabas Medical Center (SBMC), guidelines of the American College of Obstetricians and Gynecologists are followed for the 100-gram, 3-hour OGTT test. Gestational diabetes mellitus is established when 2 or more plasma glucose levels meet or exceed the fasting, 1 hour, 2 hour, or 3 hour limits. The current protocol at SBMC requires patients to complete the entire test. We examined the amount of time saved and unnecessary tests eliminated if the OGTT had been stopped when the criteria were met before completing the entire test.

**Design:** All patients who underwent the 100-gram, 3-hour OGTT in 2016 at SBMC, a community hospital, were retrospectively reviewed. Patient plasma was tested by using the Cobas 8000 modular analyzer using the hexokinase enzymatic reaction.

**Results:** A total of 163 patients underwent the 100-gram, 3-hour OGTT in 2016. Forty-five were excluded for not completing the examination, leaving 118 patients included in our study. Eighty-nine patients had normal test results and 29 met the criteria for GDM. Twenty-six patients met the criteria before 3 hours, and 3 met the criteria at hour 3. The criteria for GDM were met by 12 patients at hour 1; 7 patients at hour 2; and 3 patients at hour 3.

**Conclusions:** Stopping the OGTT when the criteria were met before 3 hours would have saved 51 total hours and eliminated a total of 36 unnecessary tests.

**The Effect of Extreme Outdoor Temperatures on Specimen Integrity**  
(Poster No. 102)

Ryan Campbell, MD  
(campbellryan2@gmail.com); Kimberley Sanderson, BSMT; Susan LeSourd, MSOM; Bert Johnson, BSMT; Ericka Olgaard, DO. Department of Pathology and Laboratory Services, University of Arkansas for Medical Sciences, Little Rock.

**Context:** Clinics send specimens to the laboratory via courier, which may close before specimen pick-up. Specimens may be held in Department of Transportation–approved metal containers outside the clinic for up to 2 hours. Specimen stability and integrity were evaluated to determine what, if any, effect summer heat could have on these specimens.

**Design:** Two plasma separator specimen tubes were drawn on 21 volunteers. One set of tubes (control group) was stored at ambient temperature and the other set was placed in a metal box with an ice pack outside an external door to simulate clinic specimen boxes. The outdoor temperature averaged 95°F. After 2 hours, a comprehensive metabolic panel (CMP) was performed on each tube on a Beckman Coulter DxC (Brea, California).

**Results:** A Student t test compared the paired CMP data. Variation in glucose and alkaline phosphatase between the control and experimental tubes was statistically significant, showing an average of 1.5 mg/dL less glucose \((P = 0.008)\) and 0.67 IU/L more alkaline phosphatase \((P = 0.05)\) in the samples exposed to heat. To account for biological and analytic variation, a standard deviation index (SDI) was calculated for each pairing, with SDI values of 1.5 mg/dL and 0.67 IU/L. The current protocol at SBMC requires patients to complete the entire test. We examined the amount of time saved and unnecessary tests eliminated if the OGTT had been stopped when the criteria were met before completing the entire test.

**Conclusions:** Although statistically significant, there was no clinically significant variation in CMP results. The 4 outliers showed no pattern and were attributed to normal variation > 2 SD expected of the method. The quality and integrity of samples properly stored for courier pick-up should not be affected by extreme ambient temperatures.
**New Paradigms for Reporting Syphilis Screening With the Introduction of Multiplex Immunoassays**

(*Poster No. 103*)

**Eric Statz, MD (statze@upmc.edu); Sarah Wheeler, PhD; Michael Shurin, MD, PhD. Department of Pathology, UPMC, Pittsburgh, Pennsylvania.**

**Context:** Algorithms for syphilis screening include “forward-testing” with a nontreponemal test (eg, rapid plasma reagin [RPR]) followed by a treponemal test, and “reverse-testing” in the opposite order. The BioPlex 2200 Syphilis Total and RPR (combination) is a multiplex immunoassay with concurrent testing, raising questions about reporting algorithms and new interferences.

**Design:** We compared the UPMC reverse-screening modality by using the BioPlex Syphilis IgG immunoassay (Bio-Rad, Hercules, California) with the combination assay (Bio-Rad, San Diego, California) and Sure-Vue RPR test (Inova Diagnostics, San Diego, California) with the combination assay (Bio-Rad). We tested 61 specimens, with 19 of 61 also tested by the serodisc Treponema pallidum hemagglutination assay (Fujirebio, Malvern, Pennsylvania). Clinical information categorized results as treated, false positive, negative, positive, or indeterminate.

**Results:** Treponemal assays showed 100% concordance for the initial 21 positive and 20 negative samples tested. RPR assays demonstrated 100% concordance for negative samples and 90.5% concordance for Sure-Vue-positive samples. We then tested 20 likely false-positive specimens (BioPlex Syphilis IgG-positive, Sure-Vue RPR-negative) and categorized results by using clinical information. By current testing, 10 were considered treated and 10 were false positives. Using the combination assay, 1/20 was false positive. Overall, 11/20 changed categories and the new diagnoses better reflected clinical information.

**Conclusions:** The combination assay provides automated results comparable to current in-house testing with increased specificity in cases with likely false-positive results by current testing. It presents new options for forward versus reverse testing algorithms. We will report treponemal and nontreponemal results simultaneously with appropriate interpretation, as both forward and reverse testing algorithms have known limitations.

---

**Next-Generation M-Protein Detection: Helping Pathologists to Be Mass Spectrometrists**

(*Poster No. 104*)

**David L. Murray, MD, PhD (murray.david@mayo.edu); Mindy Kolhagen, MLT; Angela Dispenzieri, MD; Surendra Dasari, PhD. Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota.**

**Context:** Our clinical laboratory has been using gel electrophoretic methods since 1967 to detect, quantitate, and isotype M-proteins. Recently, we have demonstrated and validated a new mass spectrometric method (MASS-FIX) capable of replacing gel electrophoresis.

---

**Atorvastatin Enhances Humoral Immune Response to Pneumococcal Pneumonia Vaccination in Healthy Volunteers**

(*Poster No. 105*)

**Tyler Wildes, BS1 (twildes@uf.edu); Kyle Dyson, BS1; Henrietta Fassanya, BS1; Adam Graggin, BS1; Jonathan Shuster, PhD1; Mark Brantley, MD,1 Departments of 1Medicine, MD-PhD Program; 2Health Outcomes and Biomedical Informatics; 3Medicine, Division of Pulmonary, Critical Care, and Sleep Medicine, University of Florida, Gainesville.**

**Context:** Pneumococcal pneumonia vaccination is recommended for at-risk individuals, healthy children, and adults older than 65 years. While current schedules provide limited protection, generating a robust immune response remains a concern. Atorvastatin, an HMG-CoA reductase inhibitor with limited toxicity and cost, has a well-described immunomodulatory role. Previous studies indicate that statins promote a type 2 T-helper cell immune response, which is important for effective humoral immunity. Therefore, we investigated the effect of atorvastatin on vaccination with Pneumovax23.

**Design:** After screening, 22 healthy volunteers were selected for this study. Subjects were excluded on the basis of prior pneumococcal vaccination, allergies, pregnancy, elevated creatinine, body mass index greater than 32, and elevated aspartate transaminase and alanine transaminase. Subjects were randomized to receive either lactose or 40 mg atorvastatin on days 0. Subjects received intramuscular Pneumovax23 on day 7, and immune responses including serotype-specific antibody titers were followed up until day 28.

**Results:** At baseline, there were no significant differences in blood pressure, heart rate, triglycerides, and cholesterol. By 3 weeks post vaccine, total pneumococcal antibody titer was significantly elevated in the atorvastatin group compared to placebo ($P < .05$). When analyzing serotypes, the atorvastatin group had a significant elevation in 4 of the 14 measured serotype-specific antibody titers (serotype 1, $P < .001$; 7, $P = .005$; 9v, $P = .01$; 18c, $P = .006$). Interestingly, lymphocyte count was significantly decreased in the atorvastatin group when compared to placebo ($P < .001$).

**Conclusions:** Atorvastatin provides a significant enhancement of antibody response to Pneumovax23. Current investigation of serum cytokines by Luminox and peripheral lymphocyte subsets by flow cytometry will inform mechanistic investigation.

---

**Plasmablastic Lymphoma of the Adrenal Gland in a Patient With Well-Controlled HIV**

(*Poster No. 106*)

**Roshan Mahabir, MD, PhD, MPH1 (roshan.mahabir@mountsinai.org); Sushma Ravirala, MBBS1; Kevin Xu, BS2; Aida Taye Bellistri, MD3; Wen Fan, MD, PhD3; Abdelsalam Sharabi, MD,1 Departments of Pathology, St. Luke's Roosevelt, New York, New York; Departments of...
Plasmablastic lymphoma (PBL) is a highly aggressive B-cell lymphoma subcategorized as CD20+/CD0 diffuse large B-cell lymphoma (DLBCL) with plasmablastic features commonly seen in the oral cavity of HIV-positive young men and immunocompromised patients, but is increasingly being reported in immunocompetent individuals and extraoral sites. PBL has been shown to favor the gastrointestinal tract, skin, and lymph nodes in immunocompetent individuals. We present a case of PBL in a 51-year-old HIV-positive man who is well maintained on HAART, who is known to have anxiety disorder and a renal mass incidentally found on CT following workup for an accident. In this patient, presurgical testing showed a minimum deviation of catecholamines, and resection of the adrenal gland showed a 3.0 × 2.5 × 1.5-cm firm, pale white mass with areas of hemorrhage that grossly appeared to involve the surrounding tissue. Histologic examination of the mass in relation to the adrenal gland showed a pleomorphic mix of discohesive lymphoid cells with abundant cytoplasm, vesicular chromatin, and centrally placed nucleoli that did not involve the adrenal parenchyma. Immunohistochemical studies revealed the tumor cells were positive for MUM1, c-MYC, and EBV and negative for CD138, CD20, CD3, CD5, CD56, and HHV-8. Ki-67 was positive in 80% of tumor cells. The diagnosis of PBL is challenging given the overlapping features of adrenocortical carcinoma, lymphomas, and anaplastic plasma cell myelomas. This case demonstrates the importance of clinical history and radiologic differential diagnoses in this rare tumor especially given the associated poor prognosis (Figure 269).

Amiodarone-Induced Thyrotoxicosis Treated With Total Thyroidectomy

(Poster No. 107)

Tracy R. Shachner, DO (tshachner@utmck.edu); Christopher T. Clark, MD. Department of Pathology, University of Tennessee Medical Center, Knoxville.

Amiodarone is a class III antiarrhythmic agent commonly used to treat tachyarrhythmias. Because amiodarone contains 37% iodine by weight and is structurally similar to the thyroid hormone thyroxine, it can affect the metabolic pathways of thyroid hormones, causing both hypothyroidism and hyperthyroidism. The frequency of amiodarone-induced hypothyroidism and amiodarone-induced thyrotoxicosis (AIT) are dependent on the iodine status of the population. In the United States, amiodarone-induced hyperthyroidism is much more common than AIT, with AIT occurring in only 3% of patients treated with amiodarone. AIT may present in 2 forms: type 1 occurs in patients with preexisting thyroid disease, and type 2 occurs in patients with previously unremarkable thyroid glands as the result of a destructive inflammatory process. In AIT type 2, amiodarone is believed to have a direct toxic effect on the thyroid, causing release of iodothyronines. AIT is usually treated medically, though surgical excision can be performed as a last resort for medically refractory cases. We report an unusual case of a patient with AIT type 2 that was refractory to medical treatment. He underwent a total thyroidectomy for definitive treatment. Microscopic examination of the thyroid showed degenerated follicular cells with aggregates of foamy macrophages and inflammatory cells within thyroid follicles, consistent with AIT type 2 (Figure 270, A through D). We present this unusual case to bring attention to the characteristic histologic findings of AIT type 2, an entity that is not commonly seen in the United States and is not commonly treated by total thyroidectomy.

Metastatic Breast Carcinoma Within a Thyroid Oncocytic Follicular Carcinoma

(Poster No. 108)

Emily L. Wickersham, DO (emily.mientus@gmail.com); Karen S. Strenge, MD. Department of Pathology, Madigan Army Medical Center, Tacoma, Washington.

Tumor-to-tumor metastasis is rare, particularly in the thyroid. Thyroid metastases from various primary sites have been described, particularly renal cell carcinoma, lung carcinoma, breast carcinoma, and colonic carcinoma. Follicular adenomas and papillary thyroid carcinomas are the most common thyroidal recipients for tumor-to-tumor metastases. There have been 42 reported cases of metastatic breast cancer to the thyroid and 28 cases of tumor metastases to thyroid neoplasms; however, no known prior cases of metastatic breast carcinoma to an oncocytic-type follicular carcinoma have been reported. We report the case of a 64-year-old woman with breast carcinoma metastasizing to a thyroid follicular carcinoma. Our patient...
had a longstanding history of a right-sided goiter and recent diagnosis of right breast invasive mammary carcinoma of no special type. Owing to compressive symptoms and recent breast cancer diagnosis, the thyroid goiter was biopsied and revealed groups of cells suggestive of a follicular neoplasm. Right hemithyroidectomy revealed metastatic breast carcinoma within a follicular carcinoma, oncocytic (Hurthle cell) type. Positive immunohistochemistry for ER (Figure 271, B) and GATA-3 (Figure 271, C) and negativity for TTF-1 (Figure 271, D) confirmed the breast origin of the morphologically distinct second population of invasive glandular cells (Figure 271, A). Distinguishing secondary thyroid metastases from a primary thyroid malignancy is important for patient’s treatment and prognosis. An additional primary malignancy is resected and has a better prognosis, whereas a metastasis to the thyroid has a worse prognosis and is only removed for compressive symptoms and/or local control of aggressive disease.

Solitary Fibrous Tumor of the Thyroid With High-Grade Transformation

(Poster No. 109)

Derek J. Danner, MD (djdanner@bcm.edu); Nitin Marwaha, MD; Chris Finch, MD; Thomas Wheeler, MD; Shilpa Jain, MD. Department of Pathology & Immunology, Baylor College of Medicine, Houston, Texas.

Solitary fibrous tumor (SFT), a rare spindle cell neoplasm, usually develops in the pleura. SFTs arising in the thyroid are rare. A 41-year-old woman with an enlarging left neck mass for 2 years presented to the emergency department with shortness of breath and dyspahgia. The neck imaging showed a heterogeneous mass arising from the left thyroid lobe, which was causing shift of the trachea with narrowing of the airway. An image-guided fine-needle aspiration and biopsy were performed, followed by resection. The aspirate smears and core needle biopsy demonstrated spindle cells arranged in patternless pattern with collagenous stroma and thin-walled vessels. An immunohistochemical workup was performed and tumor cells were positive for CD34, Bcl-2, Pax-8, with nuclear positivity for STAT6. The diagnosis of SFT arising in thyroid gland was rendered. The resection specimen showed a well-circumscribed 9.5-cm solid mass, with a firm, tan-white cut surface. The histologic findings of the tumor were consistent with SFT with areas of high-grade transformation at the periphery of the lesion. These areas were cellular with moderate atypia, higher mitotic activity (4/10 high-power fields), and higher Ki-67 proliferative index of 15%. Two lymph nodes were negative for tumor. SFTs arising in the thyroid are rare with fewer than 30 cases reported, and STAT6 is a useful marker for small biopsy. High-grade transformation of the SFT of thyroid gland is extremely rare. The transformation at the periphery of the lesion. These areas were cellular with moderate atypia, higher mitotic activity (4/10 high-power fields), and higher Ki-67 proliferative index of 15%. Two lymph nodes were negative for tumor. SFTs arising in the thyroid are rare with fewer than 30 cases reported, and STAT6 is a useful marker for small biopsy. High-grade transformation of the SFT of thyroid gland is extremely rare. The histologic findings of the tumor were consistent with SFT with areas of high-grade transformation at the periphery of the lesion. These areas were cellular with moderate atypia, higher mitotic activity (4/10 high-power fields), and higher Ki-67 proliferative index of 15%. Two lymph nodes were negative for tumor. SFTs arising in the thyroid are rare with fewer than 30 cases reported, and STAT6 is a useful marker for small biopsy. High-grade transformation of the SFT of thyroid gland is extremely rare. The histologic findings of the tumor were consistent with SFT with areas of high-grade transformation at the periphery of the lesion. These areas were cellular with moderate atypia, higher mitotic activity (4/10 high-power fields), and higher Ki-67 proliferative index of 15%. Two lymph nodes were negative for tumor. SFTs arising in the thyroid are rare with fewer than 30 cases reported, and STAT6 is a useful marker for small biopsy. High-grade transformation of the SFT of thyroid gland is extremely rare.

Utility of Whole Genome Single Nucleotide Polymorphism Microarray and Targeted Somatic Mutations in Evaluation of Histologically Equivocal Adrenal Cortical Neoplasm

(Poster No. 111)

Okechukwu Nwogbo, MD (onwogbo@augusta.edu); Suash Sharma, MD; George Wang, MD; Benjamin Johnson, BS; Ashis Mondal, PhD; Chetan Pundkar, PhD; Alka Chaubey, PhD; Ravindra B. Kolbe, MD, PhD. Department of Pathology, Medical College of Georgia at Augusta University, Augusta.

Histopathologic diagnosis of low-grade adrenal cortical carcinoma can be difficult. It is distinguished from a large adenoma by using a combination of criteria as described by Weiss, Van Slooten, or Hough. We describe a 6.0-cm, 80-g cortical tumor identified on adrenalectomy in a 57-year-old woman. The tumor displayed variably sized nests, foci of moderate nuclear pleomorphism with easily identifiable nucleoli (Fuhrman grade-3), <25% clear cells, partly disrupted reticulin architecture, and a Ki-67 labeling index of up to 5%, concerning for low-grade adrenal cortical carcinoma. Mitotic activity was up to 3/50 high-power fields; and no atypical mitoses, diffuse architecture, necrosis, venous invasion, sinusoidal invasion, or capsular invasion were identifiable to fully meet the Weiss criteria for adrenal cortical carcinoma. The whole genome single nucleotide polymorphism microarray was performed on the DNA isolated from formalin-fixed paraffin-embedded blocks following manufacturer’s protocol (OncoScan assay, Affymetrix Inc, Santa Clara, California). The raw data were analyzed in Chromosome Analysis Suite 3.0 software and were matched to in silico formalin-fixed paraffin-embedded reference sets. This platform consists of 274,000 probes including 74 somatic mutations from 9 genes (BRAF, KIAA1549, IDH1, IDH2, PDGFRA, PDGFB, CTNNB1, PIK3CA, NRAS, and TP53). The results demonstrated TP53 mutation, mosaic loss in chromosome 3 (CTNNB1 gene), and monosomy 15; these findings supported the diagnosis of low-grade adrenal cortical carcinoma as per TCGA analysis. We describe an effective technology for investigating histologically difficult cases. This report emphasizes the value of decisive molecular alterations in arriving at the critical threshold of establishing a diagnosis of low-grade adrenal cortical carcinoma (Figure 273).

Metastatic Papillary Thyroid Microcarcinomas: Clinicopathologic Features of an Otherwise Indolent Disease

(Poster No. 110)

Sigfred Lajara, MD (slajara@montefiore.org); Stacia Semple, MD; Samer Khader, MD. Department of Pathology, Montefiore Medical Center, Bronx, New York.

Context: Papillary thyroid microcarcinomas are tumors that measure 1.0 cm or less. The increased incidence is likely due to improvement in diagnostic modalities. Factors associated with aggressive behavior are still not fully understood. Our study aims to characterize the clinicopathologic parameters of metastatic papillary thyroid microcarcinomas.

Design: Surgical pathology reports from 2013 to 2017 with the diagnosis of “papillary thyroid microcarcinoma,” and without concurrent macrocarcinoma were obtained (n = 148). Twelve metastatic cases were available for slide review.

Results: Among 148 cases, 14 (9.5%) had lymph node metastases. The mean age was 52 years, with a female to male ratio of 1.8. Eleven (73%) cases had at least an atypical cytologic diagnosis, with 8 (53%) being suspicious or malignant. One case was negative. Two cases were incidentally discovered on lymph node dissection for squamous cell carcinoma. The tumor sizes ranged from 0.3 to 1.0 cm, with a median of 0.8 cm. Eight cases were multifocal and 4 were bilateral. One had minimal extrathyroidal extension. Three cases had more than 5 positive lymph nodes; 5 had extranodal extension. On slide review, 6, 4, and 2 cases had classical, follicular, and tall cell morphologies, respectively. Three were partially encapsulated, while the remaining cases were unencapsulated. Nine were associated with dense hyalinized sclerosis.

Conclusions: Although usually indolent, almost 10% of papillary microcarcinomas presented with metastatic disease, in which most were detected owing to abnormal cytologic diagnoses. Most had densely sclerotic background, and none were completely encapsulated. These findings are consistent with recently published literature and warrant further investigation.
Intraoperative Diagnosis of Parathyroid Tissue

(Poster No. 112)

Joyce Ren, MD (joyce.ren@stonybrookmedicine.edu); Alan Heimann, MD; Sonya Hwang, MD; Sui Zee, MD; Jinguan Liu, MD, PhD. Department of Pathology, Stony Brook University Hospital, Stony Brook, New York.

Context: Intraoperative diagnosis of the parathyroid gland is commonly performed for clinically suspected parathyroid adenoma or thyroid lesions. In most cases, pathologists can make a diagnosis with reasonable certainty; however, on a case-by-case basis, definitive diagnosis of parathyroid tissue continues to pose challenges on frozen section.

Design: Surgical cases for which intraoperative diagnosis of parathyroid tissue was performed during the past 5 years at our institution were reviewed. Cases with a discrepancy between the intraoperative and final diagnoses, or for which the intraoperative diagnosis was deferred to permanent section, were collected. Cases where the uncertainty of the intraoperative diagnosis was purely due to insufficient tissue or to artifacts were excluded.

Results: Of the 238 cases, 15 had uncertainty on frozen section. Indications for the surgery included hyperparathyroidism in 14 cases and thyroid mass in 1 case. The reasons for uncertainty included the presence of follicular architecture of the tissue in 8, oncocytic cytology in 3, nonfollicular lesions within thyroid parenchyma in 2, altered architecture due to prior procedure in 1, and reason that was not indicated in 1 case. Immunohistochemical studies were performed for 9, intraoperative parathyroid hormone levels were reported in 2, and consultations were obtained for 5 cases.

Conclusions: Challenging intraoperative diagnosis of parathyroid tissue is most frequently associated with atypical or unexpected architectural or cytologic changes, which renders distinguishing parathyroid tissue from thyroid tissue difficult. In the setting of lack of relevant clinical information, making an intraoperative diagnosis of parathyroid versus thyroid tissue remains a challenge for surgical pathologists.

Correlation Between Touch Impprint and Core Needle Biopsy for Diagnosing Thyroid Nodules

(Poster No. 114)

Ramayee Periakaruppan, MD1; Mehran Taherian, MD1 (mehranra@buffalo.edu); Austin Miller, PhD1; Wei Tan, MS1; Sara Pokharel, MD, PhD1; Hassan Arshad, MD2; Mihai Merzianu, MD3. Departments of 1Pathology and 2Surgery, Roswell Park Comprehensive Cancer Center, Buffalo, New York; 3Department of Pathology, University at Buffalo, Buffalo, New York.

Context: Core needle biopsy (CNB) with rapid on-site evaluation with selected cores’ touch imprints (TPs) is the primary diagnostic method for patients with thyroid nodules in our institution. Studies comparing diagnostic yield of fine-needle aspiration and CNB exist but correlation of CNB-TP diagnoses is lacking. We evaluated the CNB-TP concordance when reviewed by 2 pathologists.

Design: All CNBs performed for thyroid nodules between 2002 and 2017 were reviewed and diagnoses coded by using Bethesda system. The cases with TP and CNB performed by different pathologists were selected for evaluation. CNB and TP diagnoses were compared with each other and with the excision results. Significant discordance was defined as BDC change from 1–3 to 4–6 or vice versa.

Results: Biopsies came from 681 patients with 746 nodules and 517 (69.3%) underwent excision. A total of 487 TPs (65.3%) were read by a different pathologist with overall 71.3% TP-CNB concordance rate. The discordant rate was higher in observers with the least number of cases (Table). TP significantly upgraded the diagnosis in 2.9%. There was a strong positive correlation between TP and CNB evaluated by different pathologists were selected for analysis. CNB and TP diagnoses were compared with each other and with the excision results. Significant discordance was defined as BDC change from 1–3 to 4–6 or vice versa.

Conclusions: A relatively high CNB-TP discordance rate was identified in this cohort. TP diagnostic downgrade is likely explained by sampling, but upgrade may be related to observer bias and/or experience.

Gland-Poor Secretory Carcinoma of Thyroid With Mediastinal Involvement and Biphasic Histology

(Poster No. 115)

Shabnam Samankan, MD1 (shabnam.samankan@yahoo.com); Sheila Sait, PhD2; Vishal Gupta, MD, Mihai Merzianu, MD3.1Department of Pathology, University at Buffalo, New York; Departments of 2Pathology and 3Head & Neck Plastic Surgery, Roswell Park Comprehensive Cancer Center, Buffalo, New York.

Primary secretory carcinoma of thyroid gland (SCT) was recently described, with similar phenotype-genotype to its salivary counterpart. We present a gland-poor SCT with mediastinal involvement and...
thyroid carcinoma foci were away from the tumor in a chronic lymphocytic thyroiditis background. The diffuse/solid and trabecular/ cribriform patterns showed ovoid nuclei, prominent or conspicuous nucleoli, and eosinophilic cytoplasm with vacuolization. Mitotic rate was 1/10 high-power fields; no tumor necrosis was present. Two separate papillary thyroid carcinoma foci were away from the tumor in a chronic lymphocytic thyroiditis background. The diffuse/solid and trabecular/ cribriform patterns showed ovoid nuclei, prominent or conspicuous nucleoli, and eosinophilic cytoplasm with vacuolization. Mitotic rate was 1/10 high-power fields; no tumor necrosis was present.

### Immunohistochemical (IHC) Stains and Fluorescence

<table>
<thead>
<tr>
<th>Stain</th>
<th>SCT Diffuse/ Solid (75%)</th>
<th>SCT Cribriform/ Trabecular (20%)</th>
<th>SCT Glandular (5%)</th>
<th>Papillary Thyroid Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>TTF1</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Thyroglobulin</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Pax8</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Mammaglobin</td>
<td>+/ +</td>
<td>+/ +</td>
<td>+/ +</td>
<td>+/ +</td>
</tr>
<tr>
<td>Gat3</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>BraF-IHC</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>CK7</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Mitochondria</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Not done</td>
</tr>
<tr>
<td>ETV6 FISH</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

---

**Correlation of Histopathologic Identification of Fungal Organisms With Mycology Cultures and Identification of Diagnostic Discrepancies**

(Poster No. 117)

Lily Tran, MD (lily.tran@uchospitals.edu); Angella Charnot-Katsikas, MD; Kathleen G. Beavis, MD; Vera Tesic, MD. Department of Pathology, University of Chicago, Illinois.

**Context:** Histopathologic identification of fungal organisms affords a fast, presumptive diagnosis; however, morphologic recognition of certain pathogens can be challenging. Fungal identification and presence or absence of tissue invasion are questions faced by pathologists when presented with surgical specimens suspected of harboring infections. Few studies have compared the diagnostic accuracy of fungal detection through histopathologic examination versus the gold standard of microbiologic culture. Discrepant results can lead to unnecessary, delayed, or incorrect treatment. This study examines the prevalence and types of discordant cases to establish the need for improved fungal identification to improve patient care.

**Design:** A 10-year retrospective study was performed to compare the diagnostic accuracy between histologic examination of surgical pathology specimens and corresponding microbiologic cultures in the identification of fungal organisms.

**Results:** We identified 319 surgical pathology specimens with fungal organisms present on histologic examination. Among these specimens, 199 cases (62%) had no cultures obtained and 13 (4%) had no fungal growth on cultures. A total of 107 specimens (34%) demonstrated growth of fungal organisms on culture; of these, 101 cases (94%) had concordant results between surgical pathologic evaluation and cultures. Six cases (6%) had discrepant diagnoses. Discordant results stemmed from misidentification (n = 4), presence of a contaminant (n = 1), and incorrect terminology (n = 1) (Table).

**Conclusions:** Discordant fungal identification was identified in 6% of surgical specimens with corresponding cultures. A standardized approach for reporting fungal organisms from histopathology might minimize erroneous species identification and improve patient care.

<table>
<thead>
<tr>
<th>Age, y/Sex</th>
<th>Specimen</th>
<th>Surgical Pathology Diagnosis</th>
<th>Special Stains</th>
<th>Culture Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>39/F</td>
<td>Sinus</td>
<td>Candida</td>
<td>GMS</td>
<td>Scedosporium apiospermum</td>
</tr>
<tr>
<td>47/F</td>
<td>Sinus</td>
<td>Mucor</td>
<td>N/A</td>
<td>Aspergillus fumigatus</td>
</tr>
<tr>
<td>47/F</td>
<td>Arm drébridement</td>
<td>Rhizopus</td>
<td>GMS</td>
<td>Rhizopus</td>
</tr>
<tr>
<td>39/M</td>
<td>Nasal mass</td>
<td>Mucor</td>
<td>N/A</td>
<td>Rhizopus</td>
</tr>
<tr>
<td>38/F</td>
<td>Esophagus</td>
<td>Candida</td>
<td>N/A</td>
<td>Saccharomyces cerevisiae</td>
</tr>
<tr>
<td>66/M</td>
<td>Glans penis</td>
<td>Candida</td>
<td>GMS, PAS</td>
<td>Alternaria</td>
</tr>
</tbody>
</table>

**Aspergillus niger Causing Severe Exogenous Fungal Endophthalmitis: A Case Report With Pretreatment and Posttreatment Histology**

(Poster No. 118)

Anas Bernieh, MBBS (8abernieh@umc.edu); John Green, MD; Lisa Stermpak, MD. Departments of 1Pathology and 2Ophthalmology, UMMC, Jackson, Mississippi.

A 44-year-old man sustained a traumatic injury to his left eye due to a tree branch. Initially, he was treated with steroids but his condition deteriorated and he developed infectious keratitis with severe anterior...
chamber inflammation. Moxifloxacin was added but he progressed to secondary glaucoma. During anterior chamber washout, a spherical mass of inflammatory debris was removed and sent for histology, which showed severe acute inflammation, many narrow septate fungal hyphae with orderly acute angle branching and pigment were identified (Figure 274, A). The patient was seen the following day and noted to have a new hypopyon. He was now diagnosed with endophthalmitis, underwent anterior chamber paracentesis, and received an intraocular injection of vancomycin and ceftazidime. Culture collected from this procedure grew Aspergillus niger. As a result, he received an intravitreal injection of amphotericin B and oral voriconazole for fungal endophthalmitis. Subsequently, he developed corneal perforation and underwent full-thickness corneal transplant. The cornea was sent for histology and again fungal hyphae were identified. Nonetheless, owing to globus formation and loss of acute angulation (Figure 274, B), there was initial concern for mucoraceous organism. Upon review by the medical microbiologist, these findings were attributed to treatment effects of the antifungal agent and were consistent with the original diagnosis of A niger. This case demonstrates the importance of the surgical pathologist in recognizing the effects of antifungal treatment on fungal architecture in histologic sections.

Importance of Multiple Stool Specimen Evaluation by Enzyme Immunoassay in Chronic Giardiasis

Poster No. 119

Miles J. Mcdonough, BA (mcdnm2@uw.edu); Benjamin T. Bradley, MD, PhD; Matthew M. Yeh, MD, PhD; Kyi-Toe Tham, MD; Deepti M. Reddi, MD. Department of Pathology, University of Washington Medical Center, Seattle.

Giardiasis is a common cause of enteric parasitic infection. In the duodenum, histologic findings similar to those of celiac disease are seen in Giardia infection. We present the case of a patient with polyclonal hypergammaglobulinemia, dermatitis herpetiformis, celiac disease, and chronic giardiasis. The patient is a 51-year-old man who was incidentally found to have high serum total protein and low albumin levels. The protein electrophoresis showed polyclonal hypergammaglobulinemia and β-γ bridging. With an elevated erythrocyte sedimentation rate the patient’s stool was evaluated and was positive for Giardia lamblia cysts. The patient failed to respond to the 10-month treatment of metronidazole, tinidazole, and nitazoxanide and developed a pruritic lamblia cysts. The patient failed to respond to the 10-month treatment of metronidazole, tinidazole, and nitazoxanide and developed a pruritic.

**Potential Benefits of Screening for Urinary Tract Infection With the Sysmex UF-1000i Urine Flow Cytometer**

Poster No. 120

Quoc Nguyen, MD1 (quoc.nguyen@vchn.org); Sulakshana Ranjan, MD2; Deborah Sweet, MS2; Shiquan He, MS2; Jessica Dodge, MD.3

1Department of Pathology, Danbury Hospital, Danbury, Connecticut; 2Department of Pathology, The University of Texas Health Science Center at San Antonio; 3Research Institute, Western Connecticut Health Network, Danbury.

Context: Urine culture is the gold standard to confirm the diagnosis of urinary tract infection; however, up to 80% of urine samples yield negative results on culture. In this study, we explore a new screening method, using the Sysmex UF-1000i urine flow cytometer, to potentially reduce cost and save time that otherwise would have been spent on unnecessary urine cultures.

Design: Data from urine samples that underwent urinalysis and culture at Danbury Hospital laboratory in March 2016 were collected and analyzed. The bacterial counts from the Sysmex UF-1000i were used to determine the cutoff value that would yield a sensitivity of approximately 95% for predicting urine cultures that would grow >10,000 CFU/mL. This cutoff value was then used to calculate the urine culture positivity rate, as well as potential time and cost savings.

Results: Of the 697 urine samples that underwent urinalysis and culture, 186 grew >10,000 CFU/mL and 115 grew >100,000 CFU/mL. A bacterial count cutoff of ≥65 bacteria/µL yielded a 94.6% sensitivity and a 43.6% specificity for predicting urine cultures that grew >10,000 CFU/mL, and a 99.1% sensitivity and a 39.9% specificity for predicting urine cultures that grew >100,000 CFU/mL. Using this cutoff value, 233 urine samples would not have been reflexed to culture; this would yield a urine culture positivity rate of 37.9% versus 16.5%, save $2085/month, and save 6.8 hours/month.

Conclusions: By using a cutoff of ≥65 bacteria/µL, the urine culture positivity rate would increase, cost would decrease, and medical technologists’ time would be saved, all while providing a high sensitivity.

Hyphae in Invasive Coccidioidomycosis

Poster No. 121

Gloria H. Sura, MD (gloria.sura@gmail.com). Department of Pathology, Louisiana State University, New Orleans.

Context: Coccidioides immitis and Coccidioides posadasii are commonly found in the dry climates of the Southwestern regions of North America. These molds dwell in soil in a mycelial phase forming arthroconidia. Arthroconidia are highly infectious and can easily be disseminated into the air upon soil disturbance and cause disseminated pulmonary disease once inhaled. Hyphae and arthroconidia are only rarely detected in histopathology examination. Pathologists may inappropriately consider infection by a second hyaline mold when encountering hyphae among Coccidioides species spherules. We will highlight the histologic features of Coccidioides species in tissue infections, emphasizing production of hyphae and arthroconidia.

Design: We reviewed 30 clinical cases of coccidioidomycosis accumulated from various laboratories. Eight cases were skin, 16 cases were pulmonary, 4 cases were soft tissue, 1 case was blood, and 1 case was a paravertebral abscess.

Results: Spherules were identified in all cases with hyphae/arthroconidia and additionally identified in about 17% of cases: a Coccidioides species pulmonary mycetoma, a bronchial washing, 2 caviary lung lesions, and in Gram stain of blood.

Conclusions: Arthroconidia have been described in vivo almost exclusively in pulmonary cavities and cerebrospinal fluid shunts. We identified hyphae production in Coccidioides species infection in our clinical cases from pulmonary sources and blood. It appears that Coccidioides species may produce mycelia when growing in liquid such as CSF or blood as a result of liquid material such as granuloma contents. Pathologists should not be confused when encountering hyphae or arthroconidia in histologic preparations of Coccidioides species infections particularly from pulmonary or cerebrospinal fluid sources.
Nonpositive Bottle of a Two-Bottle Blood Culture Set: Reincubation Versus Termination Upon Detection of Positivity in the Other Bottle

(Poster No. 122)

Daniel Shapiro, MD (dshapiro@nyuwinthrop.org); Roger Siletti, PhD. Department of Pathology, NYU University Winthrop Hospital, Mineola, New York.

Context: A single blood specimen consists of an anaerobic bottle and an aerobic bottle, which are incubated up to 5 days before being reported as no growth. Some studies suggest that the duration of incubation could be reduced from 7 to 5 days without any loss of sensitivity in bacteremia detection. Several authors have demonstrated that more contaminants are detected after 5 days than significant microorganisms. If the number of polymicrobial blood specimens at NYU Winthrop Hospital is significant, reincubation may be warranted.

Design: Blood cultures collected between July 15, 2015 and July 15, 2017, and processed on the BACTEC system were reviewed retrospectively for the number of organisms isolated in each bottle up to incubation day 5. Those that exhibited polymicrobial growth were compared to positive growth bottles as a whole. The mode of distribution was used to analyze the most commonly isolated organisms.

Results: Of 2761 total positive blood cultures, 41 (1.5%) were polymicrobial. Of the 41 polymicrobial cultures, 6 contained 3 organisms and the remaining 35 contained 2 organisms. The most common organisms identified were Klebsiella pneumoniae, coagulase-negative Staphylococcus, Escherichia coli, and Enterococcus.

Conclusions: Because of the very low number of polymicrobial-positive blood cultures at the NYU Winthrop Hospital, it is not necessary to continue incubation of the second bottle once the first bottle has demonstrated growth.

Vancomycin MIC Creep in Staphylococcus aureus in Indian Subcontinent

(Poster No. 123)

Malvika Srivastava, MD1 (docmalvika@gmail.com); Nagmani Singh, BSc; Anurag Bansal, MD. Pathology, Departments of 1Microbiology and Immunology and 2Lab Operations, Quest Diagnostics India, Gurgaon, India.

Context: Strains of Staphylococcus aureus, which are methicillin-resistant, are termed as MRSA and show resistance to antibiotics like β-lactam drugs. Infections by these organisms are treated with glycopeptides like vancomycin, teicoplanin, and linezolid. A phenomenon called “MIC creep” has been observed in vancomycin where the strain remains susceptible to vancomycin but there is increase in the minimum inhibitory concentration of vancomycin against MRSA strain remains susceptible to vancomycin but there is increase in the

Design: Blood cultures collected between July 15, 2015 and July 15, 2017, and processed on the BACTEC system were reviewed retrospectively for the number of organisms isolated in each bottle up to incubation day 5. Those that exhibited polymicrobial growth were compared to positive growth bottles as a whole. The mode of distribution was used to analyze the most commonly isolated organisms.

Results: Of 2761 total positive blood cultures, 41 (1.5%) were polymicrobial. Of the 41 polymicrobial cultures, 6 contained 3 organisms and the remaining 35 contained 2 organisms. The most common organisms identified were Klebsiella pneumoniae, coagulase-negative Staphylococcus, Escherichia coli, and Enterococcus.

Conclusions: Because of the very low number of polymicrobial-positive blood cultures at the NYU Winthrop Hospital, it is not necessary to continue incubation of the second bottle once the first bottle has demonstrated growth.

A Comparison of WT1 Expression in Peripheral Blood by Molecular Testing and in Bone Marrow by Immunohistochemistry

(Poster No. 124)

Ridin Balakrishnan, MD (rbalakri@montefiore.org); Gloria Ramos Rivera, MD; Yanhua Wang, MD, PhD. Department of Anatomic and Clinical Pathology, Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, New York.

Context: Wilms tumor protein (WT1) has been targeted for leukemia-specific immunotherapy in acute leukemia, chronic lymphocytic leukemia (CML), and myelodysplastic syndromes (MDS). Studies have shown that high levels of WT1 expression in acute leukemia are associated with lower complete remission rates and reduced overall and disease-free survival. We studied the correlation of WT1 mutation by molecular testing on peripheral blood with WT1 expression in bone marrow samples by immunohistochemistry (IHC) while comparing the cytogenetics and clinical outcome.

Design: Myeloid leukemia patients with specific WT1 mutation status (7 positive and 10 negative) were selected from October 2015–March 2017. Bone marrow biopsies from these patients were then stained for WT1 IHC. The presence of WT1 mutation, cytogenetics, and clinical outcomes were compared.

Results: Three of 7 bone marrow samples in patients positive for WT1 mutation on peripheral blood were also positive on IHC, while 1 of 7 bone marrow findings on patients without the WT1 mutation were positive. The sensitivity was 43%, specificity 86%, positive predictive value 75% and negative predictive value 60%.

Conclusions: The patients with a positive WT1 mutation on bone marrow and peripheral blood were in early acute myeloid leukemia phase. This is a small cohort study and the findings require further investigation and might lead to an association of the WT1 mutation and the chronicity of this entity. WT1 identification on peripheral blood gives an opportunity to further classify these patients and could potentially be of importance for prognosis and follow-up while drastically reducing the comorbidity of bone marrow biopsy by replacing it with a noninvasive procedure.

Double Ring Chromosome 21: A Novel Cause of Down Syndrome and Alternative Mechanism for an Interstitial Deletion in a Ring Chromosome

(Poster No. 125)

Josephine Aguilar-Jakthong, MD1 (jjakthong@mednet.ucla.edu); Fabiola Quintero-Rivera, MD, 2Departments of 1Pathology and 2UCLA Clinical Genomic Center, Pathology and Laboratory Medicine at UCLA, Los Angeles, California.

Ring chromosomes are rare cytogenetic findings and are associated with intellectual disability (ID) and congenital abnormalities depending on the material lost usually at the telomere of each arm. Most ring chromosomes arise de novo. An interstitial deletion of a ring is rare. The proband is an 18-year-old man, with 1 maternal normal half-sister. Maternal side of the patient had a history of ID, a stillbirth with cleft lip. At birth, he had bilateral cleft lip/palate and mild dysmorphic features resembling Down syndrome. Later, speech and language development delay and ID were noted. Outside studies revealed 1 de novo ring chromosome 21 (chr.21, Figure 275). Chromosomal microarray analysis (CMA) showed 2 nonsyndromic, copy number deletions of chr.21, one is interstitial and the other is terminal of ~4.2 Mb and 7.3 Mb, respectively. CMA also revealed the presence of a normal diploid segment of the chr.21 that intersperses these 2 losses. Karyotype

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>MIC &lt; 0.5</th>
<th>MIC = 1</th>
<th>MIC = 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pus samples</td>
<td>40</td>
<td>44</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory samples</td>
<td>8</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Blood samples</td>
<td>6</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Urine samples</td>
<td>2</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>
identified a mosaic male with 2 different structural rings; most cells have a single ring, and a small number have a double ring, thus consistent with 3 copies of chr.21q. Fluorescence in situ hybridization (FISH) confirmed the low-level mosaic trisomy 21, thus allowing our patient’s clinical follow-up with standard protocols for Down syndrome. Ring chromosome and interstitial deletion of the same chromosome is rare. We did not exclude the possibility of another mechanism, such as the presence of an inversion on chr.21 that occurred before ring formation. However, FISH on metaphase chromosomes from the parents and the proband is necessary to determine if an inversion of chr.21 is present.

Microsatellite Instability in Colorectal Carcinoma: Does Sex Matter?

(Poster No. 126)

Dmytro Shapochka, MD; Oleksiy Selezniov, PhD; Tetyana Shapochka, MD; Angela Turkina, MD; Oksana N. Sulaieva, PhD (oksana.sulaieva@gmail.com). Departments of ‘Molecular Pathology and Histopathology, Laboratory of Pathology CSD Health Care, Kyiv, Ukraine.

Context: The aim of this study was to evaluate sex differences in microsatellite instability frequency and clinicopathologic features of colorectal carcinoma (CRC).

Design: A total of 177 patients (88 females and 89 males) with CRC who underwent microsatellite instability (MSI) testing by immunohistochemistry were included in this retrospective study.

Results: The overall incidence of MSI-high (MSI-H) status among observed patients with CRC was 14.7%. The frequency of MSI-H status was significantly higher in men (25.35%) than women (10%) (P = .04). The MSI-H status was associated with the younger age (P = .002) in men. In most cases, MSI was due to lack of MLH1+PMS2 expression (64%). MLH1 deficiency was higher in men than women (70.6% versus 50%). In contrast, women more often demonstrated deficiency of MSH2 + MSH6 (37.5% versus 11.8%). Lack of MSH2 and MSH6 expression, as well as isolated block of PMS2 expression, was associated with higher tumor grade (P < .001). MSI-H status was related to specific (mucinous or nonmucinous) histologies of CRC (P < .001) that in most cases were found in men at age up to 50 years (P = .03). Assessment of MSI-H status in relation to CRC staging showed lower frequency of metastasis in patients with MSI-H status than in patients with microsatellite-stable CRC (P = .002) regardless of sex.

Conclusions: The higher frequency of MSI-H status in men was associated with specific mismatch-repair enzyme expression, histology, and metastasis risk, which stimulates further investigation of sex-specific mechanisms of CRC.

Concomitant IDH1 and Braf (Non-V600E) Mutations in Malignant Melanoma

(Poster No. 127)

Rumeal D. Whaley, MD (rwhaley@iu.edu); Cecilia Ramirez-Santrich, MS; Mehdi Nassiri, MD. Department of Pathology and Laboratory Medicine, Indiana University School of Medicine, Indianapolis.

One-third of melanomas harbor more than one mutation. Most mutations occur in the BRAF gene (V600, 36%). The second most common mutated gene is NRAS (21%). IDH1 mutations are present in 3% of melanomas. It is rare for BRAF mutations to occur outside of the V600 hotspot. Here we present the case of 2 patients with metastatic melanoma found to have concomitant mutations of IDH1 and BRAF (non-V600E). Patient A was a 71-year-old man and patient B was a 62-year-old man. Both received adjuvant interferon for cutaneous melanoma, but did not complete the recommended 1-year treatment. Patient A progressed with lung metastases. Patient B progressed with orbital, abdominal, and spinal metastasis. Sequencing was performed from extracted DNA by using TrueSeq Amplicon Cancer Panel (Illumina, San Diego, California) on MiSeq instrument. Results were confirmed with PCR. Patient A’s lung metastasis had IDH1 (c.394C->T, p.R132C, COSM28747), BRAF (c.1397G->T, p.G466V, COSM451), and NRAS (c.182A>G, p.Q61R, COSM584) mutation. Patient B’s lymph node metastasis had IDH1 (c.394C->T, p.R132C, COSM28747) and BRAF (c.1798_1799delGTTinsAA, p.V600K, COSM475) mutation. IDH1 mutation in malignant melanoma is a rare occurrence. BRAF G466V has only been reported in 3 cases thus far. IDH1 inhibitors are being evaluated in clinical trials for tumors harboring the mutation. There are targeted therapies for BRAF mutations but the efficacy is based on trials of BRAF V600 mutations. The FDA-approved BRAF inhibitors may be ineffective against BRAF non-V600 mutants, while MEK inhibitors and pan-RAF inhibitors may be efficacious. The presence of these mutations offers more potential for drug treatments.

Correlation Between PD-L1 22C3 Expression and Molecular Profile in Non–Small Cell Lung Cancers

(Poster No. 128)

Catherine M. Nicka, MD (catherine.m.nicka@hitchcock.org); Laura J. Tafe, MD. Department of Pathology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire.

Context: Eligibility for immunotherapy with pembrolizumab in advanced-stage non–small cell lung cancer (NSCLC) patients is based on low PD-L1 tumor expression. We aimed to correlate PD-L1 expression with tumor histology and molecular profile.

Design: During a period of 19 months, 209 NSCLC patient samples were successfully tested for PD-L1 expression. Immunohistochemistry was performed by using 22C3 pharmDx kit, and the tumor proportion score (TPS) was recorded (<1%, negative; 1%-49%, low expression; ≥50%, high expression). Samples were tested for somatic mutations by using the AmpliSeq v2 and the FusionPlex next-generation sequencing panels, and ALK FISH.

Results: Tumors included 145 adenocarcinomas (ADCs), 53 squamous cell carcinomas (SqCCs), and 11 poorly differentiated NSCLCs not otherwise specified (NOS). Most patients were current or former smokers. PD-L1 TPS was negative in 42.6% (99/209), low in 32.5% (68/209) and high in 24.9% (50/209). The TPS was independent of the tumor histology. In the 145 ADCs, 10 EGFR, 3 ALK, 8 BRAF, and 52 KRAS mutations were identified. Thirty-five percent of tumors with high PD-L1 expression harbored a KRAS mutation, as compared to no expression (24%) and low expression (25%) tumors. In addition, there was a trend toward higher PD-L1 expression in KRAS/TP53 co-mutated tumors (23.8% high, 17% low, 10.5% no expression).

Conclusions: There is a trend toward higher PD-L1 expression in ADC with KRAS and KRAS/TP53 co-mutations, a known association with smoking. PD-L1 expression is useful to stratify patients for immunotherapy eligibility. In our patients treated with immunotherapy, response data are still accruing.

Does Expression of mir-149 Effect Progression and Survival in Non–Small Cell Lung Cancer Patients?

(Poster No. 129)

Waqas Mahmud, MD (waqas.mahmud@rush.edu); Prih Rohra, MD; Jayjay Blanco, MD; Anam Naumaan, MD; Lela Buckingham, PhD. Department of Pathology, Rush University Medical Center, Chicago, Illinois.

Context: miR-149, a microRNA, has been implicated in cancerogenesis and tumor progression. It down-regulates FOXM1, a transcription factor, shown to be a measure of poor prognosis in non–small cell lung cancer (NSCLC). Another predictor of low survival rates is high standard uptake value (SUV) in positron emission tomography. In this study, we aim to investigate relationships between miR-149 expression and recurrence/progression of NSCLC and correlation between miR-149 expression and SUV.

Design: Formalin-fixed, paraffin-embedded tissue and FDG-PET scan data from 57 patients with primary stage I-II NSCLC were included in this study. Demographics were obtained from electronic medical records. RNA was isolated and gene expression of miR-149 was measured by RT-qPCR. Kaplan-Meier analysis was used to determine progression and survival among high- and low-expressing miR-149 tumors. Pearson coefficient was used to determine a correlation between SUV and miR-149 expression.

Results: Mean age of these patients was 71.3 years. Thirty-four (59.5%) were female. Seventeen patients (29.8%) were deceased. Cases with lower miR-149 expression had marginally better overall survival than those with high miR-149 expression (median 107.9 months, 95% CI: 0.0–219.9, versus 54.4 months, 95% CI: 48.1–61.3, P = .12). Glycolytic activity of the tumor (maxSUV and minSUV) was marginally lower in the low-expressing miR-149 cases (Pearson coefficient –0.10 and 0.13, P > .4 and Mann-Whitney U tests, respectively). The TPS was independent of the low-expressing miR-149 cases (Pearson coefficient –0.10 and 0.13, P > .4 and Mann-Whitney U tests, respectively).

Conclusions: We previously observed that miR-149 can be detected in cell-free RNA. Hence, miR-149 might potentially contribute to liquid biopsies for management of NSCLC. Further analysis of additional cases is required to determine its effectiveness in predicting prognosis.
**TNRFSF14 Gene Expression Predicts Progression-Free Survival in Follicular Lymphoma**

(Poster No. 130)

Pavandeep Gill, MD1 (pavandeep.gill@albertahealthservices.ca); Danielle Oh, MBCB; Ariz Akhter, PhD1; Meer-Taher Shabani-Rad, MD2; Adnan Mansoor, MD2; Douglas Stewart, MD2; Etiene Mahe, MD3. Departments of 1Pathology and Laboratory Medicine and 2Medicine, University of Calgary, Alberta, Canada; 3Department of Hematology, Monash Health, Melbourne, Australia.

**Context:** Follicular lymphoma (FL) is a clinically and biologically heterogeneous disease. Recent data have suggested a role for abnormalities of the TNRFSF14 gene, either secondary to 1p36 deletion, or resulting from sequence level mutation. Such abnormalities have been noted to portend inferior outcomes in FL patients; data exploring the potential relationship between TNRFSF14 gene expression and clinical behavior are lacking.

**Design:** As part of a larger registry-based study, we evaluated the TNRFSF14 gene expression in a series of FL. Patients were diagnosed between 2004 and 2010 and received chemoimmunotherapy through the Tom Baker Cancer Centre. Total tumor RNA was isolated from archival formal-fixed, paraffin-embedded tissue blocks (QIAGEN RNeasy, Hilden, Germany). TNRFSF14 gene expression assessment was performed with the NanoString nCounter Analysis System (NanoString, Seattle, Washington), using a custom probeset, with gene expression normalization relative to a series of housekeeping genes. Statistical analyses were performed by using SPSS (v24, IBM, Armonk, New York).

**Results:** Sufficient materials were available from 163 patients; relevant clinicopathologic data are presented in the Table. TNRFSF14 gene expression below median was associated with inferior progression-free survival by univariate and multivariate analyses (HR, 1.7; 95% CI, 1.04–2.82; p = 0.03), controlling for age, sex, grade, stage, and FL International Prognostic Index risk category. TNRFSF14 gene expression was not predictive of overall survival.

**Conclusions:** Our data support previous reports highlighting the importance of the TNRFSF14 gene in FL. The nature of the TNRFSF14 gene abnormalities in FL, and the observed impact on outcomes, suggests a tumor suppressor function.

<table>
<thead>
<tr>
<th>Clinicopathologic Parameter</th>
<th>Result (N = 163)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range)</td>
<td>56 (29–85)</td>
</tr>
<tr>
<td>Sex, male:female</td>
<td>55%/45%</td>
</tr>
<tr>
<td>Stage at presentation</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>8%</td>
</tr>
<tr>
<td>II</td>
<td>10.5%</td>
</tr>
<tr>
<td>III</td>
<td>41.4%</td>
</tr>
<tr>
<td>IV</td>
<td>40.1%</td>
</tr>
<tr>
<td>Pathologic grade at presentation</td>
<td></td>
</tr>
<tr>
<td>Low (1–2/3)</td>
<td>72.4%</td>
</tr>
<tr>
<td>High (3)</td>
<td>19%</td>
</tr>
<tr>
<td>Undetermined</td>
<td>8.6%</td>
</tr>
<tr>
<td>Follicular Lymphoma International Prognostic Index risk category</td>
<td></td>
</tr>
<tr>
<td>Low (FLIPI score 0–1)</td>
<td>40.7%</td>
</tr>
<tr>
<td>Intermediate (FLIPI score 2)</td>
<td>37%</td>
</tr>
<tr>
<td>Poor (FLIPI score &gt;2)</td>
<td>22.2%</td>
</tr>
</tbody>
</table>

**KRAS, TP53, and PTEN Mutations Are Frequently Detected in Pancreatic Ductal Adenocarcinomas**

(Poster No. 131)

Tiffany G. Sheu, MD1 (tgsheu@houstonmethodist.org); Anam Omer, MD2; Kristi Pepper, MB(ASCP)2; Jessica Thomas, MD, PhD, MPH; Randall Olsen, MD; Kumar Krishnan, MD, MD3. Departments of 1Pathology and Genomic Medicine and 2Medicine, Houston Methodist, Houston, Texas; 3Department of Medicine, Harvard Medical School, Massachusetts General Hospital, Boston.

**Context:** Pancreatic cancer, particularly pancreatic ductal adenocarcinoma, causes significant morbidity and mortality. Despite advances in treatment, most patients present with advanced disease and have very poor outcomes. In patients who undergo curative resection of pancreatic cancer, many develop either recurrence or progressive disease by the time of surgery. Several recent studies have reported various gene mutations in pancreatic cancers; however, pancreatic ductal adenocarcinoma has not been well studied. The purpose of our investigation was to use next-generation sequencing to identify the key underlying genetic mutations in pancreatic ductal adenocarcinomas.

**Design:** A retrospective review of patients at our institution with pancreatic cancer diagnosed from October 2014 to January 2017 was performed. The pathology reports and histology slides were reviewed, and 13 cases of pancreatic ductal adenocarcinoma were selected for study. Representative tumor was macrodissected, genomic DNA was extracted by using standard methods, and next-generation sequencing was performed to identify somatic mutations in 50 genes that are commonly mutated in human cancer.

**Results:** All 13 cases of invasive pancreatic ductal adenocarcinoma had T3N1 grade disease, with most being stage IIIB. Somatic mutations of 1 or more genes were identified by next-generation sequencing in 12 of 13 cases. The most frequently mutated genes were KRAS, TP53, and PTEN.

**Conclusions:** This study identified a high incidence of gene mutations within pancreatic ductal adenocarcinoma. These findings may inform patient care decisions using targeted therapies or predicting prognosis.

**Recurrent/Residual Solitary Epithelioid Histiocytoma (Reticulohistiocytoma) in the Eyelid**

(Poster No. 132)

Rachael Nakfoor, MD (rachel.nakfoor@uhhospitals.org); Nafiseh Janaki, MD; Mohadese Behtaj, MD; Kord Honda, MD; Marta Couce, MD, PhD. Department of Pathology, University Hospitals Cleveland Medical Center, Cleveland, Ohio.

Solitary epithelioid histiocytoma (SEH), previously called reticulohistiocytoma, is a rare neoplasm with dermal histiocytic infiltration, occurring in any body site. We present the case of a 41-year-old man with a history of nonspecific nodules in the digits and a persistent swollen eyelid. The eyelid was biopsied and the lesion extended to margins of resection, recurring 4 months later. Microscopically, these were well-demarcated lesions, centered in the dermis, consisting of infiltrative epithelioid histiocytes with abundant eosinophilic ground-glass cytoplasm, prominent nucleioli, occasional multinucleated cells with abundant interspersed neutrophils, and eosinophils (Figure 276, A and B). Immunohistochemically, tumor cells were diffusely positive with CD68, Factor XIIa, with occasional positive staining for S100 (Figure 276, C and D) and no immunoreactivity for Melan-A, HMB-45, EMA, desmin, AE1/AE3, SOX-10, and CD1a, favoring a diagnosis of SEH. SEH is thought to be macrophage derived and its main differential diagnosis is melanoma. Clinically, SEH exhibits benign behavior and rarely recurs. To date, only 2 cases of SEH involving the eyelid have been reported, one of which was recurrent. Multicentric reticulohistiocytosis involving the eyelid has also been reported. This entity differs clinically and immunophenotypically, and refers to a systemic, occasionally paraneoplastic disease, with multiple cutaneous and mucosal nodules (in the head and neck and digits) and arthropathy. Although our patient also had nodules in the digits, these were interpreted as pyogenic granulomas and were never
biopsied. The current case likely represents recurrent/residual SEH; however, multicentric reticulohistiocytosis cannot be entirely excluded.

**Human Papillomavirus–Associated Inverted Papilloma of the Conjunctiva: Case Report and Review of Literature**

*(Poster No. 133)*

Paige C. Woodham, MD (woodhamp@musc.edu); Mary S. Richardson, DDS, MD; Evelyn T. Bruner, MD. Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston.

Conjunctival papillomas are characteristically benign exophytic lesions composed of squamous epithelium overlying a fibrovascular core. A small number harbor epithelial dysplasia, and human papillomavirus (HPV) may play a role in pathogenesis. Conversely, inverted papillomas of the conjunctiva are extremely rare with only 11 reported cases in the literature, 2 of which displayed carcinomatous transformation. Of those reported cases, only 1 was described as HPV associated. We report a case of a 62-year-old man who presented with a right superior bulbar conjunctival lesion. The differential diagnosis included squamous cell carcinoma, papilloma, and lymphoma. An excisional biopsy was performed. Microscopically, papillomatous nests of transitional-type epithelium were seen in an endophytic growth pattern with variable numbers of goblet cells (Figure 277, A and B). No high-grade cytologic atypia or invasive single nests into the stroma were detected. p16 staining exhibited strong, diffuse positivity (Figure 277, C), and Ki-67 showed a low proliferation index, limited to the basal layers. HPV DNA in situ hybridization was performed and was positive for high-risk HPV subtypes. The lesion, therefore, was best characterized as high-risk HPV-associated inverted papilloma. Though data are lacking on clinical behavior of this entity in the conjunctiva, re-excision was recommended. The lesion, therefore, was best characterized as high-risk HPV-associated inverted papilloma. Though data are lacking on clinical behavior of this entity in the conjunctiva, re-excision was recommended.

**Uveal Melanoma With GNAQ R183Q Mutation in the Setting of Bilateral Nevus of Ota**

*(Poster No. 135)*

Kyle Fraser, MD (kyfraser@ucsd.edu); Jonathan Lin, MD, PhD; Christina Di Loreto, MD; Wesleigh Edwards, MD; John Thorson, MD, PhD. Department of Pathology, University of California San Diego, La Jolla.

Uveal melanomas are the most common primary ocular tumor and are associated with distinct genetic mutations. Mutations in the genes encoding the guanine nucleotide–binding protein Ga subunit (GNAQ and GNA11) are frequently found in uveal melanomas. Most GNAQ/ GNA11 mutations in uveal melanomas are missense variants, changing the glutamine at amino acid position 209 to leucine (Q209L) or proline (Q209P). An R183Q (arginine to glutamine) mutation has also been observed in a small subset of uveal melanomas carrying Q209 mutations or R183 mutations in GNAQ/GNA11 are unclear. We identified a 34-year-old woman with bilateral nevus of Ota and ocular surface melanosis who presented with loss of visual acuity and was found to have uveal melanoma by fine-needle aspiration vitrectomy in 2014. She was treated with brachytherapy and eventual enucleation owing to relapsed disease. Tumor DNA from her enucleation was analyzed for genetic mutations and chromosomal rearrangements. Examination of the enucleation demonstrated a uveal melanoma in a background of choroidal melanosis. SNP-based cytogenetic testing revealed no chromosomal 3 deletions. Next-generation sequencing identified a GNAQ R183Q mutation with a variant allele fraction of 70%. The natural history of this patient’s presentation illustrates an unusual case of uveal melanoma arising at an early age in a background of bilateral nevus of Ota with ocular melanosis. These findings raise the possibility that uveal melanomas with the rare R183Q mutation may have a distinct clinicopathologic profile as compared to uveal melanomas with the more common Q209 mutations (Figure 278).

**Atypical Cellular Neurothekeoma of the Eyelid: A Rare Presentation of a Recurrent Neoplasm**

*(Poster No. 134)*

Sarmad H. Jassim, MD (sjassim@metrohealth.org); Amer Khiyami, MD; Stephen Semach, MD. Department of Pathology, MetroHealth Medical Center, Cleveland, Ohio.

Cellular neurothekeoma is a rare dermal neoplasm of presumed fibrohistiocytic lineage. We report the case of a patient with recurrent upper eyelid tarsal cellular neurothekeoma and address the histopathologic and immunohistochemical challenges. The patient was a 23-year-old woman who presented with a recurrent mass at the right upper eyelid tarsal margin. Her past medical history included asthma and breast fibroadenomas. The patient presented with complaints that “this stye will not go away.” Patient’s past surgical history included local steroid injections and management for possible eyelid chalazion. The patient subsequently underwent 2 eyelid surgeries to remove multiple hard round nodules extending up off the tarsus. Histologically, the eyelid tumor demonstrated a multinodular and whorled growth pattern. The cells were arranged in nests and sheets of epithelioid cells in a dense sclerotic collagenous background, admixed with scattered osteoclastic giant cells. The neoplastic cells were diffusely positive for CD68, CD138, SMA, and vimentin and focally positive for nuclear P63. The neoplastic cells were negative for S100, among other immunohistochemical stains including melanoma markers and different keratins. The specimen was subsequently reported positive for NCI-C3. Cellular neurothekeoma is a rare benign eyelid dermal neoplasm that can mimic multiple benign and malignant eyelid tumors. Careful evaluation of characteristic histologic features is a clue to diagnosis to avoid comprehensive and sometimes unnecessary immunohistochemical staining. It is critical to recognize the benign nature of this atypical neoplasm to avoid extensive eyelid surgery.
A YouTube–Based Introductory Course on Gross Examination for Incoming Pathology Residents: An Institutional Experience

(Poster No. 136)

Kunwar Singh, MD (kunwar.singh@mountsinai.org); Shyam Prapa-pati, DO; Dominick Guerrero, MD; Mark T. Friedman, DO. Department of Pathology, Mount Sinai Health System, New York, New York.

Context: Gross examination of surgical specimens provides valuable information for diagnosis and is a crucial portion of the pathology report. Therefore, great emphasis is placed on dissection skills and important information for diagnosis and is a crucial portion of the pathology course on gross examination fundamentals.

Design: Invitations to volunteer in the online course were sent to incoming residents in the month before the start of their training. The course followed a microlearning model, consisting of 3 succinct lessons (1. Specimen Workflow; 2. Descriptive Terms; and 3. Reports and Documentation), each containing a lecture and questions. Multiple choice questions were administered before and after the course to measure baseline knowledge and the impact of the course. The lectures were recorded with audio voiceover and then uploaded to YouTube.

Results: All the incoming residents completed the course before the start of residency training. The average score for the postcourse test was greater than the average score for the precourse test, 95.8% and 87.5%, respectively. User data collected revealed the residents were able to access the course from Windows PC, Mac, and smartphone devices, while geodat showed some residents participated from outside the region and even outside the country.

Conclusions: The course served its purpose in introducing fundamentals in gross examination and documentation for surgical pathology specimens. The course was created and disseminated by using commercially available free Web-based services. Residents were able to access the course from various devices and performed well on their postcourse test.

Initial Pathologic Modality in the First-Time Diagnosis of Cancer

(Poster No. 137)

Gabriel E. Morey, MD, MPH (gmorey@houstonmethodist.org); Ross A. Miller, MD; Paul A. Christensen, MD; Dina R. Mody, MD. Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Texas.

<table>
<thead>
<tr>
<th>Primary Tumor Site</th>
<th>Total Cases, n</th>
<th>Initial Diagnosis Made on Cytology, n</th>
<th>Initial Diagnosis Made on Histology, n</th>
<th>Initial Diagnosis Made on Cytology, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder</td>
<td>61</td>
<td>12</td>
<td>49</td>
<td>20</td>
</tr>
<tr>
<td>Bone and soft tissue</td>
<td>19</td>
<td>7</td>
<td>8</td>
<td>53</td>
</tr>
<tr>
<td>Ear, nose, throat</td>
<td>27</td>
<td>3</td>
<td>24</td>
<td>11</td>
</tr>
<tr>
<td>Gastrointestinal, upper</td>
<td>39</td>
<td>10</td>
<td>29</td>
<td>26</td>
</tr>
<tr>
<td>Gastrointestinal, lower</td>
<td>102</td>
<td>6</td>
<td>96</td>
<td>6</td>
</tr>
<tr>
<td>Genitourinary (nonrenal)</td>
<td>22</td>
<td>5</td>
<td>17</td>
<td>23</td>
</tr>
<tr>
<td>Gynecologic (nonovarian)</td>
<td>78</td>
<td>9</td>
<td>69</td>
<td>12</td>
</tr>
<tr>
<td>Heart, mediastinum, pleura</td>
<td>11</td>
<td>2</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>Hematologic</td>
<td>79</td>
<td>36</td>
<td>43</td>
<td>46</td>
</tr>
<tr>
<td>Hepatobiliary</td>
<td>35</td>
<td>21</td>
<td>14</td>
<td>60</td>
</tr>
<tr>
<td>Renal</td>
<td>73</td>
<td>7</td>
<td>66</td>
<td>10</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>143</td>
<td>95</td>
<td>48</td>
<td>66</td>
</tr>
<tr>
<td>Ophthalmic</td>
<td>12</td>
<td>9</td>
<td>3</td>
<td>75</td>
</tr>
<tr>
<td>Ovarian</td>
<td>30</td>
<td>14</td>
<td>16</td>
<td>47</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>49</td>
<td>35</td>
<td>14</td>
<td>71</td>
</tr>
<tr>
<td>Retropertitoneal</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Salivary gland</td>
<td>6</td>
<td>2</td>
<td>4</td>
<td>33</td>
</tr>
<tr>
<td>Skin</td>
<td>7</td>
<td>3</td>
<td>4</td>
<td>43</td>
</tr>
<tr>
<td>Thyroid</td>
<td>35</td>
<td>21</td>
<td>14</td>
<td>60</td>
</tr>
</tbody>
</table>

Proportion of Cases Initially Diagnosed on Cytology, by Primary Site

The Importance of Pathology Education After the Preclinical Years: A Structured Approach to Teaching Medical Students Gynecologic Pathology

(Poster No. 139)

Catherine Gonsalves, MD (c.gonsalves@ufl.edu); Maira Gaffar, MD; Jennifer Reppucci, DO; Jesse Kresak, MD; Ashwini Esnakula, MD; Ashwin Akki, MD; Julia Ross, MD, PhD; Marie Rivera-Zengotita, MD. Department of Pathology, University of Florida, Gainesville.

Context: Often, medical students are not offered structured pathology rotations, hindering their understanding of the specialty.

Mobile Phone Adapter for Photomicrographs: A New Beginning in Digital Pathology?

(Poster No. 138)

Binny Khandakar, MBBS, MD1 (binny.khandakar@mountsinai.org); Rifat Mannan, MD2; Roshan Mahabir, MD2; Malary Mani, MD3; Songyang Yuan, MD, D3. Department of Pathology, Mount Sinai St. Luke’s Roosevelt Hospital, New York, New York; Department of Pathology, The Johns Hopkins Hospital, Baltimore, Maryland; Department of Pathology, Mount Sinai Health System, New York, New York.

Context: Photomicrographs are very important in academic medicine, literature, and telepathology. We are in the new era of digital photomicrographs. Smart phones (SPs) have become a principal form of convenient, easily accessible, high-resolution camera. We analyzed the utility of mobile phone adapter (MPA) for photomicrography.

Design: The study was conducted with 2 SPs with the same camera configuration, 1 MPA, and 50 slides. A single representative photomicrograph was taken simultaneously for each slide, one by free hand (free-hand group [FHG]) and another by using adapter (adapter group [AG]). Surveys were created for assessing image quality: focus, sharpness, clarity, brightness, contrast, color, overall image quality, presentation, and publication use. A semiquantitative scoring on 1 to 4 scale (poor, 1; bad, 2; good, 3; excellent, 4) was used for analysis. Surveys were circulated among in-house (internal survey [IS]) and outside pathologists (external survey [ES]). An average image attribute score (AIAS) was determined.

Results: The average time for picture acquisition was more in FHG (9.6 seconds versus 0.47 seconds, P < .05). AIAS of all attributes was more for AG than FHG in both IS (3.4 versus 2.2, P < .05) and ES (2.9 versus 2.4, P < .05). Both surveys reflected a better overall image quality for AG (IS = 3.4 versus ES = 3.0) than FHG (IS = 2.2 versus ES = 2.4). MPA can be a very effective tool for photomicrography. It is useful, time-saving, and yields a high-quality image. It can replace the need for large, sophisticated, micrograph setup, providing pathologists with an inexpensive handy tool for instant high-quality images.

Abstracts e195
The literature has not fully explored the lack of standardization and effectiveness of these rotations. Our institution requires 1 day of pathology during the third-year gynecology clerkship, where students sit with the residents, fellows, and attendings as they work through the day’s caseload. Owing to the variability in case volume from day to day, medical students had a range of involvement and exposure to gynecologic pathology. The aim of this study was to structure a rotation that would allow each student to have a similar experience.

**Design:** An electronic survey was distributed to residents, fellows, and attending physicians before standardization. The change consisted of a focused gynecologic pathology curriculum: a pretest to gauge knowledge, a presentation focused on common entities, a posttest to assess understanding, and a slide study set. Upon completion, the students had scope time with a pathologist. Two months after implementation, the electronic survey was completed again. Test scores and survey results were collected and analyzed.

**Results:** From the survey, the intervention was deemed an improvement, as students were more engaged and teaching methods were more effective. The results of the pretest versus the posttest showed a 40% improvement (average score rose from 40% to 80%) after reviewing the presentation and slide study set.

**Conclusions:** Medical student exposure to pathology during their clinical years is critical. We offer this significant improvement in medical students’ test scores and survey results as evidence that structured pathology education is valuable.

**A Rare Metaplastic Breast Carcinoma Mimicking Telangiectatic Osteosarcoma on Fine-Needle Aspiration**

(Reporter No. 140)

Ammar Matloob, MD (ammamar.matloob@mountsinai.org); Diane Du, MD. Department of Pathology, Icahn School of Medicine at Mount Sinai, New York, New York. Metaplastic breast carcinoma (MBC) with chondro-osseous differentiation is very rare (<0.05% of breast malignancies). Most cases show 2 distinct cell populations: ductal or squamous carcinoma and chondro-osseous components. We present a case of MBC mimicking a telangiectatic osteosarcoma. A 79-year-old woman presented with a 2.5-cm right breast mass. Sonograms showed a well-circumscribed, multicystic mass with septae. Ultrasound-guided fine-needle aspiration was performed. Cytosmear showed scanty polygonal, stromal, and multinucleated giant cells with nuclear hyperchromasia, pleomorphism, and moderate amount of slightly granular cytoplasm. The background was bloody with scattered dense amorphous material. A cell block revealed malignant stromal and osteoclastic giant cells with anaplasia and avid mitosis. In addition, there were abundant blood-filled cystic spaces lined by atypical cells and focal osteoid rimmed by osteoblasts. No carcinoma component was found. Immunohistochemically, the malignant cells were positive for vimentin, CD163, and p53, but negative for CK7, AE1/3, p63, EMA, Oscar, CK5, S100, ER, and PR. A fine-needle aspiration diagnosis of sarcomatous lesion suggestive of MBC with osseous differentiation was established. Subsequently, right mastectomy was performed. It showed a multicystic round mass, filled with dark blood and debris containing thin septae lined by atypical cells. Scattered malignant osteoclasts, stromal cells, and osteoblasts were present, the latter rimming the osteoid. In this case, although a thorough examination did not reveal any carcinomatous components, strong p53 and weak Oscar immunoreactivities in small areas of spindle cells are diagnostic of MBC with osseous differentiation, which mimics telangiectatic osteosarcoma.

**Professionalism in the Age of Social Media:**

A Curriculum for Pathology Trainees

(Reporter No. 141)

Julie K. Karp, MD (julie.karp@jefferson.edu); Alexis R. Peeden, MD. Department of Pathology, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania.

**Context:** As social media becomes ubiquitous, explicit discussions of professional behavior on social media should be incorporated into training and continuing education of pathologists.

**Design:** We developed a curriculum for pathology trainees exploring social media professionalism. The curriculum was presented to trainees in an anatomic and clinical pathology residency program during two 1-hour conferences. In the first conference, with institutional review board exemption, a precurricular survey was administered to assess trainees’ attitudes toward social media. Cases of medical unprofessionalism from news outlets and relevant publications in the medical literature were discussed. Simulated, pathology-oriented social media posts with potentially unprofessional content were then discussed. In the second conference, trainees were shown how to update their Facebook privacy settings, and the institutional social media policy was reviewed by the institution’s social media and public affairs manager. A postcurricular survey was then administered.

**Results:** The precurricular survey revealed that 70% and 40% of trainees accessed social media at least monthly and daily, respectively. Most used Facebook, with other social media sites used less commonly. Most (75%) reported that their social media accounts were private and most (60%) were aware of the institutional social media policy. In the postcurricular survey, 100% reported that their social media accounts were private and 100% were aware of the institutional social media policy.

**Conclusions:** A curriculum focused on social media professionalism provided an interactive forum in which trainees could share how they use social media. The curriculum improved trainees’ use of social media privacy settings and knowledge of the institutional social media policy.

**Computational Pathology in Medical Curriculum in the Era of Personalized Medicine: Impetus for Impact**

(Reporter No. 142)

Ritcha Saxena, MBBS, MD (ritcha.saxena@yahoo.org); Ritwik R. Saxena, 1Department of Pathology, American University of Bridgeport, Bridgeport, Connecticut; 2Department of Biomedical Engineering, Delhi Technological University, Delhi, India.

**Context:** From slides to digitization to sequencing to cognitive computing, pathology has undergone a constant advancement for years. While the evolution has reformed many existing educational paradigms, the maximum potential of pathology informatics is yet unrealized in medical education. Computational pathology, an emerging technologic advancement, brings the role of pathologists to the very heart of precision medicine–based clinical care by melding the realms of digital pathologic and radiologic imaging, immunohistochemistry, molecular pathology including omics, with electronic health records. We aim to introduce its fundamentals in undergraduate education.

**Design:** In a team-based learning setup, students were provided diagnostic pathology, digital pathology, genetic and imaging data, pertaining to solid tumors of various organ systems, and were required to compile the data and design algorithms using SQL and Java interface, to build an elementary database. Online resources and the institutional IT expert assisted with basic informatics training. Algorithms were validated by instructors and assessed for reliability and usability.

**Results:** Student feedback revealed this system was an exciting and dynamic process that was fun as well as informative, leading to enhanced learner enthusiasm and achievement, as evidenced by block examination results. Evaluation through readiness assessment tool illustrated improved team knowledge acquisition.

**Conclusions:** Introducing computational pathology at an early stage of budding physicians’ training would potentially result in imparting a more comprehensive picture of the disease, timely direction of their focus toward precision medicine, and easier retrieval and application of massive volumes of information. In the era of big data, this would enable future physicians to make the best possible medical decisions.

**Presentation Skills Training for Residents:**

Knowing and Reaching Your Audience

(Reporter No. 143)

Sigfred Lajara, MD (slajara@montefiore.org); Sabrina Racine Brezisiek, MD, PhD; Hugo Kaneki Nakahama, MD; Michael Prytowsky, MD, PhD. Department of Pathology, Montefiore Medical Center, Bronx, New York.

**Context:** Pathology residency is largely focused on acquiring knowledge and diagnostic skills. Being part of the health care team, effective communication is paramount, yet formal presentation skills are rarely addressed during training. Recognizing this, we implemented workshops that adhere residents practiced their presentation skills. Knowing what to say and how to say it largely depends on knowing your audience. Therefore, a session was developed where residents practiced presenting to 3 main audiences: pathologists, clinicians, and medical students.

**Design:** To simulate the different scenarios, 3 volunteers agreed on 2 interesting (1 anatomic and 1 clinical) pathology cases. Each tailored their presentations to 1 of 3 scenarios: case discussion among pathologists, multidisciplinary conference with clinicians, or a didactic session with medical students. Feedback was given to each presenter,
A 15-Year Multi-Institutional Retrospective Analysis on the Morphologic and Immunohistochemical Pattern of Seminoma and Nonseminomatous Germ Cell Tumors

(Poster No. 144)

Ammar Matloob, MD (ammar.matloob@mountsinai.org); Fahad Khan, MD; Xulei Liu, MD. Department of Pathology, Icahn School of Medicine at Mount Sinai, St. Luke’s - Roosevelt Hospital, New York, New York.

Context: Seminoma and nonseminomatous germ cell tumors are notable for their responsiveness to chemotherapy, but seminoma mixed lesions have a worse prognosis.

Design: This is a 3-institution, 15-year retrospective study including 374 patients with radical orchietomy (July 2002–September 2017). Morphologic and immunohistochemical pattern of seminoma versus nonseminomatous germ cell tumors were analyzed.

<table>
<thead>
<tr>
<th>Seminoma Versus Nonseminomatous Germ Cell Tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testicular Tumor</td>
</tr>
<tr>
<td>Seminoma</td>
</tr>
<tr>
<td>Nonseminomatous germ cell tumors</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Results: A total of 374 testicular germ cell tumors containing seminoma (74.6%) and nonseminomatous germ cell tumors (25.4%) were reported with or without the use of immunostains in the diagnostic workup. Immunostains were used in 30% of these cases, and its use was correlated with the type of seminoma and nonseminomatous germ cell tumors (46.6%). Thirty-two percent of the cases using immunostains were diagnosed as nonseminomatous germ cell tumors, in comparison to 22.4%. CD30 immunostain was the most commonly used in 76% of cases, 65% of which were negative. CD117 was the second most commonly used in 72.9%, with 96.3% positive. Patients’ age varied from 22 to 55 years with a median age of 34 years (IQR 22–50). Fifty-three percent of the cases were on the left side (n = 196). The median size of the seminoma was 3.5 cm (IQR 2.20–5.50 cm). Seventy-eight percent of the cases were staged as pT1, 18% were staged as pT2, 2% were staged as pT3, and 2% were not reported (Table).

Conclusions: Immunostains were not commonly used in the diagnosis of seminoma versus nonseminomatous germ cell tumors at our institution(s). When immunostains were used, there was a higher detection rate of nonseminomatous germ cell tumors.

A Simulated Environment for Pathology Education

(Poster No. 145)

Anders R. Meyer, MD (meyer.anders@gmail.com); Kumaraen Cooper, MBChB, DPhil. Department of Pathology, University of Pennsylvania, Philadelphia.

Context: Pathology educators struggle to put trainees in a position of decision-making before their assumption of full responsibility as attending pathologists. Trainees routinely come to sign-out having formed a differential diagnosis, but, owing to limitations on tissue and resources, are often not fully responsible for ordering ancillary tests that might refine the differential diagnosis. Furthermore, pathology educators are without a means for acquiring objective data on trainee progress.

Design: We sought to design an interactive, Web-based system that would allow pathology trainees to define a histologic differential, order immunohistochemistry and fluorescence in situ hybridization, and submit a final diagnosis or differential. Additionally, we endeavored to create an objective scoring system that might allow pathology educators and trainees to gauge progress and comparative performance among trainees.

Results: Using the Python programming language, we created a Web-based portal that achieved the above-stated goals. Participants log in, are directed to view a case, enter a histologic differential diagnosis, and then have the opportunity to order ancillary tests. Akin to real-life, stains can be ordered in batches and there is a simulated turnaround time of 1 to 3 days. Once complete, the participant enters a final differential diagnosis. The Web site records the tests ordered and provides a simulated turnaround time. To evaluate the quality of the differential diagnoses, we developed a scoring system based on accuracy, precision, and histologic overlap.

Conclusions: The addition of a simulated pathology sign-out experience may be a useful adjunct in pathology education and can provide educators and trainees with objective data on their progress.

Reduction of Unnecessary Blood Draws in a Community Hospital

(Poster No. 146)

Stephanie Welsh, MLS(ASCP); Ann McCord, BS, MT(ASCP); Kaitlynn Zitek; Whitney Wedel, MD; Adam J. Horn, MD (ahorn@marylanning.org). Department of Pathology/Laboratory, Mary Lanning Healthcare, Hastings, Nebraska.

Context: Drawing extra blood tubes “just in case” has been a common practice (so-called rainbow draw). Recent literature shows this to be of little value; however, these studies have focused on larger academic and tertiary care centers. Our facility is an independent, rural-based regional hospital with an ingrained culture of routine rainbow draws on all inpatients. We sought to evaluate the outcomes from a reduction in extra tubes drawn.

Design: Unused sodium citrate tubes were selected as a surrogate marker of a rainbow draw and numbers of unused tubes were tracked pre and post intervention. Education was provided to phlebotomists and clinical staff. Conservative (citrate tubes x2) and liberal (citrate tubes x4) estimates of unused tubes were extrapolated. Re-draw rates were monitored post intervention.

Results: An average of 41 extra citrate tubes were drawn per day pre intervention; 3 extra per day were drawn post intervention. The re-draw rate was less than 3%. An annualized 13,824 fewer citrate tubes were drawn post intervention, with 37,464 fewer tubes in the conservative group and 55,296 in the liberal group. Cost savings ranged from $2670 to $5340 in materials and disposal and approximately 4.5 hours/week in phlebotomy time. The volume of blood not collected ranged from the equivalent of 195 units to 390 units.

Conclusions: Our findings support a safe reduction in routine rainbow draws with a potential benefit of cost and time savings. The substantial volume of blood not collected warrants additional investigation for possible effects on iatrogenic anemia.

Establishing a System to Assess the Economic Advantages to “In-House” Testing in Molecular Infectious Diseases

(Poster No. 147)

D. Y. Goldstein, MD (dogoldst@montefiore.org); Momka Narlieva, MS; Lucia Wol gast, MD; Amy Fox, MD, MS. Department of Pathology, Montefiore Medical Center, Bronx, New York.

Context: Laboratory utilization addresses not only the appropriate- ness of clinical ordering but also the use of hospital resources including those used for send-out reference testing as well. Oftentimes there is tremendous value to considering in-house testing as it may unify processes, expand services, and provide economic incentives to the institution. We undertook to produce a set of tools and techniques to address the appropriateness of in-house testing for various analytes.

Design: Initial data collection was necessary to enable an understanding of testing performed by reference laboratories. To this end, a workflow was configured where requests for reference laboratories generated a generic laboratory information system (LIS) test. This placeholder test ultimately allowed documentation of specific tests ordered as well as the interfaaced result. Once these data were captured by the LIS they could be specifically queried to assess individual test volume, and cost and revenue data reviewed. In addition, spreadsheet
Critical Histopathologic and Histochemical Features in Differentiating Extramammary Perianal Paget Disease From the Intraductal Mimickers

( Poster No. 148)
James J. Saller, MD1 (sallerjames@gmail.com); Aradesh Hakam, MD2; Lei Lou, MD2; Kun Jiang, MD, PhD.1 1Department of Pathology, Moffitt Cancer Center, Tampa, Florida; 2Department of Pathology, the Second Hospital, Hebei Medical University, Shijiazhuang City, China.

Context: Extramammary perianal Paget disease (EMPPD) is characterized by intraepithelial mucin-containing plump neoplastic cells that are morphologically similar to epidermal Toker and Toker-like keratinocytes (ETATLks). EMPPD remains notorious for its high risk of missed diagnoses and overdiagnosis, and frequent recurrence after excision. Our review of EMPPD specimens has demonstrated crucial histomorphologic and immunohistochemical characteristics that could help differentiate EMPPD from its mimickers and improve patient outcome.

Design: Clinicopathologic and immunohistochemical features of 12 EMPPD cases were summarized. Histomorphologic inspection and ancillary tests (mucicarmine, GCDP, GATA3, CDX2, P40, CK5/6, CK7, and CK20) were compared to those observed in the mimickers of EMPPD, principally ETATLks.

Results: EMPPD originates from skin adnexal primaries and rarely from visceral adenocarcinomas. EMPPD cells show mucin-congestion and signet-ring morphology, distributed near and along the basement membrane of squamous epithelium. This “ballooned” cytology is also seen in ETATLks, which presents a challenge even to an experienced pathologist. Our study showed that immunostaining offers minimal clarity, as both EMPPD and its mimickers can be labeled by CK7 and GATA3, except in EMPPD cases related to visceral malignancies. Our investigation identified 4 characteristic features in determining/excluding EMPPDs: EMPPD was characterized by mucicarmine-labeled, focally compressed eccentric crescent-shaped nuclei, whereas centrally located round nuclei and intercellular bridges are characteristic of (mucicarmine-negative) ETATLks.

Conclusions: EMPPD frequently presents as an insidious and persistent perianal process, with an underrecognized malignant potential. Criteria inferred by the 4 abovementioned key features may improve accuracy in diagnosing EMPPD, and consequently improve management and outcomes in patients with EMPPD.

Laboratory Methodology Testing Change Due to Increase in HIV Screening in Emergency Department

( Poster No. 149)
Renuka Malenie, MD1 (malenie15@ecu.edu); Swati Satturwar, MD2; Nada Fadul, MD3; Ciara Dority, MPH4; Timothy Keeler, MD5; Chris Miller, MT(ASCP), MS1; Richard J. Baltaro, MD, PhD.1 1Departments of 1Pathology and Laboratory Medicine, 2Internal Medicine, Division of Infectious Diseases, and 3Emergency Medicine, Vidant Medical Center, Greenville, North Carolina.

Context: The Centers for Disease Control and Prevention (CDC) released human immunodeficiency virus (HIV) testing recommendations in 2006. They were implemented in our emergency department in March 2017.

Design: Opt-out HIV testing was implemented for patients between 18 and 65 years of age requiring blood work with no previous documented HIV testing in their electronic medical record. Testing was performed as per CDC algorithm. Aim was to incorporate the increased testing in the laboratory workflow by using the existing resources to detect HIV-positive patients and link them to long-term care while in the emergency department.

Results: To improve the workflow, the laboratory switched from manual testing by Alere Determine HIV-1/2 Ag/Ab Combo to automated testing on Abbott platform. Abbott i-1000 AG/Ab Combo. Between March 2017 and February 2018, more than 7000 HIV tests were performed, which is an average of 591 tests/month compared to a previous average of 10 tests/month. Testing has increased more than 58 times as compared to tests done in the previous 2 years. Nineteen HIV-positive specimens were identified by antigen/antibody combination immunoassay and confirmed as HIV-1 by antibody immunoassay. Among the 14 newly diagnosed, 12 were linked into HIV care; 2 known positives were relinked to care from emergency department owing to improved turnaround time.

Conclusions: Our study demonstrates the feasibility of incorporating routine HIV testing within existing laboratory infrastructure by just changing the testing methodology. Although laboratory workload increased, it helped in early HIV detection and appropriate and timely long-term care services. Plans include expanding testing among adolescents and using similar methods to integrate hepatitis C testing. Authors Fadul, Dortche, Reeder, Miller, and Baltaro received grant or research support from Gilead’s FOCUS Program.

Diagnosing Harvey: An Anatomic Pathology Department’s Response to a Disaster Situation

( Poster No. 150)
Daniel J. Duohon, MD (djduohon@houstonmethodist.org); Jim Cook, MBA, MT(ASCP)DLM; David W. Bernard, MD, PhD; Mary R. Schwartz, MD. Department of Pathology and Genomic Medicine, Houston Methodist Hospital, Houston, Texas.

Context: Limited data exist regarding an anatomic pathology division’s preparedness and response to disaster situations. The goal of this project is to provide recommendations on preparedness, action, and recovery efforts to be applied to anatomic pathology services throughout the world.

Design: A PubMed literature search was performed using the terms pathology, laboratory medicine, and disaster response. Existing hospital and departmental policies regarding disaster preparedness and assessments of laboratory performance during and following Hurricane Harvey were reviewed. Personal accounts were obtained from staff, trainees, and attending physicians.

Results: The implementation of preparedness procedures following Tropical Storm Allison allowed central anatomic pathology services to maintain operations, with few interruptions, throughout the entirety of the disaster. Personnel staffing was maintained, with some hospital staff spending multiple nights in the hospital. Flooded roadways delayed transportation of specimens and cases from some sites. During the disaster, the main priorities were the safety of patients and staff, and maintaining quality and timely care of patients. The recovery period presented many challenges in the weeks that followed, with personal calls on hospital staff and patients.

Conclusions: The effects of a disaster cannot be understated. Centralization of processes, accessible record systems, and devotion to practice are valuable tools to combat a disaster. It is impossible to predict when a disaster, natural or man-made, will occur. Therefore, it is imperative for pathology services to have policies and procedures in place to ensure the safety of patients and staff, the quality and integrity of departmental performance, and measures to recover following a disaster.

Changing the Ordering Habits for Influenza Screening and Its Effect on the Accuracy of Influenza Detection in a Large, Urban Tertiary Care Emergency Department

( Poster No. 151)
Katie L. King, MD (katie.king1@bswhealth.org); Rachael Marvell, MLS; Raul Benavides, MD. Department of Pathology, Baylor University Medical Center, Dallas, Texas.

Context: In the emergency department, rapid influenza diagnostic tests, though suboptimal, are frequently used to detect influenza. The medical leadership at Baylor University Medical Center decided to change influenza testing to nucleic amplification test (NAT) to more accurately identify influenza, especially for isolation purposes. For each emergency patient who required admission for influenza during a pilot period, a Seripha enzyme immunoassay (EIA) and a Solana NAT were performed. For all other emergency patients, no influenza screening test was performed, and the patient was discharged with Tamiflu. To track effectiveness, the volume of EIAs and discrepant results (EIA versus NAT) were followed.
Design: The number of EIAAs performed in the emergency department per day was recorded both before and after the policy change. Additionally, for each patient tested with negative results, the results of EIA versus molecular tests were recorded and compared.

Results: See Figure (Figure 279) depicting EIA ordering. During the pilot period, the Sofia EIA was negative 127 times. Of those 127 tests, Solana was positive 14 times (11.02% false-negative rate). Additionally, the rate of EIA ordering decreased from 25.6/day to 10.7/day (58.2% decrease).

Conclusions: Sofia (the EIA) has a false-negative rate of 11.02% as compared to the NAT Solana. This policy change resulted in fewer occult influenza-infected patients being admitted to the hospital without isolation precautions. Molecular/NAT testing is preferred for ruling out flu for admitted patients. As a result, Baylor University Medical Center changed to NAT testing only for influenza after the pilot period concluded.

Biomarker Testing Survey for Microsatellite Instability/Mismatch Repair
(Poster No. 152)

Carolina Strosberg, MD1 (carolinastrosberg@gmail.com); Manoj Gadara, MD1; Masoumeh Ghayouri, MD1; Kun Jiang, MD, PhD1; Samer Saleem, MD1; Ardeshr Hakam, MD1. Departments of 1Pathology and 2Pathology-International Visitor Scholarship Program, H. Lee Moffitt Cancer Center, Tampa, Florida.

Context: Microsatellite instability (MSI) is caused by deficiency of DNA mismatch repair (MMR) enzymes. MSI status can be accessed via polymerase chain reaction (PCR) testing of tumoral microsatellite loci or by immunohistochemistry testing for deficiency of MMR proteins (MLH1, MSH2, MSH6, PMS2). MSI-high/MMR-deficient tumors are typically hypermutated and highly responsive to immunotherapy with PD-1/PD-L1 inhibitors.

Design: An online survey was sent that included 9 questions regarding biomarker testing of MMR enzymes. About 80 oncologist/medical professionals responded to the questions.

Results: Most clinicians typically perform MSI/MMR testing at diagnosis (67.9%); 11.5% do not perform at all; and 6.4%, 10.3%, and 3.9% perform before initiating first, second, and third line of therapy, respectively. Immunohistochemistry is the most common method used for MSI/MMR analysis and PCR the least preferred. Most clinicians interviewed are somewhat comfortable interpreting the results, 40%, versus 36% being very comfortable. MSI/MMR testing is mainly ordered as based on clinical judgment of individual cases (57%). Age, family history, and possible Lynch syndrome are the most frequent patient characteristics taken into consideration when ordering MSI/MMR testing.

Conclusions: Clinicians order MSI/MMR as based on clinical judgment in individual cases, especially in young patients and patients with possible Lynch syndrome. MSI/MMR is being ordered in 80% of metastatic solid tumors, possibly reflecting new FDA indications for PD-1/PD-L1 inhibitors. Standardization of test results seems to be a desirable feature, and reimbursement for MSI/MMR testing has not been an issue encountered by ordering clinicians.

Pelvic Lymphadenectomy Submission Practices in a Large Academic Institution
(Poster No. 153)

Melanie H. Hakar, DO (melaniel.hakar@northwestern.edu); Kruti P. Maniar, MD. Department of Pathology, Northwestern University, Chicago, Illinois.

Context: Lymph node examination is an established criterion for staging in endometrial cancer. Nodal disease is detected in 5%-10% of nodes in the approximately 40,000 new cases of endometrial carcinoma in the United States each year. Identification of nodal disease is critical, as patients with nodal metastases have poorer survival and increased risk of local recurrence.

Design: We evaluated grossing procedures for lymph node specimens from hysterectomies performed for endometrial carcinoma. Previous policy was submission of only lymphoid tissue without residual adipose tissue. The procedure was changed to include submission of all residual adipose tissue. We performed a retrospective analysis of relevant cases received 6 weeks before and after the change.

Results: We identified 30 lymphadenectomy specimens for endometrial cancer, 13 from before the procedure change and 17 from after (Table). Significantly more specimens were entirely submitted after the procedure change versus before (15/17 versus 5/13, P = .007, Fisher exact test), indicating compliance with the new policy. The average number of lymph nodes per case was significantly greater after the change (13.2 versus 5.9, P = .005, Student t test). The average additional number of blocks per case to submit the remainder of adipose tissue was 4.1 (range, 0–16). None of the additional nodes were positive for tumor.

Conclusions: We sought to ascertain whether the submission of lymphadenectomy specimens in their entirety had a significant effect on the total number of nodes examined. We conclude that entirely submitting all adipose tissue from lymphadenectomies significantly increases the number of lymph nodes available for assessment.

<table>
<thead>
<tr>
<th>Lymphadenectomy Specimens</th>
<th>Before Policy Change</th>
<th>After Policy Change</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No. of cases</td>
<td>13</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>No. of cases with lymph node specimens entirely submitted</td>
<td>5</td>
<td>15</td>
<td>.007</td>
</tr>
<tr>
<td>Average lymph nodes per case</td>
<td>5.9</td>
<td>13.2</td>
<td>.005</td>
</tr>
</tbody>
</table>

Diagnosis of PD-L1 Assay Using Whole-Slide Imaging Compared to Light Microscopy
(Poster No. 154)

Justin Rueckert, DO (justin.rueckert@uwhealth.org); Pamela C. Gibson, MD; Douglas Taatjes, PhD; Nicole Bouffard, BS; Jennifer Gordon, BA; Abiy Ambaye, MD. Department of Pathology and Laboratory Medicine, University of Vermont Medical Center, Burlington.

Context: Incorporation of whole-slide imaging (WSI) into routine pathology practice is being investigated in many settings, including immunohistochemistry (IHC) analysis. Immune checkpoint inhibitor therapies, including programmed death–ligand 1 (PD-L1), are gaining clinical interest by offering patients additional treatment options. PD-L1 IHC is validated for use at the University of Vermont Medical Center. The main aim of our study is to compare the analysis of PD-L1 IHC by light microscopy to WSI. We hypothesized both modalities to be equivalent for analysis.

<table>
<thead>
<tr>
<th>Results of Light Microscopy Scores Compared to WSI Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light Microscopy</td>
</tr>
<tr>
<td>&gt;50% (n=13)</td>
</tr>
<tr>
<td>1%–50% (n=18)</td>
</tr>
<tr>
<td>&lt;1% (n=42)</td>
</tr>
</tbody>
</table>

Design: After completing Dako’s online PD-L1 interpretation program, 2 pathologists and 1 pathology resident analyzed 73 cases where PD-L1 IHC was performed. The cases were analyzed both by light microscopy and WSI with a minimum interval of 2 weeks between analyses. A consensus result for each case and each modality was defined as when 2 of the 3 reviewers agreed. If none of the reviewers agreed, the result was considered “no match.” The light microscopy consensus result was considered the gold standard. A k coefficient and the corresponding 95% confidence interval were used as a measure of agreement between the 2 modalities.

Results: The k coefficient was calculated as 0.72 and the 95% confidence interval was calculated as 0.55 to 0.89 (Table).
Conclusions: Our results indicate a substantial level of agreement between light microscopy and WSI analysis for PD-L1 IHC. The WSI interpretation of 2 cases was discordant by 2 levels of interpretation (interpreted as >50% on light microscopy and <1% on WSI). The overall trend observed was to underscore PD-L1 IHC interpretation by WSI.

Are All Frozen Sections Indicated for Intraoperative Consults? A Critical Appraisal
(Poster No. 155)

Jaswinder Kaur, MD (jkaurm89@gmail.com); Varsha Manucha, MD. Department of Pathology, University of Mississippi Medical Center, Jackson.

Context: Frozen sections (FSs), important in management of surgical patients, must be used when results have a direct consequence on operative procedures. An accuracy of 97.8% with 0.1% clinically significant errors makes FSs valuable; however, FSs are labor intensive, costly, and must be used judiciously. Below we analyzed indications of FSs in our institute.

Design: Samples from 2017 FSs were designated to appropriate services. FS rationale was categorized as indicated for margin evaluation, establishing presence/nature of lesion, and tissue sufficiency evaluation. Other reasons not having immediate consequence to treatment at time of surgery or immediately after were designated “questionable/not indicated.”

Results: Of 952 specimens that underwent FS analysis, approximately 30% were requested by otolaryngology, followed by neurosurgery (13%), mostly for establishing nature of lesion or margin evaluation. Thirty-three gynecology cases were with questionable indications, 4 of which were benign ovarian cysts, 23 entirely cystic ovarian neoplasms, and 6 thickened endometrium. In the latter 2, representative sections favored benign or focally borderline and complex hyperplasia, respectively; final diagnosis was deferred to permanent. Additionally, 2 benign abdominal cysts and 1 multinodular goiter (diagnosis supported by radiology) in our opinion required no FS analysis (Table).

Conclusions: Most FSs at our institution are for appropriate reasons, comforting pathologists that the service is being used acceptably. However, pathologists are cautious about rendering a definitive diagnosis on large cystic lesions in which diagnosis is limited to representative sections. This is most applicable in gynecologic specimens, thereby questioning the utility of performing FSs in such specimens.

<table>
<thead>
<tr>
<th>Surgical Service</th>
<th>Total</th>
<th>Indicated (%)</th>
<th>Not indicated/Questionable indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head and Neck</td>
<td>251 (26.4%)</td>
<td>250 (99.6%)</td>
<td>Multinodular goiter-1</td>
</tr>
<tr>
<td>Bone &amp; Soft tissue</td>
<td>121 (12.7%)</td>
<td>121 (100%)</td>
<td></td>
</tr>
<tr>
<td>Neurosurgery</td>
<td>124 (13.0%)</td>
<td>124 (100%)</td>
<td></td>
</tr>
<tr>
<td>Abdominal</td>
<td>100 (10.5%)</td>
<td>122 (98%)</td>
<td>Benign cysts -2</td>
</tr>
<tr>
<td>Skin</td>
<td>91 (9.6%)</td>
<td>91 (100%)</td>
<td></td>
</tr>
<tr>
<td>Gynecologic</td>
<td>90 (9.5%)</td>
<td>57 (63.3%)</td>
<td>Ovarian cysts -4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ovarian cystic neoplasms -23</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Thickened endometrium -6</td>
</tr>
<tr>
<td>Thoracic</td>
<td>70 (7.4%)</td>
<td>70 (100%)</td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td>70 (7.4%)</td>
<td>70 (100%)</td>
<td></td>
</tr>
<tr>
<td>Organ recovery</td>
<td>18 (1.9%)</td>
<td>18 (100%)</td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>13 (1.4%)</td>
<td>13 (100%)</td>
<td></td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>4 (0.4%)</td>
<td>4 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

So Much to Do With So Little: A Quality Improvement Study to Make Good Quality Cell Blocks
(Poster No. 156)

Nitin Marwaha, MD (nitin.marwaha@me.com); Vijayalakshmi Padmanabhan, MD, MPH. Department of Pathology, Baylor College of Medicine, Houston, Texas.

Context: Cell blocks are widely used in cytology for aiding in fine-needle aspiration biopsy diagnosis and for ancillary testing. This quality improvement (QI) study was initiated to correct and improve the adequacy and quality of the cell blocks with FNA cases. The objective of this study is to use the Institute of Healthcare Improvement (IHI) tools for QI including the Ishikawa diagram, the PDSA cycle, and make a change in practice using a systematic approach.

Design: An Ishikawa diagram was prepared with input from multiple people to study potential reasons for cell blocks with low cellularity. Baseline data were collected on 30 cases from pathology database to assess adequacy of cell blocks. A PDSA cycle was made (Plan), a change was made in the practice (Do), and postchange data were collected in 30 cases (Study). The change included collecting at least 2 designated additional passes, in addition to needle rinses for cell blocks.

Results: Multiple potential causes for low cellularity were identified. Before the change, 15 of 30 cases (50%) had noncontributory cell blocks due to low cellularity. After the change, only 9 of 30 cell blocks (30%) were noncontributory with a median of 2 designated passes and average of 1.8 passes/cell block.

Conclusions: Using the IHI tools like the Ishikawa diagram and using the PDSA cycle, we studied the problem, implemented a change, and measured the improvement. Persistently asking for designated passes for a cell block preparation leads to better cell block yield and cellularity, which helps in making the diagnosis and ancillary testing.

Does Mandatory Quality Control in Surgical Pathology Result in Better Overall Quality?
(Poster No. 157)

Devin R. Broadwater, MD (broadwaterdevin@gmail.com); David T. Lynch, MD. Department of Pathology, SAUSHEC, San Antonio, Texas.

Context: Quality control (QC) in surgical pathology is an increasingly important topic with no standardized approach. Institutions are required to create their own methods to ensure quality diagnostic reports. We report our institution’s QC method outcomes and recommendations to improve overall quality.
Design: Our institution requires 100% QC by a second pathologist of prostate, breast, lung, and liver specimens, regardless of diagnosis, and all tumor resections. Other QC is at the discretion of the staff pathologist. During a 4-week study period, pathologists recorded specimen data (tissue type and diagnosis) and agreement status on a standardized document. Dermatopathology, cytology, and hematopathology QC were excluded, since they are signed out by subspecialists.

Results: Of 2996 total cases reviewed, 104 cases had QC data available (3.5% of total cases). Prostate was the specimen most frequently receiving QC (34 cases, 32.7%), followed by breast (22 cases, 21.2%). There were 70 complete agreements (67.3%), 29 minor report changes without a change in diagnosis (27.9%), 4 minor disagreements (3.8%), and 1 major disagreement (1.0%). Discrepancy types are displayed in the Table with most occurring in prostate tissue (41.2%). There is no statistical difference between required and nonrequired QC discrepancy rates (36% and 24%, respectively; \( P = .4 \) (Table).

Conclusions: Systematic approaches can be used to decrease the quantity of QC discrepancies. Identifying the types of discrepancies is a necessity. Recognizing that typographic and required report elements are our most common discrepancies, we recommend thorough proofreading. Our data suggest that required QC does not result in statistically higher detection of discrepancies, compared to nonrequired.

Optimizing Urine Drug Test Utilization Through Data-Driven Targeted Interventions

(Simone Arvisais-Anhalt, MD) (Poster No. 158)

Simone Arvisais-Anhalt, MD1 (simone.arvisais-anhalt@phhs.org); Ibrahim Hashim, PhD2; Michael Ward, BSc2; David Barnes, BSc2; Caroline McQueen, BSc2; Wende Wolls, BSc2; Melanie Kim, BSc2; Erinda Young, BSc2; Jyoti Balani, MD1; Alagajraru Muthukumar, PhD2; Ravi Sarode, MD1; Ellen Arau, MD1. Departments of 1Pathology, 2IR Ancillary Systems, 3IR Electronic Medical Records, and 4Pathology Core Lab, UT Southwestern Medical Center, Dallas, Texas.

Context: We suspected that our urine drug-testing menu was suboptimal because our internal laboratory was not receiving the expected number of opiate confirmation tests. Therefore, we created a data-driven laboratory utilization study to determine clinicians’ ordering practices.

Design: We queried laboratory data from January 1, 2016, to July 1, 2017, for urine drug testing, reviewed the tests available, and collected information about the providers and departments, test results, combinations of tests ordered together, turnaround time relative to patient discharge date, and cost.

Results: We determined that clinicians predominately ordered 3 different combinations of urine drug screening tests for opiate, cannabinoids, benzodiazepine, amphetamine, cocaine, barbiturate, and phencyclidine testing: (1) Urine 7-Drug Screen Test, (2) Urine 7-Drug Screen + Reflex Opiate Confirmation Test, and (3) Urine 7-Drug Screen + Send-out Overdose Panel (testing drugs of abuse and pharmacologic drugs). Test combination 3 was primarily ordered by neurosurgery/neurology departments with 65% of results reported after patient discharge. When asked why they were ordering a large overdose panel, they stated they used that test in lieu of a urine 7-drug confirmation test, as that choice was unavailable in our electronic medical records.

Conclusions: This study revealed an unanticipated ordering practice because of lack of options for appropriate drug confirmation testing. The drug menu was simplified by implementing a new 7-drug screen with targeted reflex confirmation testing that is predicted to save $47K annually with improved turnaround time. This study illustrates how pathologists can leverage big data to simplify the testing menu, offer appropriate testing options, and reduce health care costs.

Reclassification of Hyperplastic Polyps Based Solely on Histomorphologic Criteria

(Poster No. 159)

Sanaz Ainechi, MD (sainechi@gmail.com); Richard Judelson, MD; Xiaoxin Zhu, MD; Xiaofei Wang, MD. Department of Pathology, University of Massachusetts Medical School, Worcester.

Context: Sessile serrated adenomas (SSAs) and hyperplastic polyps (HPs) share overlapping histomorphologic features and occasionally are challenging to distinguish. Recent trend toward the lower threshold for SSA diagnosis, as well as pathologists’ knowledge of their ominous outcome, resulted in a higher ratio call for SSA in the proximal colon. We sought to study the magnitude of histopathologic findings in reclassification of HPs after removing the compromising information including anatomic location, size, and other relevant clinical information.

Design: We reevaluated previously diagnosed HPs, which were randomly selected from 2006 to 2011 at our institution. None of the selected cases had synchronous neoplasm (adenoma, SSA, traditional serrated adenoma, or colorectal carcinoma). Slides were reviewed by an expert GI pathologist according to the definition of the 2010 World Health Organization Classification of Tumors.

Results: Among 298 screening colonoscopies, a total of 487 polyps were initially diagnosed as HPs. On our review 111 were reclassified as SSA (22.8%) and 376 remained unchanged (77%). SSAs were more likely to be proximal (66%) including 4 SSAs with low-grade and 1 with high-grade dysplasia. Two traditional serrated adenomas were identified in the distal colon. There were no significant differences in patient characteristics between those with reclassified SSAs and those who had HPs.

Conclusions: Our data show that a significant proportion of previously reported right-sided HPs may be SSAs. There were no significant differences in our ratio of reclassified SSAs, in comparison to published studies. Knowledge of anatomic location or size of polypl has limited value in influencing the GI pathologist.

Crucial Use of Immunohistochemistry for H pylori Detection in Stomach Biopsy: The New Gold Standard

(Liye Suo, MD, PhD (suo@bcm.edu); Vijayalakshmi Padmanabhan, MD, MPH; Shilpa Jain, MD. Department of Pathology, Baylor College of Medicine, Houston, Texas.

Context: There is no consensus on the method of H pylori detection: H&E alone versus using special stains (Giemsa) or immunostains on every stomach biopsy. The aim of this study was to investigate the role of immunohistochemistry (IHC) in H pylori detection rate and associated with follow-up.

Incidences of H pylori and Immunohistochemistry (IHC) Study Ordering Rates in Stomach Biopsy

(Poster No. 160)

Liye Suo, MD, PhD (suo@bcm.edu); Vijayalakshmi Padmanabhan, MD, MPH; Shilpa Jain, MD. Department of Pathology, Baylor College of Medicine, Houston, Texas.

Context: There is no consensus on the method of H pylori detection: H&E alone versus using special stains (Giemsa) or immunostains on every stomach biopsy. The aim of this study was to investigate the role of immunohistochemistry (IHC) in H pylori detection rate and associated with follow-up.

Design: Laboratory information system was searched for all stomach biopsy cases between January 2015 and January 2017. The pathology report, including histology, routine Diff-Quick stain, and selected IHC results, was compared for different pathologists at a single institution. The density of H pylori was further graded on IHC as high density and rare/low density.

Results: A total of 2021 stomach biopsies were signed out by 4 pathologists. The IHC ordering rate is significantly different (\( P = .05 \)) among the 4 pathologists with significantly different (\( P < .05 \)) percentage of total H pylori–positive cases (41%–12.9%; Table). In total, 74 cases from 74 patients had the diagnosis of rare/low density H pylori organisms by IHC with negative or equivocal results from Diff-Quick stain. Histologically, 18% of cases showed active gastritis, 69% with mild chronic inactive
Does Anesthesia Type (Conscious Sedation Versus General Anesthesia) Matter for Endobronchial Ultrasound-Guided Fine-Needle Aspiration Specimen Adequacy: A Quality Assurance Study

(Poster No. 162)

Malekh Alshaikhmohamed, MD (alshaikh@bcm.edu); Pralay K. Sarkar, MD; Vijayalakshmi Padmanabhan, MD. Department of Pathology, Baylor College of Medicine, Houston, Texas.

**Context:** Endobronchial ultrasound-guided (EBUS) fine-needle aspiration is a minimally invasive procedure used for real-time imaging and tissue sampling. It is used mainly in diagnosis and staging for lung cancer and in detecting other causes of mediastinal and hilar lymphadenopathy. Adequate sedation is a crucial part of the procedure. At our institution, general anesthesia (GA) is arbitrarily used when the patient needs close monitoring, had poor past tolerance to bronchoscopy, small and/or high-stake lesion, and in patients who need a complete survey, allowing for more time and cough control. The aims of this study was to determine differences in sample adequacy with conscious sedation (CS), which we also frequently use, and GA for a cytology diagnosis in EBUS-guided fine-needle aspiration (FNA) specimens.

**Design:** Data were obtained from 58 specimens from 40 patients. All procedures were performed by 1 pulmonologist, and on-site cytology evaluation was performed by cytology fellows. Adequacy was defined by ability to make a specific diagnosis or by presence of adequate lymphoid cells. Parameters studied included sex, specimen adequacy, number of passes, lesion size, diagnosis, and cytology biopsy correlation.

**Results:** A total of 58 cases, 29 in each group (GA and CS), were identified. Student's t test was used to determine P value (Table).

<table>
<thead>
<tr>
<th></th>
<th>General Anesthesia</th>
<th>Conscious Sedation</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>17</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Specimen adequacy</td>
<td></td>
<td></td>
<td>0.8</td>
</tr>
<tr>
<td>Adequate</td>
<td>23</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Less than optimal</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Unsatisfactory</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>CytoLOGY result</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Negative for malignancy</td>
<td>18</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Positive for malignancy</td>
<td>8</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Indeterminate</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Nondiagnostic</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Lesion mean size</td>
<td>1.1</td>
<td>0.9</td>
<td>.64</td>
</tr>
<tr>
<td>No. of passes, mean (SD)</td>
<td>6.5 (1.38)</td>
<td>6.7 (2.09)</td>
<td>.43</td>
</tr>
<tr>
<td>Median No. of passes</td>
<td>7</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Cytology-biopsy correlation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>15</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>No biopsy provided</td>
<td>13</td>
<td>17</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** Our study shows no difference in EBUS-guided FNA specimen adequacy, based on anesthesia type. While GA is preferred for some patients, it is more expensive, time-consuming, and may have limited availability with contraindications and adverse effects. CS is relatively less expensive, safe, and should be considered as an equivalent alternative option.