South Bay Pathology Society

December 2015

Disclosures
December 7, 2015

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

Presenters:

Claude Burdick, MD
Thuy Nguyen, MD
Charles Lombard, MD
John Higgins, MD
Laura Hofmeister, MD
Alana Shain, MD
Kimberly Allison, MD
Christine Louie, MD
Teri Longacre, MD
Soo-Ryum Yang, MD
Eduardo Zambrano, MD
Sanjay Kakar, MD
Jenny (Peng) Li, MD
Dita Gratzinger, MD, PhD

Activity Planners:

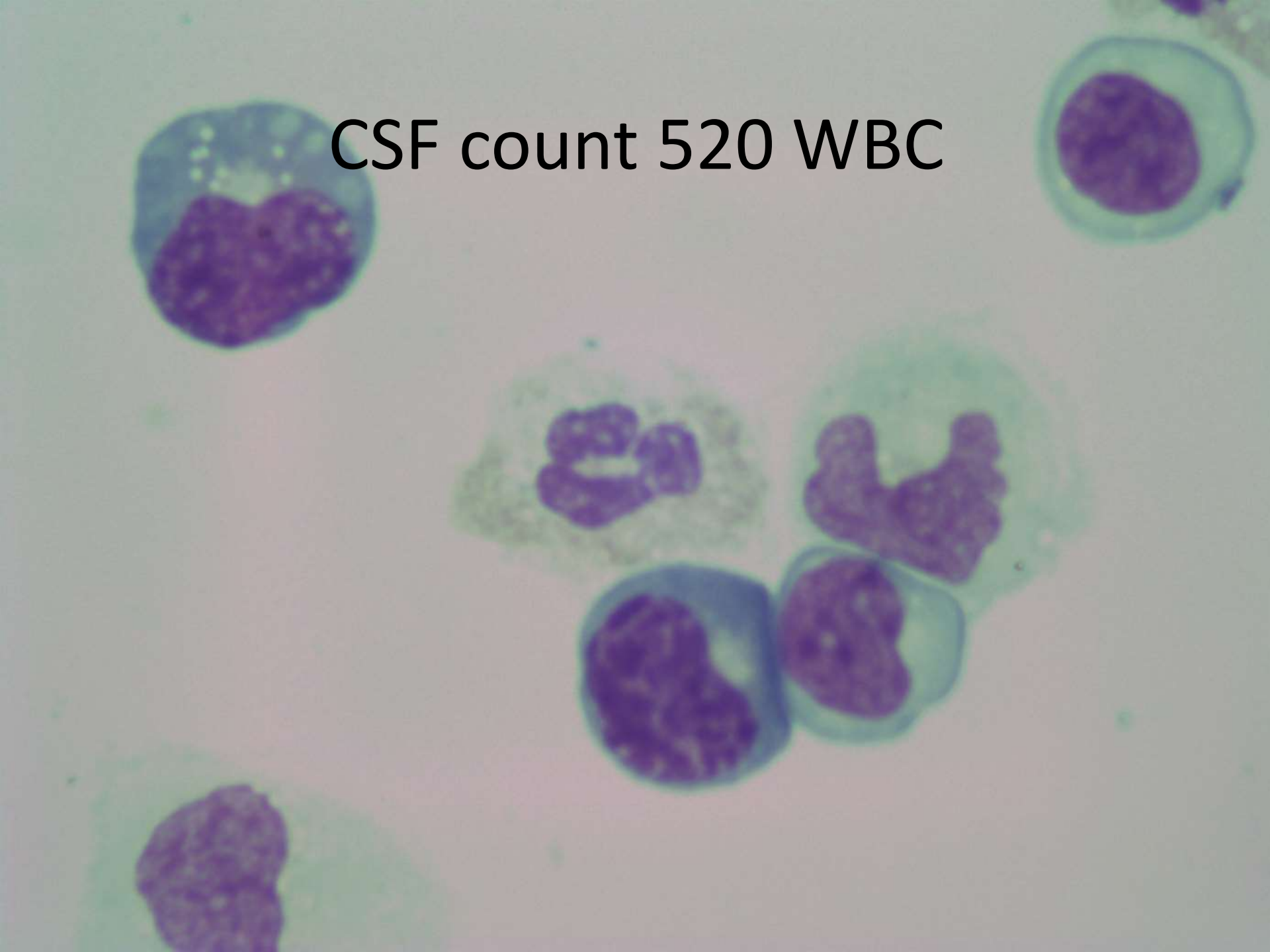
Kristin Jensen, MD
Ankur Sangoi, MD
William Rogers, MD

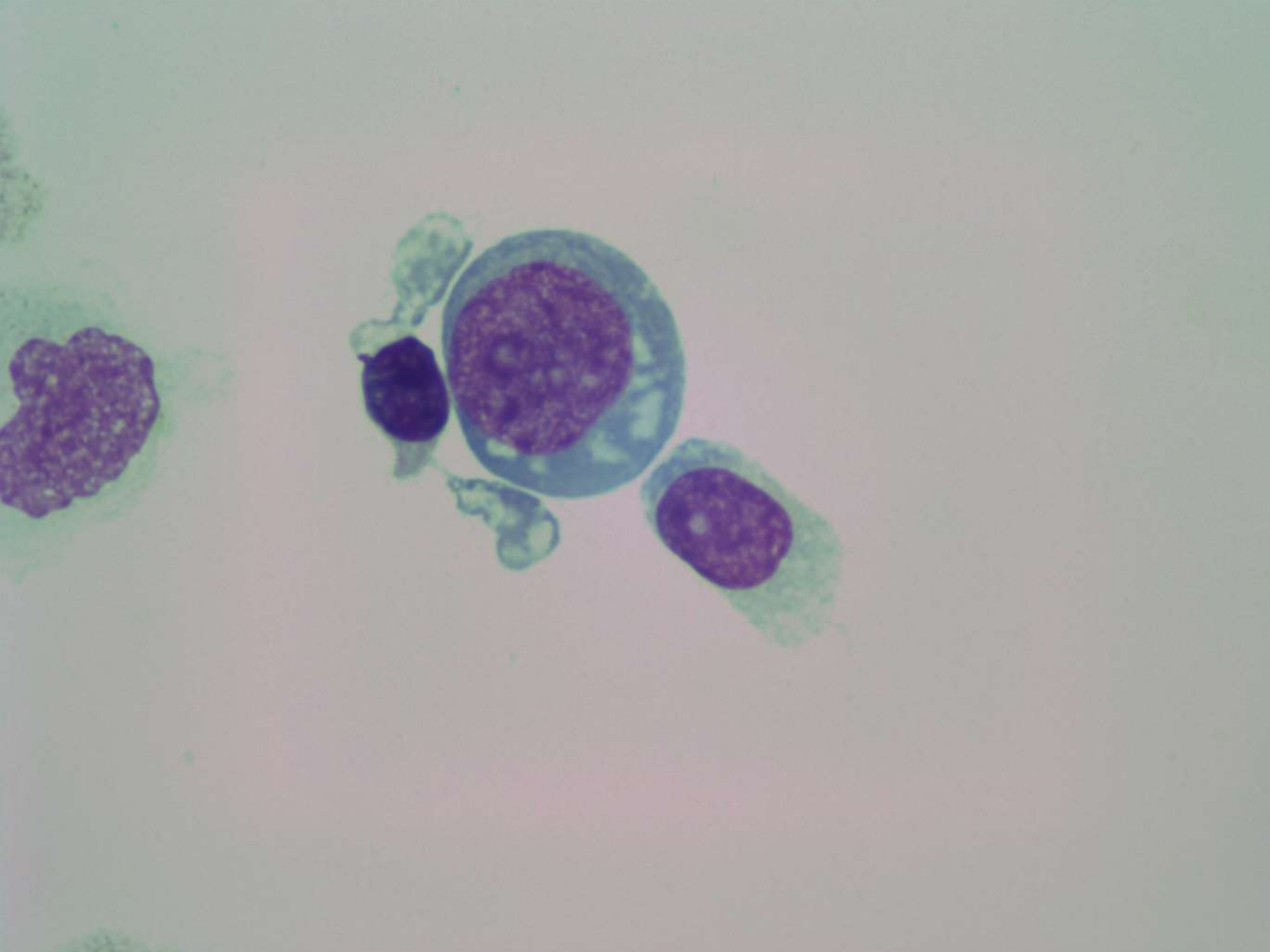
SB 6001

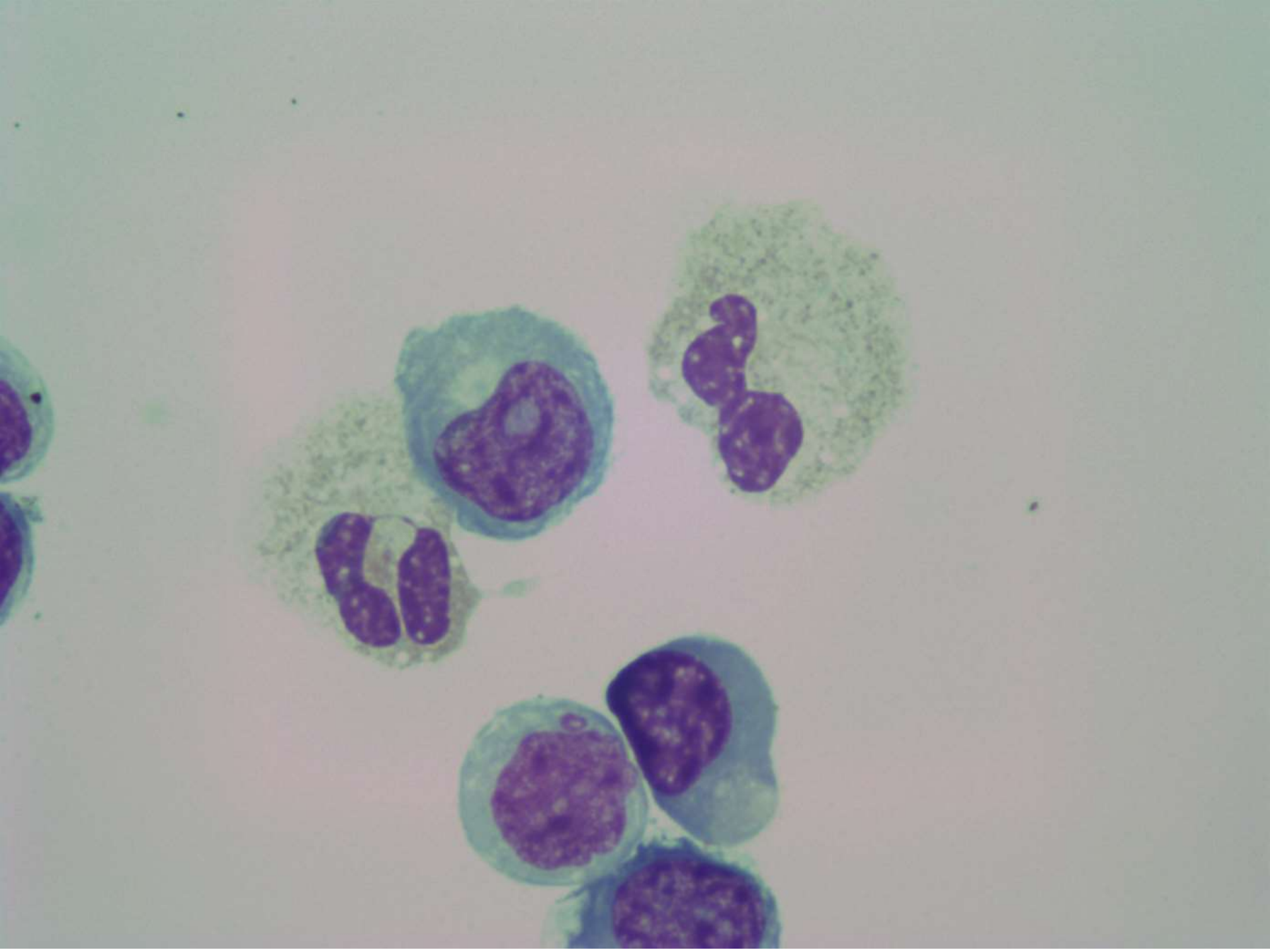
- 55-year-old male with sudden onset of convulsions, disorientation, and staggering gait. CSF cytology submitted.

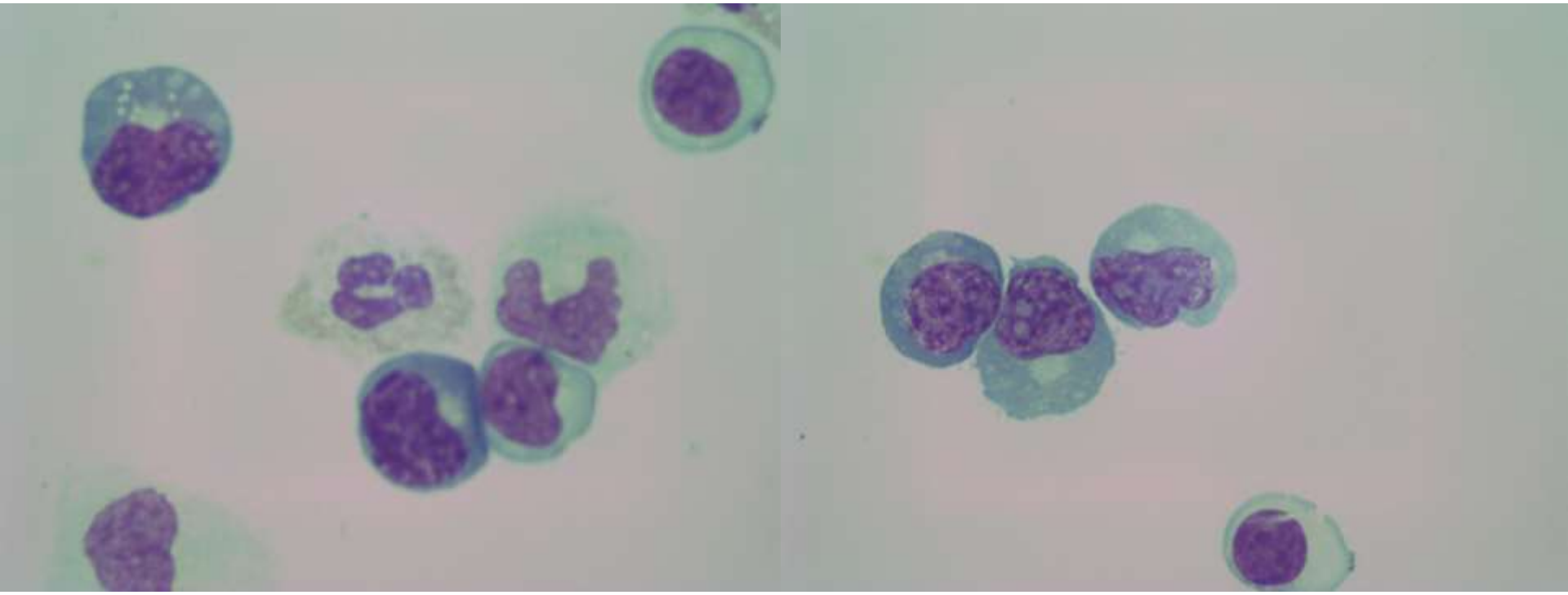
- **Claude Burdick; St. Rose Hospital**

CSF count 520 WBC









Diagnosis??

West Nile Virus

- Discovered in Uganda 1937
- First head of state:

Was Elizabeth II

Present Head of State

Yowari Musaveni

For the past 29 years

WNV: Mosquito Born Virus

- Corvids are v. susceptible: crows, jays, some raptors and sparrows.
- Dogs and cats are resistant
- Horses are susceptible
- Chickens are not sickened, and so are used as sentinels
- About 1% of infected humans become sick.

Cultural and Linguistic Factors

Consider disparities beyond race, ethnicity and language

Importance of WNV

- Arrived in US in 1999 in NYC
- 3 Largest neuroencephalitis epidemics: 2002,2003, 2012-Each with 3000 NeuroInv cases
- 10 years to 2009, 780,000 infections-Now > Mil
- ¼ get “West Nile Fever” similar to Dengue
- Of those, <1% get Neuroinvasive disease.
- Of those, 10% die.
- 40% of Patients with Neuroinvasive disease can have symptoms up to 8 years post disease.

Diagnosis

- Usually order “West Nile Virus IgM antibody.
- This is a MAC-ELISA test (M antibody capture)
- If positive, patient has the disease. Requires 4 to 10 days after viremia (fever).
- In early cases, draw acute and convalescent s.
- False positives occur with other flavoviruses: Jap B, Yellow Fever, StLe. Separated by PRNT or Plaque Reduction Neutralization Test (CDC)

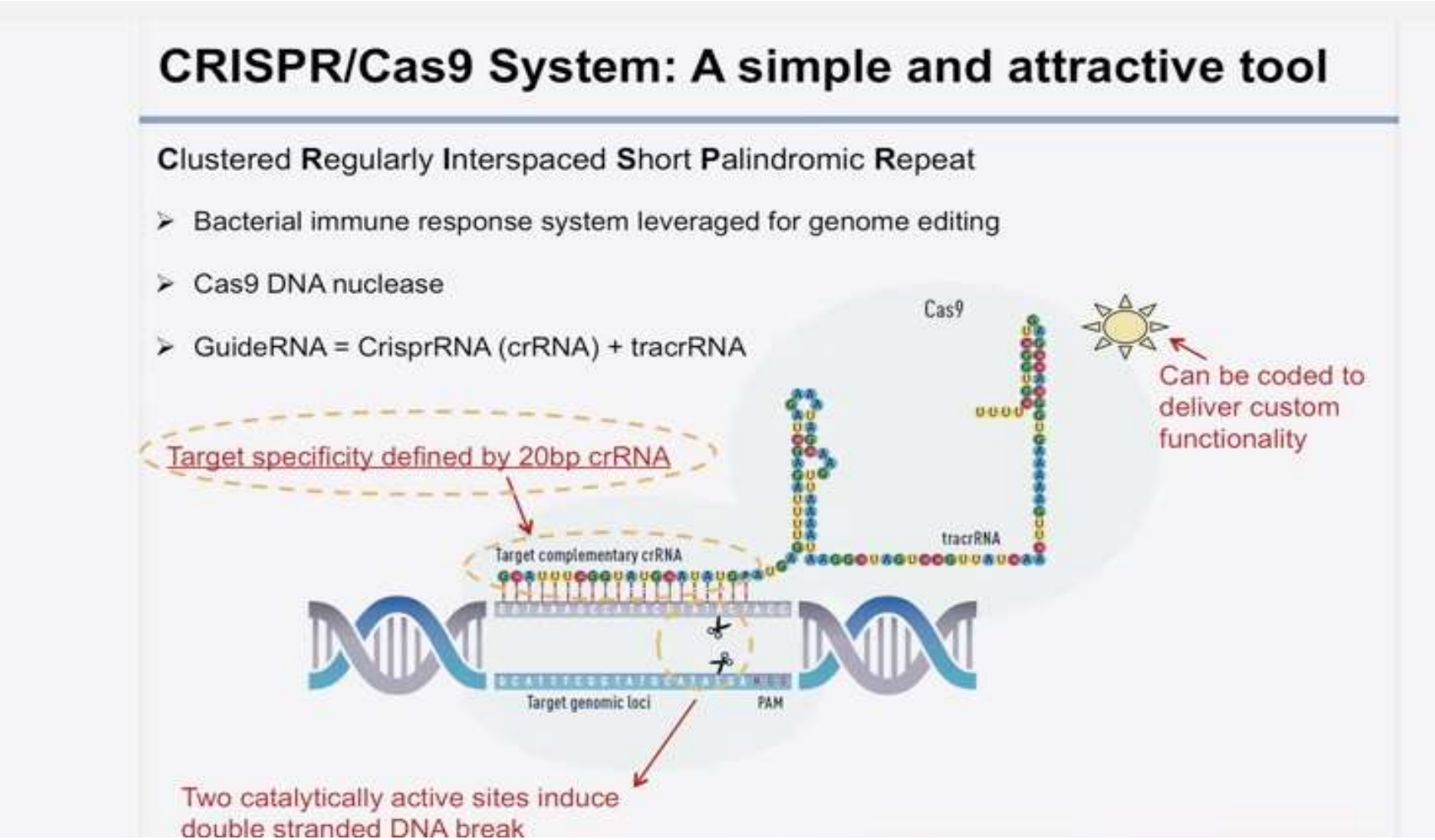
Surveillance for WNV, 2015

County	Dead Birds	Human Cases	Sentinal Chickens
Alameda	16	0	0
Contra Costa	11	1	18
Santa Clara	231	8	5
San Francisco	0	0	0
San Mateo	22	0	0
Los Angeles	92	163	137
ALL OF CALIFORNIA	1323 in 22 counties	637, 38 fatal-No BA	442

Eradication Potential

- For rapid breeding species, like mosquitoes, “Gene Drive” technology has the potential to alter the genome to eliminate the arthropod as a host and vector: Malaria, Dengue, Yellow Fever, West Nile Virus.
- A gene drive ensures that nearly all offspring inherit an altered gene, so that it spreads rapidly through a population.

HOW IT WORKS


CRISPR/Cas9 System: A simple and attractive tool
Clustered Regularly Interspaced Short Palindromic Repeat
Bacterial immune response system leveraged for genome editing
Cas9 DNA nuclease
GuideRNA = CrisprRNA (crRNA) + tracrRNA
Cas9
Can be coded to deliver custom functionality
Target specificity defined by 20bp crRNA
tracrRNA
Target complementary crRNA
Target genomic loci
PAM
Two catalytically active sites induce double stranded DNA break

BIG TIME BIOETHICAL PROBLEM

- Wyss Institute (Harvard/MIT): Did foundation work. “All work is done on laboratory strains.”
- Anthony James of UC Irvine announced last week that he has wild type Culex Pipiens from India ready for release that can eliminate Falciparum Malaria in India, probably in 2 years.
- What to Do???

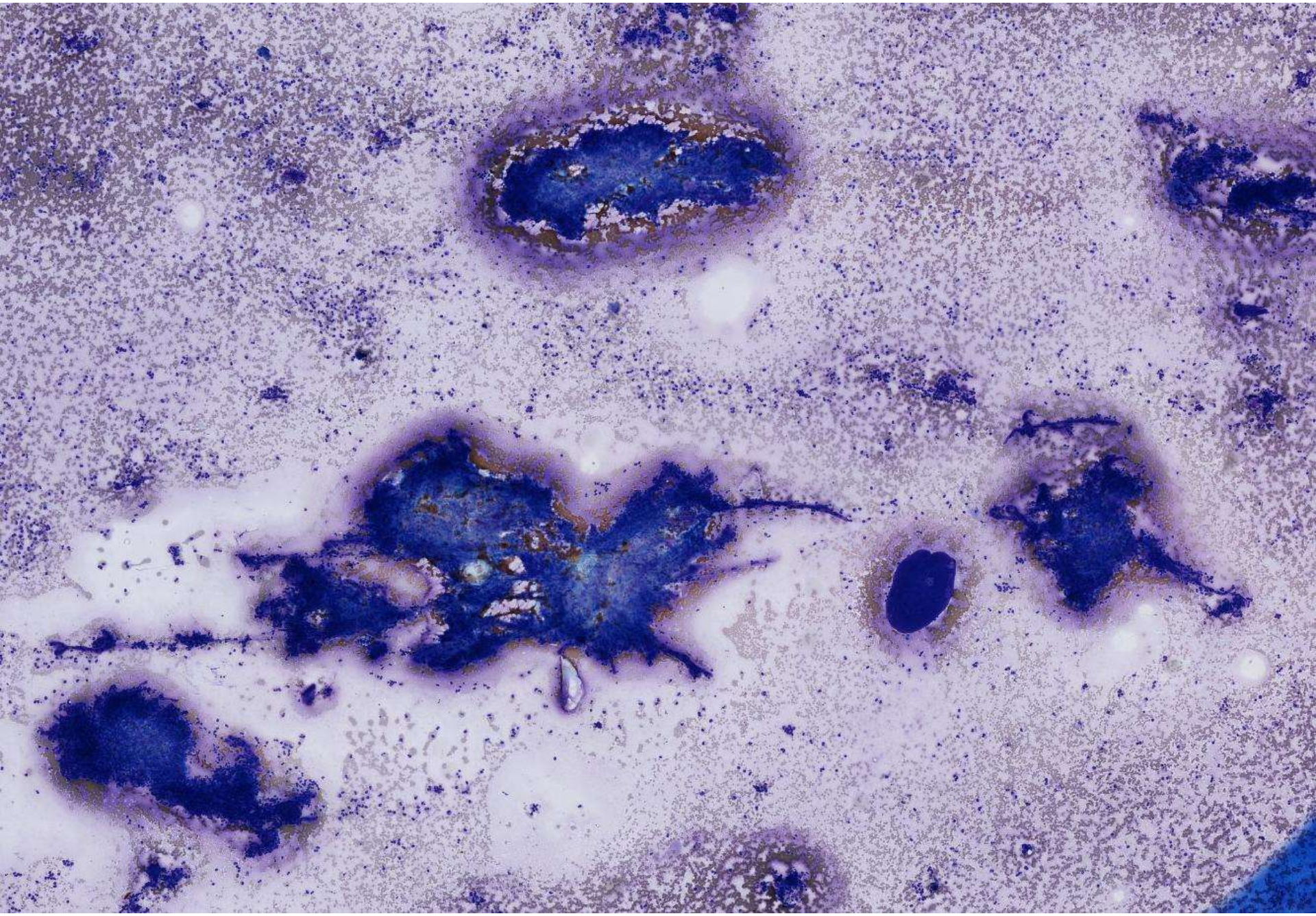
National Academy of Sciences Summit

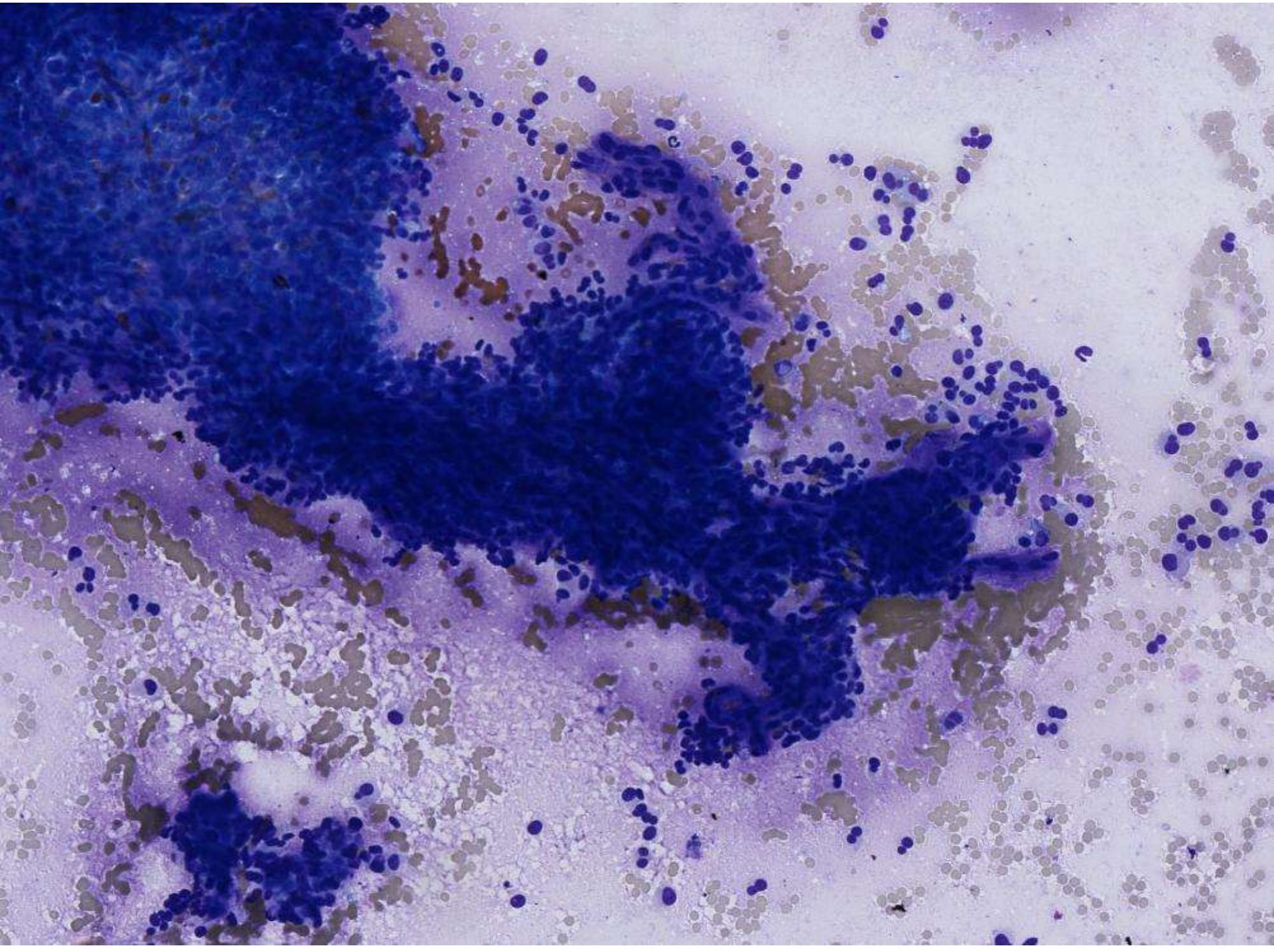
- STARTED YESTERDAY IN WASHINGTON DC
- FINISHED TODAY
- I DON’T KNOW WHAT THEY DECIDED

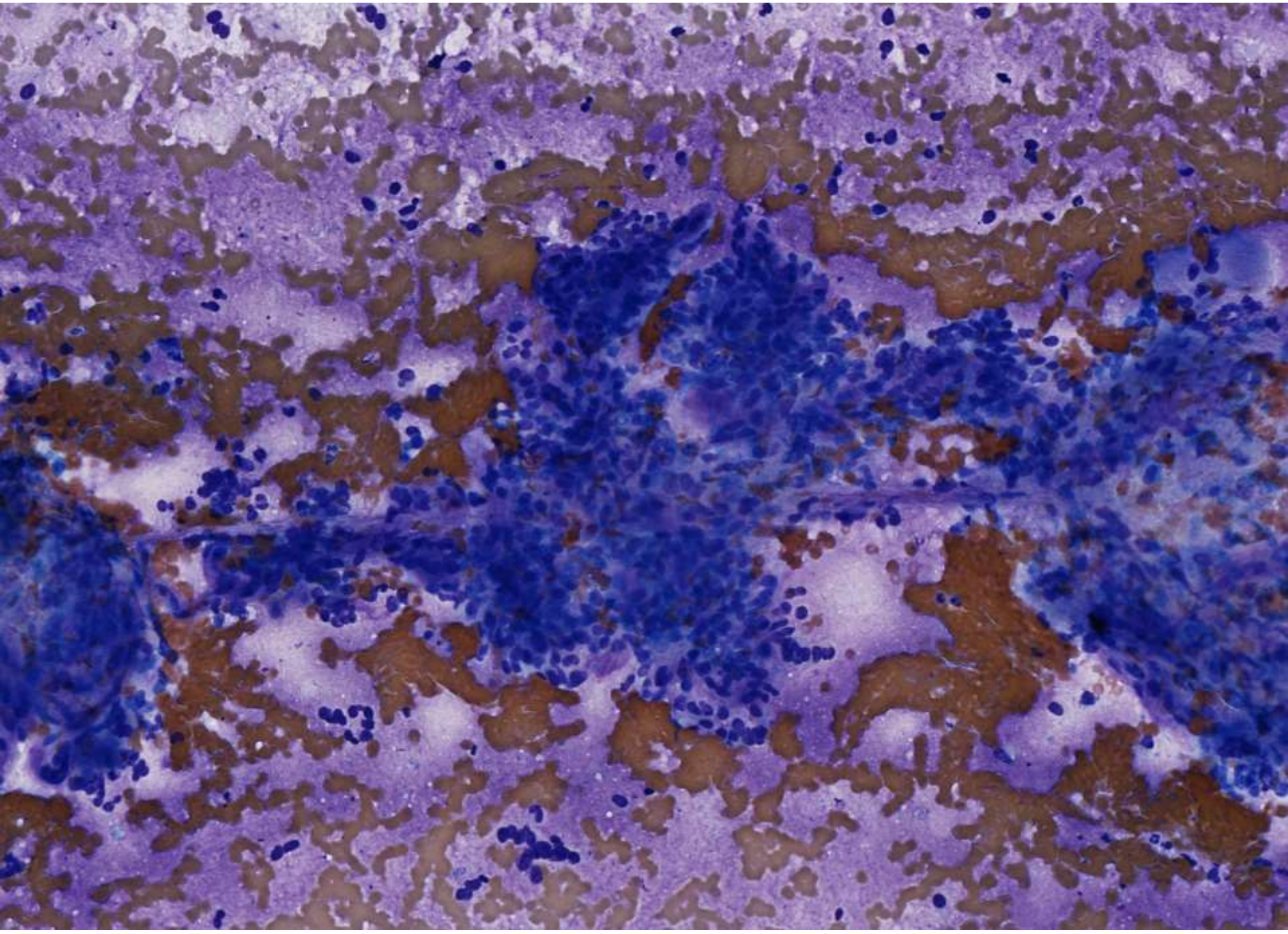
SB 6002

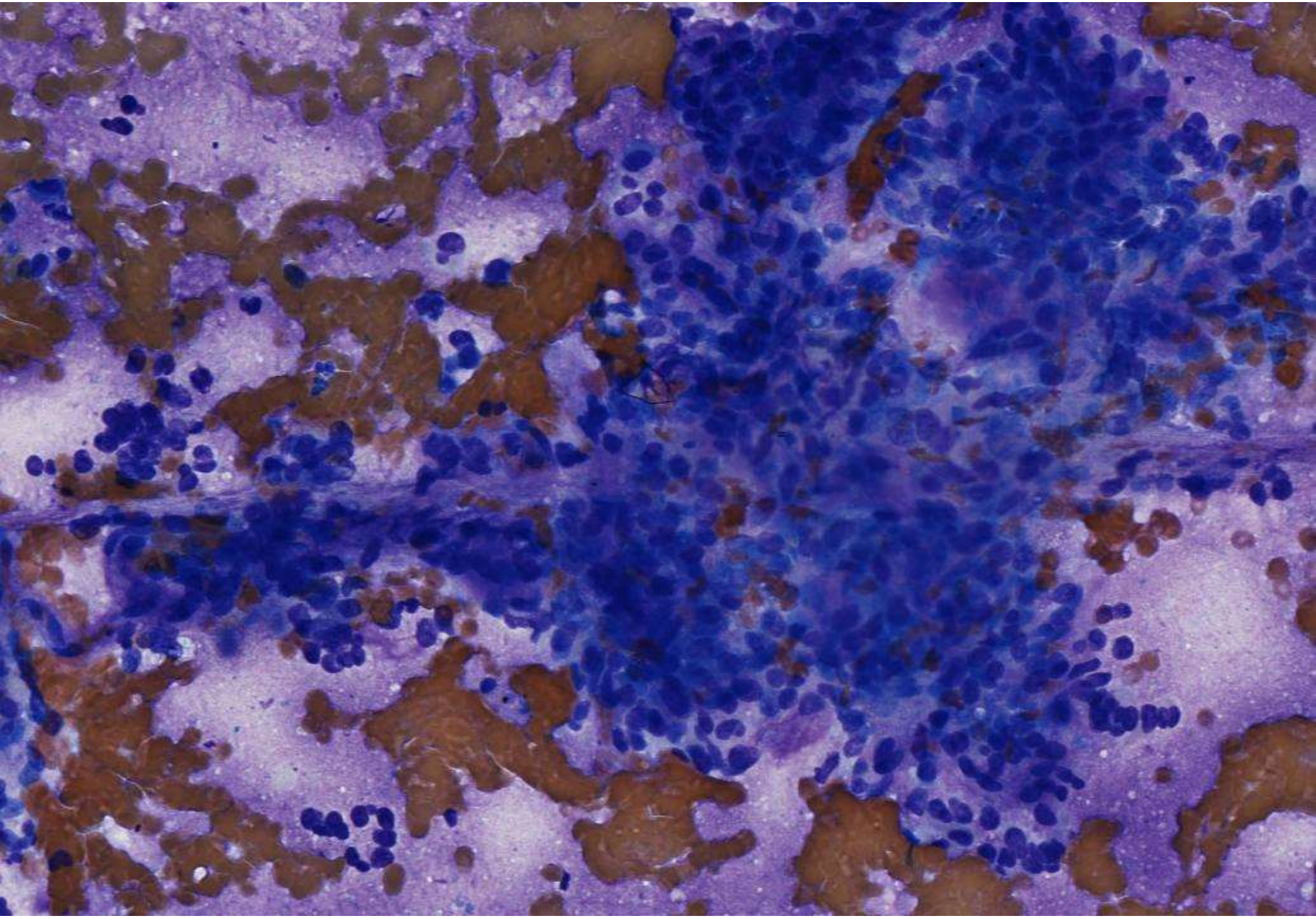
- 33-year-old female with 7.5cm cystic mass in head of pancreas found on ultrasound evaluation for radiating abdominal pain worse after meals. FNA performed

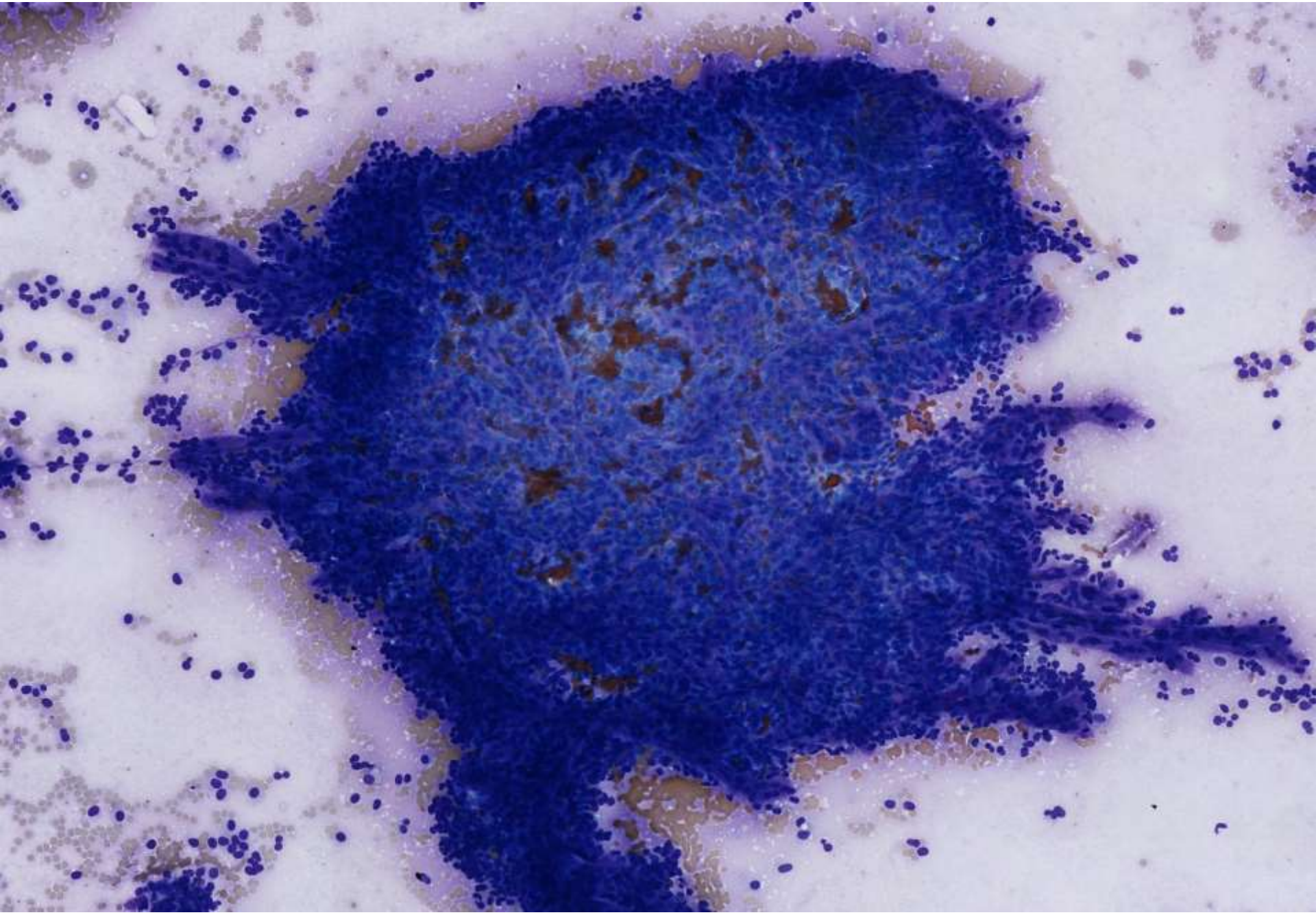
- **Thuy Nguyen; Mills Peninsula**

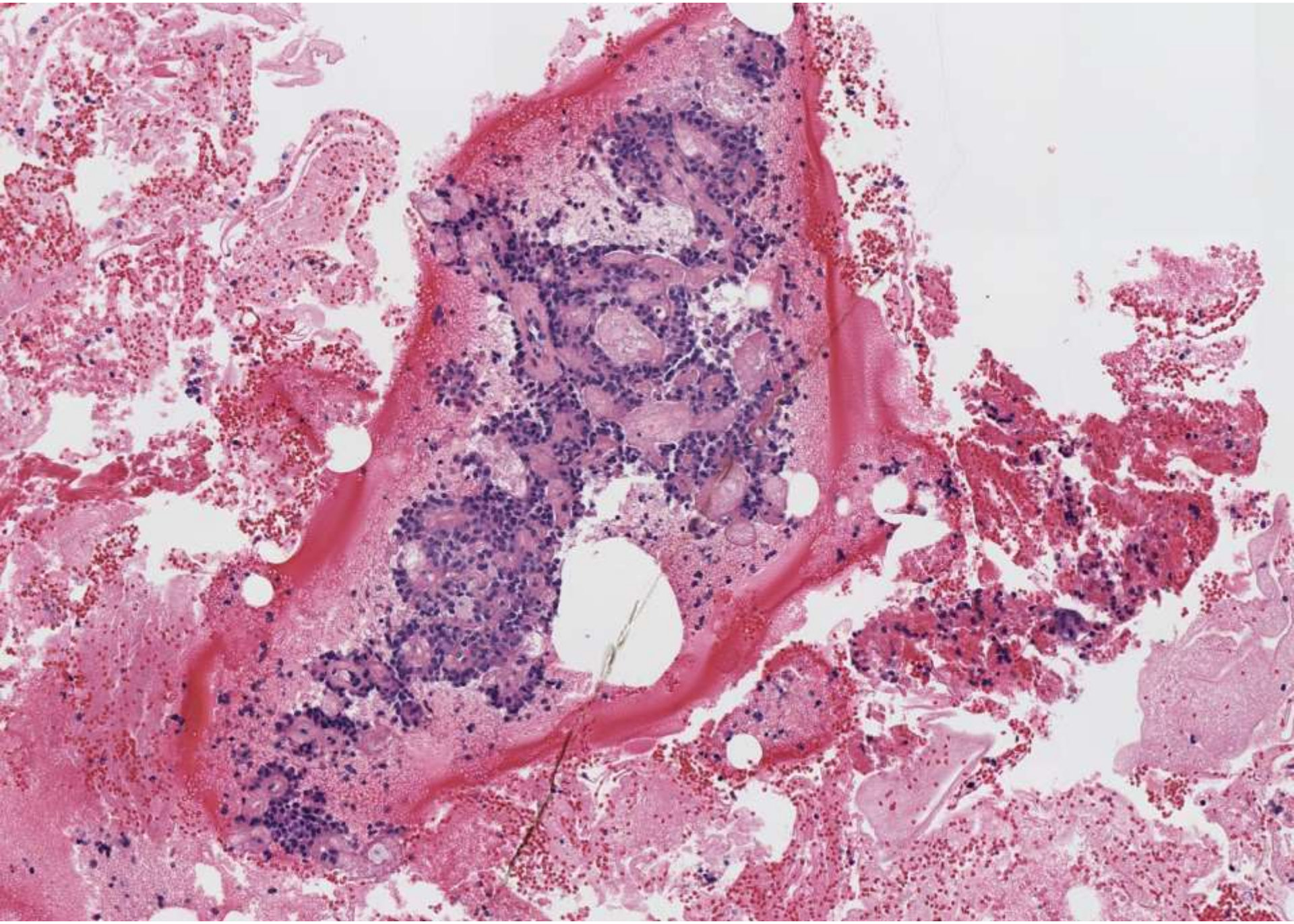








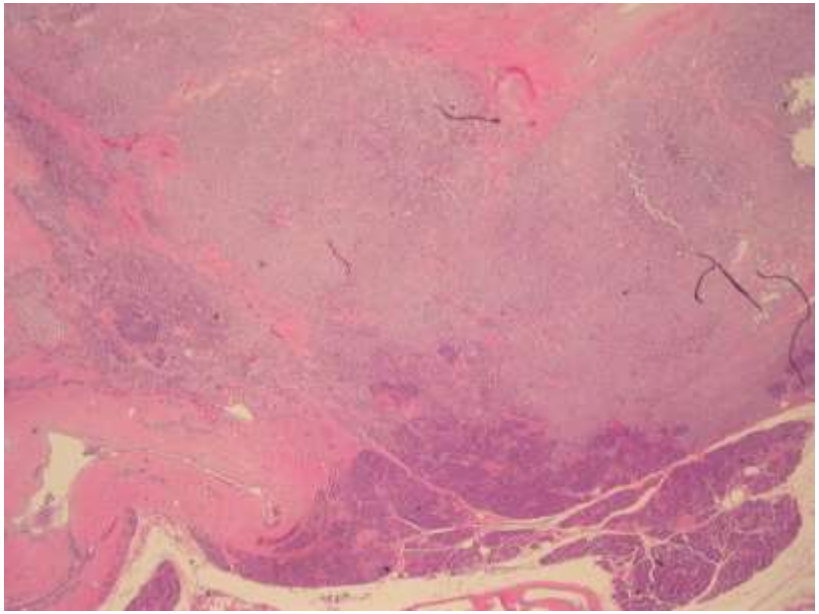


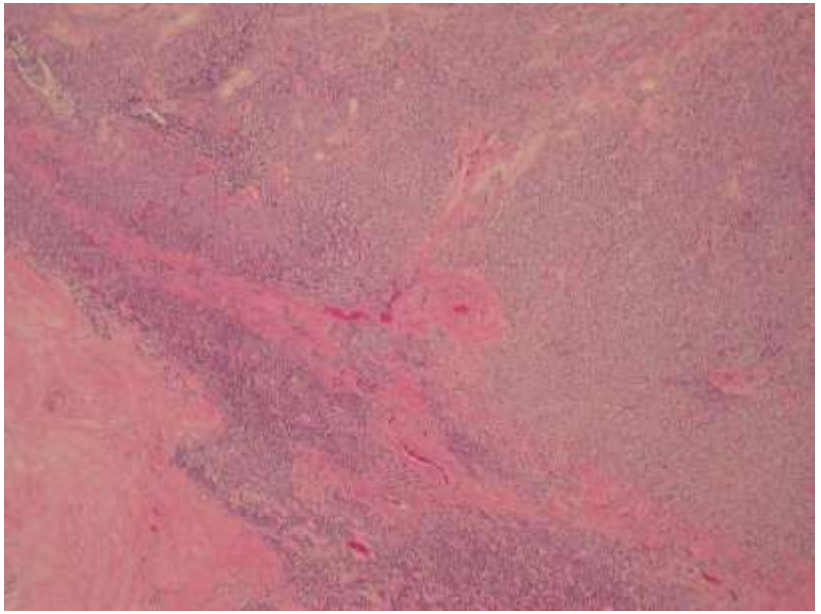


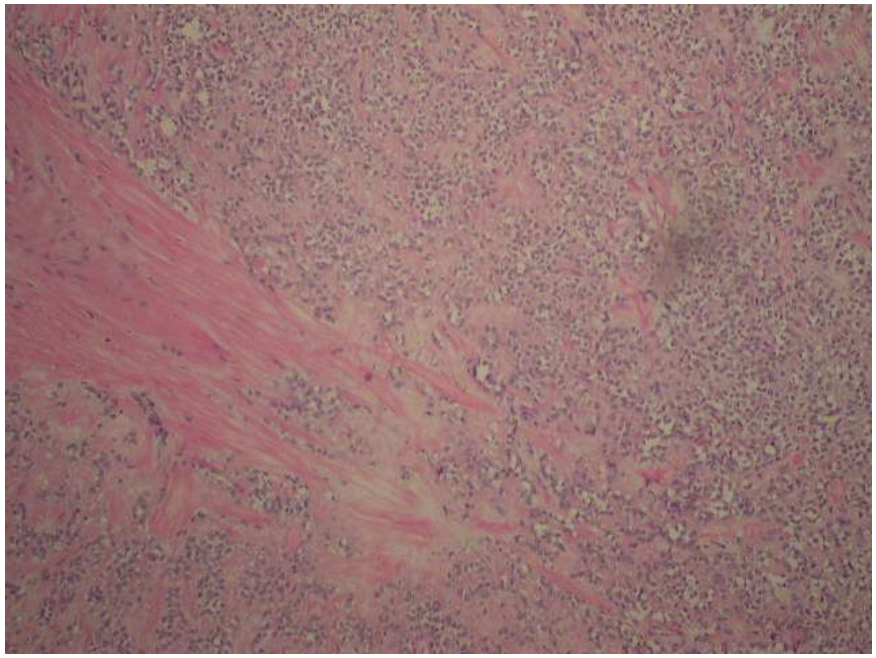
Diagnosis??

Case

- 33 year old woman presents with abdominal pain
- Found to have increased amylase
- Ultrasound shows a 7.5 cm mass in the head of pancreas







FNA

- Cell block stained:
  - Negative:
    - Chromogranin
  - Positive
    - Vimentin
    - CD10

Solid Pseudopapillary Neoplasm (SPN)

- Low grade malignancy
- Poorly cohesive monomorphic epithelial cells forming solid and pseudopapillary structures
- Not truly papillary or truly cystic
- 1-3% of non-endocrine pancreatic neoplasms
- Epidemiology:
  - Mean age 30-35 years
  - Greater than 90% women
  - Not associated with clinical syndrome
  - SPN in males
    - Average age at diagnosis is older ~ 50
    - Studies showed SPN is more solid in males

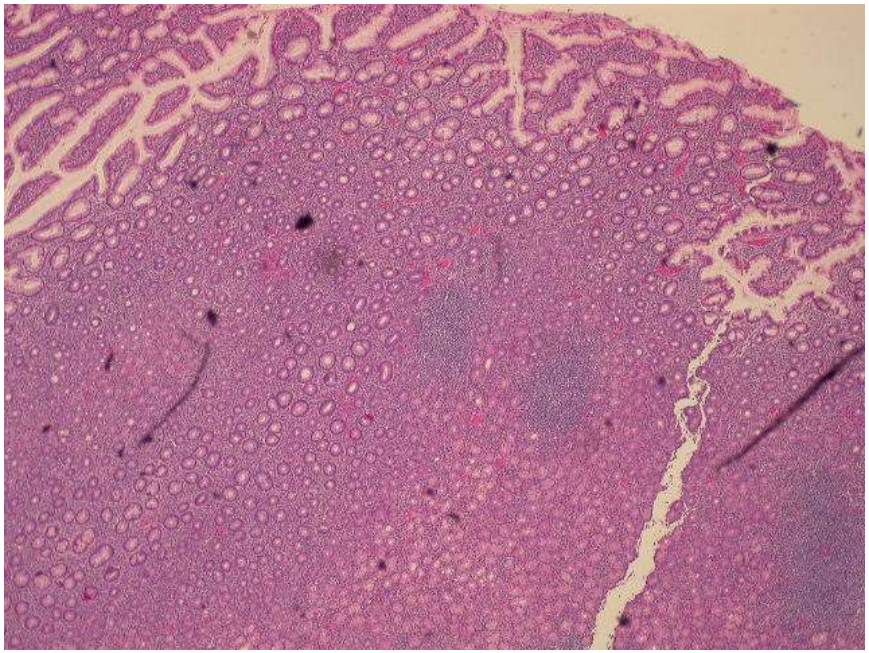
Helpful IHC Stains

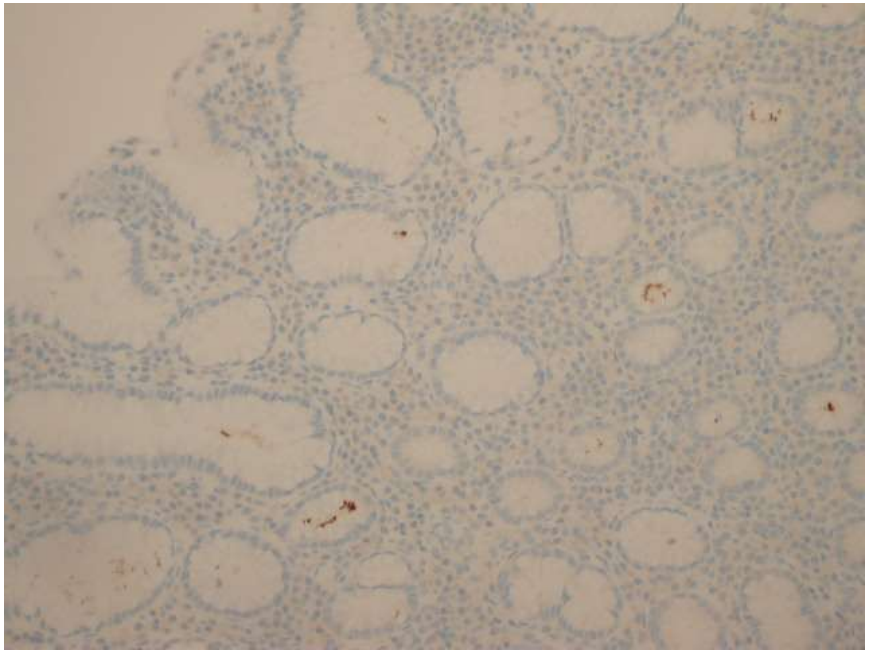
- Can be difficult to distinguish from pancreatic neuroendocrine tumor on cytology specimen
- Positive
  - Vimentin
  - CD10
  - PR
  - Nuclear staining for beta-catenin
- Negative for E-cadherin membranous staining

Treatment/Prognosis

- Complete surgical excision, including metastasis
- Poor prognostic factors:
  - Venous invasion
  - High nuclear grade
  - Necrosis
- Patients survive even with mestatases
  - Study that followed 37 patients with SPN from 1970-2008 showed:
    - 1 died of SPN due to extensive distant metastases at diagnosis
    - Of the 36 who underwent resection, none died of SPN
    - 1 developed a recurrence 7.7 years after resection, was treated with gemcitabine and remains alive after recurrence

Stomach Margin Section





Helicobacter pylori immunostain

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Burford H, Baloch Z, Liu X, et al. E-cadherin/beta-catenin and CD10: a limited immunohistochemical panel to distinguish pancreatic endocrine neoplasm from solid pseudopapillary neoplasm of the pancreas on endoscopic ultrasound-guided fine-needle aspirates of the pancreas. Am J Clin Pathol. 2009 Dec;132(6):831-9.

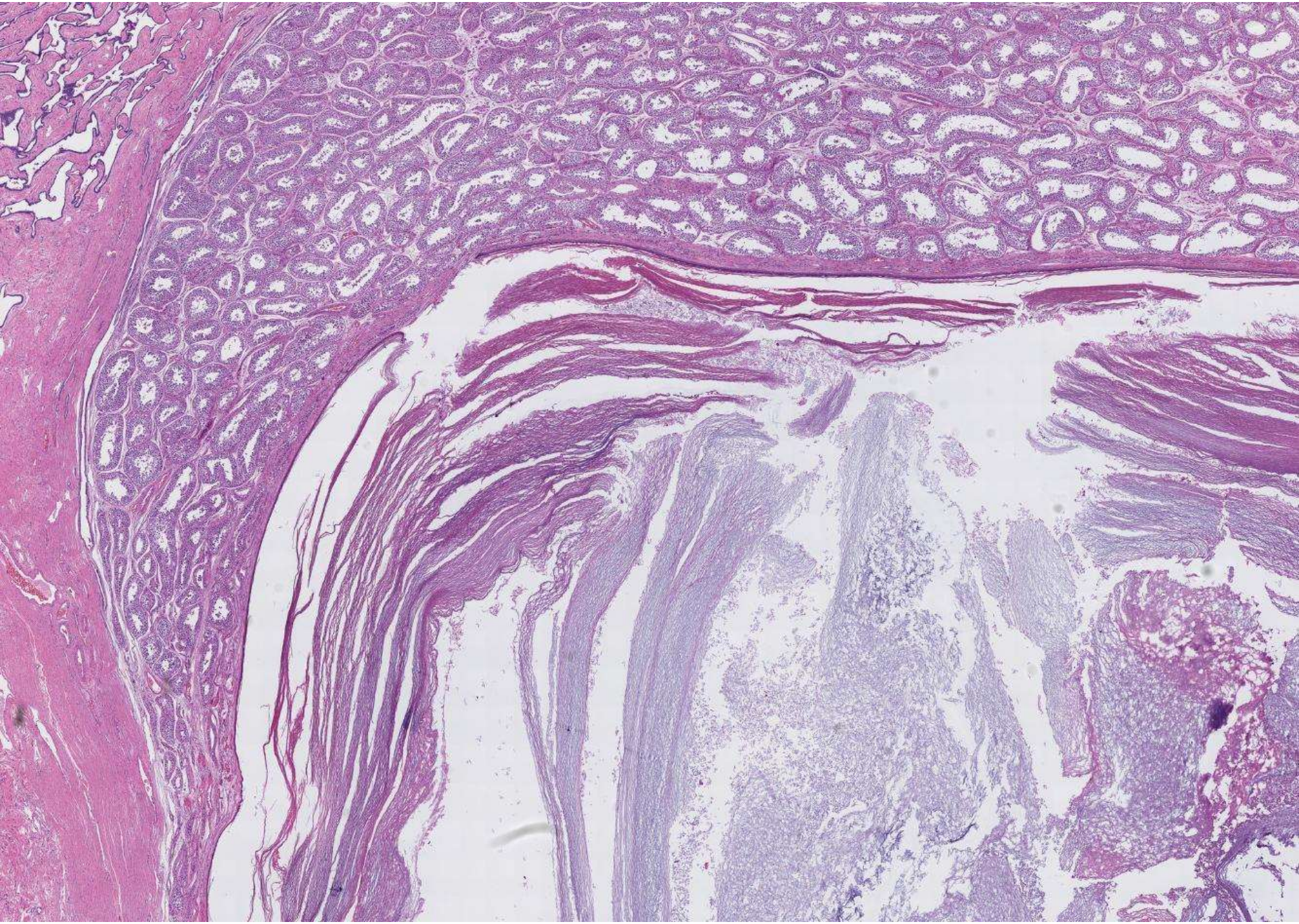
Reddy S, Cameron JL, Scudiere J, et al. Surgical Management of Solid-Pseudopapillary Neoplasms of the Pancreas (Franz or Hamoudi Tumors): A Large Single-Institutional Series. J Am Coll Surg. 2009; 208(5): 950–959.

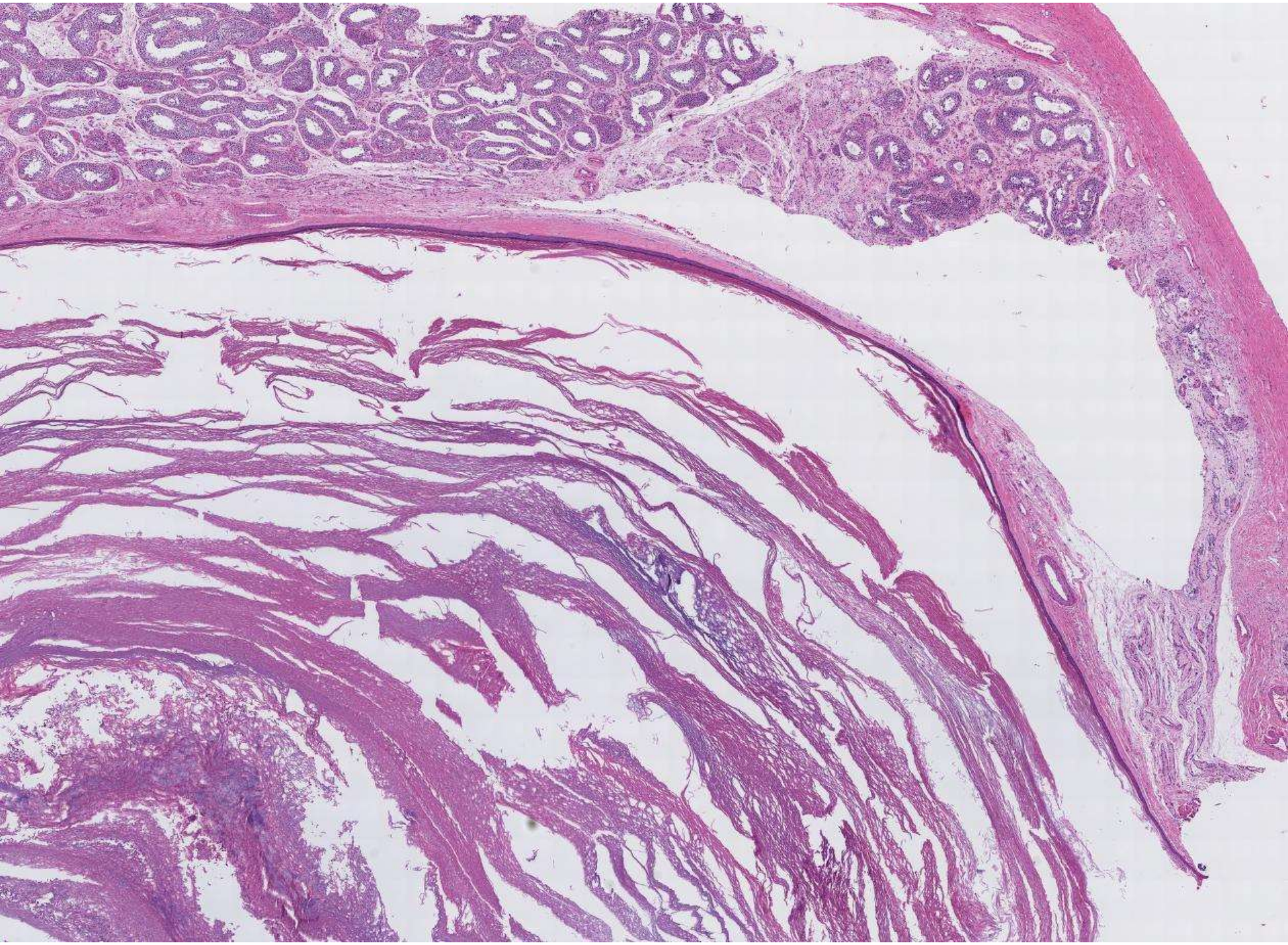
Sur YK, Lee JH, Kim JK, et al. Comparison of MR imaging features of solid pseudopapillary neoplasm of pancreas between male and female patients. Eur J Radiol. 2015 84(11):2065-70.

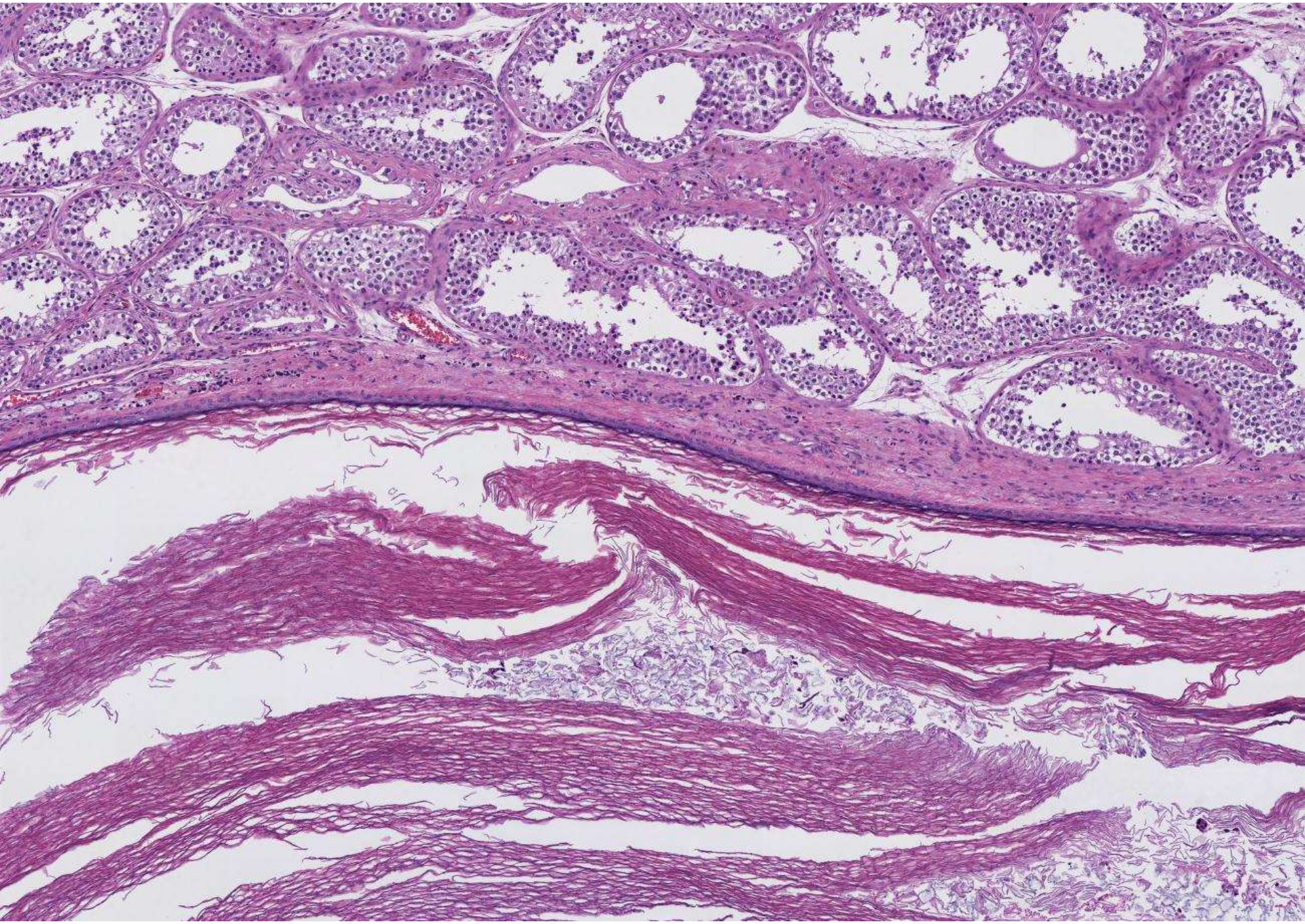
SB 6003

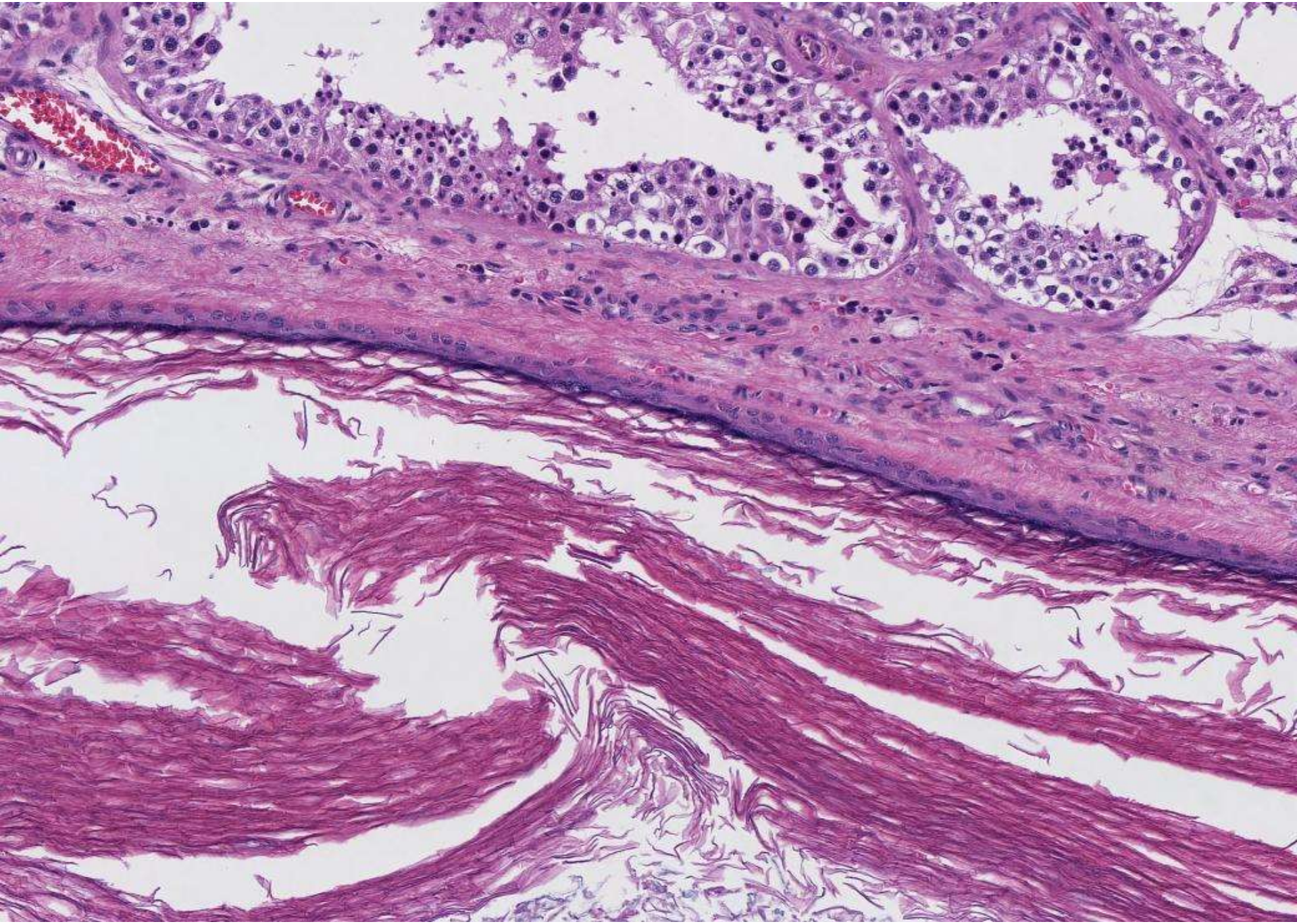
- 32-year-old male with 2.4cm testicular mass.

- **Charles Lombard; El Camino Hospital**

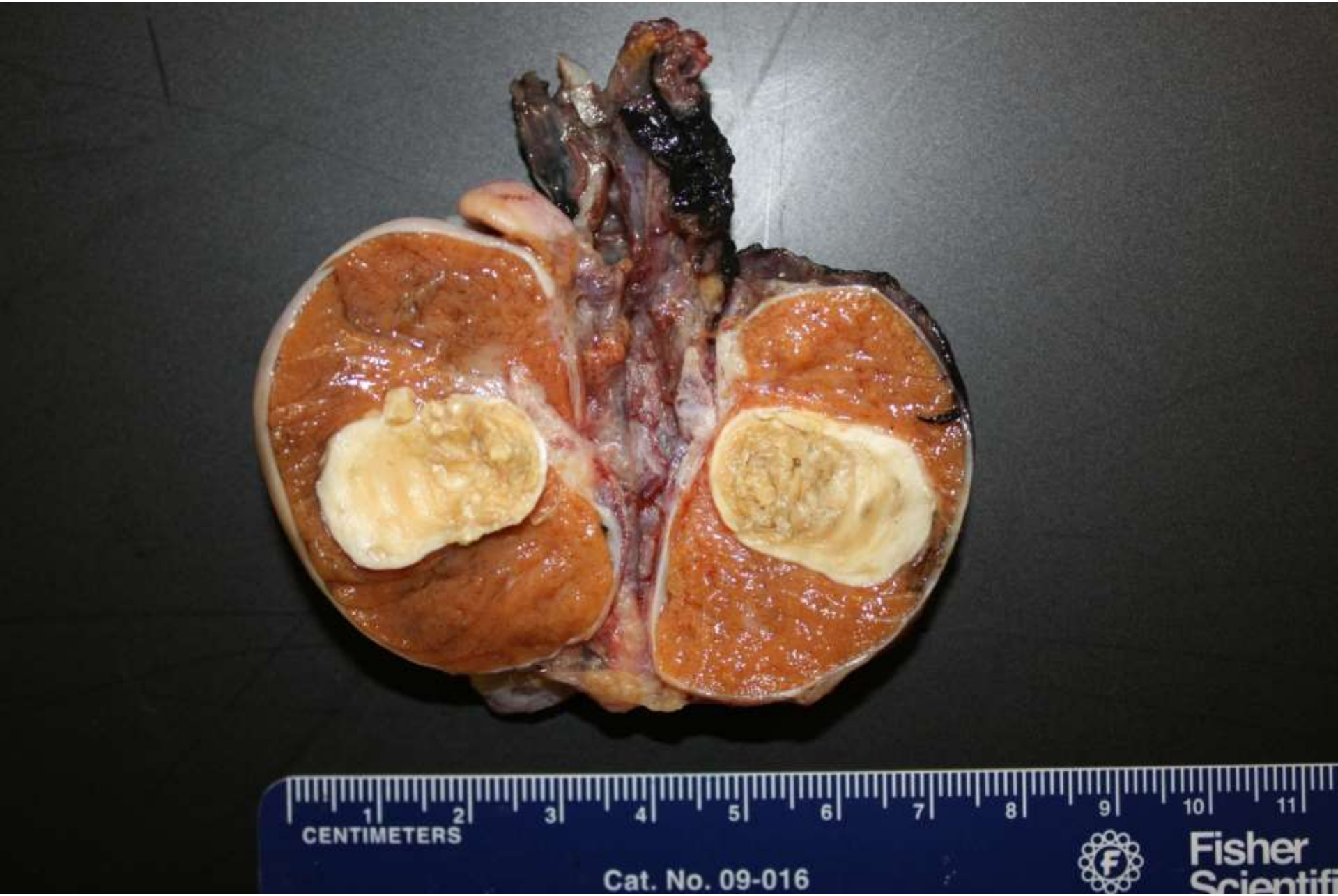








Diagnosis??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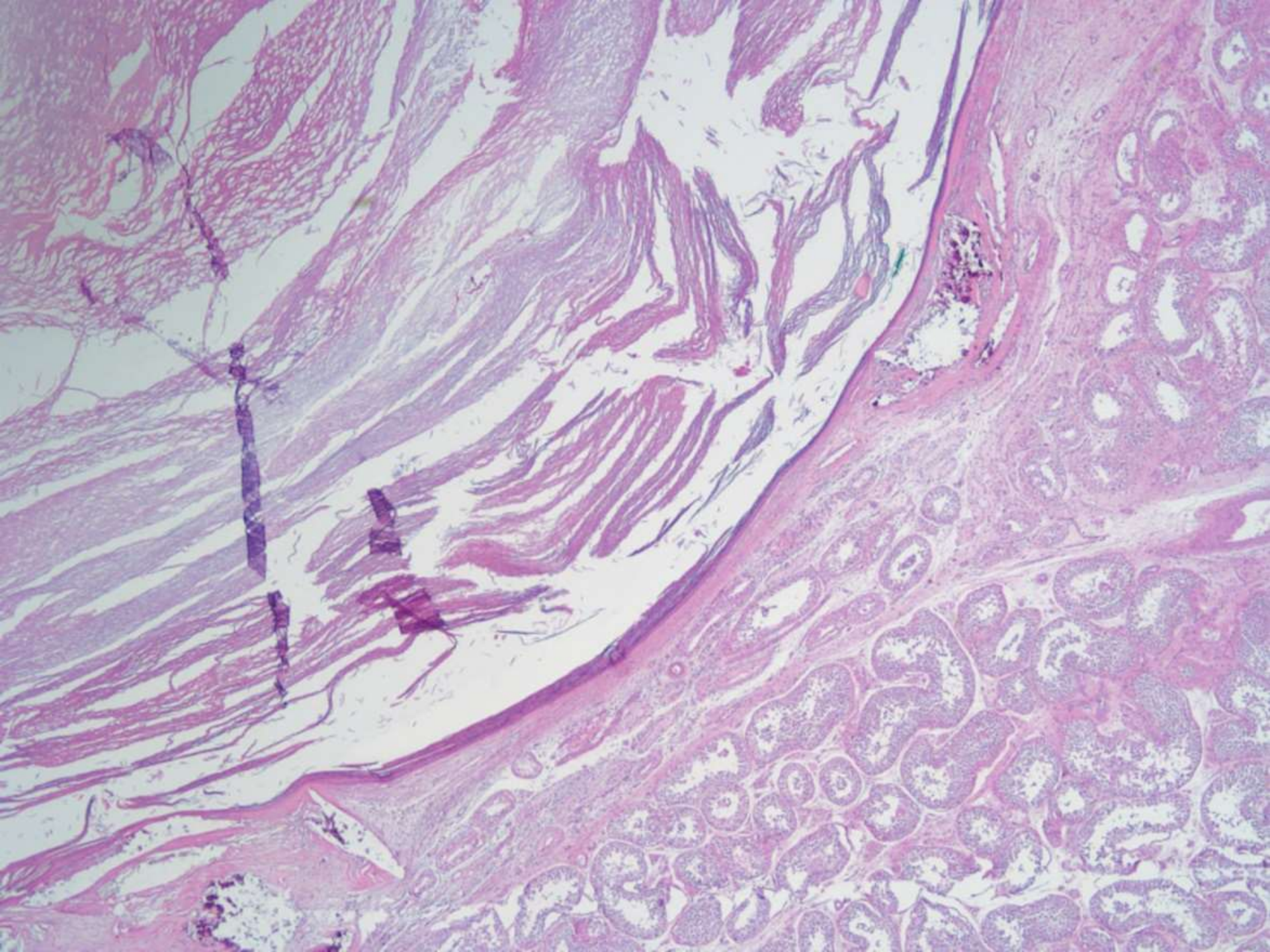
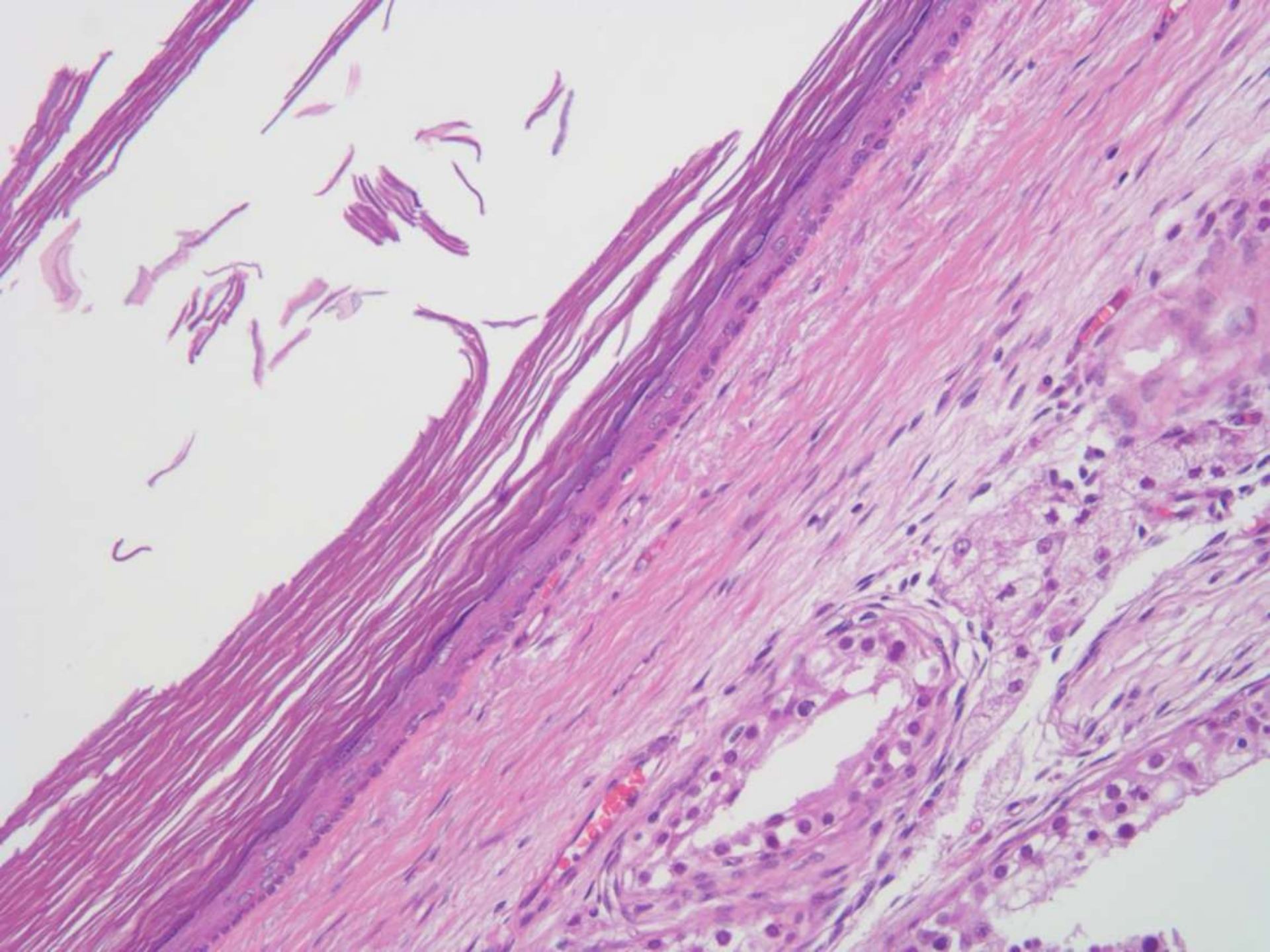




Testicular Epidermoid Cyst

- 1% of all testicular tumors
- Price histologic criteria
  - Intraparenchymal cyst filled with keratinous debris
  - Benign squamous epithelial lining
  - No teratomatous elements or dermal adnexal elements)(sebaceous/hair) in cyst wall or in testis
    - No intratubular germ cell neoplasia
  - Remaining testis +/- atrophy
  - No parenchymal scars

Price: J Urol 102:708-713;1969. Epidermoid cysts of the Testis.

Testicular epidermoid cyst Histogenesis

- Monodermal monophasic variant of teratoma
- Cystic dilatation of rete testis with metaplasia
- Squamous inclusion cyst
- Embryonic rest

Clinical data favoring teratoma variant

- Age of patients parallels that of germ cell tumors
- Like germ cell tumors, more common in causasians
- Lesions are found outside the area of the rete testis

Molecular studies favoring neoplastic etiology of epidermoid cysts of testis

- LOH on chromosomes 9p and 12q are common in GCT of testis
- Epidermoid cysts harbor allelic loss at these loci supporting a neoplastic process, although their low frequency suggests they are genetically different from malignant GCT's.

Younger et al: "Molecular evidence supporting the neoplastic nature of some Epidermoid cysts of the testis". APLM 2003;127:858-60.

Chromosome 12p Abnormalities

- Chromosome 12p abnormalities are seen in the vast majority of testicular germ cell tumors in adults and are present in all histologic subtypes.
- Neither isochrome 12p nor 12p amplification were observed in epidermoid cysts.
- Overall, 88% of testicular teratomas had chromosome 12p abnormalities

Cheng et al: “FISH analysis of chromosome 12 P. abnormalities is useful for distinguishing epidermoid cysts of the testis from fewer mature teratoma. Clin CA Res: 2006;12(19): 5668-72.

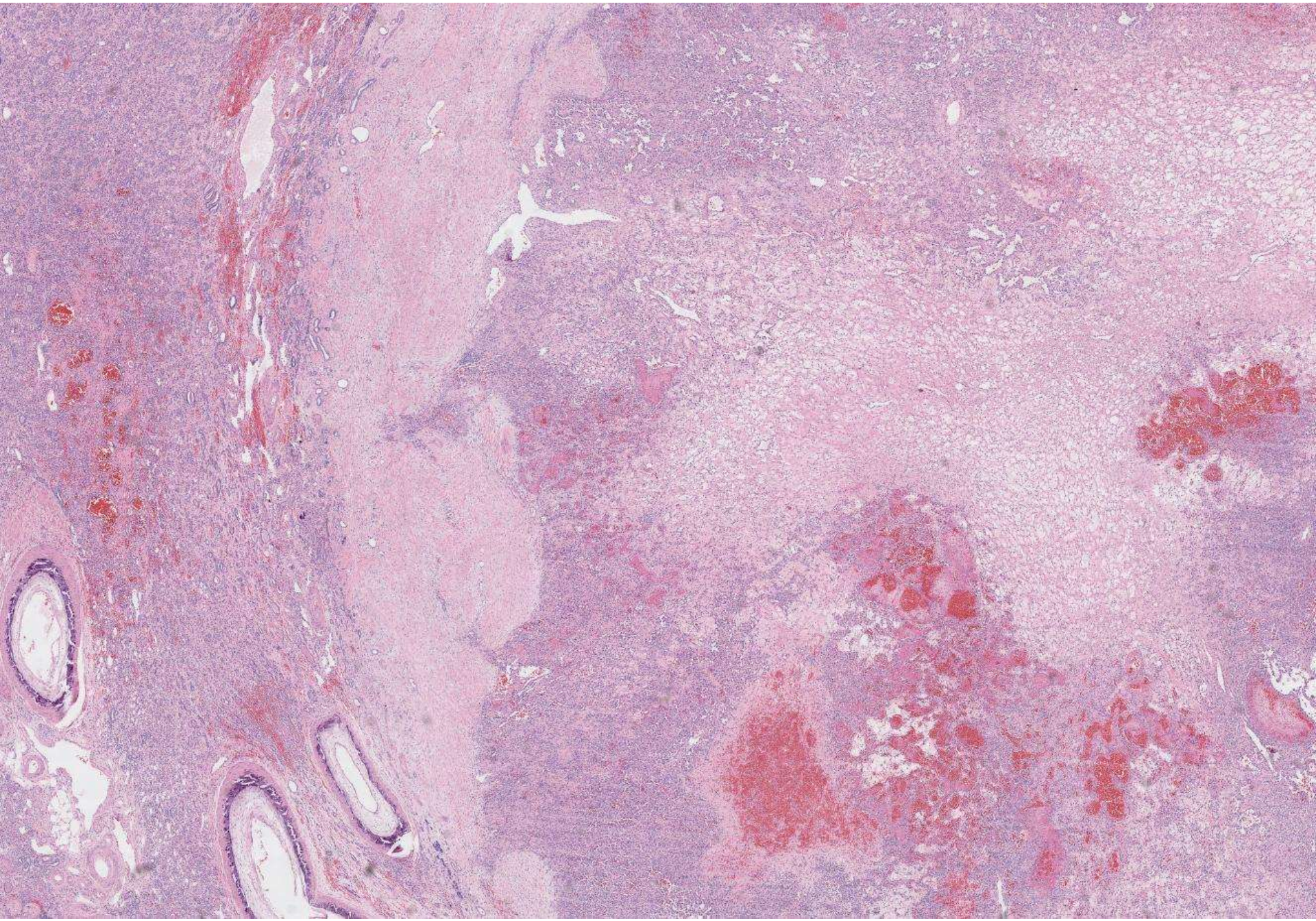
Summary

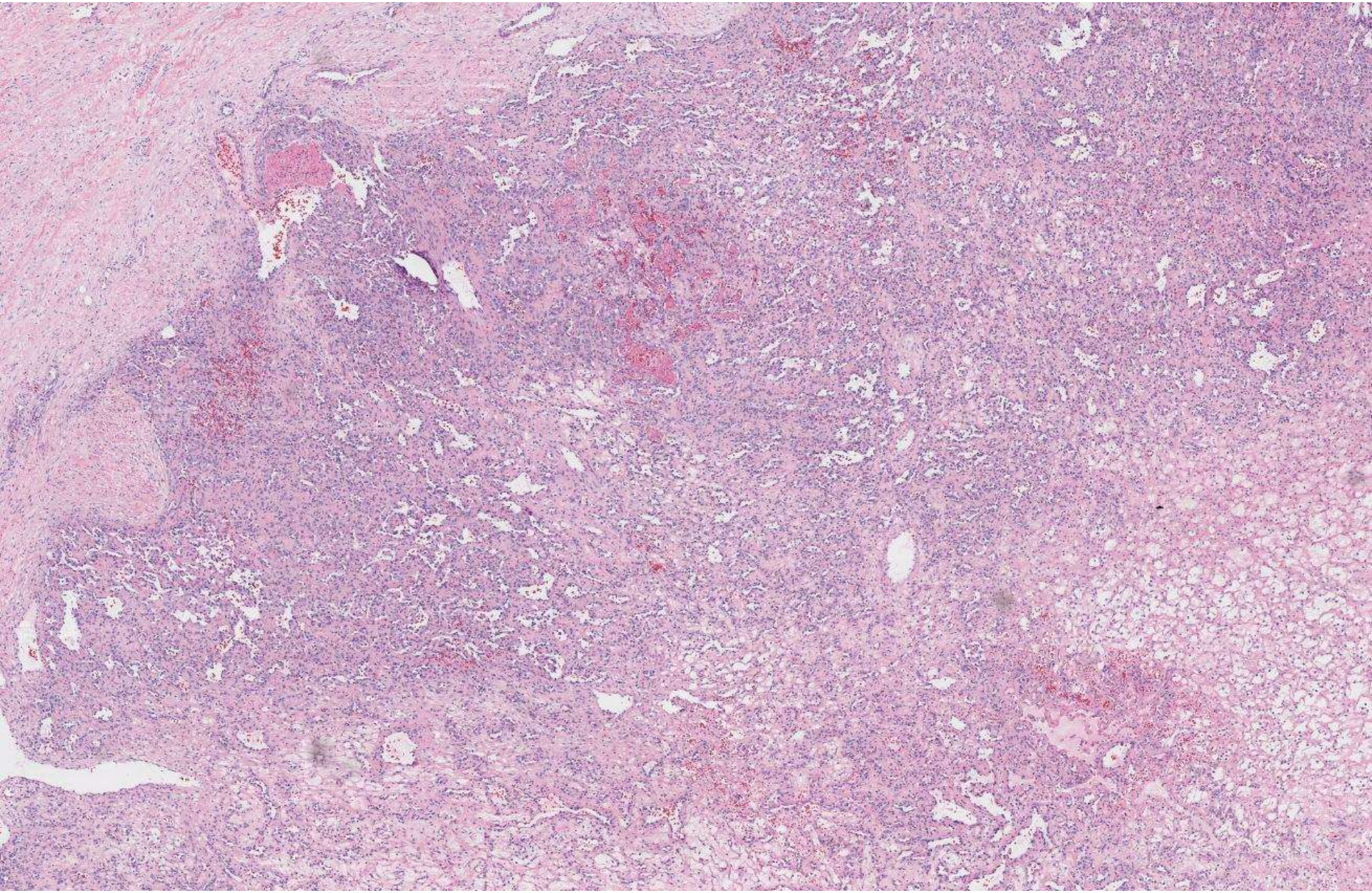
- Although controversial, most favor the concept that the epidermoid cyst of the testis represents a neoplastic process.
- However, when these lesions fulfill the Price histologic criteria, they have a benign clinical course.

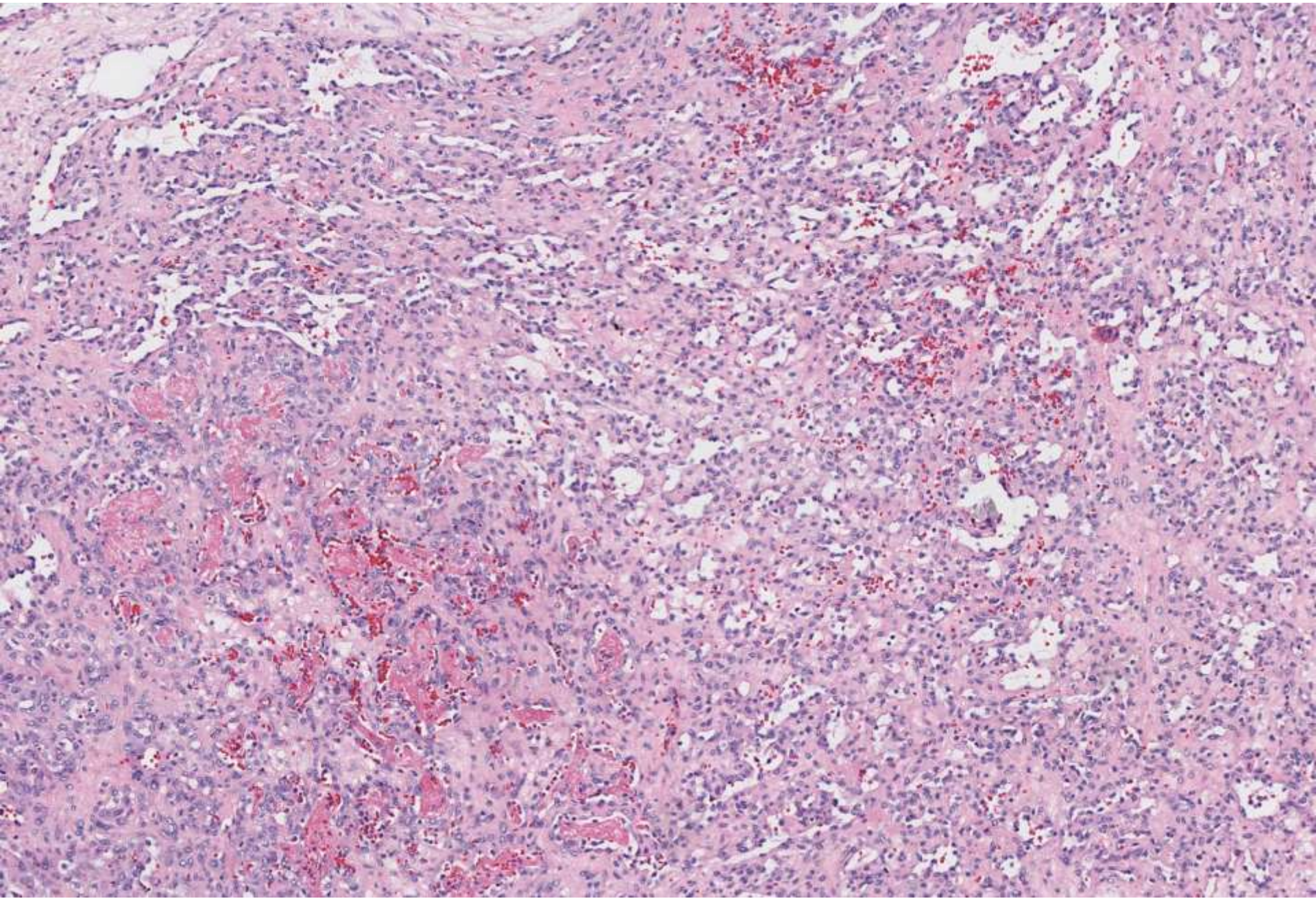
SB 6004

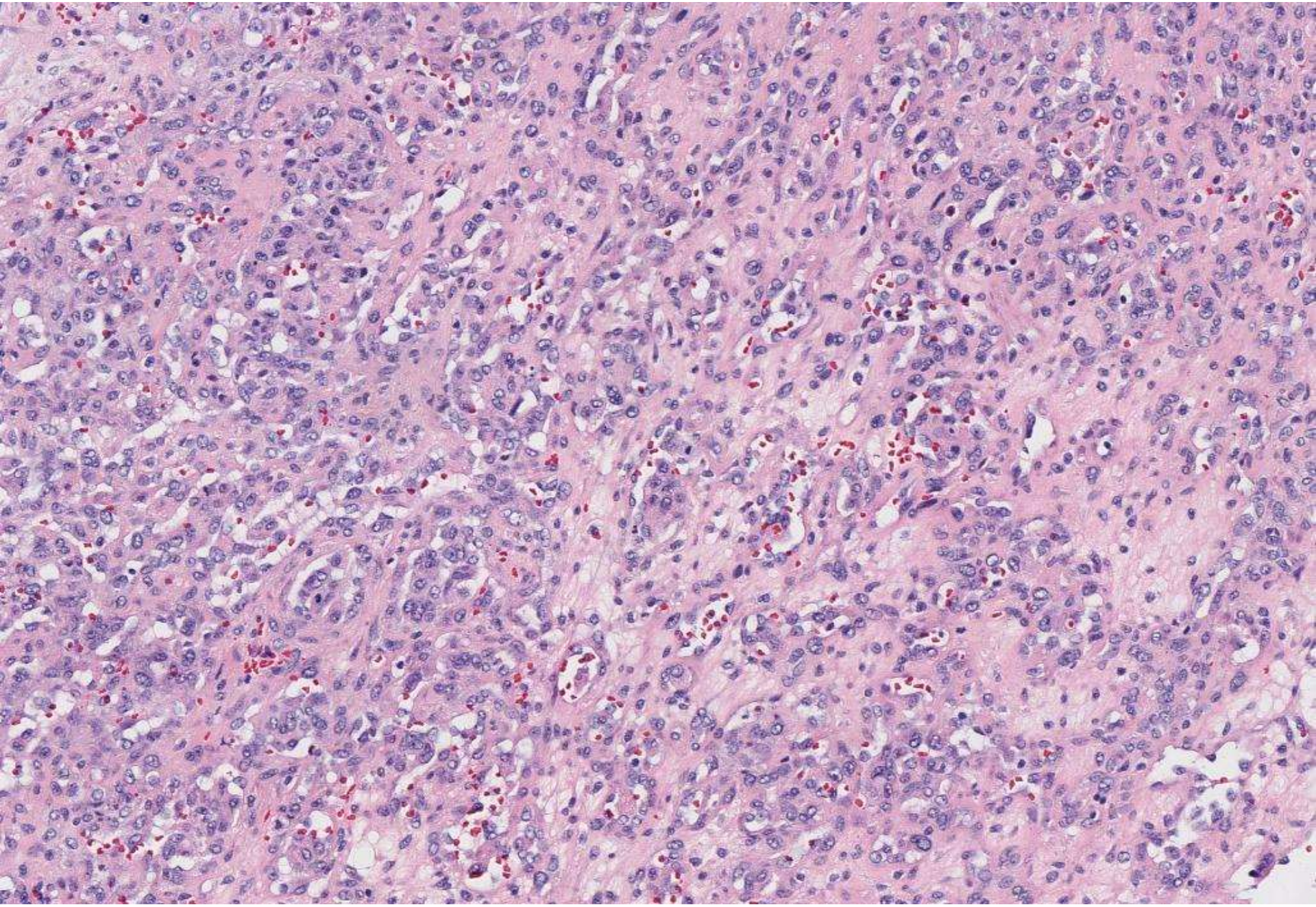
- 11-year-old girl with ESRD and a left renal mass in her native kidney.

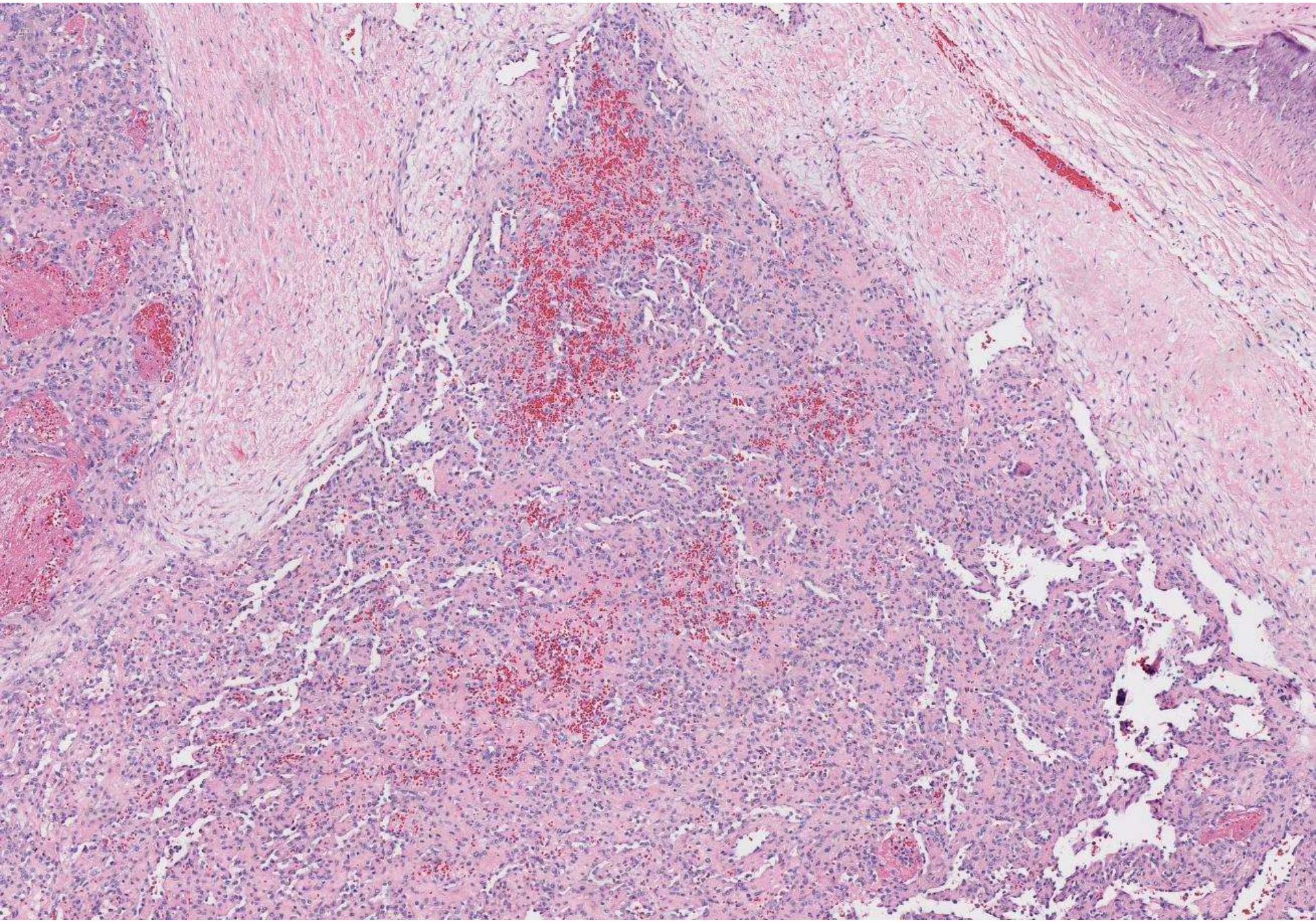
- **John Higgins; Stanford**

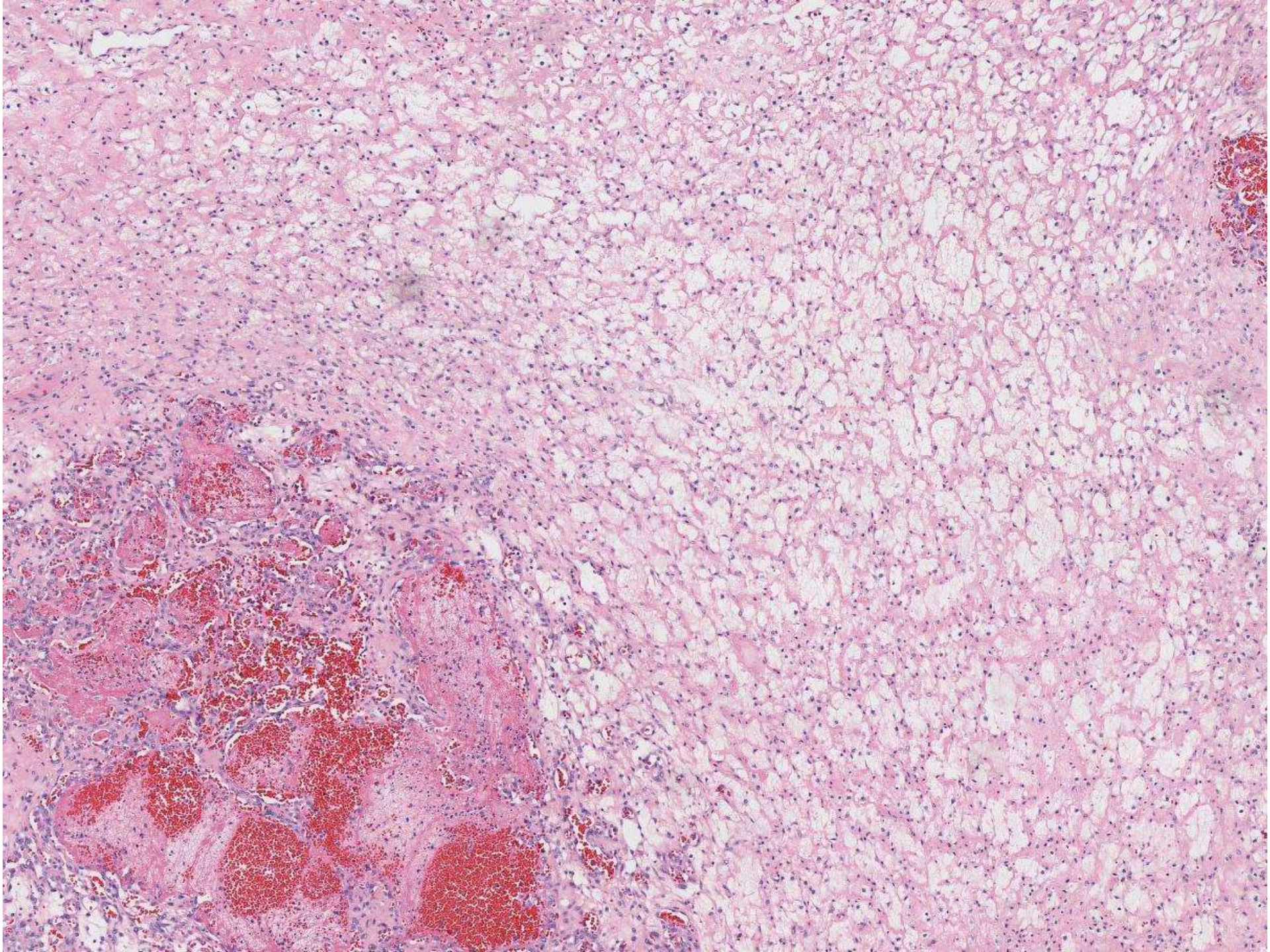








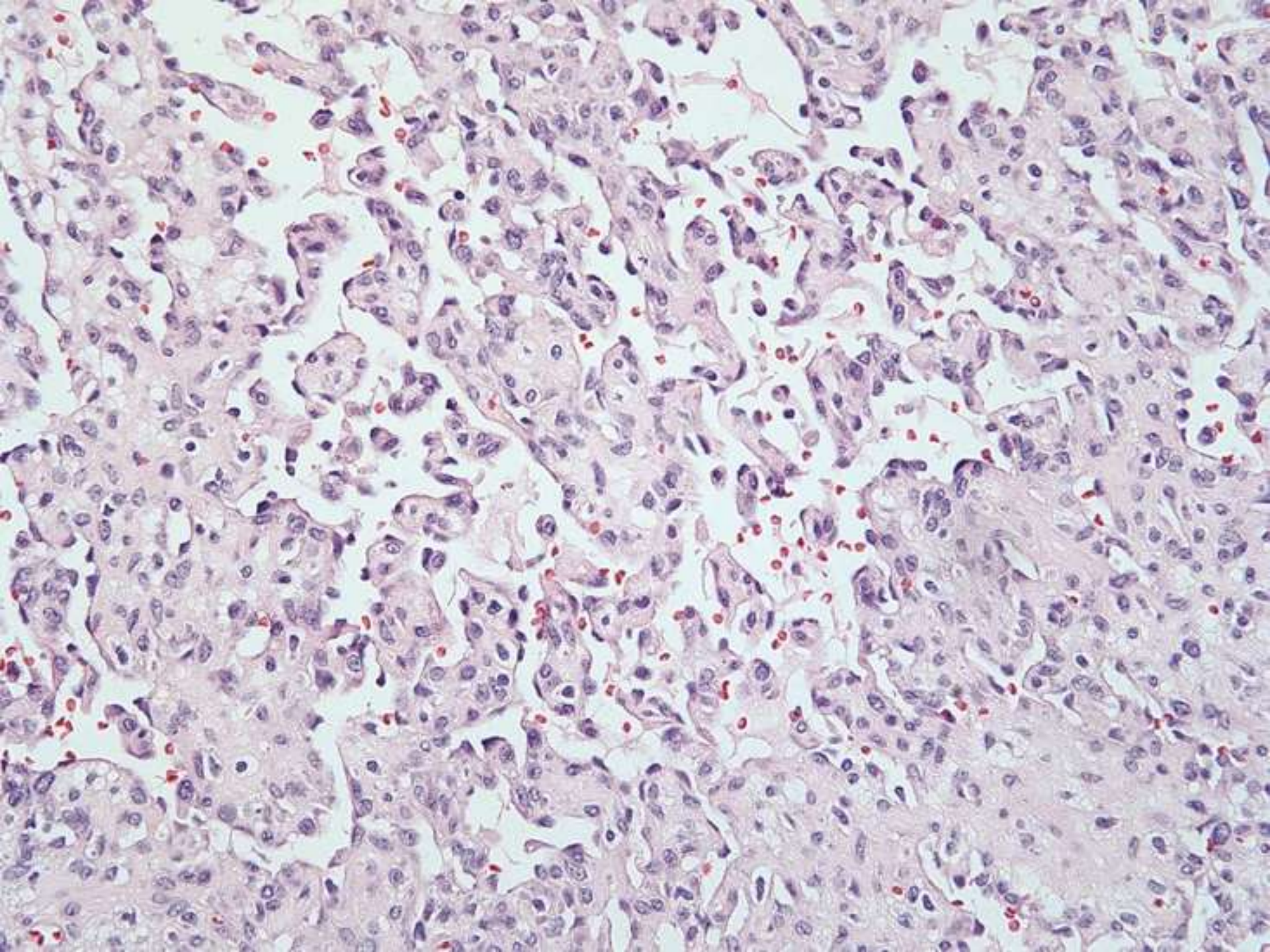


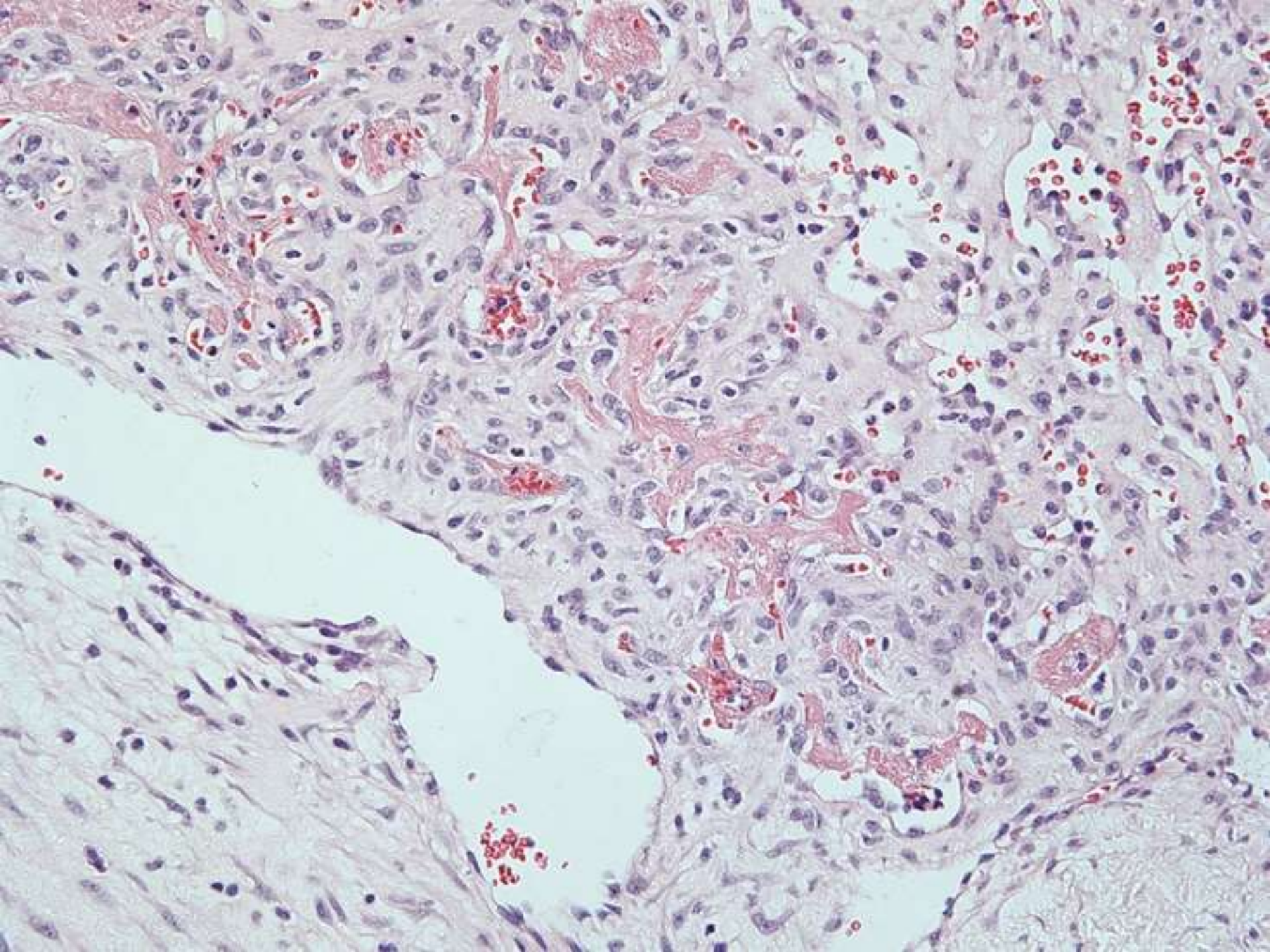


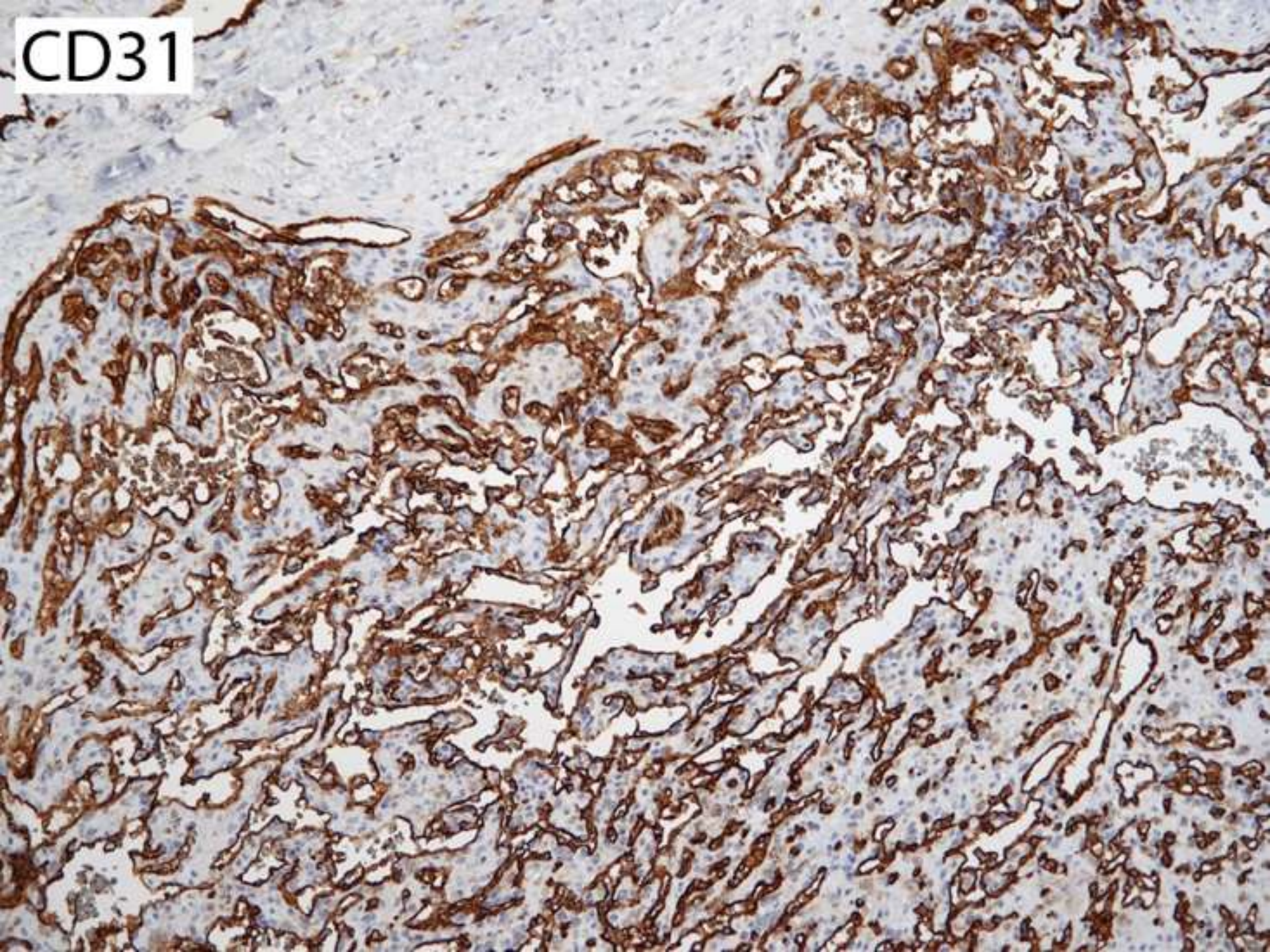
Diagnosis??

Additional history

- Underwent deceased donor transplant in 2009 for ESRD due to FSGS
- Developed early recurrence
- Treated with plasmapheresis x3 per week
- Underwent graft nephrectomy in 2010
- Underwent CAPD but developed peritonitis and switched to hemodialysis

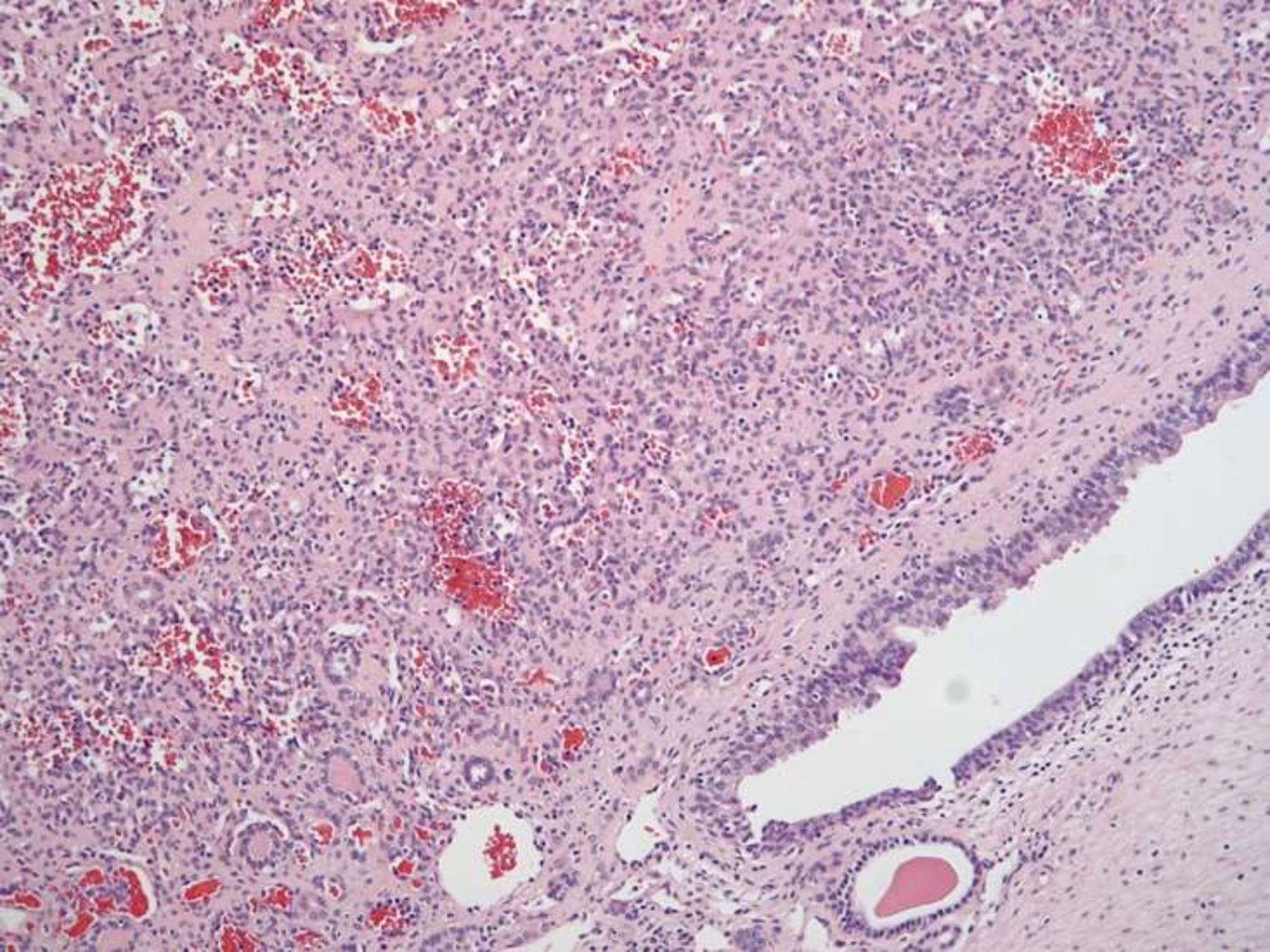





CD31

Renal vascular tumors/tumor-like lesions

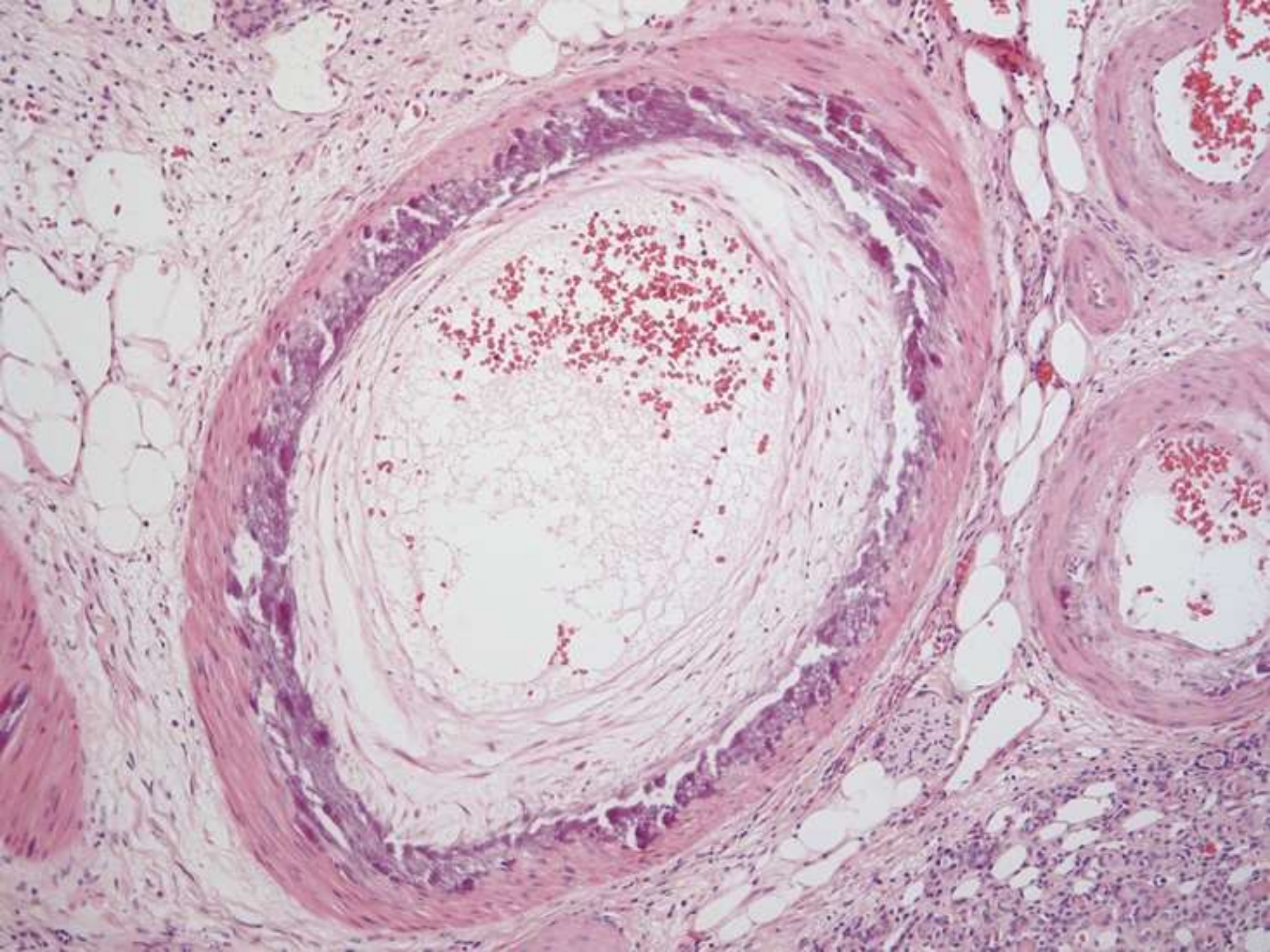
- Capillary hemangioma
- Anastomosing hemangioma
- Arteriovenous malformation
- Angiosarcoma
- Masson lesion

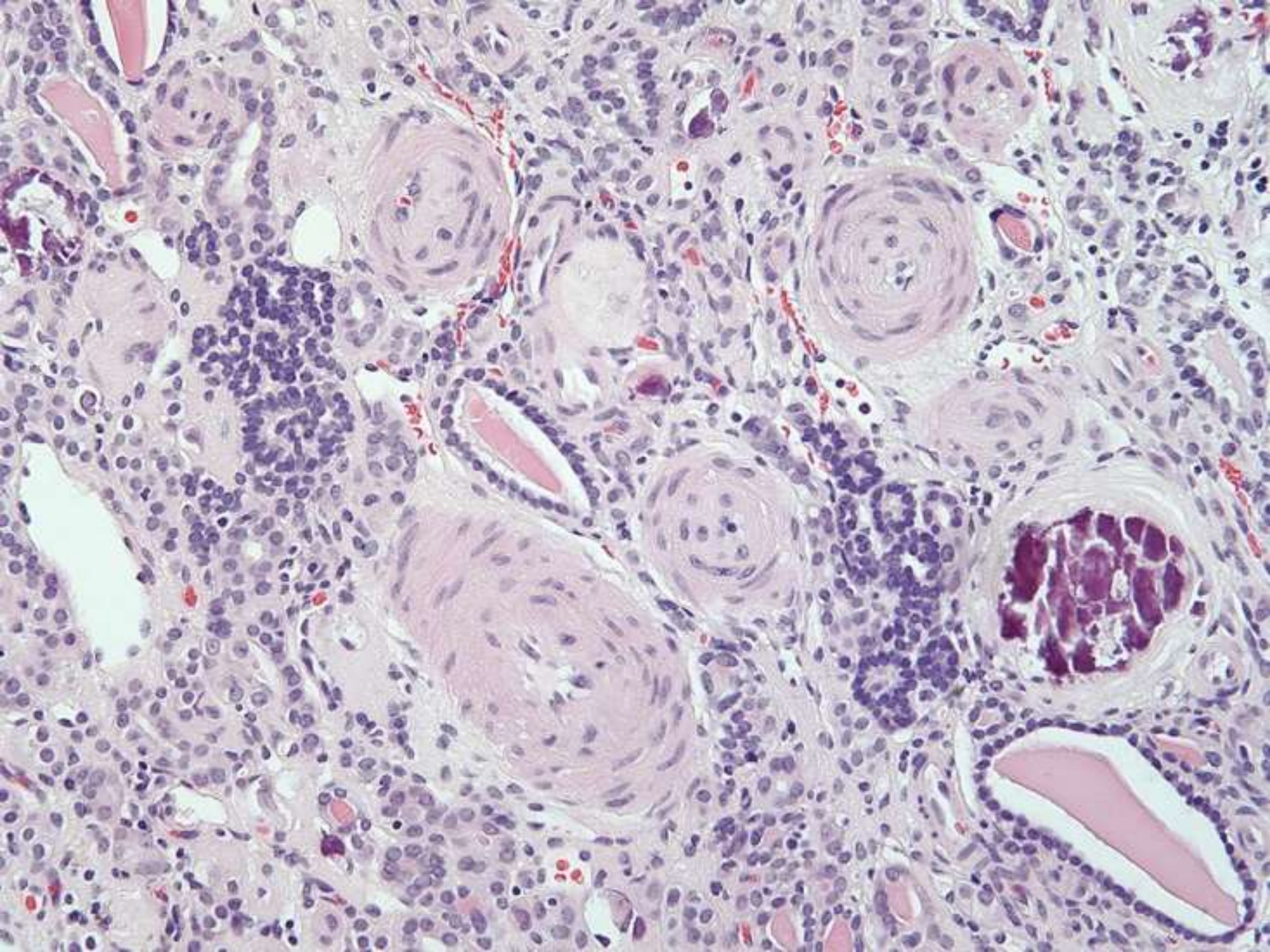


Anastomosing hemangioma of the genitourinary tract: a lesion mimicking angiosarcoma.

Montgomery E, Epstein JI. *Am J Surg Pathol.* 2009 Sep;33(9):1364-9.

- 6 tumors
  - 4 men (66%) and 2 women
  - age from 49 to 75 years (median, 59.5)
  - involving the kidney and renal hilum (4, 66%) and testis (2)
  - Tumors ranged from 1.3 to 1.7 cm (median, 1.6 cm) and were grossly well-marginated with a hemorrhagic mahogany spongy appearance
  - no recurrences or metastases in 5 cases (range: 8 to 36 mo; median 12 mo, mean 15 mo), and 1 patient was lost to follow-up
- unique neoplasm with a proclivity for the kidney. Its anastomosing appearance can lead to concern for angiosarcoma but, despite small numbers and limited follow-up in our series, evidence to date supports that the lesion is benign





Haemangiomas in kidneys with end-stage renal disease: a novel clinicopathological association.

Kryvenko ON, Haley SL, Smith SC, Shen SS, Paluru S, Gupta NS, Jorda M, Epstein JI, Amin MB, Truong LD. *Histopathology.* 2014 Sep;65(3):309-18.

- Twenty ESRD nephrectomies from 16 patients (aged 9 months-68 years)
- Haemangiomas appeared as a single mass (15), two masses (one), three masses (one), four masses (two) and eight masses (one) per kidney
- Tumours measured 0.2-3.5 cm. Four patients had bilateral haemangiomas
- All tumours were in the medulla and often abutted renal sinus fat
- All except one of the tumours were anastomosing haemangiomas, showing isolated or interconnected sinusoidal capillary-sized vascular channels lined by a single layer of benign cuboidal endothelial cells, separated by loose stroma with spindle cells
- One tumour was a cellular capillary haemangioma
- Anastomosing haemangioma appears as a distinctive clinicopathological entity developing in kidneys with ESRD, with or without ACKD

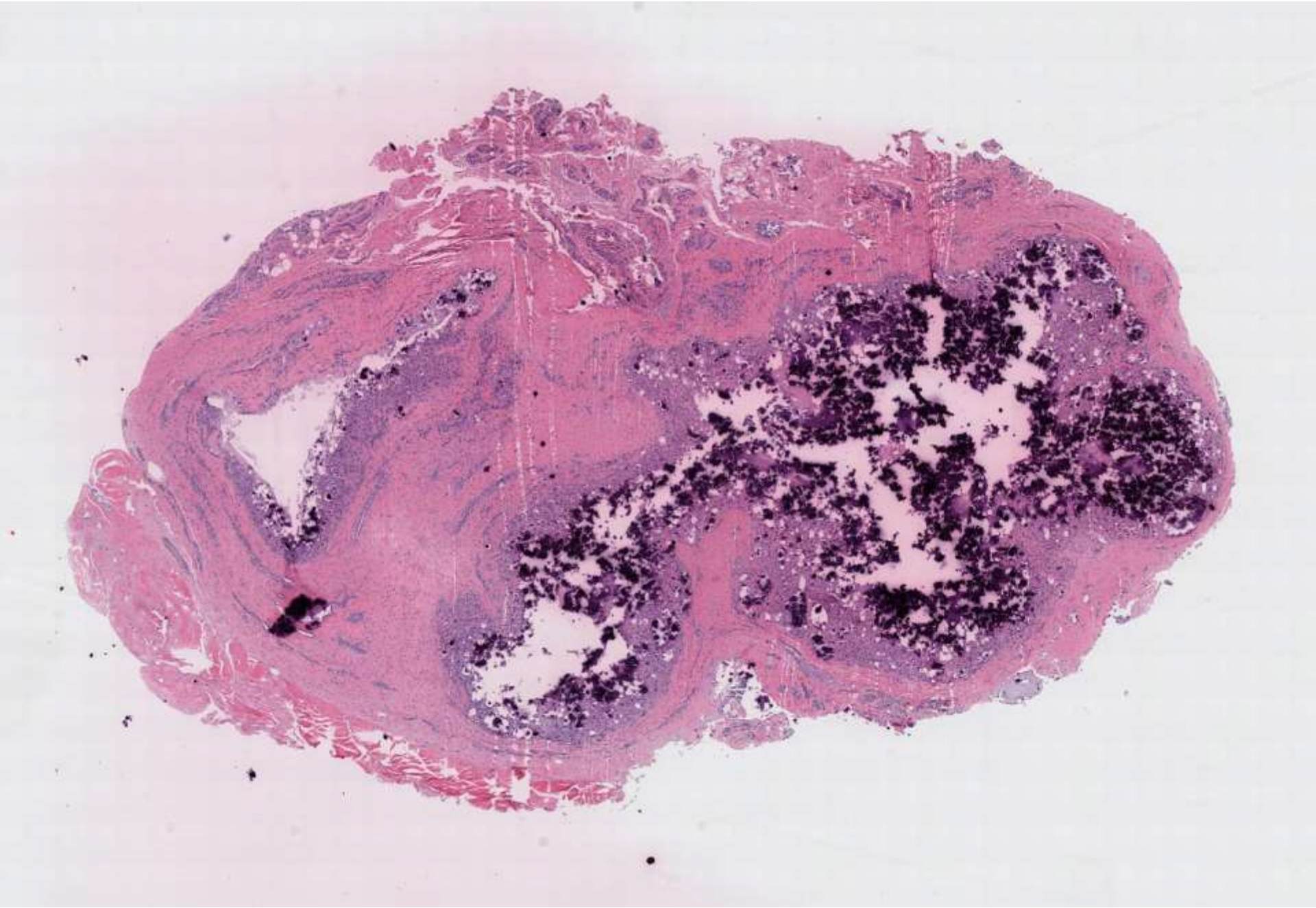
Follow-up

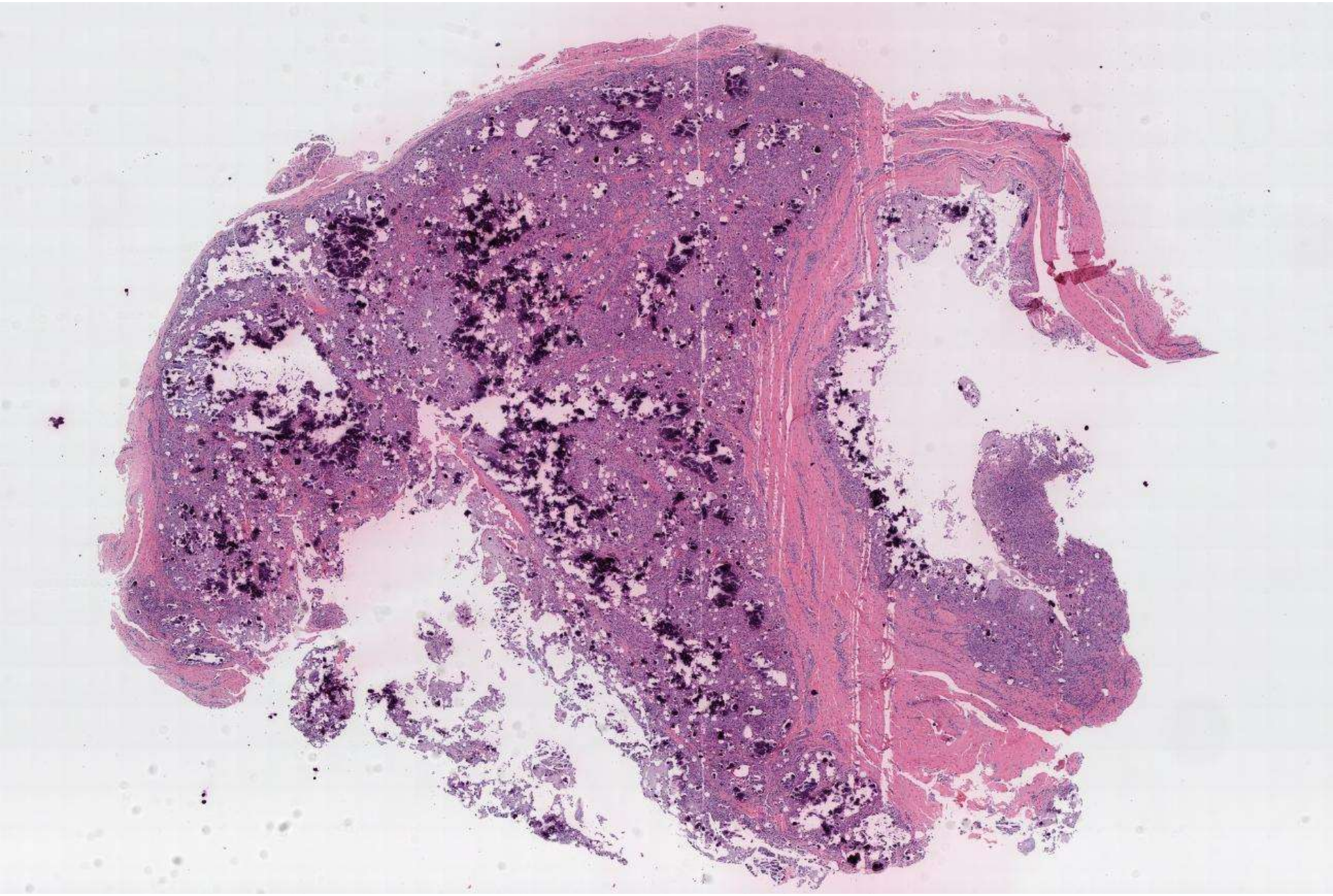
- Left native nephrectomy 7 months ago – NED
- Second renal transplant (deceased donor) 3 months ago – redeveloped nephrotic range proteinuria immediately after transplant and is receiving daily plasmapheresis and IVIG qod

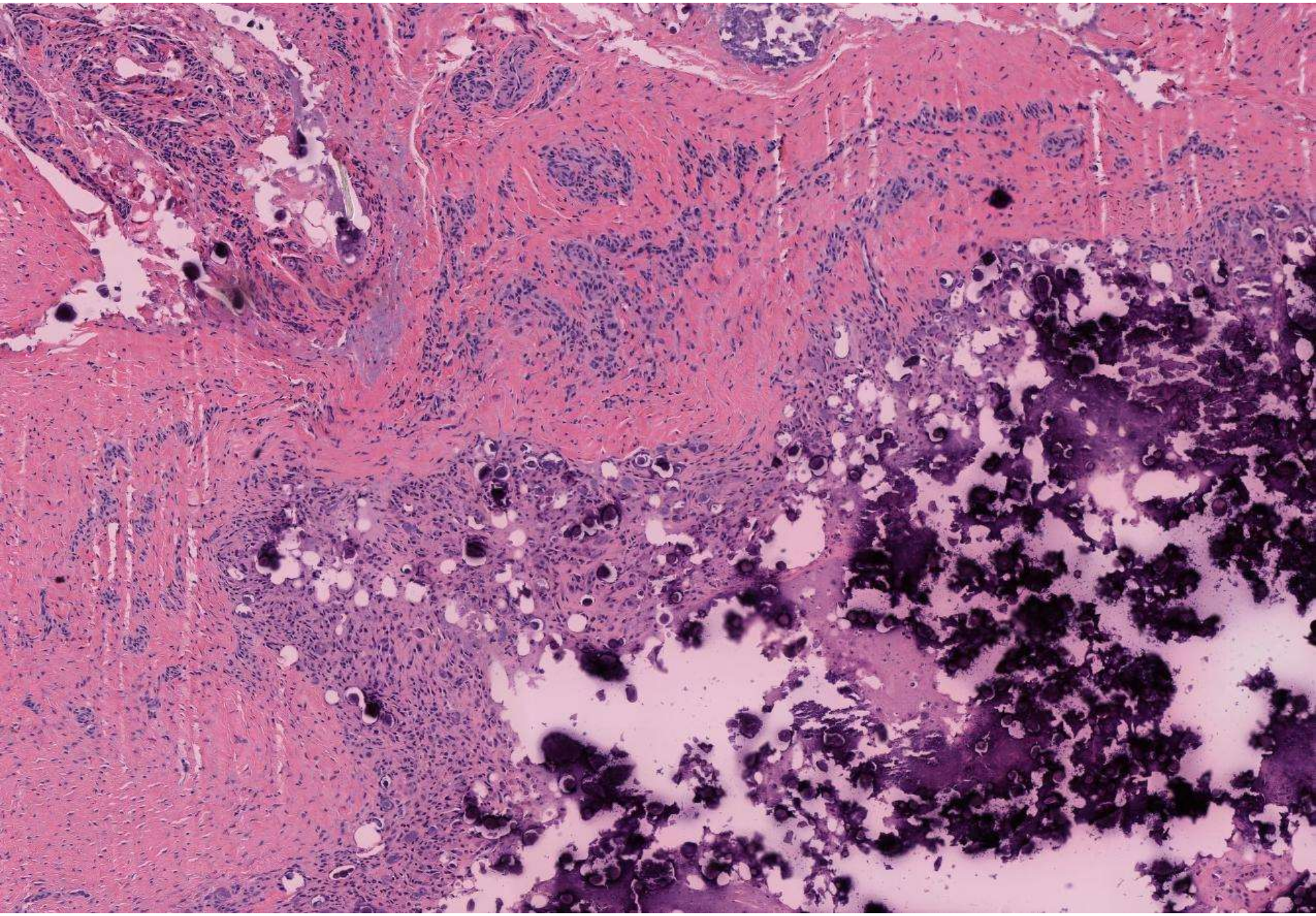
SB 6005

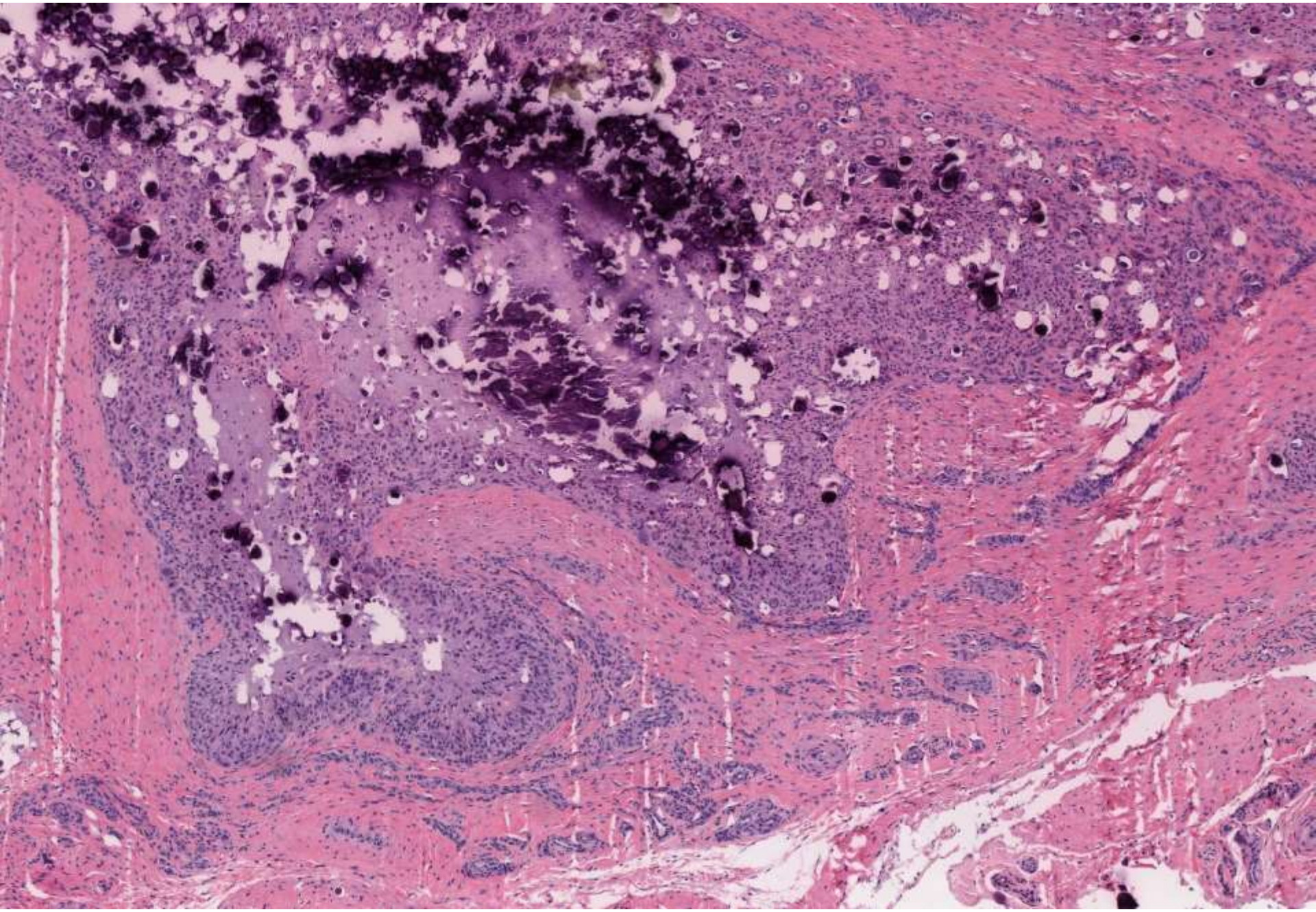
- 65-year-old right-handed Caucasian female with a right index finger nodule which has slowly enlarged over 2 years.

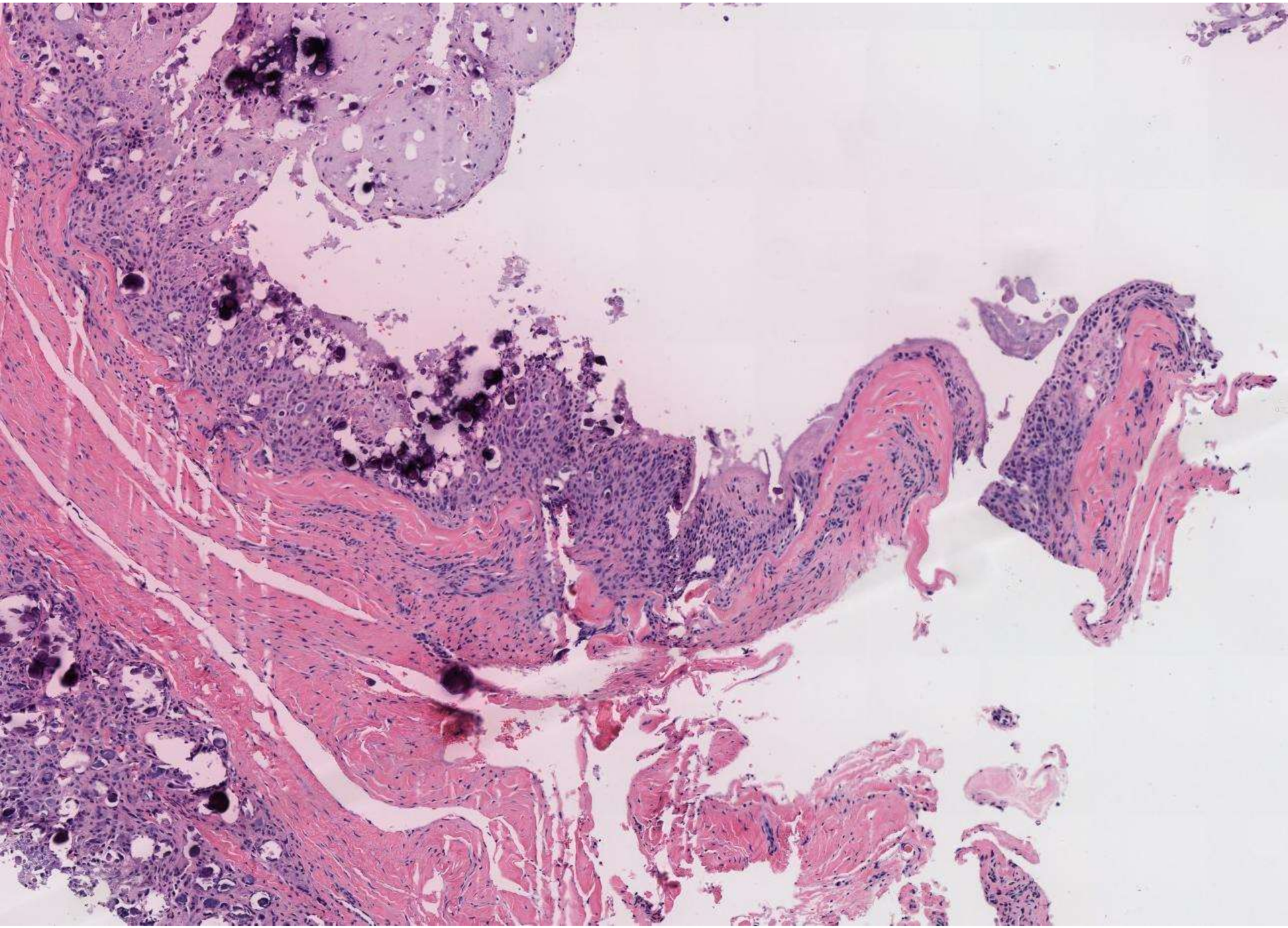
- **Laura Hofmeister; Santa Clara Kaiser**

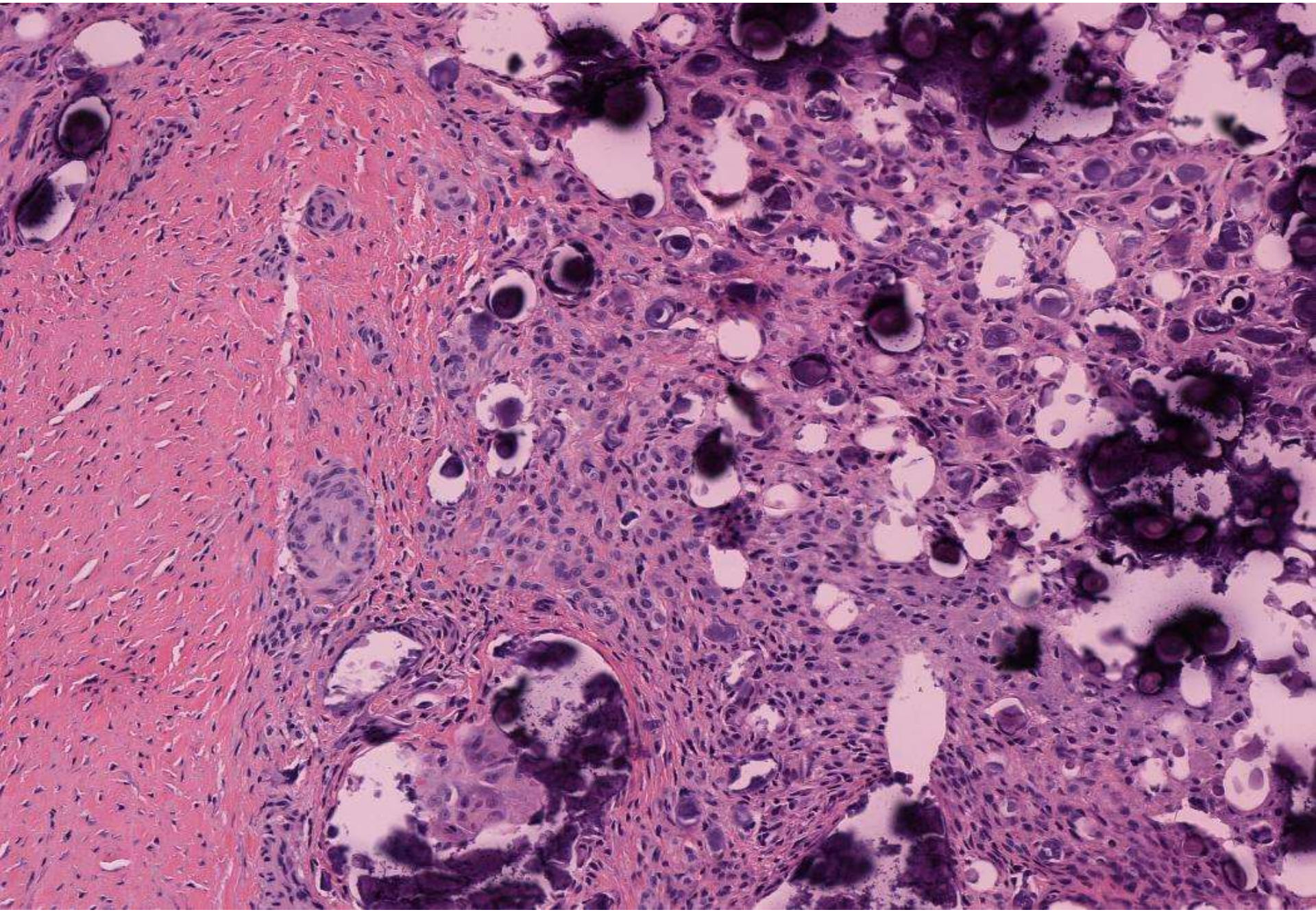












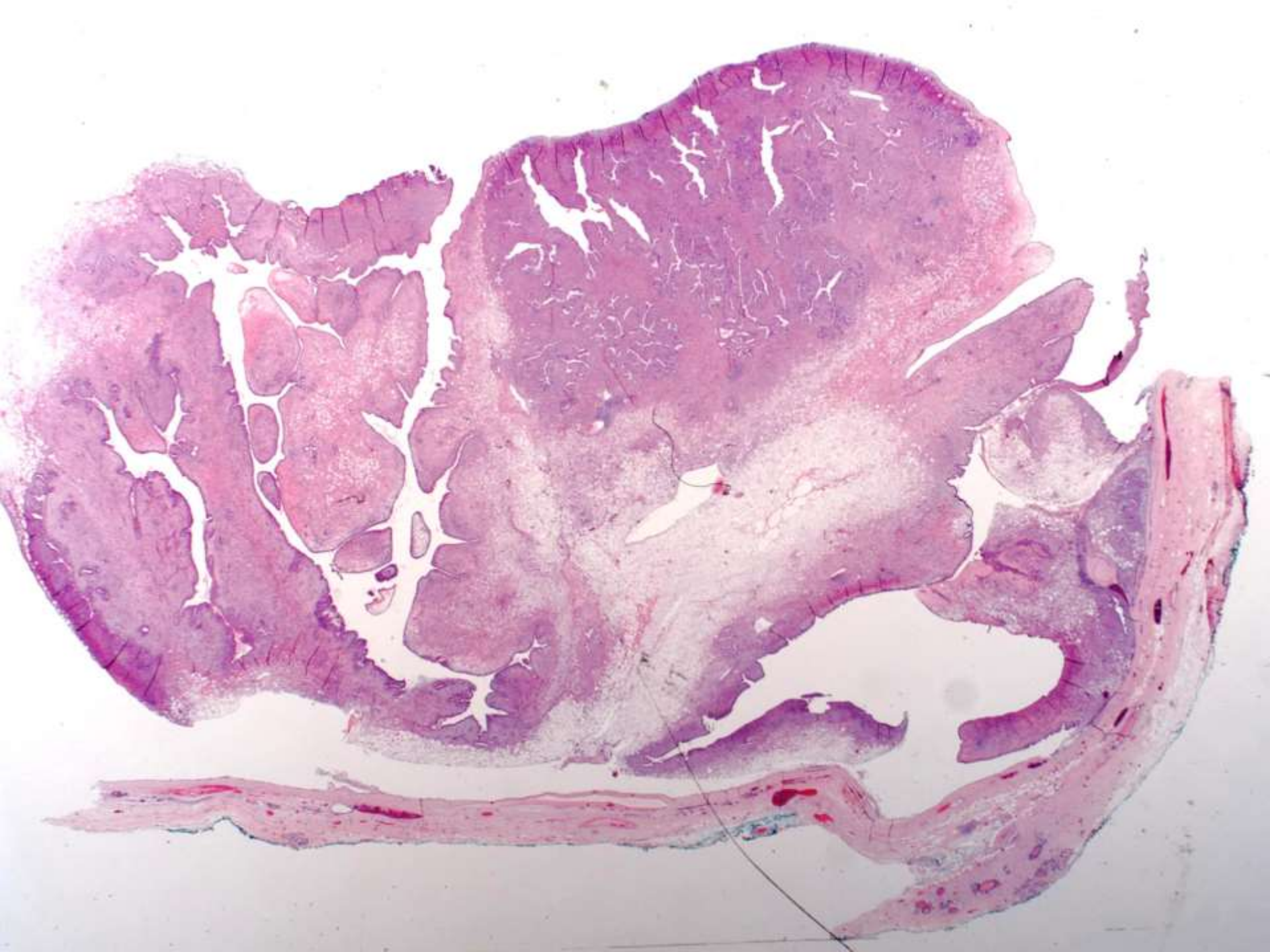
Diagnosis??

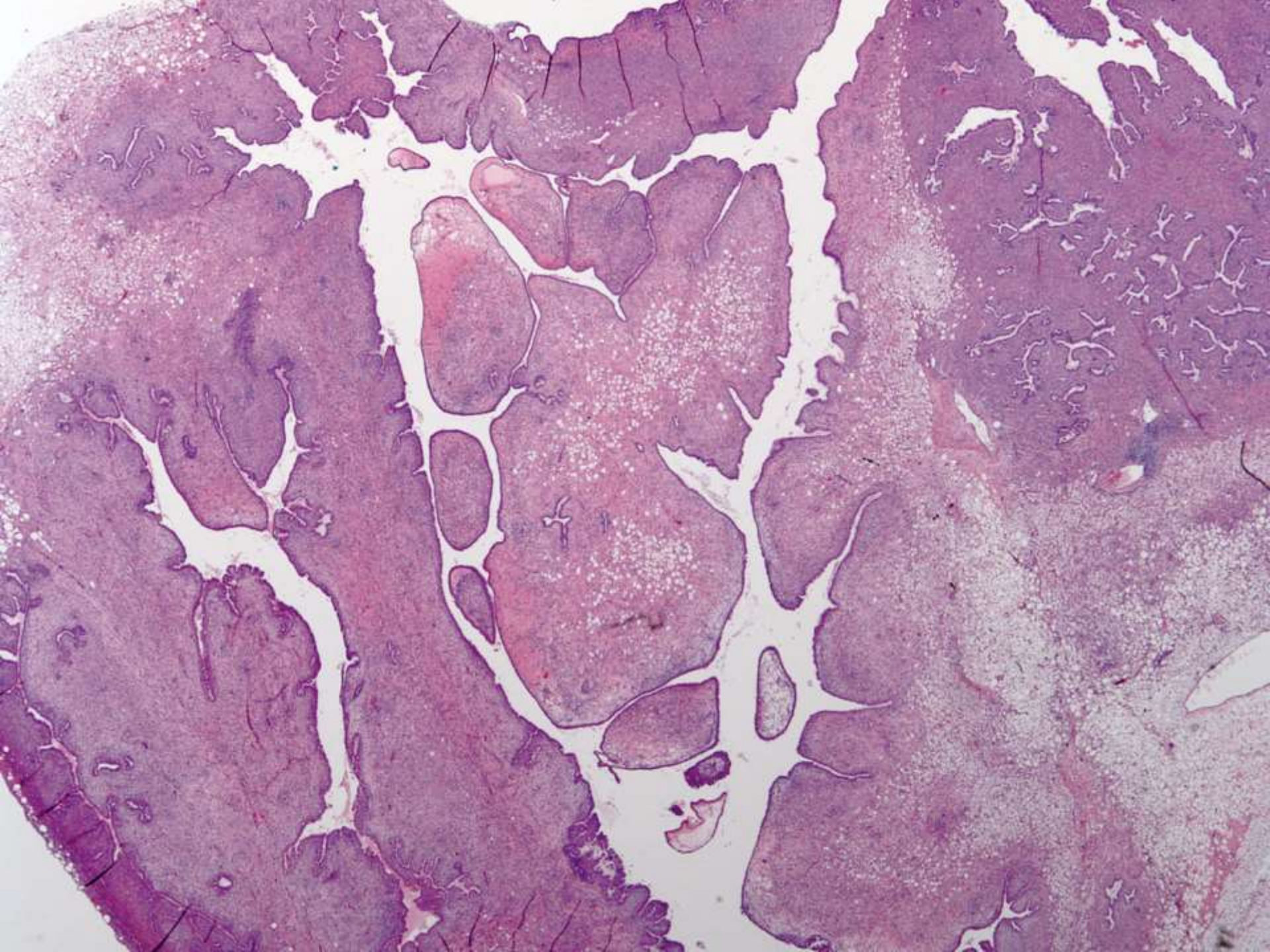
Case Discussion

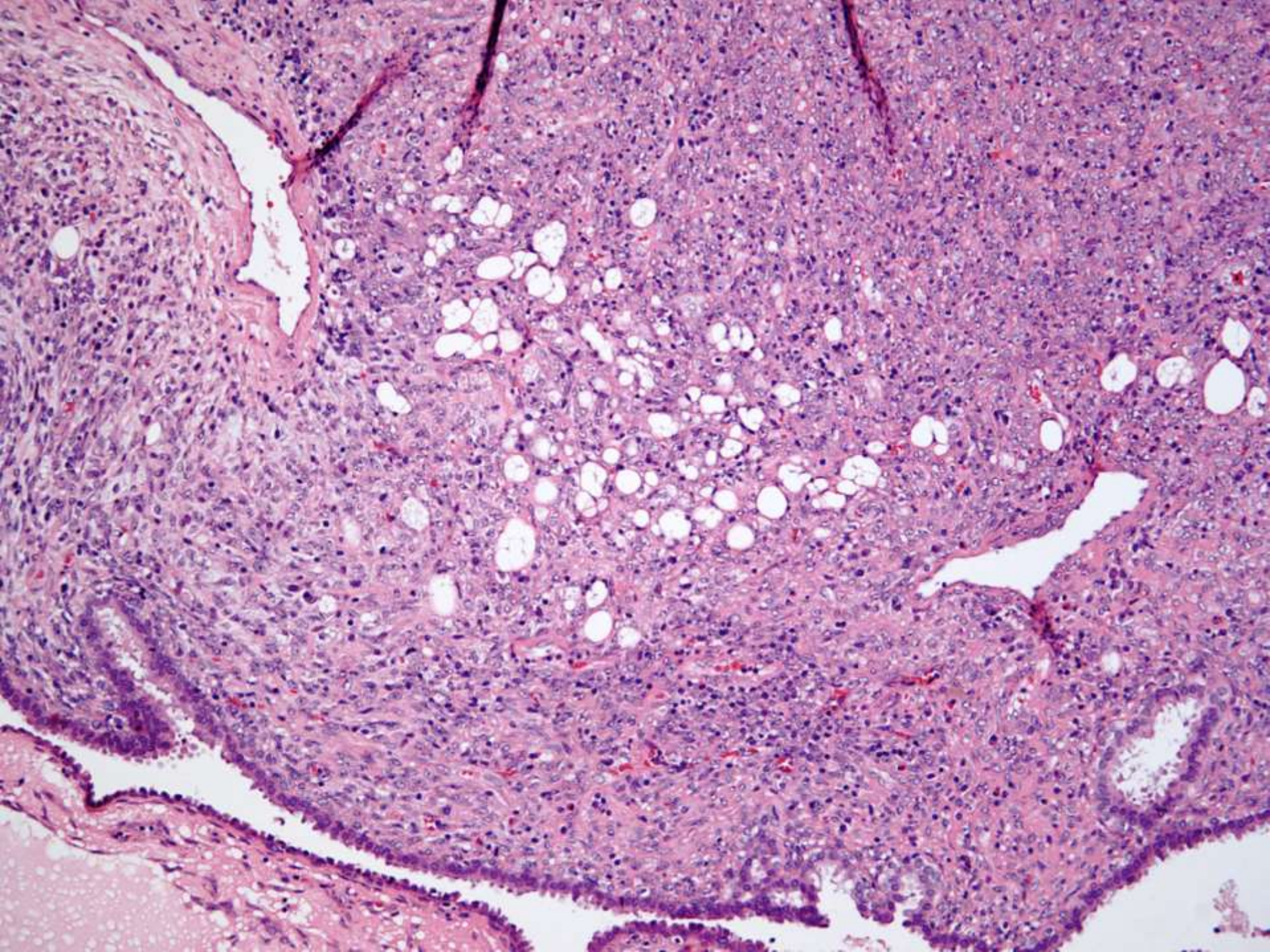
SB 6006

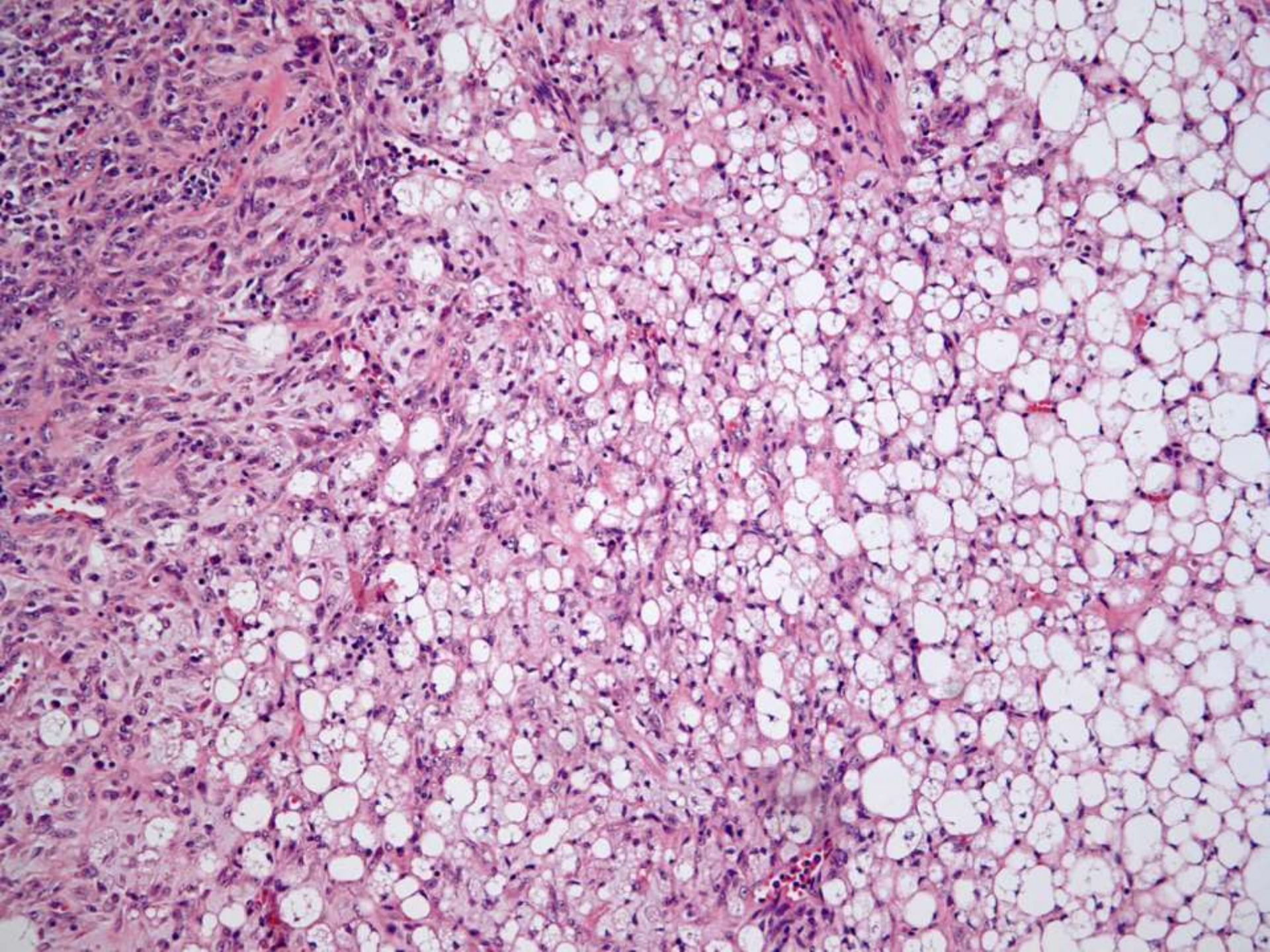
- 46-year-old female with 5cm breast mass.

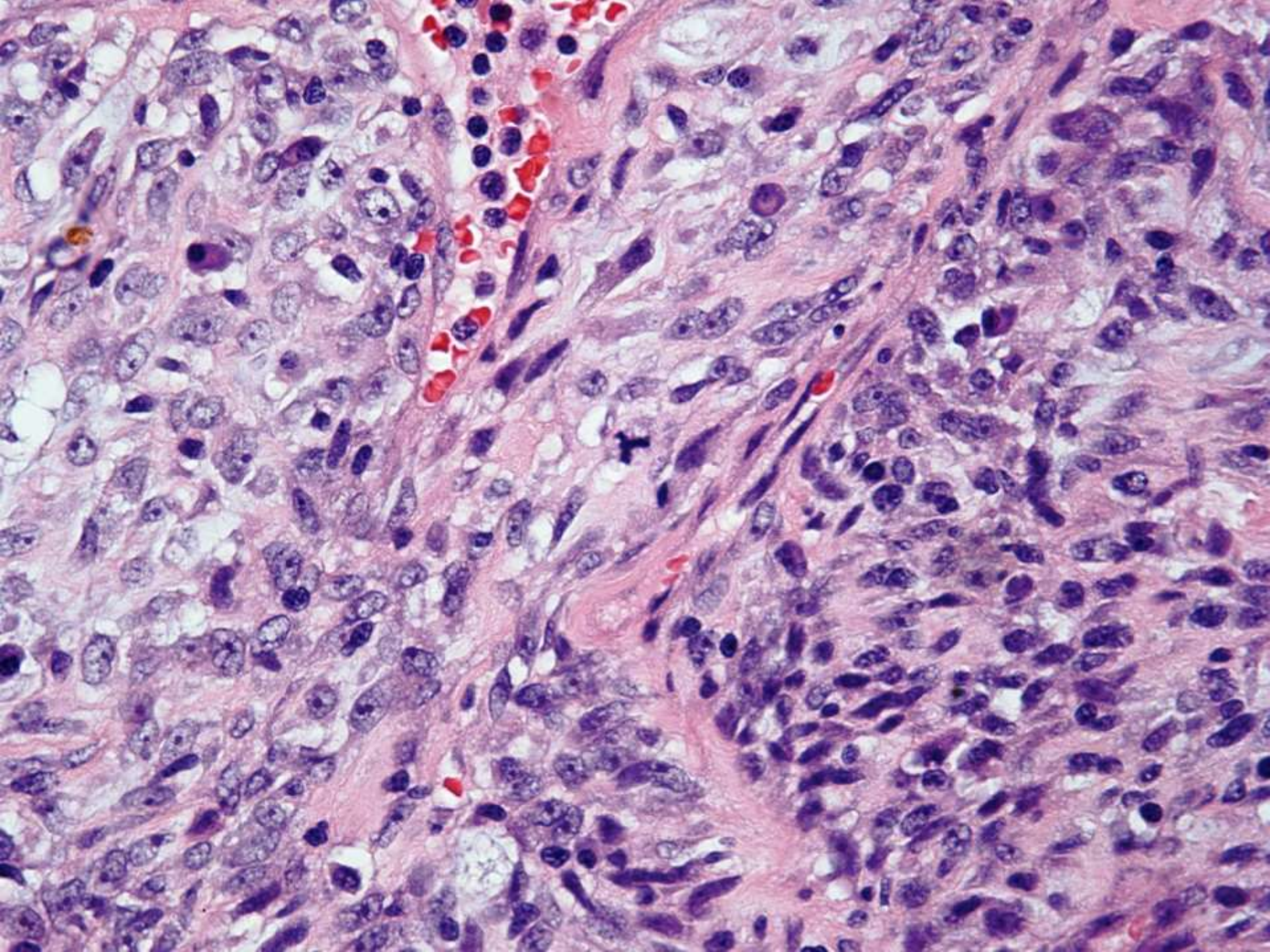
- **Alana Shain/Kimberly Allison; Stanford**

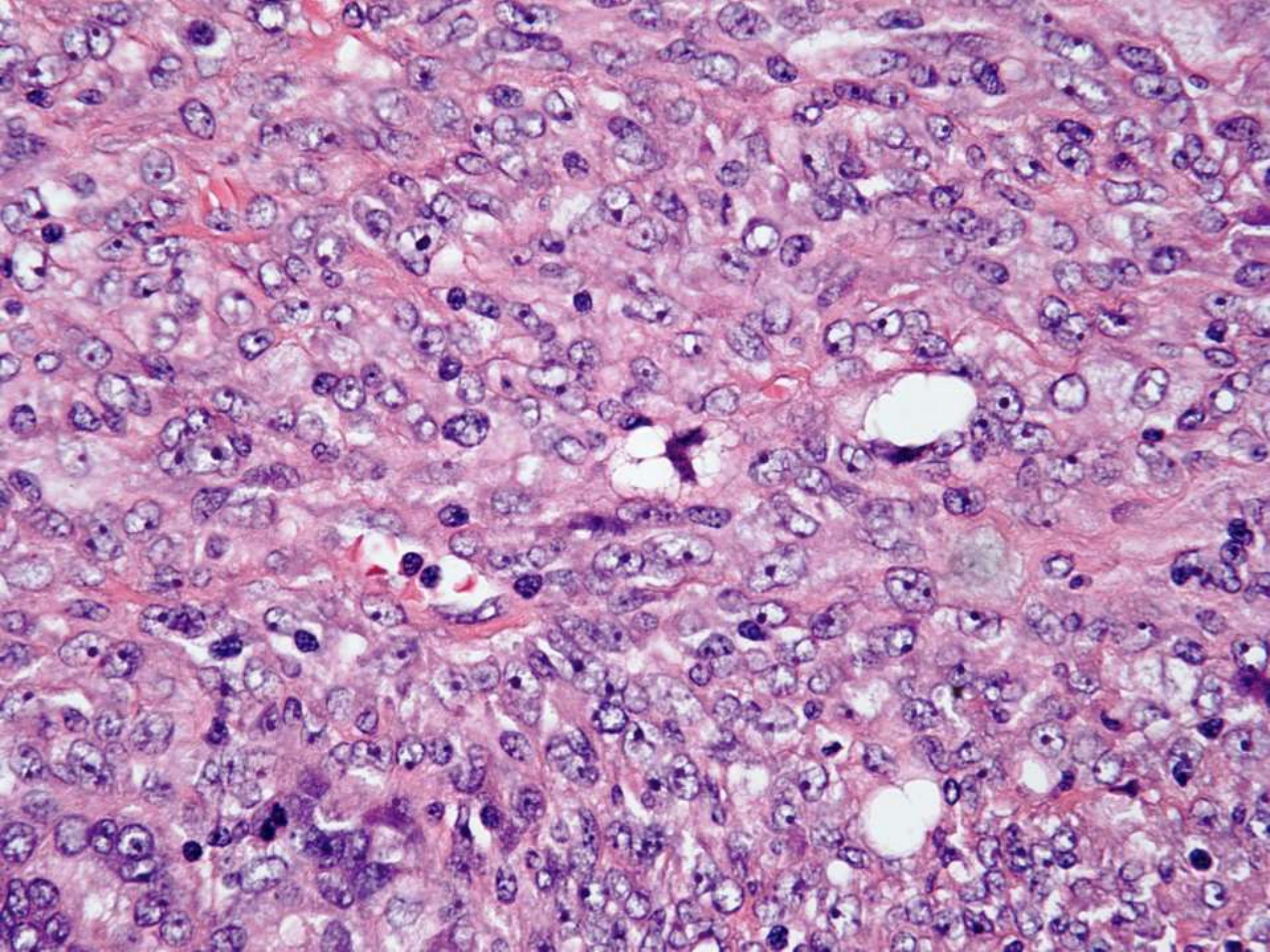


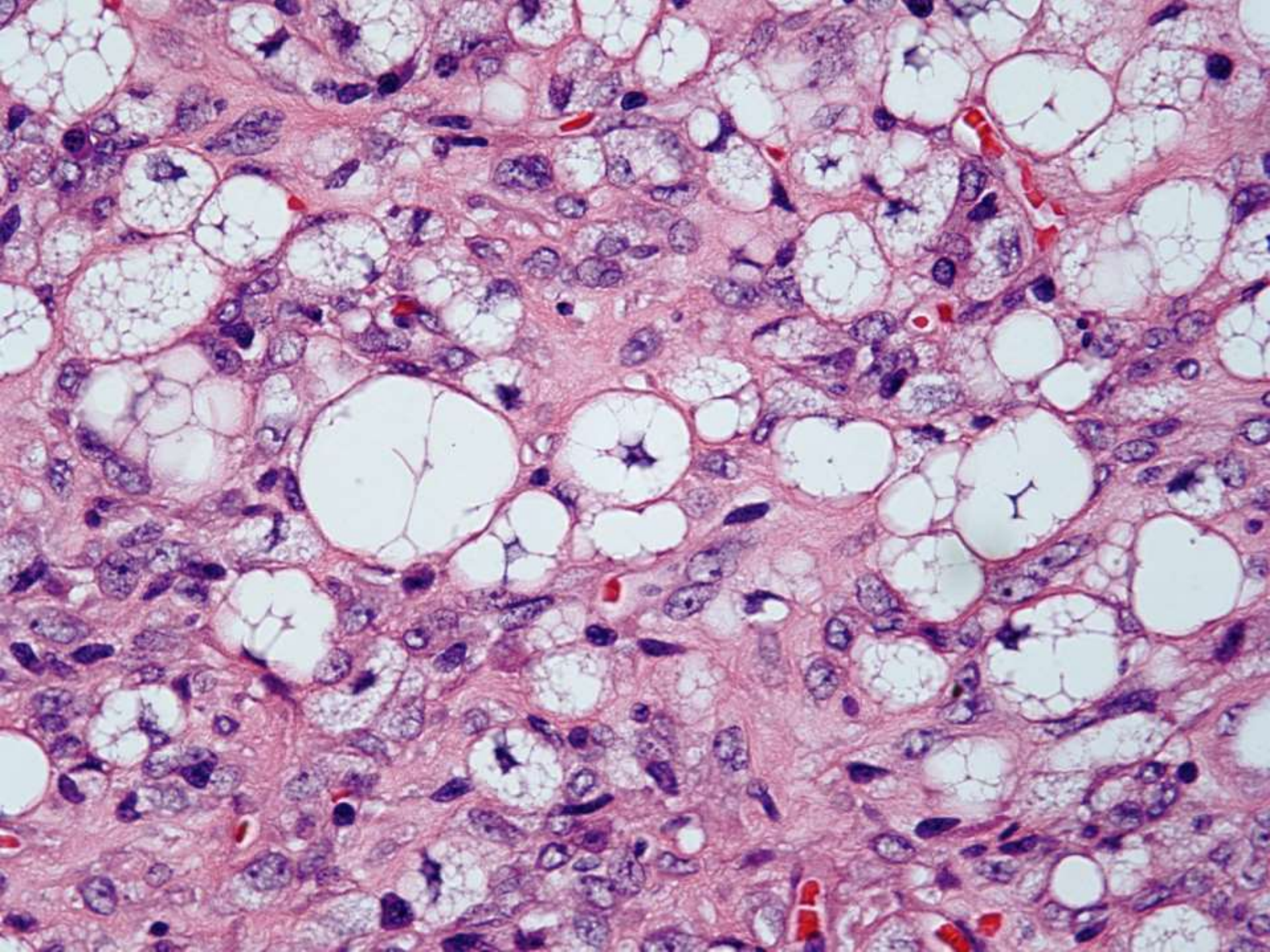












Diagnosis??

SB 6006
Malignant Phyllodes Tumor with Liposarcomatous Differentiation

Alana Shain, MD/Kimberly Allison, MD
Stanford University

Case courtesy Dr. David Wheeler
(Tuscon Medical Center, Tuscon AZ)

First, published on November 2, 2011 as 10.1136/jclinpath-2011-200368
Original article

Predicting clinical behaviour of breast phyllodes tumours: a nomogram based on histological criteria and surgical margins

Puay Hoon Tan,[1] Aye Aye Thike,[1] Wai Jin Tan,[1] Minn Minn Myint Thu,[1] Inny Busmanis,[1] HuiHua Li,[2] Wen Yee Chay,[3] Min-Han Tan,[4] The Phyllodes Tumour Network Singapore*

- Some **variability** in diagnostic criteria
  - Stromal overgrowth (>1 40x field without epithelium)
  - High mitotic index (>10/10 mitotic figures/10 hpf)
  - Sarcomatous stroma (nuclear pleomorphism & atypia)

- Surgical **margins** critical

Heterologous differentiation:

Liposarcoma, osteosarcoma, chondrosarcoma, rhabdomyosarcoma, fibrosarcoma, angiosarcoma

Tan et al. JCP 2012

Tool for Predicting Recurrence

Singapore General Hospital
SingHealth

http://mobile.sgh.com.sg/ptrra/

Phyllodes Tumour Recurrence Risk Assessment

Welcome to the Singapore General Hospital's Department of Pathology risk assessment tool for estimating a person's recurrence free likelihood following a histologic diagnosis of breast phyllodes tumour.

This tool is based on a study undertaken at the Singapore General Hospital (Tan PH et al. J Clin Pathol. 2012 Jan;65(1):69-76.)

This tool was designed for use by healthcare professionals. If you are not a healthcare professional, you are encouraged to discuss the results with your doctor.

Please read the SGH Nomogram Terms of Use before proceeding with this tool.

Detailed information on this risk assessment tool is available [Definitions for nomogram].

Risk assessment tool

Atypia

Does the tumor show stromal cytologic atypia ○ None or mild ○ Moderate ○ Marked

Mitoses

How many mitoses are visible per 10 high powered fields? Mitoses per 10 hpf 0

Overgrowth

Is there stromal overgrowth seen? ○ Absent ○ Present

Surgical margins

Are the margins histologically involved (positive)? ○ Negative ○ Positive

Can we use MDM2 FISH?

- Malignant phyllodes tumors with liposarcomatous differentiation (38 cases, 10 with blocks available)
- Evaluated ***MDM2* and *CDK4* amplification**
- **0/10 cases** showed amplification by **FISH**

Conclusion

MPTs with heterologous liposarcomatous differentiation

lack characteristic molecular alteration of soft tissue ALT/WDLS

Lyle PL et al. Histopathology 2015

Management

Breast conserving therapy without adjuvant therapy for all phyllodes tumors

Margins still **controversial**

Malignant phyllodes can be considered for **radiation** (Barth et al)

- Status post margin-negative, breast conserving resection
- Adjuvant radiation therapy
- **Decreased rate of local recurrence (0% vs 21%)**

Barth RJ et al. Ann Surg Oncol 2009

References

Austin R M, Dupree W B. 1986. Liposarcoma of the breast: a clinicopathologic study of 20 cases. Human pathology 17 (9): 906-913.

Barth R J, Wells W A, Mitchell S E, Cole B F. 2009. A prospective, multi-institutional study of adjuvant radiotherapy after resection of malignant phyllodes tumors. Annals of Surgical Oncology 16 (8): 2288-2294.

Lyle P L, Bridge J A, Simpson J F, Cates J M, Sanders M E. 2015. Liposarcomatous differentiation in malignant phyllodes tumors is unassociated with MDM2 or CDK4 amplification. Histopathology, Accepted article.

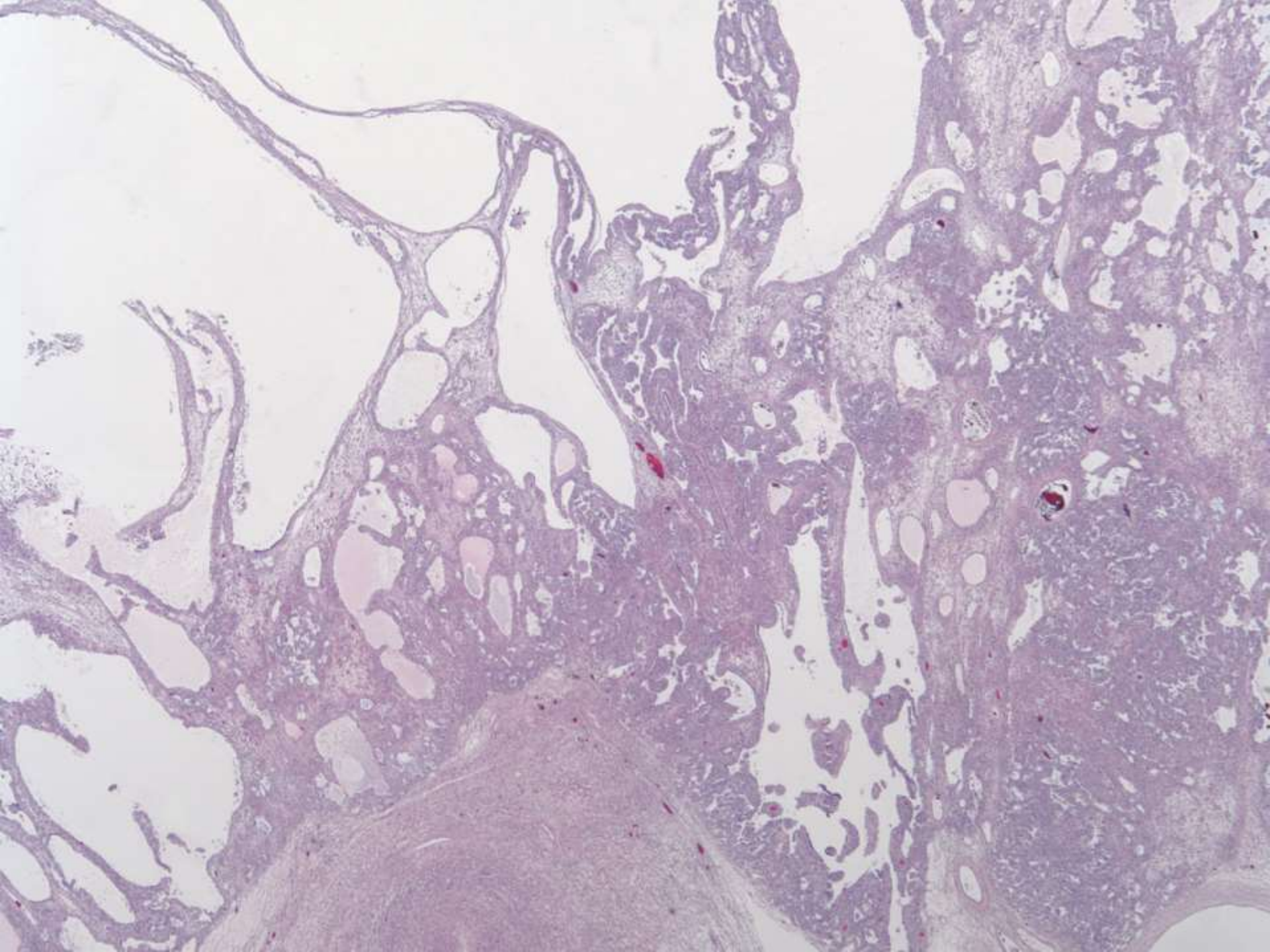
Powell C M, Rosen P P. 1994. Adipose differentiation in cystosarcoma phyllodes. A study of 14 cases. The American journal of surgical pathology 18 (7): 720-727.

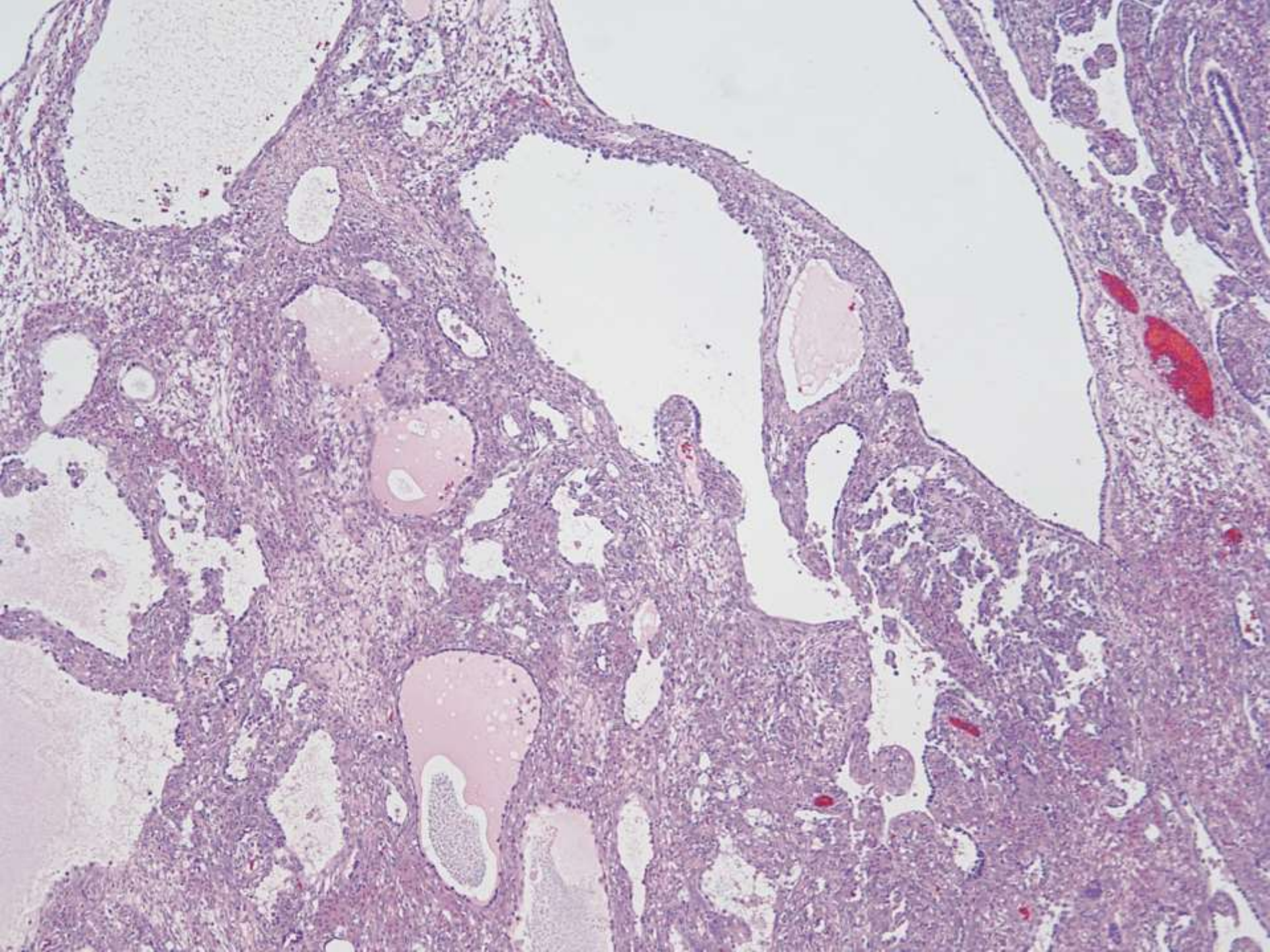
Tan P H, Thike A A, Tan W J, Thu M M, Busmanis I, Li H, Chay W Y, Tan M. 2012. Predicting clinical behaviour of breast phyllodes tumours: a nomogram based on histological criteria and surgical margins. Journal of Clinical Pathology 65 (1): 69-76.

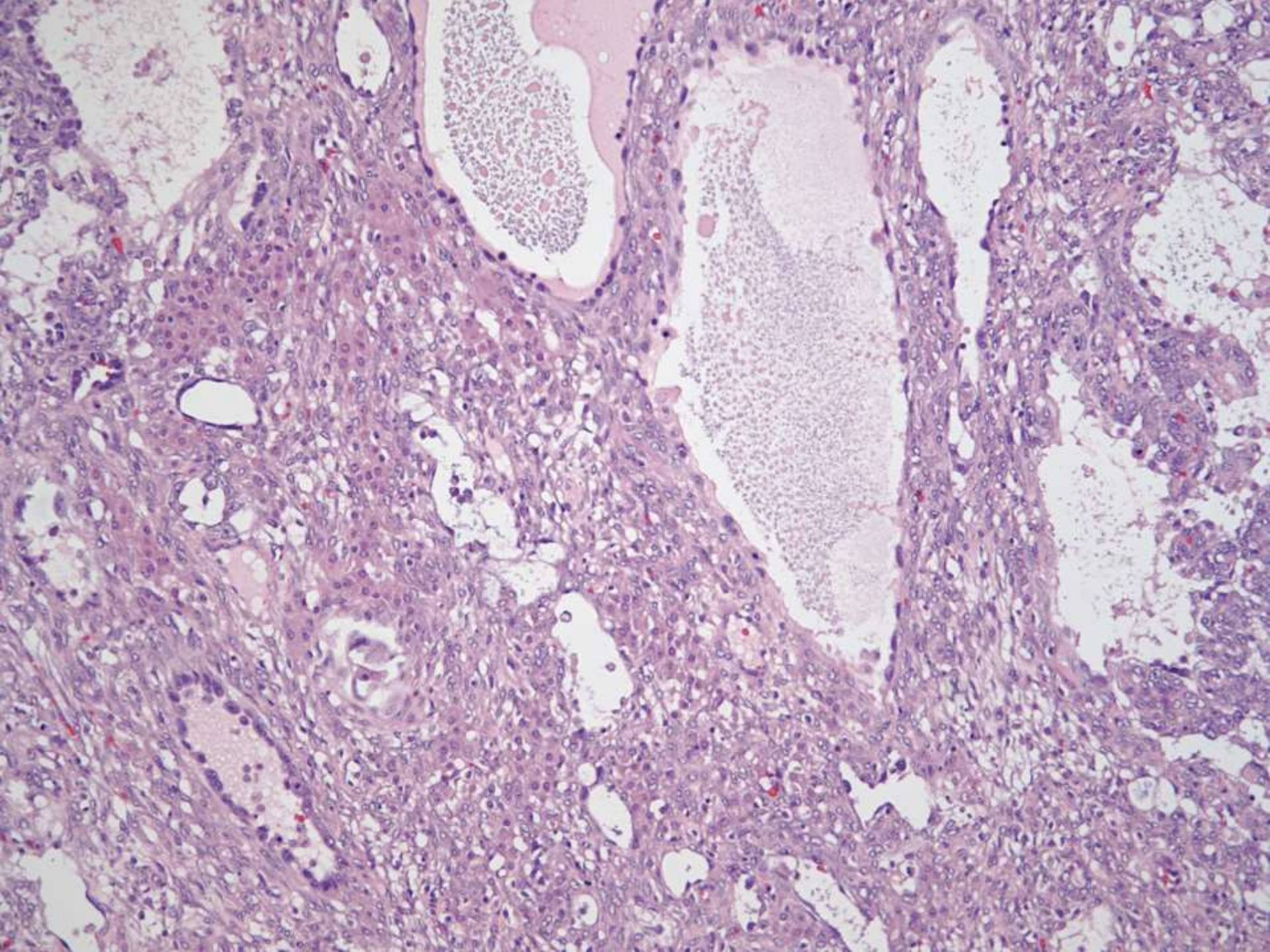
SB 6007

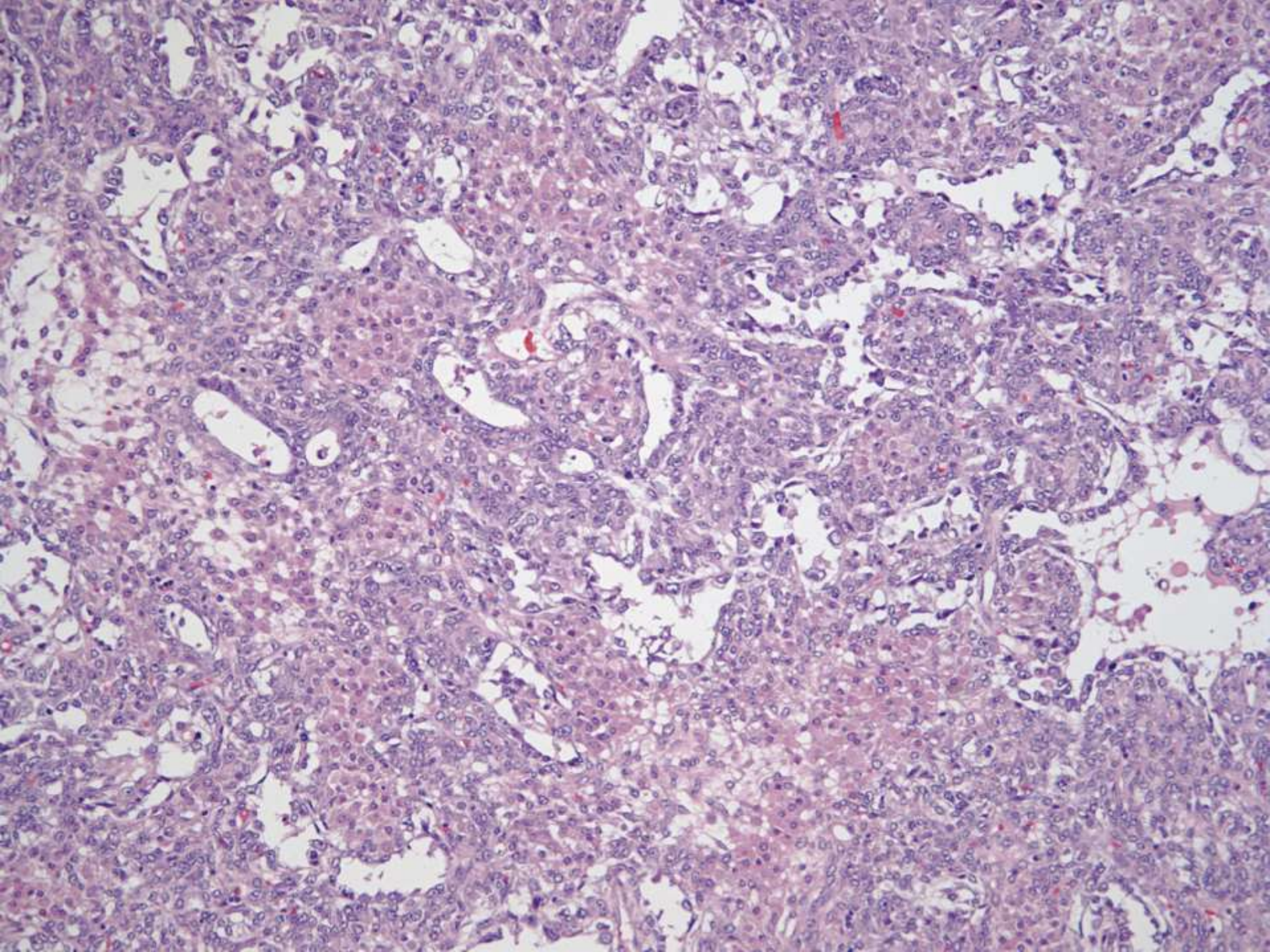
- 25-year-old female, 29 weeks pregnant, with unilateral 18.5cm ovarian mass.

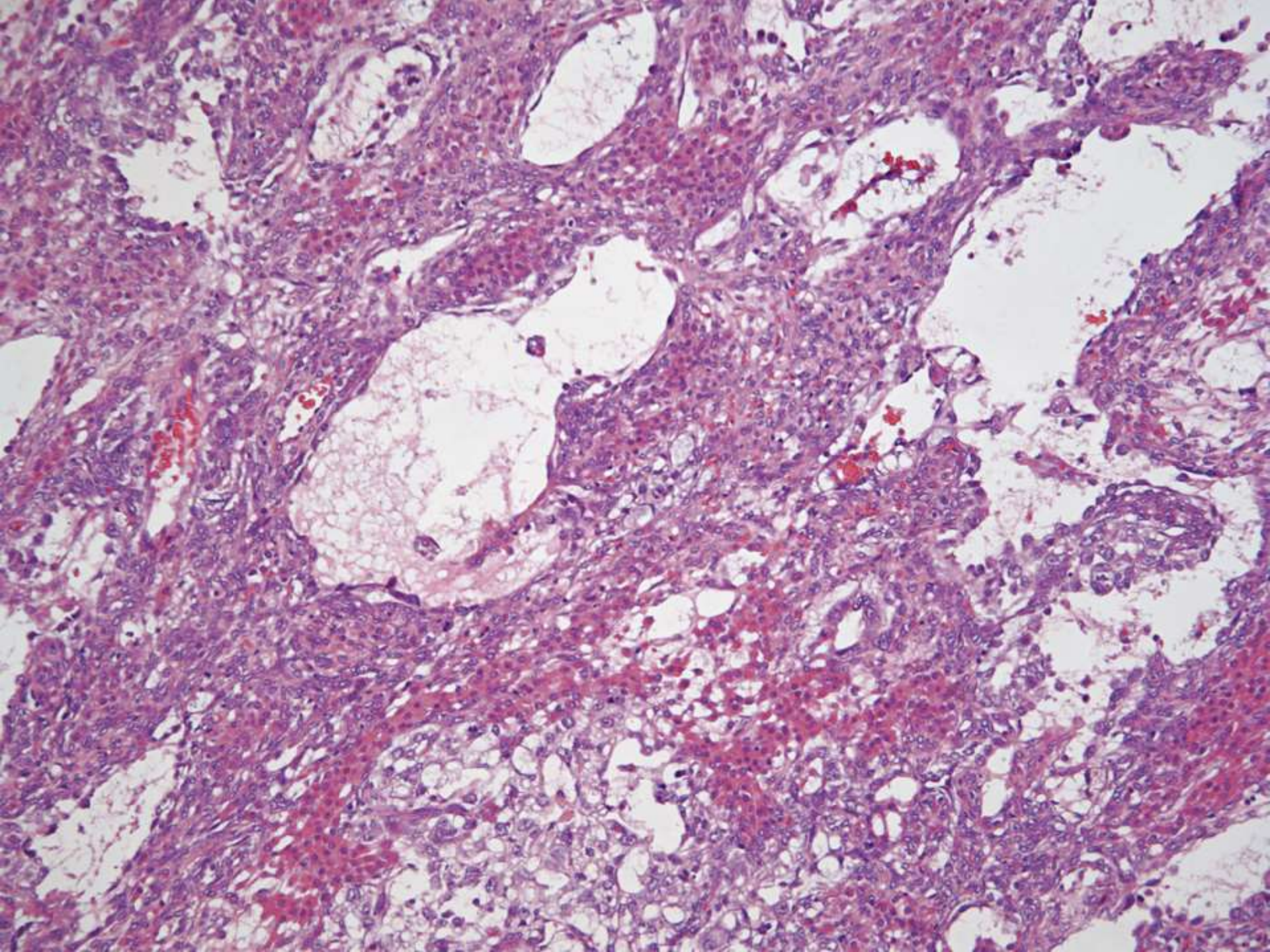
- **Christine Louie/Teri Longacre; Stanford**







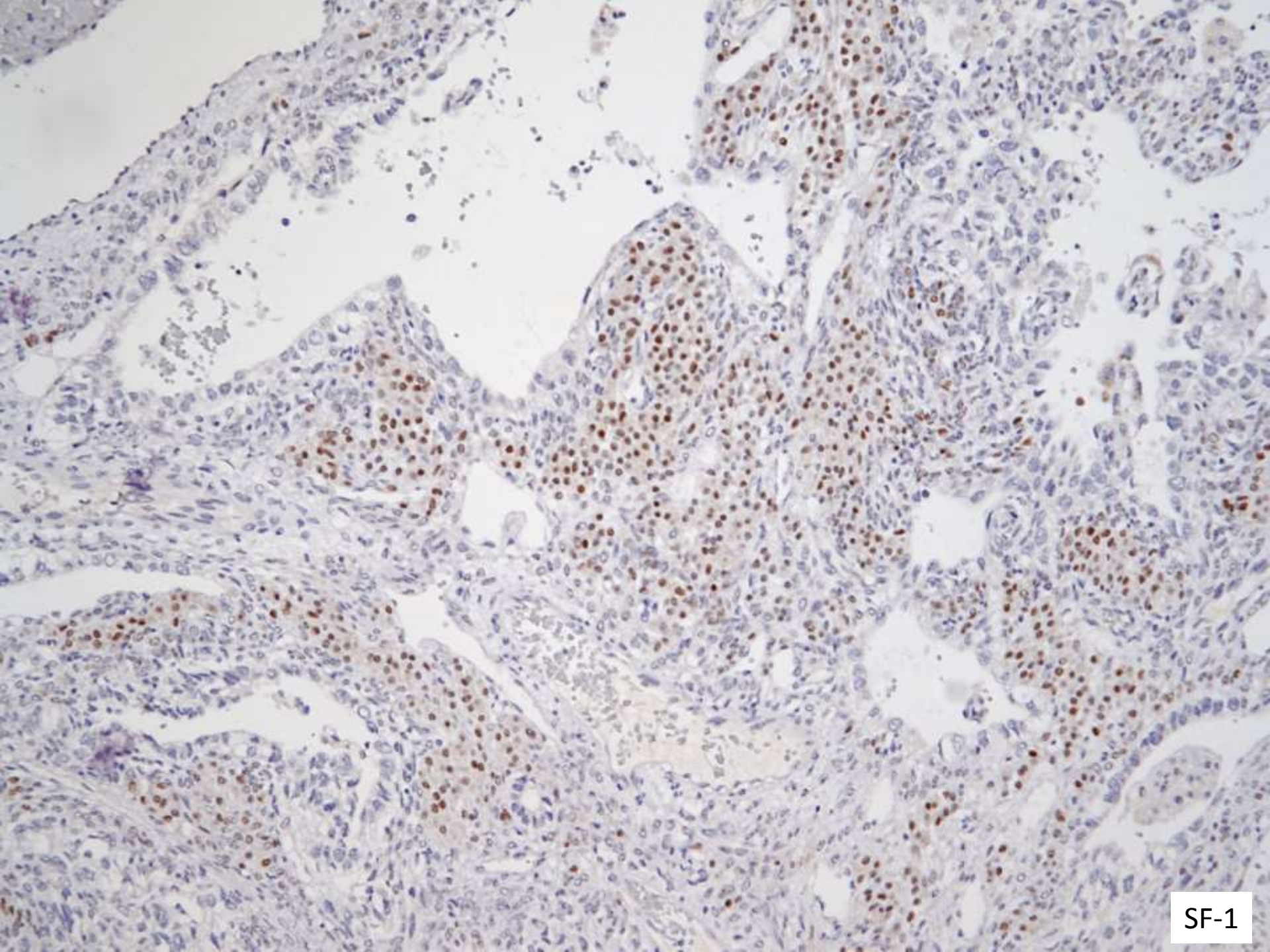




Diagnosis??

Differential Diagnosis

- Sertoli-Leydig tumor
- Juvenile granulosa cell tumor
- Clear cell carcinoma
- Endometrioid adenocarcinoma
- Yolk sac tumor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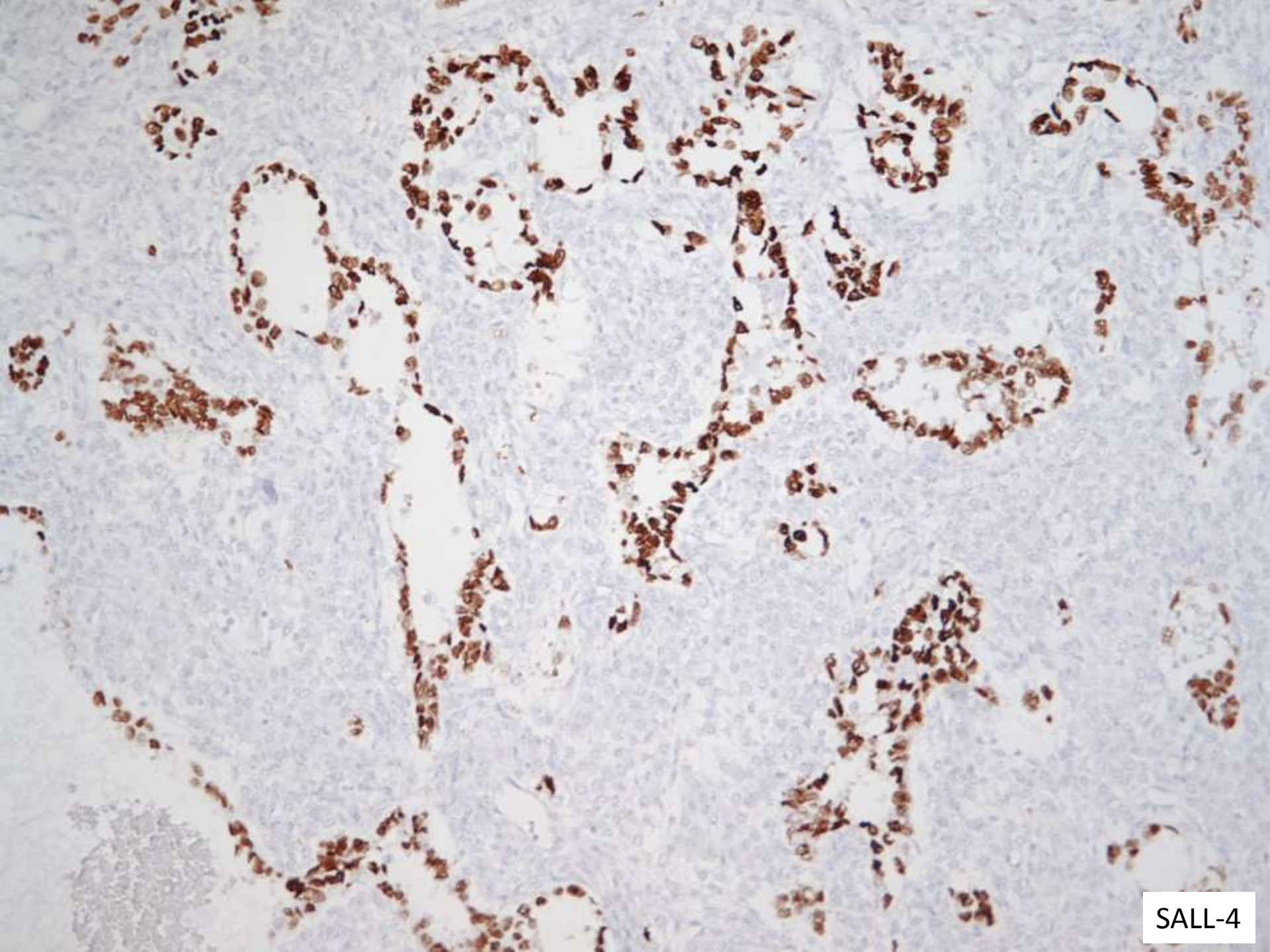
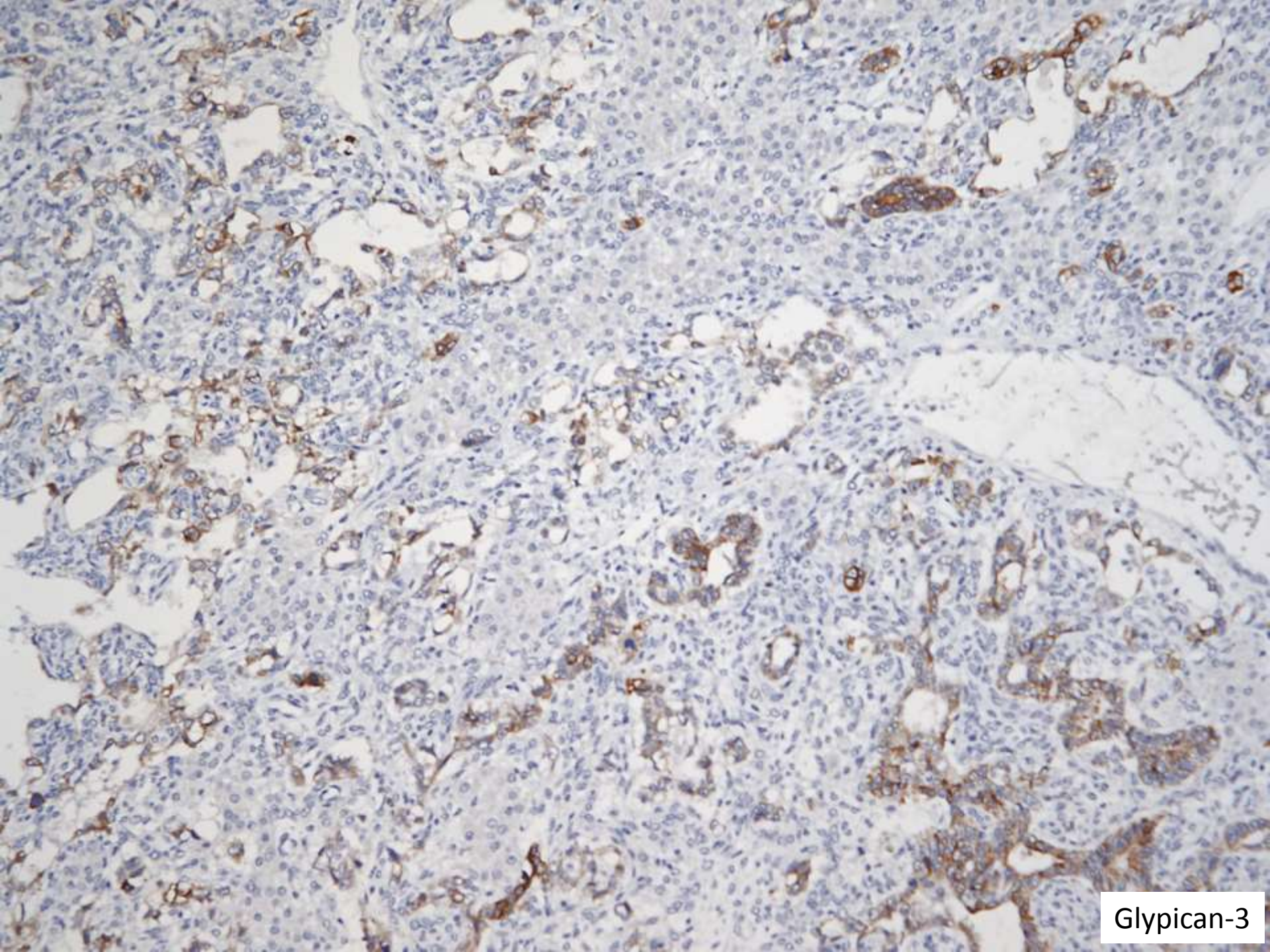

SALL-4


Glypican-3

Yolk Sac Tumor

Yolk Sac Tumor

- Malignant germ cell neoplasm
- Often occurs in ovary in pure form
- Young women
- Typically presents as unilateral, rapidly growing pelvic mass
- Rupture or torsion occurs in ~10%

Curr Oncol Rep (2014) 16:415
DOI 10.1007/s11912-014-0415-z

GYNECOLOGIC CANCERS (NS REED, SECTION EDITOR)

Management of Gynecological Cancers During Pregnancy

Sileny N. Han · Magali Verheecke · Tineke Vandenbroucke · Mina Mhallem Gziri · Kristel Van Calsteren · Frédéric Amant

- Surgery and chemotherapy; no radiation
- Our case – baby was delivered at time of surgery

THE JOURNAL OF
Obstetrics and Gynaecology Research

The official Journal of Asia and Oceania Federation of Obstetrics and Gynaecology
Japan Society of Obstetrics and Gynecology

doi:10.1111/j.1447-0756.2010.01254.x

J. Obstet. Gynaecol. Res. Vol. 36, No. 5: 1137–1141, October 2010

Ruptured ovarian endodermal sinus tumor diagnosed during pregnancy: Case report and review of the literature

Mongkol Benjapibal, Pattama Chaopotong, Chairatana Leelaphatanadit and Atthapon Jaishuen

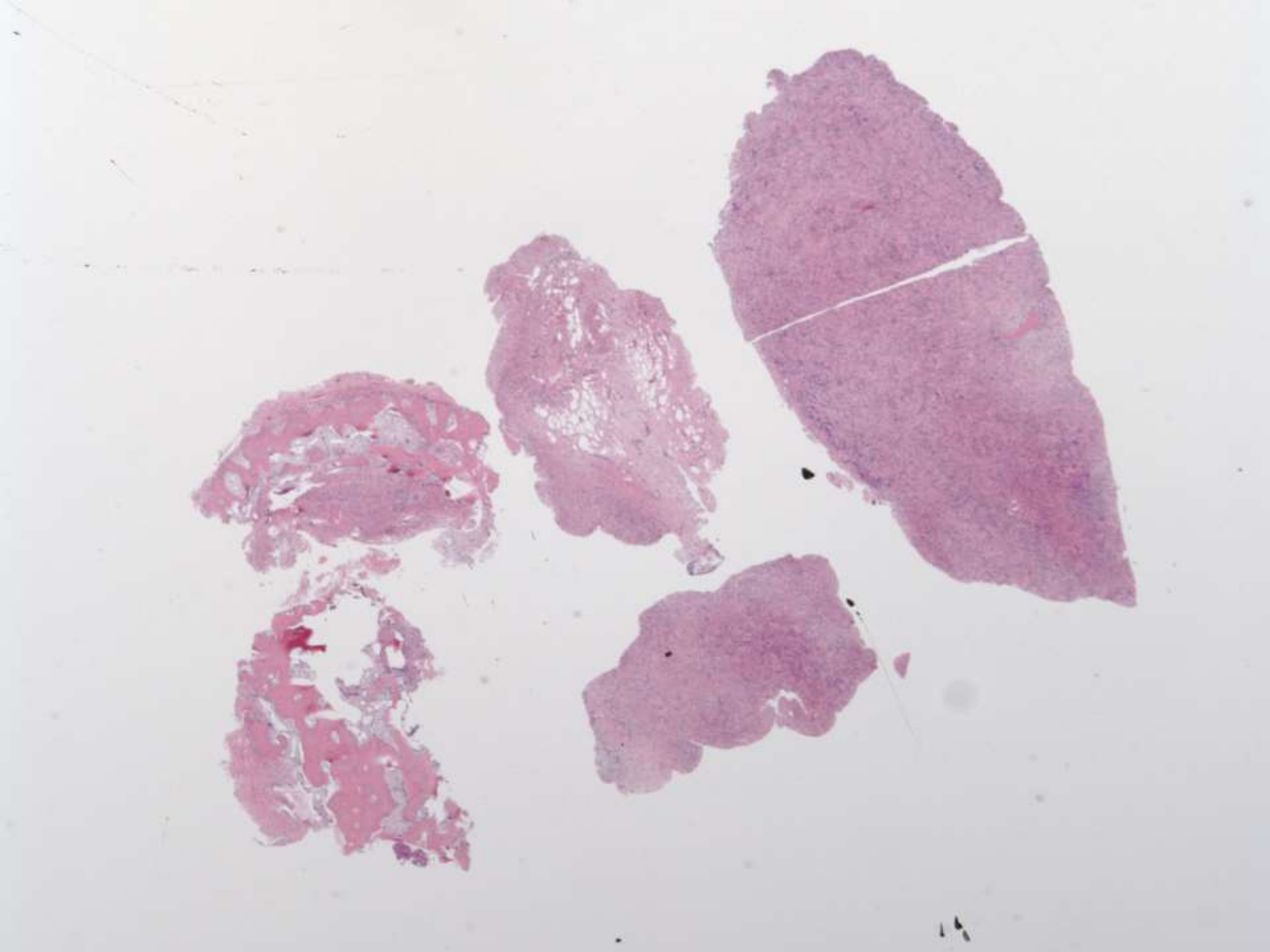
Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

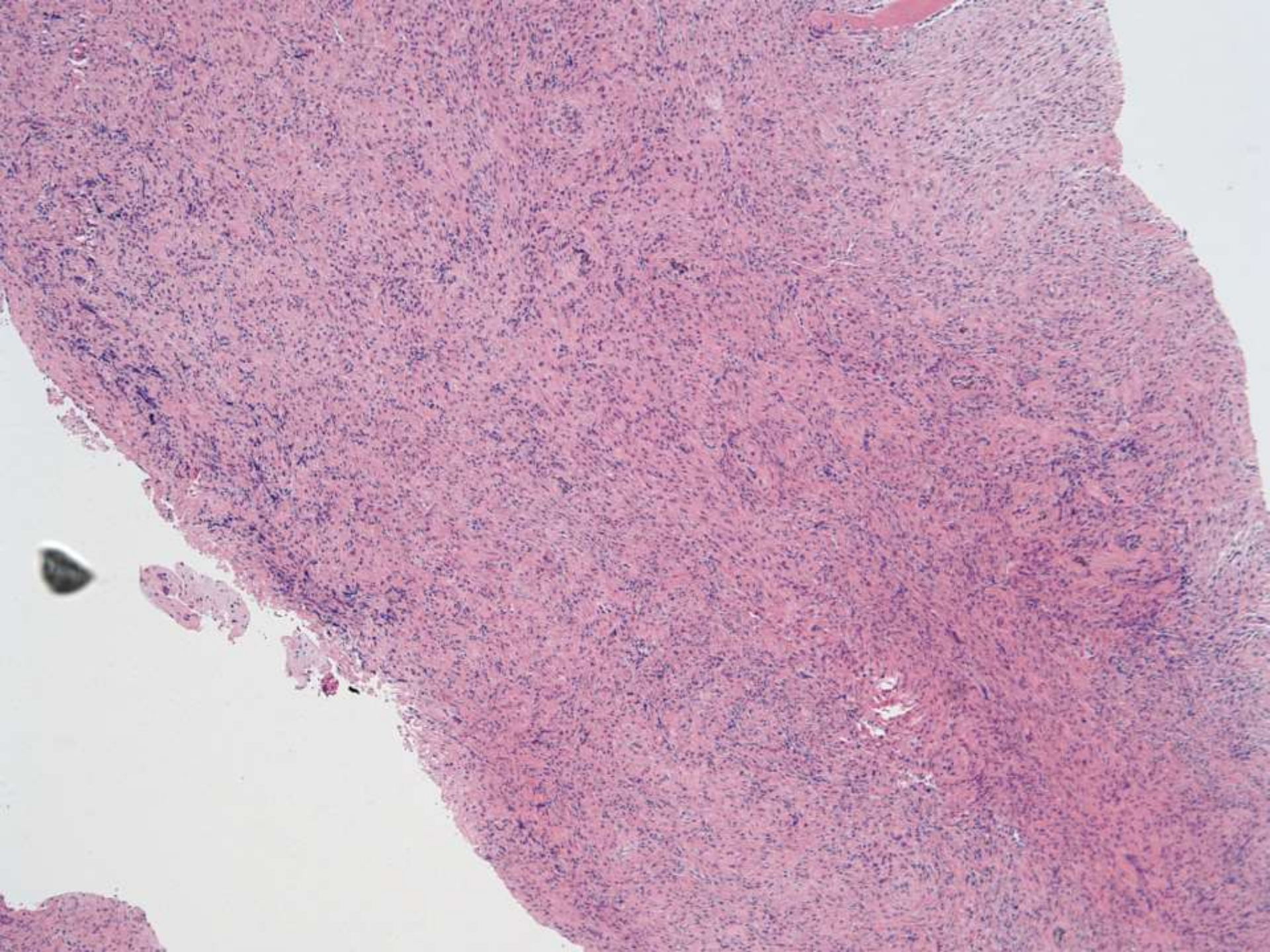
- Yolk sac tumor found during pregnancy is rare
- Surgery and chemotherapy
- Most cases of chemotherapy had healthy babies (only a handful)

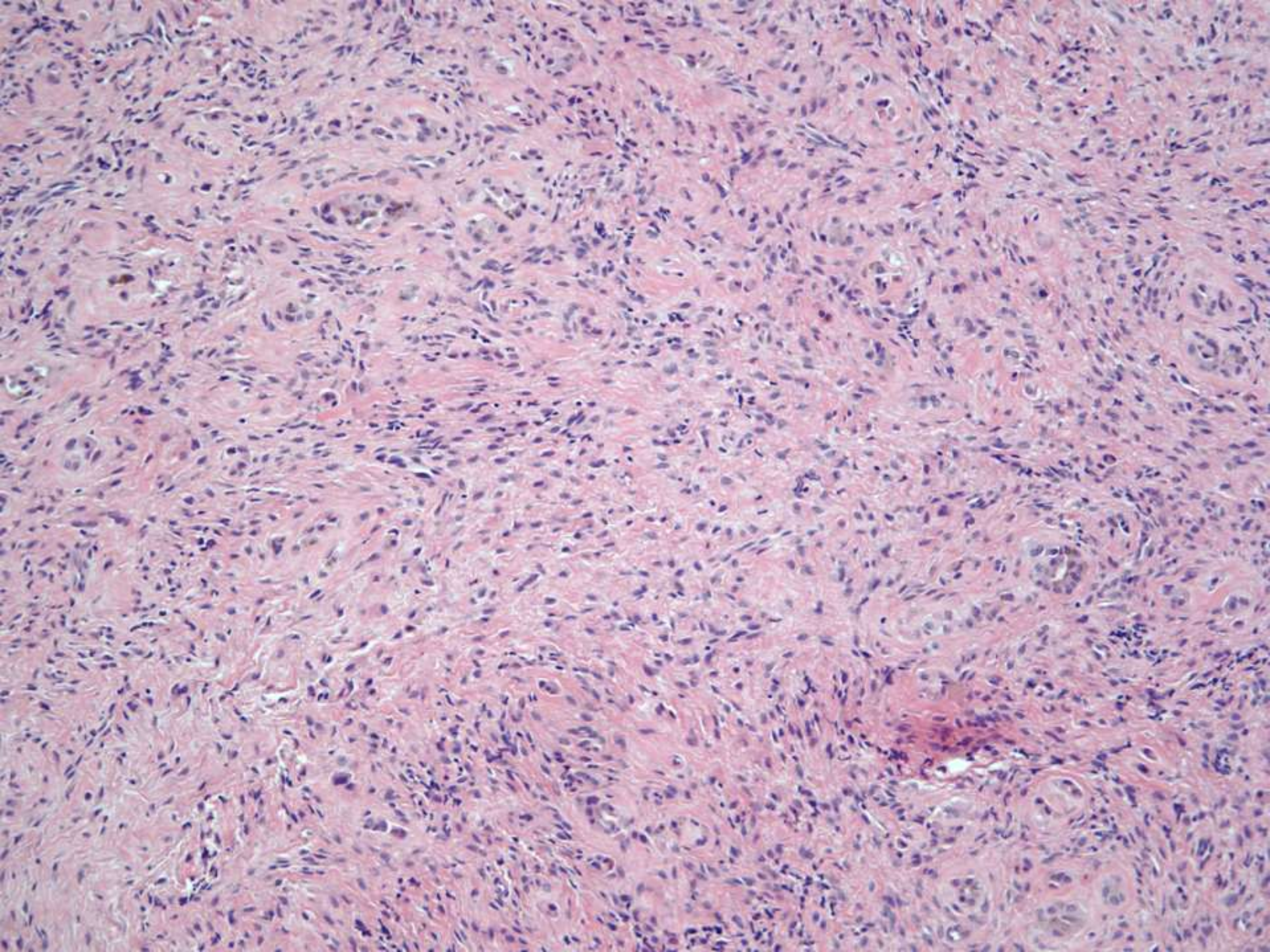
SB 6008

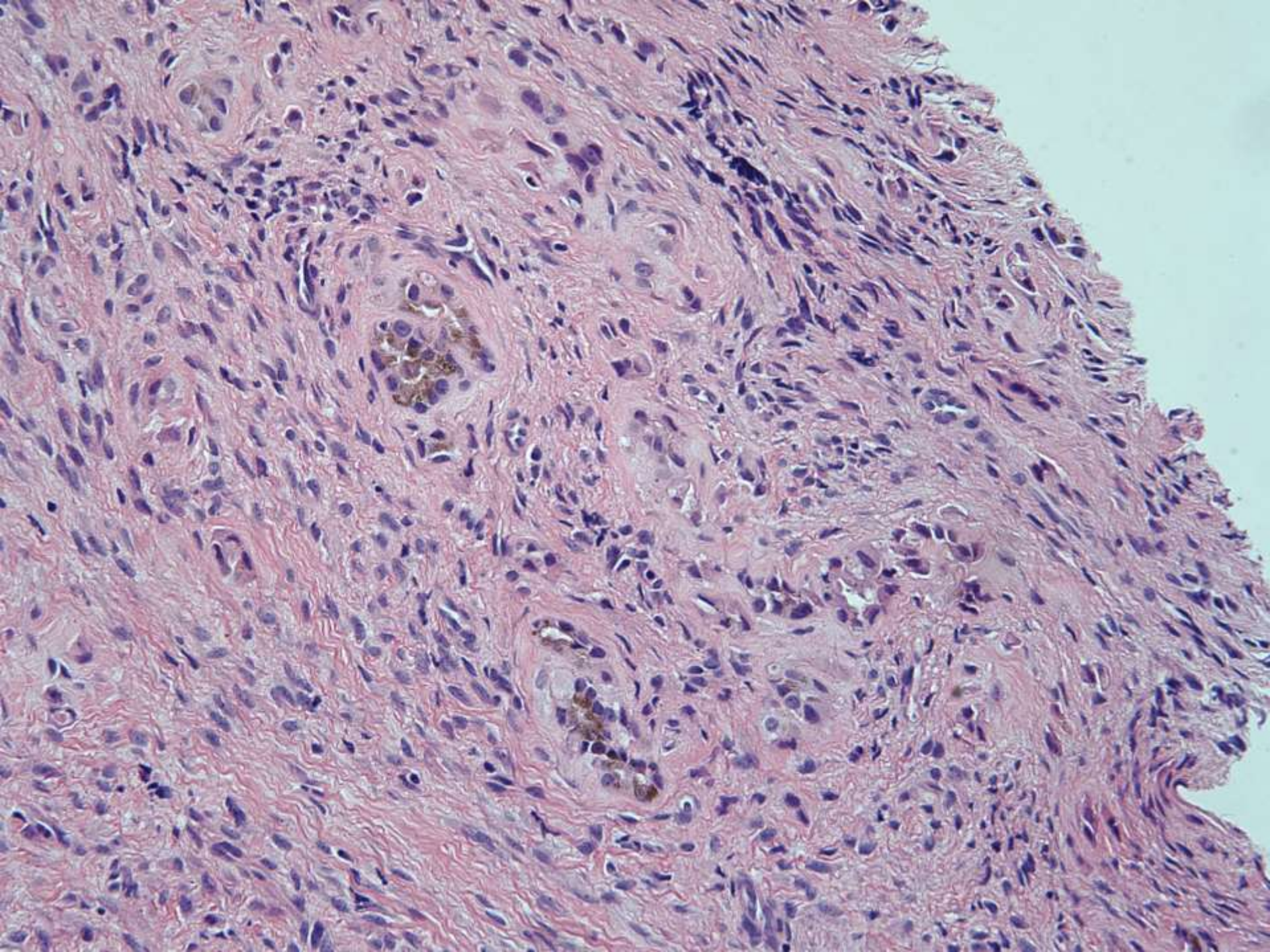
- 6-month-old baby girl with 2-month history of cystic mandibular lesion on CT. The lesion has been growing in size and now measures 1.4cm.

- **Soo-Ryum Yang/Eduardo Zambrano; Stanford**

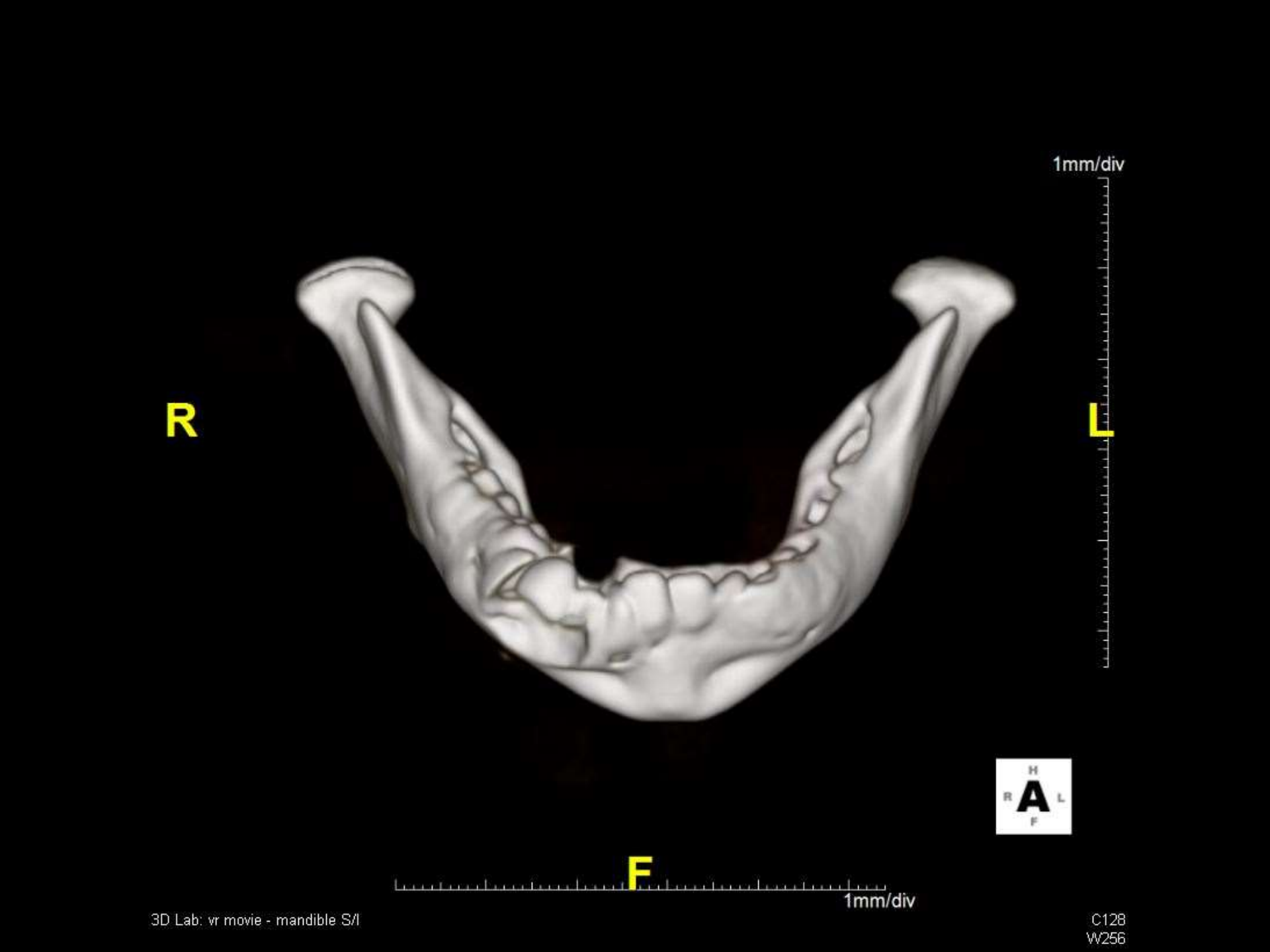








Diagnosis??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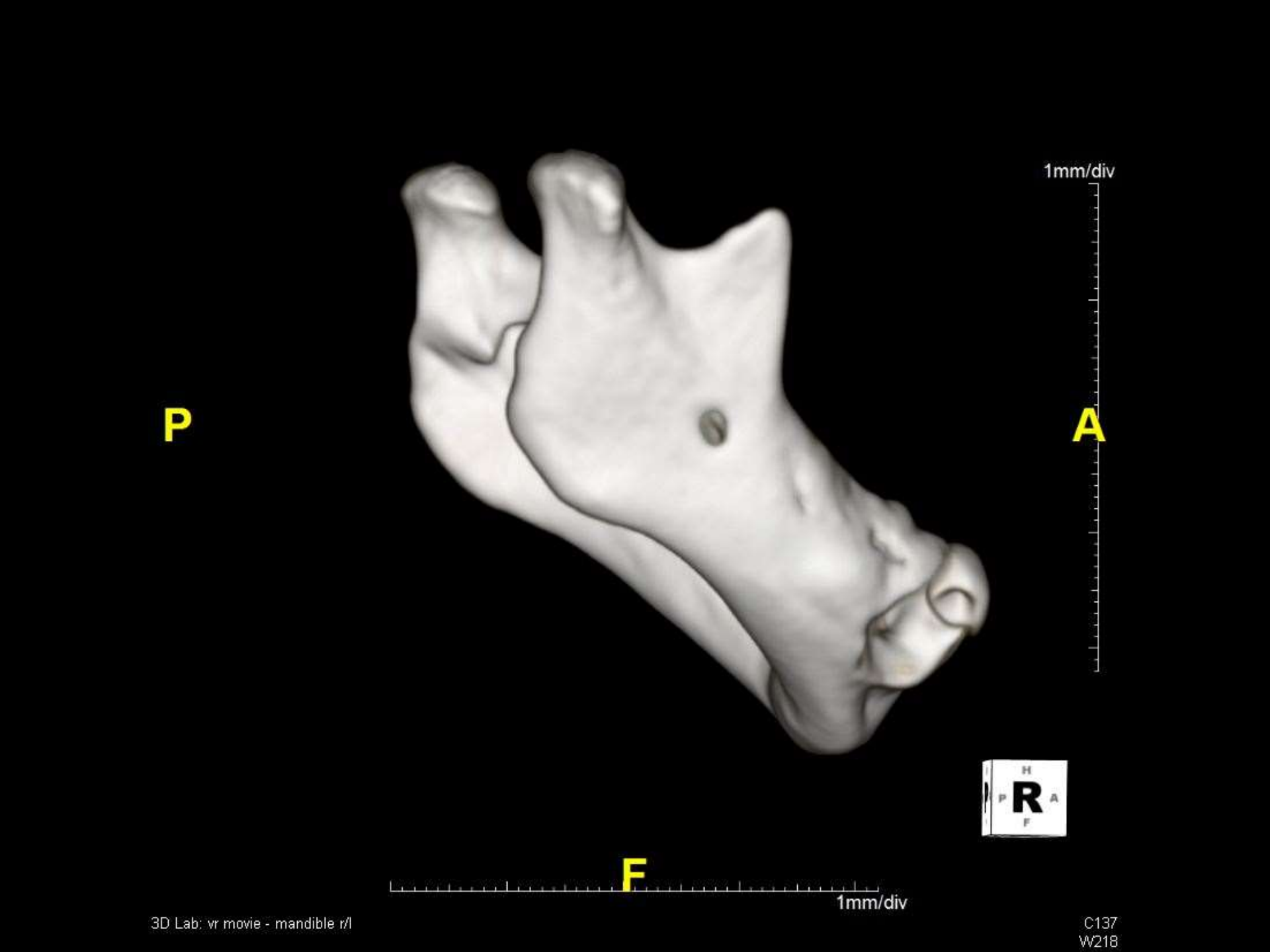
3D Lab: vr movie - mandible S/I
C128
W256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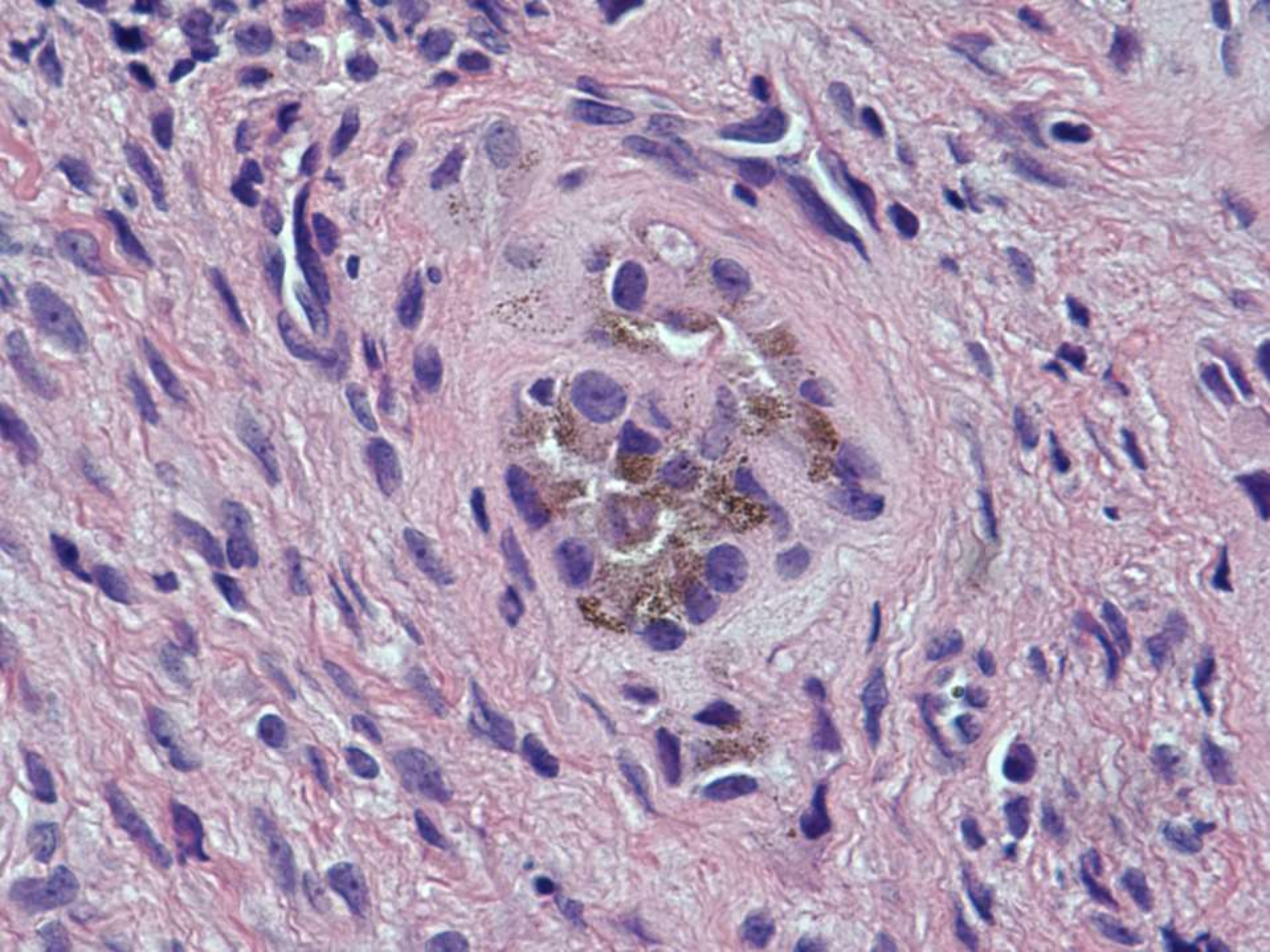

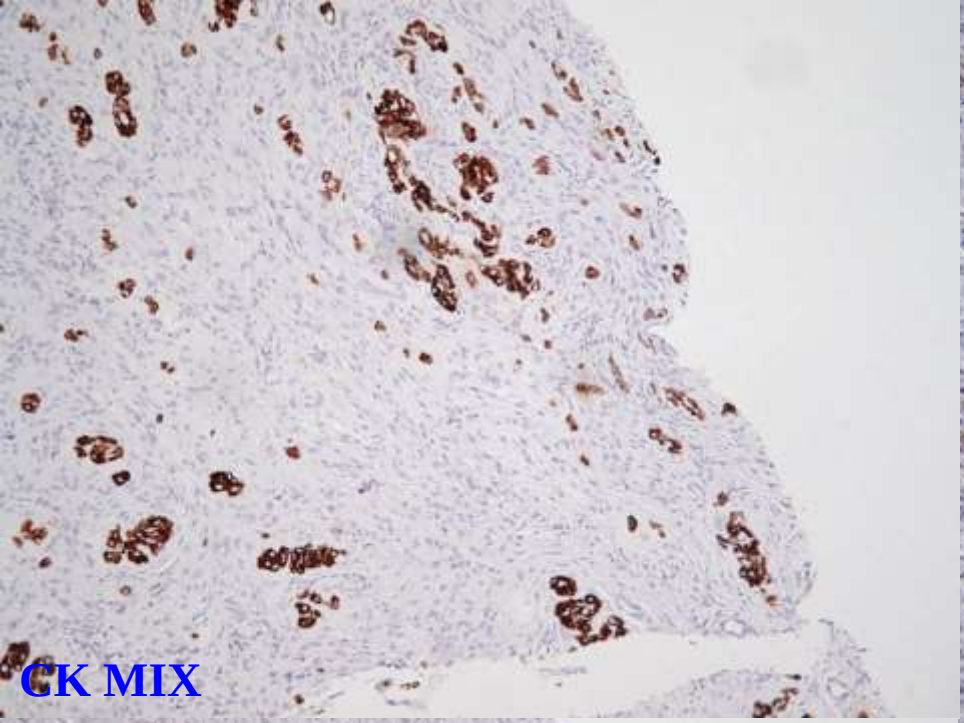
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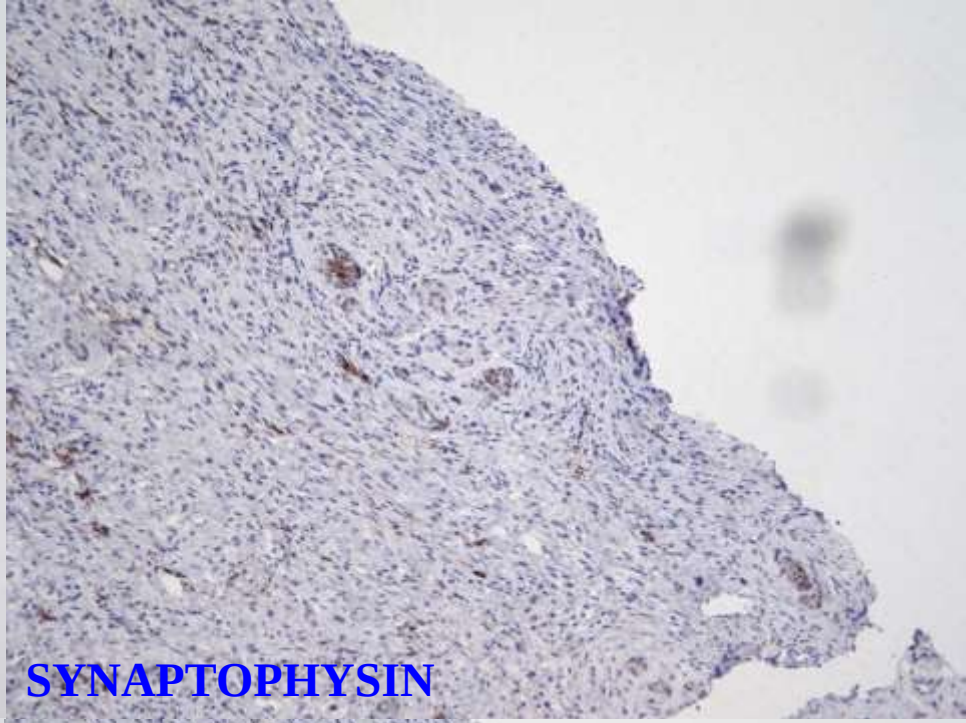
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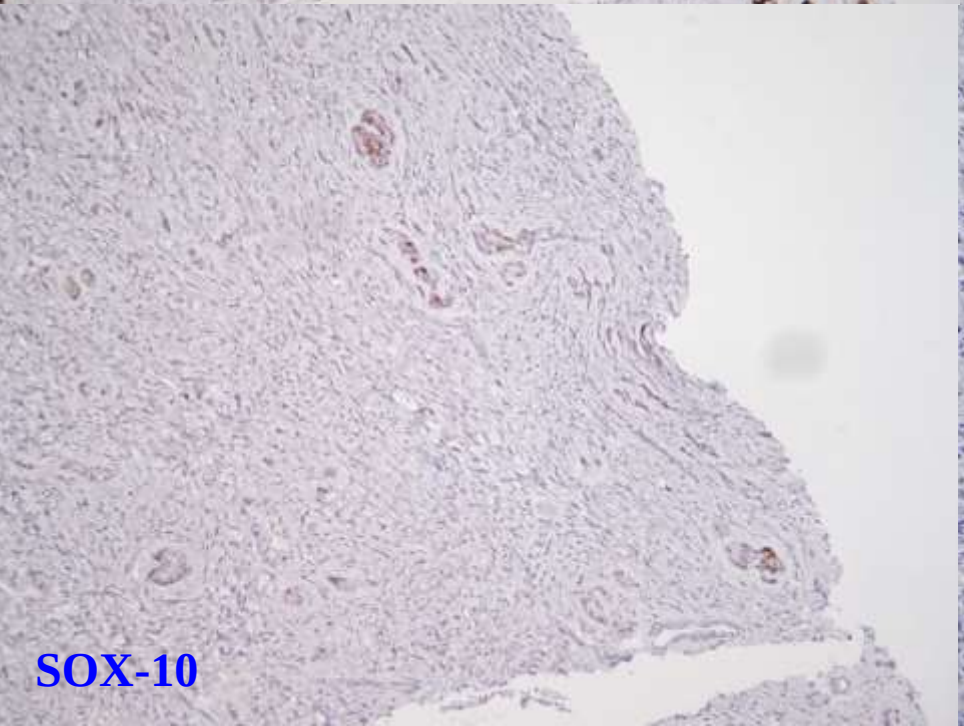
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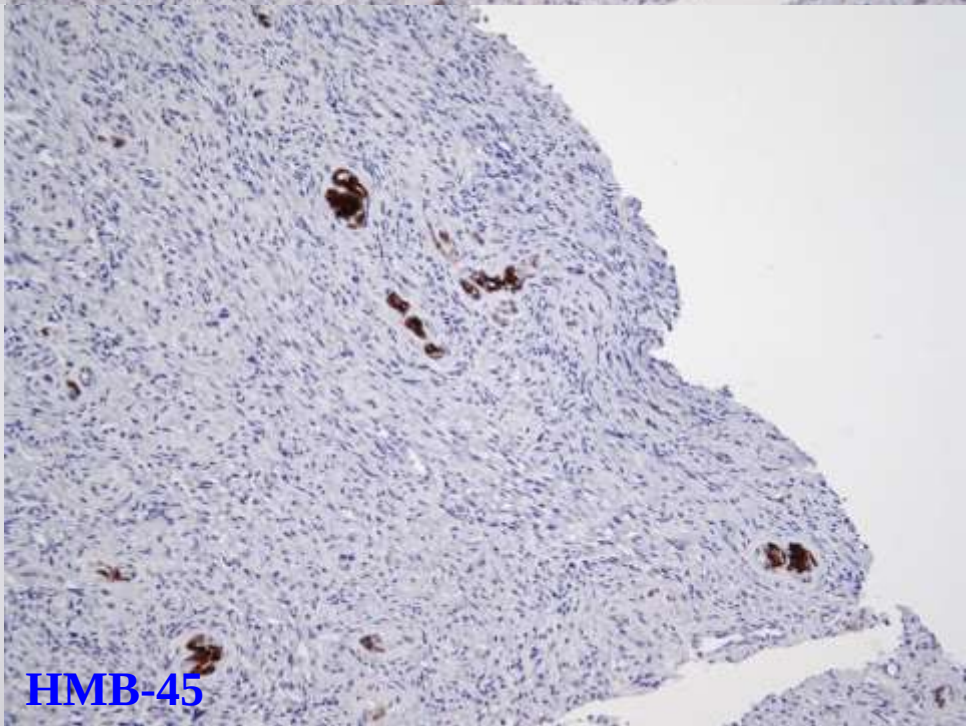
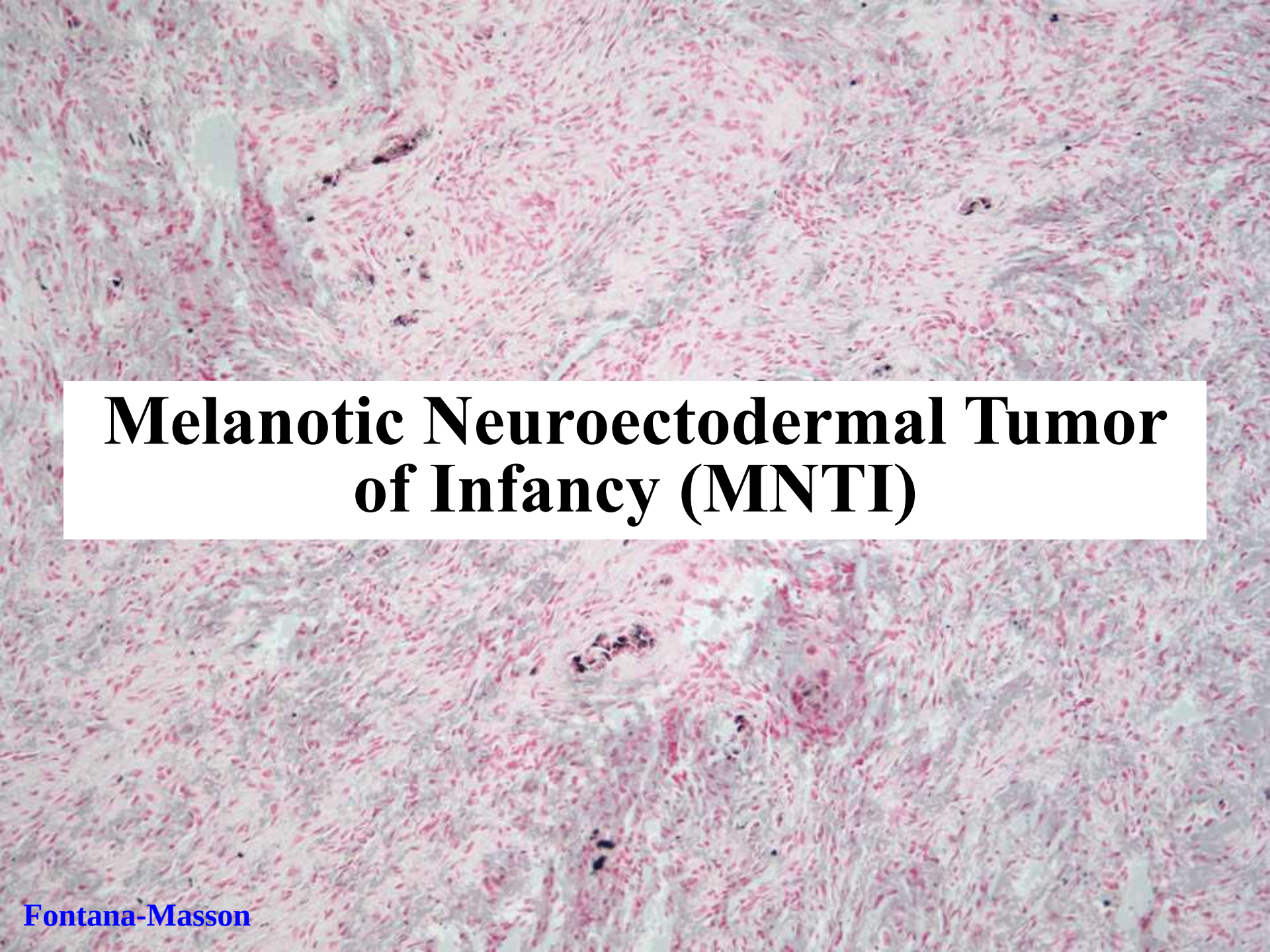

HMB-45

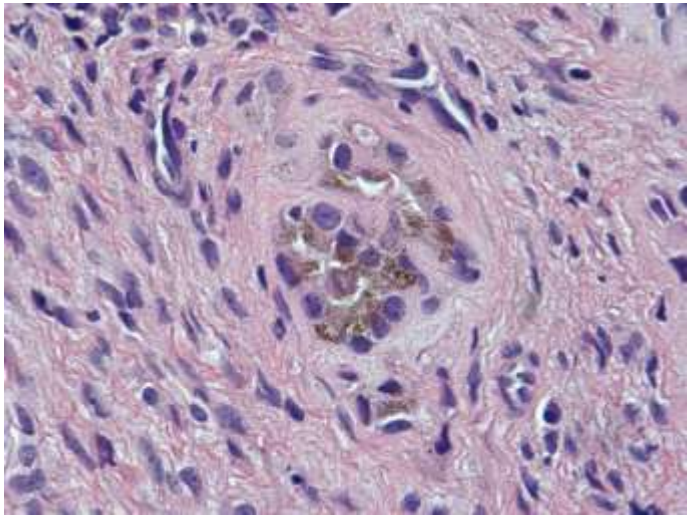


Melanotic Neuroectodermal Tumor of Infancy (MNTI)

Fontana-Masson

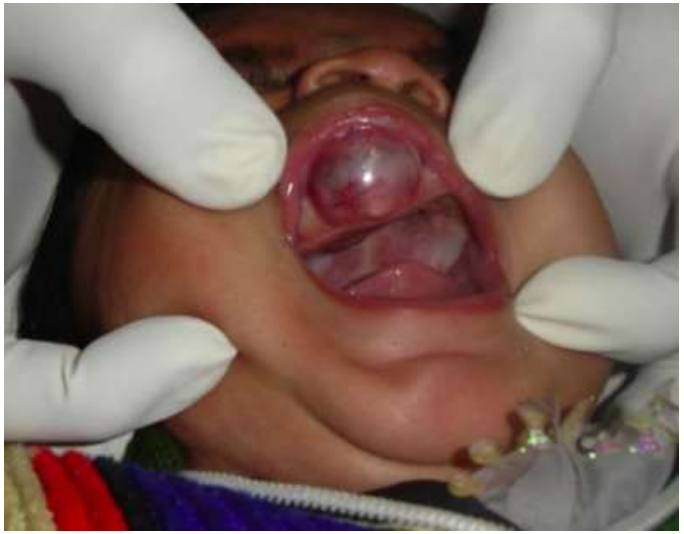
Diagnostic Findings

- Large cells
  - Eosinophilic cytoplasm with nucleoli and melanin
  - IPOX: CK, HMB45, SOX10, synaptophysin
- Small cells
  - Primitive neuroepithelial cells with scant cytoplasm
  - IPOX: synaptophysin, CD56, NSE
- Malignant: 5-10%

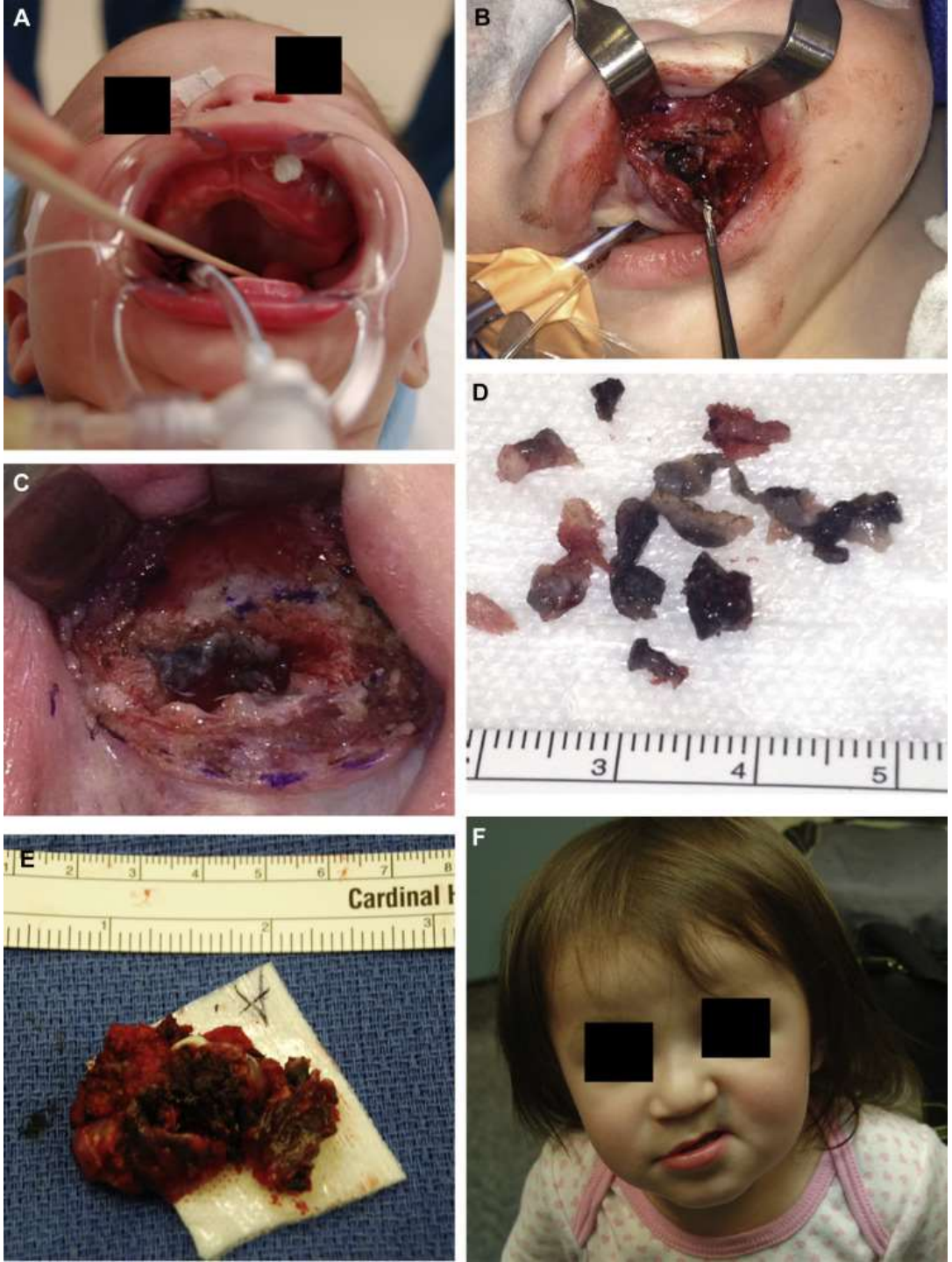


Clinical Presentation

- 1918: “congenital melanocarcinoma” in a 2-month-old
  - Proposed to originate from neural crests
- Age: <1 year (3-6 months)
- Gender: male > female (1.48)
- Location:
  - Craniofacial region
    - Maxilla (80-68%)
    - Skull (10%)
    - Mandible (6%)
    - Brain (4%)
  - Other sites: testes, ovaries, mediastinum
- Labs: urinary VMA



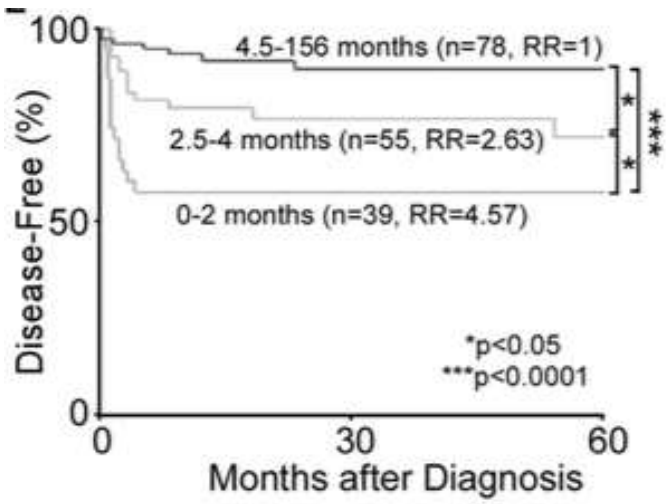
Gupta et al. 2015



Rachidi et al. 2015

Treatment and Prognosis

- Treatment
  - Adequate surgical resection +/- chemotherapy
  - Surveillance
- Recurrence: 10-15%
  - Multifocal disease
  - Incomplete resection
  - Bone marrow involvement
  - **Age at diagnosis**
- Metastasis: 5%
- Malignant: Median time of survival: < 1 year



Differential diagnosis

- Infants
  - Congenital epulis
  - Gingival cyst of newborn
  - Congenital eruption cyst
- Pediatric
  - Odontogenic tumors: Odontoma, ameloblastoma
  - Non-odontogenic tumors: Osteoma, JOF, CGCG
- Melanin-positive cells
  - Teratoma with retinal differentiation
  - Melanoma
- “Small round blue cell tumors”

Patient Follow-up

- 6/15:
  - Biopsy of lesion
  - Diagnosis of MNTI
- 7/15: Enucleation of the mass
- 8/15:
  - Patient doing well
  - Meeting milestones
  - Q6 CT scan for recurrence

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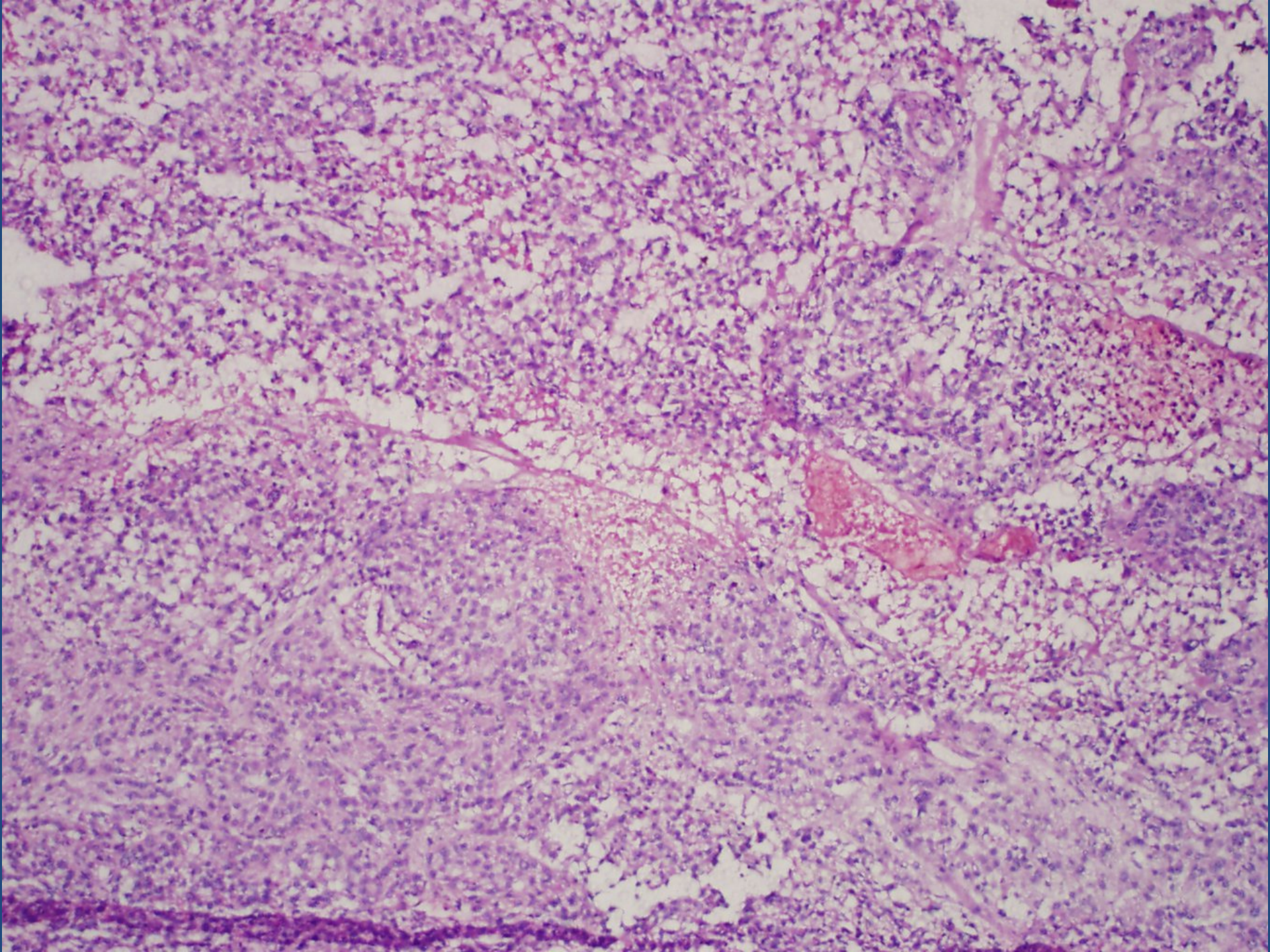
- http://surgpathcriteria.stanford.edu/srbc/melanotic-neuroectodermal-tumor-of-infancy/

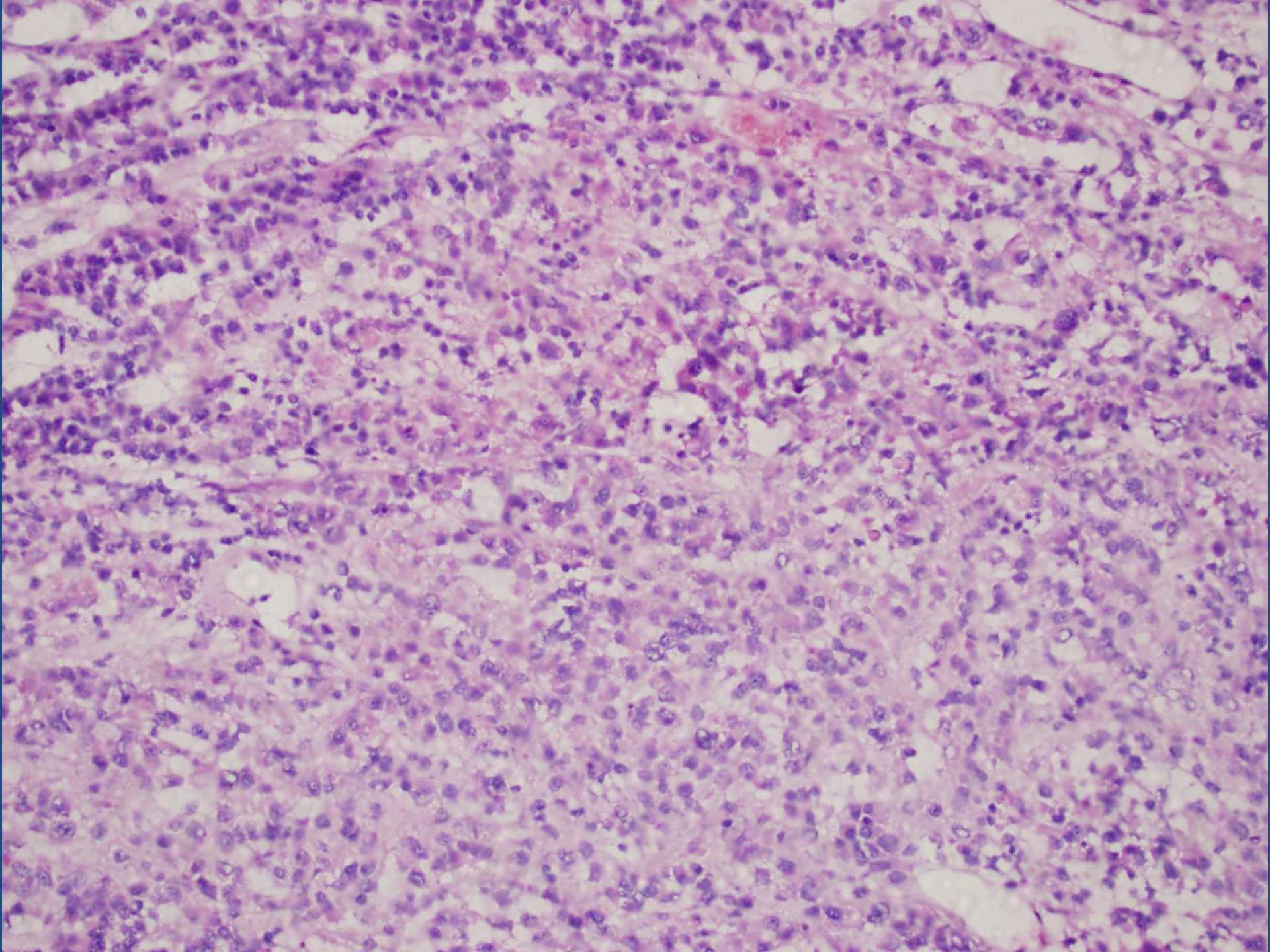
Questions?

SB 6009

- 48-year-old male with 5cm anterior mediastinal mass found on CT scan done as part of work-up for persistent cough. No past/current tumor at any other site. Intraoperatively, a left thymic mass was identified densely adherent to hilar area of lung with direct invasion of lymph nodes and left phrenic nerve.

- **Sanjay Kakar; UCSF**

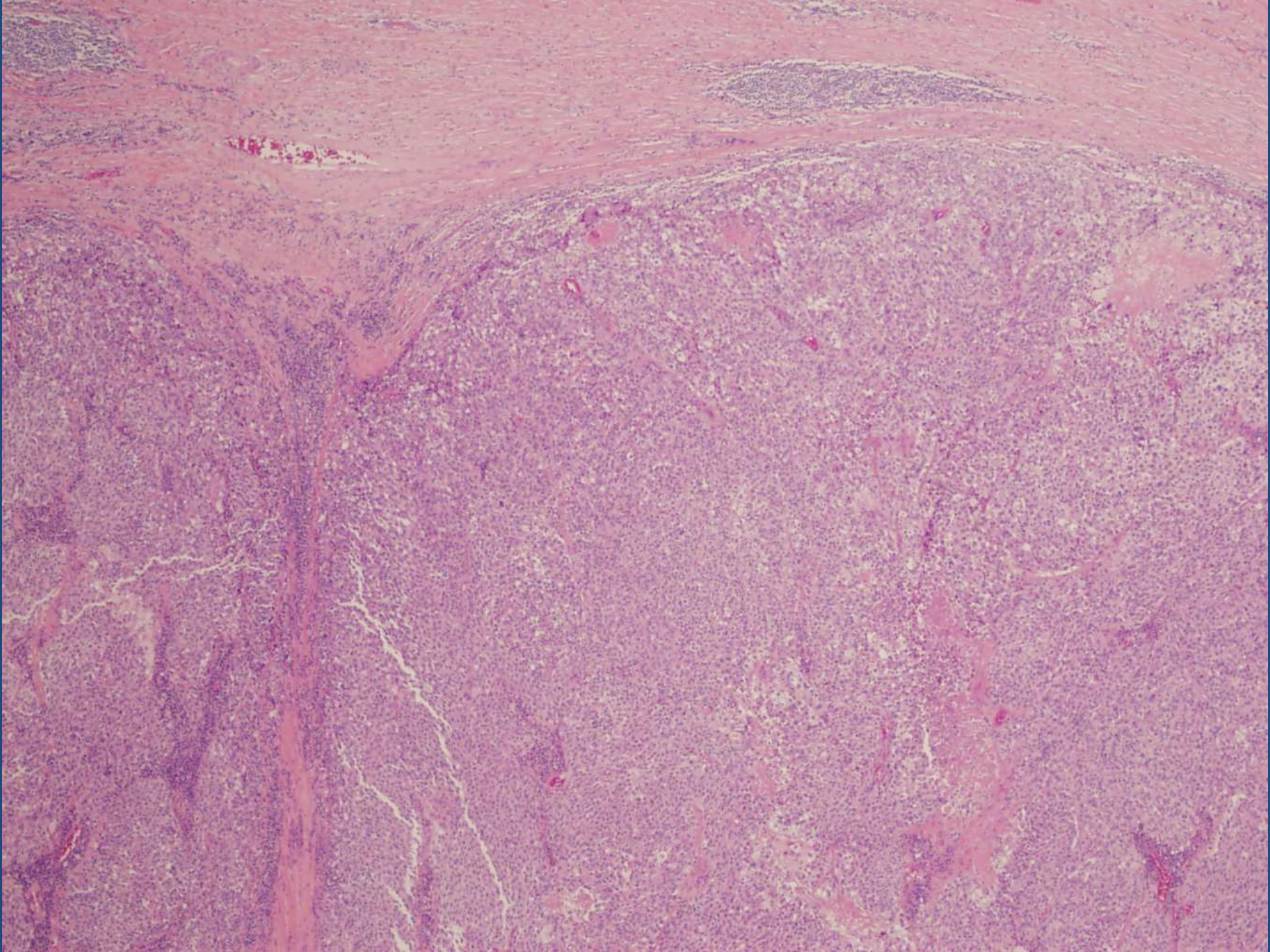


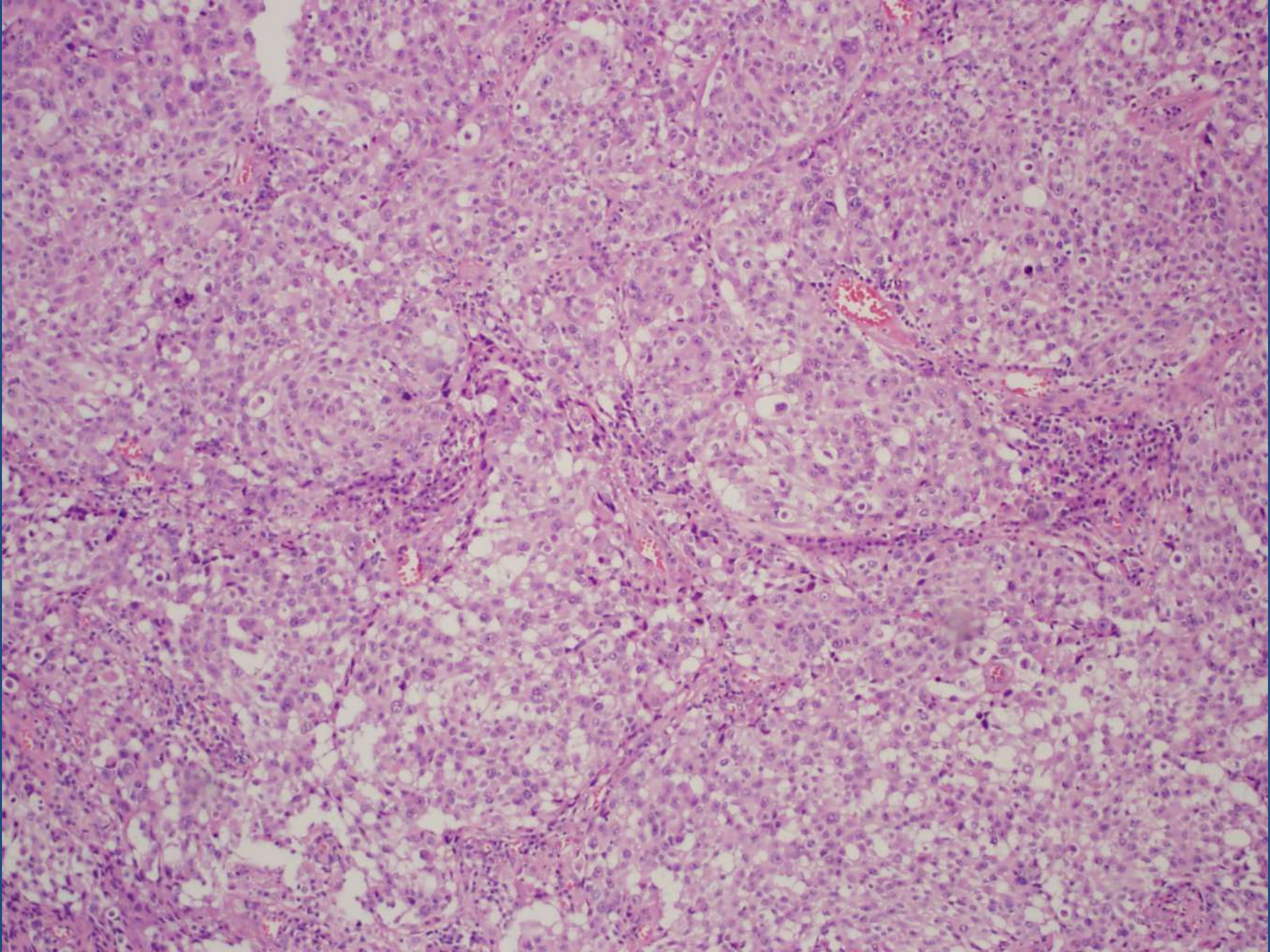


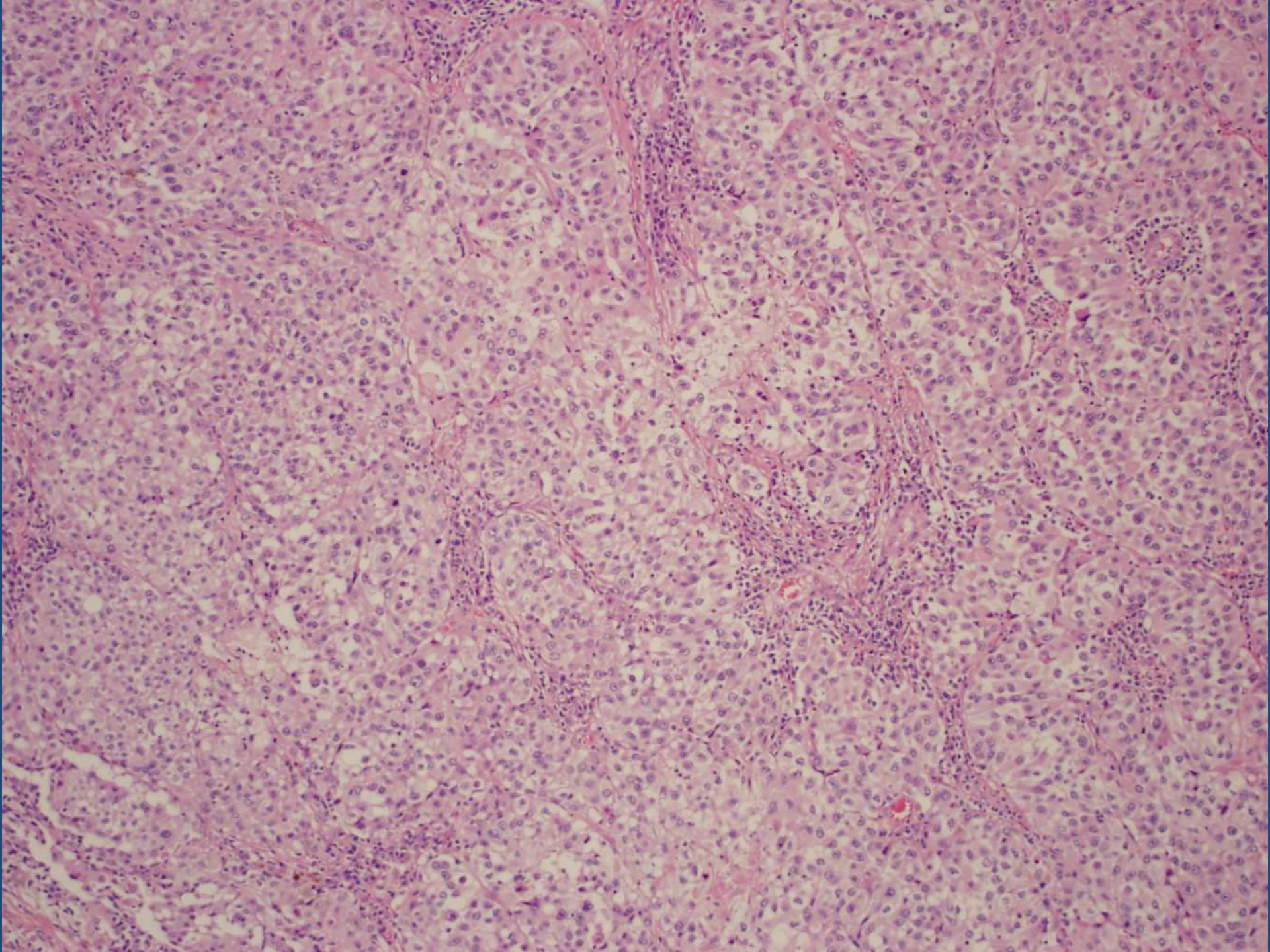
Frozen section diagnosis

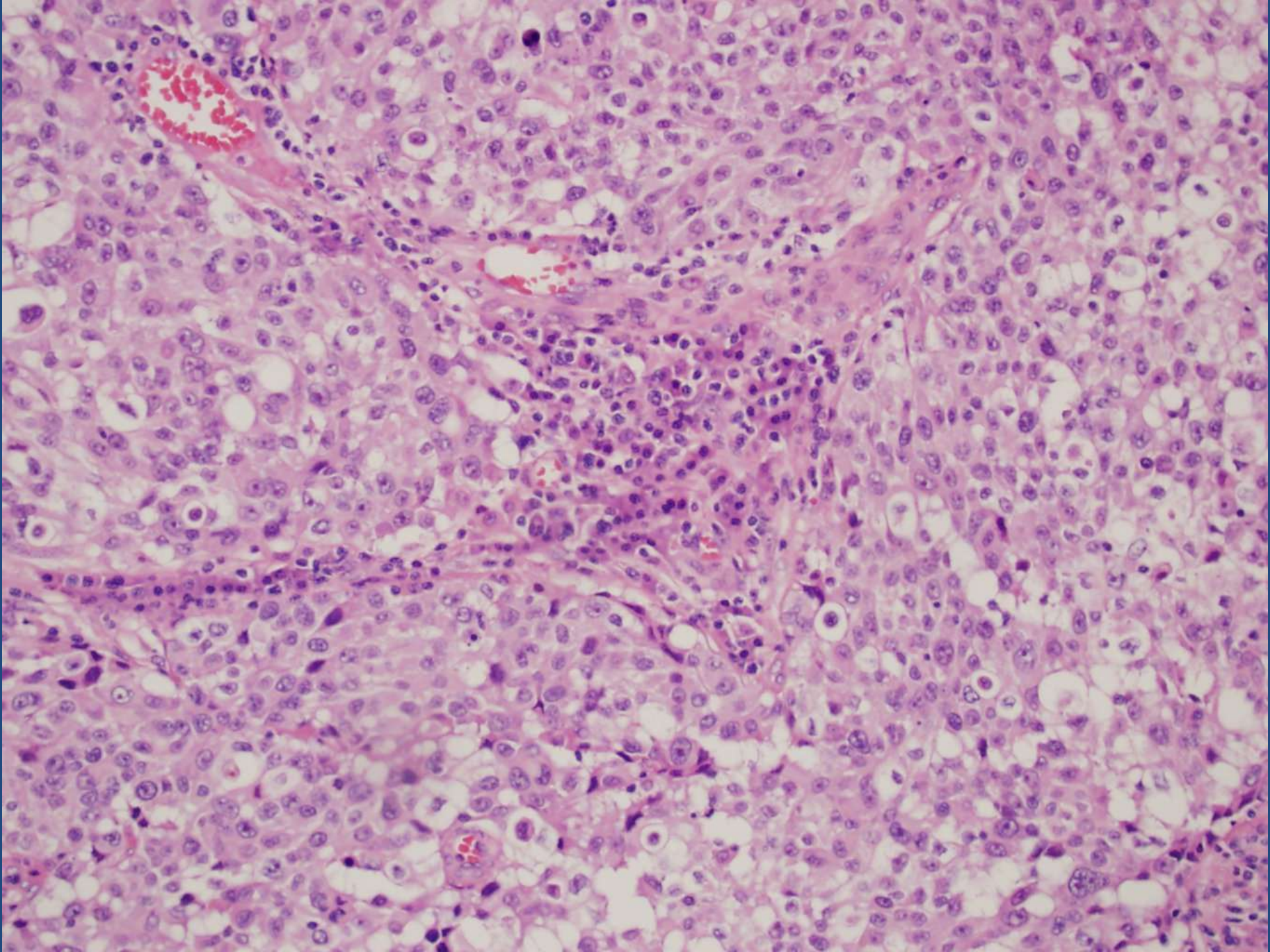
- Malignant neoplasm, further typing will be performed on review of permanent sections
- In response to a question by the surgeon: ‘differential diagnosis includes invasive/ malignant thymoma’

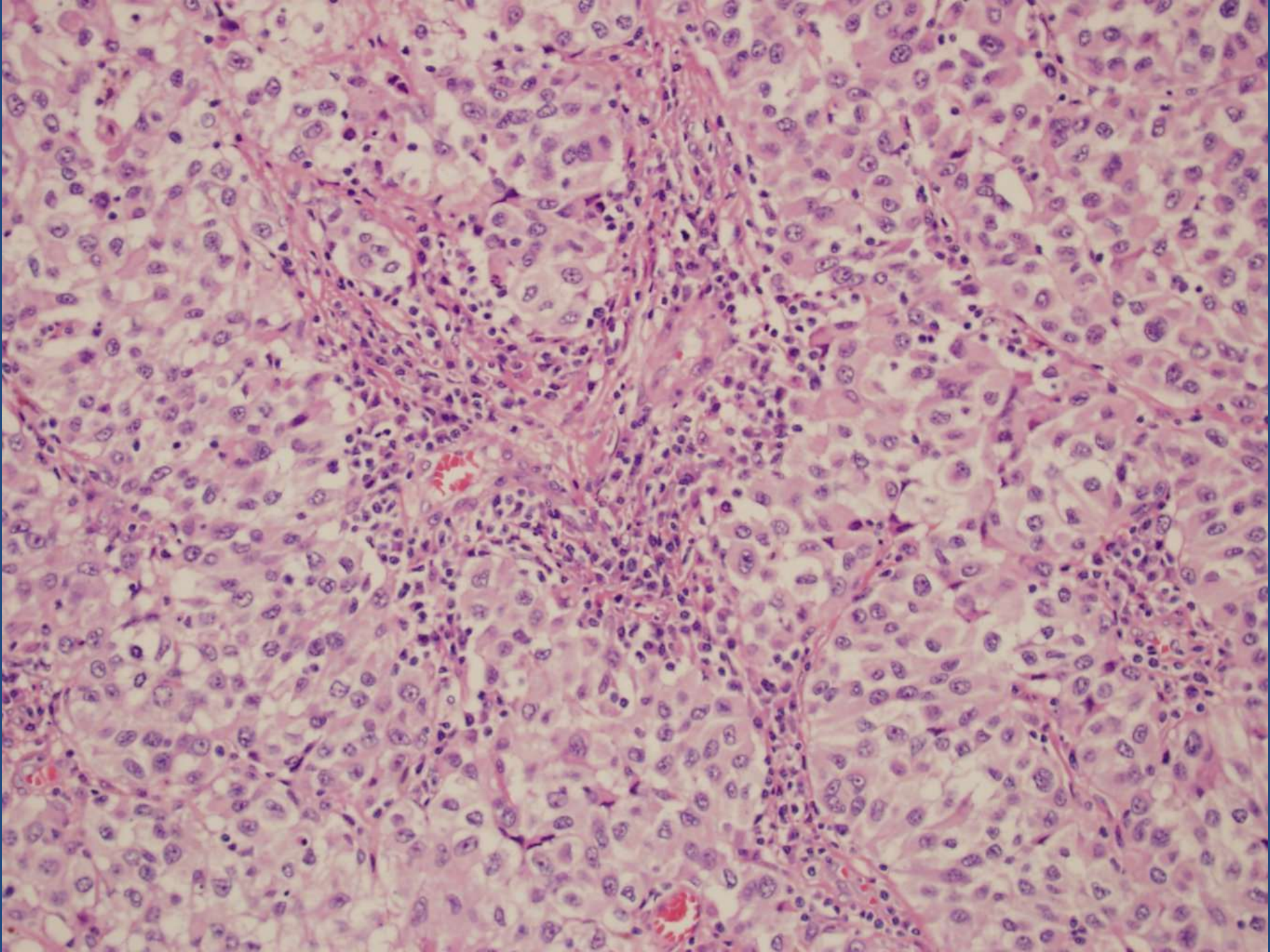
Permanent sections

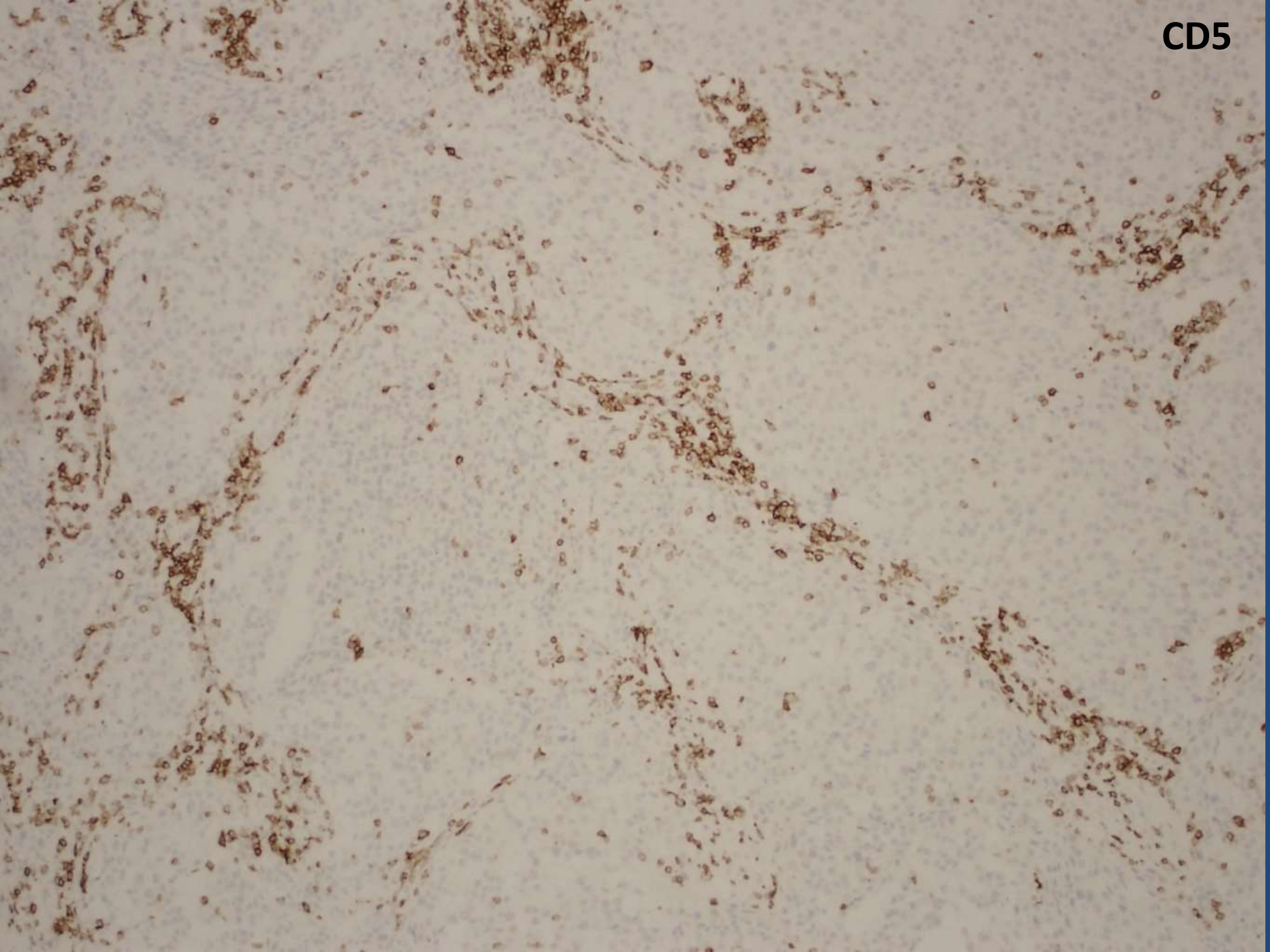


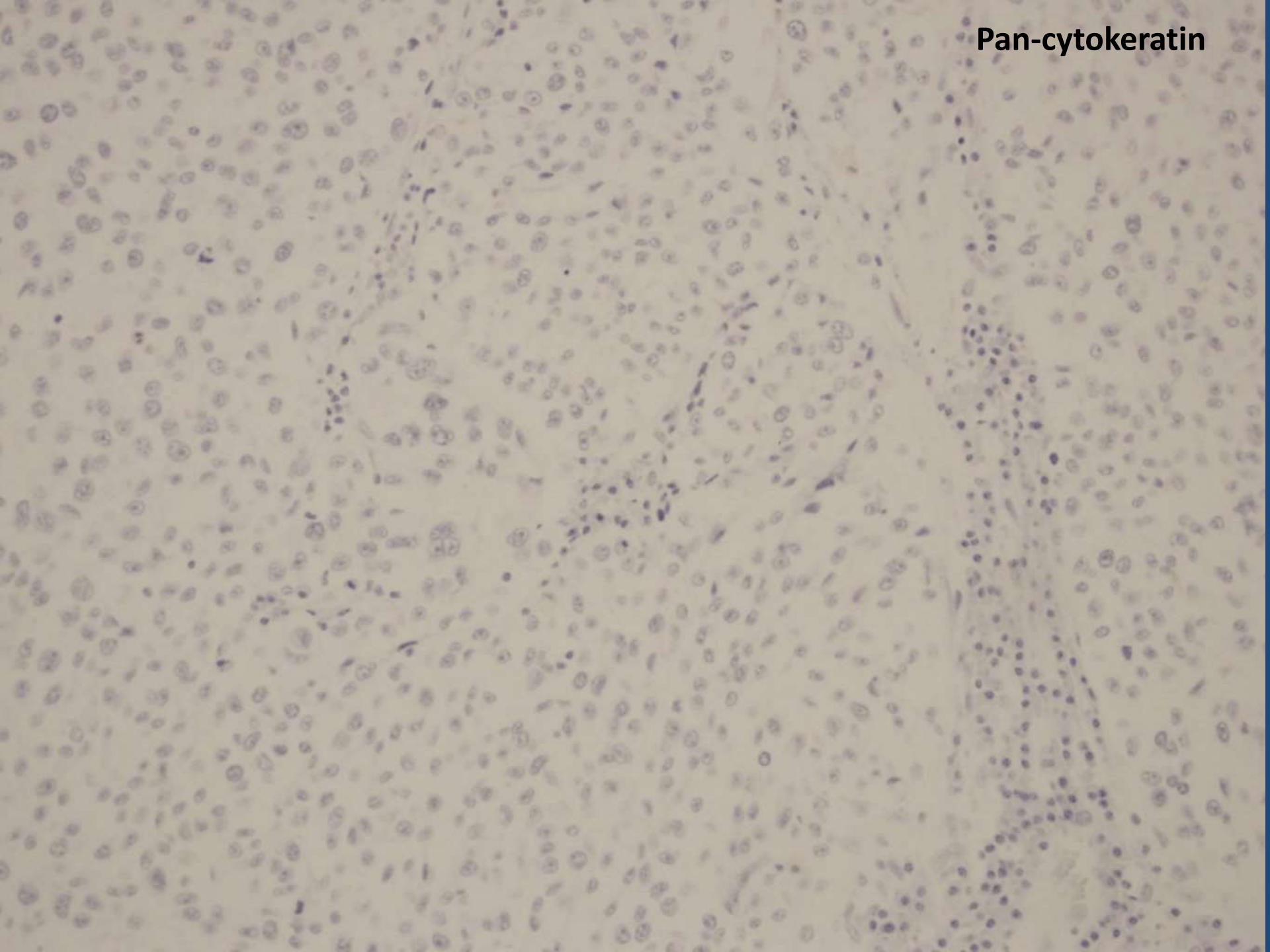








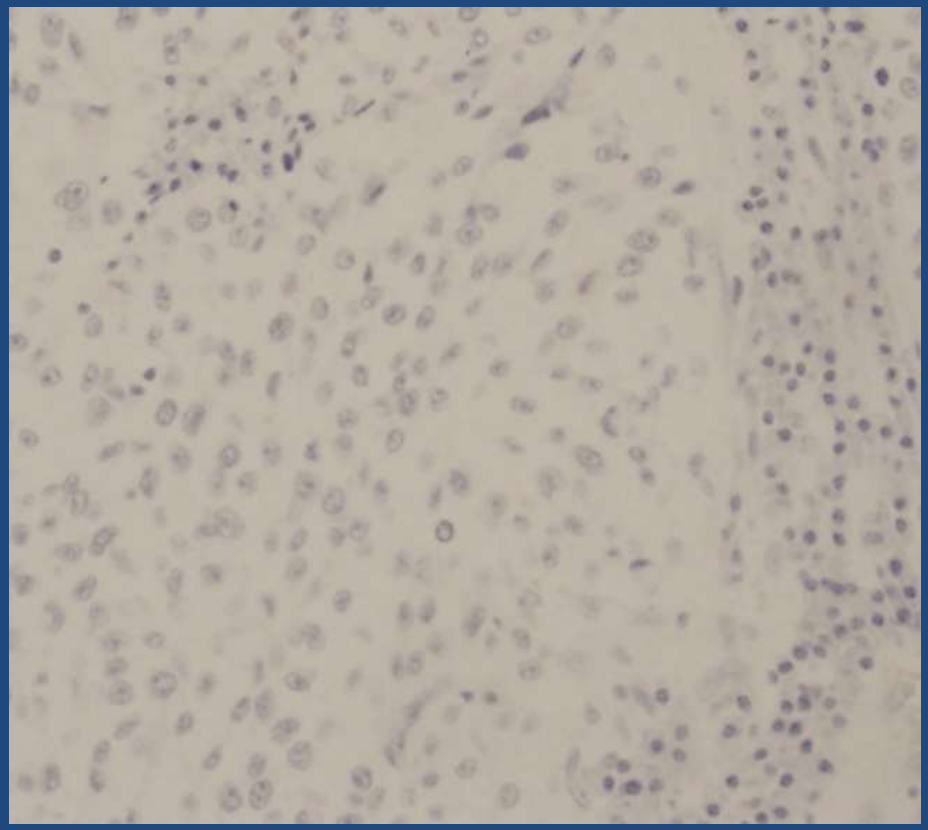

CD5

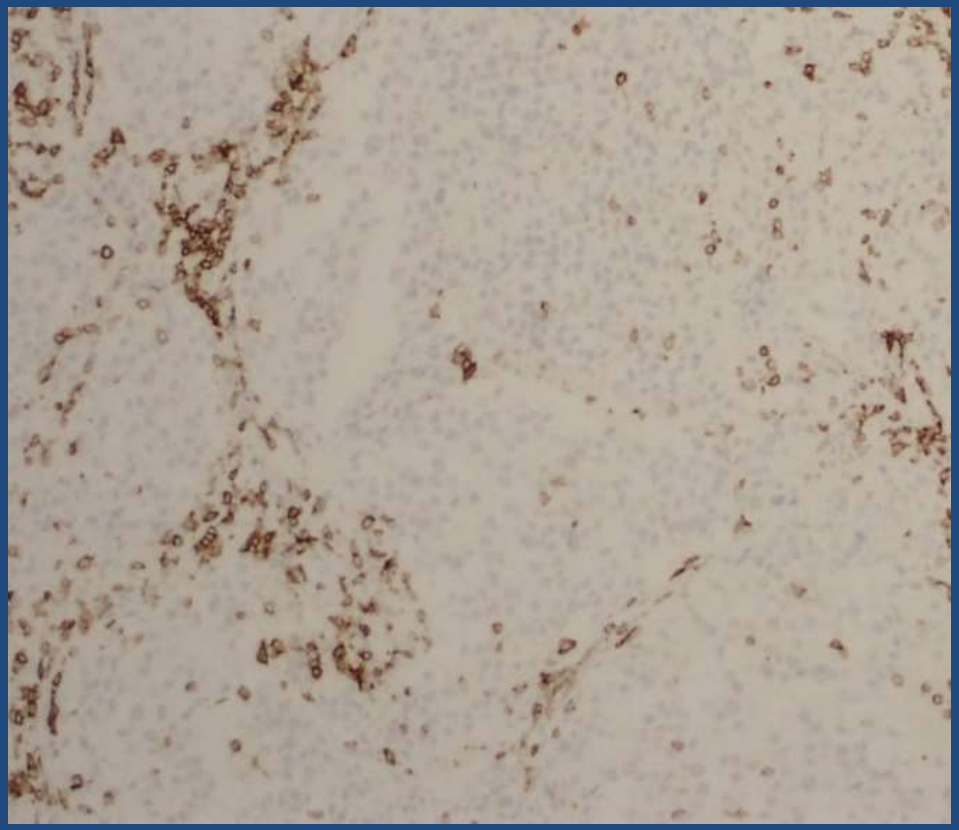

Pan-cytokeratin

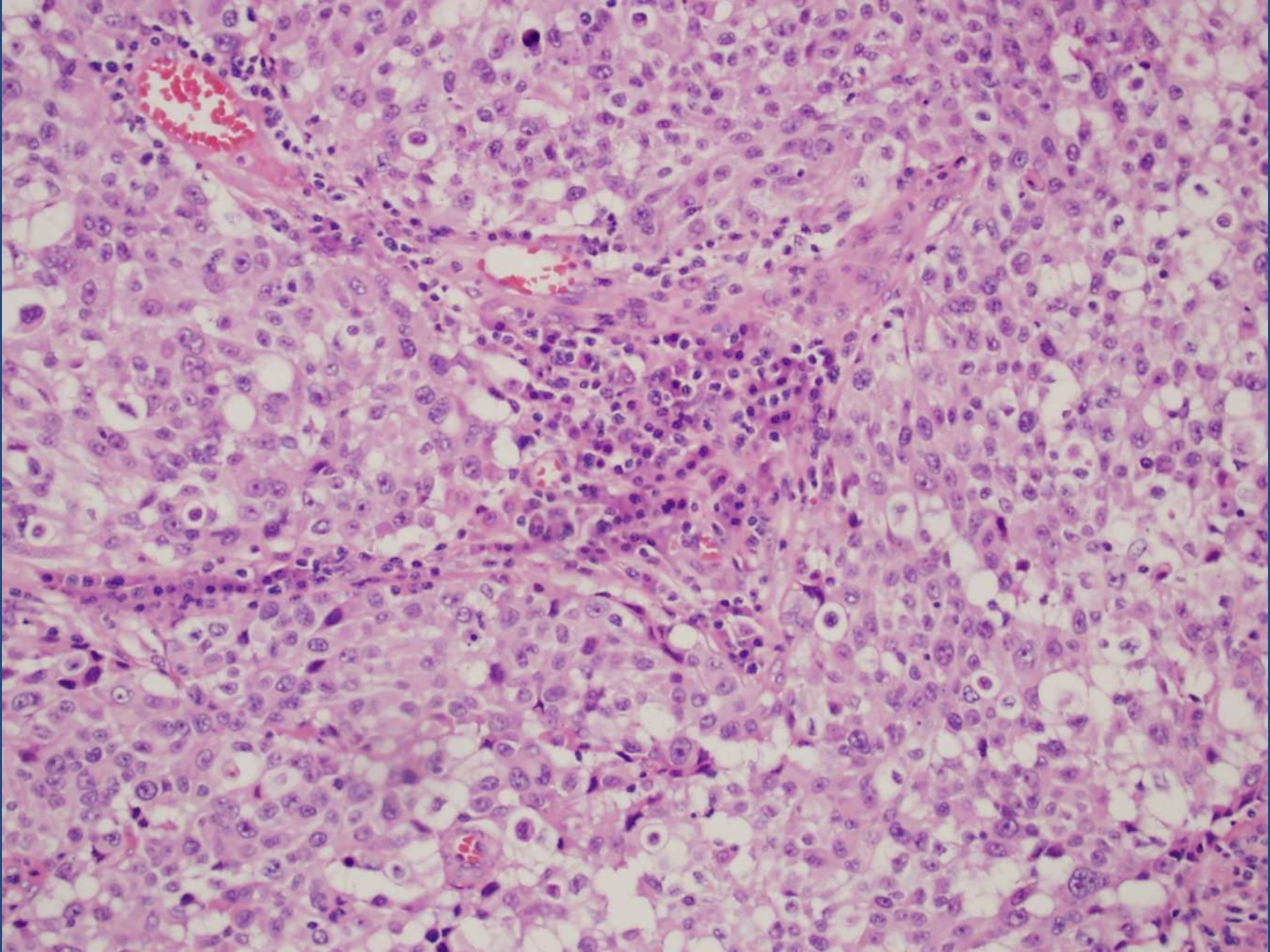
Diagnosis??

Differential diagnosis

- Epithelial thymoma/thymic carcinoma
- PanCK, CD5, CD117: negative







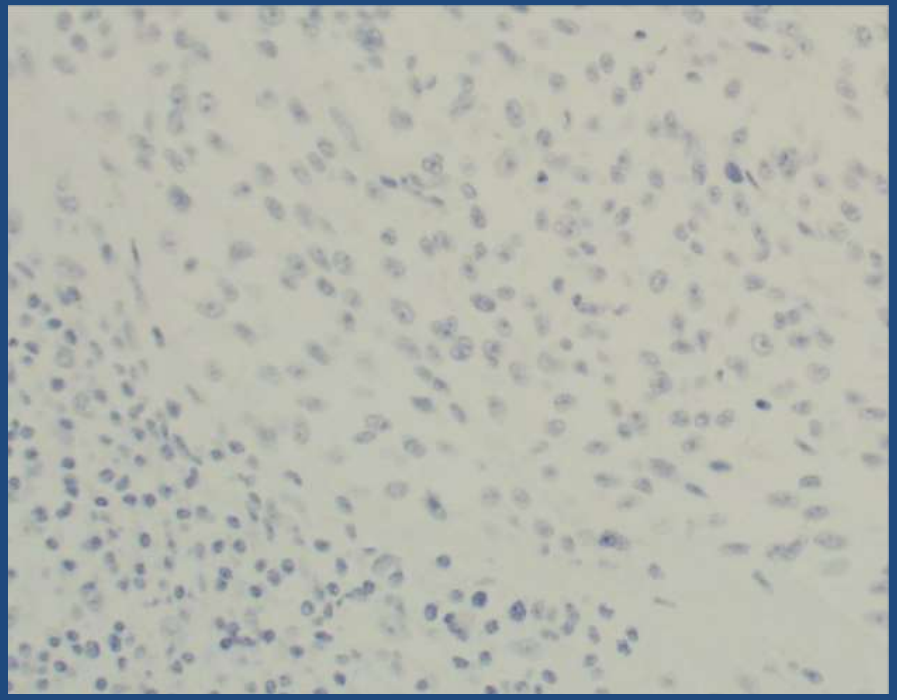
Differential diagnosis

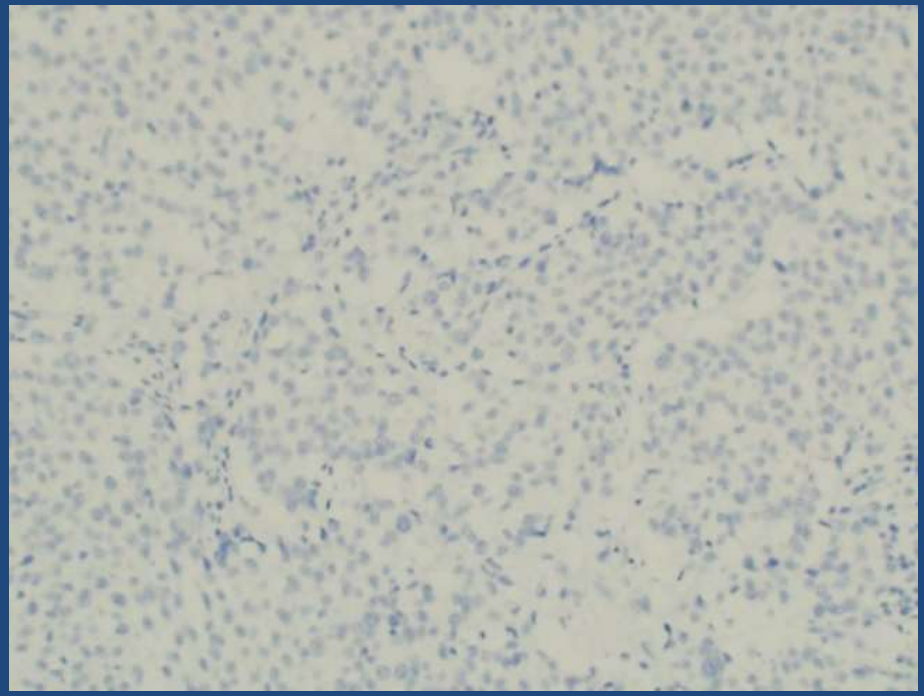
Germ cell tumor

- PLAP, OCT4, D2-40: negative

Thymic NET, paraganglioma

- NE markers: negative





Differential diagnosis

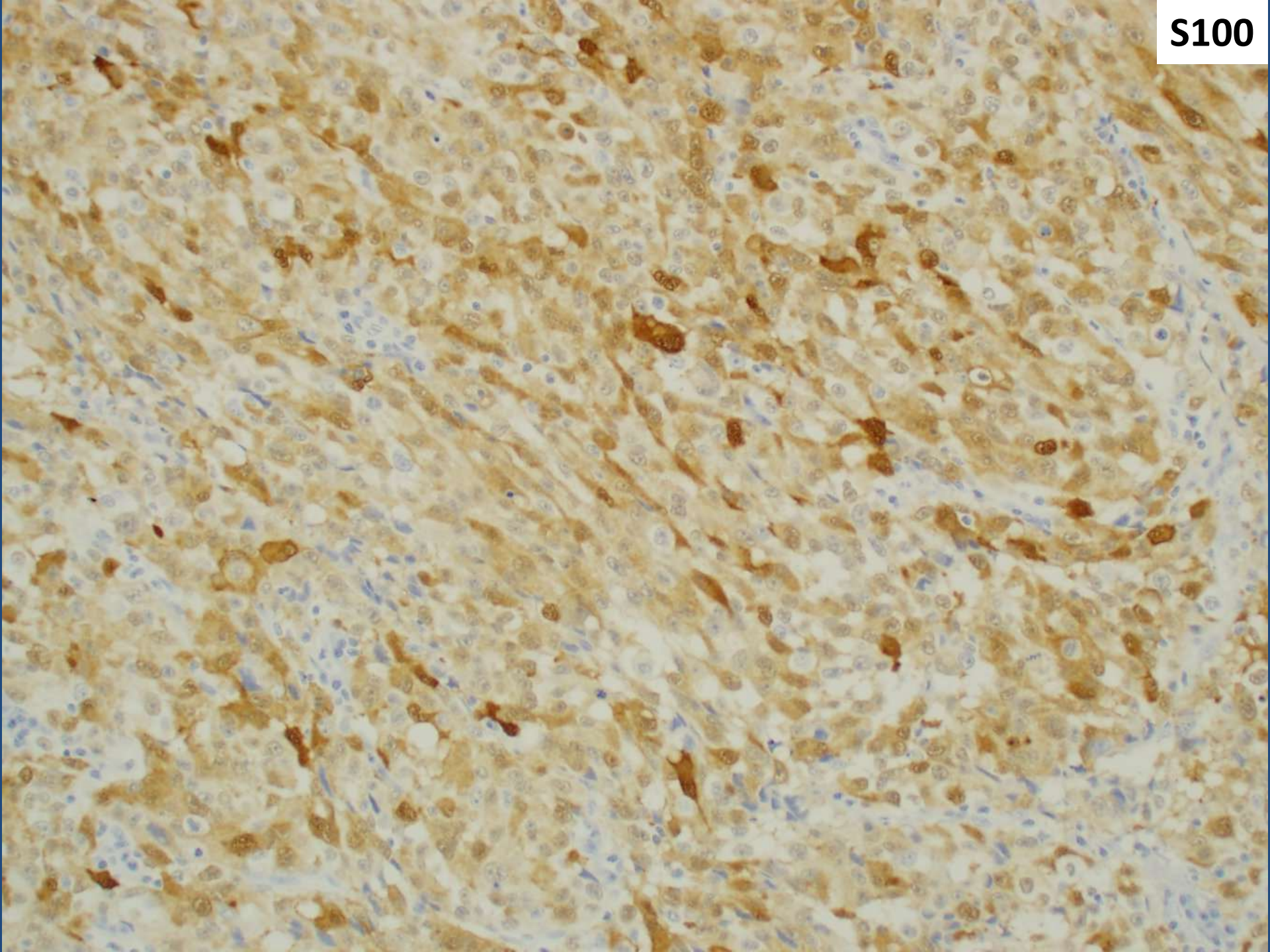
- **Lymphoma**

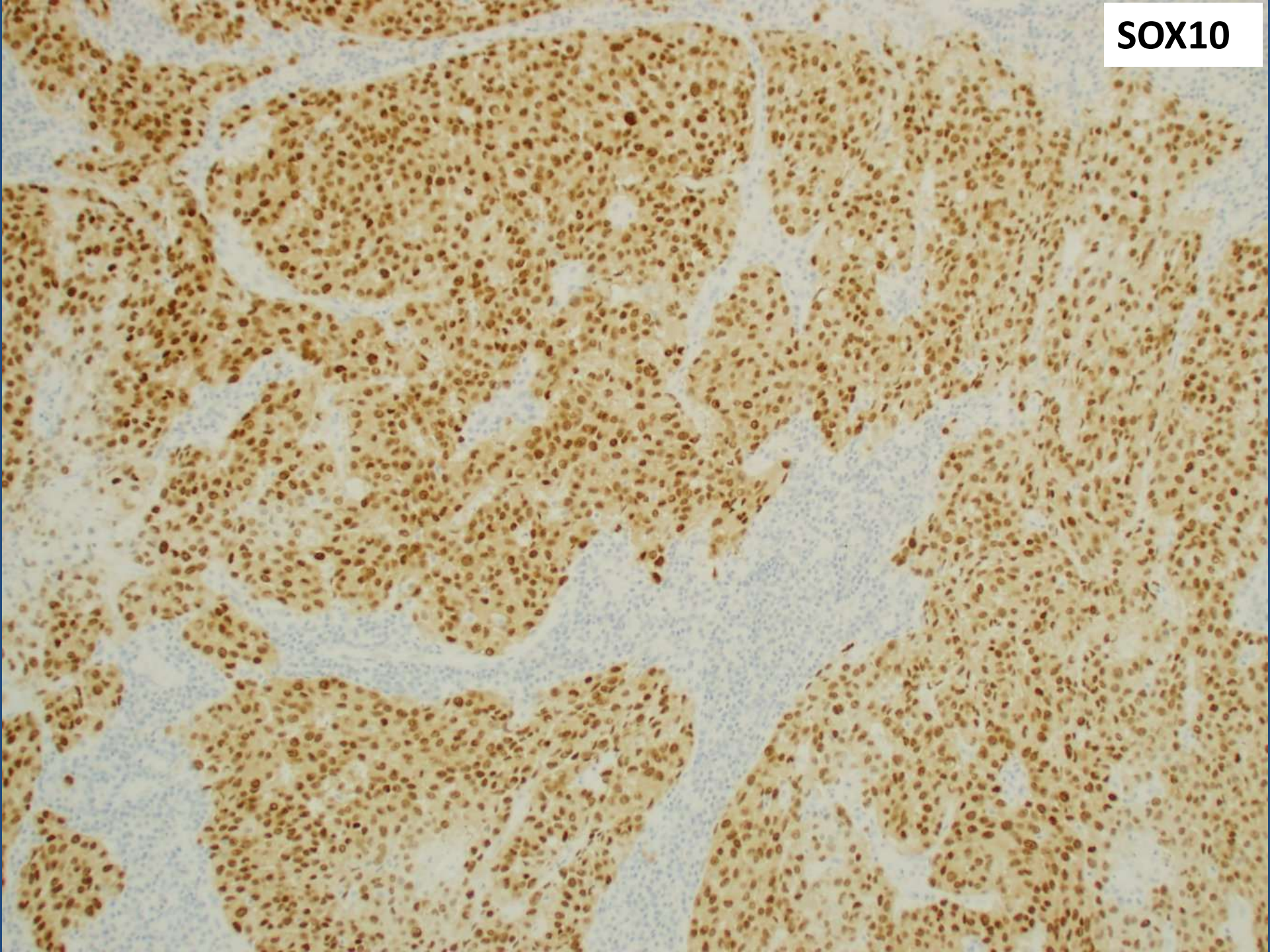
  CD45, CD3, CD20 negative
- **Perivascular epithelioid tumor**

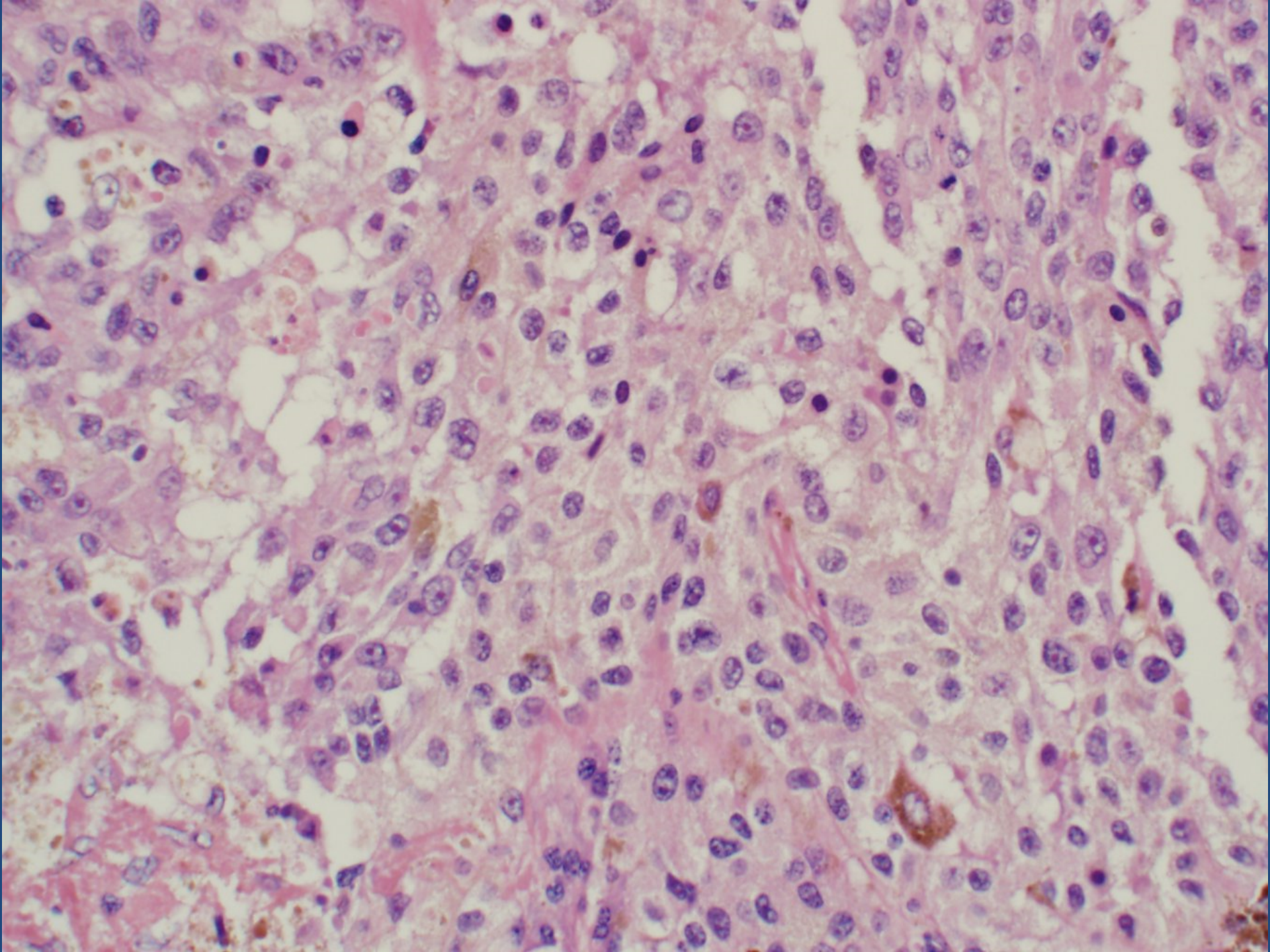
  Desmin, SMA negative
- **Melanoma**

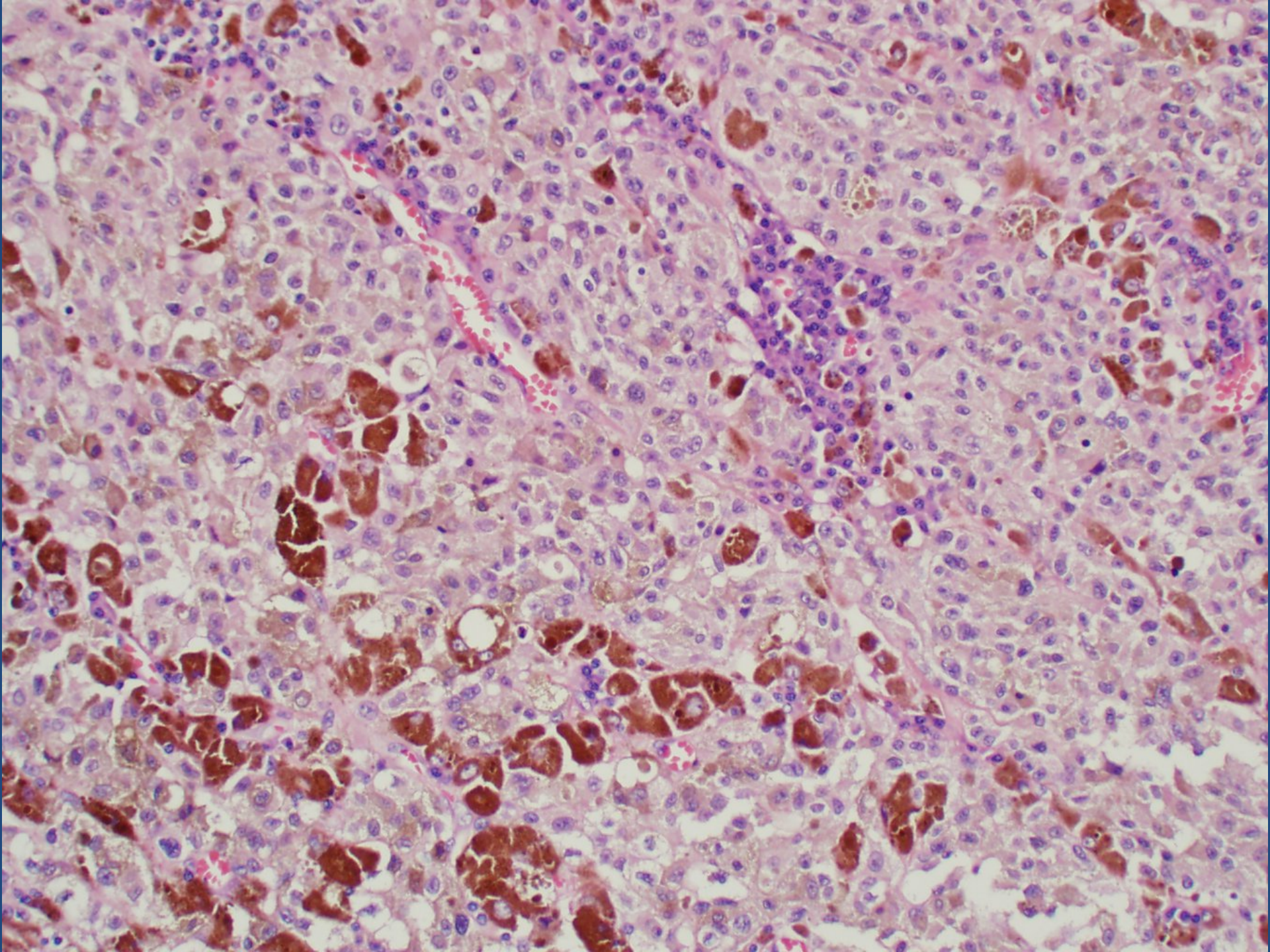
Melanomas at South Bay

South Bay 1959-2013	Total cases: 103
Skin	50
Soft tissue	9
GI sites	8
Nasal/Paranasal	5
Lymph node, eye	4 each
Mediastinum	1


S100


SOX10





Malignant melanocytic neoplasm

Mod Pathol. 1999 Mar;12(3):329-32.

Benign nevus cell aggregates in the thymus: a case report.

Parker JR[1], Ro JY, Ordóñez NG.

Int J Surg Case Rep. 2011;2(8):239-40. doi: 10.1016/j.ijscr.2011.01.010. Epub 2011 Mar 3.

Primary malignant melanoma presenting as superior mediastinal mass.

Kalra A[1], Kalra A, Palaniswamy C, Gajera M, Rajput V.

Ann Thorac Surg. 1999 Mar;67(3):851-2.

Malignant melanoma presenting as a mediastinal mass.

Lau CL[1], Bentley RC, Gockerman JP, Que LG, D'Amico TA.

Malignant melanocytic neoplasm
Melanoma or Clear Cell Sarcoma

Case Rep Oncol. 2014 May 14;7(2):306-9. doi: 10.1159/000363180. eCollection 2014.

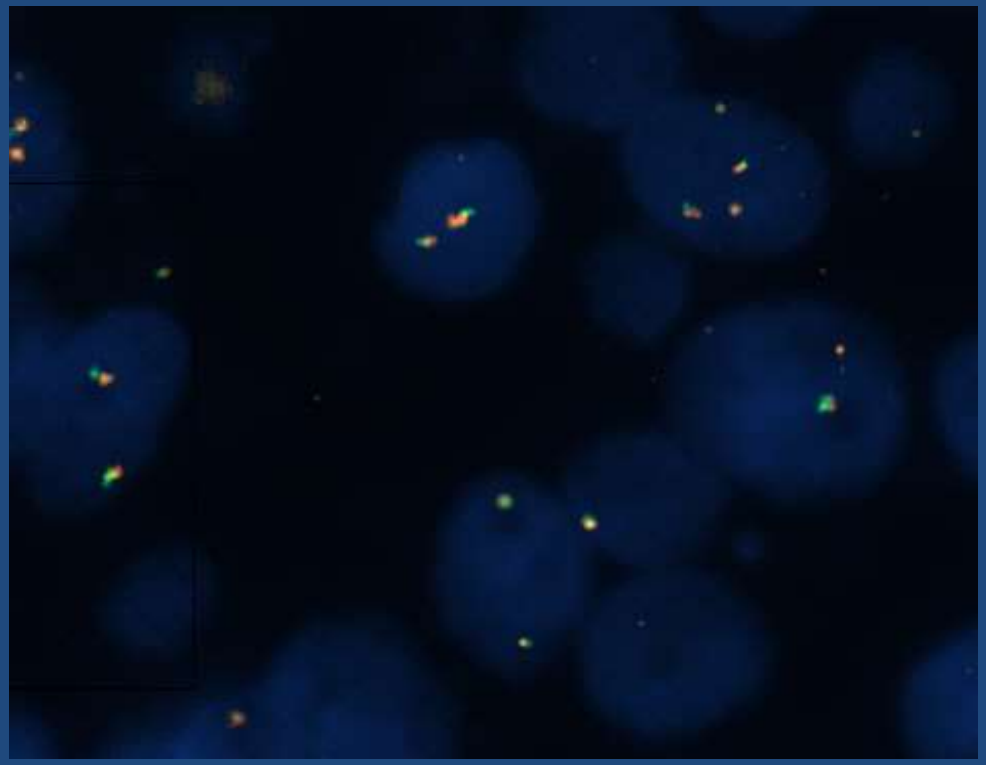
Primary clear-cell sarcoma in the mediastinum.

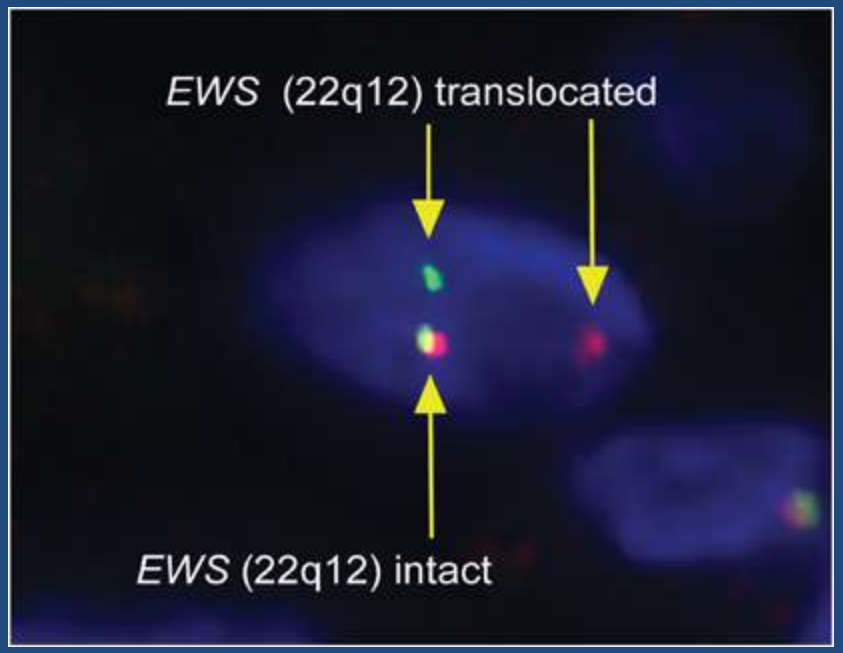
Tanaka Y[1], Yoshimasu T[1], Oura S[1], Hirai Y[1], Kawago M[1], Okamura Y[1].

Malignant melanocytic neoplasm

	Melanoma	Clear cell sarcoma
CD117	Positive 60-70%	Negative
t(12;22) Fusion of *EWS* (22q12) and *ATF1* (12q13) t(2;22)	Absent	70-80%
BRAF mutation	~50%	Absent
NRAS mutation	~15%	Absent

FISH: EWS break apart probe



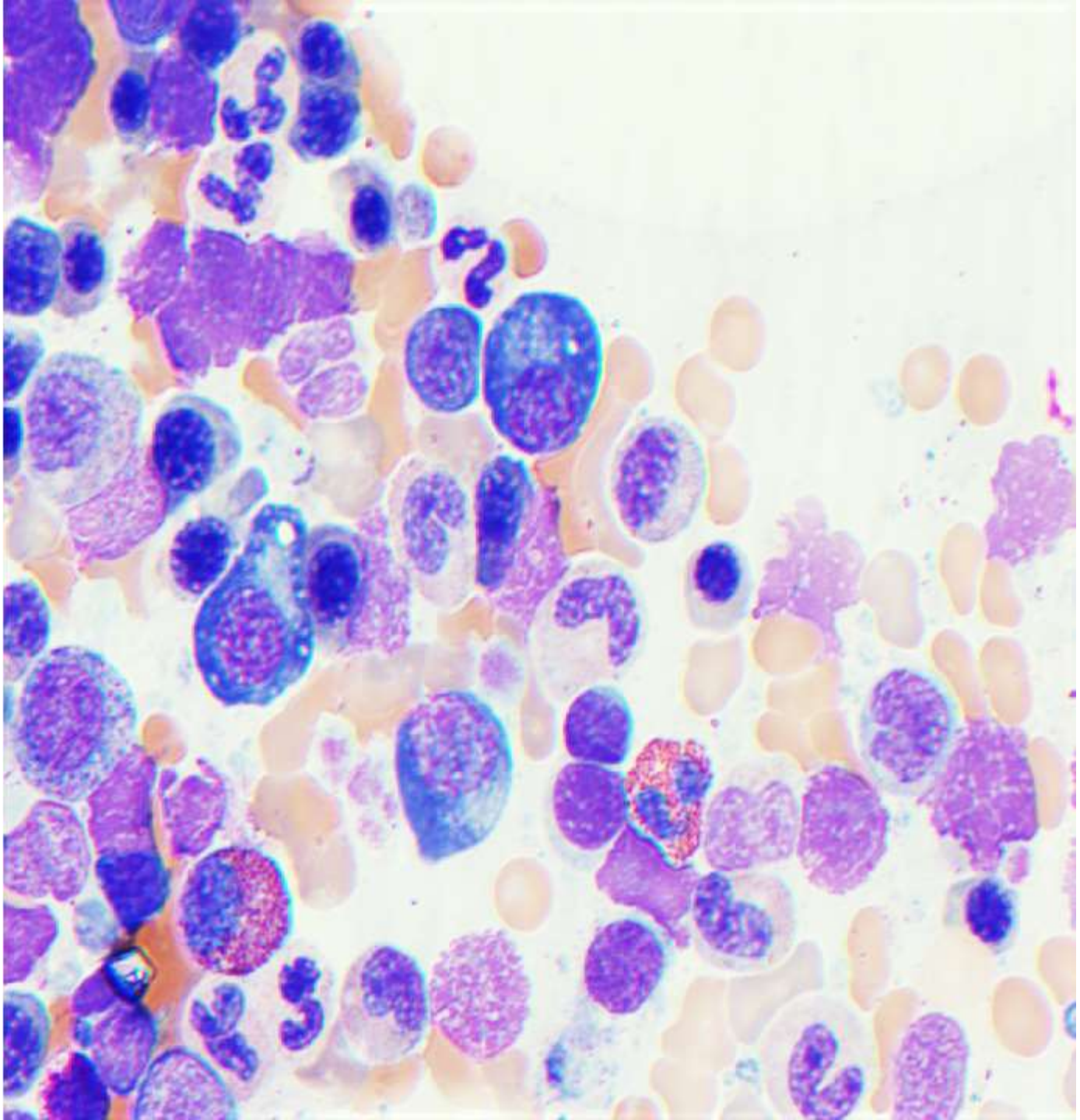


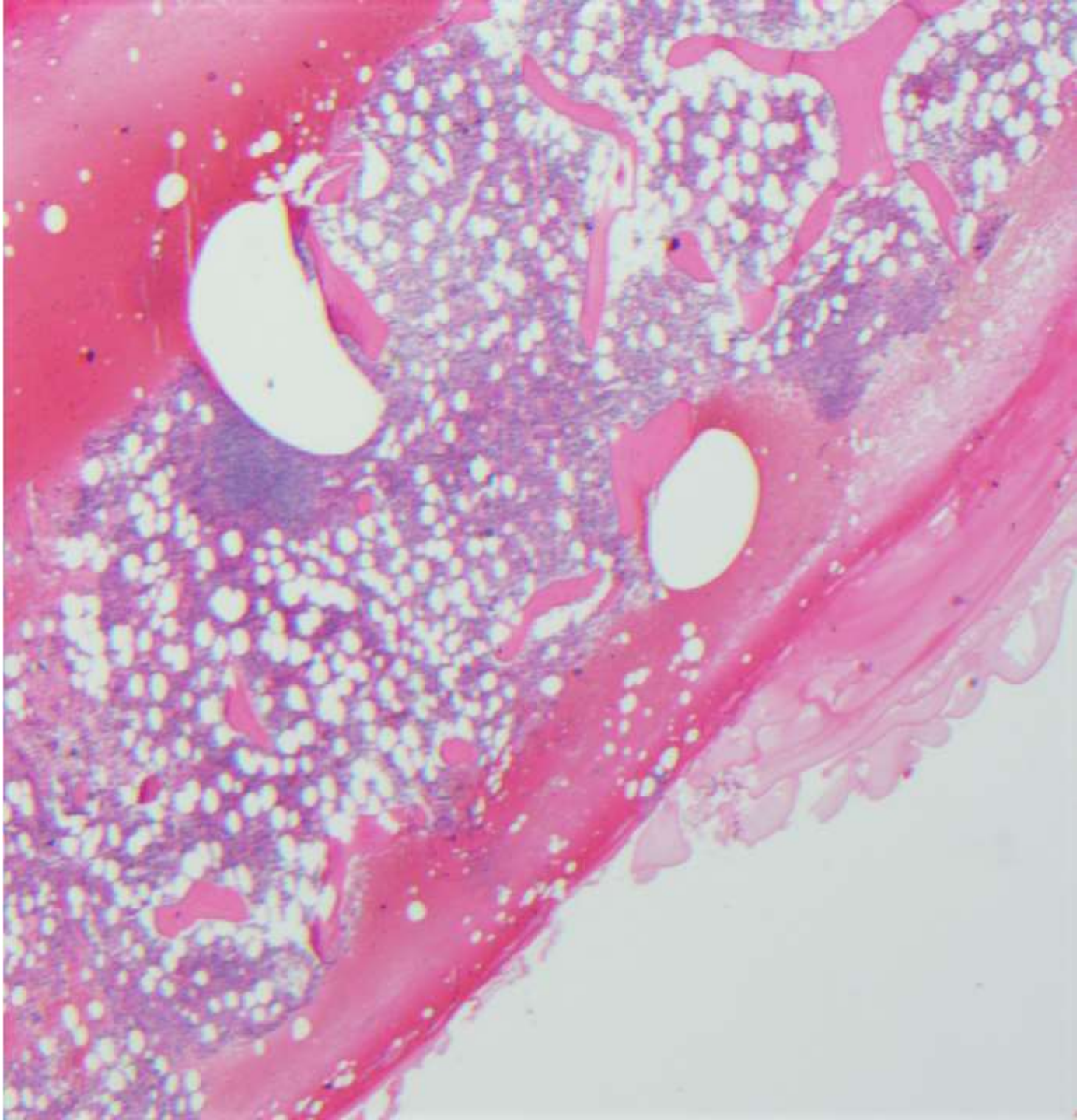
Malignant melanocytic neoplasm, likely malignant melanoma

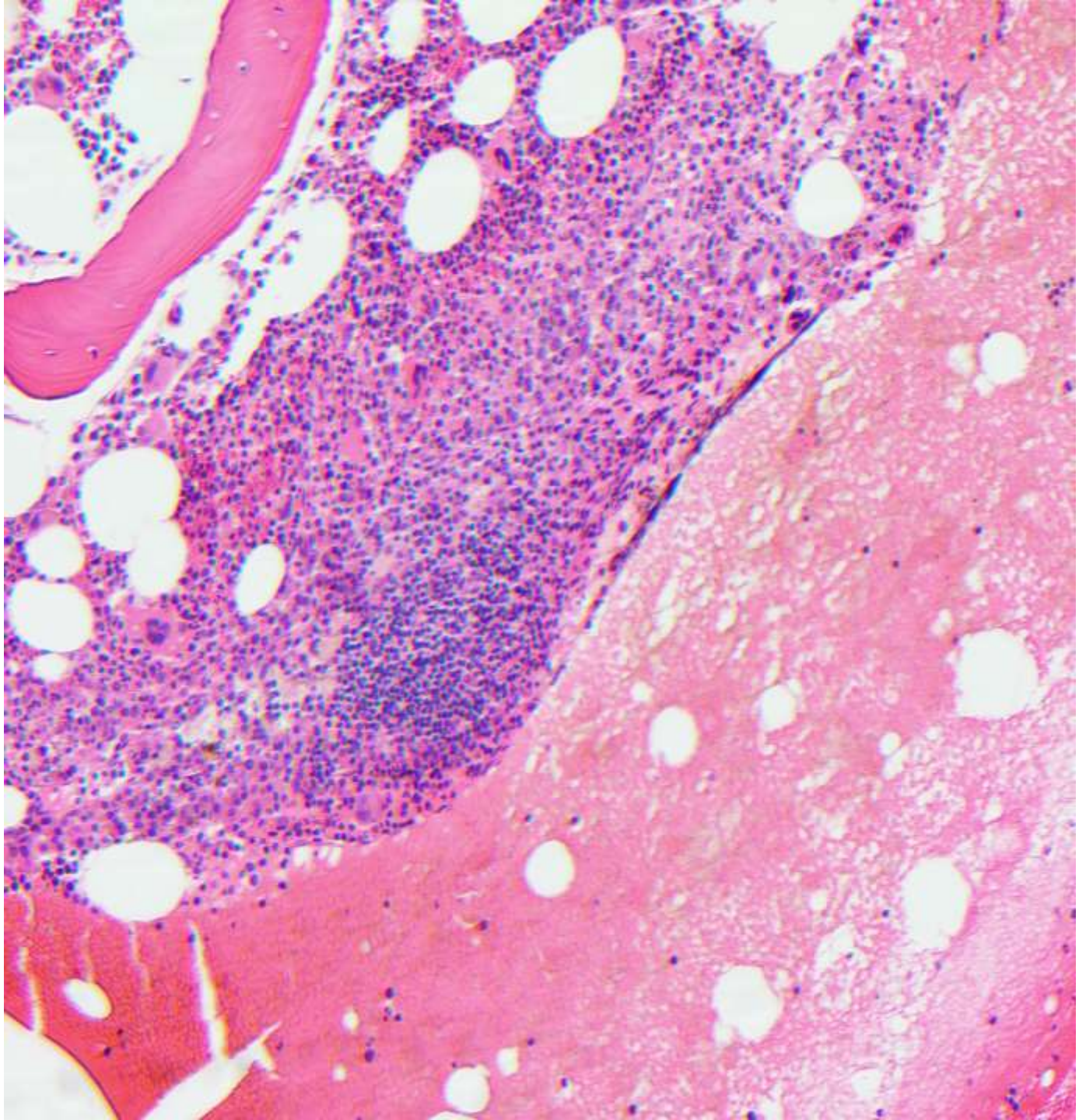
SB 6010

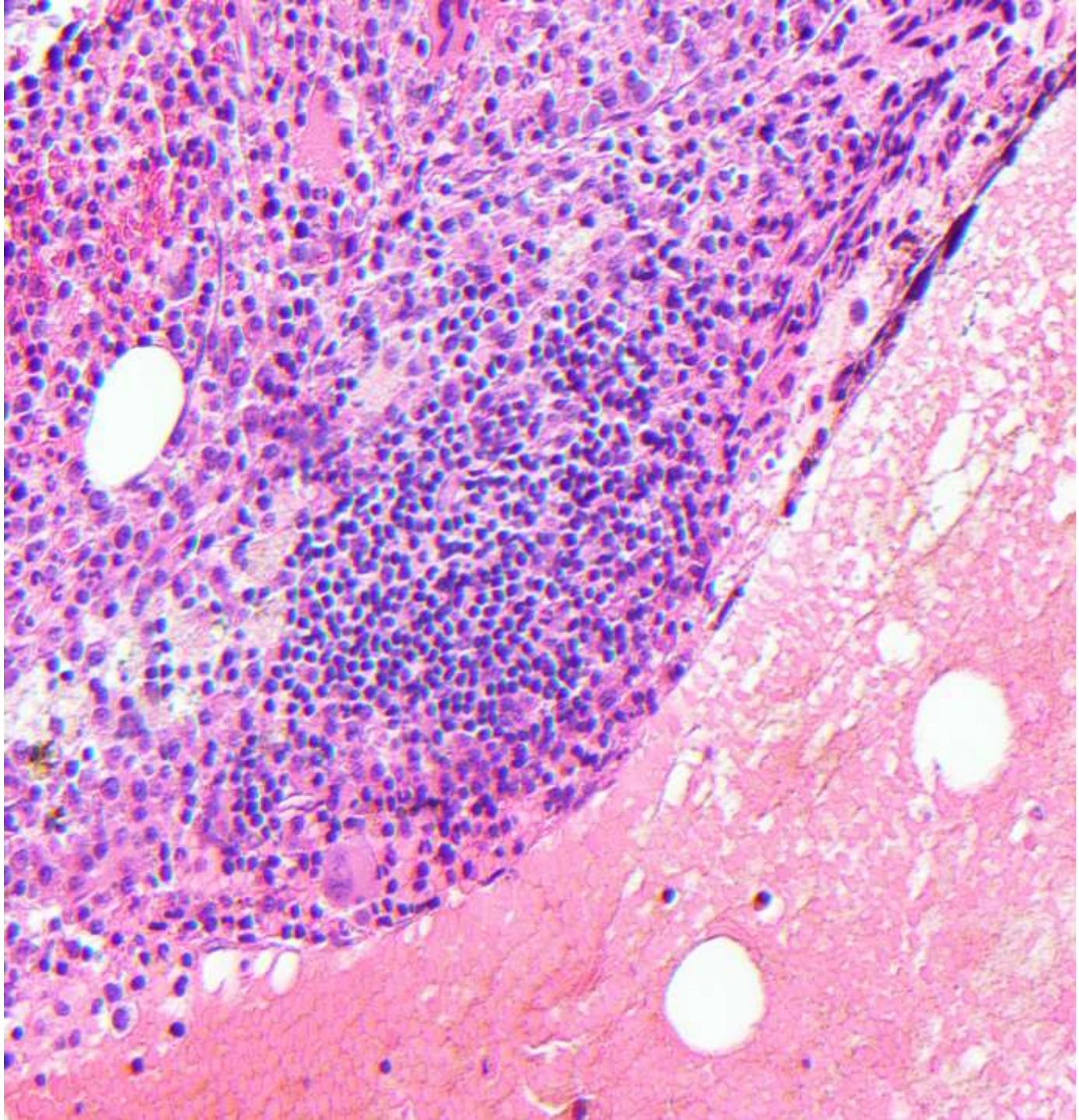
- 54-year-old male with elevated lambda light chain monoclonal IgA and polyneuropathy. Bone marrow biopsy performed.

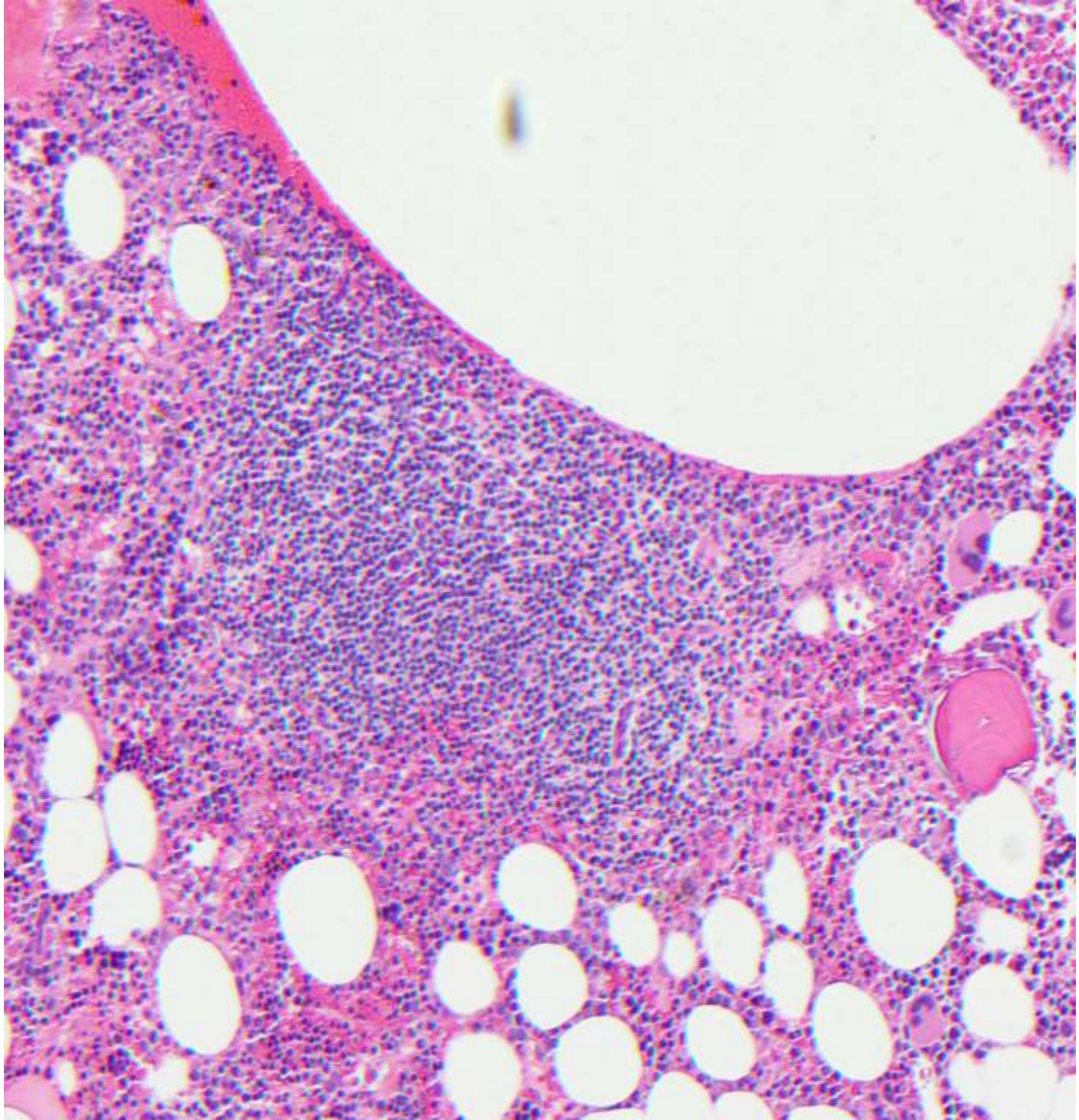
- **Peng Li/Dita Gratzinger; Stanford**

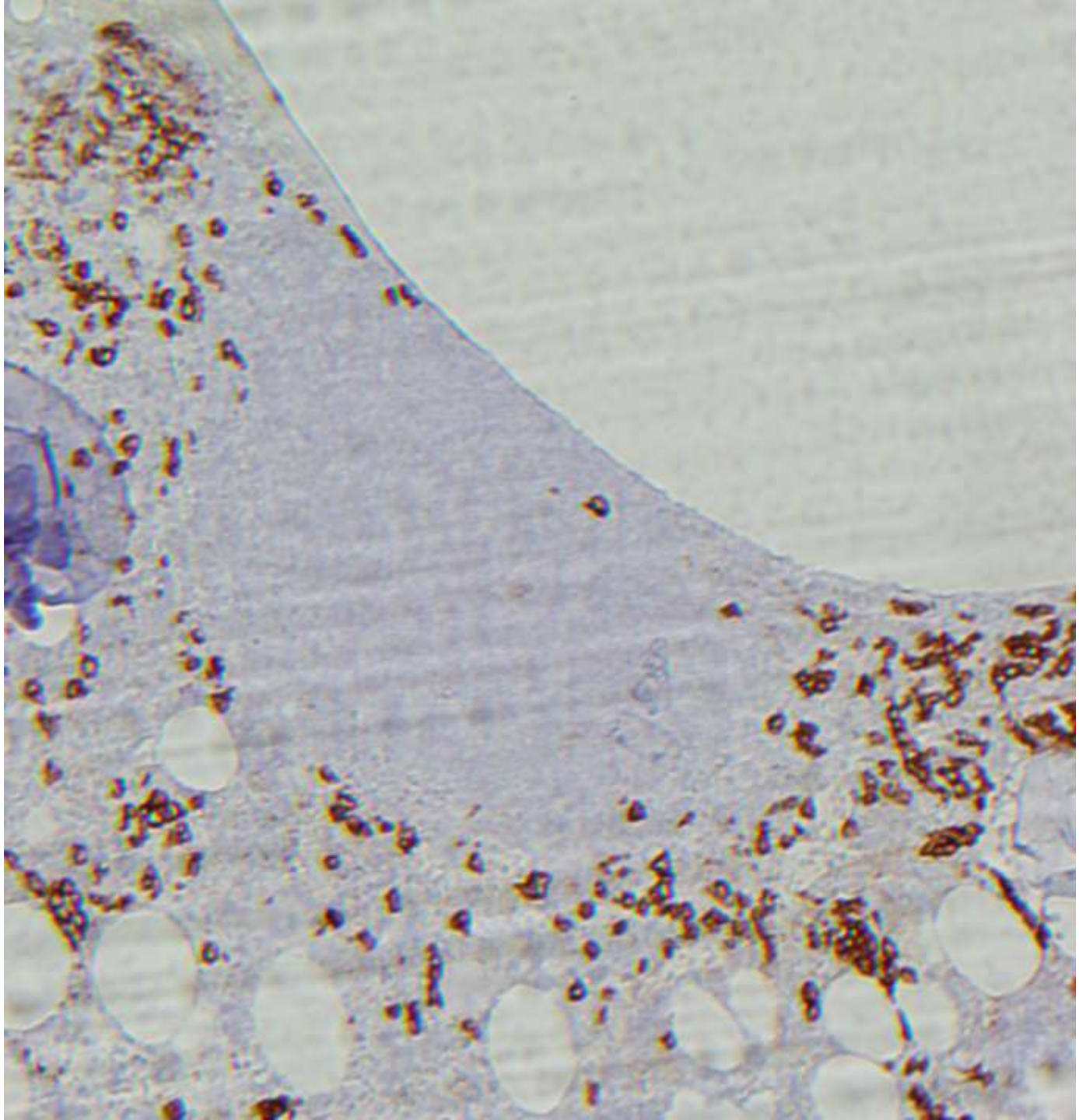










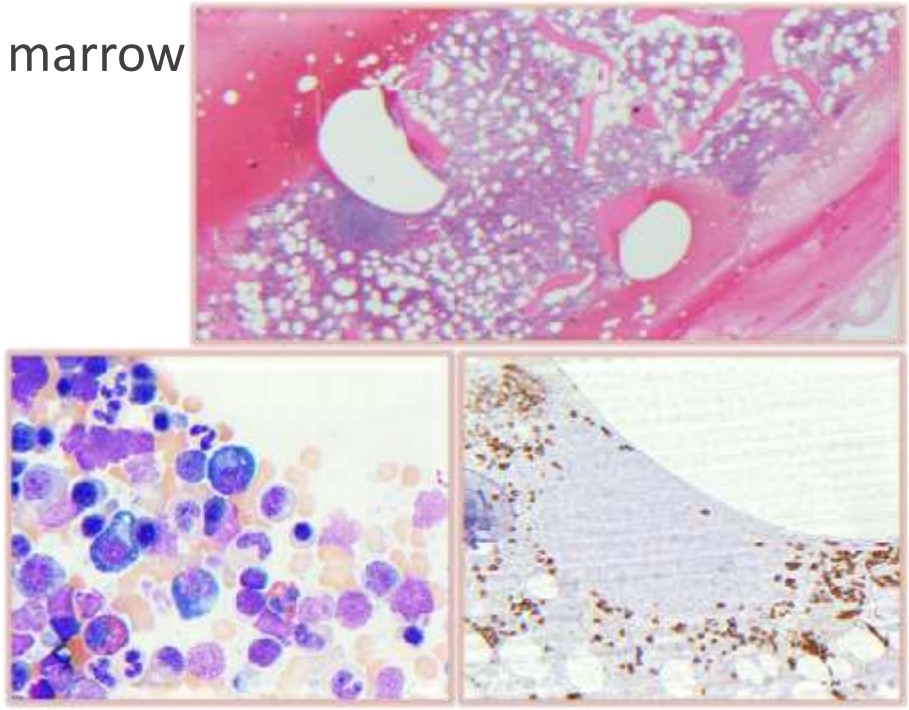


CD138

Diagnosis??

Summary of Morphologic Findings

- Multiple lymphoid aggregates in marrow
  - Small and well-circumscribed
- Increase in plasma cells
  - Overall less than 5%
  - Around lymphoid infiltrates
- Normal trabecular bone



Differential Diagnoses

- POEMS
- MGUS
- Castleman disease
- Low grade B cell lymphoma (marginal zone lymphoma or lymphoplasmacytic lymphoma)

Brief History

- 54-year-old gentleman
- Polyneuropathy
- Organomegaly
- Endocrinopathy
- Monoclonal plasma proliferative disorder
- Skin changes

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- 54-year-old gentleman
- Polyneuropathy
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- Skin changes

Poems Syndrome

Presence of 2 major criteria, including a **monoclonal plasma cell proliferative disorder** and **polyneuropathy**

In addition to the existence of 1 minor criterion listed below

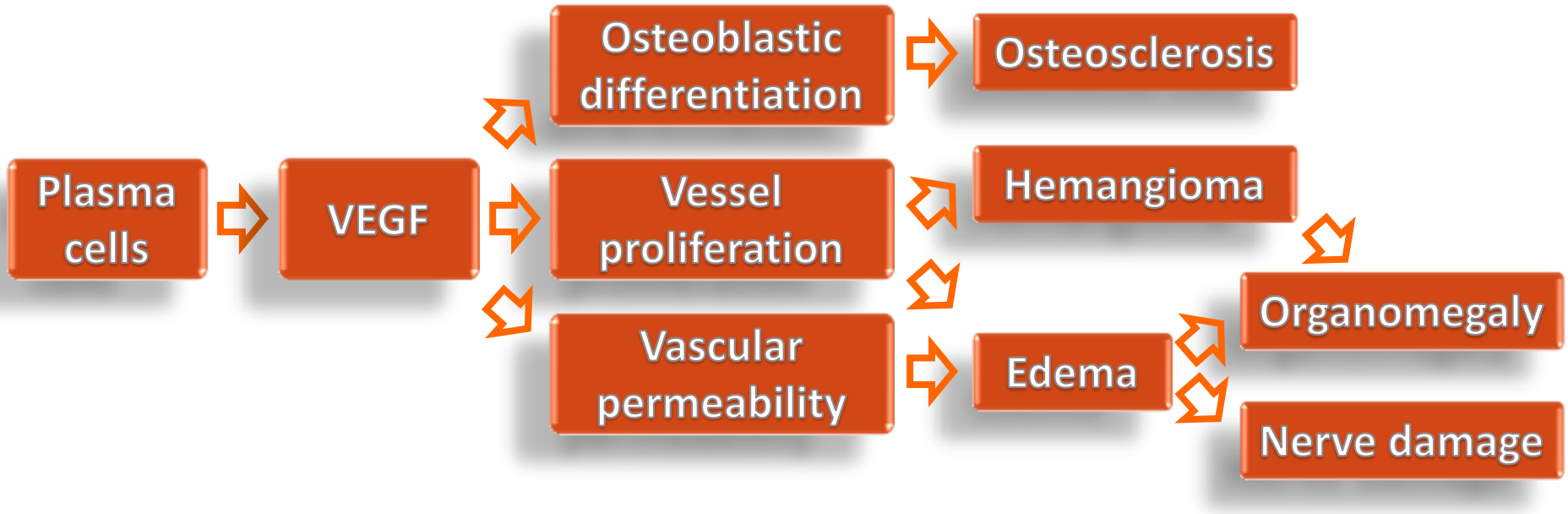
- ❑ Sclerotic bone lesions
- ❑ Organomegaly
- ❑ General edema
- ❑ Endocrinopathy
- ❑ Papilledema
- ❑ Skin changes

POEMS Syndrome Epidemiology

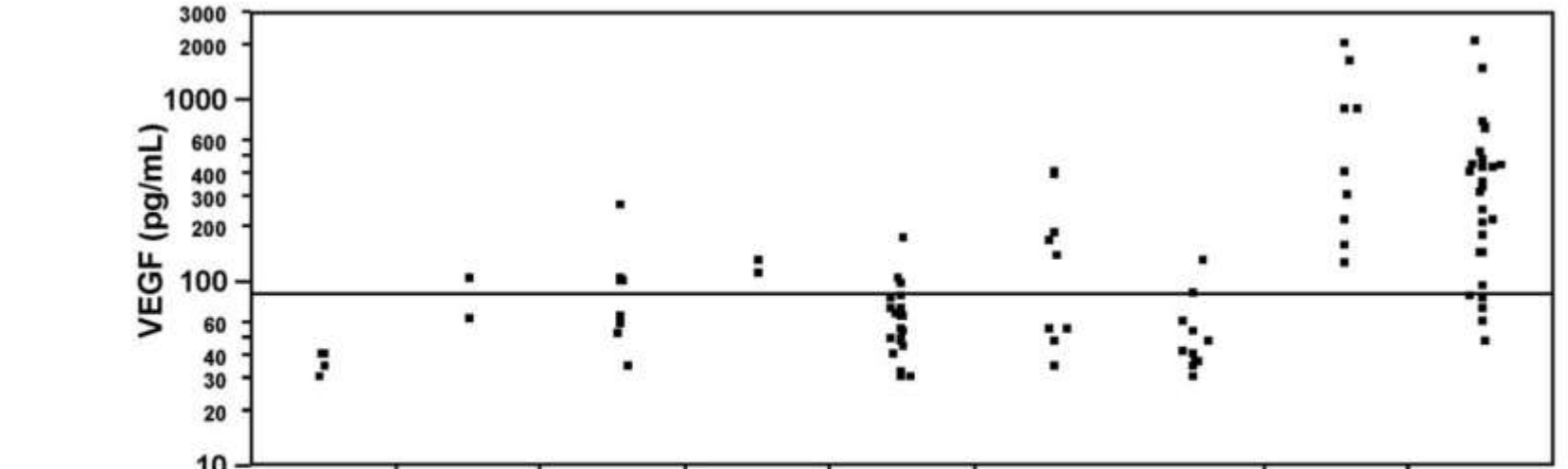
- Several hundred case reports
- The incidence may be underreported because the syndrome may be unrecognized
- M:F = 2.5:1
- Most frequently in the fifth and sixth decade of life (Mean age at onset of 48 years for man and 59 years for woman)

POEMS Pathogenesis

- A rare systemic disease with paraneoplastic manifestation



POEMS Pathogenesis VEGF



Diagnosis	AL N=4	MGUS N=2	MM N=9	CLS N=2	PN N=29	CTD N=9	Other N=12	CD N=9	POEMS N=29
Median VEGF, pg/mL	38	86	68	124	50	142	45	412	355
IQR, pg/mL	32-42	64-109	57-106	113-136	31-72	53-292	38-81	195-1285	147-462

Light chain amyloidosis

Capillary leak syndrome

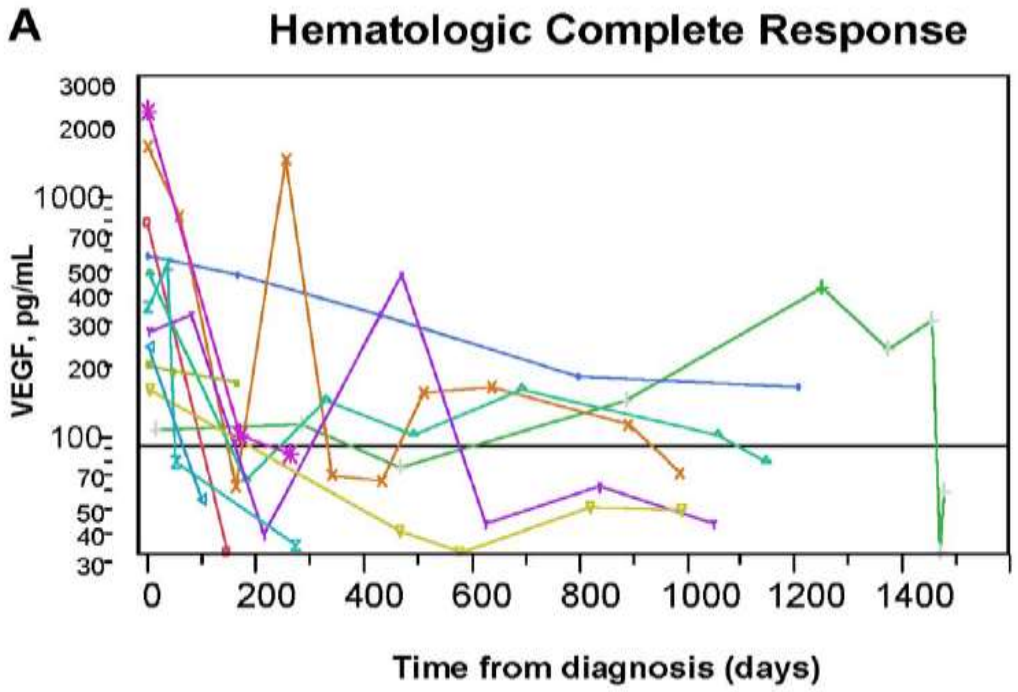
Peripheral neuropathy

Connective tissue disease

Castleman disease

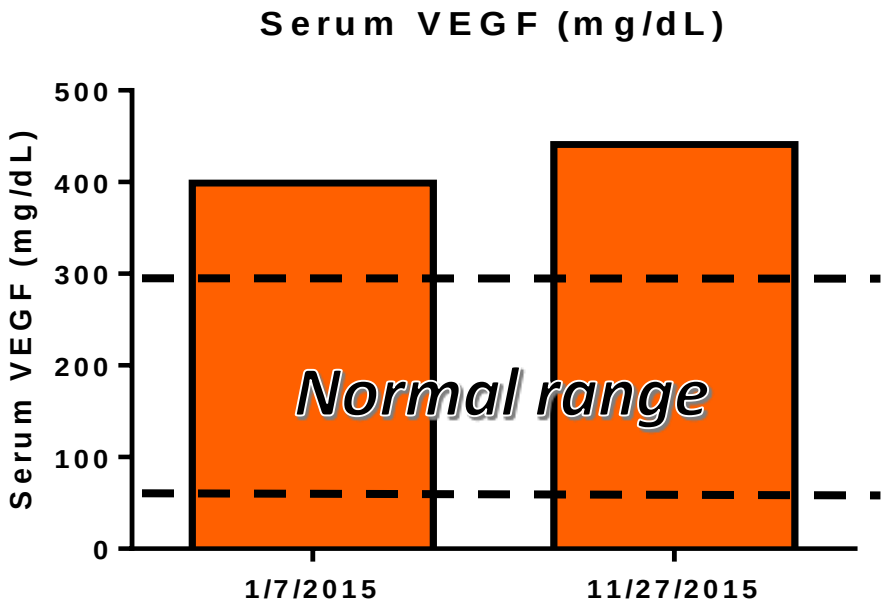
D'Souza, Blood 2011

POEMS Pathogenesis VEGF



D'Souza, Blood 2011

POEMS Pathogenesis VEGF in This Case



POEMS Bone Marrow Pathology

Osteosclerotic myeloma or monoclonal gammopathy of unknown significance

- Less than 5% plasma cells
- Plasma cell aggregates around lymphoid infiltrates
- Lambda light chain restriction
- Usually IgG or IgA
- Vessel proliferation and edema
- Osteosclerotic lesions

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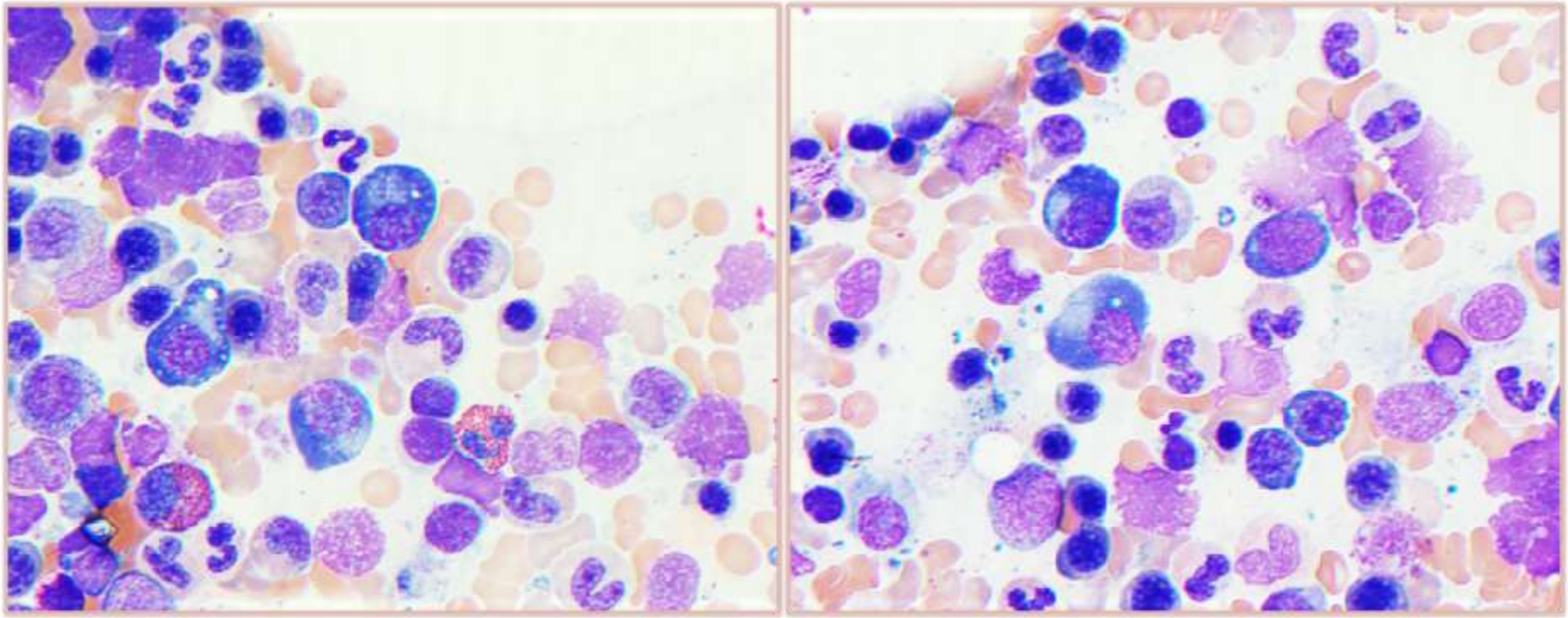
POEMS and Plasma Cell Myeloma



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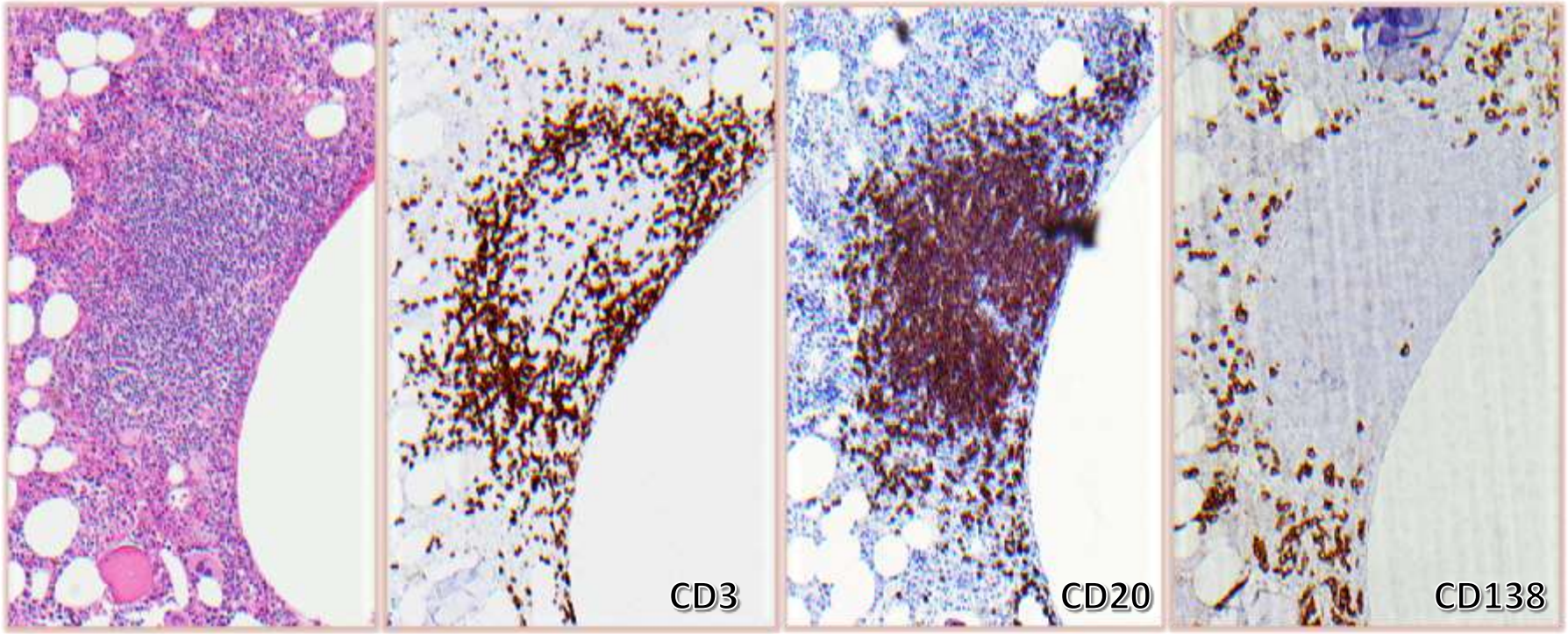
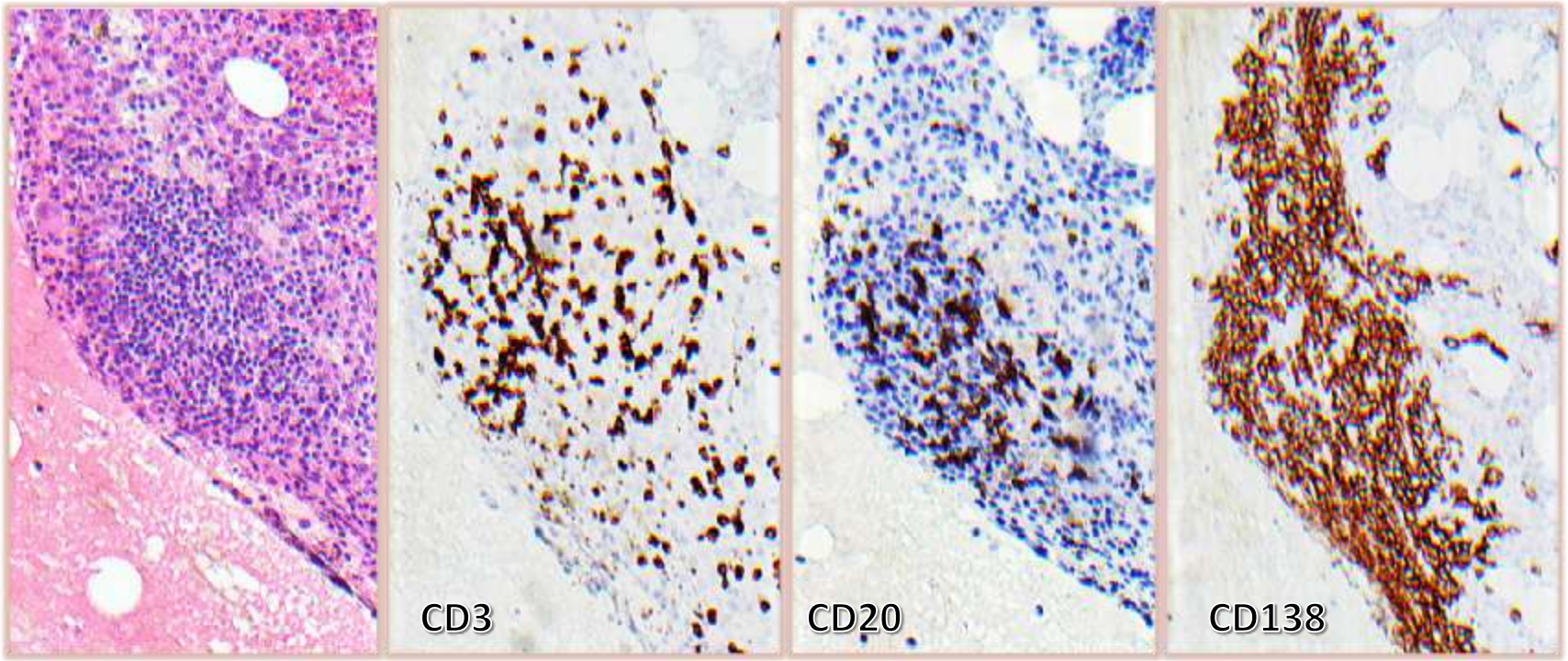


POEMS and Plasma Cell Myeloma



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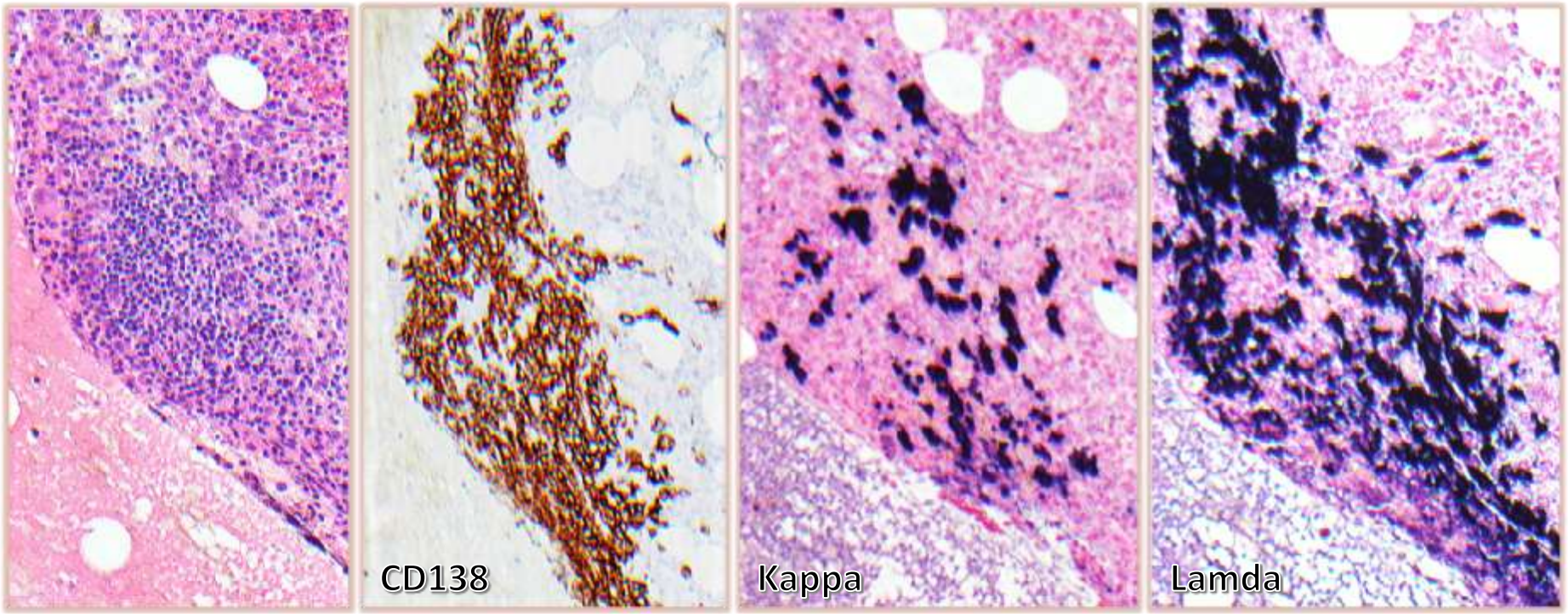
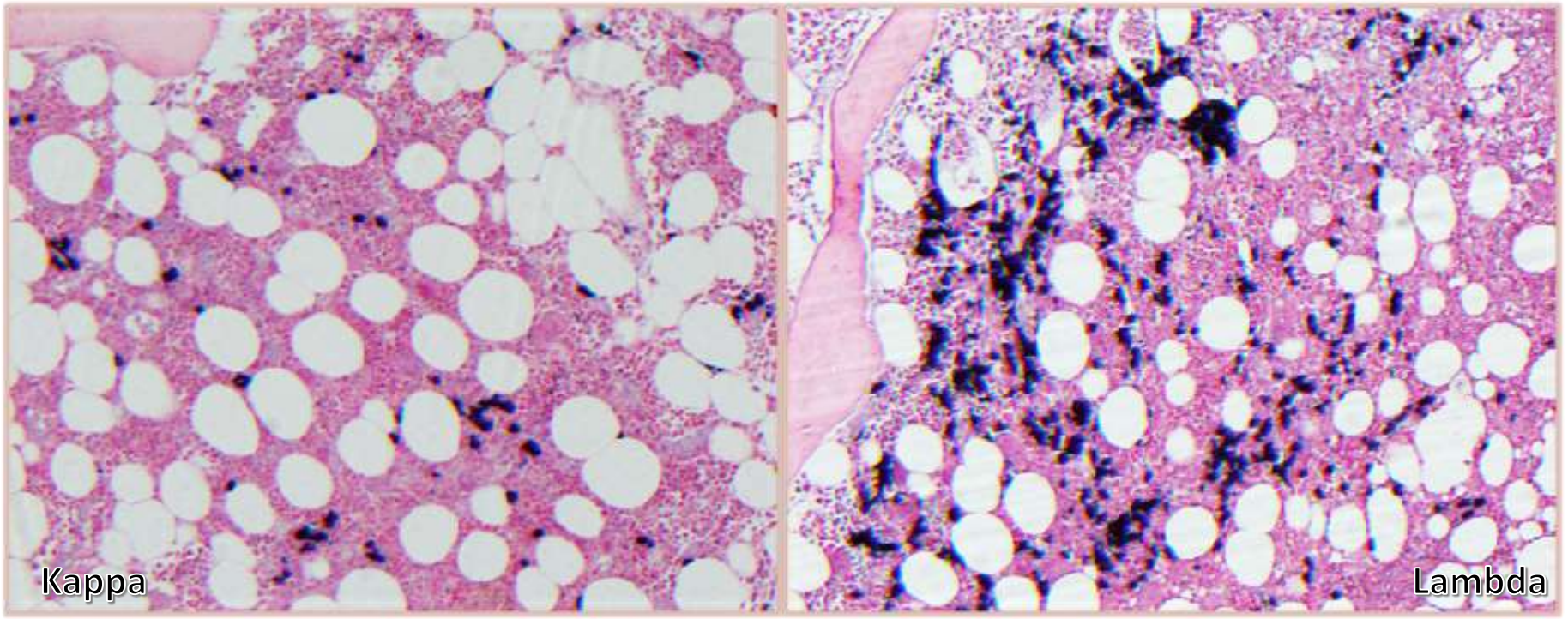
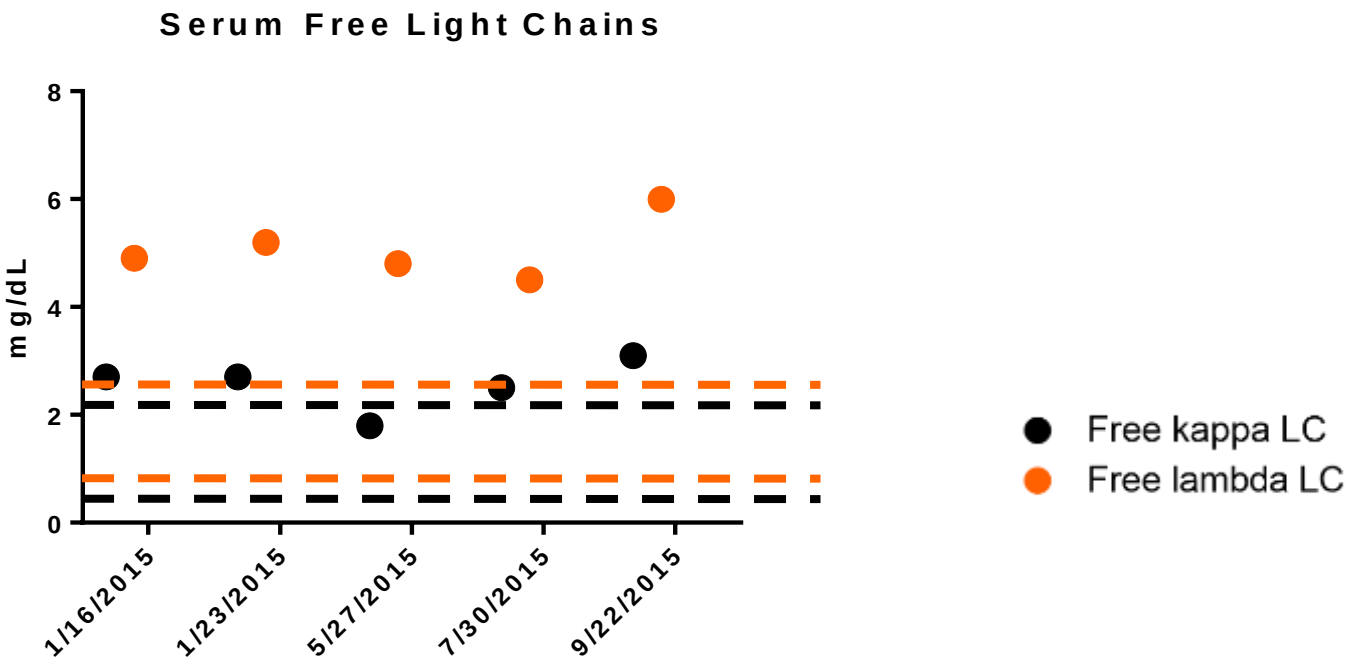
POEMS and Plasma Cell Myeloma



POEMS and Plasma Cell Myeloma



POEMS and Serum Lambda FLC



POEMS Bone Marrow Pathology

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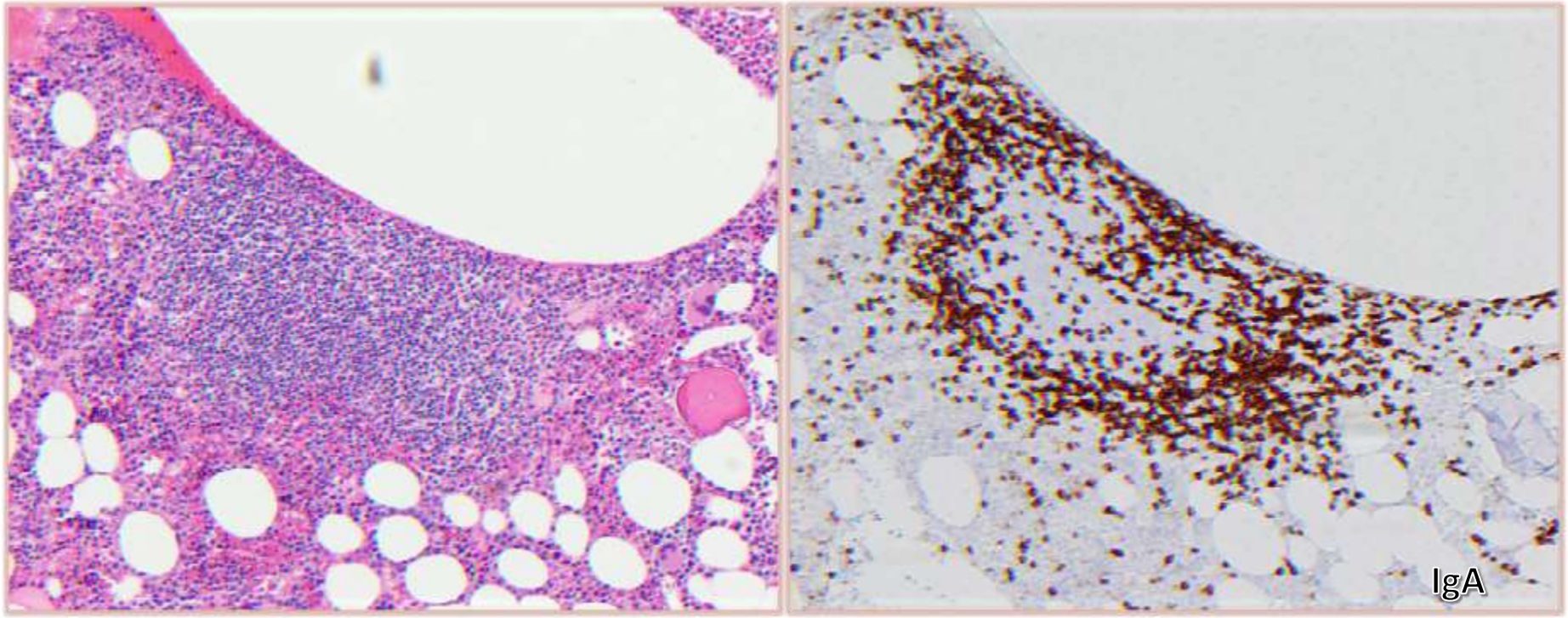
POEMS and Plasma Cell Myeloma



POEMS Bone Marrow Pathology

Osteosclerotic myeloma or monoclonal gammopathy of unknown significance

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POEMS Bone Marrow Pathology

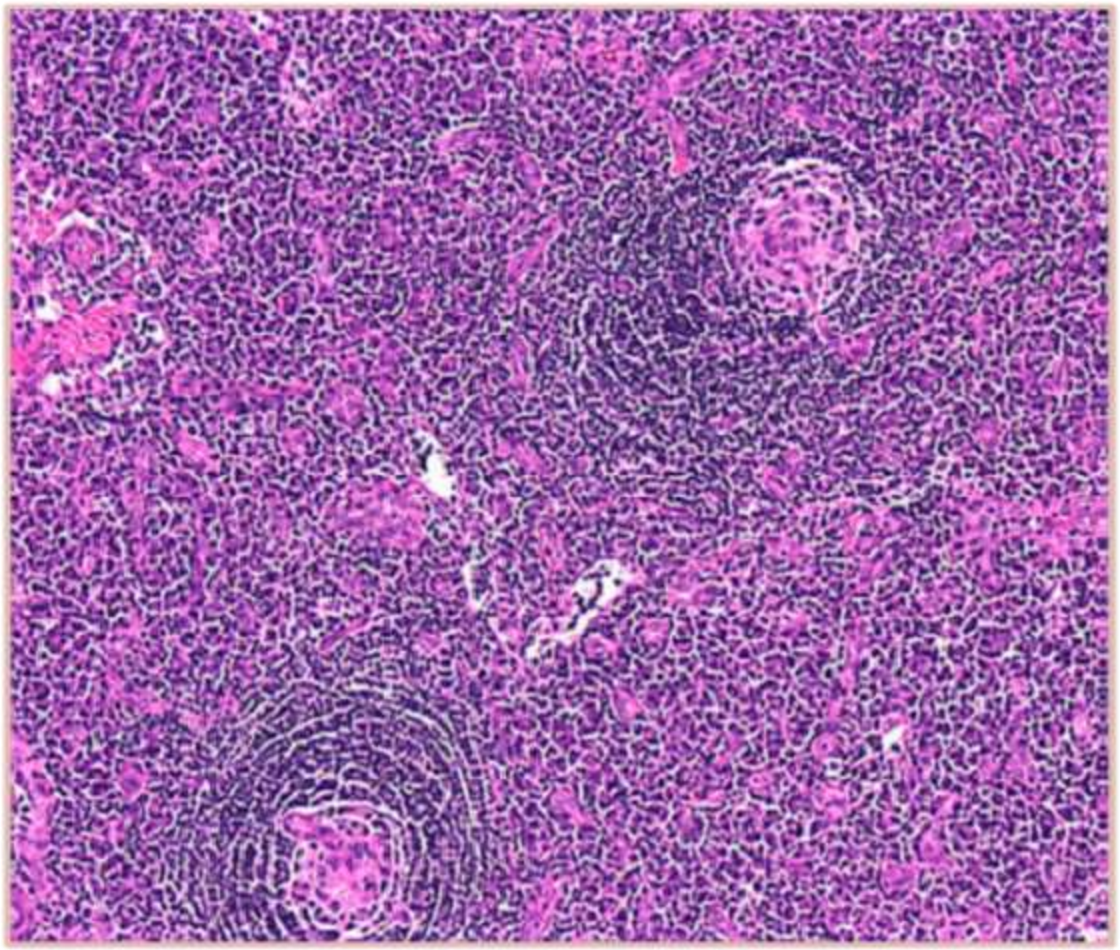
Osteosclerotic myeloma or monoclonal gammopathy of unknown significance

- Less than 5% plasma cells
- Plasma cell aggregates around lymphoid infiltrates
- Lambda light chain restriction
- Usually IgG or IgA
- Vessel proliferation and edema, not present
- Osteosclerotic lesions, not present

POEMS Organomegaly

- Hepatosplemomegaly
- Lymphadenopathy
- Enlargement of the lymph nodes and spleen is secondary to changes consistent with Castleman disease (giant angiofollicular hyperplasia, multicentric plasma cell variant)
- Approximately 15% of patients with POEMS syndrome have concomitant evidence of Castleman disease.

POEMS Organomegaly

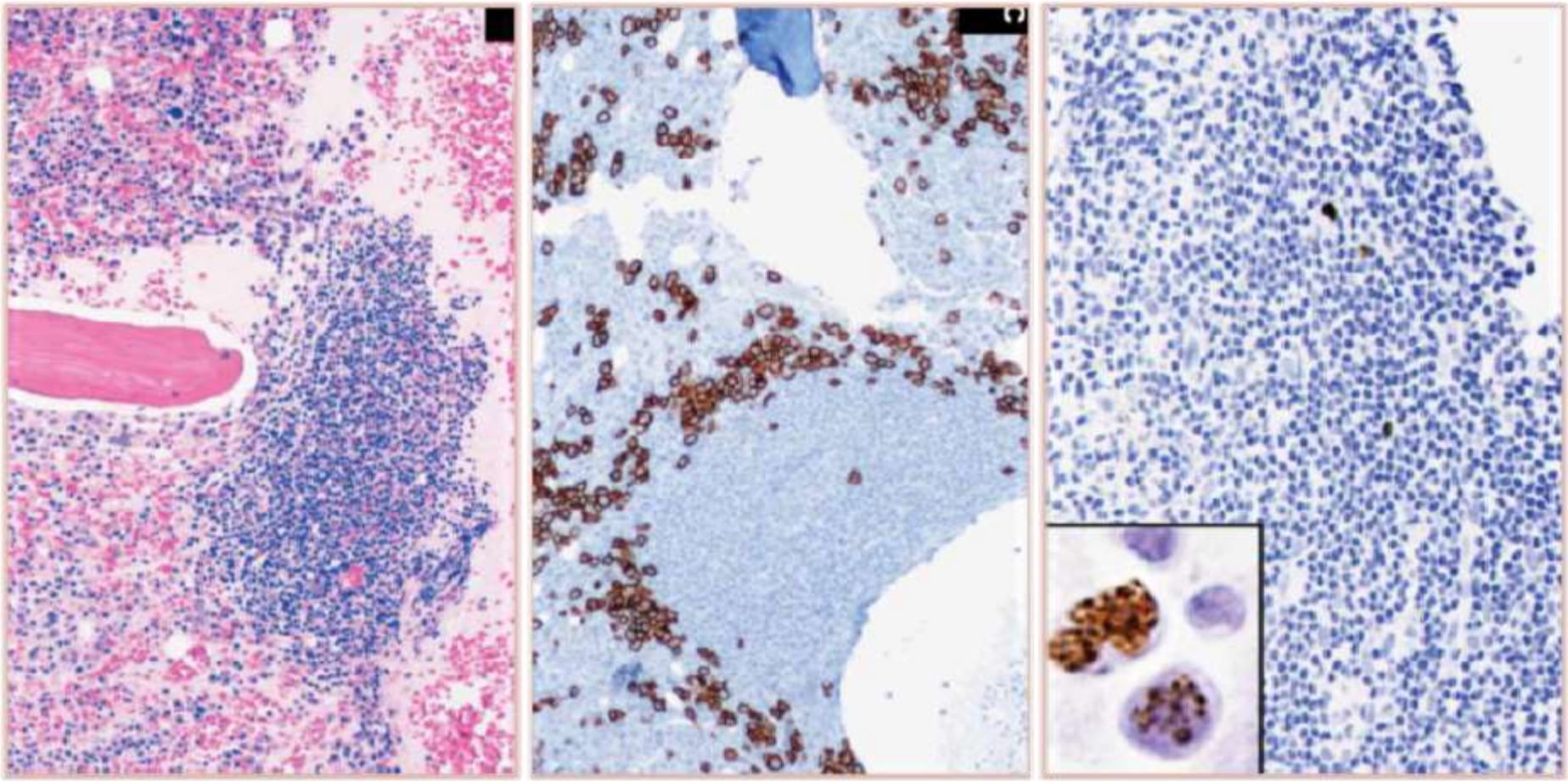


POEMS syndrome
Castleman features in cervical lymph node

- ❑ HHV8-
- ❑ Monotypic plasma cells

Andhavarapu, blood, 2013

POEMS and Castleman Disease



Venkataraman, Am J Clin Pathol. 2013

POEMS Organomegaly

- Hepatosplemomegaly
- Lymphadenopathy
- Enlargement of the lymph nodes and spleen is secondary to changes consistent with Castleman disease (giant angiofollicular hyperplasia, multicentric plasma cell variant)
- Approximately 15% of patients with POEMS syndrome have concomitant evidence of Castleman disease.
- HHV8- in this case, no evidence of multicentric Castleman features

POEMS Endocrinopathy

- Gonadal dysfunction
- Thyroid dysfunction
- Abnormal glucose metabolism
- Adrenal insufficiency

POEMS Endocrinopathy

- Gonadal dysfunction
- Thyroid dysfunction, hypothyroidism in this case
- Abnormal glucose metabolism
- Adrenal insufficiency

POEMS Skin Changes

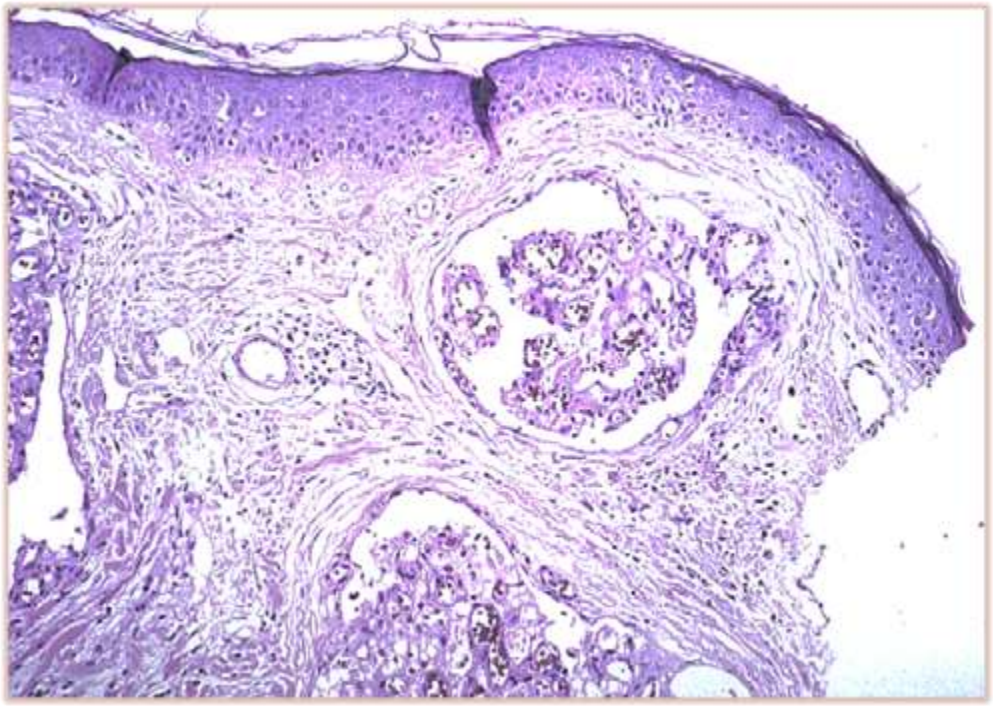
- Diffuse hyperpigmentation (90%)
- Hypertrichosis (80%)
- Skin thickening (77%)
- Hemangioma, may progress rapidly
- Whitening of the proximal nails and possible clubbing
- Sweet-like lesions
- Vasculitis

POEMS Skin Changes

- Diffuse hyperpigmentation (90%), present in this case
- Hypertrichosis (80%)
- Skin thickening (77%)
- Hemangioma, may progress rapidly, present in this case
- Whitening of the proximal nails and possible clubbing
- Sweet-like lesions
- Vasculitis

POEMS Skin Changes, Hemangioma

- Glomeruloid hemangioma
- Distinctive vascular proliferation rich in hyaline globules
- Highly suspicious for Castleman disease and POEMS



Rosai, Surgical Pathology 10th edition

Take Home Message

- Presence of a **monoclonal plasma-proliferative disorder** and **polyneuropathy,** in addition to 1 minor criterion
- Less than 5% plasma cells
- Plasma cell aggregates around lymphoid infiltrates
- Lambda light chain restriction
- Osteosclerotic lesions
- Elevated serum VEGF

Thank you

Questions?