Disclosures
Aug 6, 2018

Dr. Christine Louie has disclosed a financial relationship with Grail, Inc. (consultant). Dr. Christian Kunder has disclosed a financial relationship with Gilead Sciences (spouse is employee and stock owner). Dr. Jeff Simko has disclosed a financial relationship with Bristol Meyers Squib (consultant), and 3D (advisor) and South Bay Pathology Society has determined that these relationships are not relevant to the clinical cases being presented. The following planners and faculty had no financial relationships with commercial interests to disclose:

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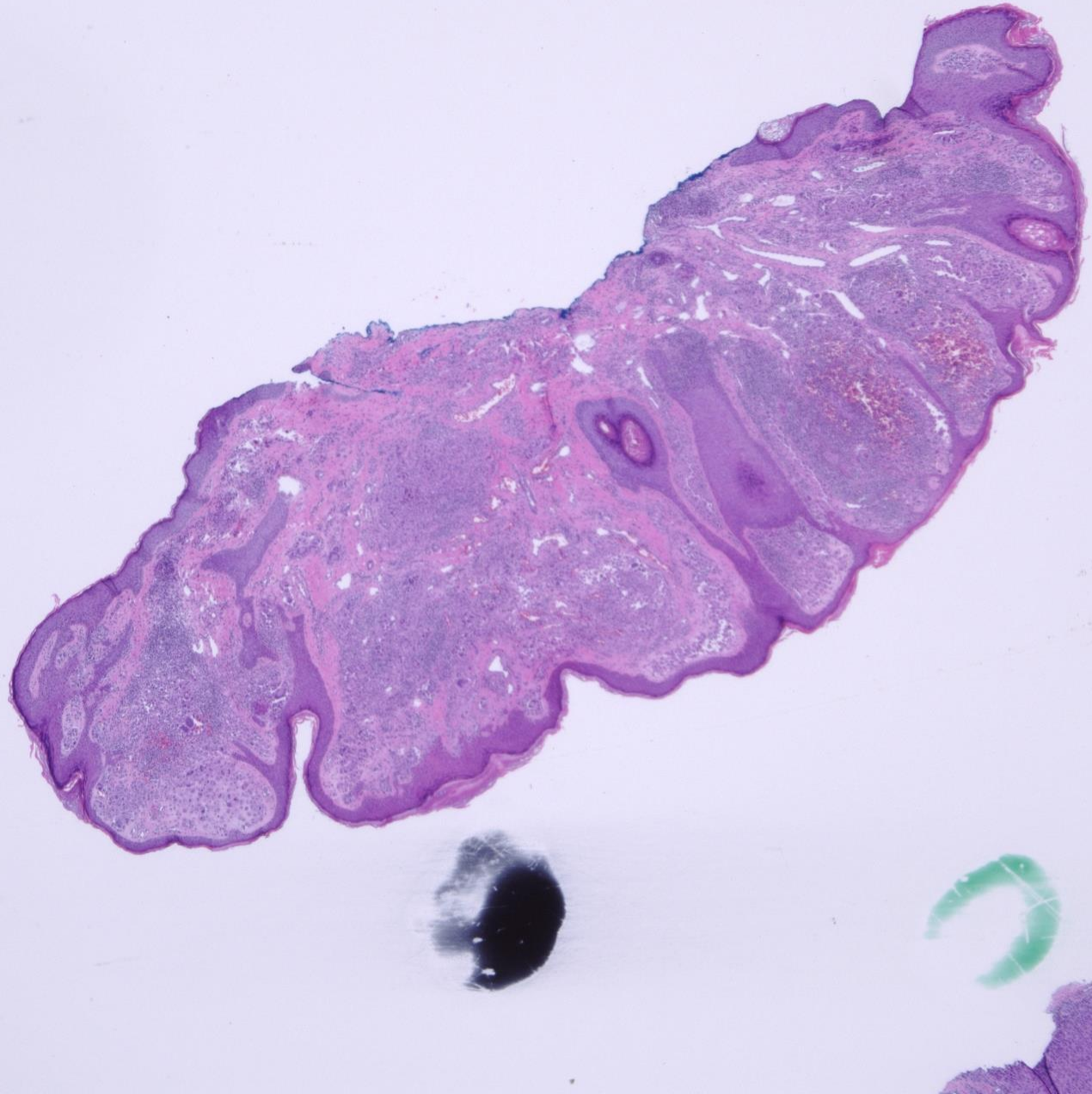
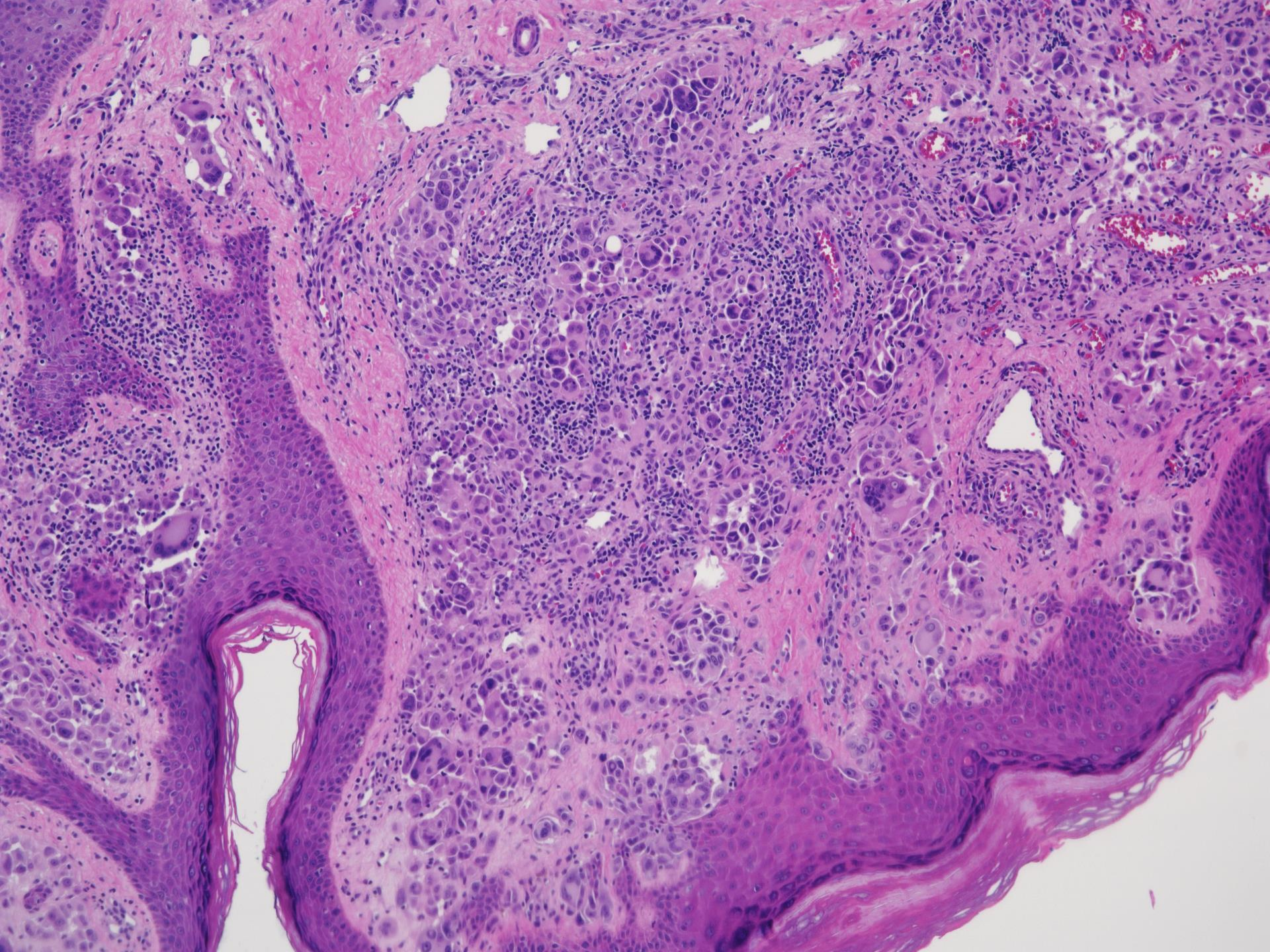
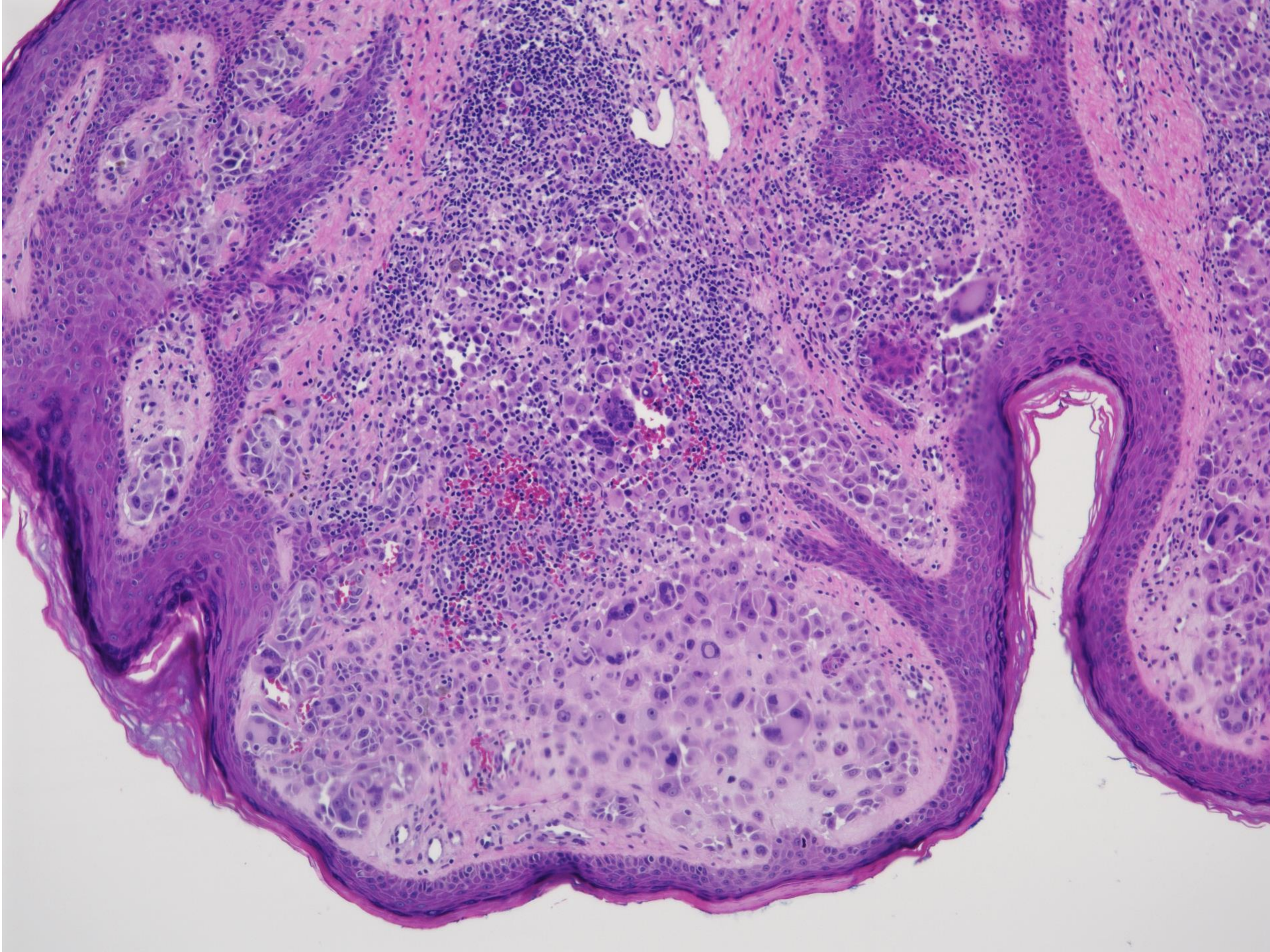
SB 6291

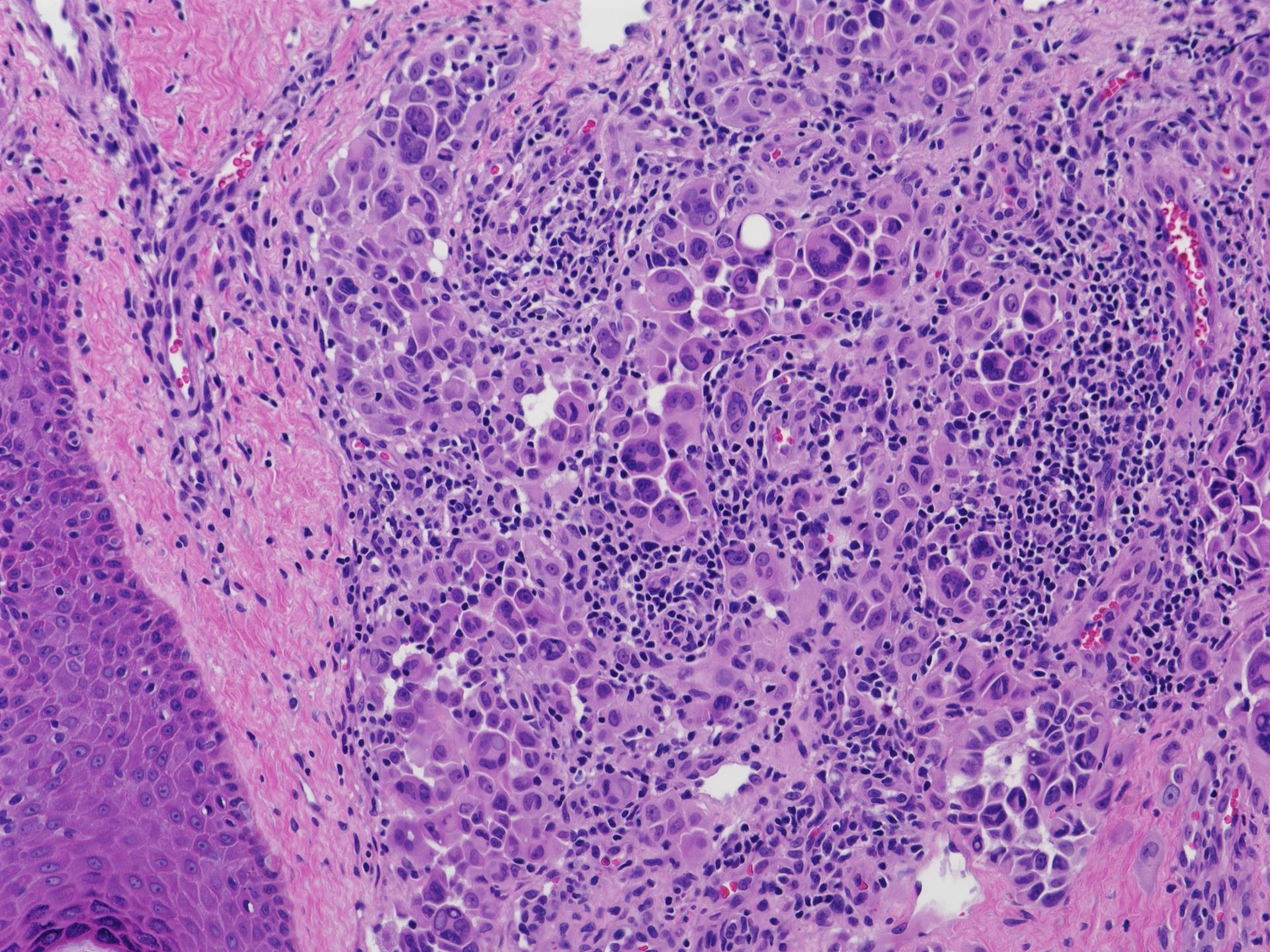
Sebastian Fernandez-Pol/Kerri Rieger; Stanford

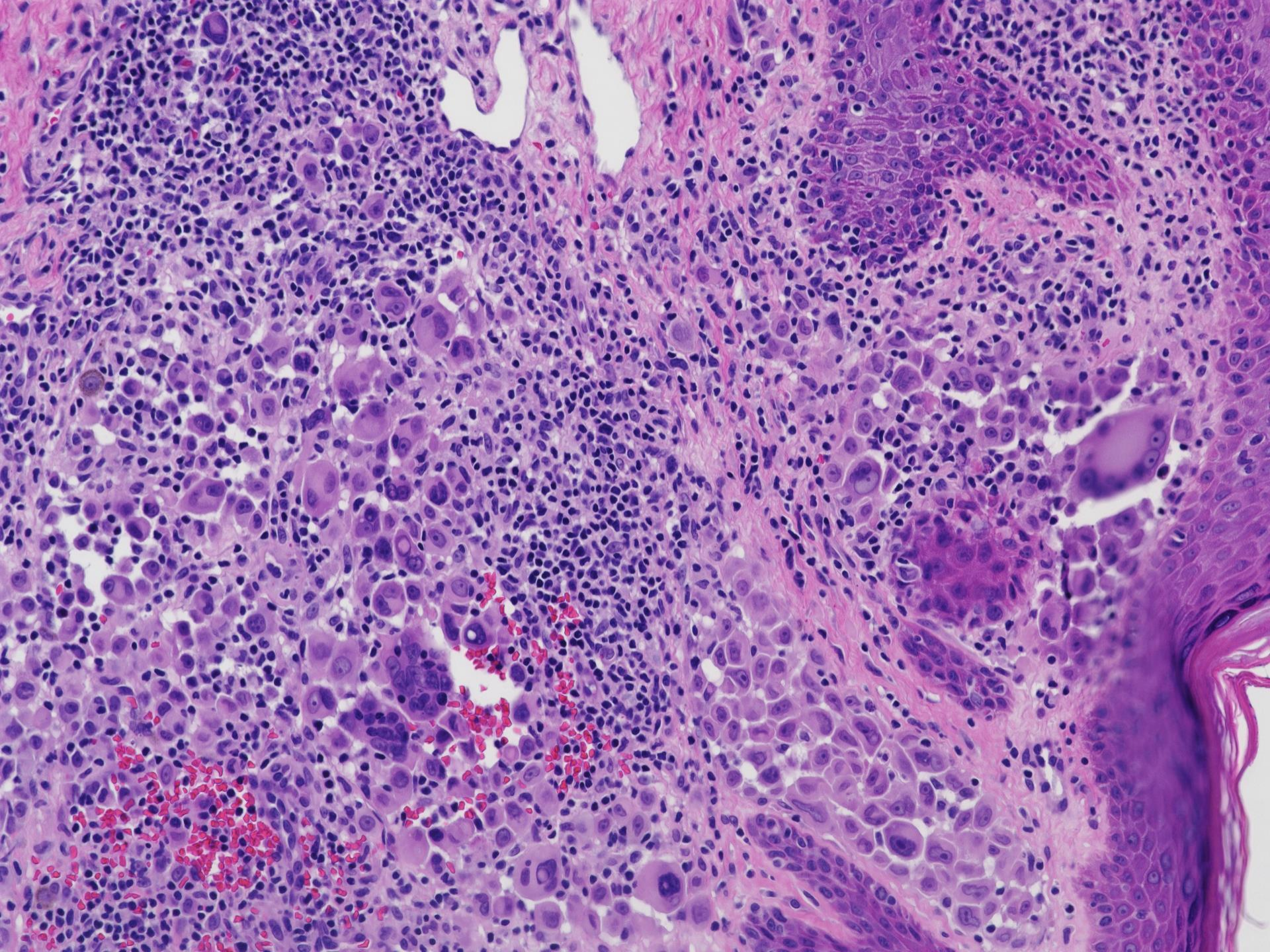
2-year-old with likely pyogenic granuloma.



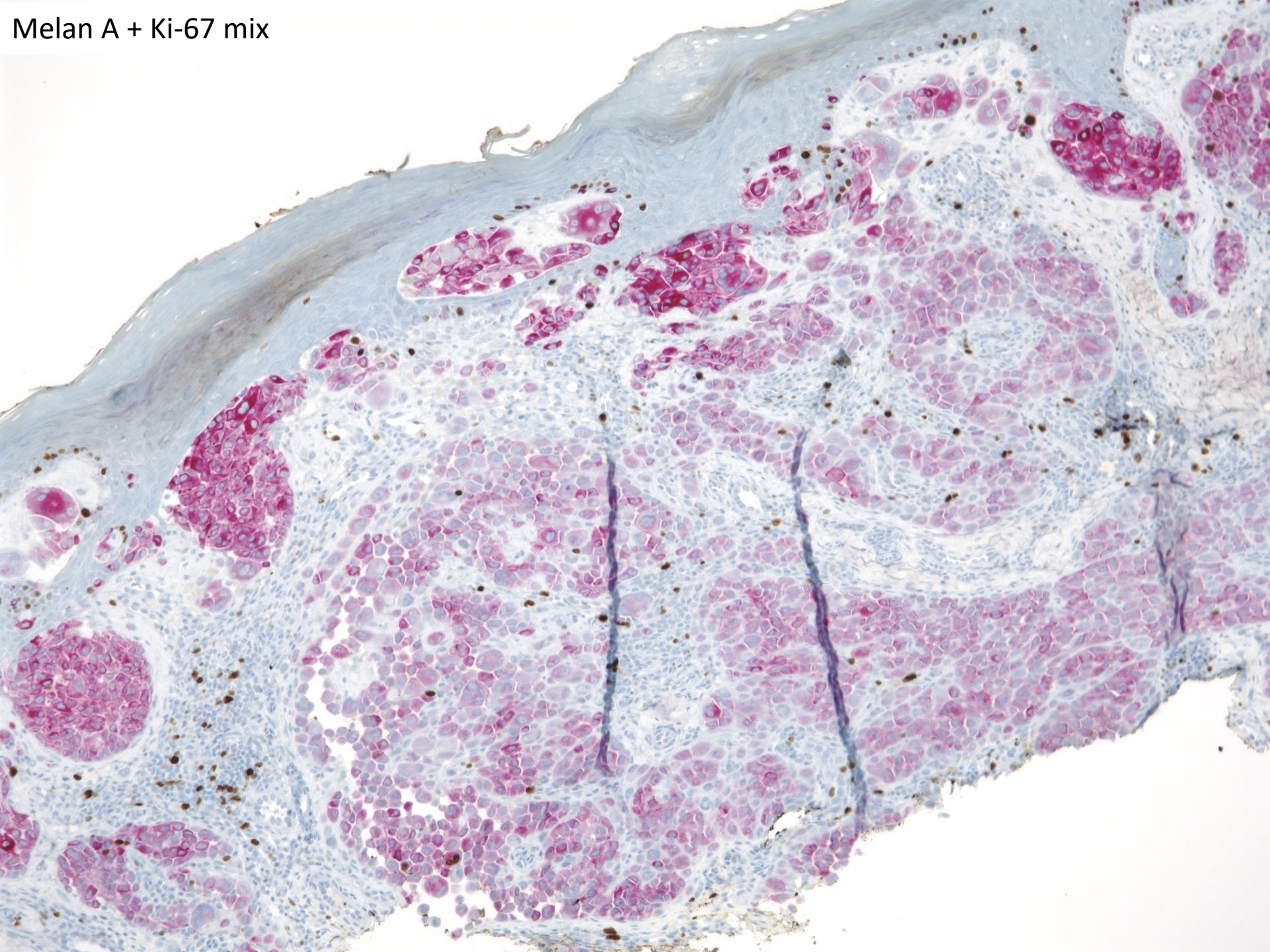


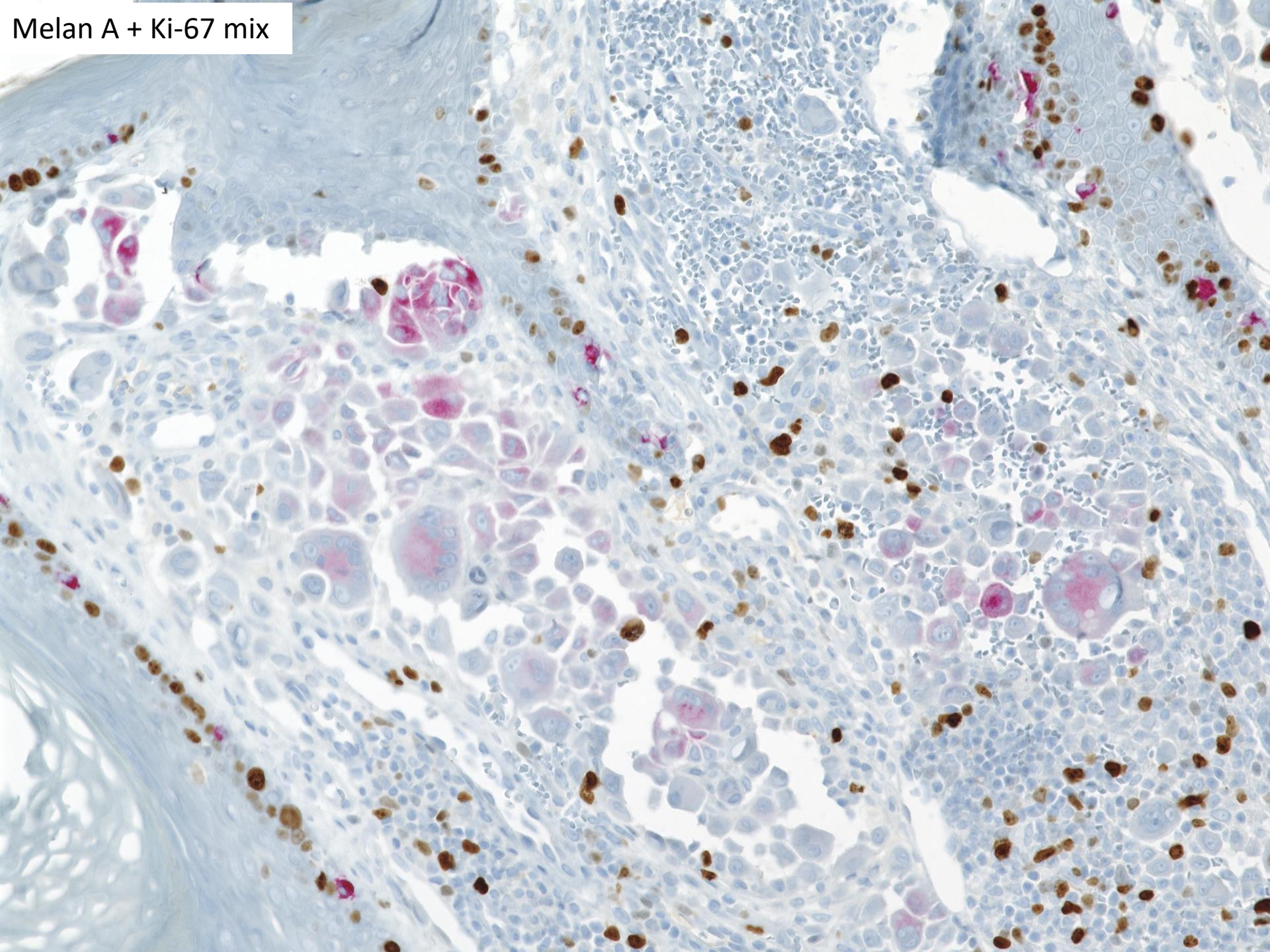


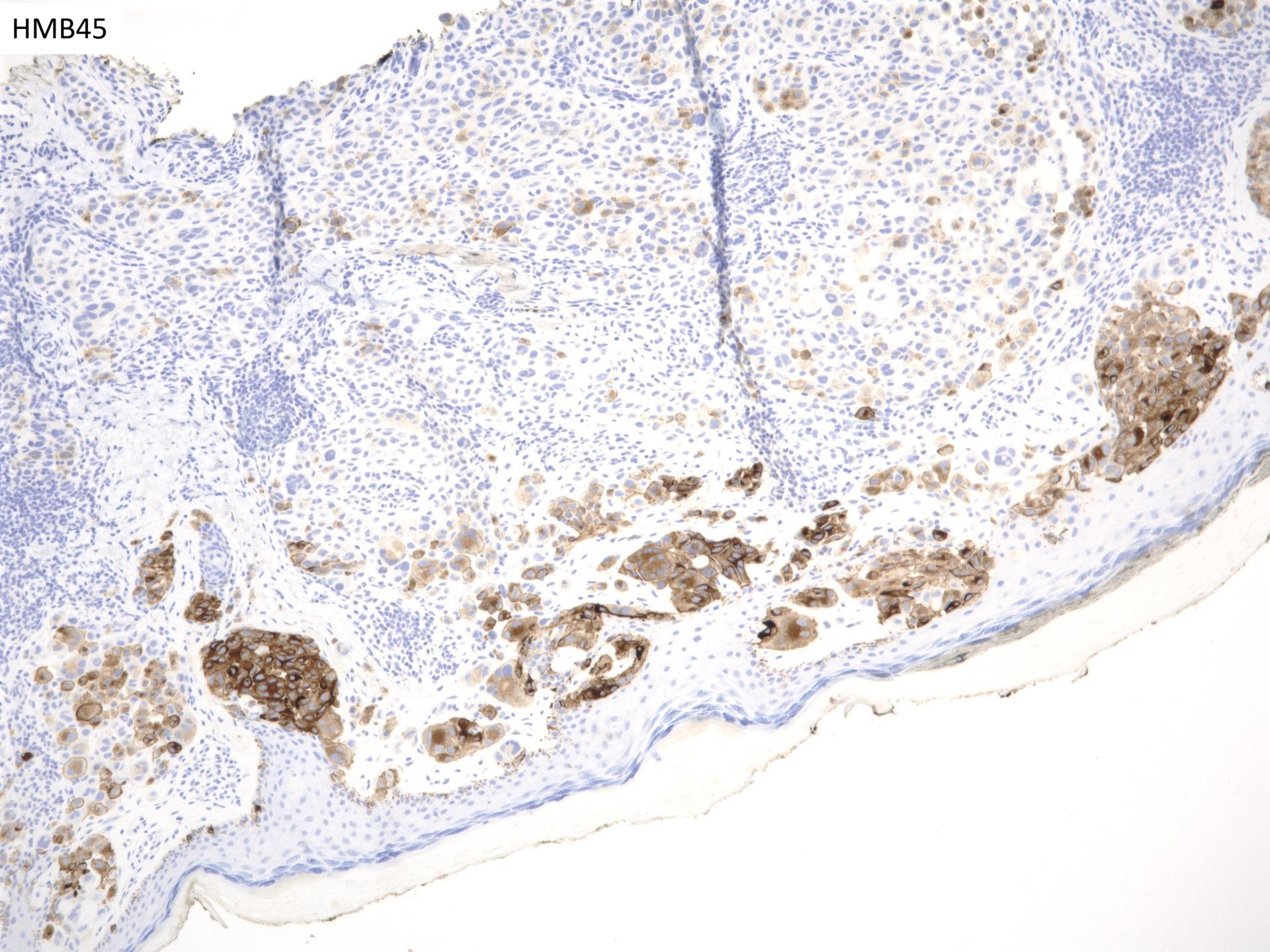




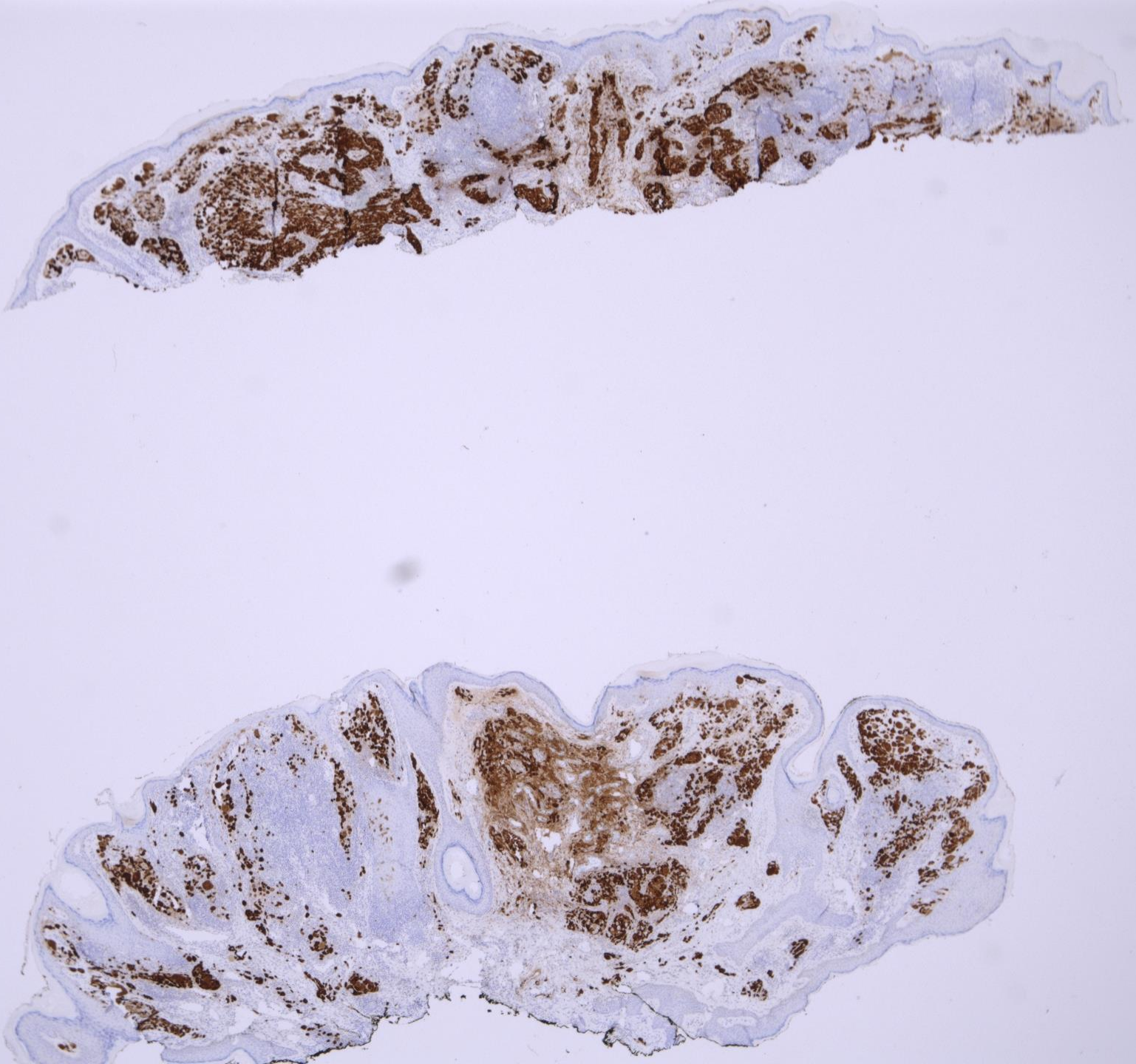
Melan A + Ki-67 mix

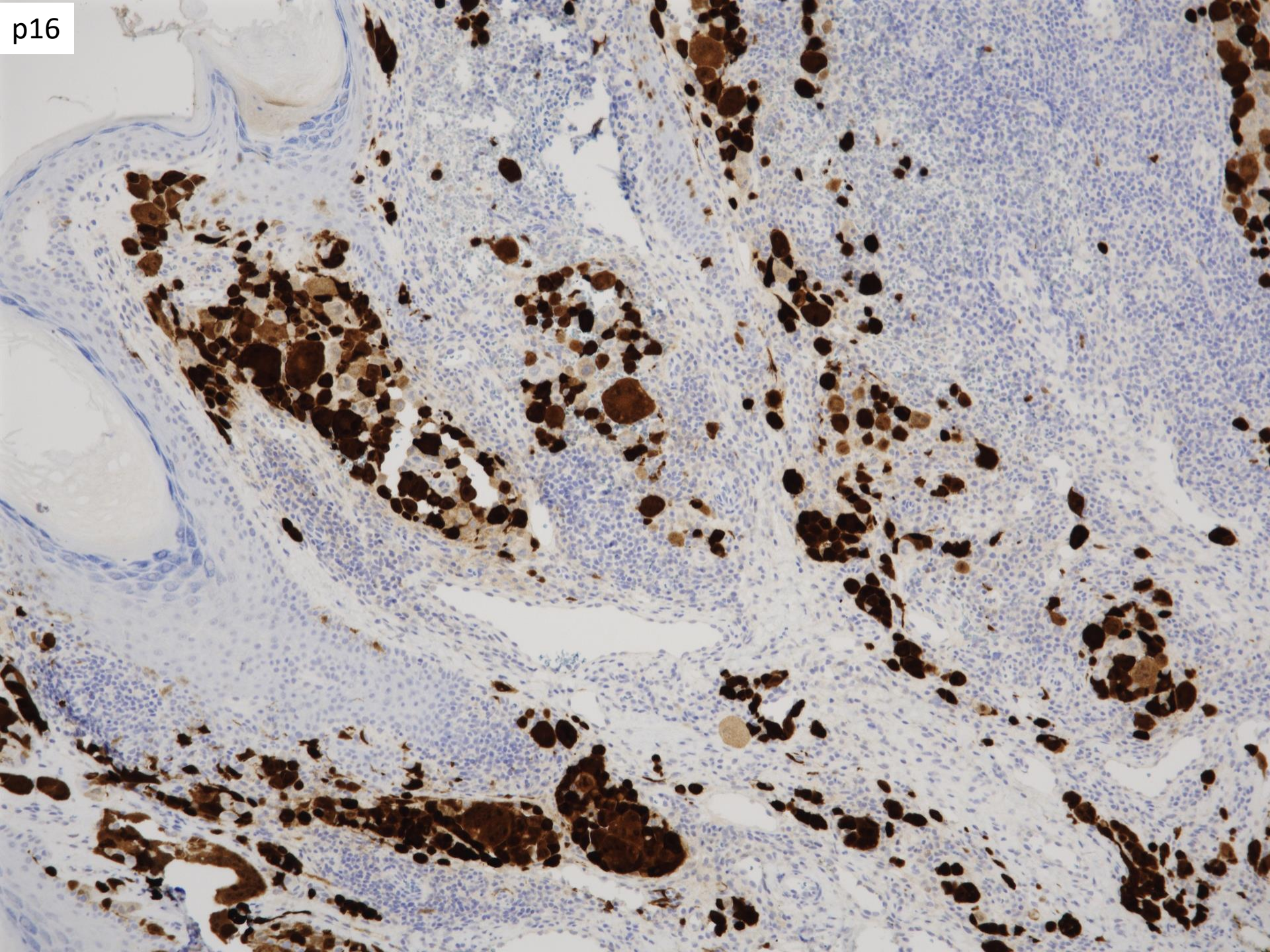



Melan A + Ki-67 mix


HMB45

p16

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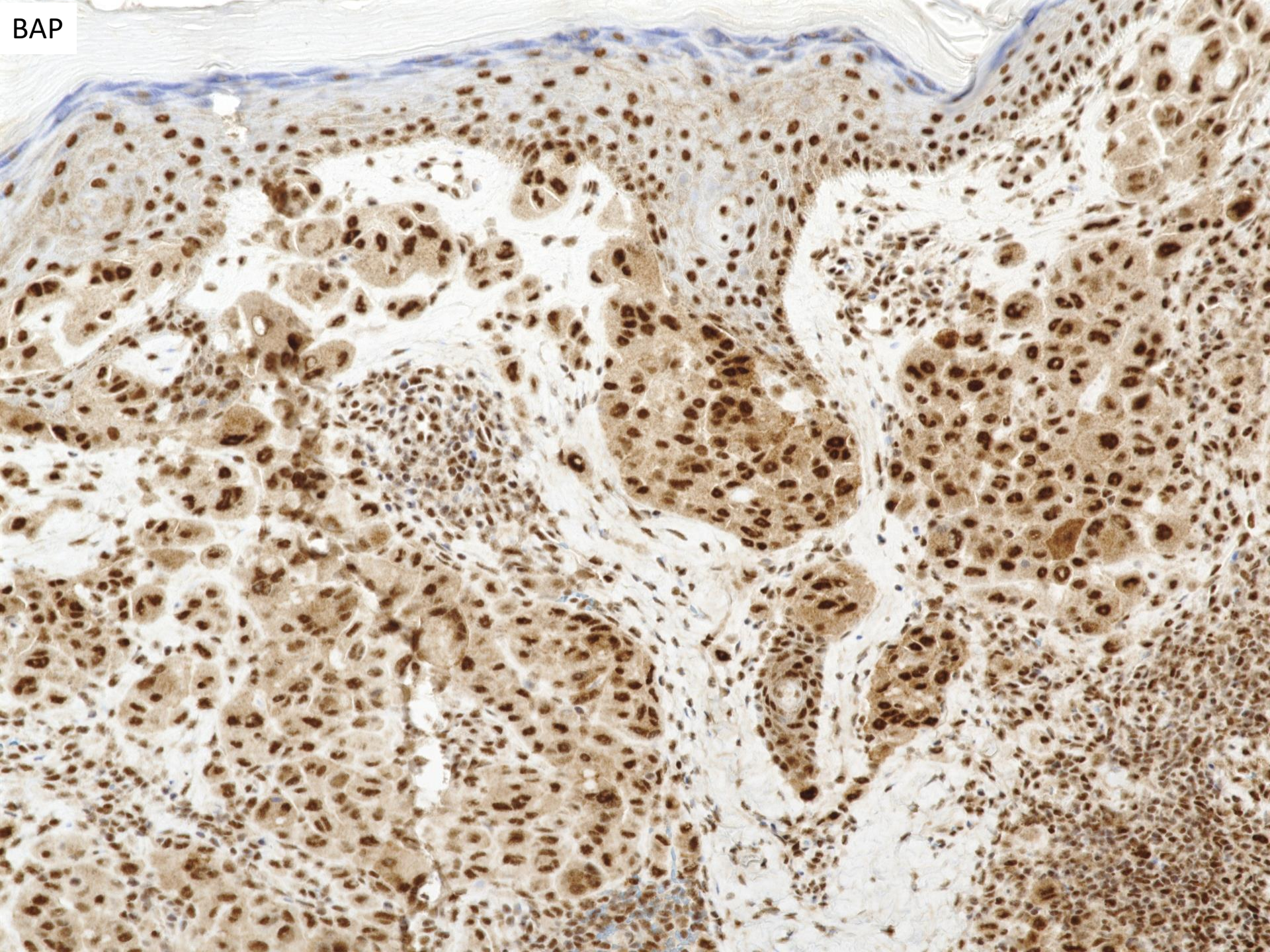

BAP

DIAGNOSIS?

Differential diagnosis

Spitzoid melanocytic neoplasms:

1. Spitz nevi - benign tumors
2. Atypical Spitz tumors - tumors of uncertain malignant potential
3. Spitzoid melanomas - malignant tumors, with metastasizing and lethal potential

Important features of this case

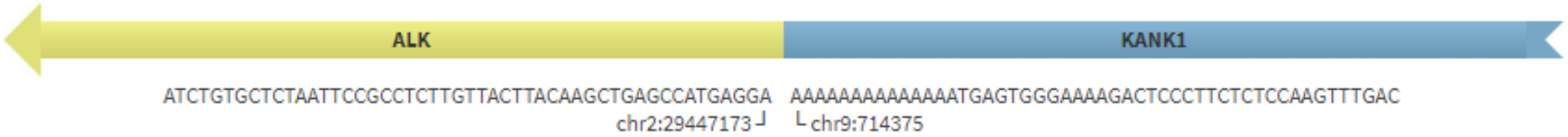
- **Concerning features:**
  - Cytologic atypia
  - Presence of 4 dermal mitotic figures (mitotic index 3/mm^2), one of which was towards the deep aspect of the lesion (none were atypical)
- **Reassuring features:**
  - Patient's young age
  - Preservation of p16 expression
  - Dermal gradient of HMB45 expression
- **Favor atypical Spitz tumor**

Additional ancillary studies

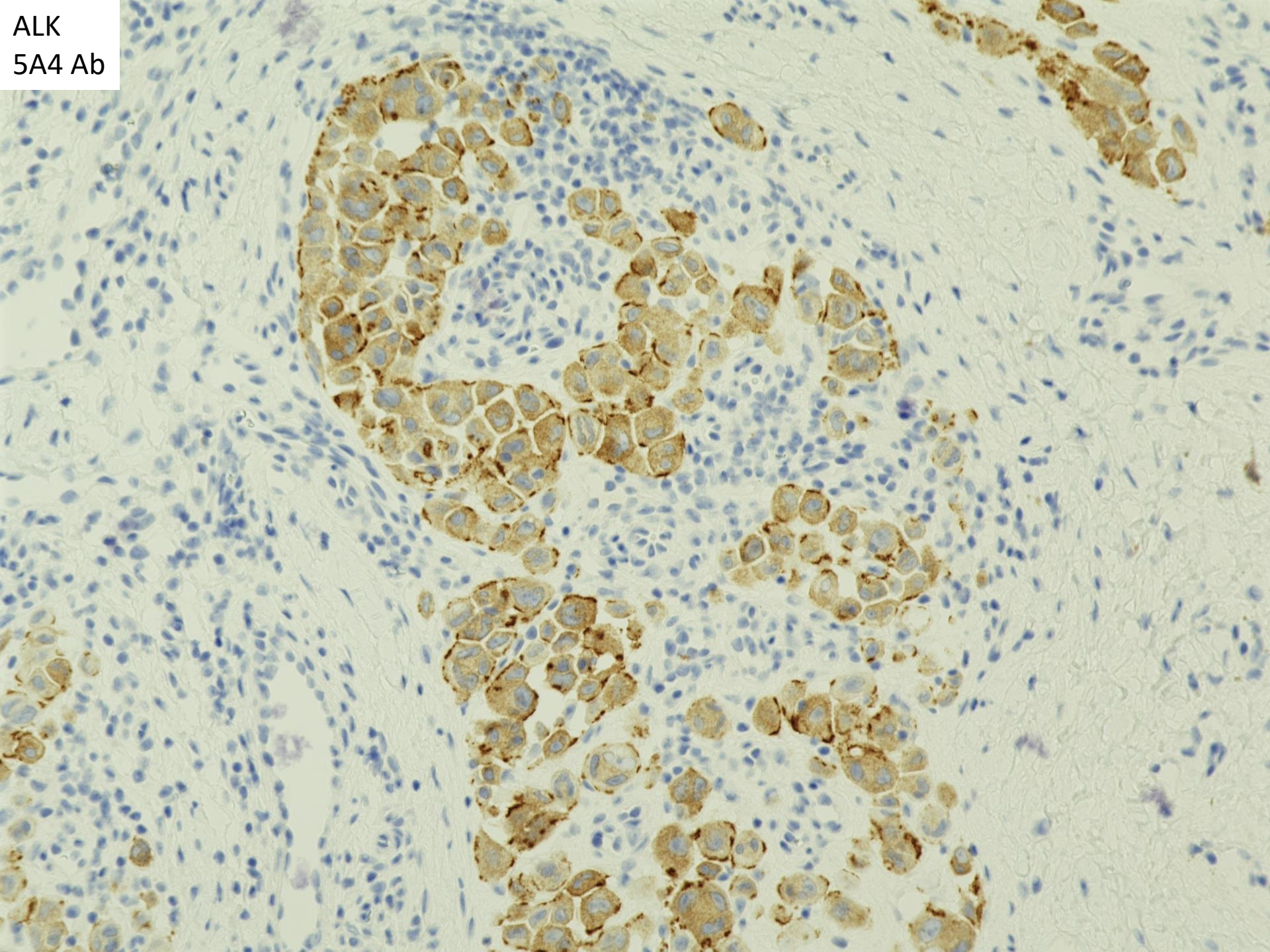
- Perform melanoma FISH studies to detect abnormalities associated with melanoma
  - Borderline positive
- Perform next generation sequencing assay
  - Negative for *TERT* promoter mutation

Stanford Solid Tumor Actionable Mutation Panel (STAMP)

KANK1-ALK fusion



In frame mRNA transcript that encodes a chimeric protein with a constitutively activated kinase.


ALK
5A4 Ab

Genetics of Spitz tumors

- Kinase-rearranged (in 72 of 140 or 51.4% of spitzoid neoplasms):
  - Receptor tyrosine kinases
    - **ALK (10%)**, ROS1, NTRK1, and RET
  - Serine-threonine kinase BRAF

- *HRAS*-mutant sclerosing Spitz nevi

- *BAP1* loss Spitz tumors

- Spitzoid melanomas with homozygous deletions of p16

Kinase fusions in Spitzoid melanocytic neoplasms

- Kinase fusions are detected across the entire spectrum of Spitz lesions
  - Benign Spitz nevi
  - Atypical Spitz tumors
  - Rare spitzoid melanomas

- Suggests that the fusions likely occur early in the pathogenesis of the tumors and are not sufficient for malignant transformation

Clinical, Histopathologic, and Genomic Features of Spitz Tumors With *ALK* Fusions

Iwei Yeh, MD, PhD, Arnaud de la Fouchardiere, MD, PhD,† Daniel Pissaloux, PhD,† Thaddeus W. Mully, MD,* Maria C. Garrido, MD, PhD,* Swapna S. Vemula, MS,* Klaus J. Busam, MD,‡ Philip E. LeBoit, MD,* Timothy H. McCalmont, MD,* and Boris C. Bastian, MD, PhD**

- 32 Spitz tumors with ALK fusions
  - 6 Spitz nevi
  - 22 atypical Spitz tumors
  - 4 spitzoid melanomas
- Age range 5 months to 64 years (median=12 y)
- Female predominance (21 female, 11 male)
- Exophytic papules on the extremities (~50%), also trunk and head and neck

Clinical, Histopathologic, and Genomic Features of Spitz Tumors With *ALK* Fusions

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- None of the patients' tumors recurred, including the 4 patients with spitzoid melanoma who were each followed for >1 year
- No Spitz tumors with ALK fusions are yet reported to have widely disseminated

Follow up

- Re-excision ~4 months later with no residual tumor
- Did not pursue sentinel node biopsy
- Continue clinical monitoring
- No evidence of disease at ~8 months

Summary

- Cytogenetic and molecular studies are useful in the subclassification of atypical Spitz lesions
  - FISH
  - Next generation sequencing – *TERT* promoter

- ALK fusions are estimated to be present in ~8% of Spitz nevi, ~5% of atypical Spitz tumors, and ~1% of spitzoid melanomas

- ALK-rearranged Spitz lesions (even Spitzoid melanomas) may behave indolently, though further study is needed

References

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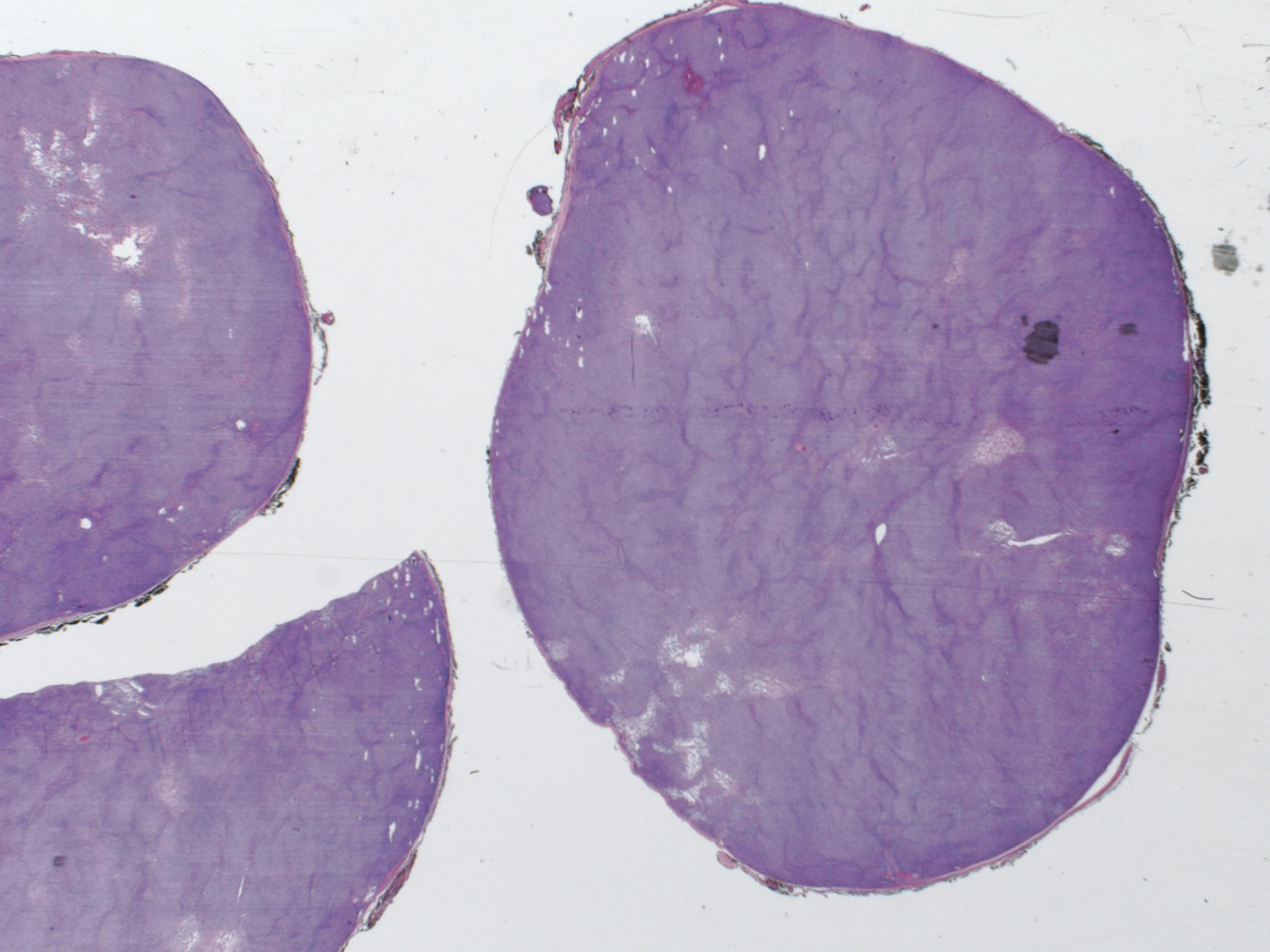
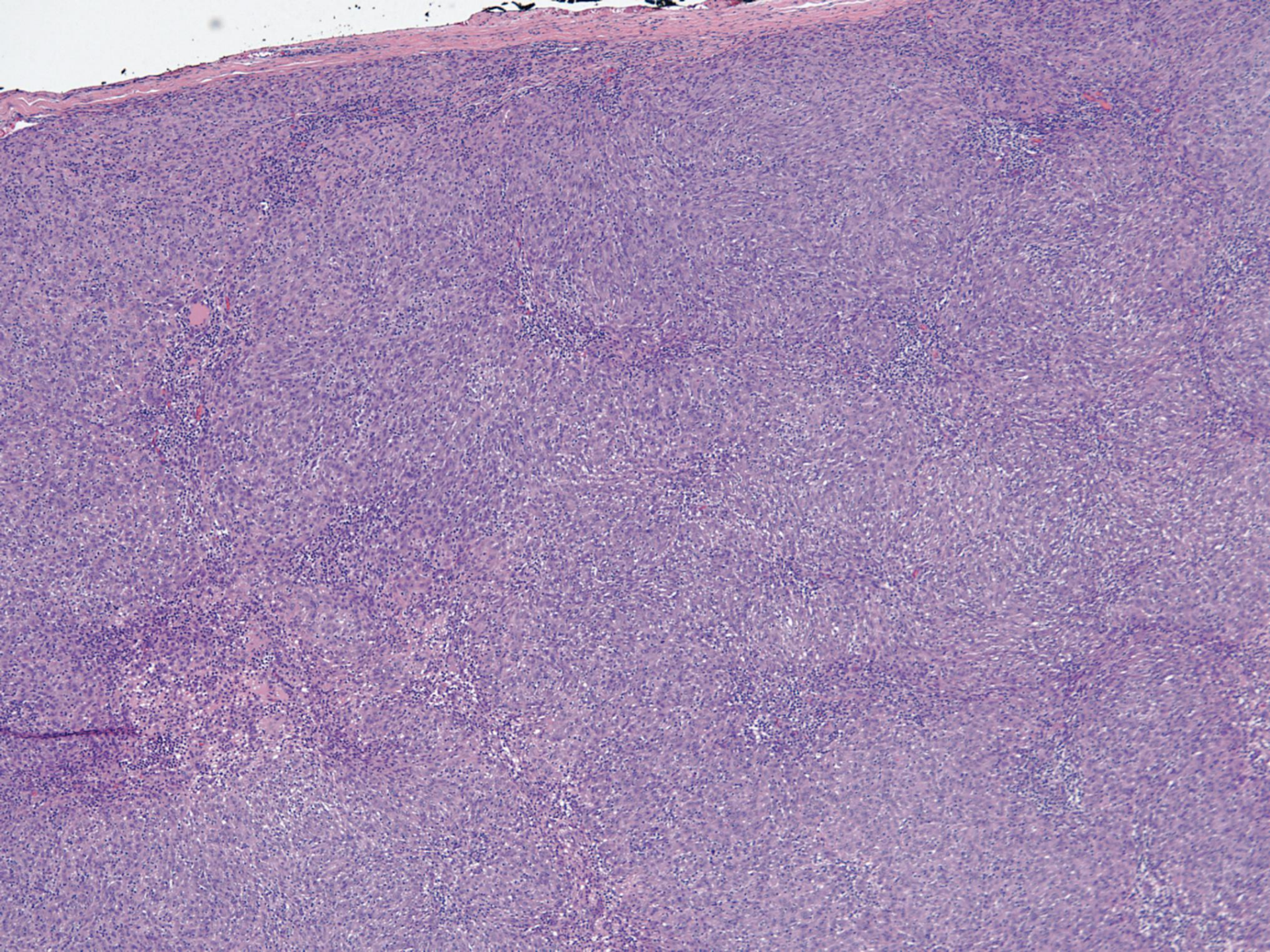
- Yeh I, de la Fouchardiere A, Pissaloux D, Mully TW, Garrido MC, Vemula SS, et al. Clinical, histopathologic, and genomic features of Spitz tumors with ALK fusions. Am J Surg Pathol. 2015;39:581–591.

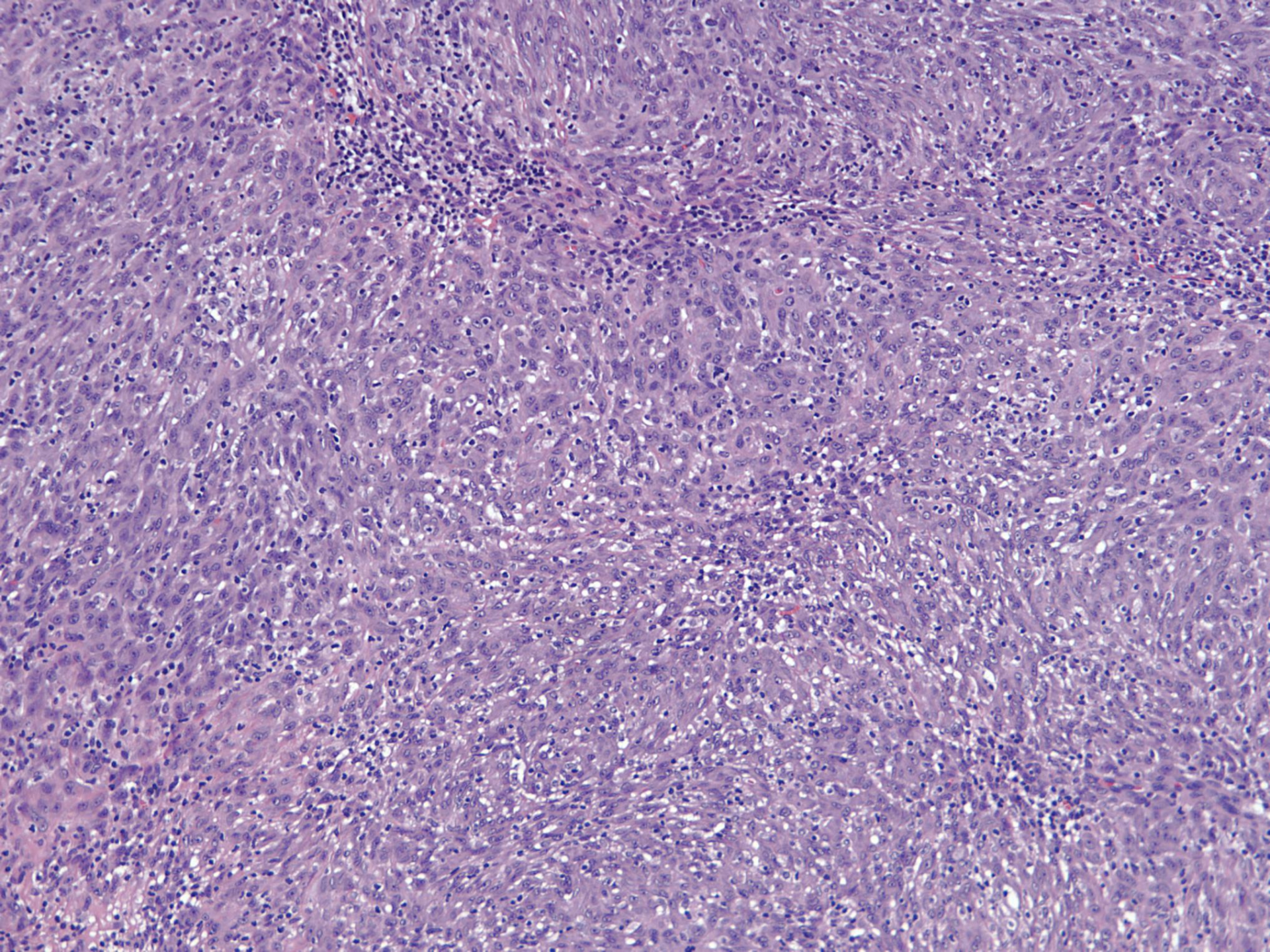
SB 6292

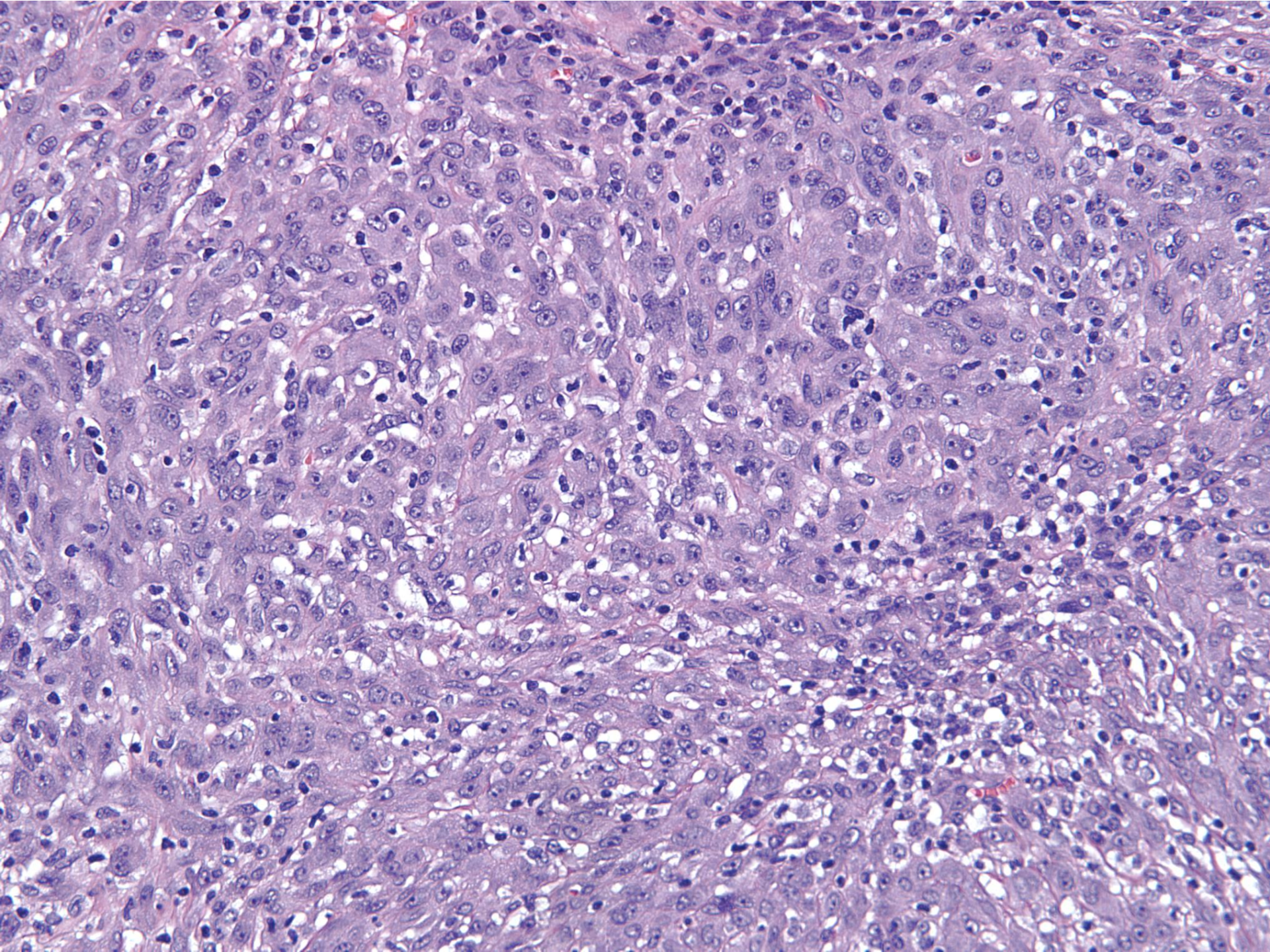
Sebastian Fernandez-Pol/Christian Kunder; Stanford

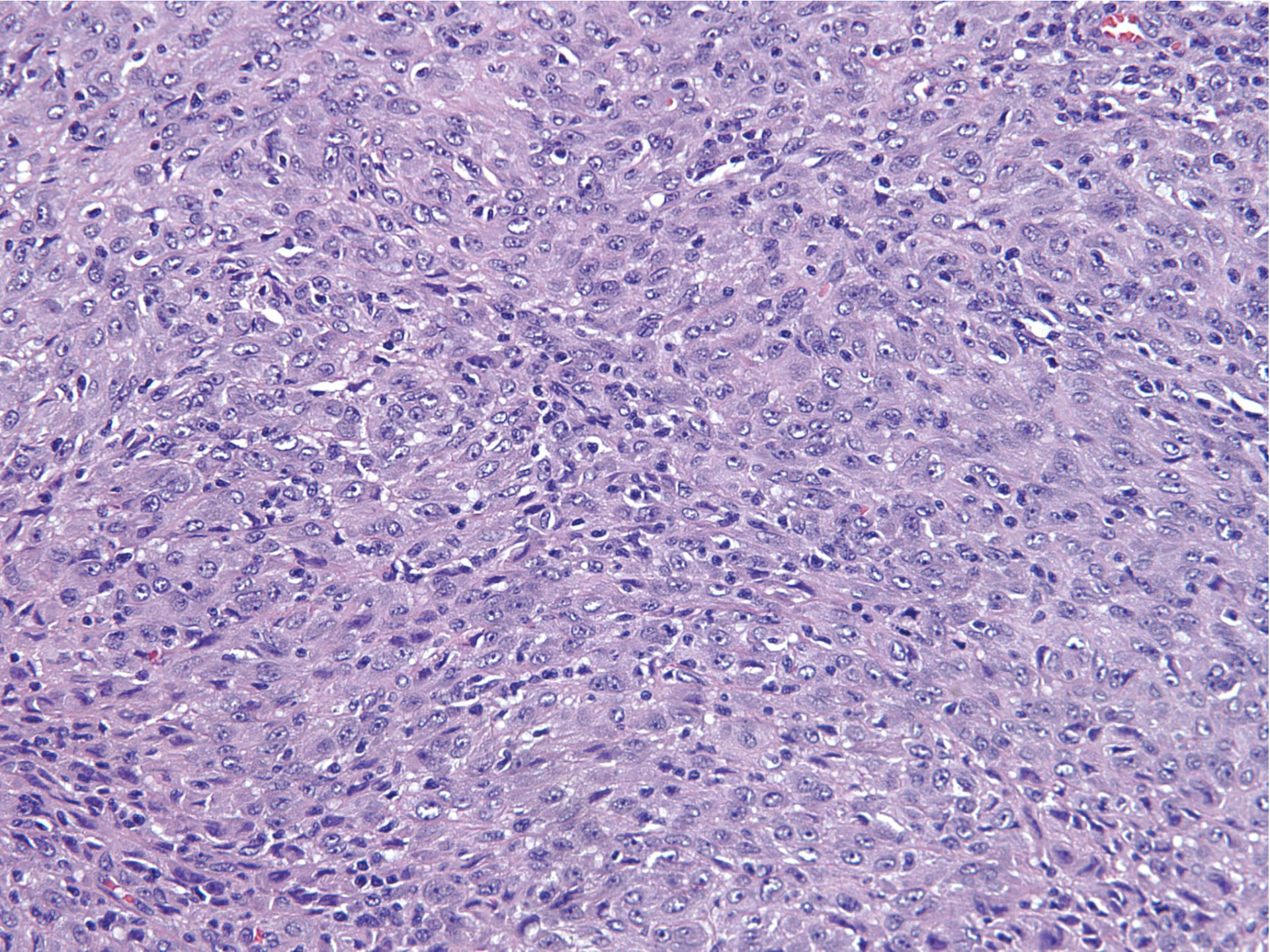
31-year-old man with right upper eyelid lesion.

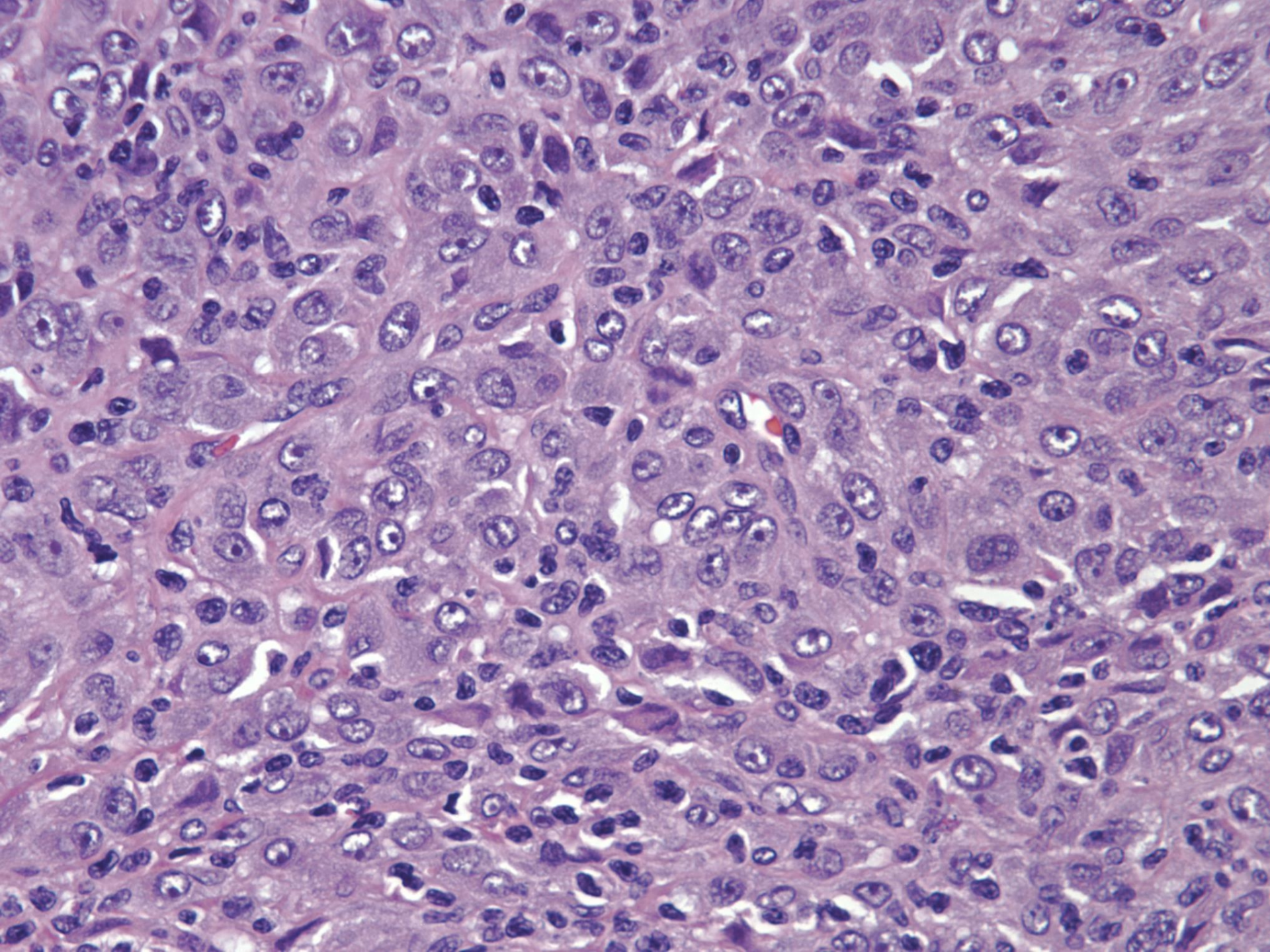


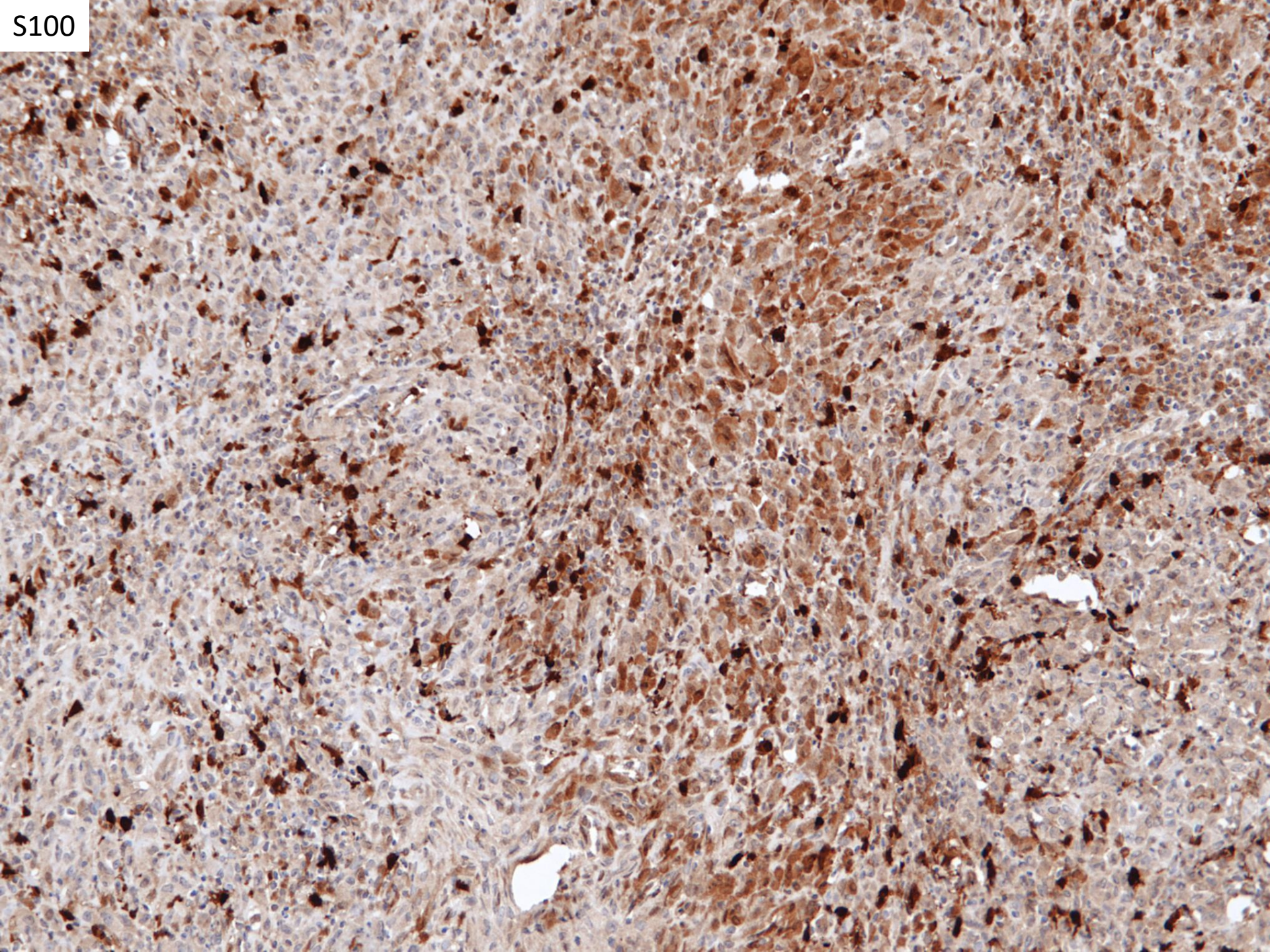


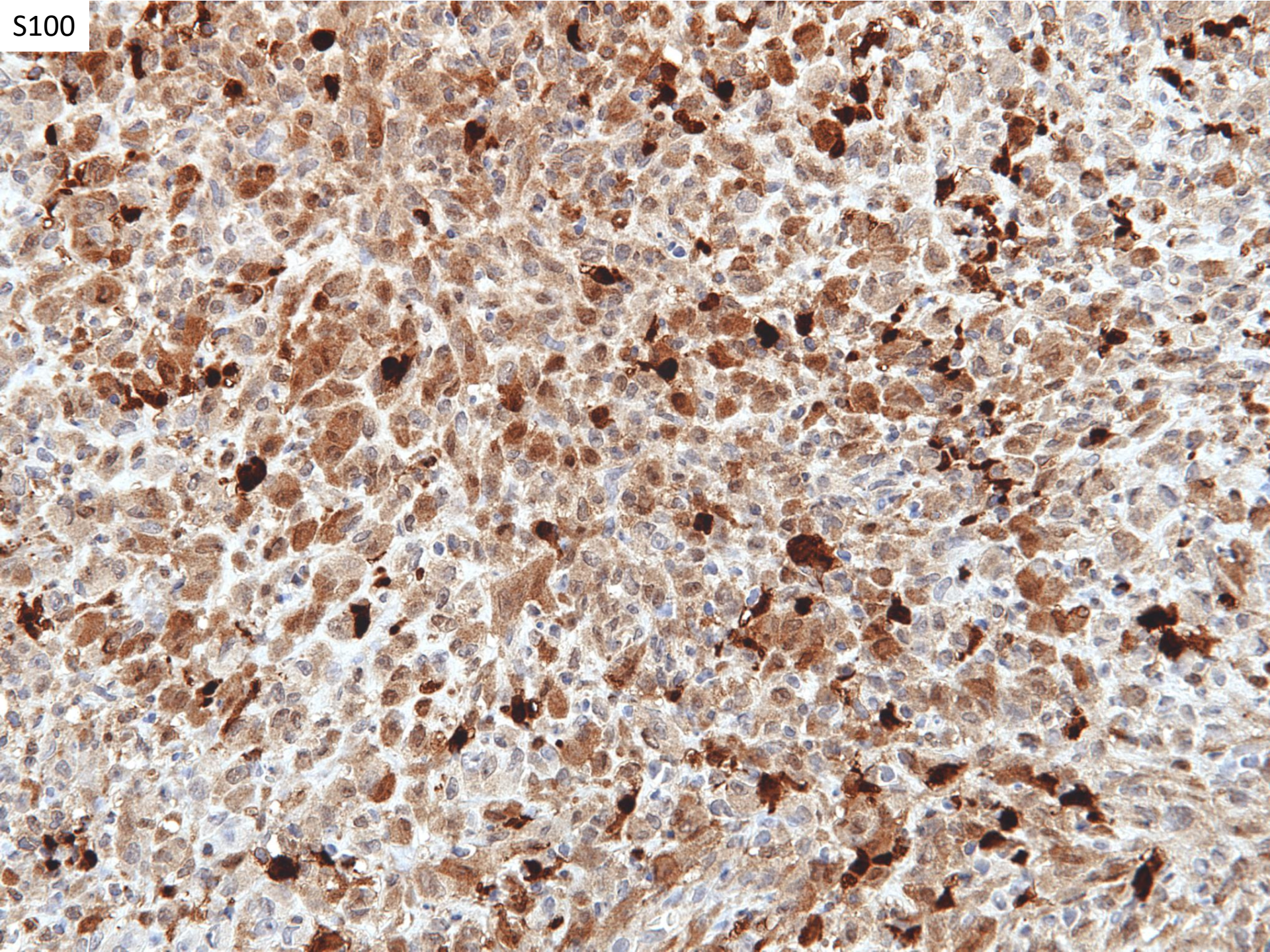









S100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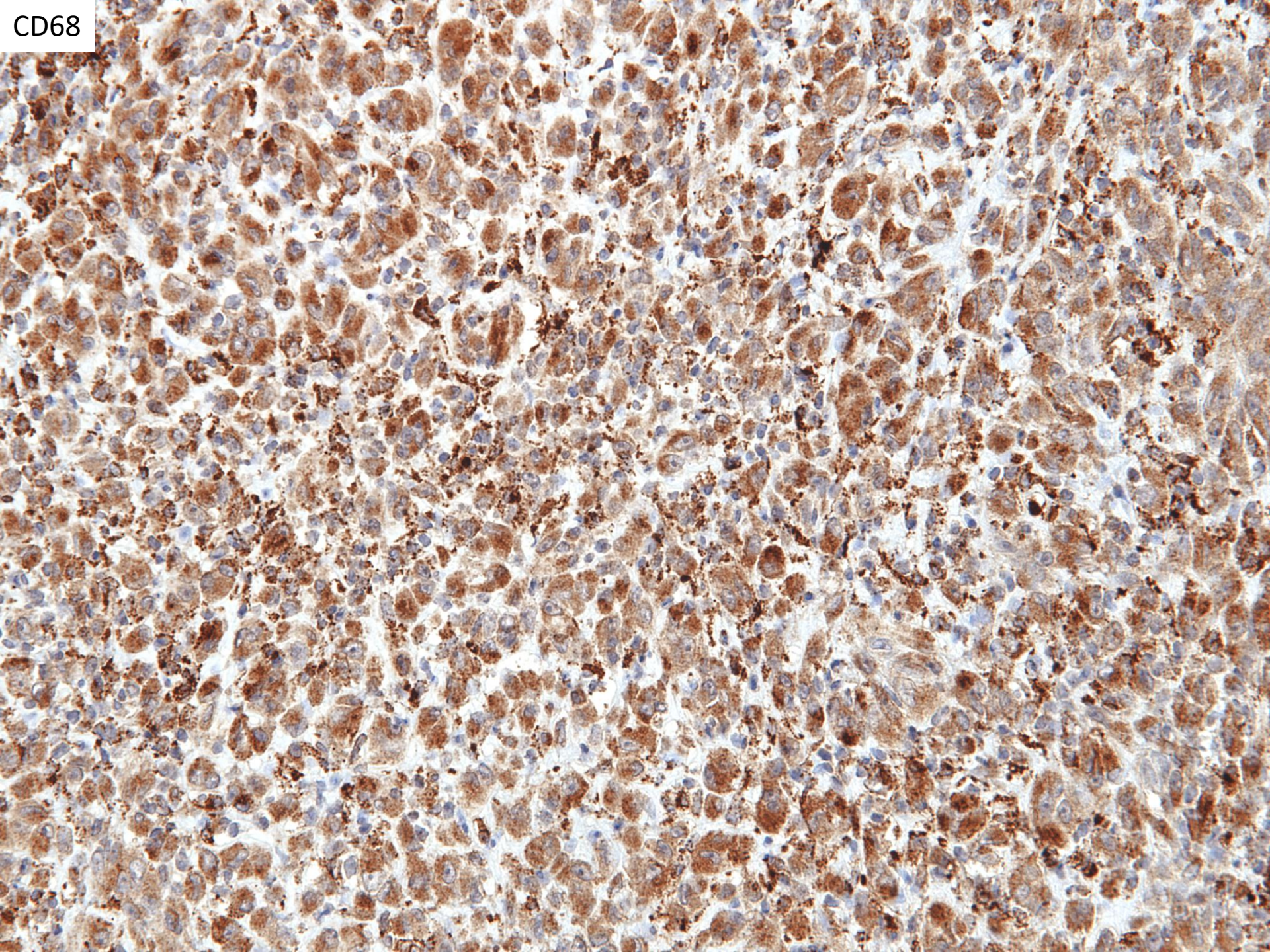
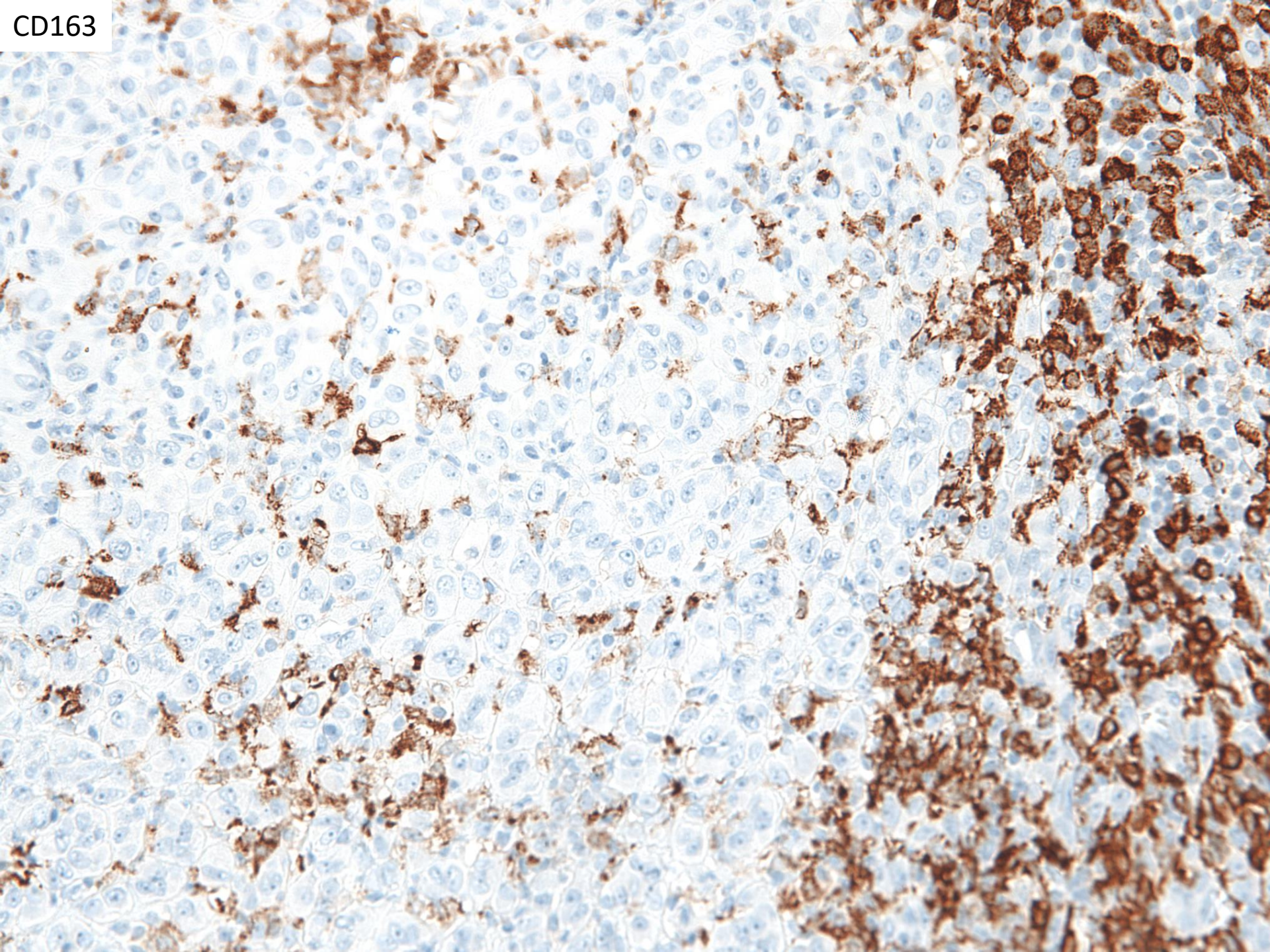
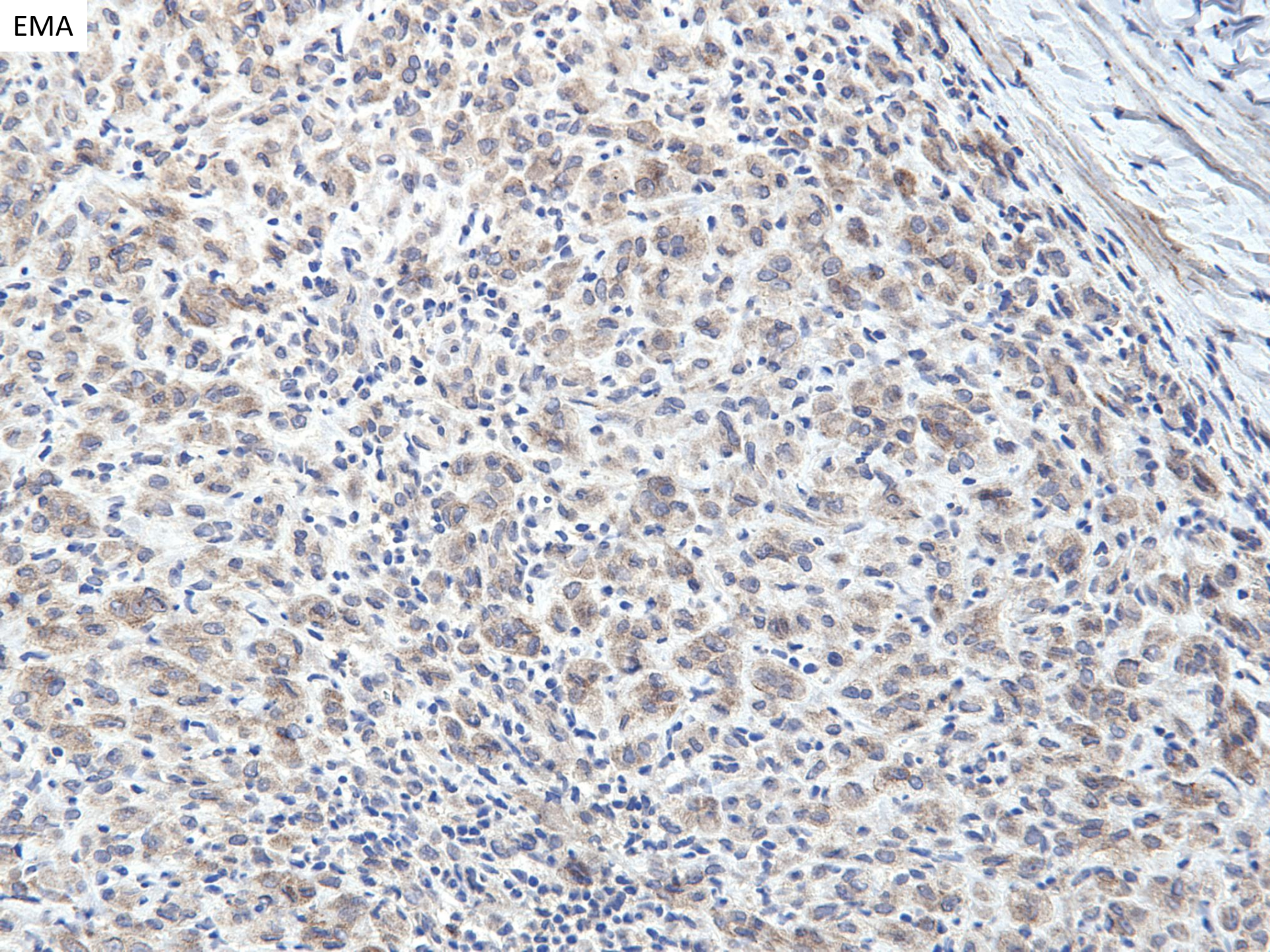
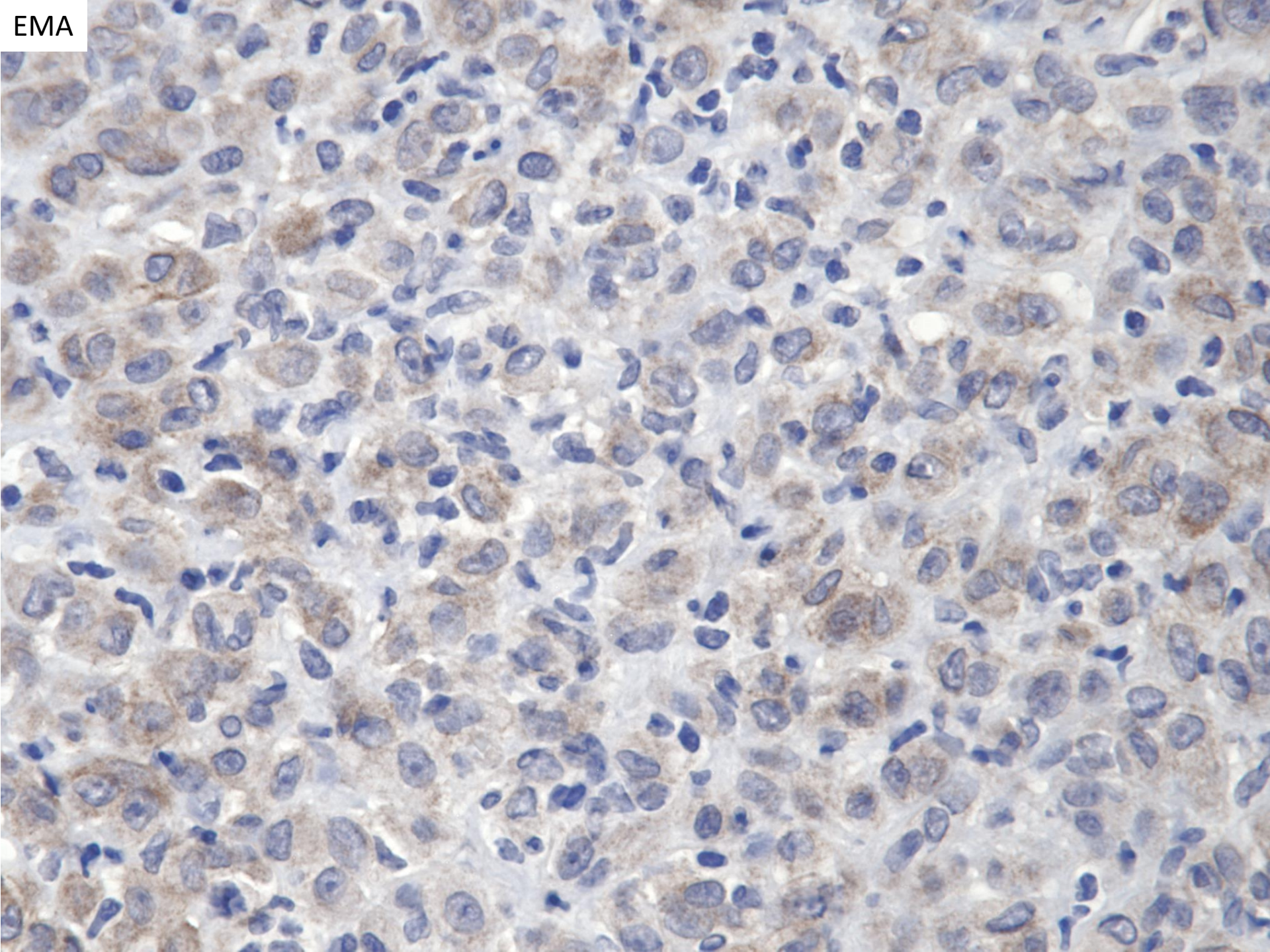

CD68


CD163


EMA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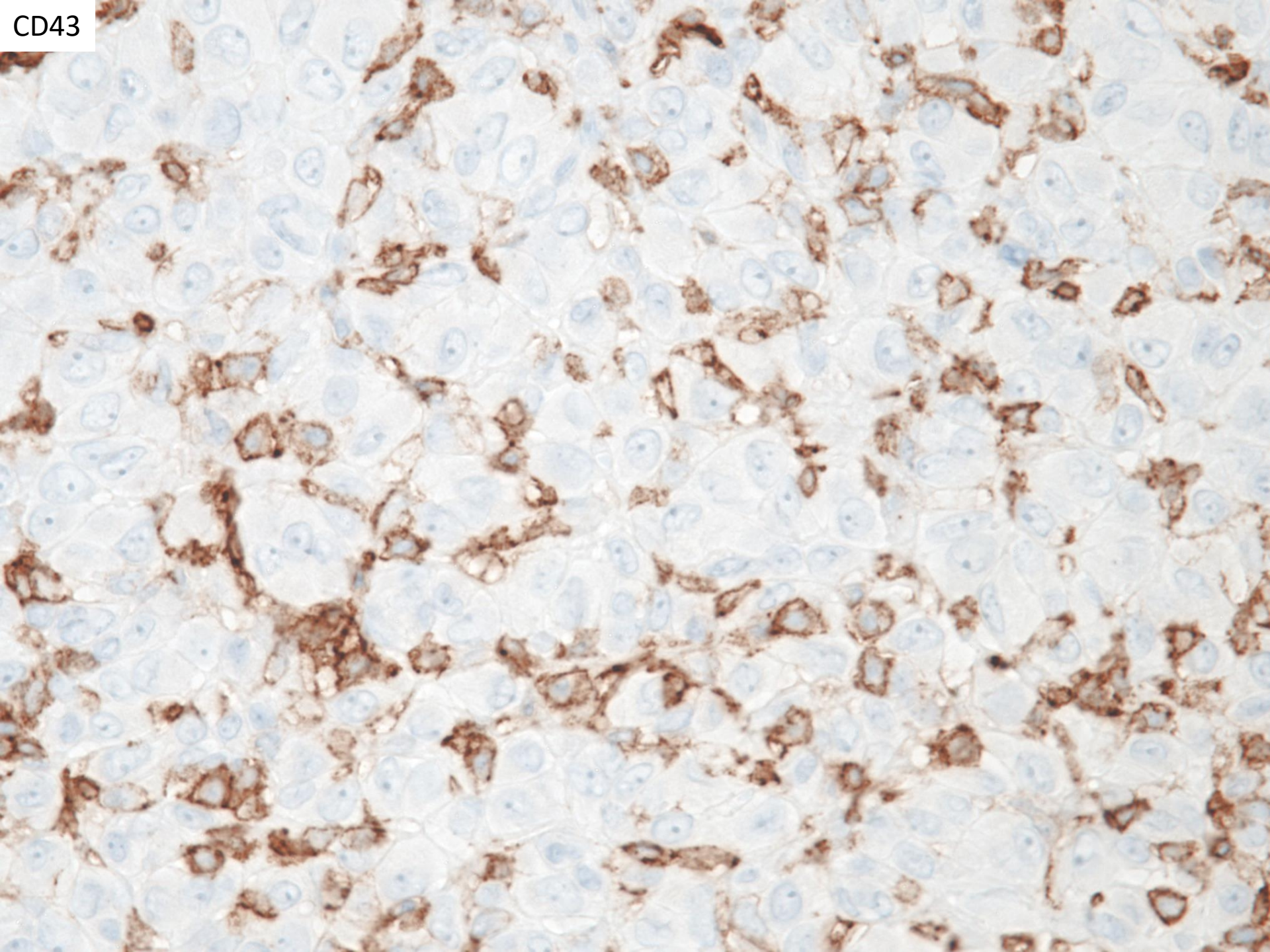
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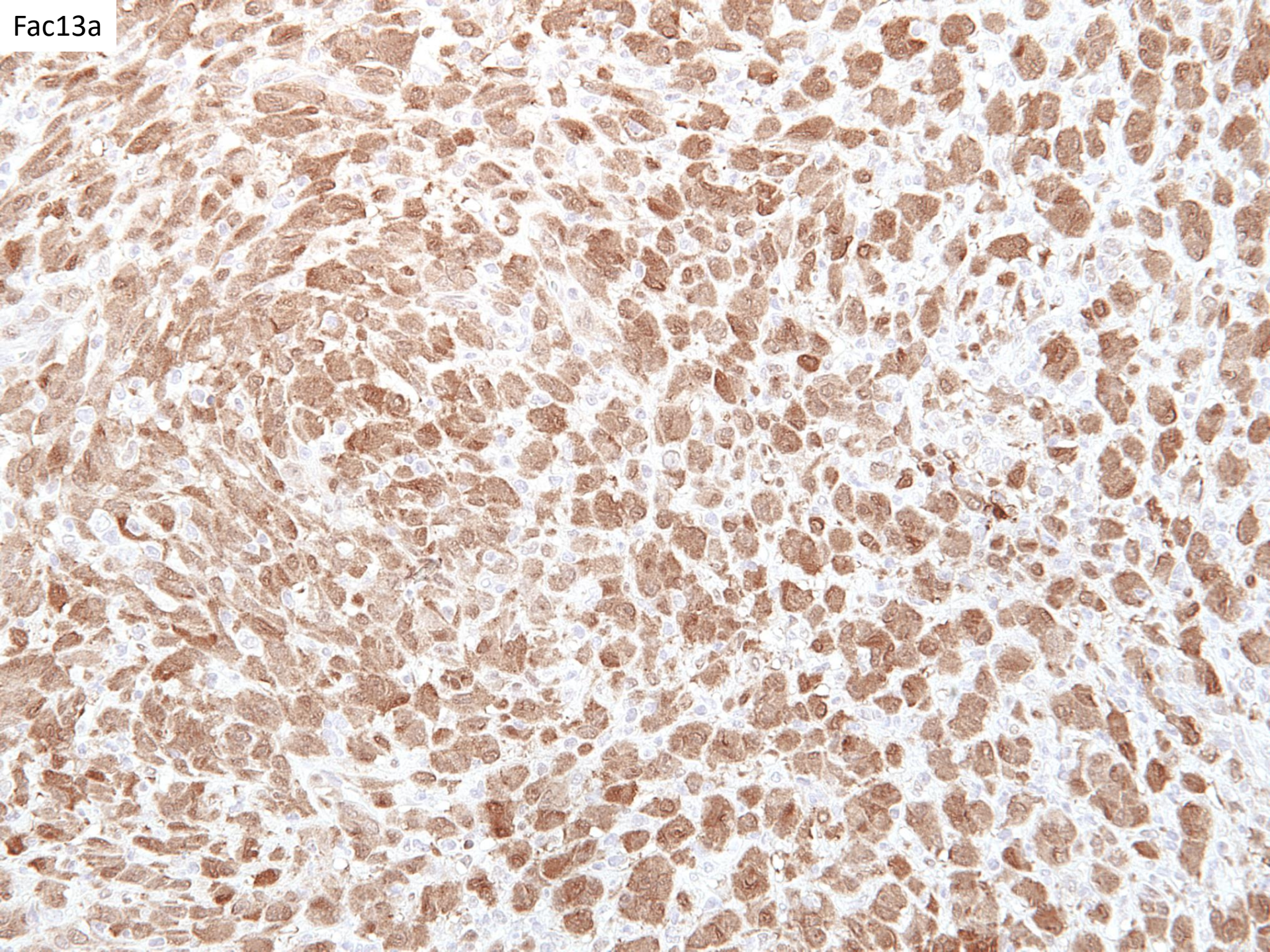

Fac13a

Negative stains

- AFB, FITE, and GMS stains are negative.

Melan A	CD23	CD21
Pancytokeratin,	CD3	BRAF V600E
ALK-1	CD4	CD20
CD34	CD8	SOX-10
p63	Calponin	CD14
CD15	CD1a	desmin
CD30	Langerin	ActS/SMA
CXCL13	CD43	CD117
INI (retained)	GFAP	EBV

Cytogenetic studies

- FISH negative for clonal separation of 5‘ and 3' *EWSR1* signals

- FISH negative for clonal separation of 5’ and 3’ *ALK* signals

DIAGNOSIS?

Differential diagnosis

Histiocytic neoplasms:

- **Follicular dendritic cell sarcoma –** excluded by negative CD21, CD23, and CXCL13

- **Erdheim-Chester disease –** excluded by morphology (not foamy), expression of EMA, and negative CD163

Benign fibrohistiocytic tumors:

- **Epithelioid fibrous histiocytoma**

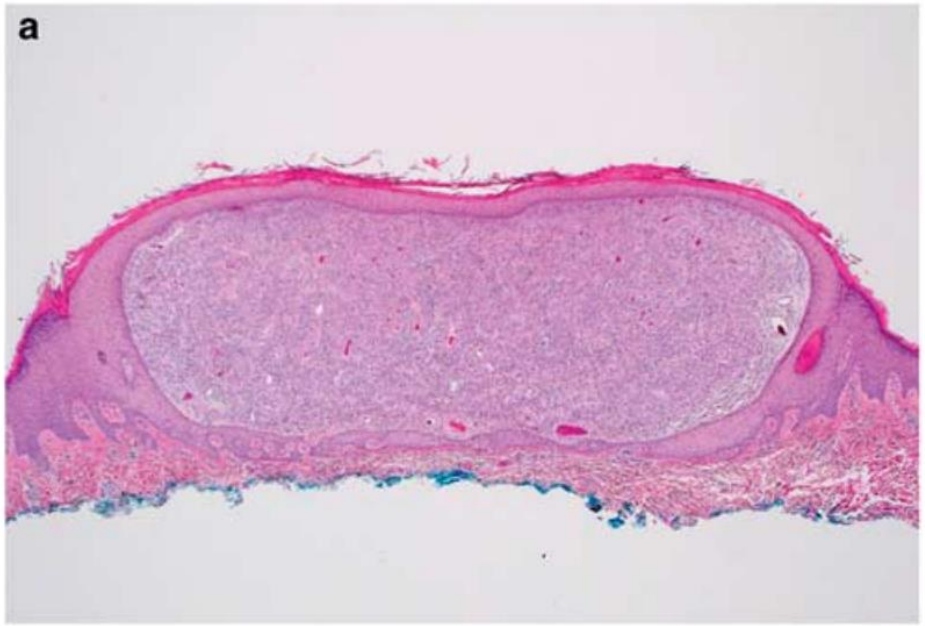
- **Cutaneous syncytial myoepithelioma**

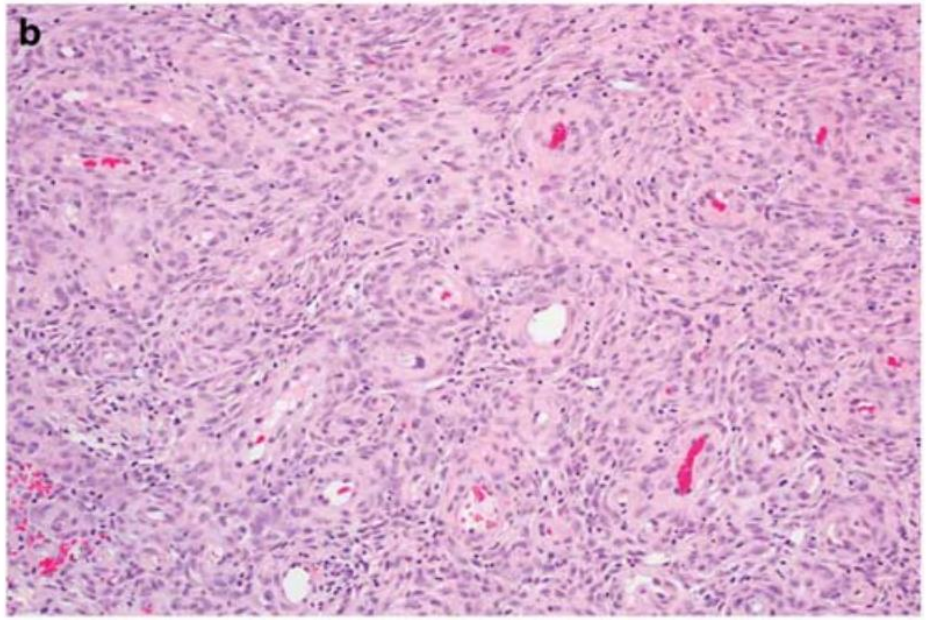
Epitheloid fibrous histiocytoma

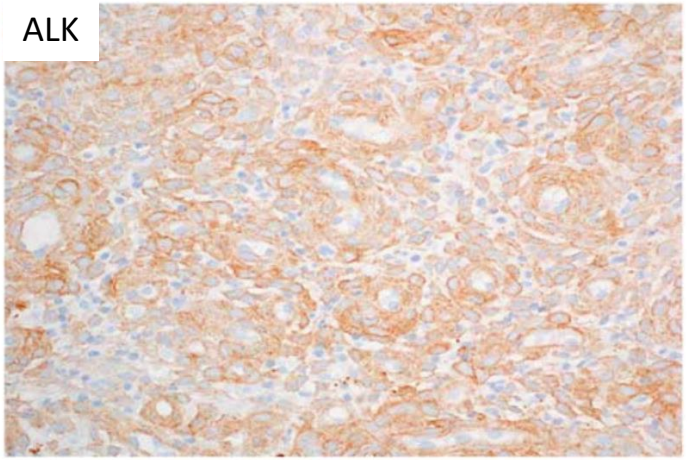
- Used to be considered a variant of benign fibrous histiocytoma/dermatofibroma with >50% epithelioid cells

- The detection of *ALK* rearrangements in most cases argues that epithelioid fibrous histiocytoma is likely different from benign fibrous histiocytoma

Epithelioid fibrous histiocytoma

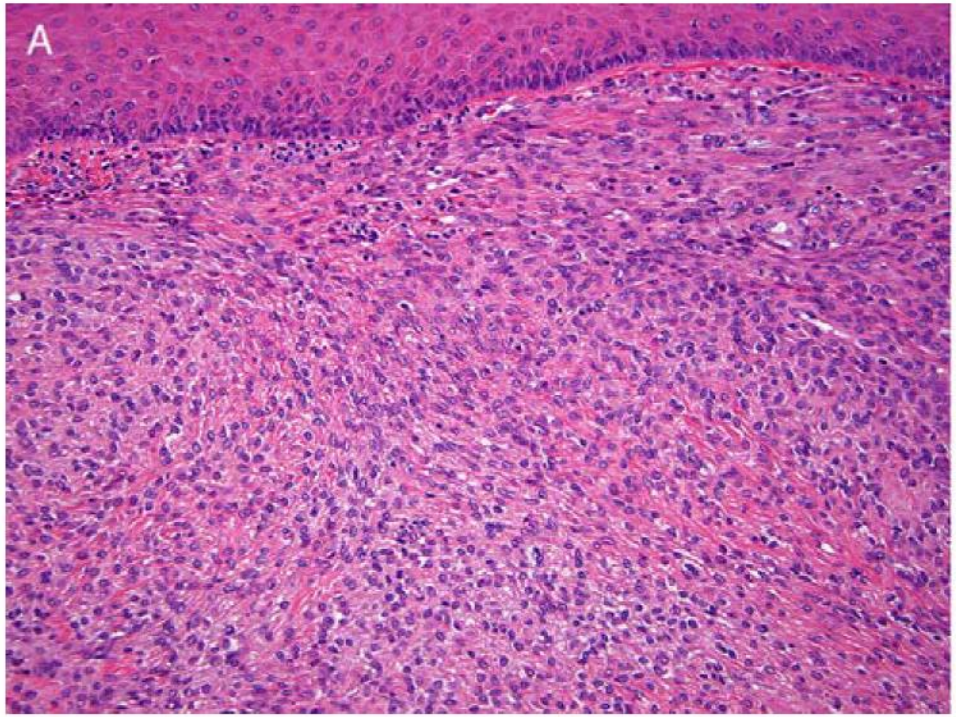


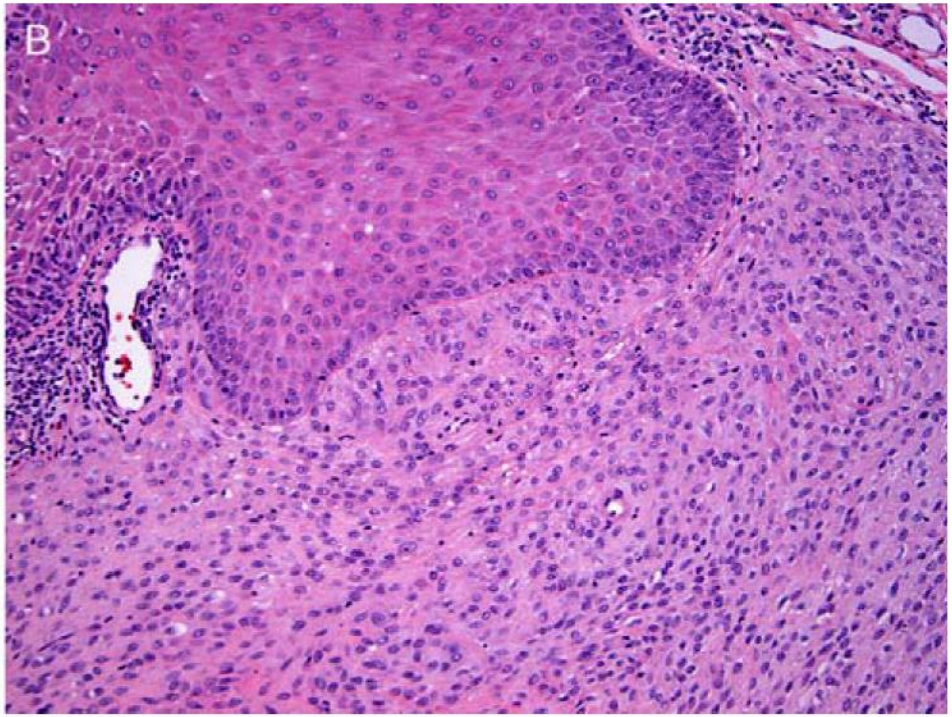




Doyle L.A., Mariño-Enriquez A., Fletcher C.D., Hornick J.L. ALK rearrangement and overexpression in epithelioid fibrous histiocytoma. Mod. Pathol. 2015;28:904–912.

Cutaneous syncytial myoepithelioma





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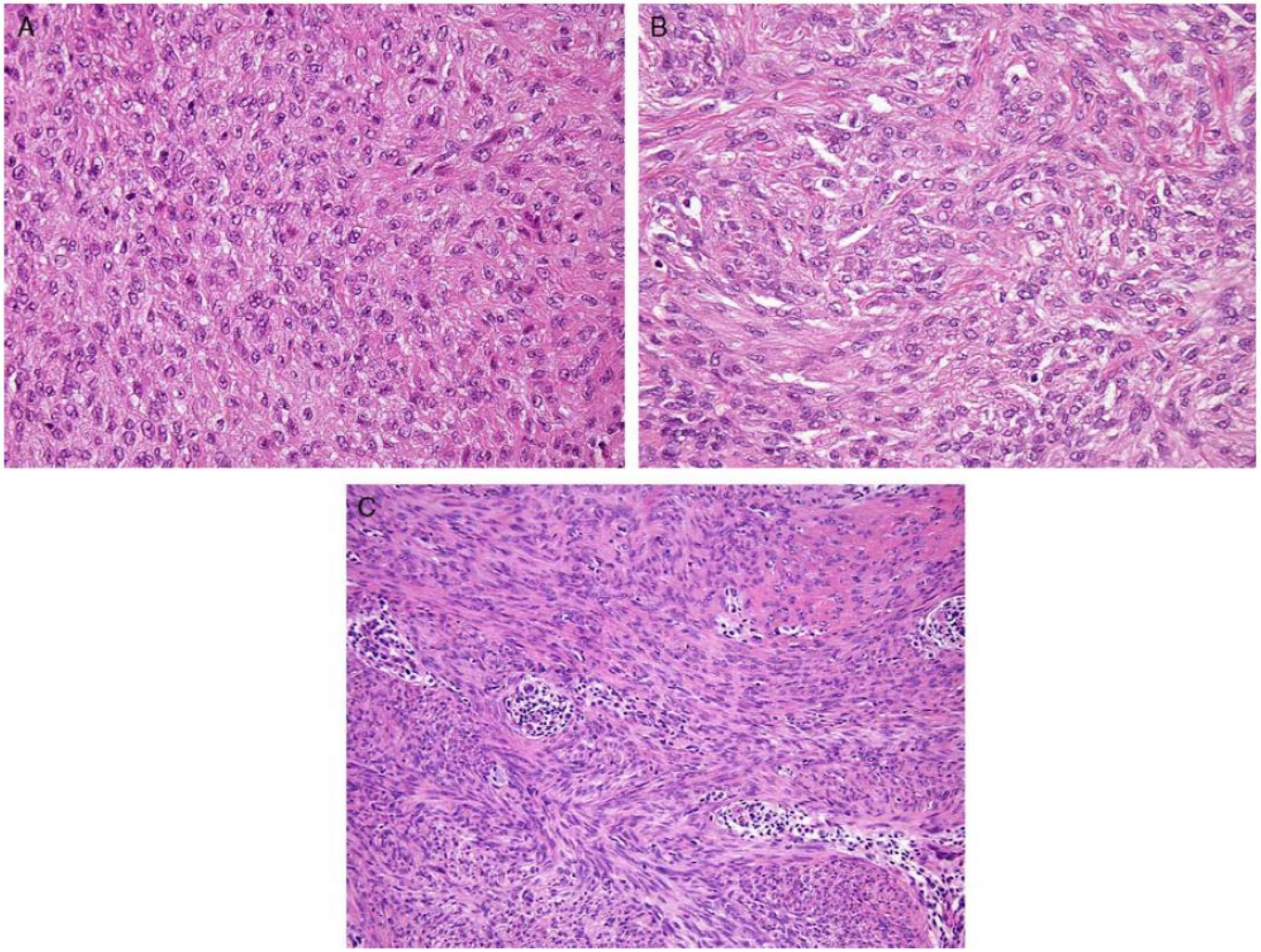
Cutaneous syncytial myoepithelioma



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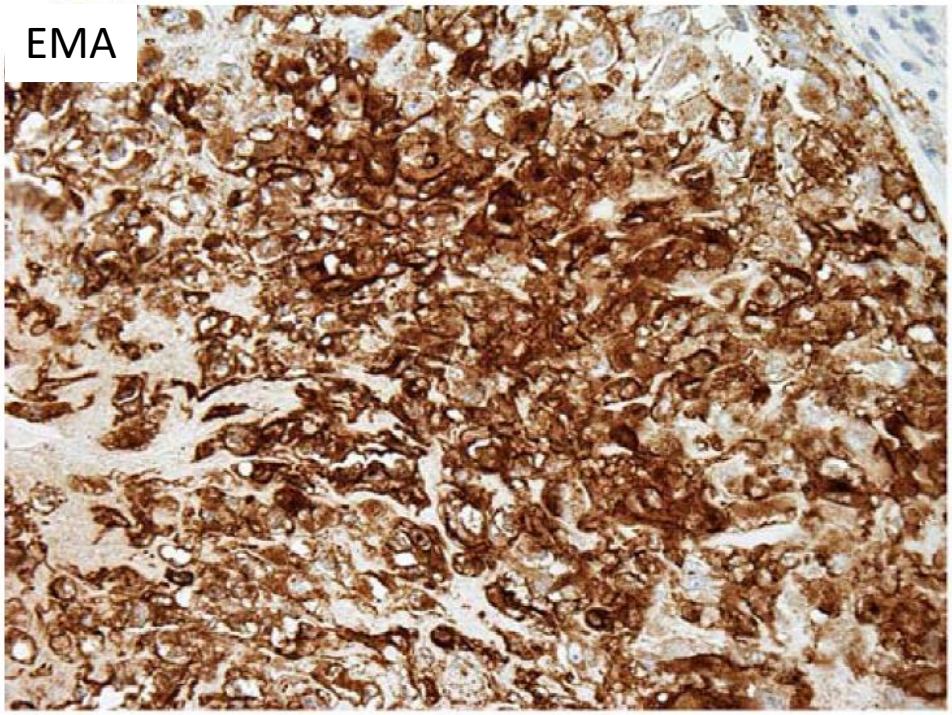
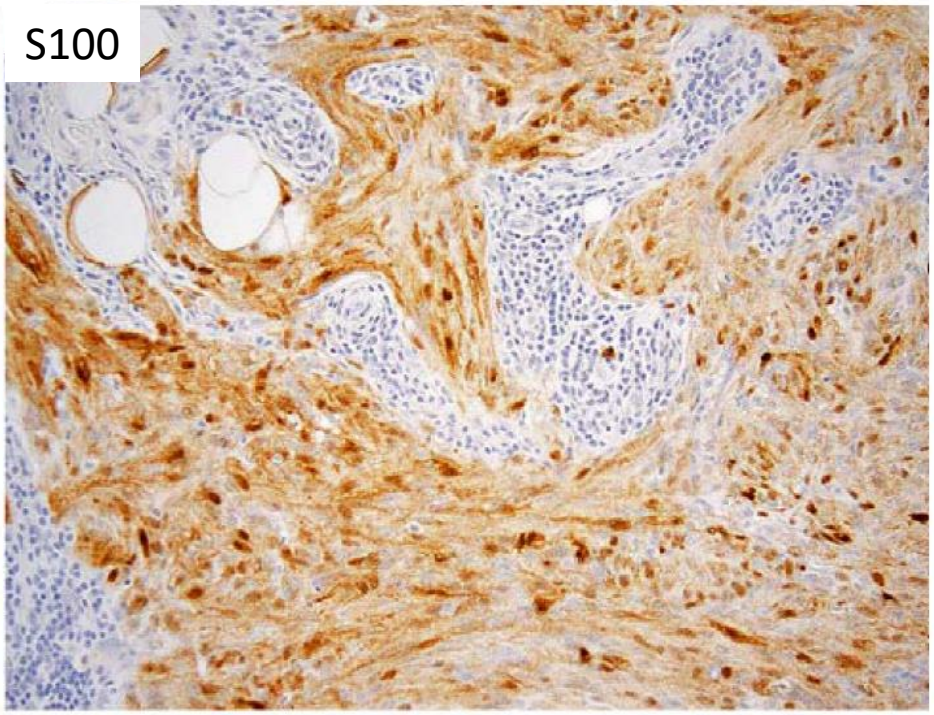
Cutaneous syncytial myoepithelioma

All tumors showed diffuse positivity for EMA and S-100





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Cutaneous syncytial myoepithelioma

- Described initially in 2004
- More completely characterized in 2013
- **Immunohistochemistry:**
  - All diffusely positive for EMA
  - Majority showed diffuse staining for S-100 protein (5 showing focal staining)
  - GFAP+ (14/33)
  - SMA+ (9/13)
  - p63+ (6/11)
  - *EWSR1* rearrangement (14/17)

	Epithelioid fibrous histiocytoma	Cutaneous syncytial myoepithelioma	Our case
EMA	64%	100%	Dim
S100	Negative	100%	Negative in epithelioid cells
Factor 13a	71%	Unknown	Positive
ALK	88%	Negative	Negative
Predominant site	Lower limbs	Upper extremity	Eyelid
Cytogenetics	*ALK* rearrangements	*EWSR1* rearrangements	Negative for *ALK* and *EWSR1*
Binucleate cells	Present	Absent	Present
Clinical behavior	Benign	Benign	No follow up

Summary

- **Epithelioid fibrous histiocytoma** is probably not just a variant of benign fibrous histiocytoma
  - Vast majority of EFHs have *ALK* rearrangements

- **Cutaneous syncytial myoepithelioma** is a relatively recently described entity
  - EWSR1 translocation is seen in most or all cases

References

- Doyle LA, Fletcher CD. EMA positivity in epithelioid fibrous histiocytoma: a potential diagnostic pitfall. *J Cutan Pathol*. 2011;**38**(9):697.
- Doyle L.A., Mariño-Enriquez A., Fletcher C.D., Hornick J.L. ALK rearrangement and overexpression in epithelioid fibrous histiocytoma. Mod. Pathol. 2015;28:904–912.
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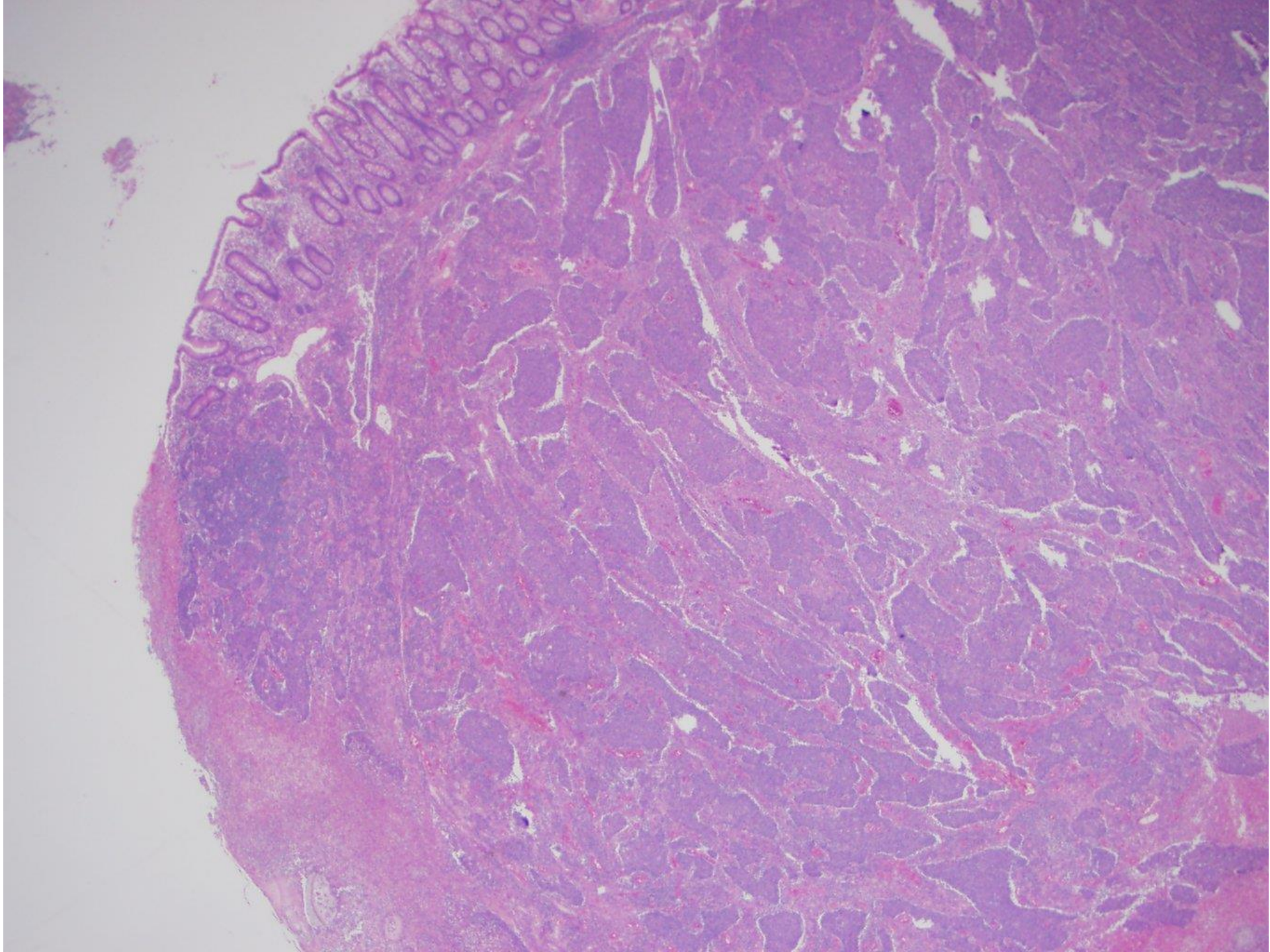
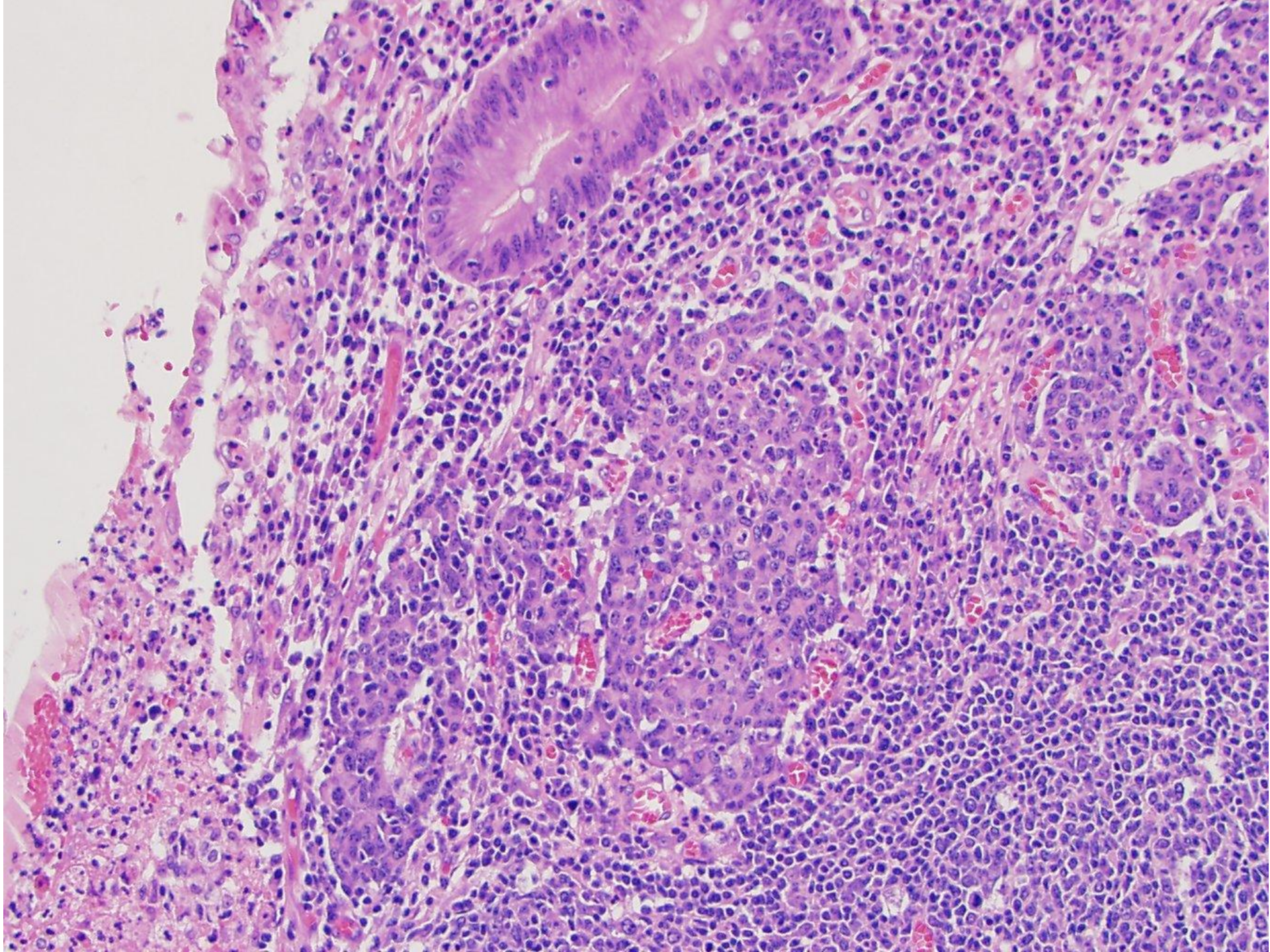
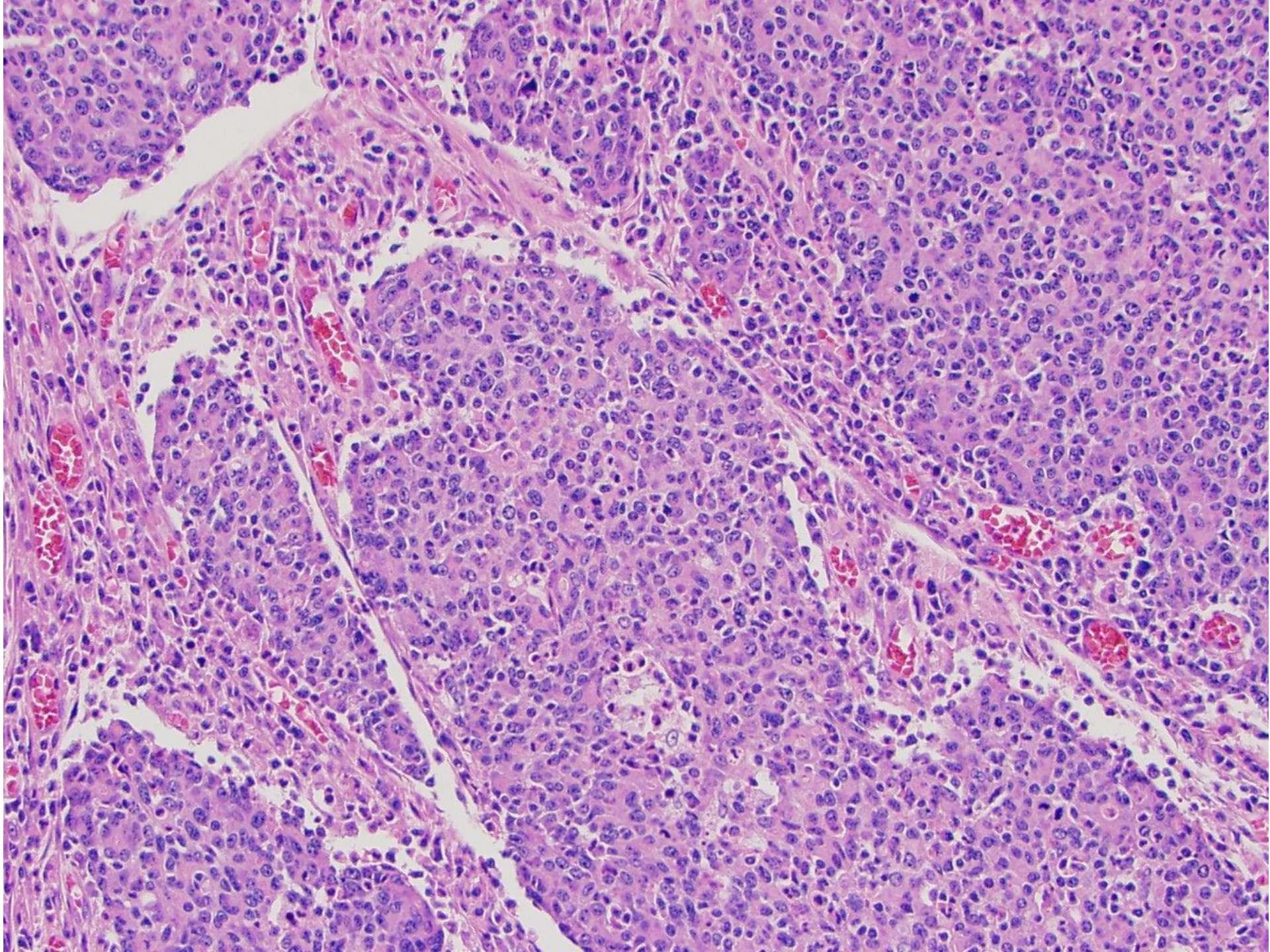
SB 6293

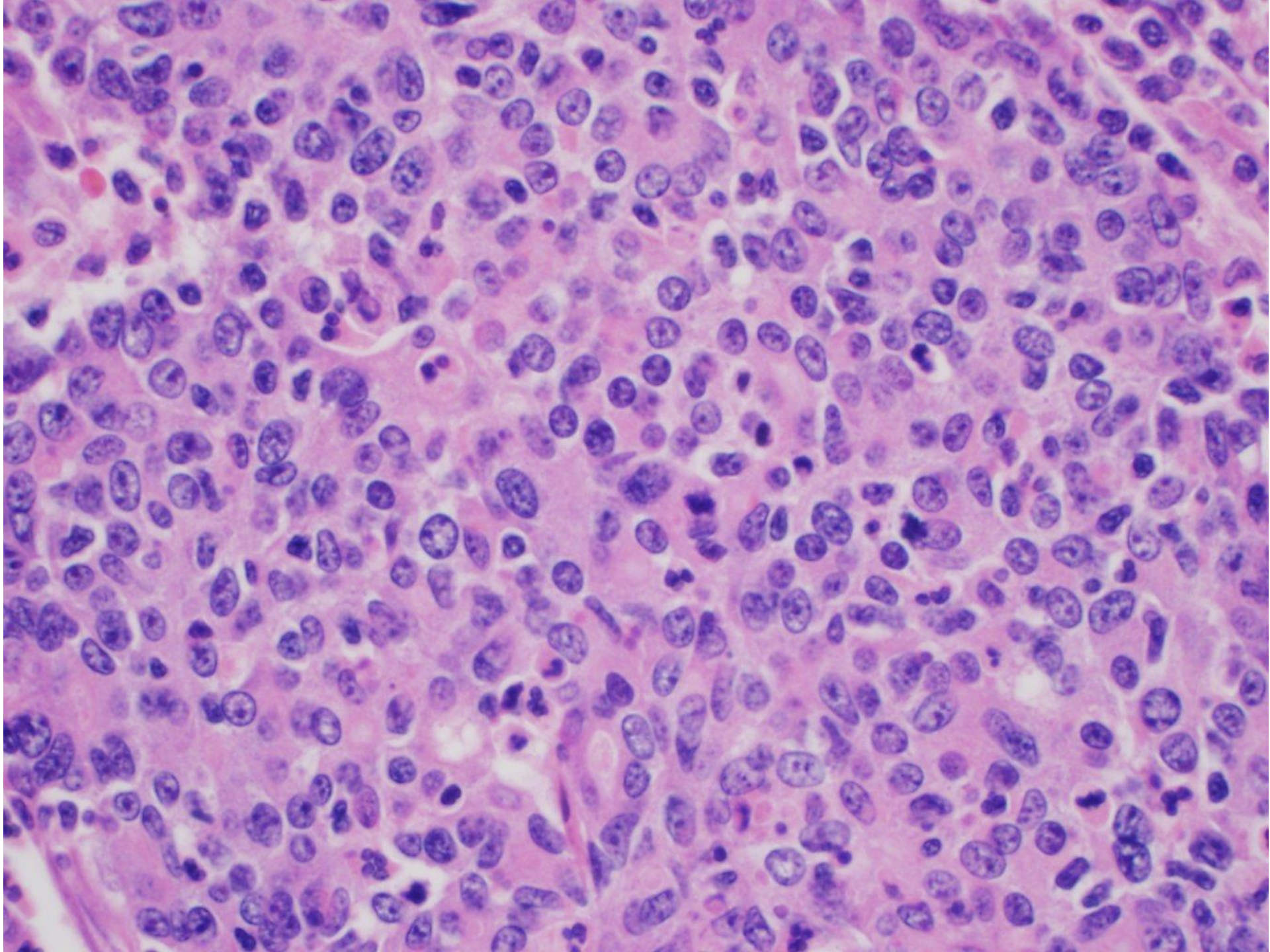
Greg Rumore; Kaiser Walnut Creek

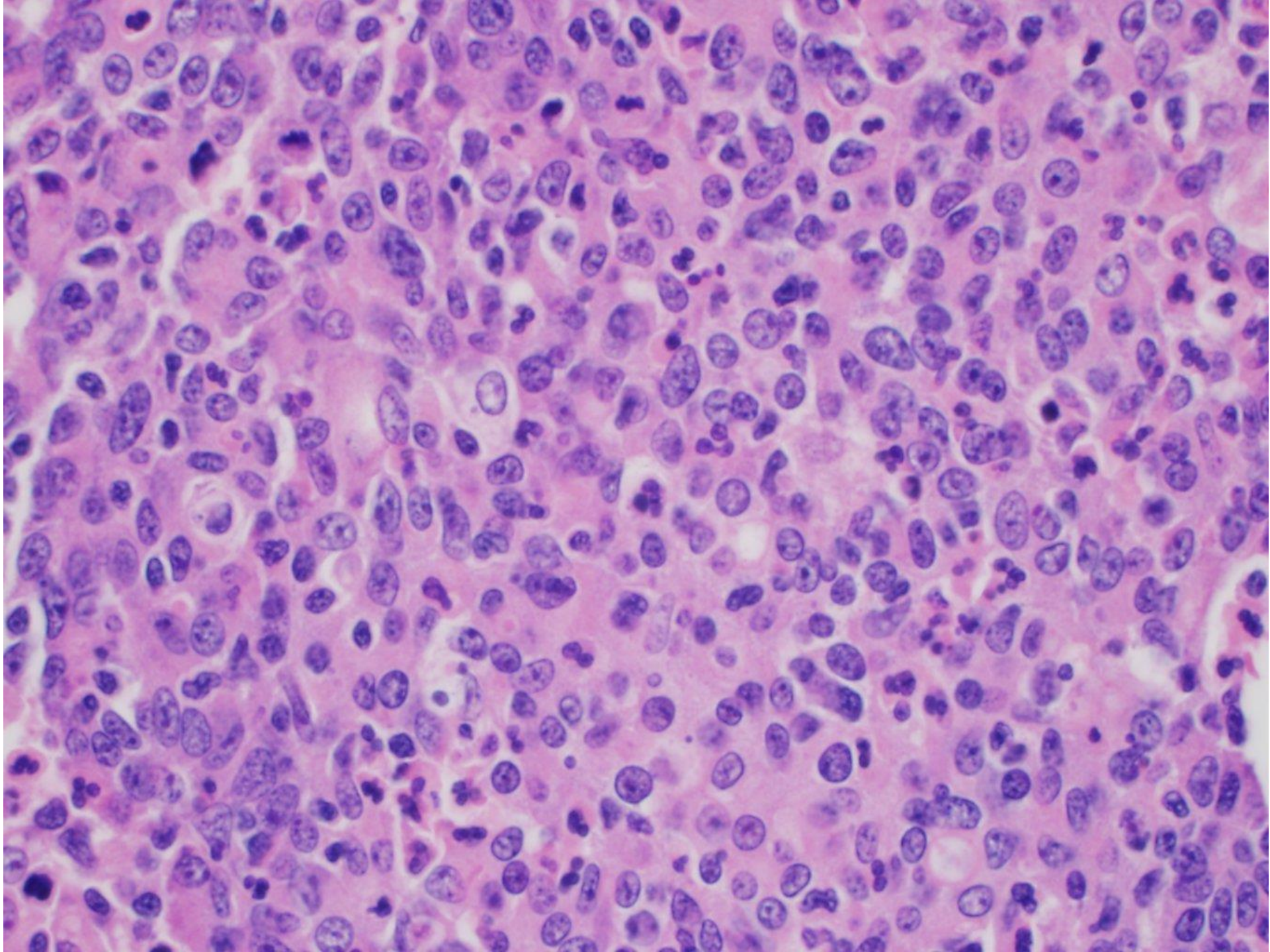
82-year-old woman with 8cm in ascending colon.

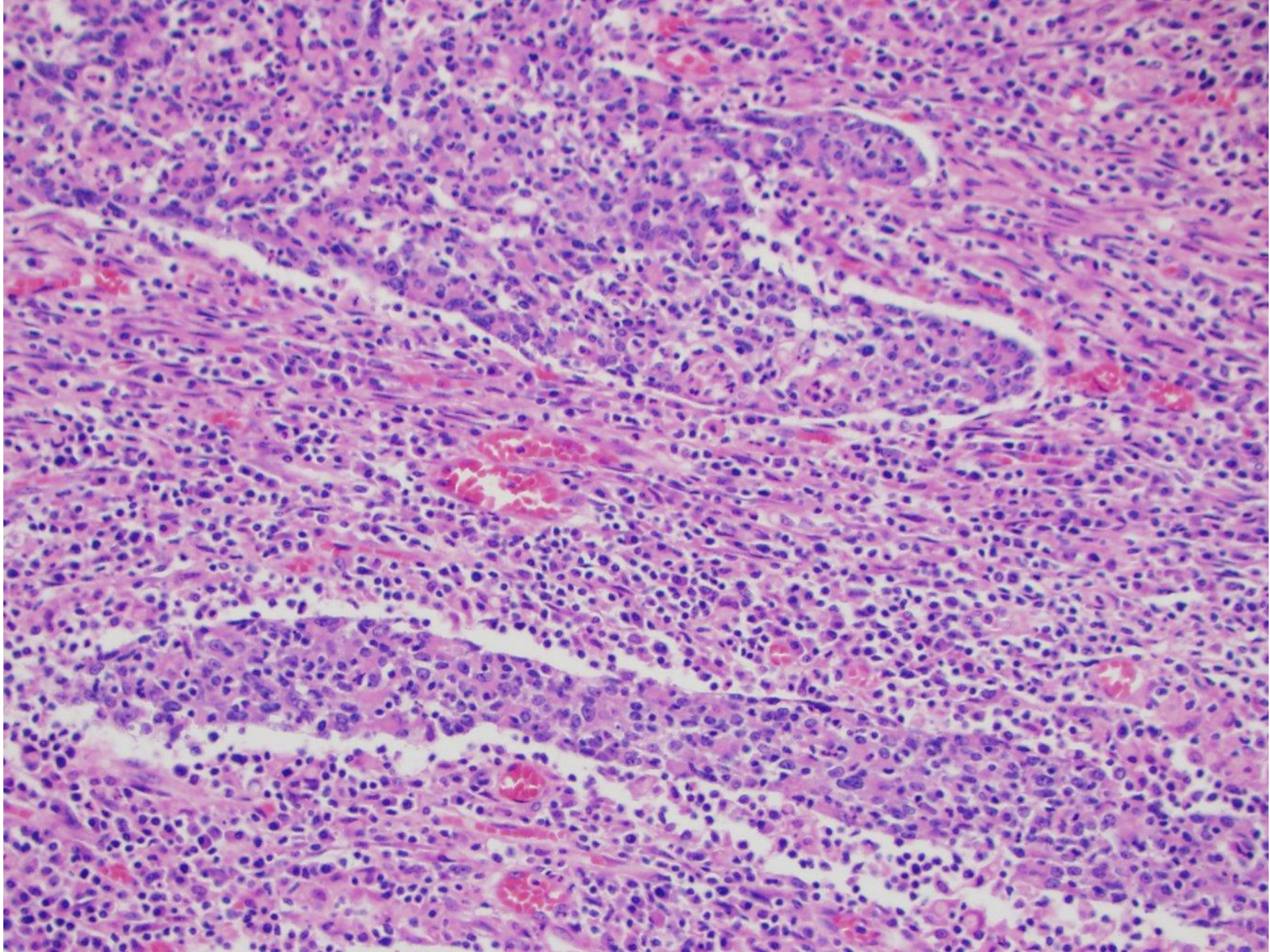




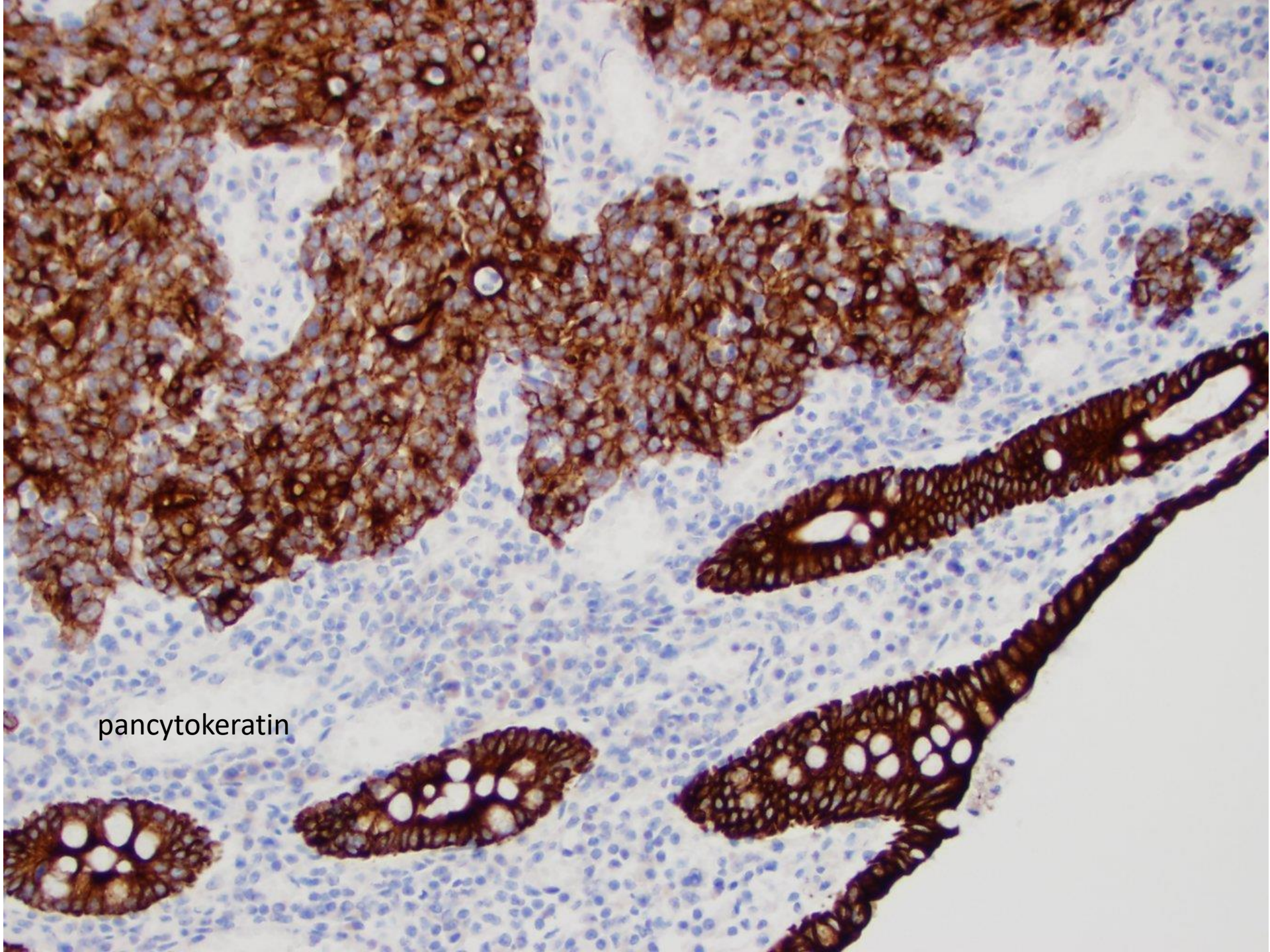


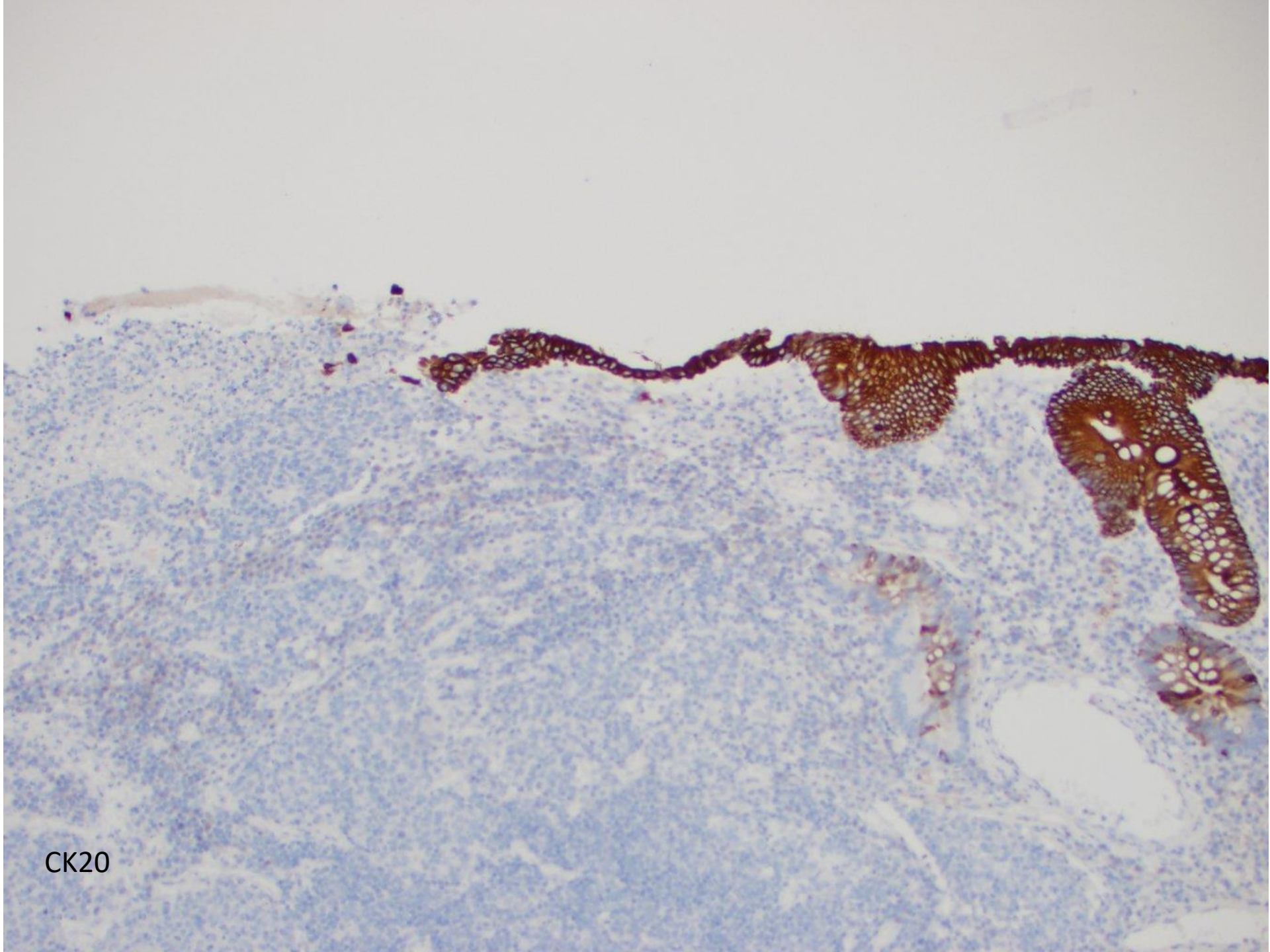






DIAGNOSIS?


pancytokeratin


CK20

Studies

- Pancytokeratin-positive
- CK7-negative
- CK20-negative
- CDX-2-focal weak positivity
- Synaptophysin-negative
- MLH1, PMS2-negative
- 66 negative lymph nodes

Medullary Carcinoma

- Solid sheets, nests and trabeculae, pushing border
- Uniform small to medium cells, vesicular nuclei, prominent nuclei
- High N/C ratio, scant-moderate cytoplasm
- Prominent lymphocytic infiltrate
- Frequently MSI unstable
- MLH1 negative (80-100%)

Medullary Carcinoma

- 70-100% right sided
- 50-100% female
- Better prognosis than poorly differentiated/ undifferentiated carcinoma
- Not graded

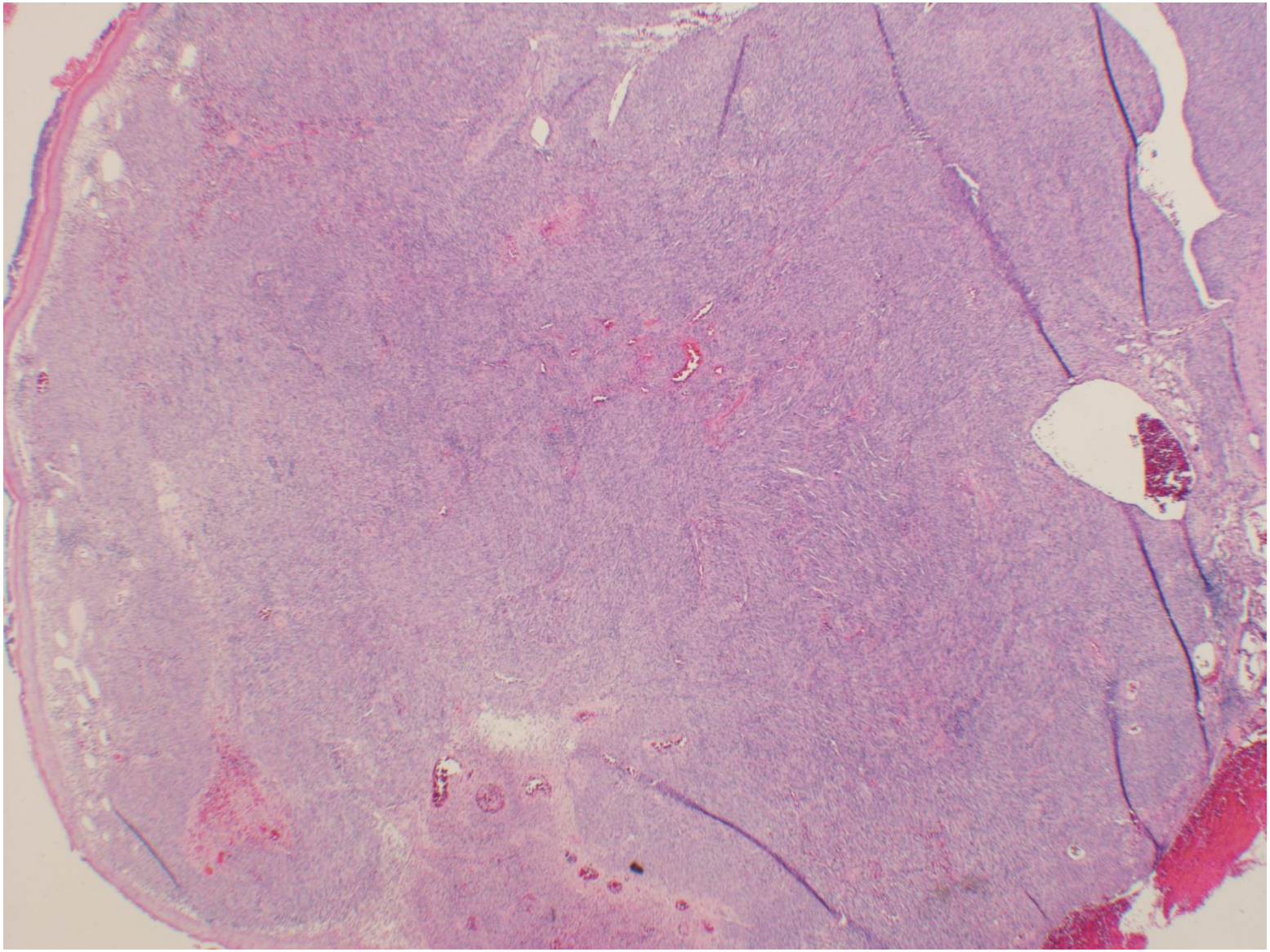
- Ref. Rouse, R., Stanford SurgPath Criteria

SB 6294

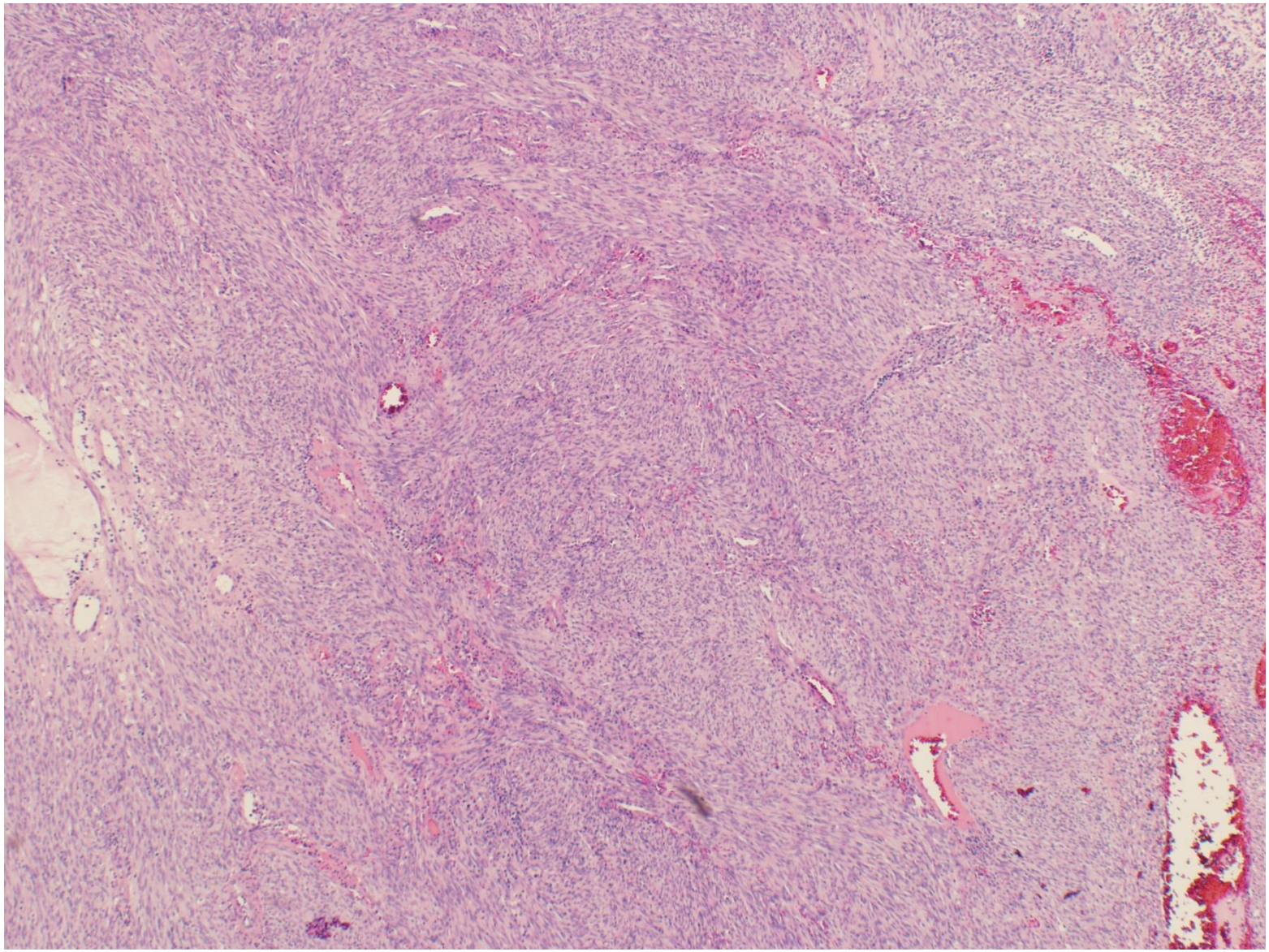
Daiva Mattis/Jeff Simko; UCSF

38-year-old man with 1cm verrucous exophytic right tonsil mass.

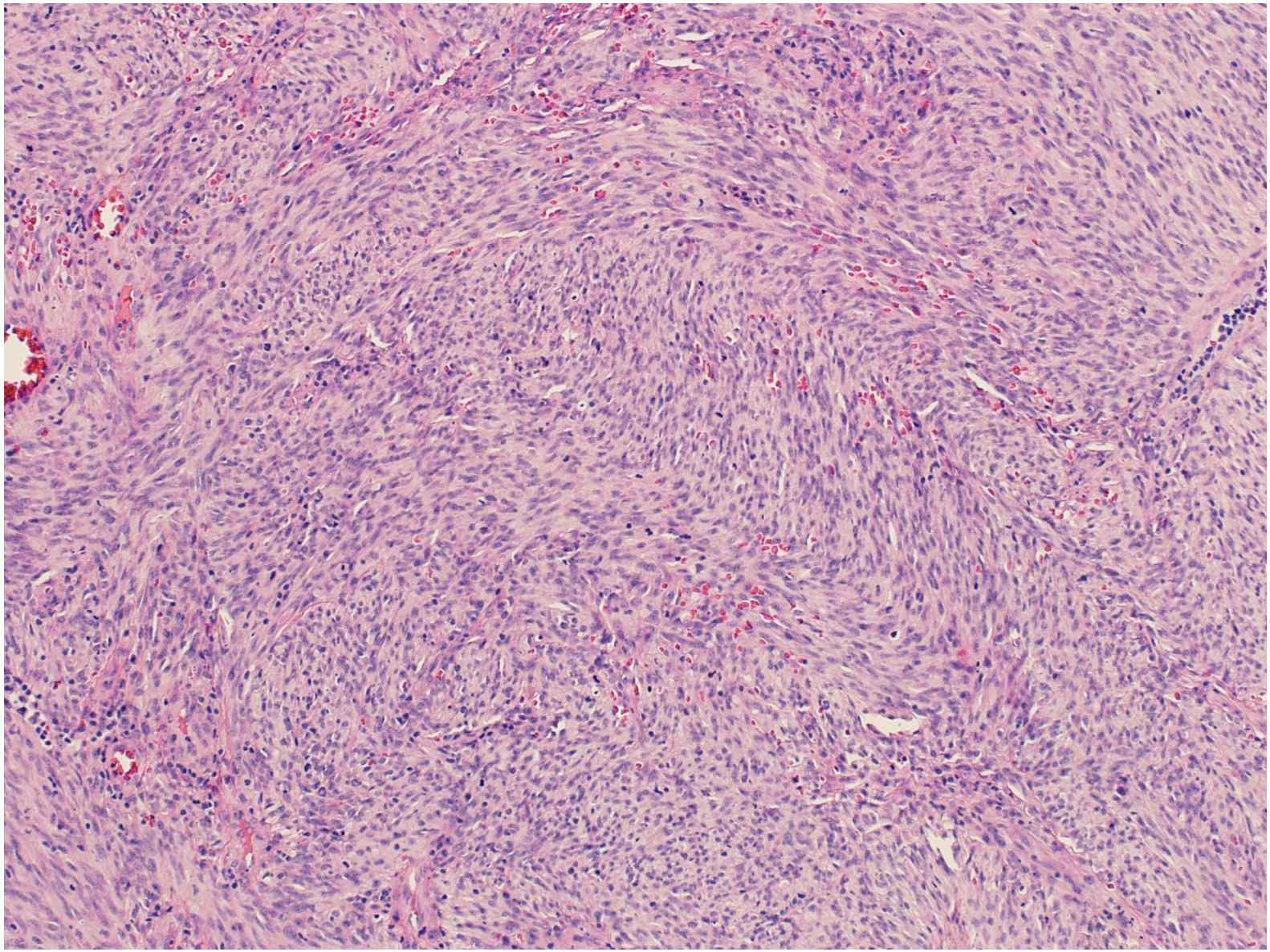
H&E Low Power



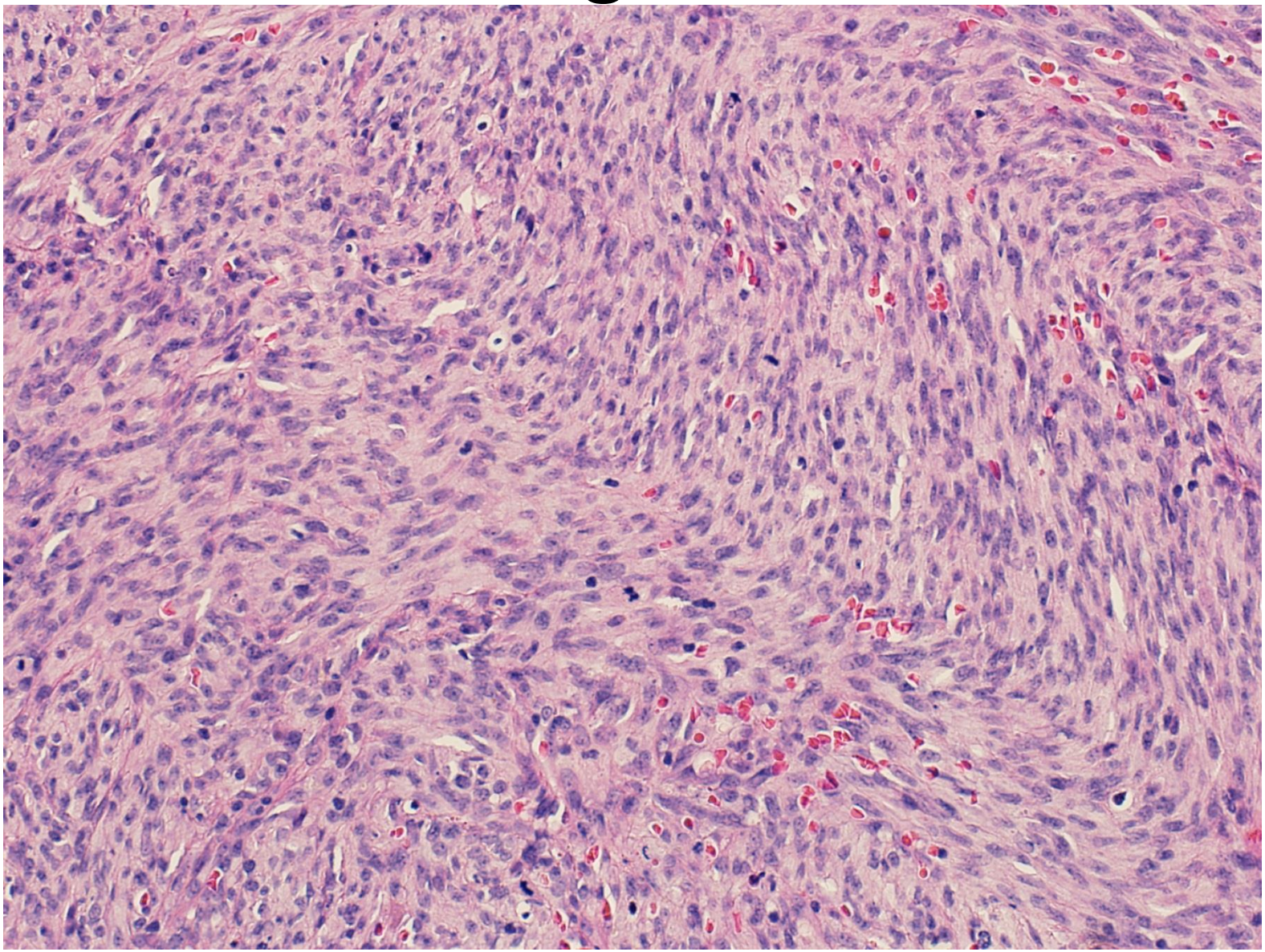
H&E Low Power



H&E Med Power



H&E High Power



DIAGNOSIS?

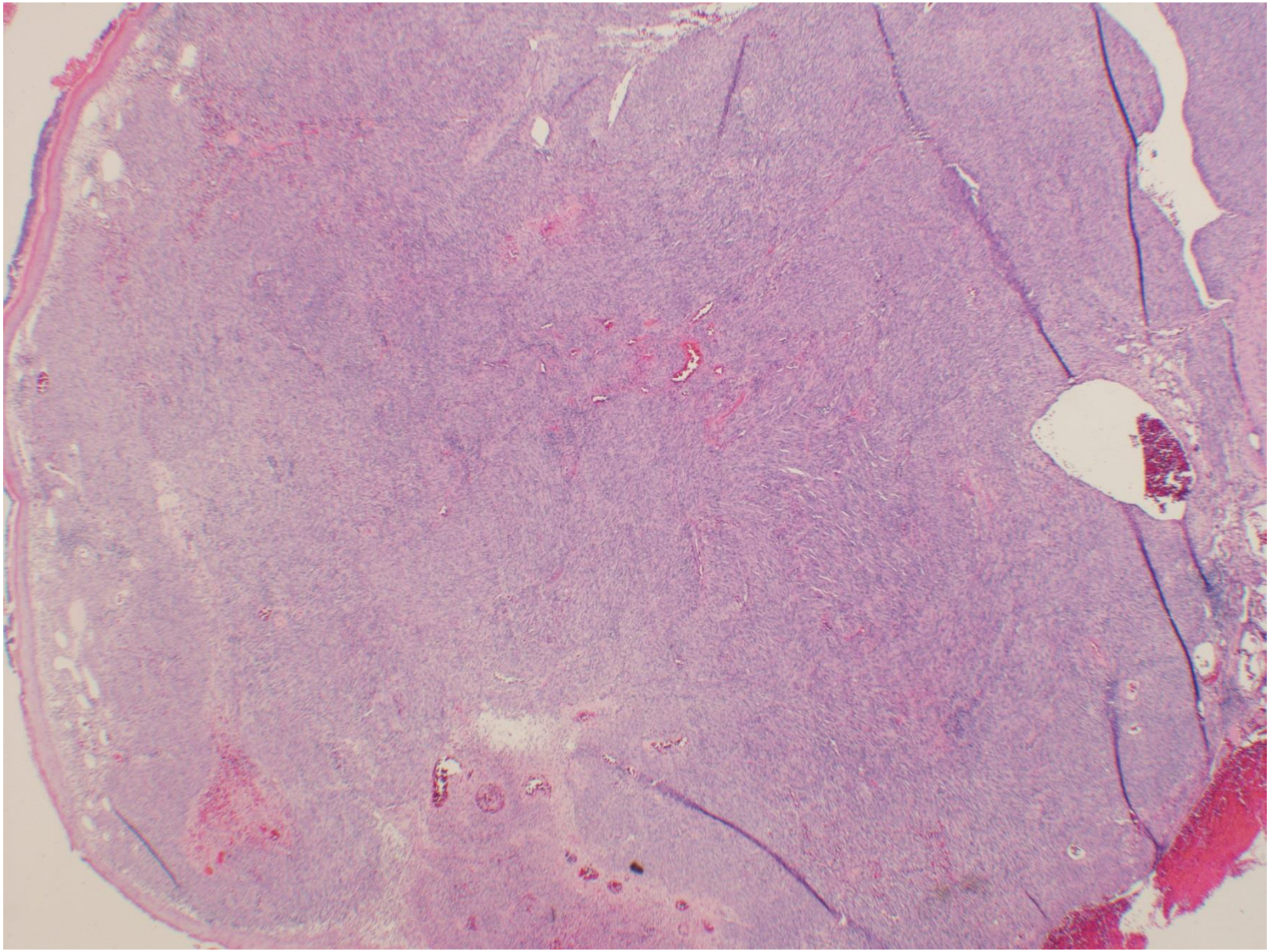
Clinical History

- **Presentation:** Foreign body sensation in right throat for approximately 1 month

- **Physical Exam:** “Papilloma” of right tonsil; large (no size in reports) exophytic “verrucous” lesion of the right tonsillar superior pole

- **Operative Note:**
  - **Procedure:** “Right tonsil mass excision”
  - **Specimen removed:** “Right tonsil biopsy”

H&E Low Power



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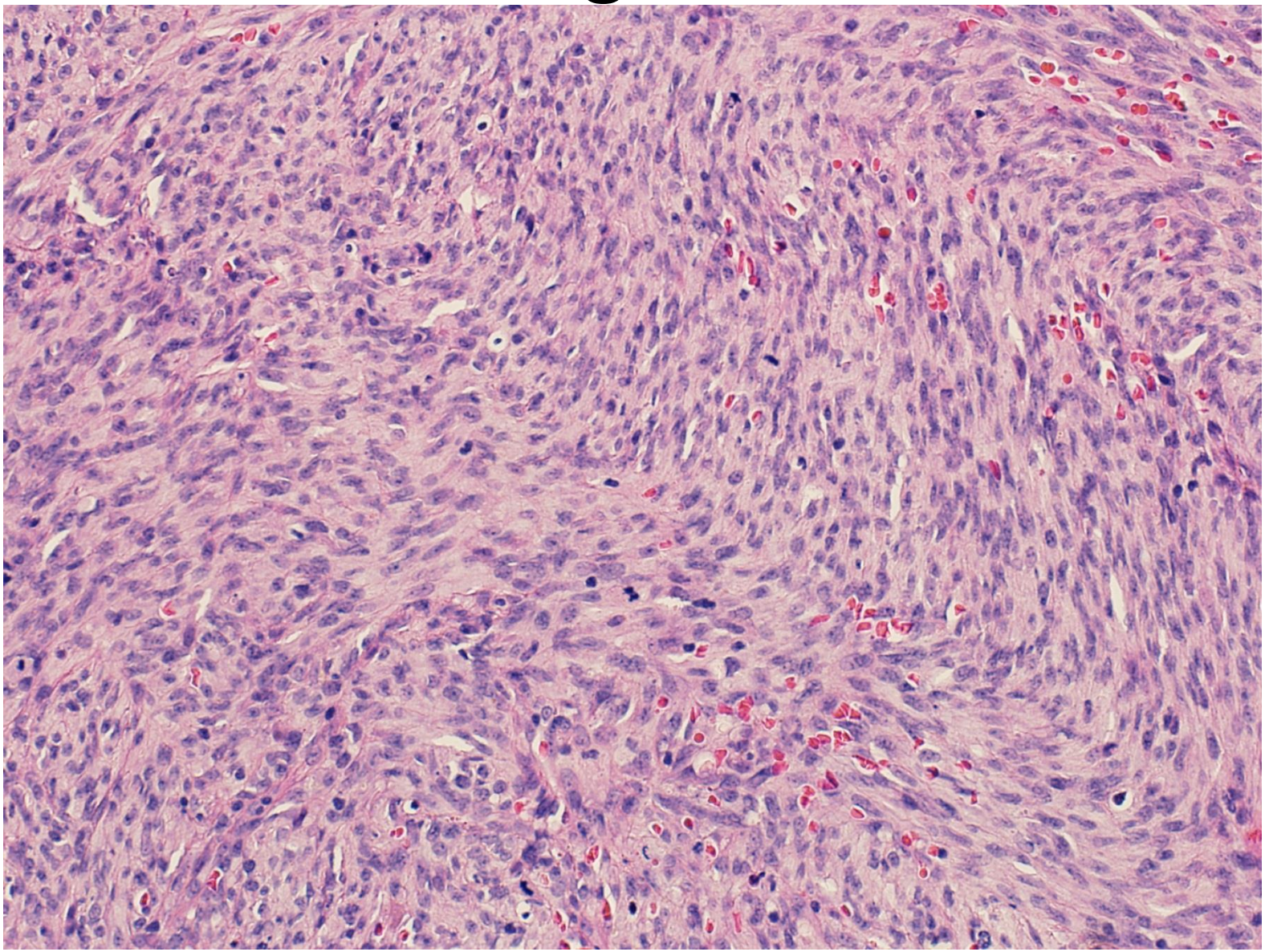


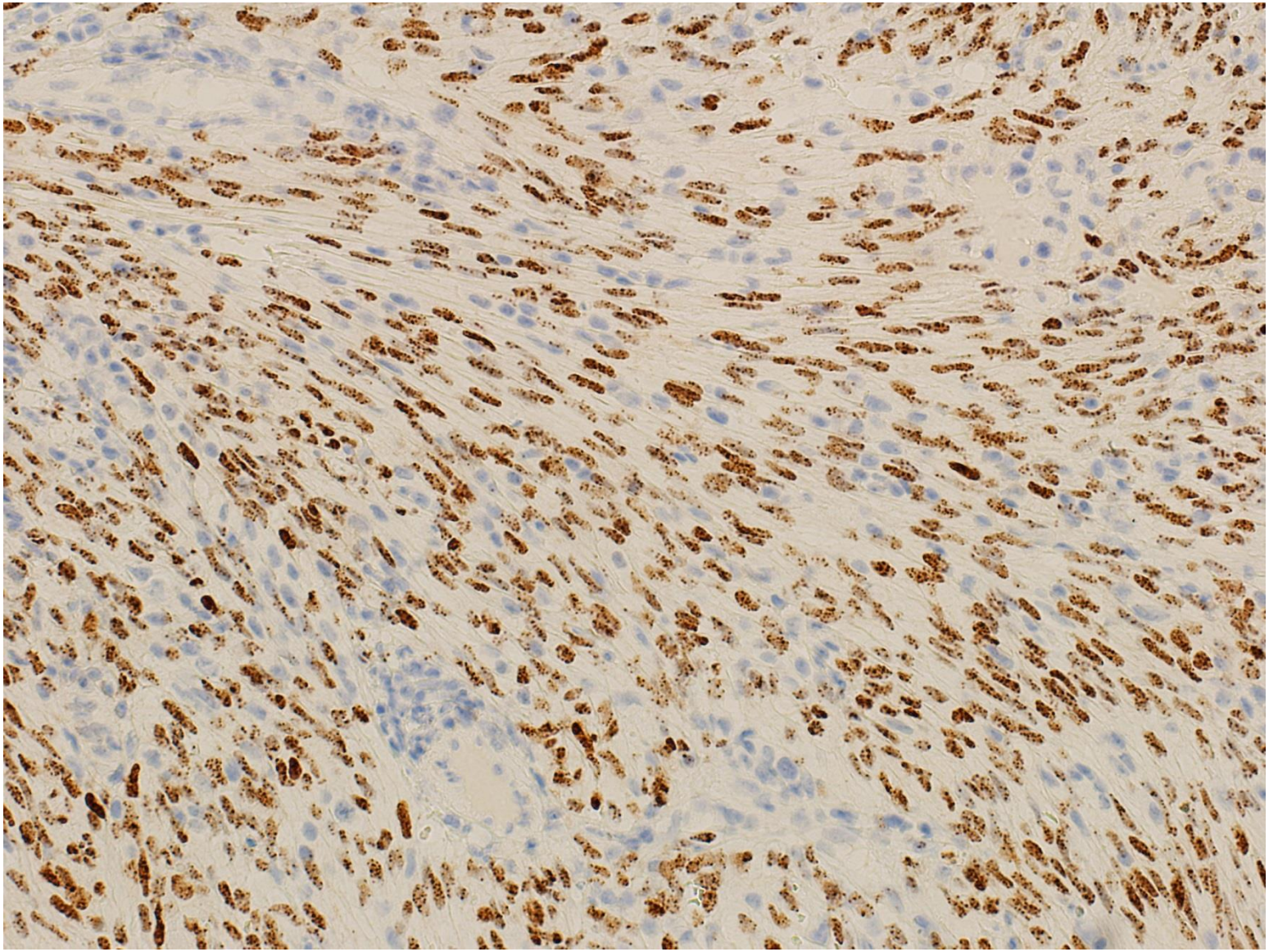
Differential Diagnosis:

- Kaposi Sarcoma
- Kaposi Sarcoma
- Kaposi Sarcoma
- Other spindle cell neoplasms
  - Sarcomatoid carcinoma
  - Spindle cell hemangioma
  - Angiosarcoma (with spindle cell morphology)
  - Haemangioendothelioma
  - Pyogenic granuloma

Verified Additional History

- Patient negative for HIV (4 repeated tests)
- History of HIV positive partner (without history of AIDS); patient taking prophylactic Truvada
- Normal CD4 count
- No history of immunosuppression

HHV8



Immunohistochemistry

- **Positive**:
  + HHV8
  + CD34
  + CD31
  + ERG
  + FLI-1
- **Negative**:
  – EBV in situ
  – CMV
  – S-100
  – MelanA
  – HMB45
  – Desmin
  – CD117
  – SMActin
  – STAT6

TABLE 1. VARIANTS OF KAPOSI'S SARCOMA.

VARIANT	RISK GROUP	MEDIAN SURVIVAL
Classic	Elderly men of Eastern European or Mediterranean origin	Years or decades
Endemic	African children and adults	Months or years
Immunosuppression-associated, or transplantation-associated	Organ-transplant recipients	Months or years
Epidemic, or AIDS-associated*	Persons infected with human immunodeficiency virus, especially homosexual or bisexual men	Weeks or months

*AIDS denotes acquired immunodeficiency syndrome.

* None of these variants fit the patient

N Engl J Med 2000; 342:1027-1038

- Diagnosis remained:

  Kaposi's sarcoma, nodular type

  – LONG comment with discussion

- Example of the diagnosis not fitting the usual clinical history

HHV8

- HHV8 is associated with neoplastic diseases
  - Kaposi's sarcoma
  - Multicentric Castleman disease
  - Primary effusion lymphoma
- Greater than 95% of KS lesions contain HHV8 viral DNA
- Horizontal transmission of HHV8 by saliva is the most common route

Cases of HIV-negative MSM KS without other risk factors

Table 2 Reports of nonepidemic Kaposi sarcoma in the literature

Authors (year)	Number of patients, age(s), location of KS
Marquart et al. (1986)	*N* = 1, 44, penis
Garcia-Muret et al. (1990)	*N* = 1, 42, disseminated: cutaneous and GI tract
Friedman-Kien et al. (1990)	*N* = 6, 32–62 (mean age 45), lower extremity and penis
Kua et al. (2004)	*N* = 1, 52, buccal mucosa
Lanternier et al. (2008)	*N* = 28, 35–83 (mean age 55), face, trunk, upper extremity, genitalia, lower extremity, genitalia
Potthoff et al. (2010)	*N* = 1, 53, trunk, lower extremity
Rashidgamat et al. (2014)	*N* = 8, 36–65 (mean age 53), upper extremity, lower extremity, penis
Hinojosa et al. (2017)	*N* = 1, 55, face, lower extremity

Reference: Vangipuram R, Tyring SK. Epidemiology of Kaposi sarcoma: review and description of the nonepidemic variant. Int J Dermatol. 2018 Jun 11.

- At least 61 cases reported:
  - Largest series with 28 patients (Lanternier F, et al. Kaposi's sarcoma in HIV-negative men having sex with men. AIDS. 2008 Jun 19;22(10):1163-8).
  - Clinically resembles classic KS, but often occurs in younger patients
  - Same treatment as classic KS; with excision and/or radiation curative

TABLE 1. VARIANTS OF KAPOSI'S SARCOMA.

VARIANT	RISK GROUP	MEDIAN SURVIVAL
Classic	Elderly men of Eastern European or Mediterranean origin	Years or decades
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Immunosuppression-associated, or transplantation-associated	Organ-transplant recipients	Months or years
Epidemic, or AIDS-associated*	Persons infected with human immunodeficiency virus, especially homosexual or bisexual men	Weeks or months

*AIDS denotes acquired immunodeficiency syndrome.

HIV-negative MSM (Nonepidemic KS): No cellular or humoral immunodeficiency, often younger, MSM, good prognosis (curative) with excision and/or radiation treatment

N Engl J Med 2000; 342:1027-1038

Patient Follow-up

- Patient seen 1 month after procedure
- Physical exam showed no additional growth
- No additional excision or radiation therapy
- Patient followed

Conclusions

- HIV-negative MSM without signs of cellular or humoral immunodeficiency is an epidemiologic form of Kaposi's Sarcoma to consider in a differential diagnosis
- Can occur in younger patients

- **Recommendation:** If classic histology with unusual clinical history, consider this epidemiologic form

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3. Francesca Pica and Antonio Volpi. Transmission of human herpesvirus 8: an update. Curr Opin Infect Dis 2007, 20:152-156.

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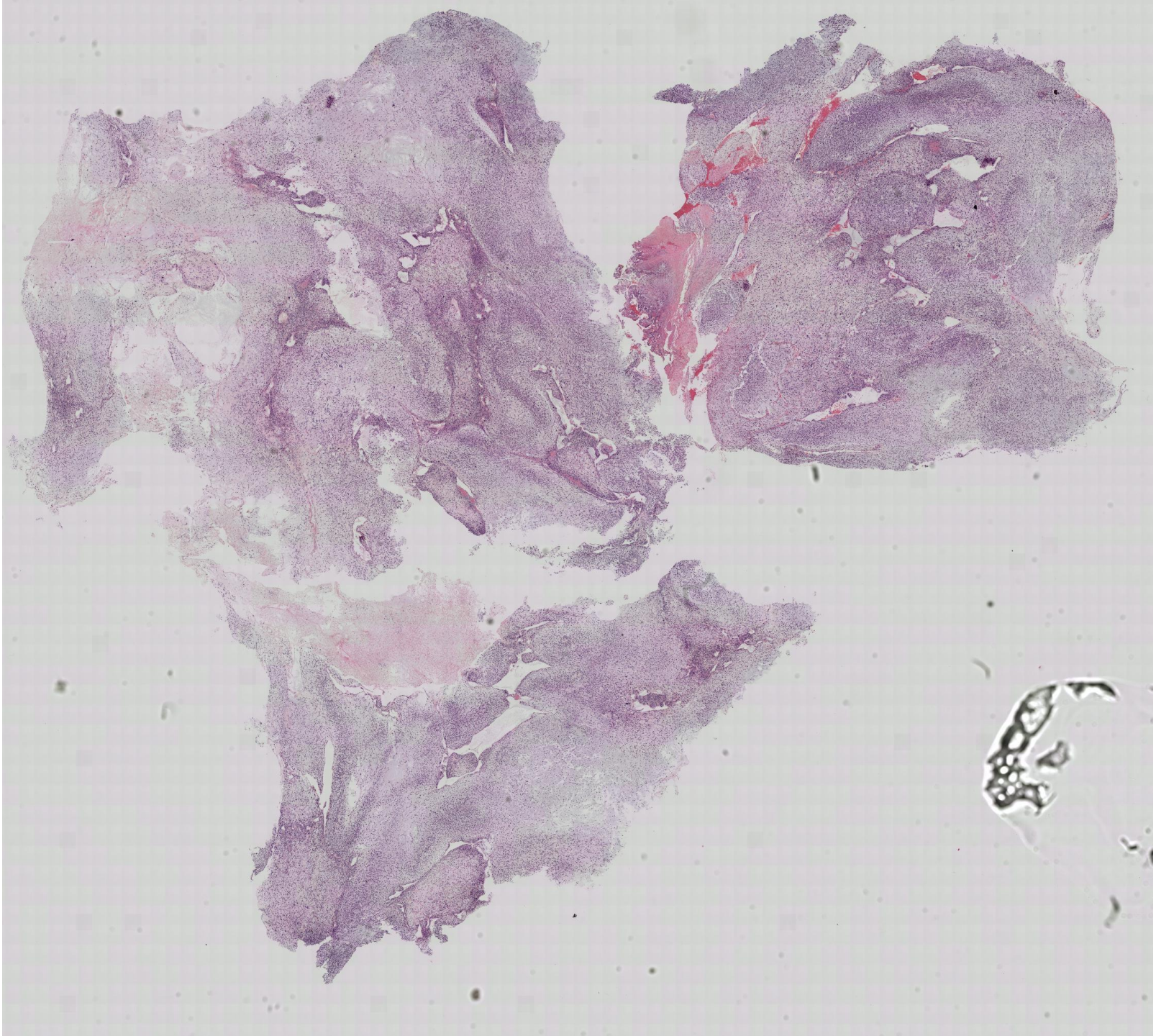
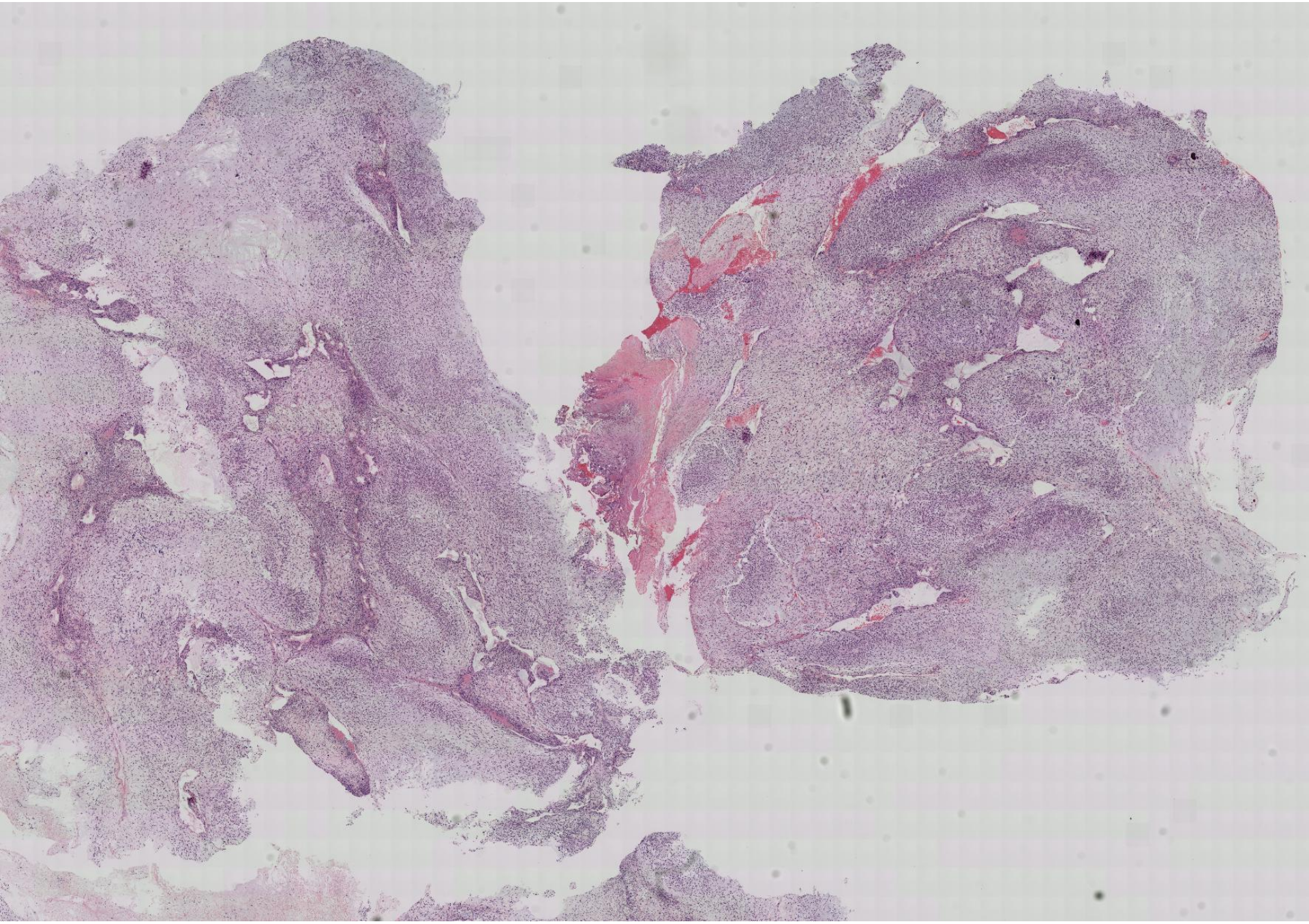
8. Yenice MG, Varnalı E, Şeker KG, Kavak A, Tuğcu V. Scrotal Kaposi's Sarcoma in HIV-negative patient: A case report and review of the literature. Turk J Urol. 2018 Mar;44(2):182-184. doi: 10.5152/tud.2017.68366. Epub 2017 Dec 11.

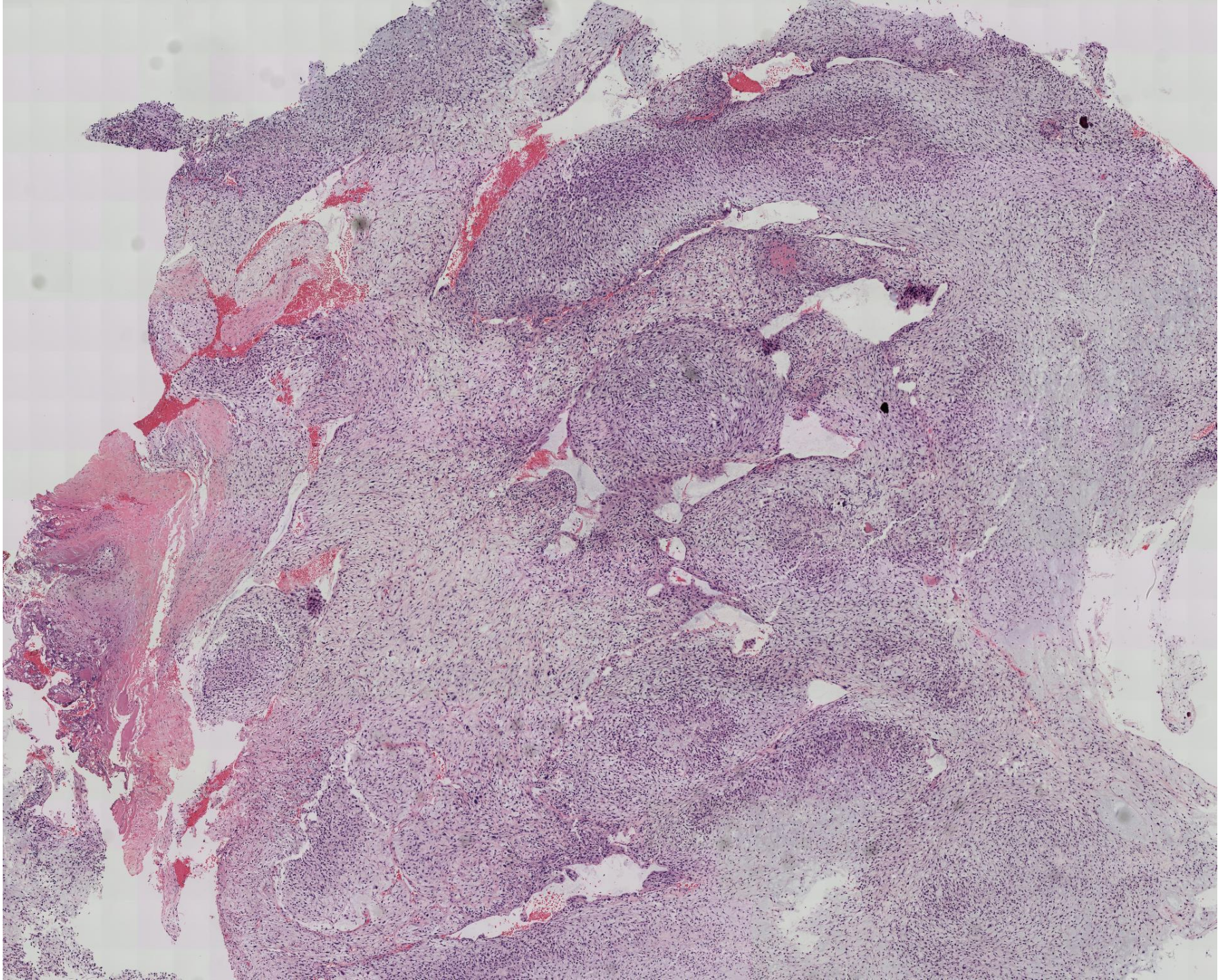
SB 6295
(scanned slide available)

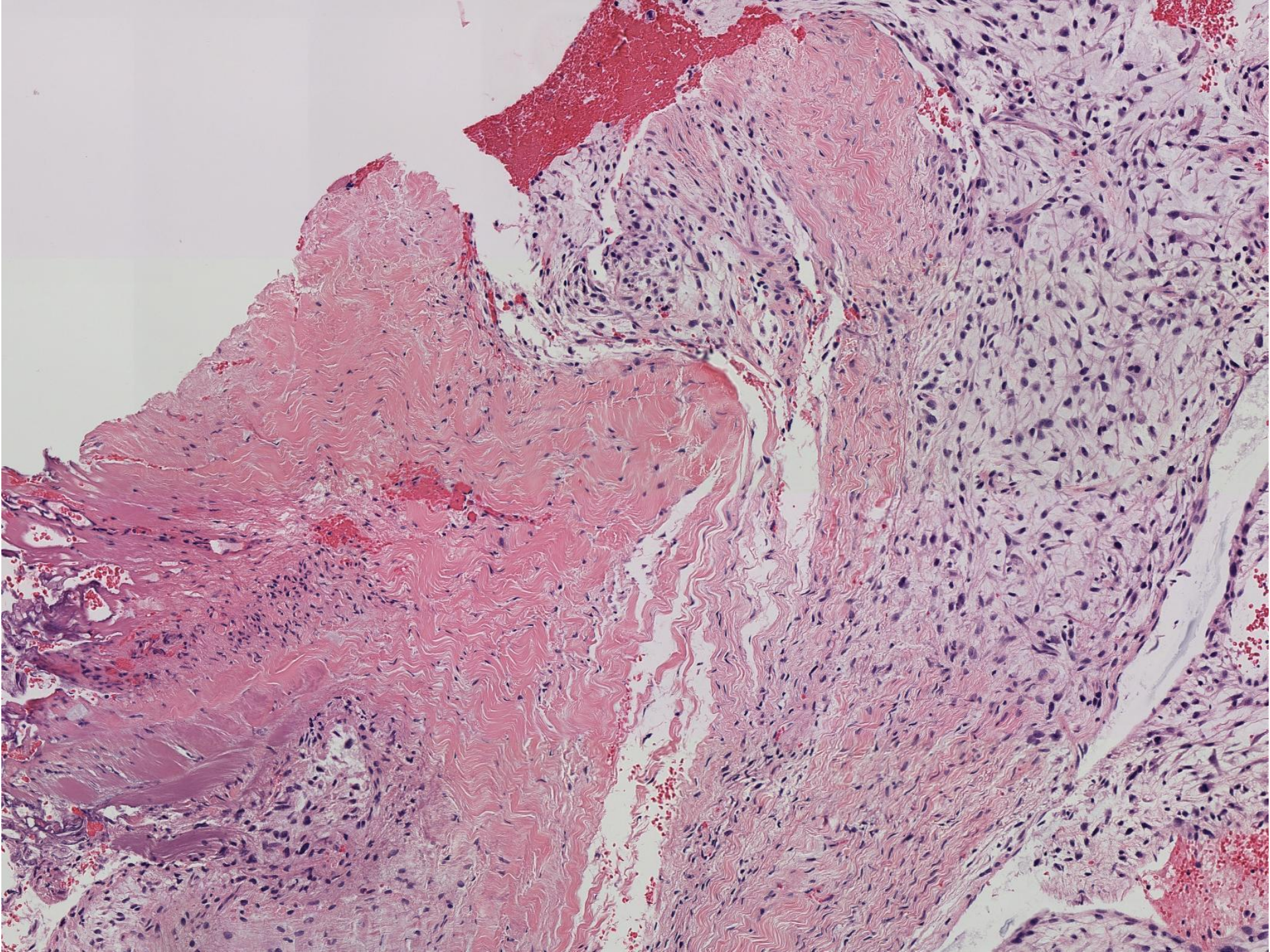
Keith Duncan; Mills Peninsula

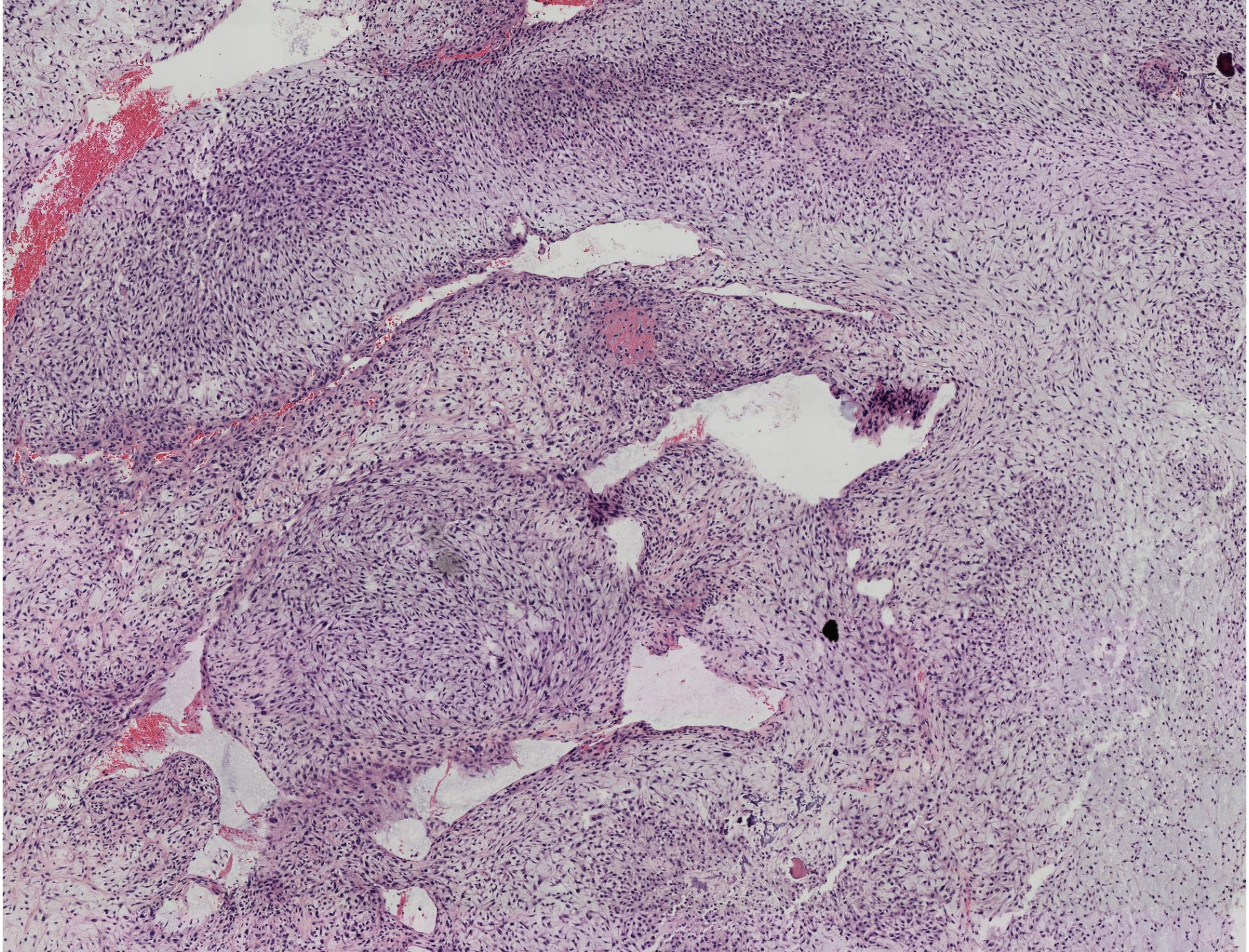
19-year-old man with right lower leg mass. PET scan: hypermetabolic focus right proximal tibia diaphysis extending into soft tissue. Excisional biopsy of soft tissue mass submitted.

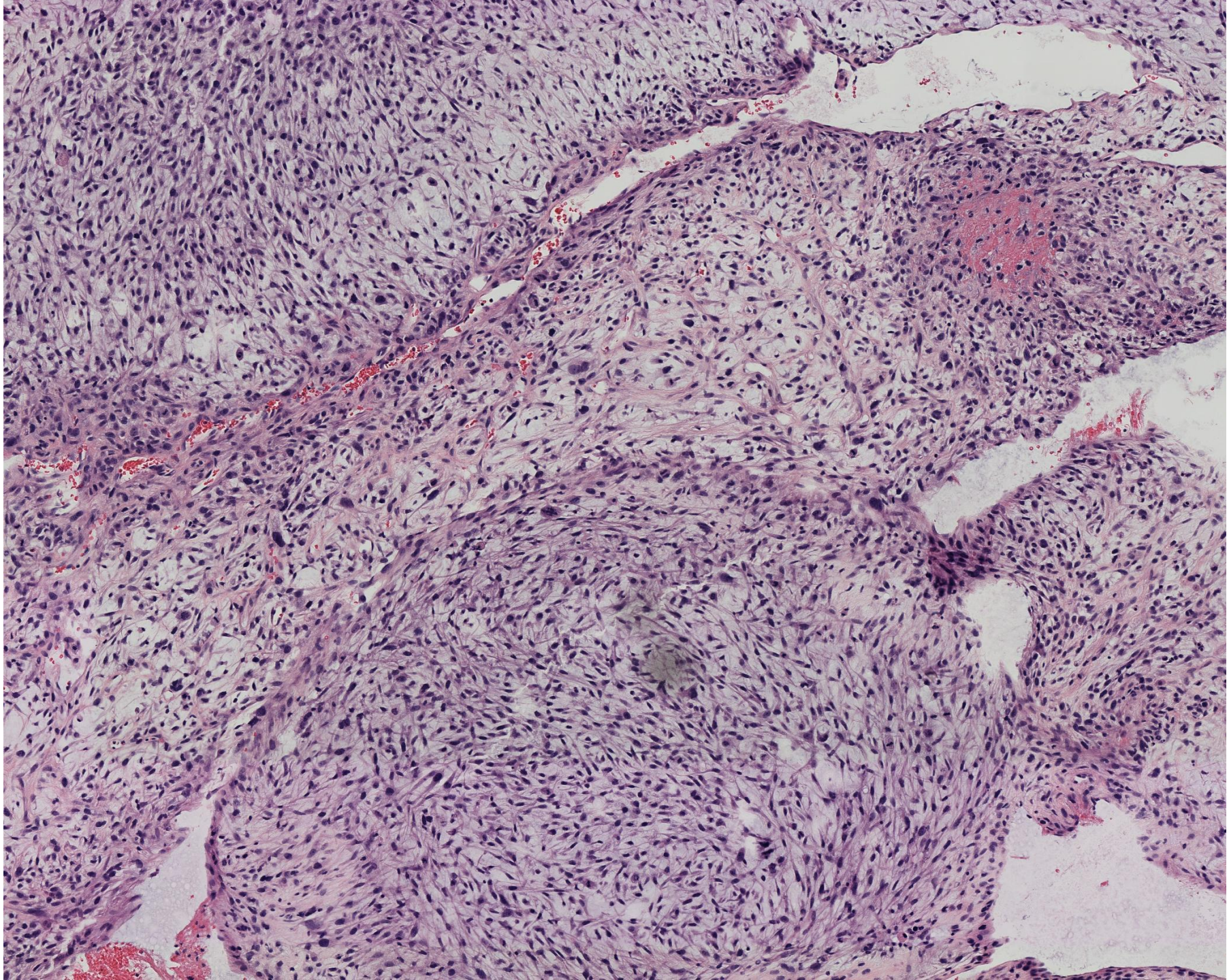


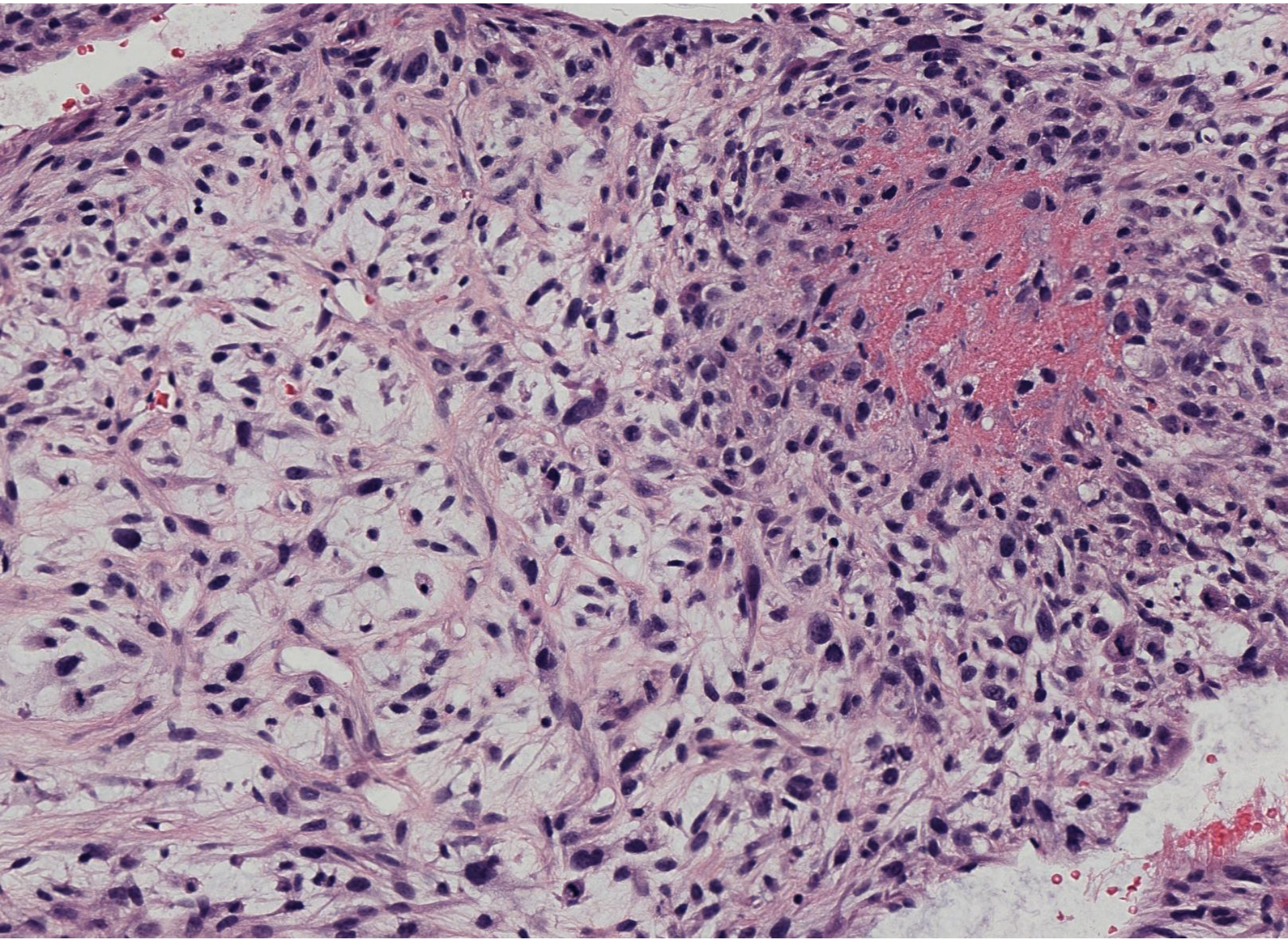


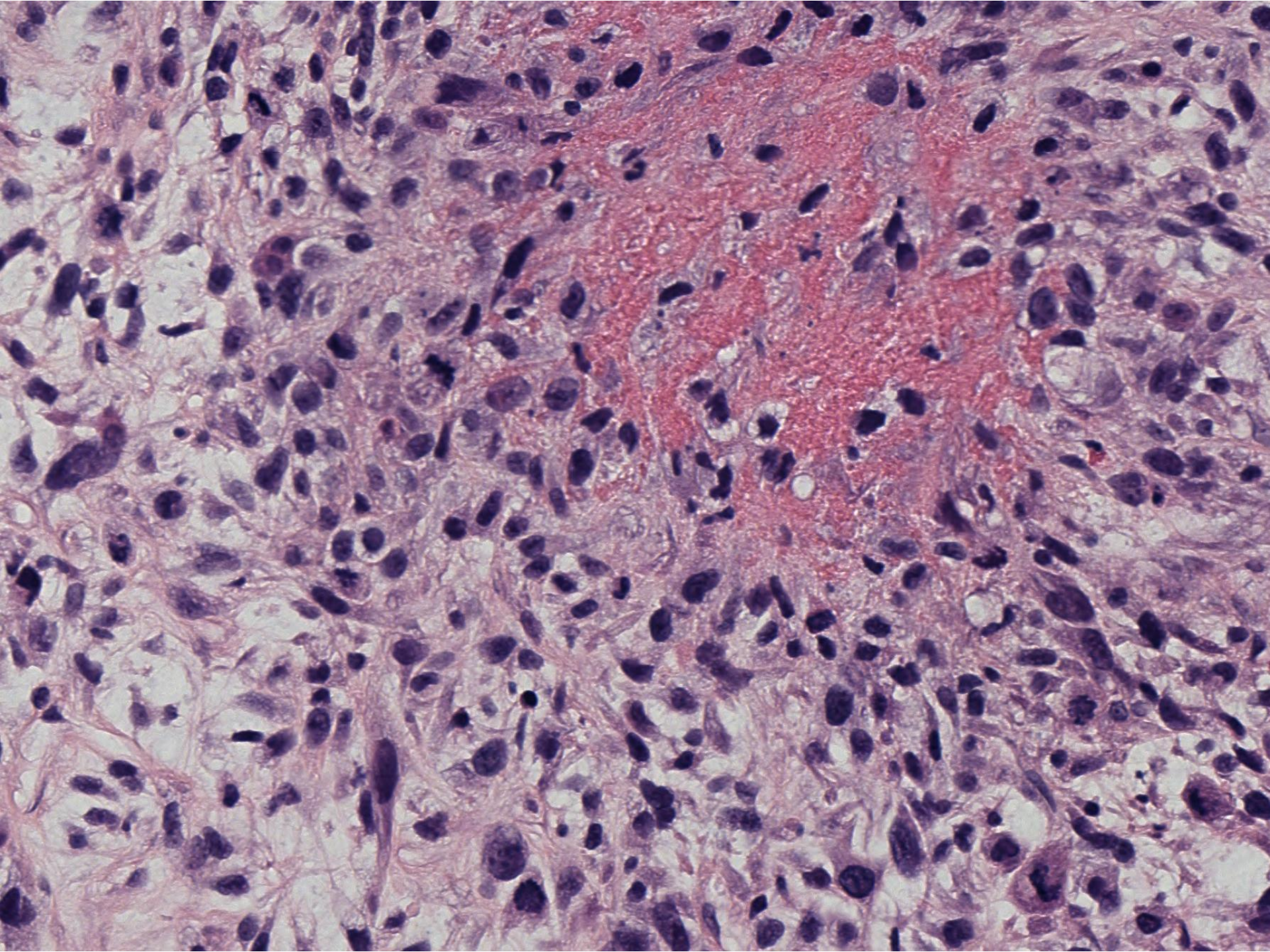












DIAGNOSIS?

MRI Impression:
5 x 10 cm aggressive appearing solid enhancing mass in the proximal tibial diaphyseal shaft with large lobulated soft tissue component, irregular permeative lysis of the tibial cortex, and mild surrounding muscle inflammation.

Differential considerations:
malignant primary bone neoplasms including Ewing sarcoma, osteosarcoma, or lymphoma.

XRAY: Subtle hazy sclerosis in the proximal right tibial diaphysis with subtle periosteal reaction

OUTSIDE OPINIONS

- DR. ANDREW VOLPE MAYO
- OSTEOSARCOMA, HIGH GRADE APPARENTLY ARISING IN TIBIA WITH 2ND SOFT TISSUE EXTENSION
- IPOX STAINS: PANCYTOKERATIN, S-100, SMA, DESMIN NEGATIVE
- LEVEL SECTIONS AT MAYO REVEALED SMALL AREAS OF CALFICIED MATRIX PRODUCTION “ESSENTIALLY DIAGNOSTIC OF OSTEOSARCOMA IN THIS CLINICAL CONTEXT”.
- He shared radiographs with his orthopedic radiologists who agreed

Stanford bottom line: High grade sarcoma

- Did not see definite osteoid in slides we provided-
- Pattern of myxoid matrix & curvilinear vessels with necrosis reminiscent of high grade myxofibrosarcoma
- They acknowledged Mayo report of osteoid and agreed that radiographic findings and patient age support dx of osteosarcoma

•Most common primary bone tumor after myeloma

•60% male; usually ages 10 - 25 years or ages 40+ with other diseases

•Associated with Paget disease, post-radiation exposure, Thorotrast administration, chemotherapy in children, fibrous dysplasia, osteochondromatosis, chondromatosis

•Not associated with trauma, although trauma may lead to discovery

•**Sites:** metaphysis of long bones (distal femur, proximal tibia, proximal humerus); occasionally diaphysis

Postradiation: 10-15 years after 40-60 Gy exposure
•**Sites of metastasis:** lung ,other bones, pleura, heart

OSTEOSARCOMA Microscopic description

- High grade spindle cell tumor that produces osteoid matrix **unconnected by cartilage**
- **Tumor cells produce neoplastic bone - basophilic thin trabeculae** of neoplastic bone resembling neoplastic osteoid - eosinophilic, homogenous, glassy with irregular contours & osteoblastic rimming
- May have ***osteoblastic***, ***fibroblastic*** or ***chondroblastic predominance***
- Osteoid may be variable in amount
- With bizarre giant cells in stroma or acellular stroma
- Vessels may have hemangiopericytoma-like features
- Cartilage may be mineralized, immature, myxoid

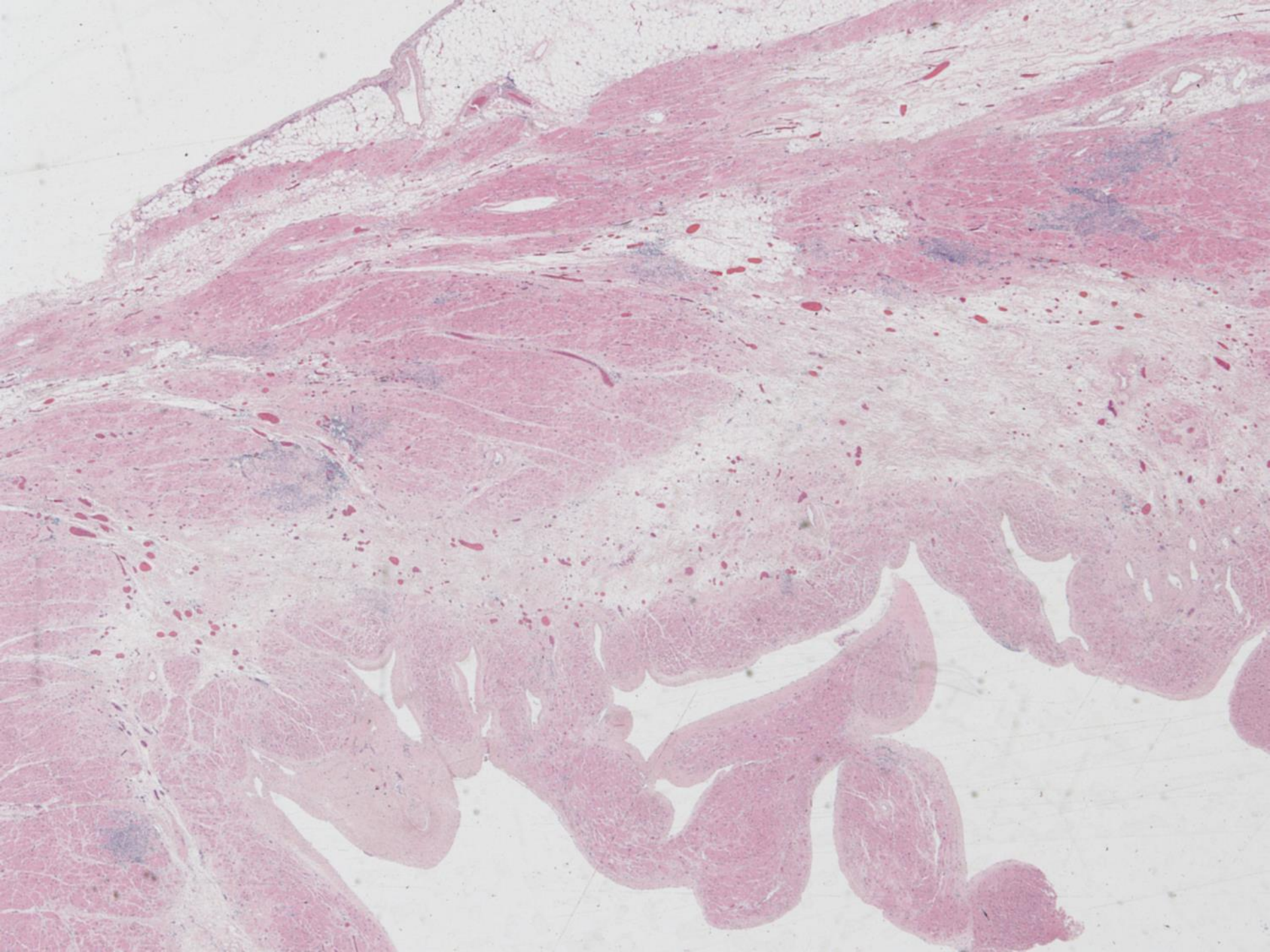
LAST FOLLOW UP AT STANFORD 6/2016

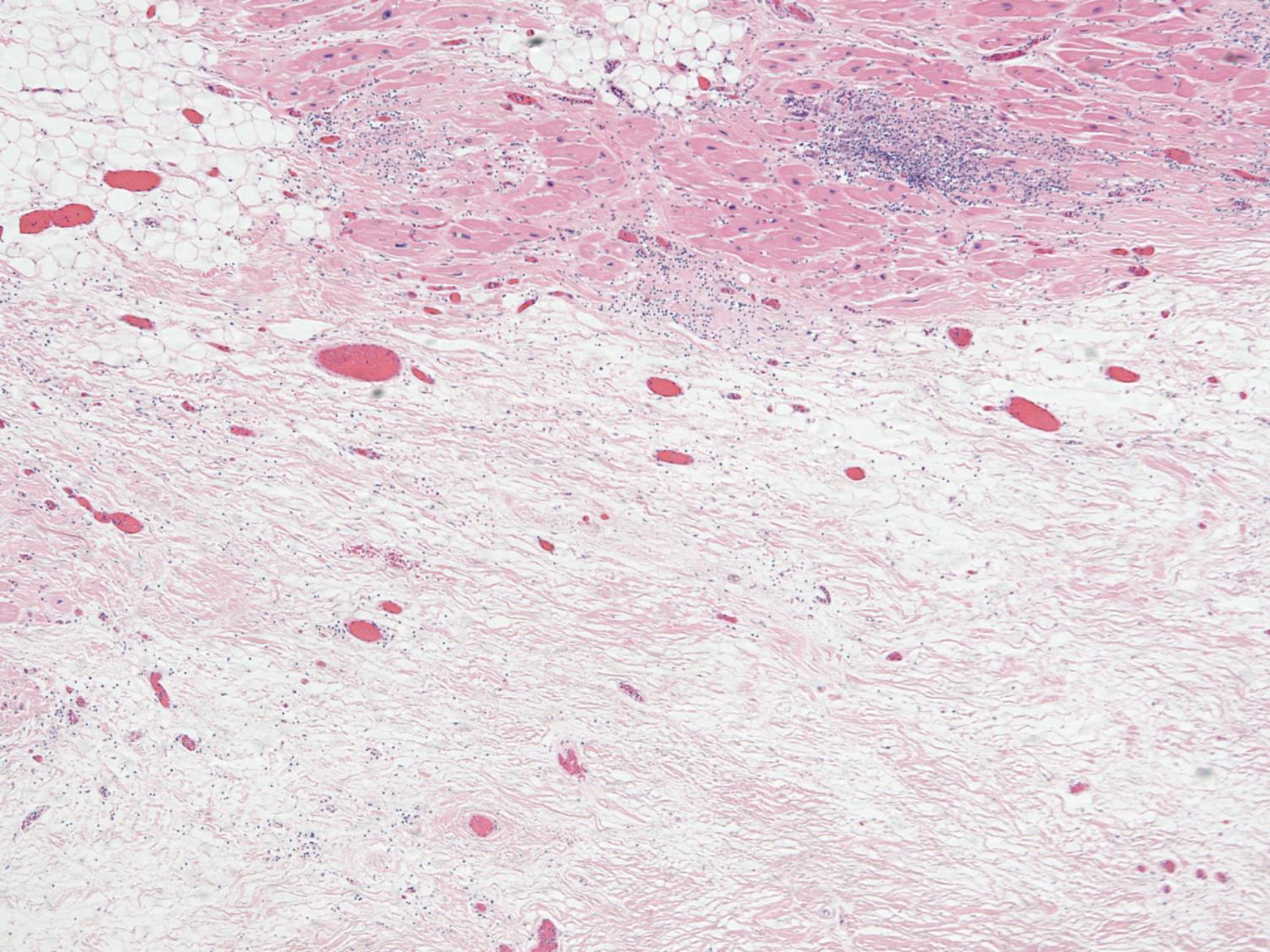
- Non-metastatic osteosarcoma right proximal tibia -completed chemotx and then underwent limb salvage sx with allograft.
- Did well post tx but allograft has not healed and he remains on crutches with no weight bearing

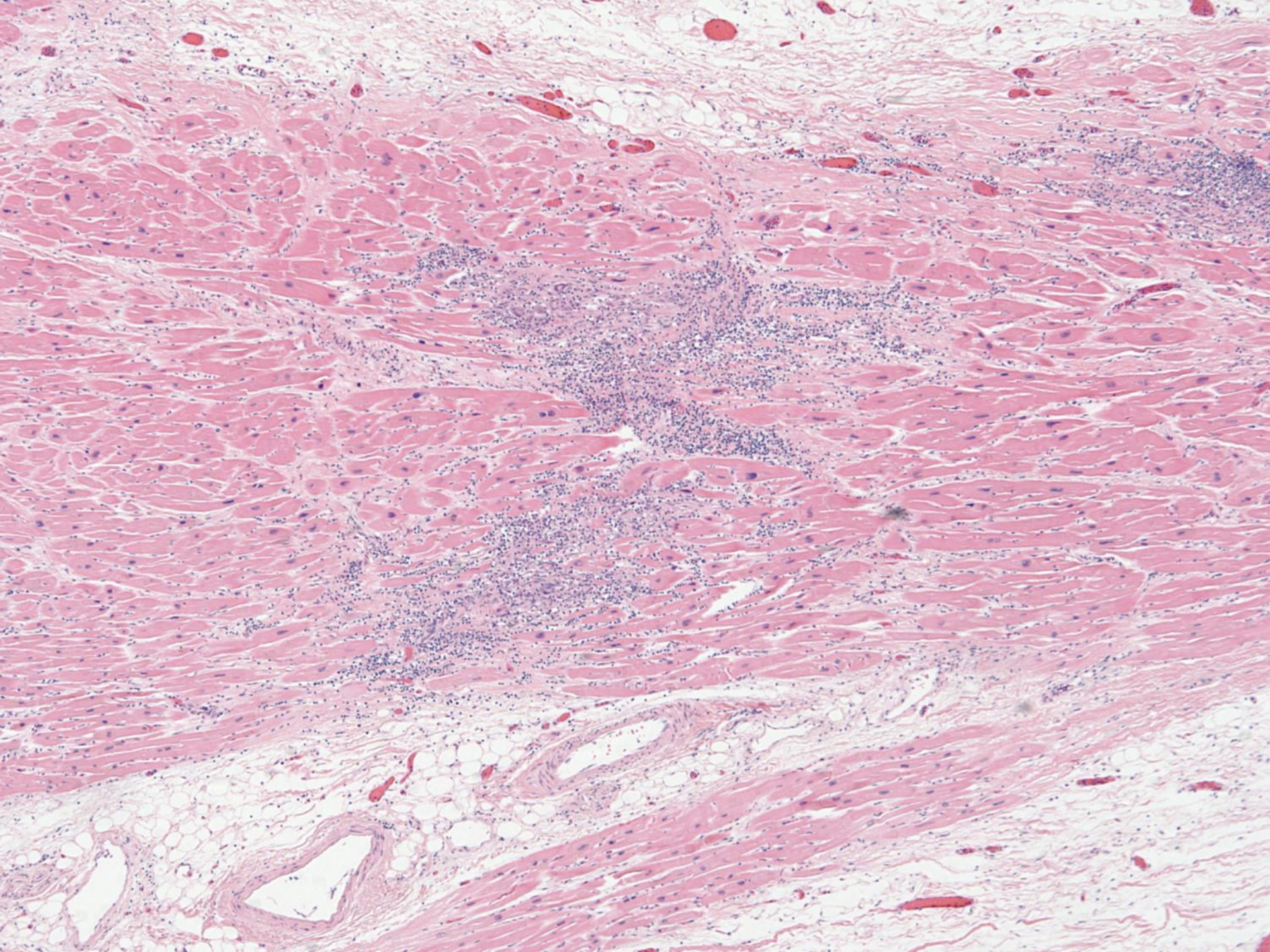
SB 6296

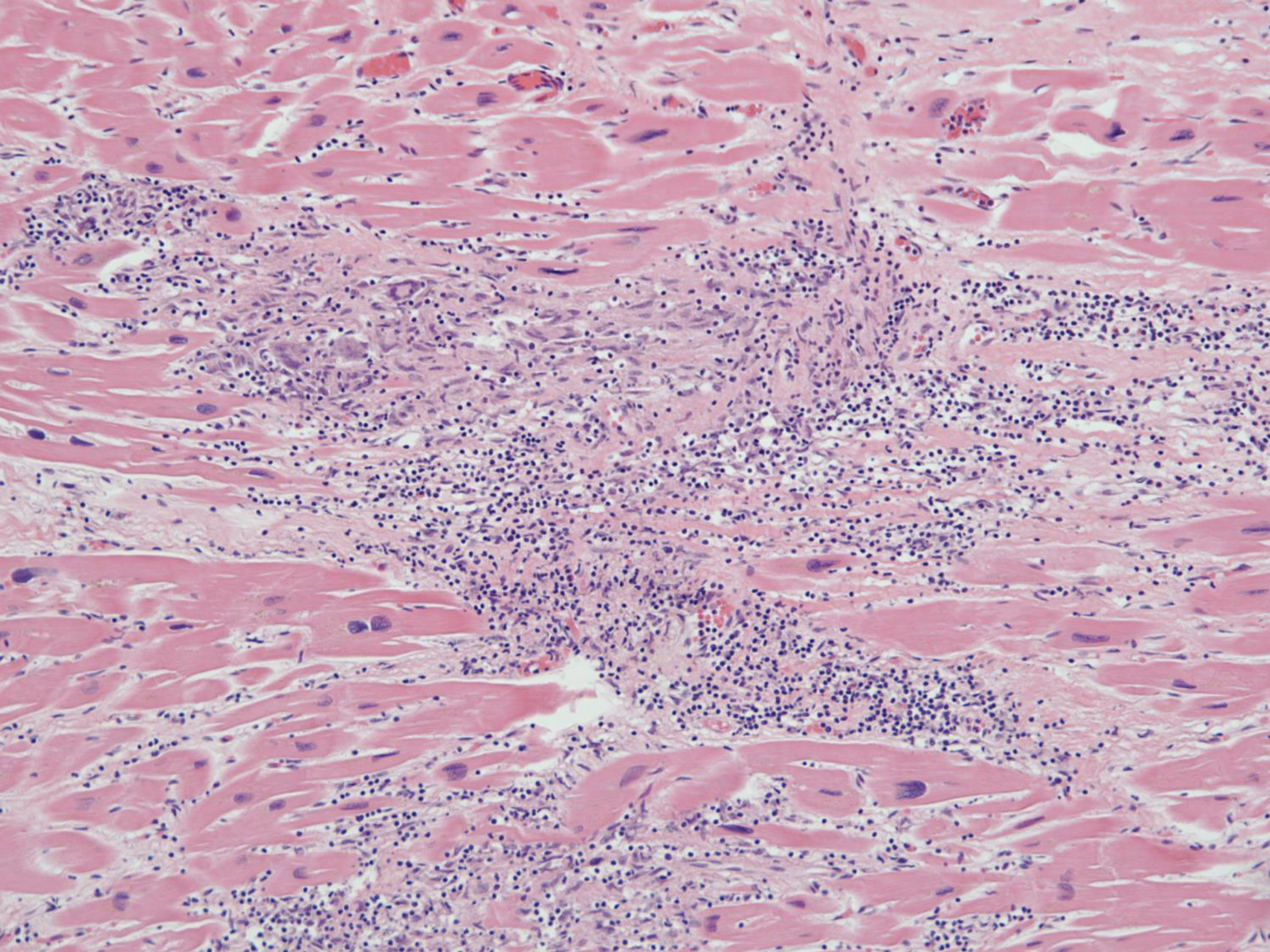
Jeff Cloutier/Christine Louie; Palo Alto VA

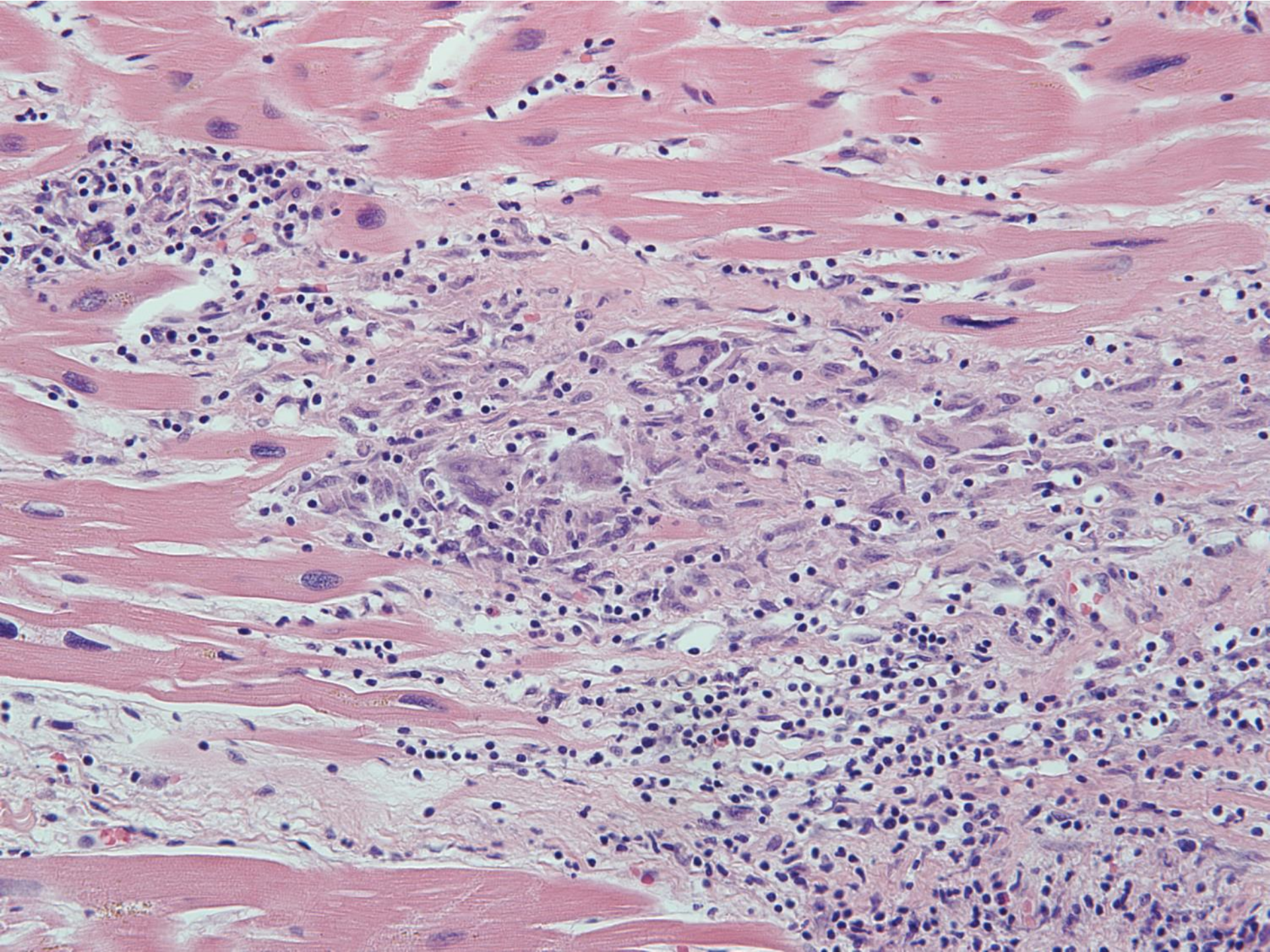
42-year-old man with T1DM and ESRD with significant coronary artery disease. Three days prior to death he underwent a 3v CABG. Although initially alert POD#1, he subsequently decompensated with worsening metabolic acidosis, culminating in PEA arrest. Sections of left ventricle are submitted at autopsy in an area grossly suspicious for MI.

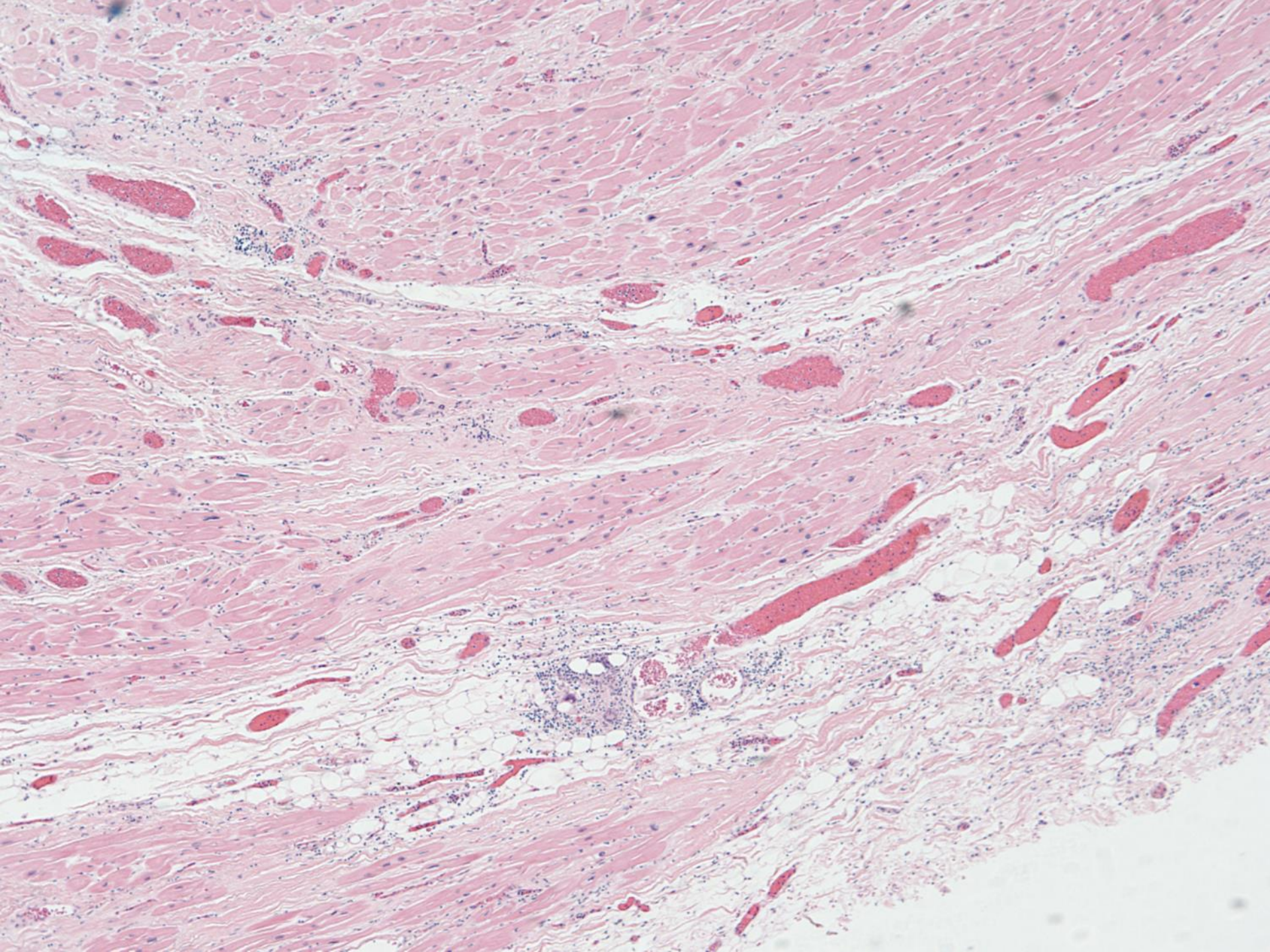


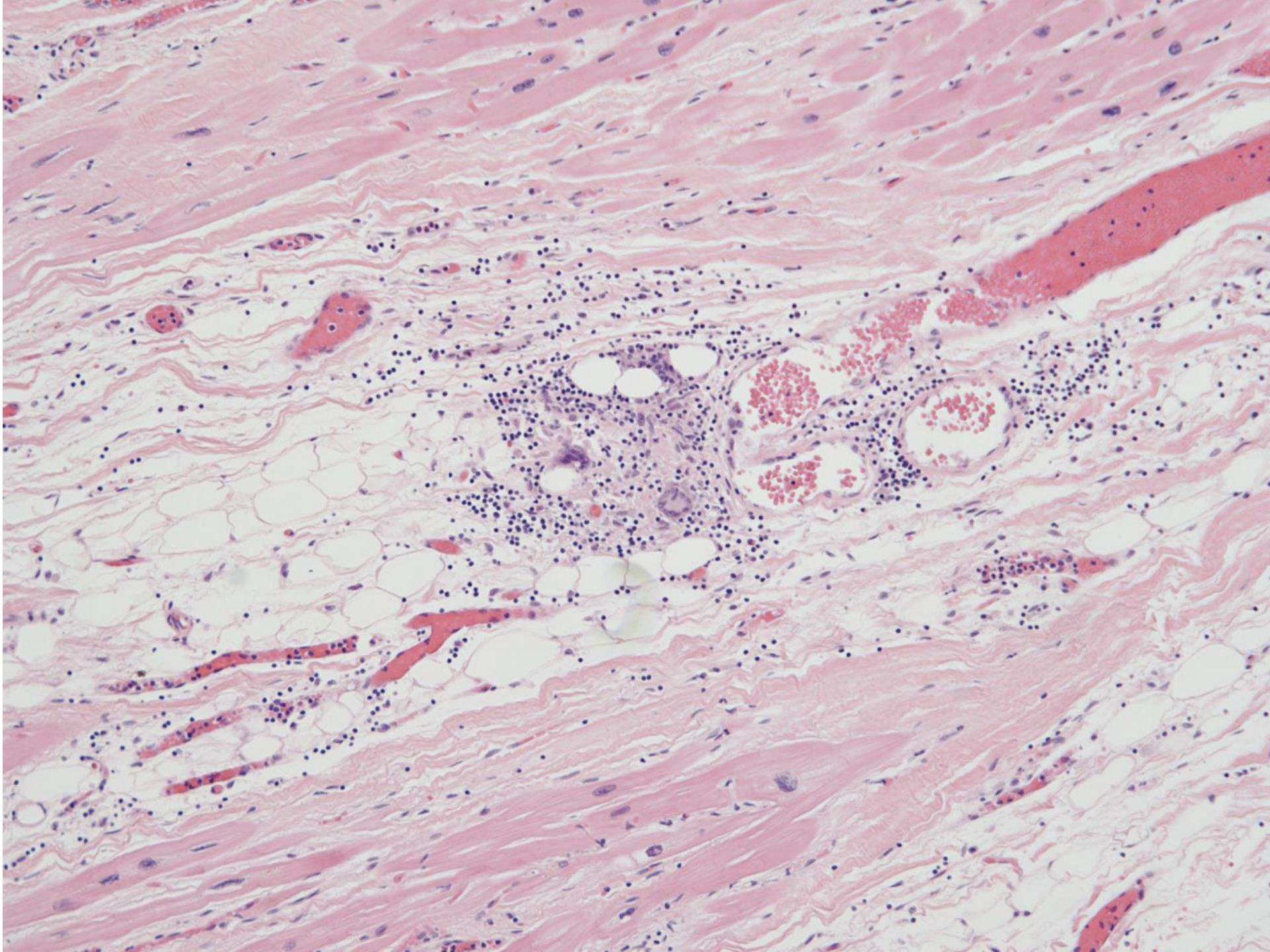








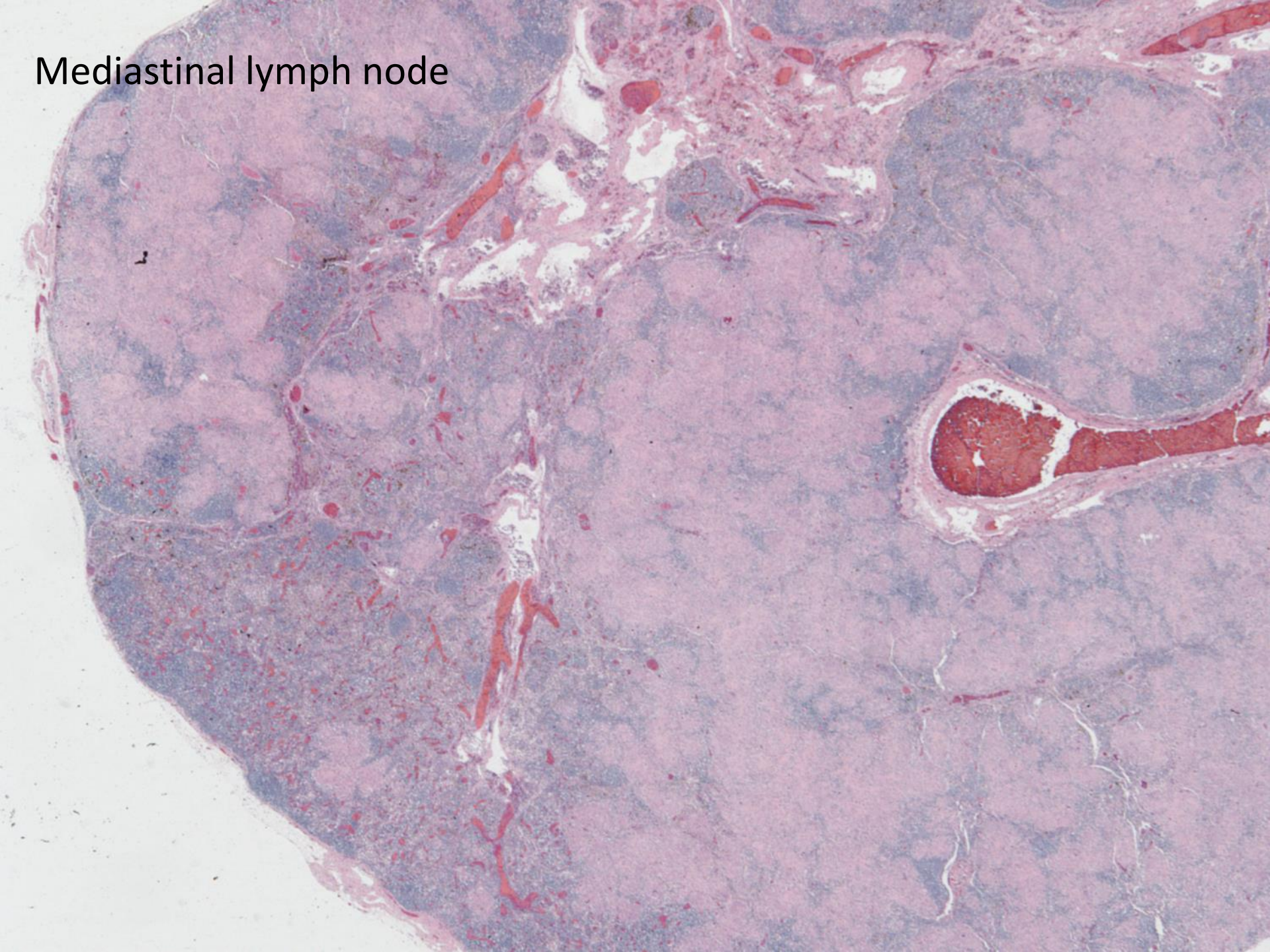


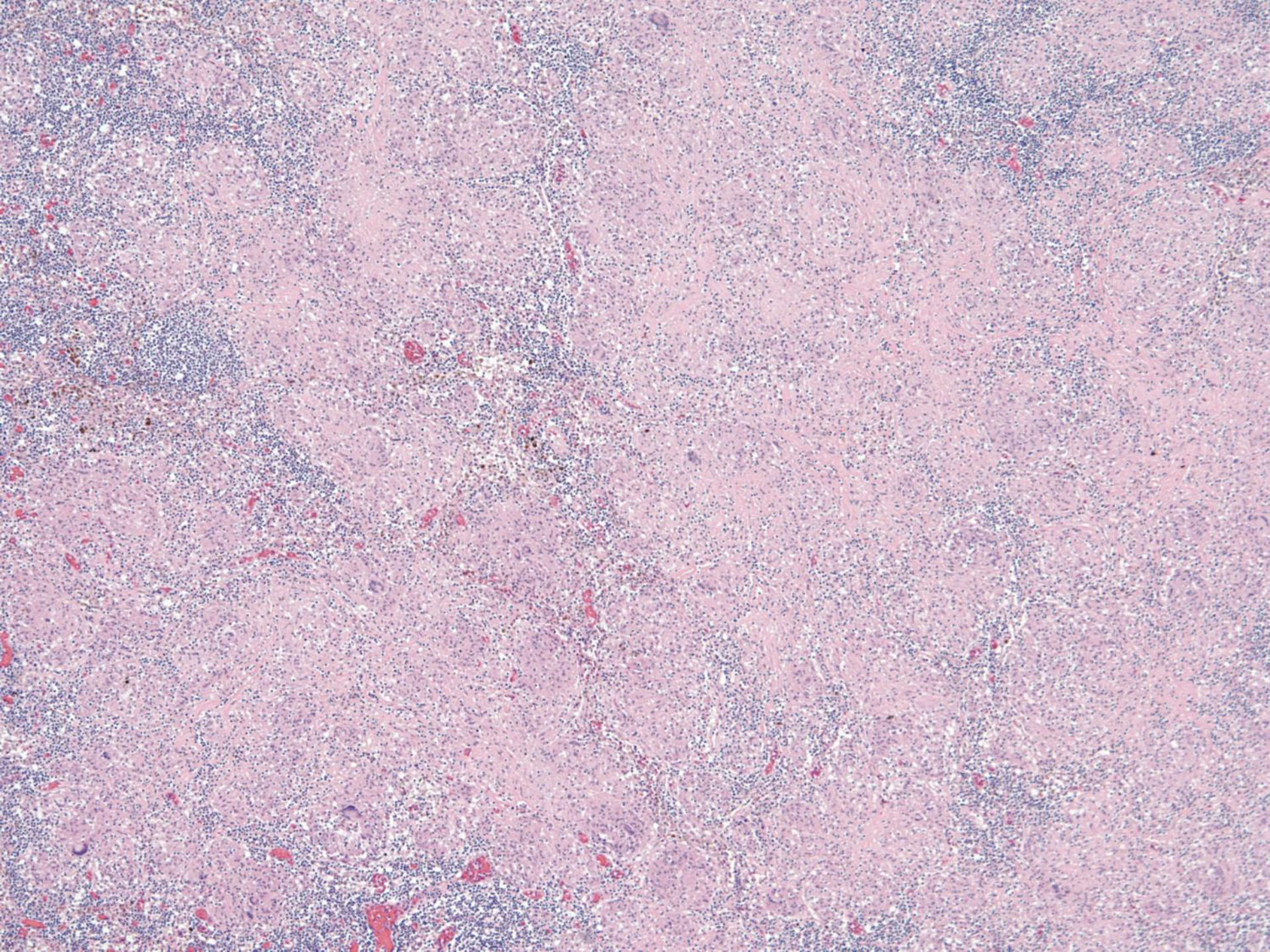


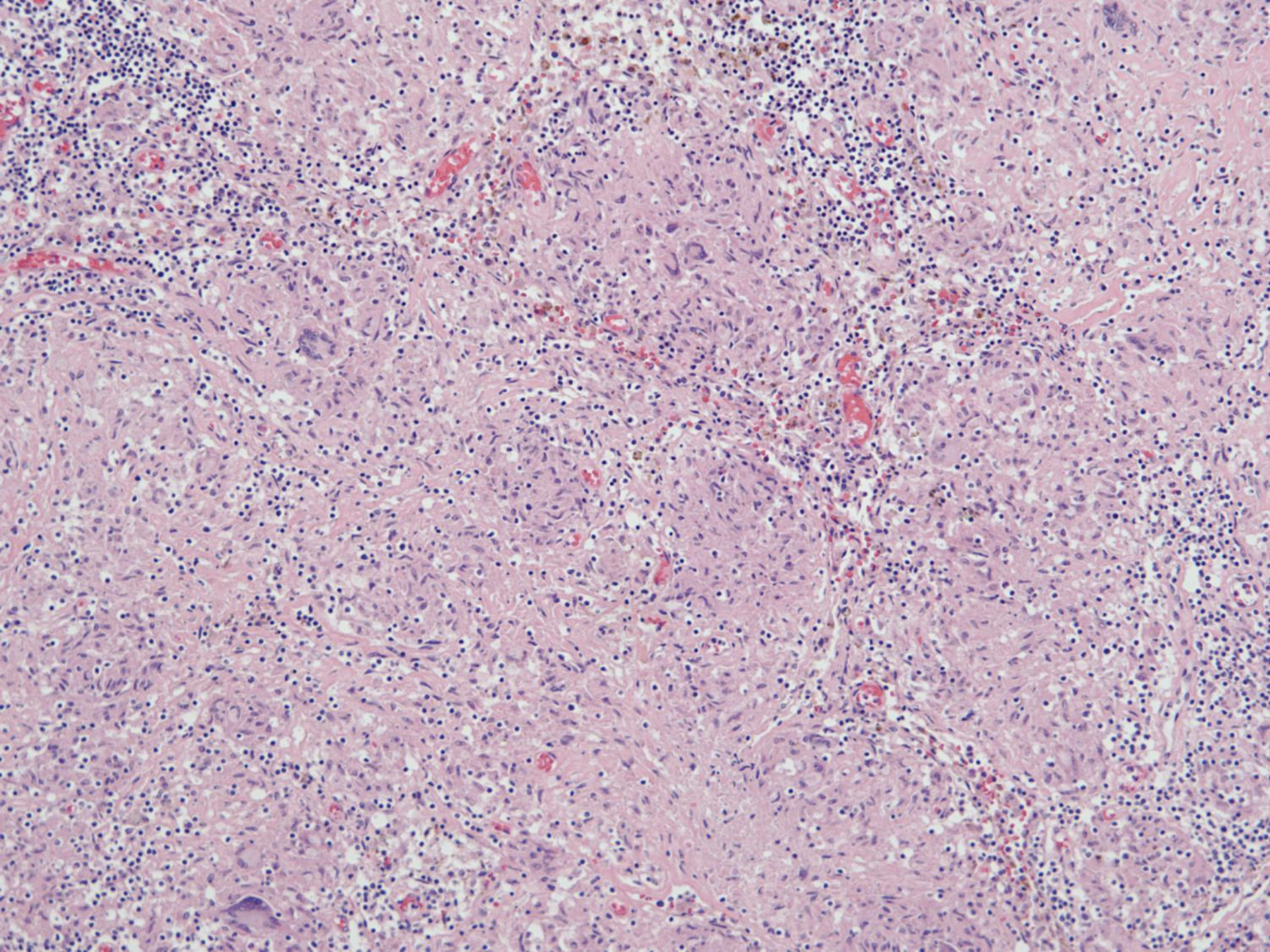
DIAGNOSIS?

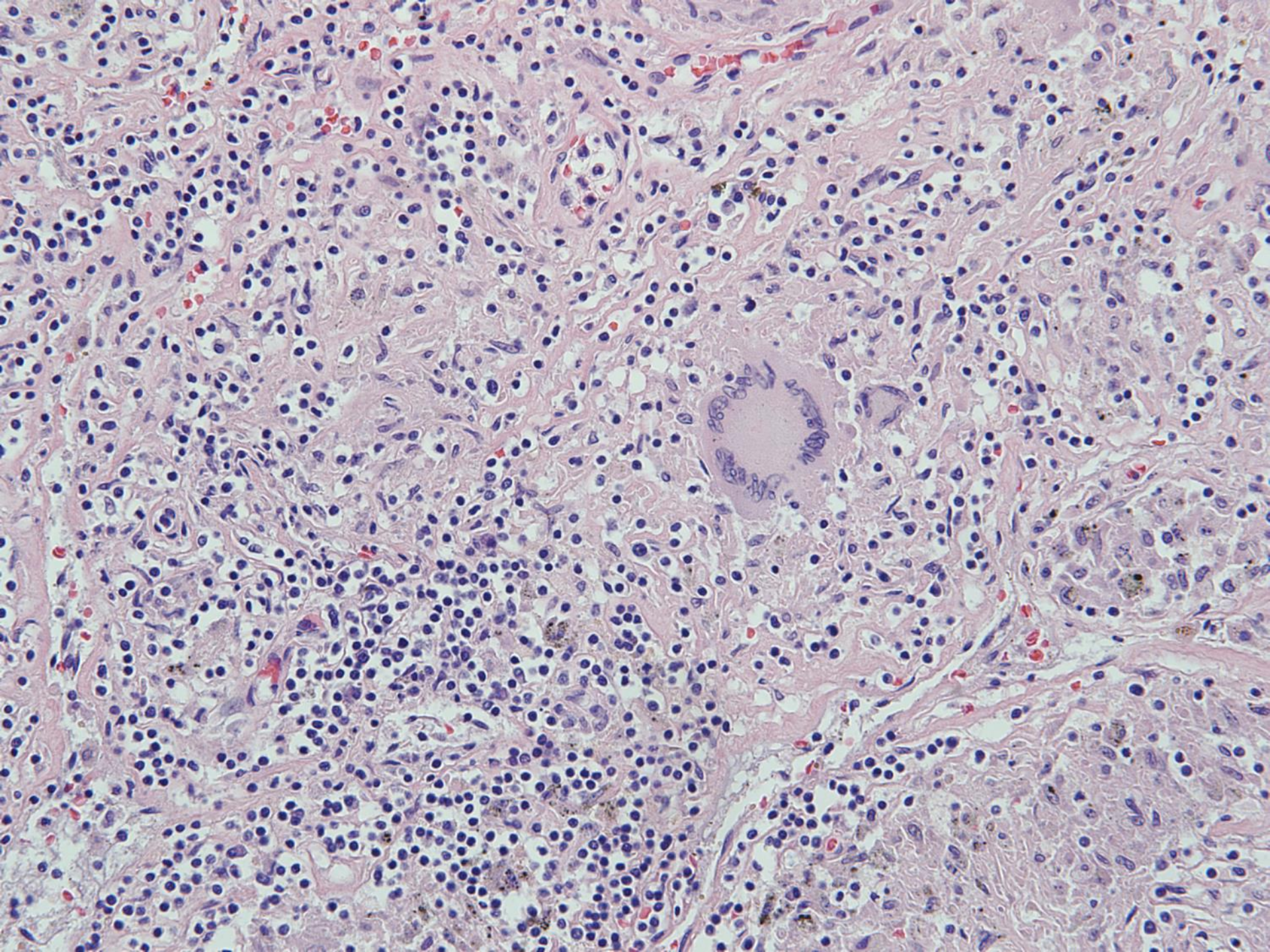
Differential diagnosis

- Giant cell myocarditis
- Infectious granulomatous myocarditis (TB, fungal)
- Foreign body granulomas
- Cardiac sarcoidosis
- Acute rheumatic heart disease
- Vasculitis processes (GCA)


Mediastinal lymph node

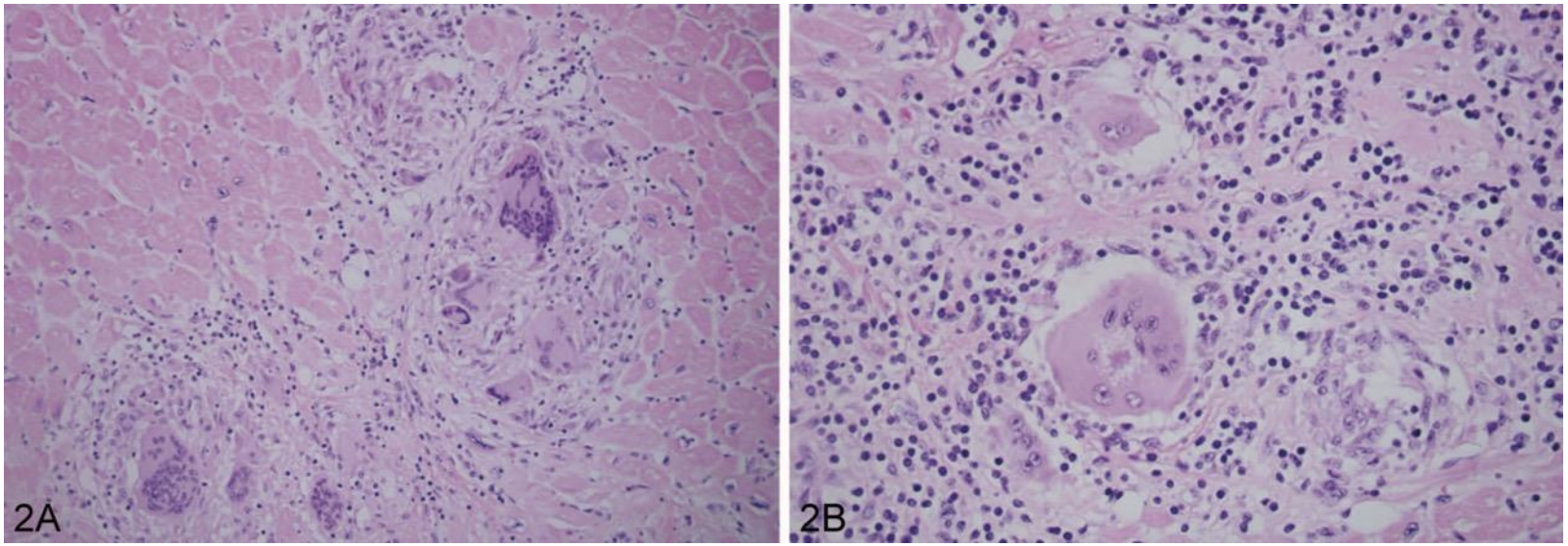






Cardiac sarcoidosis - histology

- Non-necrotizing granulomatous inflammation in transmural or focal distribution, may have pericardial extension
- Multinucleated giant cell inclusions
  - Asteroid bodies – stellate shaped with cytoplasmic clearing
  - Schaumann bodies – oval, concentrically laminated, calcifications
- Interstitial fibrosis
- Few/no eosinophils, myocyte necrosis rare



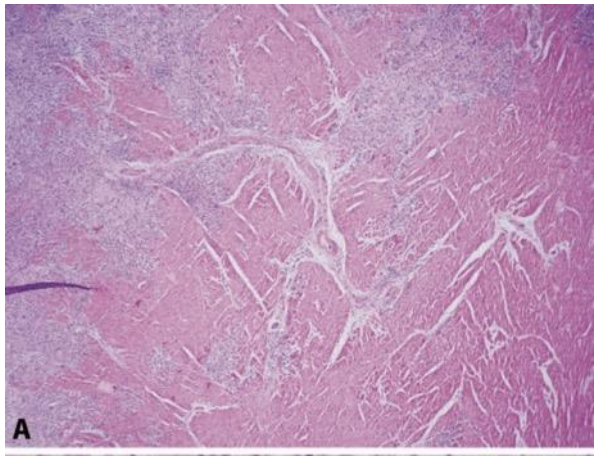
Xu J, Brooks EG. Giant Cell Myocarditis: A Brief Review. Arch Pathol Lab Med. 2016 Dec;140(12):1429-1434.

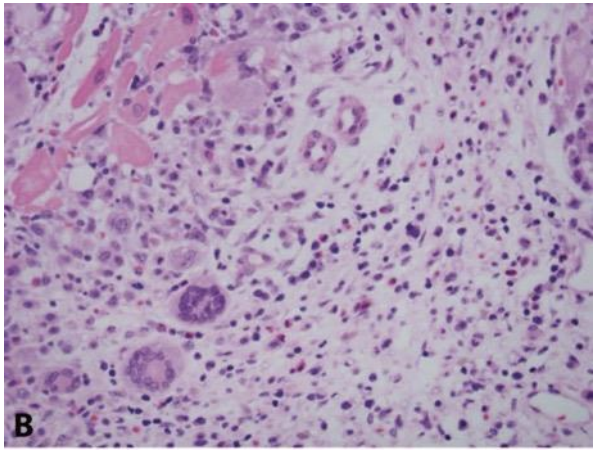
Cardiac sarcoidosis – clinical issues

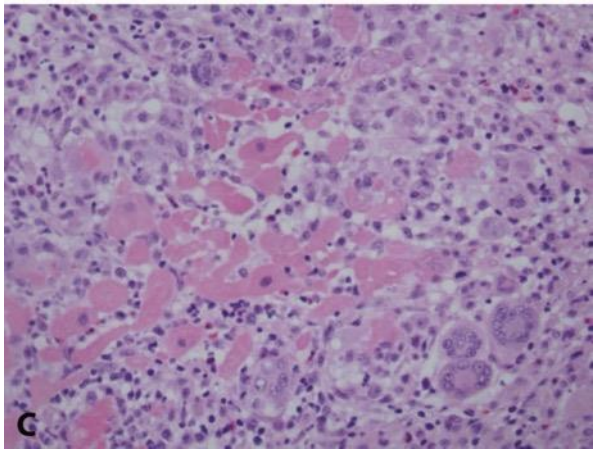
- Young/middle-aged adults (20-40s)
- F>M
- 10-35:100,000
- Conduction disturbances (AV delay, bundle branch block)
- Arrhythmias
- Congestive heart failure
- Sudden death
- Hypercalcemia

Histologic differential diagnosis

- Giant cell myocarditis
  - Multifocal serpiginous infiltrate
  - Absence of well-formed granulomas
  - Numerous eosinophils and myocyte necrosis
  - Not associated with systemic disease







Xu J, Brooks EG. Giant Cell Myocarditis: A Brief Review. Arch Pathol Lab Med. 2016 Dec;140(12):1429-1434.

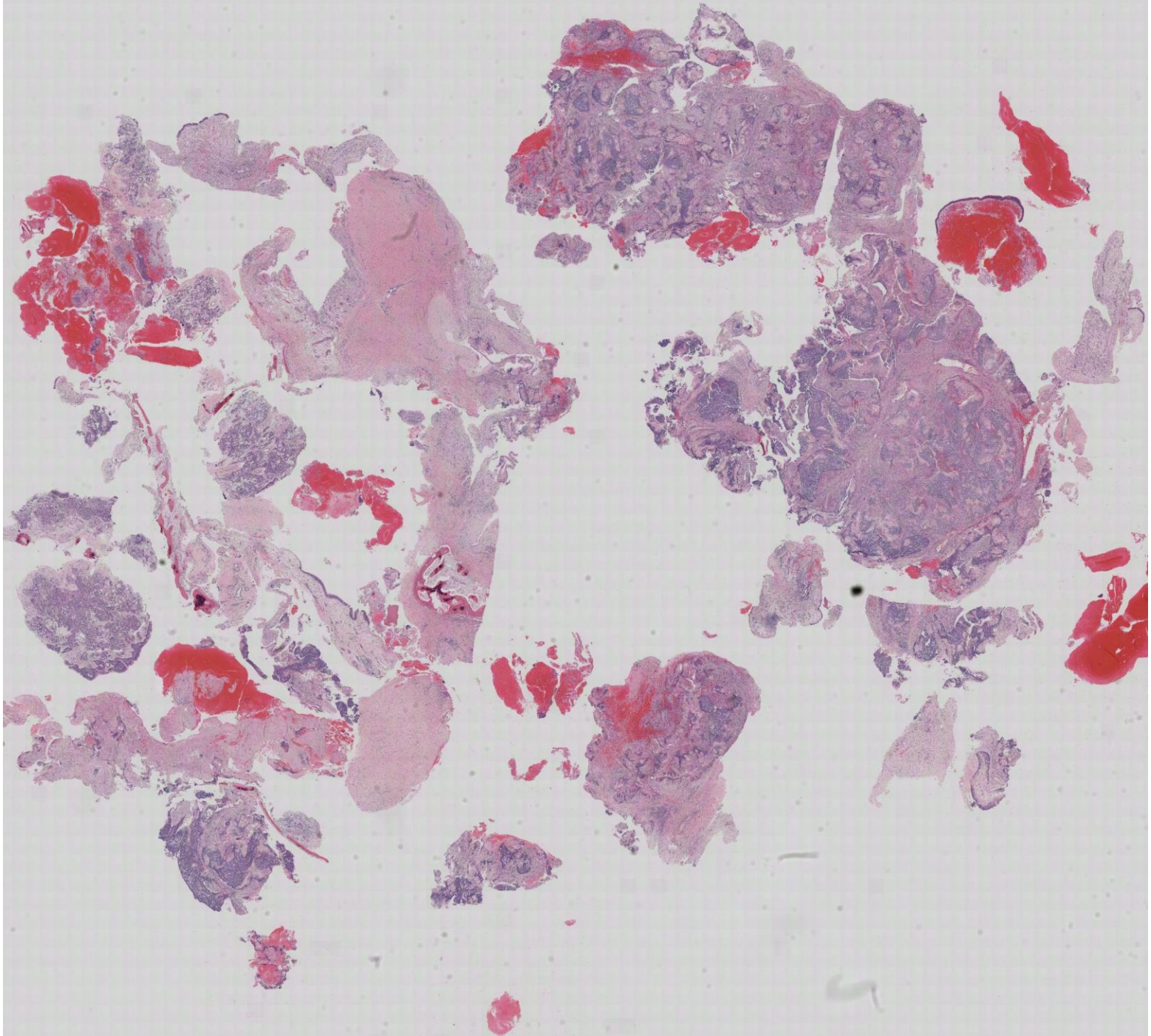
Histologic differential diagnosis

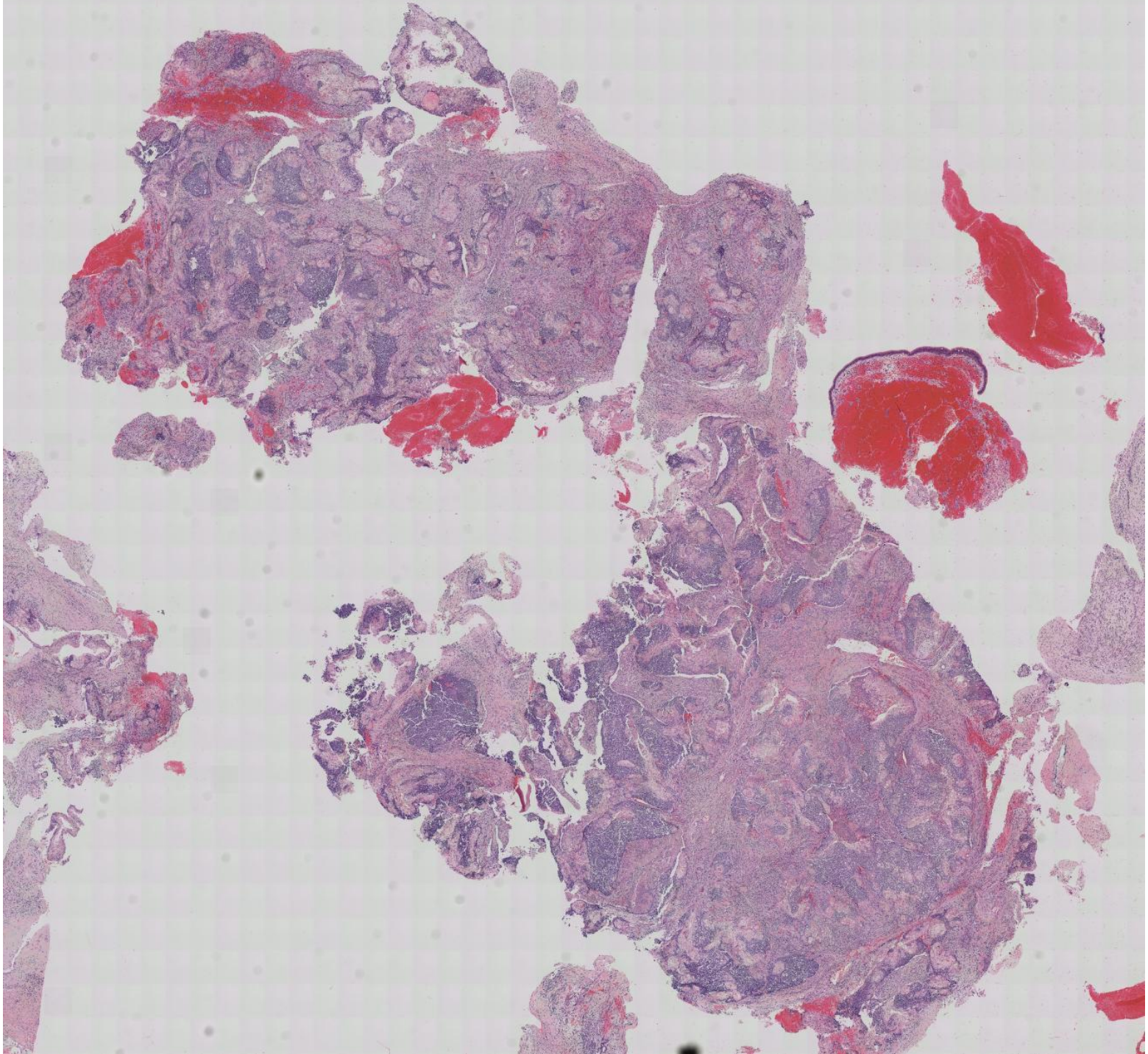
- Infectious granulomatous myocarditis
  - Granulomas with central necrosis
  - Positive special stains GMS or AFB
- Foreign body granulomas
  - Not well-formed granulomas
  - Foreign material identified under polarized light

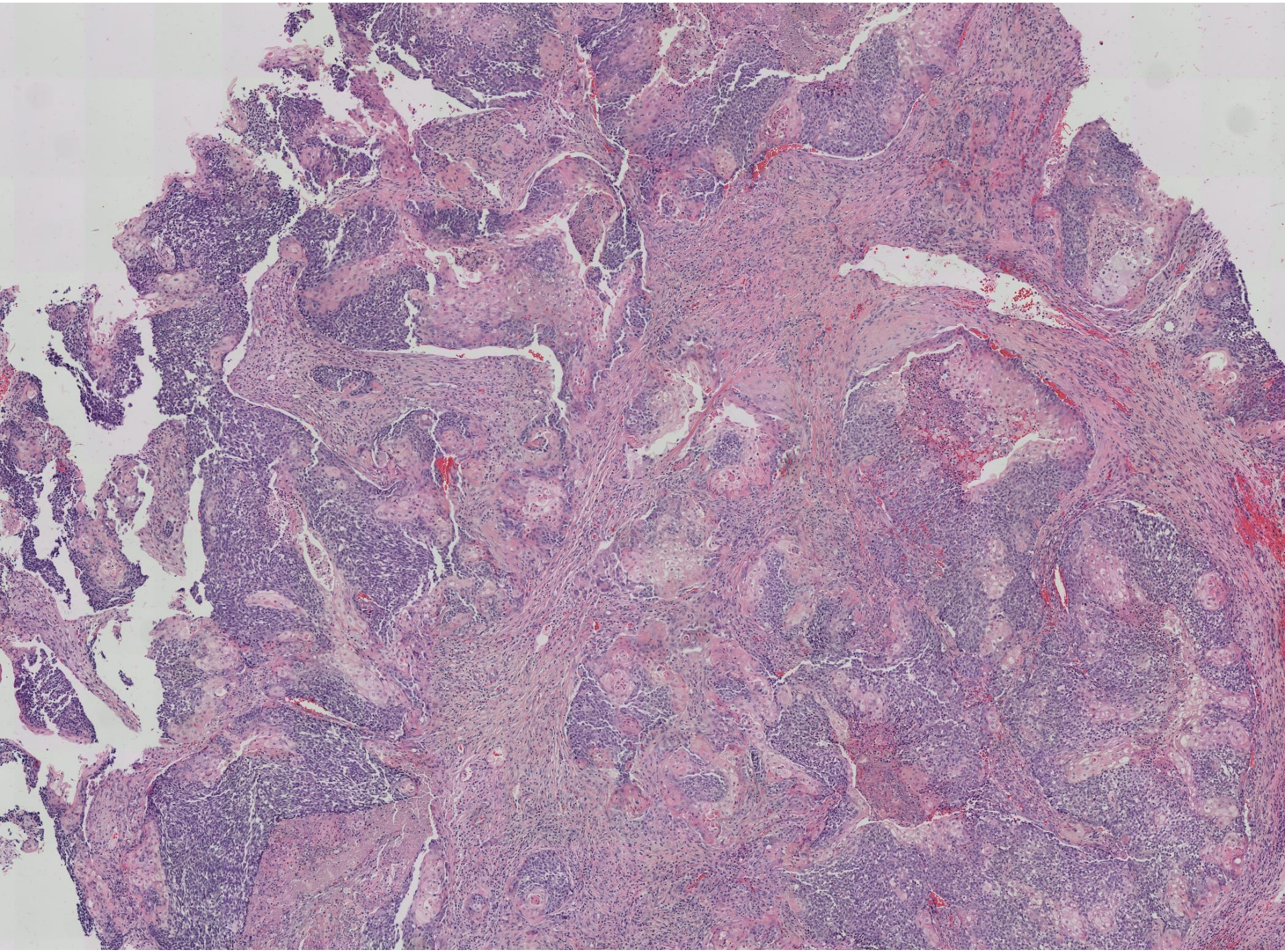
SB 6297
(scanned slide available)

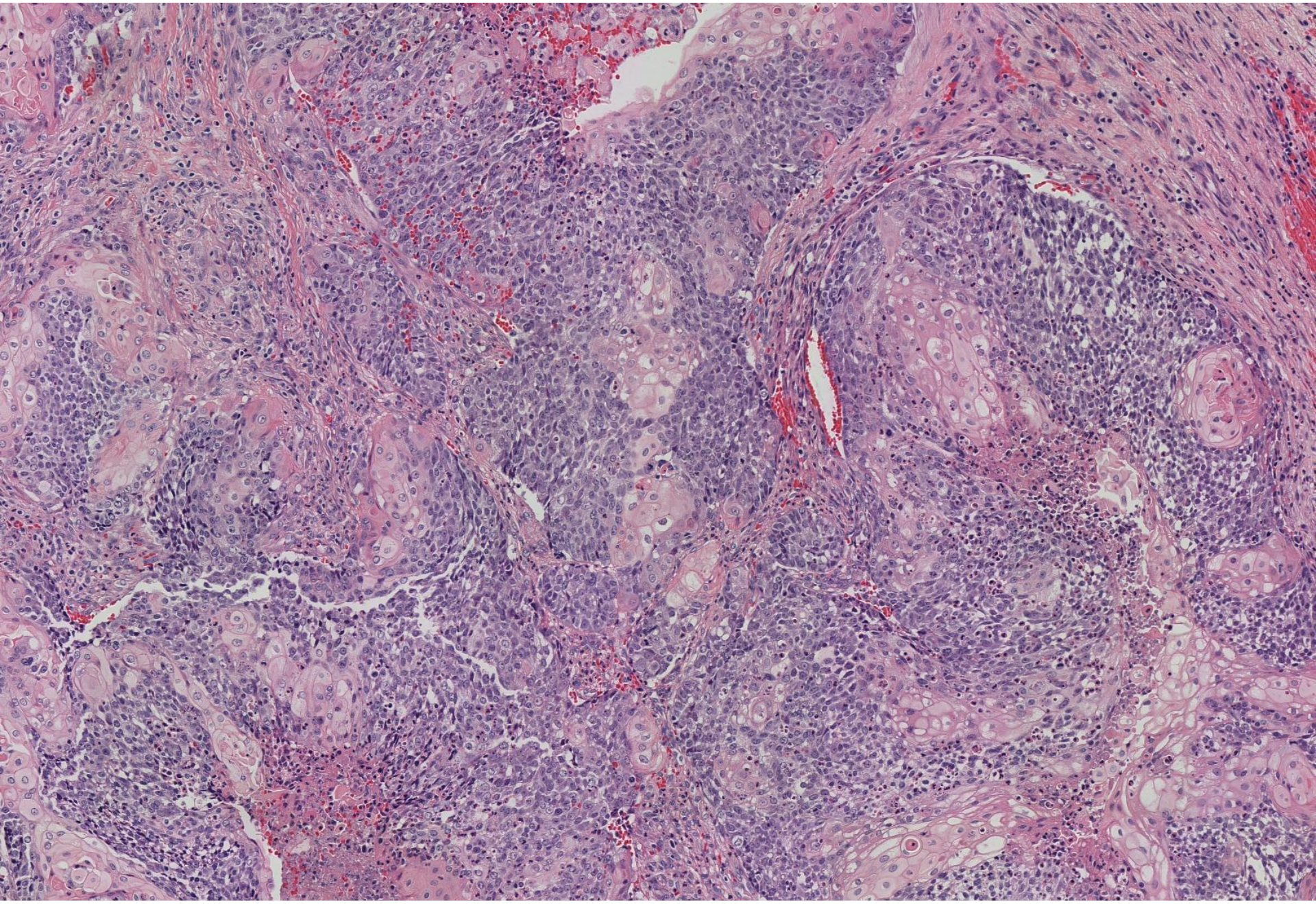
Emily Chan/Annemieke Van Zante; UCSF

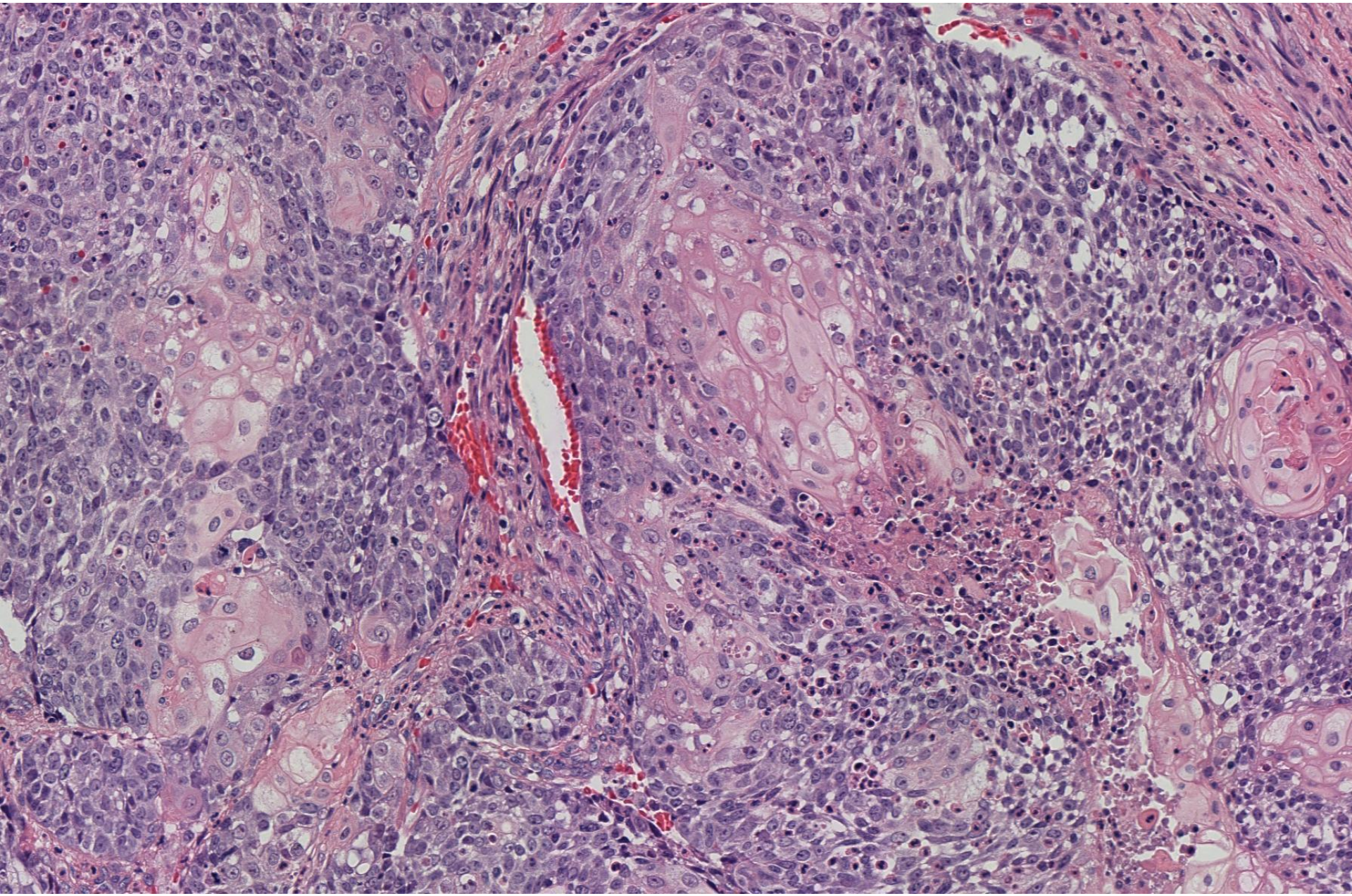
50-year-old woman presents with 2-3 months headache and worsening vision, found to have aggressive appearing right-sided sinonasal mass.

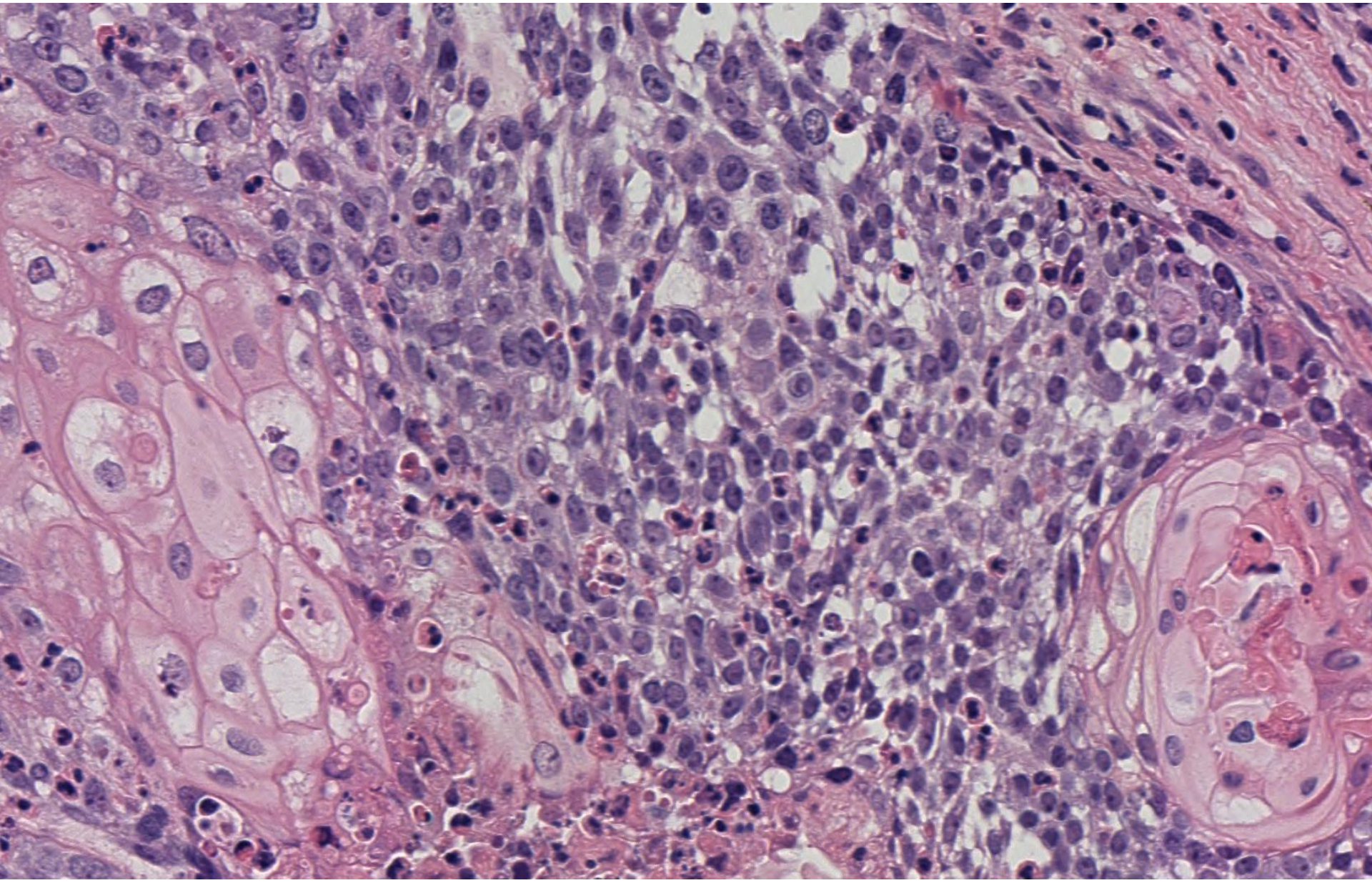


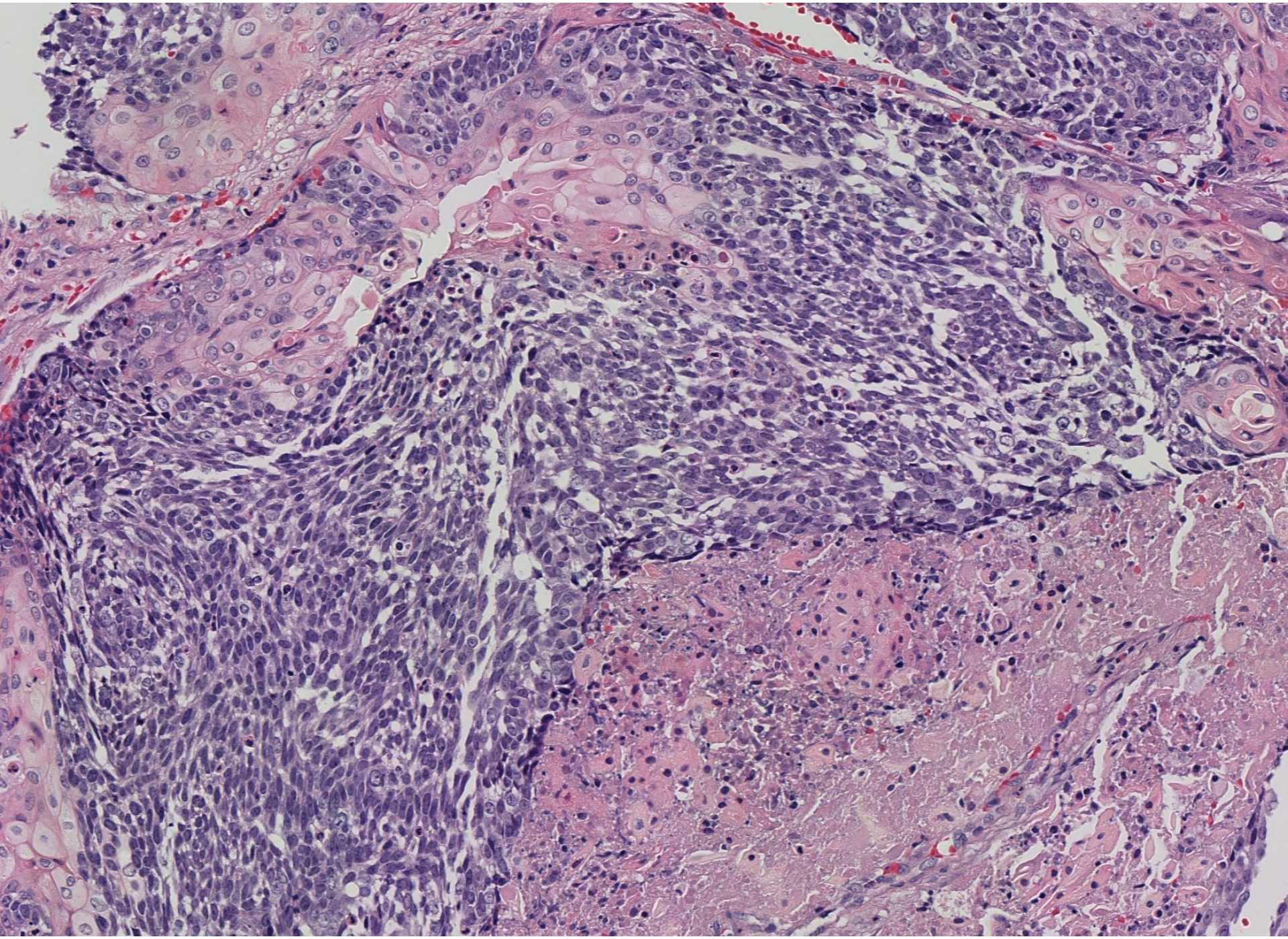


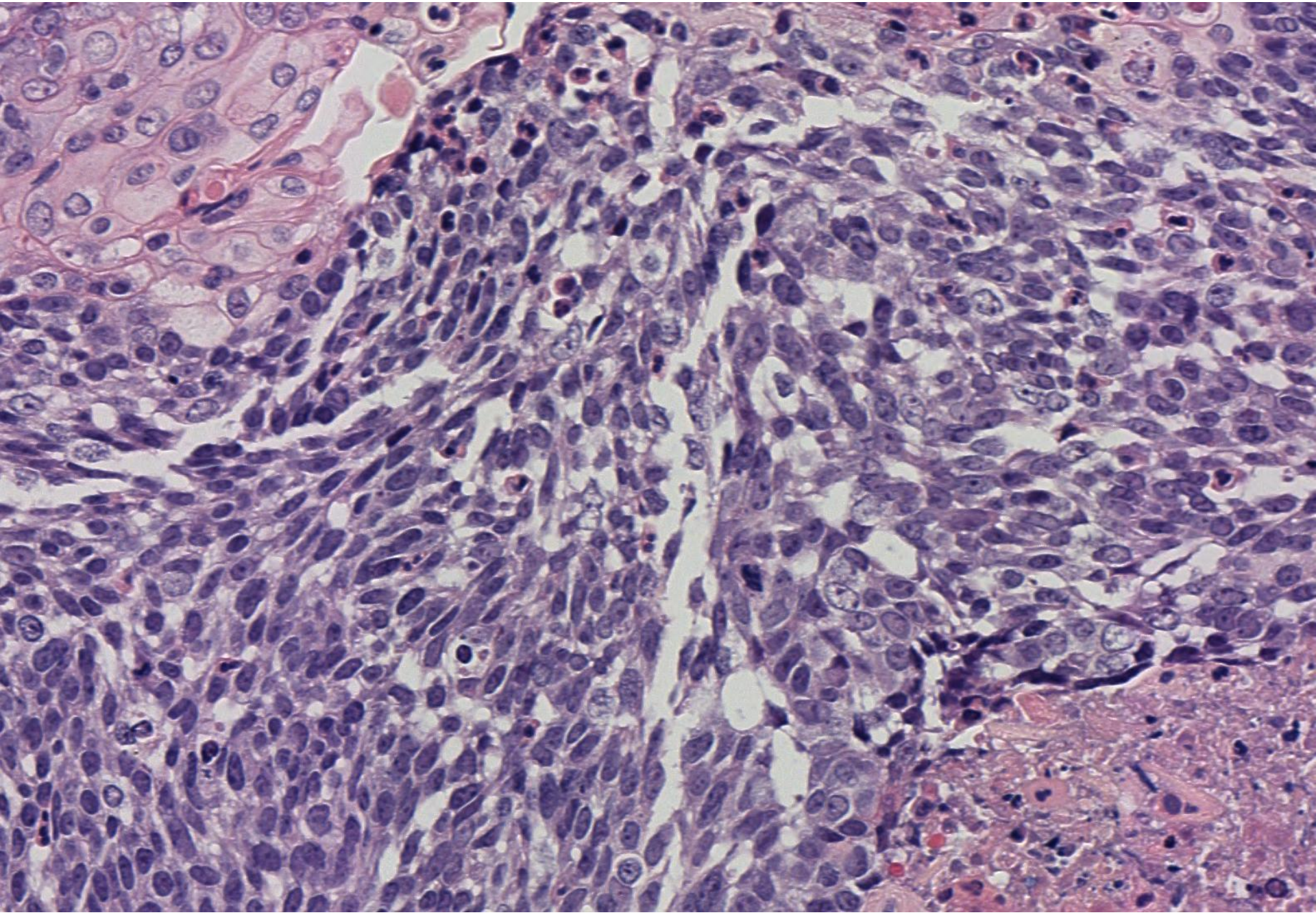




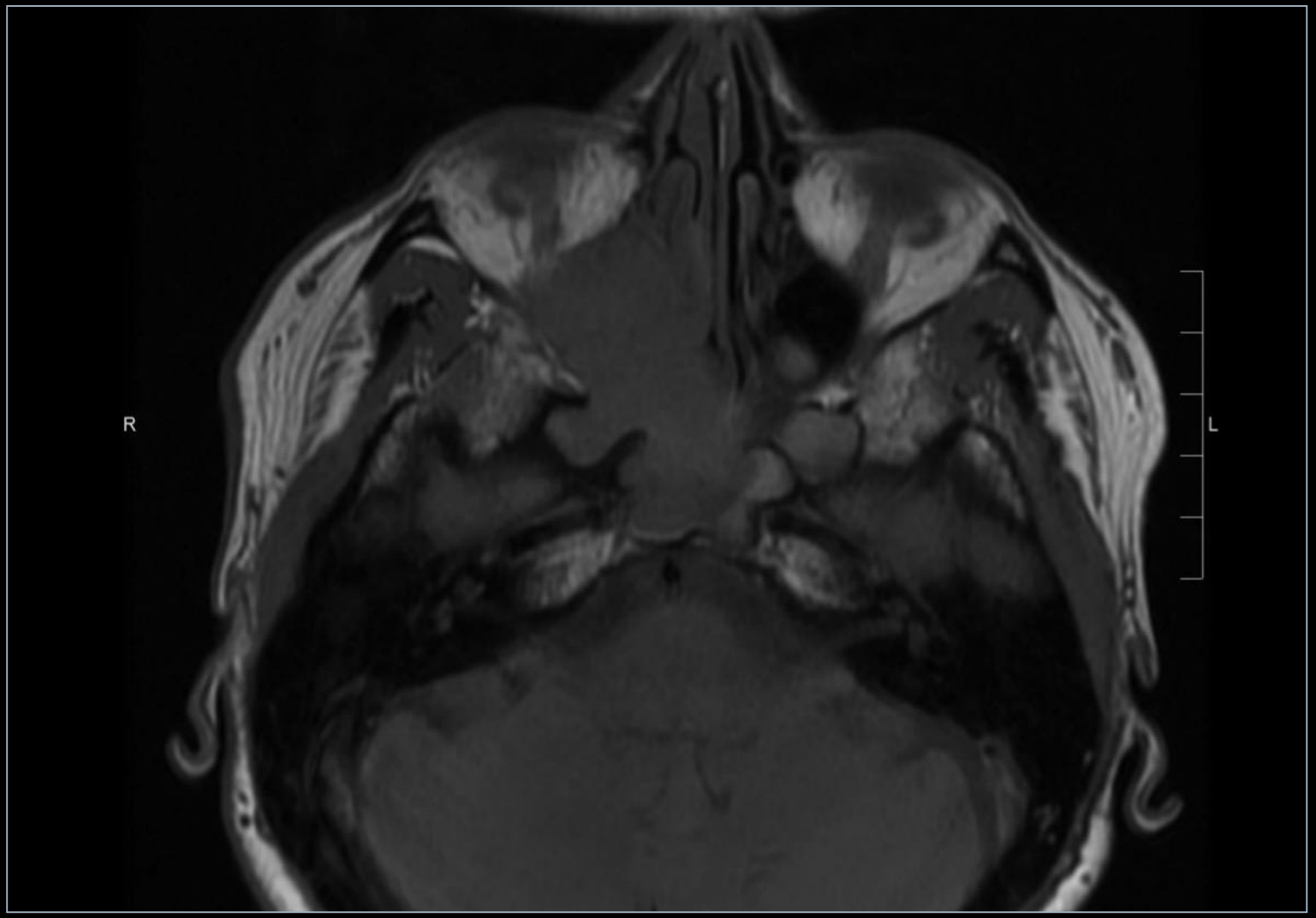








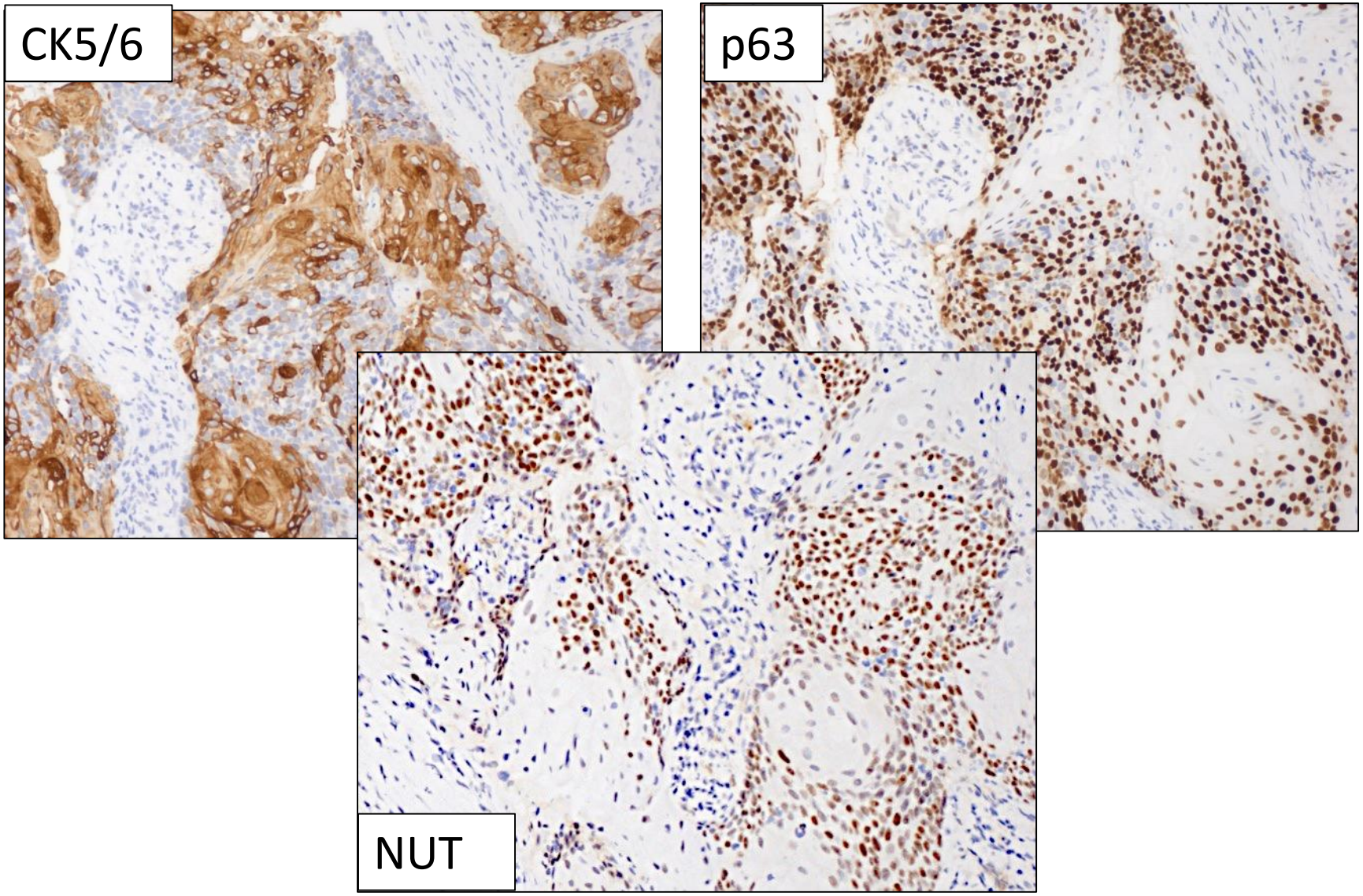
DIAGNOSIS?


R
L

Top Differential Diagnosis

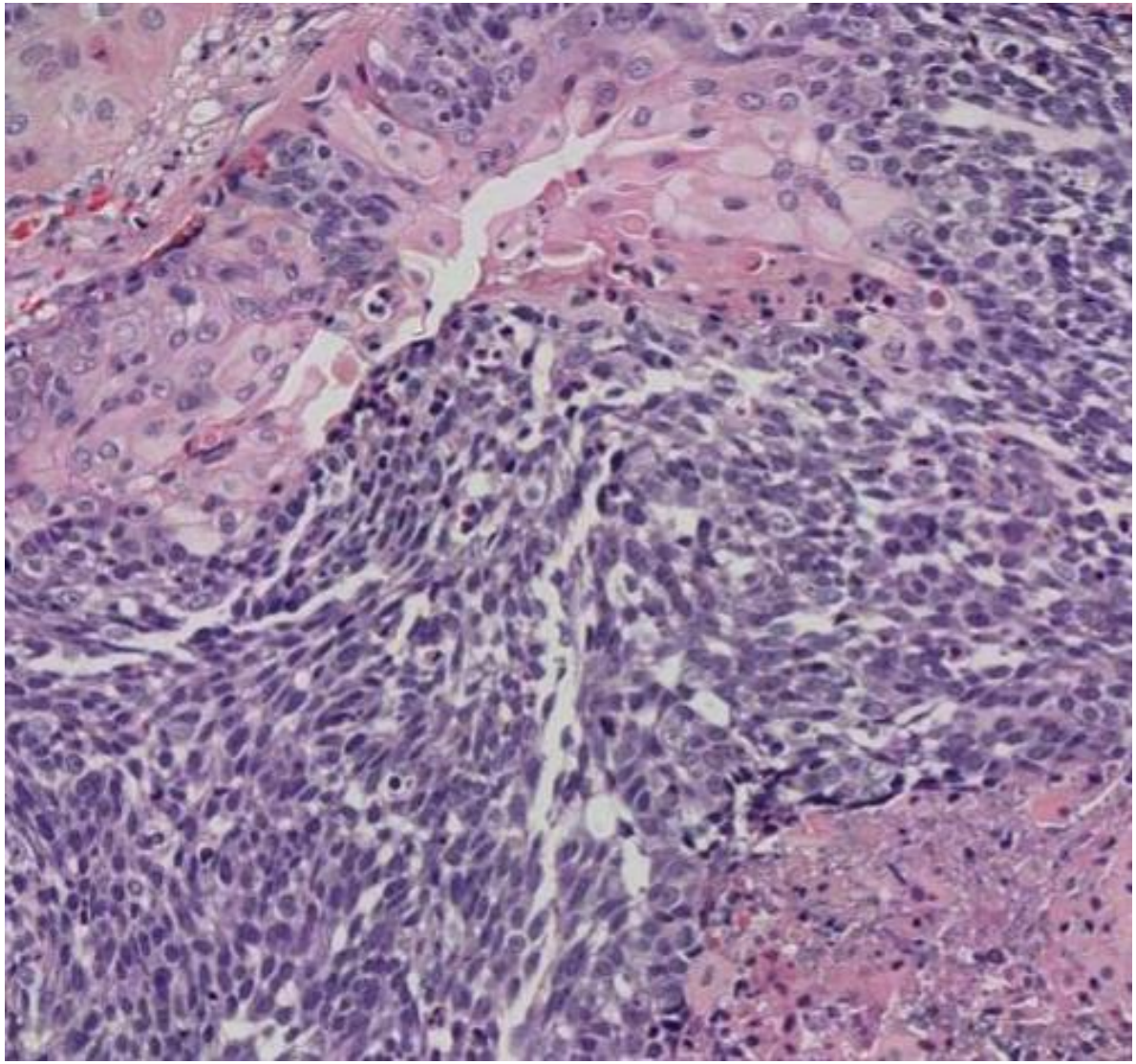
- Squamous cell carcinoma
- NUT carcinoma
- HPV/EBV driven nasopharyngeal carcinomas

IHC workup



NUT Carcinoma

- Rare neoplasm, young adults
- Location: Head and neck and mediastinum
- Highly aggressive, mean survival under 1 year
- NUT rearrangement, most often with BRD4
  - t(15:19)(q14,p13.1)
- H&E: Abrupt keratinization, relatively monotonous
- IHC: p63, CK5/6, NUT
- Potential therapies: bromodomain and histone deacetylase inhibitors



NUT Carcinoma

Key Features:

- Poorly differentiated
- Monotonous, relatively bland cells
- Abrupt keratinization
- Necrosis and mitoses

More common differential
(when you only have the blue cells)

- Melanoma
- Rhabdomyosarcoma
- SNUC/SCC/SNEC/Synovial sarcoma
- Lymphoma (NK/T Cell)
- Esthesioneuroblastoma (olfactory neuroblastoma)
- Ewing Sarcoma
- Pituitary adenoma/paraganglioma

MR SLEEP + 4 (NUT, EBV, HPV, INI)

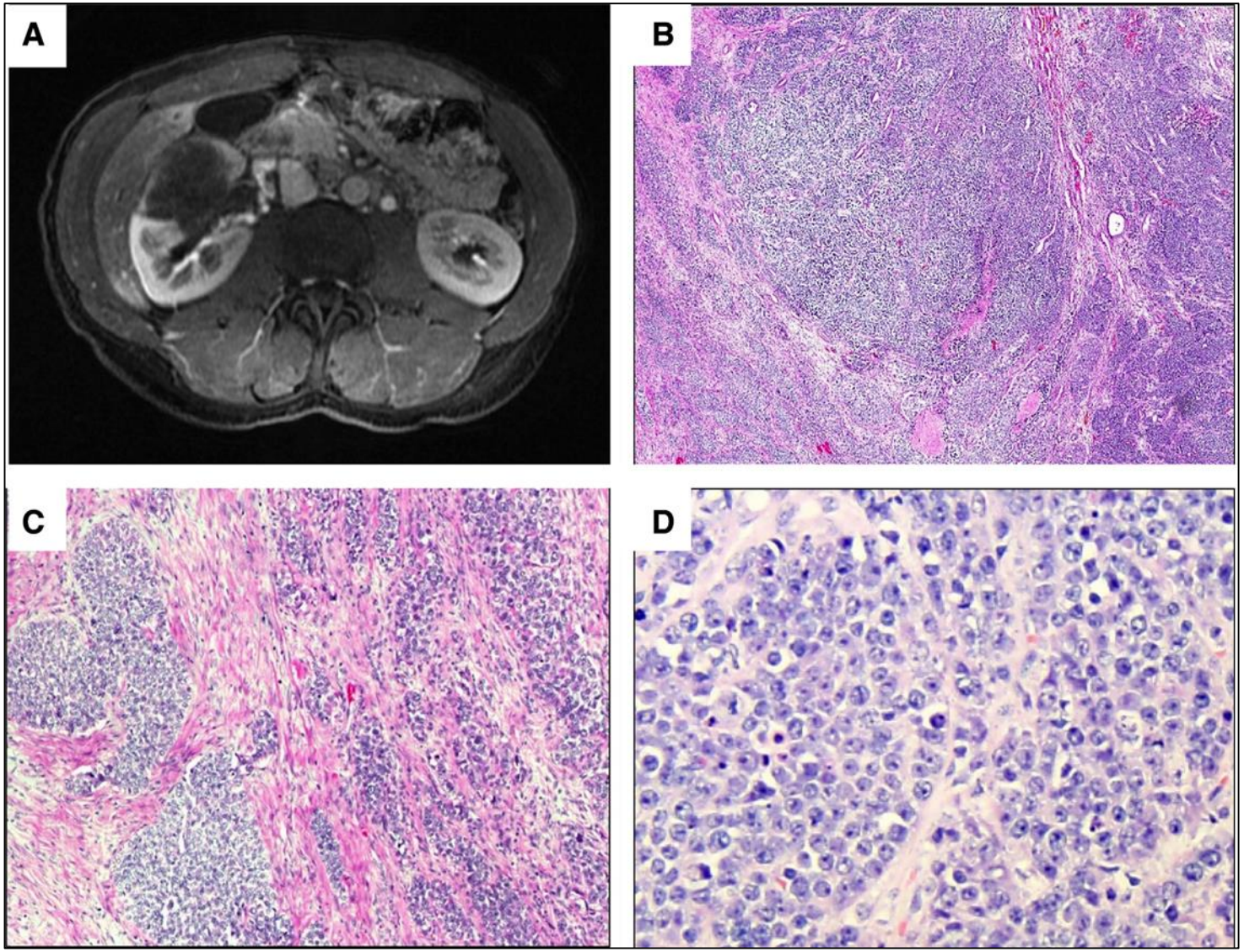
Bishop JA, Head Neck Pathol 2016, Thompson LD, Mod Pathol, 2017

When to stain:

- Midline poorly differentiated carcinoma
- Never smoker
- No EBV or HPV
- Consider NUT in other sites: larynx, salivary gland, kidney, bone, bladder, soft tissue

French, Cancer Genet Cytogenet 2011
Hellquist et al. Histopathology 2017
Agaimy et al. AJSP 2018
Dickson et al. AJSP 2018
And more…with a growing list…

Renal NUT

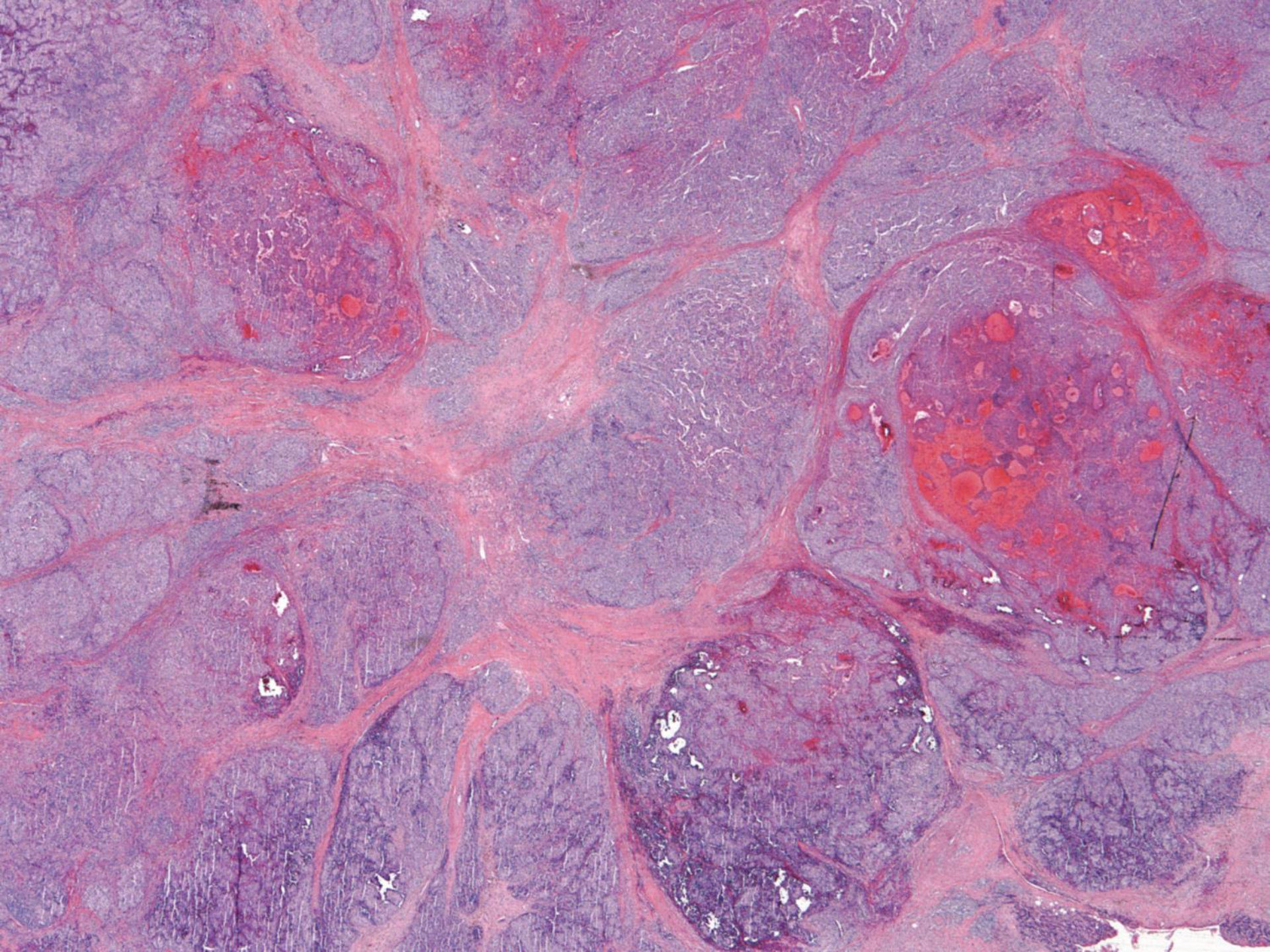


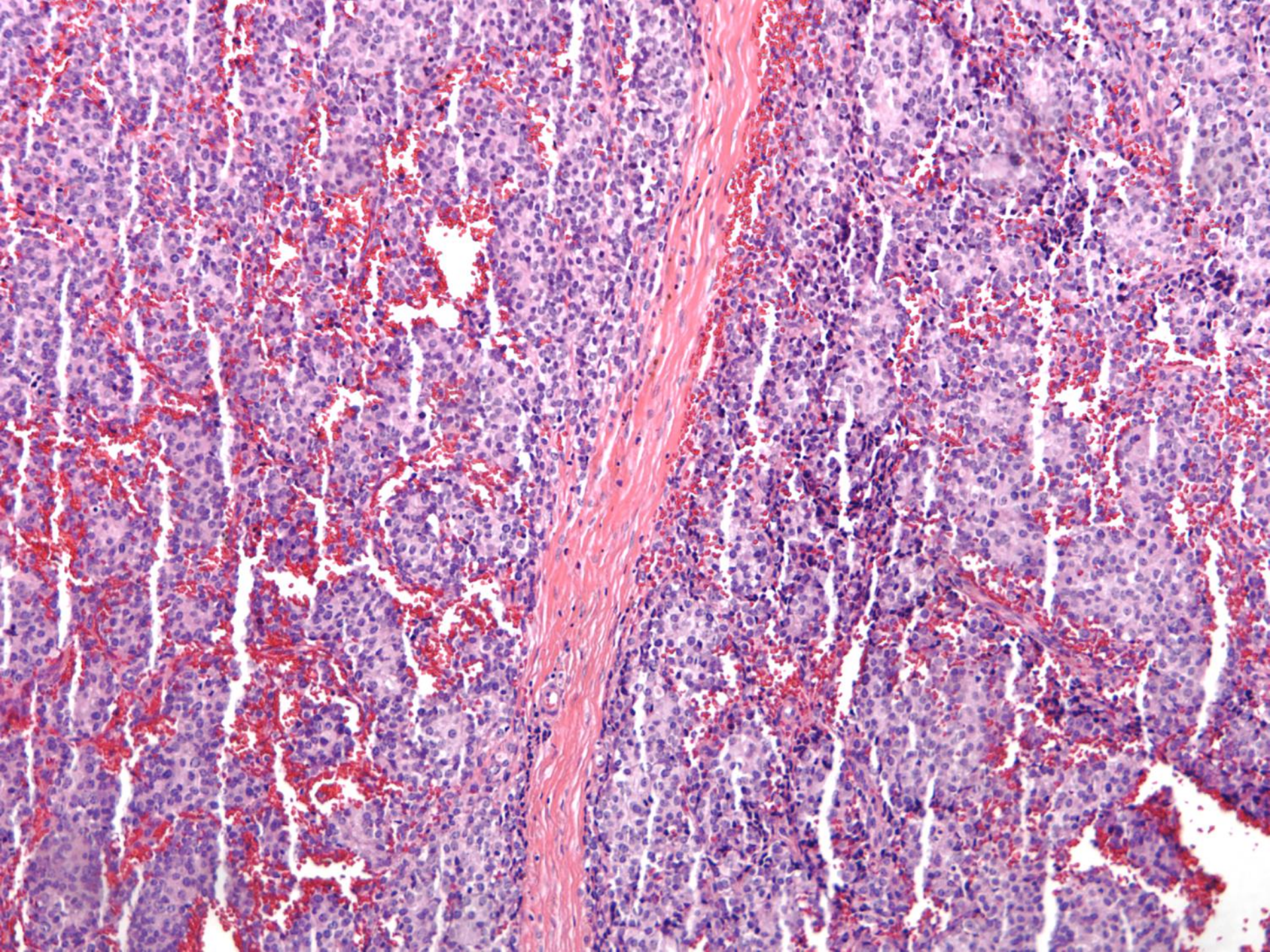
Sirohi, Garg, Simko, Grenert, Histopathology 2018

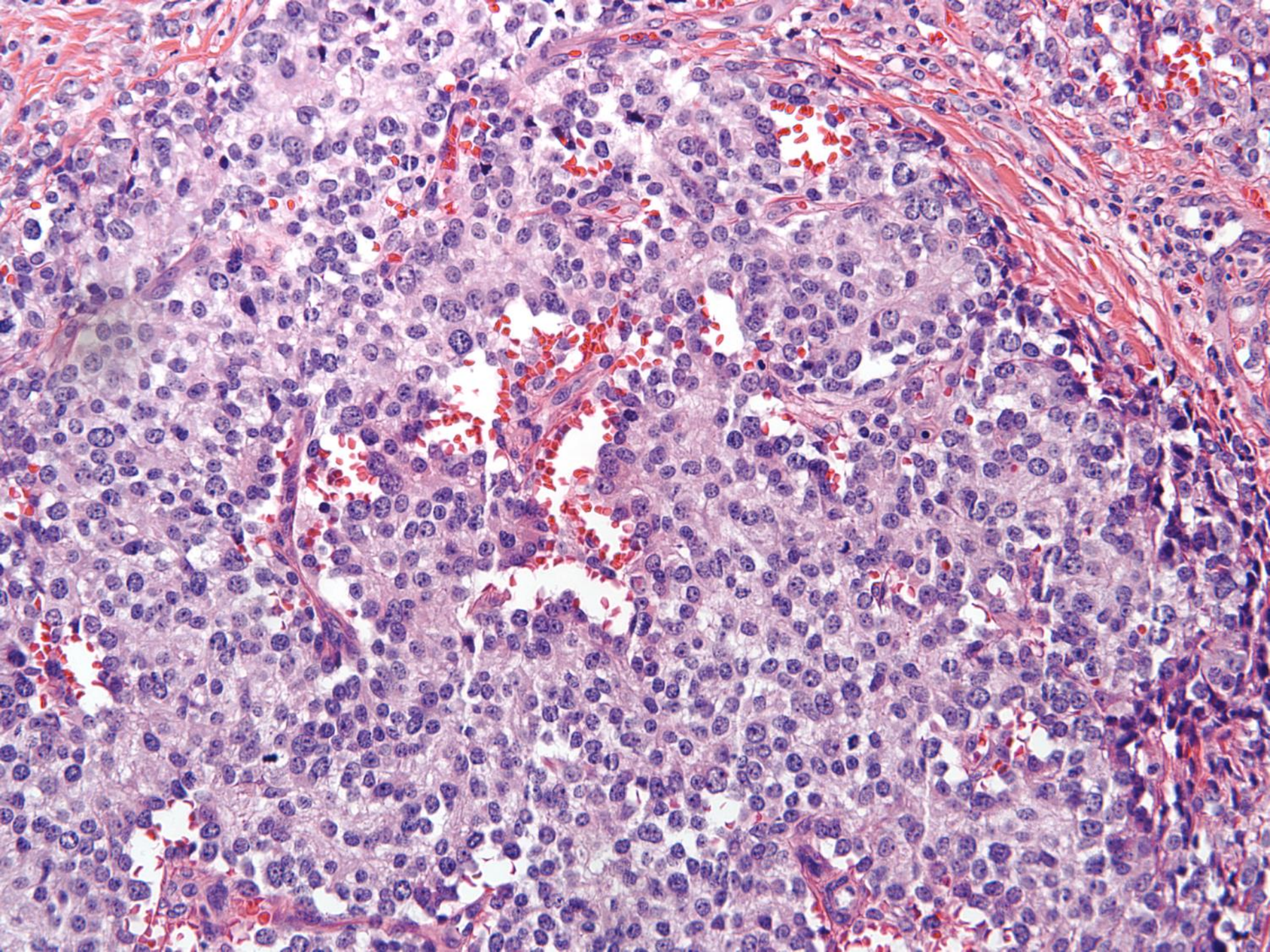
SB 6298

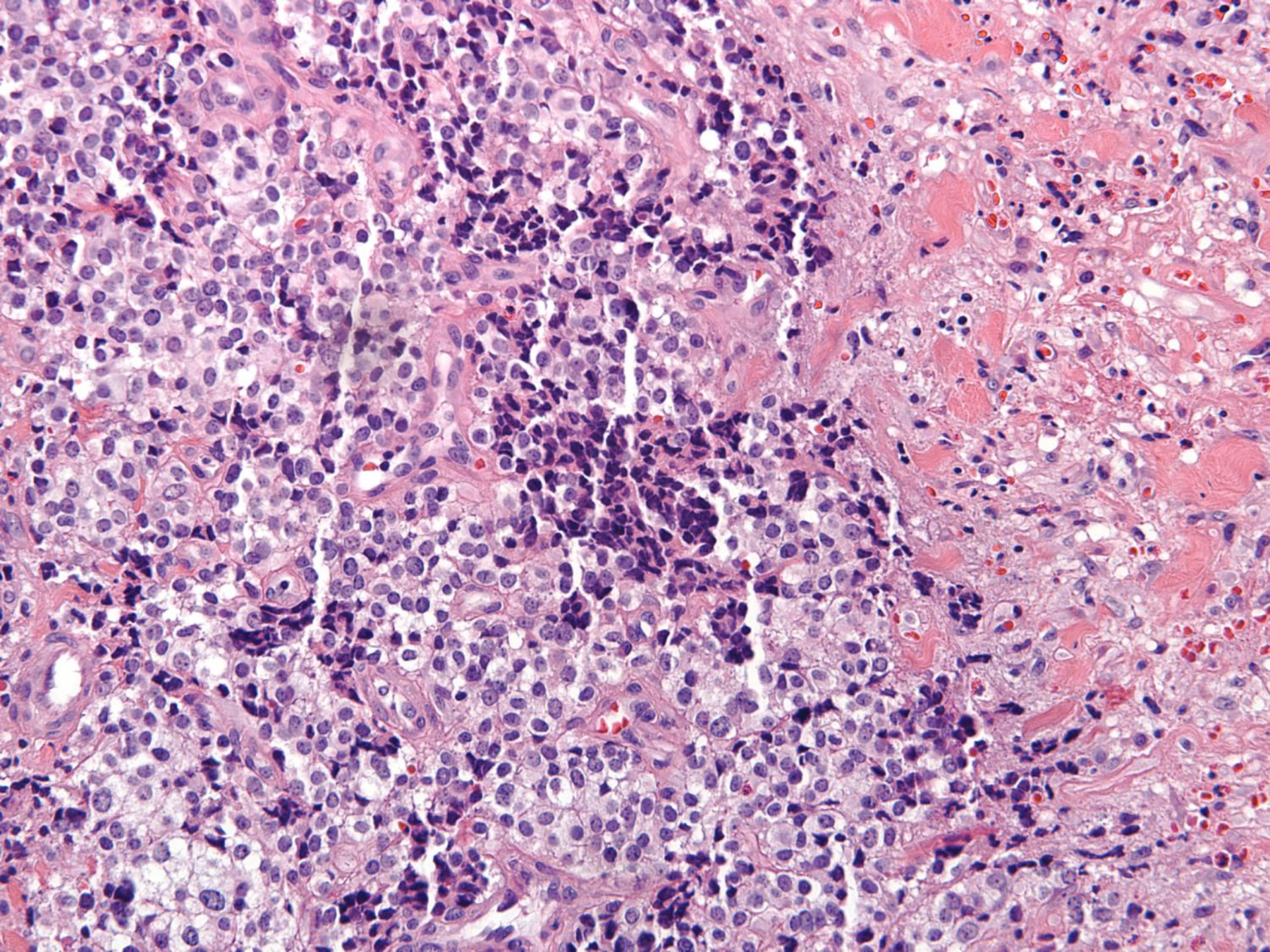
Jonathan Lavezo/Hannes Vogel/Don Born; Stanford

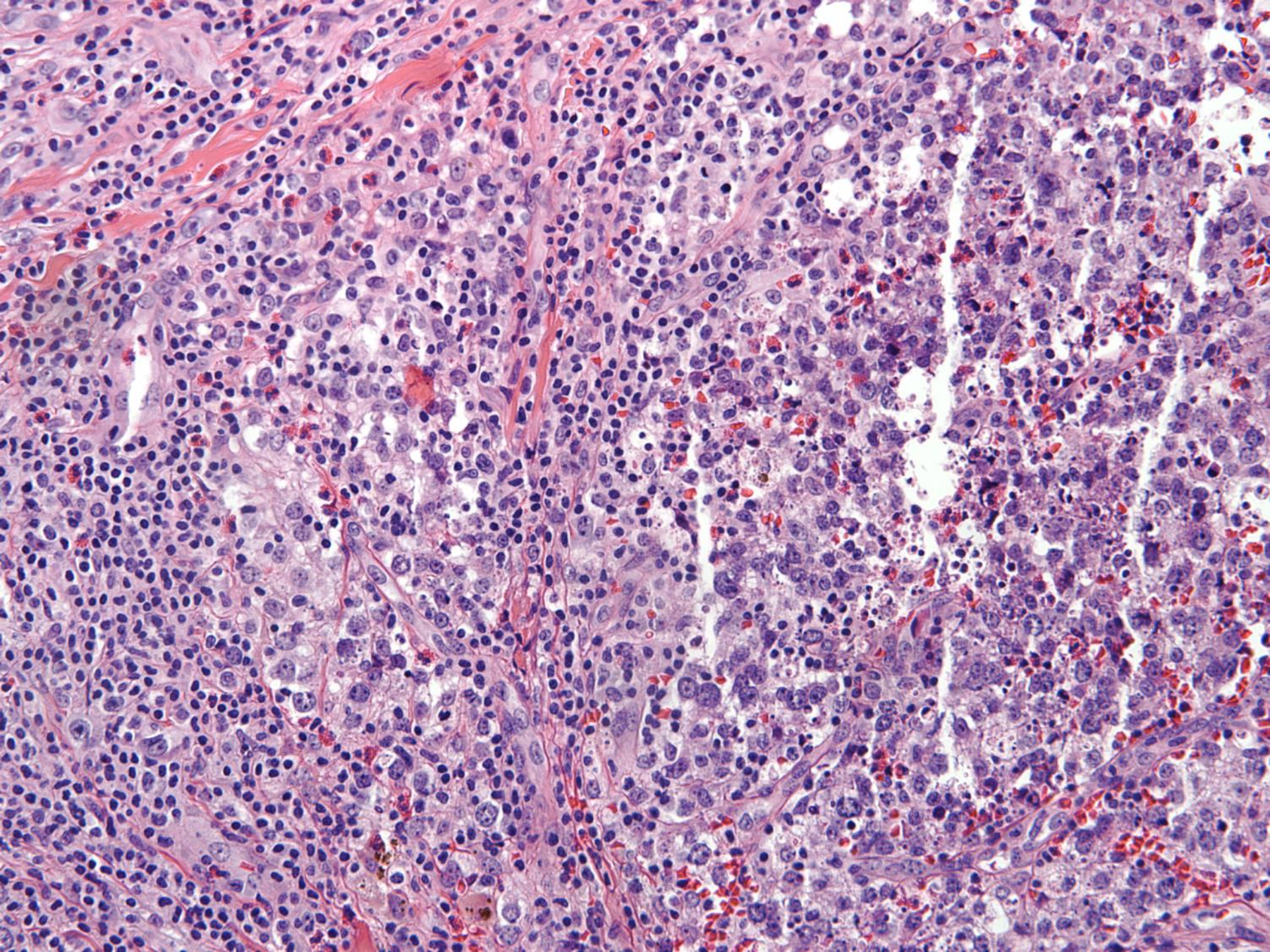
69-year-old woman with scalp mass.

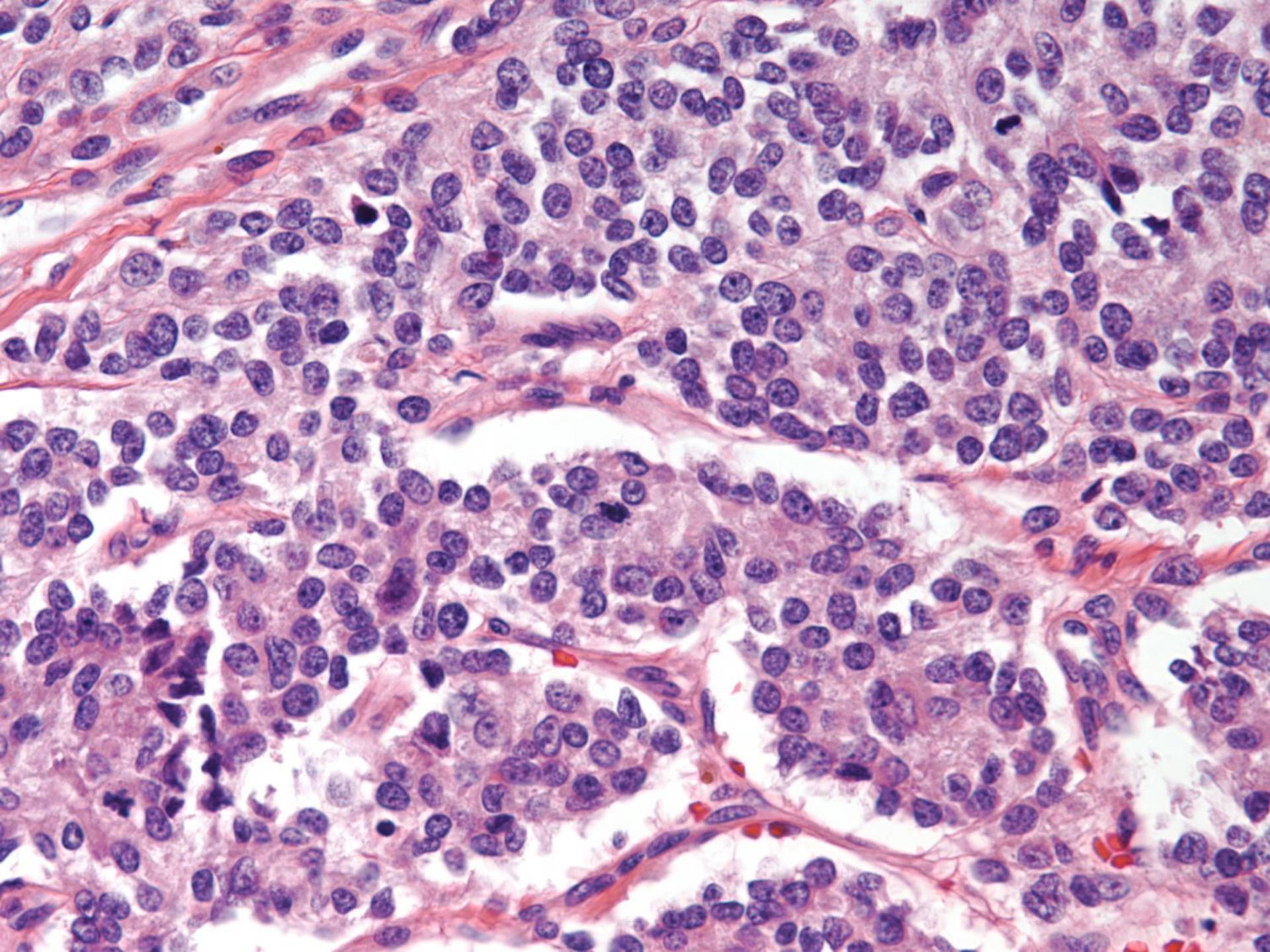


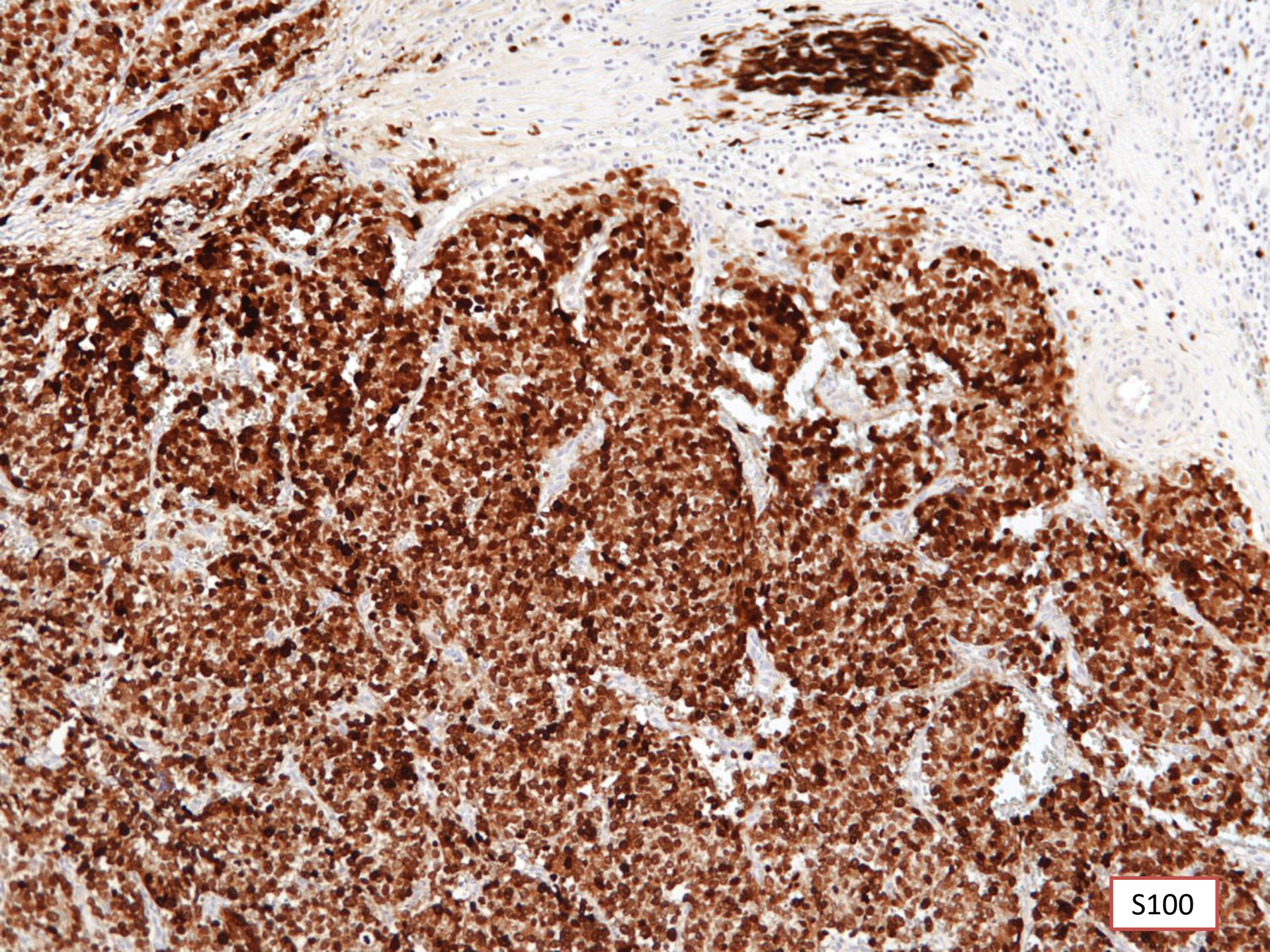




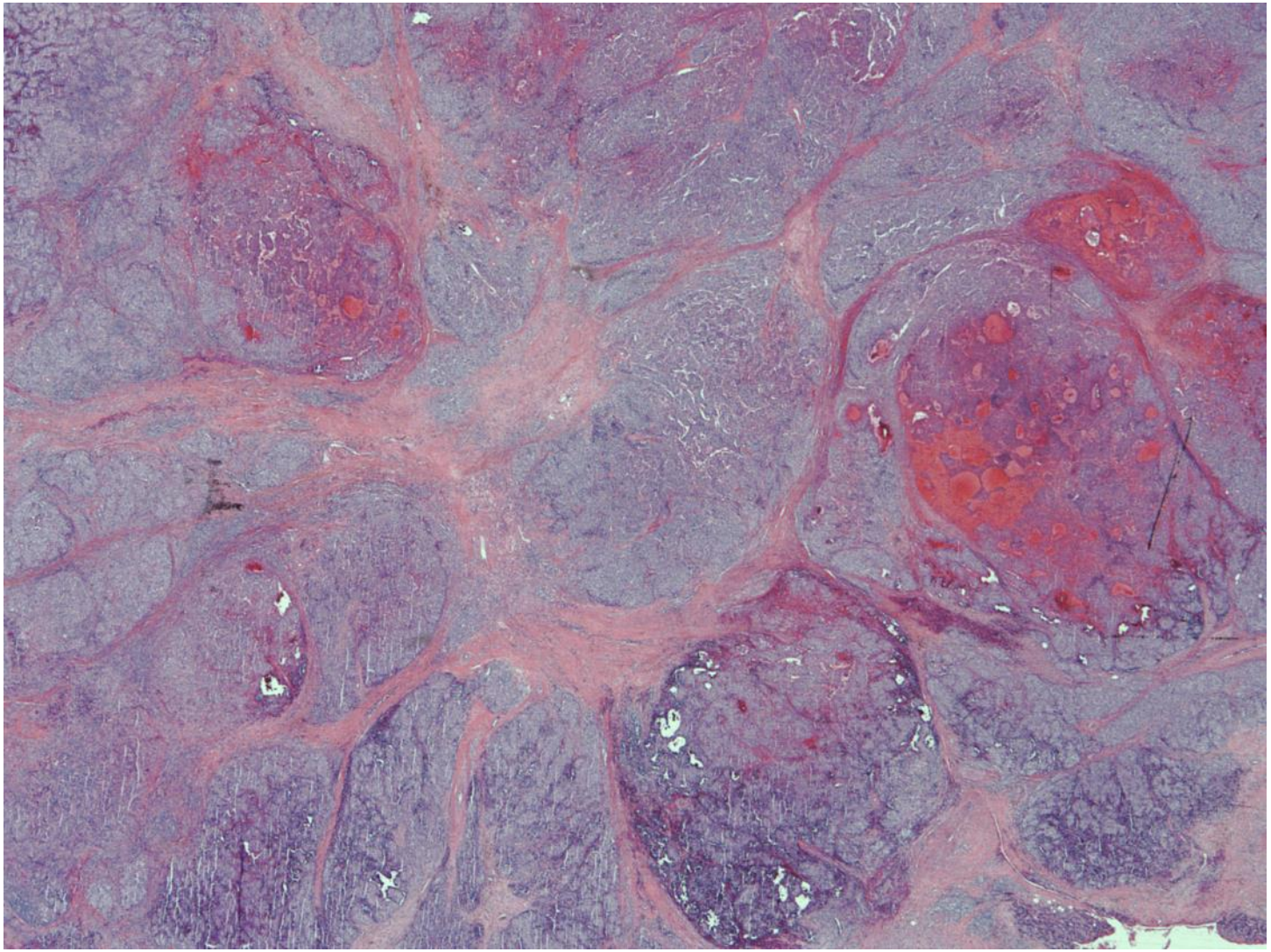


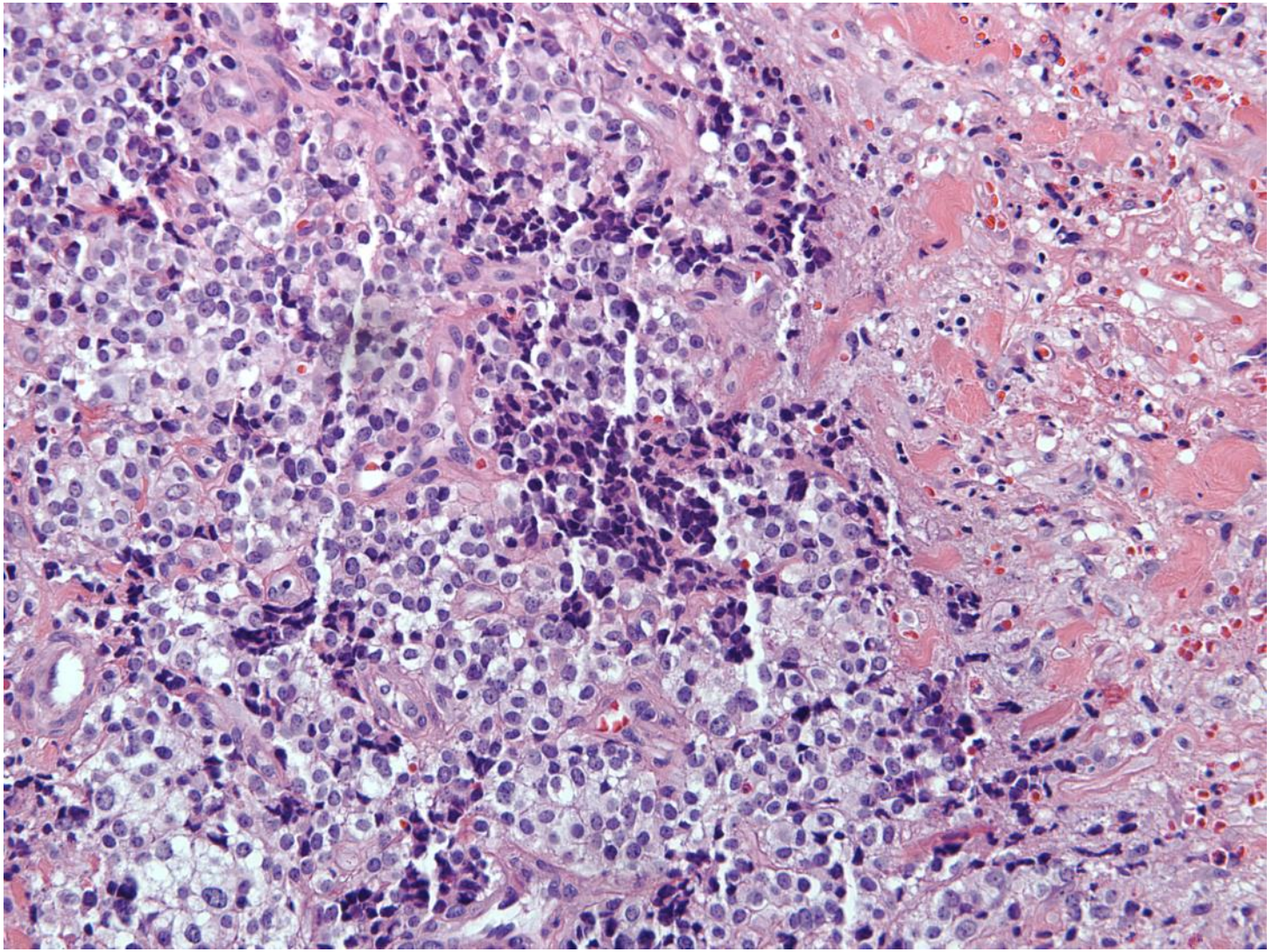





S100

DIAGNOSIS?



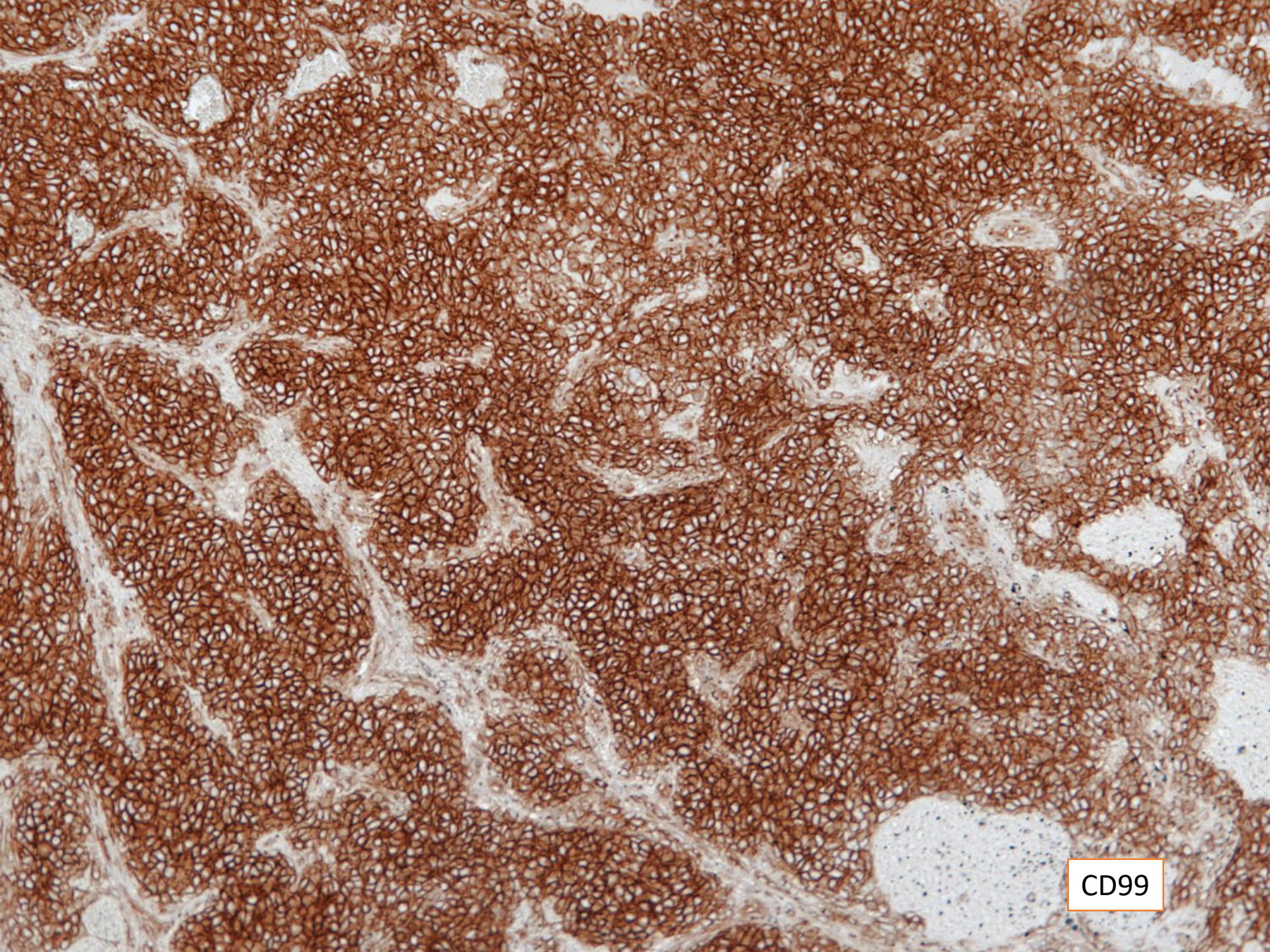


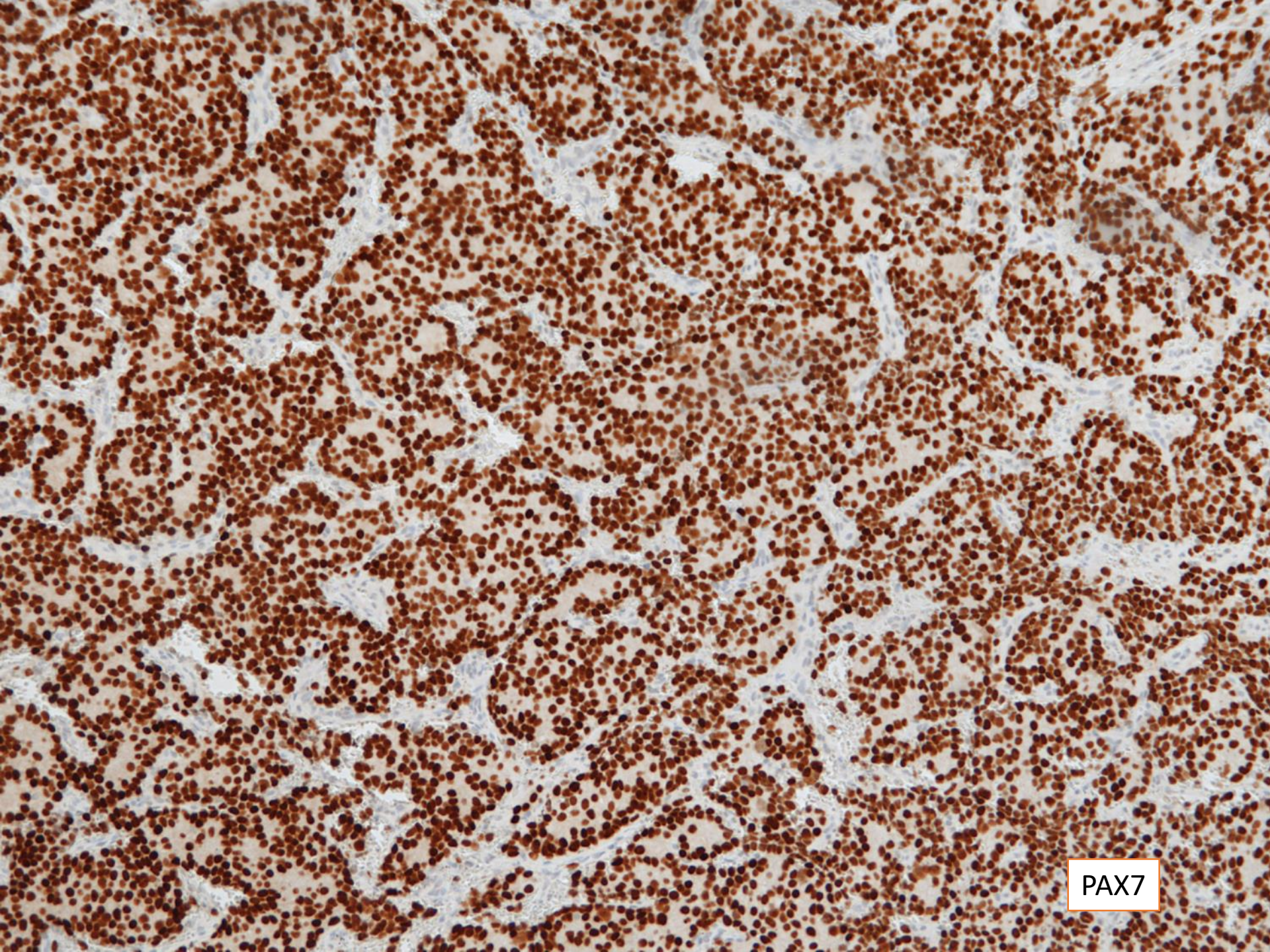
Differential Diagnosis

- Nerve sheath tumors
  - Malignant peripheral nerve sheath tumor
  - Cellular schwannoma
- Cellular Blue Nevus
- Malignant Melanoma
- Myoepithelial tumors
- Clear cell sarcoma
- Vascular tumor

Patient Clinical History

- 69 year-old female with personal and family history of breast cancer
- Noticed scalp mass in July 2017
- Grew and became painful (Nov 2017)
- Partial resection of 3 x 2 x 1.5cm vascular scalp mass (Dec 2017)
- Original pathology diagnosed as favor epithelioid malignant peripheral nerve sheath tumor
- Negative work-up for metastatic disease


CD99


PAX7

Primary Cutaneous Ewing Sarcoma

- Peripheral Primitive Neuroectodermal Tumor
- Characteristic small round cell morphology
- Atypical histologic patterns
  - Spindled, pseudoendothelialiomatous pattern with hemorrhage, sclerosing, and adamantinomatous-like
- May show aberrant S100 or keratins
- EWSR1-FLI1 rearrangement present

Primary Cutaneous Ewing Sarcoma Clinical

- Median age 17 years
- 66% in females
- Treatment
  - Surgery (ALL)
  - Adjuvant multiagent chemotherapy (69%)
  - Adjuvant chemoradiation (38%)
  - Adjuvant radiation (3%)

Primary Cutaneous Ewing Sarcoma Clinical

- Overall Survival – 93%
- 10-year probability of survival:
  - Estimated at 91% (95% CL 83-100)
- Unique outcomes with better prognosis than primary Ewing sarcoma of bone

Follow-Up

- Underwent neoadjuvant VDC
- Next steps are radiation therapy vs complete surgical excision
- No distant metastasis by PET

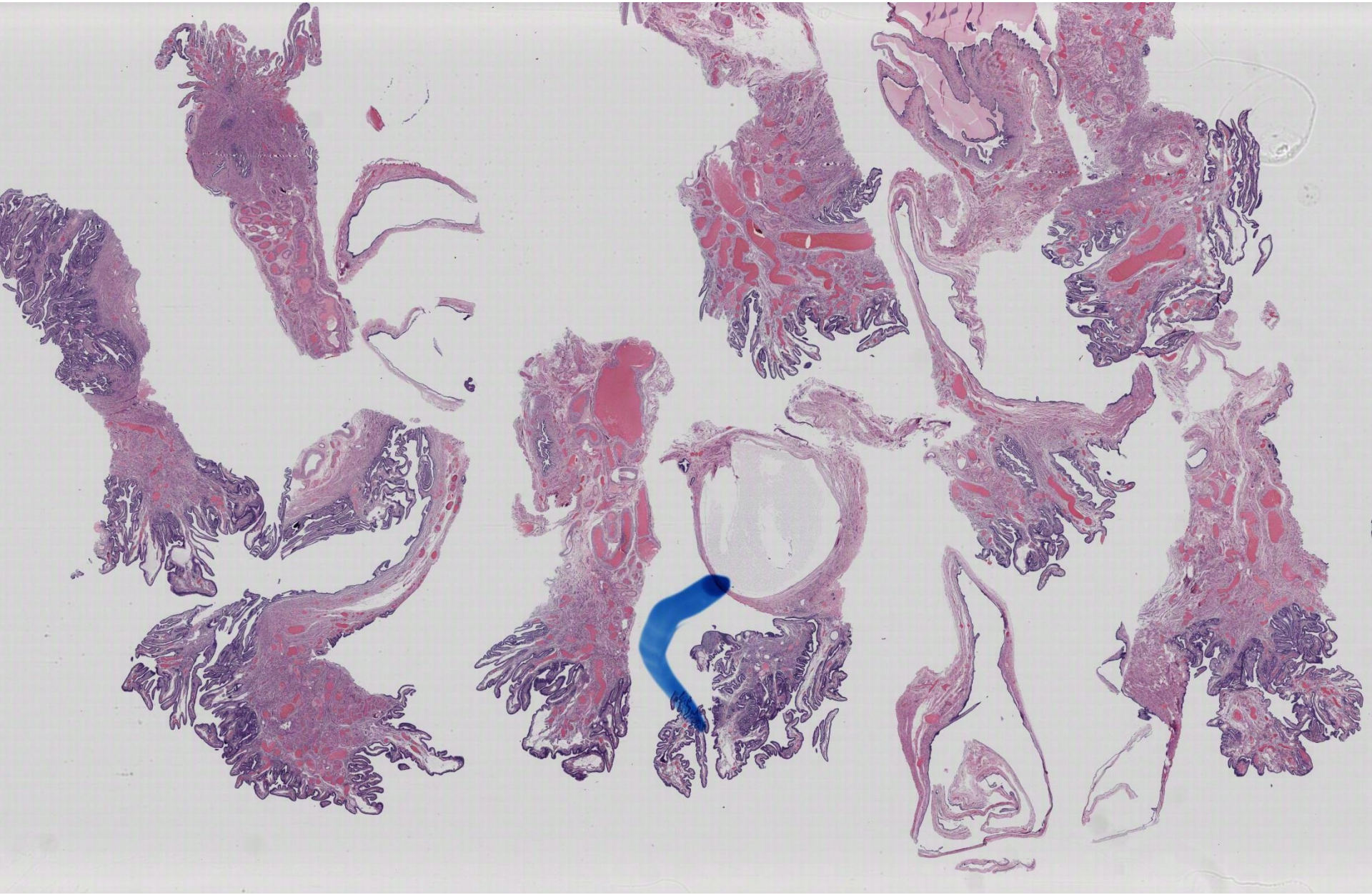
References

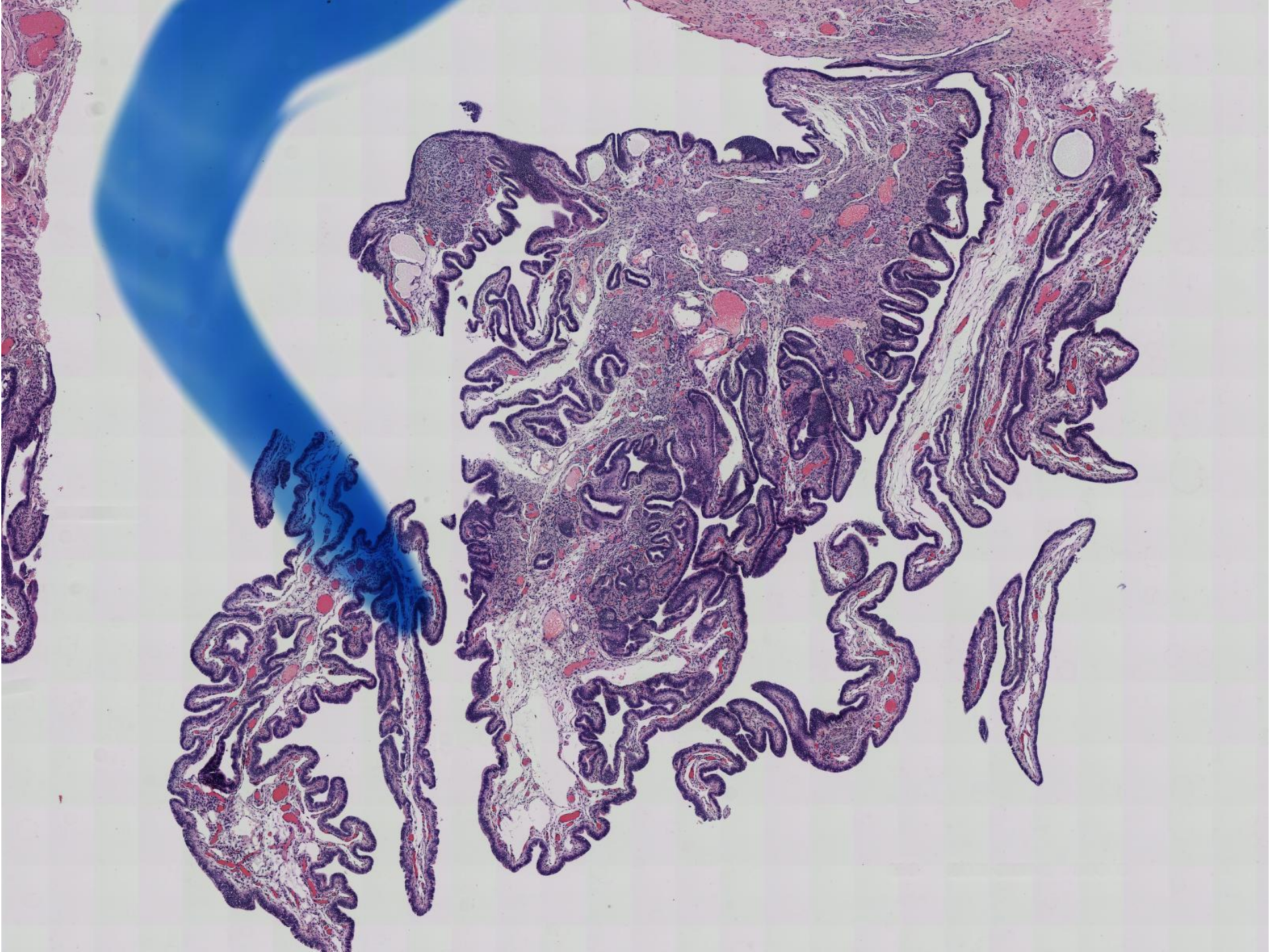
- Arnold, M.A., et al. Primary Subcutaneous Spindle Cell Ewing Sarcoma with Strong S100 Expression and EWSR1-FLI1 Fusion: A Case Report. Pediatric and Developmental Pathology. 17, 302-307 (2014)
- Delaplace, M. et al. Primary cutaneous Ewing Sarcoma: a systematic review focused on treatment and outcome. British Journal of Dermatology. 166, 721-726 (2011)

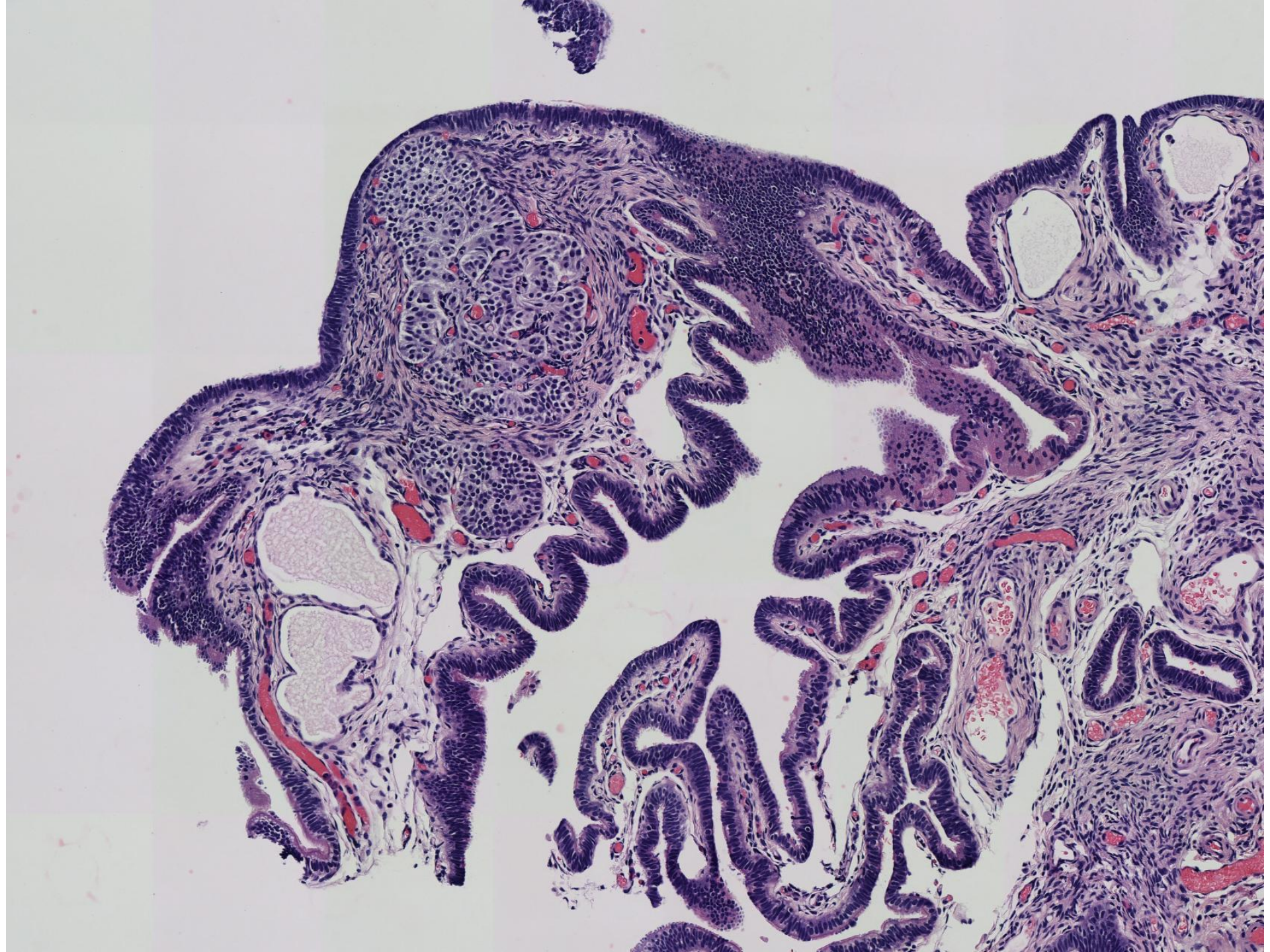
SB 6299
(scanned slide available)

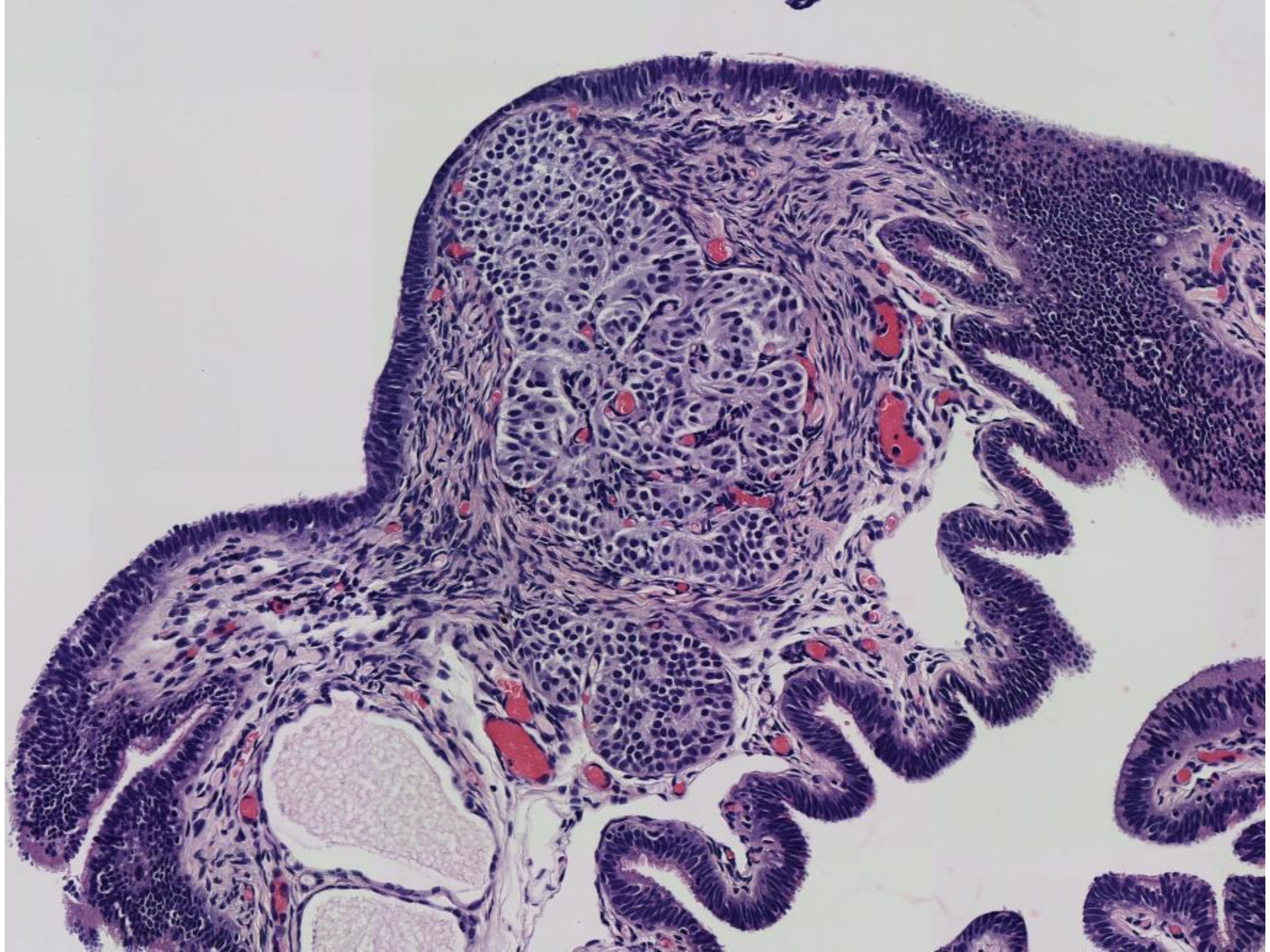
Ankur Sangoi; El Camino Hospital

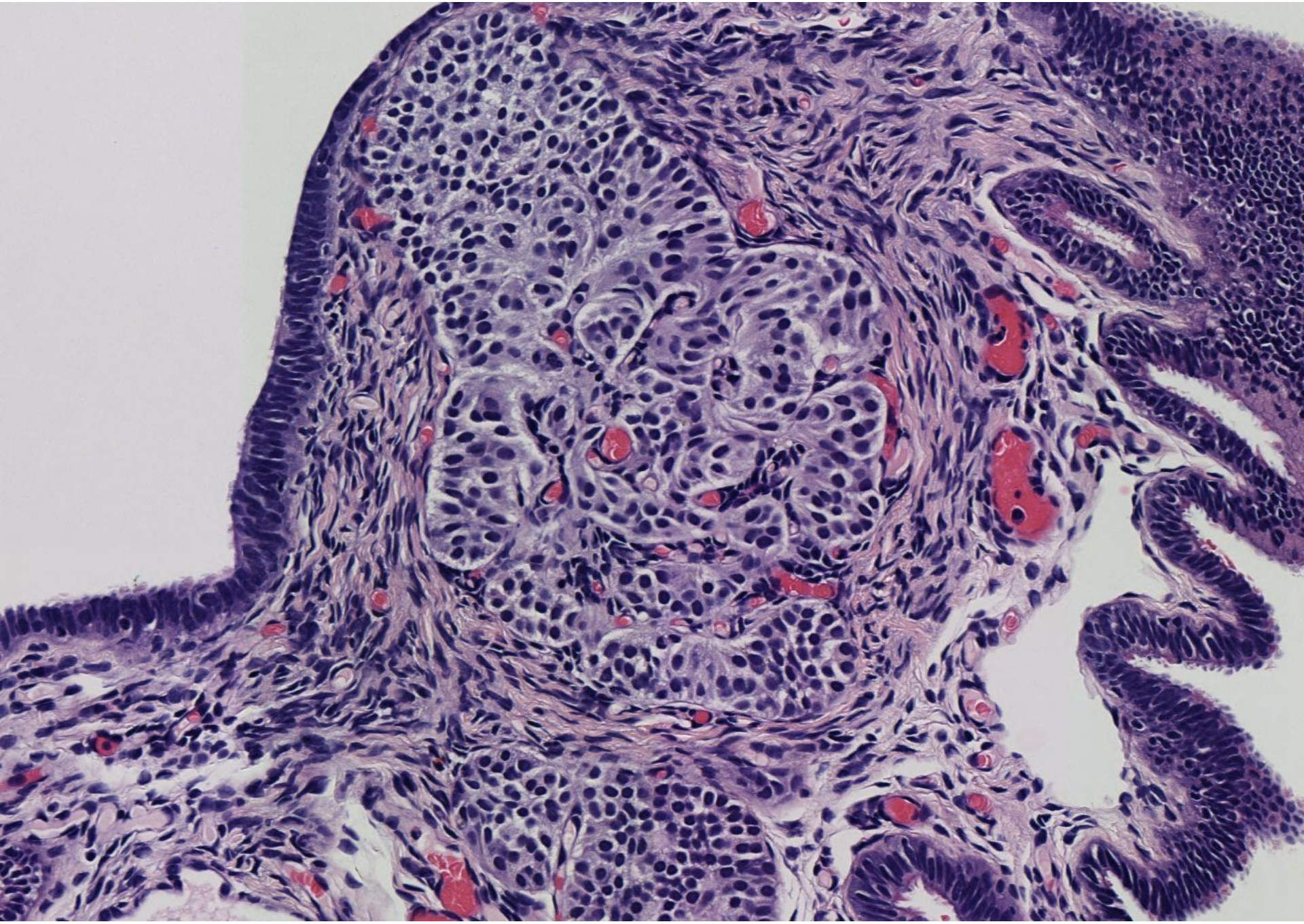
44-year-old woman with history of high stage breast cancer, found to be BRCA1 gene mutated. Undergoes risk-reducing bilateral salpingo-oophorectomy. Section of fallopian tube submitted.

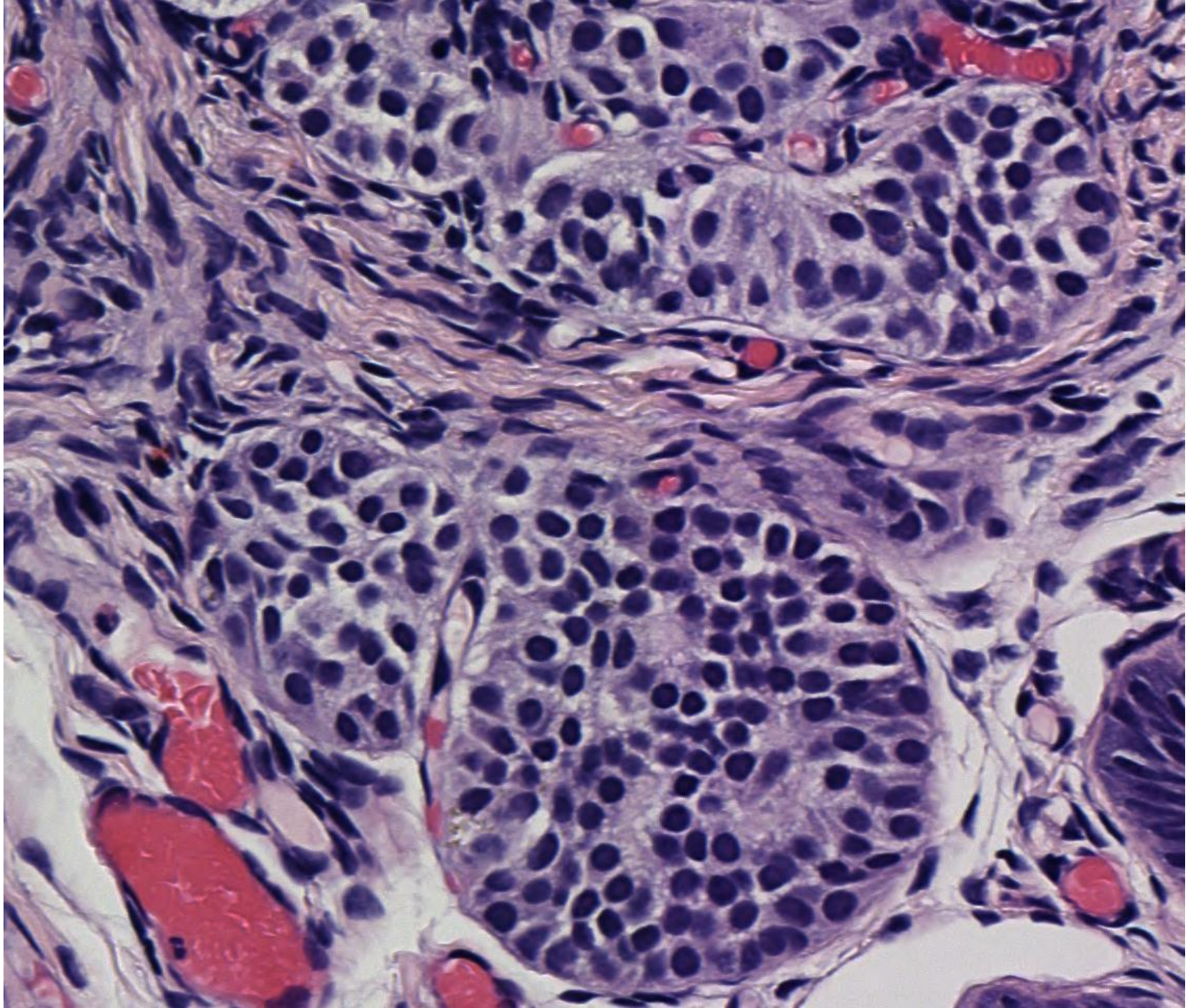


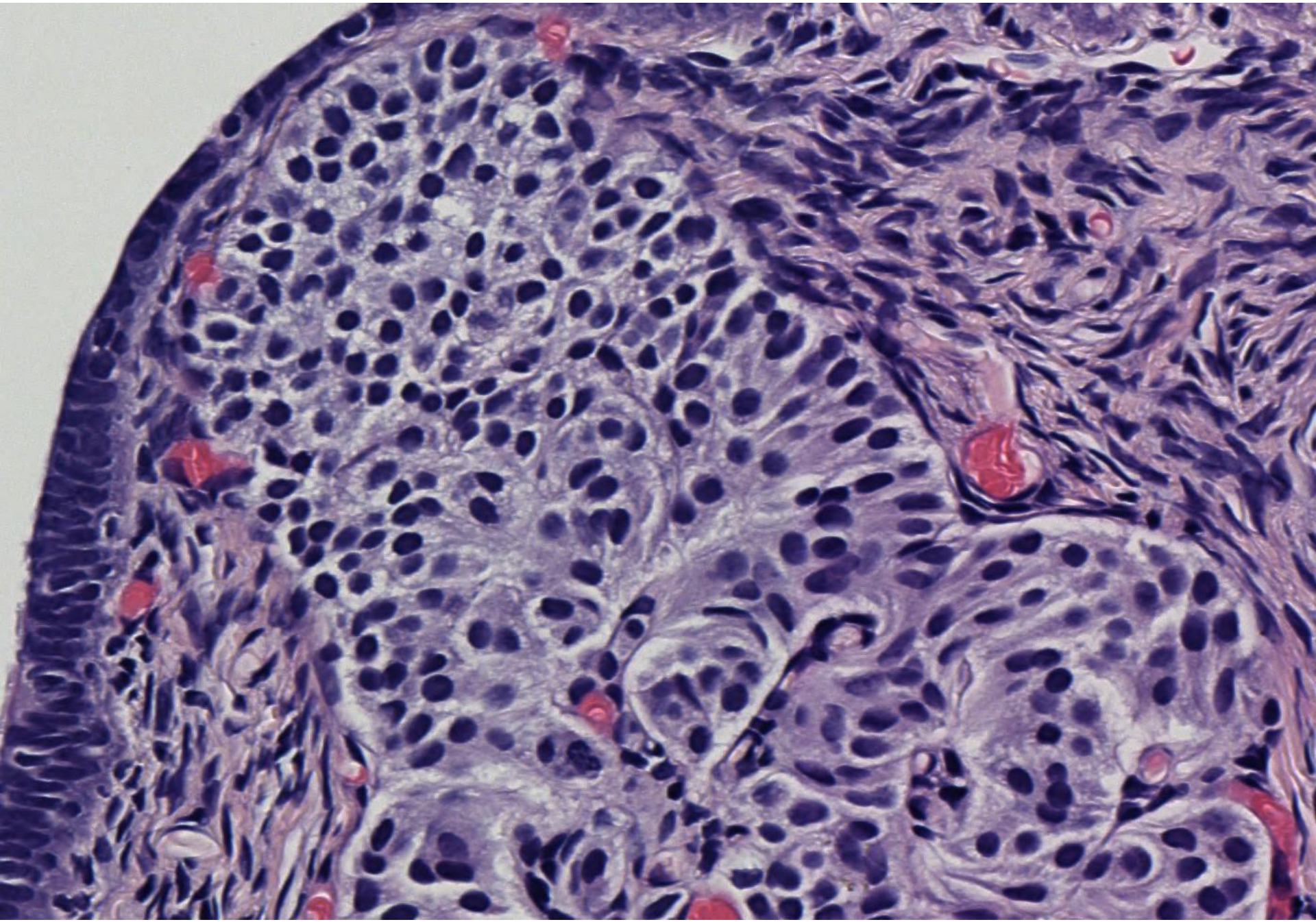








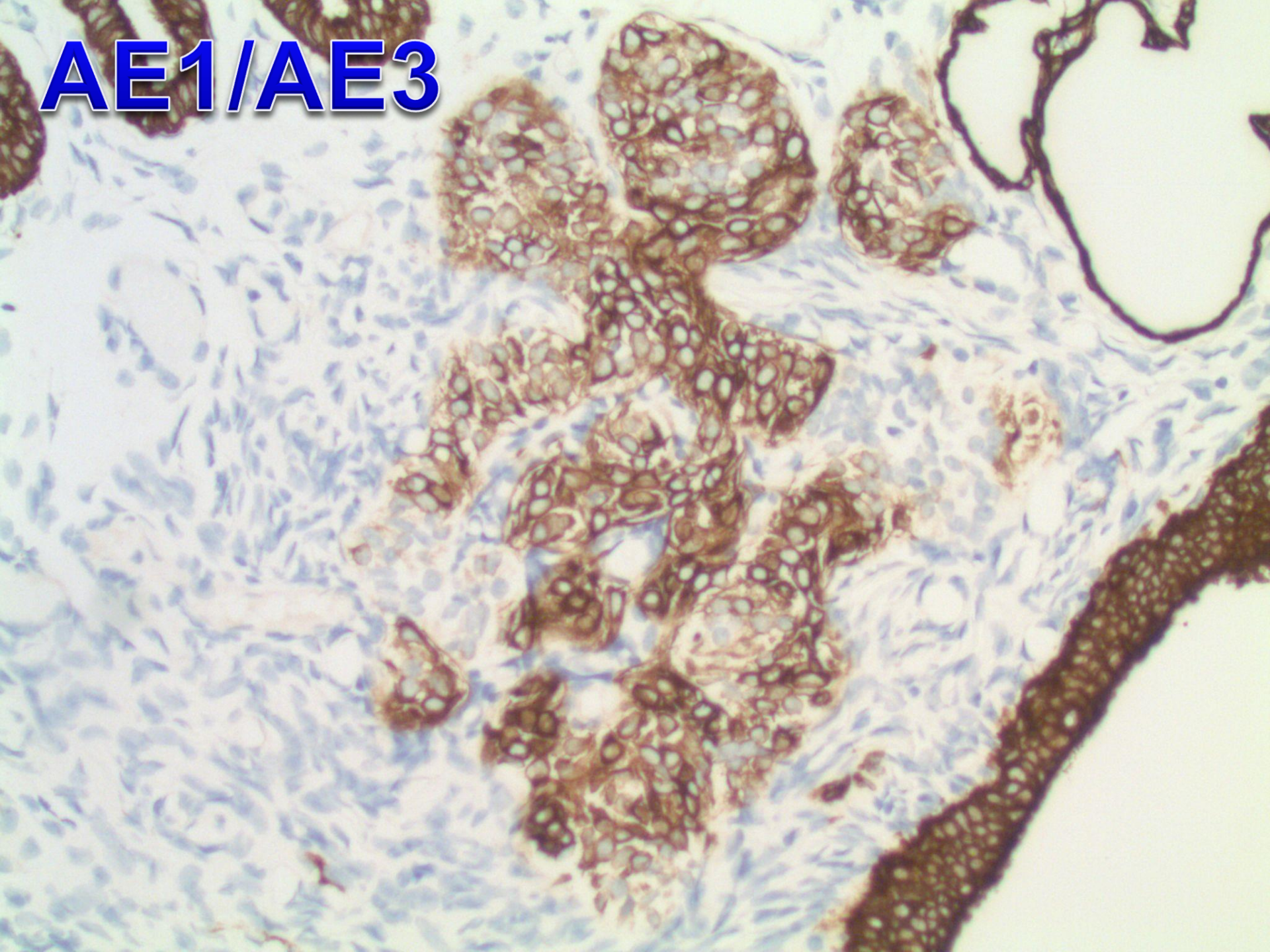


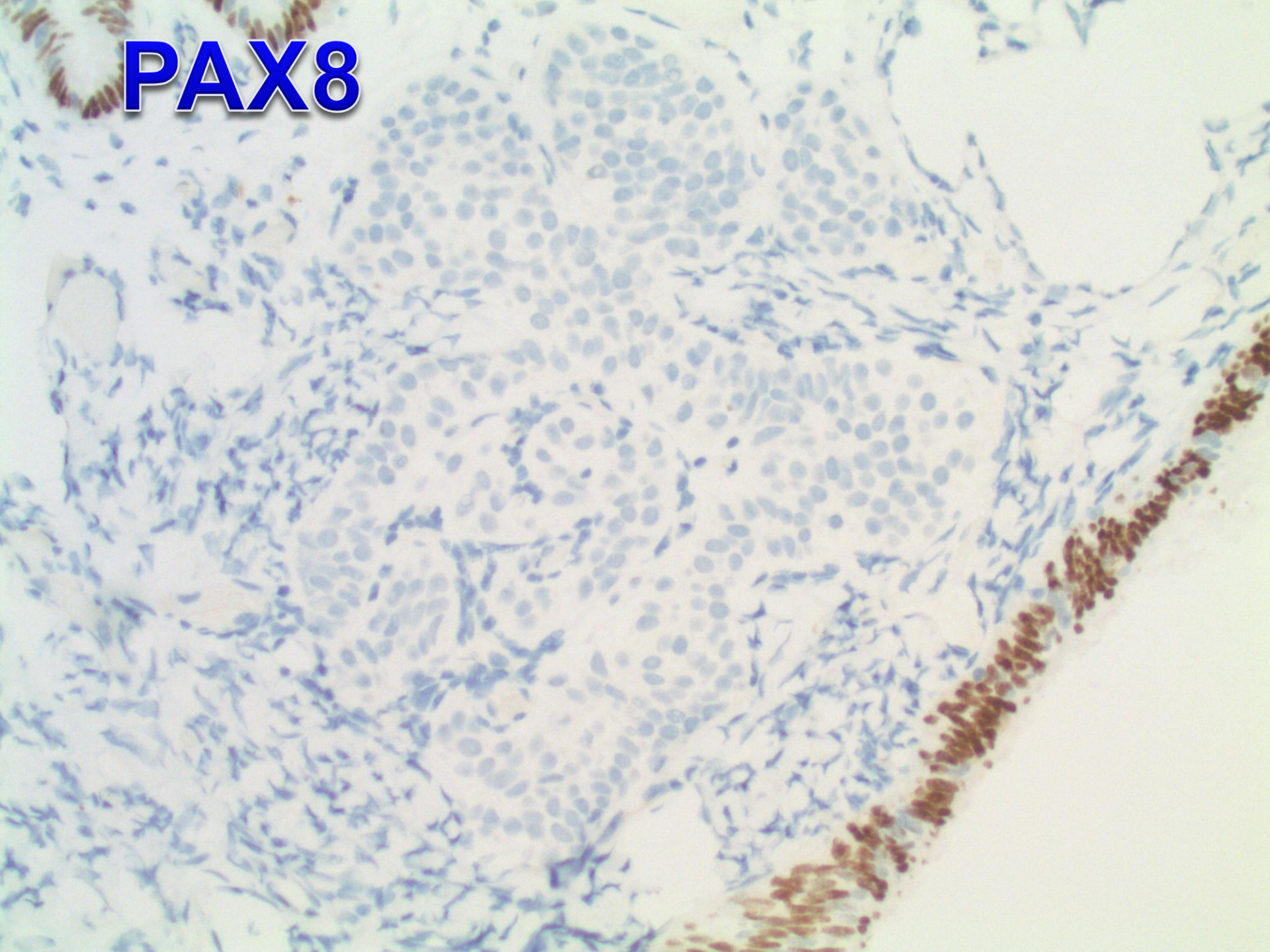


DIAGNOSIS?

DDx

- metastatic breast carcinoma
- tubal serous carcinoma
- Walthard rests
- extra-ovarian sex cord stromal proliferation
- paraganglioma
- neuroendocrine tumor


AE1/AE3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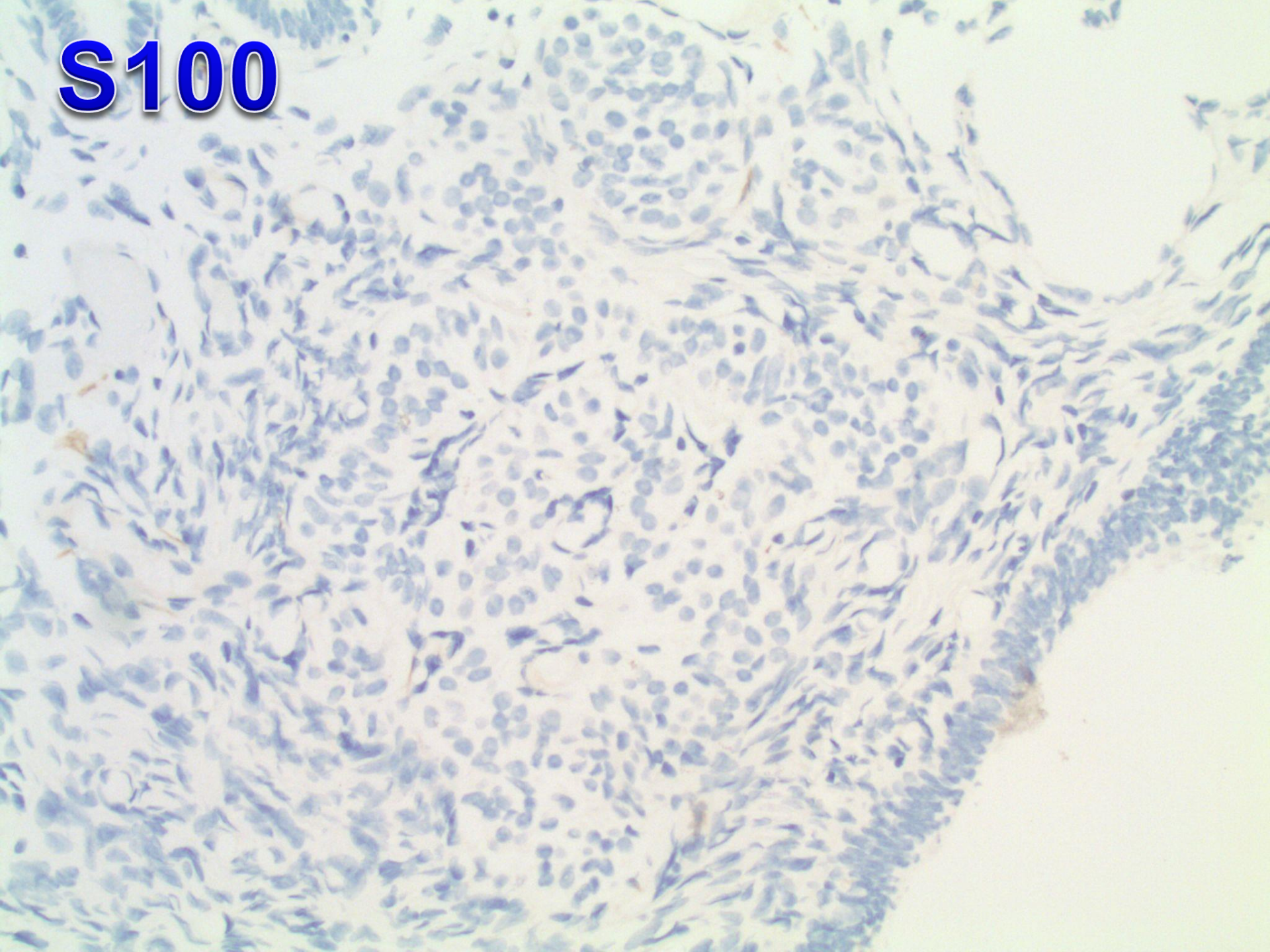
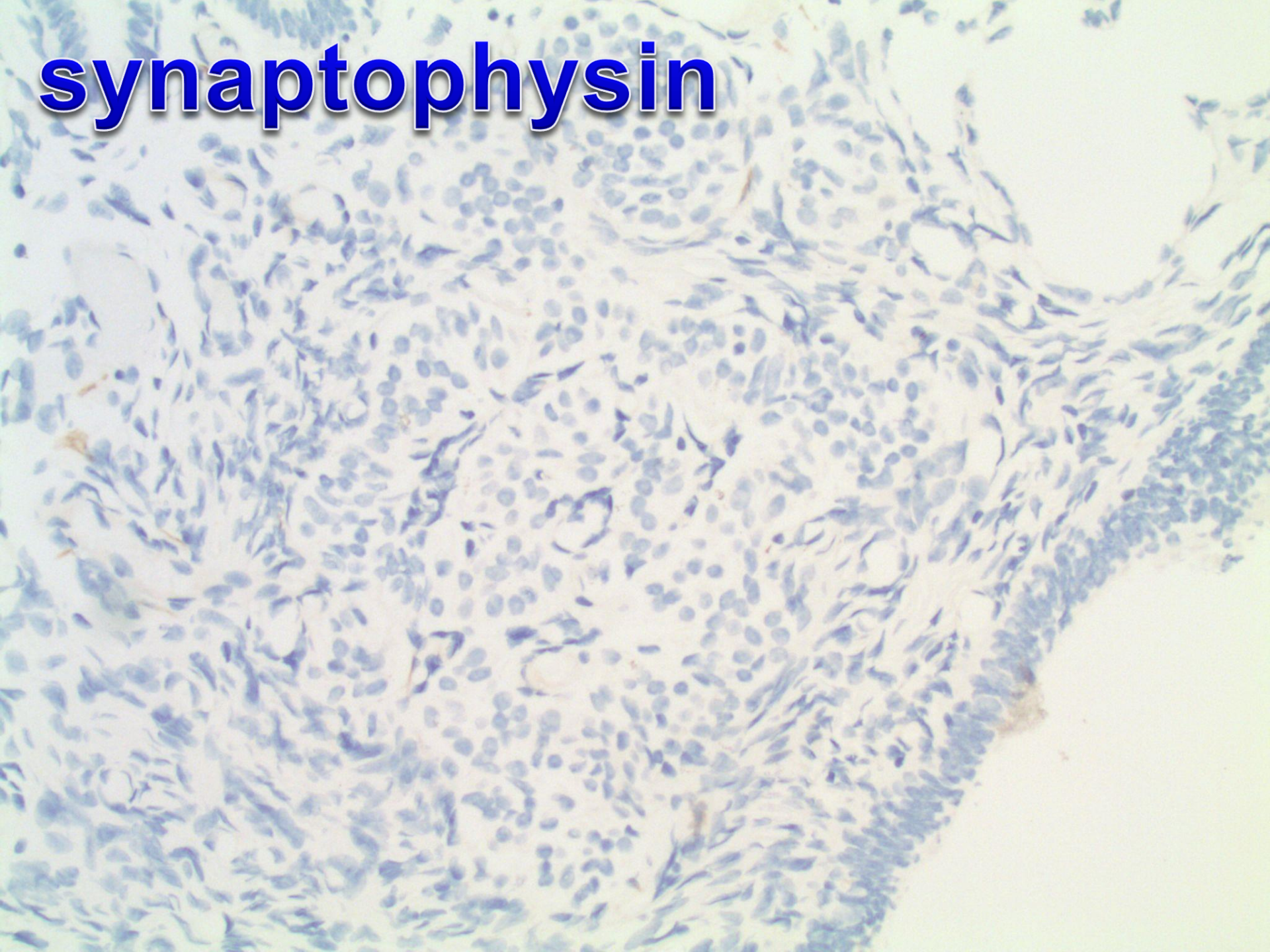
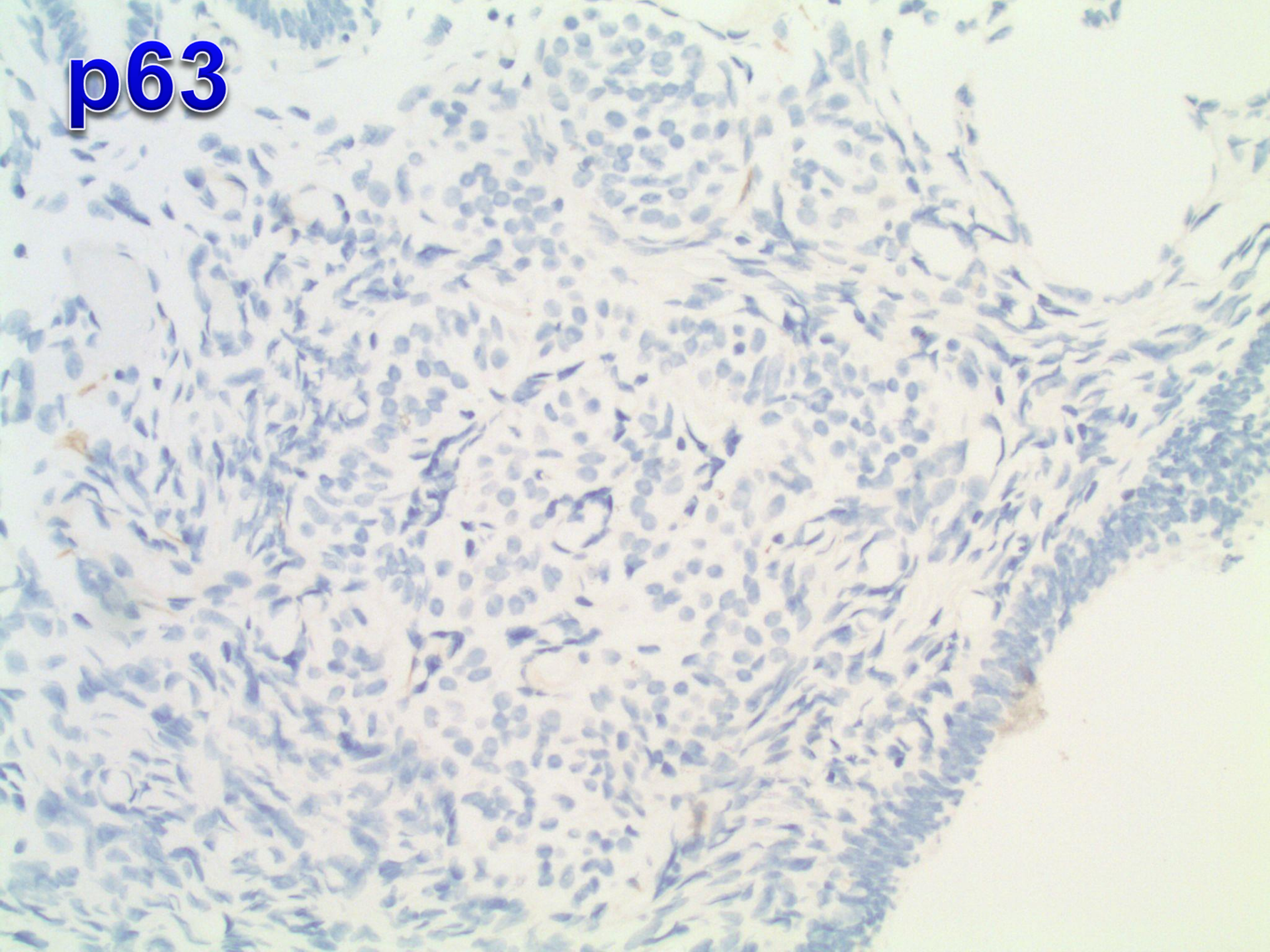
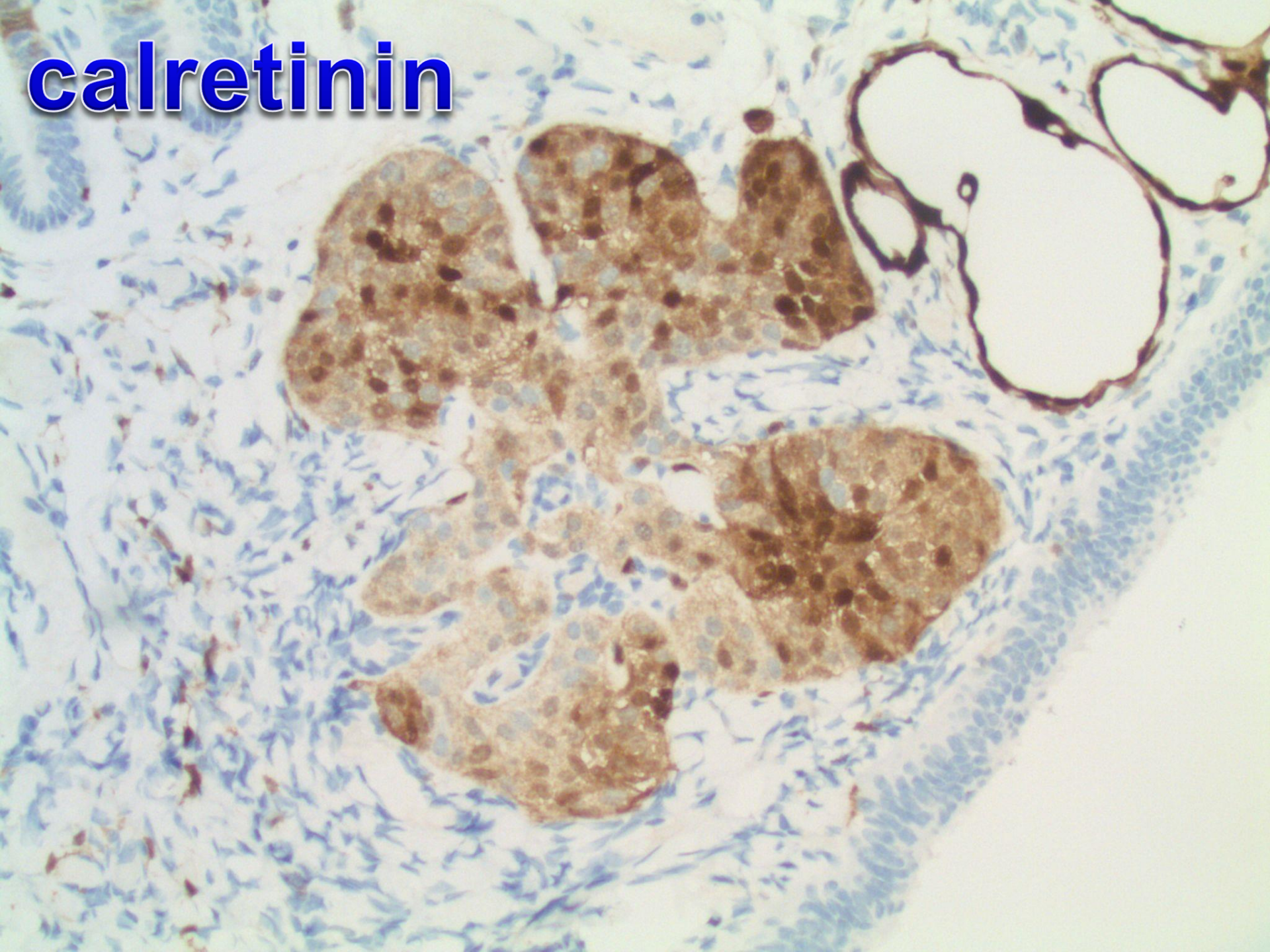
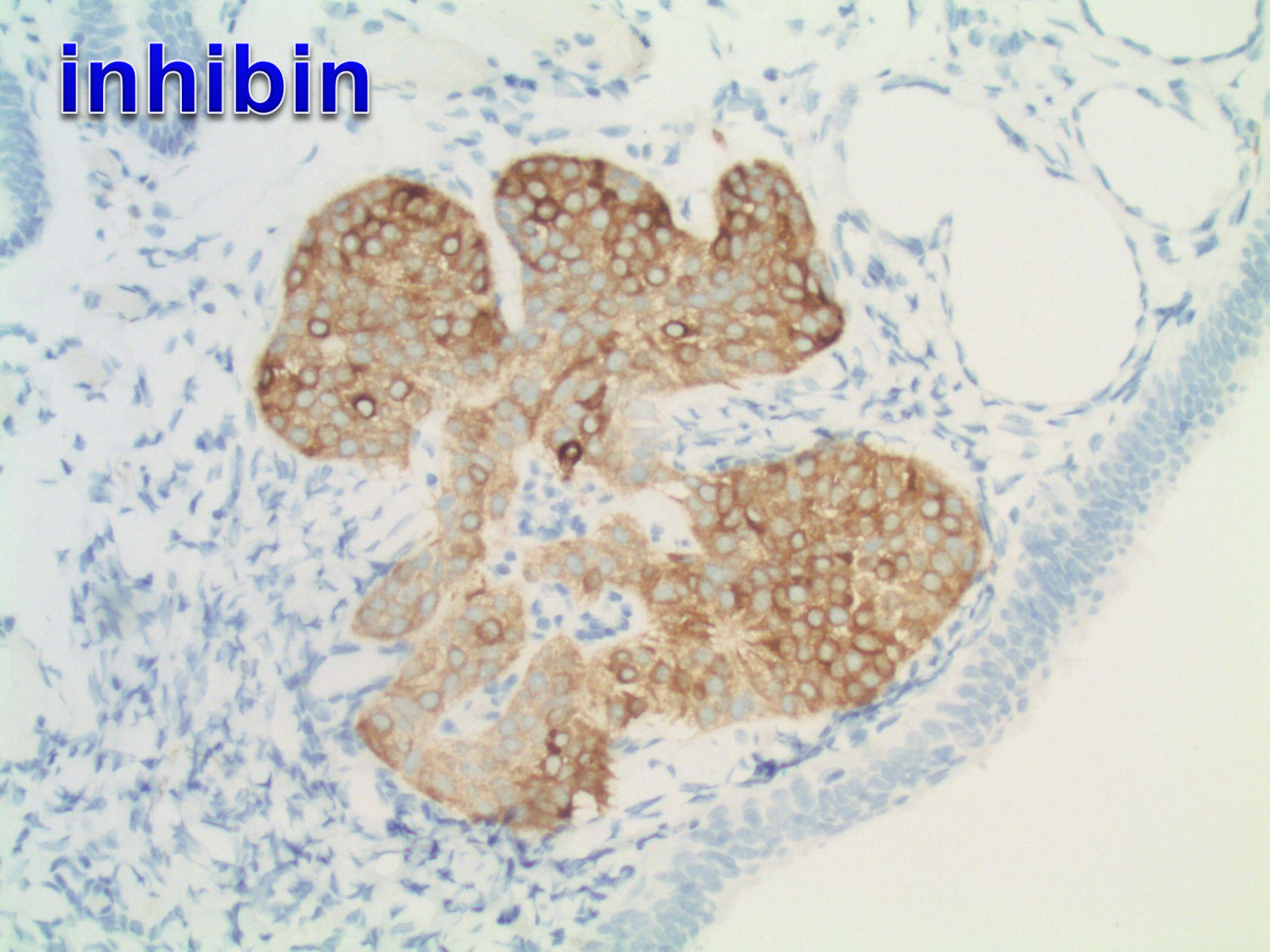
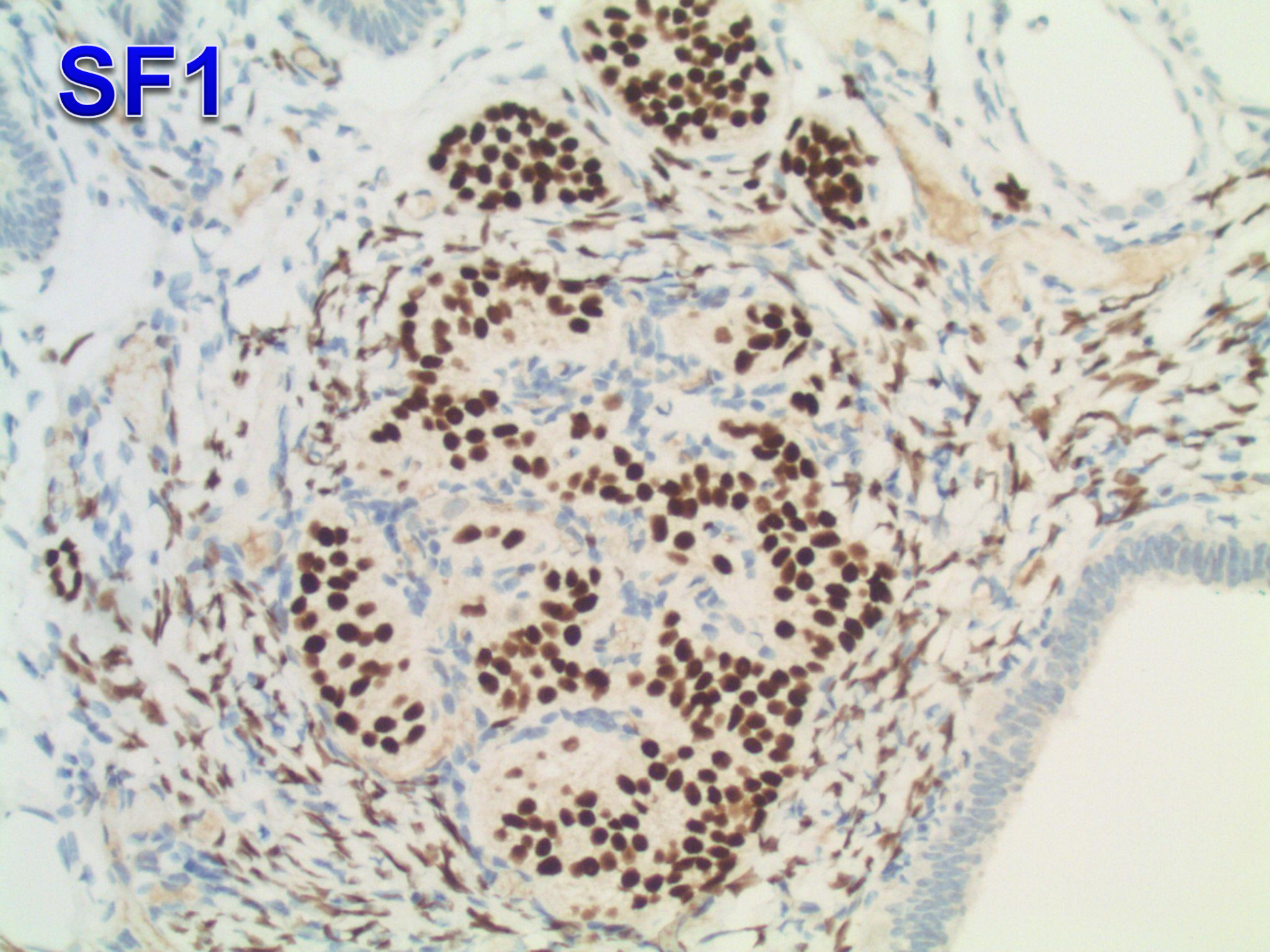

S100


synaptophysin


p63


calretinin


inhibin


SF1

Histopathology

Histopathology 2015, **66**, 555–564. DOI: 10.1111/his.12580

Microscopic extraovarian sex cord proliferations: an undescribed phenomenon

W Glenn McCluggage,[1] Colin J R Stewart,[2] Jean Iacobelli,[2] Anita Soma,[2] Kathleen R Cho,[3] Mark K Heatley,[4] Adam Boyde[5] & Blaise A Clarke[6]

[1]*Department of Pathology, Belfast Health and Social Care Trust, Belfast, UK,* [2]*Department of Pathology, King Edward Memorial Hospital, Perth, WA, Australia,* [3]*Department of Pathology, University of Michigan Medical School, Ann Arbor, MI, USA,* [4]*Department of Pathology, St James's Hospital, Leeds, UK,* [5]*Department of Pathology, University of Hospital, Cardiff, UK, and* [6]*Department of Laboratory Medicine and Pathobiology, University Health Network, University of Toronto, Toronto, ON, Canada*

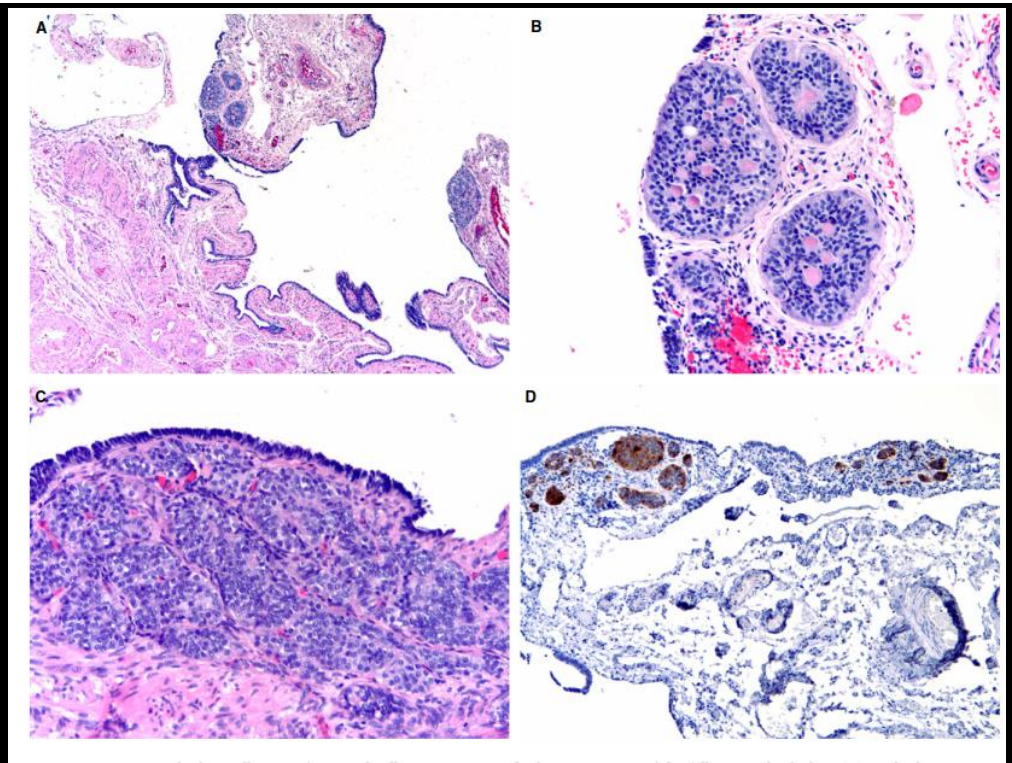


Table 1. Clinicopathological features of the cases in this study

Case	Age (years)	Indication for surgery	Operative procedure	Location of sex cord proliferations	Immunohistochemistry	Follow-up
1	58	Unknown	Bilateral salpingo-oophorectomy	Fallopian tube fimbria	Positive for inhibin and calretinin; negative for chromogranin and p63	48 months
2	39	Uterine fibroids and menorrhagia	Hysterectomy and bilateral salpingectomy	Fallopian tube fimbria	Positive for inhibin and calretinin	Recent case
3	48	Presumed acute appendicitis	Appendicectomy	Appendiceal serosa	Positive for inhibin, calretinin, WT1, and MNF116; negative for EMA and CD56	Recent case
4	23	Ovarian cysts and ? pelvic endometriosis	Bilateral cystectomies and pelvic side wall biopsy	Right pelvic side wall	Diffusely positive for inhibin, calretinin, SF1, WT1, ER, PR, and AE1/3; focally positive for CD56 and CD99; negative for p63, chromogranin, and synaptophysin	11 months
5	58	Endometrial carcinoma	Hysterectomy and bilateral salpingo-oophorectomy	Para-ovarian connective tissues and ovarian capsular adhesions	Diffusely positive for inhibin, SF1, WT1, ER, PR, and AE1/3; focally positive for calretinin, CD56, and CD99; negative for p63, chromogranin, and synaptophysin	2 years
6	39	Uterine fibroids	Hysterectomy and bilateral salpingo-oophorectomy	Fallopian tube	None performed	6 years

Microscopic Heterotopic Extraovarian Sex Cord–Stromal Proliferations: Expanding the Histologic Spectrum

Aisling Longworth, B.Sc., M.B.Ch.B, M.R.C.P., Raji Ganesan, M.B.B.S., F.R.C.Path., Adrian K.H. Yoong, M.B.B.Chir., F.R.C.Path., and Lynn Hirschowitz, M.B.B.Ch., F.R.C.Path.

Summary: Microscopic, heterotopic extraovarian sex cord–stromal proliferations have only recently been reported in the literature. We describe the largest series to date, of 30 cases of microscopic, incidentally detected, heterotopic extraovarian sex cord–stromal proliferation, in women aged 25–79 yr who had undergone surgery for a range of benign and malignant gynecologic conditions. In 14 patients the foci of proliferation comprised ovarian cortical stroma, in some cases with an ovarian fibroma-like appearance. Ten cases of adenofibroma and cystadenofibroma were also identified, including 1 Brenner adenofibroma; 2 cases comprised both ovarian cortical stroma and serous cystadenofibroma; 4 cases showed sex cord proliferation resembling microscopic adult granulosa cell tumors. Immunohistochemistry, where possible, confirmed the sex cord nature of the heterotopic proliferations. The foci of proliferation were < 1–7 mm, and most were at the fimbrial end of the fallopian tube. These proliferations are likely to be encountered with increasing frequency as we sample the adnexa more extensively. Previous reports postulated that the proliferations probably represent embryonic rests caused by anomalous migration but we suggest that incorporation of exposed ovarian parenchymal tissue into the fimbrial stroma at the time of ovulation may be another possible cause. **Key Words:** Extraovarian site—Fallopian tube—Sex cord–stromal proliferation—Immunohistochemistry.

International Journal of Gynecological Pathology
37:35–43, Lippincott Williams & Wilkins, Baltimore

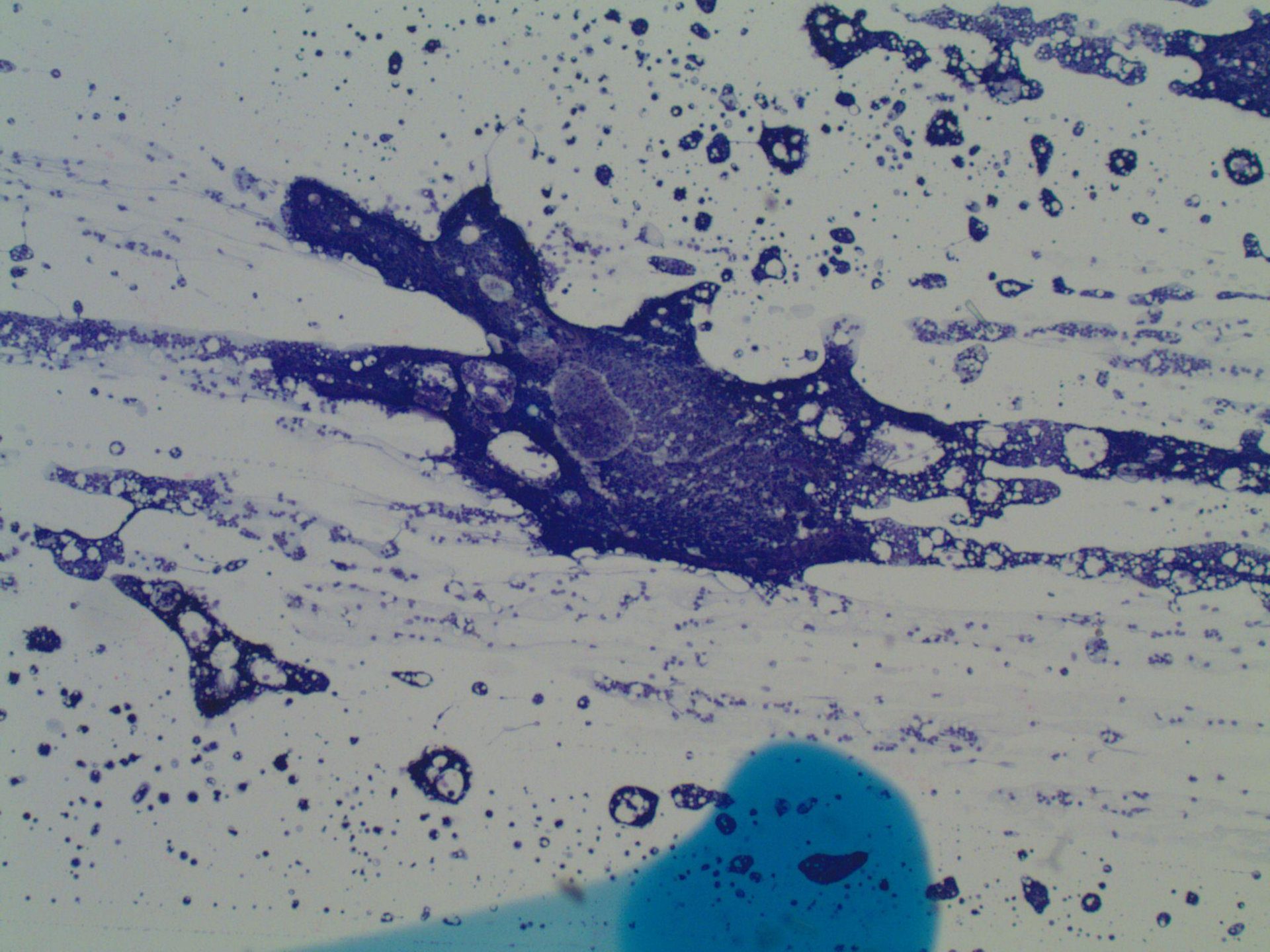
Extra-ovarian sex cord stromal proliferations

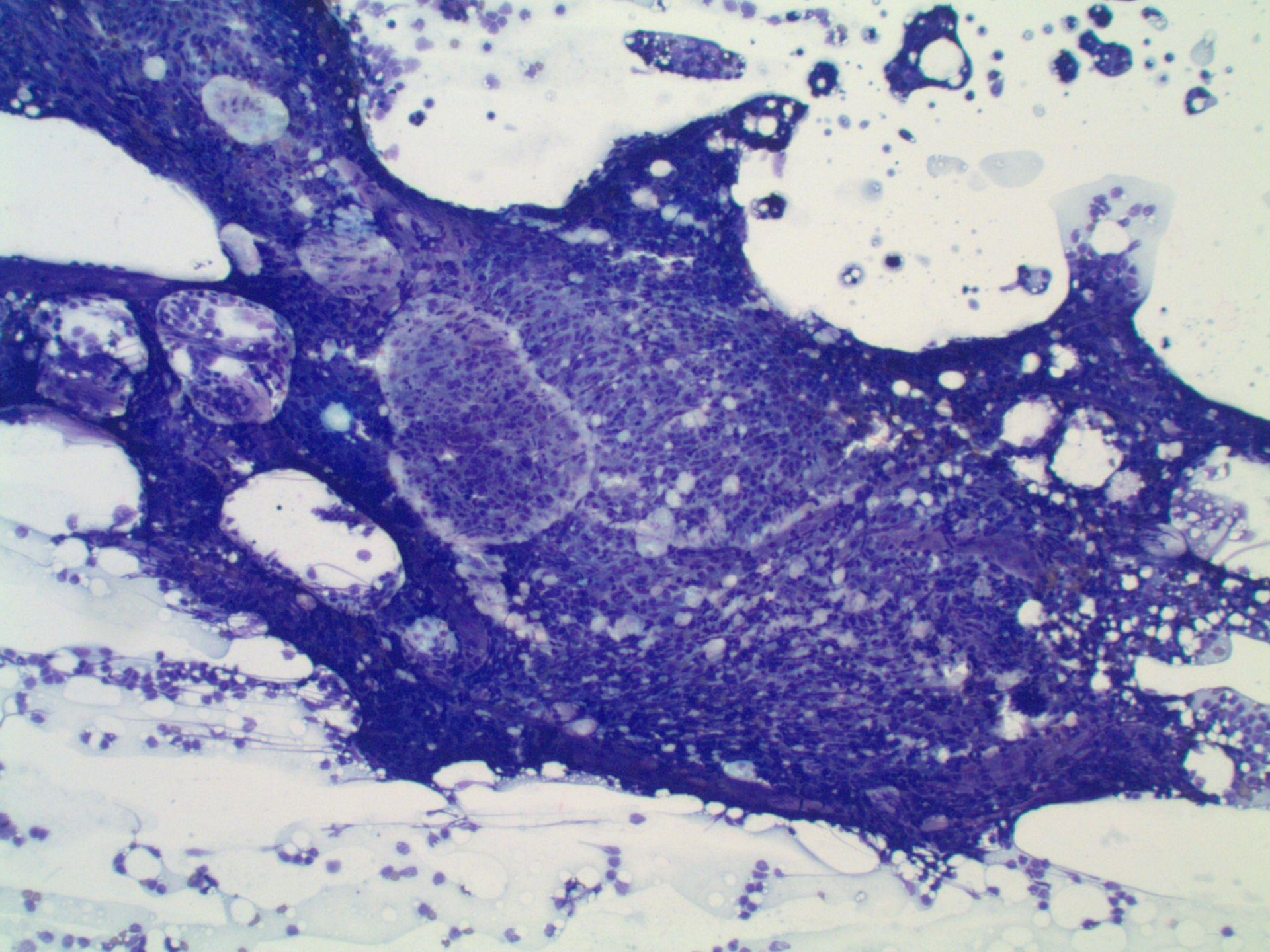
- **Historically uncommon**
  - Likely increasing frequency given more extensive adnexal histologic sampling
- **Etiology?**
  - Embryonic rests caused by anomalous migration
  - Exposed ovarian parenchymal tissue into fimbria at time of ovulation
- **Benign, incidental findings**

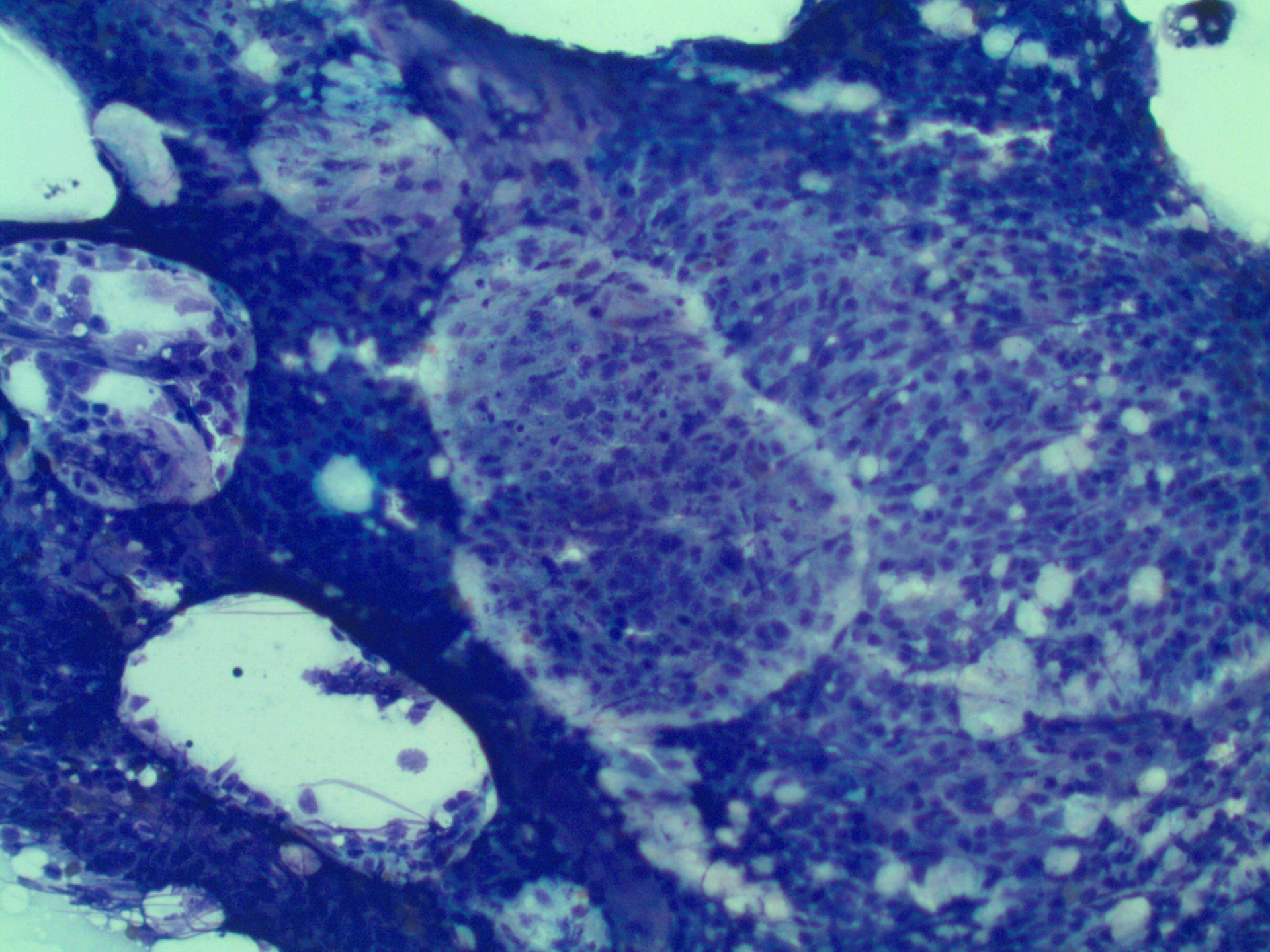
SB 6300

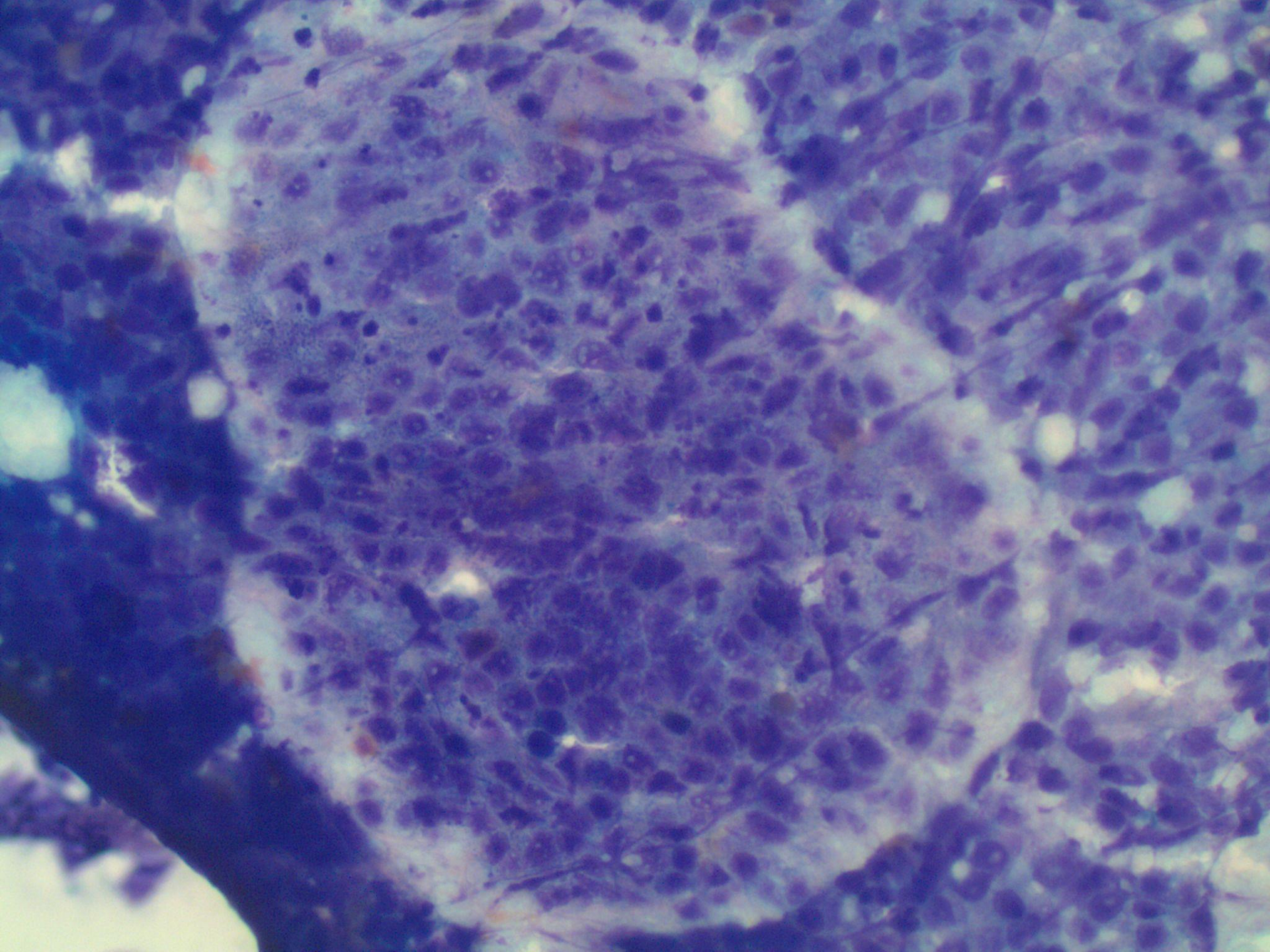
Ankur Sangoi; El Camino Hospital

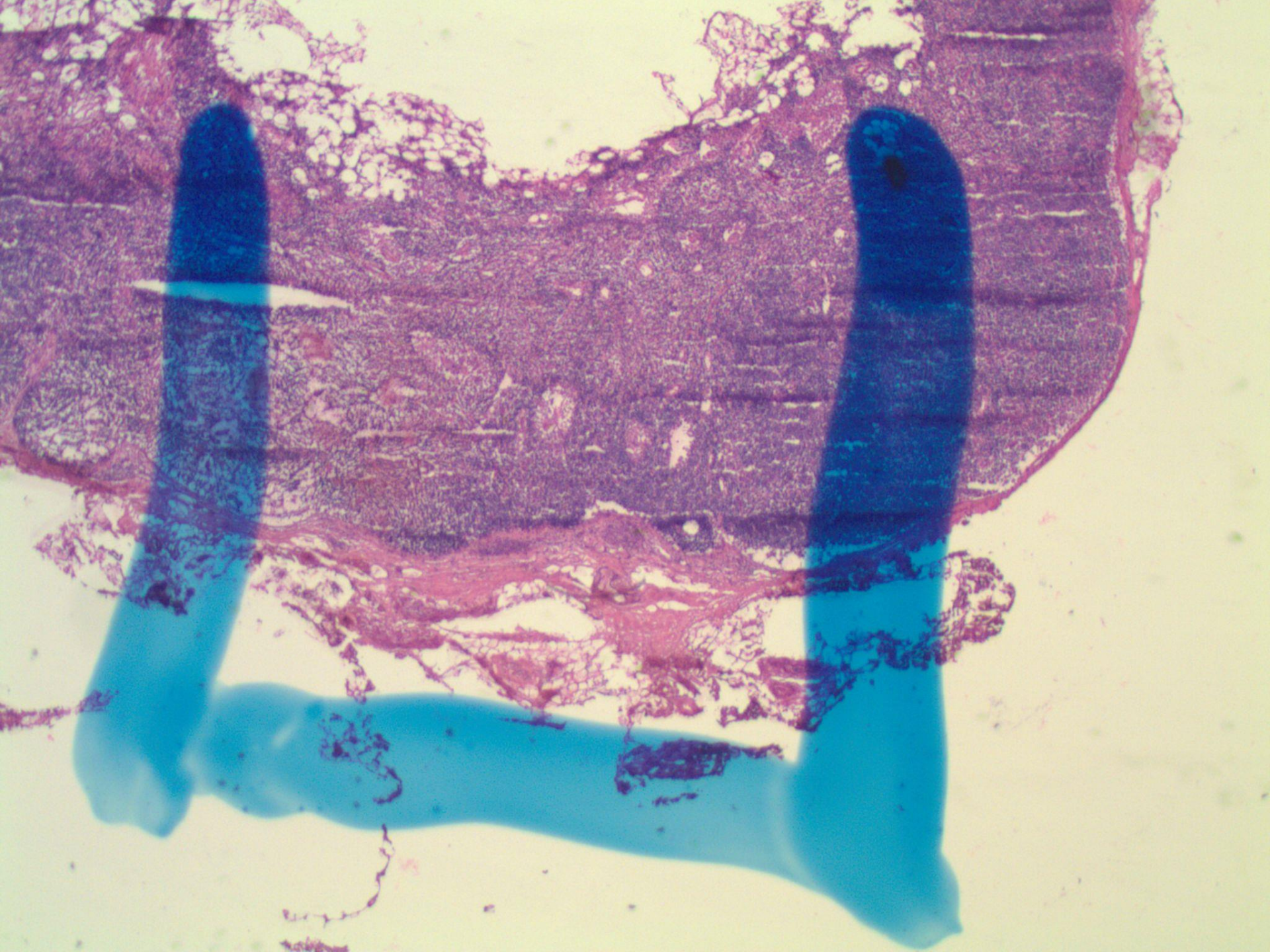
68-year-old woman with breast biopsy-proven lobular carcinoma. Given the large tumor size on imaging with abnormal appearing lymph nodes, simple mastectomy was performed. At the time of surgery, SLN biopsy was submitted for frozen section (intraoperative smears/frozen shown).

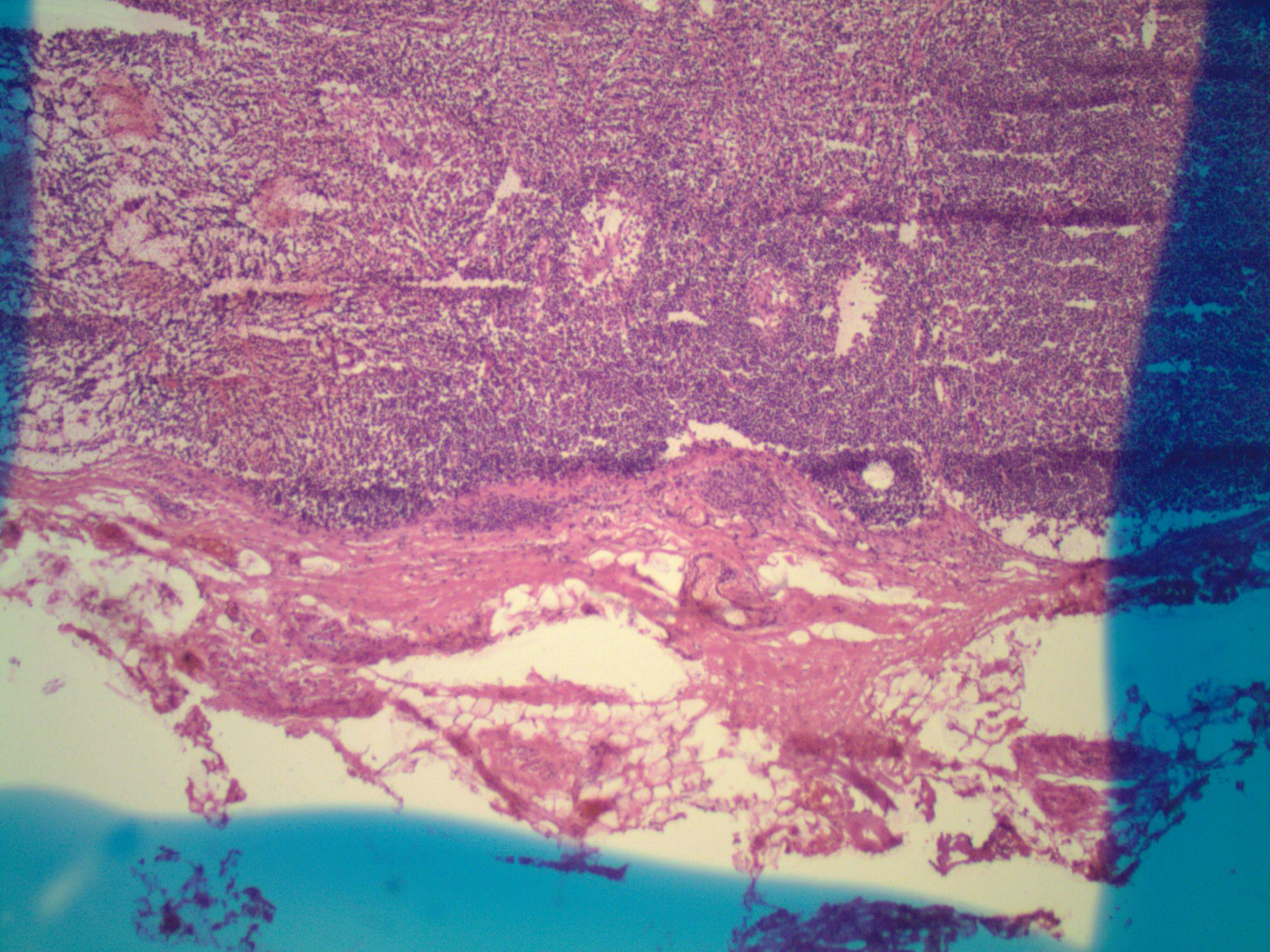


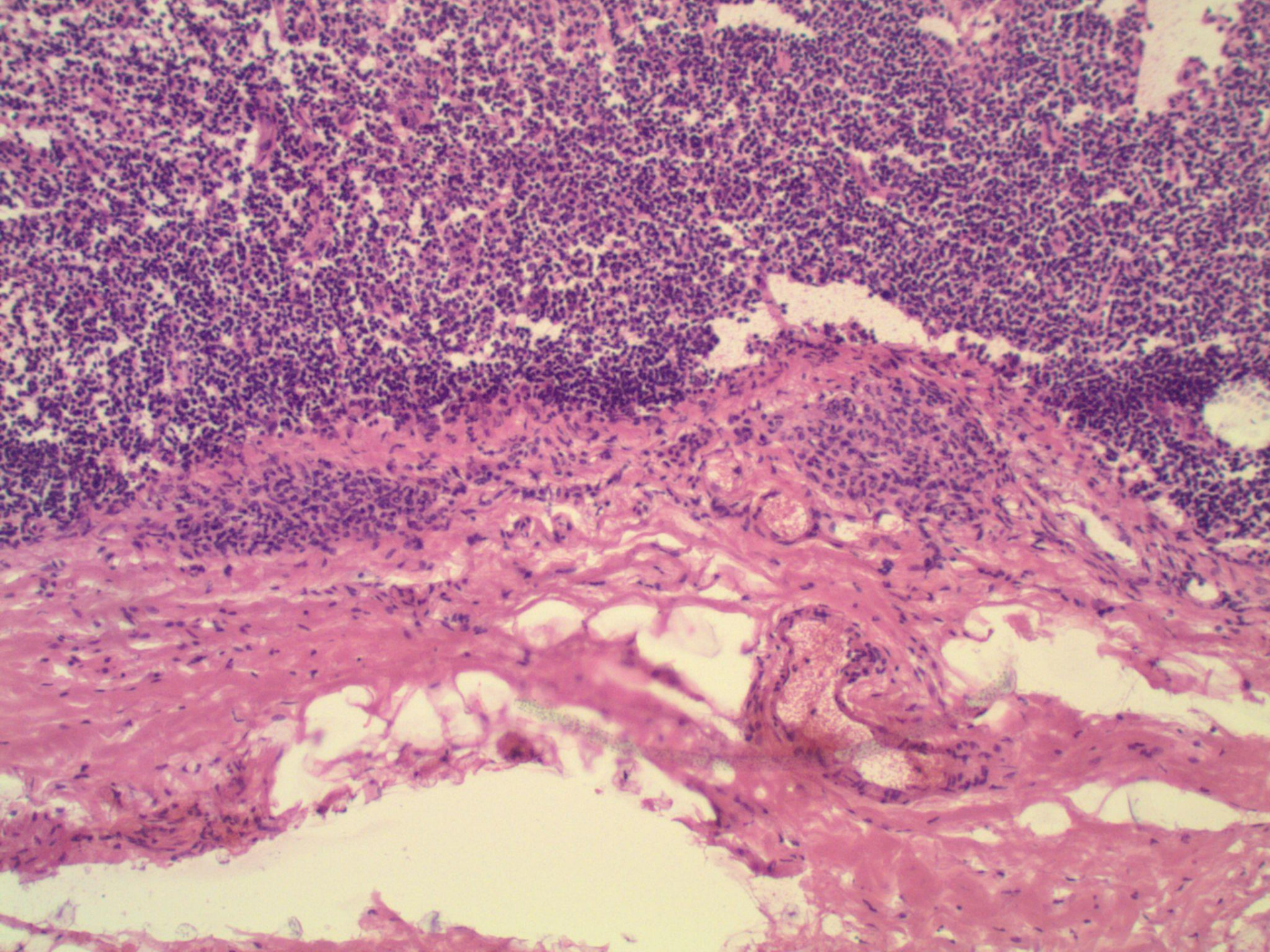








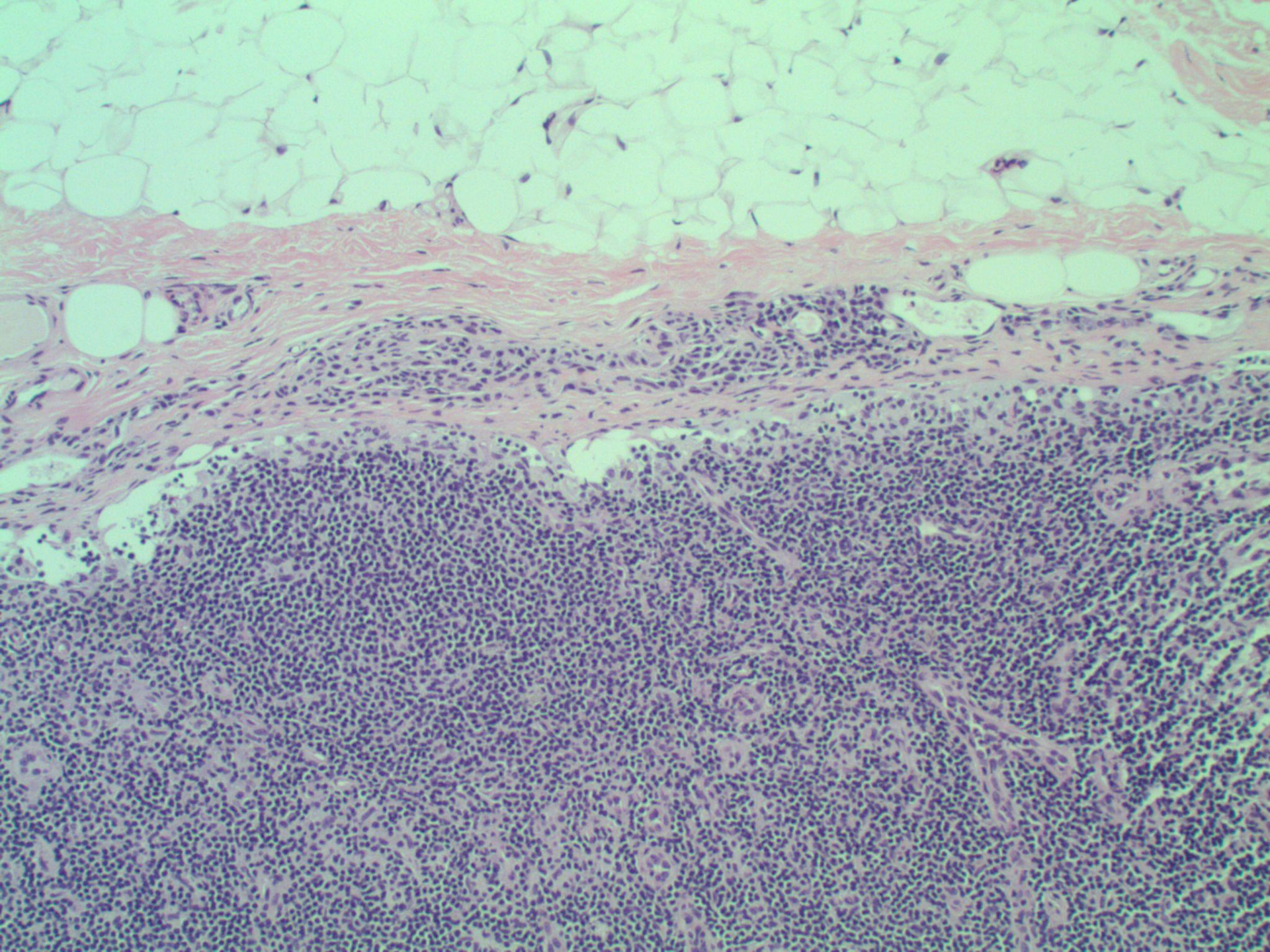


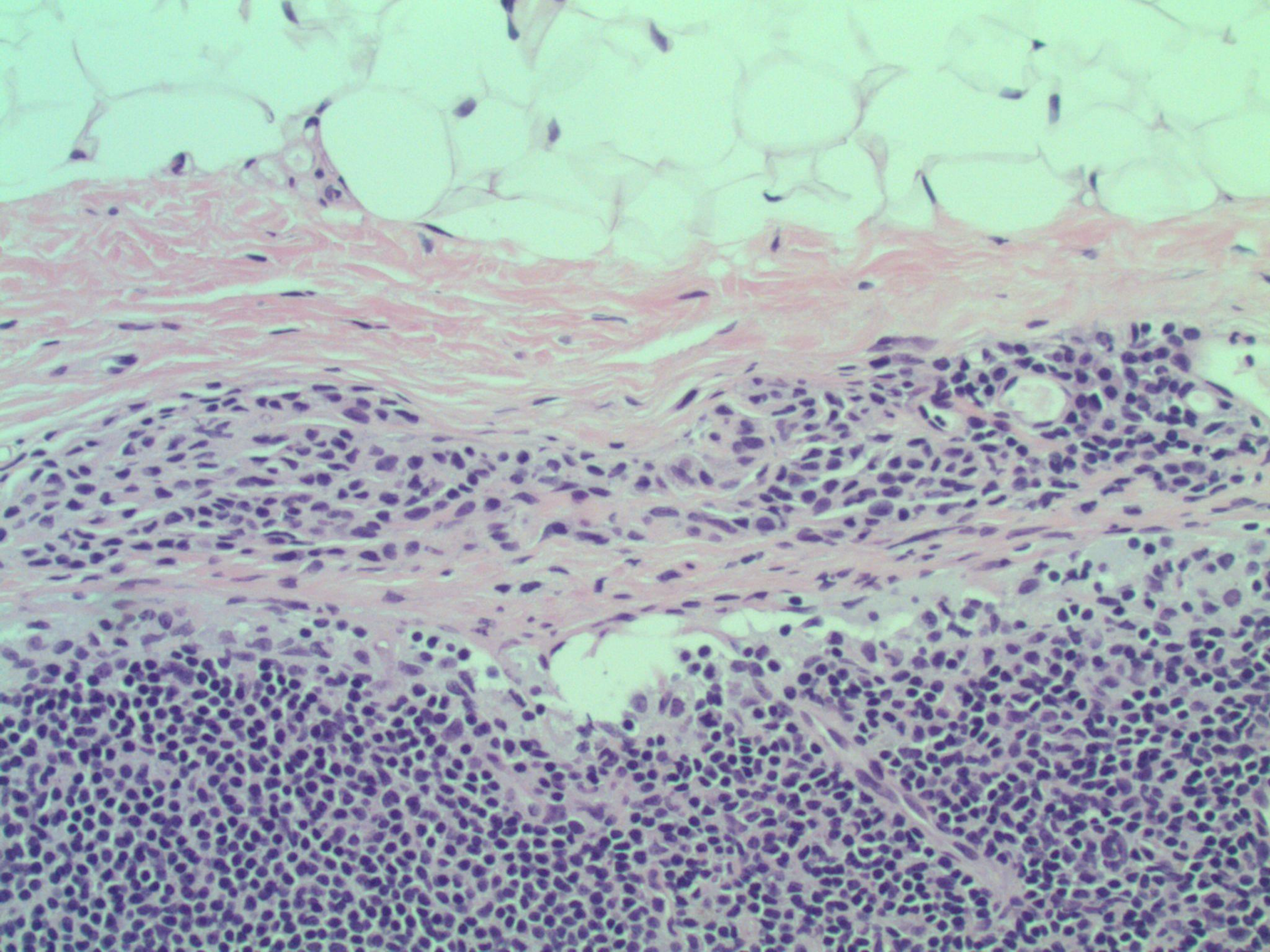


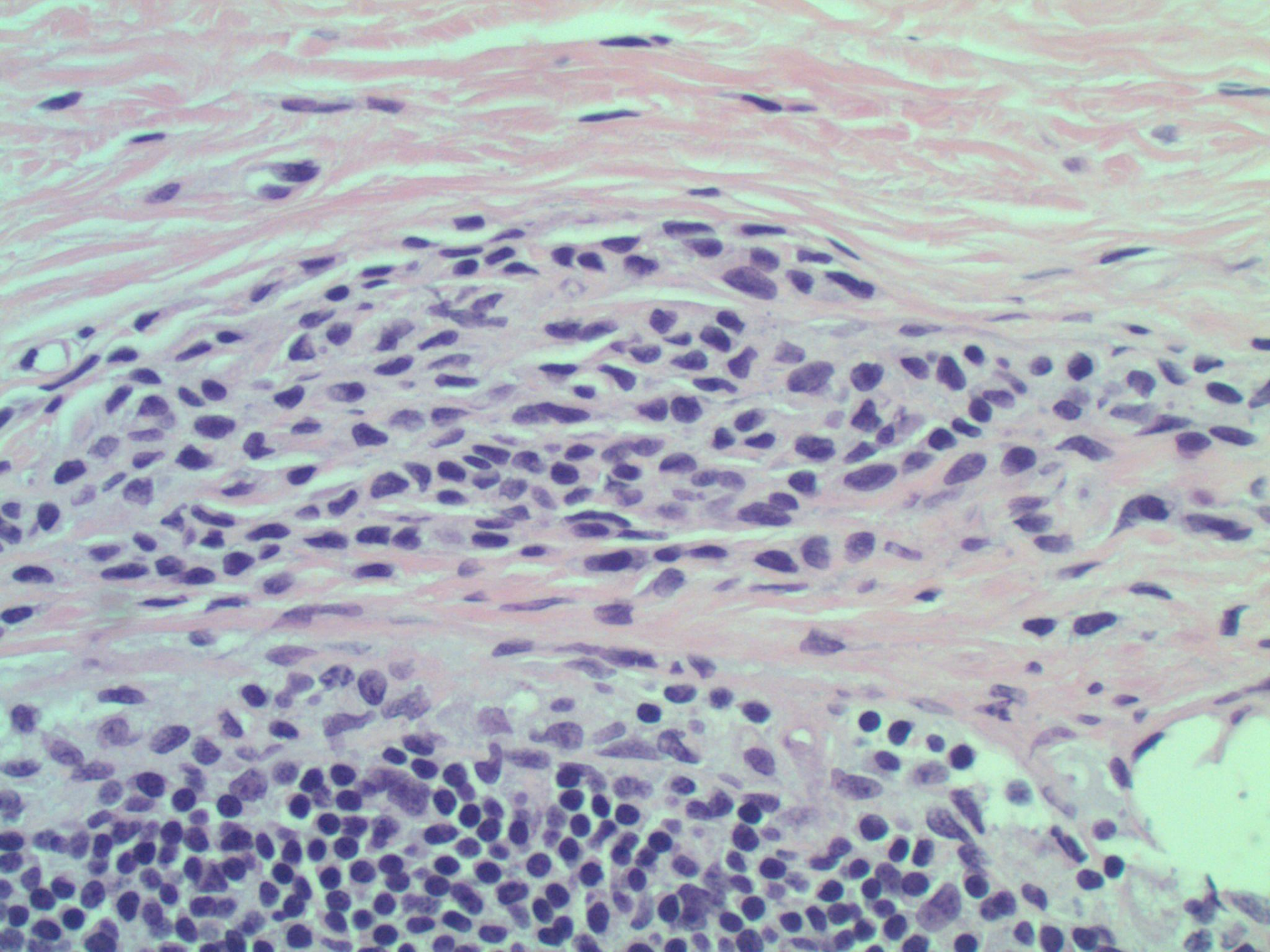
DIAGNOSIS?

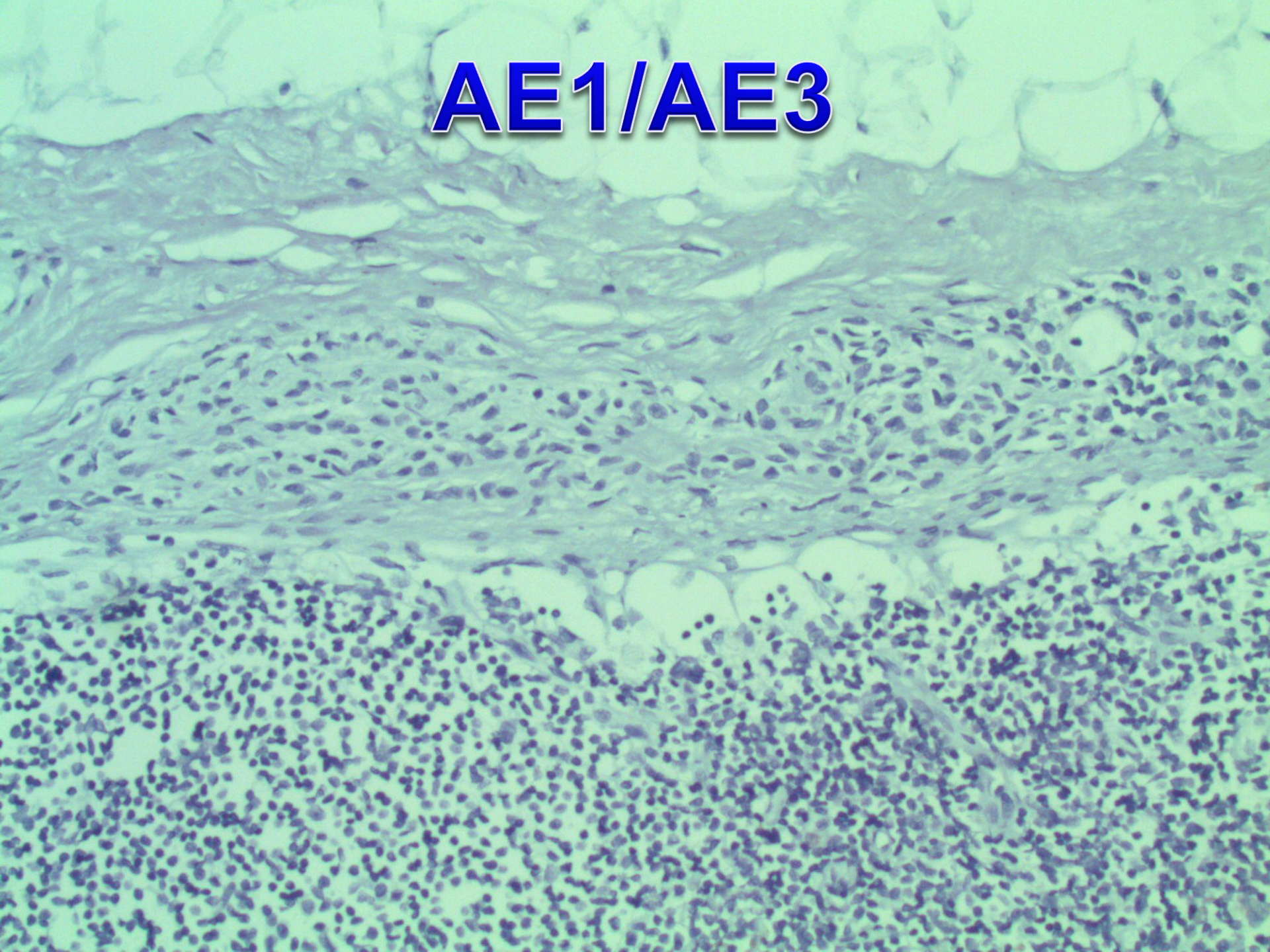
DDx

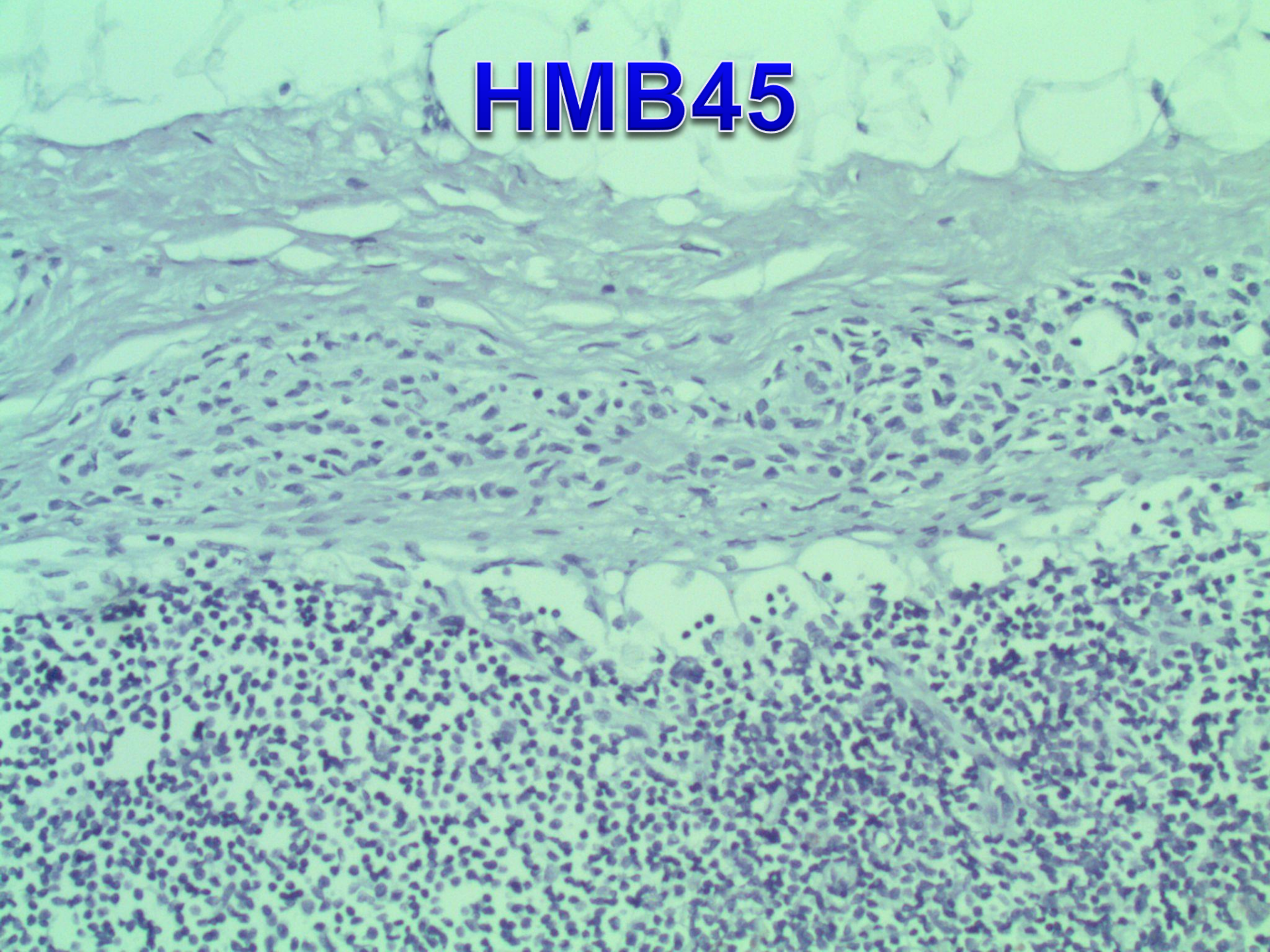
- Metastatic (micro) carcinoma
- Metastatic melanoma
- Histiocytic aggregate
- Capsular melanocytic nevus/rest

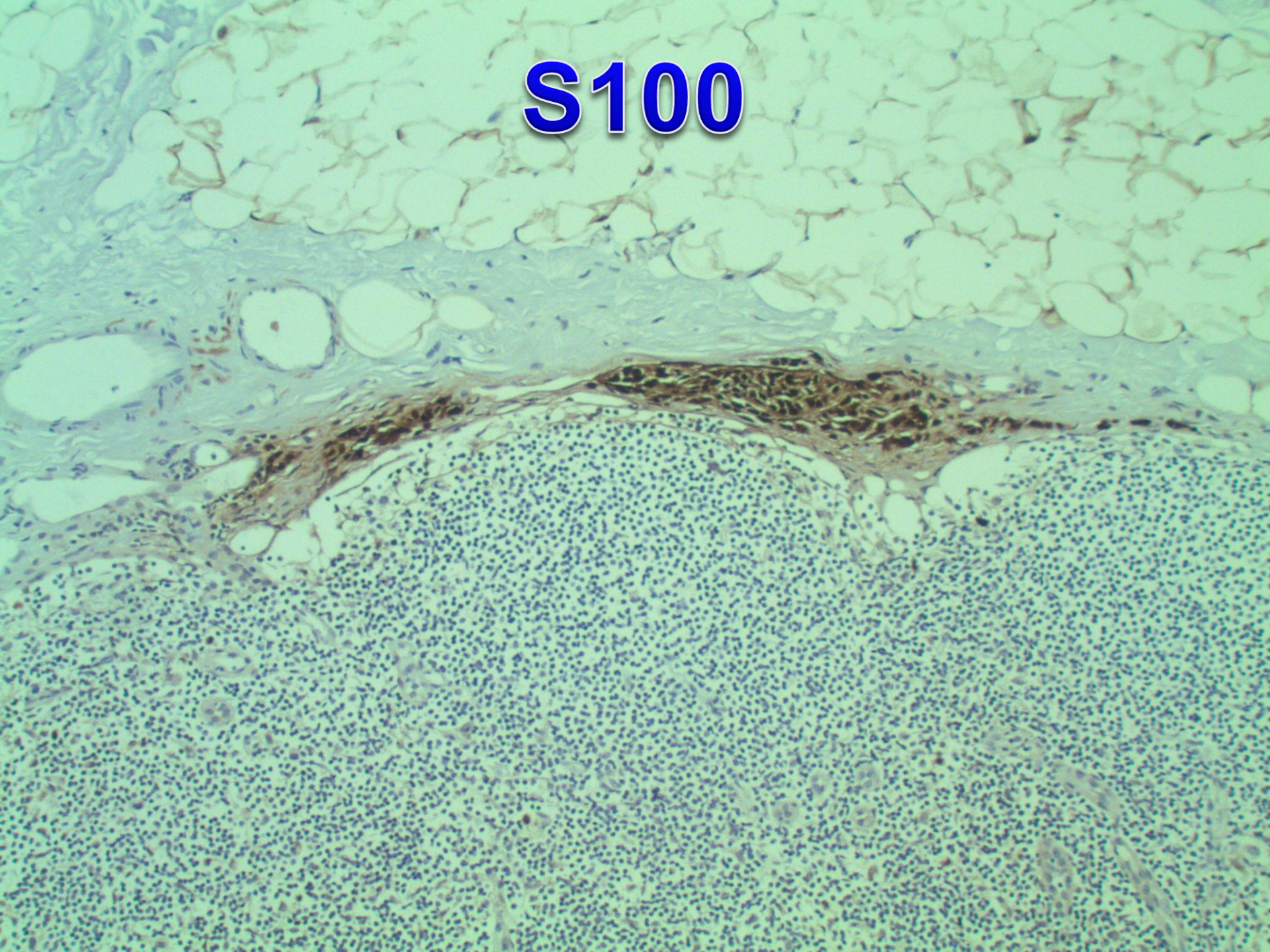


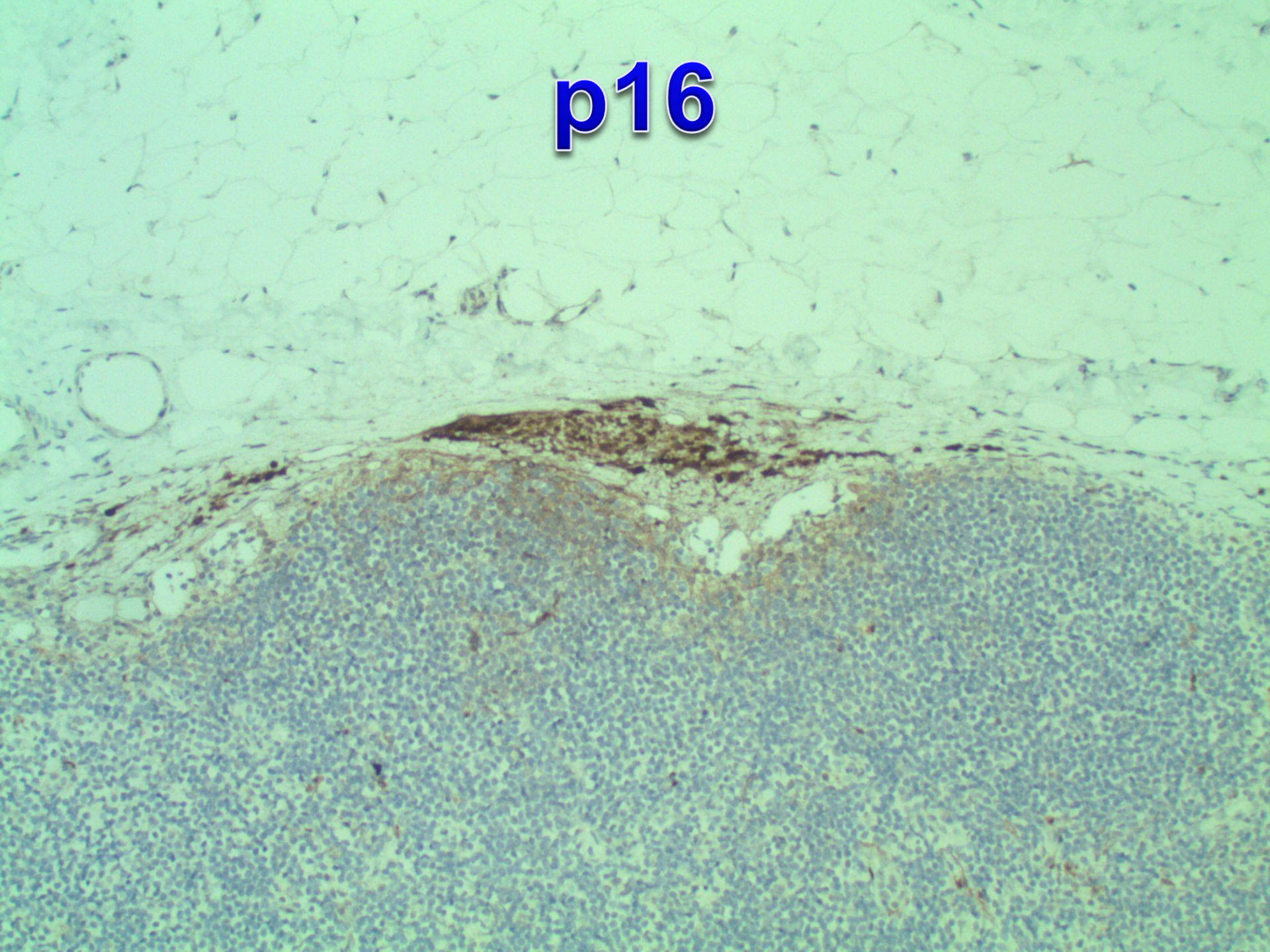





AE1/AE3


HMB45


S100


p16

Capsular nevus/rest

- **7% incidence in axillary nodes**
- Presence in SLN in melanoma patients is associated with cutaneous nevi and congenital cutaneous nevi
- May represent benign metastases from intradermal nevus in area of lymphatic drainage
- usually within fibrous capsule and trabeculae, but also within nodal parenchyma or surrounding a small vessel

CAPSULAR NEVUS: Useful IHC panel

POSITIVE

S100, SOX10, p16

NEGATIVE

AE1/AE3

HMB45 (or weak)

Low Ki67