Disclosures February 5, 2018

The following planners and faculty had no financial relationships with commercial interests to disclose:

Presenters

Hannes Vogel, MD

Jonathan Lavezo, MD

Erna Forgo, MD

Keith Duncan, MD

Kelly Mooney, MD

Kevin Ko, MD

Christine Louie, MD

Bart Singer, MD

John Higgins, MD

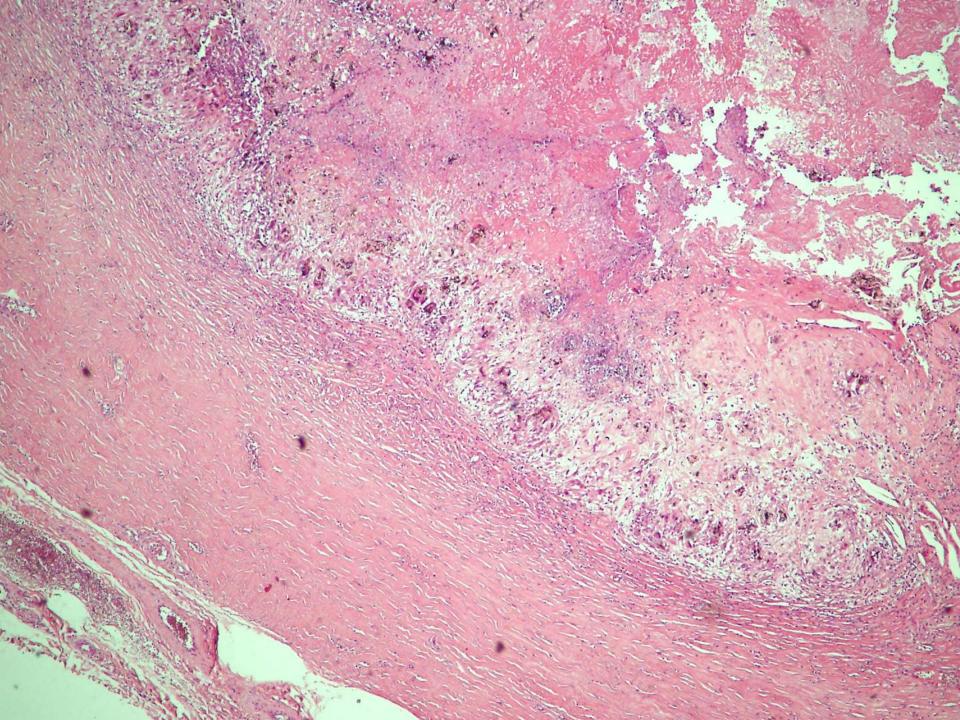
Justin Cuff, MD

Nabeen Nayak, MD

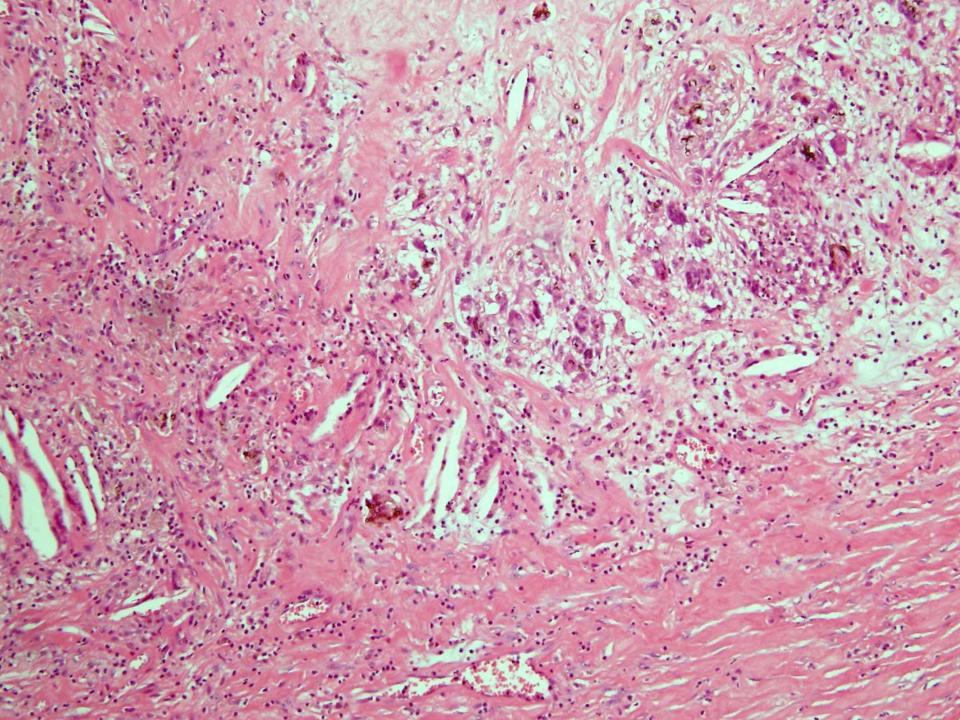
Activity Planners/Moderator: Kristin Jensen, MD Ankur Sangoi, MD Megan Troxell, MD, PhD

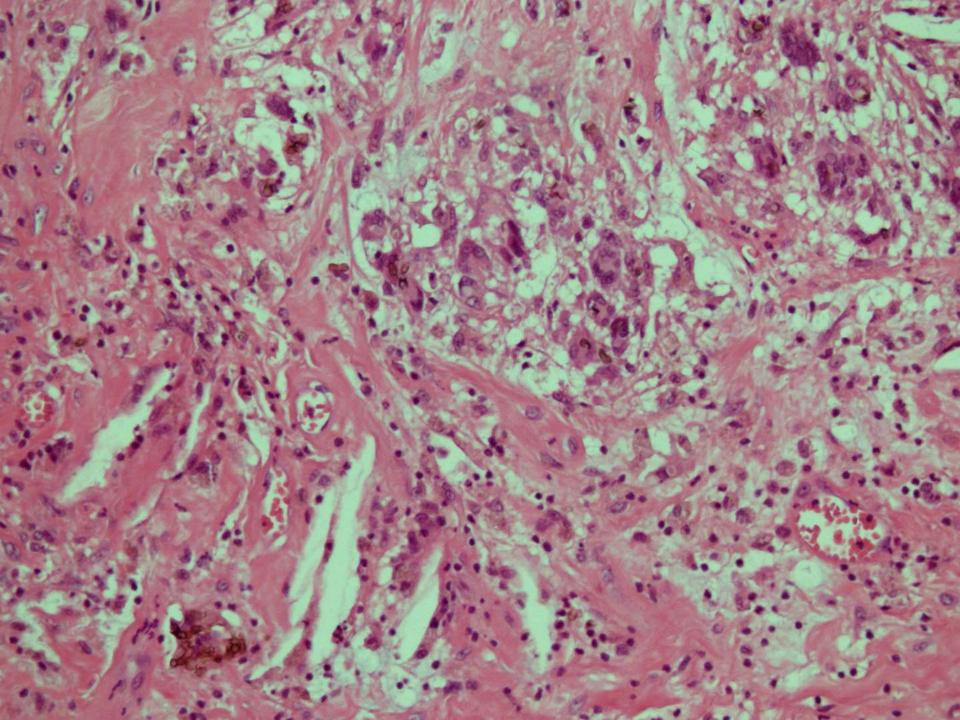
SB 6241

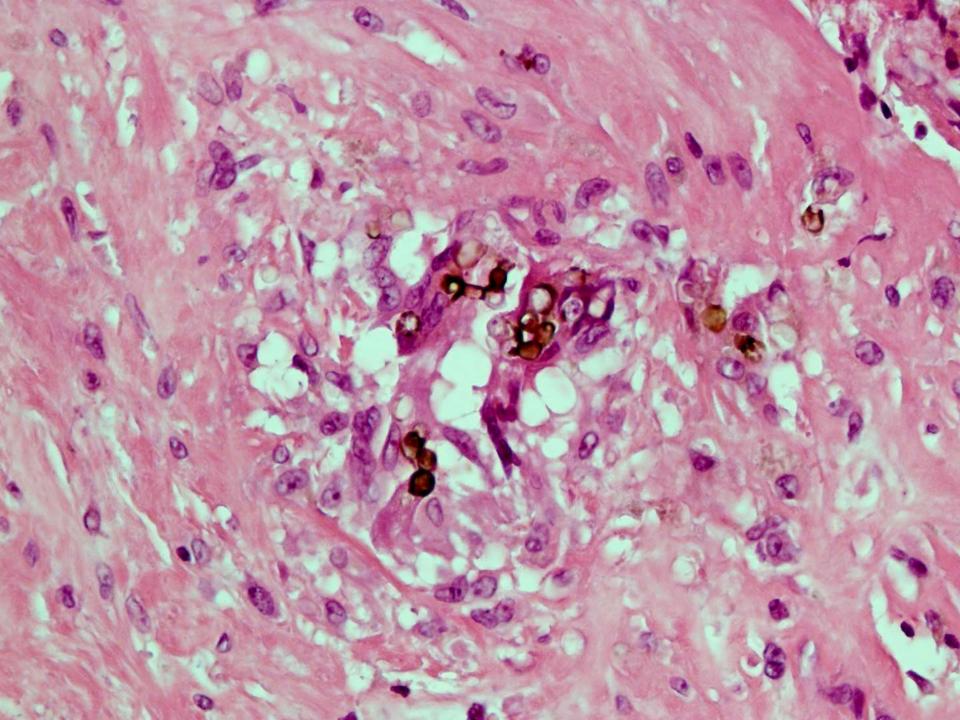
Nabeen Nayak; Sir Ganga Ram Hospital, New Dehli 71-year-old male with nodular, partly ulcerated skin lesions in both feet.

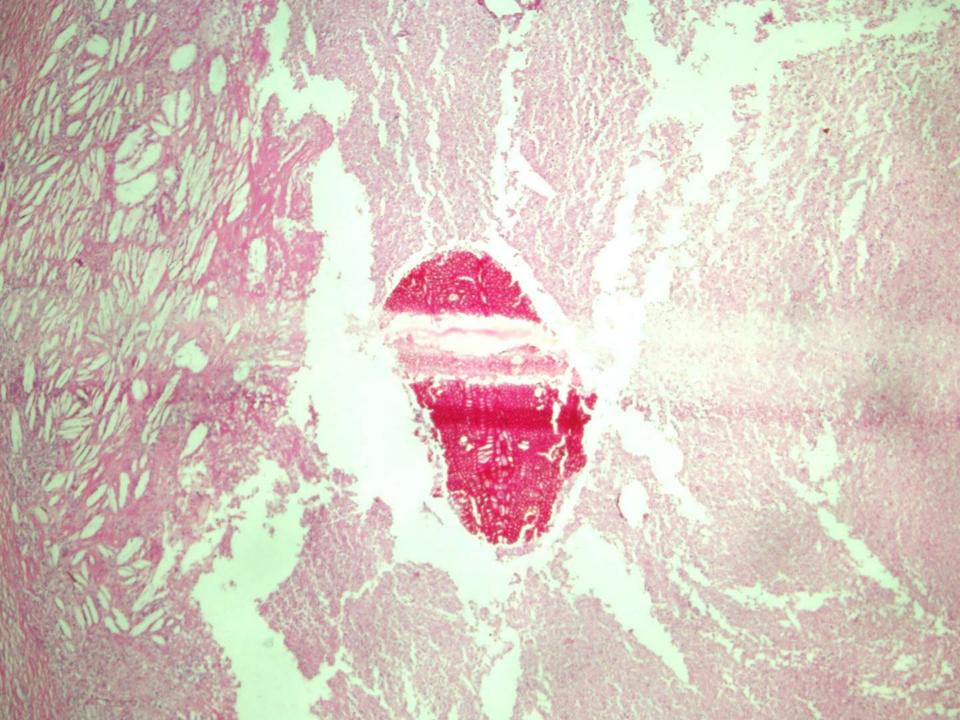


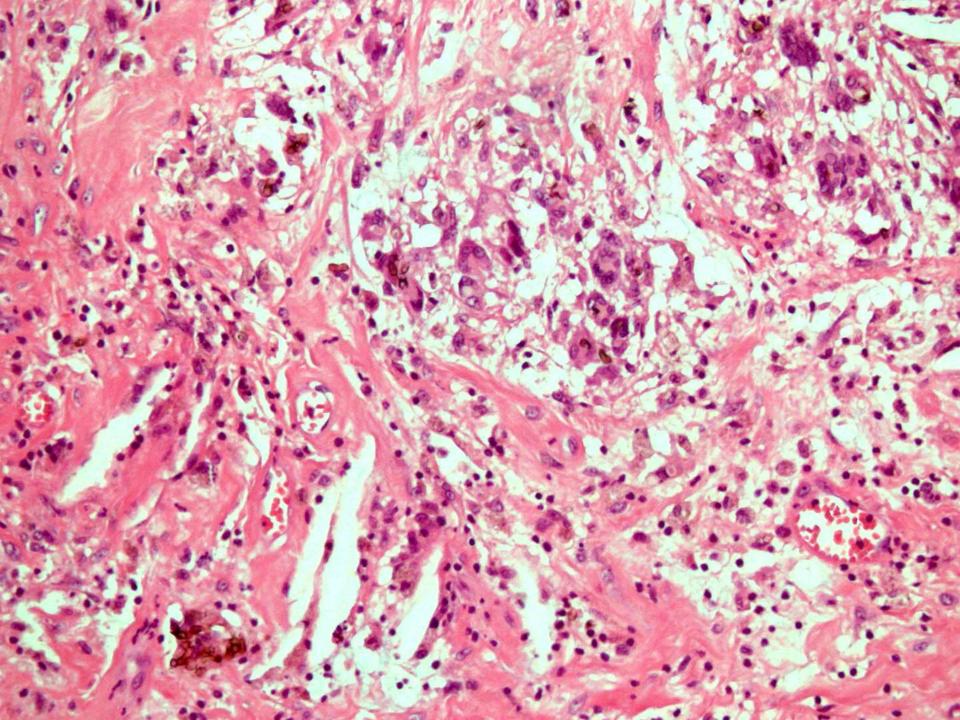
PAS stain

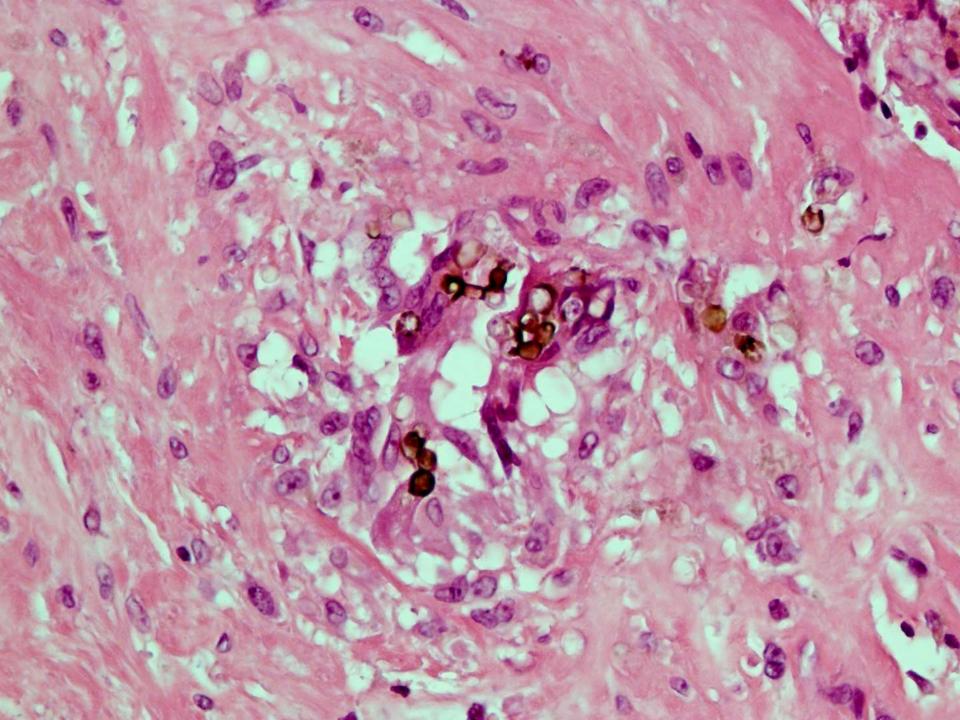


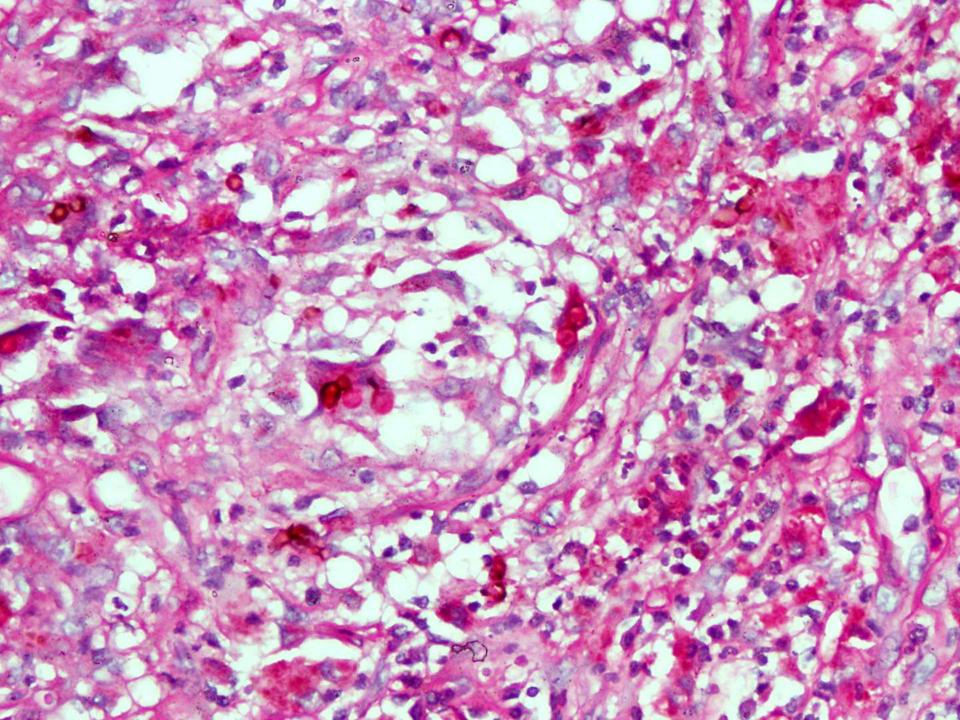


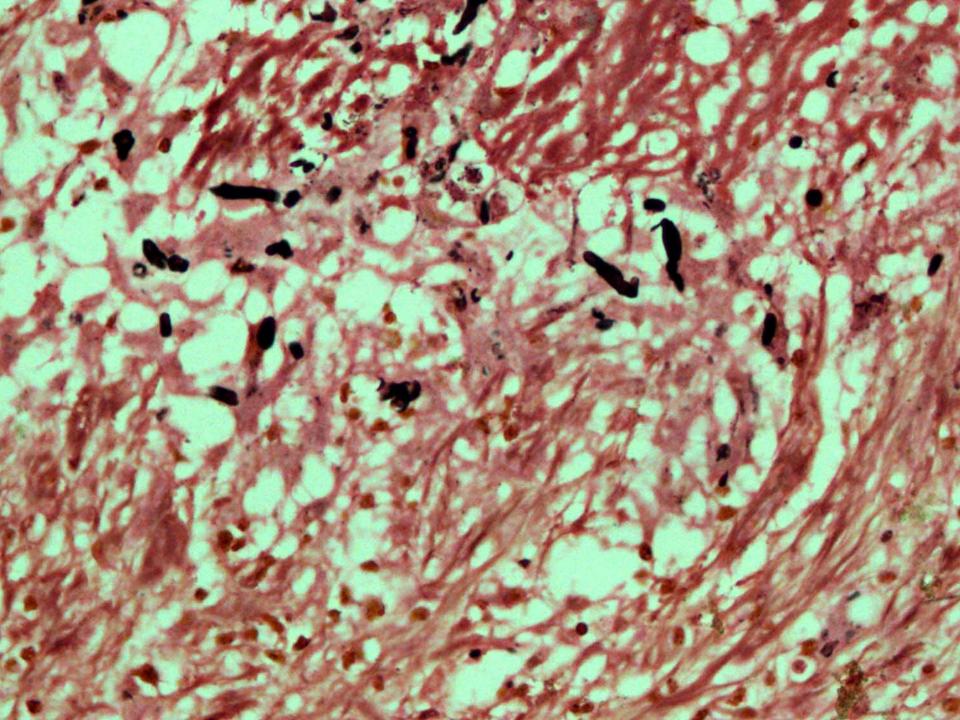


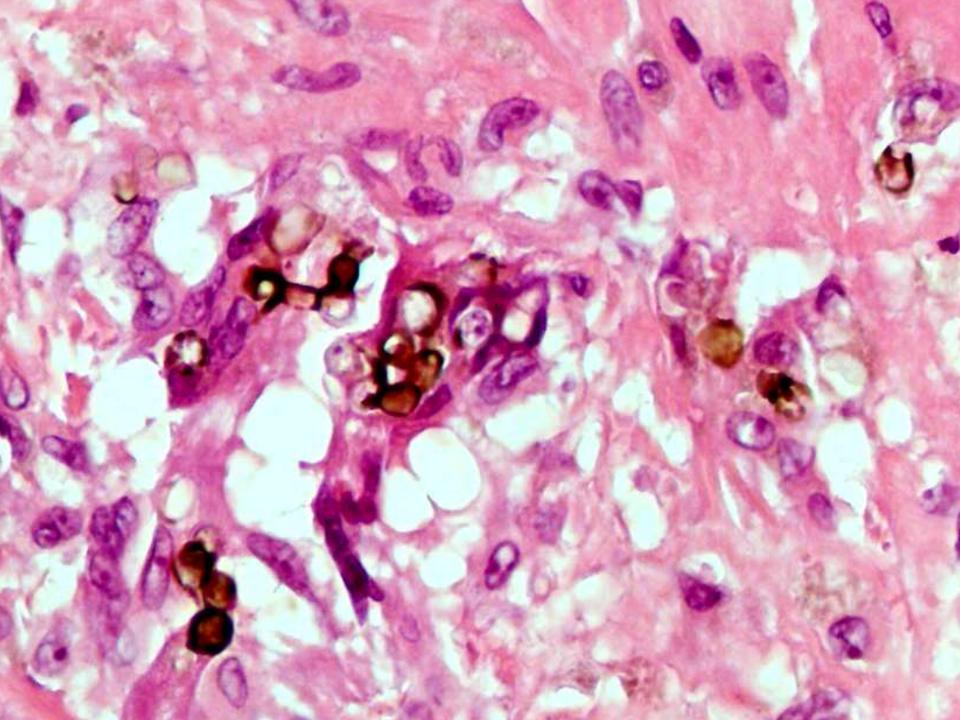






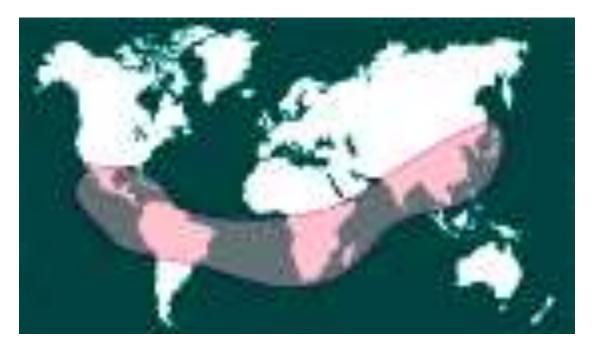






DIAGNOSIS: Chromoblastomycosis, skin and subcutaneous soft tissues of foot.

This infection, commonly affecting the skin and subcutis of the extremities, is caused by 6-7 different species of a dermatiaceous fungus, the most frequent one among which is *Funsecaea pedrosoi* (about 80% cases).



Geographical distribution of chromoblastomycosis based on CDC, and the Pub Med Base review

-The fungus grows on decayed wood, grass and leaves on the ground and is implanted in the human tissue through wounds (commonly in bare-footed farmers).

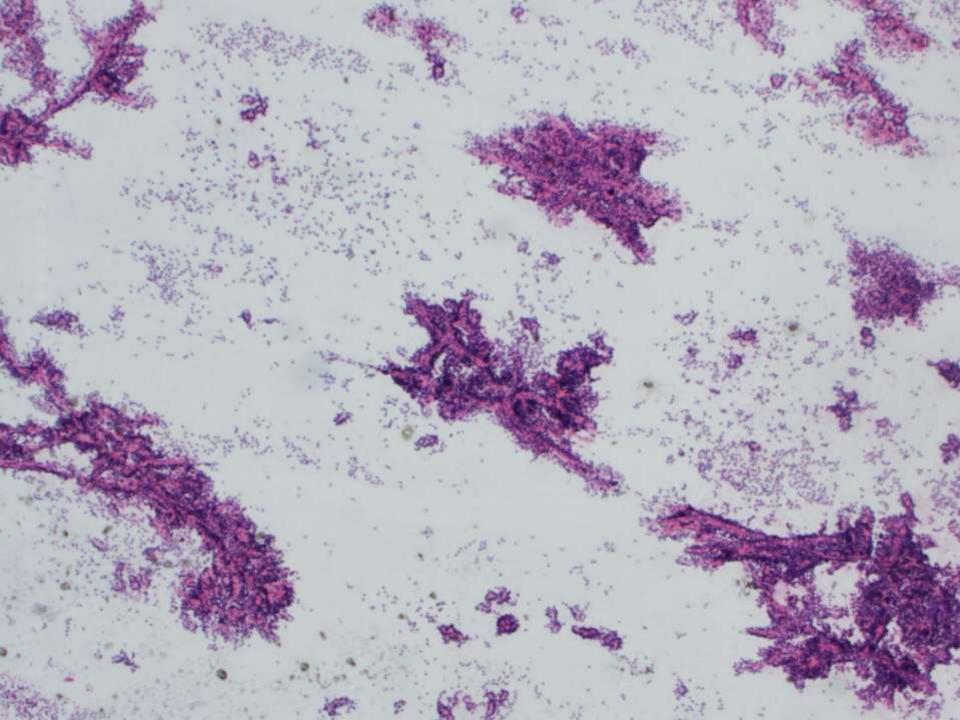
-The disease is chronic and very prolonged, fatality being extremely rare.

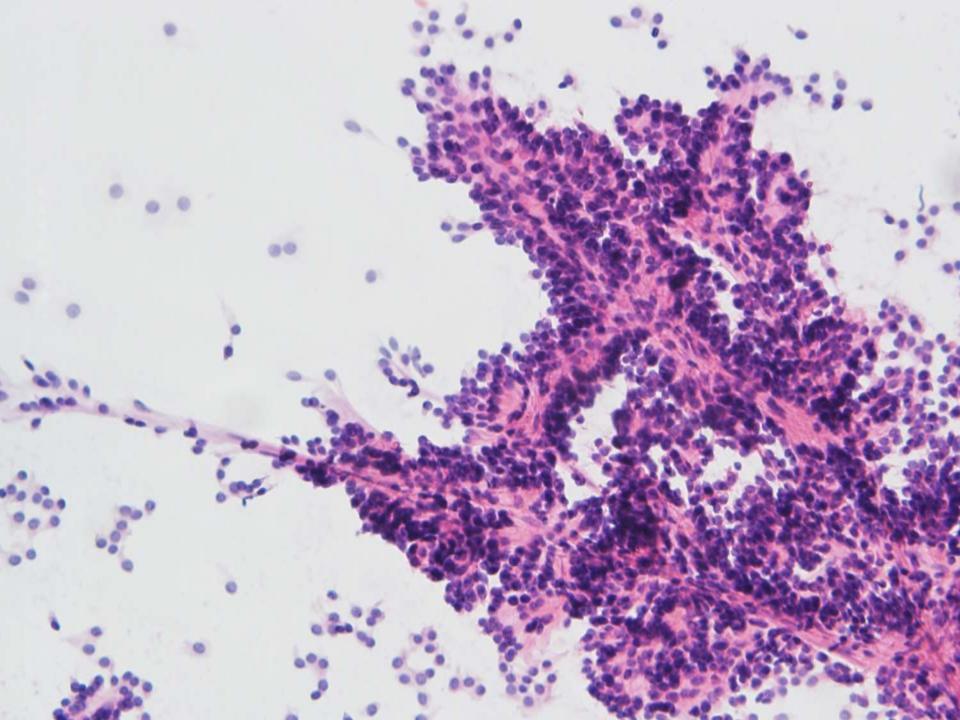
- Histological diagnosis is based on granulomatous/necrotic lesions with the so-called "Sclerotic" or "Medlar" bodies having dark brown, cigar colored round or cylindrical fungi which frequently divide by equatorial septation.

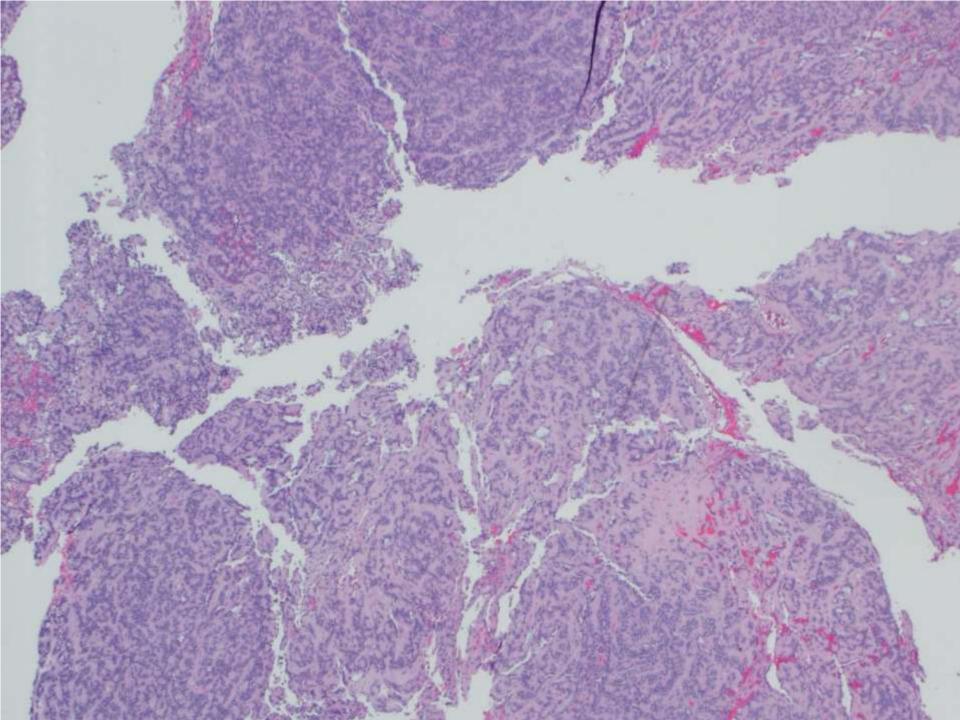
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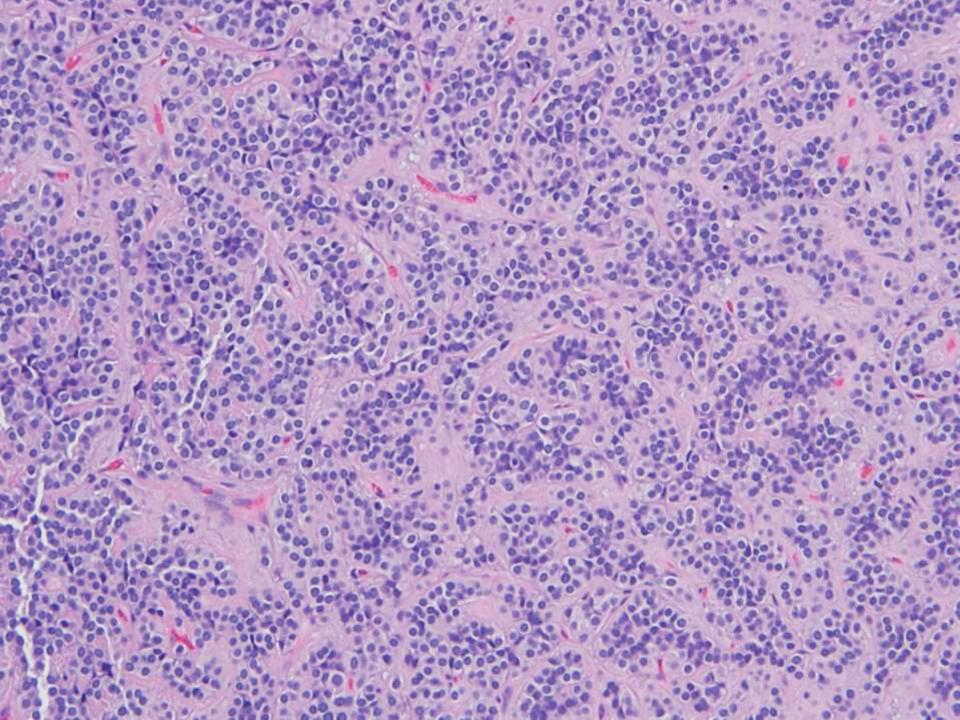
Jonathan Lavezo/Erna Forgo/Hannes Vogel; Stanford

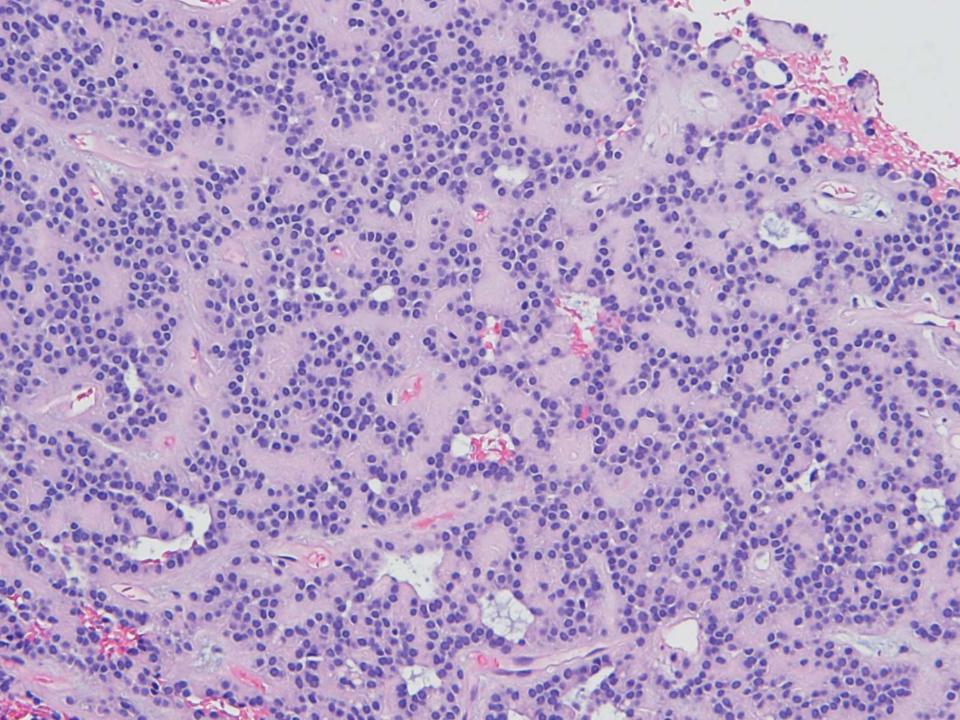
62-year-old female with an intramuscular right cervical paraspinal mass.

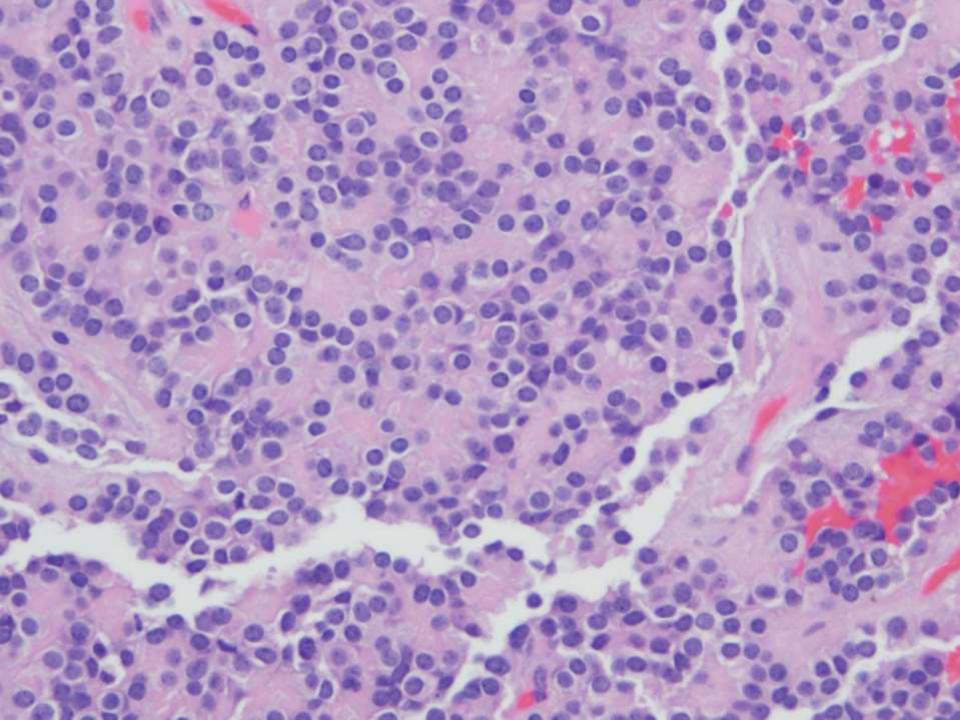


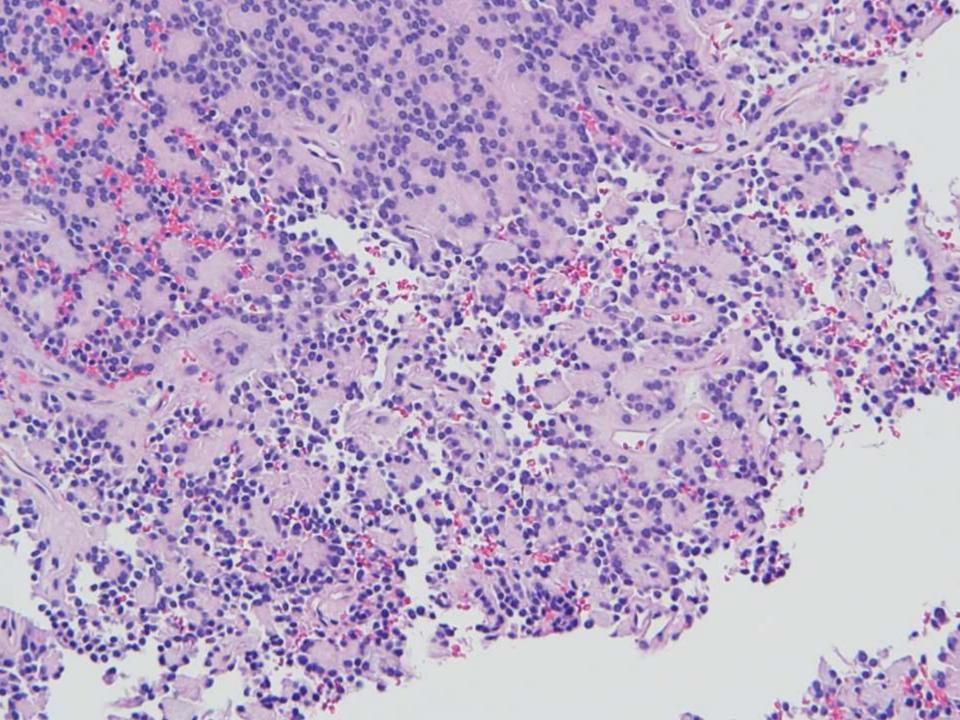






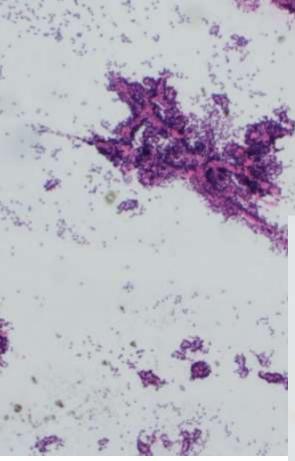


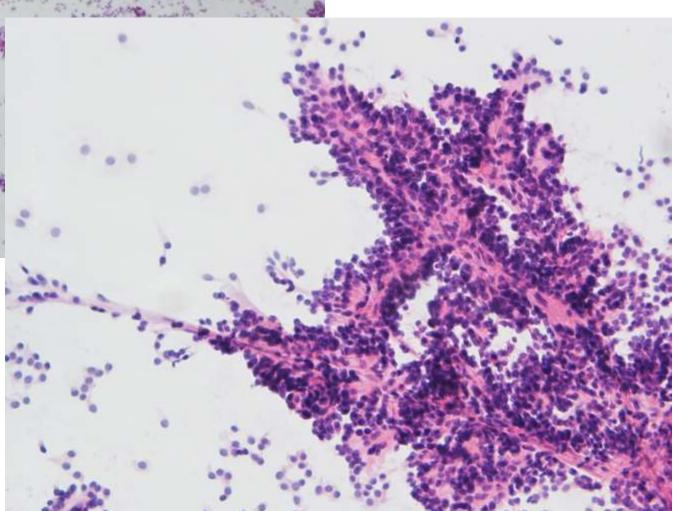


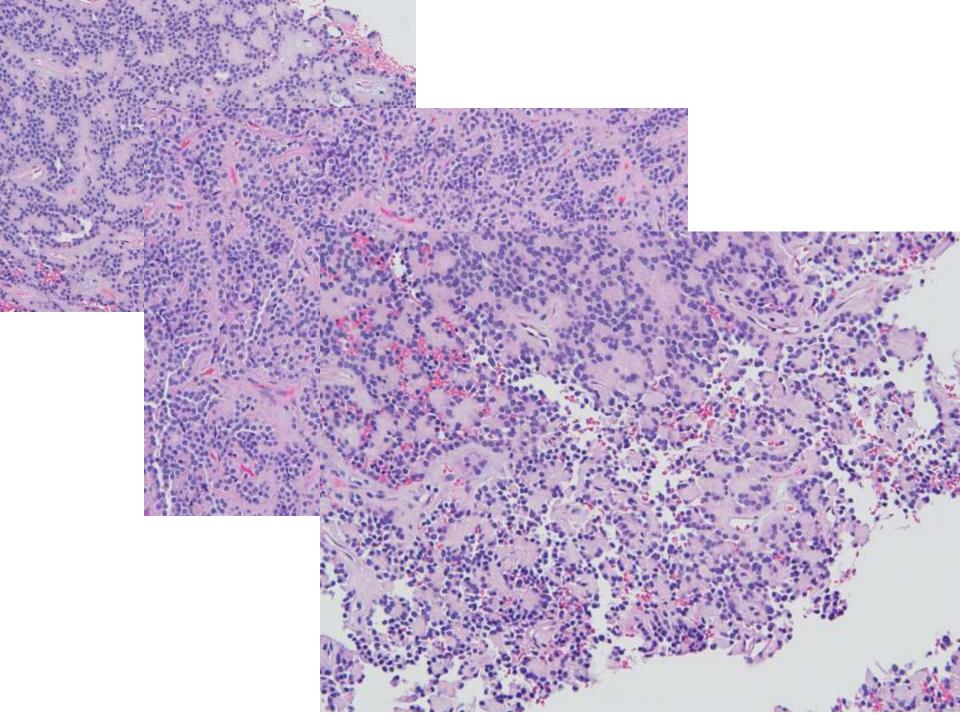


February 2018 - South Bay

Lavezo/Forgo/Vogel Stanford University

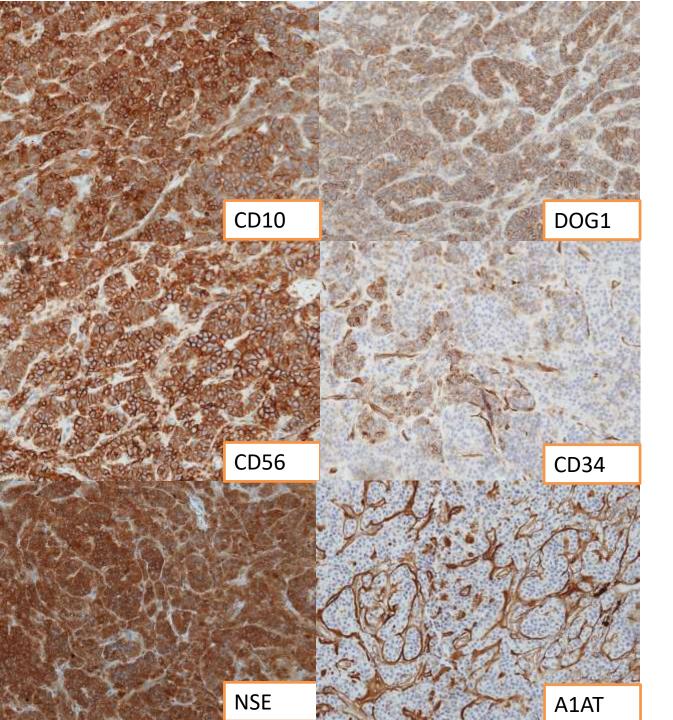




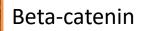


Differential Diagnosis

- Neuroendocrine tumor
- Glomus tumor
- Myxopapillary ependymoma
- Metastatic neoplasm
 - Salivary gland
 - Breast
 - Others



Negative SYNAP **CHROMO** INHIBIN PR CKMIX CK7 CK20 CAM5.2 **E-CADHERIN** P63 PAX8 TTF1 STAT6 S100 SOX10 **MELAN-A** HMB45 SMA DESMIN CALDESMON **MYOGENIN** ERG CD31



Sequencing Results

- MUTATIONAL PROFILING BY STAMP
 POSITIVE FOR CTNNB1 S37F MUTATION
 - -- POSITIVE FOR TERT PROMOTER MUTATION

Solid Pseudopapillary Neoplasm

- Low-grade malignant neoplasm
 - 0.9-2.7% of all exocrine pancreatic neoplasms
 - Predominantly in adolescent girls and young women (90% female; age range 7-79)
 - Metastases occur in 5-15% of cases
 - Usually peritoneum and liver
 - Exceptionally rare sites of metastases include lymph node and skin
 - Origin outside of the pancreas is uncommon with reports of retropancreatic, mesocolon, and ovary

Extrapancreatic Solid Pseudopapillary Neoplasm??

- Negative CT of chest, abdomen, and pelvis.
- Negative PET scan
- No residual neoplasm of post-operative MRI

References

- WHO Classification IARC Tumours of the Digestive system. Fourth Edition. 2010.
- Deshpande V. et. al. Solid pseudopapillary neoplasm of the ovary: a report of 3 primary ovarian tumors resembling those of the pancreas. Am J Surg Pathol 2010 Oct; 34(10):1514-20.
- Guo X. et. al. Extrapancreatic solid pseudopapillary tumors: A clinicopathological analysis of two cases. Mol Clin Oncol. 2016 May: 4(5): 845-850.

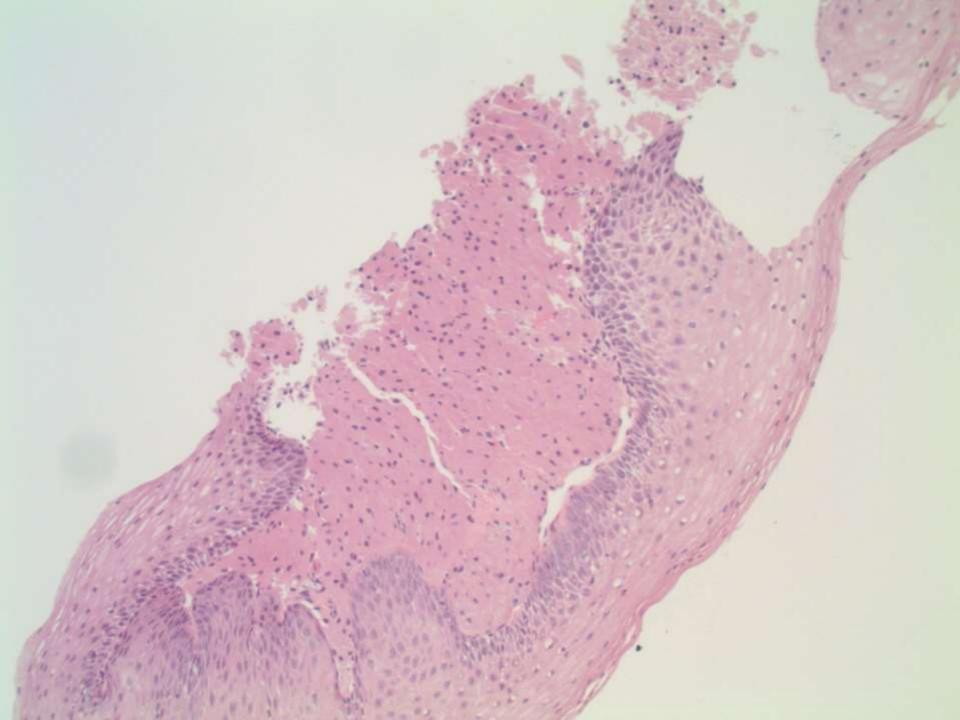
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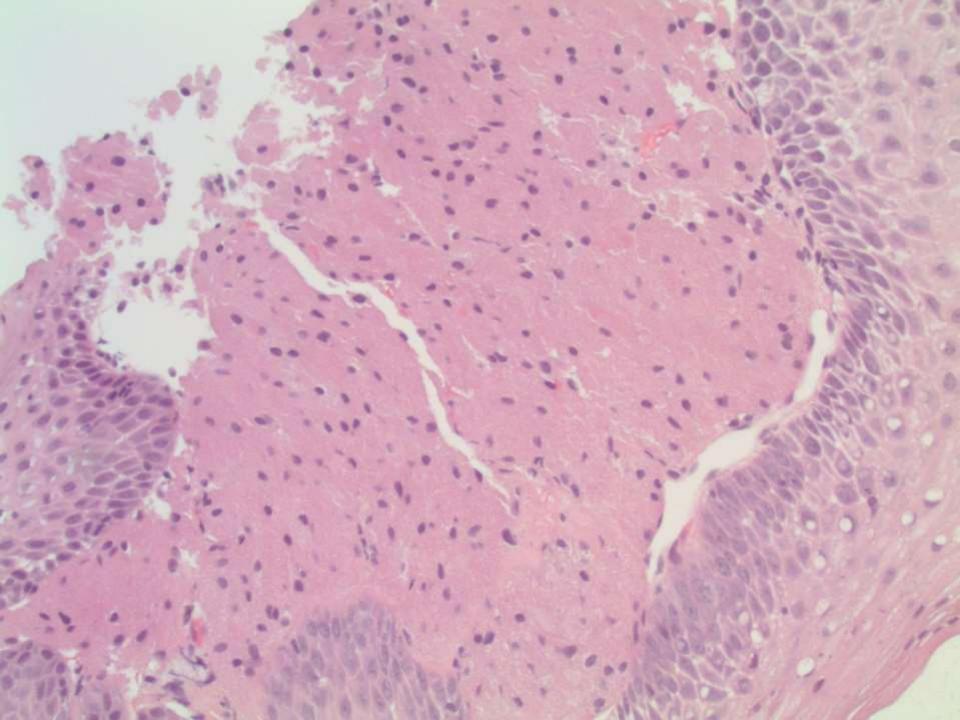
Keith Duncan; Mills-Peninsula

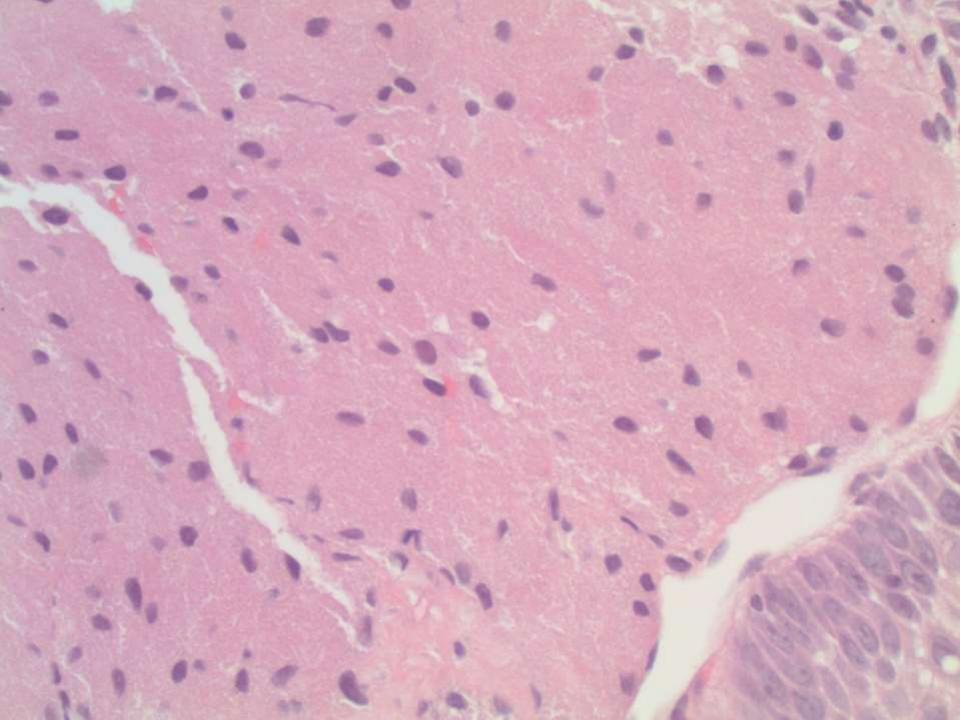
40-year-old female presents to GI doctor for upper abdominal pain. Pan-endoscopic work-up reveals small esophageal nodule which was biopsied.





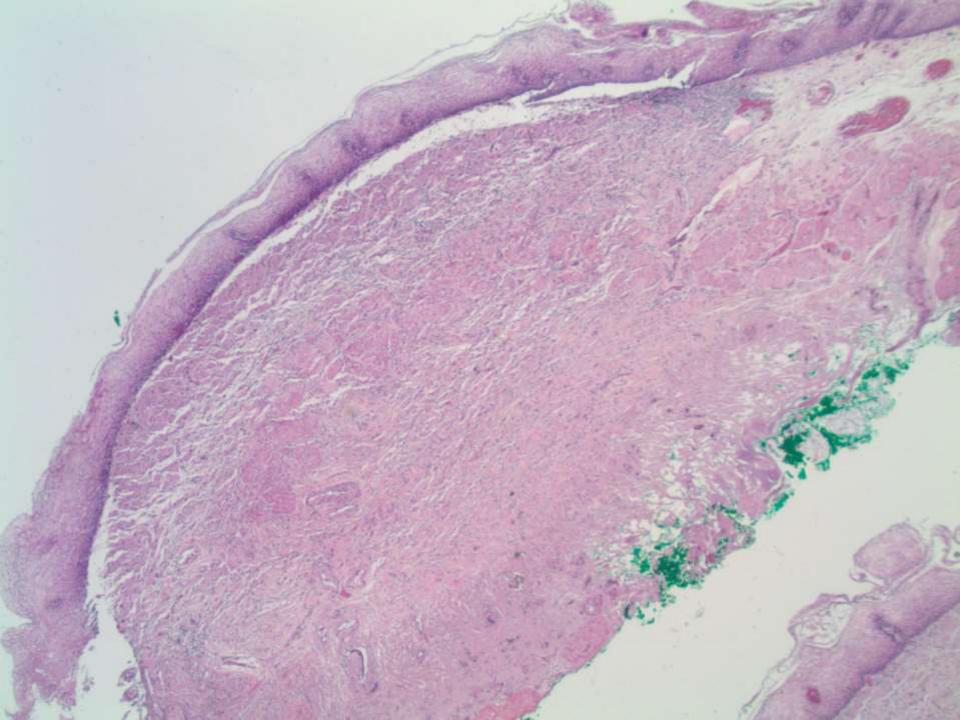


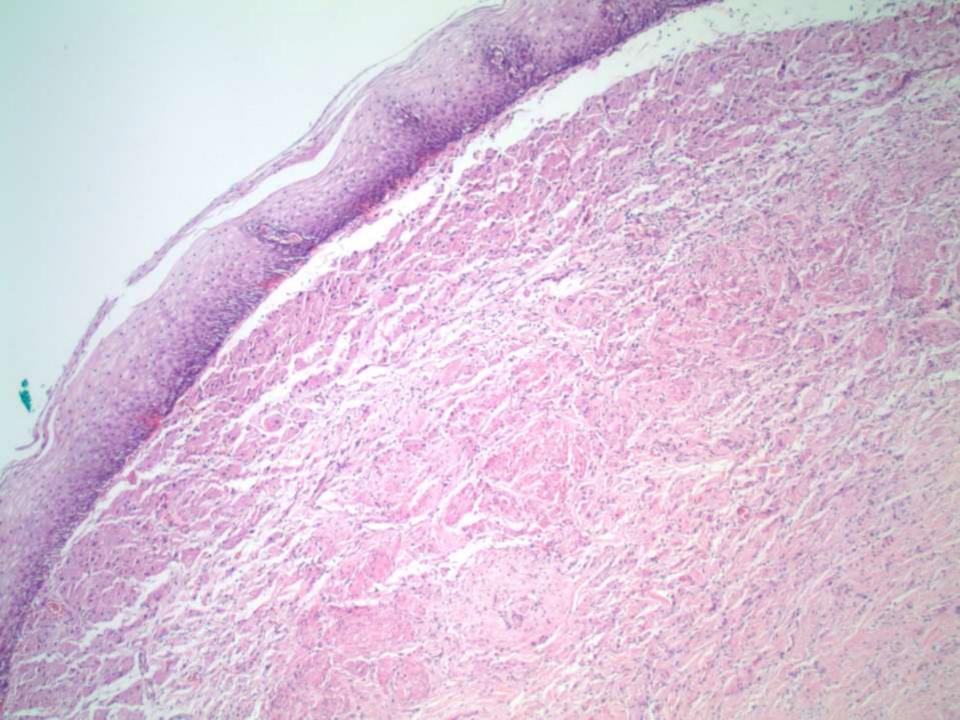


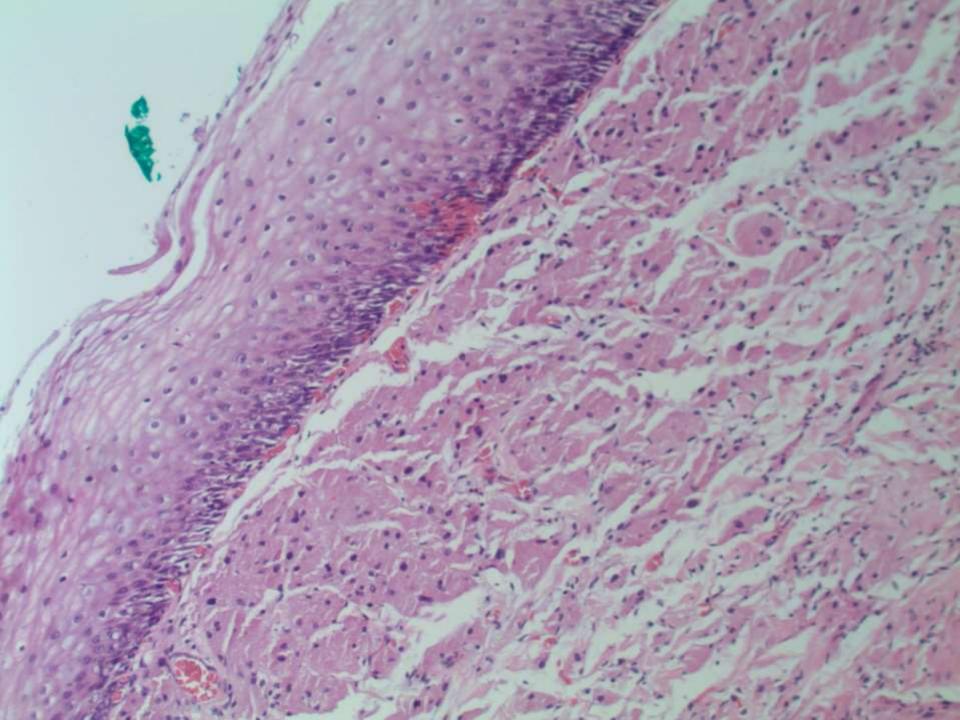


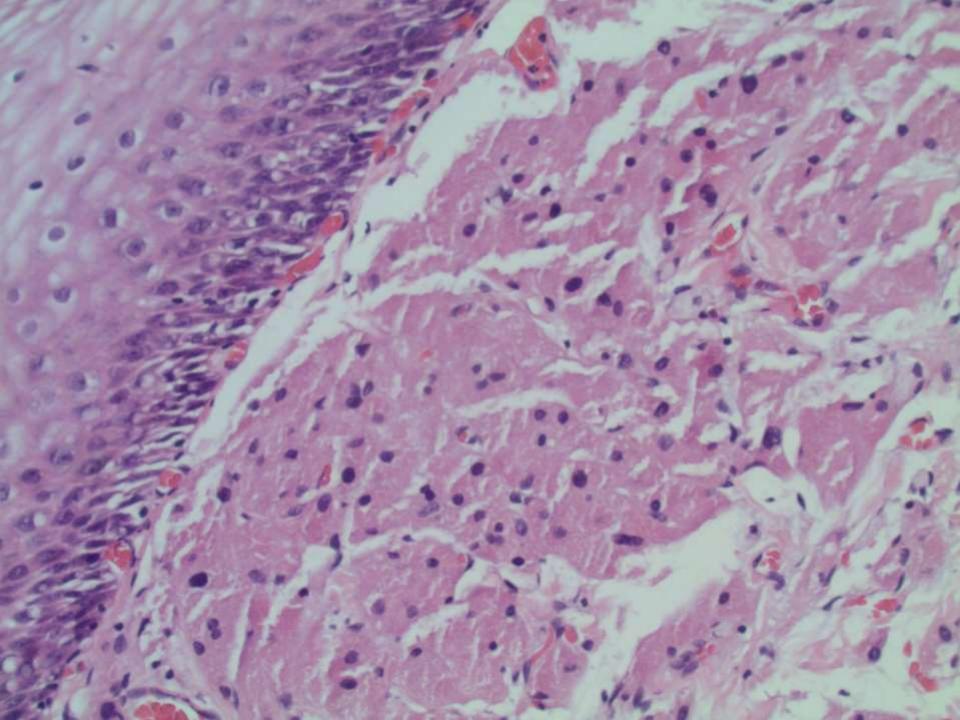


S100









Granular cell tumor of the Esophagus

- Most common site in GI tract
- #2 most common stromal tumor of esophagus after leiomyoma
- Usually incidental, in lower esophagus, 90% solitary
- May cause obstruction if large

Granular cell tumor of the Esophagus Clinical features

- Schwannian origin
- Most common in women in 40s, African American
- May be underdiagnosed on superficial biopsies
- **Endoscopy:** sessile, yellowish white, firm, intact epithelium
- 1 3% are malignant (locally recur)
 - Associated with rapid growth, > 4 cm, tumor necrosis, increased cellularity, atypia, > 2 mitotic figures/HPF

Microscopic description

- Sheets/packets of uniform epithelioid cells with abundant eosinophilic granular cytoplasm and small nuclei
- Often pseudoepitheliomatous hyperplasia, which may mimic squamous cell carcinoma on small biopsies

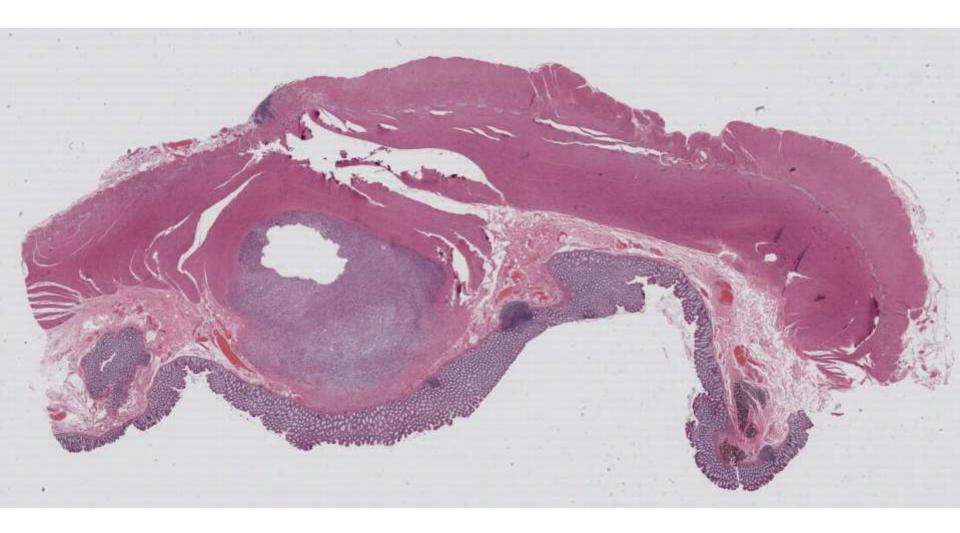
Positive stains

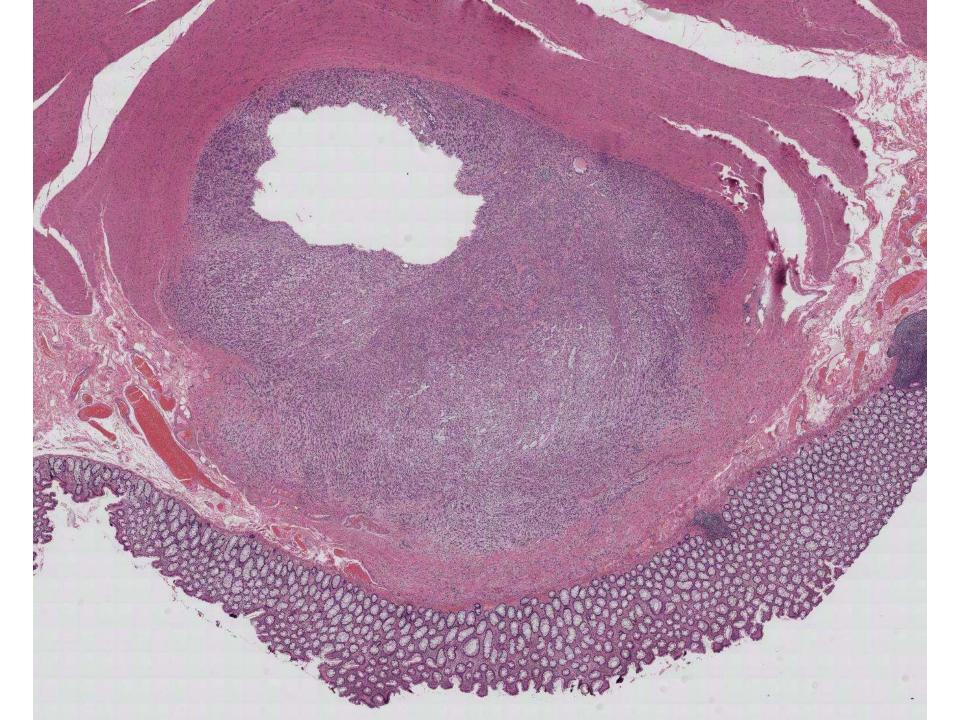
 PAS, S100, inhibin alpha subunit, CD68, calretinin

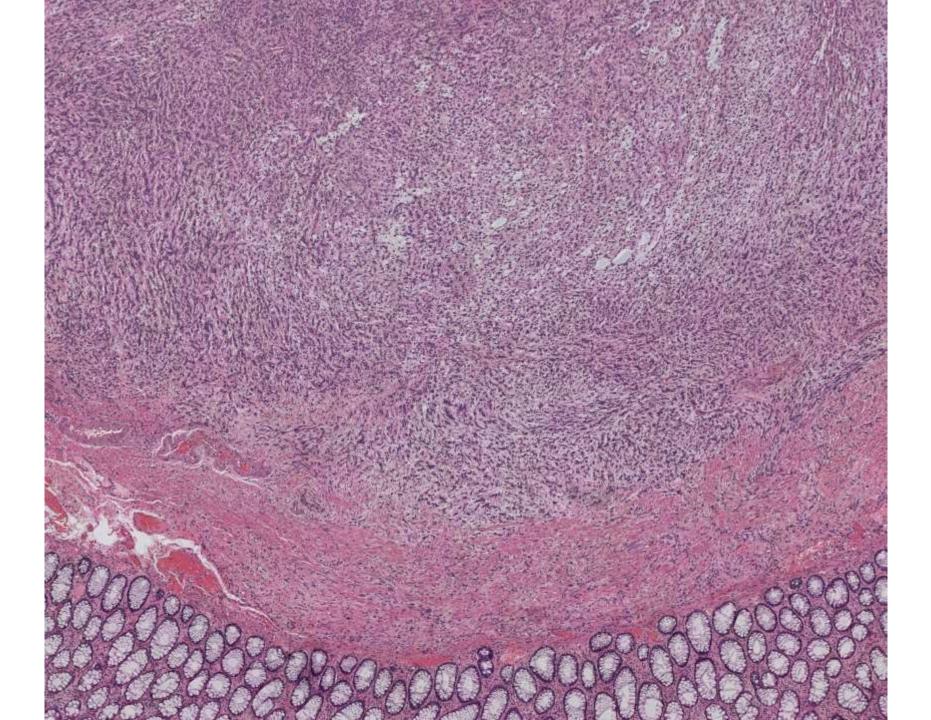
 Thumallapally et al: "Esophageal granular cell tumor: A case report and review of the literature." Cureus 8 (9): e782.

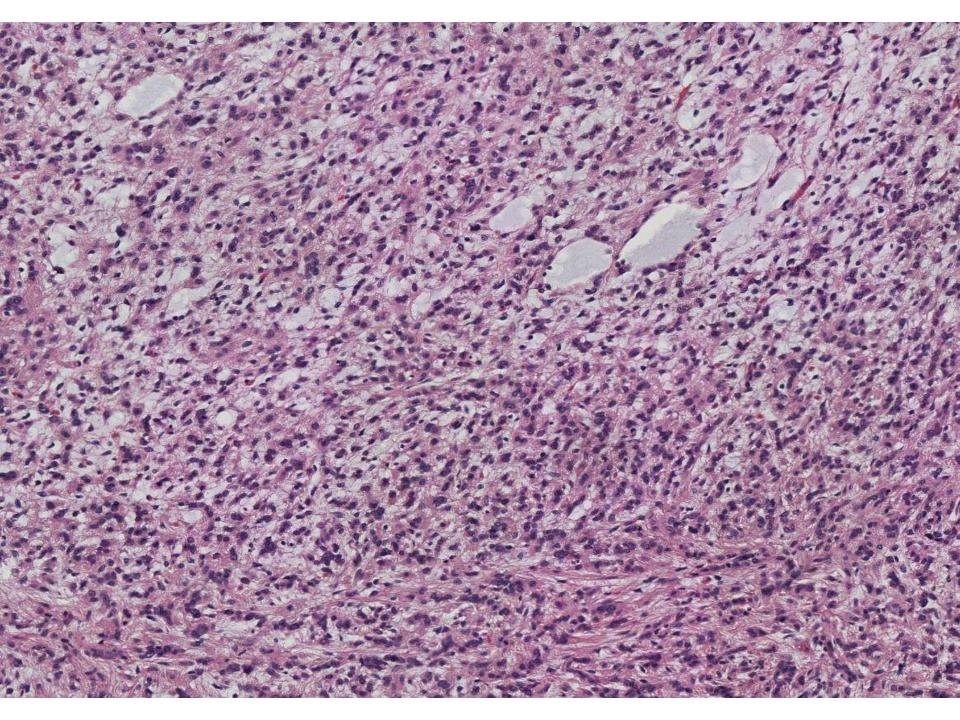
SB 6244 (scanned slide available)

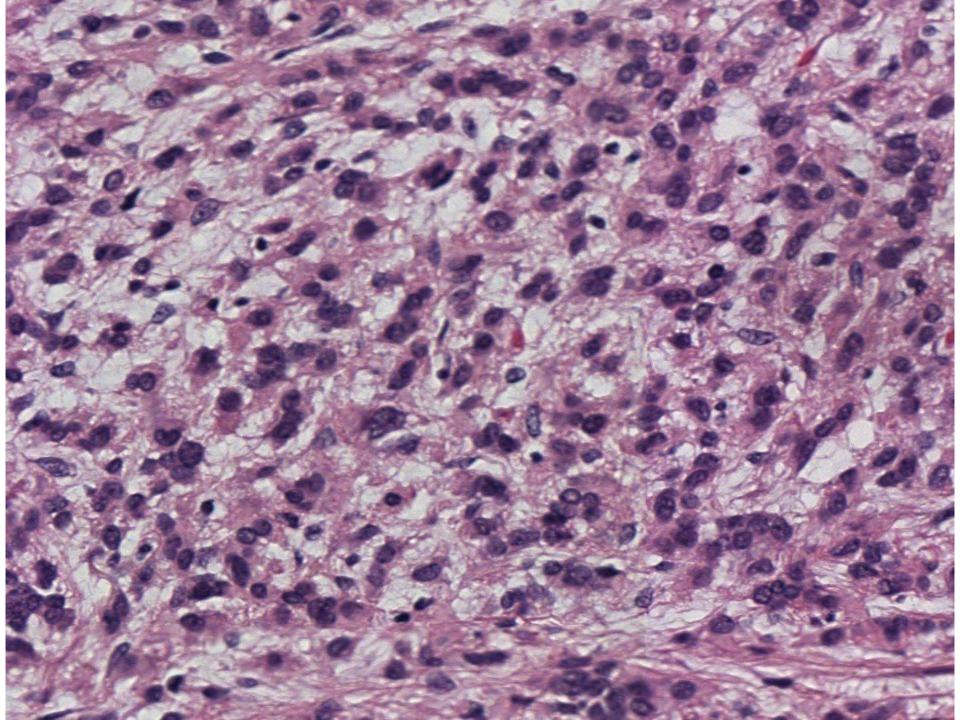
Justin Cuff; Mills-Peninsula 72-year-old female with 1.5cm sigmoid colon mass.

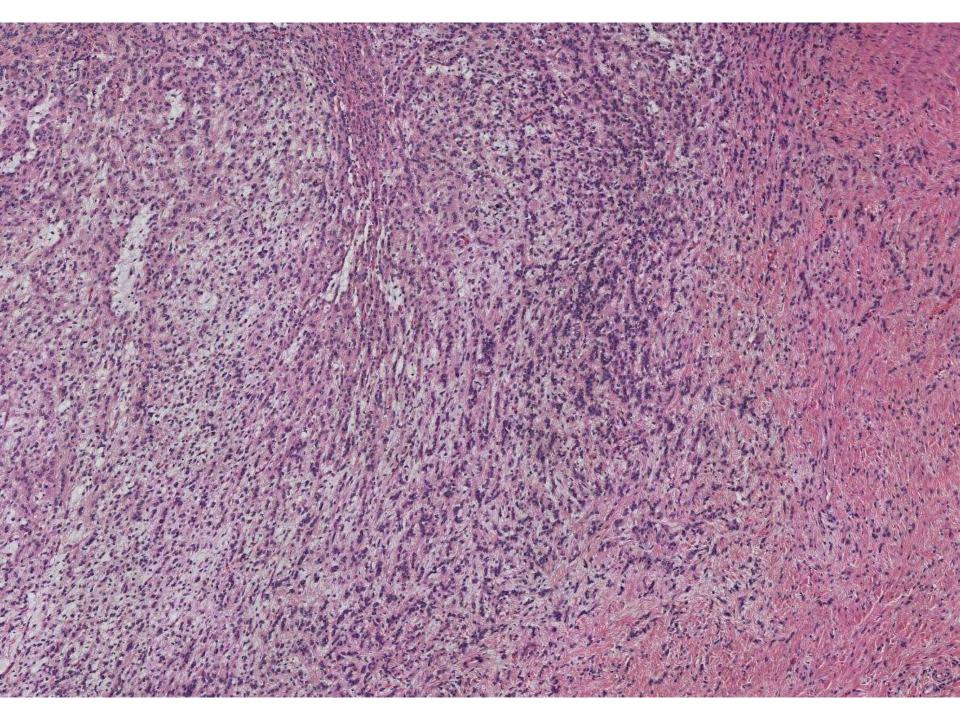


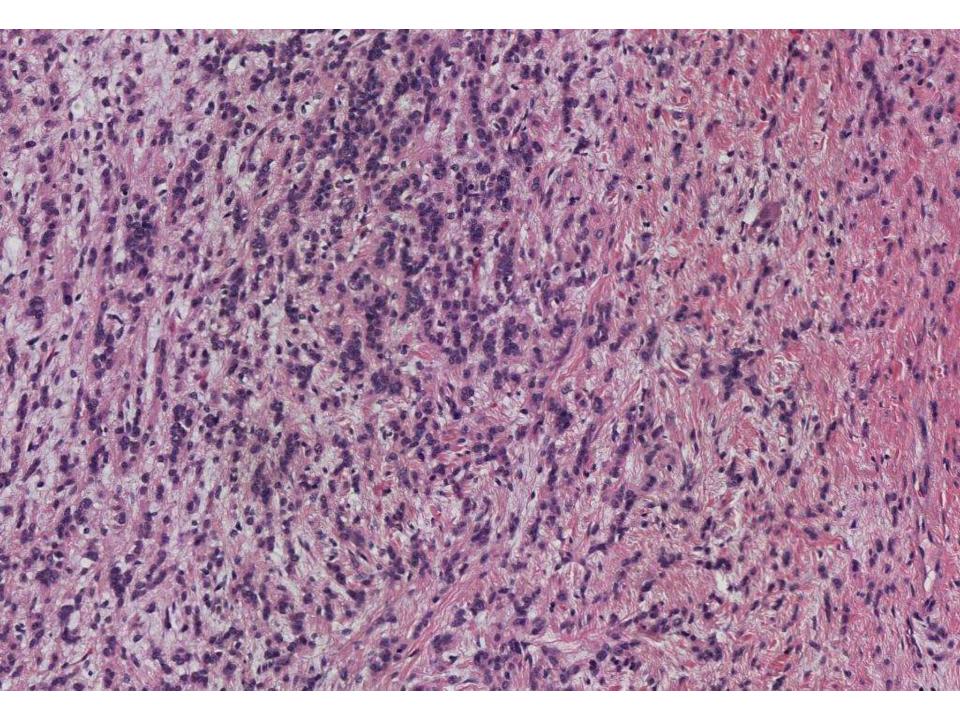


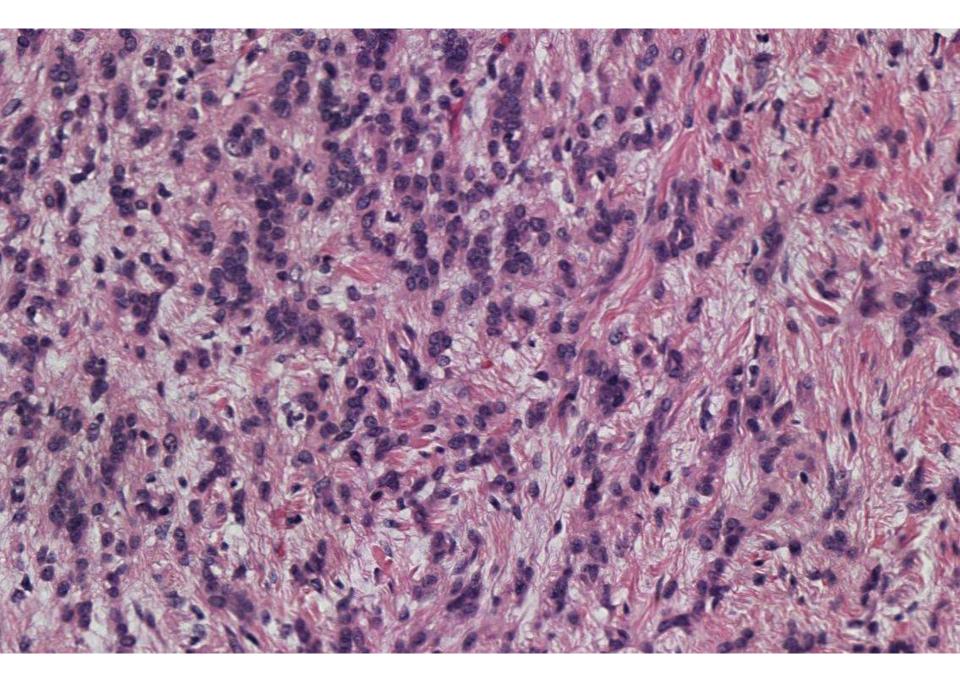












Mucosal Benign Epithelioid Nerve Sheath Tumor

- A distinct subset of mucosal peripheral nerve sheath tumors characterized by small epithelioid cells and a benign clinical course
- The largest series (n=7) shows
 - Average age at presentation 59
 - Predominantly left colon and a single bladder lesion
 - Range in size from 0.2–1.0 cm
 - May present on screening colonoscopy or during work up for a GI bleed
 - No known link to neurofibromatosis

Marc R. Lewin, MD, H. Parry Dilworth, MD, Amer K. Abu Alfa, MD, Jonathan I. Epstein, MD, and Elizabeth Montgomery, MD. *Mucosal Benign Epithelioid Nerve Sheath Tumors.* Am J Surg Pathol 2005;29:1310–1315

Benign Epithelioid Peripheral Nerve Sheath Tumors

- Epithelioid variants of nerve sheath tumors are often small, well-circumscribed, encapsulated tumors (cutaneous variants) and lack typical features of schwannoma and neurofibroma
 - Do not often show Antoni A or Antoni B
 - Lack of intra-lesional neuraxons or any association with peripheral nerves.
 - GI schwannomas lack alterations in the NF2 gene found in many sporadic, conventional schwannomas from other sites.
- Lesions that have been classified as GI schwannomas differ from the conventional somatic soft tissue schwannomas histologically by having peripheral lymphoid cuffs, lacking fibrous capsules or vascular hyalinization, and rarely showing degenerative changes

Morphology and Phenotype of BENST

- Nuclei show frequent intra-nuclear pseudo-inclusions with spindled to epithelioid cells with clear to eosinophilic fibrillary cytoplasm arranged in nests and whorls
- The epicenter of the lesions are typically in the lamina propria with extension into the superficial submucosa
- Lesions lack: a distinct lymphoid cuff, ganglion cells and have no mitotic activity
- Immunohistochemical characteristics
 - Strong and diffuse S-100 protein staining
 - Variable CD34
 - Negative CD117

Differential Diagnosis

- Melanoma
- GIST
- Carcinoma
- Carcinoid
- Leiomyoma
- Ganglioneuroma
- Perineurioma
- Mucosal schwann cell hamartoma*

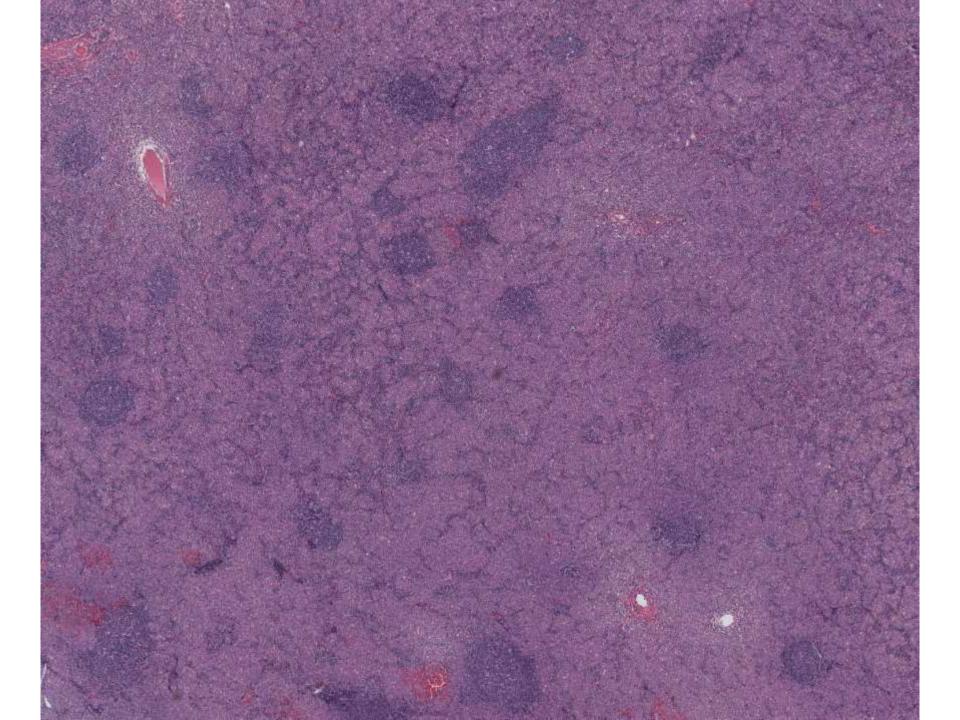
Epithelioid Variants of Peripheral Nerve Sheath Tumors

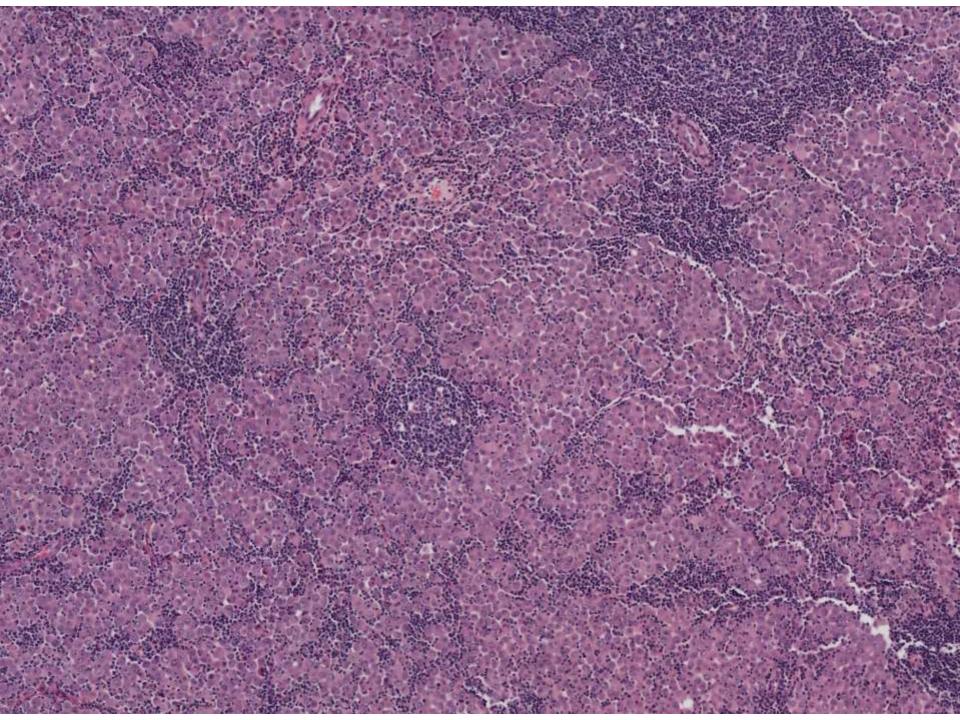
- GI tract schawannomas exhibit unique morphologic and genetic features compared to sporadic schwannomas
- Classification of these lesions as schwannomas or neurofibromas is difficult because of their rarity and location in a site where conventional-appearing schwannomas are known to exhibit both morphologic and genetic features distinct from other sporadic schwannomas.
- The main importance of this lesion is to recognize epithelioid nerve sheath tumor as a benign lesion amongst the differential diagnosis of epithelioid lesions of mucosal sites

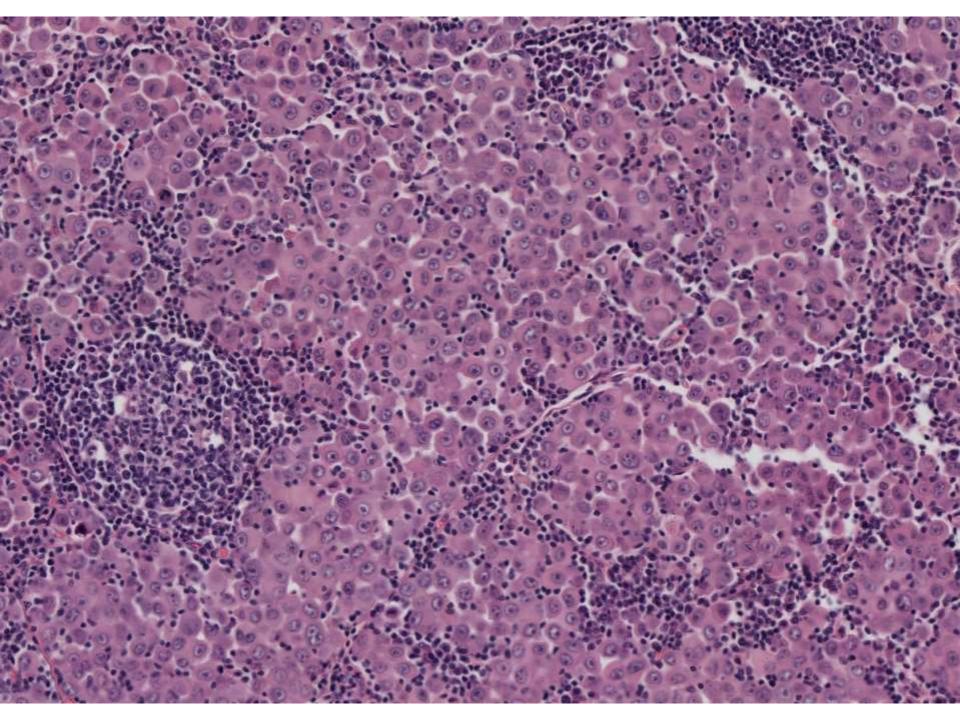
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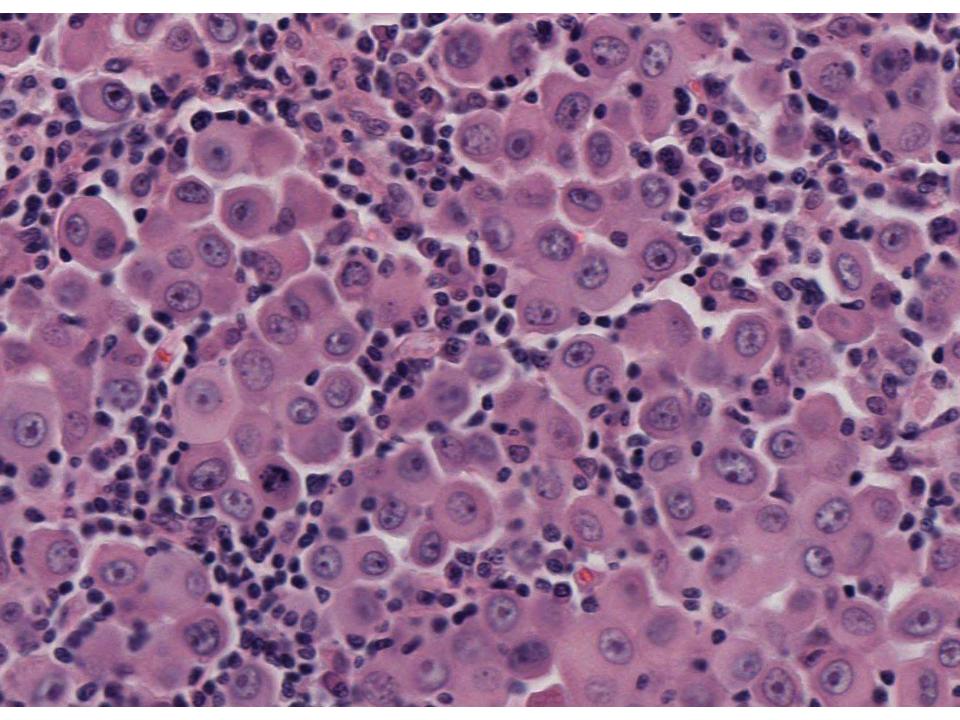
Kelly Mooney/Megan Troxell; Stanford 70-year-old female with negative mammogram one year ago, presenting with 10 pound weight loss and axillary mass.









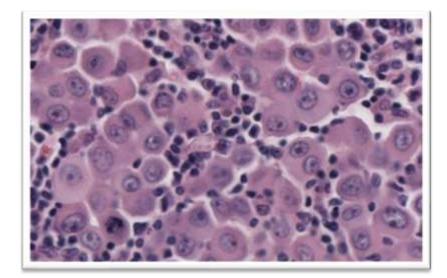


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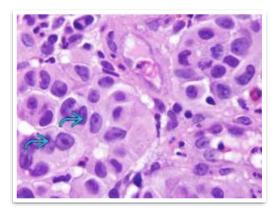
February 2018 Kelly Mooney, MD (PGY-2) / Megan Troxell, MD PhD



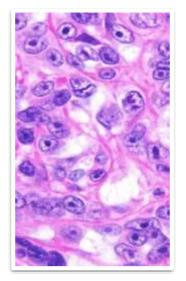




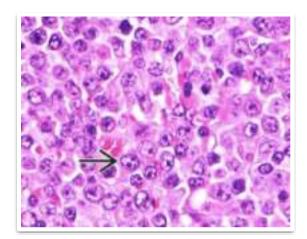
Lymph node effaced by large discohesive cells with round nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm



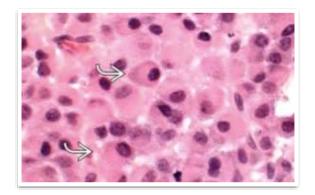
Melanoma



Clear cell sarcoma



Large B-cell **lymphoma** (Immunoblasts)



Carcinoma With apocrine features (invasive apocrine, lobular breast, salivary gland)

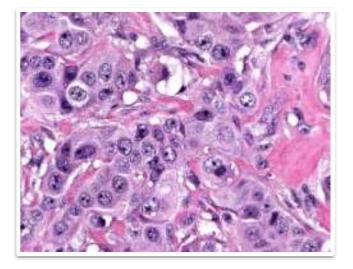
Photos from https://app.expertpath.com/

Immunohistochemical work-up

Negative:			
Melan-A	CD45	GATA-3	Positive
<i>S100</i>	CD3	BRST2 (GCDFP15)	Positive
HMB45	CD20	Mammaglobin	Focally positive
MiTF	CD10	СК7	Positive
	CD15	СК20	Negative
Desmin		СКМІХ	Positive
	CD30	Androgen receptor	Positive
Actin	BCL1	E-cadherin	Negative
	BCL2	Ki67	High (90%)
CDX2	BCL6		
TTF1	MUM1	ER	Negative (<1%)
	CD21	PR	Negative (<1%)
	PAX-5	HER2	Negative (0)

Diagnosis: Metastatic high grade carcinoma, favor pleomorphic apocrine lobular carcinoma

Differential: occult salivary gland, apocrine skin/ sweat gland



High grade salivary duct carcinoma

Pleomorphic (apocrine) lobular carcinoma

Definition: lobular carcinoma variant characterized by larger cells, more abundant eosinophilic cytoplasm (apocrine features), distinct nucleoli

Clinical: post-menopausal women

Immunohistochemistry: AR, GCDFP-15 positive, E-cadherin negative, ER/PR/HER2 negative.

Genetics: Gene expression profiling shows that the subtype is more closely genetically related to classical ILC than invasive ductal carcinoma

Outcomes: Overall, seems to be more aggressive than ILC with higher recurrence risk (12% vs 4%)

Occult breast carcinoma presenting as axillary lymph node metastasis

<1% patients present with axillary node metastasis as first clinical manifestation

Studies show that about 65% of cases of metastatic adenocarcinoma in axillary lymph nodes from occult breast carcinoma have large cells, often with apocrine features

MRI reveals abnormalities in ~60% of these patients (high false + rate)

Case follow-up

Imaging: Breast MRI & full body PET only with axillary lymphadenopathy CT and ultrasound head and neck with no masses

Genetics assay: 89% probability salivary gland/ head & neck, 7% breast

Favored breast primary (more common/ expected than occult salivary gland to axilla without neck lymphadenopathy)

Treated with neoadjuvant chemoradiation therapy/ axillary lymph node dissection with metastatic carcinoma in 3/17 sclerotic lymph nodes

Per latest clinic notes doing "fairly well"

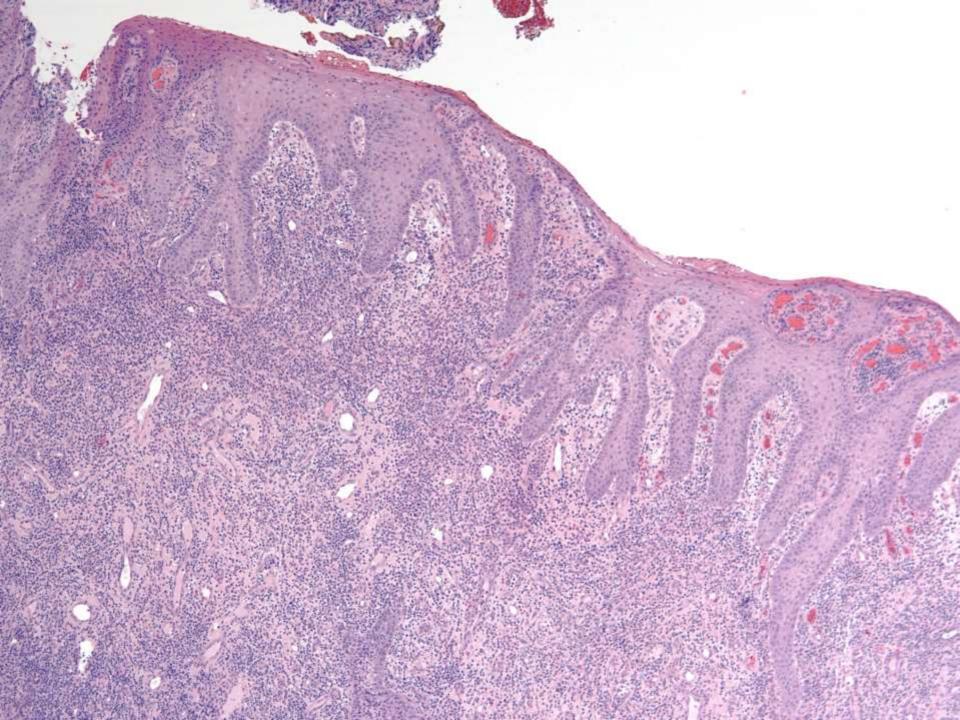
References

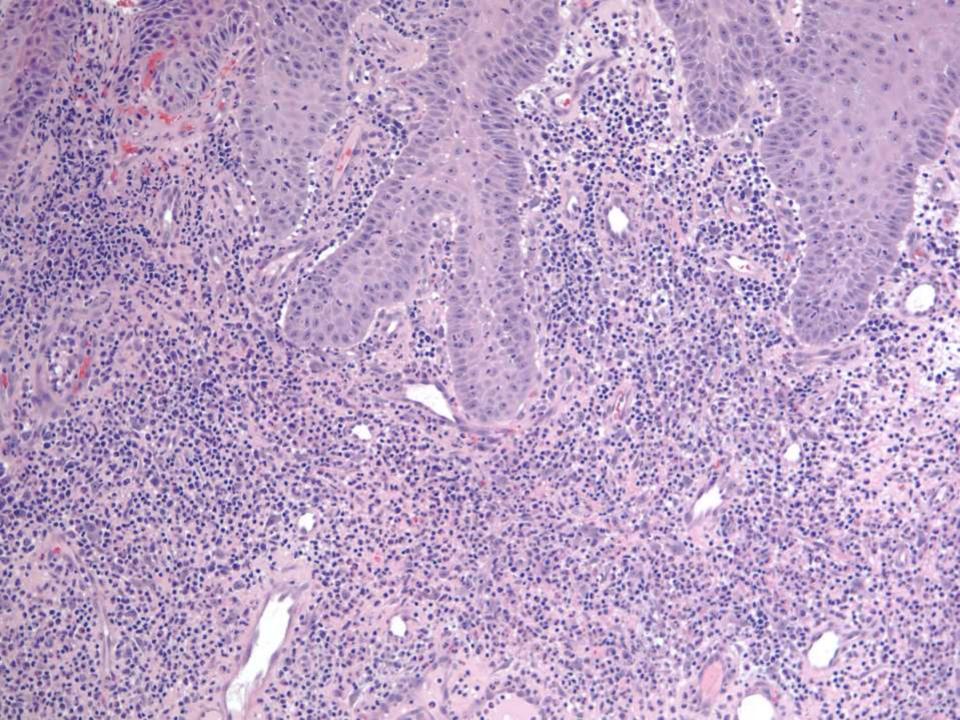
- Hoda, S.A., P.P. Rosen, E. Brogi, and F.C. Koerner. *Rosen's Breast Pathology*. Wolters Kluwer Health, 2014.
- 2. Gown AM, Fulton RS, Kandalaft P et al. Markers of metastatic carcinoma of breast origin. *Histopathology.* 2016;68(1):86-95.
- 3. Monhollen L, Morrison C, Ademuyiwa FO et al. Pleomorphic lobular carcinoma: a distinctive clinical and molecular breast cancer type. *Histopathology*. 2012;61(3):365-77

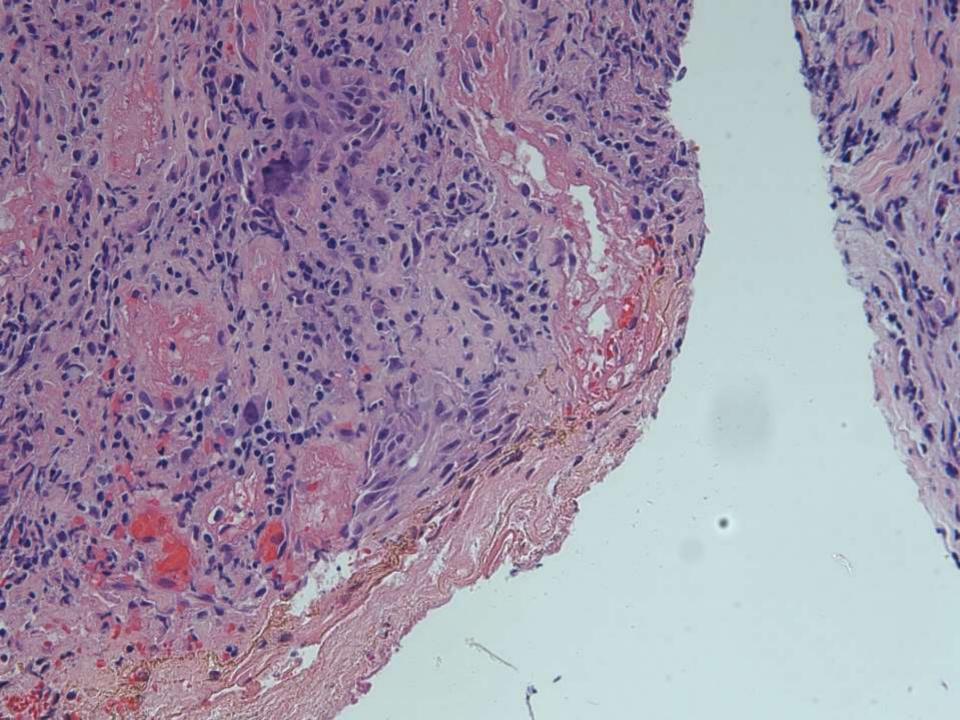
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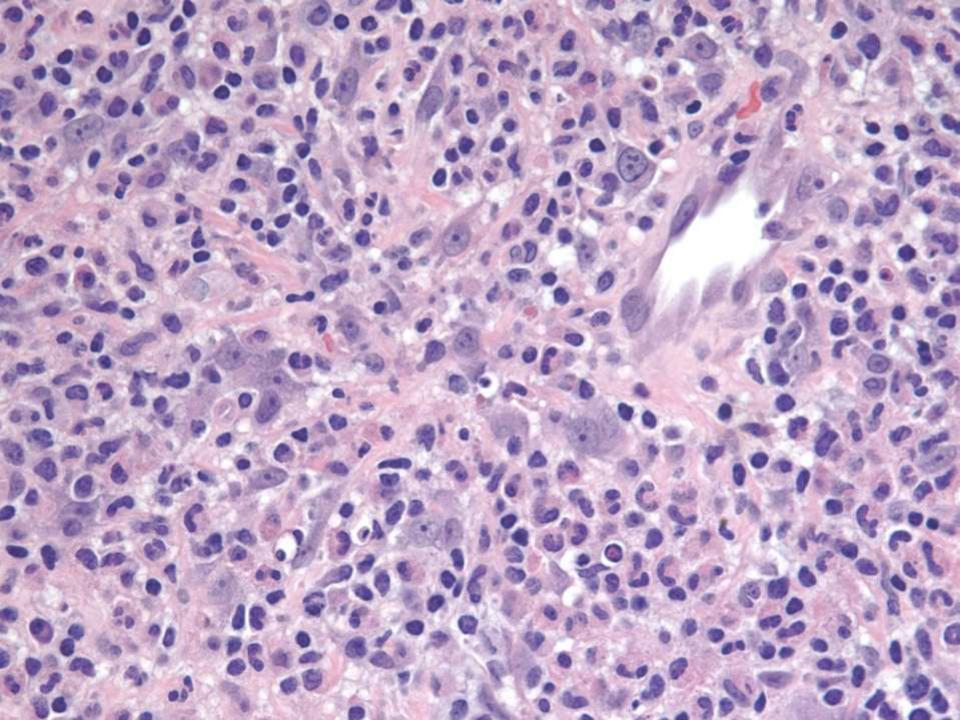
Kevin Ko/Bart Singer/John Higgins; Stanford 59-year-old male with history of HepC, HCC, s/p orthotopic liver transplant, who presented with >2cm oral ulcer for 4 weeks.







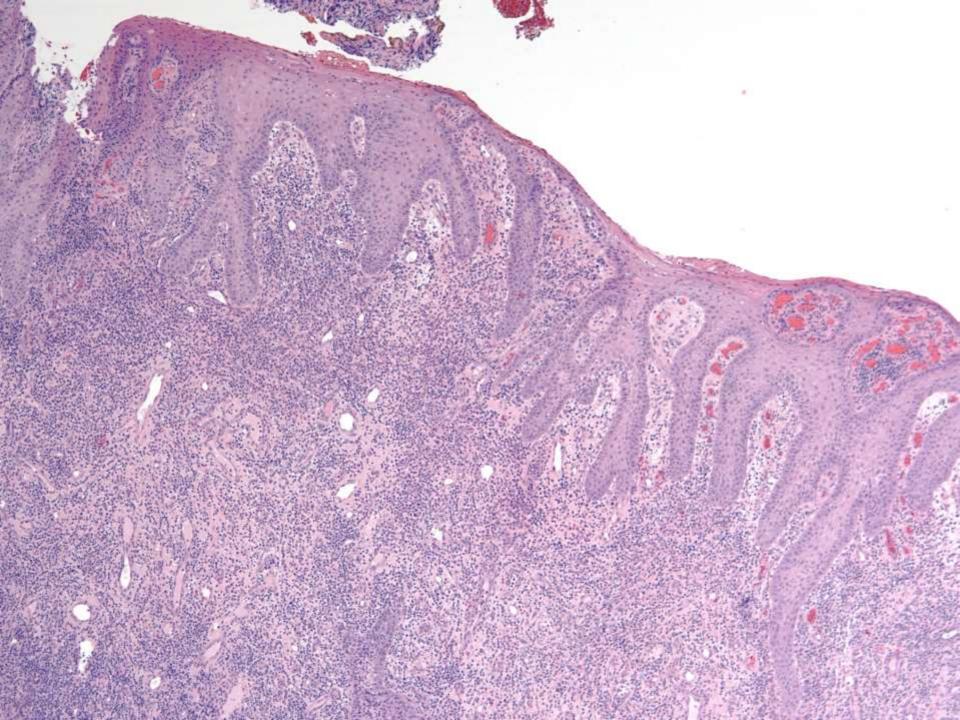


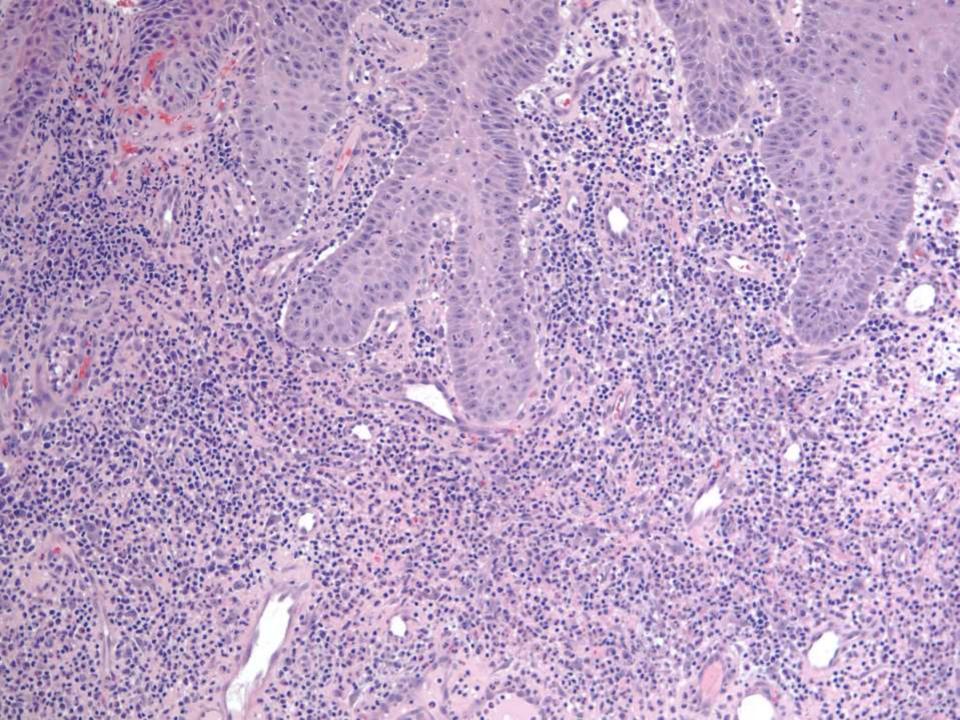


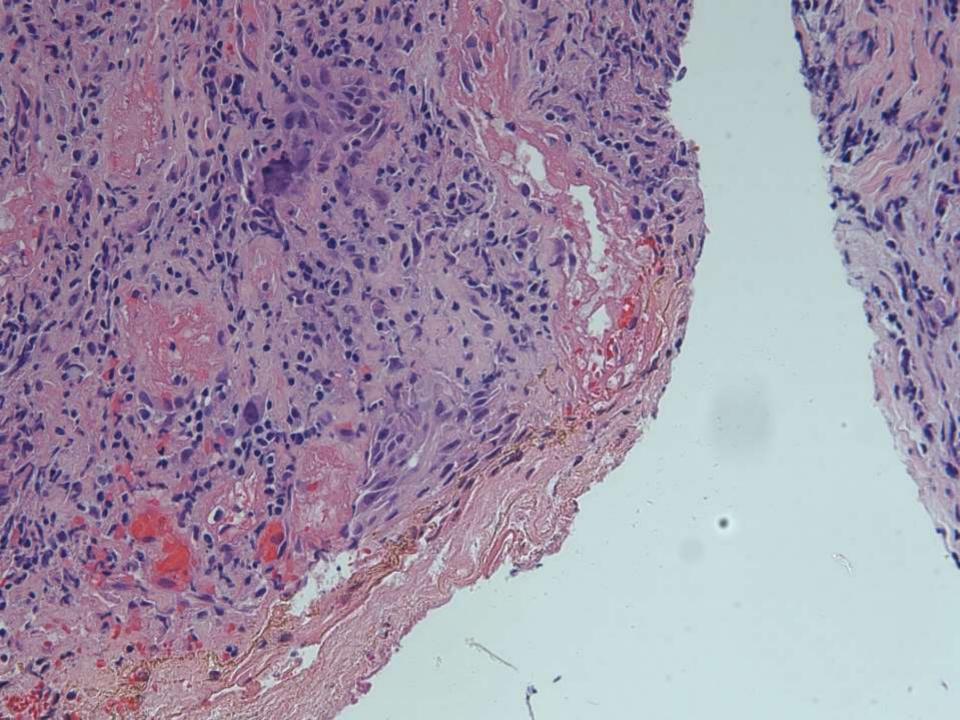
Southbay Presentation

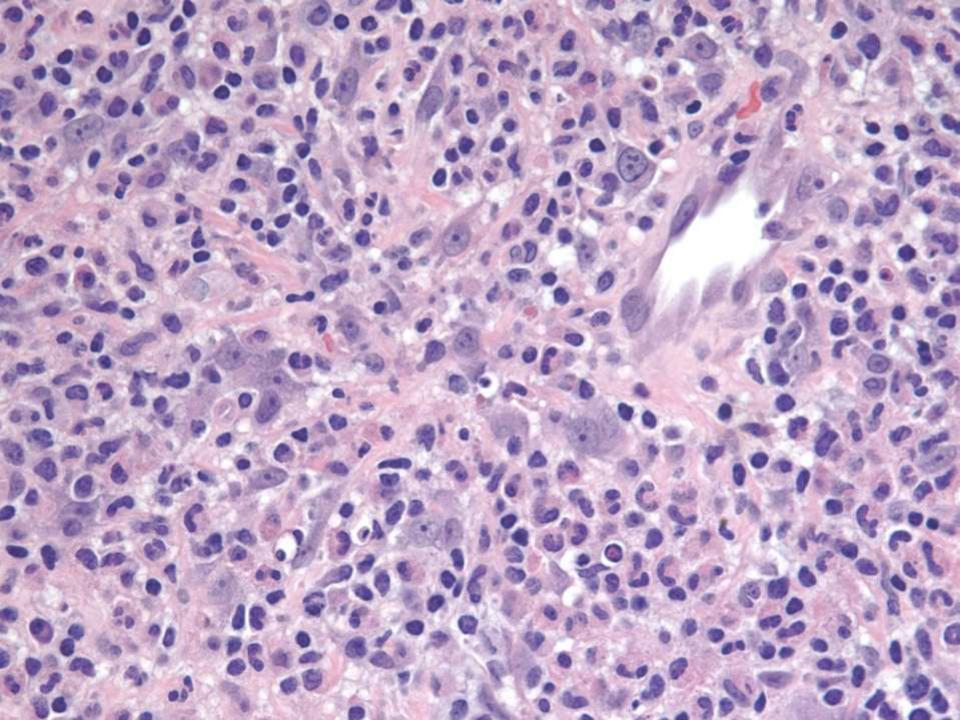
Kevin Ko/Bart Singer/John Higgins; Stanford 59-year-old male with a history of hepatitis C, HCC, s/p orthotopic liver transplant who presented with >2cm oral ulcer for 6 weeks









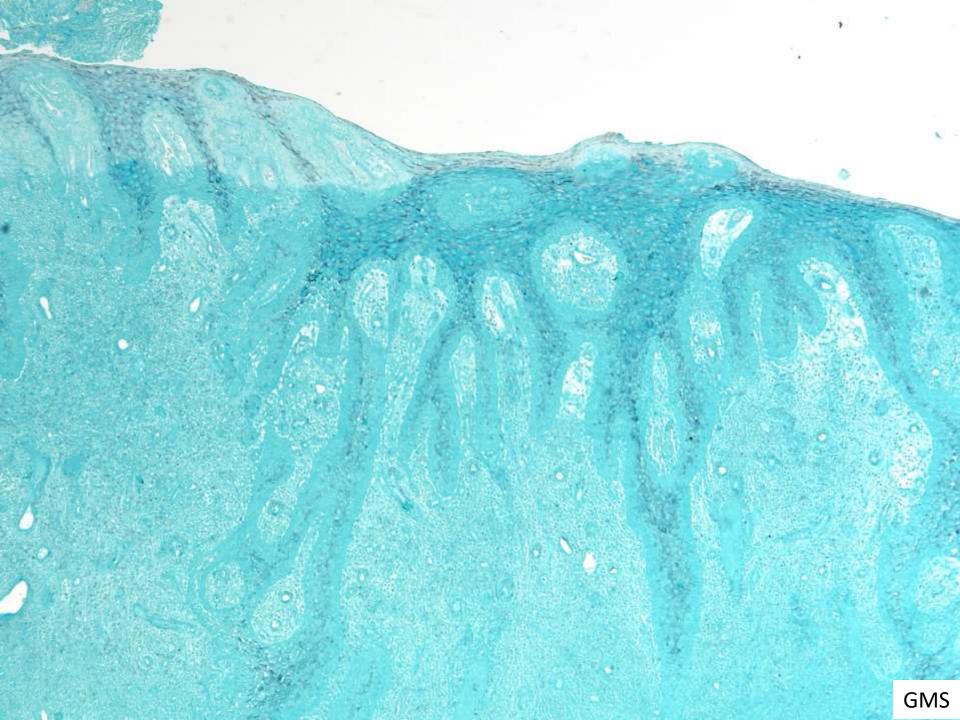


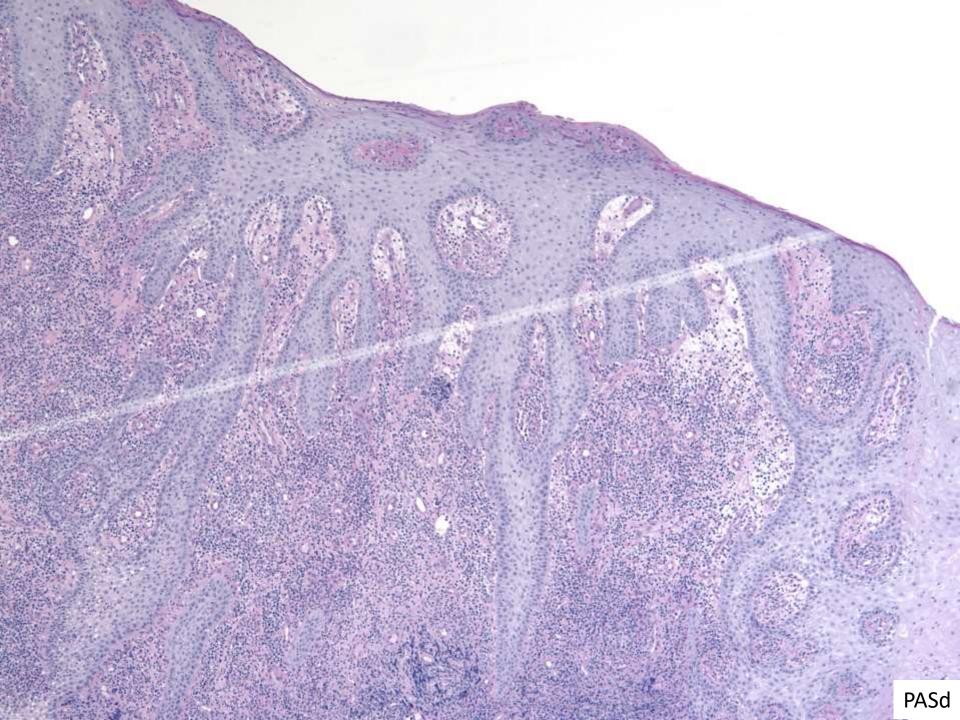
More History

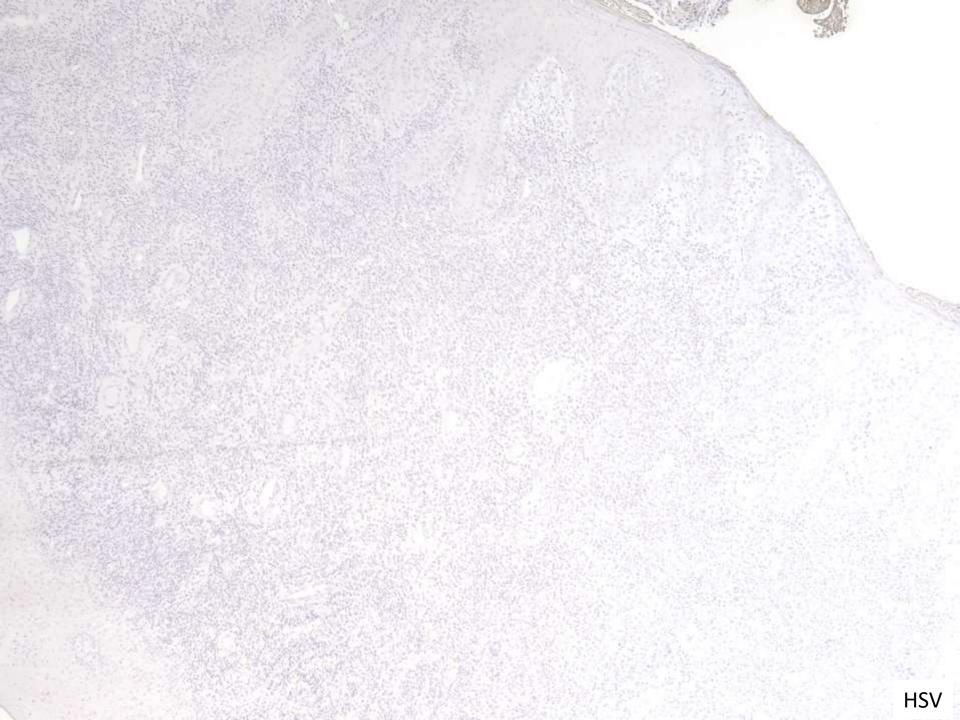
- 8/31/2017- Initial presentation/Office visit
 - CC: oral ulcer, painful, ~ 1 week
 - Started on Acyclovir 800mg TID for 13 days
 - Started on Nystatin
- 10/2/2017 ED
 - Worsening oral ulcer, ~4 weeks
 - Having difficulty eating, lost weight
 - Viscous lidocaine prescribed
- 10/10/2017- ENT clinic

Surgeon's assessment:

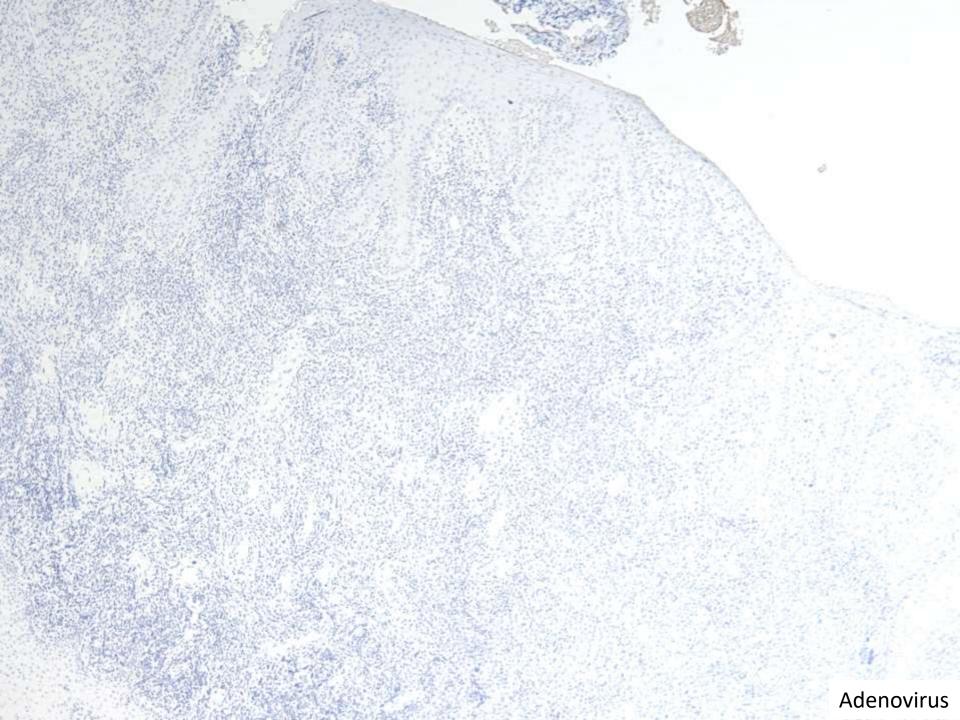
- ">2 cm ulcer with exudates and heaped up edges"
- "Clinically suspicious for malignancy"

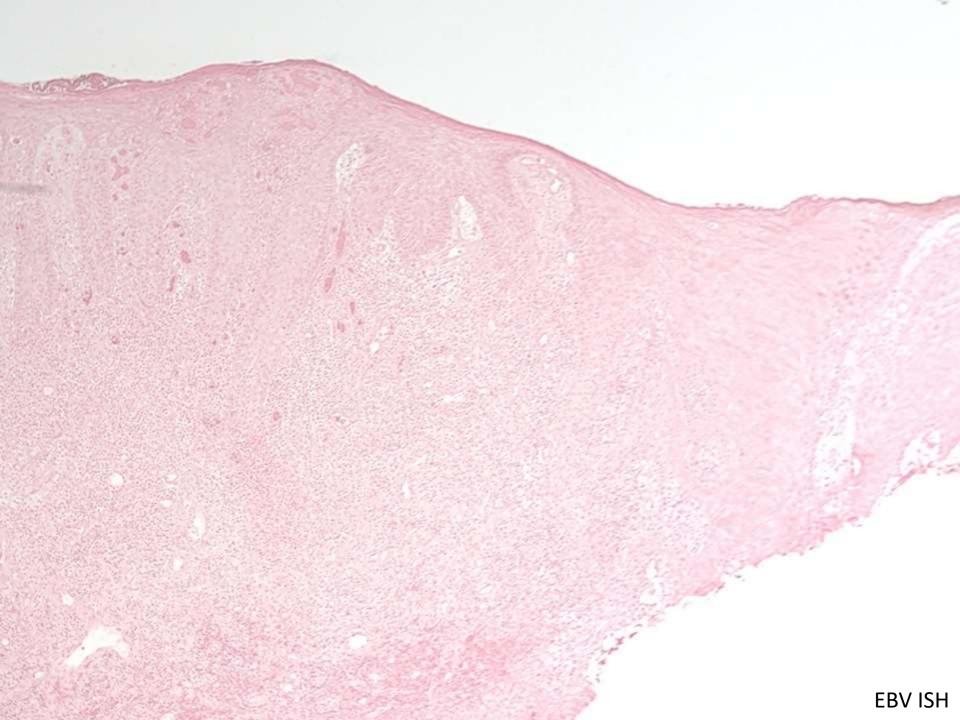


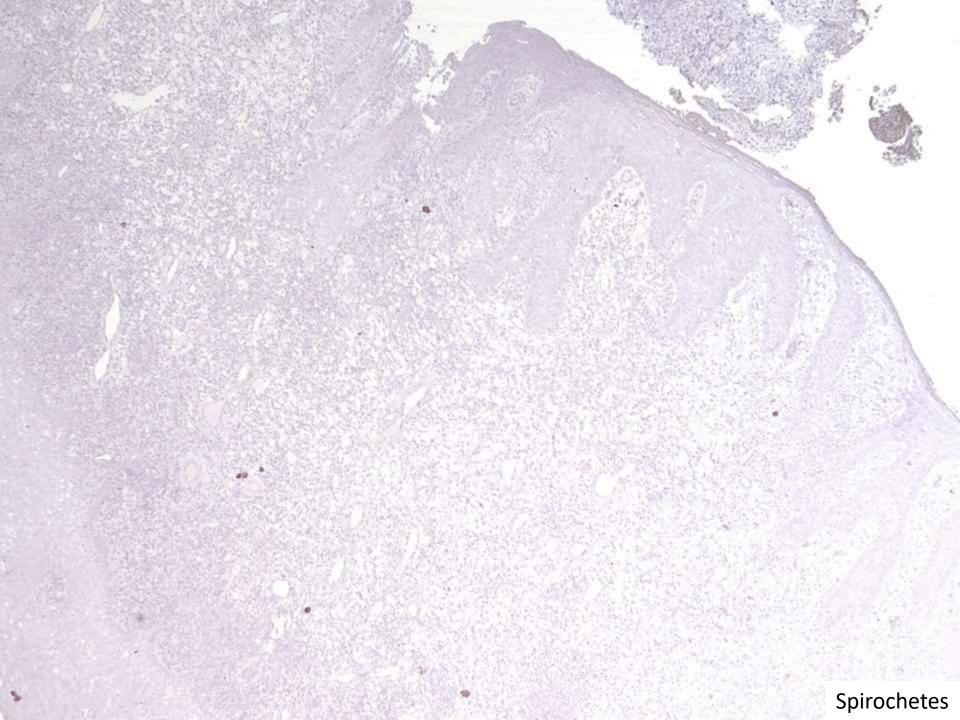












Pathology Report

COMMENT:

We note, per EPIC, the patient's history of liver transplant and reported treatment with mycophenolate. A few case reports in the literature implicate mycophenolate in causing ulcerative stomatitis in transplant recipients, possibly by direct mycophenolate-induced cytotoxicity in oral mucosa. We raise this as a possible etiology for the findings in the current biopsy and note that in the referenced case reports, decreasing mycophenolate dosing improved oral ulcerations. Clinical correlation is recommended.

- 10/27/2017-ENT clinic
- Surgeon's assessment:
 - "Recommend to transplant team to consider decreasing CellCept per pathologist's suggestion to see if ulcers resolve"

Clinic follow up: 10/30/2017



Clinic follow up: 11/09/2017



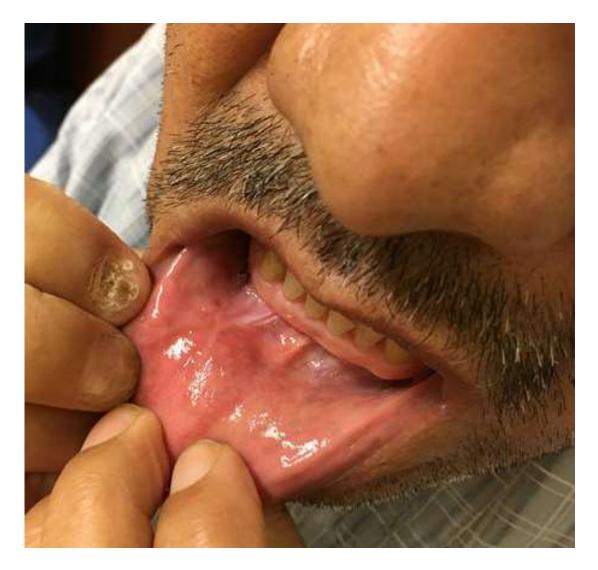
Clinic follow up: 11/16/2017



Clinic follow up: 12/21/2017



Clinic follow up: 1/25/2018



Final Diagnosis: LOWER LIP ULCER, BIOPSY

> -- Mycophenolate Mofetil-Induced Ulcerative Stomatitis

 A brief review of ulcerative stomatitis ("Aphthous Ulcers")

Ulcerative Stomatitis A.K.A "Aphthous Ulcers"

- Very common
- Etiology = unknown
 - Reported Triggers/Predisposing Factors
 - Allergies/hypersensitivity
 - Stress
 - Trauma
 - Nutritional deficiency
 - Hormones
 - Immunological factors
 - Hematological abnormalities
 - Genetic predisposition

Ulcerative Stomatitis "Aphthous Ulcers"

• 3 types

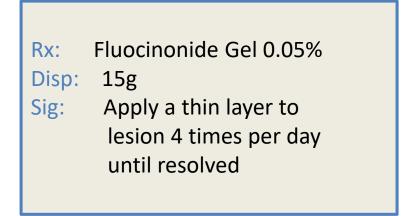
- Minor : 3-10mm, 7-14 days
- Major : 1-3cm, 2-6 weeks, +/- scar
- Herpetiform : 1-3mm, 7-10 days, multiple & tend to occur in clusters, can be mistaken for intraoral HSV
- Minor is most common
 - Only occurs on non-keratinized mucosa
 - (not gingiva or hard palate)





Diagnosis: Clinical

- Treatment:
 - No treatment
 - OTC anesthetic
 - Topical corticosteroid
 - Cauterization



- Systemic steroid (for multi-focal outbreak)

If a patient presents w/ cc of multiple recurrences, r/o the following systemic conditions.....

Celiac Disease
Nutritional Deficiency
IBS/Chrohns
IgA Deficiency
Cyclic Neutropenia
Immunocompromised Conditions

Mycophenolate Mofetil-Induced Ulcerative Stomatitis in Transplant Recipients

- First case described in the English literature in 2007
- Not well recognized until late 2015
- Initial step is to exclude infectious origin
 - HSV and CMV infections are most common culprits
- Exclude underlying dermatological or systemic diseases associated with oral ulceration

Naranjo J, Poniachik D, Cisco J, et al. Oral ulcers produced by mycophenolate mofetil in two liver transplant patients. *Transplant Proc.* 2007; 39(3):612-614

Salik J, Tang, R, Nord K, et al. Mycophenolate mofetil-induced oral ulcerations in solid organ transplant recipients: A report of 3 cases. JAAD Case Reports. 2015;1:261-3

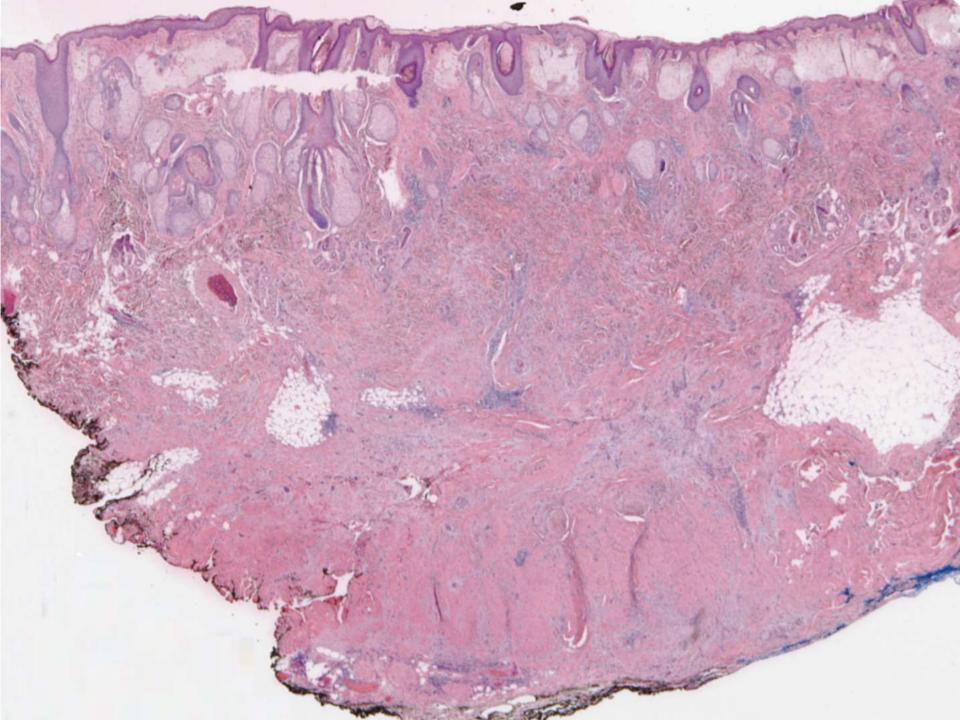
Mycophenolate Mofetil-Induced Ulcerative Stomatitis in Transplant Recipients

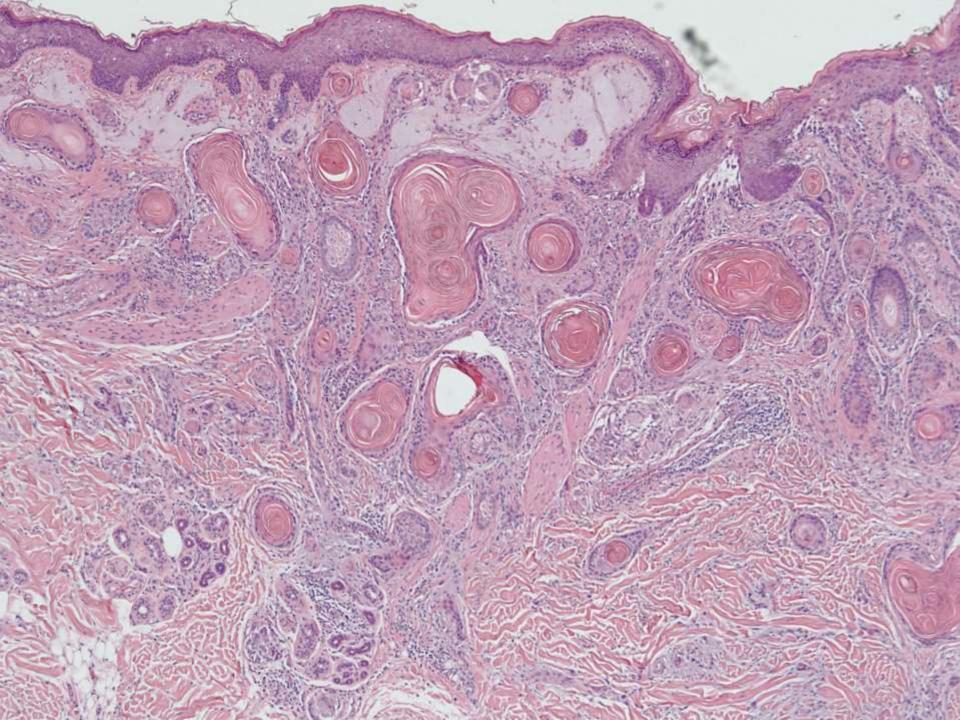
- Pathogenesis
 - Direct MMF-induced cytotoxicity in oral mucosa
 - Neutropenia-induced ulceration secondary to immunosuppression

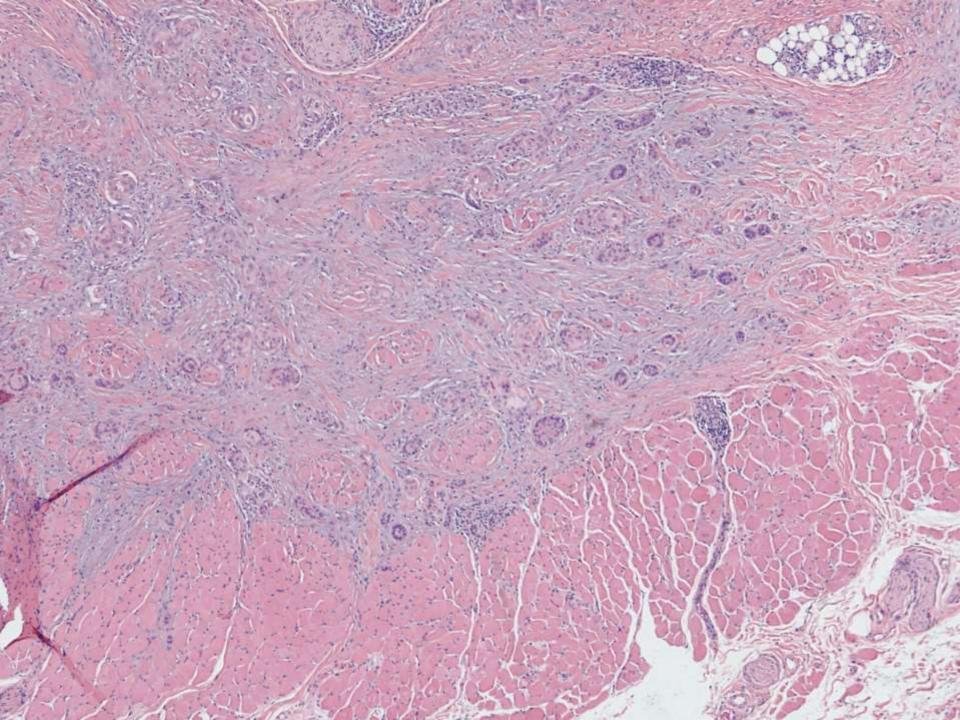
SB 6247

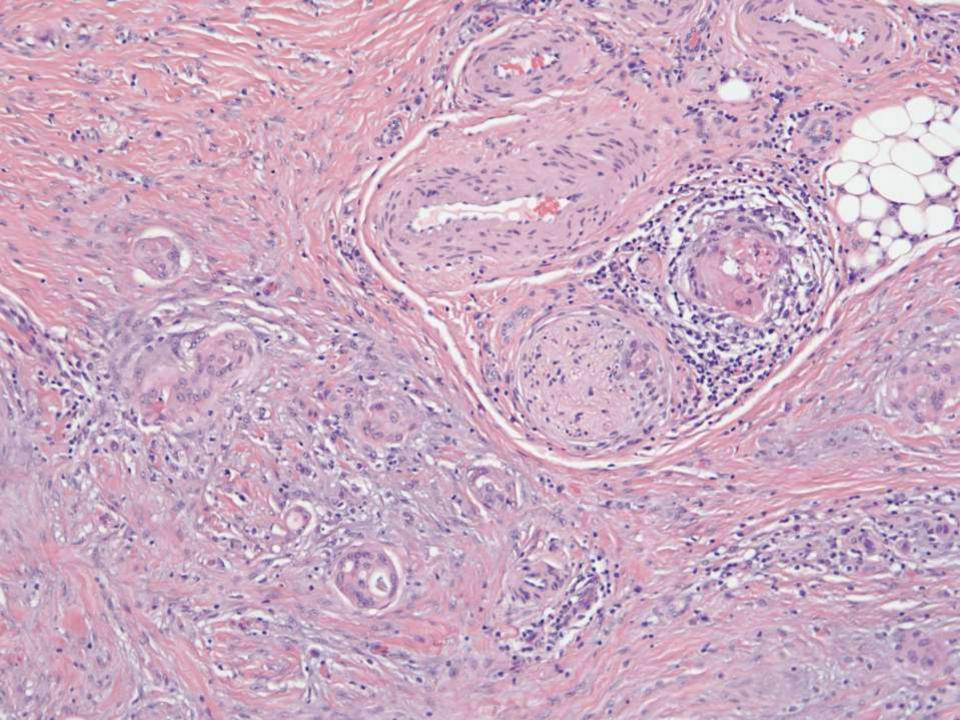
Kevin Ko/Christine Louie; Stanford/Palo Alto VA

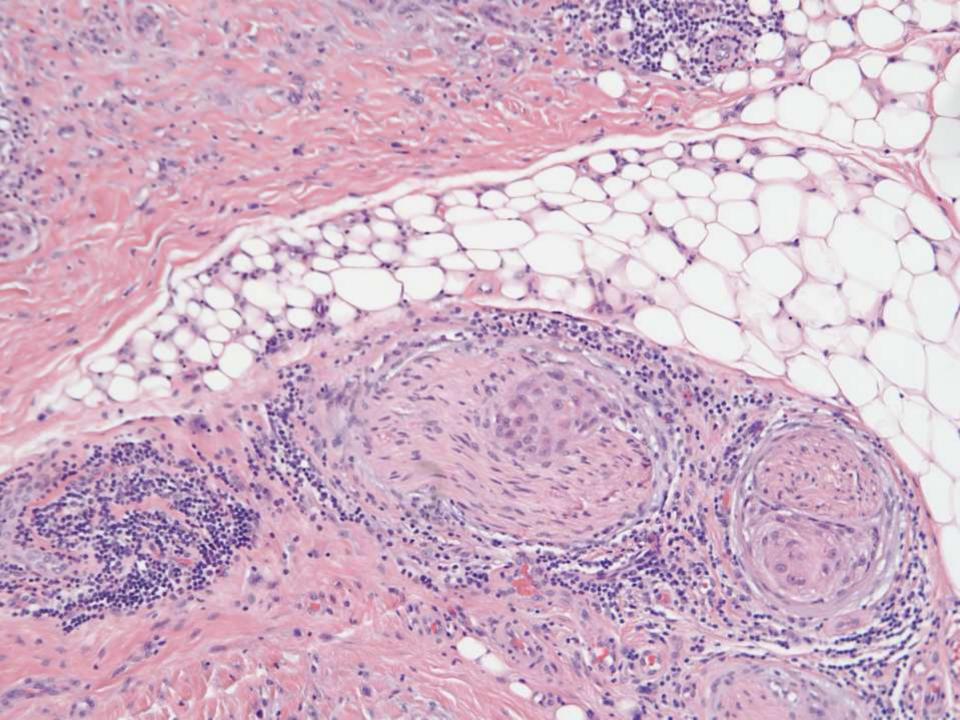
70-year-old male with depressed plaque on left forehead. Initial shave biopsy read as "squamous cell carcinoma, transected at deep margin."

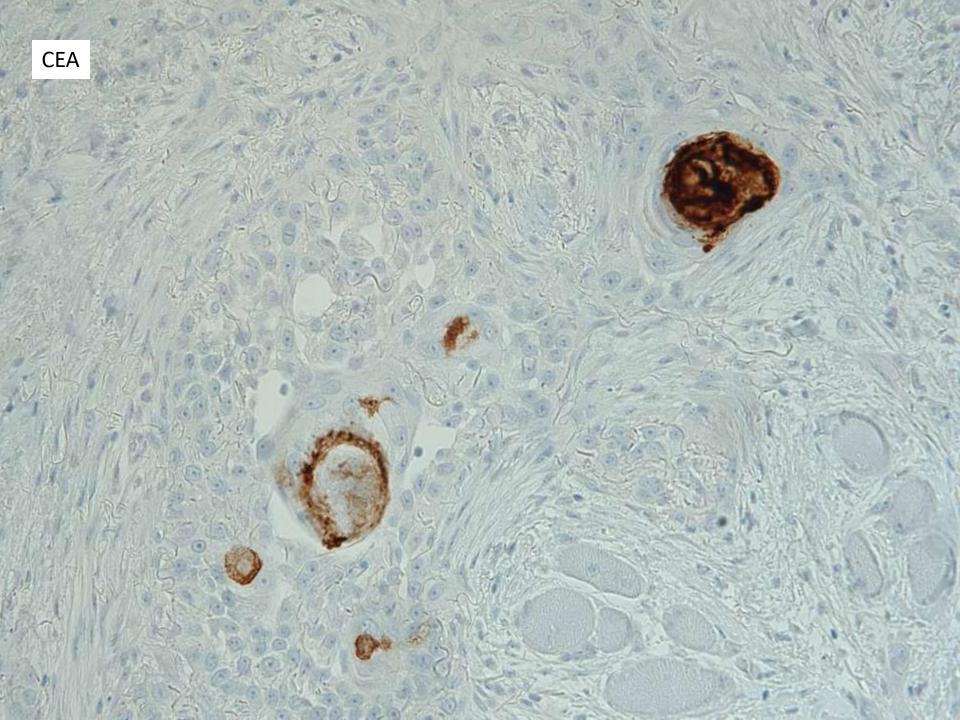






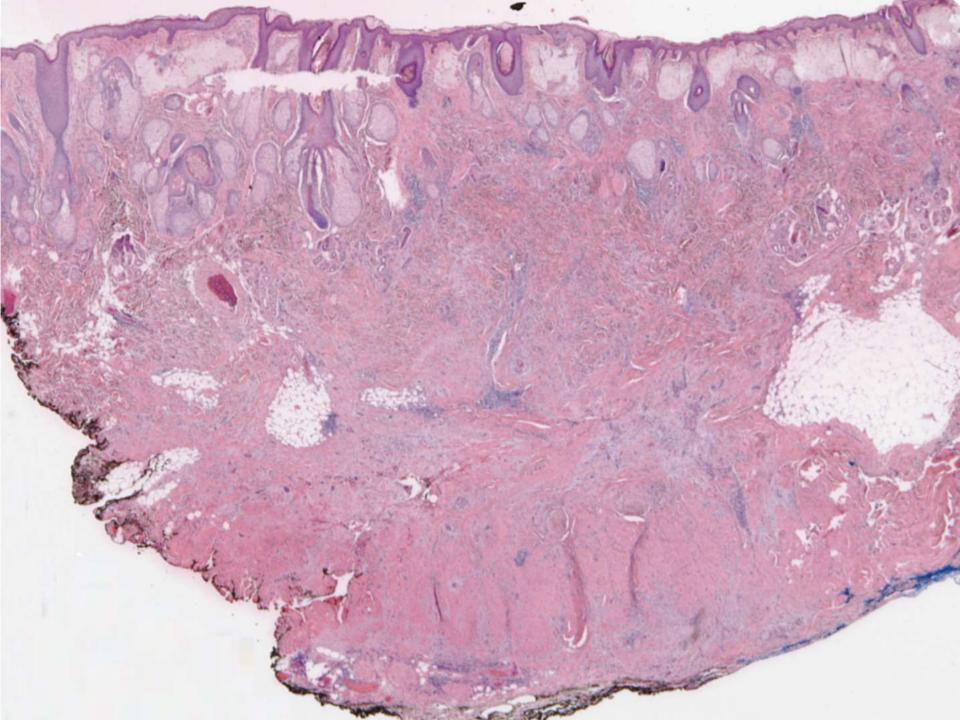


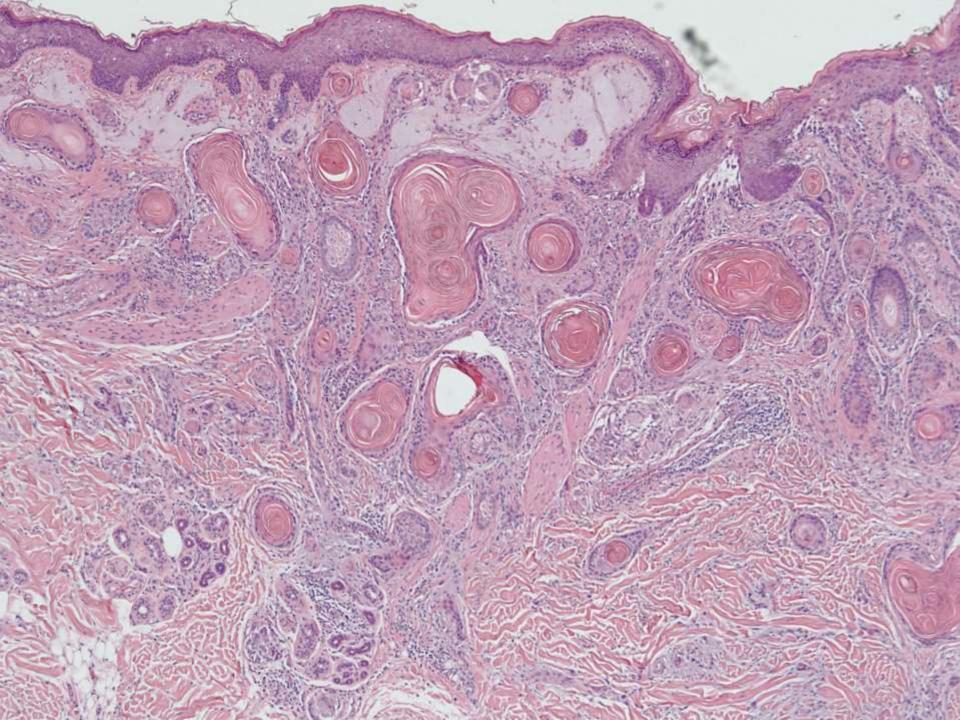


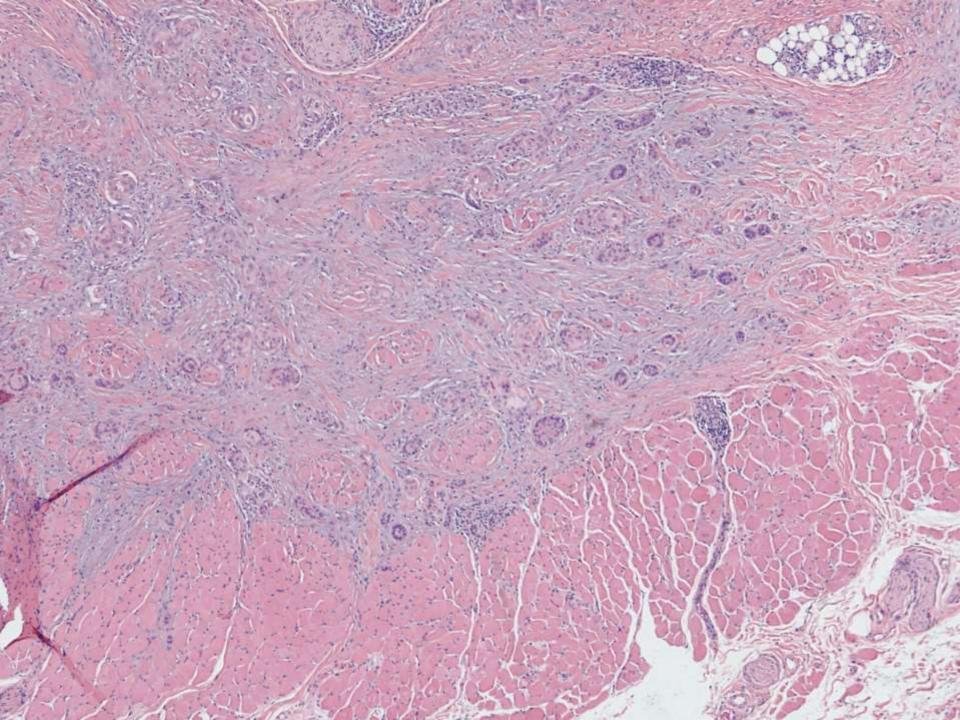


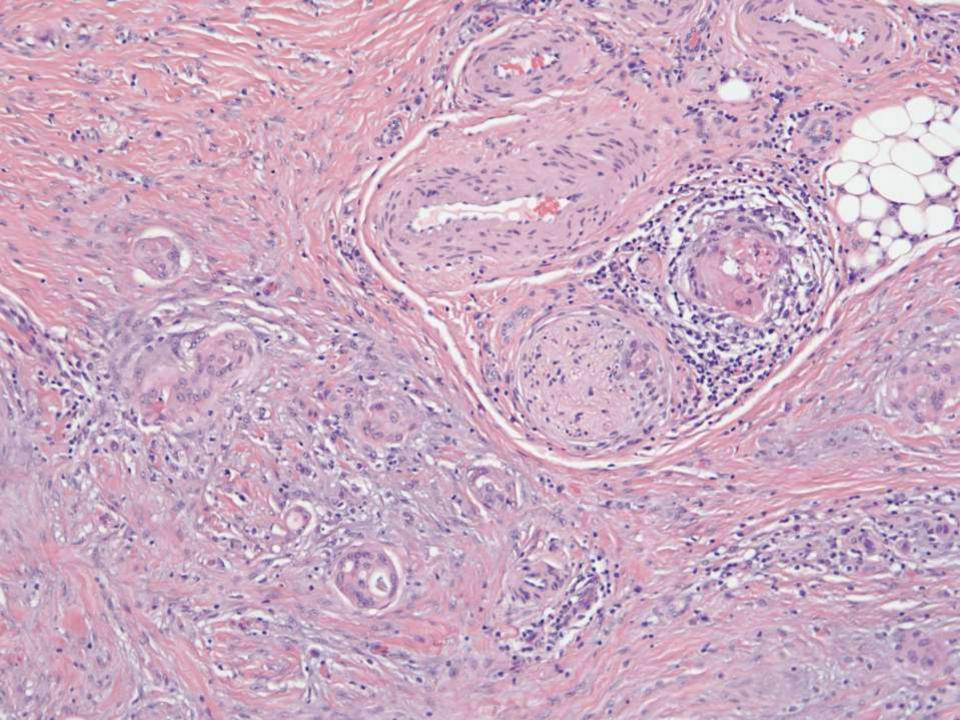
EMA

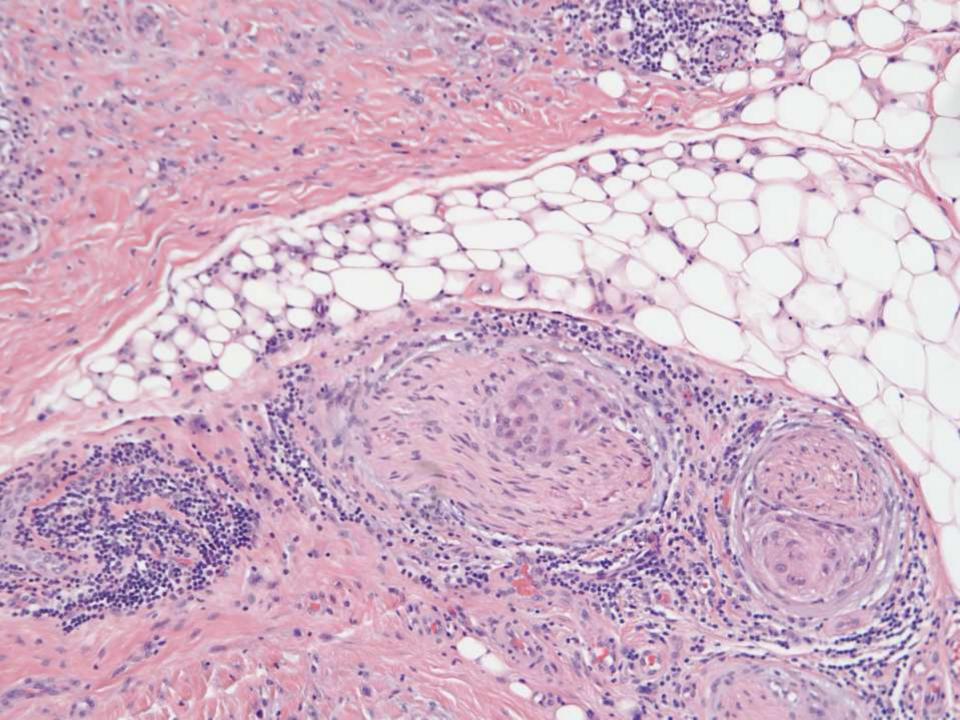
Kevin Ko/Christine Louie; Stanford; Palo Alto VA 70-year-old man with depressed plaque on the left forehead. Initial shave biopsy read as "squamous cell carcinoma, transected at deep margin"

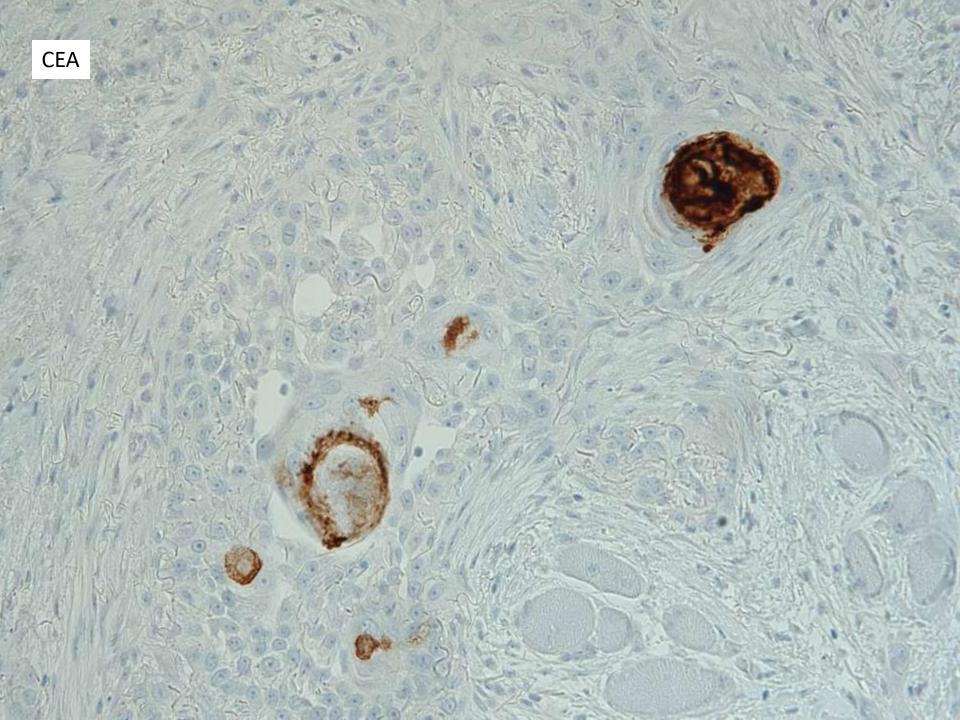












EMA

Diagnosis

• Microcystic Adnexal Carcinoma

Microcystic Adnexal Carcinoma

- Key features
 - Infiltrative adnexal neoplasm with eccrine and follicular differentiation
 - Clustering of bland-appearing, teardrop-shaped epithelial nests
 - Perineural invasion (often present in deeper areas)
 - Luminal cells: EMA+, CEA+
 - Low Ki-67

Microcystic Adnexal Carcinoma

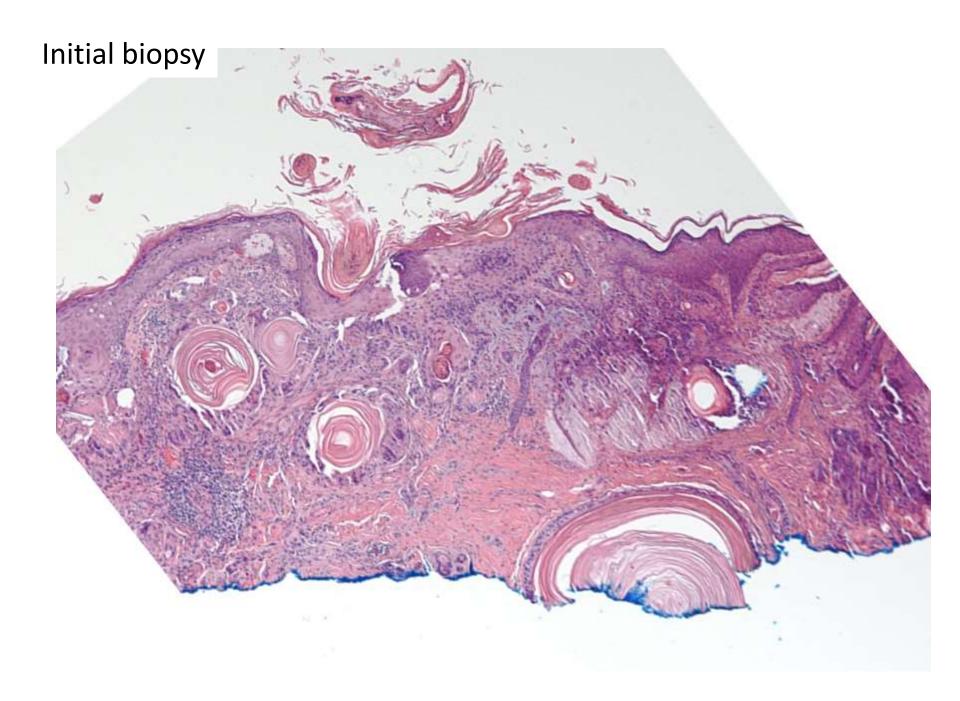
- Differential diagnosis
 - Desmoplastic trichoepithelioma
 - Luminal cells EMA negative and CEA negative
 - Lacks perineural invasion
 - Syringoma
 - Lacks evidence of follicular differentiation
 - Desmoplastic basal cell carcinoma
 - Luminal cells EMA negative and CEA negative
 - High levels of Ki67

Microcystic Adnexal Carcinoma

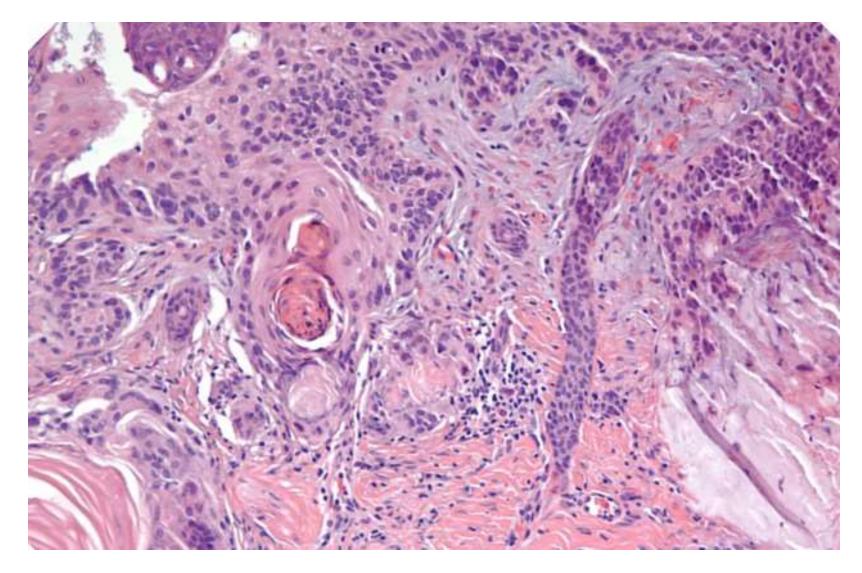
- Incidence of 1.6 to 6.5 per 10,000,000 people
- Middle-aged to older adults
- Upper lip most common
- Treatment:

- Complex excision with clear margins (Mohs)

- High incidence of local recurrence
- Rare metastases



Initial biopsy



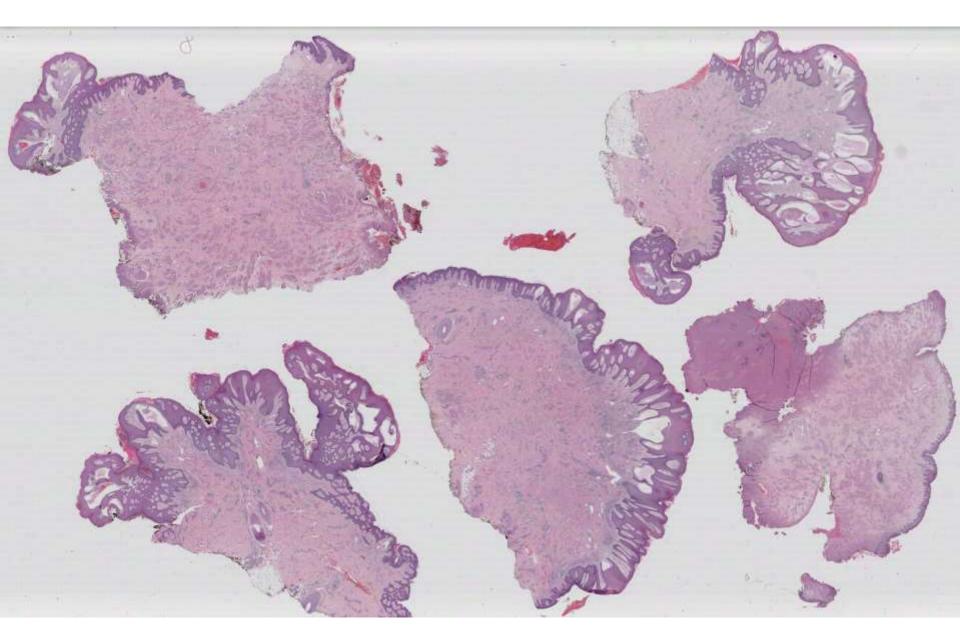
- "Inadequate biopsy techniques showing only the superficial component should be avoided"
- "A deep biopsy is mandatory for the correct diagnosis, and Mohs micrographic surgery provides the highest cure rate"

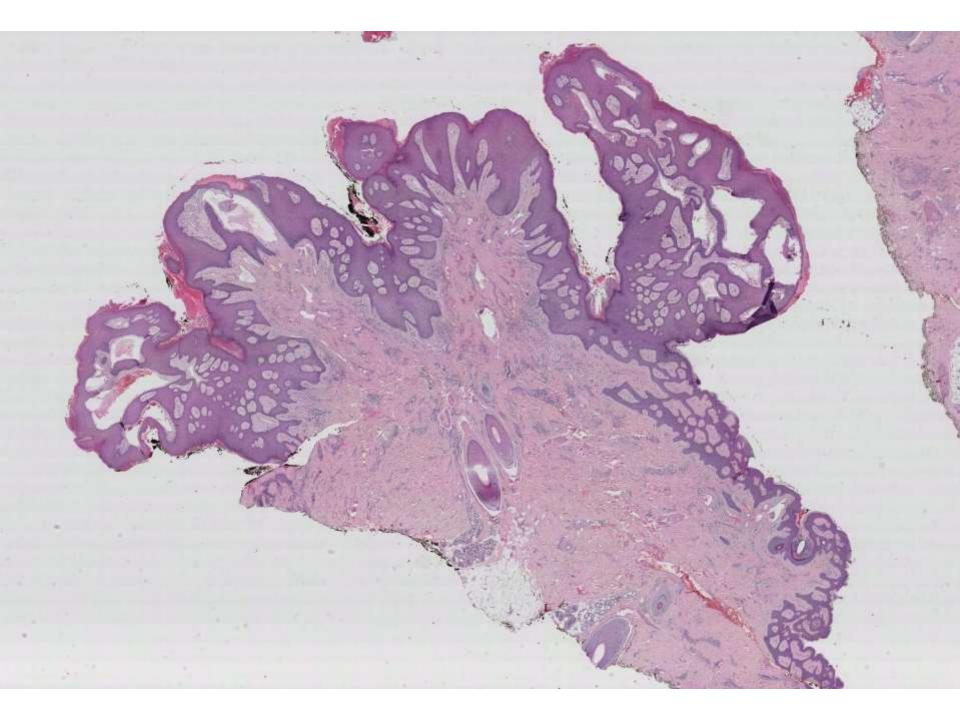
Gordon S, Fischer C, Martin A, Rosman IS, Council ML. Microcystic Adnexal Carcinoma: A Review of the Literature. Dermatol Surg. 2017 Aug;43(8):1012-1016

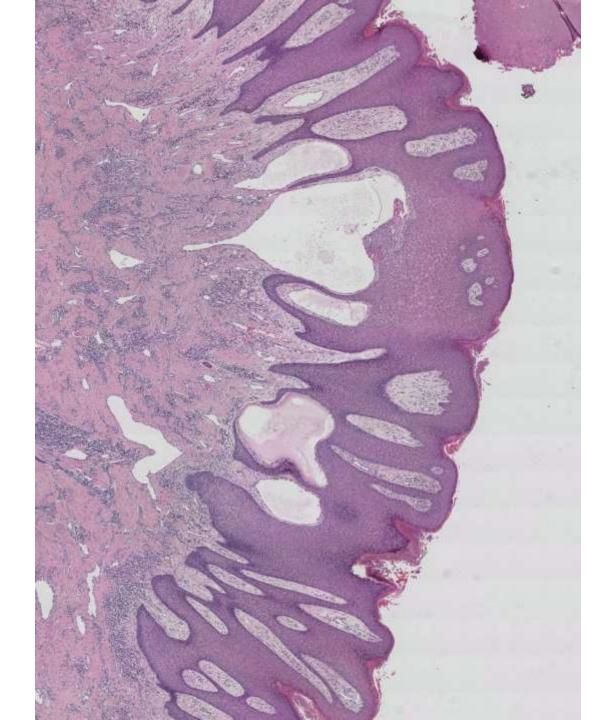
Ximena Calderón-Castrat, MD, Concepción Román-Curto, MD, PhD, Angel Santos-Briz, MD, PhD, and Emilia Fernández-López, MD, PhD. Microcystic adnexal carcinoma mimicking basal cell carcinoma. JAAD Case Rep. 2017 Nov; 3(6): 492–494.

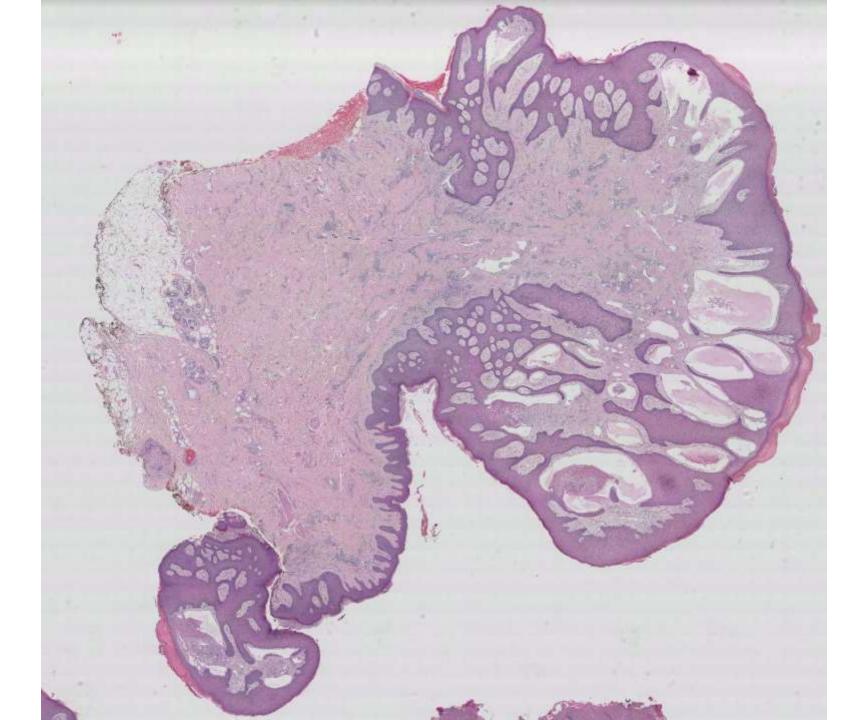
SB 6248 (scanned slide available)

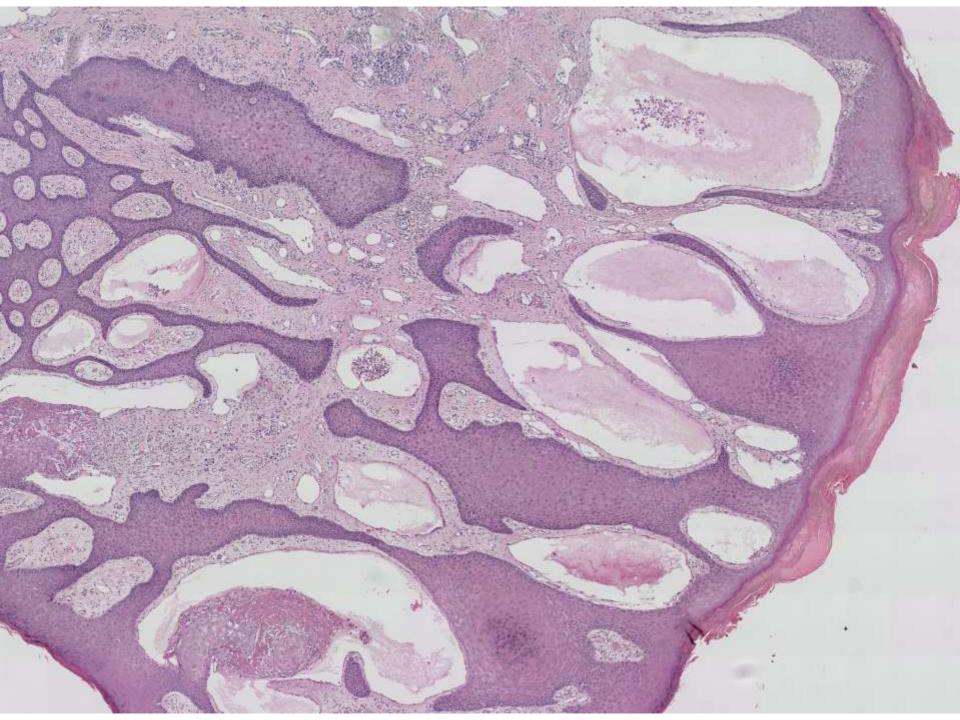
Ankur Sangoi; El Camino Hospital 54-year-old male with scrotal mass.

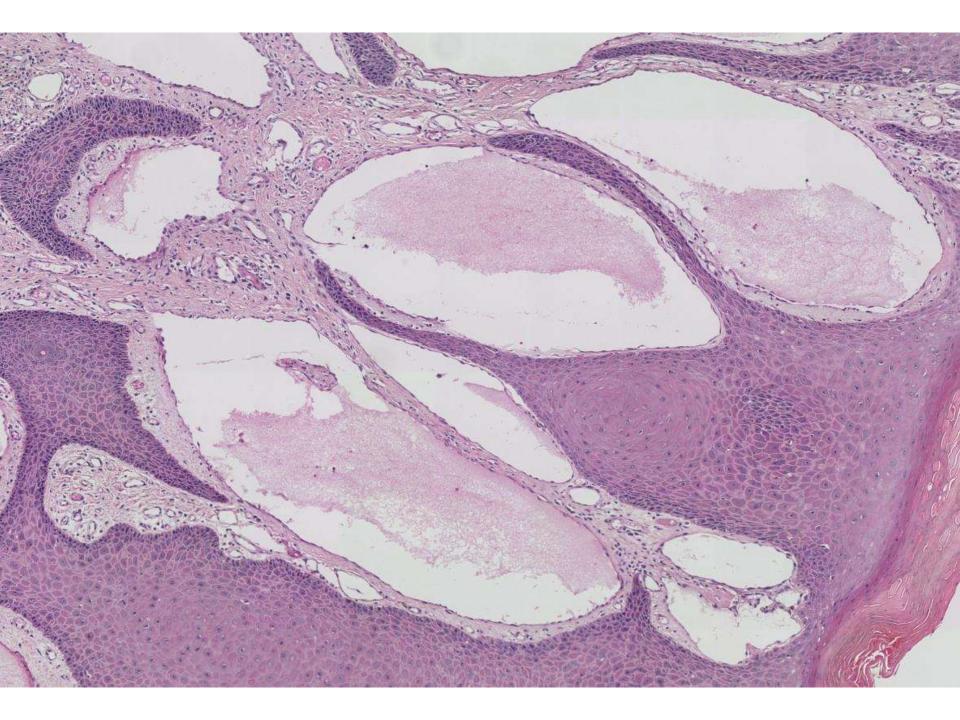


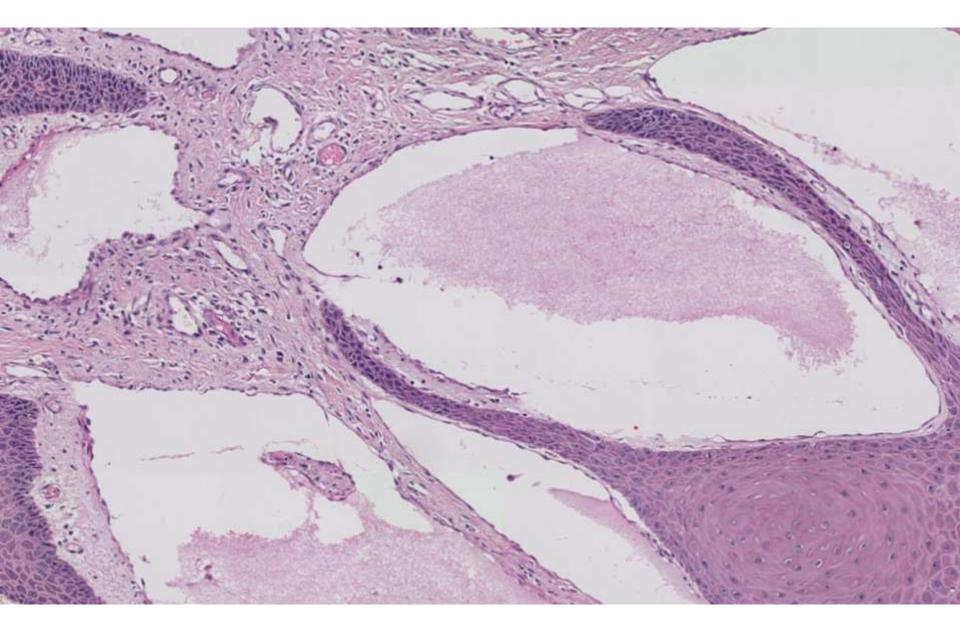


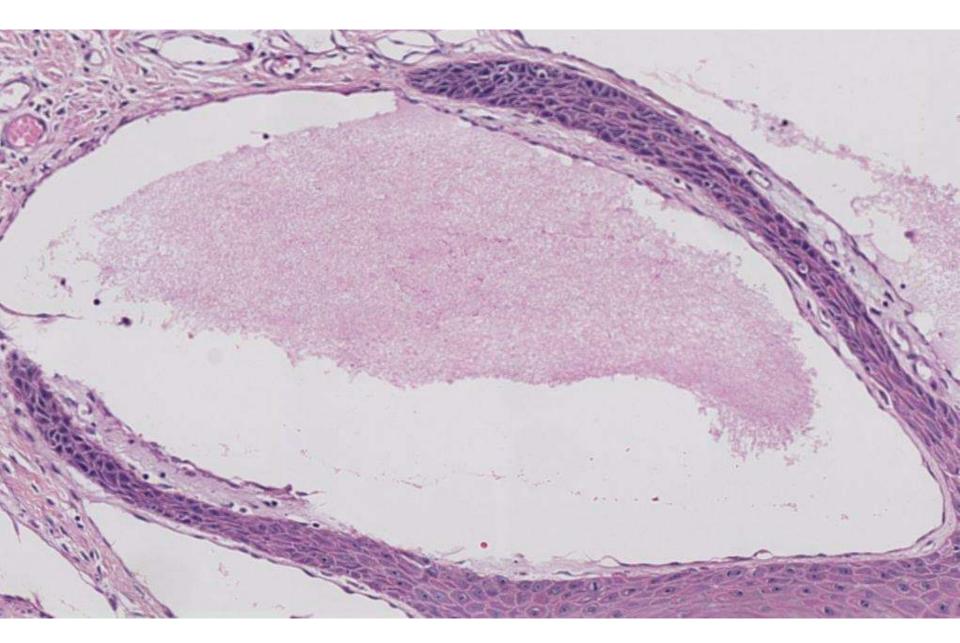








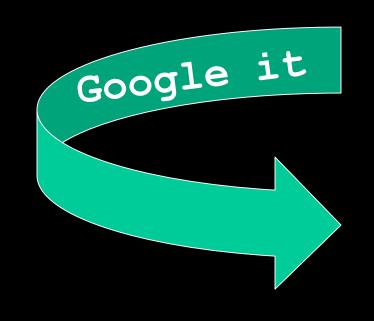




DDx

- Lymphangioma circumscriptum
- Angiokeratoma
- Hemangioma
- Glomangioma
- Lymphangiosarcoma







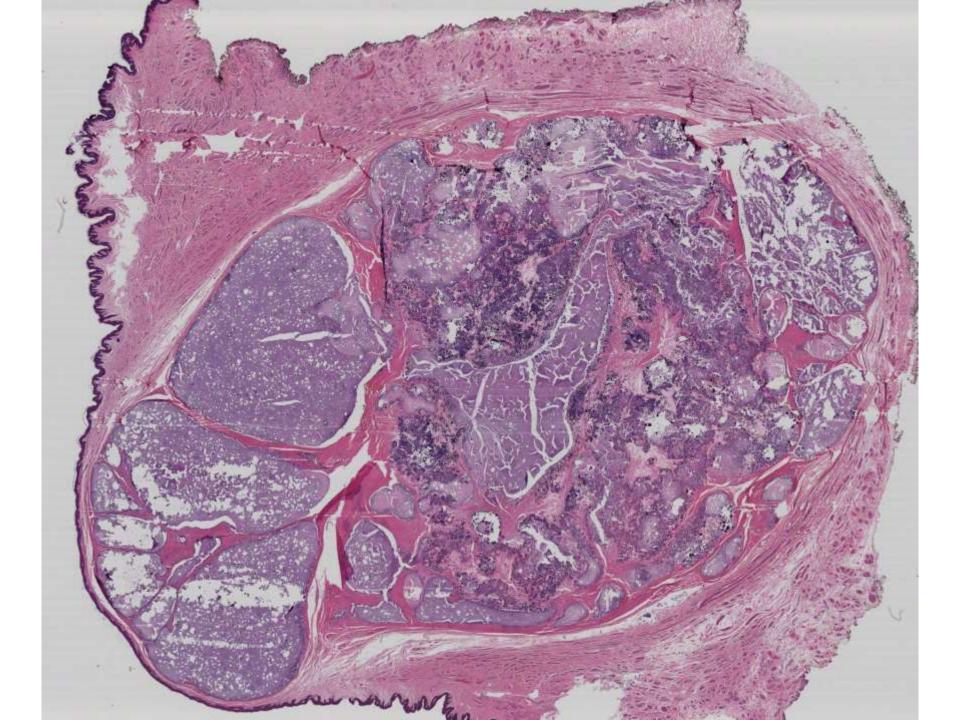
Lymphangioma circumscriptum

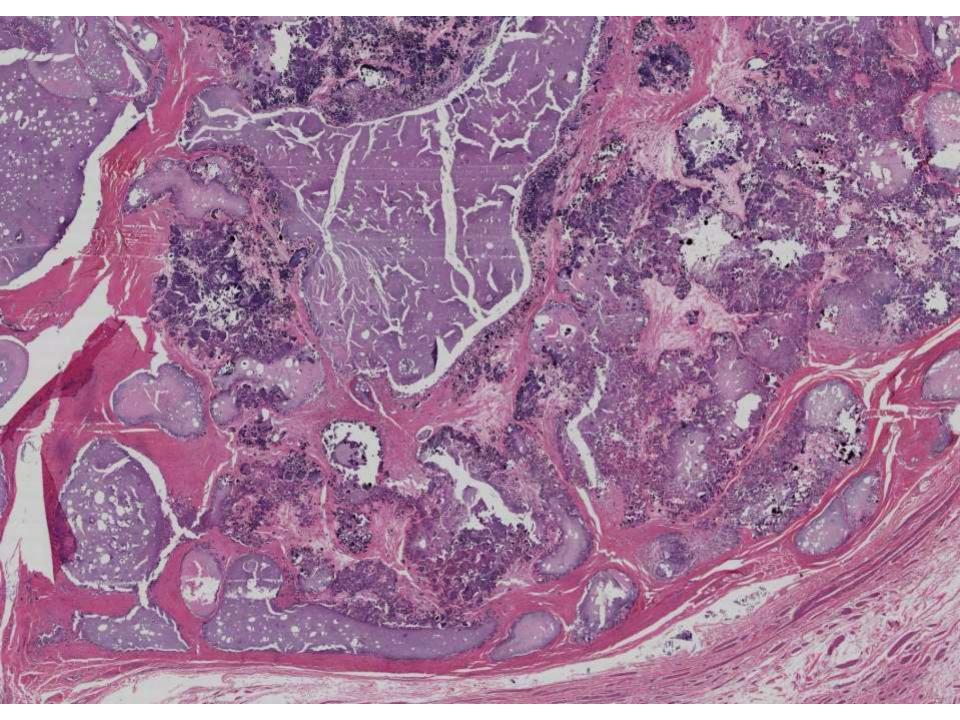
- Uncommon grouped papulovesicles
- Usually multiple, usually congenital, sometimes arising later in childhood
 – Rare in adulthood
- Deep component can exist
 - MRI often used to assess extent
- Tendency to recur after superficial excision
- Rarely → to lymphangiosarcoma (after XRT)

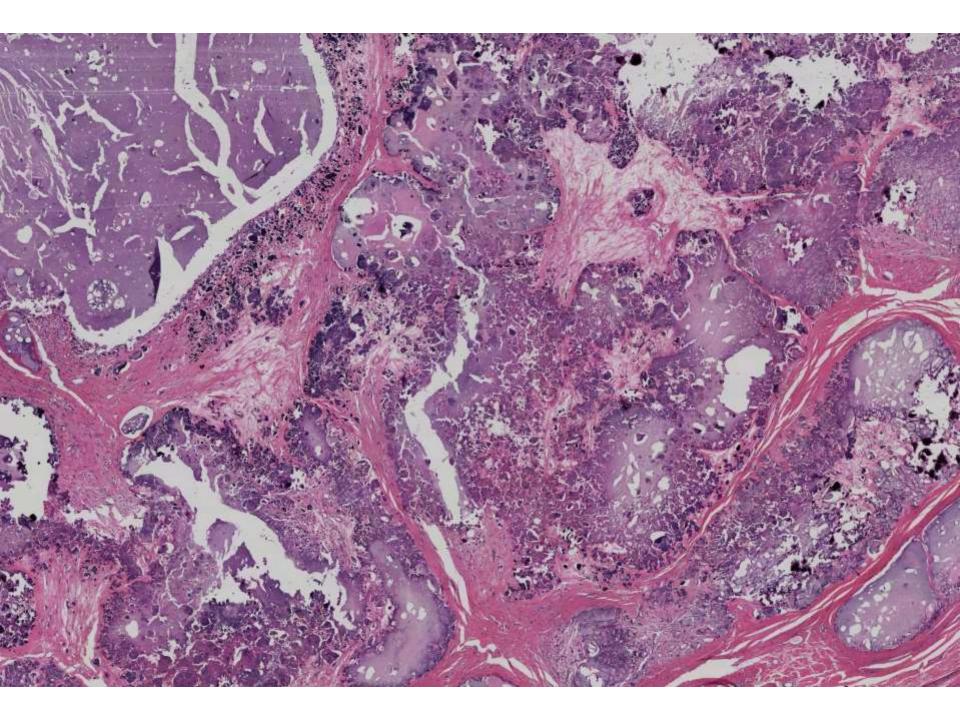
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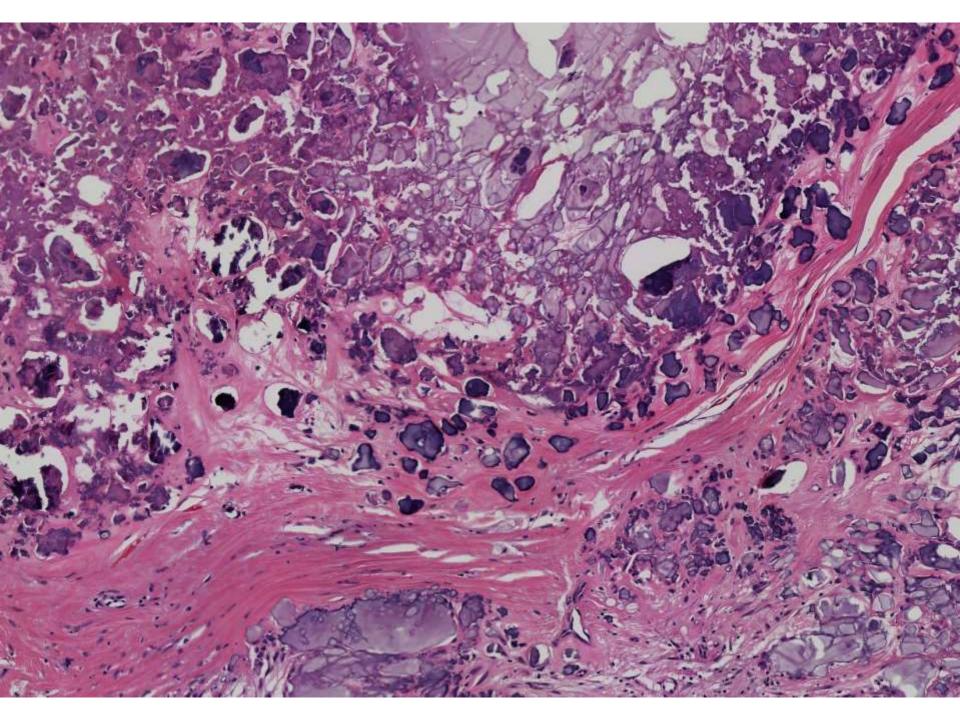
Ankur Sangoi; El Camino Hospital 47-year-old male with scrotal mass.

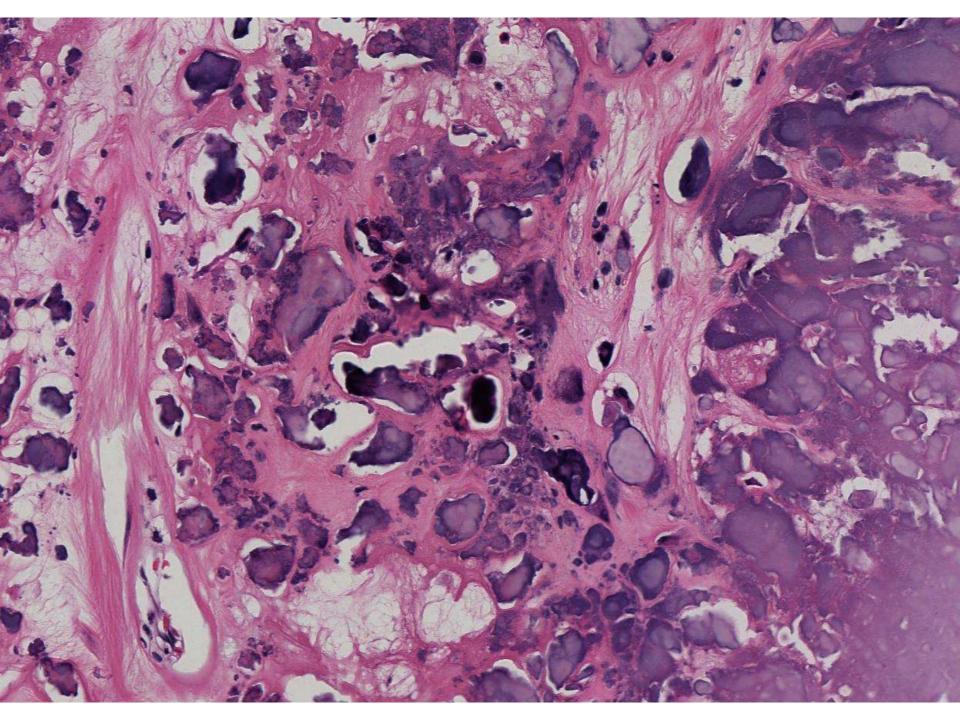














 "this entity has a very distinctive appearance with almost NO histologic differential diagnosis"



CAPTAIN OBVIOUS

DDx

- Idiopathic scrotal calcinosis
- Dystrophic calcification
 Onchocerca volvulus
- Nodular amyloidosis



idiopathic scrotal calcinosis

- Uncommon growth of brown/yellow nodules in scrotal skin
 - Ca deposits of various size + granulomatous rxn
- Typically begin in adolescence or early adulthood
 - Occurs in absence of abnormalities in Ca & PO4 metabolism
- Usually asymptomatic
 - Can have pain and infection
- Controversial risk of recurrence
 - Surgery probably still curative

Possible pathogenosis: "idiopathic" scrotal calcinosis

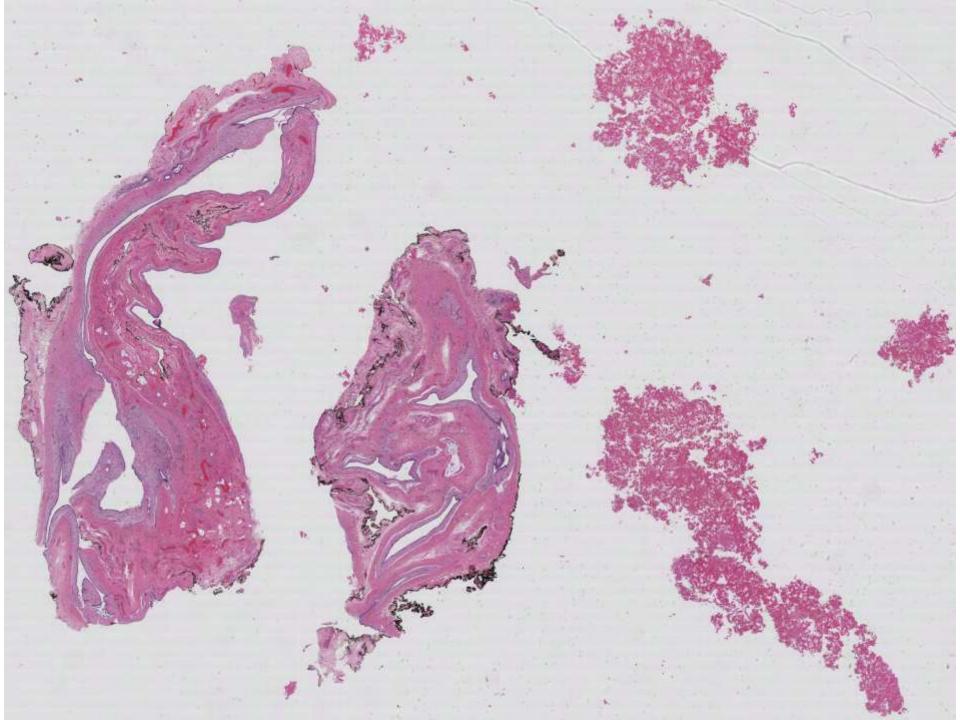
- Calcific degeneration of epidermoid cysts or eccrine sweat ducts
- Dartos muscle necrosis → dystrophic calcification
 - Similar to uterine leiomyoma calcification

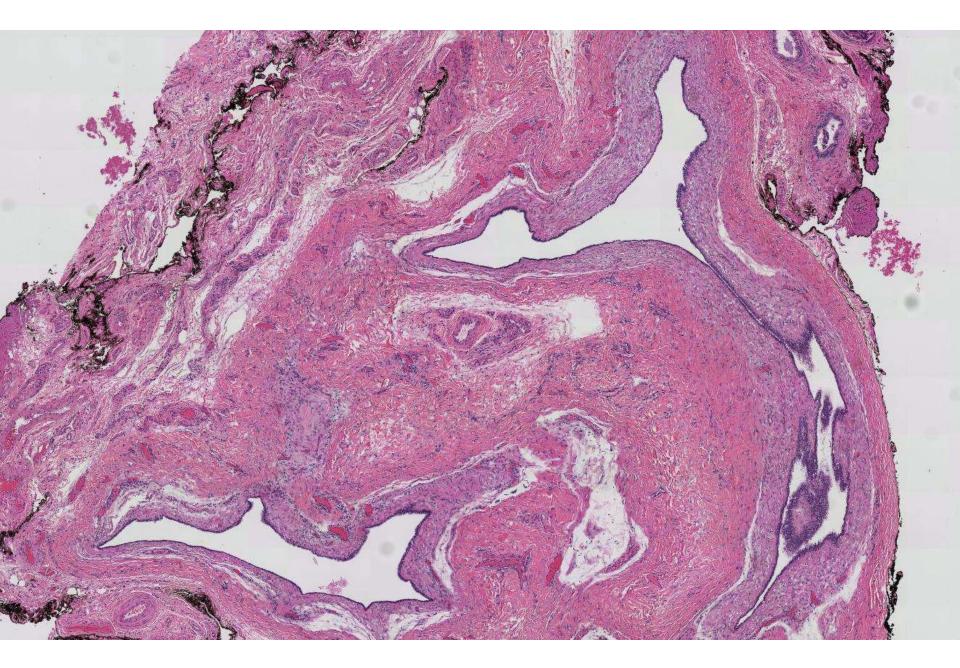
Cultural & Linguistic Competency References

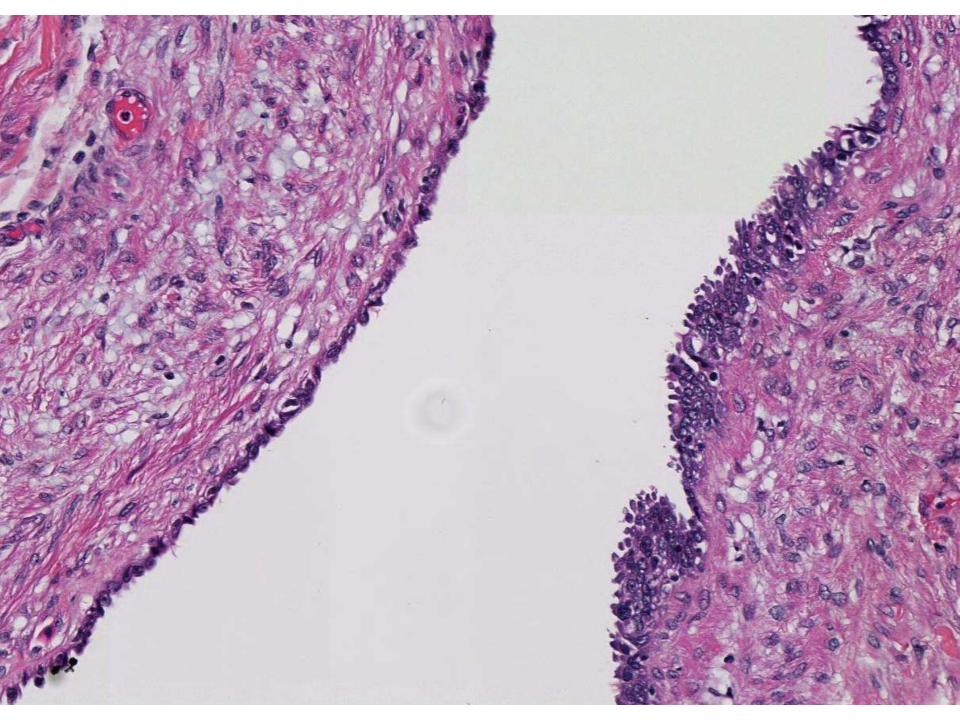
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- calcinosis: surgical treatment and histopathologic evaluation of etiology.
- Urology. 2010 Dec;76(6):1493-5. doi: 10.1016/j.urology.2010.02.001. Epub 2010 Apr
- 9. PubMed PMID: 20381842.
- Dubey S, Sharma R, Maheshwari V. Scrotal calcinosis: idiopathic or dystrophic?
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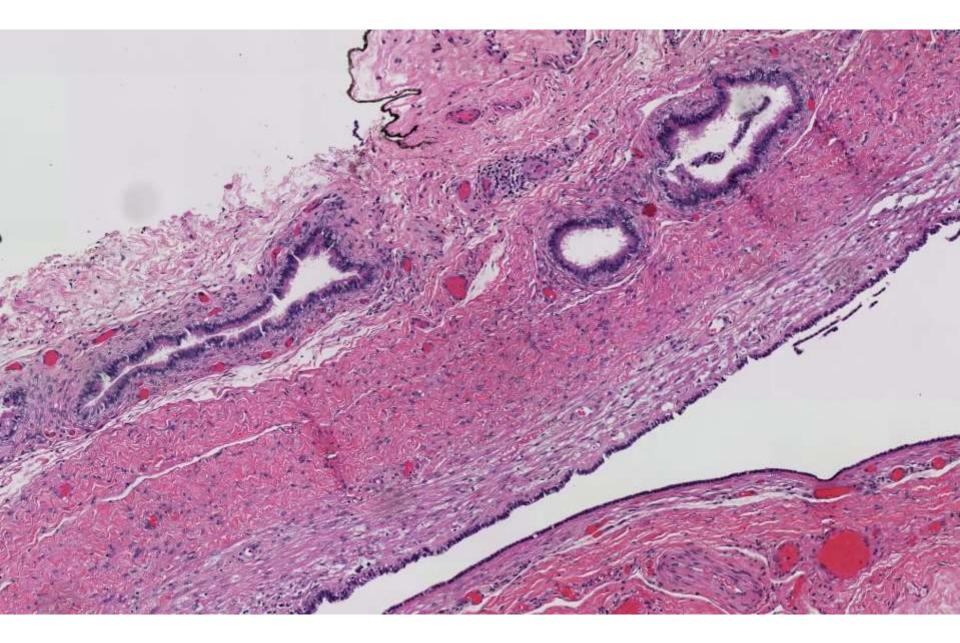
Ankur Sangoi; El Camino Hospital 24-year-old male with scrotal mass.

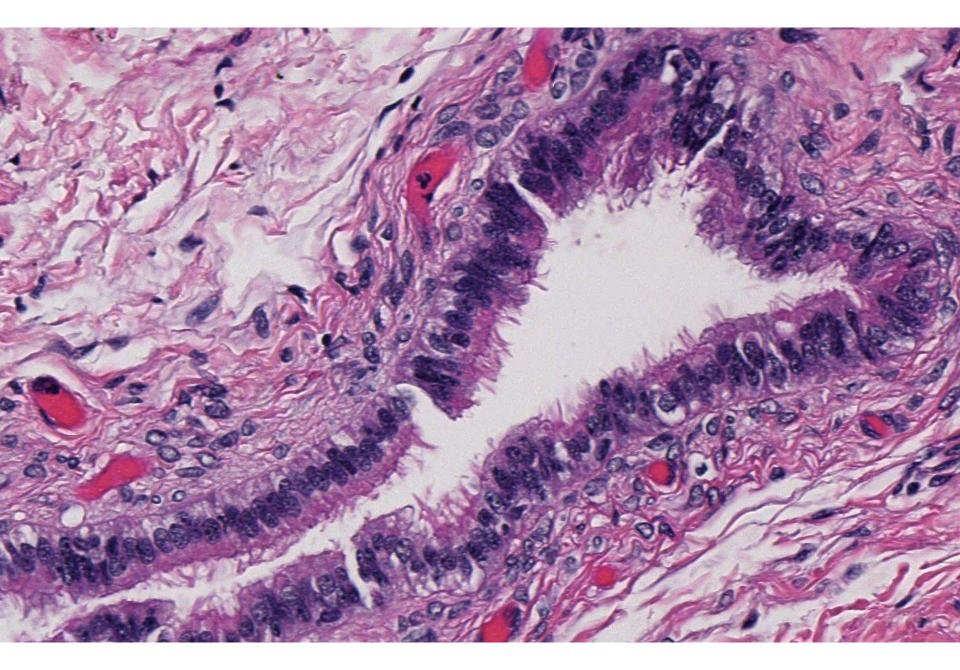


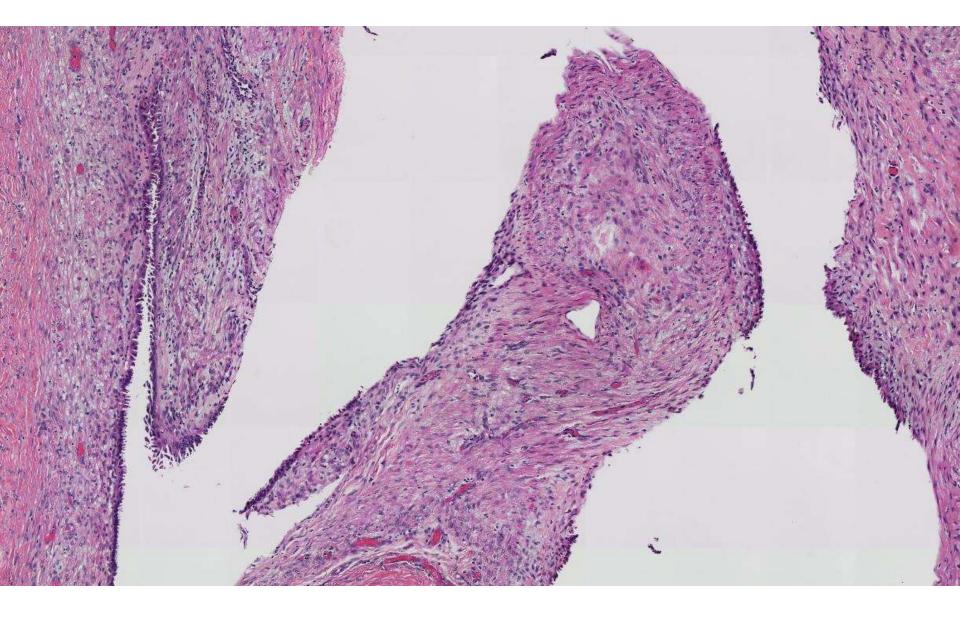


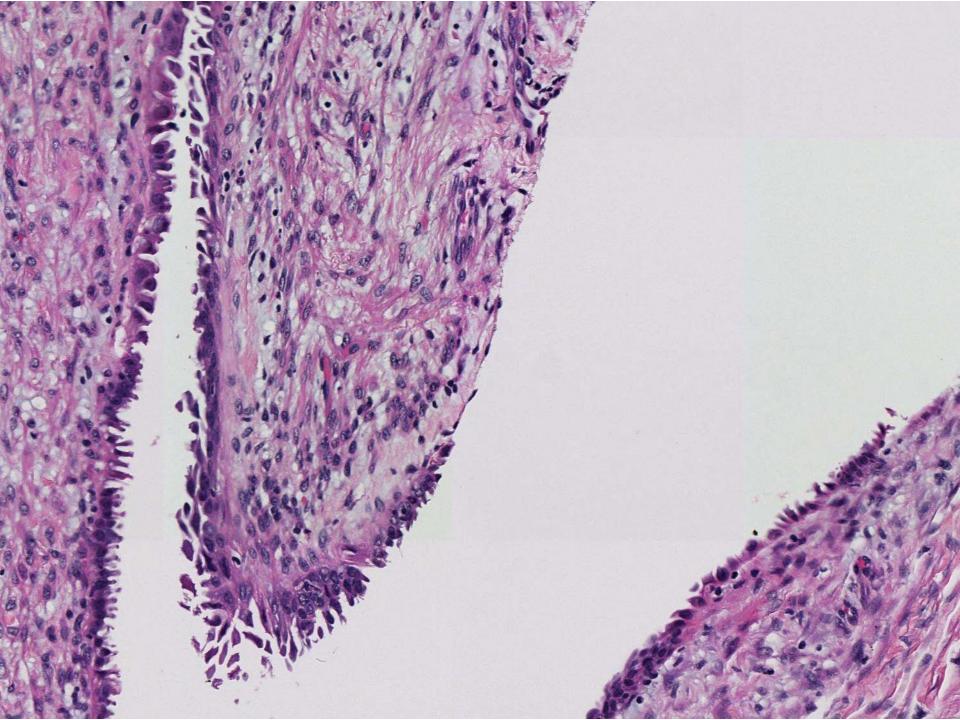


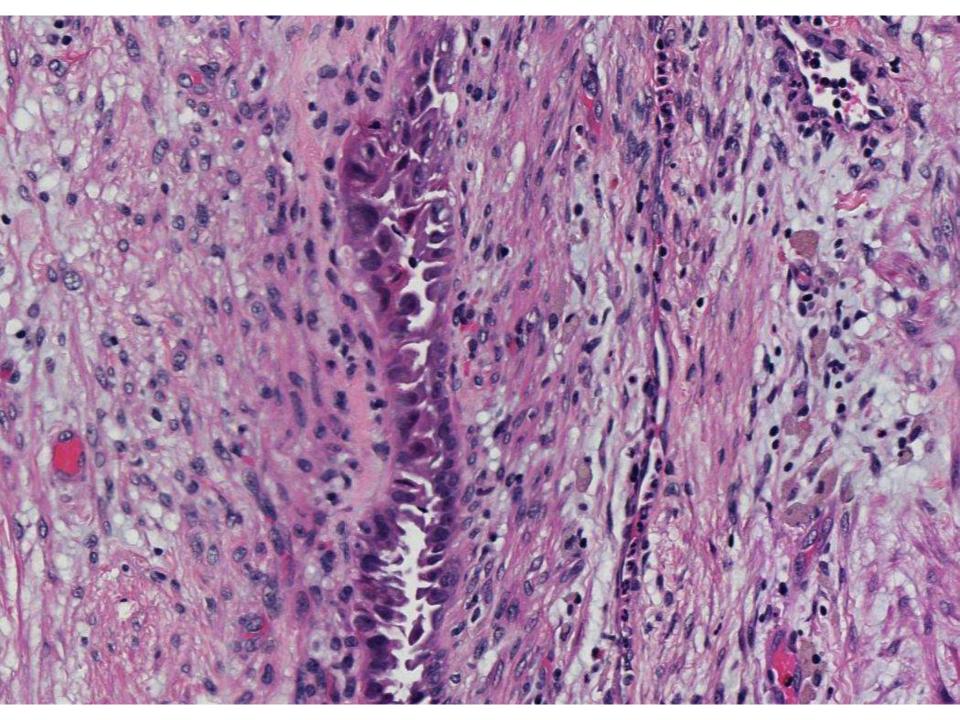












SCROTUM LESIONS (Rapini's dermpath book)

- Angiokeratoma
- Bowen's disease
- Contact dermatitis
- Candidiasis
- Calcinosis scroti
- Condyloma
- Elephantiasis
- Epidermoid cyst
- HSV
- Leiomyoma
- Lichen simplex chronicus
- Paget's disease
- Pediculosis pubis
- Sclerosing lipogranuloma

Cutaneous cysts

- Hidrocystoma
- Bronchogenic cyst
- Cystadenoma
- Dermoid cyst
- Keratinous cyst
- Follicular cyst
- Steatocystoma
- Vellous hair cyst

Cutaneous cysts

- Hidrocystoma
- Bronchogenic cyst
- Cystadenoma →
- Dermoid cyst
- Keratinous cyst
- Follicular cyst
- Steatocystoma
- Vellous hair cyst

Cutaneous cysts

- Hidrocystoma
- Bronchogenic cyst
- Cystadenoma →
 - Cutaneous ciliated cyst (cutaneous Muellerian cyst)
- Dermoid cyst
- Keratinous cyst
- Follicular cyst
- Steatocystoma
- Vellous hair cyst

Dx:

cutaneous Muellerian cyst

- Usually extremity of teenage girls

 thigh>buttock>calf>foot
- Müllerian (paramesonephric) derivation, representing a migration abnormality of fetal development (heterotopia)
- Cysts arising at other sites and in males may represent metaplasia of lining of a pre-existent simple cyst of sweat duct derivation