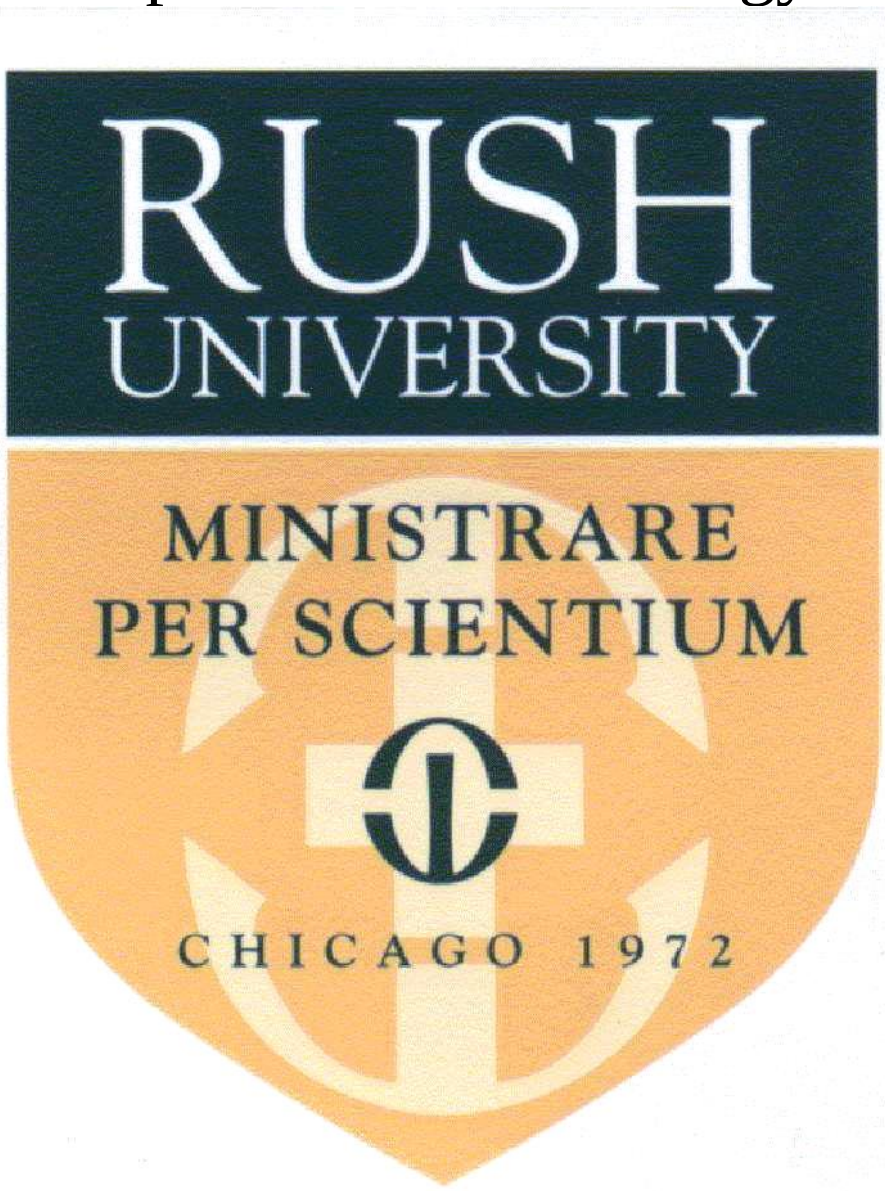
Rush University Medical Center
Department of Pathology



Illinois Registry of Anatomic Pathology
February 24, 2020

Illinois Registry of Anatomic Pathology
2/24/2020
Rush University Medical Center

CASE #1
Presenter: Brittany Cody
Attending: David Cimbaluk

CASE HISTORY: A 33-year old male of Polish descent presented to nephrology for mild proteinuria and declining renal function. He had been an 'avid' bodybuilder since the age of 15. His diet included multiple protein supplements and a very high protein diet.

His past medical history is notable only for rectal bleeding several years prior (colonoscopic exam revealed hemorrhoids).

Social history review revealed use of anabolic androgenic steroids (AAS) for a short time at the age of 15, but regular use for the last 2 years.

There is no pertinent family history.

Laboratory studies revealed the following: serum creatinine: 1.77 mg/dl, eGFR 37 ml/min, urine protein: 37 mg/dl, urine creatinine: 82, urine protein/creatinine ratio: 450 mg/g.

Serologic workup was negative.

DIAGNOSIS: Focal Segmental Glomerulosclerosis

DISCUSSION:
- Anabolic androgenic steroids are a rare but documented cause of secondary FSGS
- Primary versus secondary FSGS can be differentiated on EM by evaluating the degree of podocyte effacement
- suPAR mediates podocyte injury that leads to FSGS and may represent a future therapy target

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QUESTIONS:

1) Which of the following are potential causes of secondary focal segmental glomerulosclerosis?
   A. Genetic Mutations
   B. Viral Infections
   C. Drugs
   D. All of the above

2) Which of the following represents a circulating molecule, produced by the bone marrow which initiates the cascade of events resulting in focal segmental glomerulosclerosis
   A. IFN-γ
   B. suPAR
   C. IgA
   D. IL-2

ANSWERS: 1) D; 2) B

CASE #2
Presenter: Abdullah Almajnooni
Attending: Mark Pool

CASE HISTORY: 47-year old female with Turner syndrome presented to an outside institution with a 3 cm liver mass incidentally identified during an imaging evaluation for hematuria

DIAGNOSIS: Hepatic perivascular epithelioid cell tumor (PEComa)

DIFFERENTIAL DIAGNOSIS of Hepatic PEComa

- Hepatocellular carcinoma, clear cell variant
- Paraganglioma
- Metastatic renal cell carcinoma

- Metastatic adrenal cortical carcinoma
- Metastatic melanoma

DISCUSSION:

Key Features:

- PEComas are a family of mesenchymal tumors composed of peri-vascular epithelioid cells, with histological and immunohistochemical features of melanocytic and smooth muscle differentiation
- Associated with Tuberous sclerosis syndrome and TFE3 gene rearrangements
- The risk of malignancy exists but the criteria for malignant potential are not fully established
- Differential diagnosis is location dependent

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QUESTIONS:

1) What are the stains that would favor metastatic adrenal cortical carcinoma over PEComa?
   A. SMA (+) and CK8/18 (-)
   B. Melan-A (+) and SMA (+)
   C. Melan-A (+), and inhibin (+)
   D. HMB-45 (+) and inhibin (+)

2) Which of the following criteria is significantly associated with potential malignant behavior in PEComa?
   A. Size >5.0 cm
   B. Infiltrative margins

C. Vascular invasion
D. Necrosis

ANSWERS: 1) C; 2) A

CASE #3
Presenter: Fernando Alekos Ocampo Gonzalez
Attending: Ji-Weon Park

CASE HISTORY: A previously healthy 20-year old man presented to the emergency department with dyspnea on exertion, fever and cough with occasional white sputum for 3 days, and malaise for 7 days. He was seen at an outside clinic 3 days before, presumed to have pneumonia and started on empiric antibiotics with no improvement. On admission, patient was tachypneic, tachycardic, hypoxic and febrile, with coarse breath sounds on examination. A chest CT showed scattered areas of interlobular septal thickening and diffuse ground-glass opacities in both lungs, with associated bronchial wall thickening. Bronchoscopy was performed, with no lesions or secretions identified, and cytology revealed benign clusters of bronchial epithelial cells, scant inflammatory infiltrate and abundant lipid laden macrophages.

DIAGNOSIS: Vaping-induced lung injury

DIFFERENTIAL DIAGNOSIS of Vaping-induced lung injury
- Community acquired pneumonia
- Atypical pneumonia
- Hypersensitivity pneumonitis
- Exogenous lipoid pneumonia
- Drug toxicity (i.e. amiodarone)
- Mycobacterium avium infection.

DISCUSSION:
- Diagnosis of exclusion
- >2000 cases in the USA, >40 deaths
- Lipid-laden macrophage index a consistent BUT non-specific finding
- Oil Red-O stain difficult to perform and interpret – no recommendation to implement if not already experienced on it.
- Vitamin E acetate identified as a toxicant in majority of cases studied in CDC series.

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QUESTIONS:

1) The following is true about vaping-induced lung injury, EXCEPT:
   A. On biopsy, numerous patters of injury, including diffuse alveolar damage and organizing pneumonia have been identified
   B. Lipid-laden macrophages are a pathognomonic finding in VALI
   C. The clinical picture is dominated by respiratory and gastrointestinal findings
   D. A ‘‘probable” case can have positive infectious work-up

2) The following is true about exogenous lipoid pneumonia, EXCEPT:
   A. A foreign-body giant cell reaction is identified
   B. It is classically associated with mineral oil treatments for constipation
   C. Lipid vacuoles in macrophages are coarse
   D. Historically associated with airway obstruction secondary to masses

   ANSWERS: 1) B; 2) D

CASE #4
Presenter: Dr. Subramanya S Mallikarjunappa
Attending: Dr. Ritu Ghai

CASE HISTORY: A 17-year old obese female presented with a self-detected right sided breast mass, present for 4 months. Imaging of the breast demonstrated a solid 4 cm mass in the right breast. The patient underwent a needle biopsy followed by an excisional biopsy of the breast mass.

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DIAGNOSIS:
Extranodal Rosai Dorfman Disease of the breast

DIFFERENTIAL DIAGNOSIS:
- Inflammatory/infectious process
- Langerhans cell histiocytosis
- Non-Hodgkin's Lymphoma
- IgG4 related disease

DISCUSSION:
Histology: Diffuse sheets of lymphoplasmacytic infiltrate and large histiocytes with abundant clear to eosinophilic cytoplasm, round to oval basophilic nuclei, inconspicuous nucleoli with emperipolesis.

Large histiocytes positive for S-100, CD68, CD163 and negative for CD1a.
IgG4 mildly increased (IgG4/IgG=25%) in our case.

Pathophysiology: Suggested Autoimmune/infectious etiology, incompletely understood
Relationship to IgG4 related disease: Mixed literature reviews; some studies supporting it to be a spectrum of the same disease while others indicating that they are two different entities. More research needed to understand the relationship between the two.

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QUESTIONS:

1) A 25-year old female presented with a right breast mass. Imaging showed a 3 cm solid nodular mass in the right breast. A core needle biopsy was performed which showed a diffuse infiltrate of lymphoplasmacytic cells and large histiocytes. The histiocytes are positive for S100, CD68 and CD163. Which of the following features helps in the diagnosis of Extranodal Rosai Dorfman disease?
   A. High mitotic rate
   B. Storiform fibrosis and obliterative phlebitis
   C. Histiocytes engulfing the lymphocytes
   D. Positive fungal stains
   E. Granulomas with necrosis

2) A 30-year old female presented with a chronic swelling in the submandibular region. Physical examination shows a mildly tender mass in the right submandibular region. Imaging shows an ill-defined 3 cm mass. Biopsy of the mass shows a diffuse lymphoplasmacytic infiltrate, with storiform fibrosis and areas of obliterative phlebitis. A diagnosis of IgG4 related disease is made. Which of the following features support the diagnosis?
   A. IgG4/IgG ratio of 50%
   B. Associated salmonella infection
   C. Ki67 of 80%

D. Emperipolesis
E. CD1a positivity for neoplastic cells

ANSWERS: 1) C; 2) A

CASE #5
Presenter: Josean Ramos, MD
Attending: Lin Cheng, MD, PhD

CASE HISTORY: 55-year-old female with past medical history of tobacco smoking (20 pack-years), systemic lupus erythematosus and hypertension presented with a palpable cervical lymph node (Jan. 2018). A biopsy of the lymph node was attempted at an outside hospital which showed no evidence of malignancy. She continued to have persistent lymphadenopathy and underwent excisional biopsy of the cervical lymph node (Sept. 2018), which showed metastatic non-keratinizing squamous cell carcinoma, grade 3. During further workup, PET CT was obtained which showed a hypermetabolic well-circumscribed nodule on the left lower lobe of the lung (2.3 cm). CT-guided biopsy of the lung nodule was performed with subsequent left lower lobe wedge resection and right neck dissection. No additional foci of malignancy, involved lymph nodes or palpable masses were identified. H&E stained slides of the left lower lobe wedge resection specimen are submitted for your review.

DIAGNOSIS: Primary mammary-analogue secretory carcinoma of the lung

DIFFERENTIAL DIAGNOSIS:
- Metastatic mammary-analogue secretory carcinoma
- Primary lung tumors
  - Adenocarcinoma
  - Mucoepidermoid carcinoma
  - Acinic cell carcinoma

DISCUSSION:
- Mammary-analogue secretory carcinoma of the lung is a very rare tumor with only one other case reported in the literature
- Generally a low-grade lesion with diverse morphologic features and almost invariably eosinophilic (colloid-like) secretions
- IHC (e.g. mammaglobin and S100 protein) are sensitive but not specific for establishing the diagnosis of MASC.
- Morphologic mimics can be ruled out by characteristic ETV6 gene rearrangement

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QUESTIONS:

1) What is the most common translocation partner of ETV6 gene, seen in secretory carcinoma?
   A. MAML2
   B. NTRK3
   C. EWSR1
   D. RUNX1

2) ETV6 translocation can be seen in which of the following tumors?
   A. Mammary-analogue secretory carcinoma
   B. Congenital cellular mesoblastic nephroma
   C. Familial thrombocytopenia
   D. AML
   E. All of the above

Answers: 1) B; 2) E

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CASE #6
Presenter: Karina Furlan, MD
Attending: Ira Miller, MD, PhD

CASE HISTORY: A 48-year old female with history of right foot pain with unremarkable past medical history, except for plantar fasciitis on the right foot and intermittent pain. Over time she noticed increased pain when touching certain areas of her right ankle and foot. She had an MRI done, which showed multicentric soft tissue tumors involving the right foot and ankle. The orthopedic surgeon performed a needle biopsy which showed mature adipose tissue and increased benign vascular structures, suggestive of angiolipoma. An excisional biopsy was performed to obtain additional tissue for further evaluation. On follow up, she continued to have some pain, edema and difficulty walking. Complete resection was not possible given the multi-focal nature of the lesion.

DIAGNOSIS: Glomangiomatosis

DIFFERENTIAL DIAGNOSIS:
- Fibroblastic tumors: Solitary fibrous tumor
- Synovial sarcoma
- Vascular tumors: Glomangiopericytoma (sinonasal hemangiopericyoma), angiomatosis, glomus tumor
- Smooth muscle tumors: low-grade leiomyosarcoma

DISCUSSION:
Background
Glomangiomatosis is a benign vascular variant of glomus tumor. The majority of glomus tumors are small, benign neoplasms that occur in the dermis or subcutis of the extremities, most commonly on the nail bed. However, occasional glomus tumors may show unusual clinical features, such as large size, deep soft tissue and infiltrative growth pattern. These lesions are most commonly located in the distal extremities and are multiple and often painful (1).

Gould et al (1) first attempted a classification for glomus tumors in 1990. They studied six atypical glomus tumors and proposed the term locally infiltrative glomus tumor for cytologically bland tumors with infiltrative growth pattern and glomangiosarcoma de novo for malignant-appearing tumors with or without identifiable benign glomus.

The term glomangiomatosis was described by Folpe et al (8). It represents a benign glomus tumor with histologic features of diffuse angiomatosis with excess of glomus cells. The tumor develops from small arteriovenous anastomoses, called Sucquet-Hoyer canals and is most often identified in young adults. The lesions usually recur (1). The most common primary sites are:

ankle and foot (2–4, 8), with isolated case reports involving neural structures as sciatic and sural nerves (5,6) and paraspinal region (7).

A familial form of glomuvenous malformation is recognized, however the tumors have superficial location and histologically show dilation of vessels, instead of proliferation, with variable glomus cell component. The lesions are present at birth with slow expansion during childhood. An inherited mutation on the glomulin gene (1p21-22) resulting in loss of function and aberrant transcripts was identified in 162 families with different clinical presentations of glomuvenous malformation (12). It is believed that it segregates as an autosomal dominant disease with variable expressivity and incomplete penetration. Despite the lack of clinical similarities between glomuvenous malformation and glomangiomatosis, the histologic similarities raise the possibility of an involvement of the glomulin gene on these cases.

Glomangiomatosis is considered a benign condition with no risk of metastasis; however the multi-focal nature of the disease and the potential infiltration of surrounding structures can lead to severe limitations. Prognostically; it is not well known if these patients will have progression of the disease.

Histological Findings

- Vascular proliferation of different calibers (capillaries, arterioles and venules) with irregular configuration, positive by immunohistochemistry to CD34 and collagen type IV (9,10).
- Proliferation of round to oval cells, positive by immunohistochemistry to smooth muscle actin and/or pan-muscle actin; surrounded by basement membrane, highlighted by PAS, collagen type IV and reticulin.
- A subset of tumors immunostain positive for cytokeratins, S100 protein, desmin, vimentin, calponin and caldesmon (8, 11).

Clinical Presentation

- Early adult age
- Pain and limitation to walk
- A nodular or tumoral lesion can be appreciated clinically in some cases

Treatment

- Surgical excision; however in most of the cases a complete resection is not possible due to multi-focality
- Radiation therapy is proposed however there is poor experience and uncertain results.
- Finally, due to extenuating symptoms, some patients decide to undergo amputation

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QUESTIONS:

1) What histological features are helpful to diagnose benign glomus tumors?
   A. Spindle cell proliferation in a mono or biphasic pattern with staghorn-shaped vessels
   B. Fibroblastic proliferation in a patternless pattern interspersed with irregular vessels
   C. Proliferation of fusiform cells with blunt end-shaped nuclei and variable number of mitosis
   D. Proliferation of round to oval shaped cells with bland morphology interspersed with staghorn-shaped vessels

2) When diagnosing glomus tumors; besides smooth muscle actin immunostain, what other immunostains or special stains can show positivity?
   A. STAT-6
   B. Nuclear B-Catenin
   C. Caldesmon
   D. CD20

ANSWERS: 1) D; 2) C