

Case # 1

Presenter: Leonidas Arvanitis, MD

Attending: Ira Miller, MD, PhD

Clinical history: A 36 year old male presented with increasing back pain and a recent 20 pound weight loss. The pain radiated to the right side of abdomen. Neurological examination was remarkable for right leg weakness. A CT scan revealed an 18 cm mass near the level of L3 extending to the right kidney. A complete surgical excision was performed.

- **Diagnosis:** Melanotic schwannoma (A.K.A. psammomatous melanotic schwannoma)

Important Differential Diagnosis of deep pigmented spindle cell tumors

- Cellular Schwannoma
- Pigmented neurofibroma
- Clear cell sarcoma
- Metastatic malignant melanoma

Key morphologic features of Melanotic Schwannoma:

- Spindle cells, some of which are pigmented, arranged in fascicles and ribbons.
- Psammoma bodies
- Some tumors have mature fat cells
- Minimal atypia and low level mitotic activity
- Consistently positive for S-100 and HMB-45, while negative for synaptophysin, chromogranin, GFAP, actin and cytokeratin
- Characteristic ultrastructural findings
 - interdigitating cytoplasmic processes,
 - basement membrane formation
 - melanosomes in all stages of maturation

Discussion:

- A tumor composed of cells with both schwannian and melanocytic features
- Rare, approximately 80 reported cases
- Sporadic or associated with Carney's Complex
- Affects males and females equally with the median age of time of diagnosis being 38 years (range 10-60 years)
- Most common sites are the spinal or autonomic nerves (46%), but can also present in other locations (stomach, bone/soft tissues, heart, etc)
- 20% multifocal, 10% malignant
- Slow evolving tumors with a median interval between first symptoms and diagnosis at 3.6 years
- Most tumors are benign however a recent review revealed that many can show an aggressive behavior such as metastases and local recurrences.

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- Patients should undergo extensive genetic and endocrine testing as well as evaluation for atrial myxoma to exclude Carney Complex.
- Appropriate long-term follow-up is required for all melanotic schwannomas, as it may recur or metastasize after more than 5 years, even in the absence of overt malignant histological features.
- There are currently no criteria to predict behavior.

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Case # 2

Presenter: Luis Blanco Jr., M.D.

Attending: Paolo Gattuso, M.D.

Clinical History: 28 year old asymptomatic woman with an incidental lung mass in the left lower lobe.

Diagnosis: Sclerosing hemangioma

Important Differential Diagnosis of Sclerosing Hemangioma

- Clear cell tumor
- Pulmonary hamartoma
- Hemangioma
- Epithelioid hemangioendothelioma
- Bronchioloalveolar carcinoma
- Carcinoid tumor
- Metastatic papillary thyroid carcinoma
- Metastatic renal cell carcinoma

Key Morphologic Features

- Gross: solitary, well circumscribed mass with a heterogeneous cut surface
- Hallmark: histologic heterogeneity
- 2 cell types: cuboidal surface cells and round stromal cells
 - May show moderate to marked atypia
- 4 architectural patterns: papillary, solid, hemorrhagic and sclerotic
 - 95% display 3 patterns
 - 100% contain at least 2 patterns

Discussion:

- Sclerosing hemangioma is an uncommon pulmonary neoplasm.
- There is a female predominance, with a female to male ratio of 5:1.
- Patients are usually asymptomatic or present with hemoptysis, chronic cough or chest pain.
- A peripheral, solitary, well-circumscribed mass is usually found incidentally.
- They are derived from undifferentiated respiratory epithelium and hence the term sclerosing hemangioma is a misnomer.
 - Surface cells: positive for TTF-1, EMA, CK AE1/AE3 and surfactant proteins A and B
 - Round cells: positive for TTF-1, EMA, focally for CK 7 and CAM 5.2 and negative for CK AE1/AE3 and surfactant proteins A and B
 - The expression of TTF-1 but not surfactant proteins A and B in the round cells suggests they arise from undifferentiated respiratory epithelium.

- Electron microscopy reveals lamellar bodies in various stages of maturation in the round cells, also supporting the theory.
- Because of the histologic heterogeneity, it can mimic many benign and malignant neoplasms depending on what architectural pattern predominates.
 - It is particularly important to differentiate the papillary areas that may display marked atypia from bronchioloalveolar carcinoma.
- Sclerosing hemangioma is benign and cured by surgical excision.
 - Rare lesions with regional lymph node metastases have been reported.
 - Mortality has not been attributed to sclerosing hemangioma.

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Case # 3

Presenter: Richard Cantley, M.D.

Attending: Jerome Loew, M.D.

Clinical History: Incidentally found mass found in the spleen on radiographic imaging of a 63 year old woman with an unrelated pancreatic tumor.

- Diagnosis: Sclerosing angiomatoid nodular transformation of the spleen (SANT)

Important Differential Diagnosis of SANT

- Littoral cell angioma
- Hamartoma
- Hemangioma
- Epithelioid hemangioendothelioma
- Splenic angiosarcoma
- Kaposi sarcoma

Key Features:

- Typically found incidentally on abdominal imaging
- Grossly, it presents as a single mass with red-tan nodules intermixed with white fibrous tissue
- Microscopically, it is composed of multiple nodules with numerous slit-like vascular spaces lined by plump endothelium.
- Vascular spaces are lined by a mixture of endothelial types that recapitulate the normal red pulp vascular components

	CD31	CD8/CD68	CD34
Splenic sinusoid type	+	+	-
Systemic-vascular type	+	-	+
Small vein-like	+	-	-

- The internodular areas contain dense collagen fibers intermixed with myofibroblasts, plasma cells, lymphocytes, macrophages, and hemosiderin-laden macrophages.
- Splenectomy is curative

Discussion:

- SANT is a non-neoplastic process
- It may represent an entity within the spectrum of IgG4 sclerosing diseases
- A minority of cases of SANT show EBV+ myofibroblasts in the internodular areas of, suggesting that a subset of SANT may be related to inflammatory pseudotumor

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Case #4

Presenter: Michelle Collier, MD

Attending: Melvin Schwartz, MD

Clinical History: A 73 year old woman with hypertension admitted for new onset neutropenia (WBC 0.7) and increased serum creatinine (2.6). The patient received granulocyte colony stimulating factor rapidly increasing her neutrophil count. On hospital day 4, the patient developed hematuria and had an acute elevation in her creatinine. The patient was diagnosed with rapidly progressive glomerulonephritis and steroids were started. However, her renal function continued to deteriorate, requiring hemodialysis. She was found unresponsive, coded and died on hospital day 8. At autopsy her kidneys showed diffuse cortical petechial hemorrhages with necrotizing glomerulonephritis with crescent formation. Immunofluorescence was essentially negative for immunoglobulin or complement. Her lungs showed diffuse alveolar hemorrhage and alveolar capillaritis. Serologies were positive for p-ANCA.

Diagnosis: Microscopic polyangiitis (MPA)

Discussion: Rapidly progressive glomerulonephritis (RPGN) is a clinical diagnosis based on the findings of proteinuria, hematuria, hypertension, increased serum creatinine together with rapid progressive renal failure with the histologic correlate being glomerular crescents. RPGN is classified based on the mechanism of glomerular injury by immunofluorescence with 15% having anti-GBM antibodies, 25% immune complex mediated, and 60% are pauci-immune. The pauci-immune RPGN is divided into a renal limited form and a systemic form with kidney and other organ involvement and associated with ANCA. There are three main diseases associated with ANCA systemic small vessel vasculitis including Wegener's (granulomatous vasculitis), Churg Strauss (history of asthma and eosinophilia) and microscopic polyangiitis (pauci-immune vasculitis without granulomatous inflammation or eosinophilia). MPA involves the kidney (90%) and lung (50%).

There is a lot of evidence in the literature implicating ANCAs in the pathogenesis of MPA including a compelling case report of a pregnant woman with active MPA and transplacental passage of ANCAs to her infant causing renal dysfunction and pulmonary hemorrhage in the infant.

Recent studies have been looking into the discovery of a possible new ANCA directed at a different lysosomal and neutrophil membrane protein called LAMP-2. A possible mechanism for autoantibody formation includes infection with certain bacteria.

Neutrophils are implicated in the pathogenesis of MPA. Neutrophils and damaged neutrophils were seen in the lungs and kidneys of our patient. Our patient presented with neutropenia, possibly keeping her disease smoldering and her disease really unmasked itself when she received the colony stimulating factor and her disease quickly took a fulminant

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path. The clinical course in this case further supports a role for neutrophils and ANCAs in the pathogenesis of MPA.

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Case #5

Presenter; Dawn Bradly, MD

Attending: Shriram Jakate, MD

Clinical History: A 53 y/o Caucasian male with a history of Hepatitis B and hepatocellular carcinoma and s/p OLT one month prior presented to the ER with severe RUQ pain, jaundice, and fever (101.5° F). He was pronounced dead after developing aystole less than 6 hours later.

Diagnosis: Acute necrotizing cholangiohepatitis with *Clostridium perfringens* (gas gangrene)

Differential Diagnosis

- Autolysis
- Severe ischemic necrosis
- Severe sepsis

Key Morphologic Features

- Necrotic hepatic parenchyma
- Scattered microorganisms (bacilli)
- Lack of inflammatory infiltrate

Discussion

- Gas gangrene is a well known complication of traumatic wounds
- Most common as a soft tissue phenomenon
- Rare case reports with solid organ involvement, including the liver, pancreas, kidney, heart, bladder, uterus, and brain
- *Clostridium perfringens* is the most common gas producing organism of the *Clostridium* species
- *Clostridium perfringens*: Gram positive, spore forming, non-motile, bacillus
- Hepatic infection is thought to occur from ascension of bacteria through the biliary tree and into the liver
- Infection can progress several inches per hour and become well established in as little as 6-8 hours
- Alpha and theta toxins are major virulence factors
- Re-transplantation is treatment of choice with a relatively good prognosis (50%)
- Most patients deteriorate rapidly and die before re-transplantation can be performed
- Differential Diagnosis
 - Autolysis
 - Gross appearance: No parenchymal holes
 - Expect to see autolysis in other organs
 - Check antemortum blood culture
 - Severe ischemic necrosis
 - A.K.A. severe perfusion injury

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- Often results from arterial or venous thrombosis
- May be differentiated by ill-defined hypoechoic areas on ultrasound
- Acute process, often seen immediately after transplantation
- Severe sepsis
 - Mild infections are common within the first month post-transplantation
 - Severe infection can be a cause for morbidity and mortality
 - Hepatic infection with *Clostridium perfringens* is extremely rare, with less than 20 cases reported in the literature

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Case # 6

Presenter: Marlene Gallegos MD

Attending: Shriram Jakate MD

- **Diagnosis:** Cap polyposis

Important Differential Diagnosis of Cap polyposis

- Inflammatory bowel disease pseudopolyps
- Familial adenomatous polyposis
- Cronkhite-Canada syndrome

Key Morphological Features of Cap polyposis:

- **Gross:**
 - Common location is the rectosigmoid colon
 - Multiple polyps ranging in size from millimeters to 2 cm
 - Polyps located at mucosal folds separated by normal or edematous mucosa
 - Polyps have a mucoid and fibrinopurulent cap
- **Histology:**
 - Polyps have a cap of fibrinopurulent exudate and granulation tissue
 - Elongated, tortuous, and often distended crypts at the base of the polyps
 - Inflammatory cell infiltration in the lamina propria of polyps
 - Adjacent colonic mucosa is edematous or normal

Discussion of Cap polyposis:

- First reported in 1985 by Williams et al.
- Occurs in the 5th to 6th decade of life with a slight male predominance
- Symptoms include mucoid and bloody diarrhea, tenesmus, and abdominal pain
- Distribution from the rectum to the distal colon
 - Involves entire colon and stomach in a few cases
- Etiology is unclear, but various possible causes include: infections, mechanical stimulation by stool, and abnormal colonic motility leading to mucosal prolapse
- Lab results might reveal hypoproteinemia as a result of excess discharge of mucus
 - Hypoproteinemia resolves with resolution of cap polyposis
- Various treatments such as the administration of salazosulphapyridine, antibiotics, metronidazole and glucocorticoids have been reported
- A few cases resolved spontaneously
- Surgical resection is recommended if disease persists

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