Case #1:

**PRESENTER:** Sharif Nasr, MD  
**ATTENDING:** Igor Jovanovich, MD PhD

**CASE HISTORY:** A 40 year old female presented with intermittent right sided pelvic fullness. She has a history of Cushing’s Syndrome and a total abdominal hysterectomy and left sided salpingo-oophorectomy for menorrhagia and a benign ovarian cyst. Subsequent imaging demonstrated a large mass in the right hemipelvis and elevated CA-125 and CA19-9. Exploratory laparotomy with excision was performed.

**DIAGNOSIS:** Polypoid Endometriosis (PE)

**KEY DIFFERENTIAL DIAGNOSES:**
- Mullerian Adenosarcoma
- Benign endometrioid adenofibroma
- Endometrial stromal sarcoma
- Borderline Endometrioid tumor

**DISCUSSION:**

- **History:**
  - First described in Polypoid first described by Mostoufizadeh and Scully in 1980 detailing a variant of endometriosis that shared histological features with endometrial polyps
  - Rare diagnosis with only a few case reports
    - Largest of which in 2004 Found fewer than half of patients were taking exogenous hormones
    - Study in 2016 demonstrating two subtypes of PE, one resembling endometrial polyps and the other resembling non polypoid endometriosis.

- **Histology:**
  - Glands showing varying degrees of proliferation and possible metaplastic changes.
  - Stroma appearing proliferative phase without stromal atypia. Also varying stromal fibrosis and thick walled vessels. Irregularly spaced and cystic glands.
  - Significant stain: P16 differentiating resemblance of endometrial type PE from conventional endometriosis type PE

- **Arriving at PE:**

<table>
<thead>
<tr>
<th>PE lacks....</th>
<th>Seen in...</th>
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<tbody>
<tr>
<td>No broad fronds, nuclear atypia, or malignant stroma</td>
<td>Adenosarcoma</td>
</tr>
<tr>
<td>No ovarian stroma or cleft like papillary architecture</td>
<td>Adenofibroma</td>
</tr>
<tr>
<td>No cribiform or papillae architectures</td>
<td>Endometrioid borderline</td>
</tr>
<tr>
<td>No finger like permeative growth pattern, no invasion</td>
<td>Endometrial stromal sarcoma</td>
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</table>

- **Treatment:**
  - Treatment involves cessation of any hormonal medication that could be contributing to the growth of the mass if clinically indicated.
  - Definitive treatment is surgical.
REFERENCES:

Case #2:

**PRESENTER:** Myra Khan, D.O.
**ATTENDING:** Michael Kaufman, M.D.

**CASE HISTORY:** The patient is a 48 year old female who presented for a well-woman exam. She had a past medical history significant for left ovarian torsion and subsequent left salpingo-oophorectomy in 1984. On physical exam her primary care physician palpated a right adnexal mass. Serum studies performed demonstrated an elevated inhibin level and a normal CA 125. She then underwent an MRI that demonstrated a 4.2 cm solid mass medial to the right ovary. The patient then underwent a right salpingo-oophorectomy. An intraoperative consultation of the mass demonstrated a tumor completely separate from both the right ovary and right oviduct. Based on the location and histology, the tumor was thought to be of probable Wolffian origin.

**DIAGNOSIS:** Female Adnexal Tumor of probable Wolffian Origin (FATWO)
*Outside consult agreed by Stanford University Medical Center, Department of Pathology.*

**IMPORTANT DIFFERENTIAL DIAGNOSES:** Endometrioid adenocarcinoma of the fallopian tube, sex-cord stromal tumors such as a sertoli-leydig cell tumor, and a granulosa-theca cell tumor.

**KEY DIAGNOSTIC FEATURES:**

- **Etiology of tumor:**
  - Develops from the remnants of the Wolffian duct system; 71 cases reported
    - 9 cases of solid encapsulated tumors arising from the location of Wolffian duct remnants: the broad ligament, mesosalpinx, and para-ovary.
  - Unilateral and localized without dissemination
  - Age: 19-83; mean age 45 years
  - Patients present with abdominal pain, a palpable mass, or as an incidental finding

- **Gross:**
  - Smooth, lobulated, solid, or combination of solid and cystic
  - Pale yellow to tan cut surface and rubbery
  - 0.8 cm to 20.0 cm in greatest dimension; mean 6.0 cm
  - Larger tumors may have hemorrhage or necrosis

- **Histology:**
  - All the cells are epithelioid to spindle shaped and are arranged in tubules in varying patterns:
    - Sieve-like and cystic
    - Solid and diffuse
    - Trabecular and tubular
    - Or any of the combinations above
  - The stroma ranges from collagenous hyalinization to delicate reticulin-positive fibers
  - Some tubules demonstrate eosinophilic secretions that are PAS-positive
  - Some cells contain granules that are PAS-positive

- **Cytology:**
  - The nuclei are: round, irregular, or spindled shaped
  - The chromatin is uneven
  - Nucleoli are inconspicuous
  - Low mitotic activity (<1/10 HPF)

- **Staining profile:**
  - Positive: calretinin, CD10, cytokeratin, vimentin, and inhibin
  - Negative: EMA, CEA, PR, ER, CK20, and Ki67

- **Genetic profile:** strongly c-Kit positive

- **Malignant features:**
  - Brisk mitotic activity (10 or > mitosis per 10 HPF)
- Nuclear pleomorphism
- + CD117
- Ki67 >3.2%
- Capsular invasion
- Necrosis

**Behavior:**
- FATWO tumors with malignant features can demonstrate recurrence.
- FATWO tumors without malignant features did not demonstrate recurrence or metastasis in 15 year follow-up.
- Overall, FATWO is deemed a low malignant potential neoplasm with periodic follow-up suggested.
- Of the 71 cases reported, 8 recurred, and 2 of the 8 metastasized to the liver and lungs. However, those patients are disease free with 15 year follow-up.

**Treatment:**
- Surgical excision with follow-up.
- Malignant tumors can be treated with re-excision and tyrosine kinase inhibitors.

**Key points:**
- FATWO is diagnosed based on histological pattern, staining profile, and location.
- It is a low malignant potential neoplasm with a non-aggressive disease course. Follow-up for patients is recommended.

**REFERENCES:**

Case # 3:

PRESENTER:  Indu Agarwal, MD
ATTENDING:  Thomas Cibull, MD

CASE HISTORY:
A 34 year old male presented with a subcutaneous nodule in the right hand. The differential provided by the clinician was keratoacanthoma versus atypical infection.

HISTORY:
Dermal tumor composed of sheets of epithelioid cells, separated by capillaries. Cells had clear to eosinophilic cytoplasm, centrally-placed nucleus, without nuclear pleomorphism or mitotic figures. Occasional giant cells were seen.

DIFFERENTIAL DIAGNOSES:
- Malignant melanoma (clear cell type)
- Ballon (clear cell ) nevus
- Dermatofibroma ( clear cell type)
- Clear cell sarcoma
- Metastatic renal cell carcinoma
- Dermal clear cell mesenchymal neoplasm
- Perivascular epithelioid cell neoplasm (PEComa)

IMMUNOHISTOCHEMISTRY:
- Positive stains:
  - HMB 45, SMA, Mart-1, MiTF
- Negative stains:
  - S100, SOX10, pancytokeratin, desmin, EMA and CD163

DIAGNOSIS:  Cutaneous perivascular epithelioid cell neoplasm (PEComa)

DISCUSSION:
- PEComa:
  - Mesenchymal neoplasm composed of histologically and immunohistochemically distinctive perivascular epithelioid cells (PEC). Neoplasms show myomelanocytic differentiation by IHC.
- PEComa Family:
  - These include angiomyolipoma (AML), clear cell “sugar” tumor of the lung (CCST), lymphangioleiomyomatosis (LAM). May occur at various visceral and soft tissue sites and recently have been described on skin.
- Histopathology:
  - The architecture is nested or in sheets. Epithelioid cells demonstrate abundant clear to granular eosinophilic cytoplasm, a centrally placed nucleus, and have a tendency of perivascular distribution.
- Primary cutaneous PEComas:
  - Presents as small dermal nodule. Approximately 40 cases described.
- Immunohistochemistry of primary cutaneous PEComa:
  - Positive stains: HMB 45, MiTF, MelanA, Smooth Muscle Actin, Desmin, Caldesmon
  - Negative stains: S100, SOX10, AE1/AE3, CD163, CD68
- Prognosis and behaviour:
  - All known tumor have behaved in a benign fashion
  - No recurrences known even in tumors with increased mitotic activity
- Transcription factor E3 (TFE3) Translocation:
  - The overexpression of TFE3 occurs with a translocation involving its locus at Xp11. This has been demonstrated in alveolar soft part sarcoma, in a subset of renal cell
carcinomas, and recently demonstrated in a subset of visceral PEComas. PEComas harboring TFE3 translocation theoretically may not respond to conventional therapy inhibiting mammalian target of rapamycin (mTOR). However no known cutaneous PEComa has exhibited TFE translocations to date.

REFERENCES:

1. Bernadette Liegl, MD, Jason L. Hornick, MD, PhD, and Christopher D. M. Fletcher, MD, FRCPath; Primary Cutaneous PEComa: Distinctive Clear Cell Lesions of Skin; Am J Surg Pathol 2008;32:608–614
2. Aaron Auerbach, MD, MPH, David S. Cassarino, MD, PhD; Clear cell tumors of soft tissue; Surgical Pathology 4 (2011) 783–798
4. Eleni Ieremia, FRCPath and Alistair Robson, FRCPath, DipRCPath; Cutaneous PEComa: A Rare Entity to Consider in an Unusual Site; Am J Dermatopathol 2014;36;198–201
6. Narasimhan P. Agaram, MBBS, Yun-Shao Sung, MS, Lei Zhang, MD, MS, Chun-Liang Chen, MS, Hsiao-Wei Chen, MS, Samuel Singer, MD, Mark A. Dickson, MD, Michael F. Berger, PhD, and Cristina R. Antonescu, MD; Dichotomy of Genetic Abnormalities in PEComas With Therapeutic Implications; Am J Surg Pathol 2015;39:813–825
Case #4:

PRESENTER: Saman S. Ahmadian, MD
ATTENDING: James Padgett, MD

CASE HISTORY: The patient is an 86 year old female who presented with an asymptomatic 5.5 cm right axillary mass detected during follow up CT scan for endometrial cancer diagnosed and treated 6 months ago.

DIAGNOSIS: Follicular dendritic cell sarcoma (FDCS)

IMPORTANT DIFFERENTIAL DIAGNOSES: Histiocytic sarcoma, interdigitating dendritic cell (IDC) sarcoma, epithelioid sarcoma, Langerhan’s cell histiocytosis

KEY DIAGNOSTIC FEATURES:

- Etiology of tumor:
  - Neoplasm rising from follicular dendritic cells
  - Described for the first time in 1986

- Gross:
  - Well circumscribed mass (median size = 5 cm)

- Cytology:
  - Focally cellular and relatively cohesive clusters of epithelioid cells admixed with small lymphocytes
  - Occasional internuclear inclusions and grooves

- Histology:
  - Atypical epithelioid cells with variably distinct cell borders, moderate amount of eosinophilic cytoplasm, moderately pleomorphic nuclei and vesicular or finely granular chromatin, small but distinct nucleoli
  - Presence of binucleated or multinucleated giant neoplastic cells
  - Scant mitosis
  - Small lymphocytes interspersed between tumoral cells

- Staining profile:
  - Positive: CD21, CD23, CD35, clusterin
  - Negative: cytokeratin, histiocytic, Langerhans and myeloid markers

- Unfavorable predictive factors:
  - High grade features (mitosis, necrosis & cytological atypia), large tumor (>6cm), extranodal location (especially intra-abdominal tumor)

- Treatment:
  - Surgical excision with follow-up for primary and recurrent tumors

- Key points:
  - 11% of FDCS can be epithelioid and should be considered in the differential diagnosis of cytokeratin negative epithelioid tumors

REFERENCES:


2. WHO Classification of Tumours, Volume 2, IARC WHO Classification of Tumours, No 2, Swerdlow, S.H., Campo, E., Harris, N.L., Jaffe, E.S., Pileri, S.A., Stein, H., Thiele, J., Vardiman, J.W, IARC.

3. Ioachim’s Lymph Node Pathology Fourth Edition, by Harry L. Ioachim (Editor), L. Jeffrey Medeiros MD (Editor)

5. Rosai and Ackerman's Surgical Pathology - 2 Volume Set, 10th Edition.


Case #5:

**PRESENTER:** Elisheva Shanes, MD  
**ATTENDINGS:** Thomas Cibull, MD  
William Watkin, MD

**CASE HISTORY:** A 32-year-old female presented with several months of nausea and abdominal pain. CT of the abdomen revealed inflammation of the rectum as well as abdominal and pelvic lymphadenopathy. A sigmoidoscopy was performed and biopsies were taken. Two weeks following initial presentation the patient developed a diffuse rash.

**DIAGNOSIS:**  
Skin, left abdomen:  
- Syphilis.

Colon, random biopsies:  
- Focal active syphilitic colitis, positive for *Treponema pallidum* organisms.

**DISCUSSION:**  
- The incidence of syphilis has increased significantly in recent years  
  - The CDC’s most recent report puts the 2013 rate at double the rate in 2000.  
  - Most significant increase is in the population of men who have sex with men (MSM)  
- Syphilis and lymphogranuloma venereum can both cause colitis (STI colitis).  
- Syphilitic proctocolitis can present with hematochezia, urgency, diarrhea, or constipation, and imaging is often significant for circumferential thickening of the rectal wall and lymphadenopathy.  
  - Syphilis can cause mass lesions and be mistaken radiologically for carcinoma or lymphoma  
  - At endoscopy, the findings vary from ulcerated lesions to erythema to normal mucosa  
- While STI colitis is often treated empirically, the diagnosis may not be clinically apparent, and thus biopsies may end up on the pathologist’s desk. Keeping STI colitis in mind as a differential diagnosis is therefore prudent.  
- Differentiating between inflammatory bowel disease (IBD) and STI colitis:  
  - Distinguishing features from IBD: STI colitis features a large number of submucosal plasma cells and lacks significant architectural distortion, crypt-centric damage, and eosinophilia  
  - Overlapping Features with IBD: skip and aphthoid lesions, chronic inflammation, Paneth cells, lymphoid aggregates, fibrosis, granulomata, mucosal plasma cells  
- This case is unique in that previously reported cases of syphilitic colitis have been exclusively in HIV+ MSM. This case in an otherwise healthy, HIV-negative female could have been missed if not for a subsequent skin biopsy that was classic for syphilis. This emphasizes the importance of considering STI colitis as a differential diagnosis in GI biopsies.

**REFERENCES:**  
Case #6:

Presenter: Talent Theparee, MD
Attending: Curtis Hall, MD

A 57 year old male patient with fatigue and a past history of hypertension
- Undergoing medication adjustment due to fluctuating blood pressure (up to 170)
- Occasional abdominal cramping diarrhea with flushing
- CT scan done for suspicion of pheochromocytoma revealing an enlarged spleen with multiple hypodense foci; PET scanning showed diffused uptake
- Splenectomy was performed.

Grossly, the spleen weighed 1839 g and the splenic parenchyma was diffusely red-tan to brown, mottled, and homogenous. Histopathology revealed diffuse replacement of splenic architecture with polygonal cells with moderate cytoplasm, irregular nuclei, and occasional nucleoli that surround red blood cells and appear to form vascular spaces.

Immunohistochemical stains were done as follows:
- **Diffusely positive:** Lysozyme, CD31; **Variably positive:** CD163
- **Negative:** Myeloperoxidase, CD3, CD20, CD21, CD45/LCA, CD68 (KP1), S100, factor VIII, CD8, CD34, pancytokeratin (AE1/AE3), D2-40

**Initial diagnosis:** littoral cell hemangioendothelioma

Littoral cell hemangioendothelioma is a rare neoplasm of littoral cells, or splenic sinus endothelial cells. Littoral cell neoplasms can range from a benign angioma to angiosarcoma, with hemangioendothelioma showing some malignant features but is not overtly malignant. Immunohistochemically they express both endothelial markers (CD31, factor VIII) and macrophage markers (CD68, CD163) as well as CD21 while losing CD8 expression.

The case was also sent for outside review, with additional immunohistochemical stains as follows:
- **Positive:** CD11c, CD33, CD43, CD56, CD68 (PGM-1), NPM1 (nuclear)
- **Negative:** BRAF-V600E, FLI-1, langerin (CD207), TdT, CD14, CD64, CD117, CD123, ERG

With additional positive stains for myeloid markers, negative staining for vascular markers, and an interpretation of the histologic appearance of the neoplastic cells as diffusely infiltrating the splenic red pulp, the diagnosis was revised to: **findings consistent with myeloid sarcoma**.

Myeloid sarcoma is a neoplasm of immature hematopoietic progenitor cells with aberrant homing to sites such as the skin, lymph nodes, testis, intestines, bones, CNS, and mucosa. Myeloid sarcoma can precede, occur concurrent with, or occur after AML, MDS, or MPS. Based on lineage, myeloid sarcomas can occur with granulocytic precursors, monoblastic/monocytic precursors, or have trilineage precursors.

Myeloid sarcoma and littoral cell neoplasms can overlap in the following ways:

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<tr>
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<th>Littoral cell neoplasm</th>
<th>Myeloid sarcoma</th>
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</thead>
<tbody>
<tr>
<td><strong>Presentation in spleen</strong></td>
<td>Rare</td>
<td>Uncommon</td>
</tr>
<tr>
<td><strong>Clinical presentation</strong></td>
<td>Often incidental, splenomegaly</td>
<td>Can be incidental if no concurrent AML</td>
</tr>
<tr>
<td><strong>Morphology</strong></td>
<td>Ranges from clear vascular spaces to solid areas with spindled, round cells</td>
<td>Generally diffuse pattern, can be infiltrating, cells are round</td>
</tr>
<tr>
<td><strong>IHC</strong></td>
<td>Stains for CD31, CD68, lysozyme, CD163 Usually also positive for other endothelial markers such as Factor VIII Also CD21+</td>
<td>Can also stain similarly, depending on subset</td>
</tr>
</tbody>
</table>
References:

Littoral cell neoplasms


Myeloid sarcoma


CD31