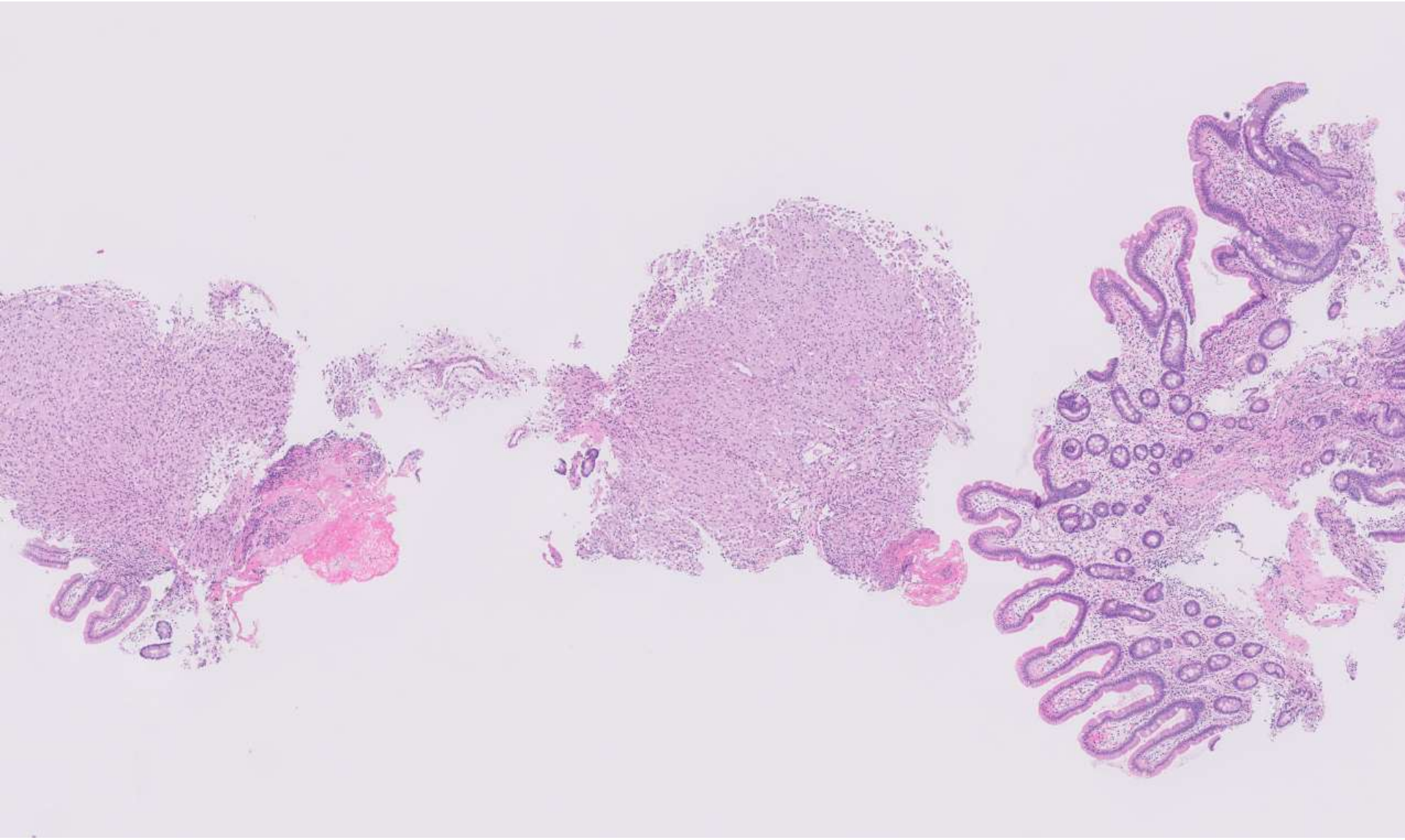
OCT 2022 DIAGNOSIS LIST

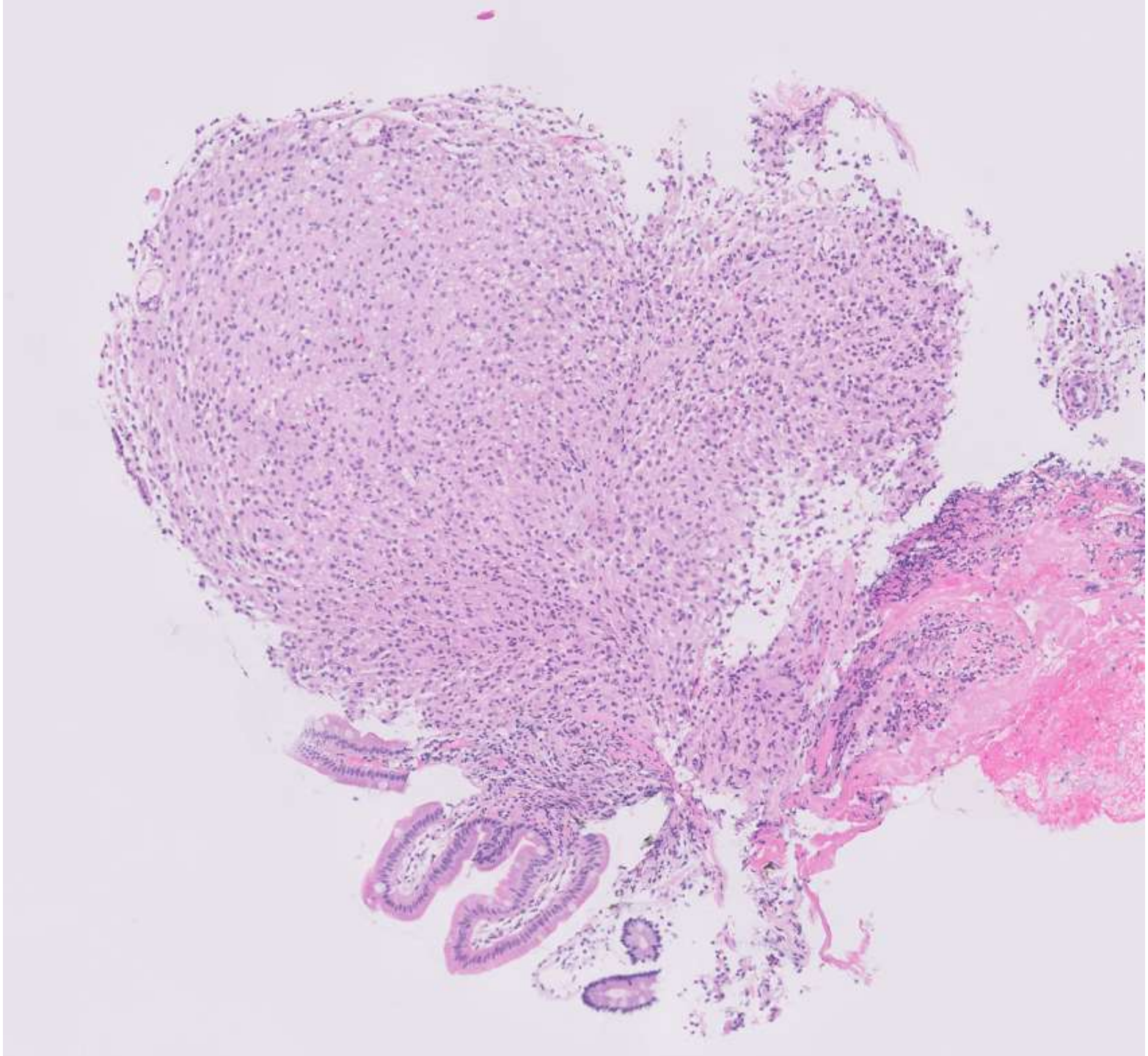
22-1001: epithelioid gastrointestinal stromal tumor (small bowel; GI path)
22-1002: pseudomyogenic hemangioendothelioma (penis; BST path)
22-1003: renal osteodystrophy (bone marrow; BST path)
22-1004: Ewing sarcoma (soft tissue; pedspath and BST path)
22-1005: Intramuscular fast-flow vascular anomaly (MAP2K1 somatic mutation) (soft tissue; pedspath and BSTpath)
22-1006: alveolar soft part sarcoma (breast, BST path)
22-1007: basal cell adenoma (salivary gland; ENT path)
22-1008: endometriosis mimicking LAMN (appendix; GI path)

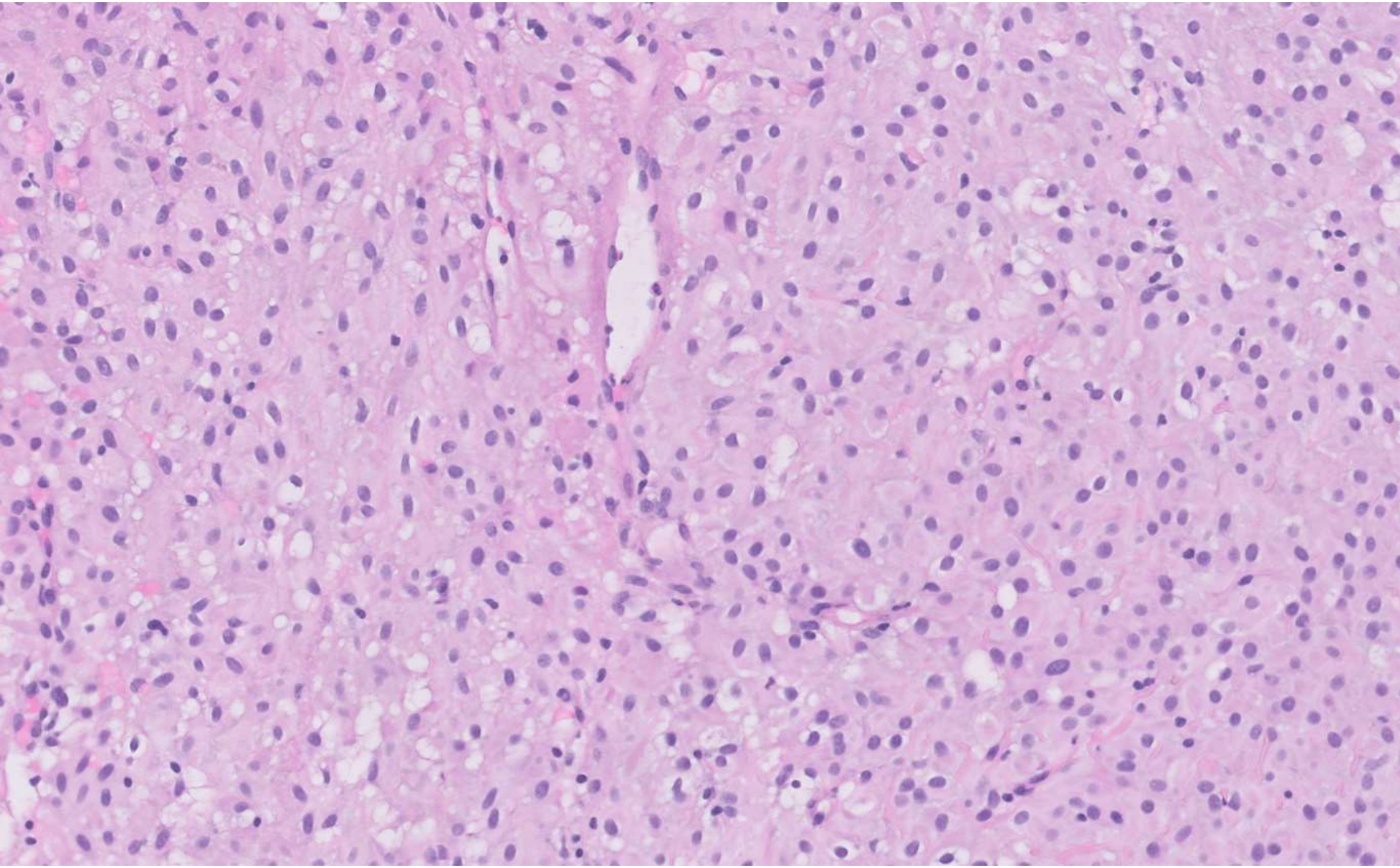
22-1001

Cindy Wang; Stanford

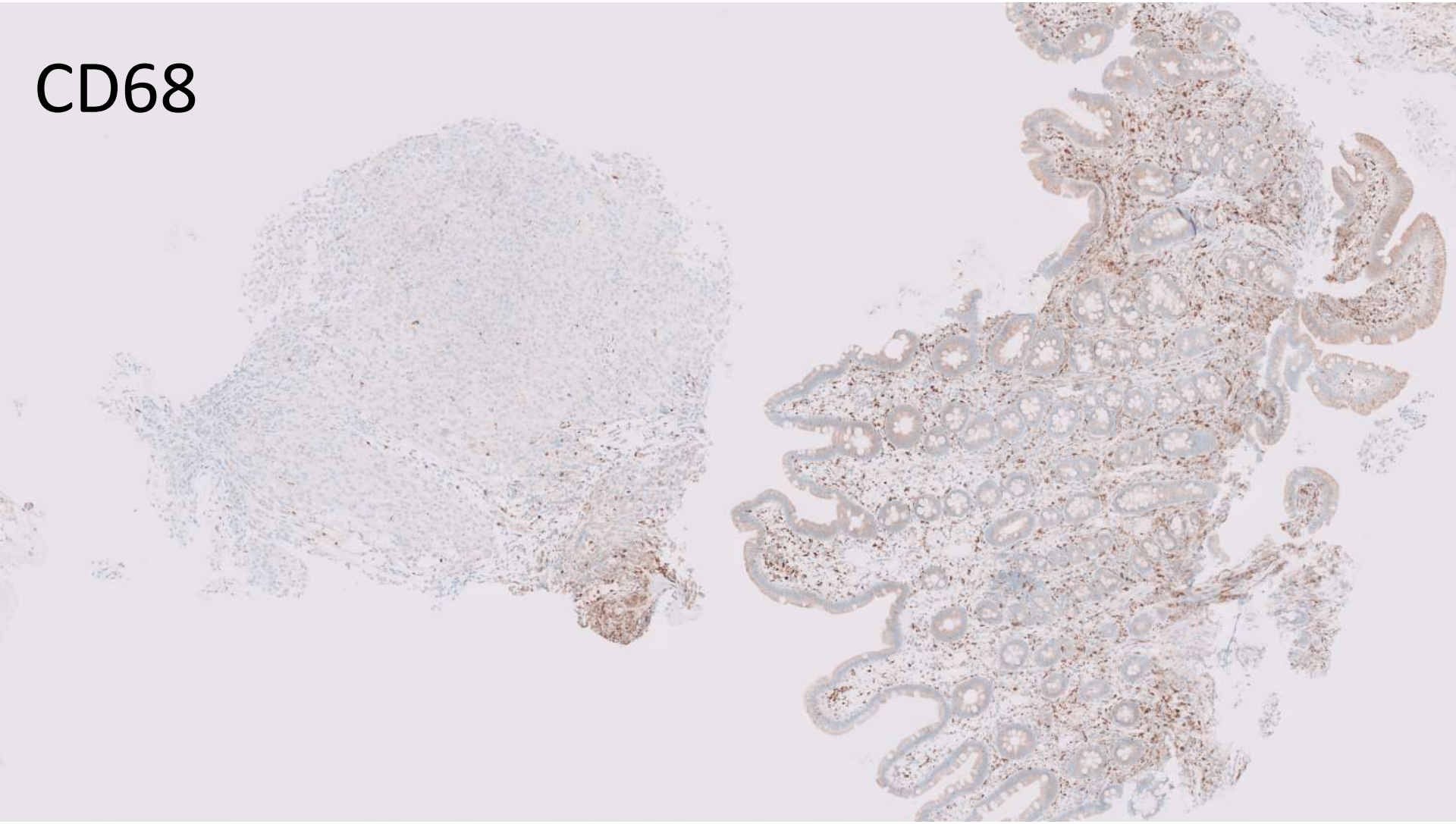
Adult with jejunal lesion, resected.







CD68



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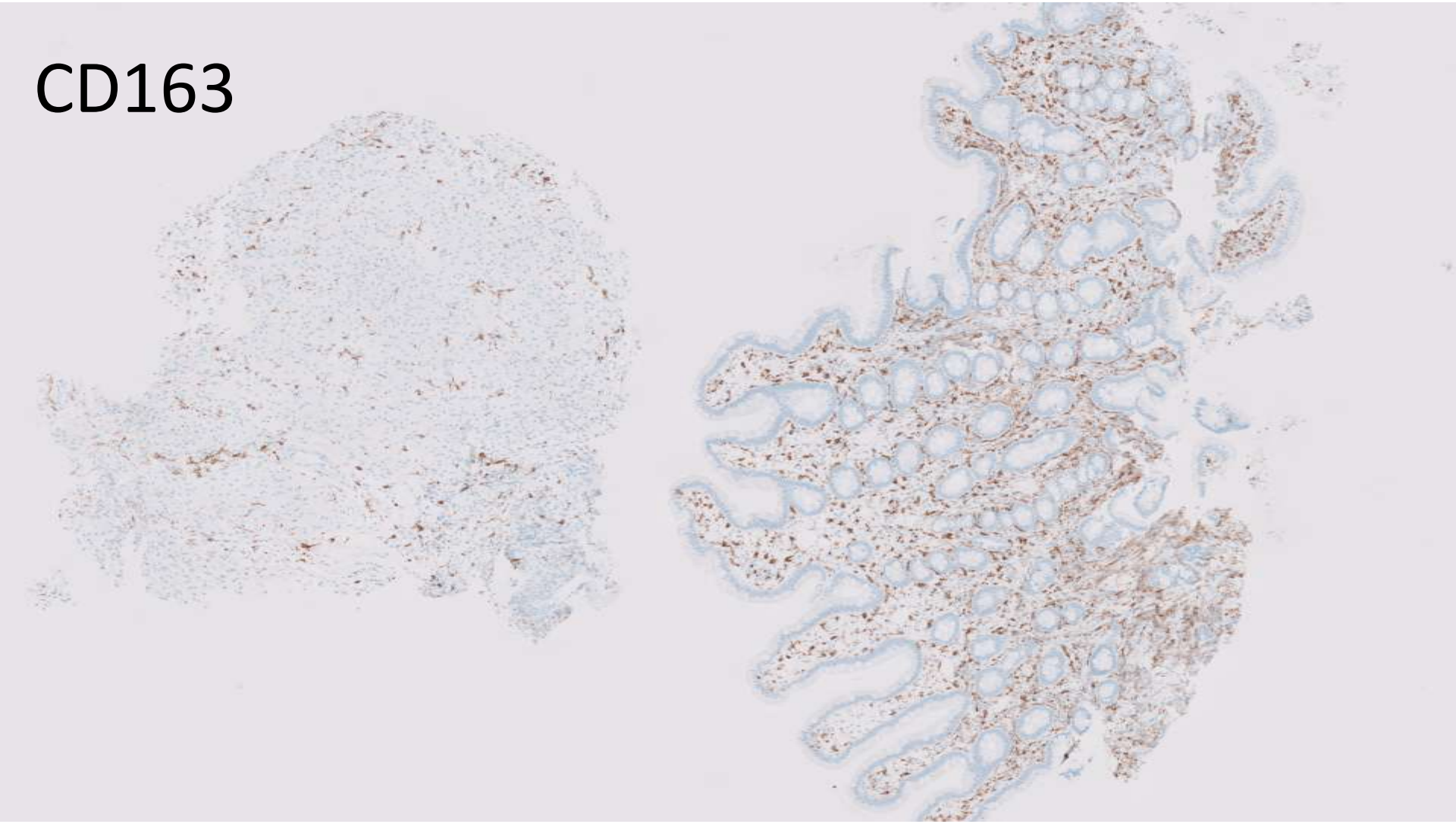
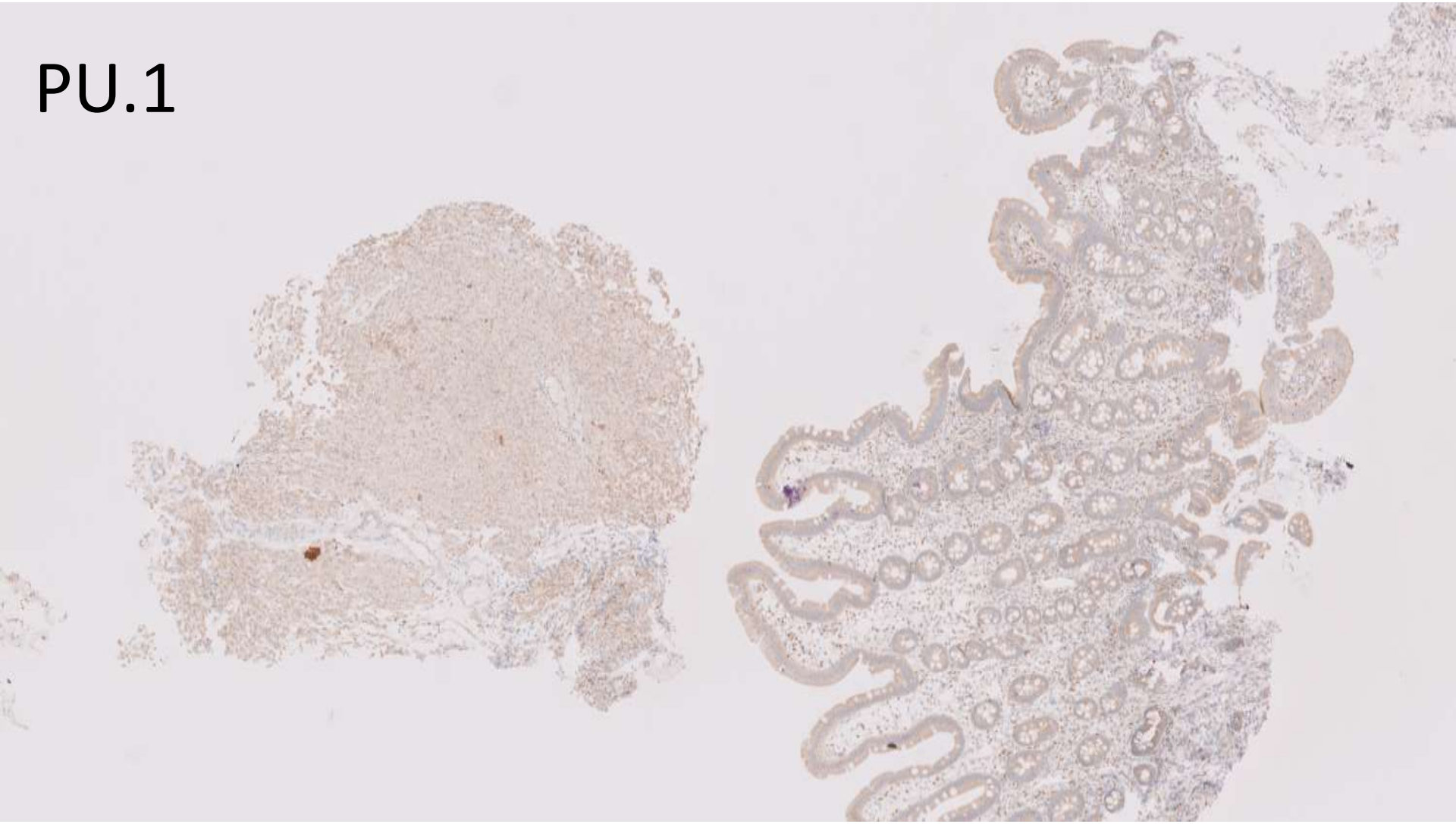


PU.1



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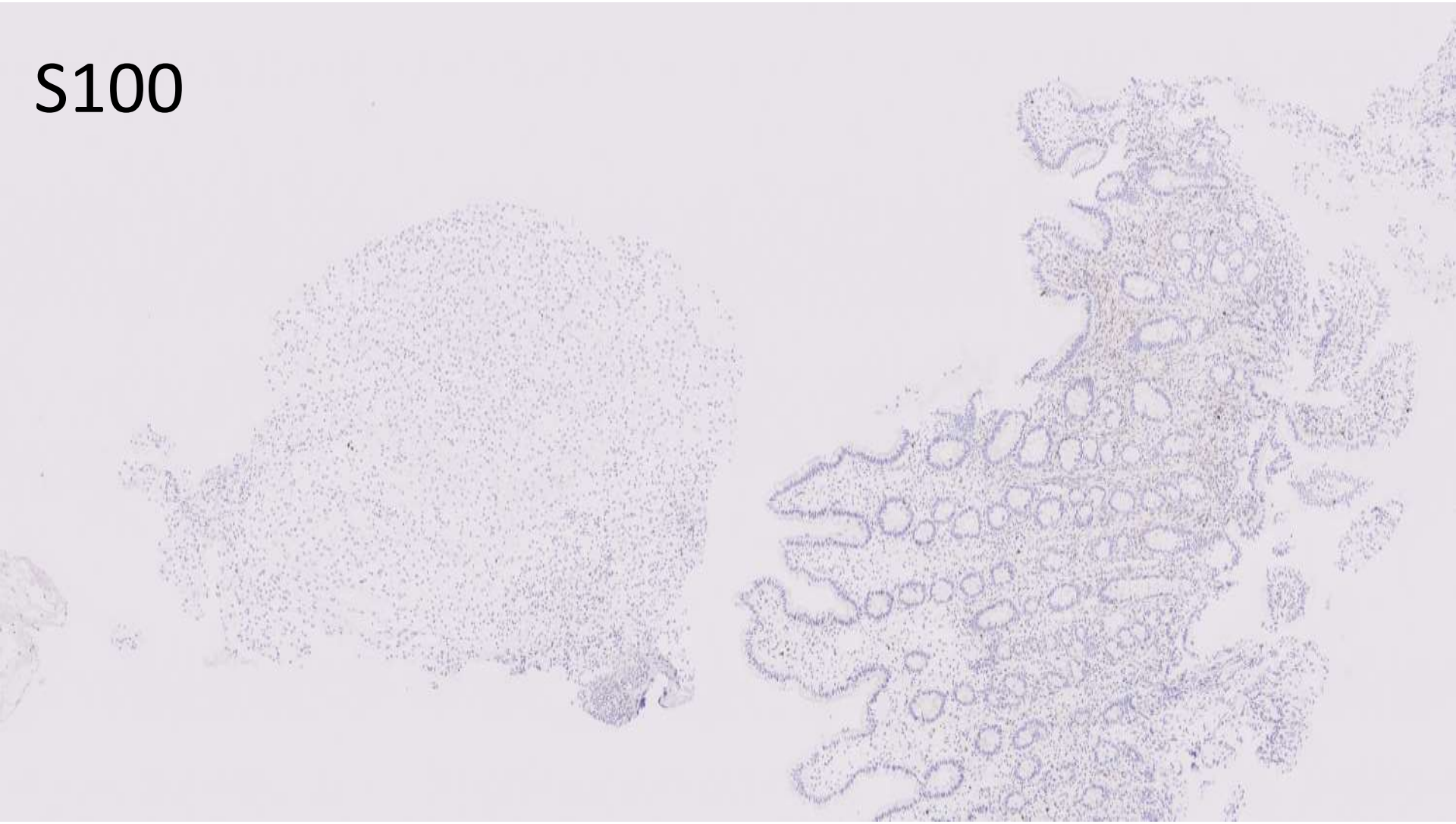

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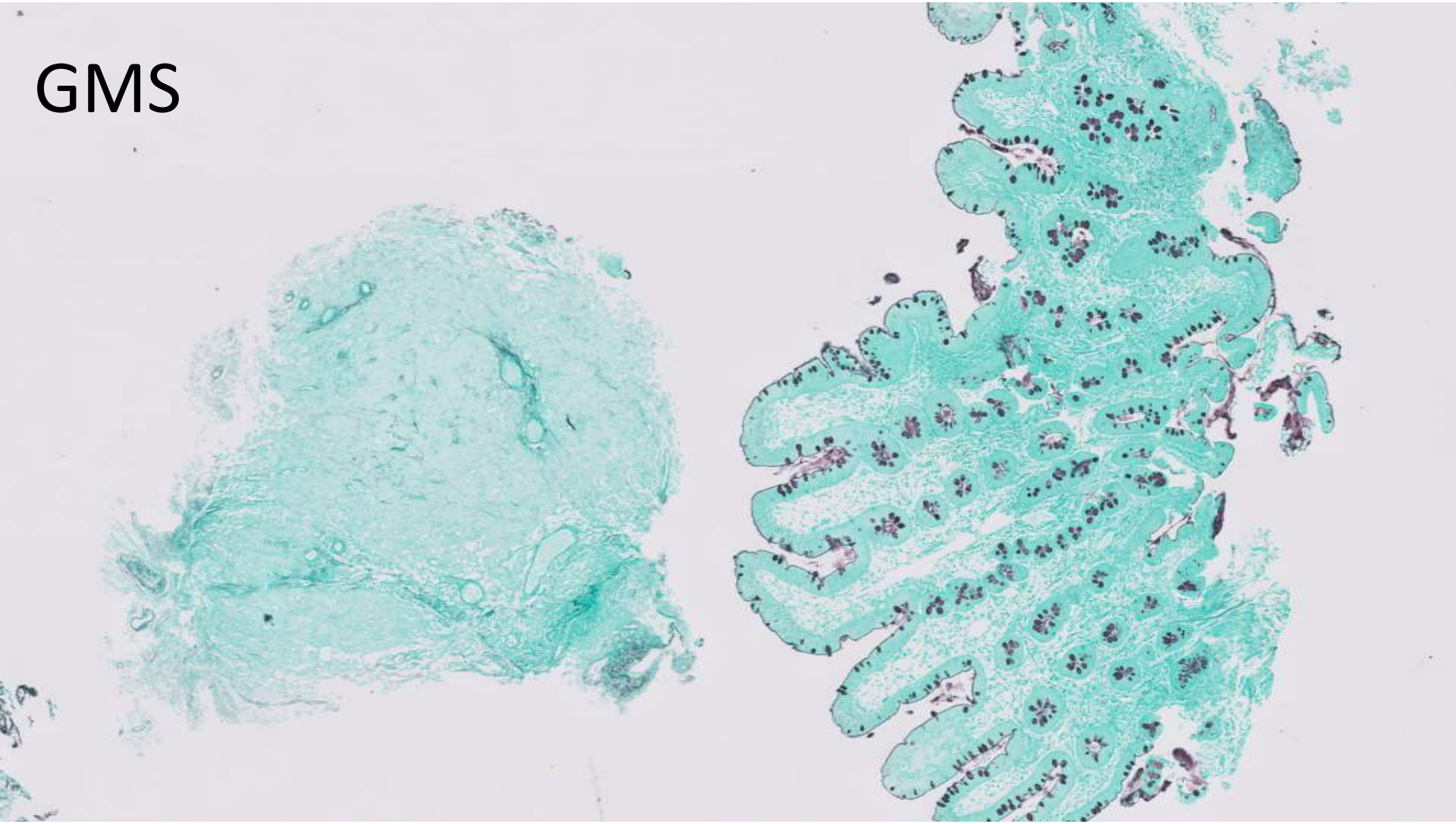
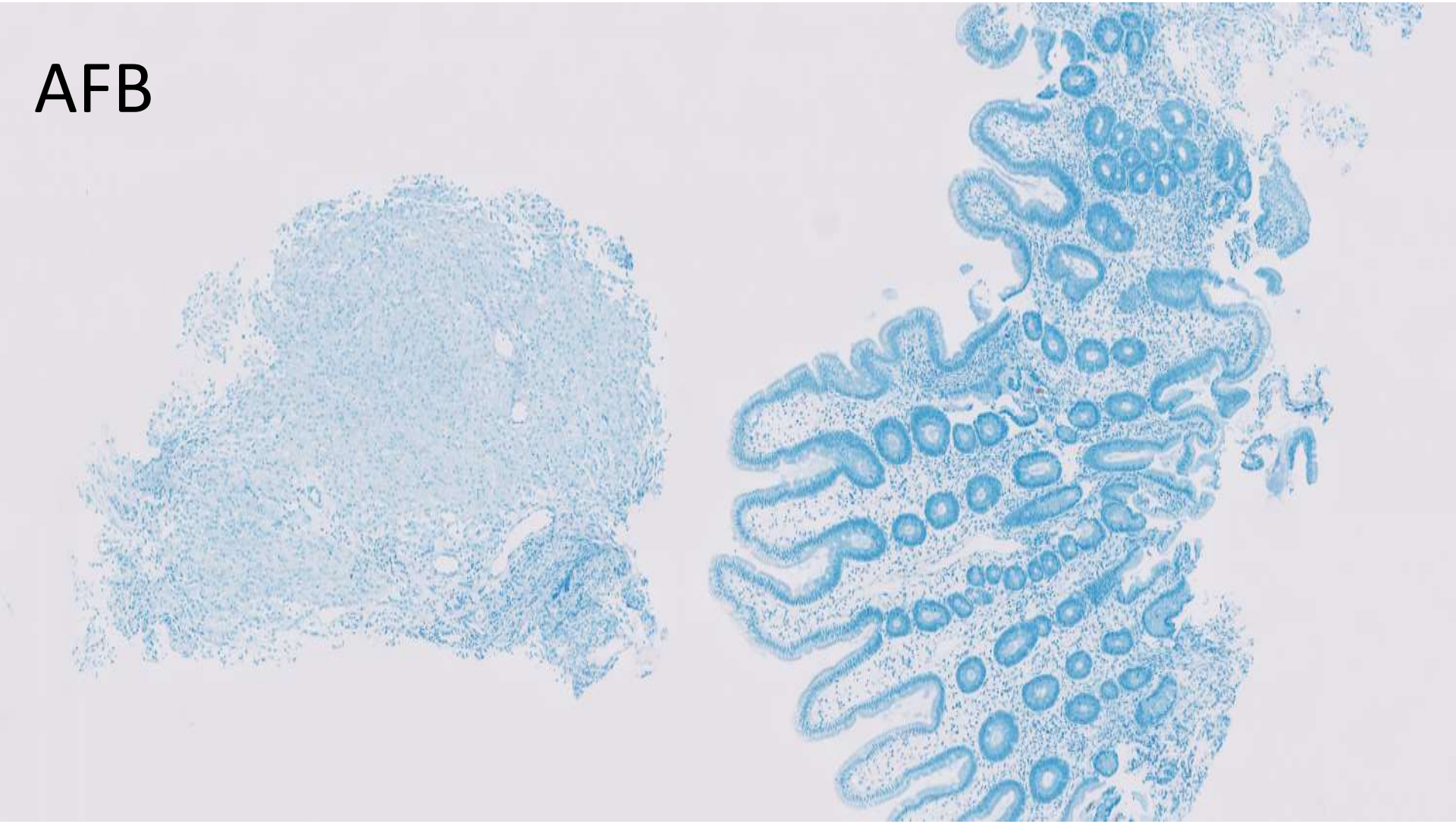


AFB



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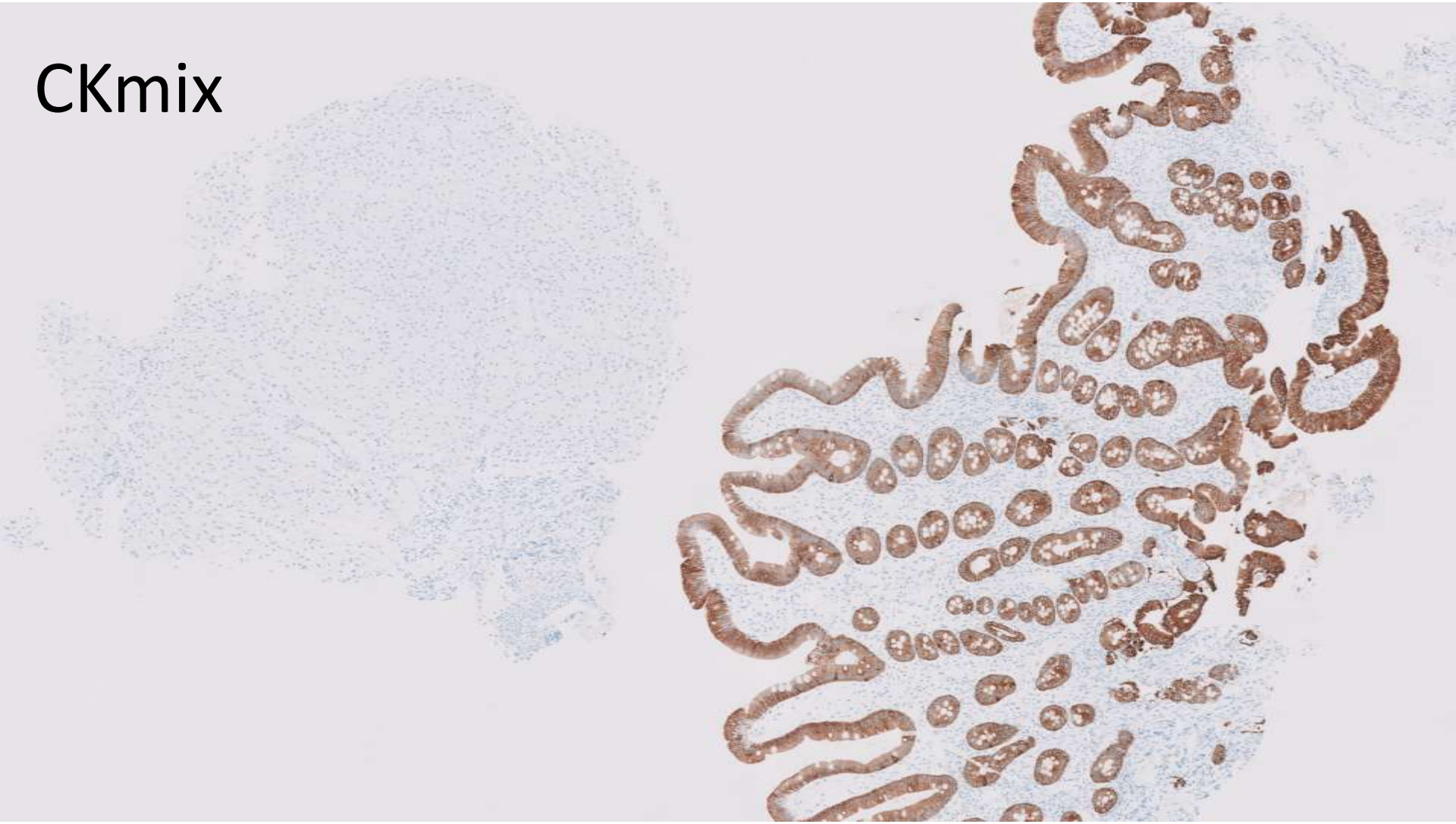

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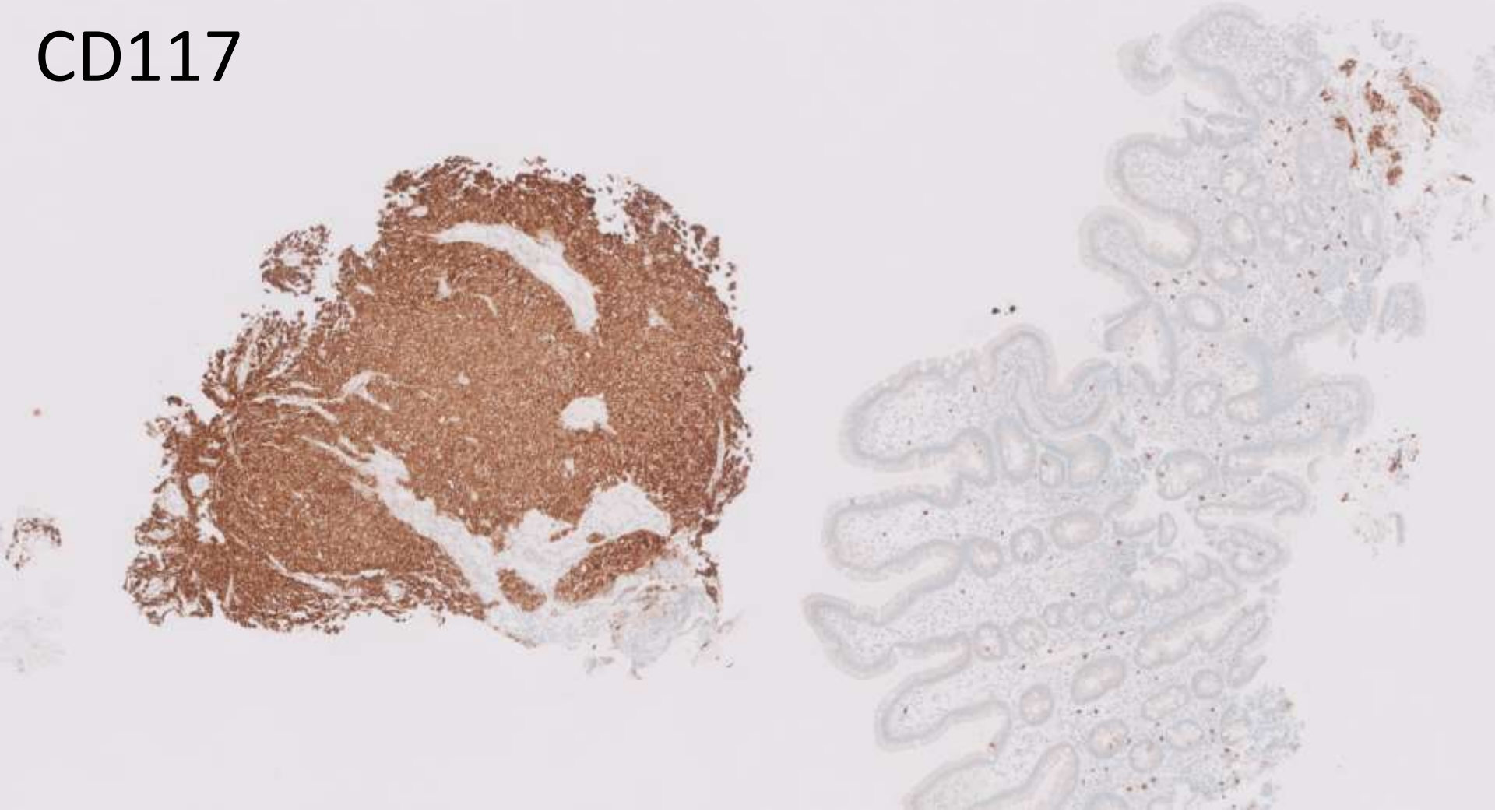

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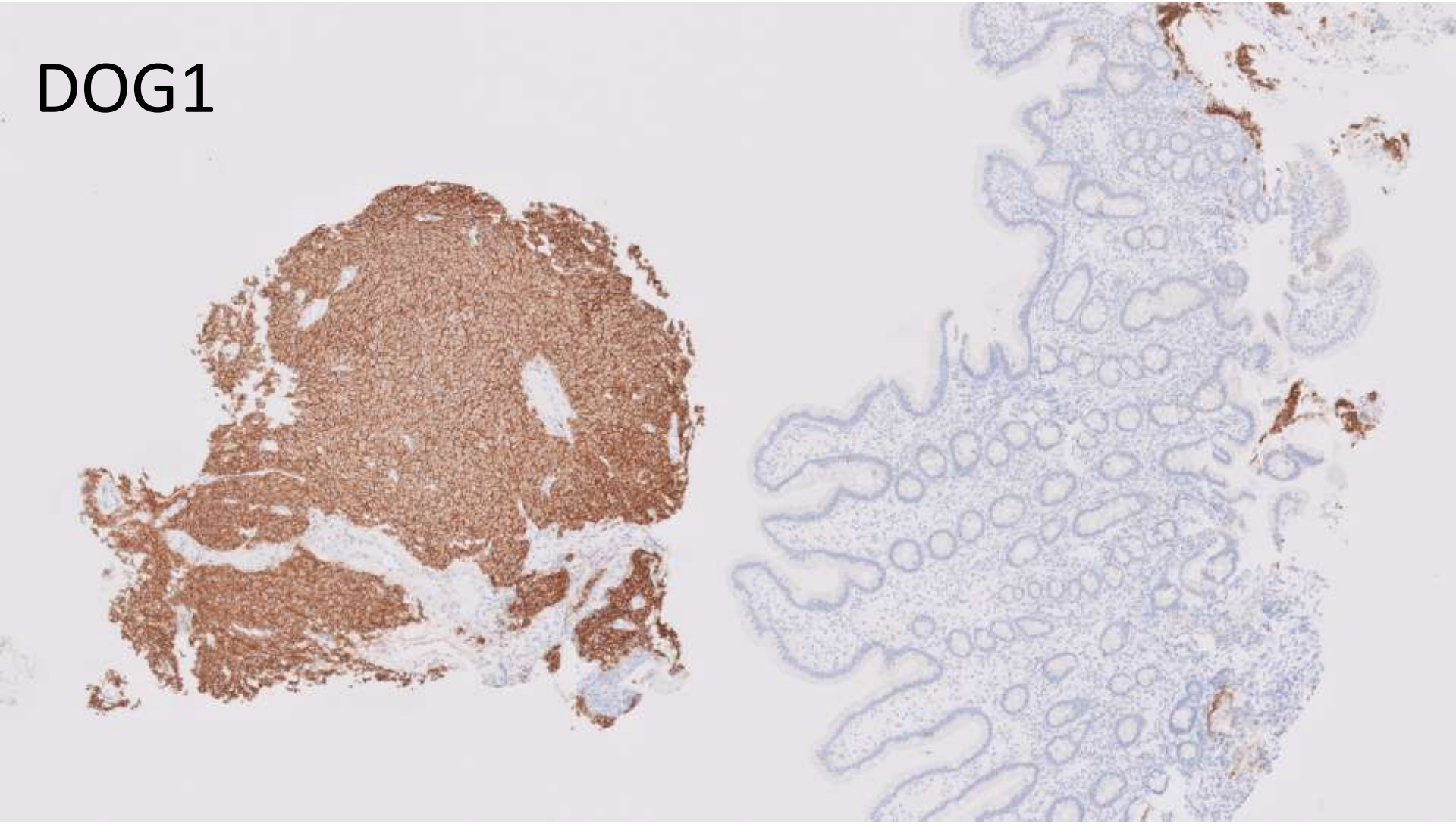
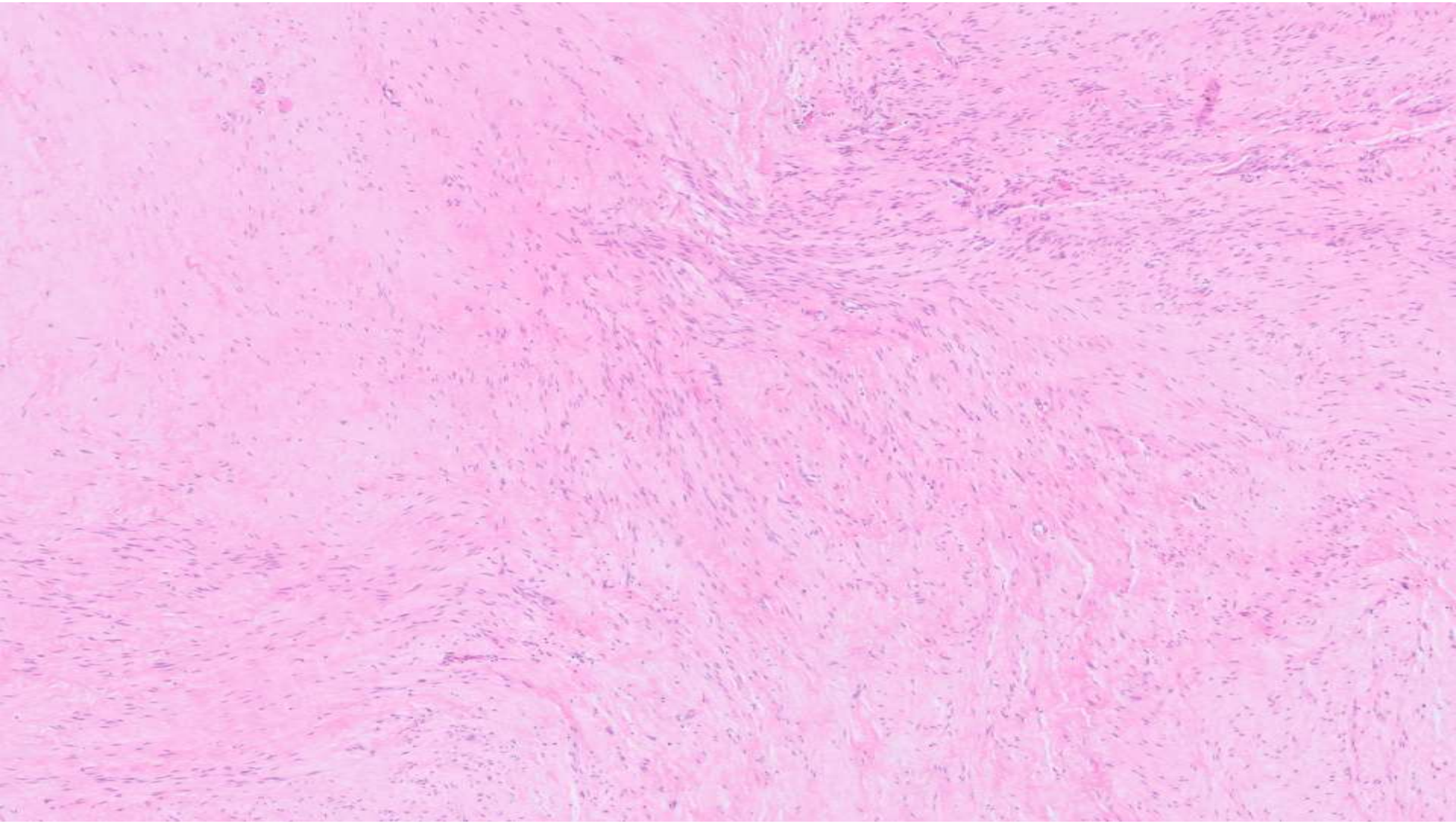
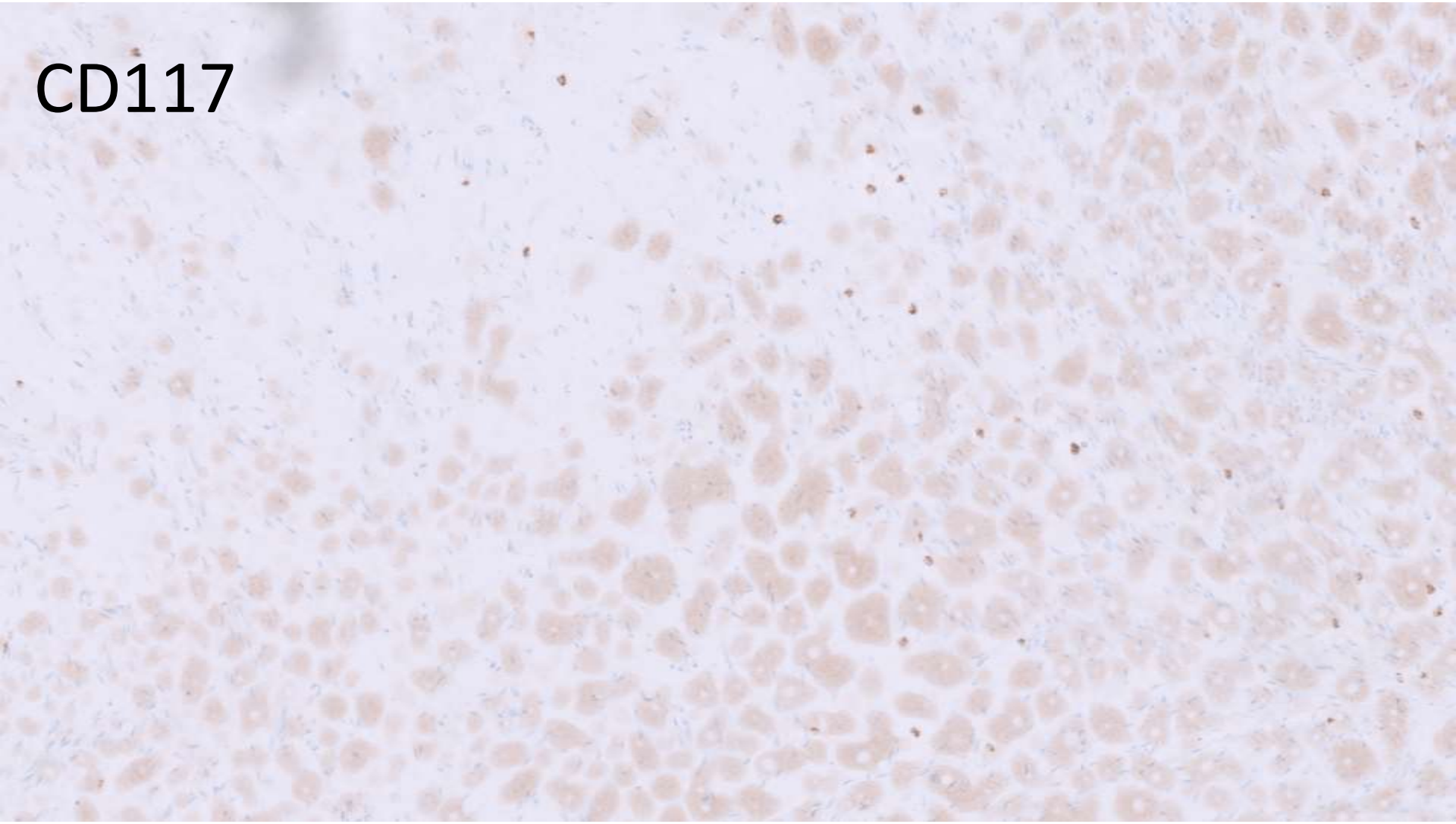


Epithelioid Gastrointestinal Stromal Tumor

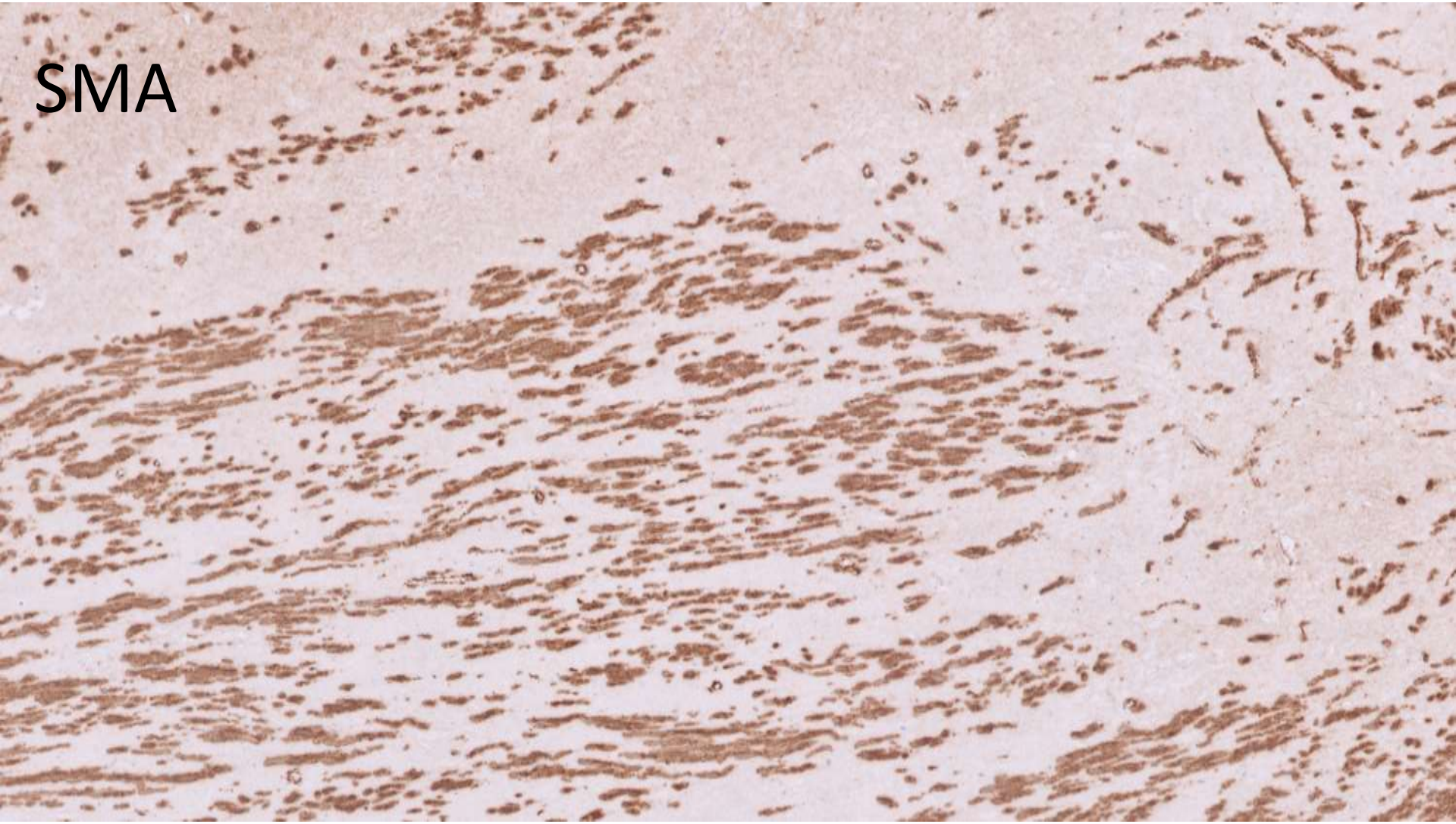
GIST Pitfalls

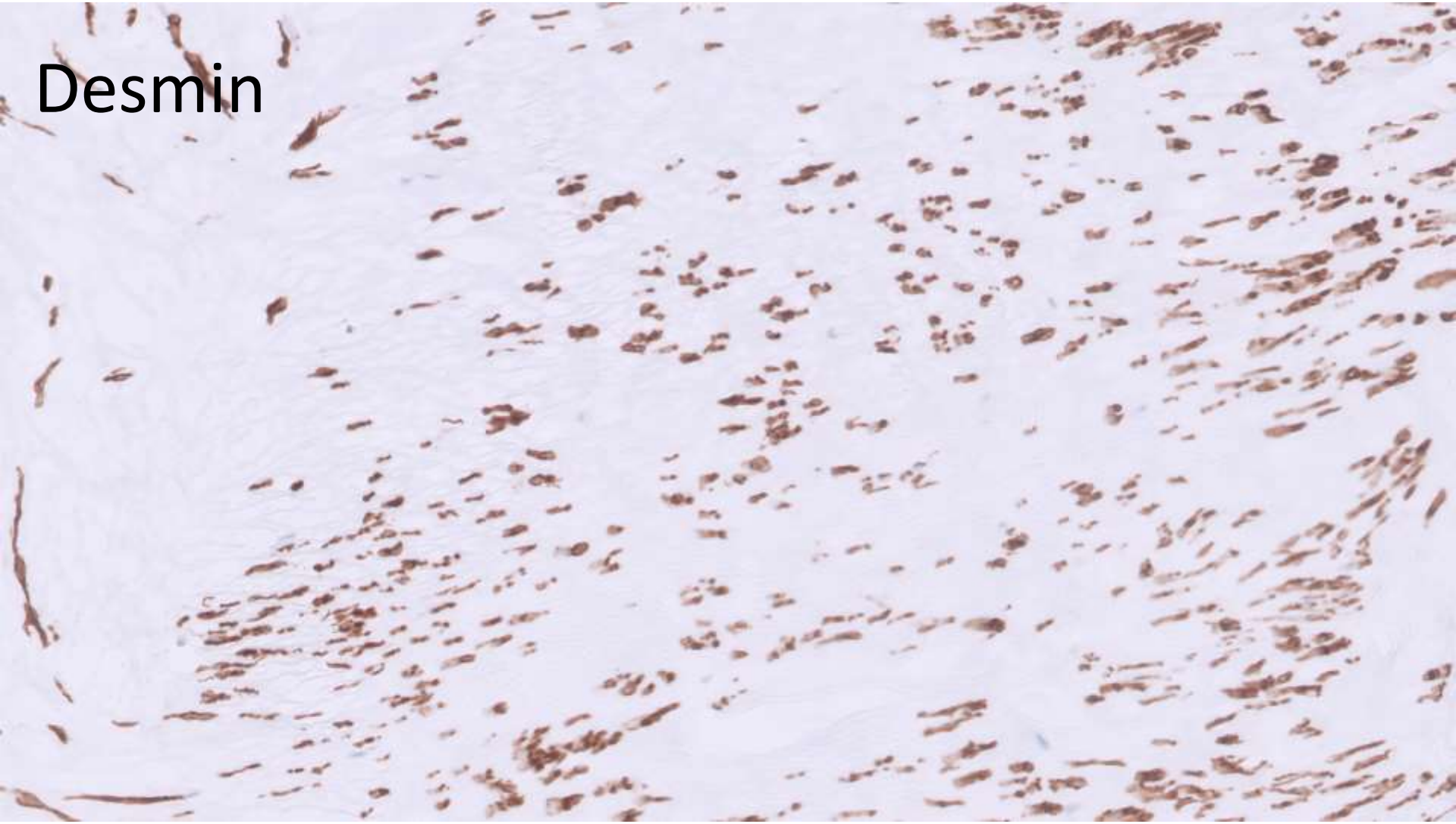
- 20-25% of all GISTs epithelioid morphology
- Small intestine and colon GISTs usually spindle cell
- SDH deficient GISTs characteristically show epithelioid morphology
- De novo or s/p imatinib therapy →dedifferentiation and/or transdifferentiation
  - epithelial, myogenic or angiosarcomatous

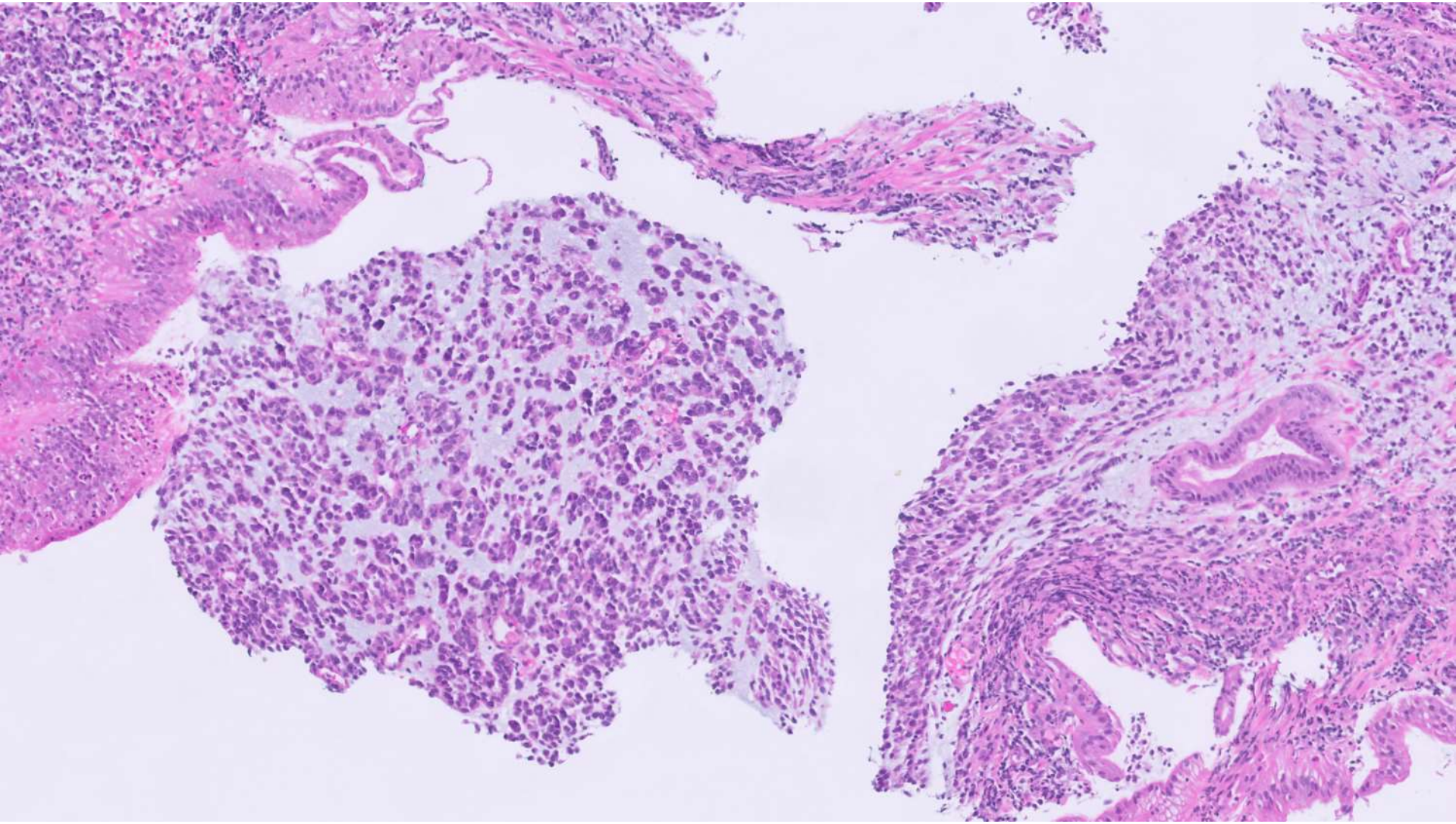


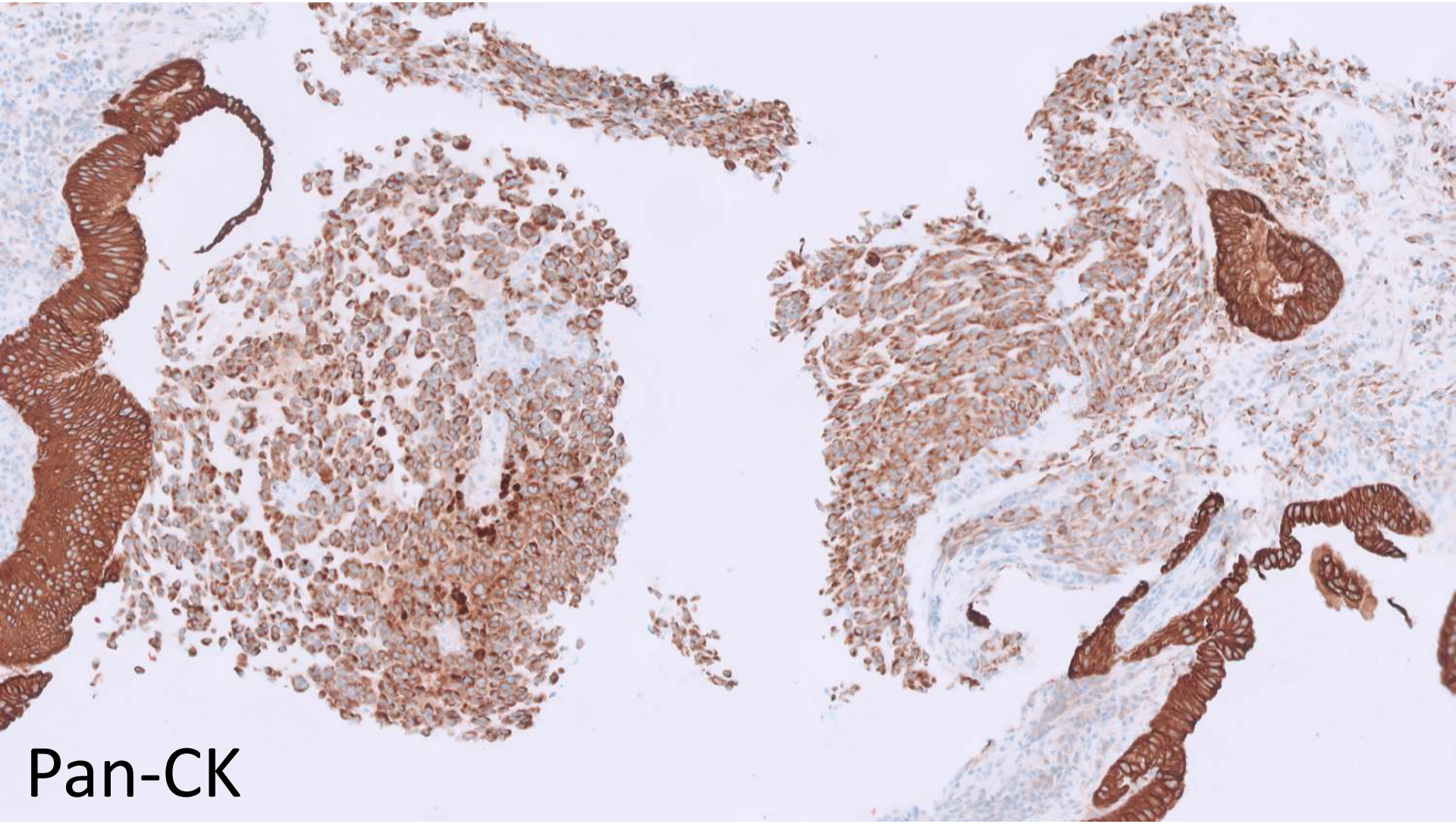

CD117


DOG1


SMA


Desmin

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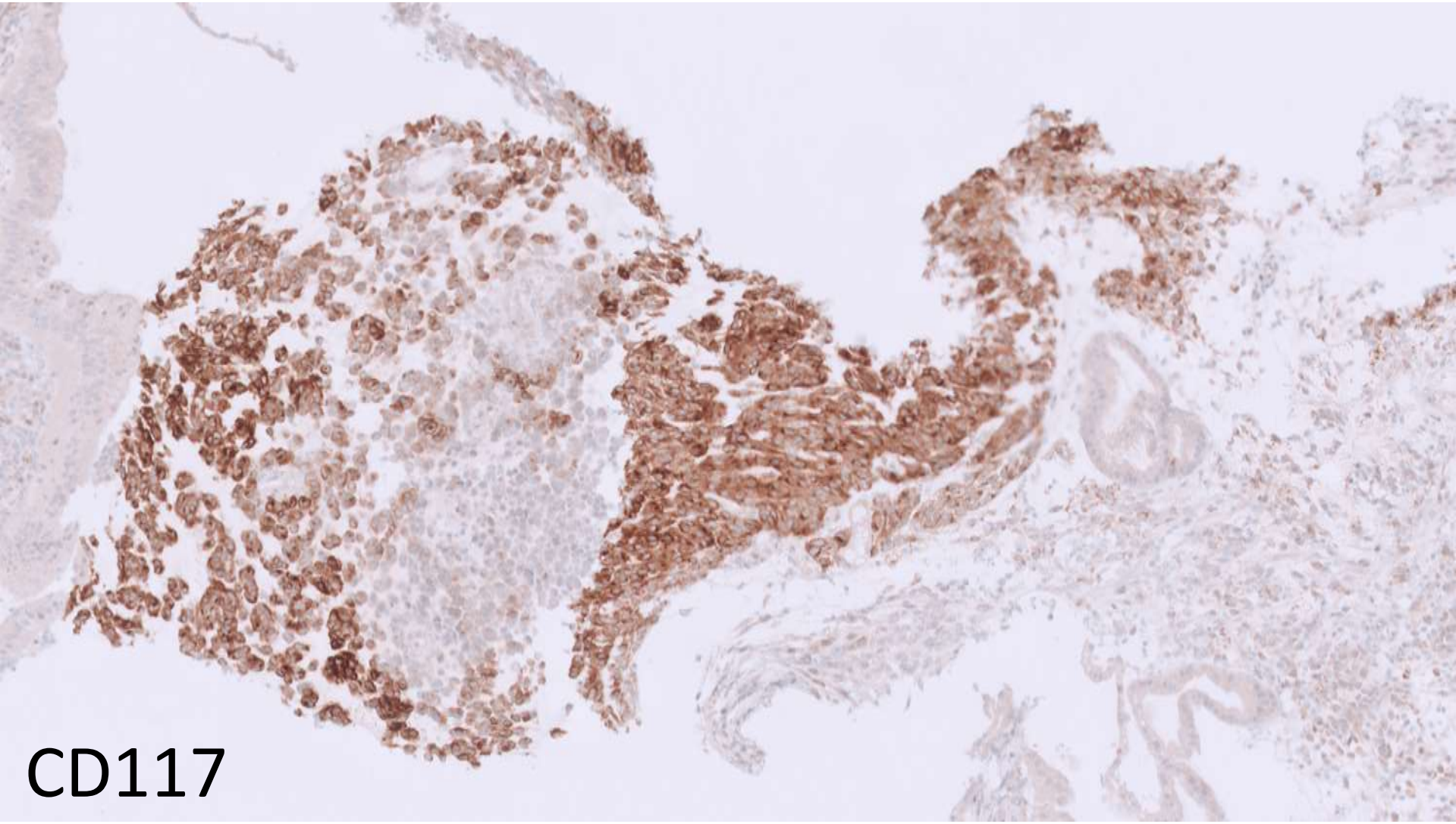
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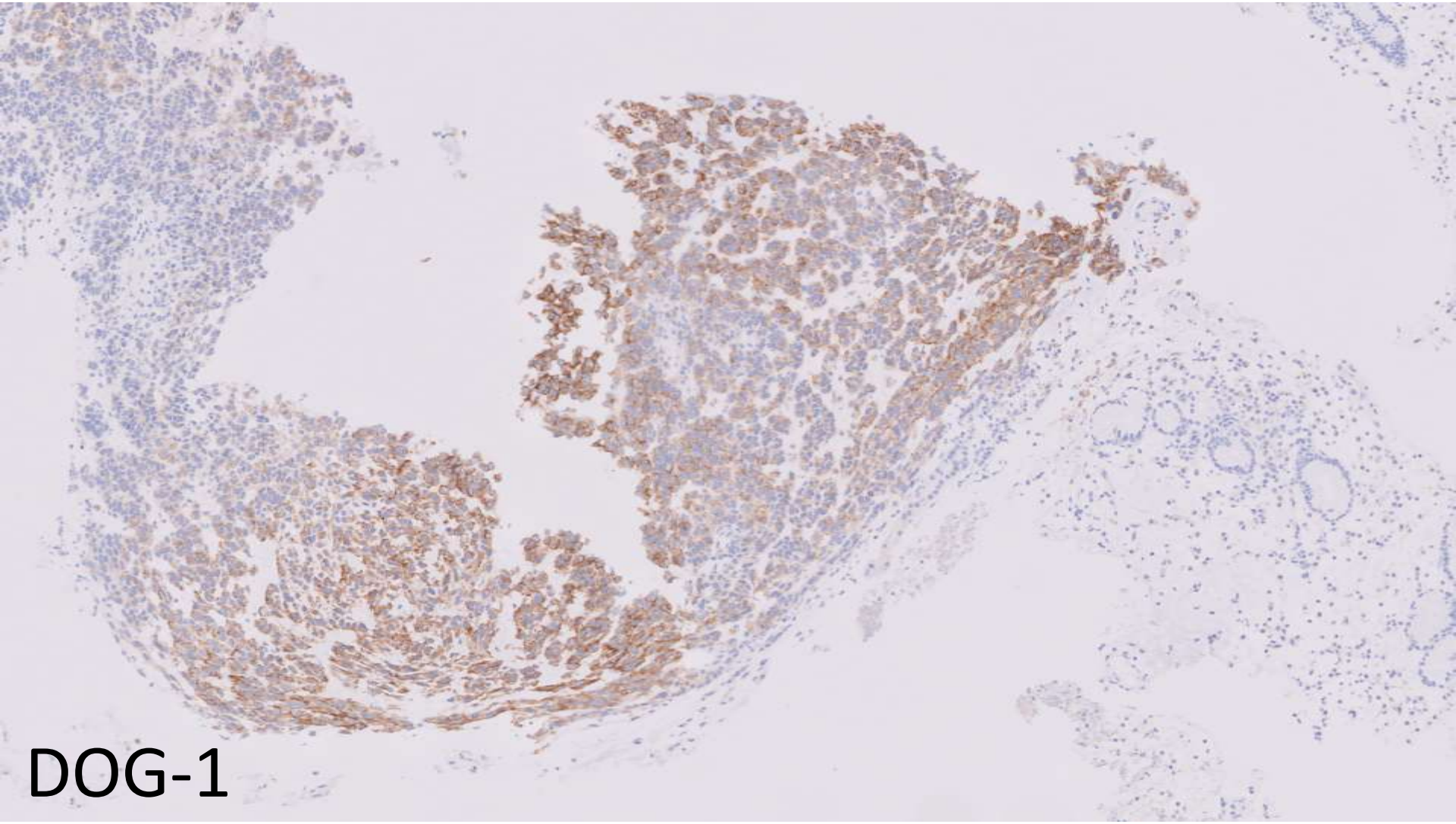
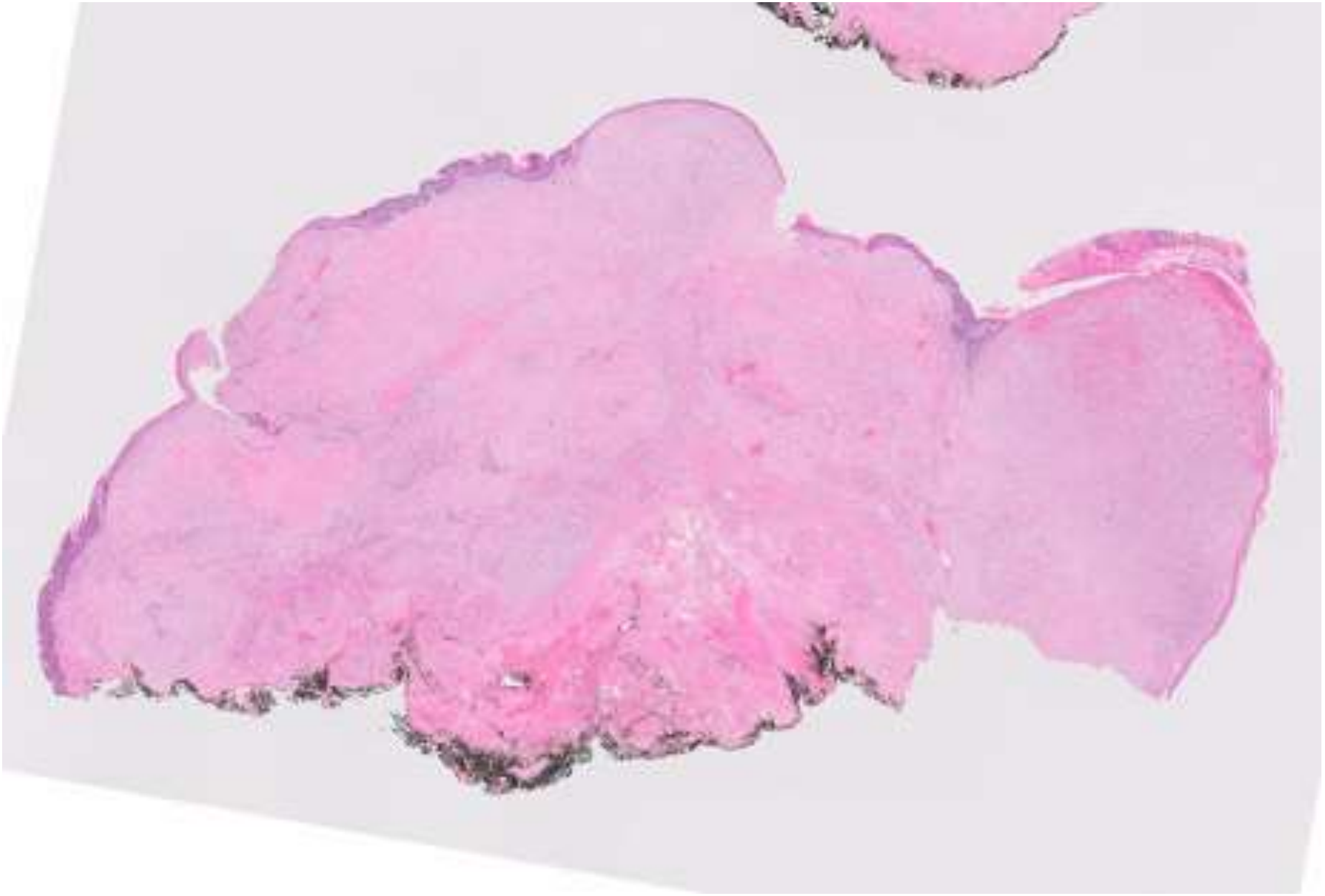
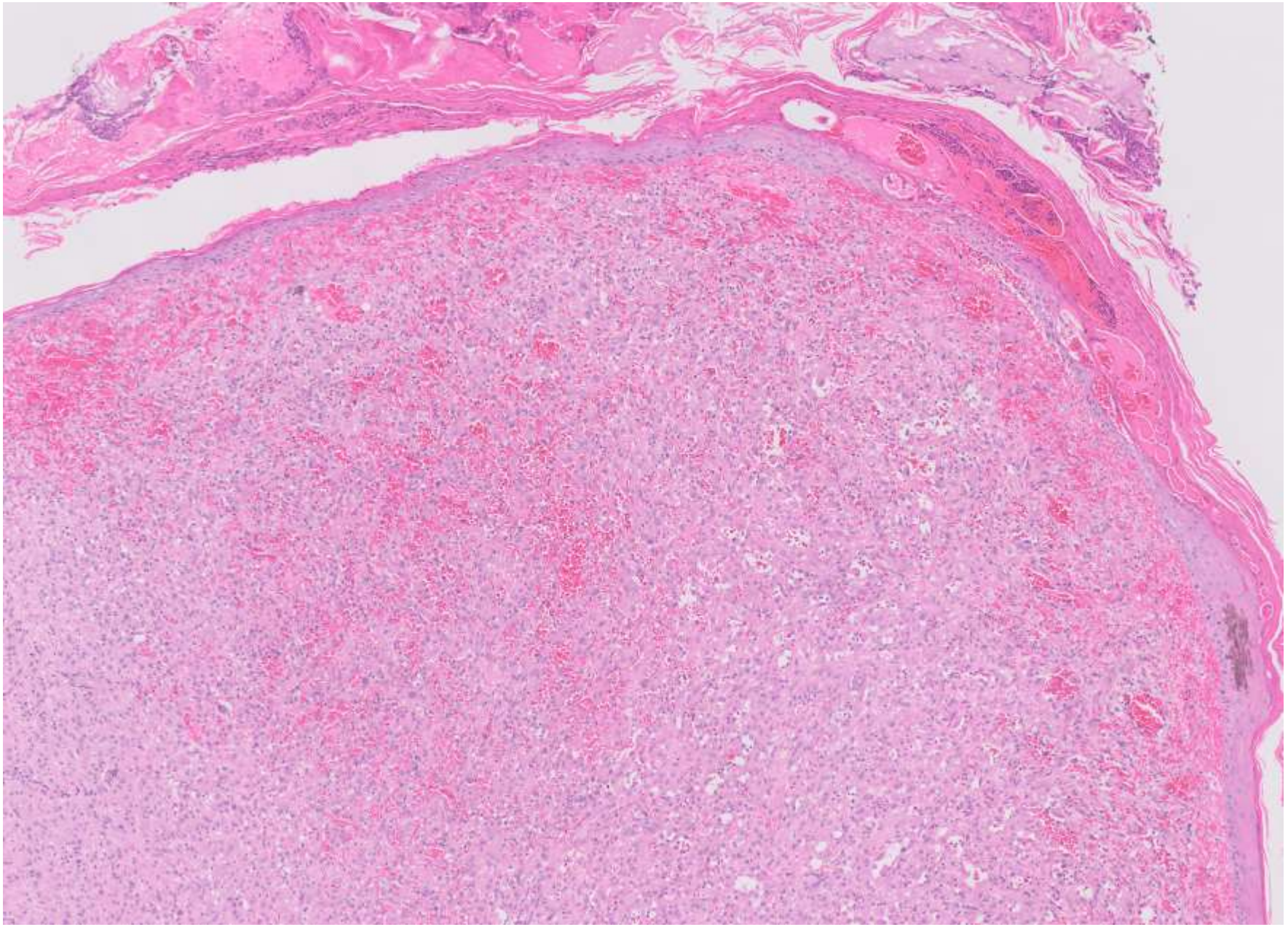

DOG-1

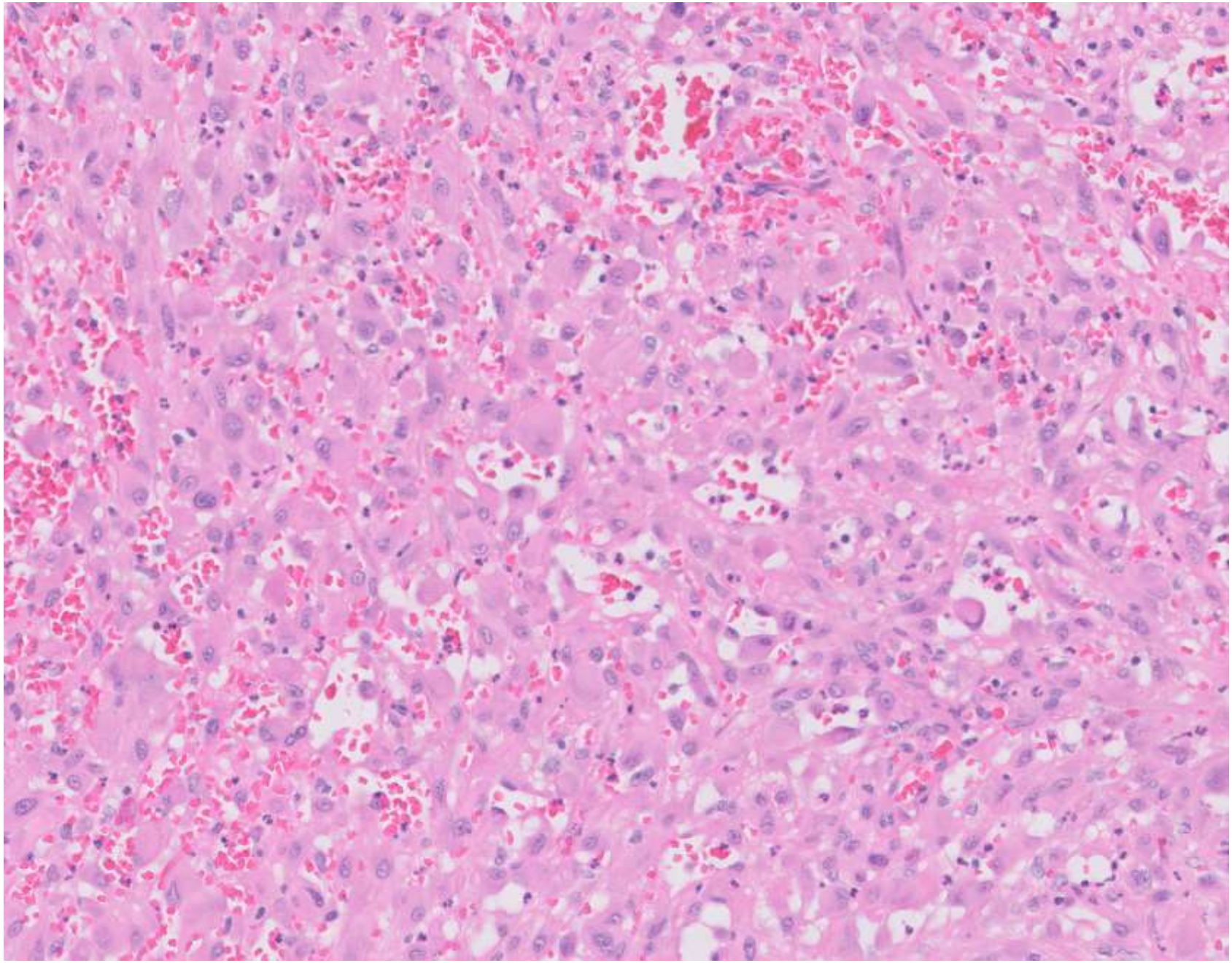
22-1002

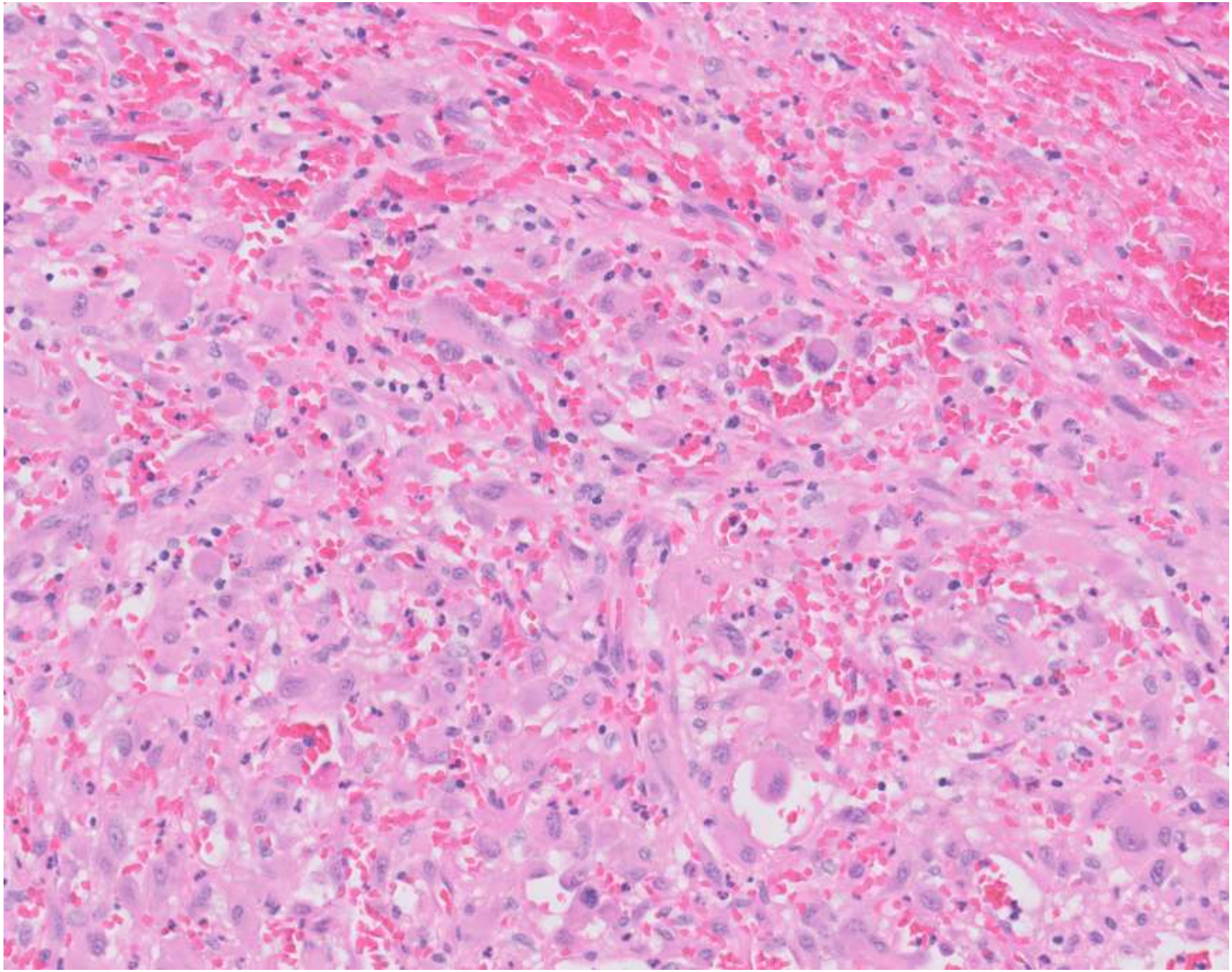
Emily Chan; UCSF

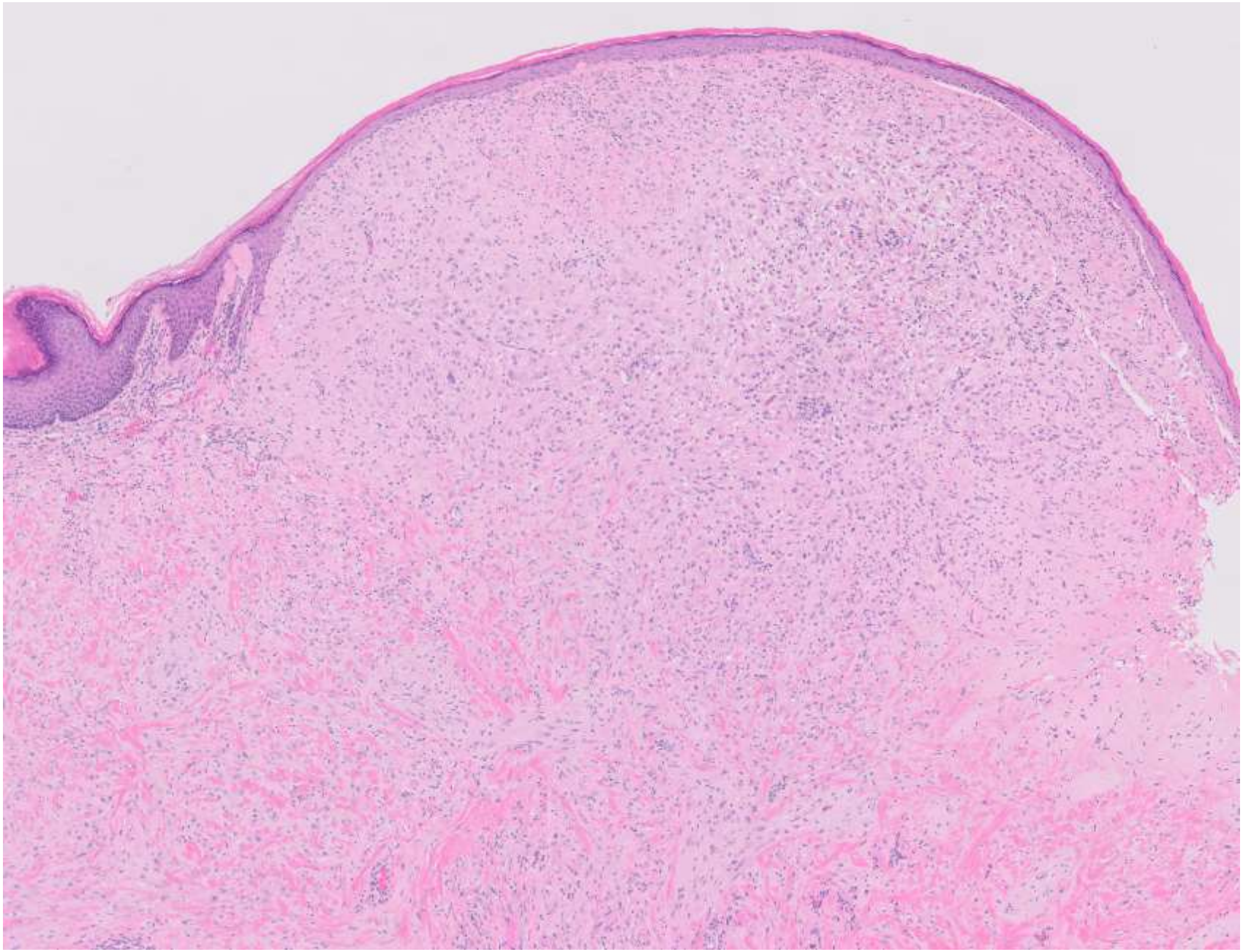
20ish M with multiple penile lesions, excisional biopsy performed.

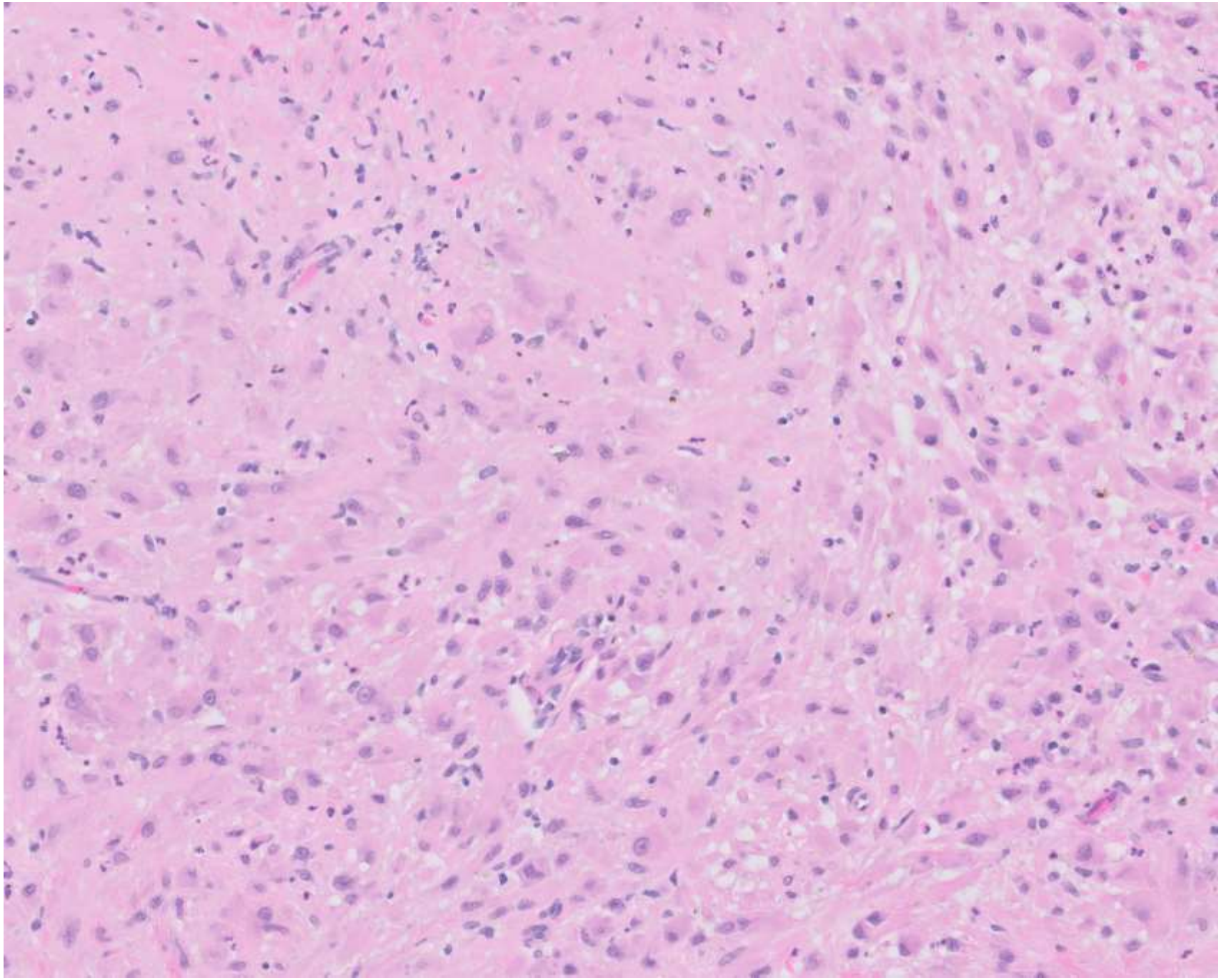


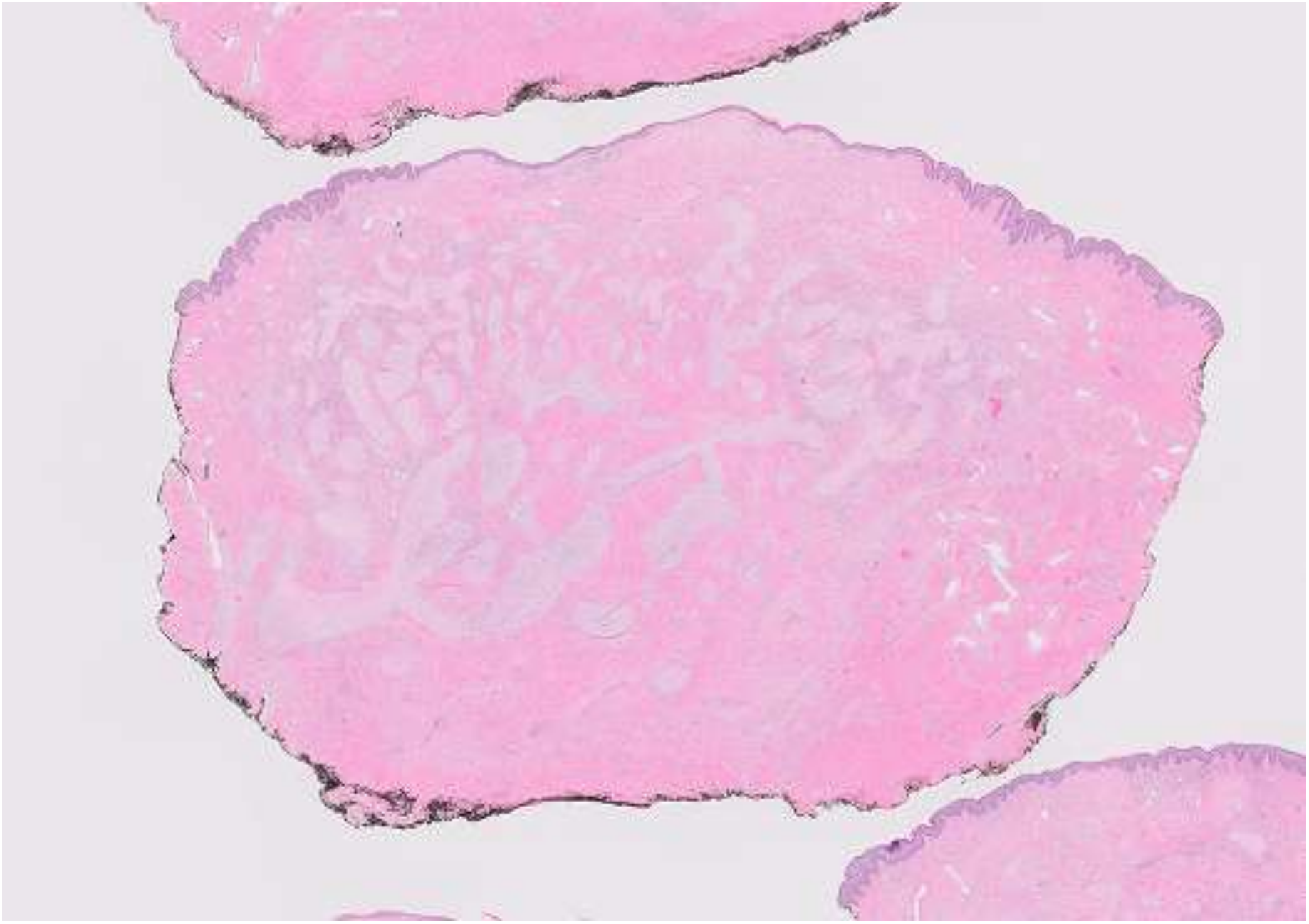


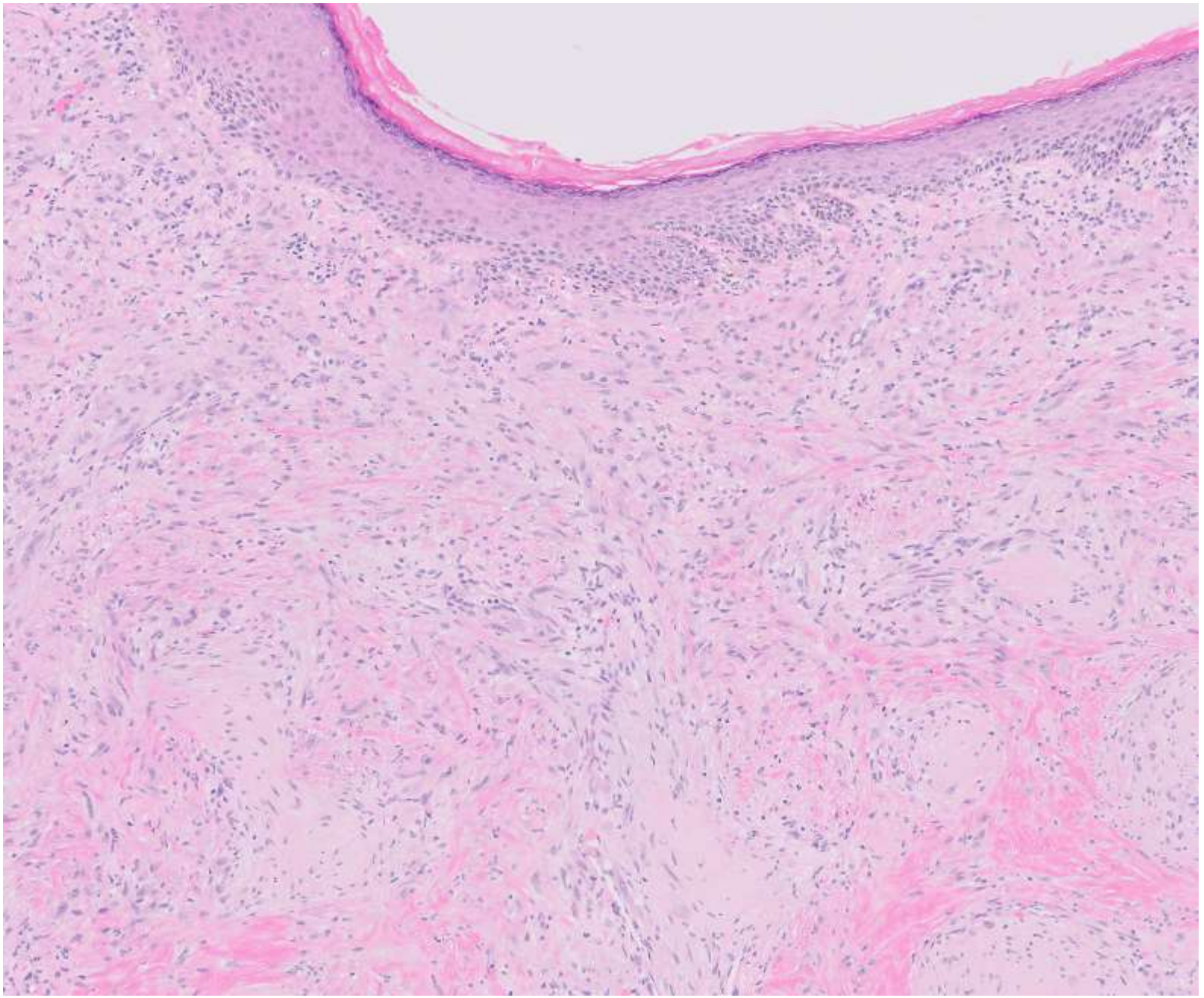


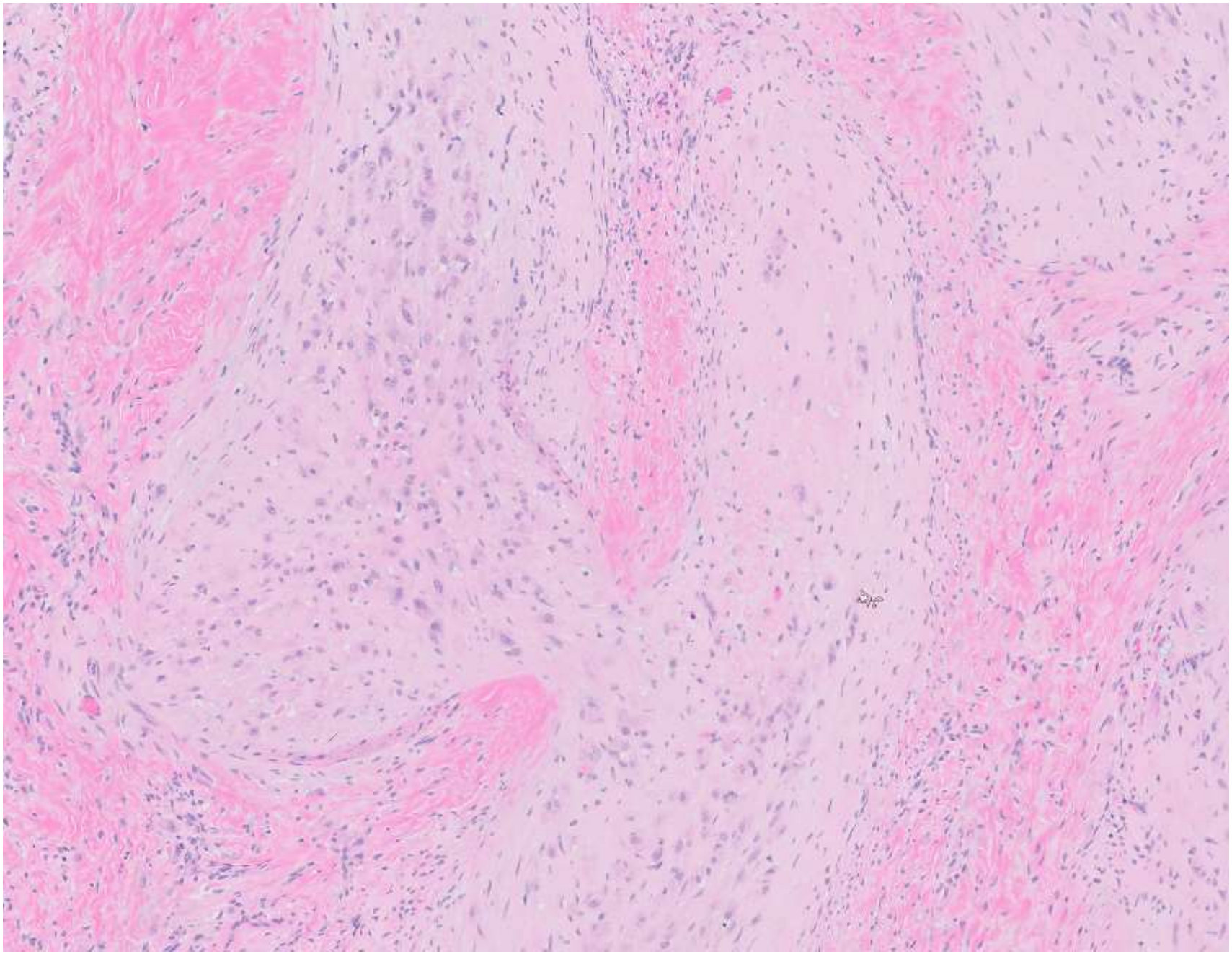


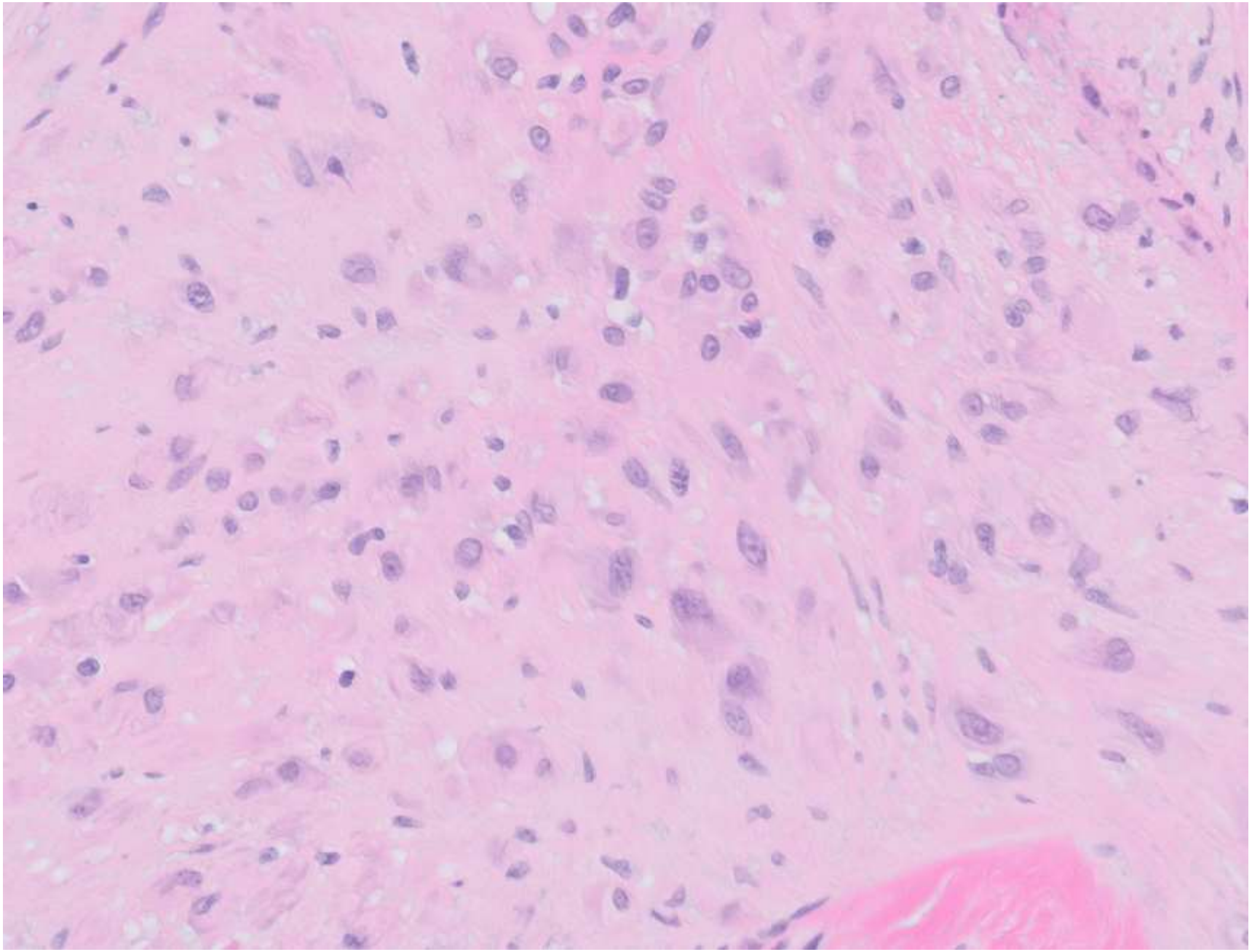


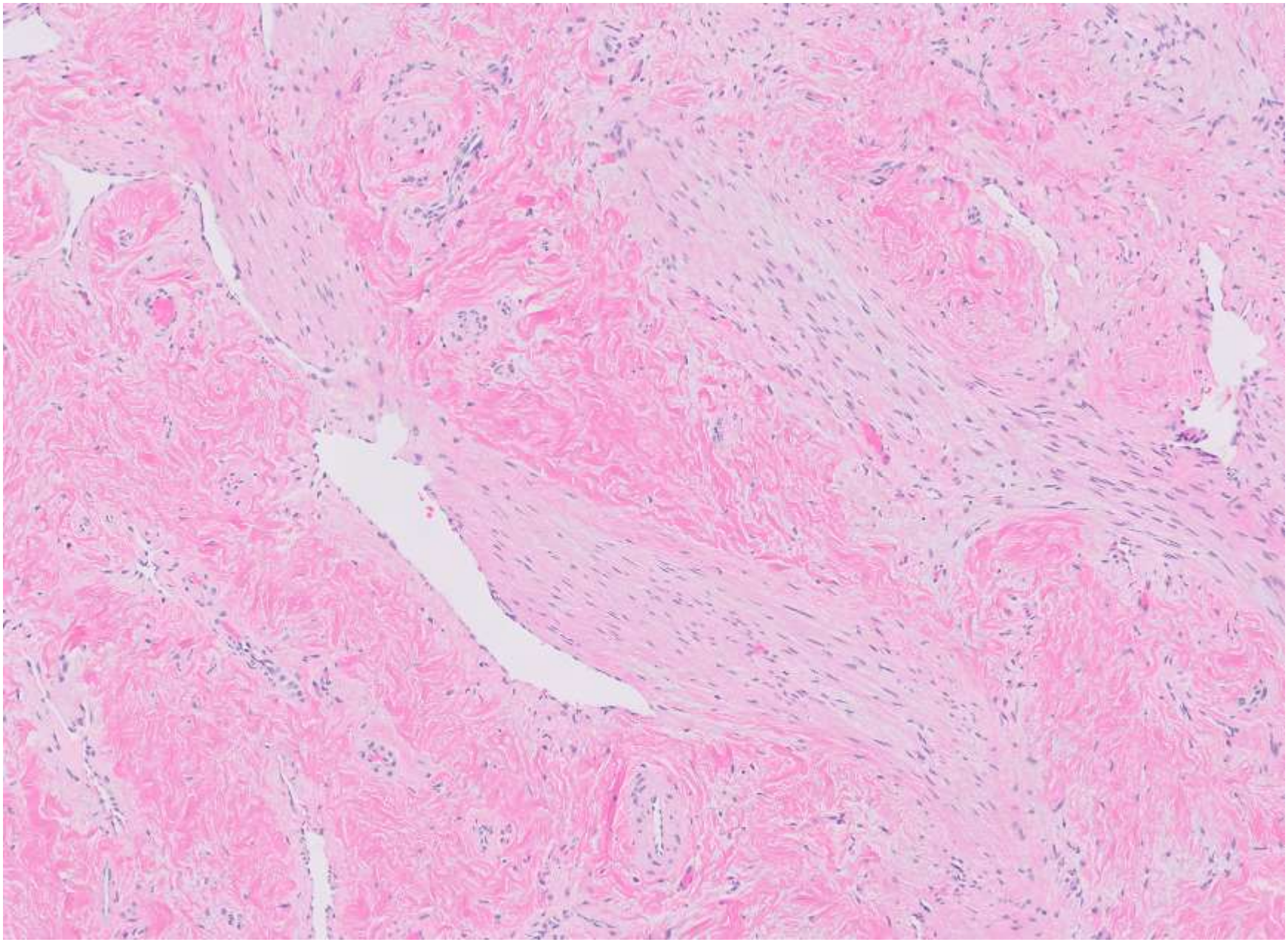




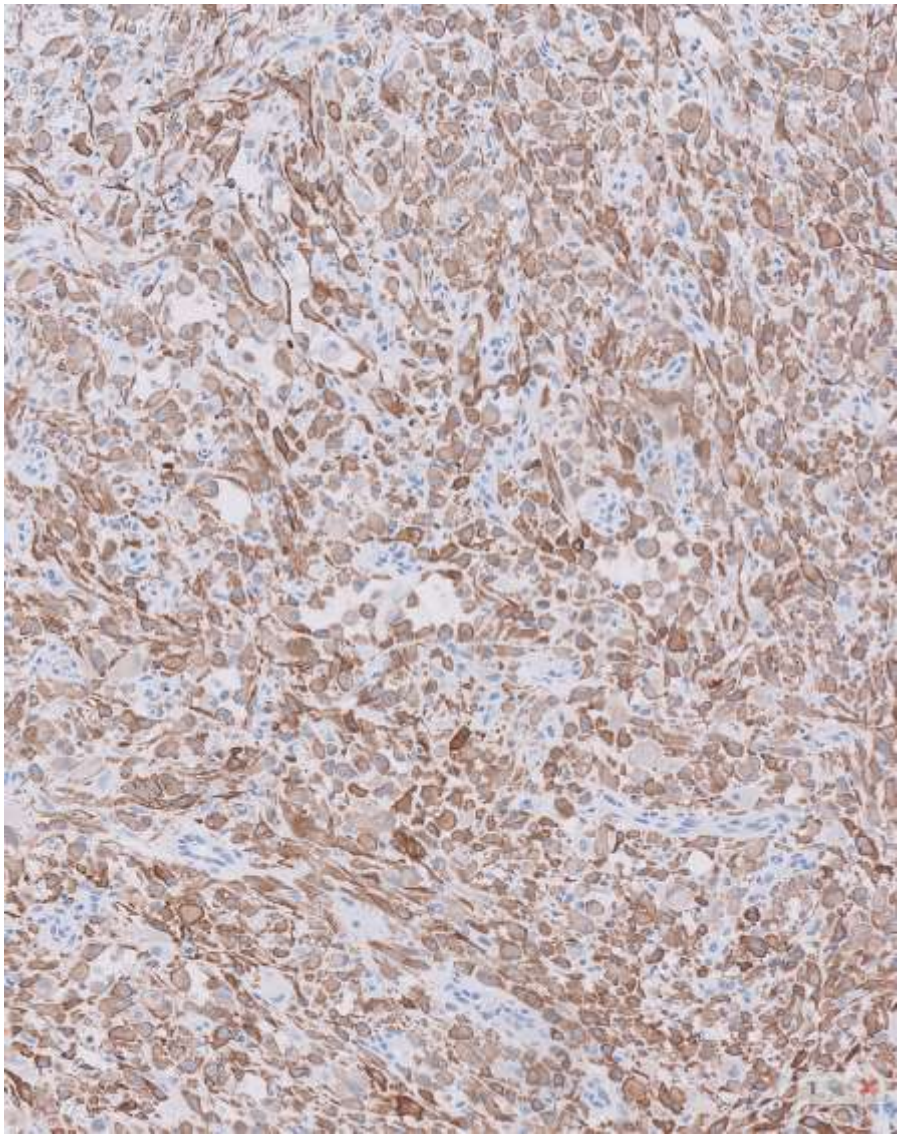


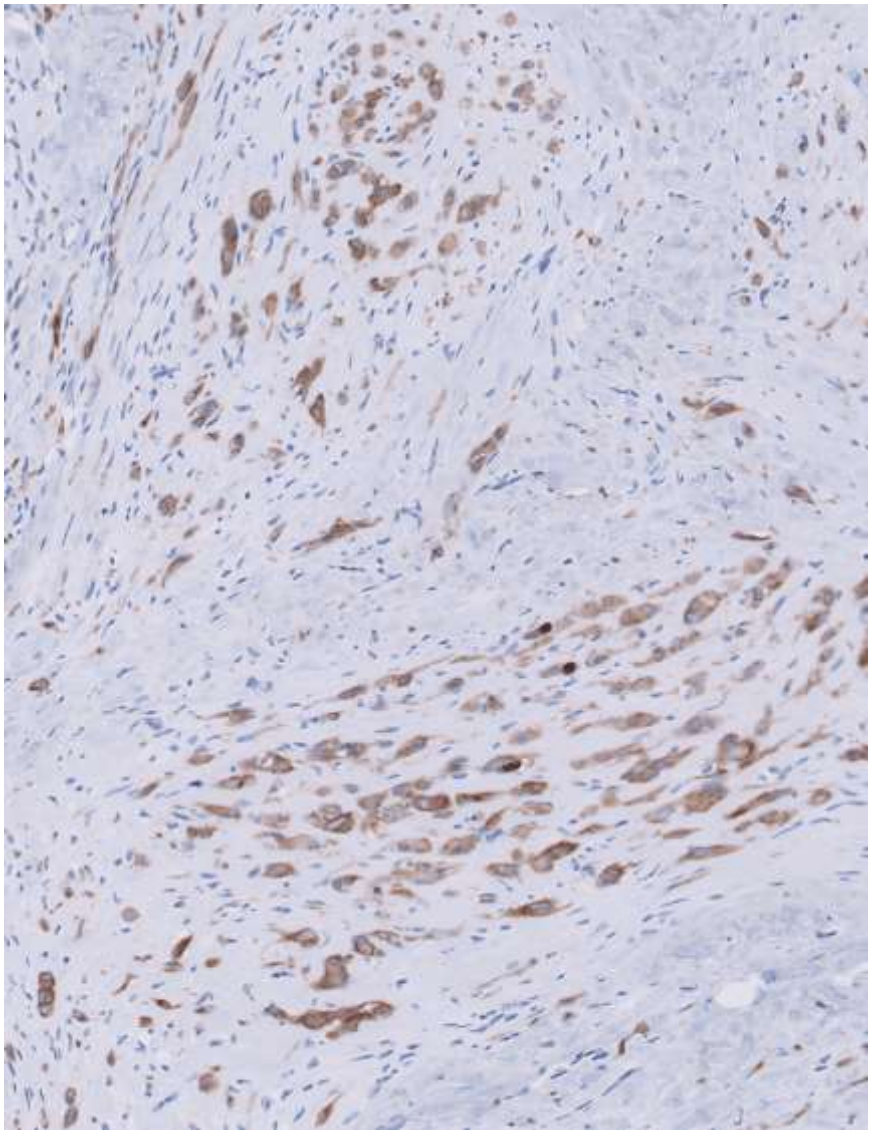




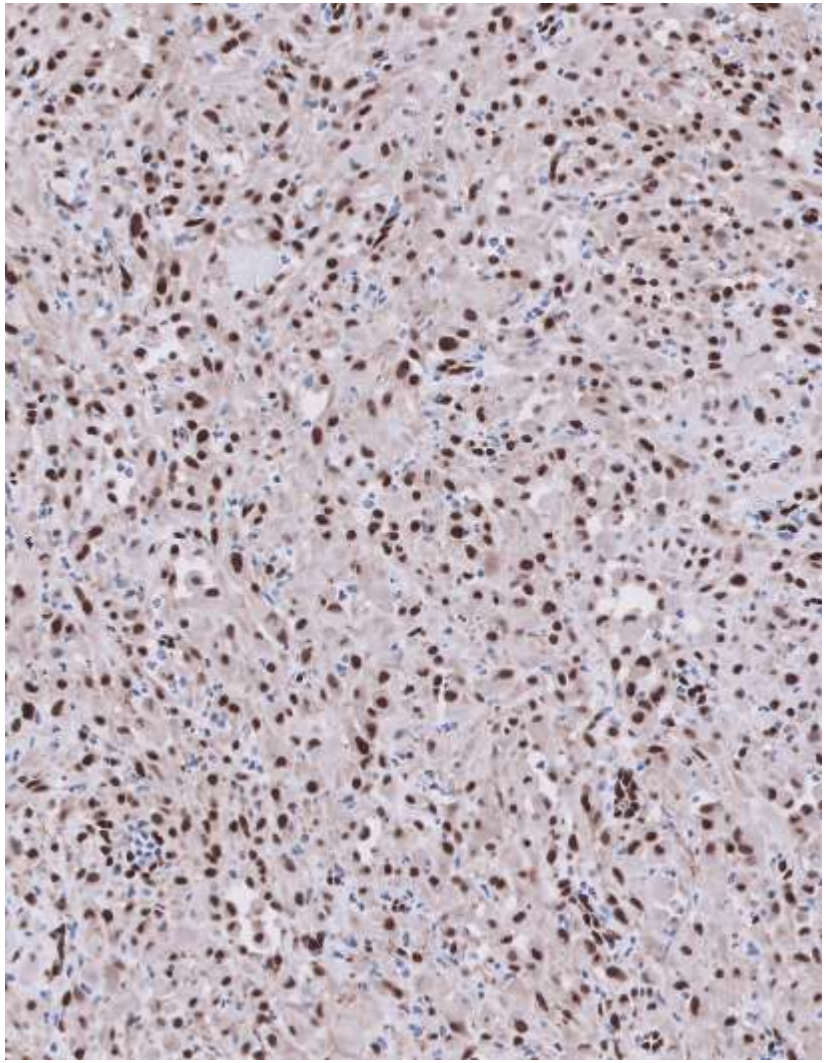


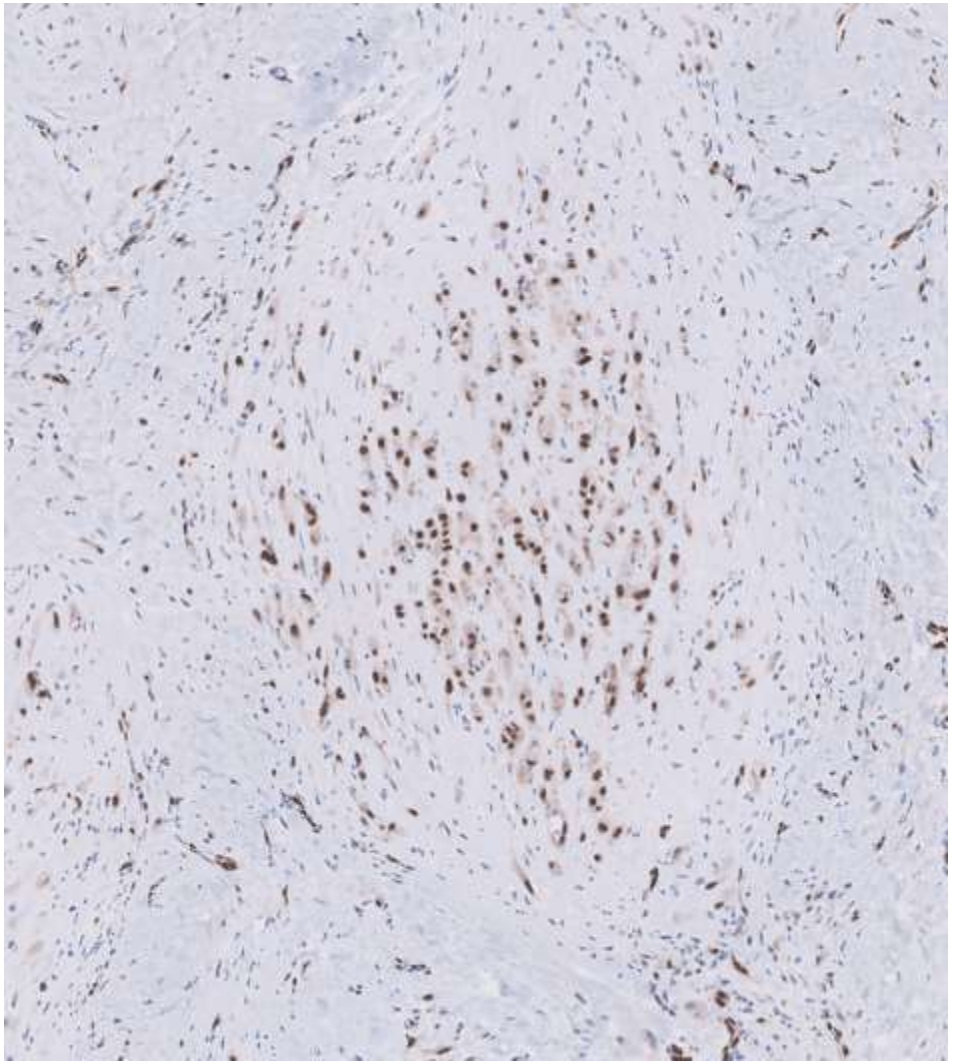
Pankeratin





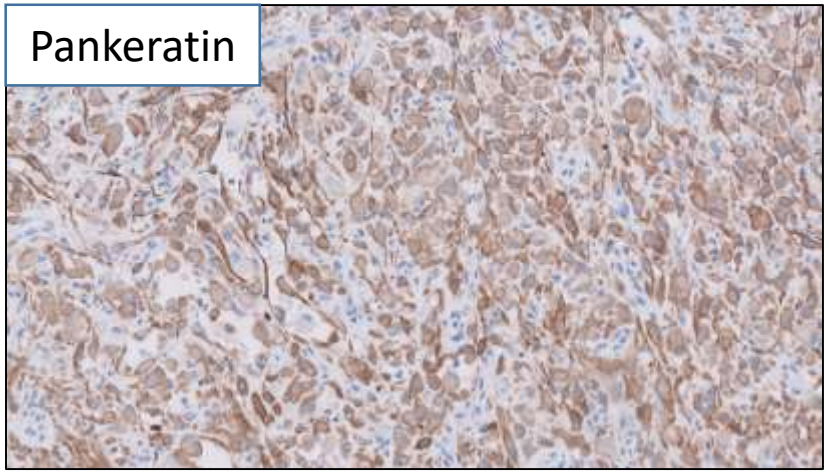
Erg

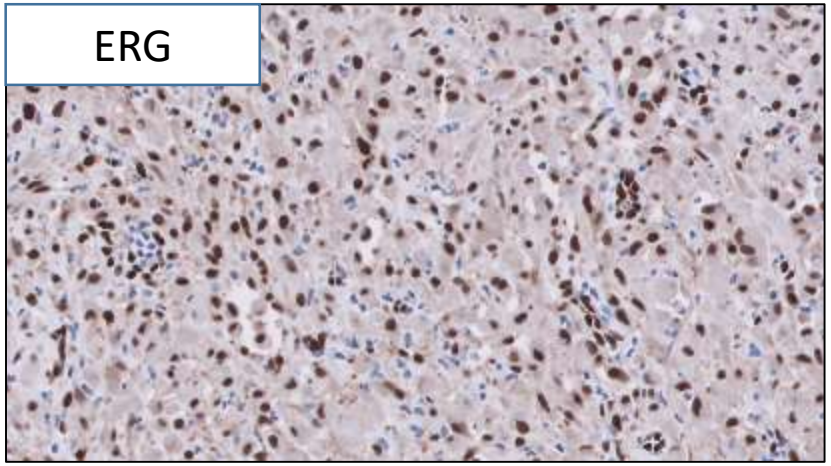




Additional Negative IHC

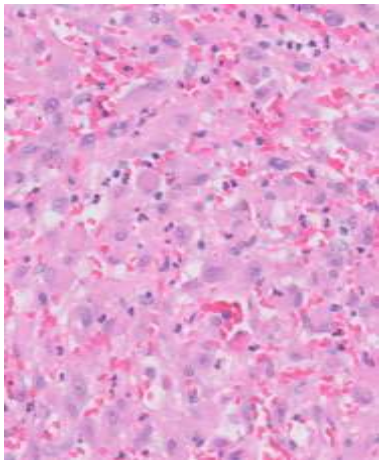
- SMA
- S100/SOX10
- ALK
- CD45
- CD68
- ALK
- CD34
- HHV8 (for Kaposi sarcoma)

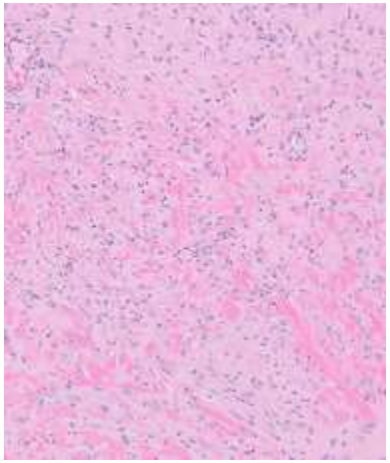


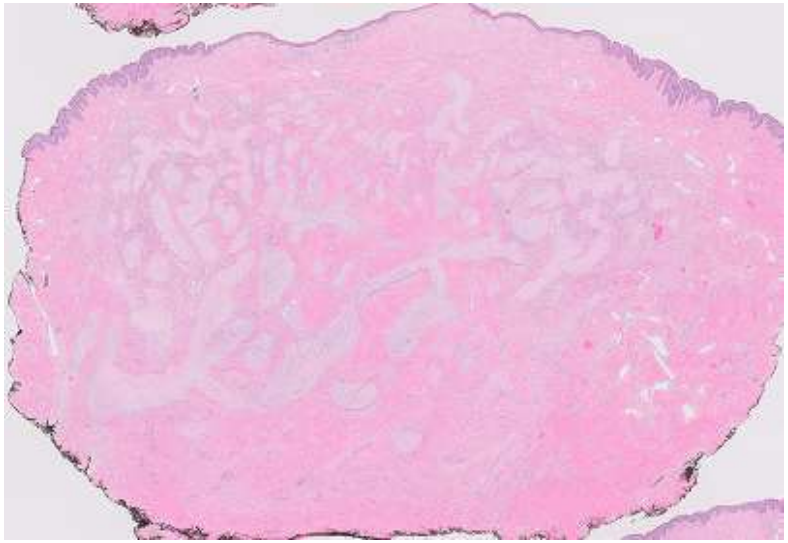


Case summary: Epithelioid endothelial neoplasm

- Multifocal, nodular, involving dermis and underlying erectile tissue
- Heterogenous morphology
- Low mitotic activity (rare up to 1 per 50 hpf)
- Intravascular growth
- Pankeratin and ERG positive but not vasoformative







Differential Diagnosis

- Epithelioid angiosarcoma
- Epithelioid sarcoma (ES)
- Epithelioid hemangioendothelioma (EHE)
- Pseudomyogenic hemangioendothelioma (PMHE)

?Epithelioid angiosarcoma

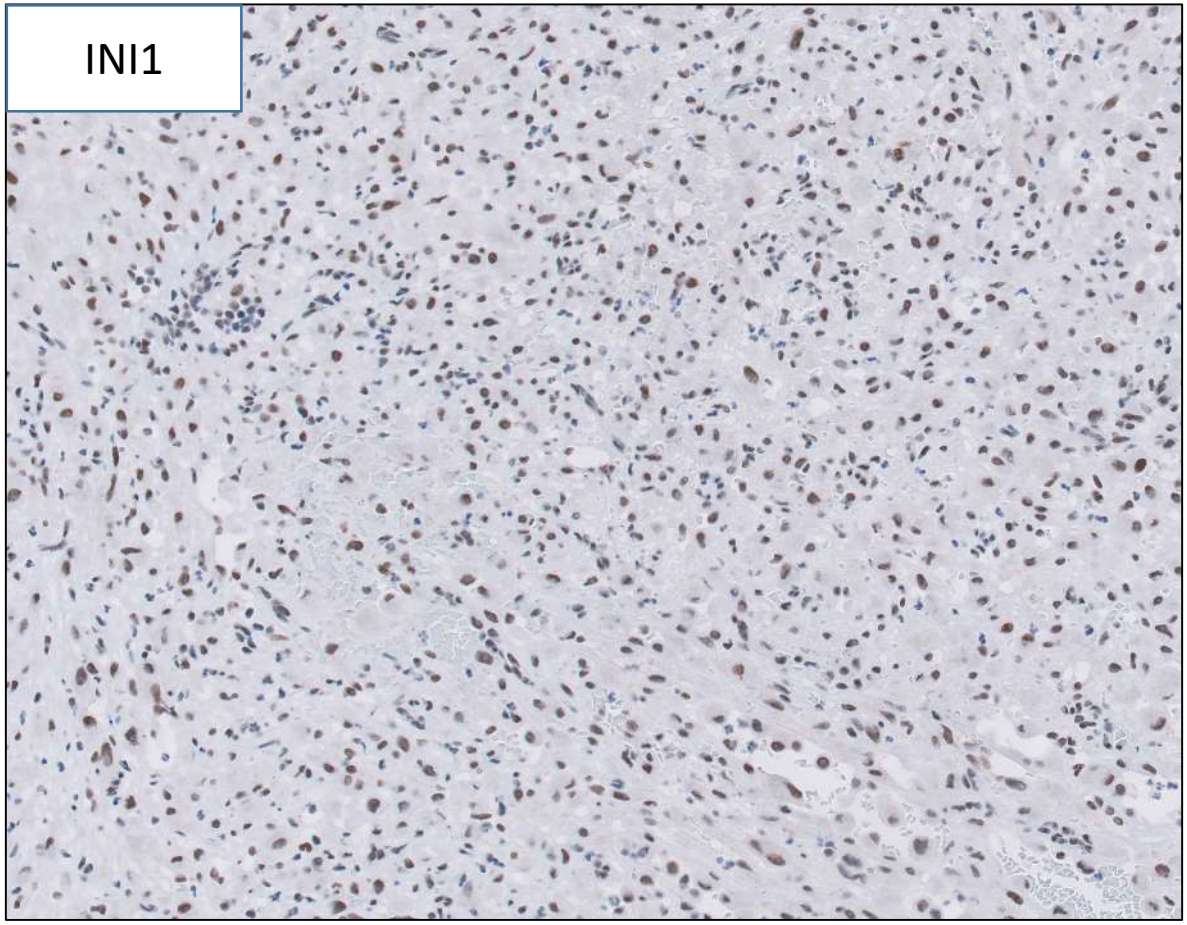
(a subset of angiosarcomas)

- Typically older patient, rapidly growing ill-defined
- Histo: Usually still shows a mix of vasoformative and non-vasoformative patterns
  - High-grade morphology, more atypical cells, mitotic activity, and necrosis
- Malignant: highly aggressive with >50% death within 1 year
- IHC: vascular markers+; can pick up keratin
- Molecular: not really helpful (genetically heterogenous with generally complex karyotypes)

?Epithelioid sarcoma (ES)

- Wide age range with “classic” and “proximal” subtypes
  - “Classic” more likely to be dermal/subq and affect young adults as multiple nonhealing ulcers
- Histo: Cellular nodules of epithelioid and spindled tumor cells with central degeneration and/or necrosis
  - Vague granulomatous appearance
- Malignant: high rate of recurrence and metastases
- IHC: Keratin positive, INI loss
  - can see ERG expression in 40-67%
- Molecular: *SMARCB1* (*INI1*) deletion (22q11)

?Epithelioid sarcoma (ES)

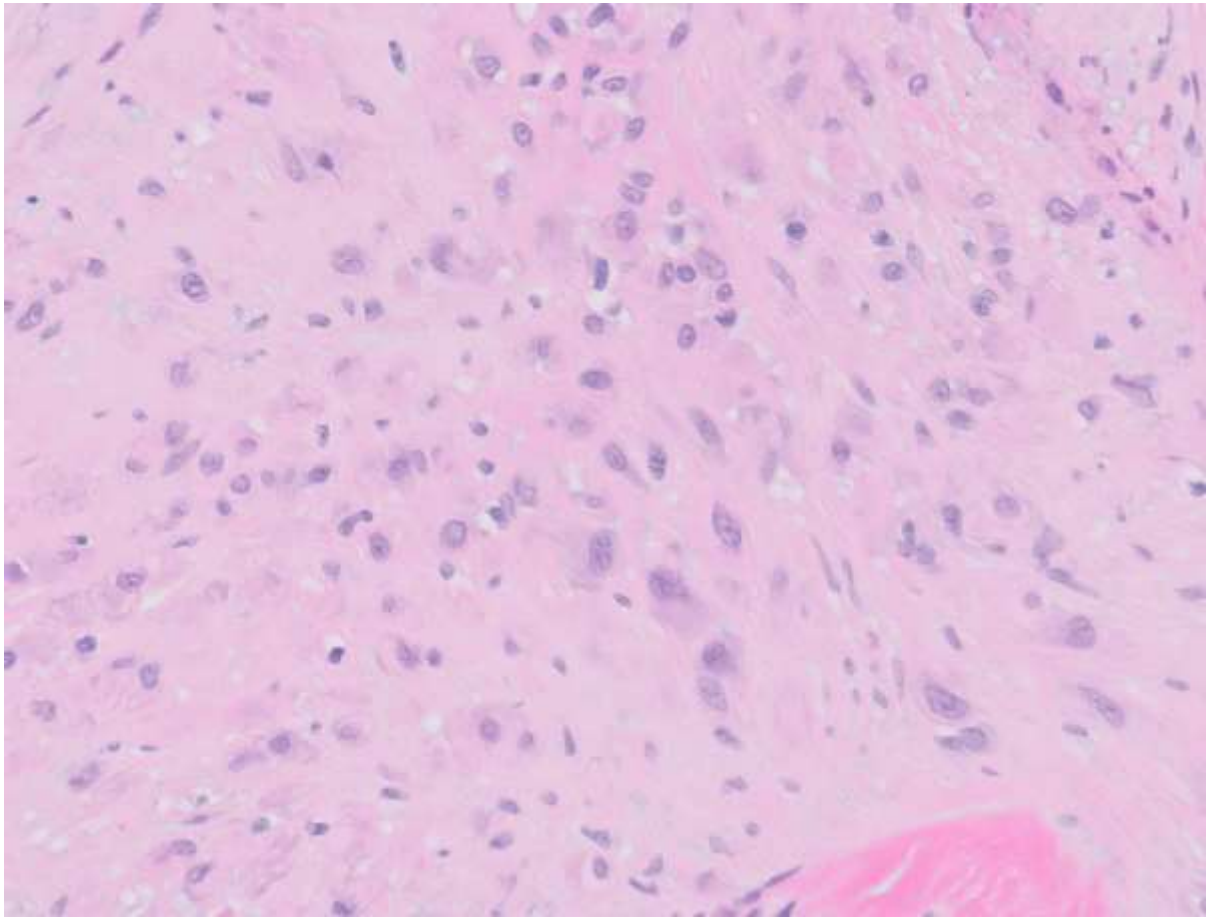


Retained (negative test result)

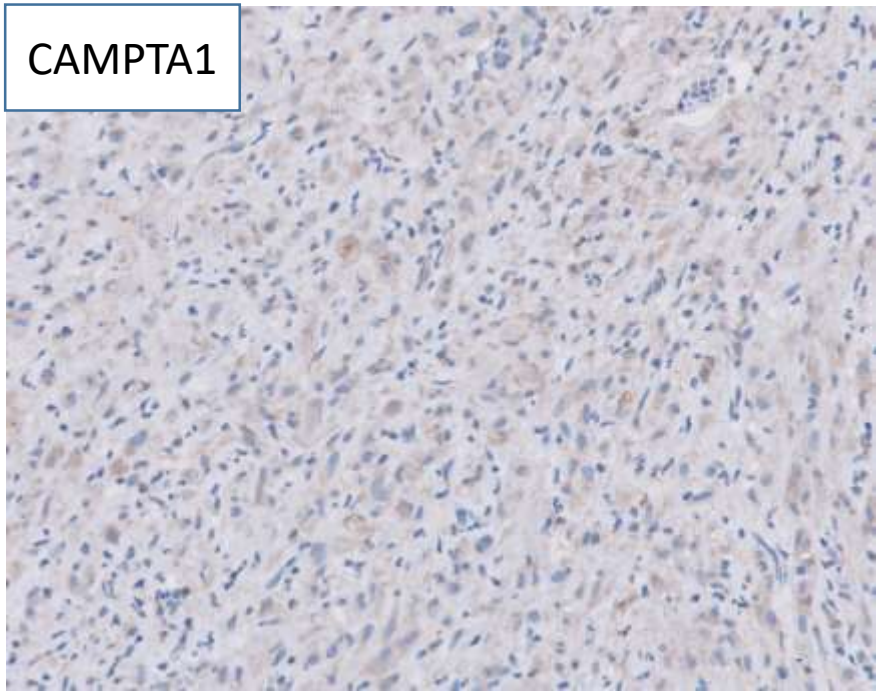
?Epithelioid hemangioendothelioma (EHE)

- 30-50 yo most common, solitary, often painful
- Histo: cords and nests of cells within a myxohyaline stroma
  - Infiltrative growth
  - Intracytoplasmic lumina common “blister cells”, lack of well-formed vascular channels
  - Involvement of larger vessels common
- Metastases in 20-30%, mortality rate 10-20% (large and with increased mitotic activity)
- IHC: CD34, CD31, FLI1 and ERG+, 40% express keratins
- Molecular: t(1;3) with *WWTR1-CAMTA1* fusion
  - Subset with *YAP1-TFE3* fusion

Blister cells and myxohyaline stroma???

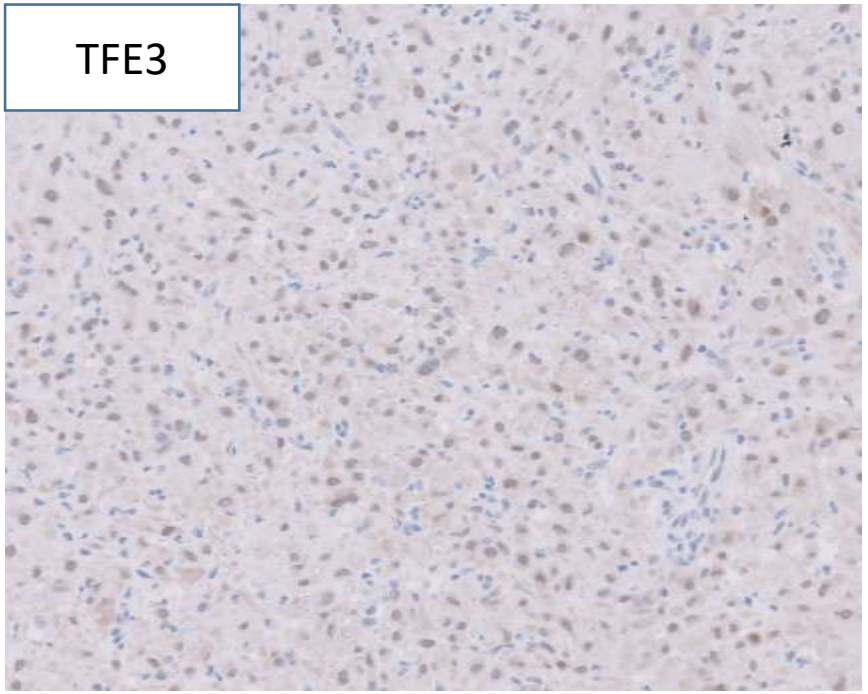


CAMPTA1



Negative (should be nuclear)

TFE3



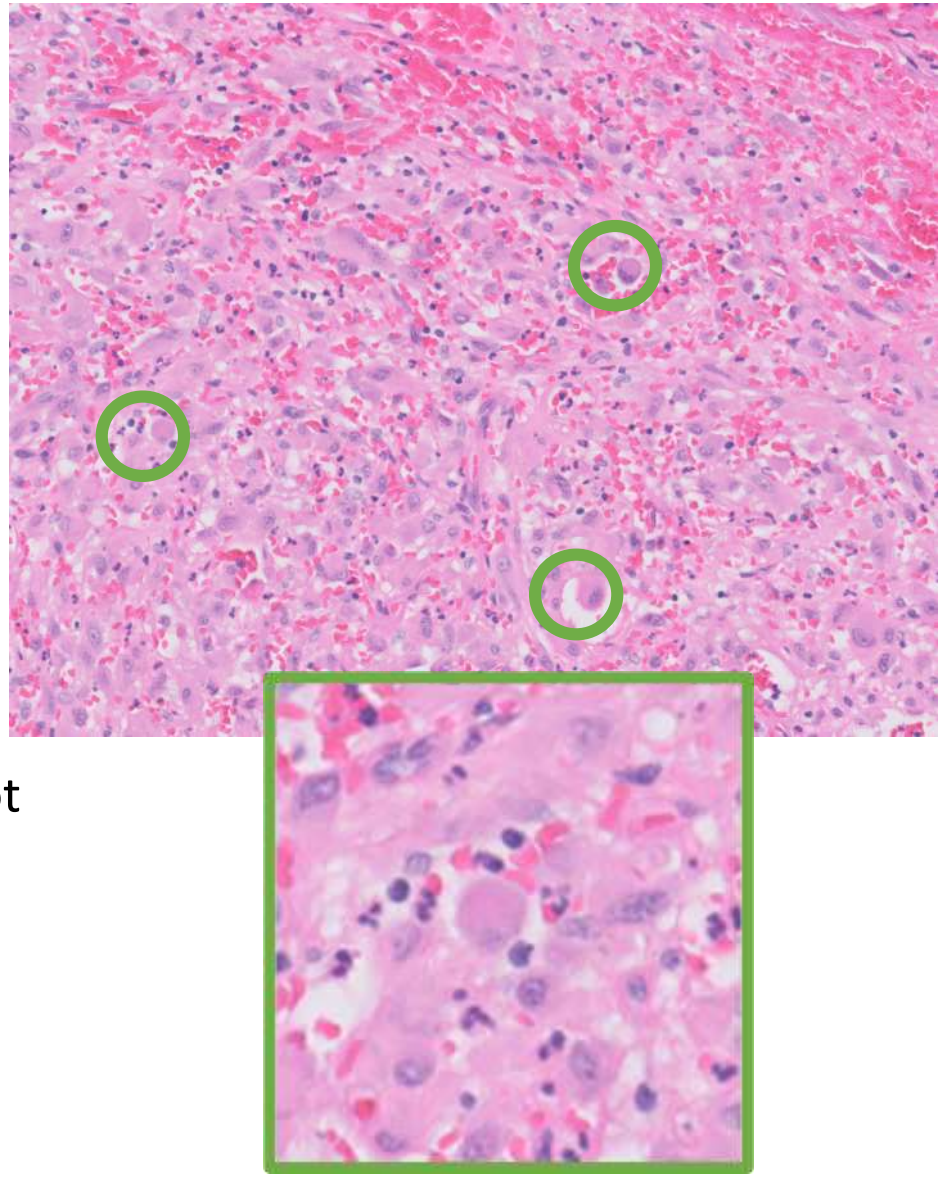
Negative (should be nuclear diffuse strong)

Pseudomyogenic hemangioendothelioma

- Young adults (mean 30 years) with male predilection
- Site:
  - Lower extremities (55%), upper limbs and trunk (20%), head and neck (5%)
  - Cutaneous/subcutaneous (75%), intramuscular (50%), lytic bone lesions (20%)
- Multicentric/multifocal nodular growth common, involving multiple tissue planes
- Borderline malignant potential
  - Approximately 60% experience early local recurrence
  - Mets uncommon (<5%), usually very late
- Molecular: T(7;19)(q22;q13) with SERPINE1-FOSB fusion

Pseudomyogenic hemangioendothelioma histology

- Ill-defined nodules, sheets, fascicles
- Plump spindled and epithelioid cells with abundant eosinophilic cytoplasm
- Relatively small uniform/bland nuclei
- Some cells may resemble rhabdomyoblasts
- Usually scant mitoses
- Absent well-developed vasoformation
- 50% contain prominent stromal neutrophils
- Diffuse keratin expression (AE1/AE3, not MNF116) and ERG; 50% positive for CD31



UCSF500 on current case:

PATHOGENIC AND LIKELY PATHOGENIC ALTERATIONS				
VARIANT	TRANSCRIPT ID	CLASSIFICATION	READS	MUTANT ALLELE FREQUENCY
SERPINE1: :FOSB fusion	NM_000602, NM_006732	Pathogenic	167	N/A

'Reads' indicates the number of unique DNA molecules sequenced. 'Mutant Allele Frequency' indicates the percentage of the reads with the respective 'Variant' and is affected by the degree of normal cell

Diagnosis: Pseudomyogenic hemangioendothelioma

ORIGINAL ARTICLES

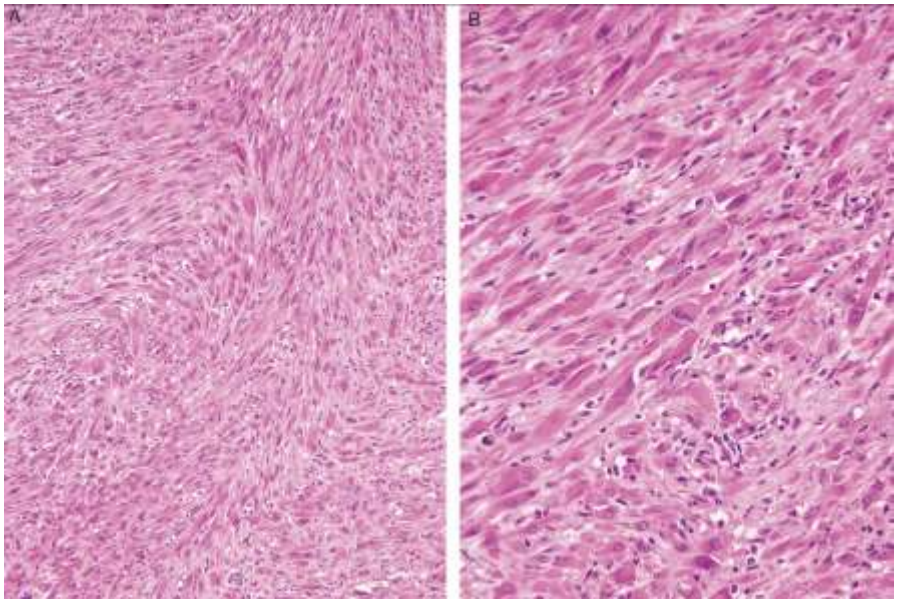
Pseudomyogenic Hemangioendothelioma

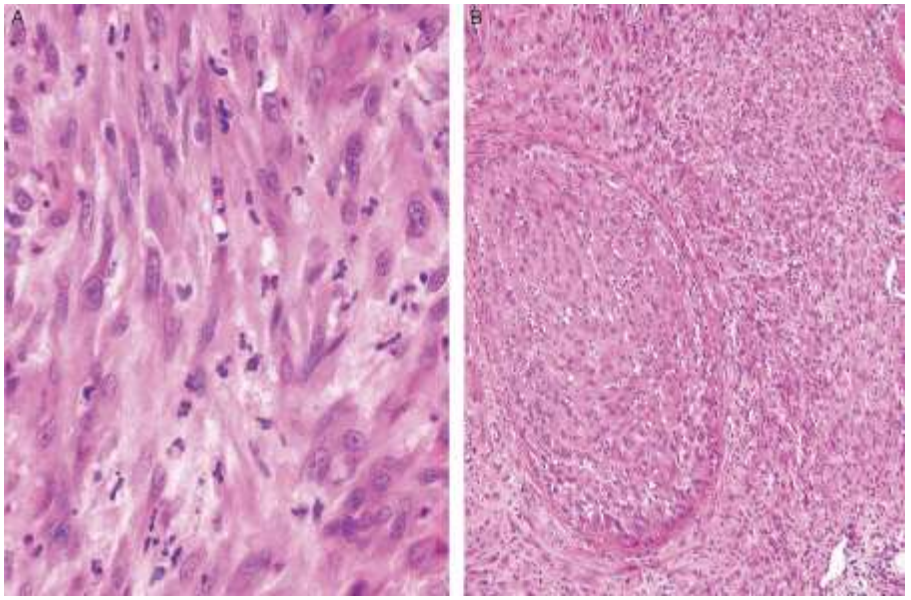
A Distinctive, Often Multicentric Tumor With Indolent Behavior

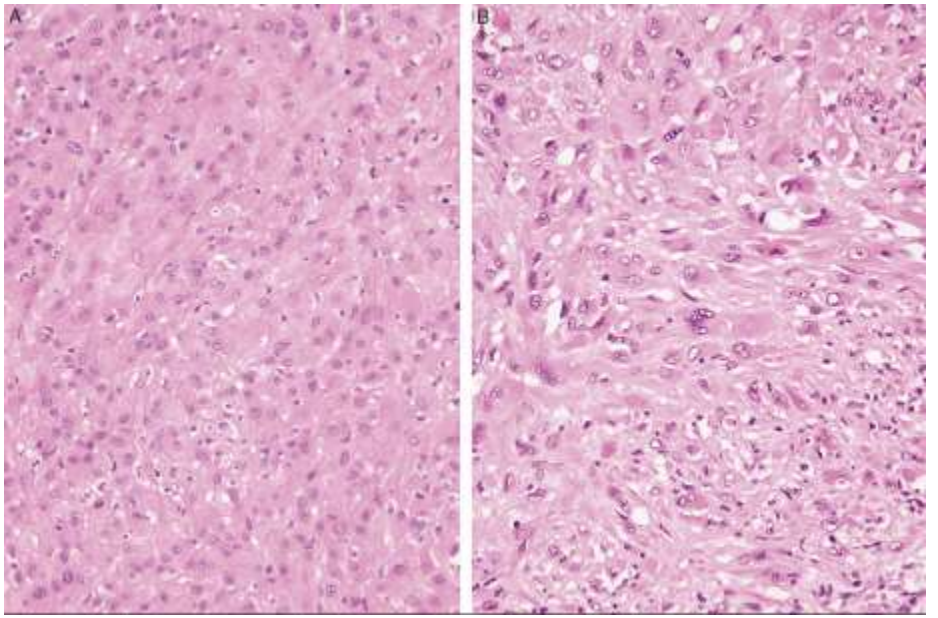
Hornick, Jason L. MD, PhD; Fletcher, Christopher D.M. MD, FRCPath

Author Information

The American Journal of Surgical Pathology: February 2011 - Volume 35 - Issue 2 - p 190-201
doi: 10.1097/PAS.0b013e3181ff0901







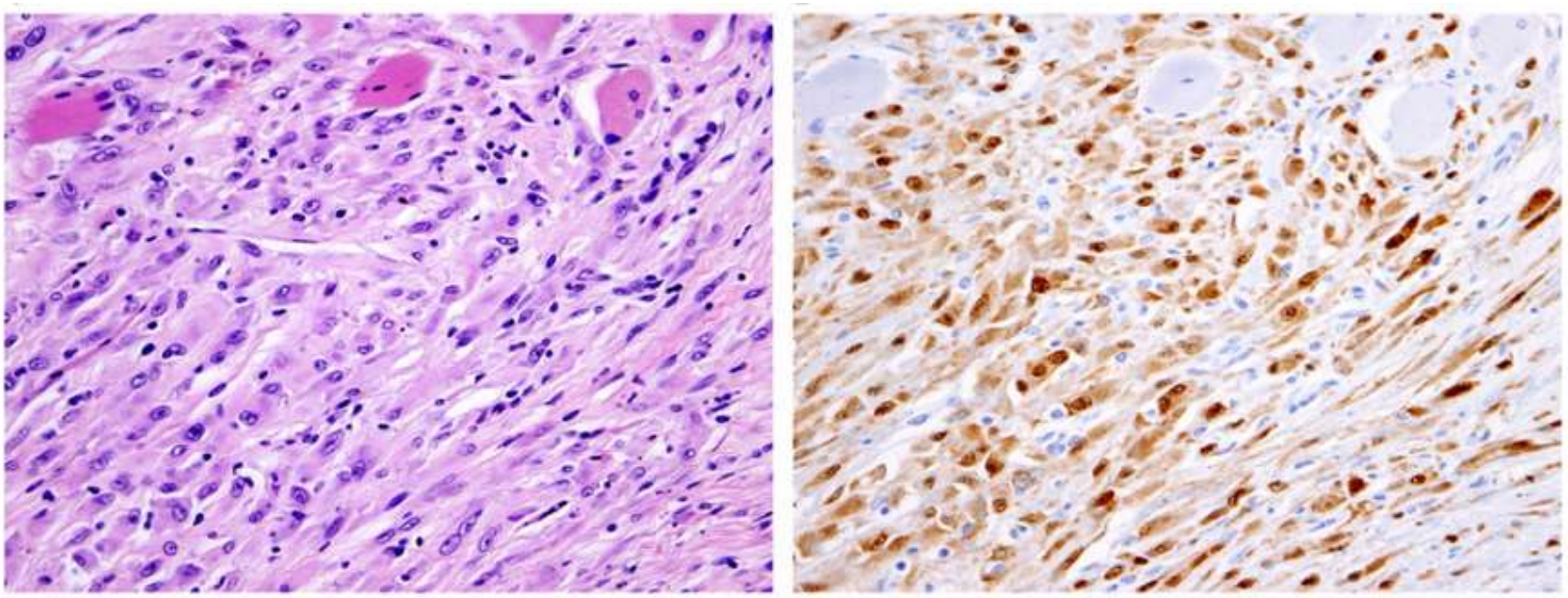
ORIGINAL ARTICLES

FOSB is a Useful Diagnostic Marker for Pseudomyogenic Hemangioendothelioma

Hung, Yin P. MD, PhD; Fletcher, Christopher D.M. MD, FRCPath; Hornick, Jason L. MD, PhD

Author Information

The American Journal of Surgical Pathology: May 2017 - Volume 41 - Issue 5 - p 596-606
doi: 10.1097/PAS.0000000000000795



Take home points: Pseudomyogenic hemangioendothelioma (PMHE)

- Consider PMHE when approached with a uniform bland soft tissue tumor with brightly eosinophilic cytoplasm
- PMHE is keratin (AE1/AE3) and ERG positive
- PMHE molecularly defined by SERPINE1-FOSB fusion
  - FOSB IHC is available in some laboratories
- Differential diagnosis of keratin and vascular marker positive infiltrative appearing tumors includes EHE, ES, and epithelioid angiosarcoma
  - Compared to these, PMHE is only borderline malignant

22-1003

Brent Tan; Stanford

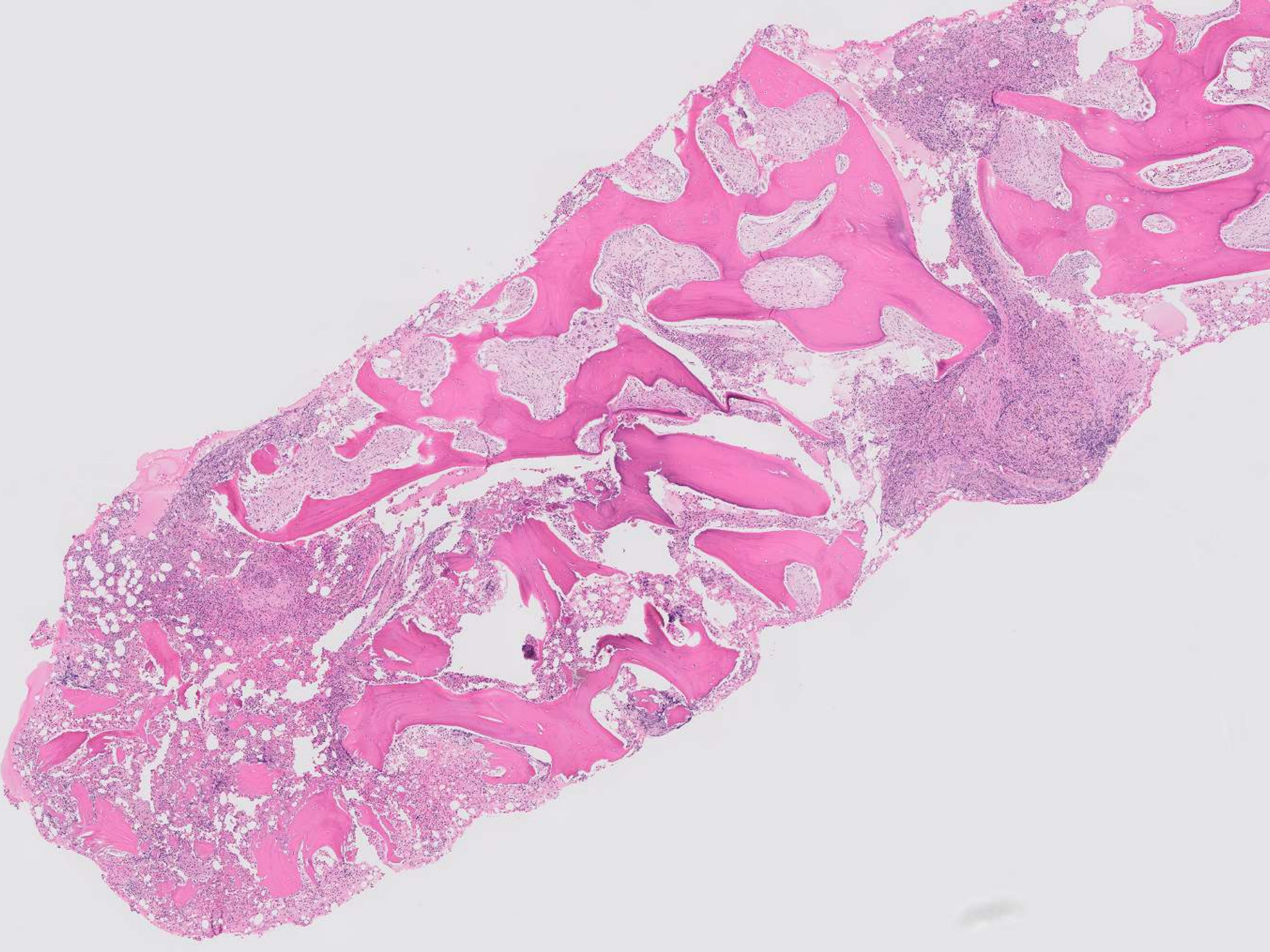
40ish M with pathologic left femur fracture, multiple lytic bone lesions throughout skeleton. Prior hip biopsy showed a giant cell rich lesion. Bone marrow biopsy performed.

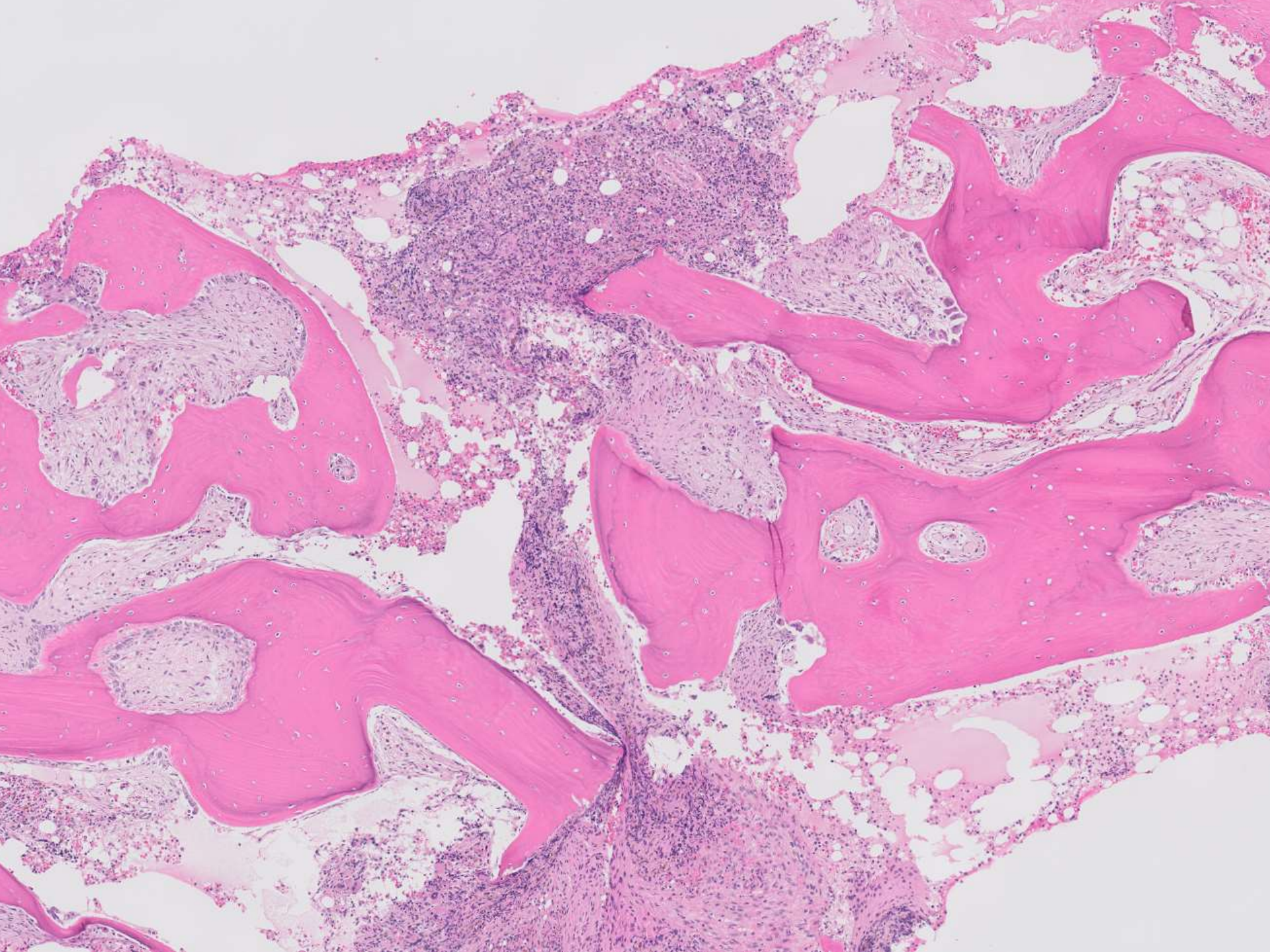
Clinical history

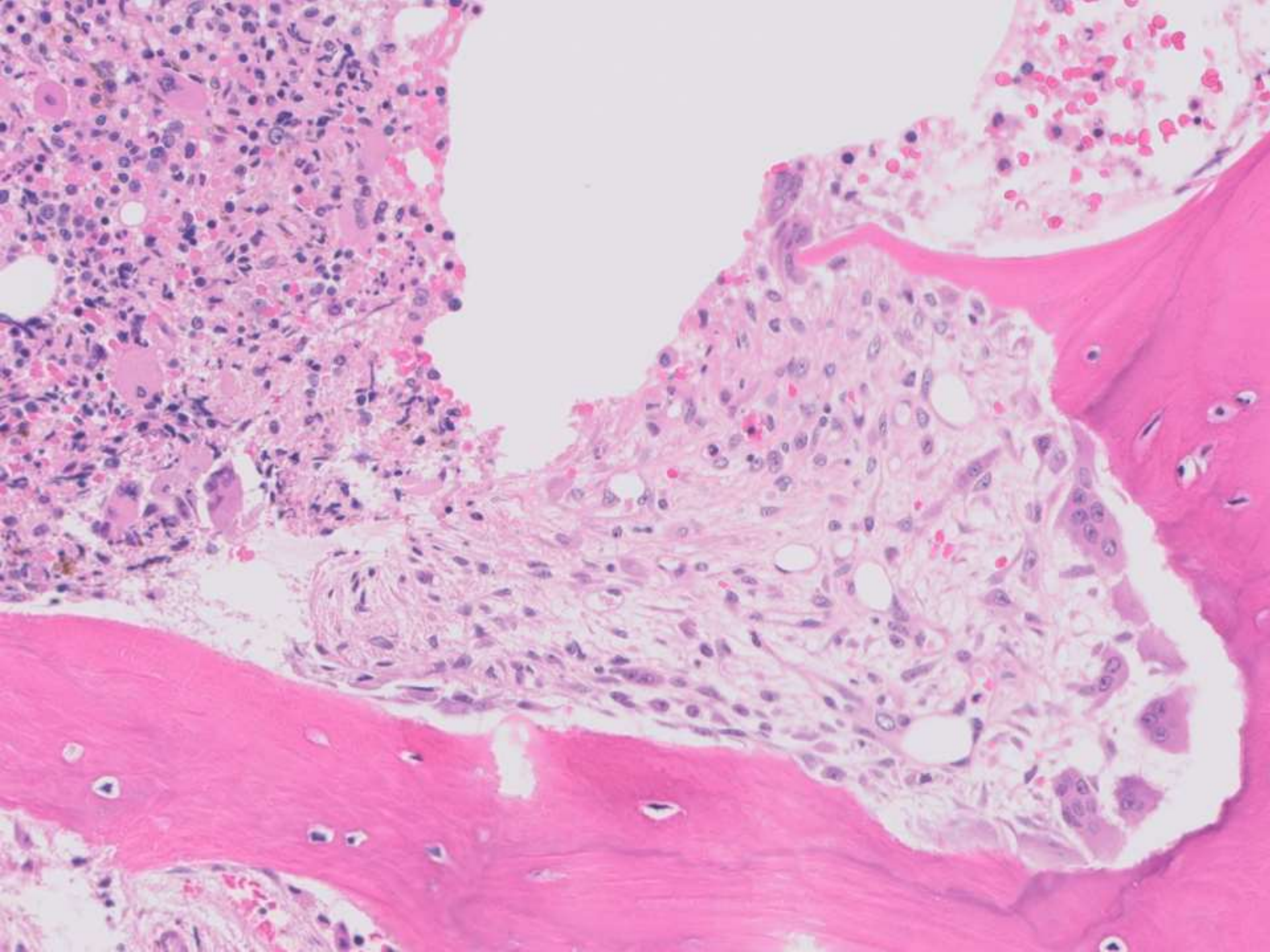
A 40ish man with a history of end-stage renal disease presented with hip pain and was found on imaging to have a pathologic left femur fracture and multiple lytic bone lesions throughout skeleton.

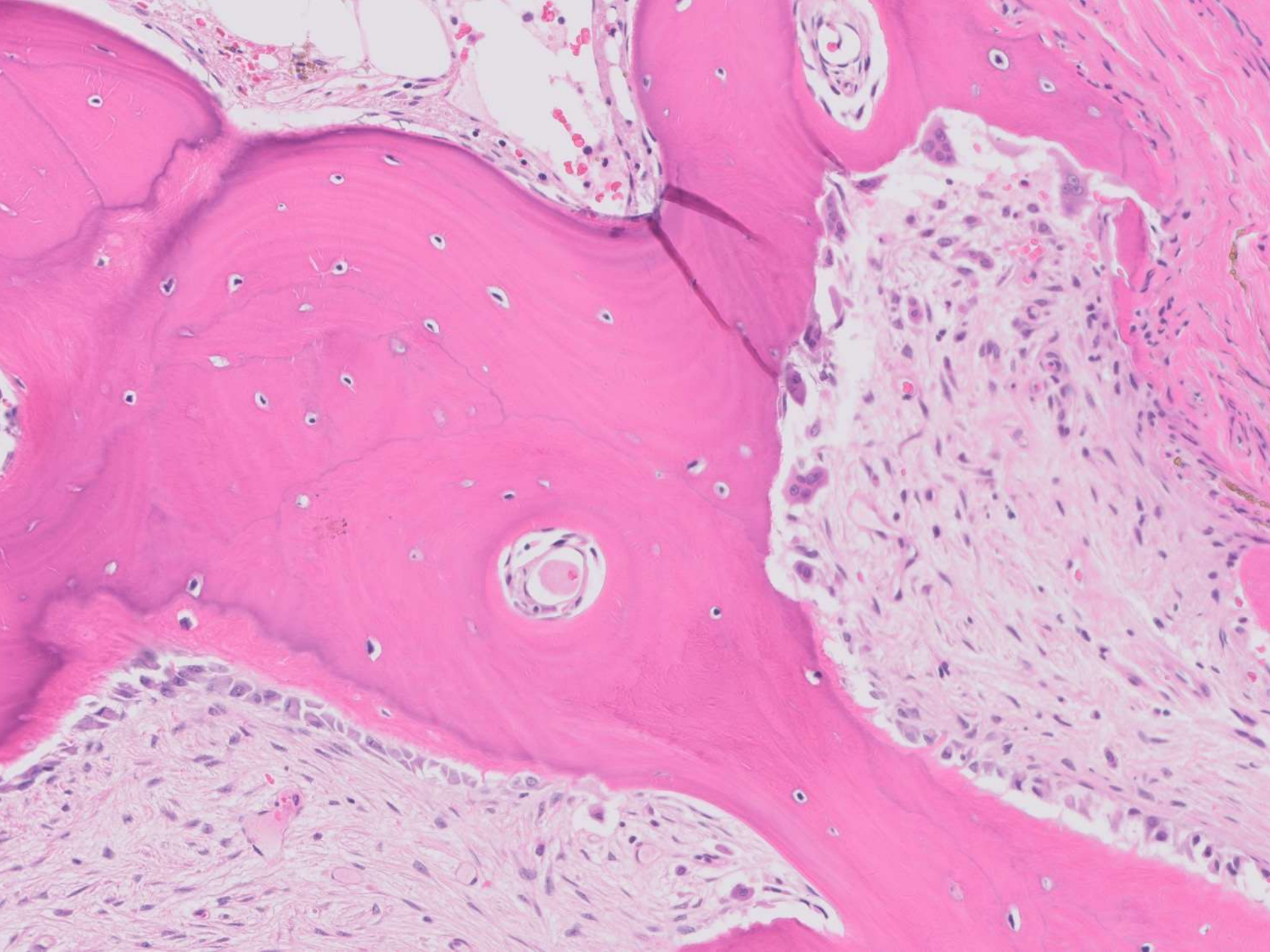
A prior hip biopsy showed a giant cell rich lesion.

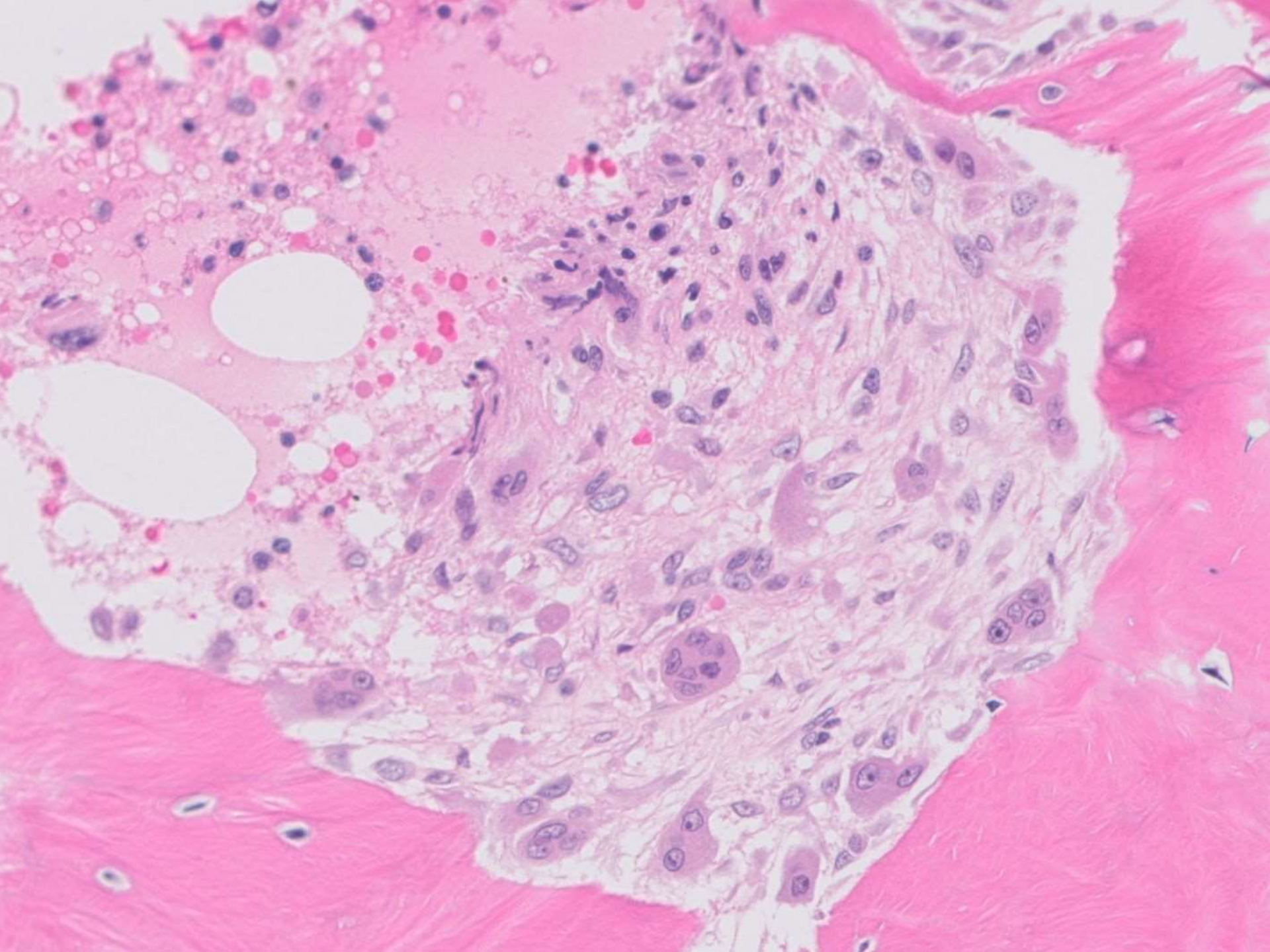
A bone marrow biopsy was performed.



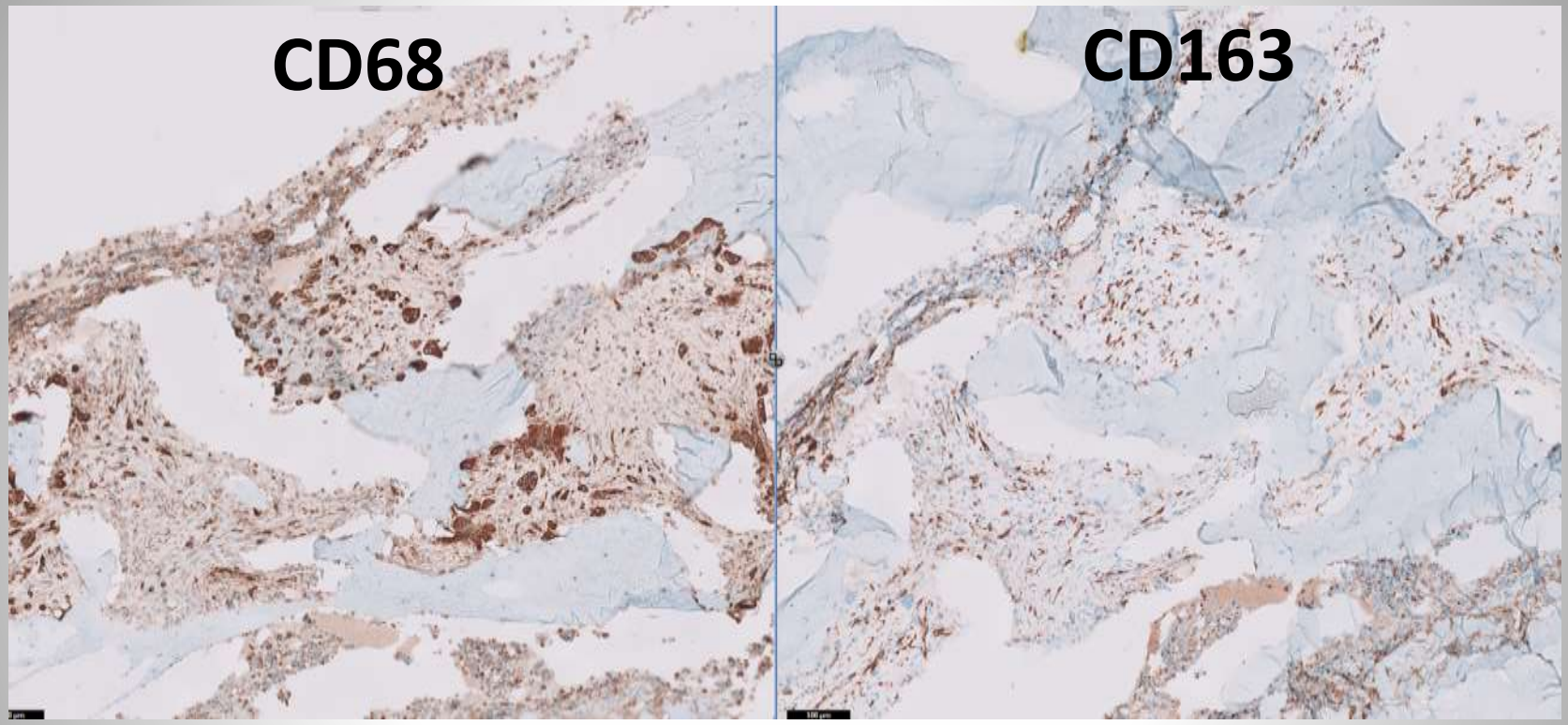








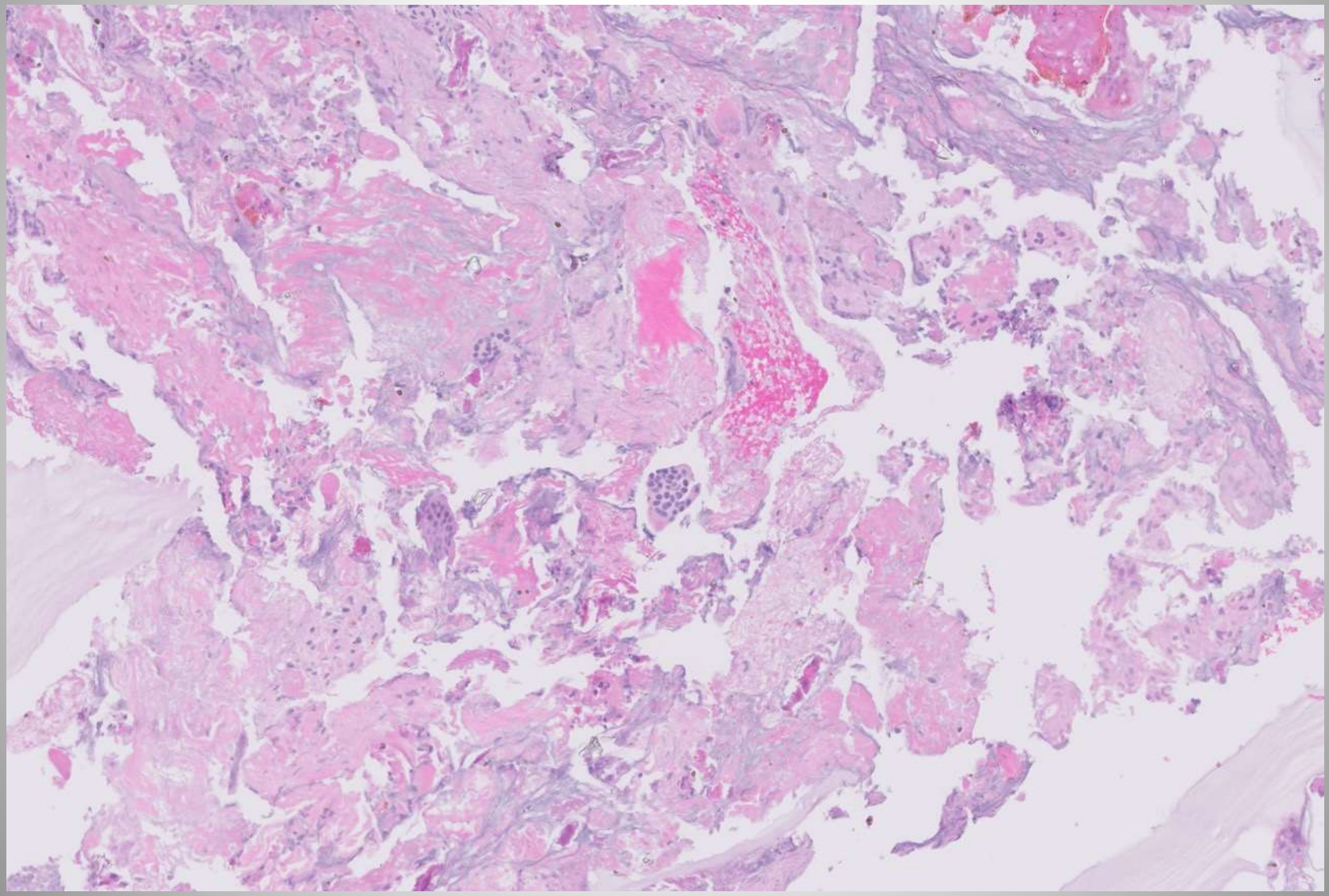
Immunostains

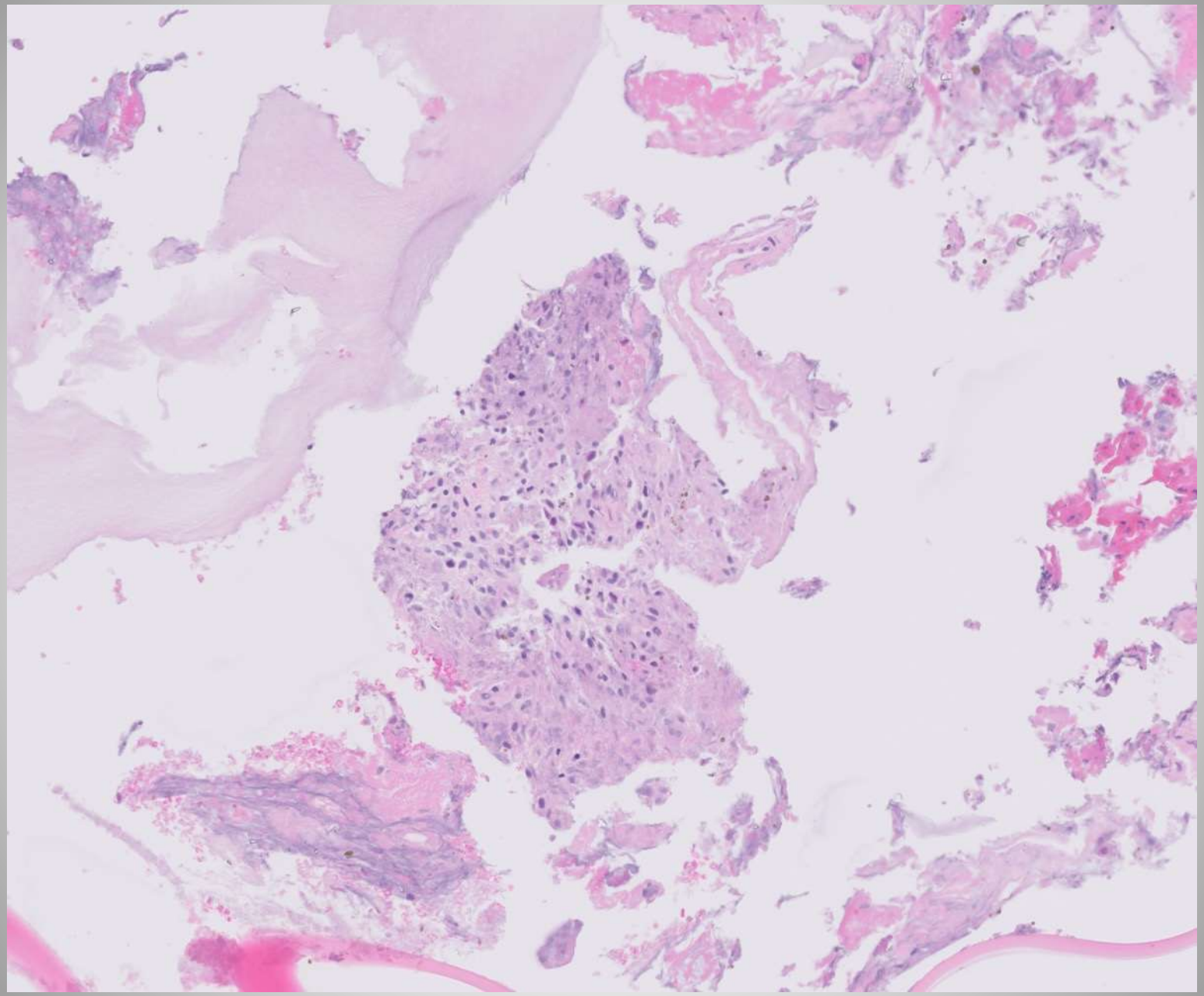


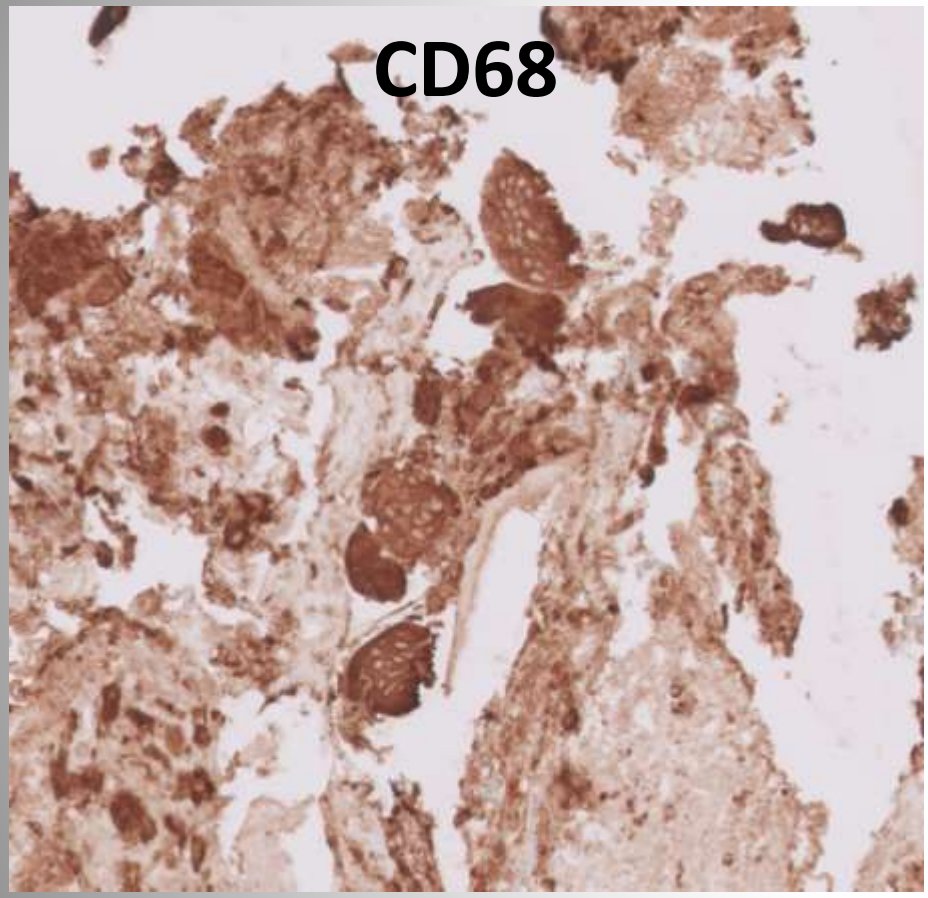
Stains for CD138, ISH kappa/lambda showed polytypic plasma cells within the hematopoietic areas

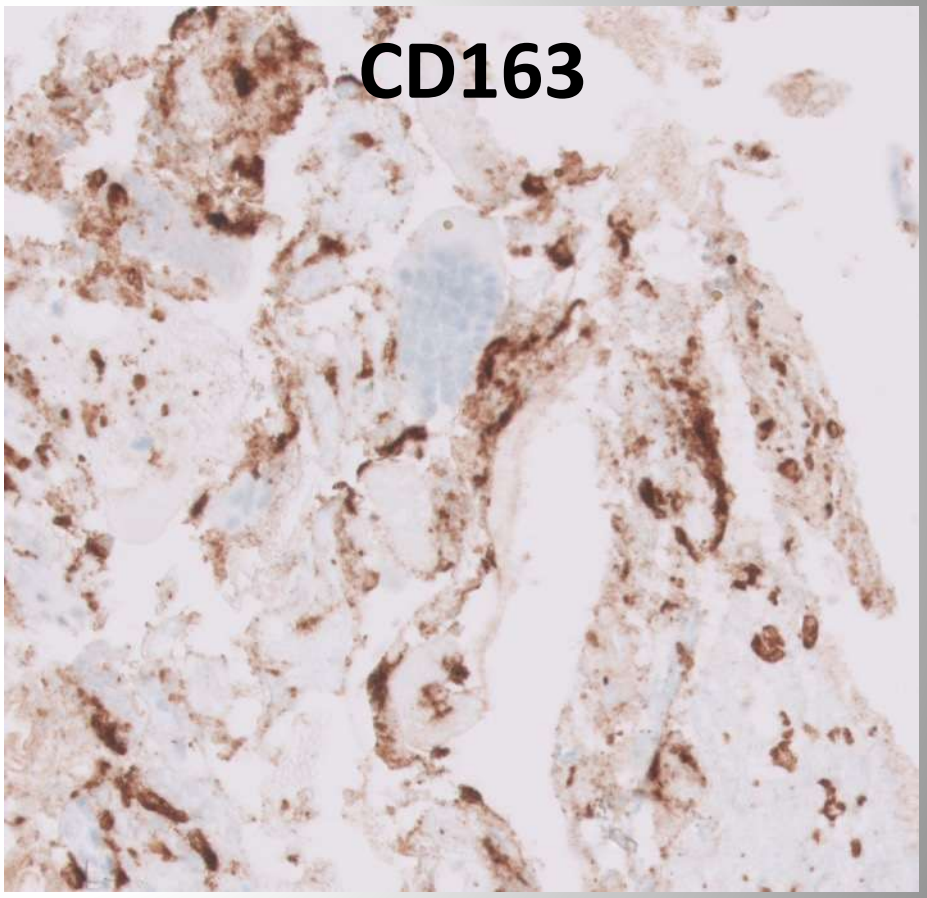
Stains for BRAF V600E, S100, cytokeratin, langerin, and melanA were negative

Hip biopsy






CD68


CD163

Laboratory studies

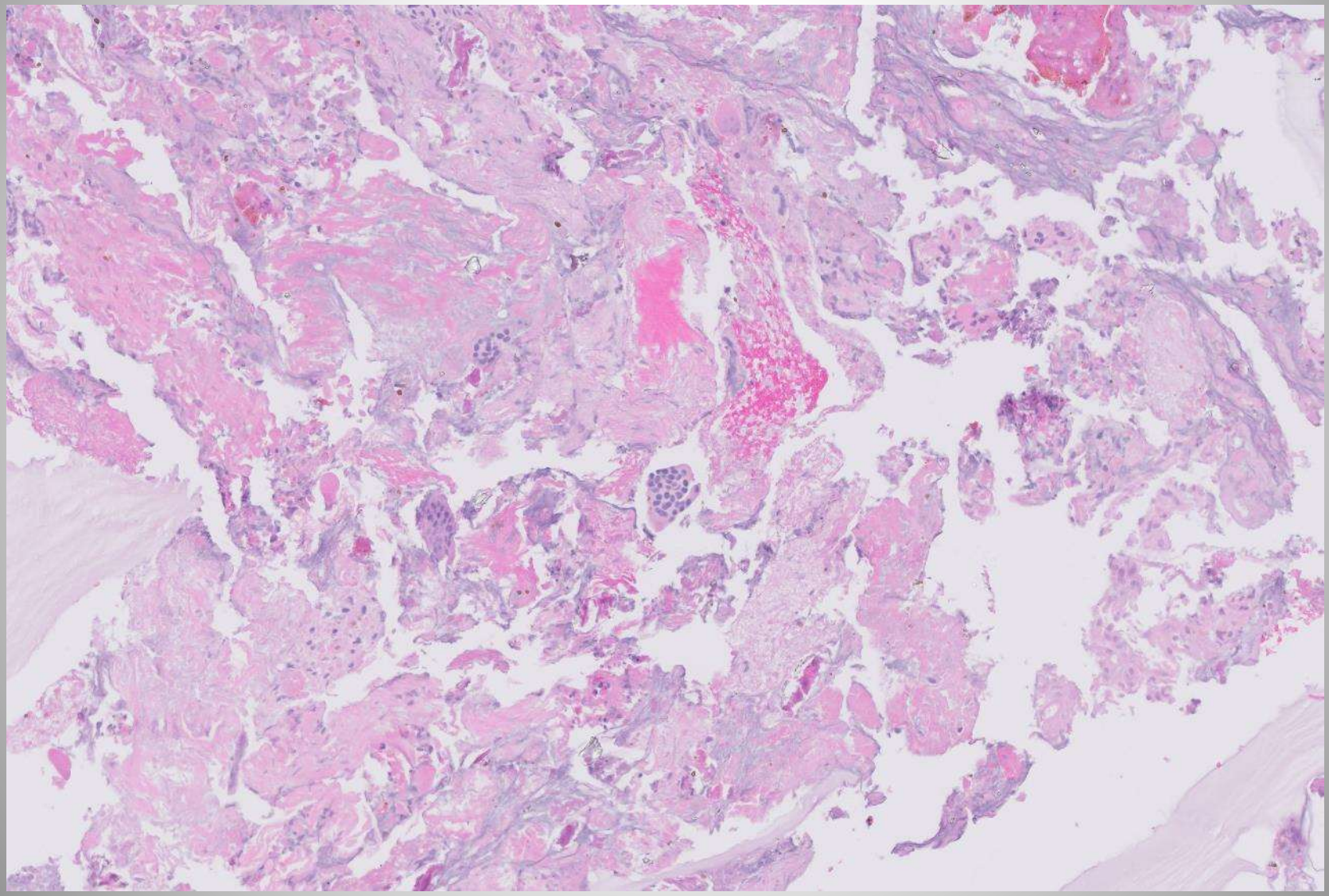
- Creatinine 7.6 mg/dL (0.67 – 1.17 mg/dL)
- Alkaline phosphatase 703 U/L (40-130 U/L)
- Parathyroid hormone 2135 pg/mL (15-65 pg/mL)
- Phosphorus 4.1 mg/dL (2.5 – 4.5 mg/dL)

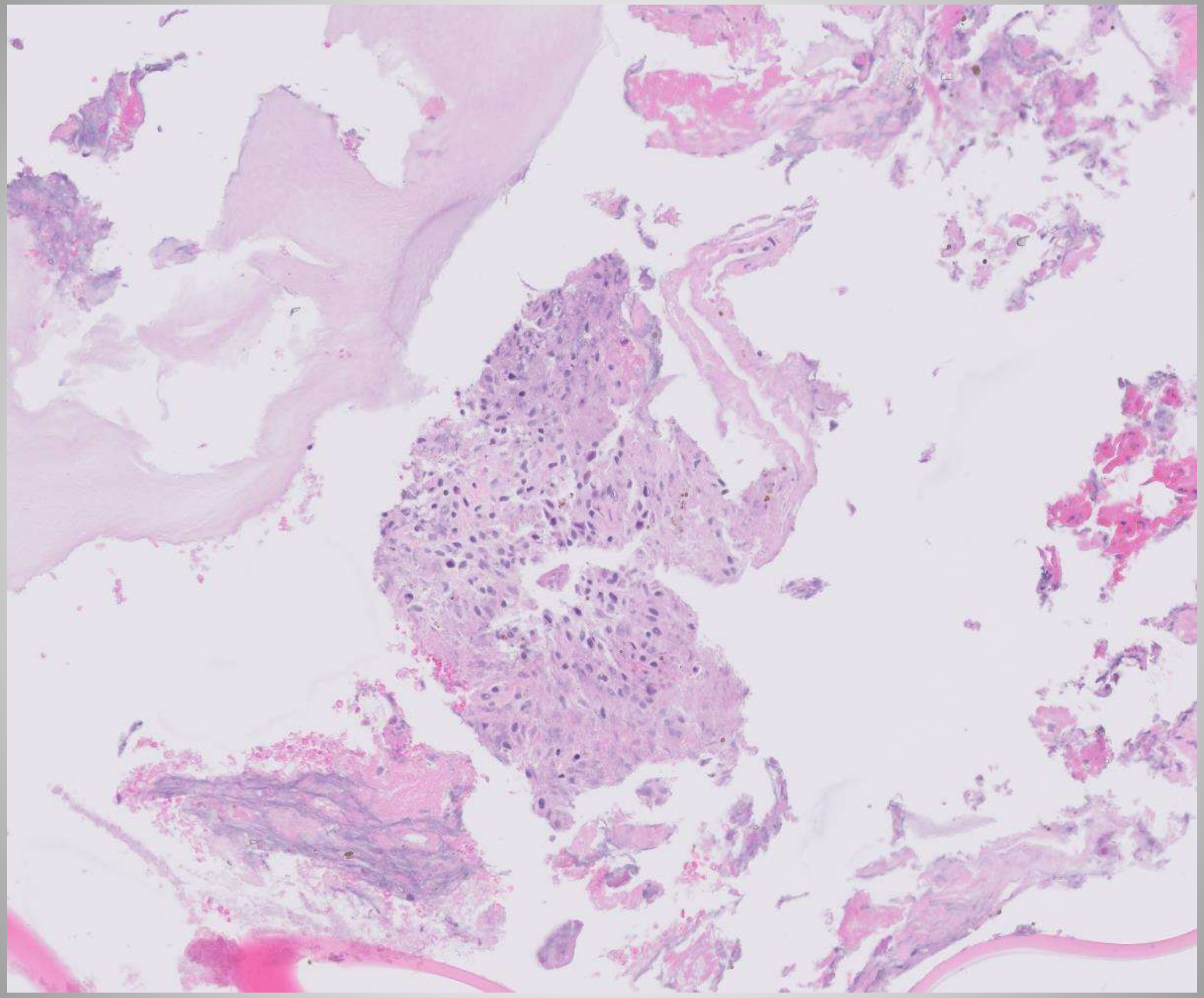
40ish man with multiple bony lesions

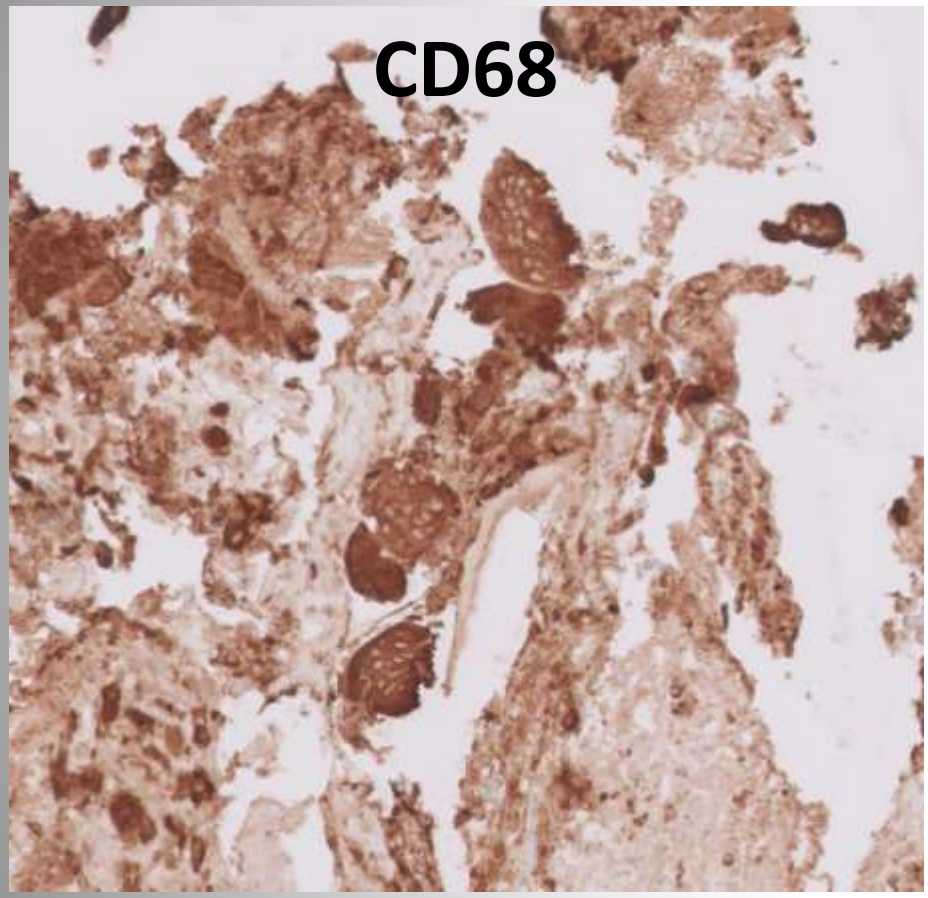
Brent Tan

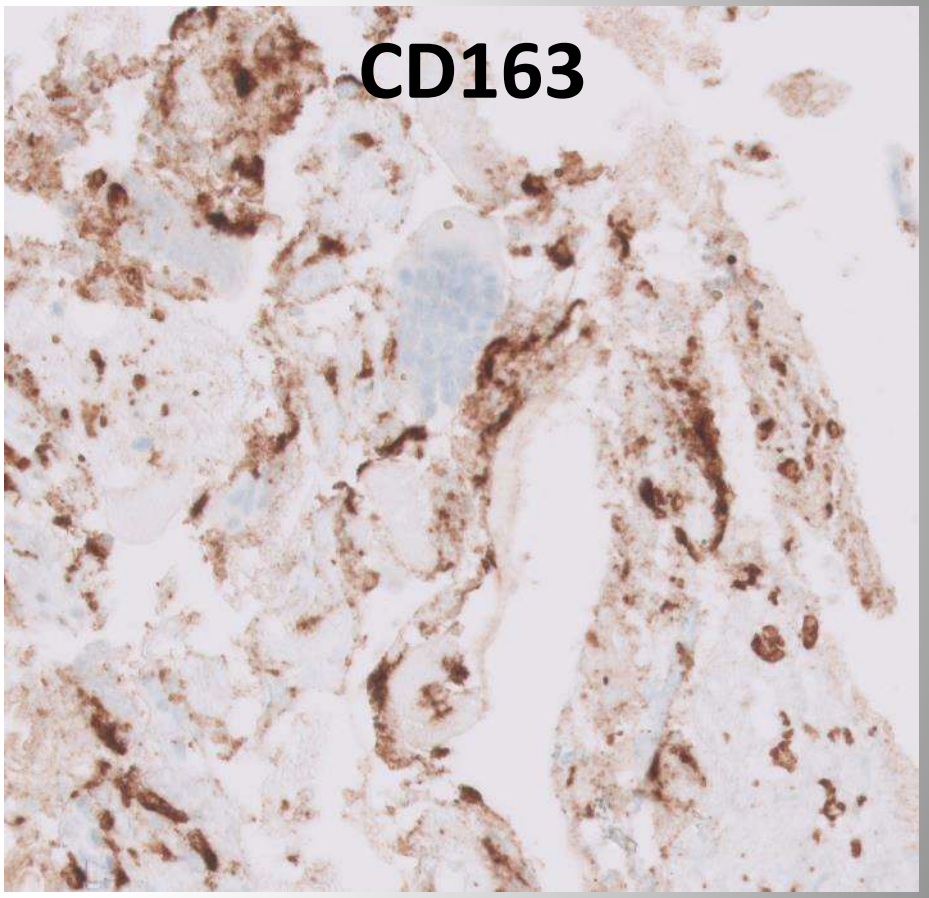
Stanford University

Hip biopsy






CD68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Renal Osteodystrophy

- Chronic renal failure leads to hyperphosphatemia and hypocalcemia

- Secondary hyperparathyroidism
  - Increased bone turnover
  - Increased osteoblast and osteoclasts
  - Endosteal and marrow fibrosis

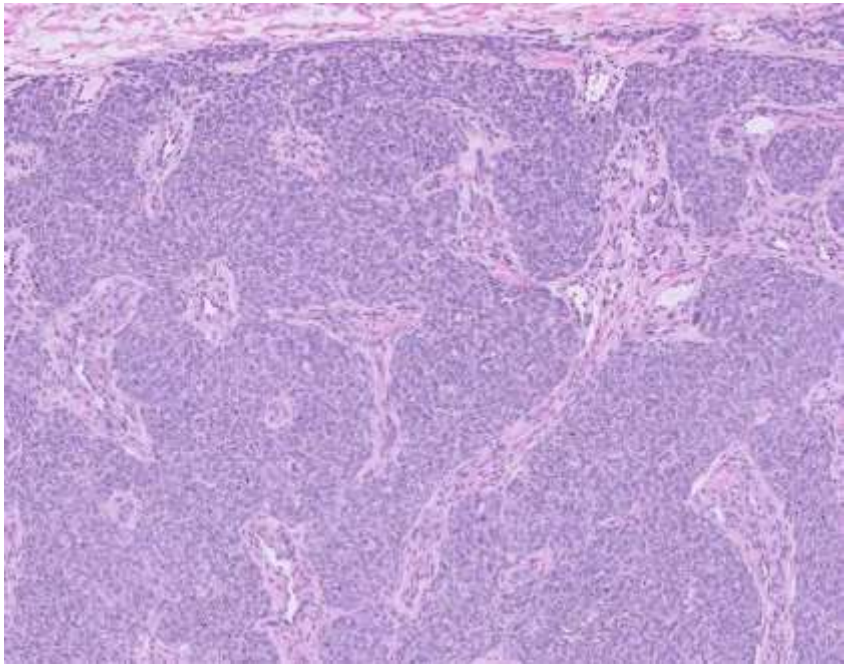
- Pathology
  - Histopathology: Rapid bone loss results in reparative vascular granulation tissue and subsequent fibrous that replaces normal marrow elements
  - Hemosiderin can impart a brown color

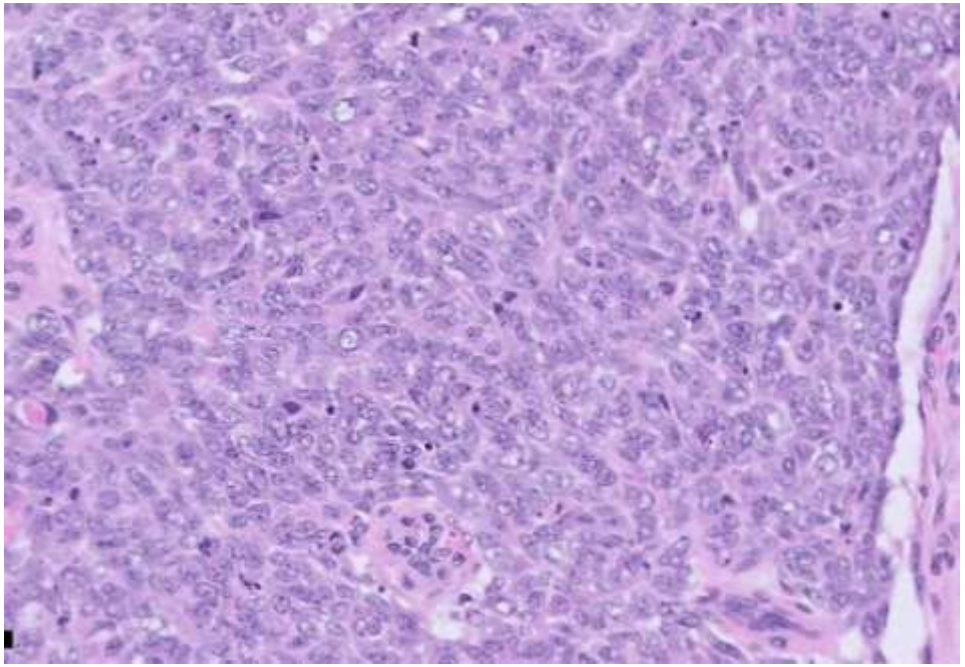
22-1004

Jiajie “George” Lu/Serena Tan; Stanford

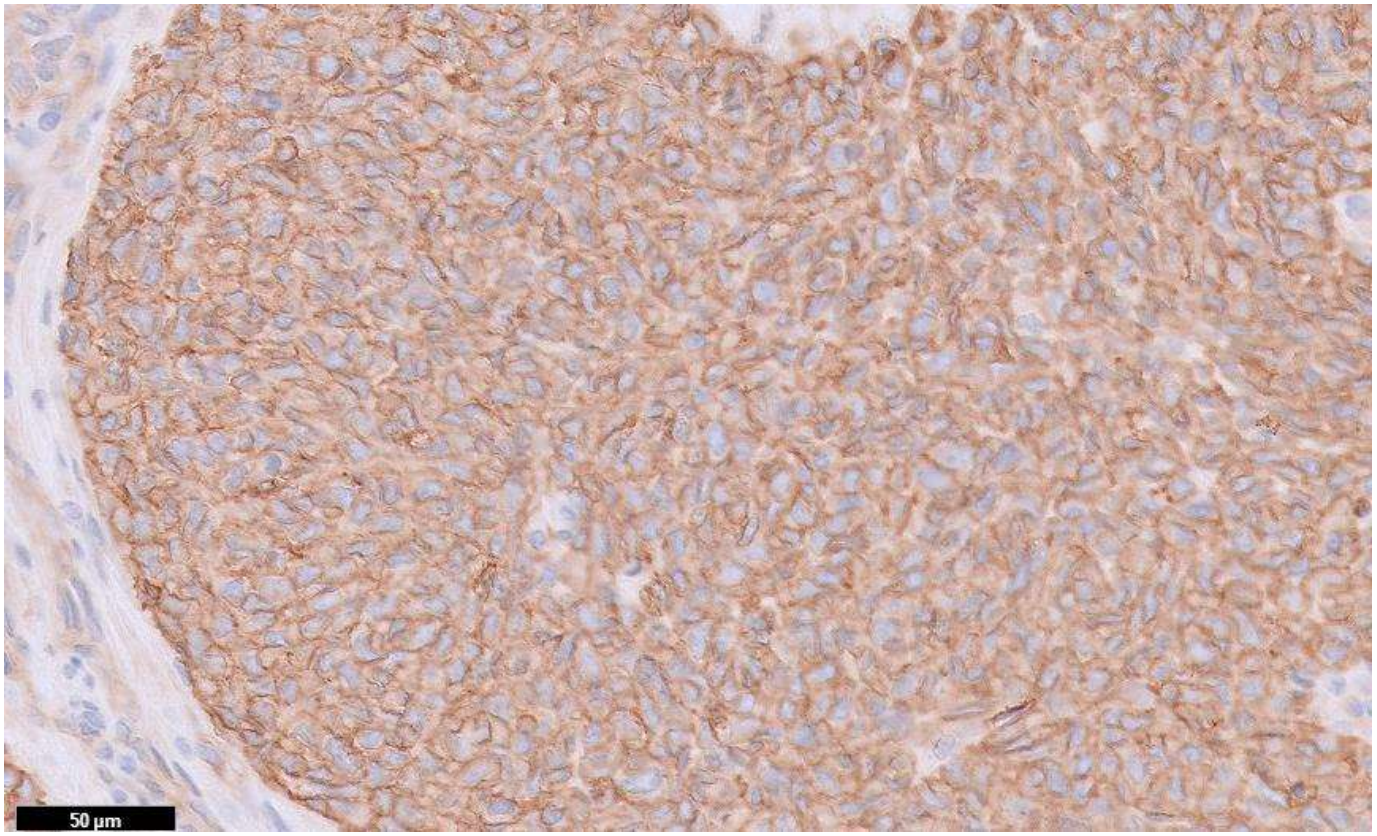
Young infant with presents with scalp mass. Case received in consultation for concern for carcinoma, following a thorough immunohistochemical and cytogenetics/FISH workup.

H&E

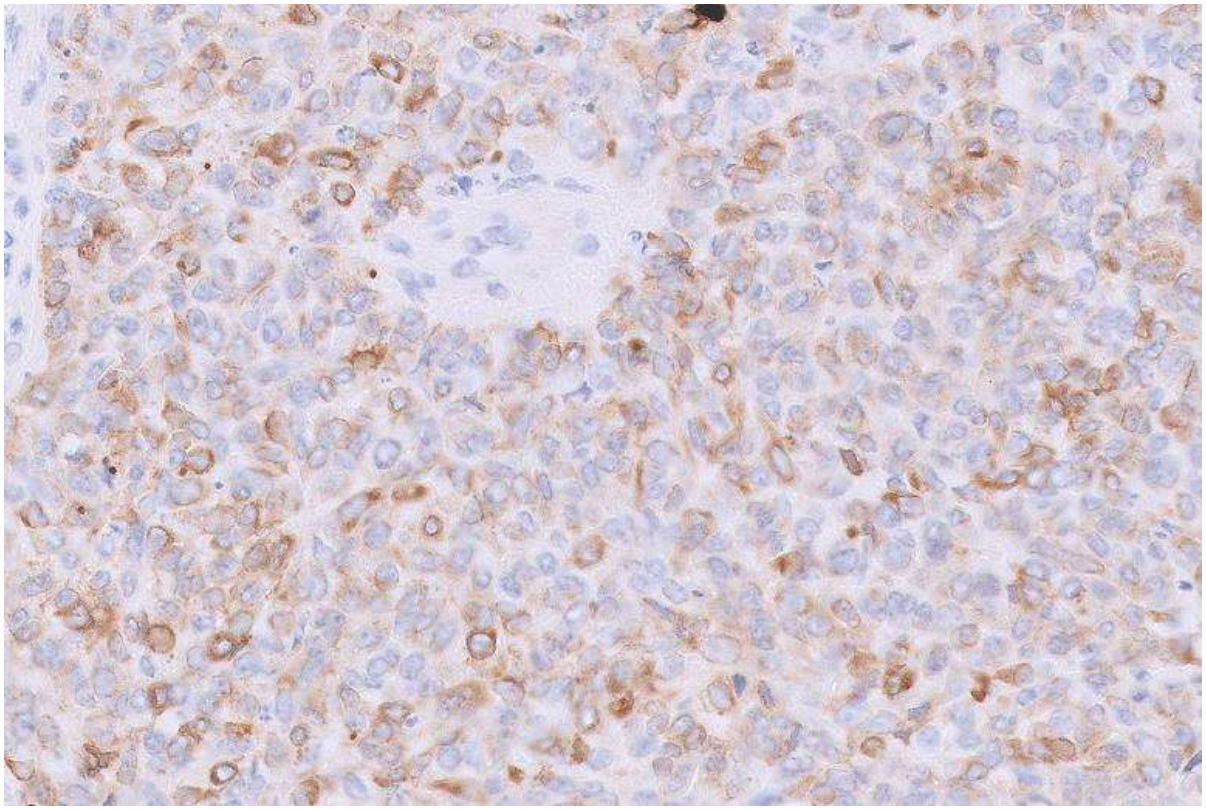




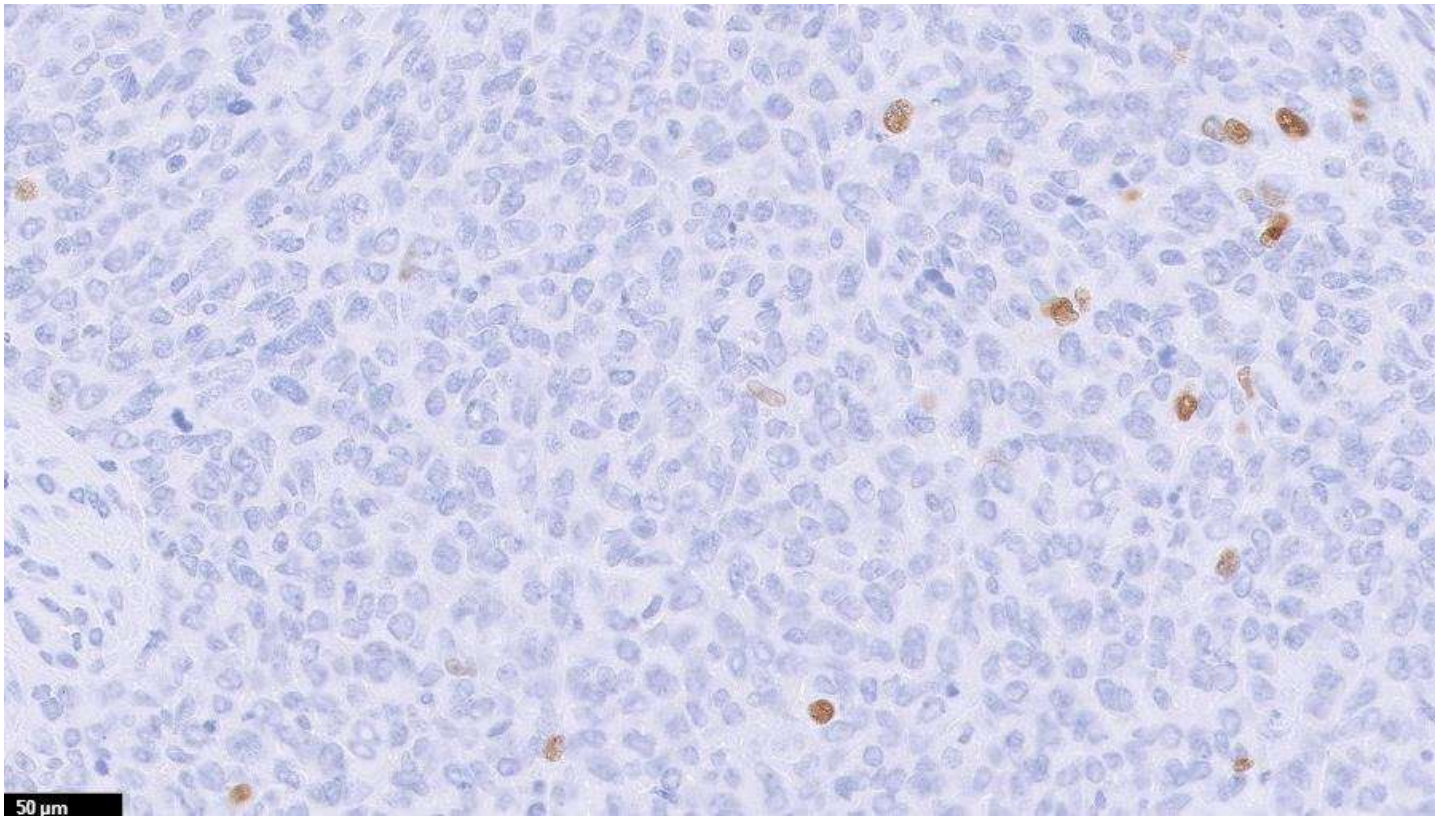
CD99



CK AE1/AE3



NKX2.2



Additional Immunohistochemistry

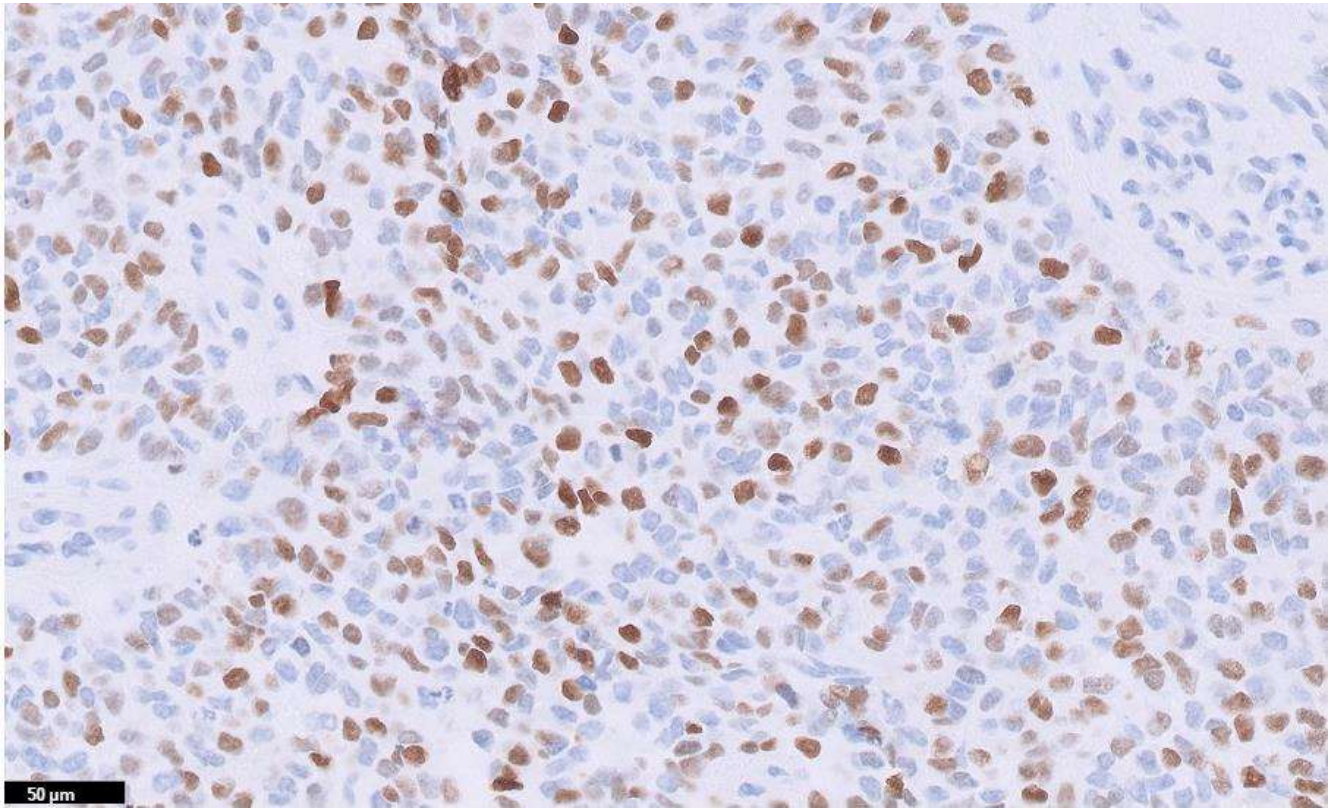
IHC	Result
Desmin	Weak/focal positive
EMA	Weak/focal positive
S100	Weak/focal positive
Calretinin	Weak/focal positive
WT1	Weak/focal positive
TLE1	Weak/focal positive
BCOR	Weak/focal positive
Myogenin	Negative
SMA	Negative
CD45	Negative
Synaptophysin	Negative
Chromogranin	Negative

IHC	Result
PHOX2b	Negative
TdT	Negative
SATB2	Negative
Calponin	Negative
CD34	Negative
NUT	Negative
INSMI	Negative
SOX10	Negative
GFAP	Negative
Claudin-4	Negative
p40	Negative
INI1	Retained

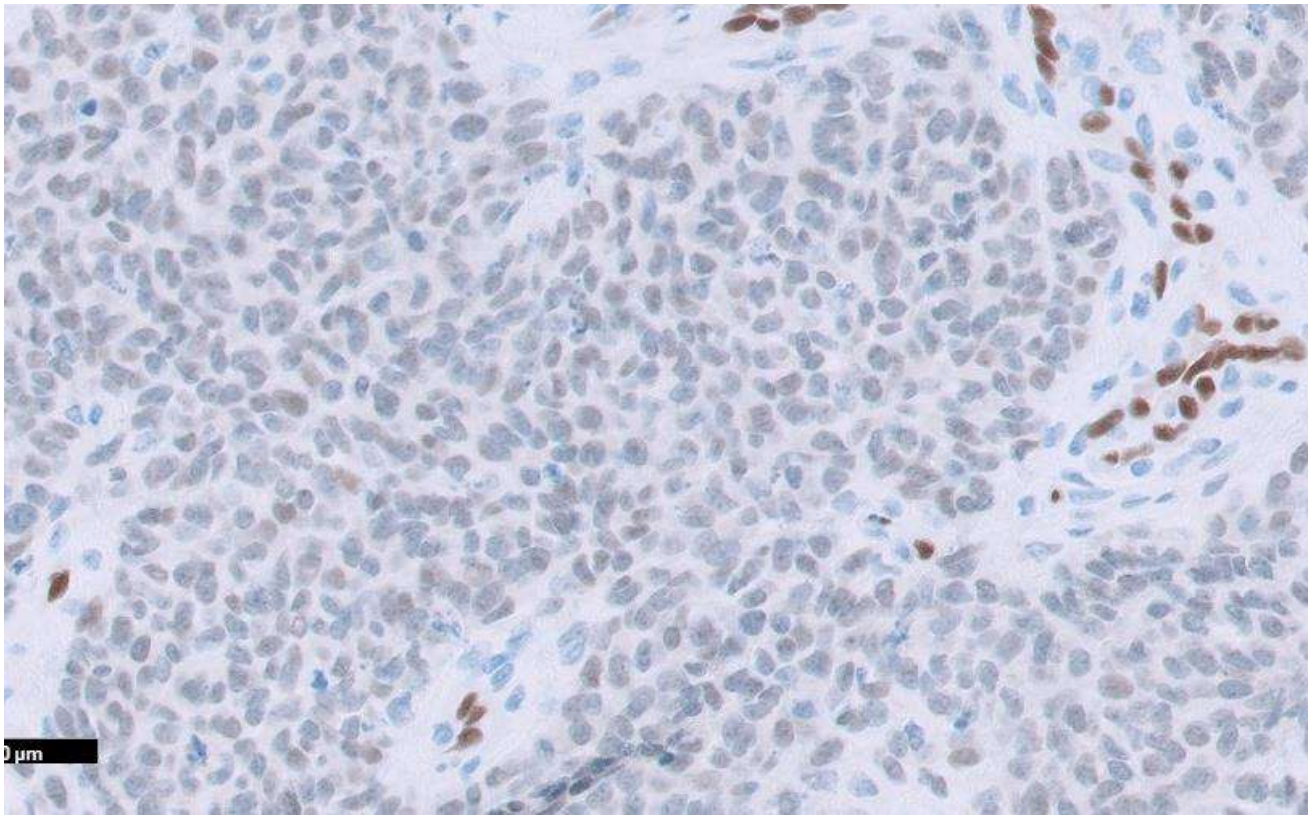
FISH Results

- Negative for rearrangements in *BCOR, TFE3, NTRK1/2/3, ETV6, YWAE, SS18, CIC, EWSR1*
- Repeat FISH at second facility again failed to demonstrate rearrangement of *EWSR1*

PAX7



ERG



NGS

Next generation sequencing (Foundation One) identified an *EWSR1-ERG* fusion as well as mutations at ATM and TNFAIP3

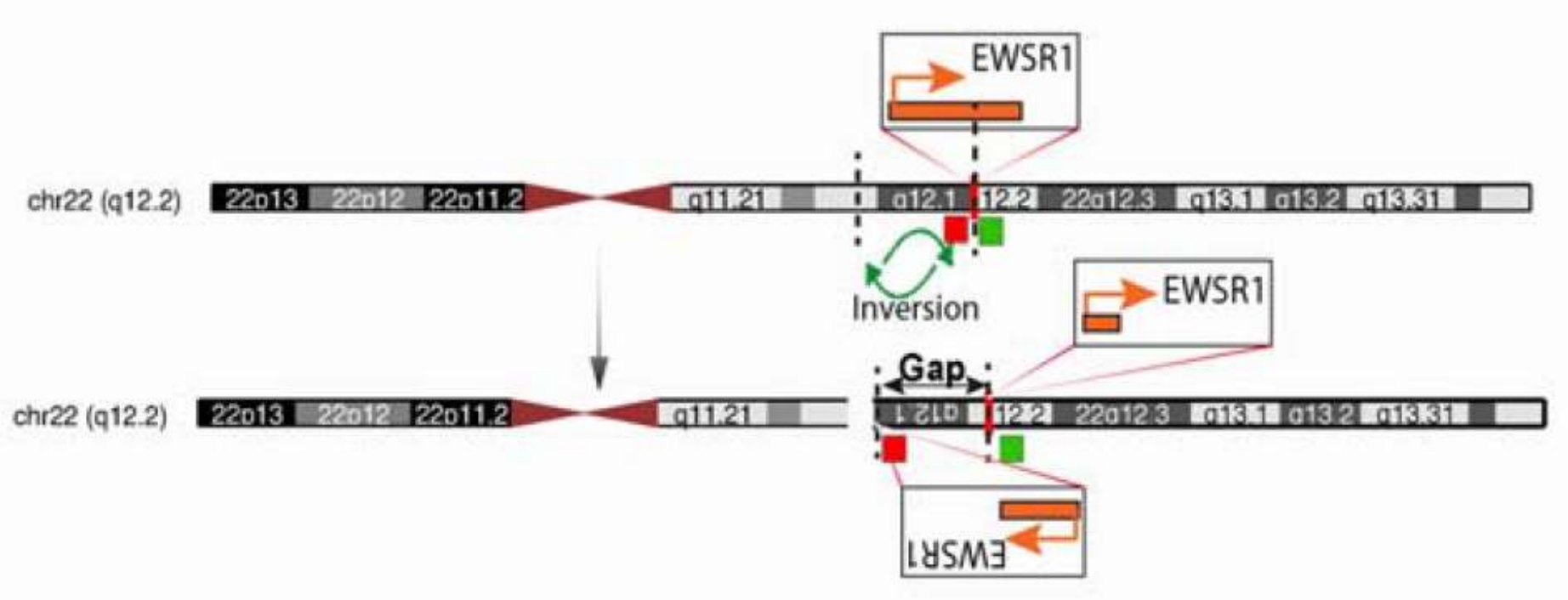
Final Diagnosis: Ewing Sarcoma with *EWSR1-ERG* rearrangement

TABLE 1. Chromosomal Translocations, Rearrangements, and Fusion Products in the Ewing Sarcoma Family of Tumors

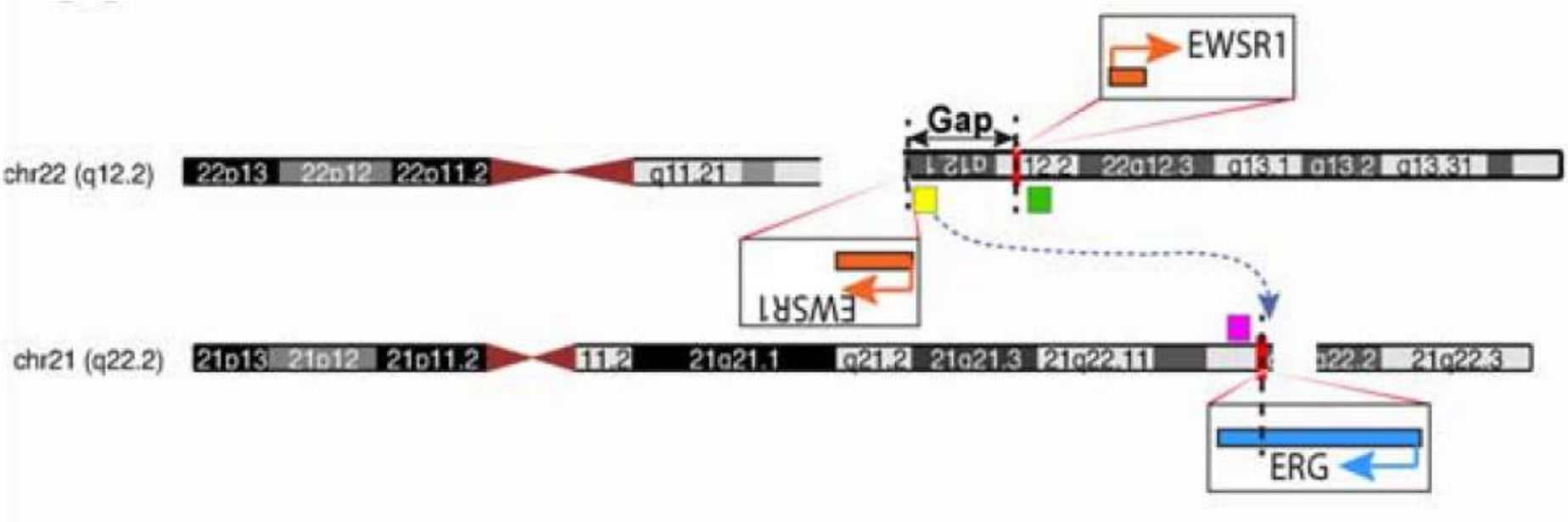
Chromosomal Rearrangement	Fusion Gene	Origin	Prevalence (%)
EWSR1			
t(11;22)(q24;q12)	*EWSR1-FLI1*	B > ST	85-90
t(21;22)(q22;q12)	*EWSR1-ERG*	B > ST	5-10
t(7;22)(q22;q12)	*EWSR1-ETV1*	ST > B	*
t(17;22)(q21;q12)	*EWSR1-ETV4 (E1AF)*	ST > B	*
t(2:22)(q35;q12)	*EWSR1-FEV*	ST > B	*
t(2;22)(p31;q12)	*EWSR1-SP3*	ST	*
t(1;22)(p36;q12)	*EWSR1-PATZ1*	ST	*
t(4;22)(q31;q12)	*EWSR1-SMARCA5*	ST	*
t(6;22)(p21;q12)	*EWSR1-POUSF1*	B	*
t(20;22)(q13;q12)	*EWSR1- NFATc2*	B > ST	*
FUS			
t(16;21)(p11;q22)	*FUS-ERG*	B > ST	*
t(2;16)(q35;p11)	*FUS-FEV*	B = ST	*
t(16;20)(p11;q13)	*FUS-NFATc2*	B	*

Kilpatrick SE et al. Adv Anat Pathol 2018; 25: 314-326

Why was the *EWSR1* FISH negative?



Chen S et al. *Genes, Chromosomes, and Cancer* 2016; 55: 340-349



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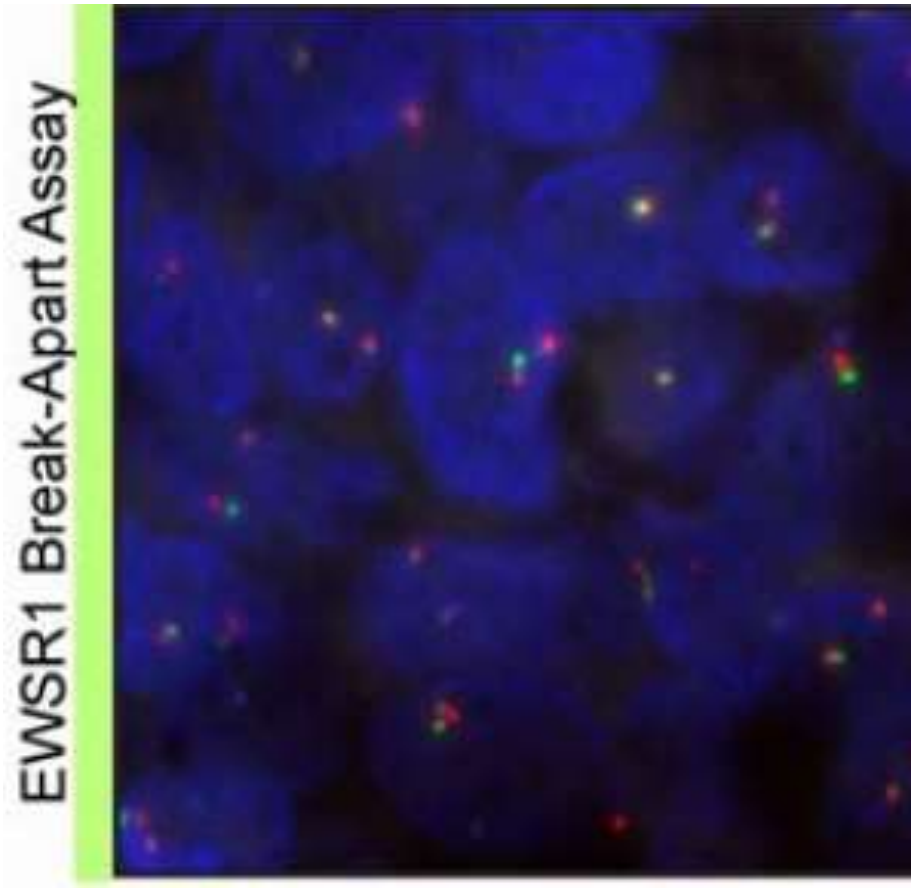
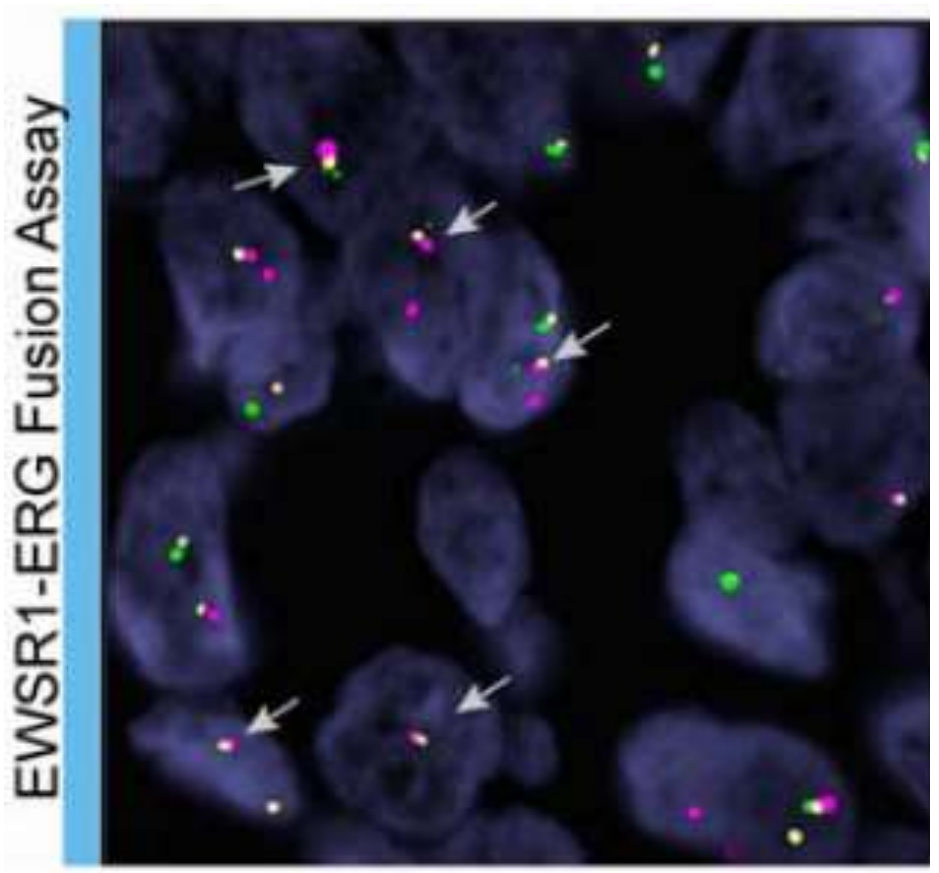
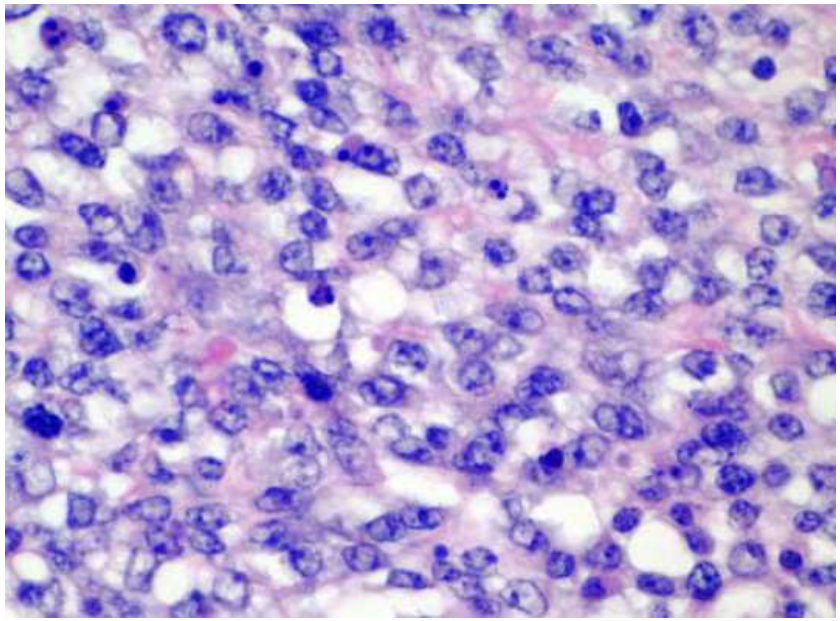




Chen S et al., *Genes, Chromosomes, and Cancer* 2016; 55: 340-349

Features Suggestive of Ewing Sarcoma

- Clinical Features:
  - Adolescent or young adult
  - Rare < 5 years of age
  - Diaphysis or metaphysis of long bones (femur, tibia, humerus)
  - Scapula, ribs, pelvic bones
  - Extraskeletal locations: Paravertebral region, chest wall, soft tissue
- Histology:
  - Round blue cells with vacuolated cytoplasm
  - Typically sparse mitoses
  - Glycogen staining with PAS stain



Kilpatrick SE et al. Adv Anat Pathol 2018; 25: 314-326

IHC Features of Ewing Sarcoma

- CD99
  - Diffuse membranous staining is characteristic
  - If not present, unlikely to be Ewing
  - However, it is nonspecific as synovial sarcoma, ALL, *EWSR1-NFATC2* translocation sarcoma, *BCOR* rearranged sarcoma, other entities may also be positive
- Cytokeratins:
  - Usually has some positivity
- PAX7[1]:
  - Sensitive, however can stain alveolar RMS, synovial sarcoma, *BCOR-CCNB3* sarcomas, small cell osteosarcoma, DSRCT
- NKX2.2[2]:
  - Sensitive and fairly specific except for neuroblastoma, some small cell/synovial sarcomas/mesenchymal chondrosarcoma/melanoma
- FLI or ERG
  - Depending on *EWSR1* translocation partner

1. Toki S et al. *Histopathology 2018;* 73: 645-652
2. Yoshida A et al. *Am J Surg Pathol 2012*; 36: 993-999.

Differential: Ewing-like Sarcomas

	Anatomic Location	Morphology	IHC	Clinical Features
CIC-DUX4 sarcoma	Deep soft tissue	Ewing-like	Patchy to weak CD99 staining	Less responsive to neoadjuvant therapy
BCOR rearranged sarcomas	Bone predominance	+/- Spindle cells, myxoid background	Less intense CD99; TLE1, CCNB3, BCOR positive	Responds to neoadjuvant, similar prognosis as Ewing
EWSR1-NFATC2 sarcoma	Skeletal sites more common	+/- Spindle cells, myxoid background	Strong CD99 and NKX2.2 staining	Resistant to Ewing specific chemotherapy

Kilpatrick SE et al. Adv Anat Pathol 2018; 25: 314-326

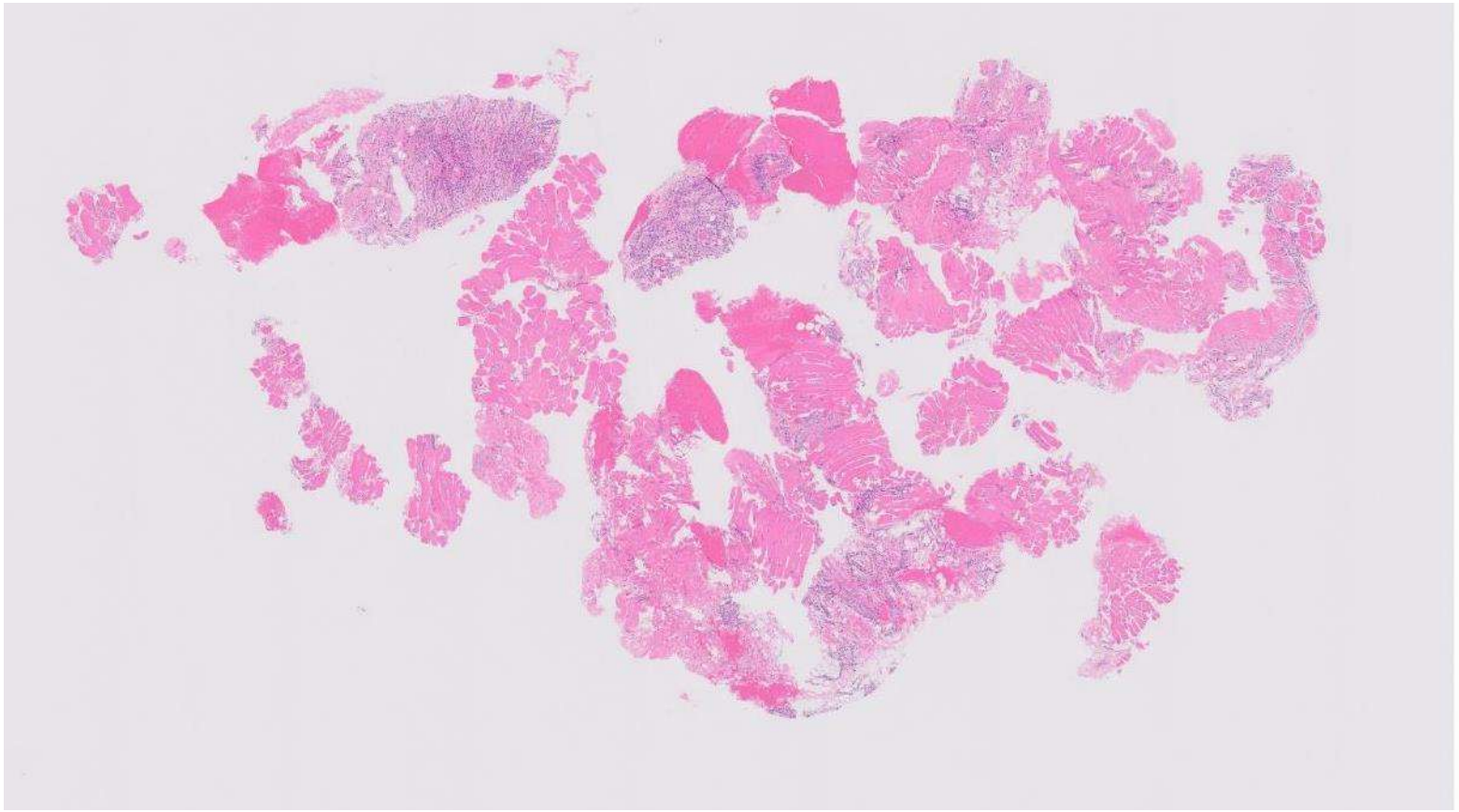
References

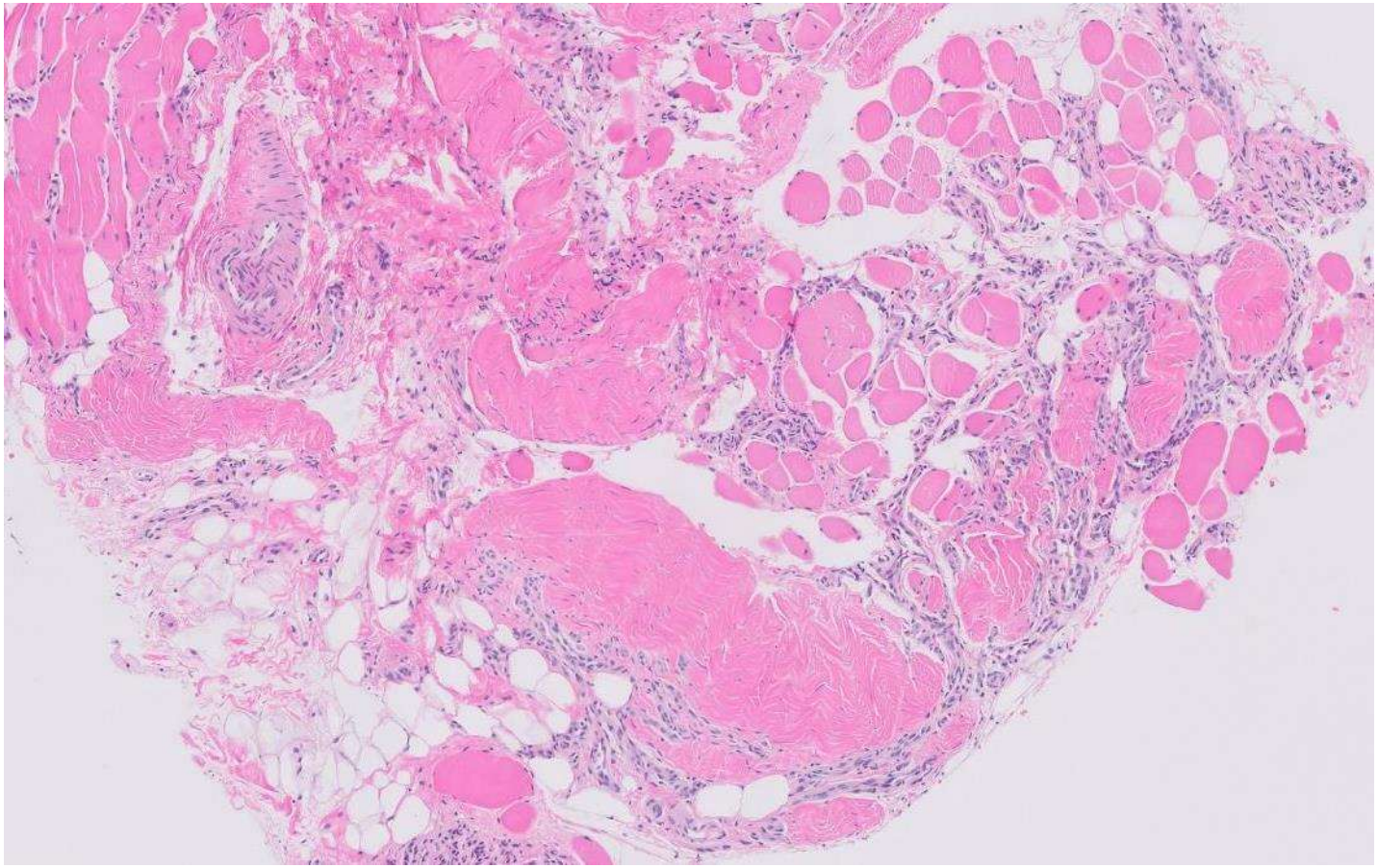
- Chen S, Deniz K, Sung YS, Zhang L, et al. Ewing sarcoma with *ERG* gene rearrangements: a molecular study focusing on the prevalence of *FUS-ERG* and common pitfalls in detecting *EWSR1-ERG* fusions by FISH. *Genes, Chromosomes, and Cancer* 2016; 55: 340-349.
- Kilpatrick SE, Reith JD, Rubin B. Ewing Sarcoma and the history of similar and possibly related small round cell tumors: from whence have we come and where are we going? *Adv Anat Pathol* 2018; 25:314-326.
- Toki S, Wakai S, Sekimizu M, Mori T, et al. PAX7 immunohistochemical evaluation of Ewing sarcoma and other small round cell tumors. *Histopathology 2018;* 73: 645-652.
- Yoshida A, Sekine S, Tsuta K, Fukayama M, et al. NKX2.2 is a useful immunohistochemical marker for Ewing sarcoma. *Am J Surg Pathol 2012*; 36: 993-999.

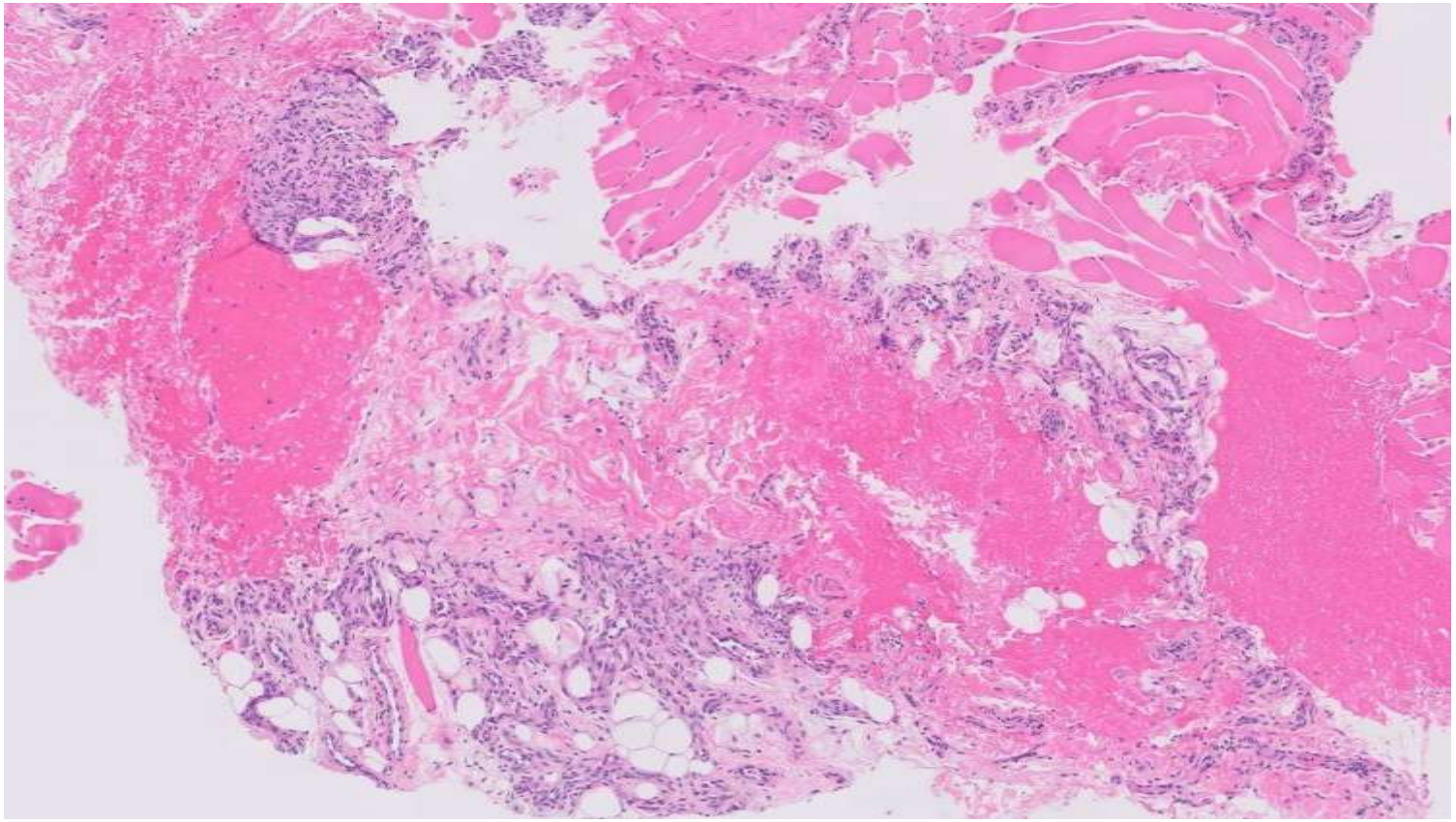
22-1005

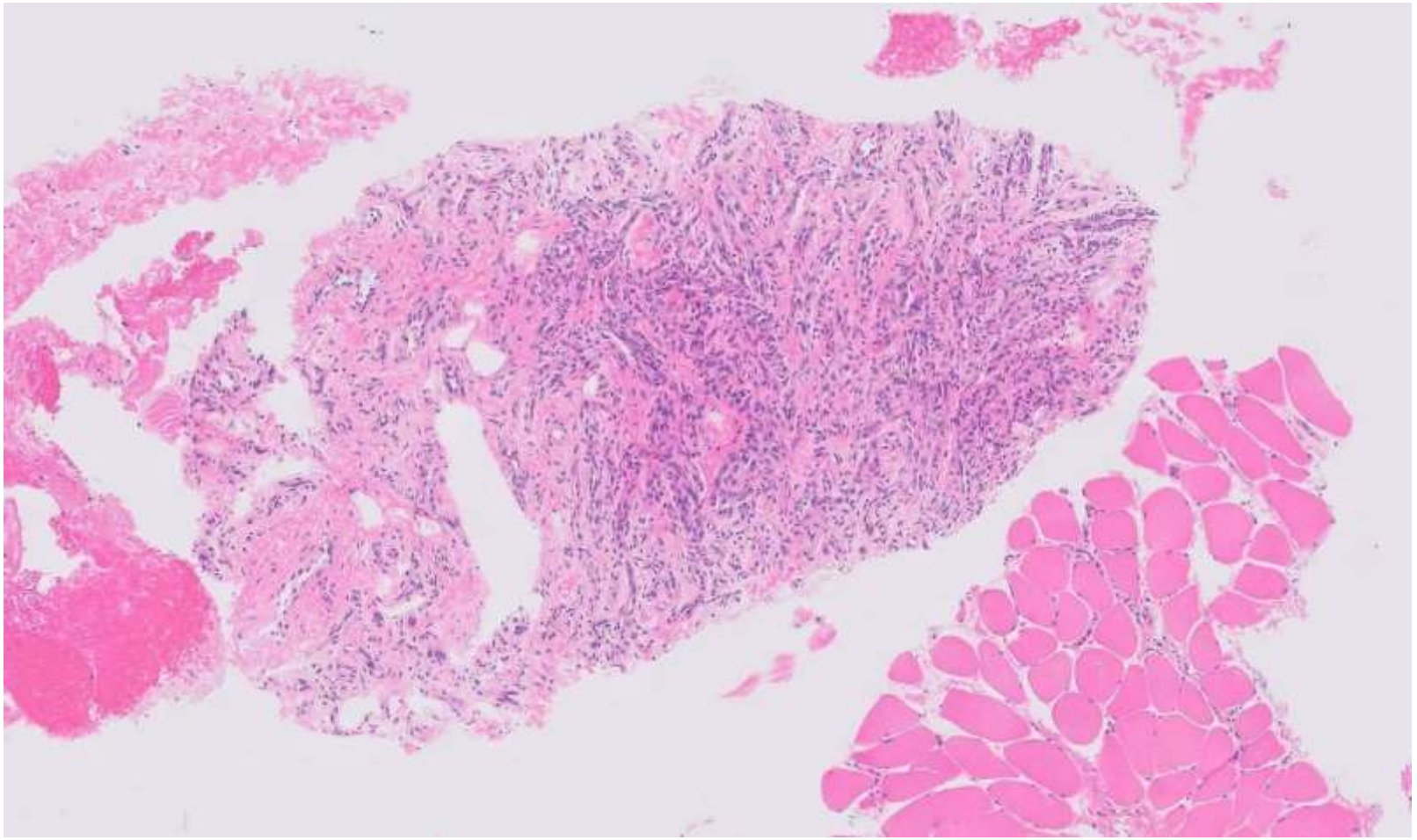
Serena Tan; Stanford

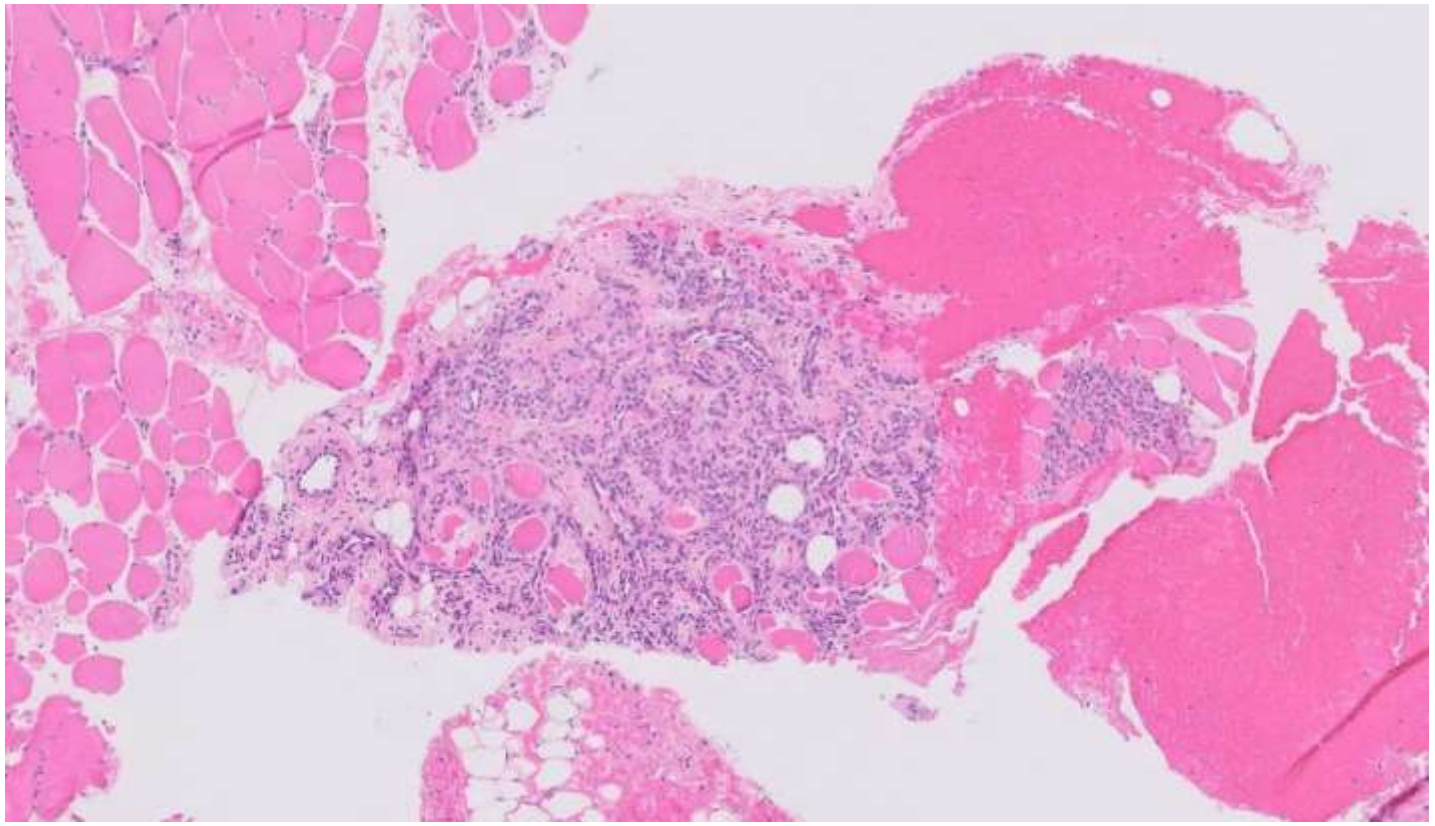
Young infant male with left chest wall mass deep to pectoralis muscle.

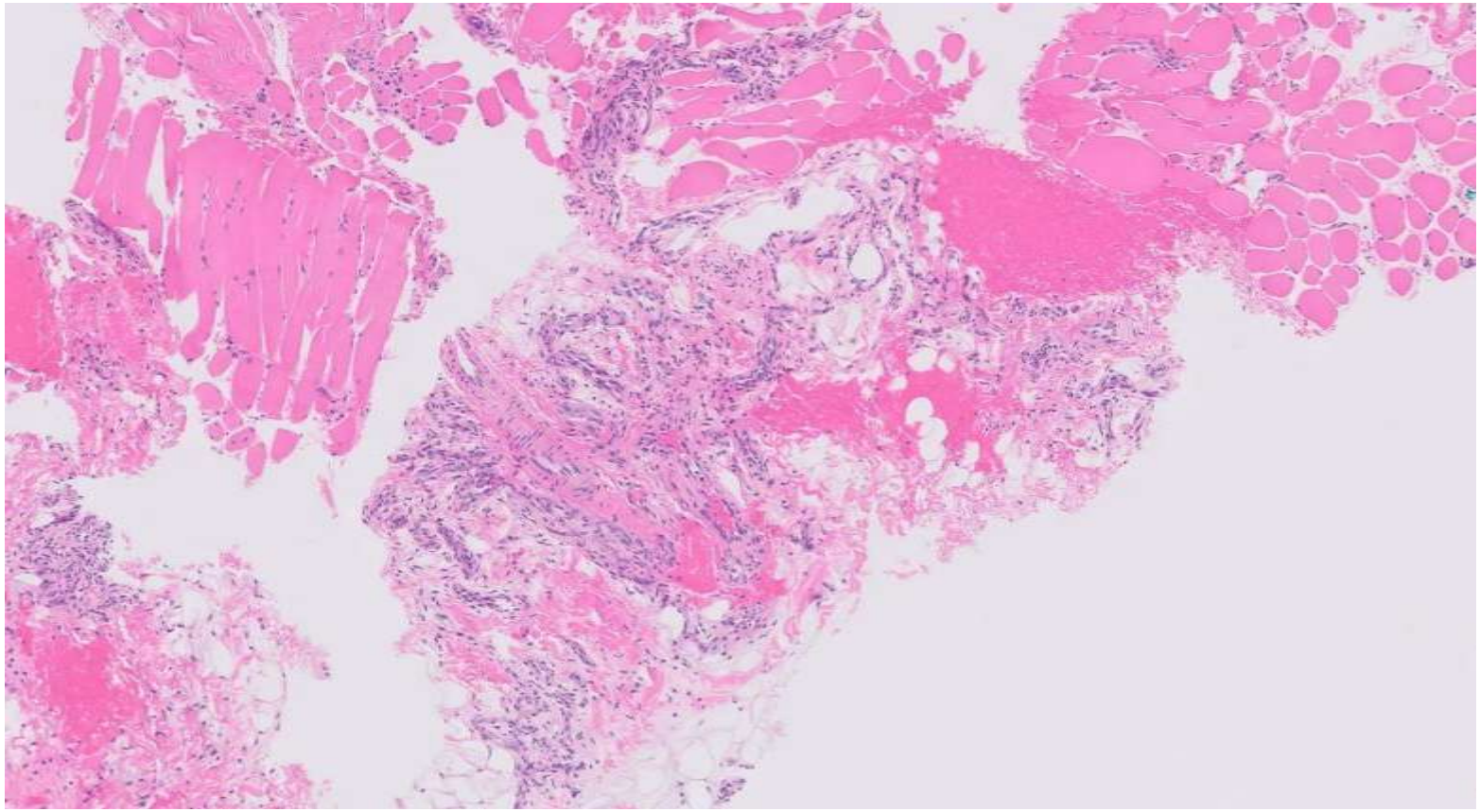


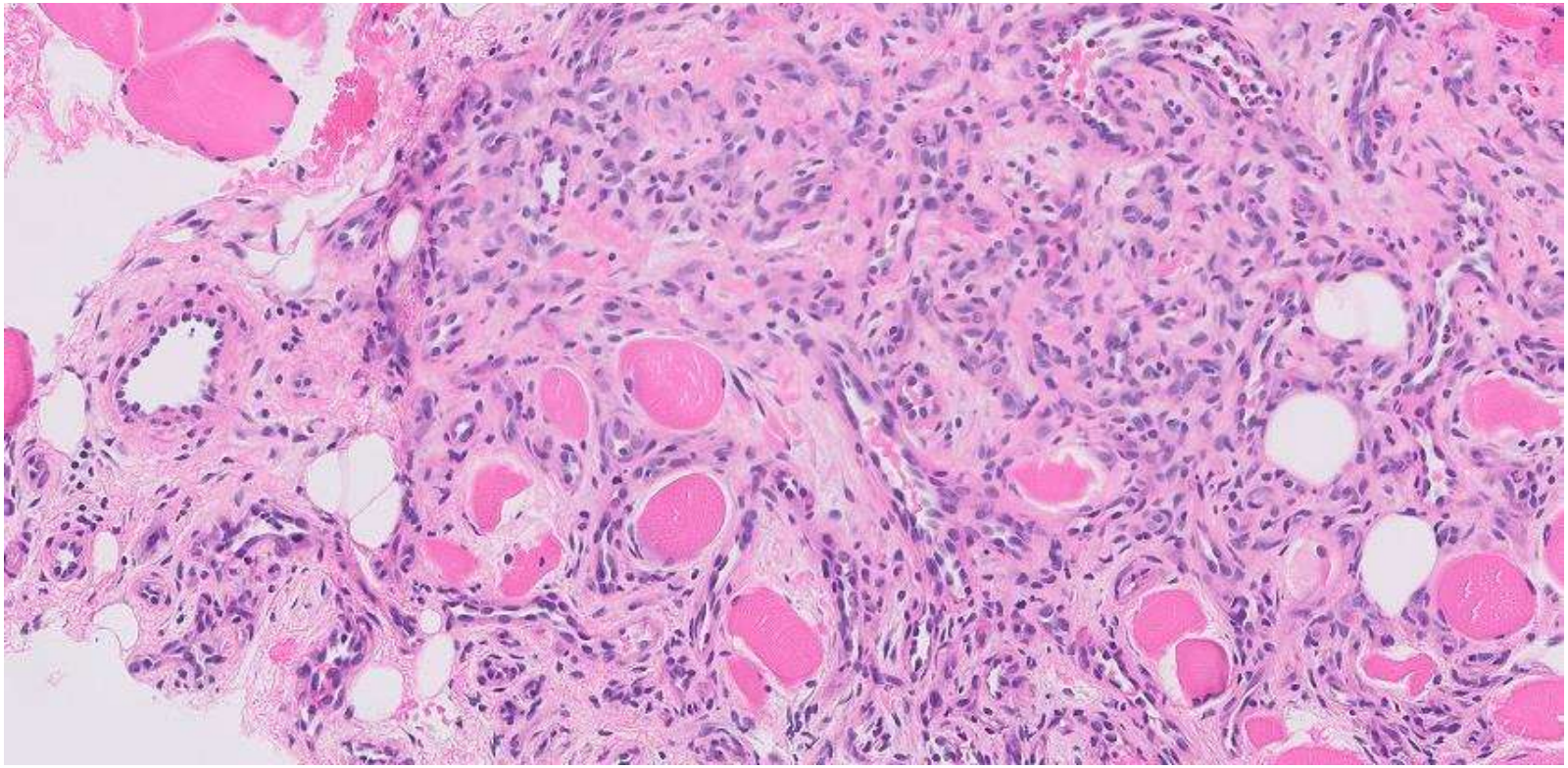


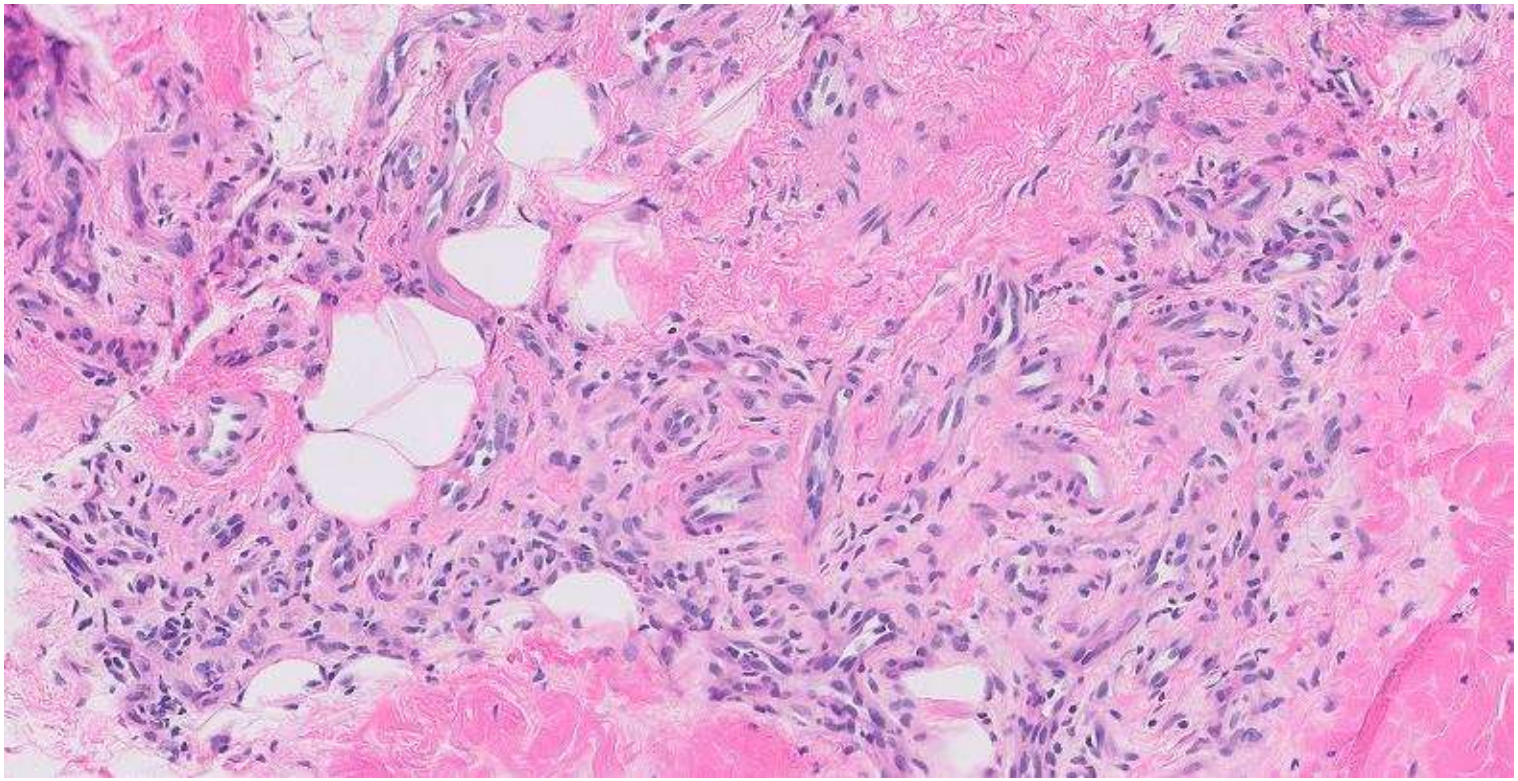












Intramuscular Vascular Anomalies

(Used to all be known as “intramuscular hemangiomas”)

Fast Flow

- Arteriovenous malformation
- Intramuscular fast flow vascular anomaly
- *PTEN* hamartoma of soft tissue

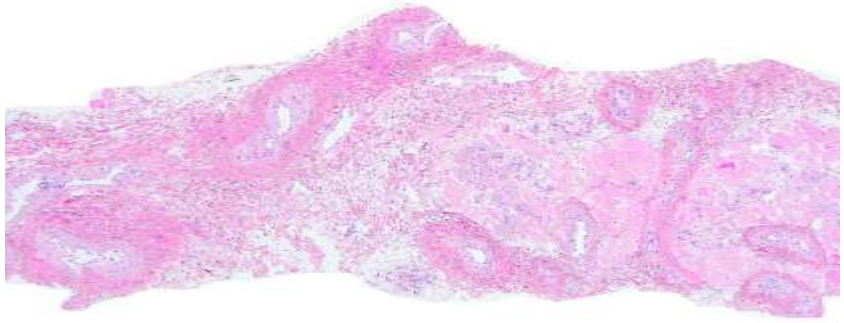
Slow Flow

- Fibroadipose Vascular Anomaly (FAVA)
- Venous malformation

“intramuscular hemangioma, capillary type”….

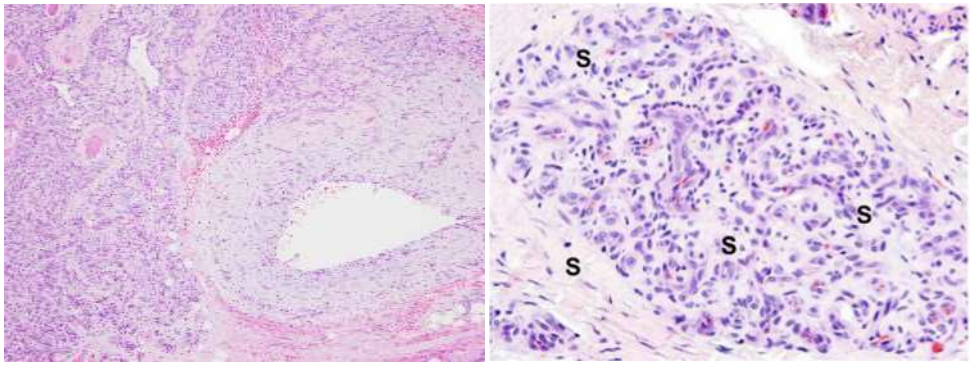
WHO Classification of Tumors, Paediatric tumors, 5th Ed (beta)

Arteriovenous malformation



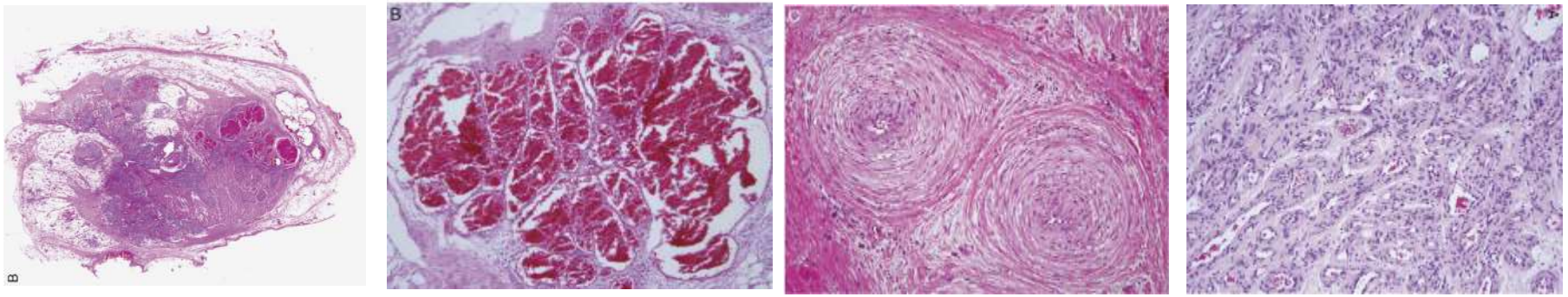
WHO Classification of Tumors, Paediatric tumors, 5th Ed (beta)

Intramuscular fast flow vascular anomaly



Angiogenesis. 2019;22(4):547-552.

PTEN hamartoma of soft tissue



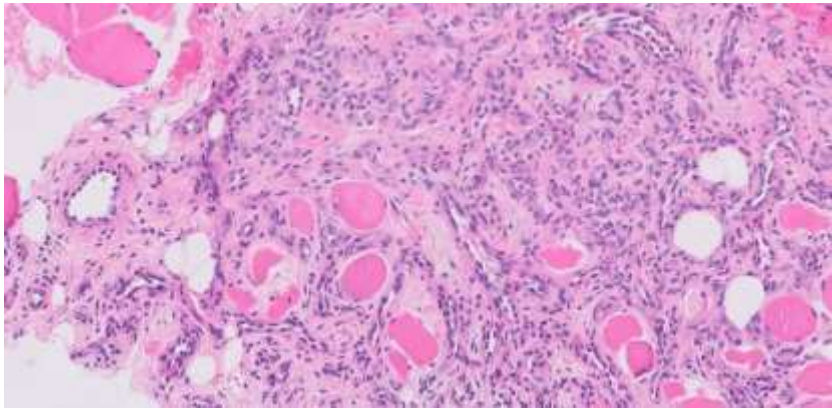
The American Journal of Surgical Pathology. 2012;36(5):671-687.

Next Generation Sequencing

Lesion	Molecular
Arteriovenous malformation	MAP2K1, KRAS
Intramuscular fast flow vascular anomaly	MAP2K1, KRAS
PTEN hamartoma of soft tissue	PTEN

- More diffuse
- Shunting between larger vessels

- More localized, well-defined "lesion"
- Small capillary sized vessels
- No obvious arteriovenous shunting



+

MAP2K1 F53_Q58delinsL MUTATION

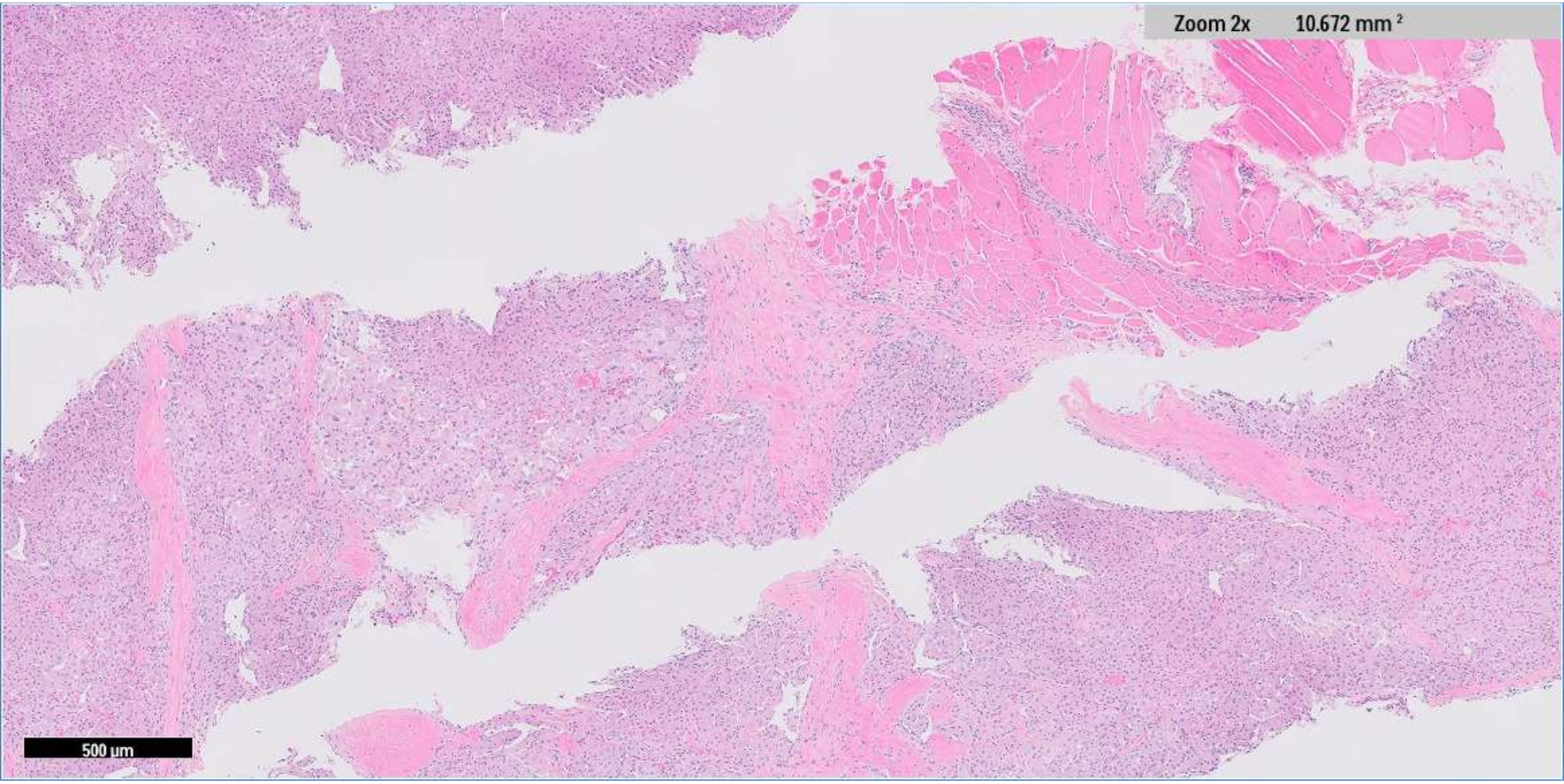
Intramuscular fast flow vascular anomaly

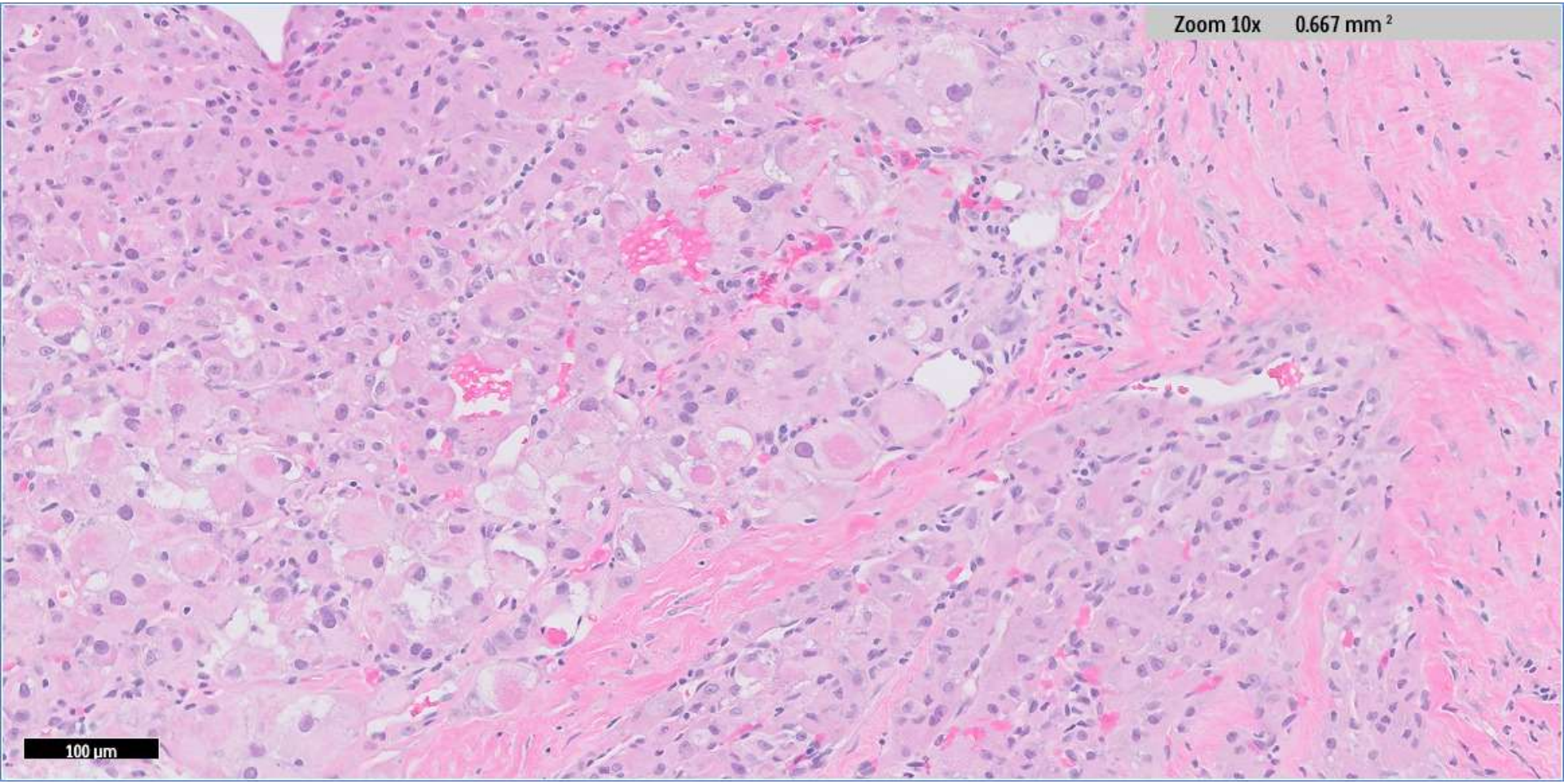
Seen in Vascular anomalies clinic
Imaging findings concordant!
Medical therapy to shrink lesion, will be followed by ablation

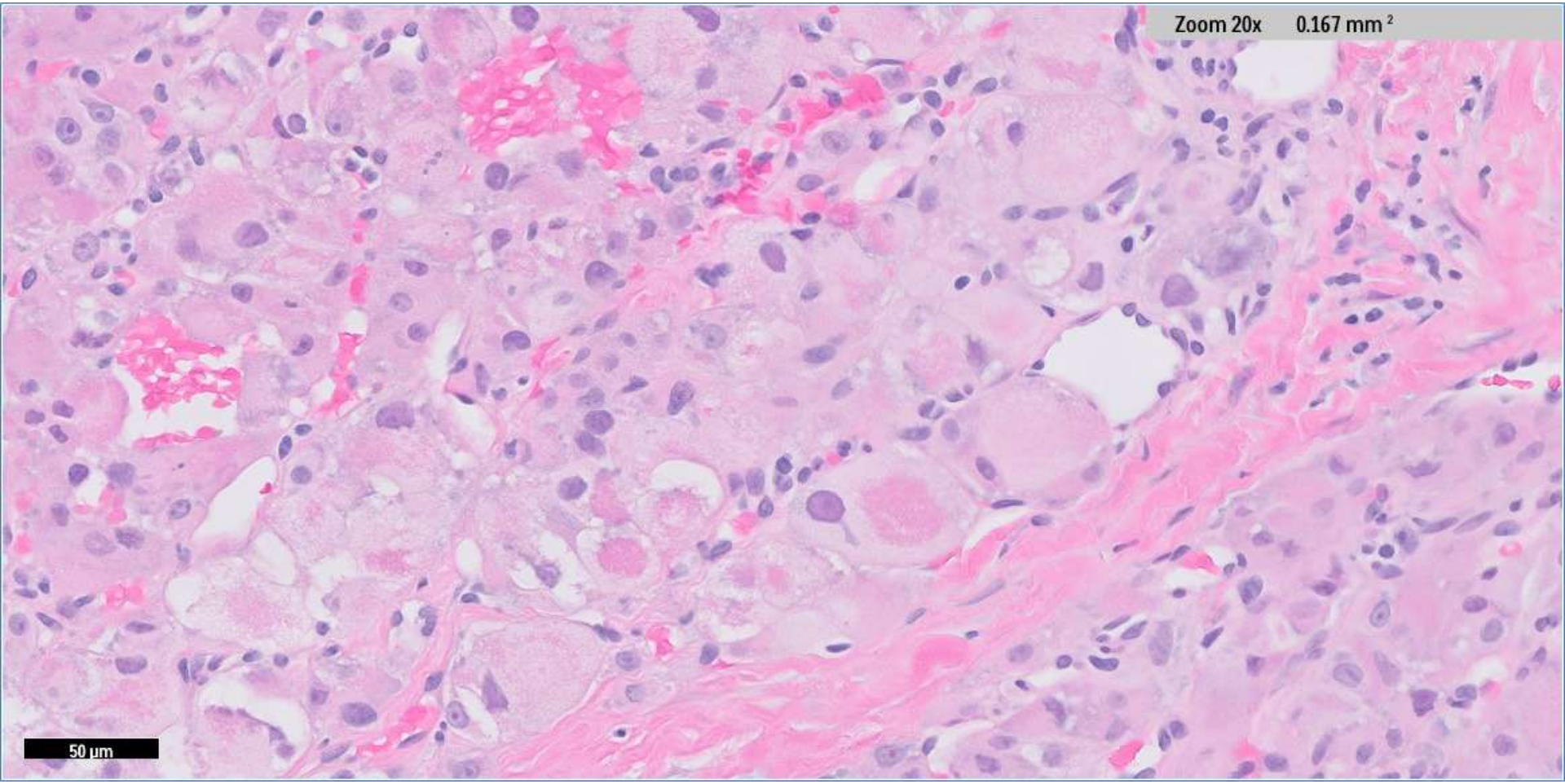
22-1006

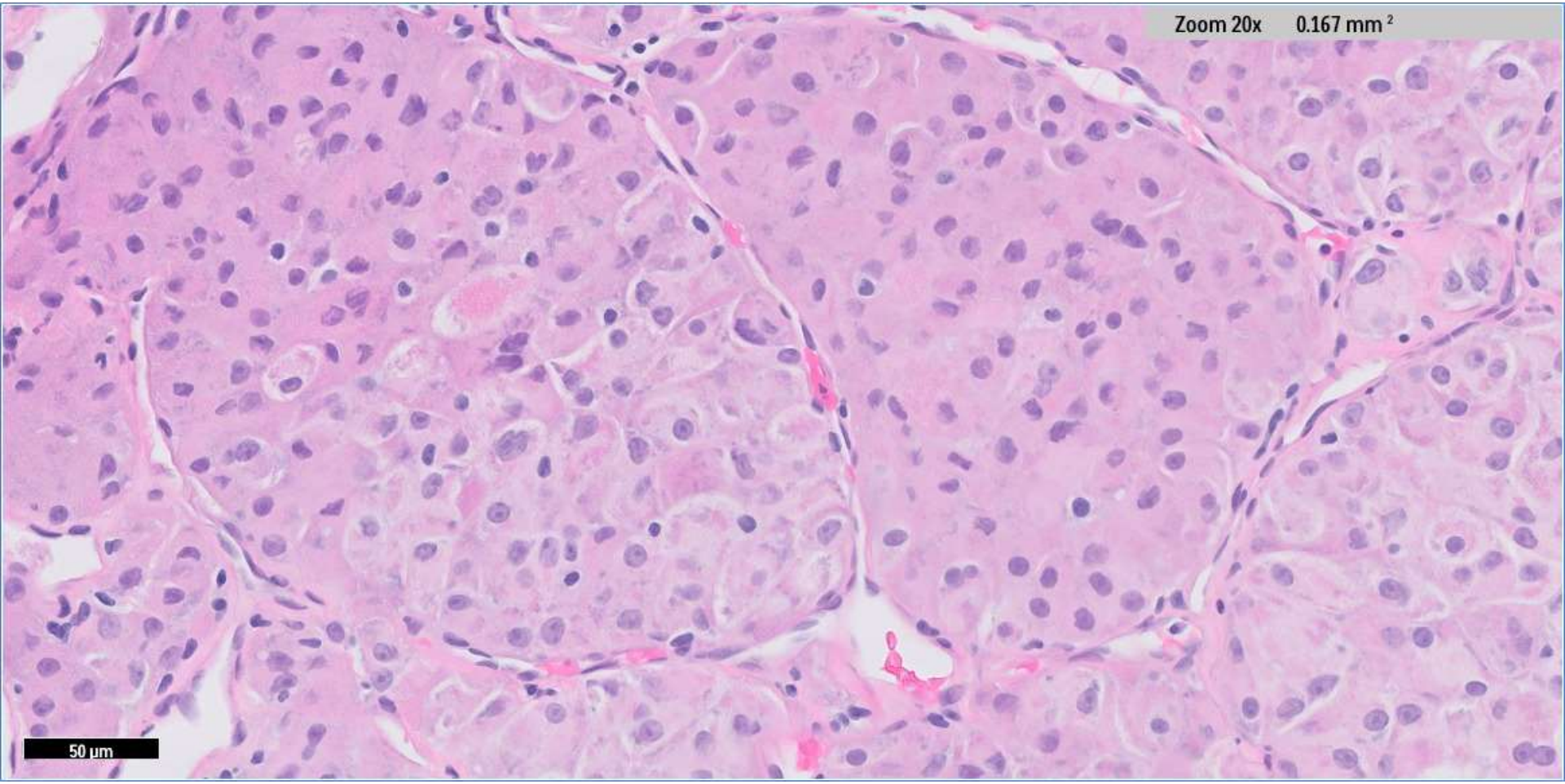
Andrew Xiao/Chris Schwartz/Steve Long; UCSF

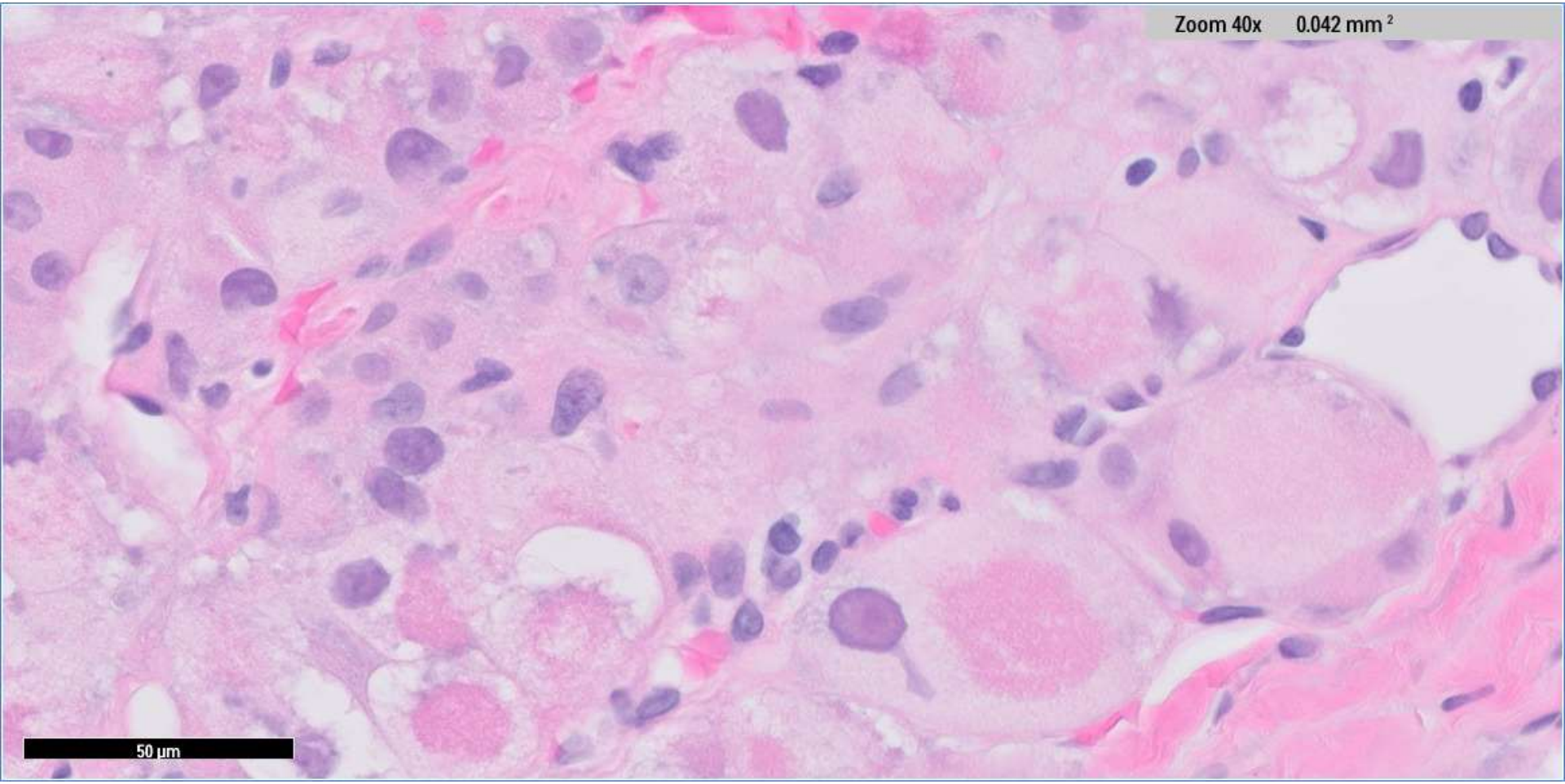
20ishF with recently identified palpable right breast mass. Ultrasound demonstrates a 37 x 15 x 33 mm hypoechoic, irregularly shaped solid mass with indistinct margins in the upper inner quadrant of the right breast. She undergoes ultrasound-guided core biopsy.

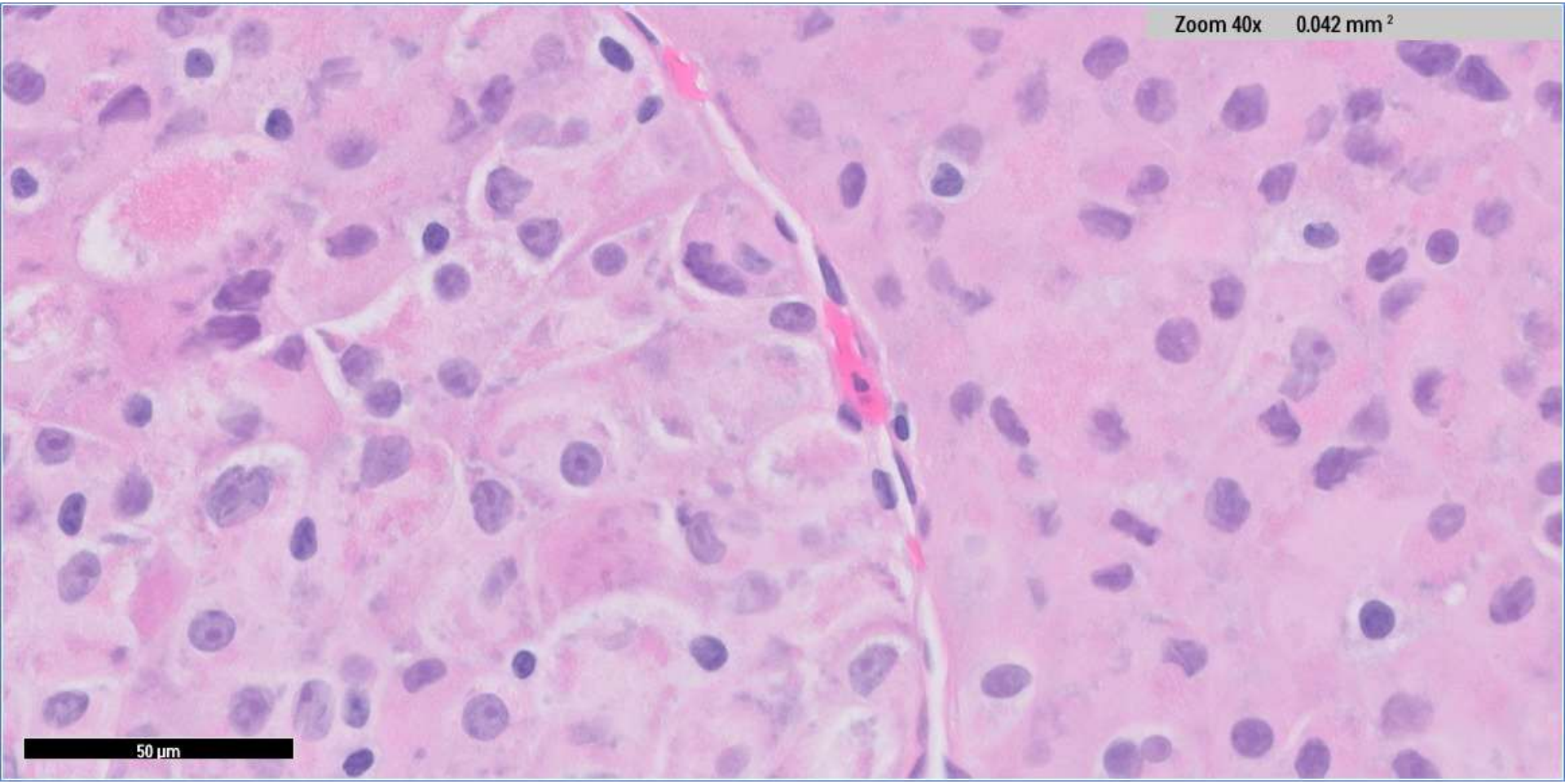

Zoom 2x
10.672 mm ²
500 µm


Zoom 10x 0.667 mm ²
100 µm


Zoom 20x 0.167 mm ²
50 µm


Zoom 20x 0.167 mm ²
50 µm


Zoom 40x 0.042 mm ²
50 µm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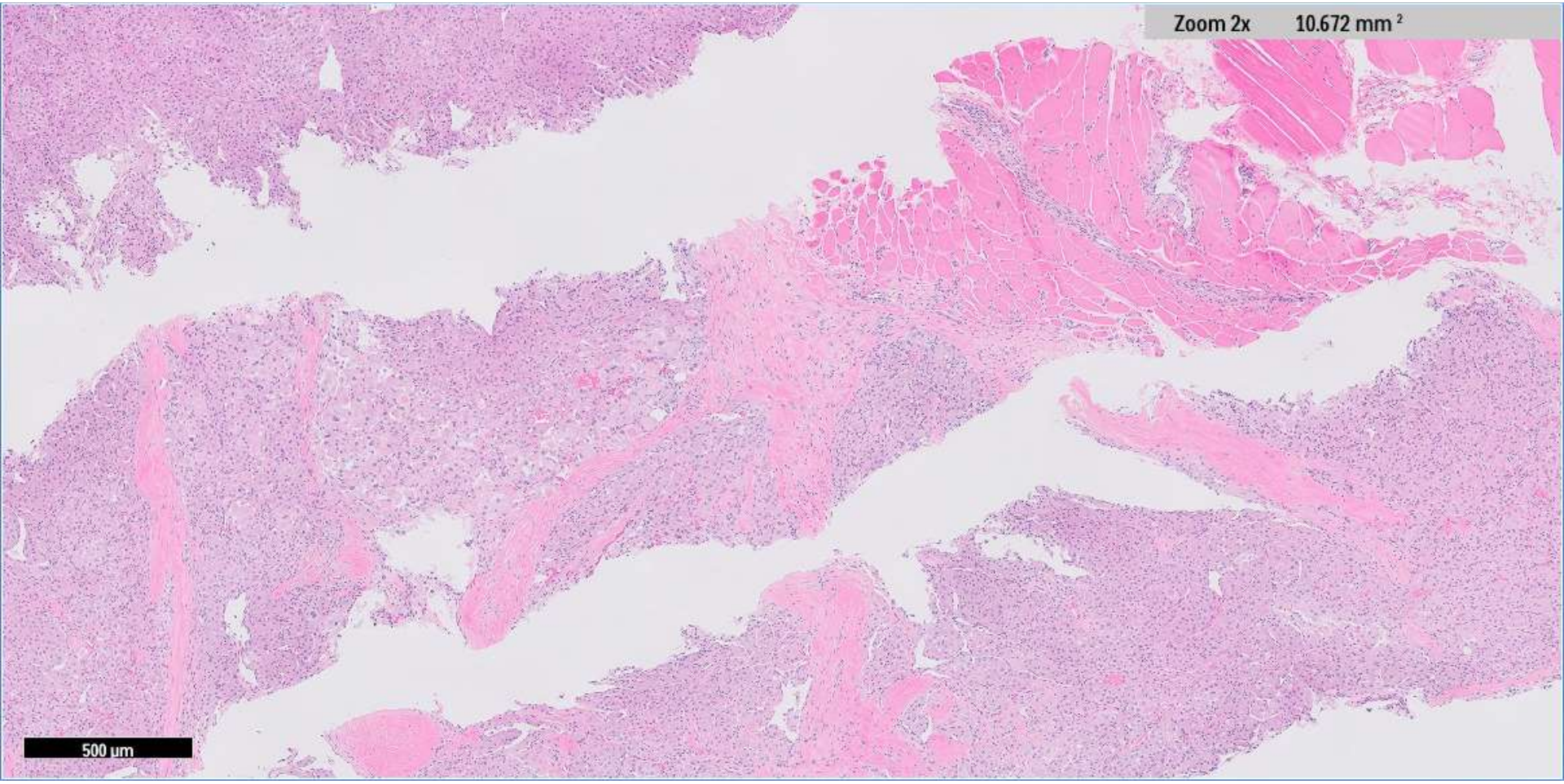
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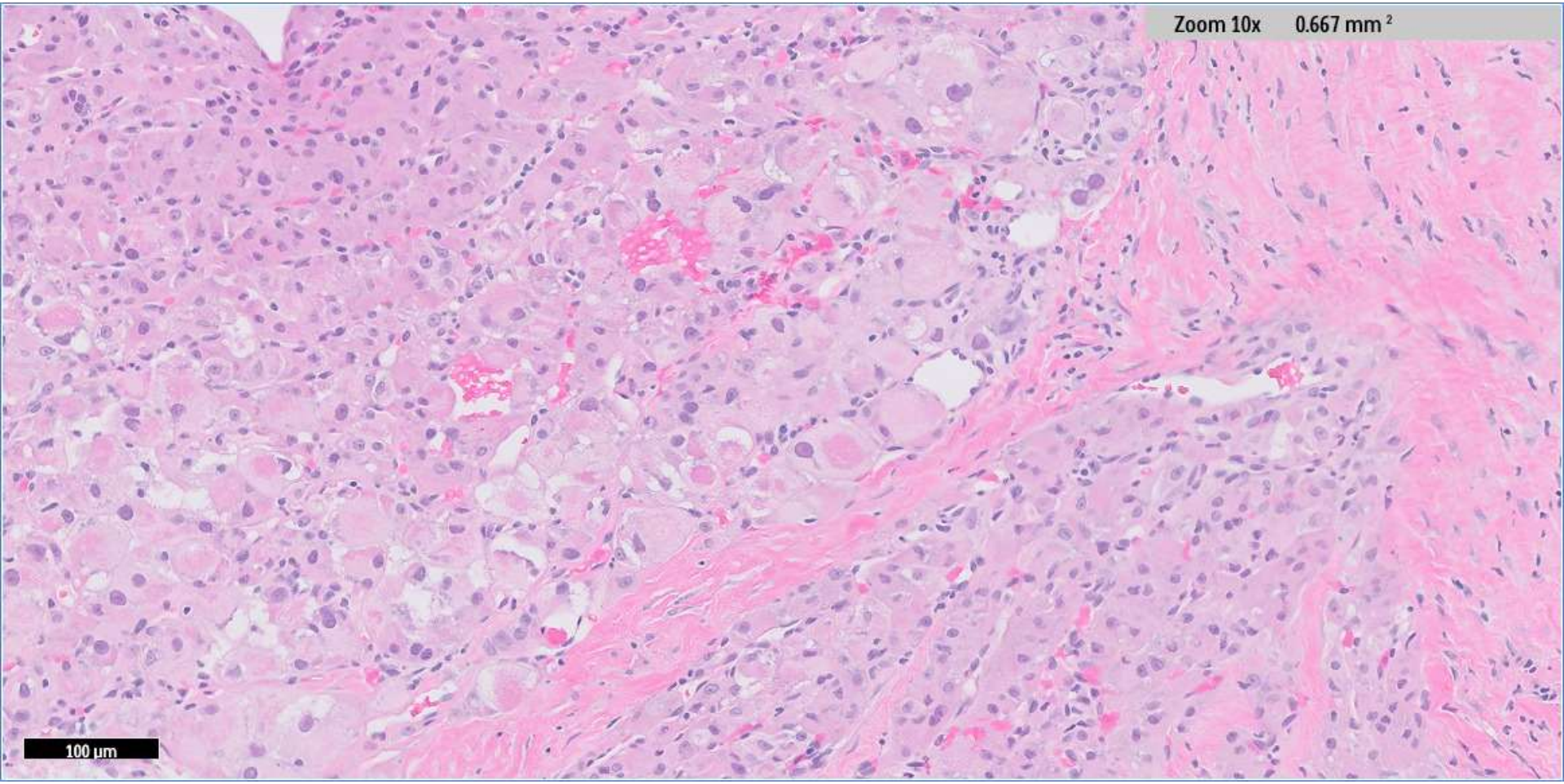
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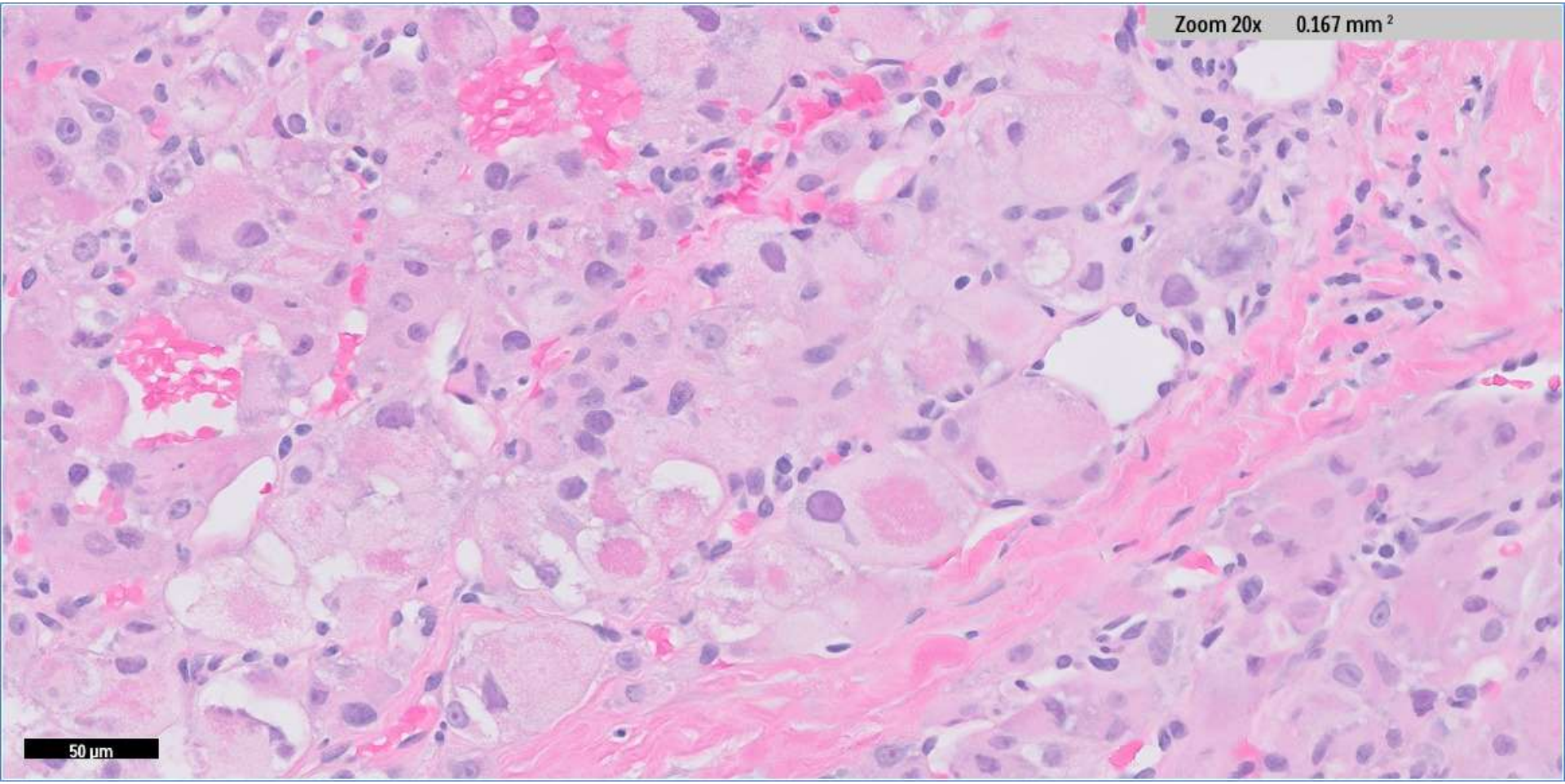
100 µm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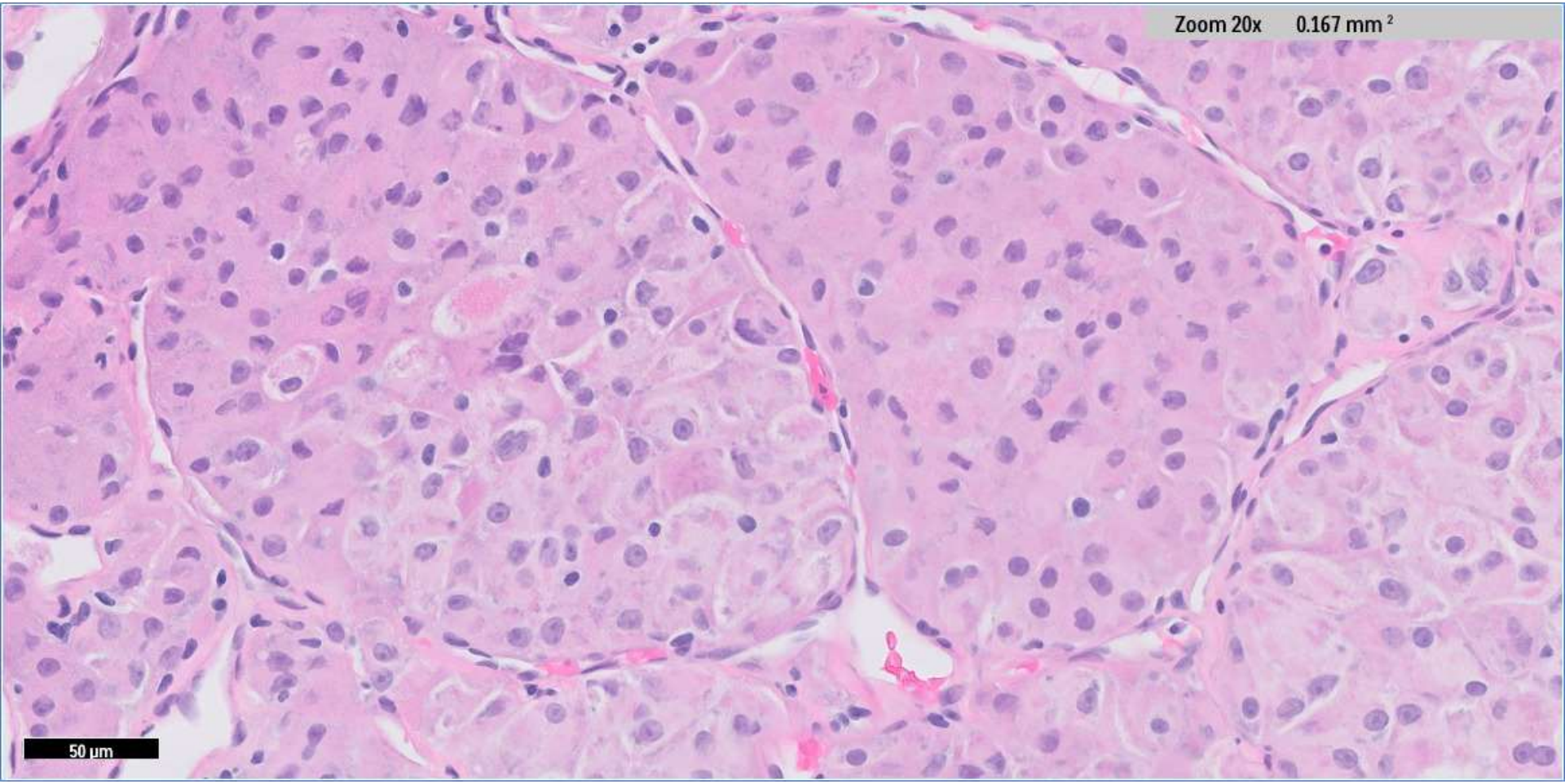
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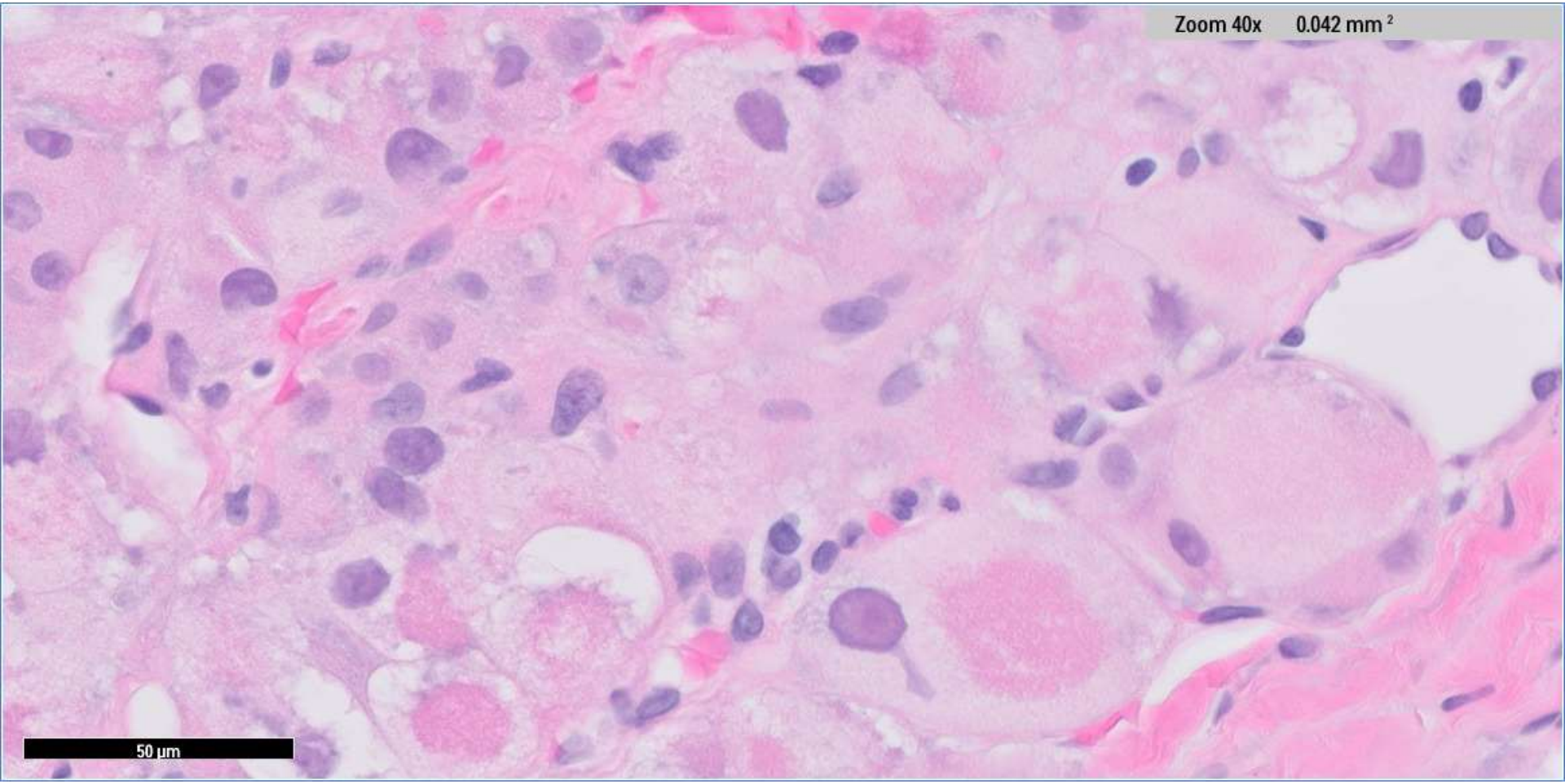
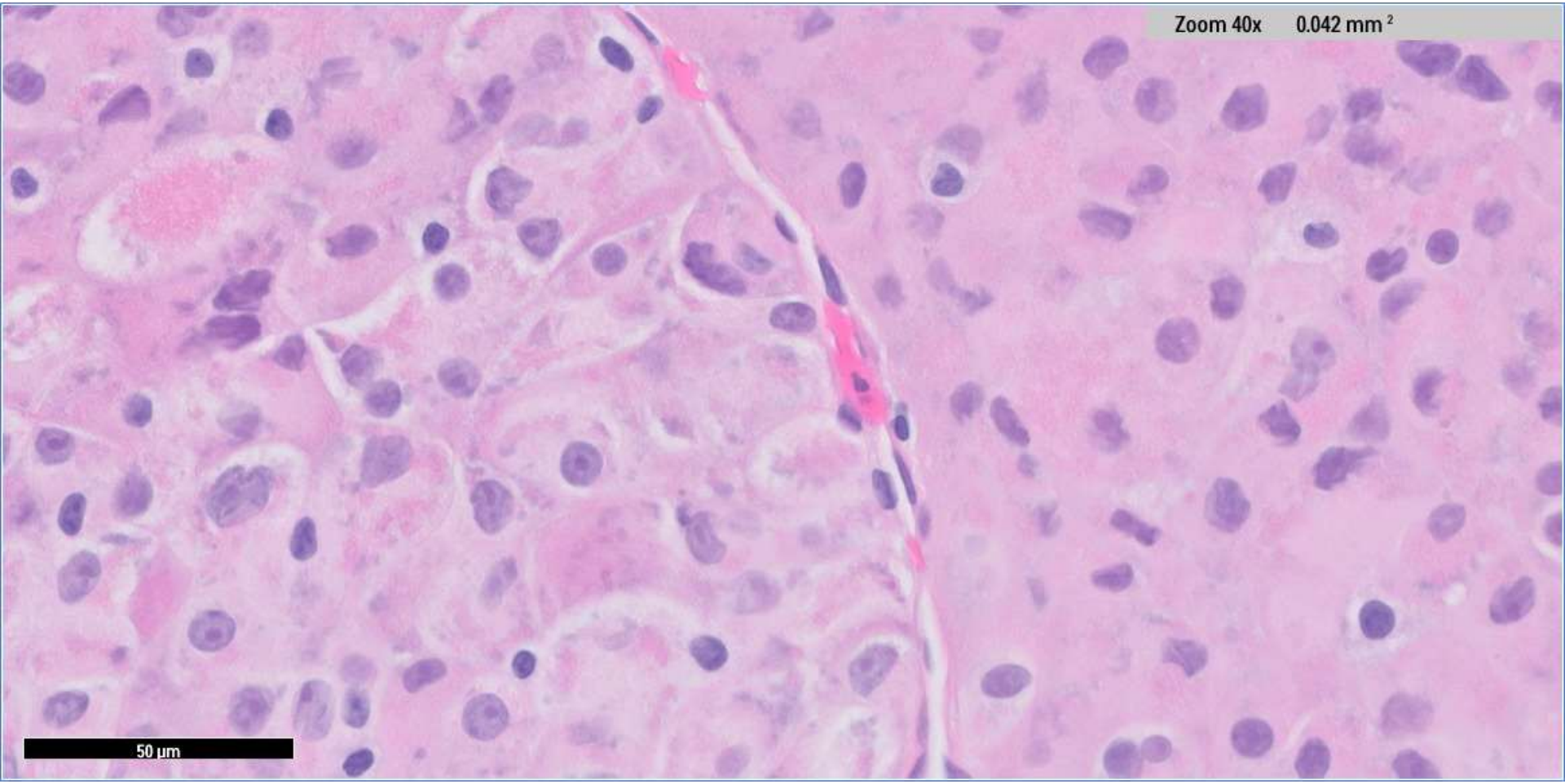
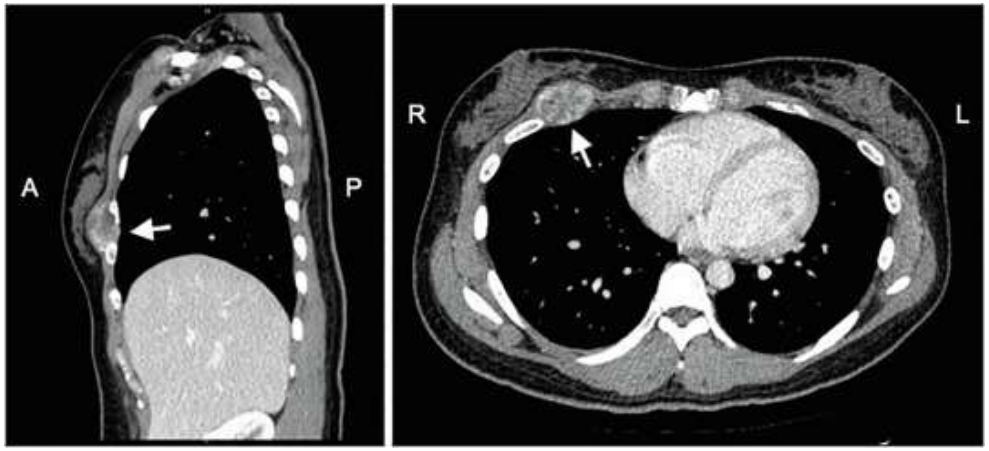

Zoom 40x 0.042 mm ²
50 µm


Zoom 40x 0.042 mm ²
50 µm

Initial Radiologic Imaging



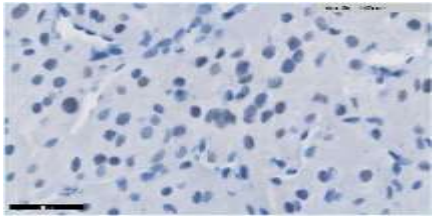
- CT:
  - Heterogeneously enhancing, oval mass involving the right pectoralis major muscle and chest wall
  - Clear fat plane separating the mass from the superficial breast tissue

Differential Diagnosis

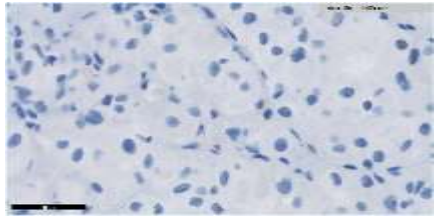
- Apocrine carcinoma of the breast
- PEComa
- Paraganglioma
- Granular cell tumor
- Rhabdomyoma
- Epithelioid smooth muscle tumor
- Rhabdomyosarcoma
- Melanoma
- Alveolar Soft Part Sarcoma
- Metastatic renal cell carcinoma

Stains

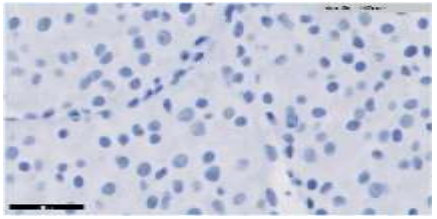
- Negative:
  - ER
  - PR
  - HER2
  - AR
  - Pan-cytokeratin
  - GCDFP-15
  - P63
  - SMM
  - S100
  - SOX10
  - PAX8
  - Synaptophysin
  - Chromogranin
  - MyoD1
  - Myogenin
  - Melan-A
  - HMB45
  - SMA
  - Desmin



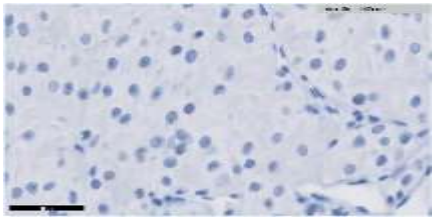
ER



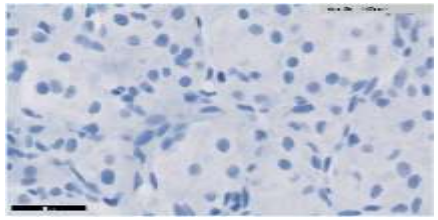
PR



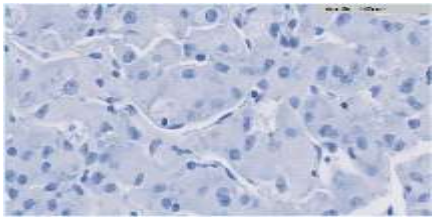
HER2



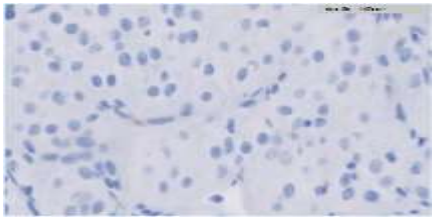
AR



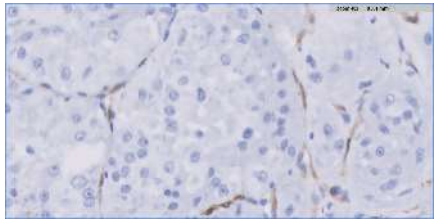
Pan-CK



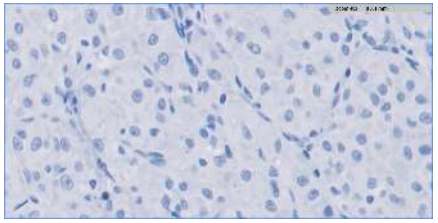
S100



MyoD1

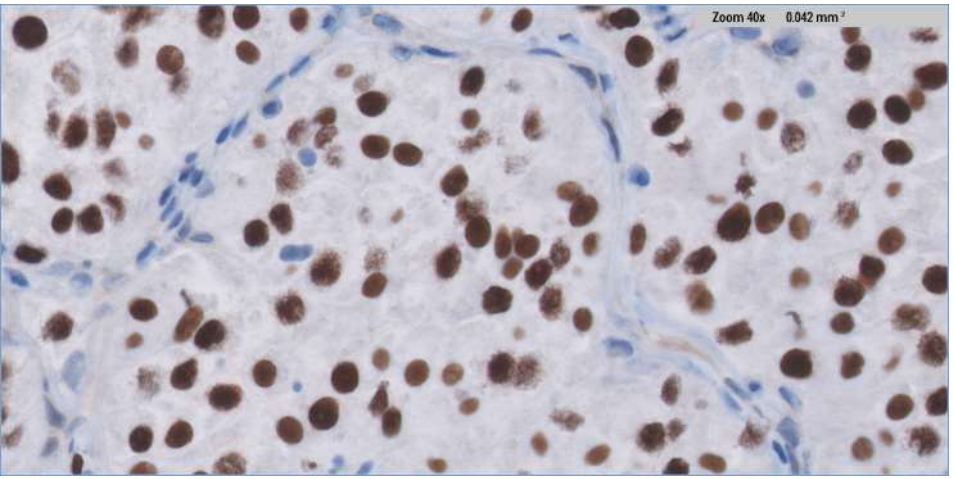


SMA

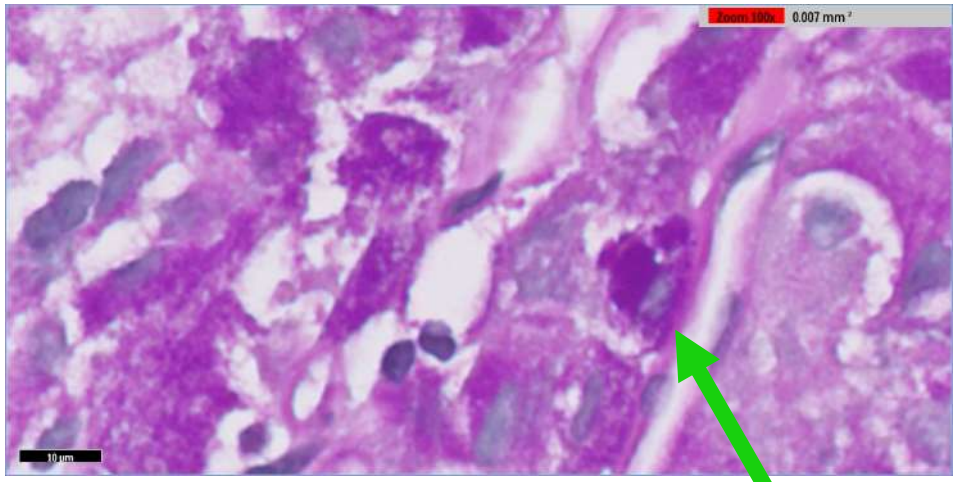


Melan-A

Stains



TFE3: positive



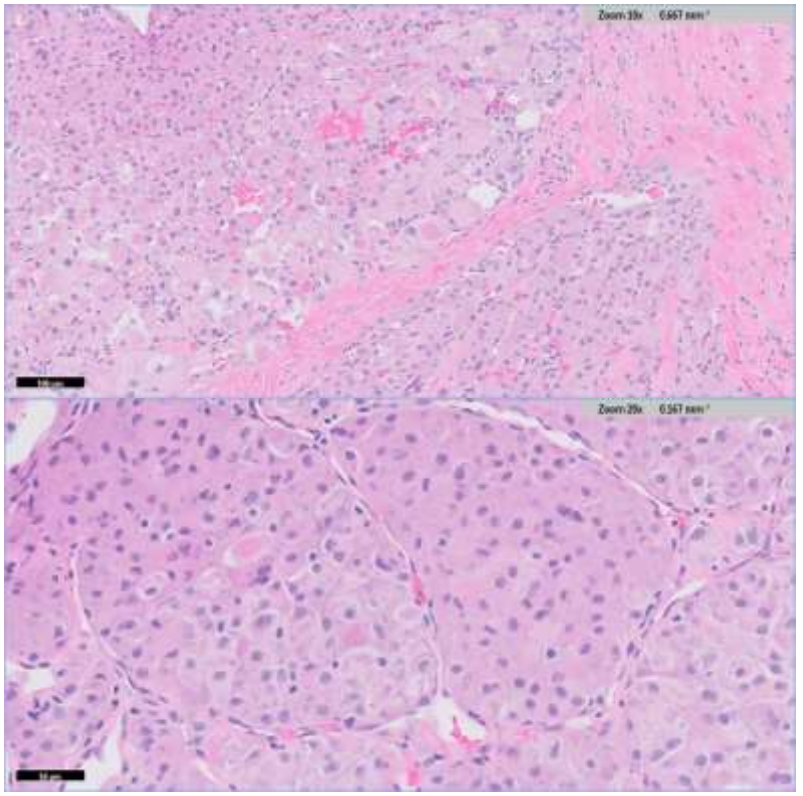
PAS: rare crystalloid formation

Diagnosis

- Alveolar soft part sarcoma (ASPS)

ASPS Key Microscopic Features

- Pseudoalveolar arrangement with centrally dyscohesive cells
  - Some variants show sheet-like growth
- Prominent compartmentalization
  - Thick, fibrous septa
  - Lobules and nests
- Cellular features:
  - Large, polygonal tumor cells
  - Ample eosinophilic, granular cytoplasm
  - Round nuclei
  - Prominent nucleoli
- Inconspicuous:
  - Mitosis
  - Necrosis



Workflow Performed

- Initial biopsy diagnosis:
  - Round cell sarcoma favor alveolar soft part sarcoma
- UCSF 500: ASPSCR1-TFE3 Fusion
- Full body PET:
  - No evidence of additional disease in the abdomen, pelvis, brain, or lower extremities,
  - Primary site: chest wall
- Treatment: resection (negative margins) & radiation

ASPS Clinical Profile

- Enigmatic differentiation & origin
  - Chimeric ASPSCR1-transcription factor E3 (TFE3) fusion protein
  - Characteristic t(X;17)(p11;q25) translocation
- Age at presentation: 15-35 years old (median: 25)
- Sex: Female predilection
- Location: Extremities ≫ trunk/pelvis/retroperitoneum, head/neck, female reproductive tract, other
- Metastasis: Lung ≫ bone, brain, other

ASPS Prognosis & Management

- Median overall survival:
  - No metastasis at diagnosis: 11 years
  - Metastasis at diagnosis: 3 years
- Treatment
  - Surgical resection
  - Positive margin: adjuvant radiation therapy
  - Metastatic:
    - Multi-targeted, tyrosine-kinase inhibitor: pazopanib, sunitinib
    - PDL-1 inhibitor: pembrolizumab

Key Points

- Include “outside” lesions in the differential
- Common demographic: Young female
- IHC: TFE3 positive
- *ASPSCR1-TFE3* fusion gene

References

- O'Sullivan Coyne G, Naqash AR, Sankaran H, Chen AP. Advances in the management of alveolar soft part sarcoma. Current Problems in Cancer. 2021;45(4):100775. doi:10.1016/j.currproblcancer.2021.100775

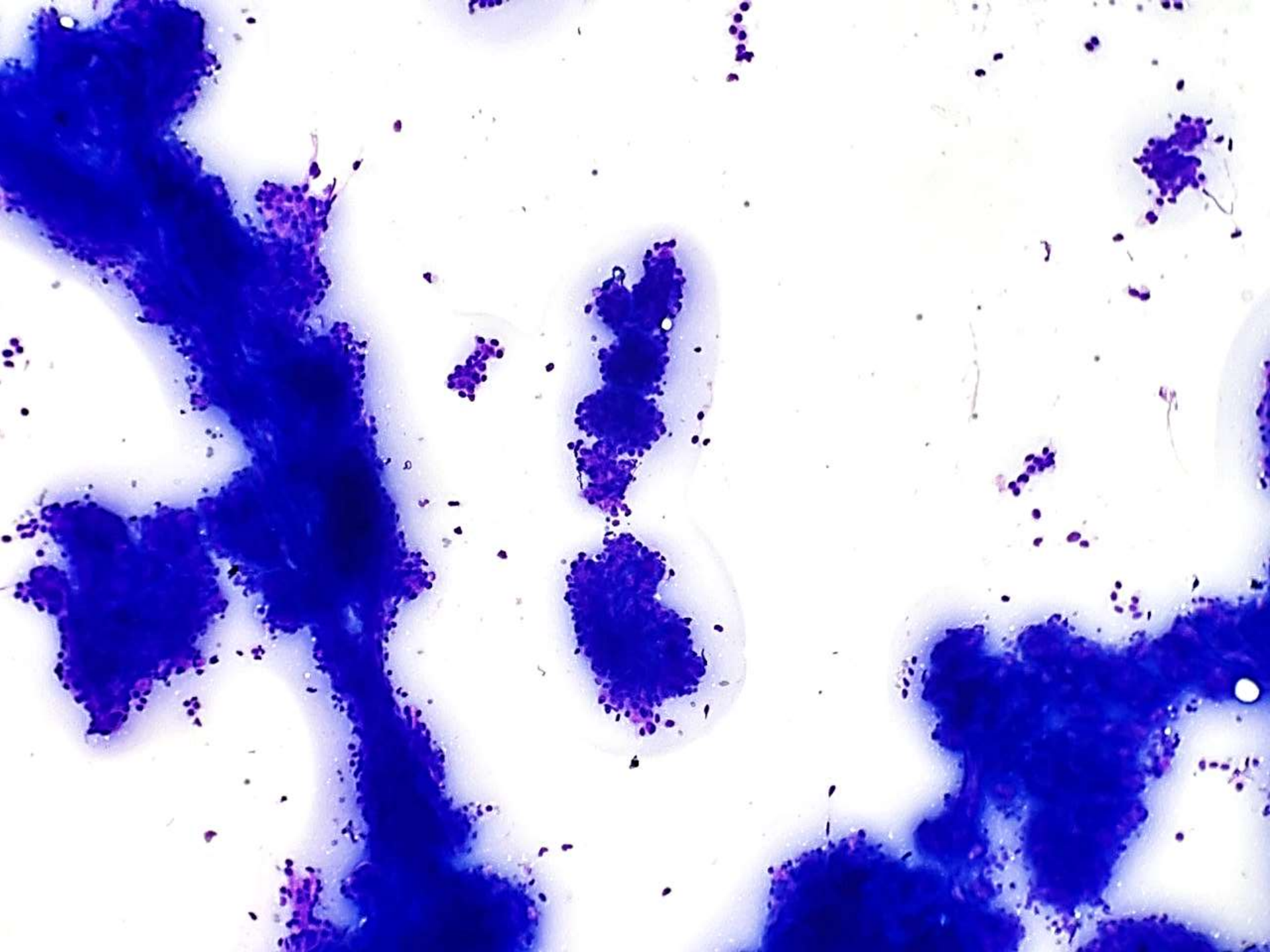
- Paoluzzi L, Maki RG. Diagnosis, prognosis, and treatment of alveolar soft-part sarcoma. *JAMA Oncology*. 2018;5(2):254-260. doi:10.1001/jamaoncol.2018.4490

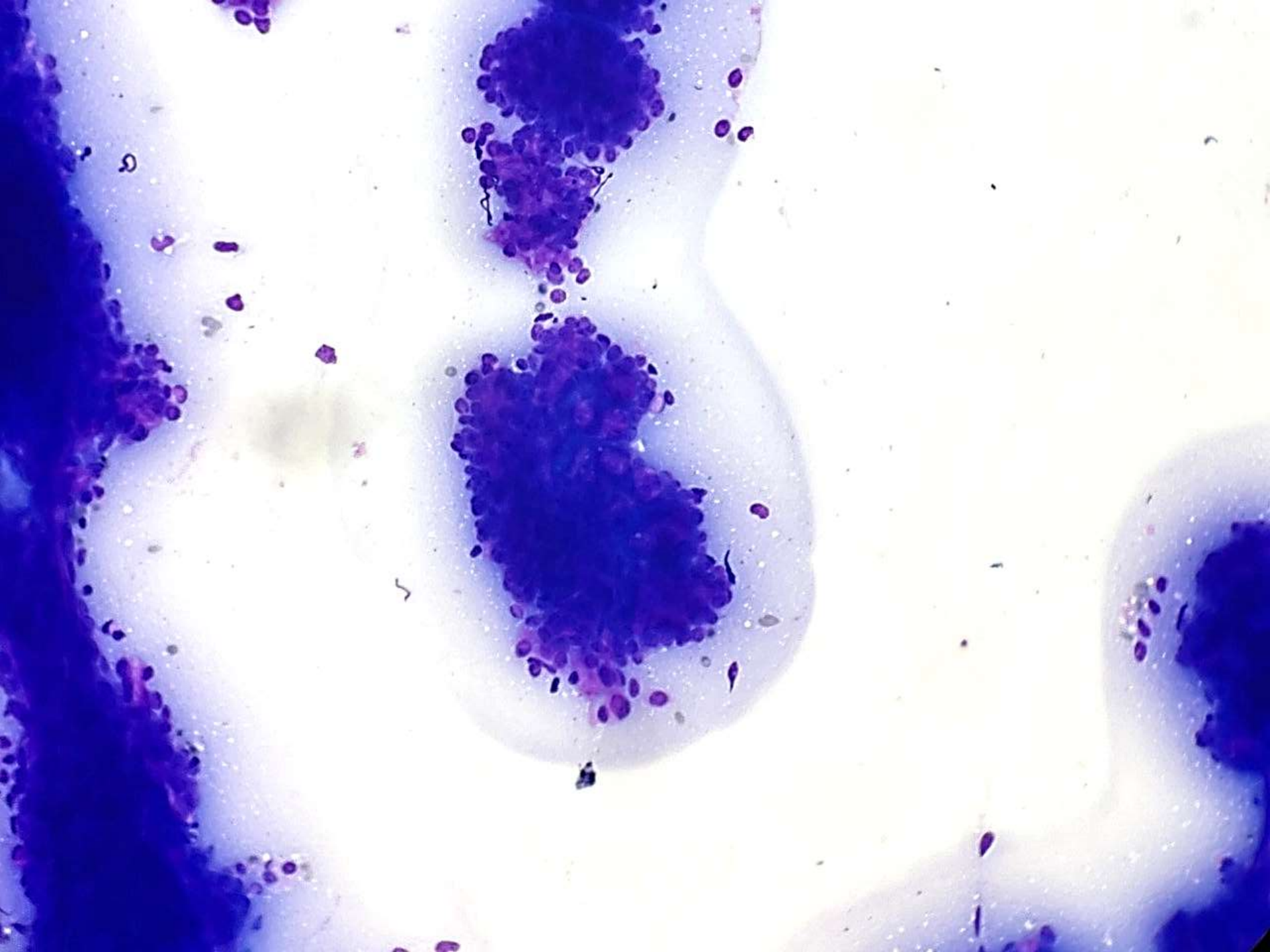
- Lu KL, Sieberg R, Freimanis RI, Greenwood HI, Schwartz CJ. Alveolar soft part sarcoma of the pectoralis mimicking a breast mass: A case report. *Human Pathology Reports*. 2022;29:300674. doi:10.1016/j.hpr.2022.300674

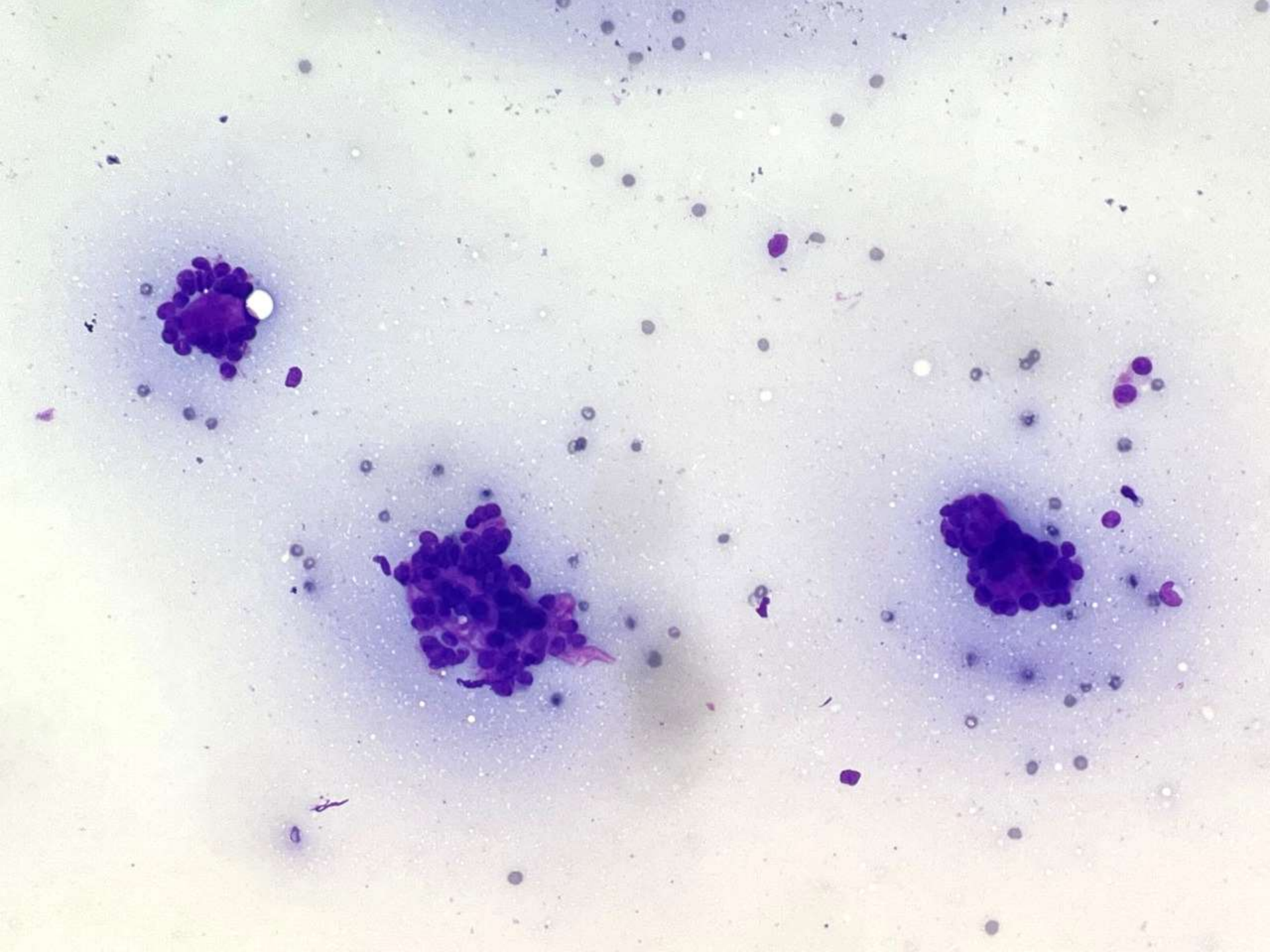
22-1007

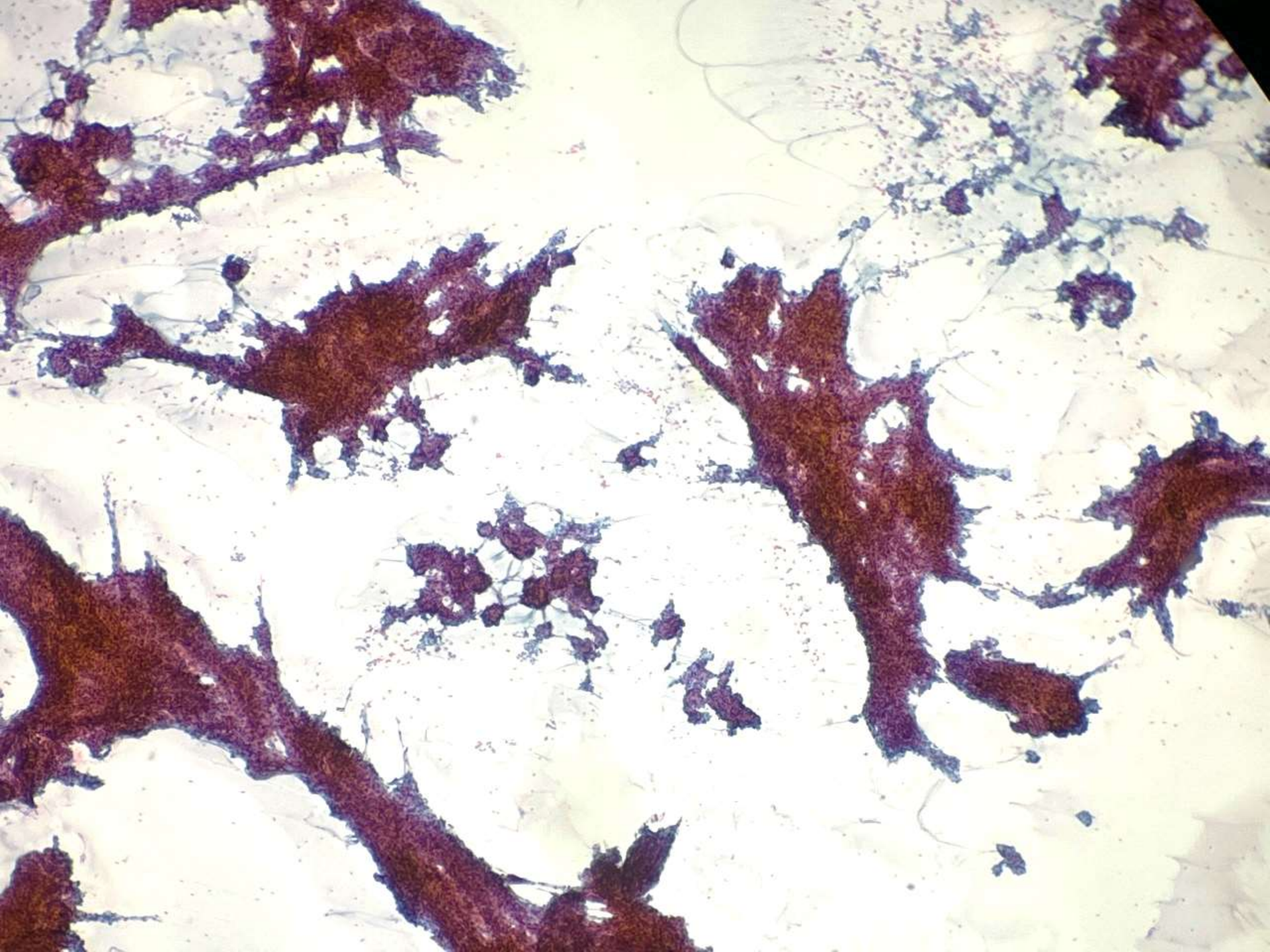
22-1007 Harris Goodman; Alameda Health

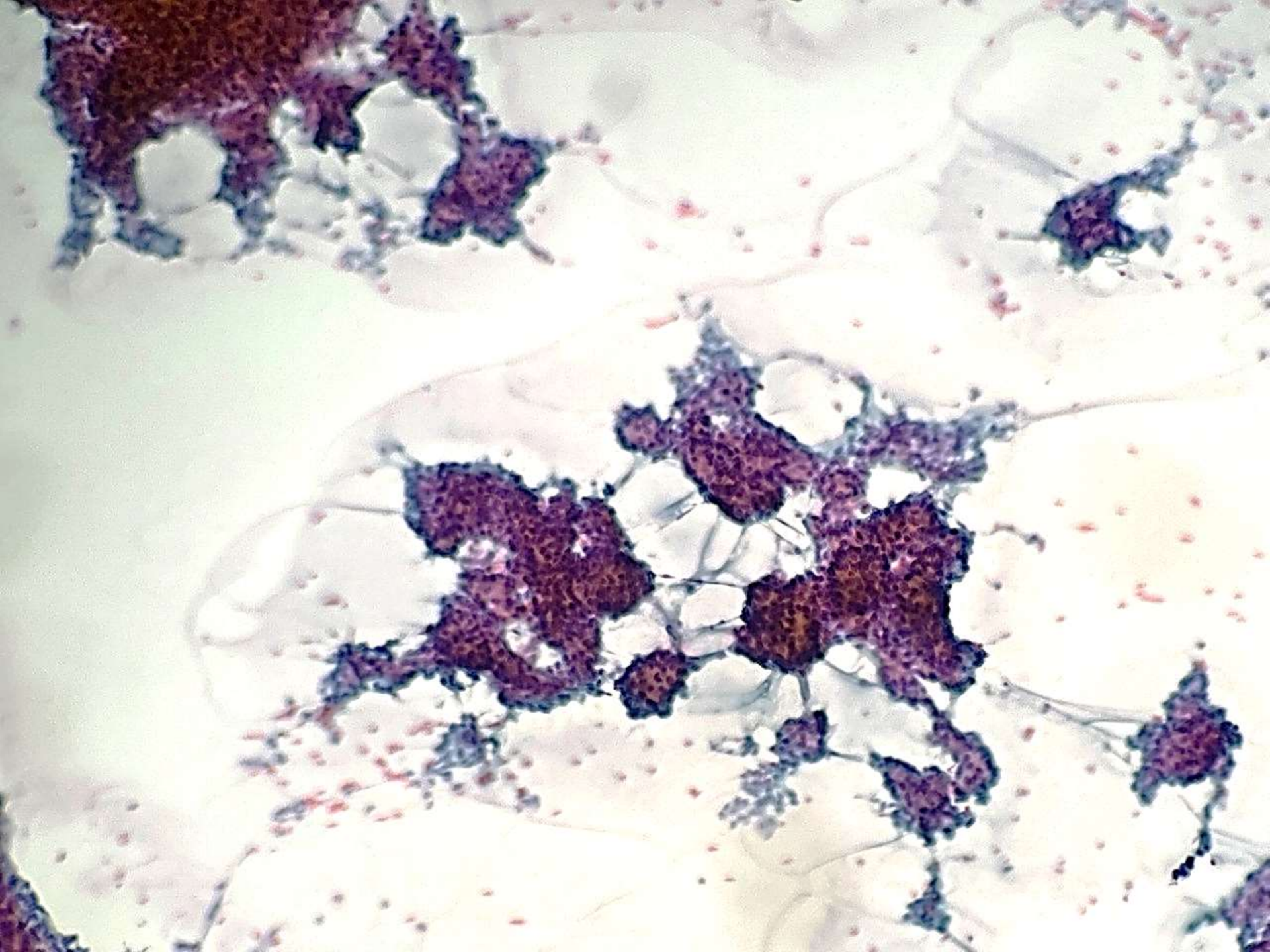
30ish F with right parotid mass, FNA performed.

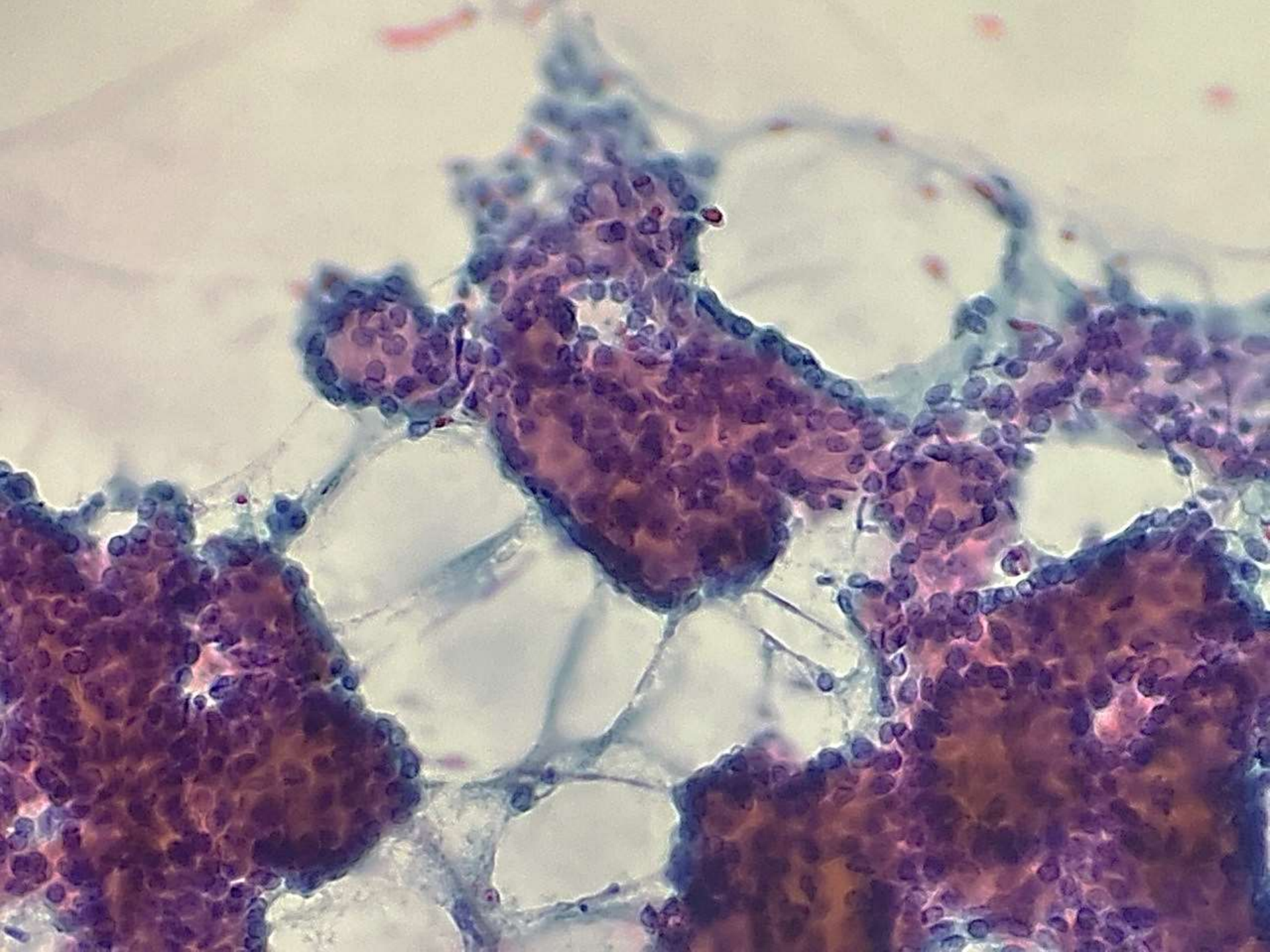












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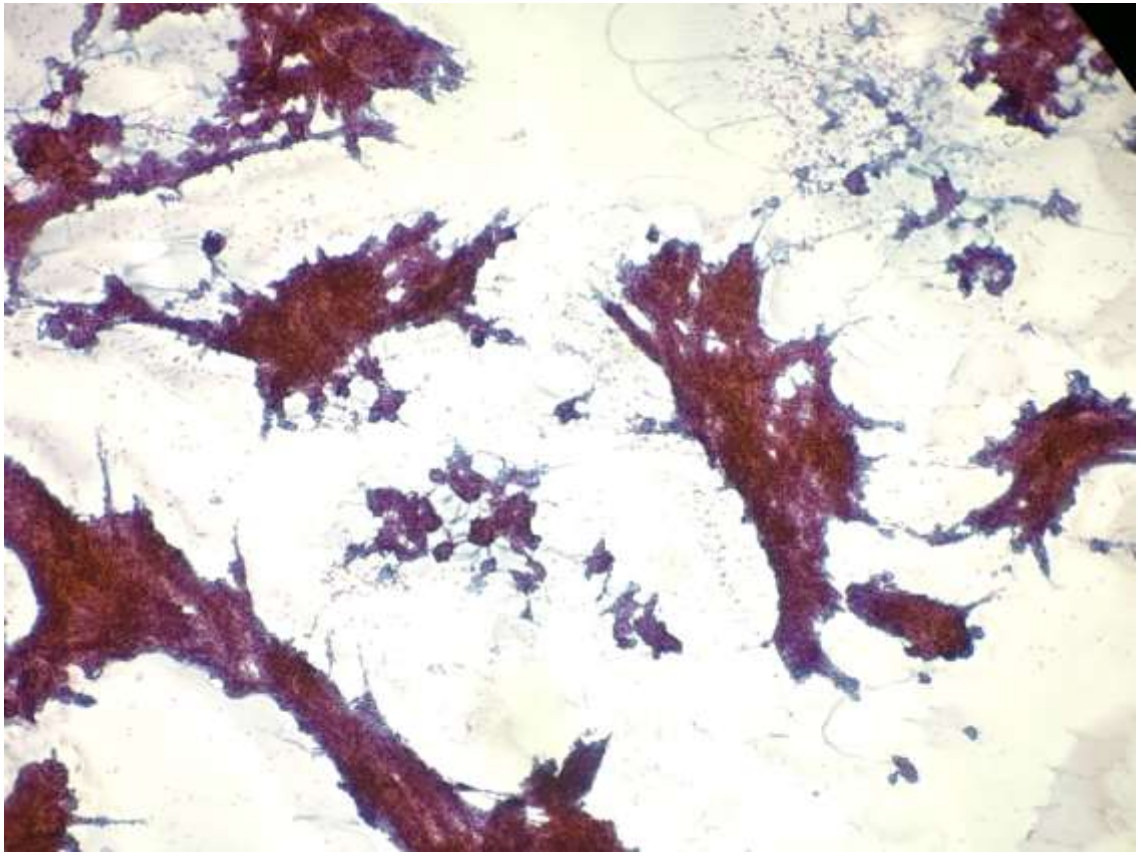

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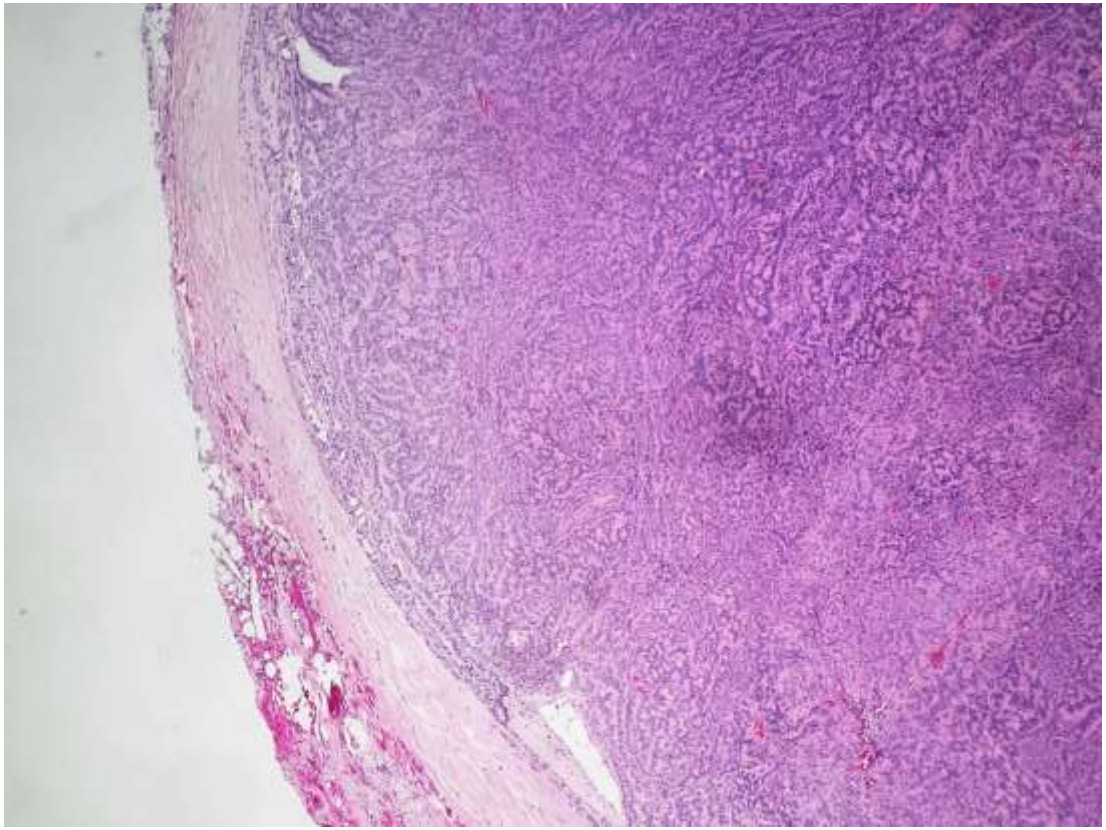

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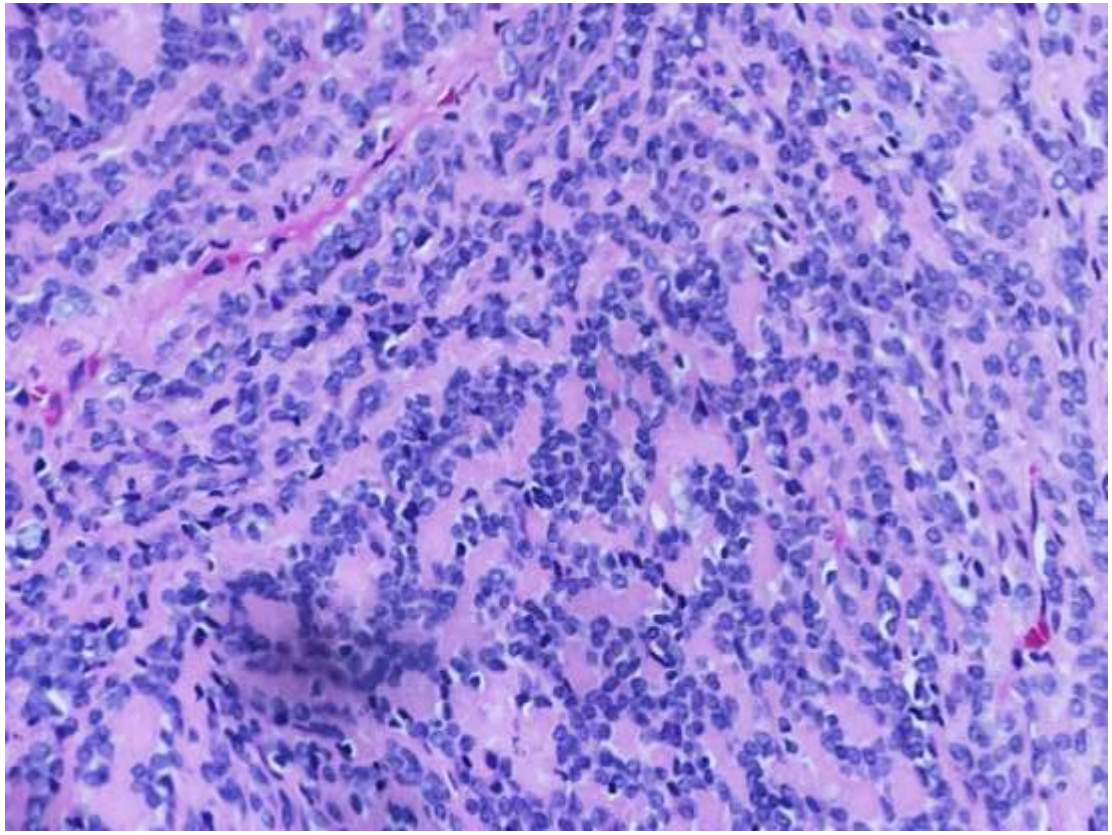


22-1007

- Salivary gland aspirates containing hyaline-type globules:
  - Cellular pleomorphic adenoma
  - Basal cell adenoma

  - Adenoid cystic carcinoma
  - Basal cell adenocarcinoma
  - Epithelial-myoepithelial carcinoma
  - Polymorphous adenocarcinoma
  - Pleomorphic adenoma
  - Metastatic basaloid squamous cell carcinoma

22-1007

- Salivary gland aspirates containing hyaline-type globules:
  - Benign lesions:
    - Cellular pleomorphic adenoma
      - Ragged chondromyxoid stroma

22-1007

- Salivary gland aspirates containing hyaline-type globules:
  - Malignant lesions:
    - Adenoid cystic carcinoma
      - Neural symptoms (e.g. pain, numbness or parathesias common).
      - 60 - 90% have characteristic and diagnostic fusion involving MYB, MYBL1 or NFIB gene.
    - Basal cell adenocarcinoma
      - Virtually indistinguishable for basal cell adenoma using FNA cytopathology.
      - May have pain, tenderness, adhesion to surrounding tissue.
    - Epithelial-myoepithelial carcinoma
      - Cytology is not reliable, has a high false negative rate (Cancer Cytopathol 2020;128:392).
      - Most cases may be misdiagnosed as pleomorphic adenoma due to overlapping cytological features.
    - Polymorphous adenocarcinoma
      - Usually intraoral.
      - 73 - 89% harbor PRKD1 E710D hotspot mutation (Nat Genet 2014;46:1166, Mod Pathol 2020;33:65, Am J Surg Pathol 2020;44:545).
      - 6 - 11% contain fusions involving PRKD1, PRKD2 or PRKD3 genes, with the fusion partners being ARID1A or DDX3X (Genes Chromosomes Cancer 2014;53:845, Mod Pathol 2020;33:65, Am J Surg Pathol 2020;44:545).
    - Metastatic basaloid squamous cell carcinoma
      - Usually men, age > 50 years, heavy smokers or drinkers.

22-1007

- References:

- Bhat, A., et. al. (2015), Basal cell adenoma of the parotid gland: Cytological diagnosis of an uncommon tumor. J Oral Maxillofac Pathol. Jan-Apr;19(1):106. https://doi: 10.4103/0973-029X.157211

  "Cytodiagnosis of basaloid tumors chiefly basal cell adenoma of the salivary gland, is extremely challenging. The cytological differential diagnoses range from benign to malignant, neoplastic to non-neoplastic lesions."

- Gupta, N., Bal, A., Gupta, A.K. and Rajwanshi, A. (2011), Basal cell adenoma: A diagnostic dilemma on fine needle aspiration cytology. Diagn. Cytopathol., 39: 913-916. https://doi.org/10.1002/dc.21576

  "Basaloid tumors are the most difficult problem in salivary gland fine needle aspiration cytology (FNAC)."

No, I am not done yet….

22-1007

- Christopher C. Griffith, MD, PhD, Reetesh K. Pai, MD, Frank Schneider, MD, Umamaheswar Duvvuri, MD, PhD, Robert L. Ferris, MD, PhD, Jonas T. Johnson, MD, Raja R. Seethala, MD
- Salivary Gland Tumor Fine-Needle Aspiration Cytology: A Proposal for a Risk Stratification Classification
- American Journal of Clinical Pathology, Volume 143, Issue 6, June 2015, Pages 839–853, https://doi.org/10.1309/AJCPMII6OSD2HSJA

22-1007

Table 2
Abbreviated Descriptions of Salivary Gland Aspiration Categories

Category	Description	Differential Diagnosis
Unsatisfactory/nondiagnostic	<4 hpf of epithelial cells and no definitive categorization can be made	
Cyst contents only	Unsatisfactory but with cyst content background (ie, histiocytes and granular debris)	
Nonneoplastic	Only benign acini and ducts or inflammatory background with only reactive epithelium	
Pleomorphic adenoma	Smears are characteristic for PA with bland ductal epithelial cells and myoepithelial cells embedded in a fibrillary myxochondroid stroma; stroma comprises at least 25% of the specimen	
Monomorphic cellular basaloid neoplasm	Neoplastic cells have scant cytoplasm with low to moderate nuclear grade; stroma comprises less than 25% of the specimen; the quality of the stroma determines the subclassification as follows:	
With fibrillary stroma	Mostly composed of cells with scant cytoplasm but with scant fibrillary stroma often with intermixed basaloid myoepithelial cells; stroma is metachromatic on Romanowsky stain	Cellular pleomorphic adenoma, epithelial myoepithelial carcinoma, basal cell adenoma/adenocarcinoma
With hyaline stroma	Stroma has a harder appearance than fibrillary stroma; neoplastic cells are usually excluded from the stroma	Basal cell adenoma/adenocarcinoma, adenoid cystic carcinoma, epithelial myoepithelial carcinoma
With mixed/other stroma	Stroma is difficult to classify as either fibrillary or hyaline; stroma may be scant to absent	Basal cell adenoma/adenocarcinoma, adenoid cystic carcinoma, epithelial myoepithelial carcinoma
Pleomorphic basaloid neoplasm	Smears show a predominantly basaloid neoplasm composed of pleomorphic nuclei suggestive of a high-grade malignancy; other high-grade nuclear features may also be seen (mitotic activity, apoptosis, nuclear membrane irregularities)	Salivary gland carcinoma with HGT, metastatic high-grade neuroendocrine carcinoma, metastatic nonkeratinizing SqCC
Warthin tumor	Smears are characteristic for WT; cellular constituents are truly oncocytic, highly cohesive, and have low to moderate nuclear grade; lymphocytes are present in the background or as lymphoid tangles mixed with epithelium; the background may be slightly mucinous or with cyst contents	
Monomorphic oncocytoid neoplasm	Cells have more cytoplasm than basaloid cells but may not represent true oncocytes; nuclear grade is low to moderate, but smears are not sufficiently characteristic of WT; prominent vacuoles excludes these categories; fine, dense granularity of an oncocyte is common but coarse foamy granularity excludes this category; background determines subclassification as follows:	
With cyst content background	Mostly histiocytes and finely granular debris comprise the background of smears	Warthin tumor, oncocytic cystadenoma
With mucinous background	Mucinous strands are present in the background; often cells with intracellular mucin can also be seen, but this is not required	Mucoepidermoid carcinoma, metaplastic Warthin tumor
With other background	Background material is not classifiable as cyst contents or mucinous; often these smears show a clean background	Oncocytoma
Oncocytoid neoplasm, coarsely granular/vacuolated cytoplasm	Neoplastic cells have prominent foamy and coarsely granular or vacuolated cytoplasm but are not characteristic of true oncocytes; in general, these smears are more dyshesive and have more naked nuclei than monomorphic oncocytoid neoplasms	Acinic cell carcinoma, mammary analogue secretory carcinoma, metastatic renal cell carcinoma
Pleomorphic oncocytoid neoplasm	Neoplastic cells have abundant cytoplasm and pleomorphic nuclei that often show other high-grade nuclear features (mitotic activity, apoptosis)	Salivary duct carcinoma, high-grade mucoepidermoid carcinoma metastatic carcinoma (adeno or squamous), metastatic melanoma

22-1007

Table 5
Consolidation of New Cytology Categories Into Classes

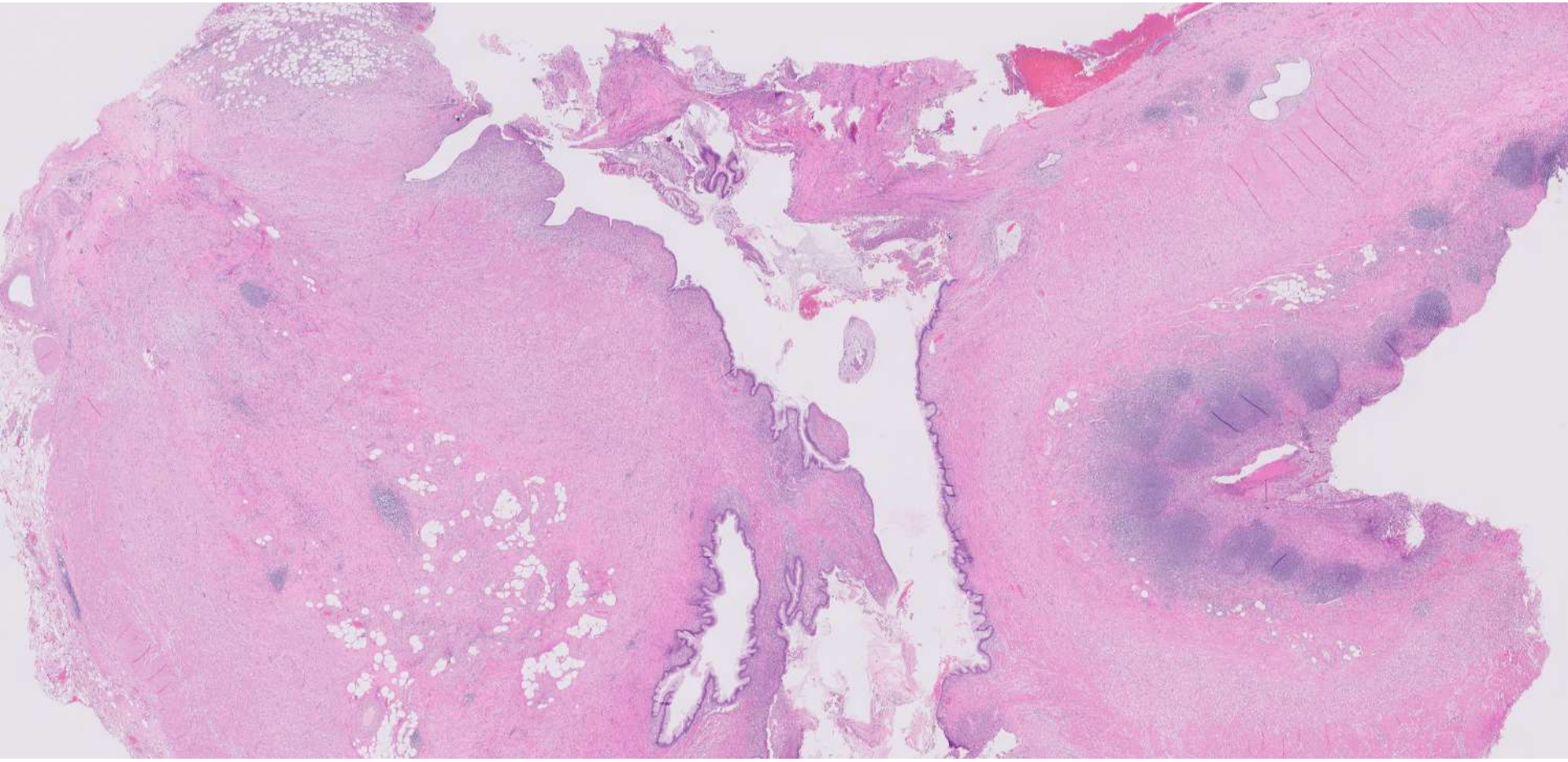
Categorization/Subcategorization	Risk of Malignancy, No./Total No. (%)	Classification	No./Total No. (%)	
			Overall Risk of Malignancy	Overall Risk of HG Malignancy
Nonneoplastic	0/25 (0)	Benign	2/103 (2.0)	1/103 (1.0)
Pleomorphic adenoma	2/49 (4.1)			
Warthin tumor	0/29 (0)			
Monomorphic cellular basaloid neoplasm with fibrillary stroma	2/13 (15.4)	NUMP	9/50 (18.0)	2/50 (4.0)
Monomorphic cellular basaloid neoplasm with hyaline stroma	3/7 (42.9)			
Monomorphic oncocytoid neoplasm with cyst contents background	0/11 (0)			
Monomorphic oncocytoid neoplasm with other background	4/19 (21.1)			
Monomorphic cellular basaloid neoplasm with mixed/other	6/10 (60.0)	Suspicious for malignancy	25/33 (75.8)	9/33 (27.3)
Monomorphic oncocytoid neoplasm with mucinous background	8/10 (80.0)			
Cellular basaloid neoplasm with coarsely granular/vacuolated cytoplasm	11/13 (84.6)			
Pleomorphic basaloid neoplasm	4/4 (100.0)	Positive for malignancy	25/25 (100.0)	22/25 (88.0)
Pleomorphic oncocytoid neoplasm	21/21 (100.0)			

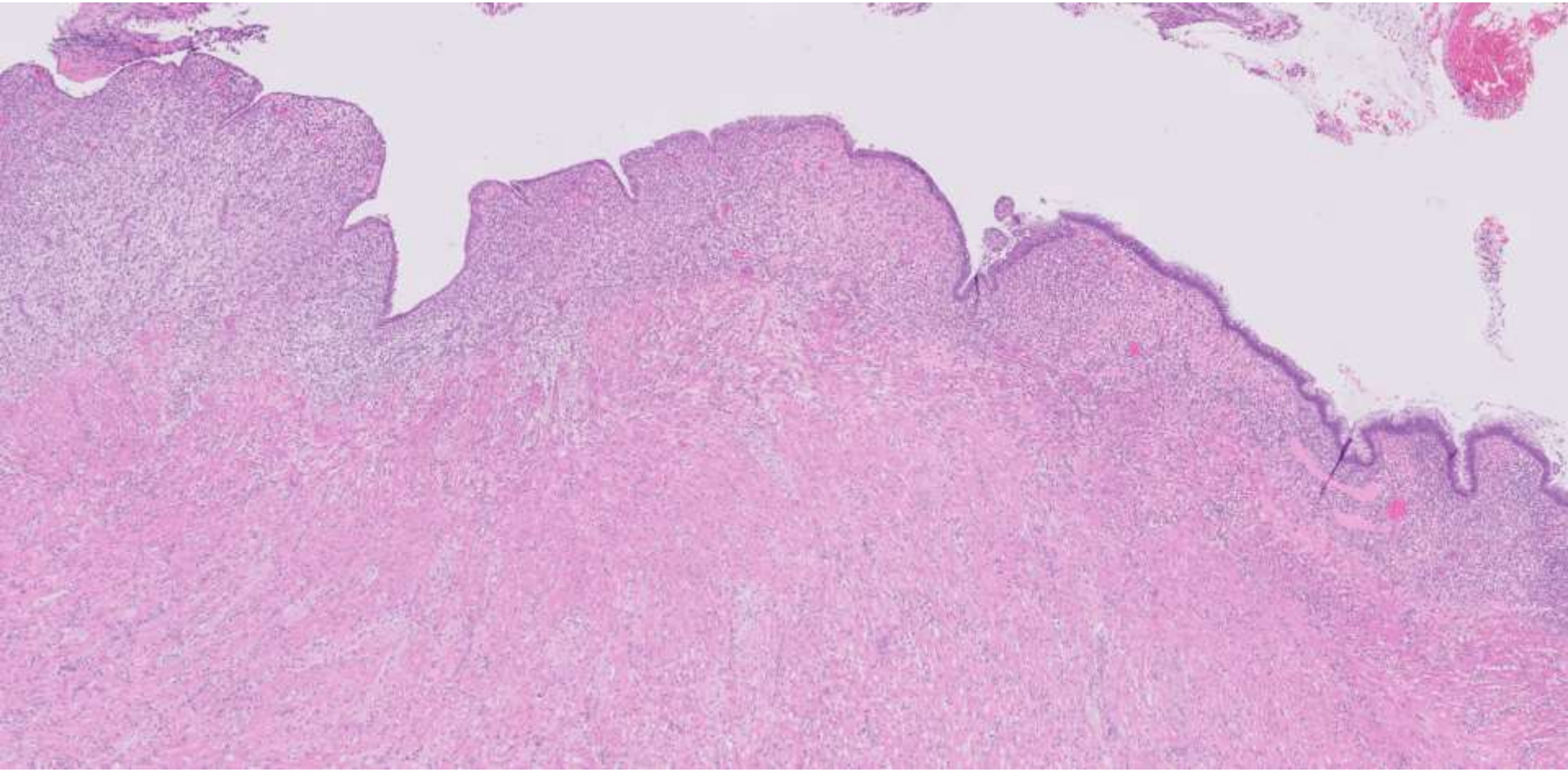
HG, high-grade; NUMP, neoplasm of uncertain malignant potential.

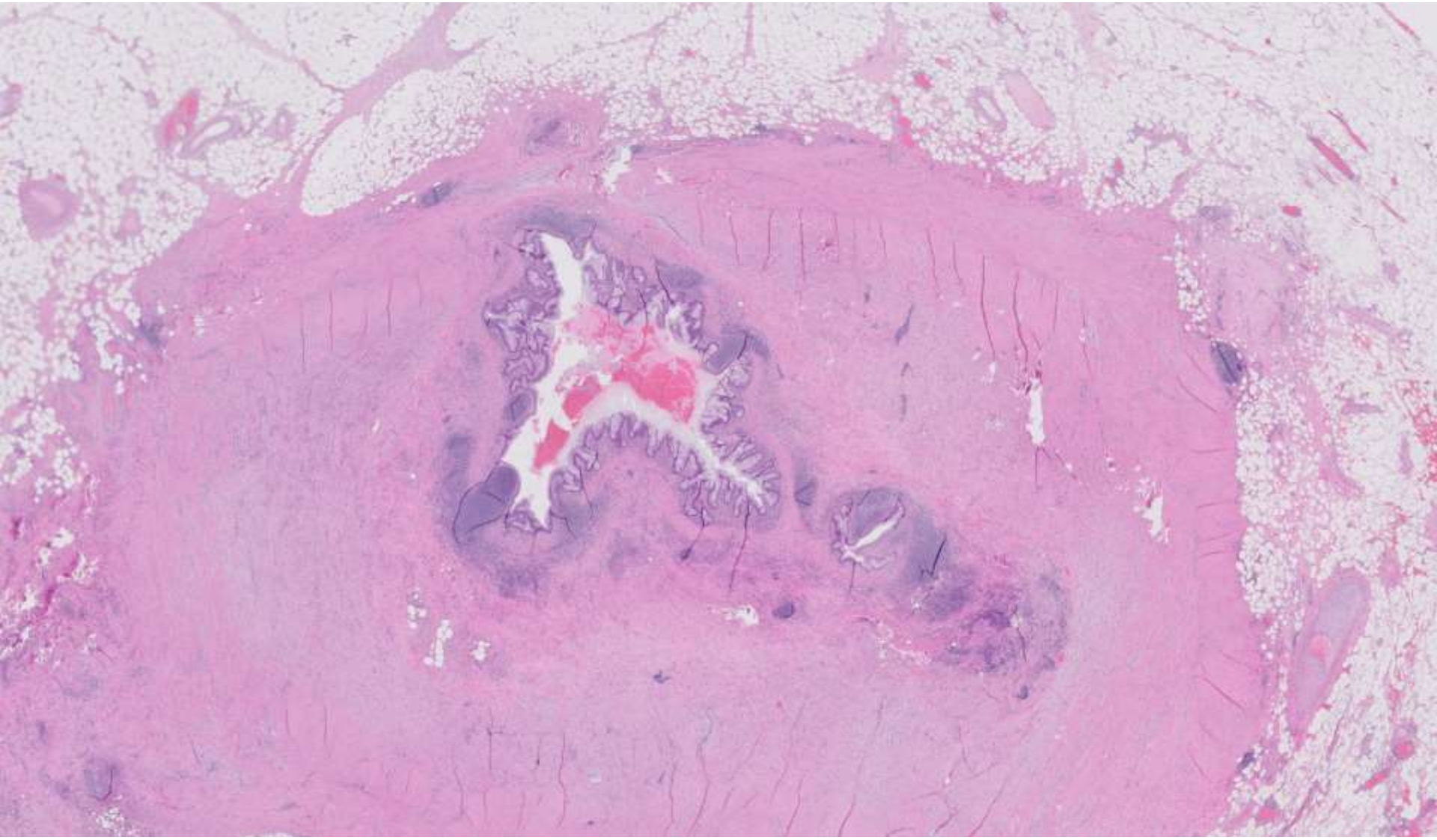
22-1008

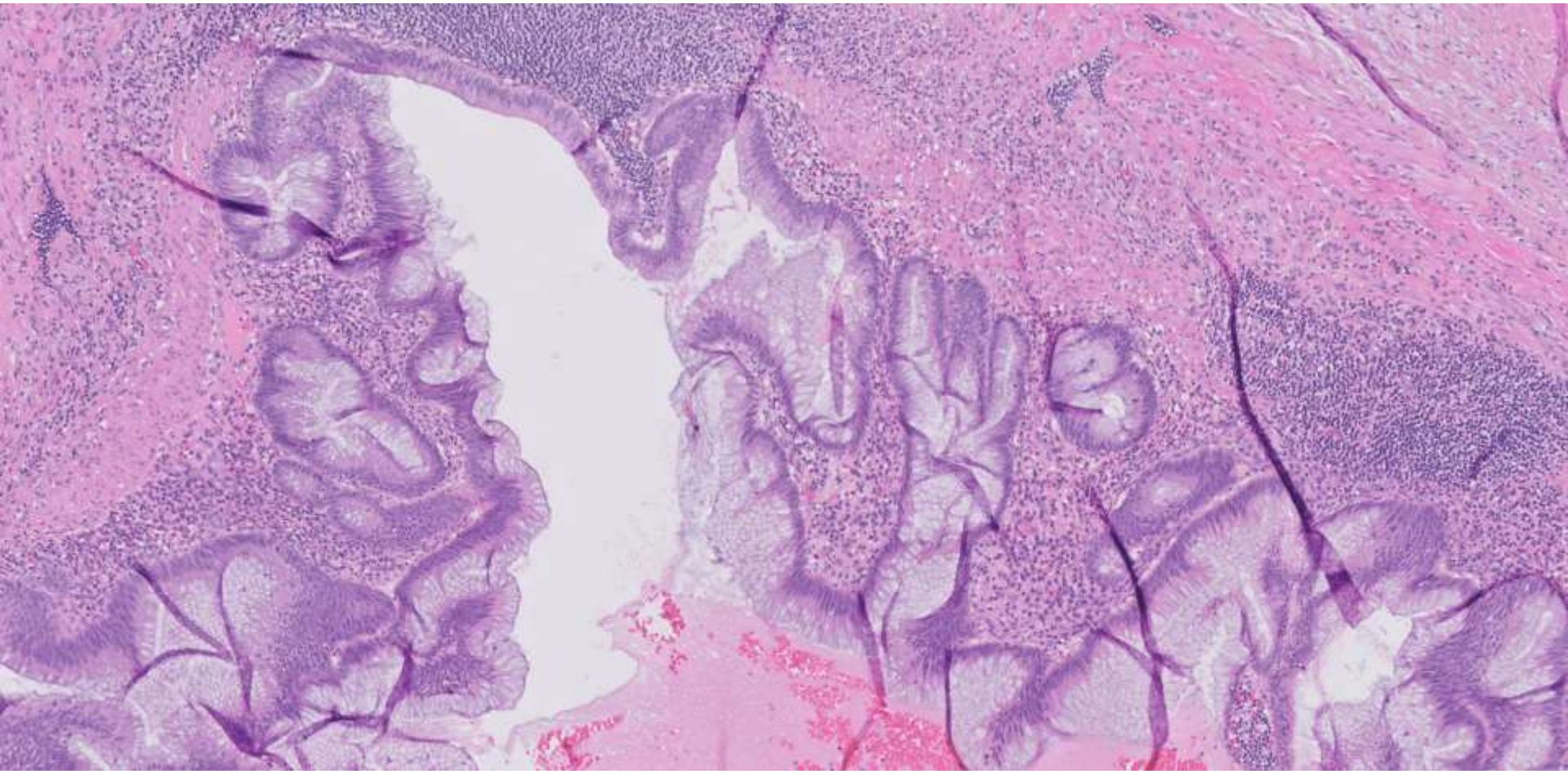
Dave Bingham; Stanford

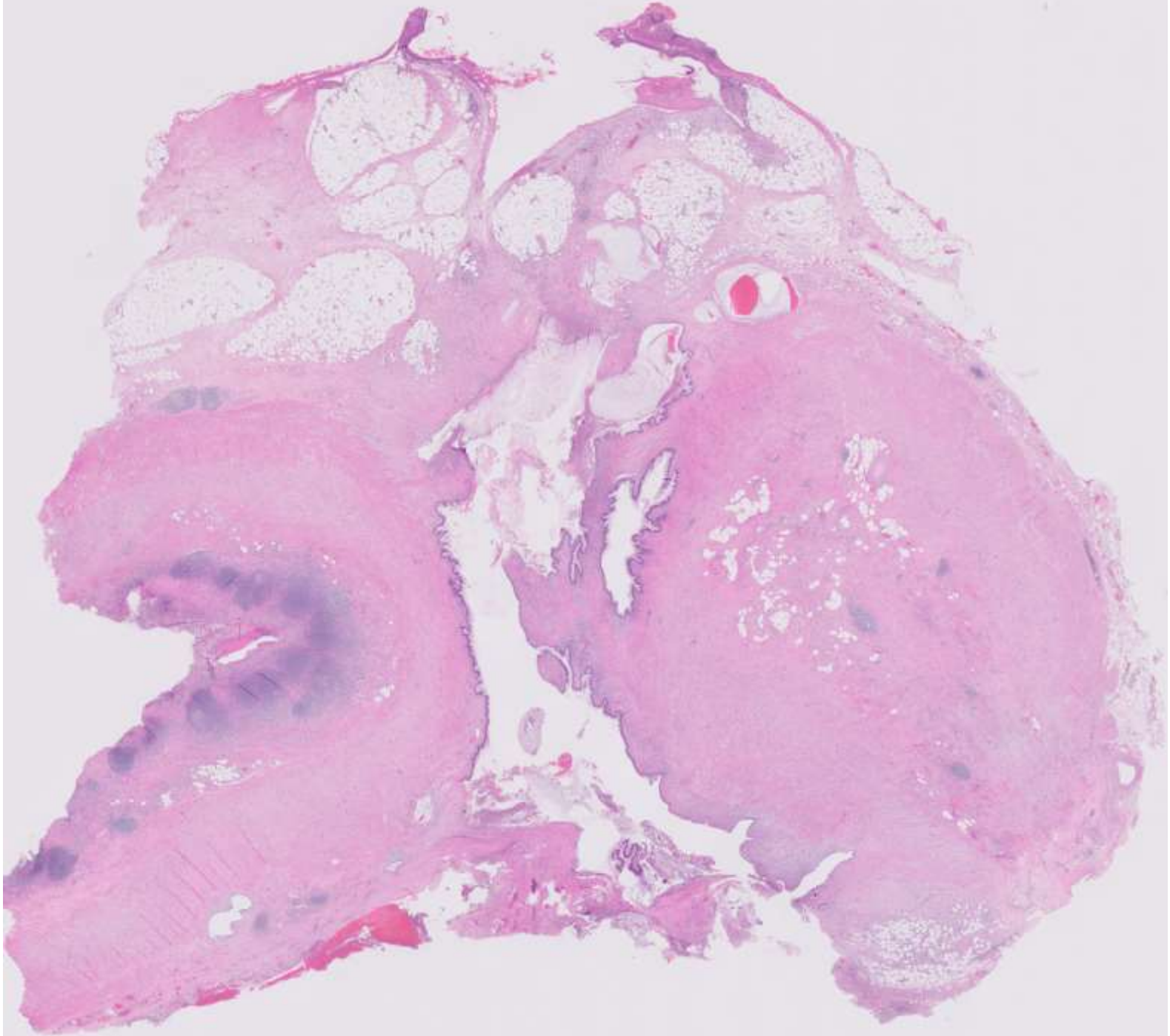
30ish F with 1-day h/o acute abdominal pain. Work-up revealed focal tenderness in the RUQ, WBC 16, and CT showing acute inflamed appendix.

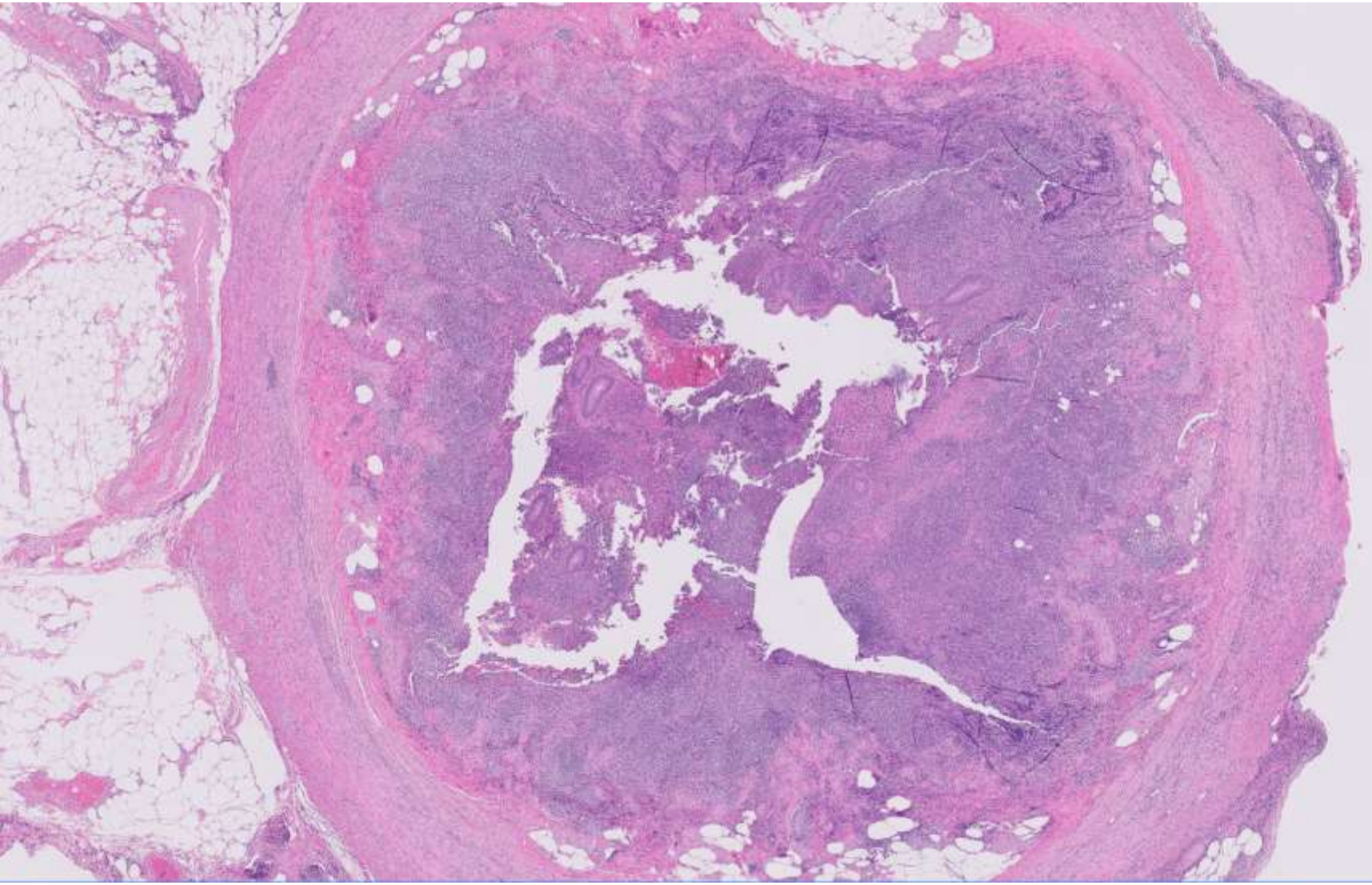


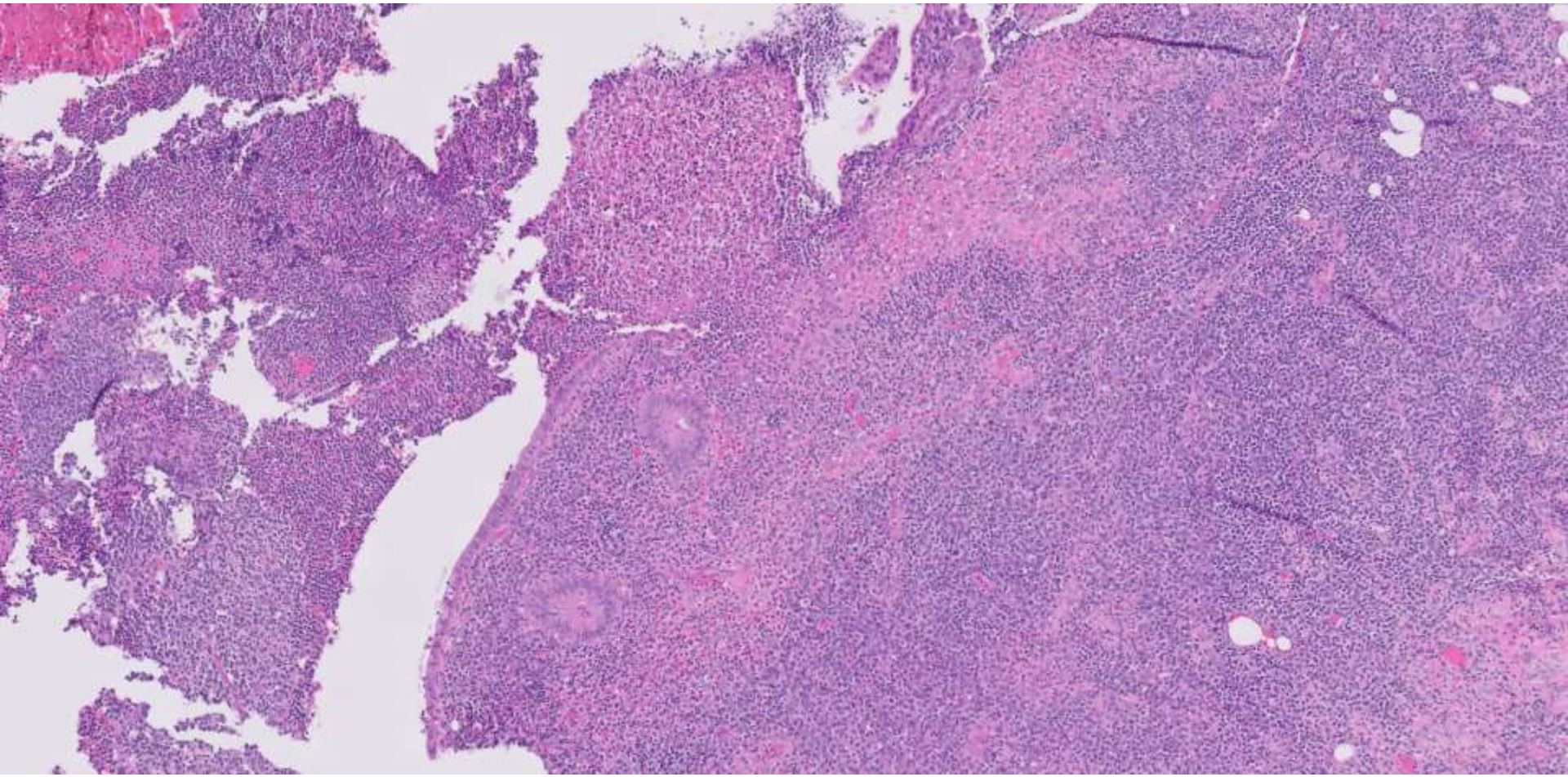


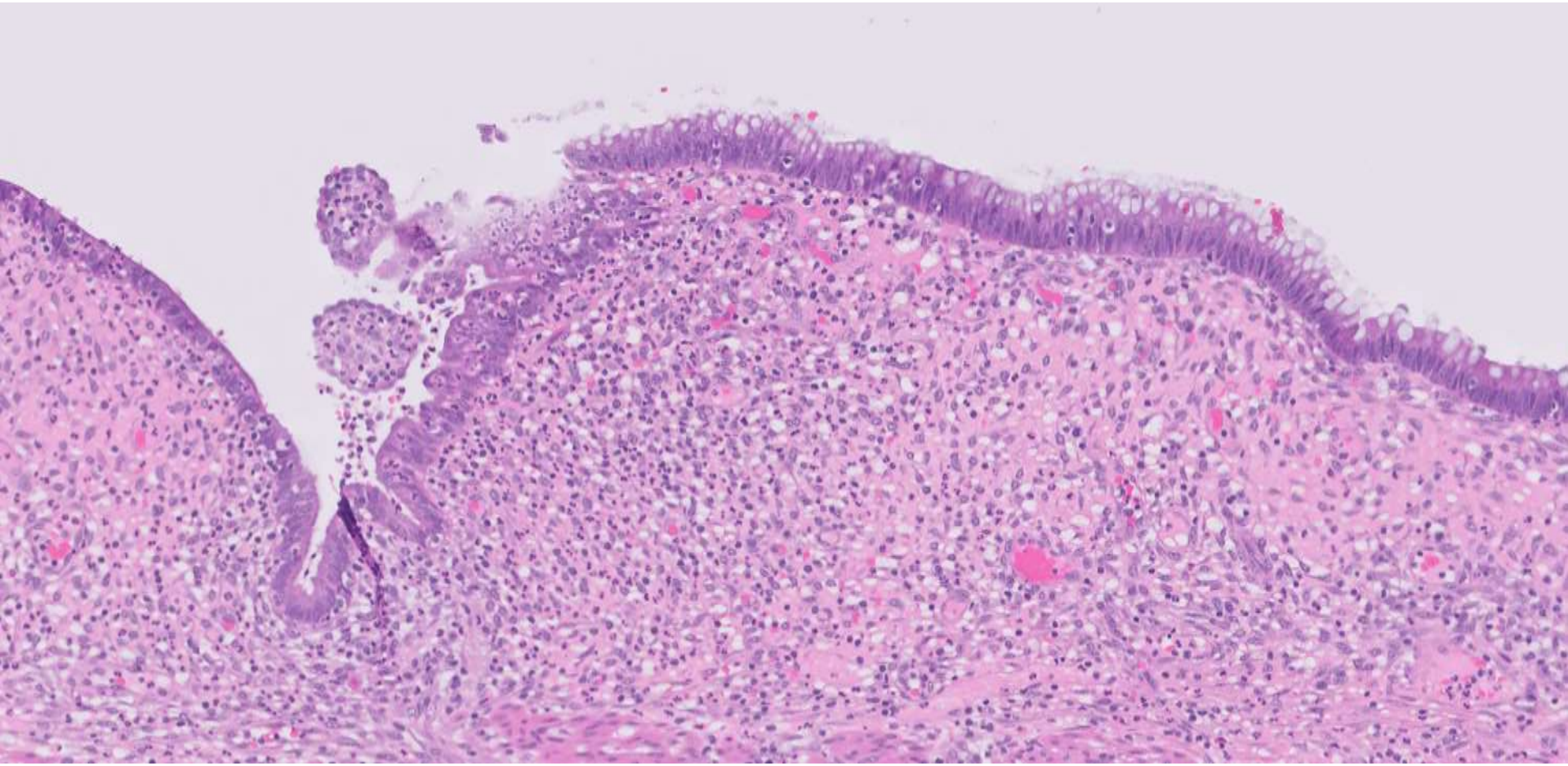










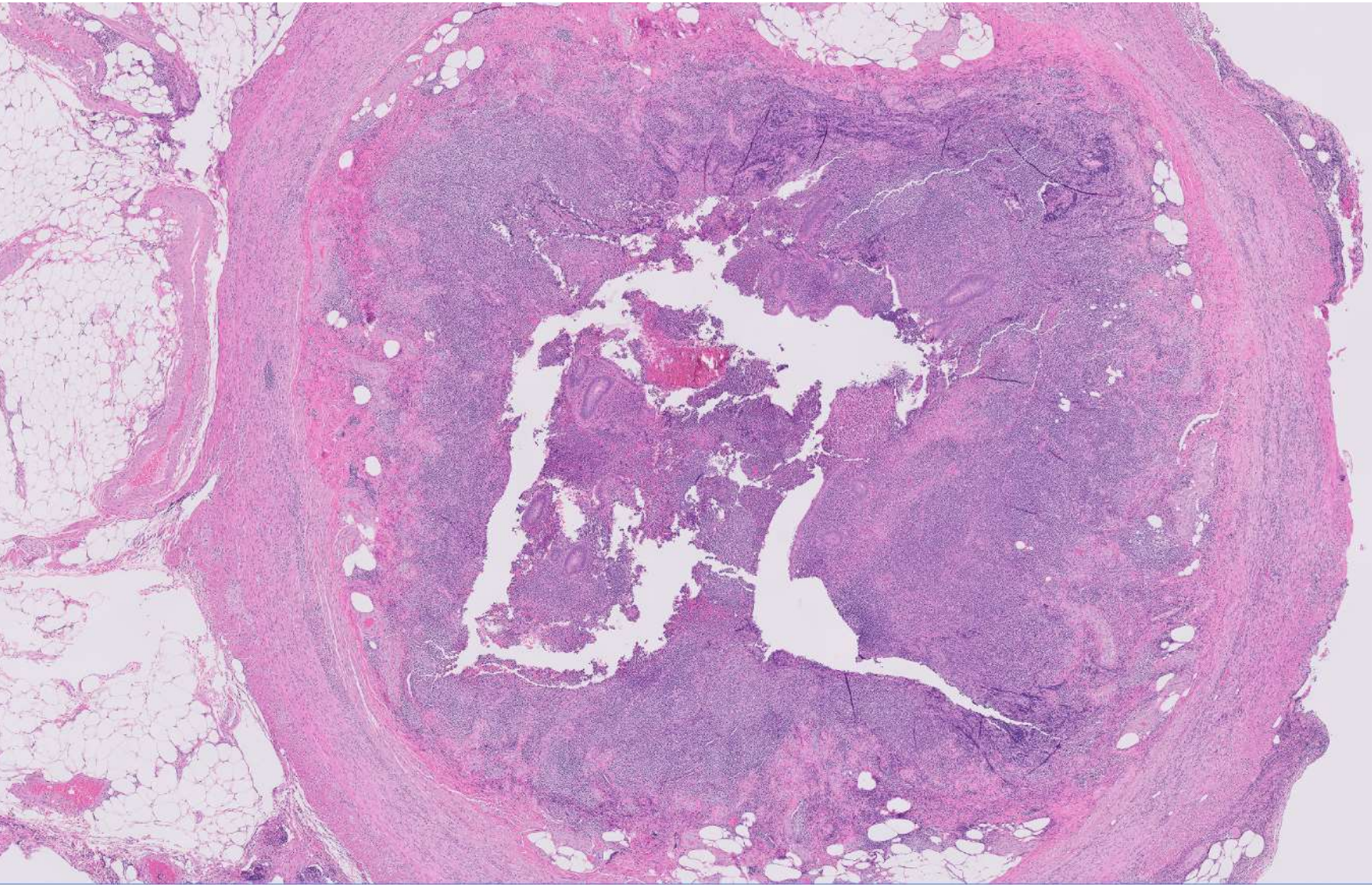


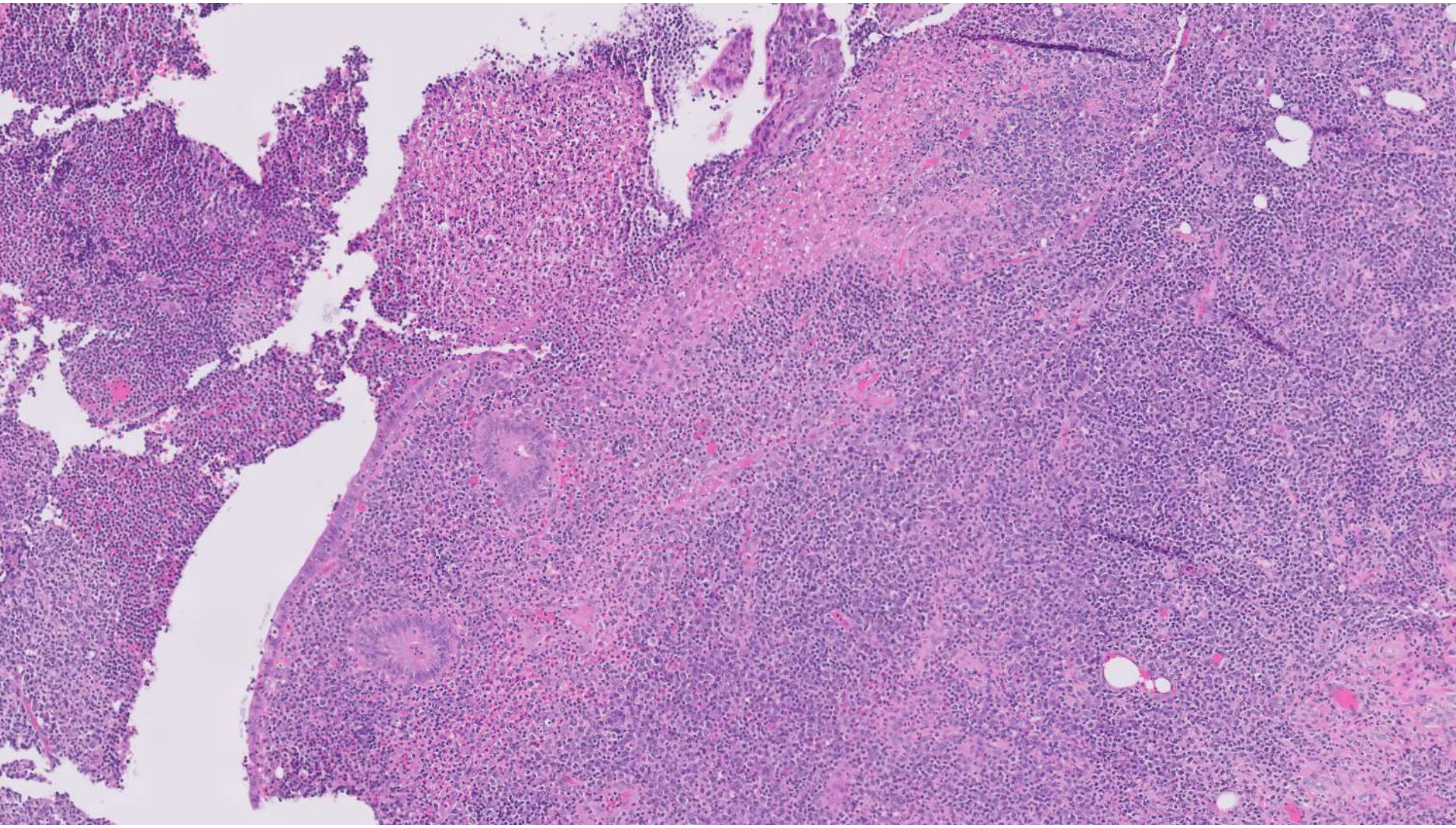
DIAGNOSIS (MICROSCOPIC):

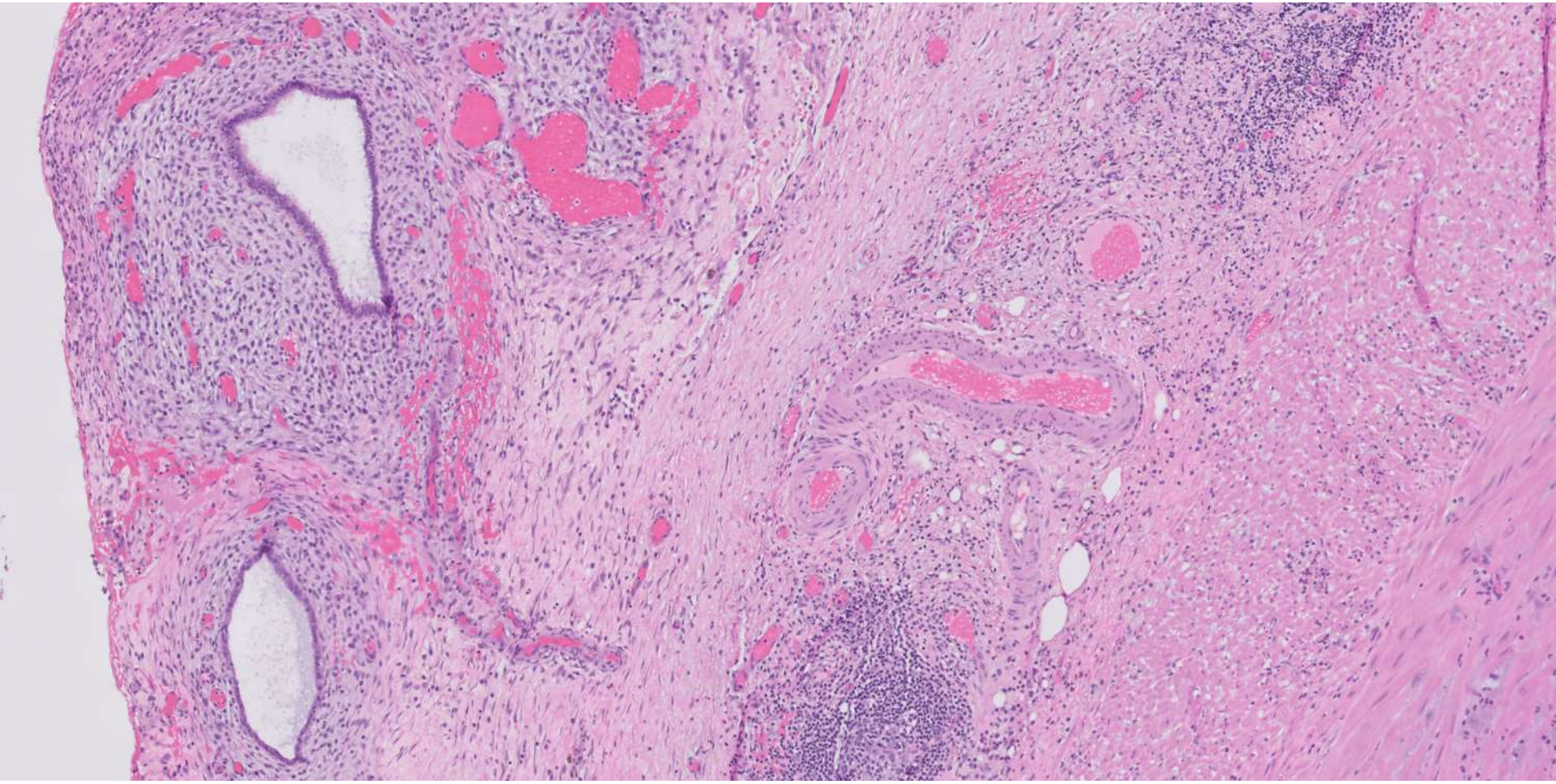
A. APPENDIX, APPENDECTOMY

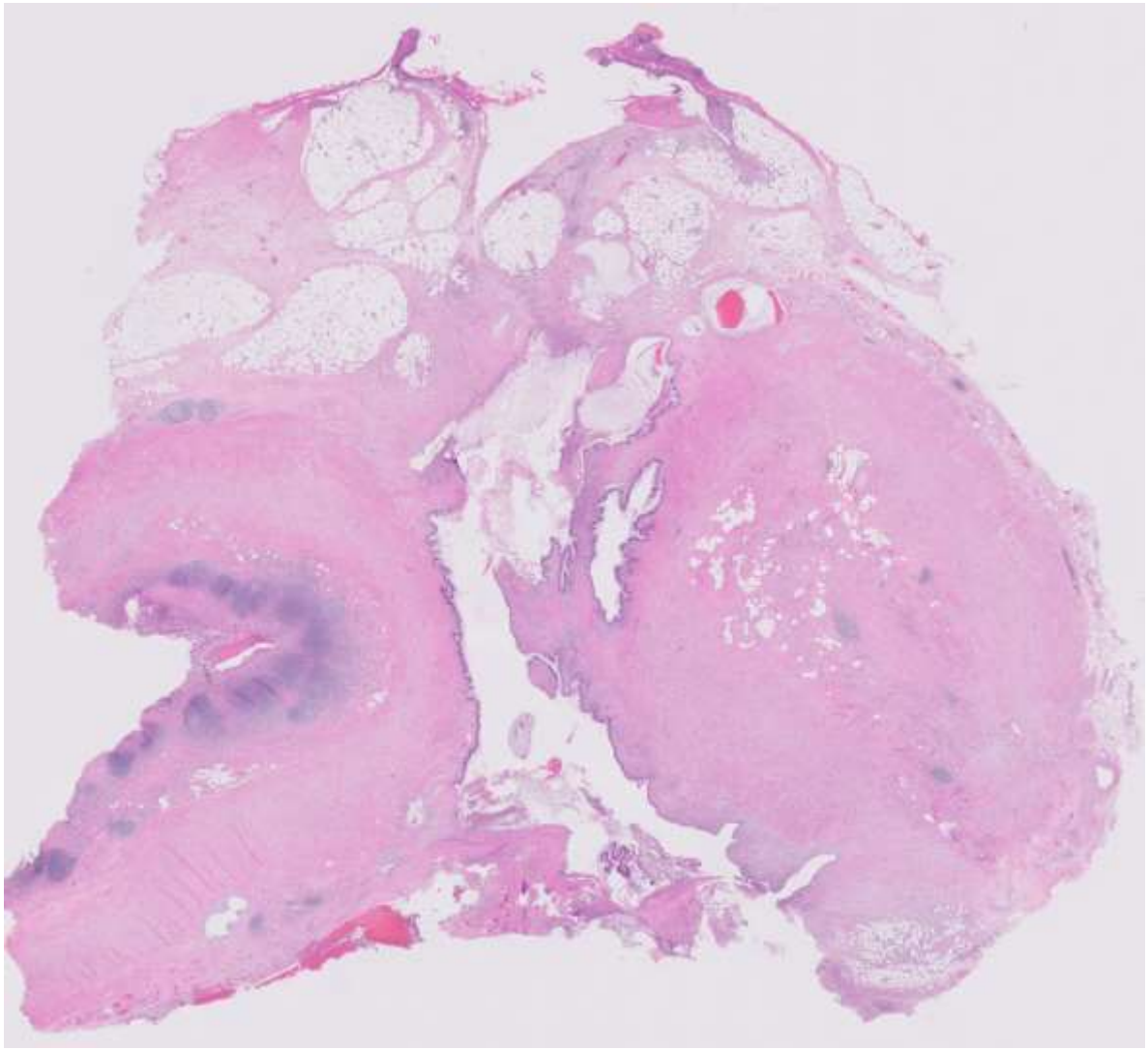
-- **ACUTE APPENDICITIS**

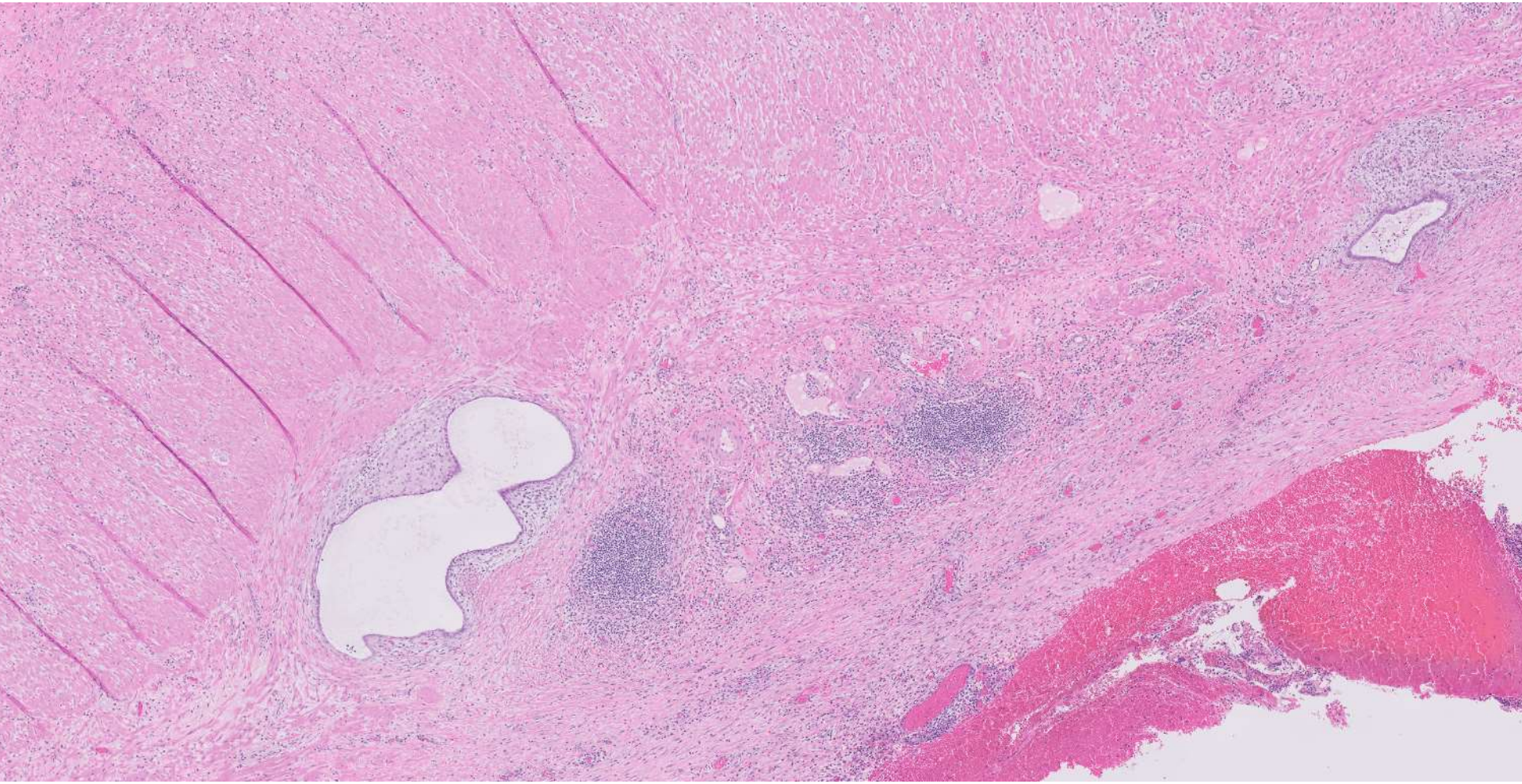
-- **ENDOMETRIOSIS WITH MUCINOUS METAPLASIA**

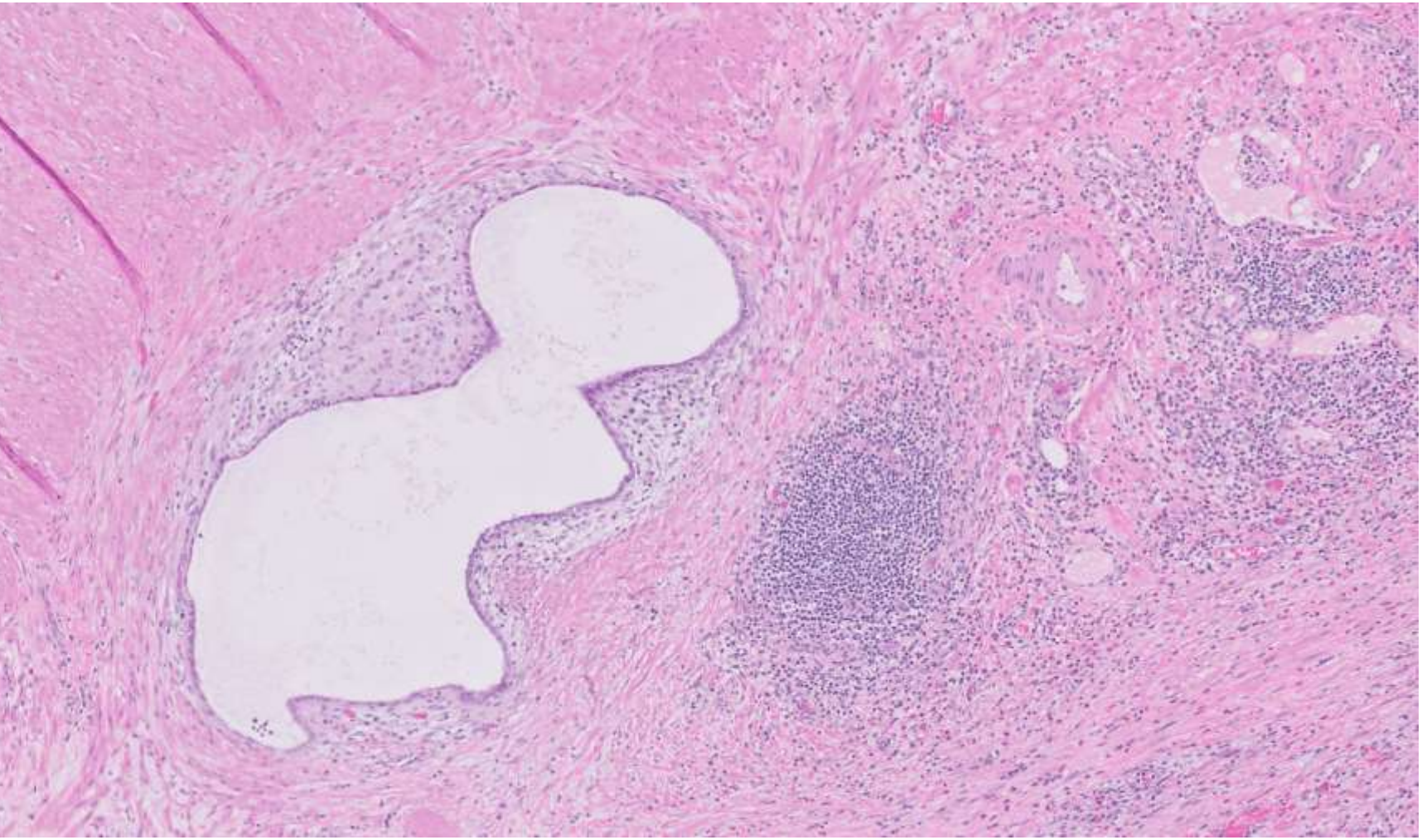


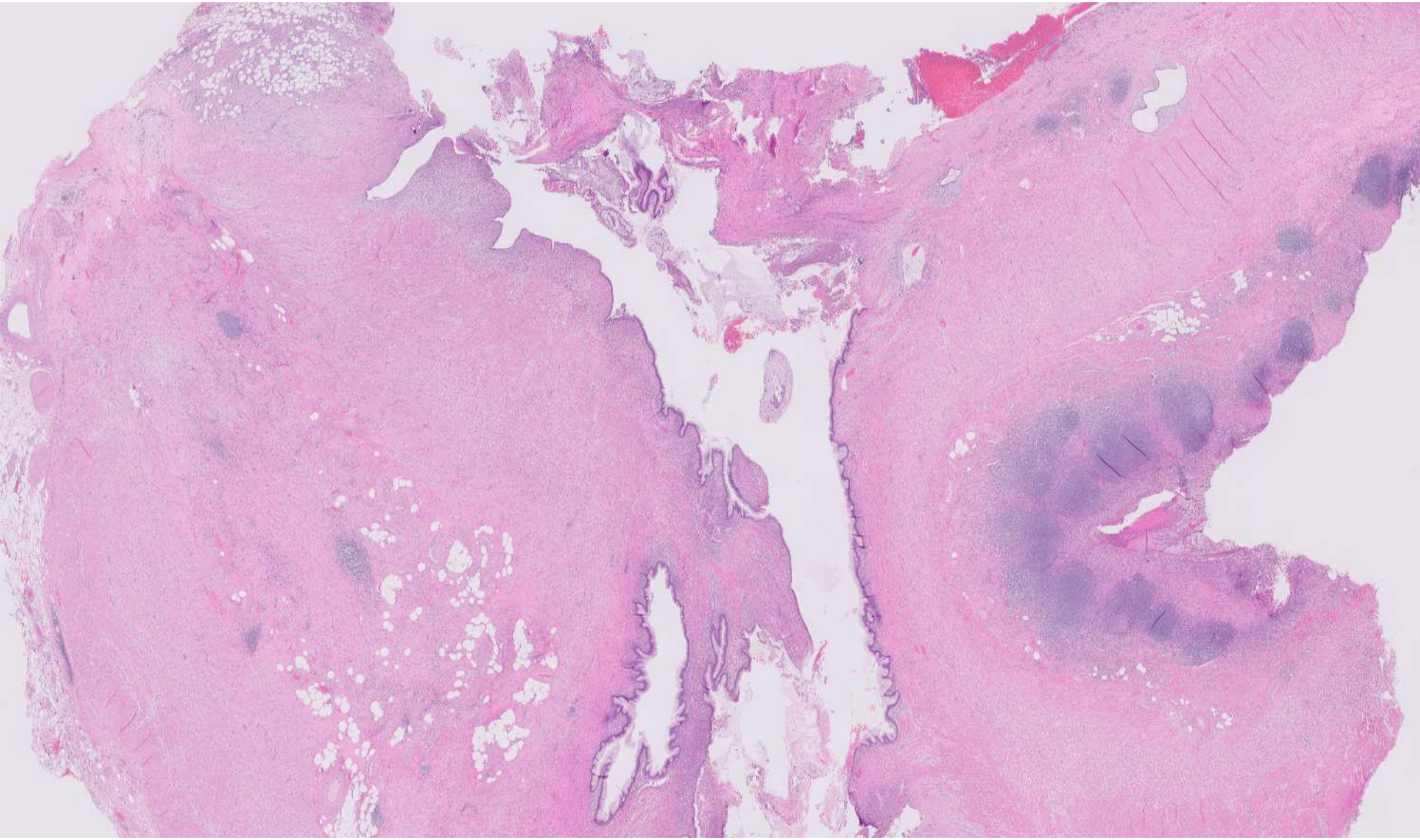


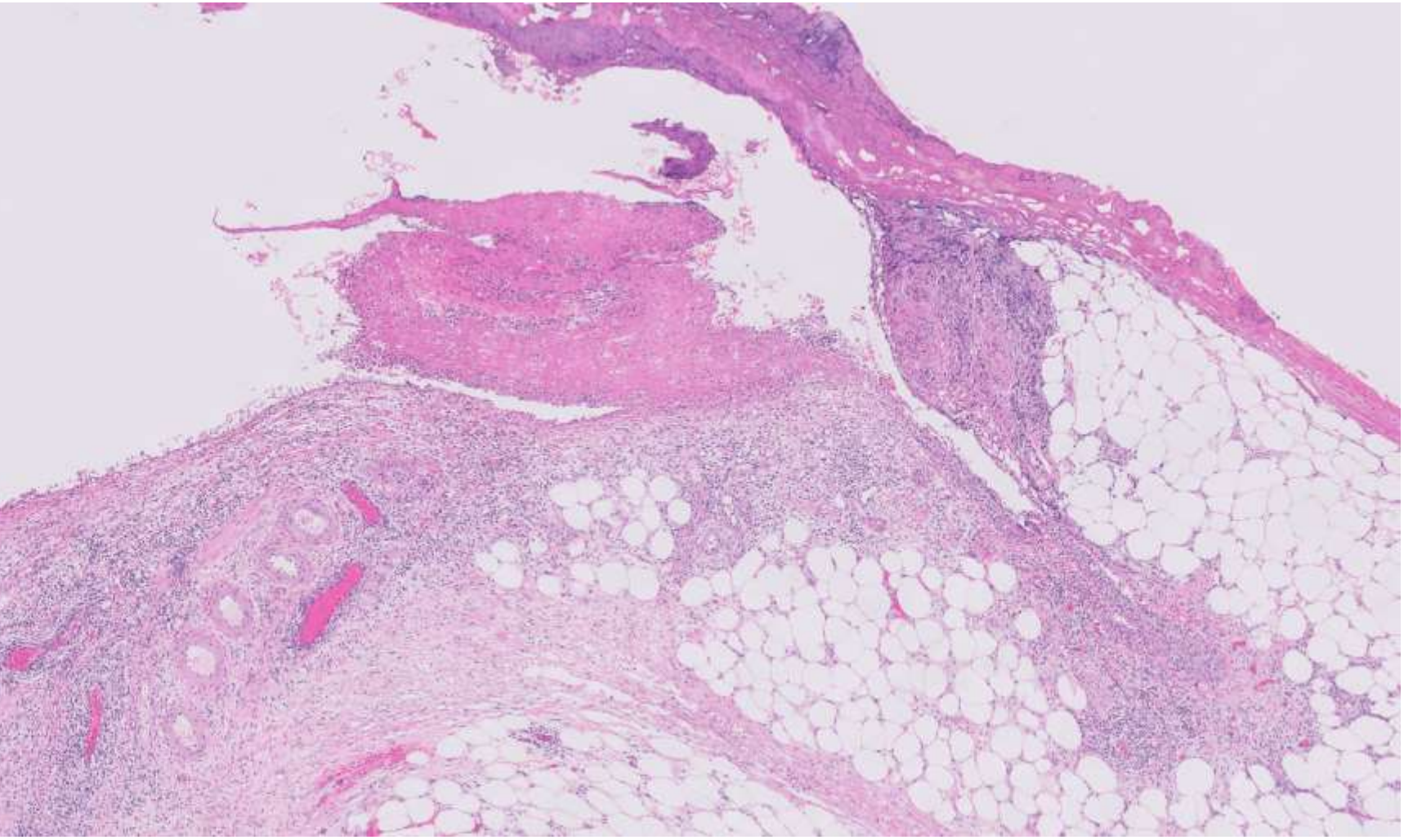


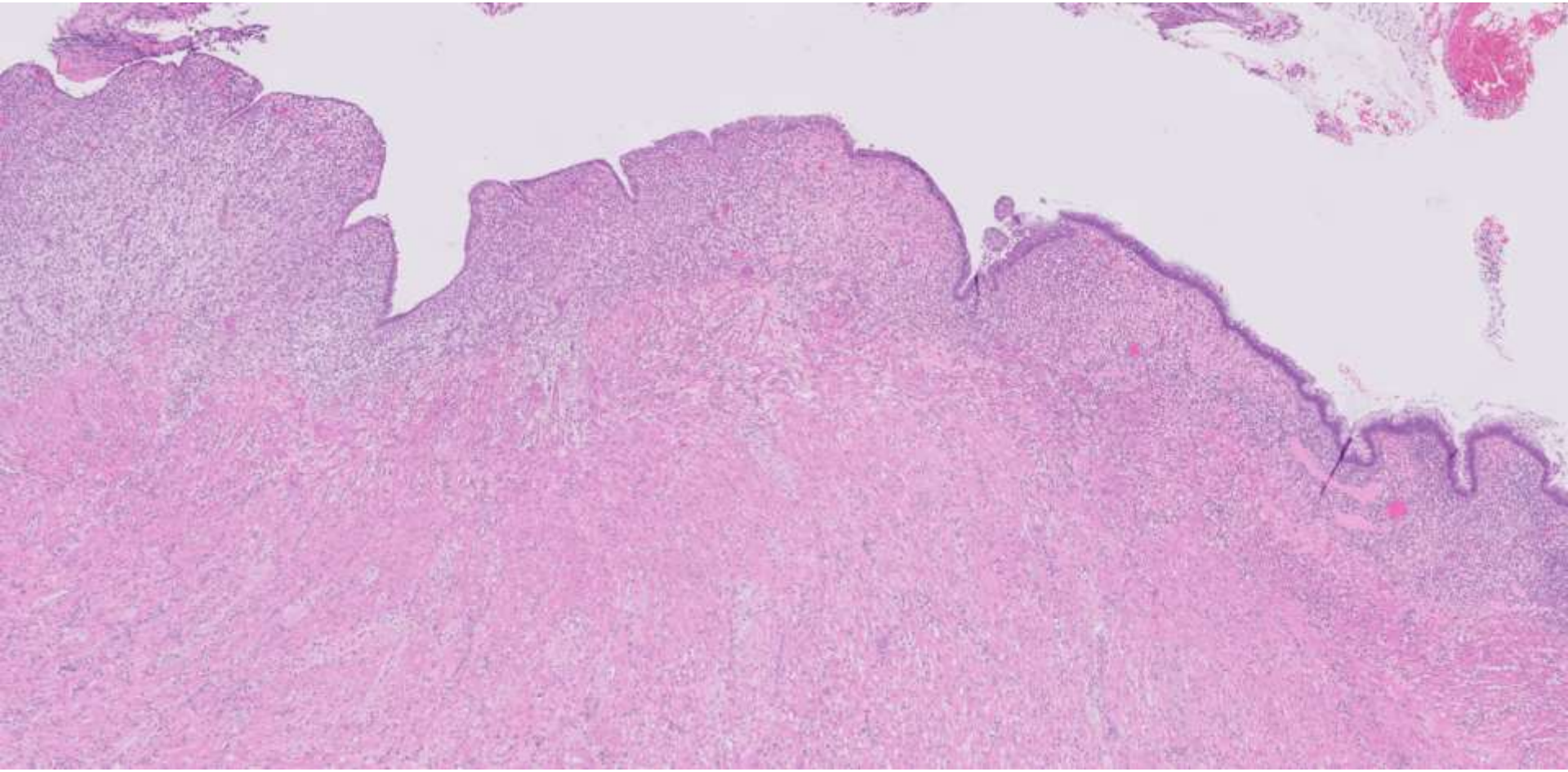


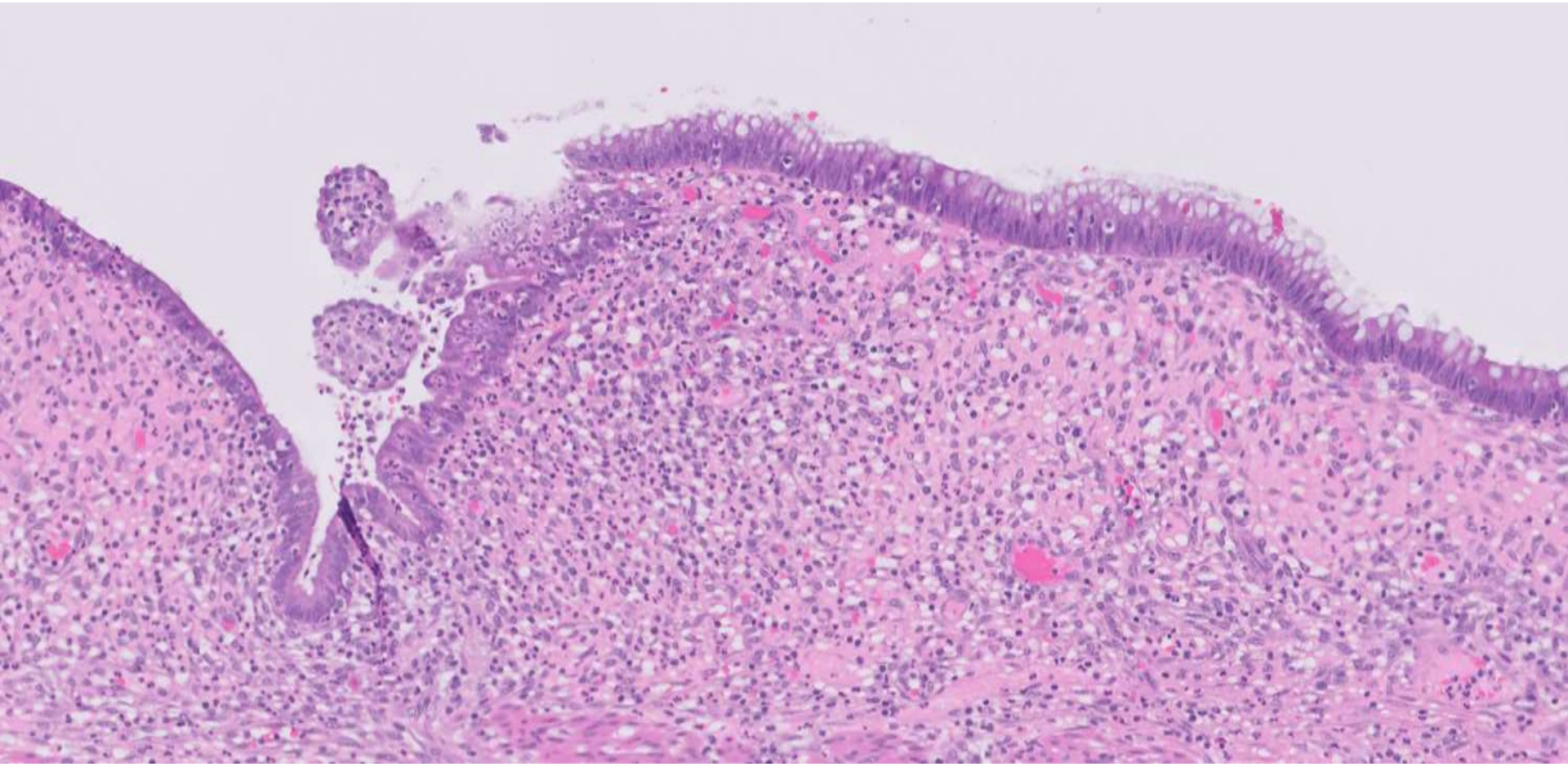


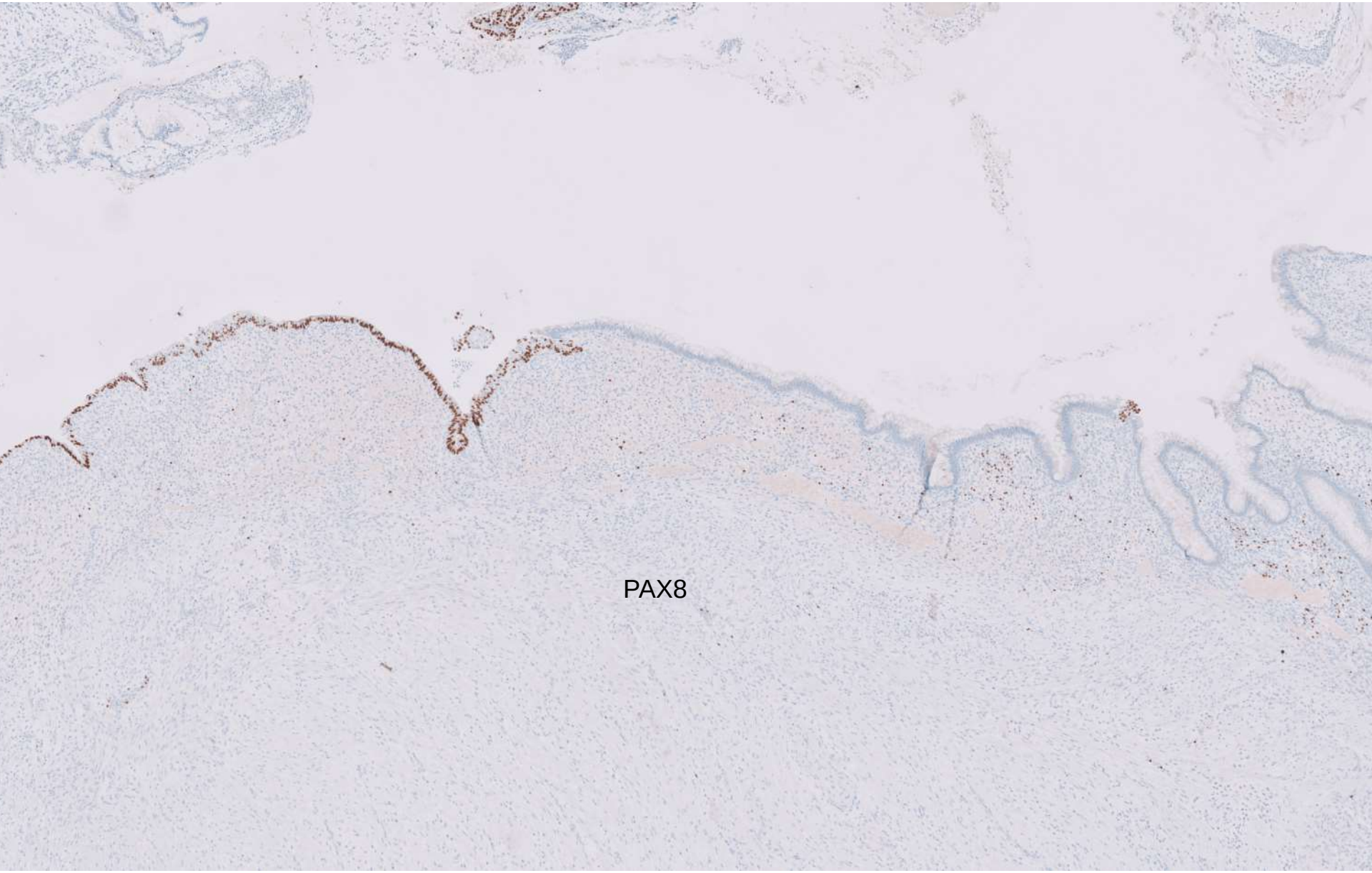


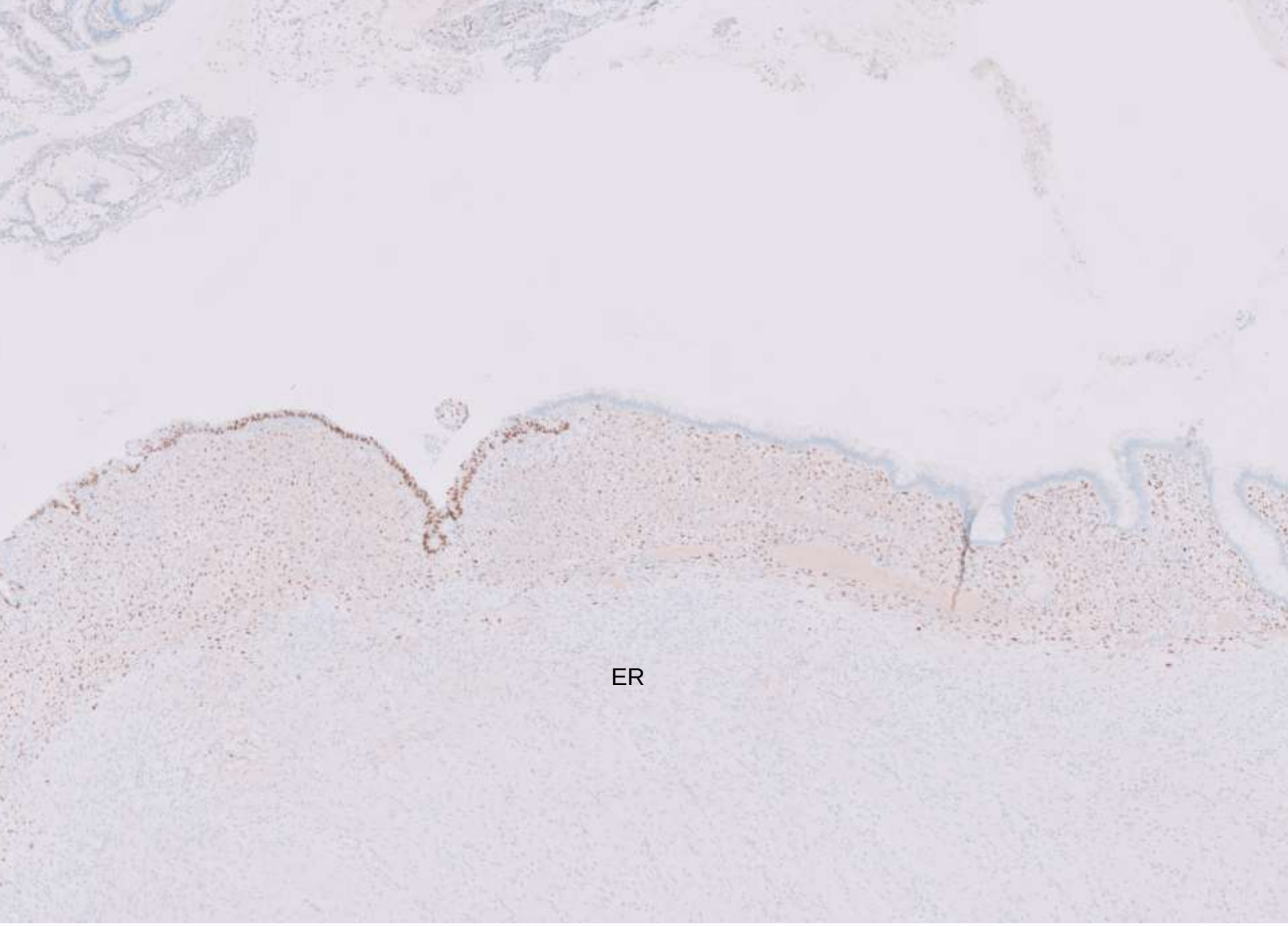


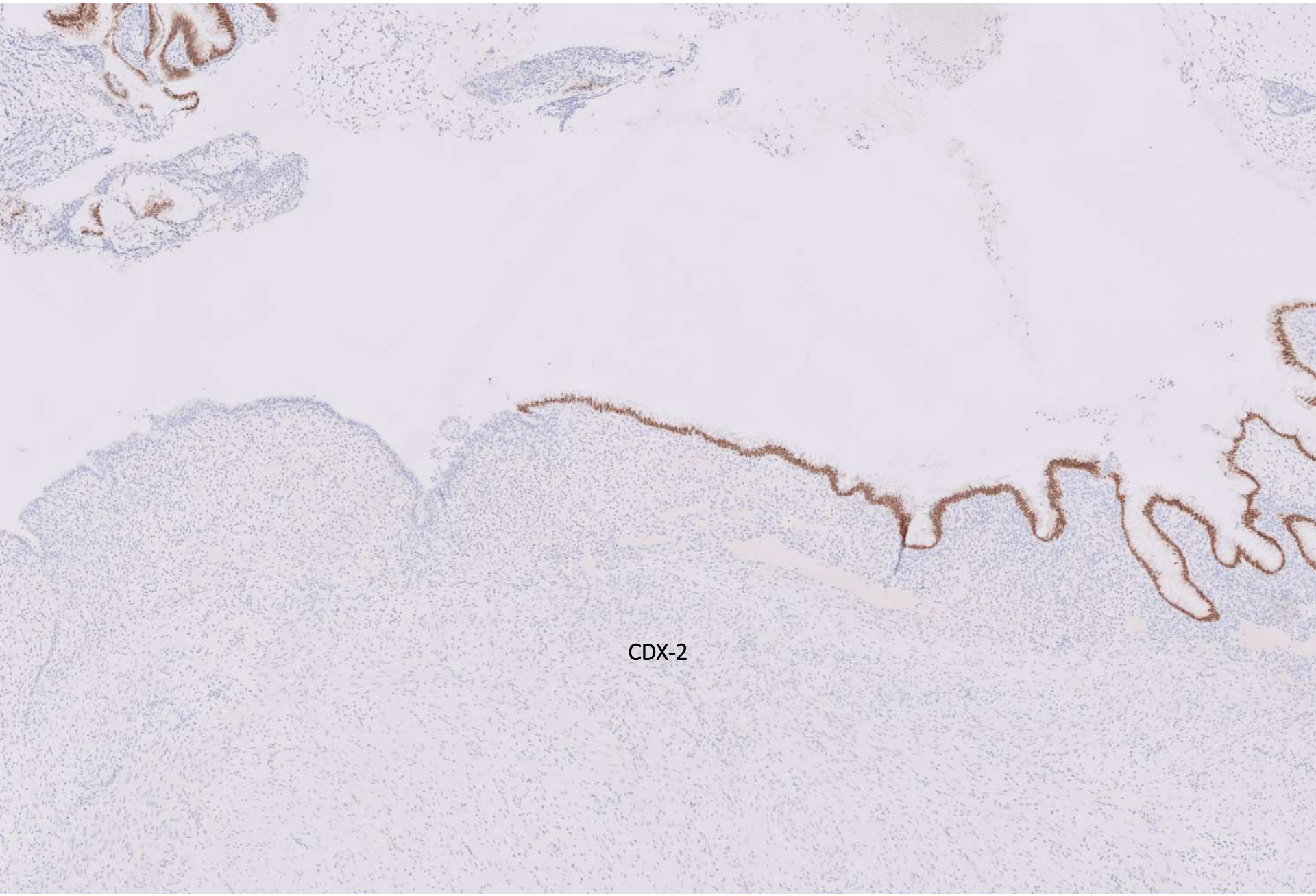







PAX8


ER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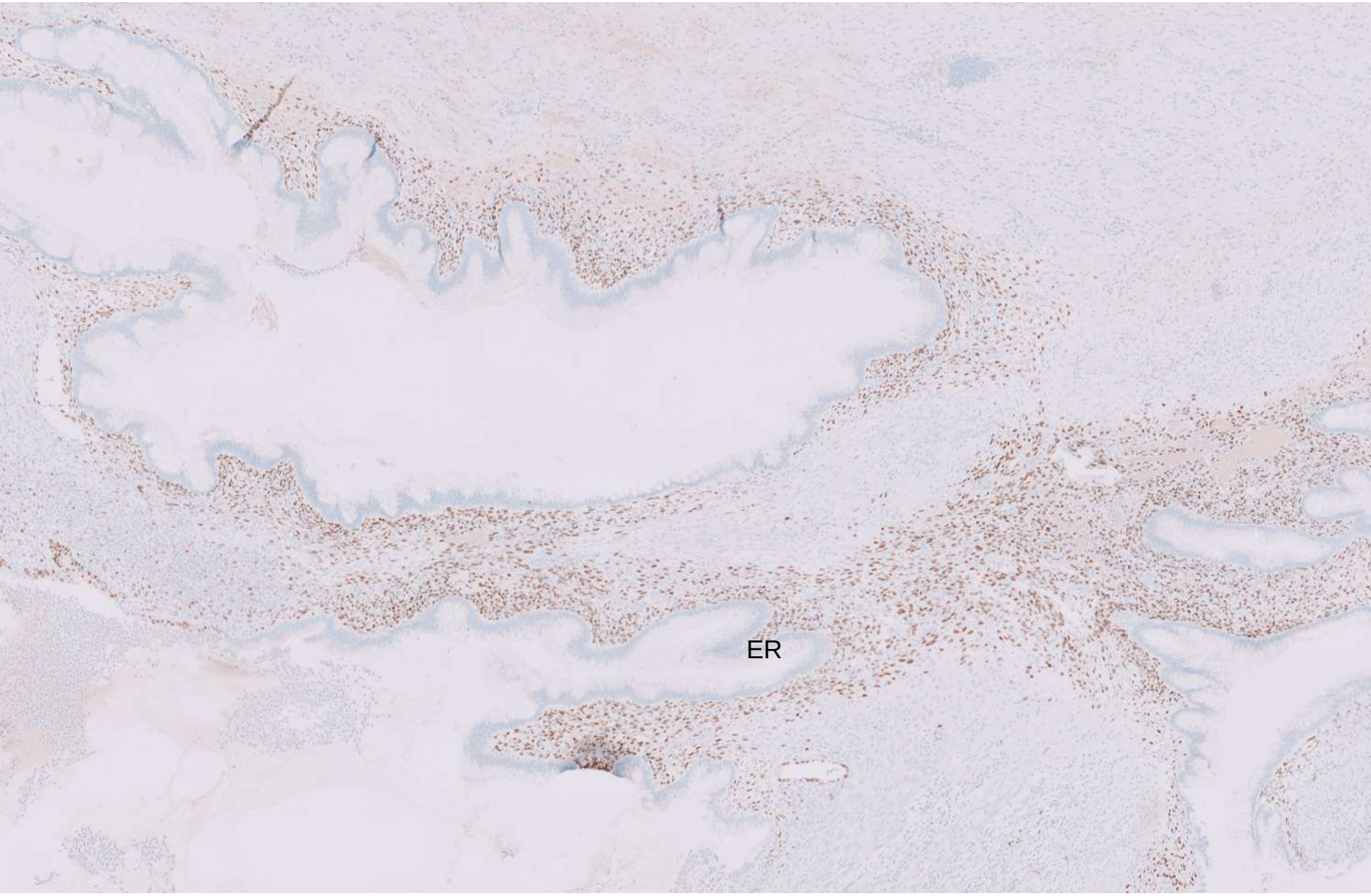
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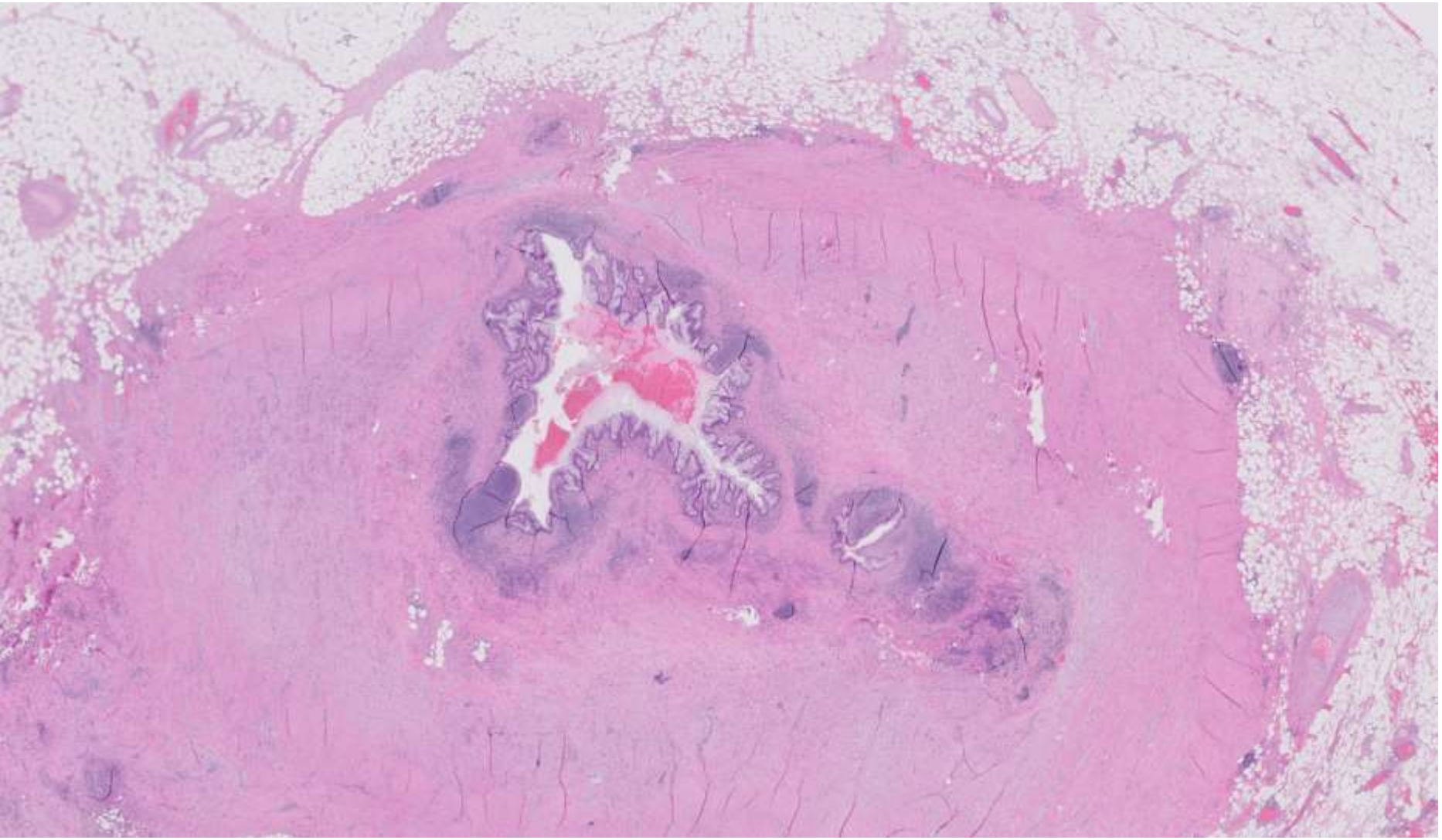

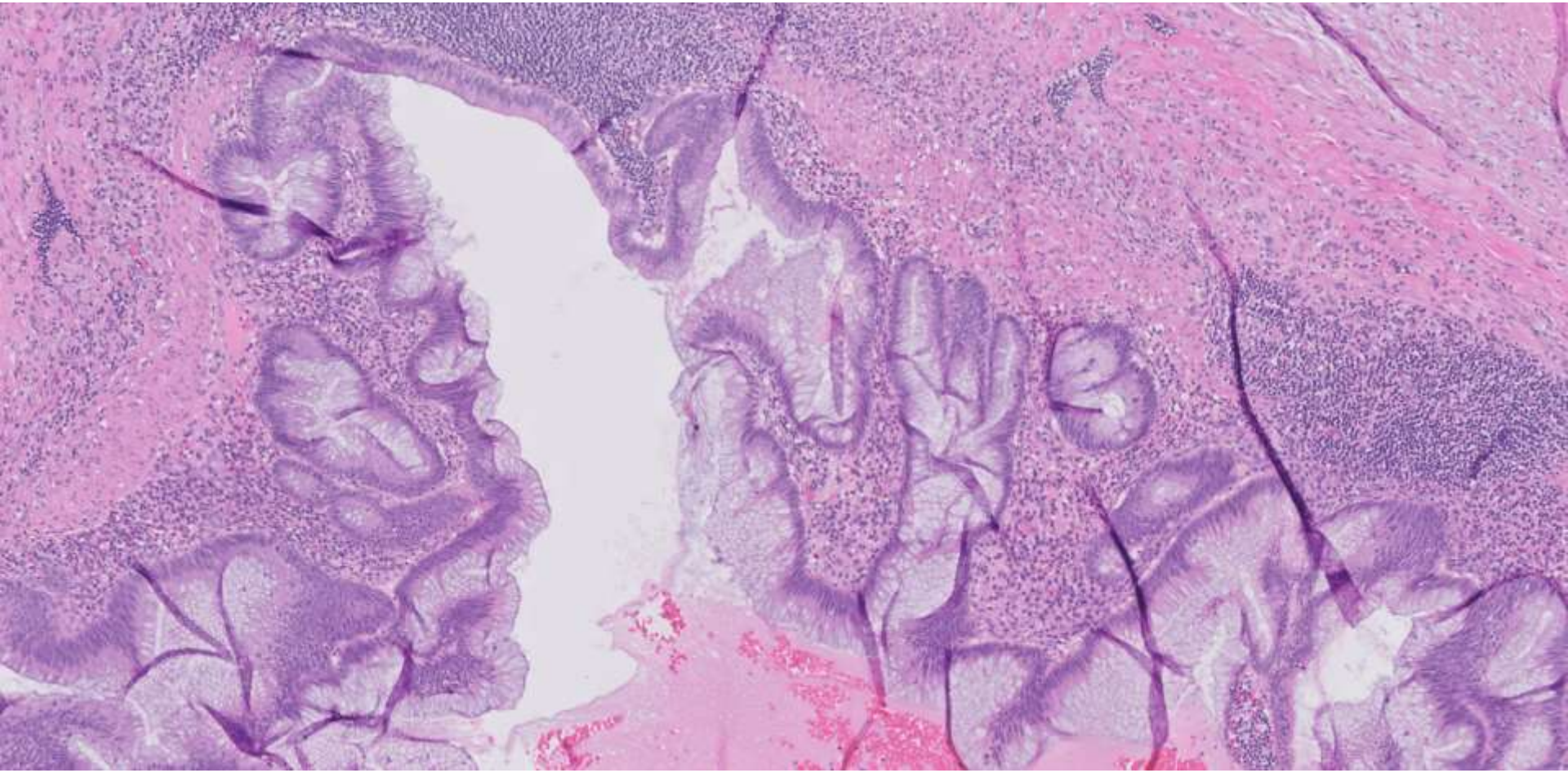

Appendiceal endometriosis with mucinous metaplasia

- Very rare, only a few reported cases
- Important because differential diagnosis includes low grade appendiceal mucinous neoplasm and appendiceal adeno CA
- Clues include usual endometriosis in some areas and lack of classic features of LAMN (e.g. presence of lamina propria)
- Diagnosis supported by ER stain

REFERENCE: Dysplastic intestinal-type metaplasia of appendiceal endometriosis: a mimic of low grade appendiceal mucinous neoplasm. Mitchell A, Dubé P, Sideris L. Diagn Pathol. 2014 Feb 21;9:39.