Disclosures
August 3, 2015

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

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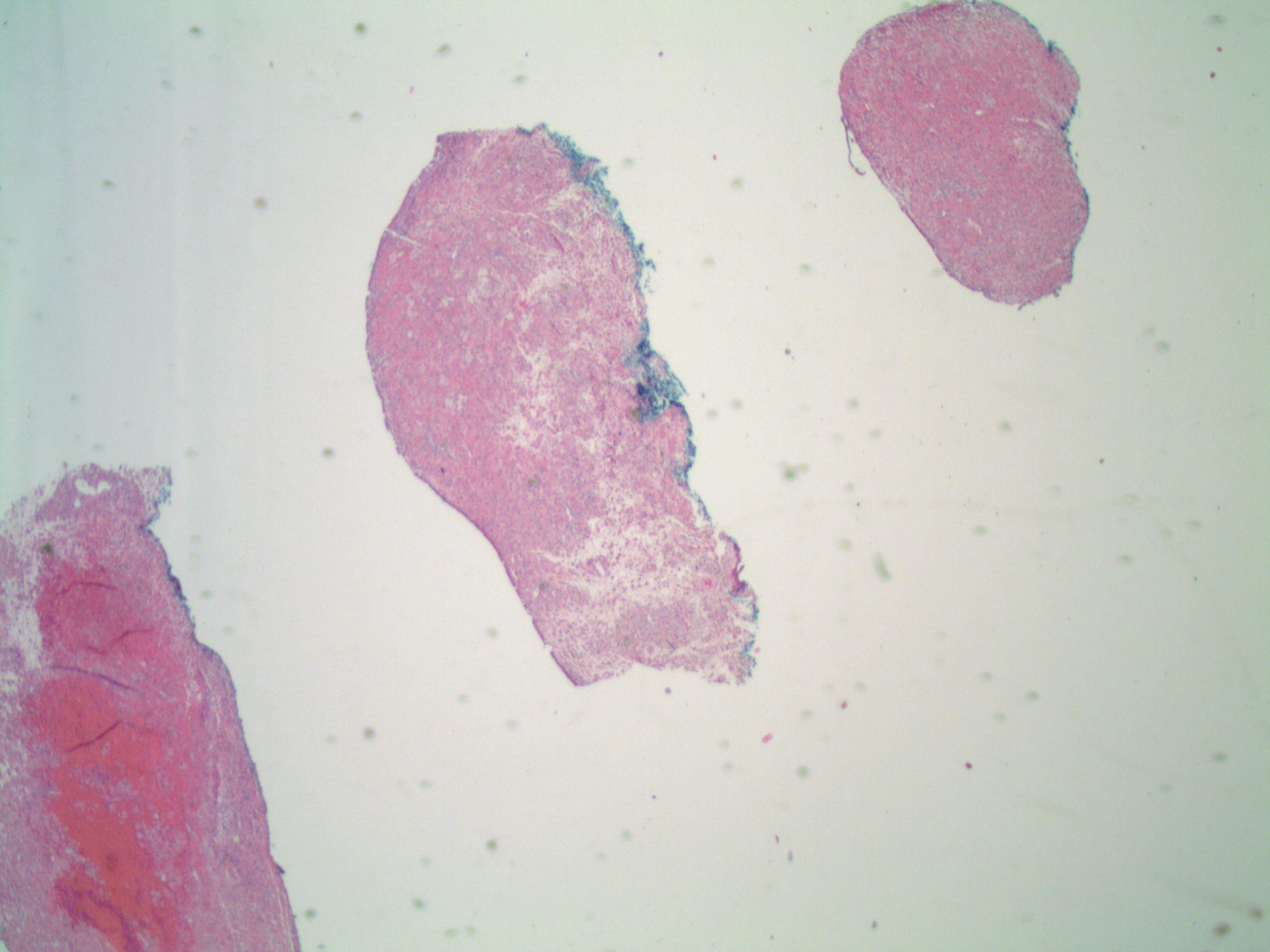
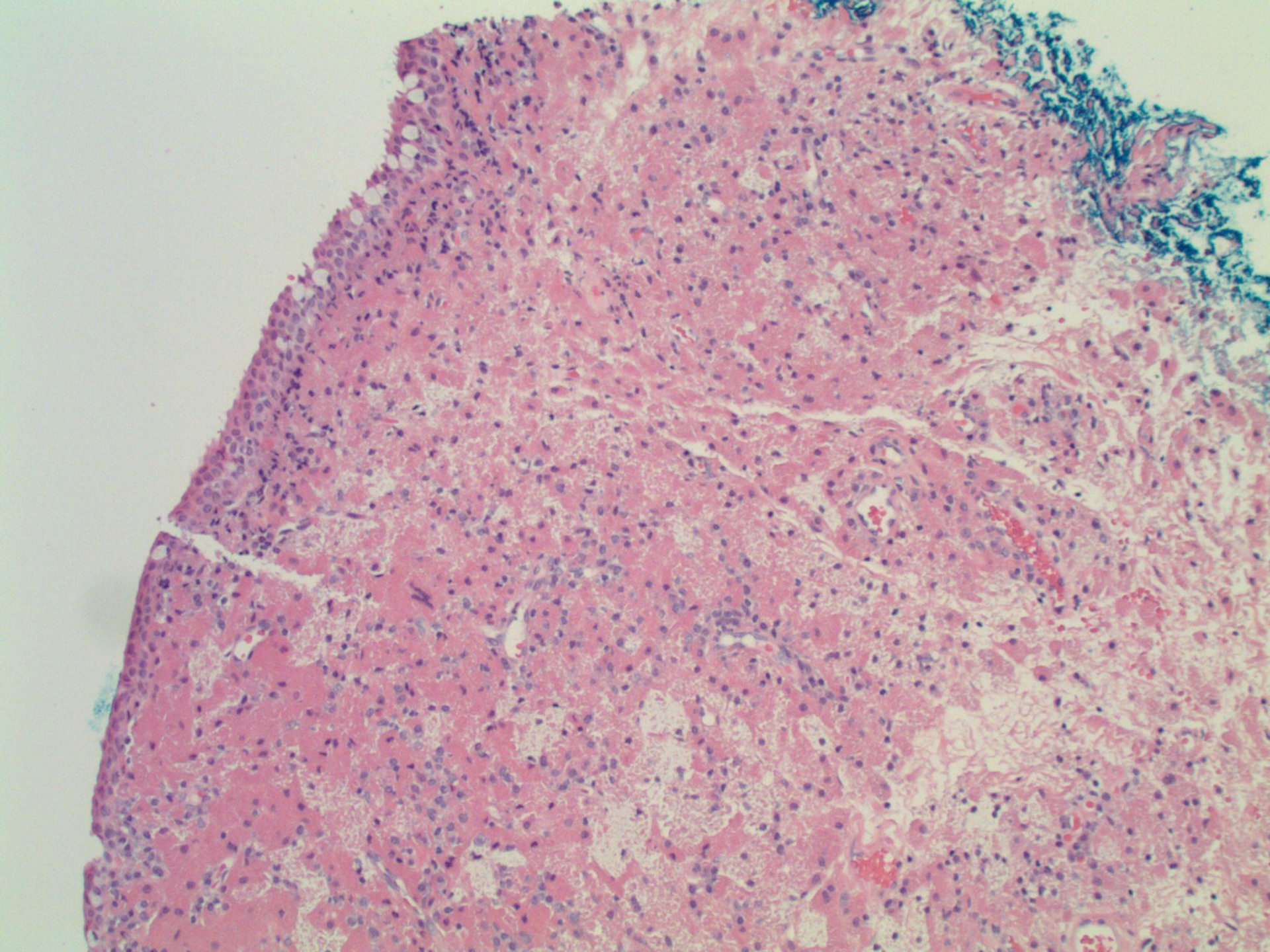
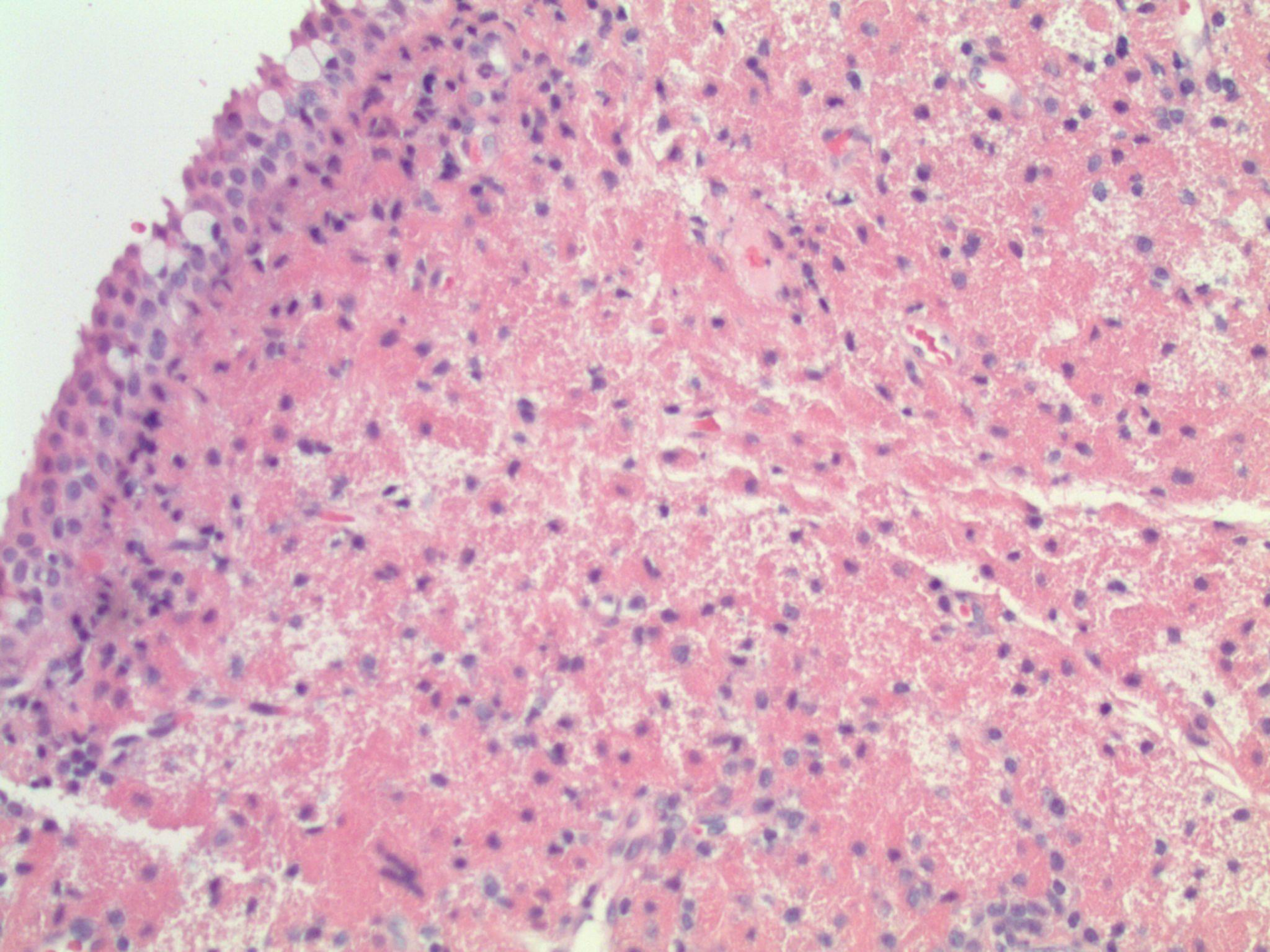
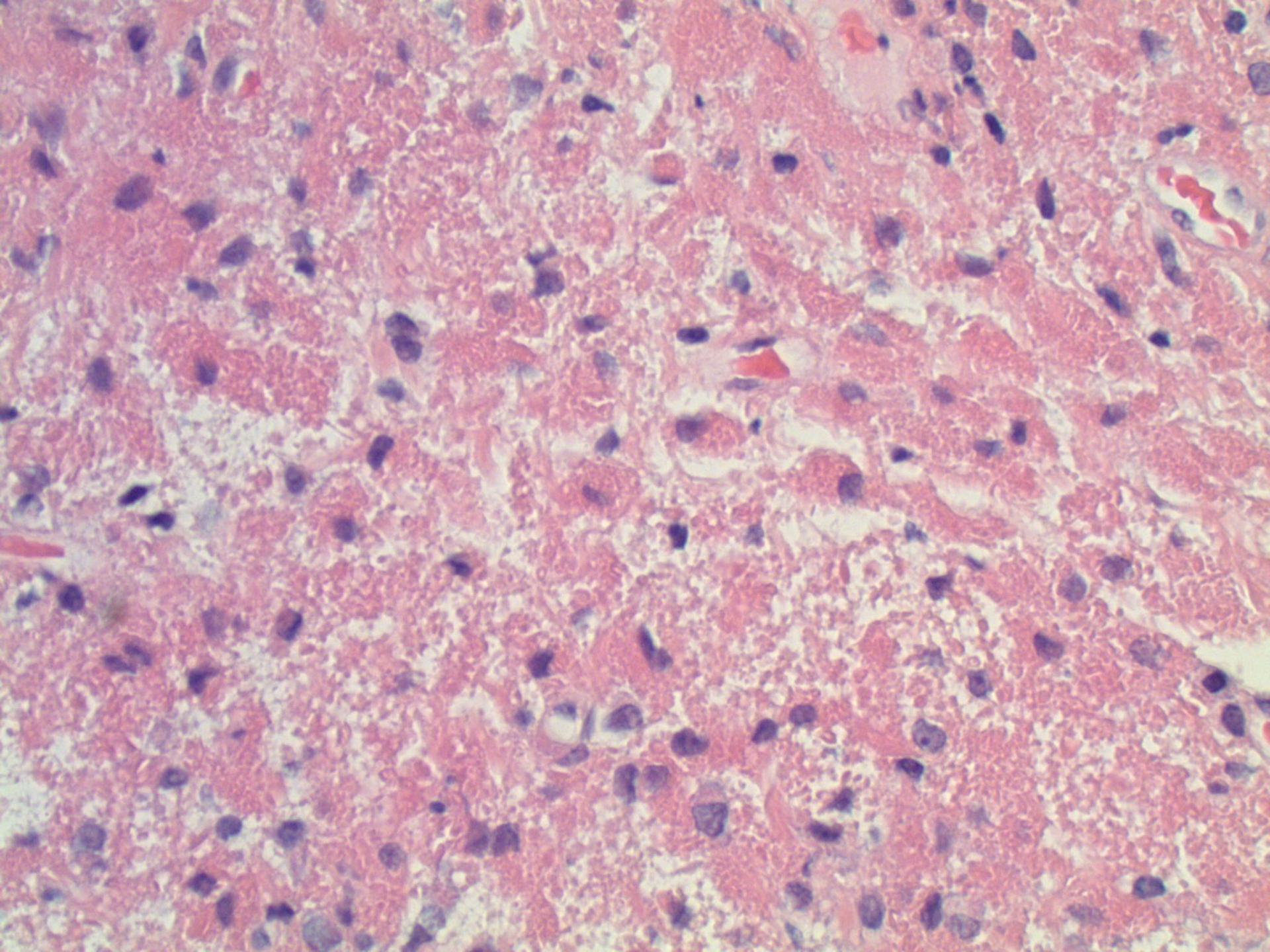
SB 5961
Ed Plowey; Stanford

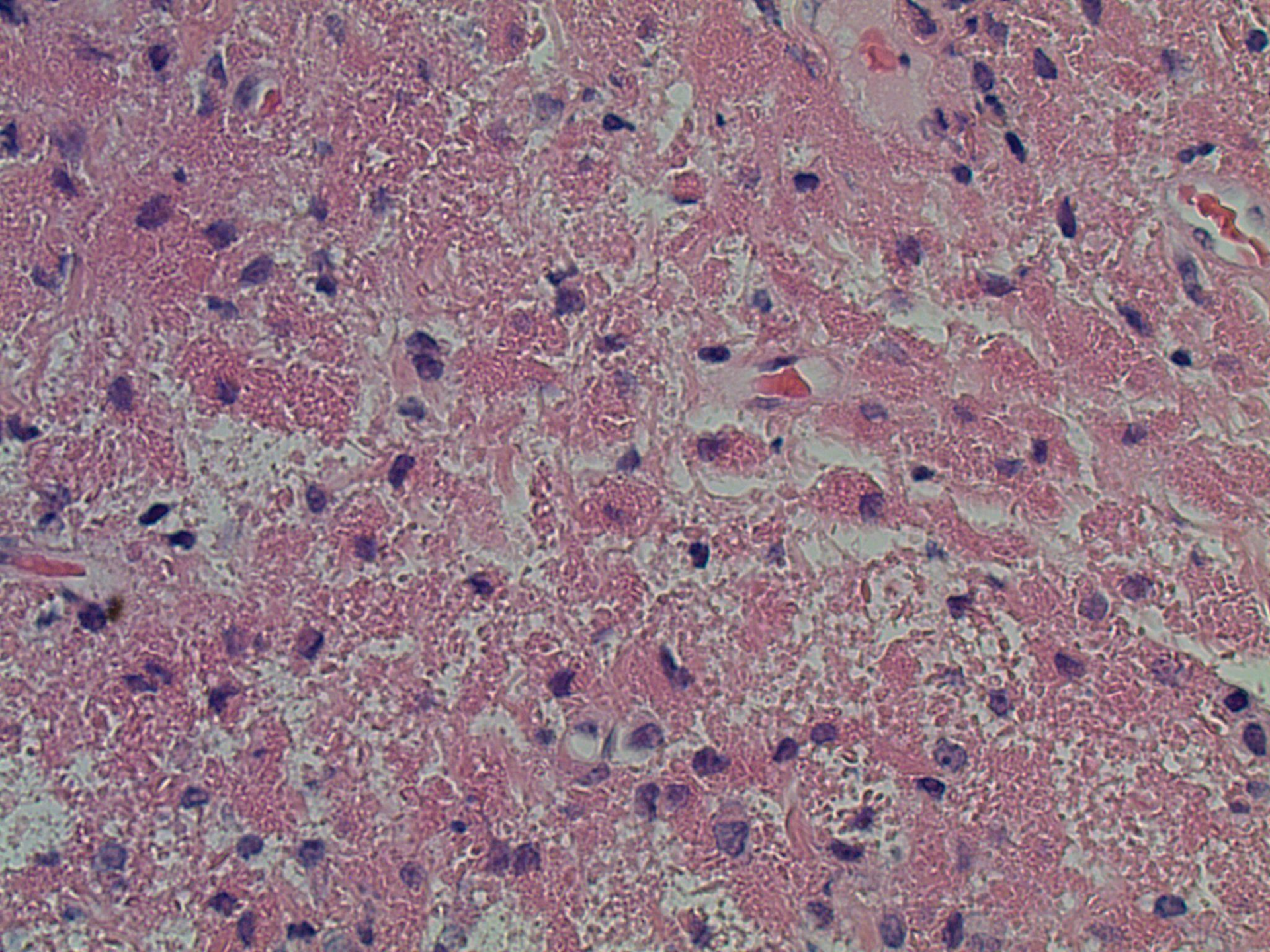
42-year-old woman with bilateral slowing enlarging inferior conjunctival fornix.











Crystal-Storing Histiocytosis of the Conjunctiva

Edward D. Plowey, MD, PhD
Stanford University School of Medicine

STANFORD
UNIVERSITY

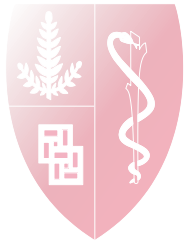
South Bay Pathology Society
August 3, 2015

Clinical History

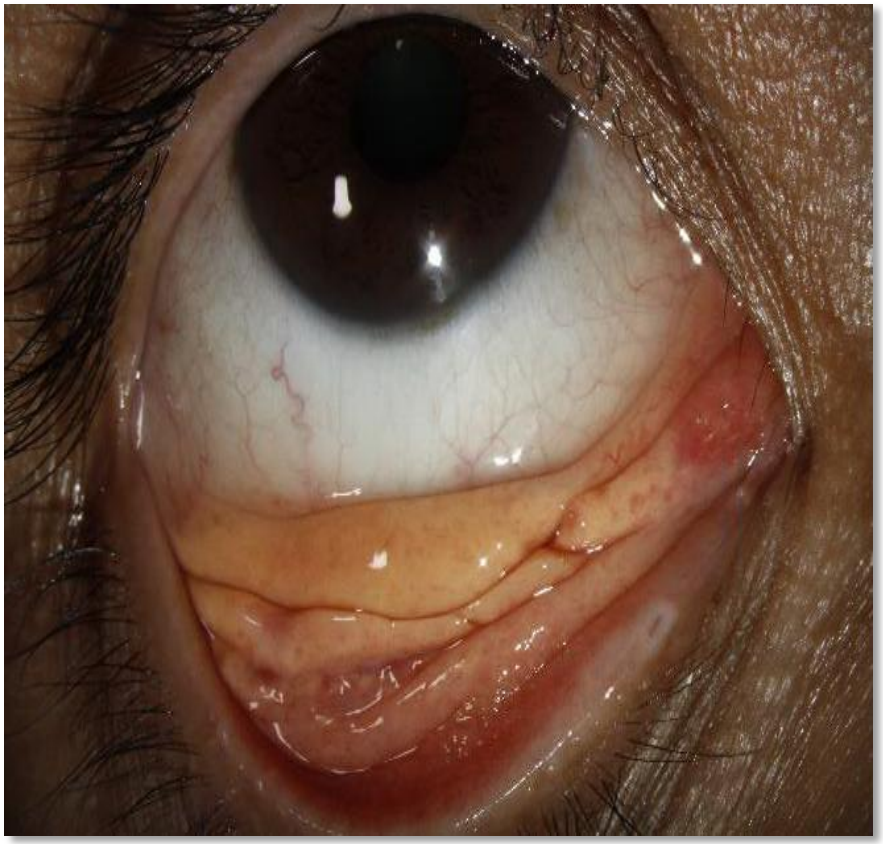
- A 42-year-old healthy woman presented with bilateral conjunctival lesions x several months
- Steady growth in the right eye conjunctival lesion
  - Associated itching and discomfort
  - She denied pain, bleeding and discharge
- PMHx: atrial fibrillation (paroxysmal x 1)
- SHx: occupation not reflected in medical record
- ROS: negative

Clinical History

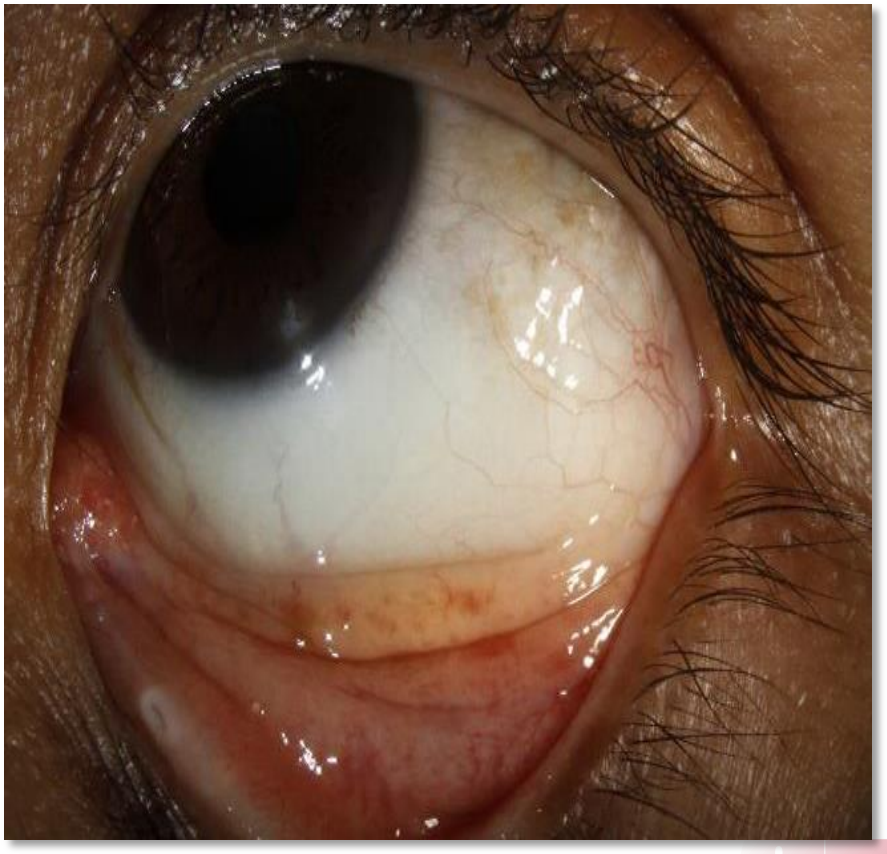
- Physical Examination
  - healthy woman with bilateral lower lid conjunctival yellow fleshy lesions along the lengths of the inferior fornices, R>L
    - Superior fornices normal; no proptosis
    - Corneas, ACs, irises, lenses normal
  - Visual acuity with correction: 20/25 -2 OD, 20/20 -1 OS
  - Intraocular pressure: 16 mmHg OD, 15 mmHg OS
  - PERRLA, EOM normal bilaterally. Confrontation visual fields were full bilaterally.
- Excisional biopsy of the right lower lid lesion



Ophthalmologic Examination



OD



OS

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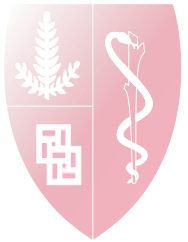
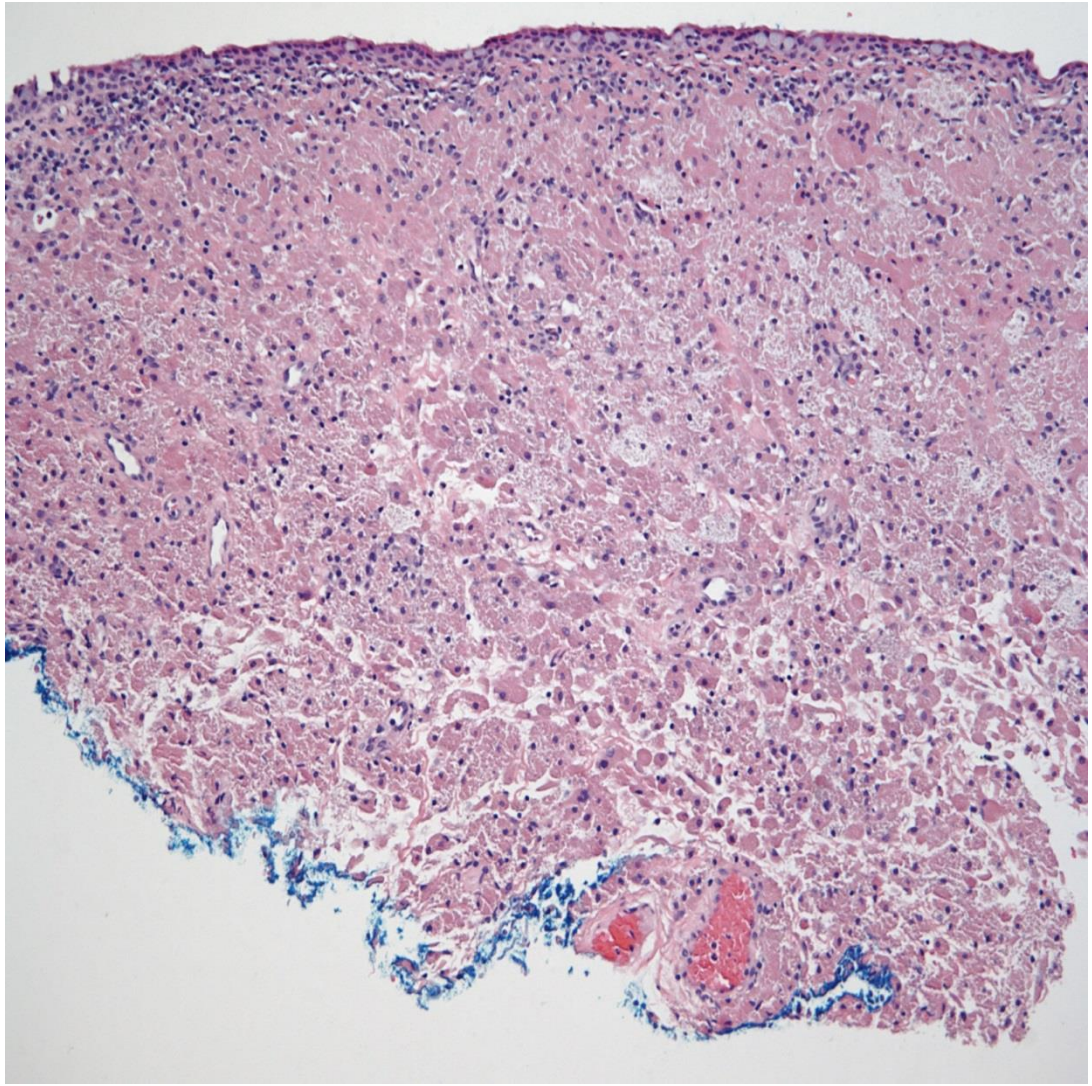
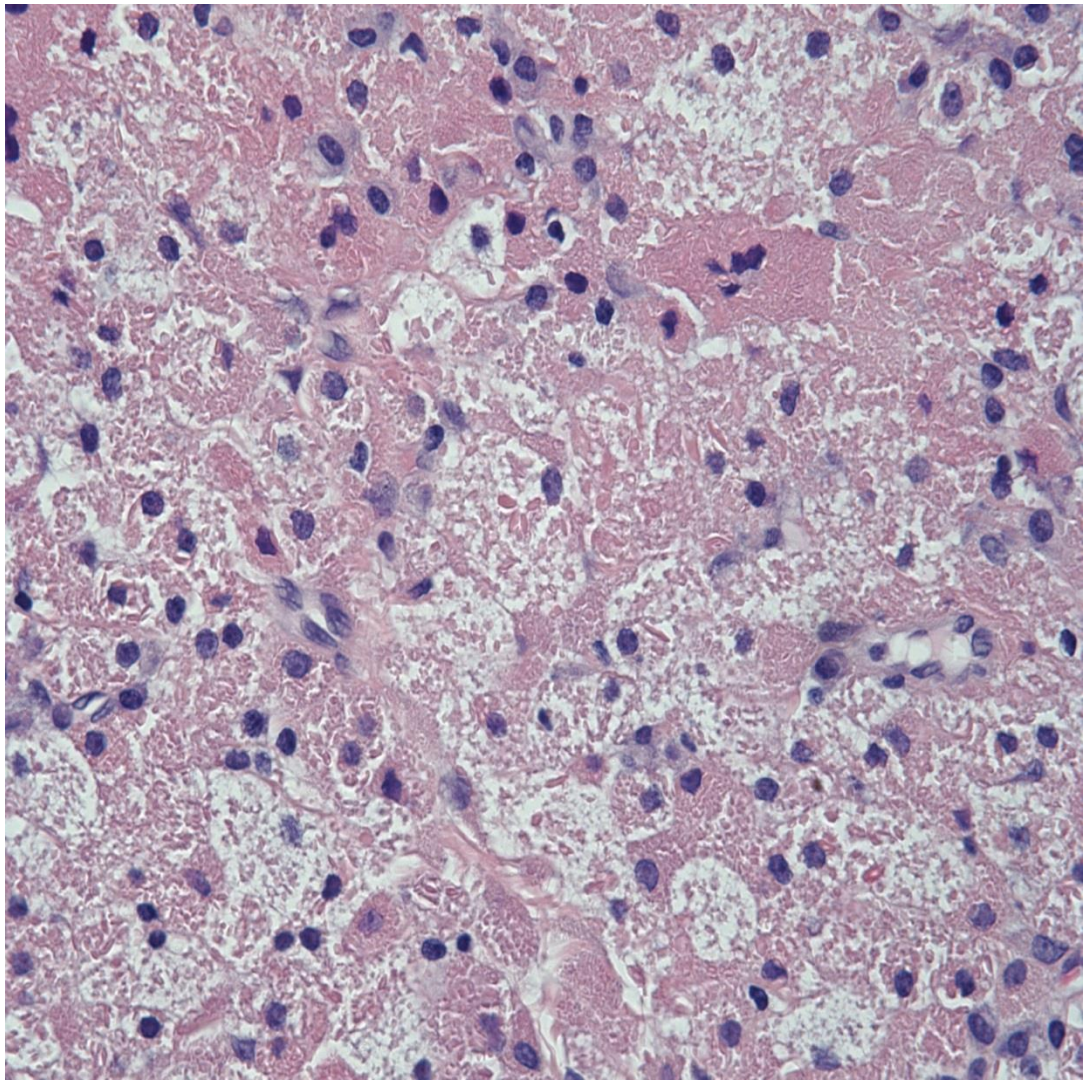


Pathology: H&E



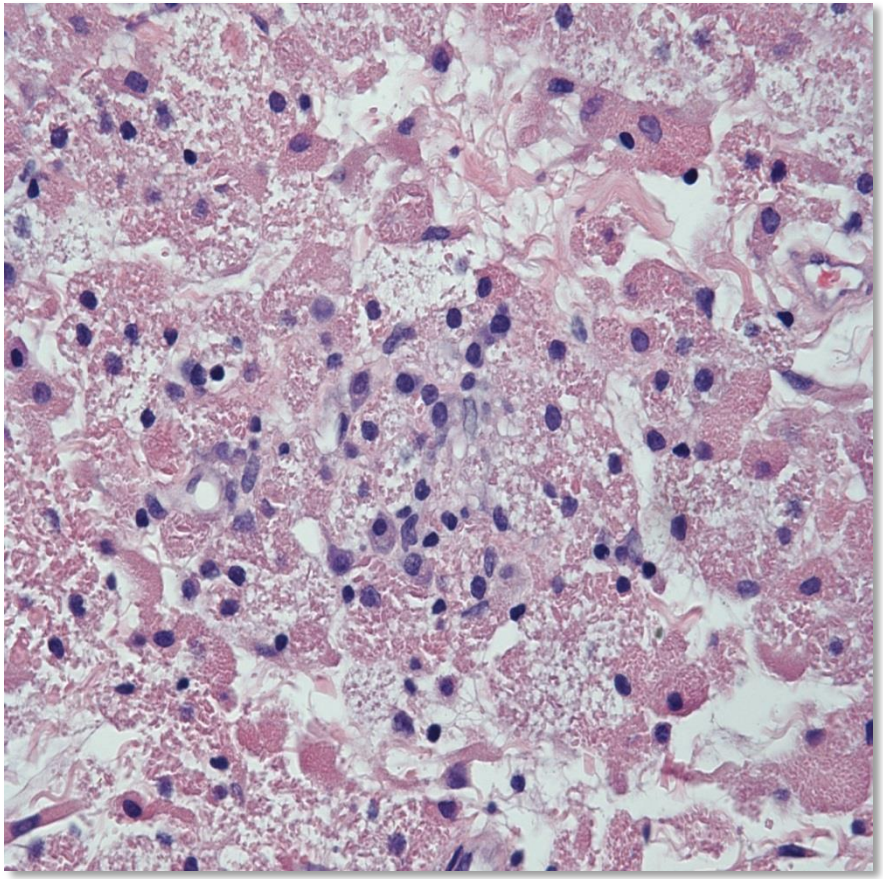
100x

Pathology: H&E



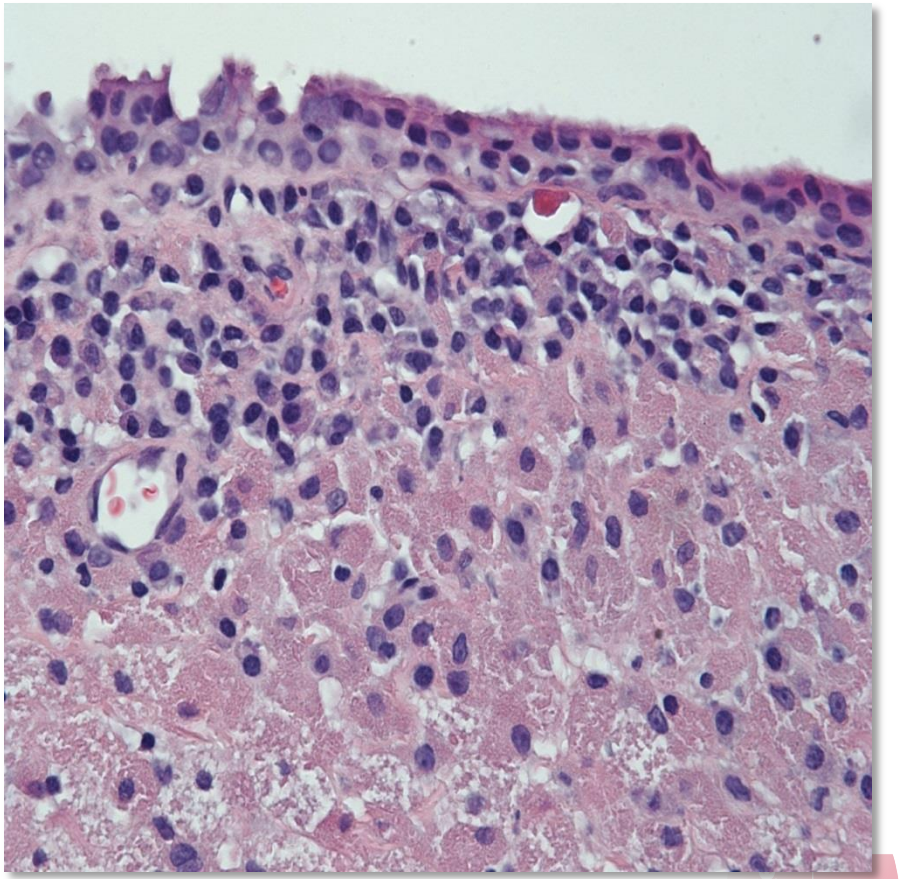
400x

Pathology: H&E



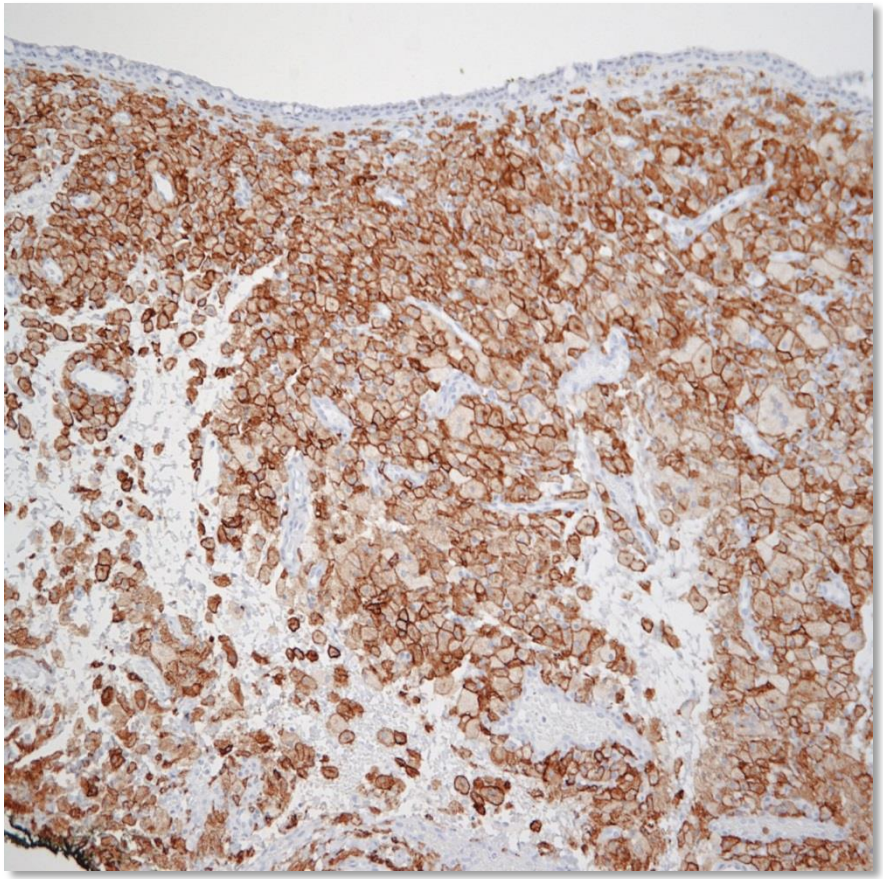
Perivascular plasma cells (400x)

No significant lymphocytic infiltrate

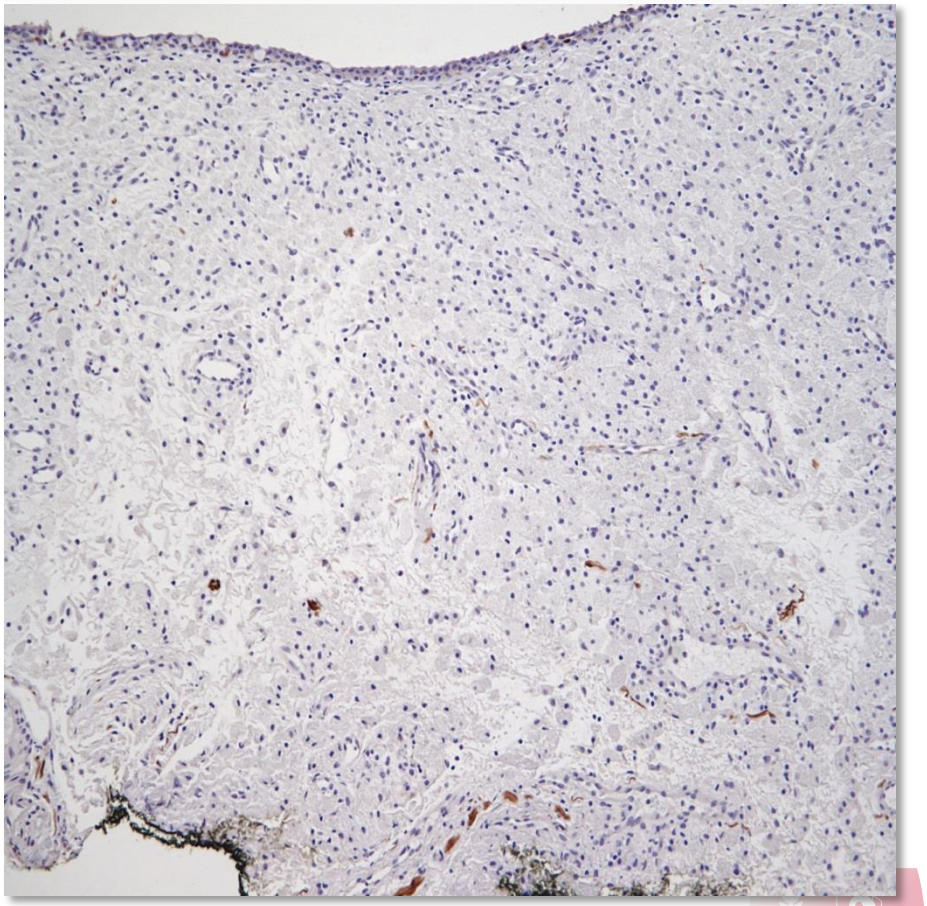


Subepithelial plasma cells (400x)

Non-Langerhans Cell Histiocytic lesion



CD163



S100

Pathology – Additional Negative Stains

CD1a, Langerin

Sox10

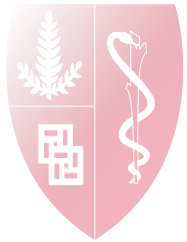
Melan-A (MiTF positive in histiocytes)

GMS, AFB, Fite

Von Kossa

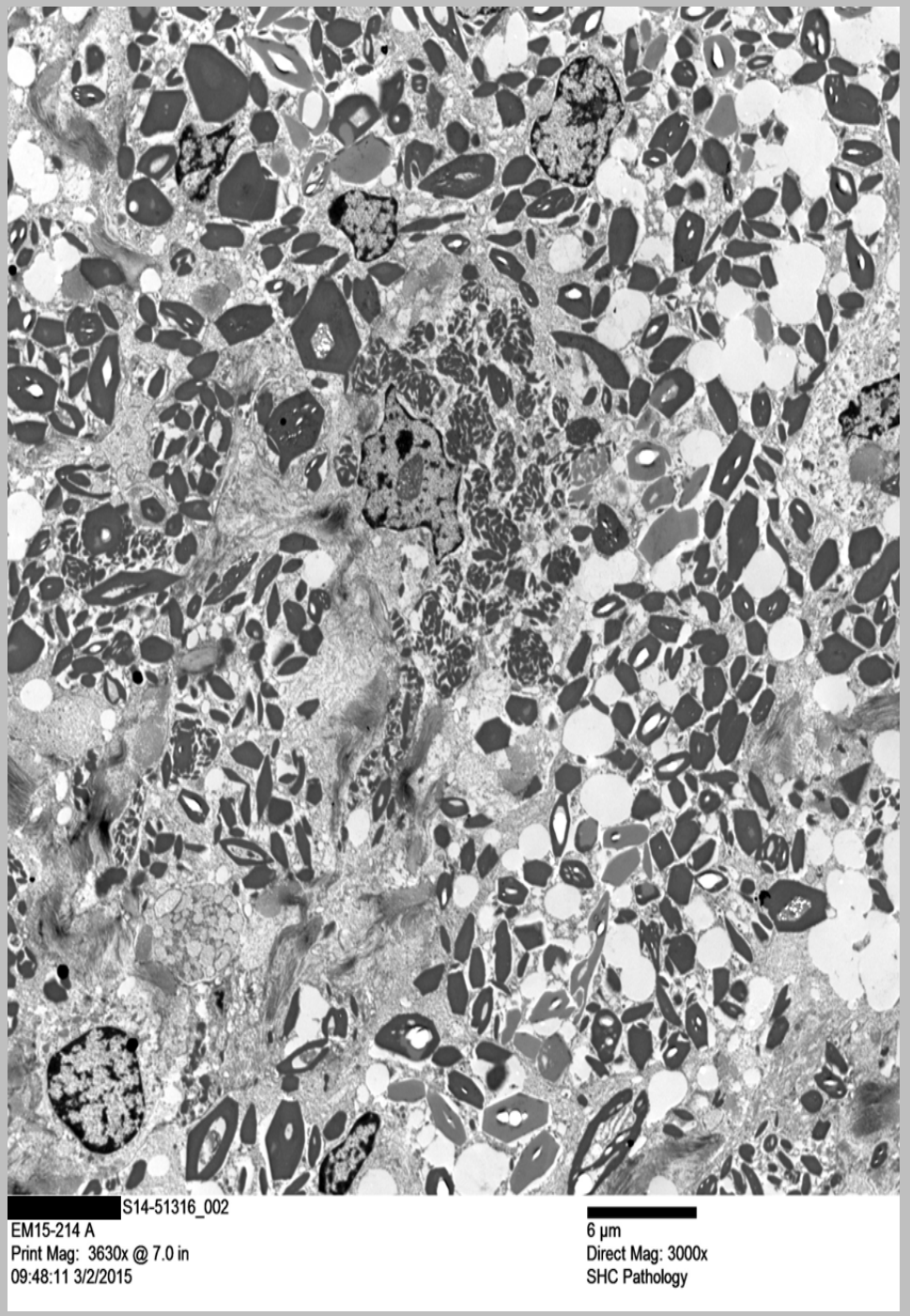
Congo red

PAS



Transmission Electron Microscopy

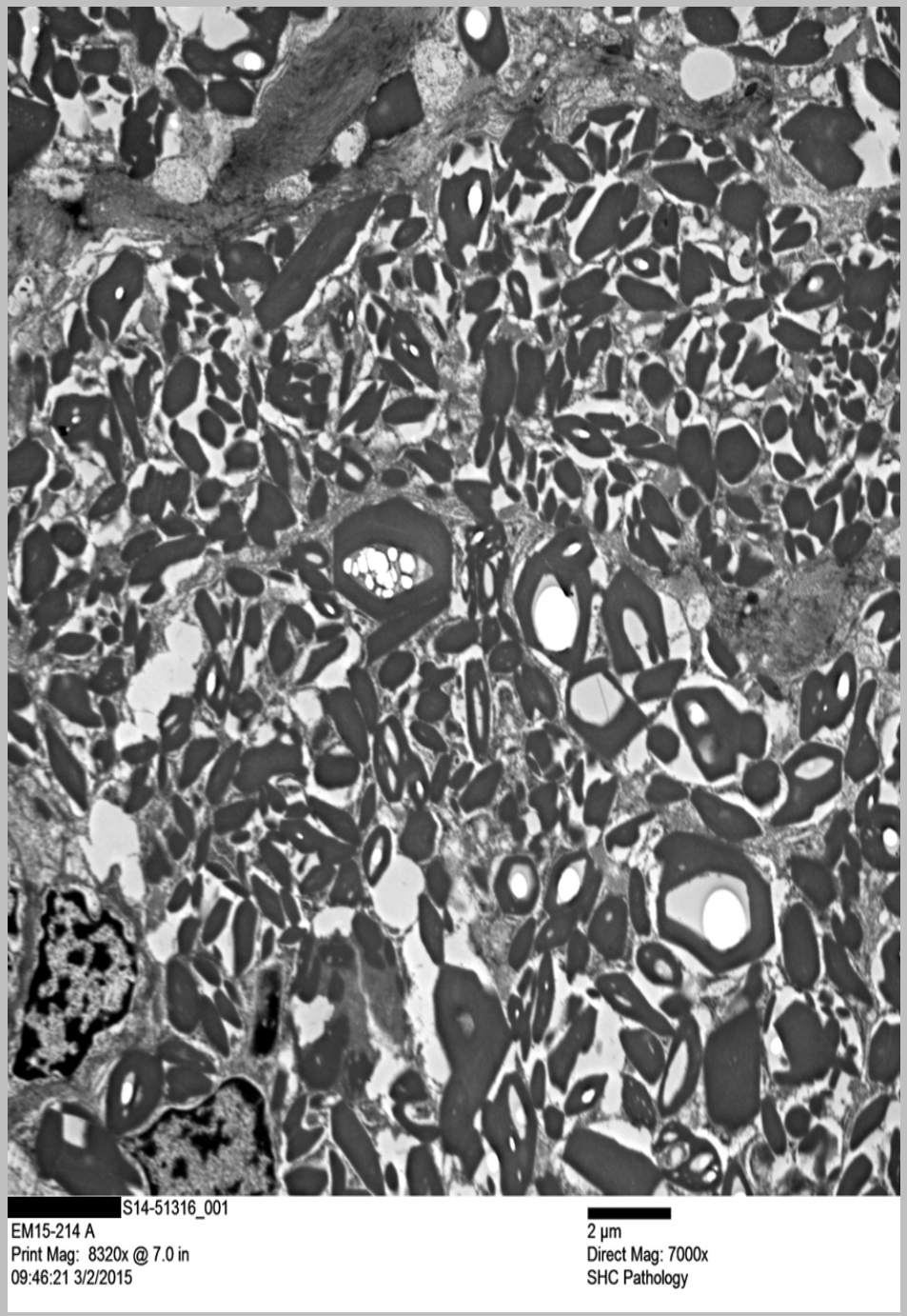
- from FFPE tissue



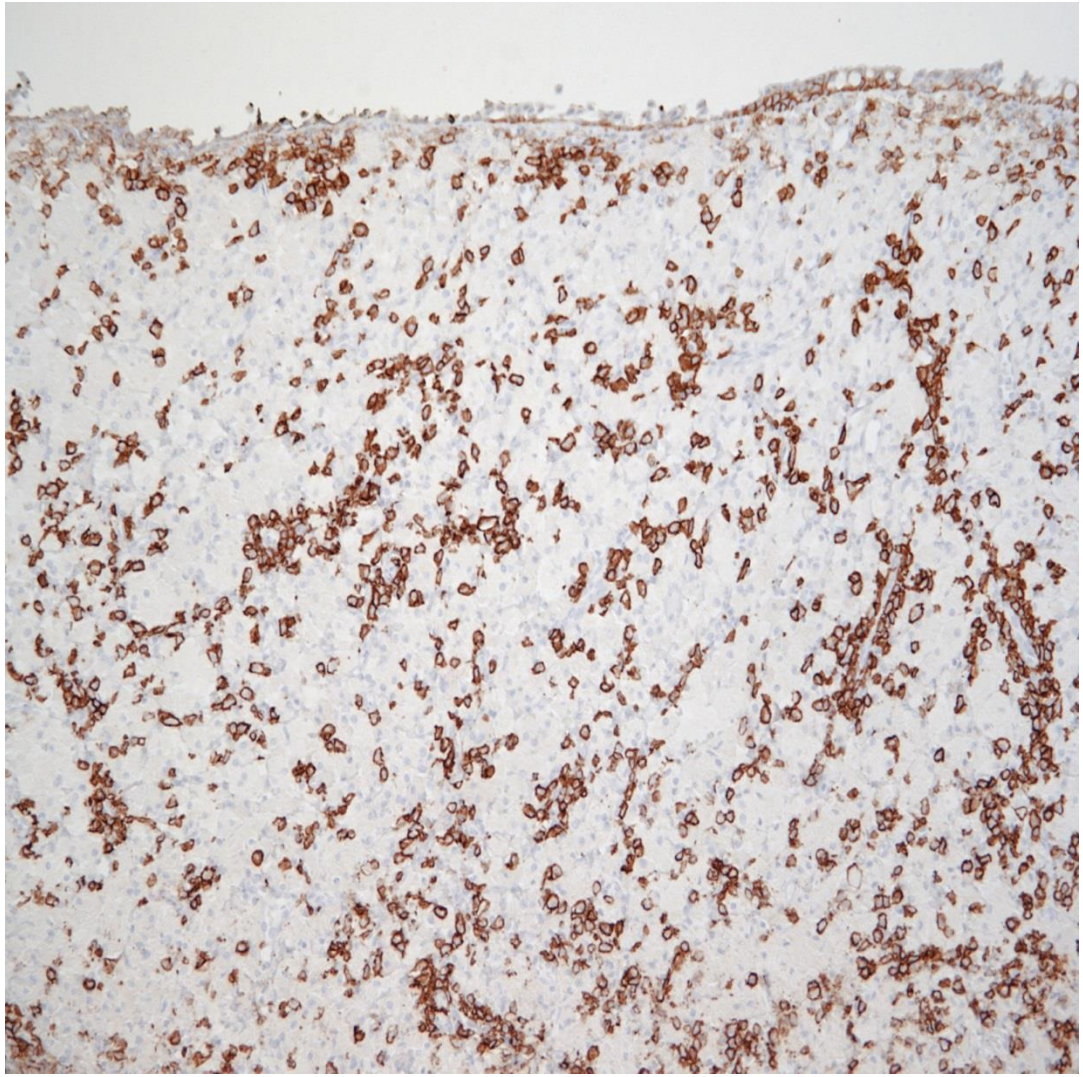
Transmission Electron Microscopy

- from FFPE tissue

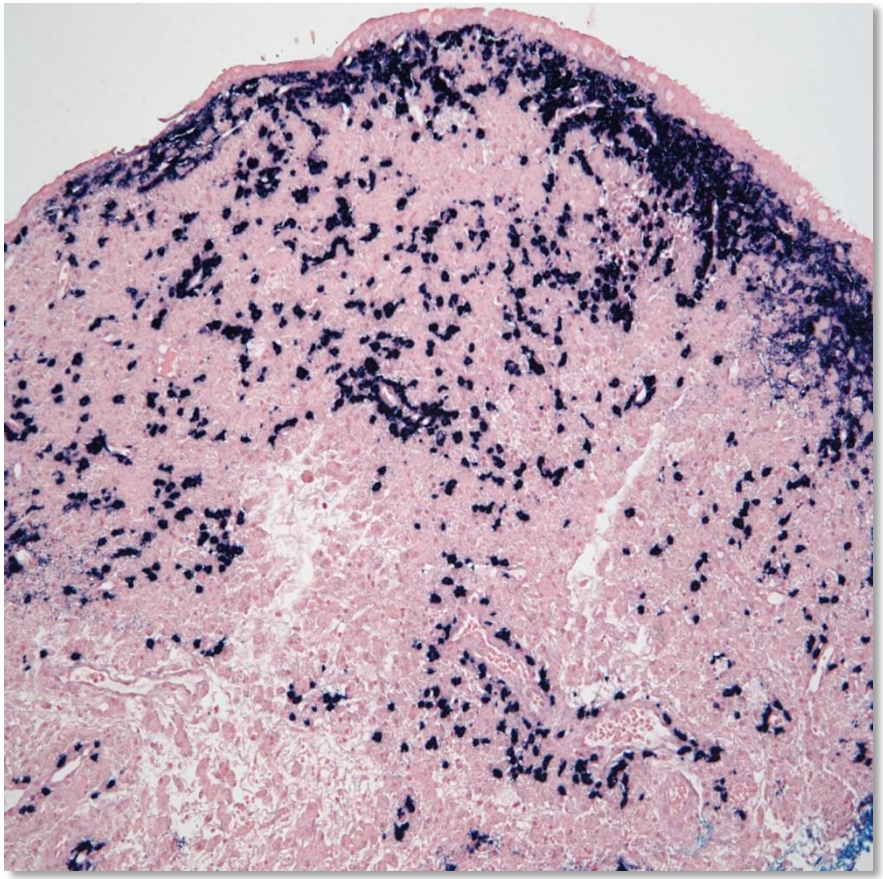
Dx: Crystal-storing histiocytosis



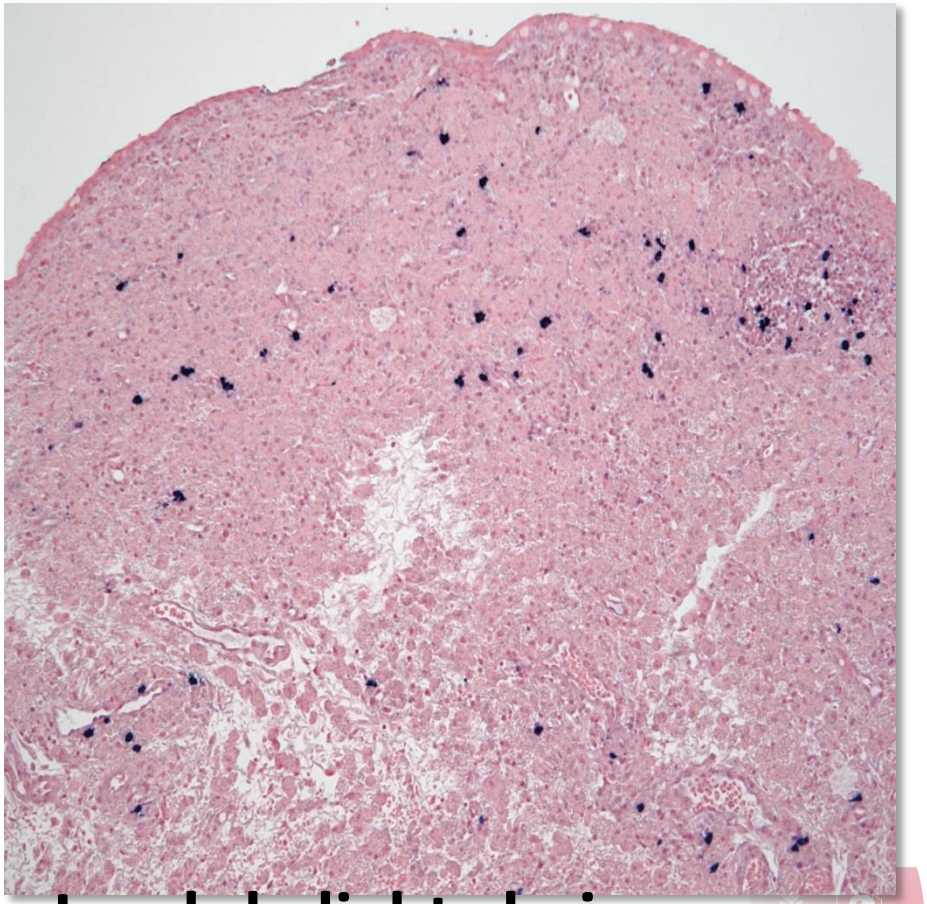
CD138



Plasma cell phenotype

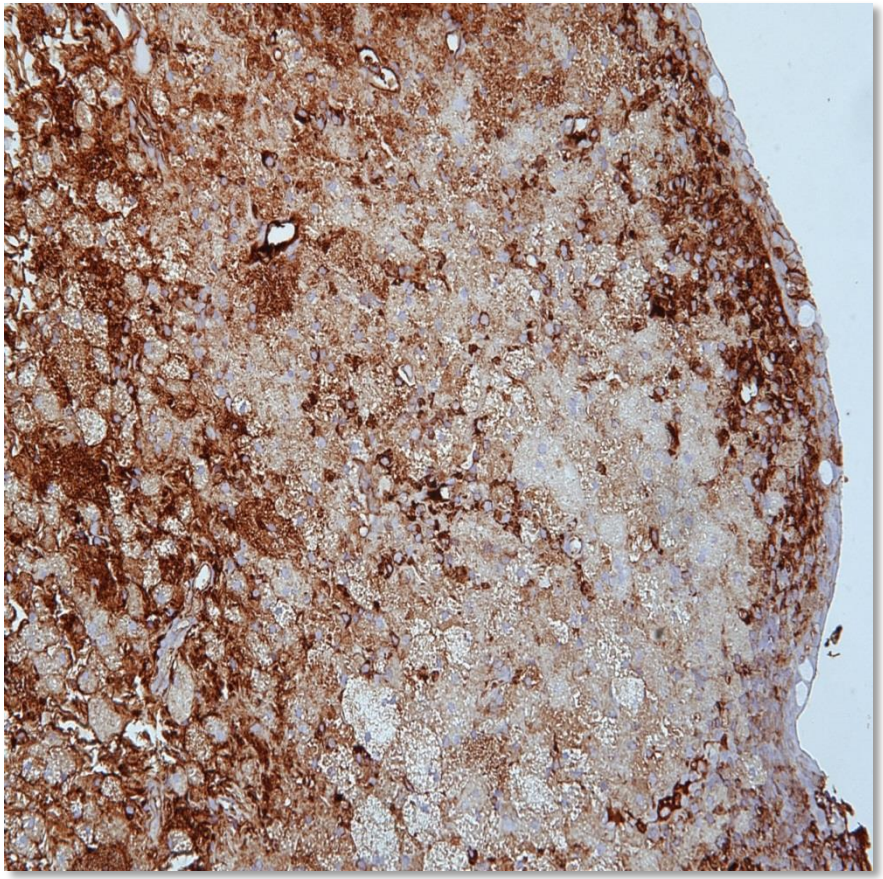


Kappa light chain ISH

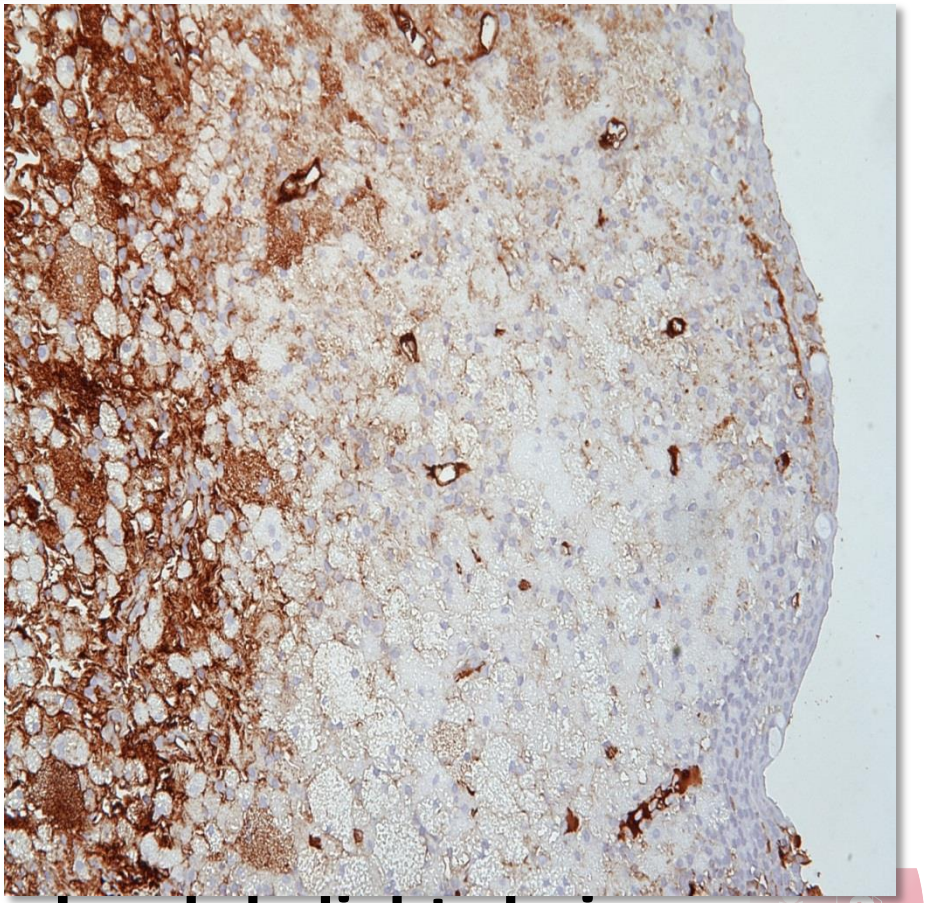


Lambda light chain ISH

Plasma cell phenotype



Kappa light chain IPOX



Lambda light chain IPOX

Pathology

- Diagnosis
  - Crystal-storing histiocytosis of conjunctival fornix
  - Kappa light chain-restricted plasma cells

- Comment:
  - CSH is strongly associated with diseases characterized by monoclonal gammopathy (plasma cell neoplasia, MGUS; 90%; Dogan et al., *Head and Neck*, 2012)
  - Some patients demonstrate extranodal marginal zone lymphoma of ocular adnexae/orbit
  - Chronic inflammatory diseases are uncommonly associated with this condition (~ 9%; Dogan et al., *Head and Neck*, 2012)
  - Rare patients show no evidence of these abnormalities (~1-2%)

Dogan et al., 2012 – Literature Review of 80 CSH Cases

- Sites of localized CSH (46 cases)
  - Head and neck (35%)
    - Eye/orbit (13%)

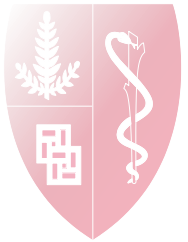
- In generalized CSH (34 cases), conjunctival involvement appears to be rare (~3%)

Dogan et al., 2012

Table 1 Proposed classification of CSH

According to etiology and/or associated disease	According to crystal
1. Hematopoietic	1. Immunoglobulin
A. Multiple myeloma	A. Type
B. Extramedullary plasmacytoma	(1) Heavy chain
C. Lymphomas	(2) Light chain
	B. Clonality
2. MGUS-Amyloid	(1) Monoclonal
	(2) Polyclonal
3. Drugs	(3) Indeterminate
A. Clofazimine	
	2. Clofazimine
4. Allergic-autoimmune	
A. Rheumatoid arthritis	3. Charcot-Leyden
B. Eosinophilic colitis	
C. Mastocytosis	4. Other
D. Hypereosinophilic syndrome	A. Cystine
	B. Silica
5. Metabolic	
A. Cystinosis	
6. Inflammatory-reactive	
A. Pulmonary infections	
B. Plasma cell granuloma	
C. Crohn's disease	
D. *Helicobacter pylori*	
7. Other	
A. Silica	

CSH crystal-storing histiocytosis, *MGUS* monoclonal gammopathy of undetermined significance



Literature review: Localized CSH in ocular adnexa and orbit

Reference	Demographic	Presentation	CSH Sites	CSH Laterality	Diagnosis (plasma cell phenotype)	Paraproteinemia
Pinkerton et al, [6]	50, Male	↓ visual acuity	Conj., cornea	Left	MM	Elevated IgG (SPEP)
Rao et al. [8]	17, Female	Papillary conjunctivitis	Upper and Lower Lids	Bilateral	None	Elevated IgG (SPEP)
Grossniklaus et al. [4]	64, Female	Blurred vision	Conj., cornea	Bilateral	? MGUS (no marrow bx)	IgA/kappa
de Alba Campomanes et al. [2]	66, Male	Left Eye Ptosis, proptosis, external ophthalmoplegia	Orbital fat, EOM	Left*	MGUS	IgG/lambda (SPEP)
Coupland et al. [1]	62, Woman	Diplopia, eyelid swelling	Lacrimal gland, conj.	Left	Recurrent EMZL, (IgM/kappa)	Negative (SPEP)
Kusakabe et al. [5]	81, Male	Slowly enlarging tumor of left	Lower eyelid, inferior	Left	EMZL (IgM/kappa)	(-)

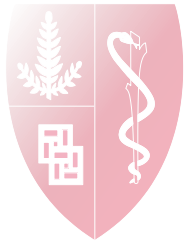
- Not reported; * patient reported to have bilateral crystalline keratopathy; MM – multiple myeloma; MGUS – monoclonal gammopathy of undetermined significance; EMZL – extranodal marginal zone lymphoma; SPEP – serum protein electrophoresis

Results potentially suggest:

- bilateral orbital CSH may be more likely associated with paraproteinemia or monoclonal gammopathy
- unilateral orbital CSH with EMZL of orbit
- more cases clearly

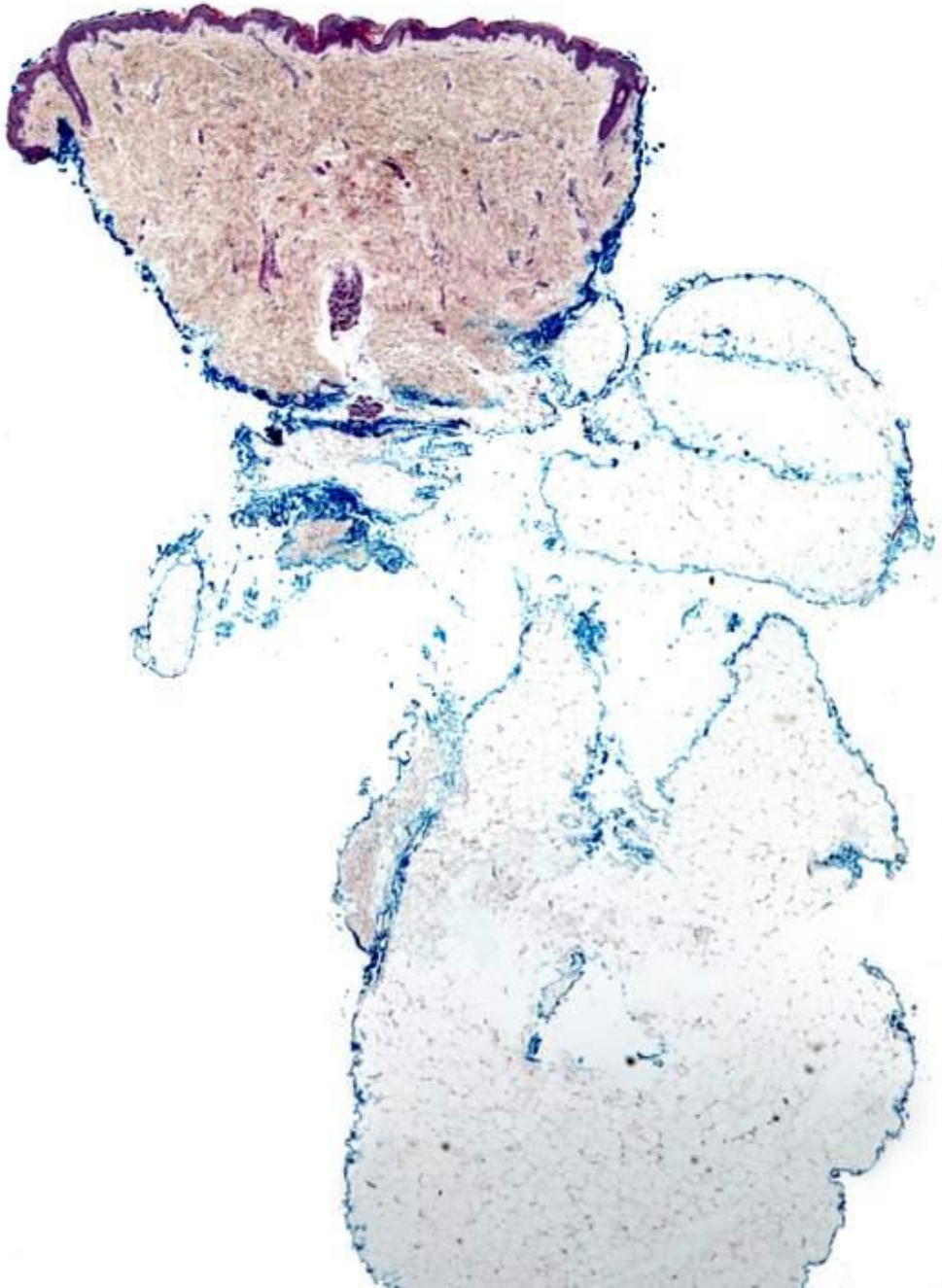
Case Follow-up

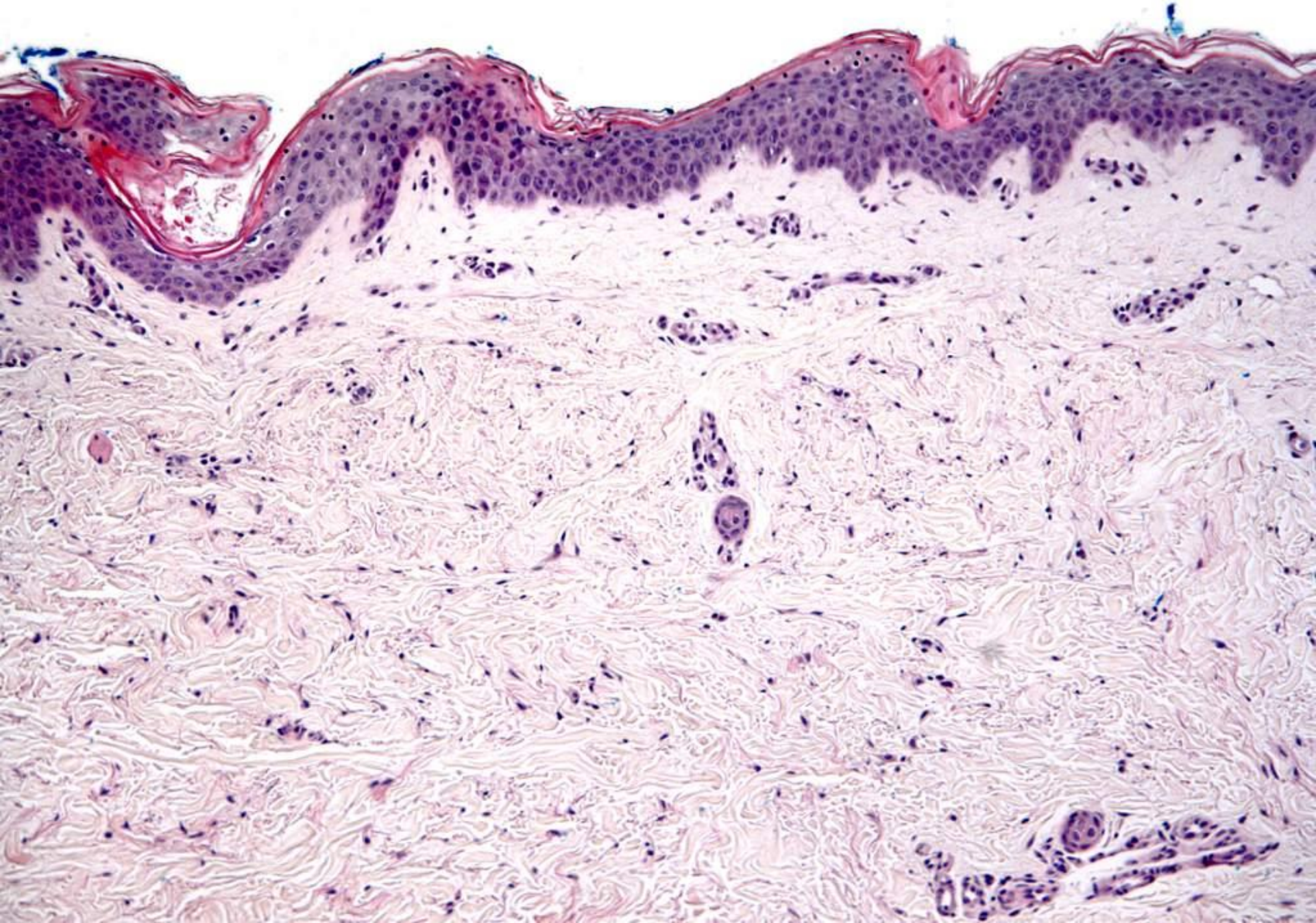
- Lymphoma and Paraprotein Workups Negative
  - CBC normal; Chemistry showed no evidence of renal failure
  - CT neck, CAP
  - MRI orbits
  - IgG panel, SPEP, UPEP, free light chain ratio, LDH, beta 2 microglobulin
- Bone marrow biopsy deferred; follow-up recommended

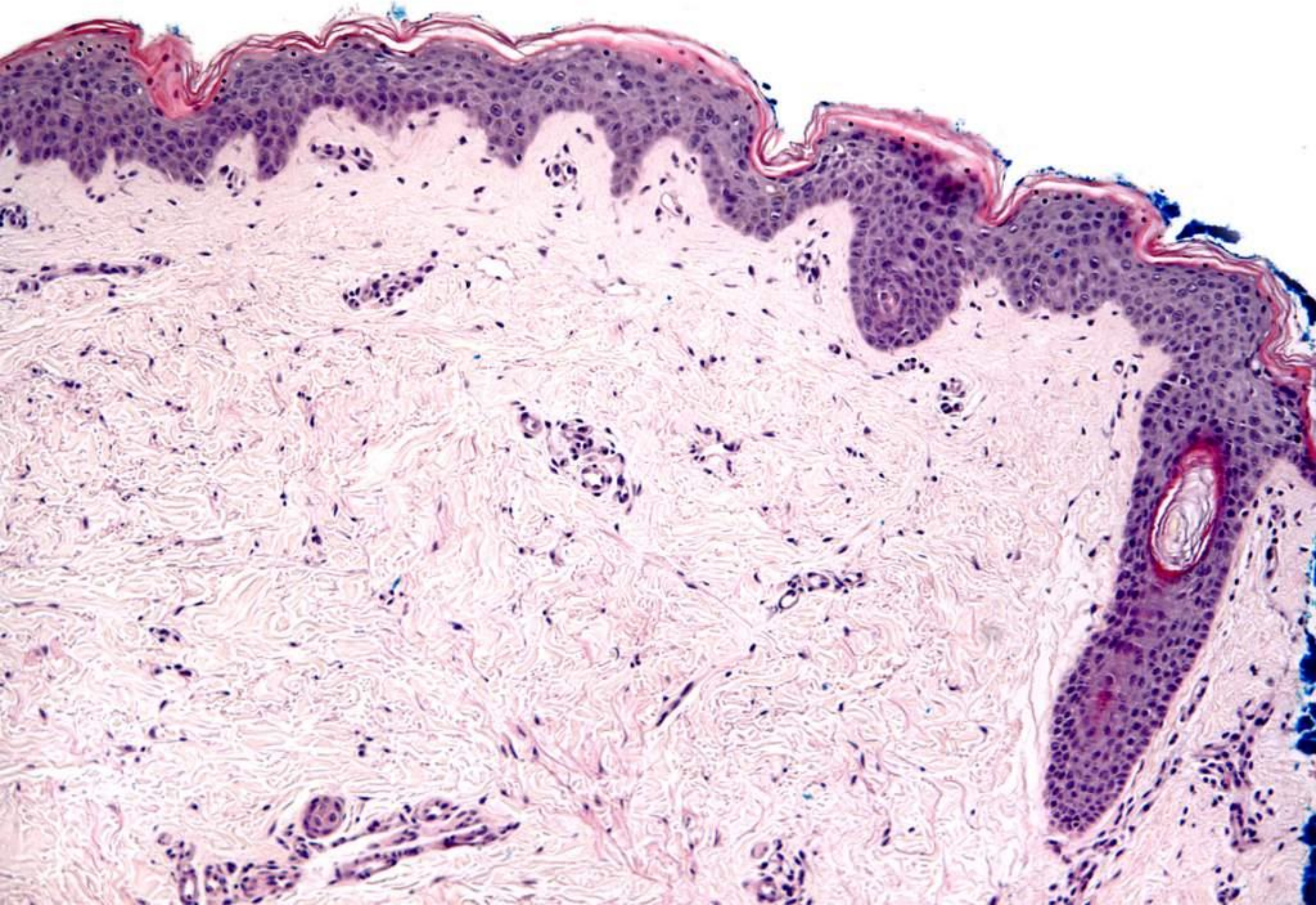


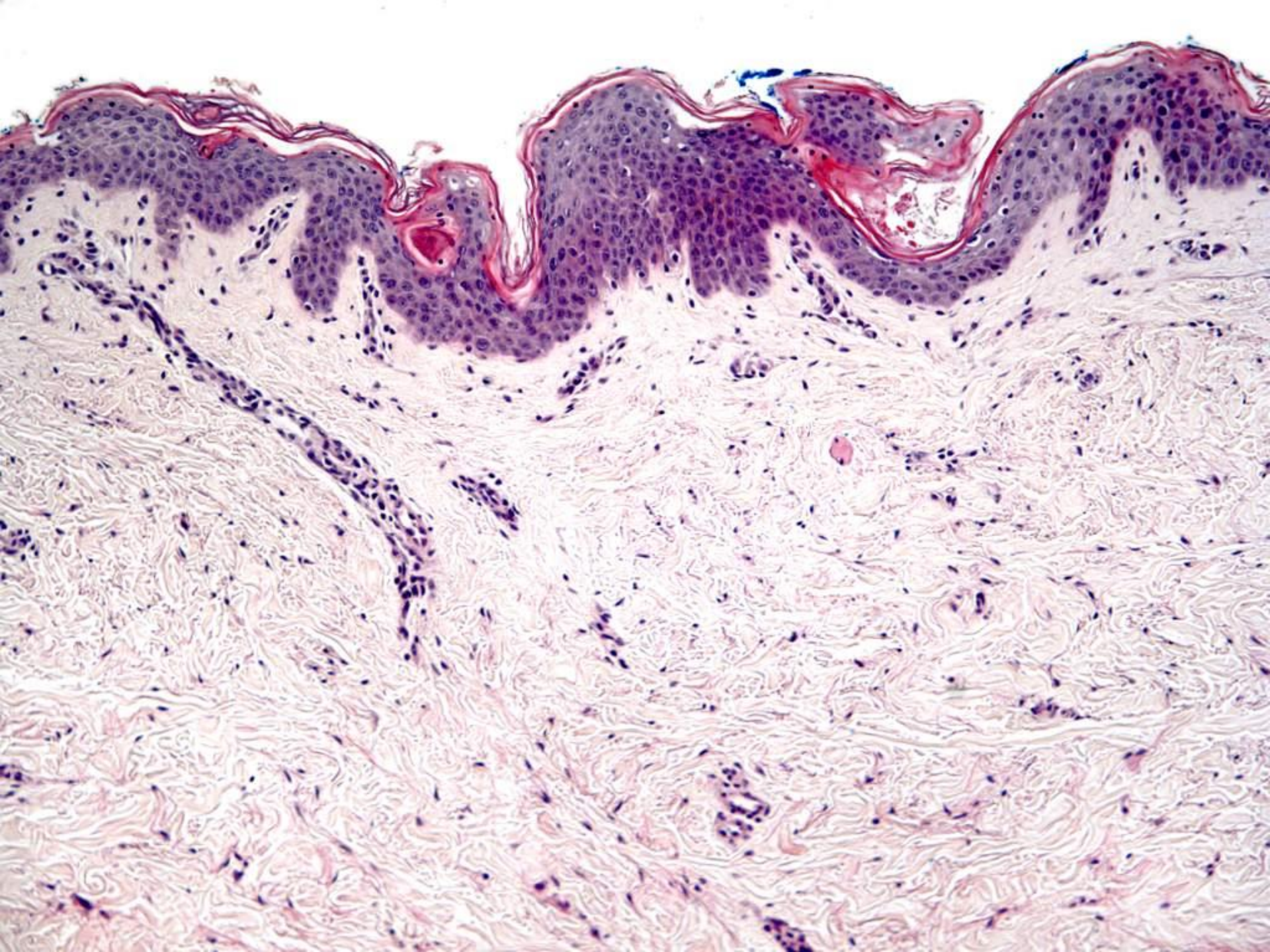
SB 5962
Uma Sundram; APMG

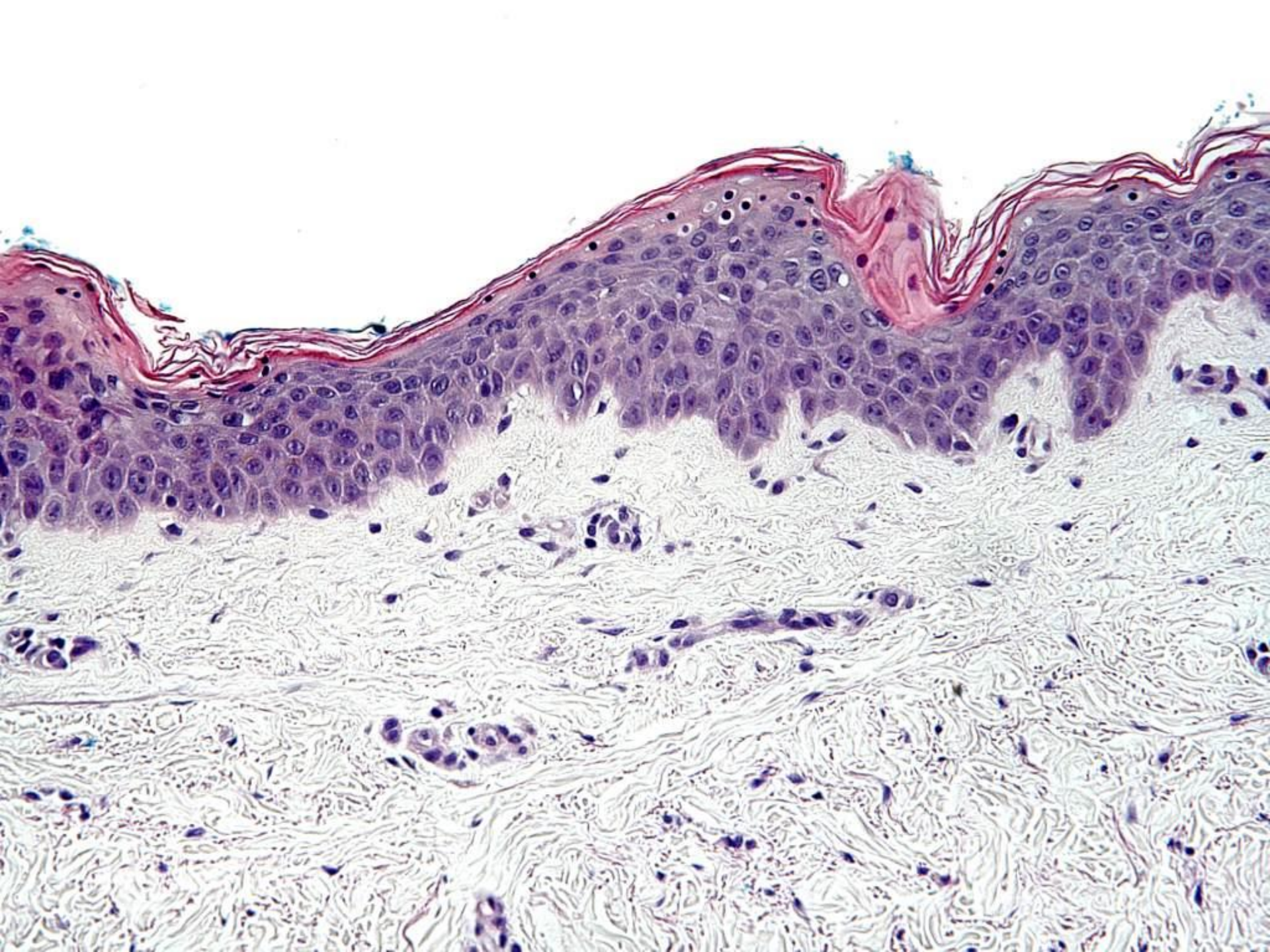
19-month-old female with new onset rash that started in diaper area and now involves proximal arms/legs and cheeks. Erythematous, blanching patches in diaper area (sparing folds) and neck, cheeks, and proximal arms/legs noted. No satellite lesions or pustules were seen. A biopsy of a right thigh lesion was performed.

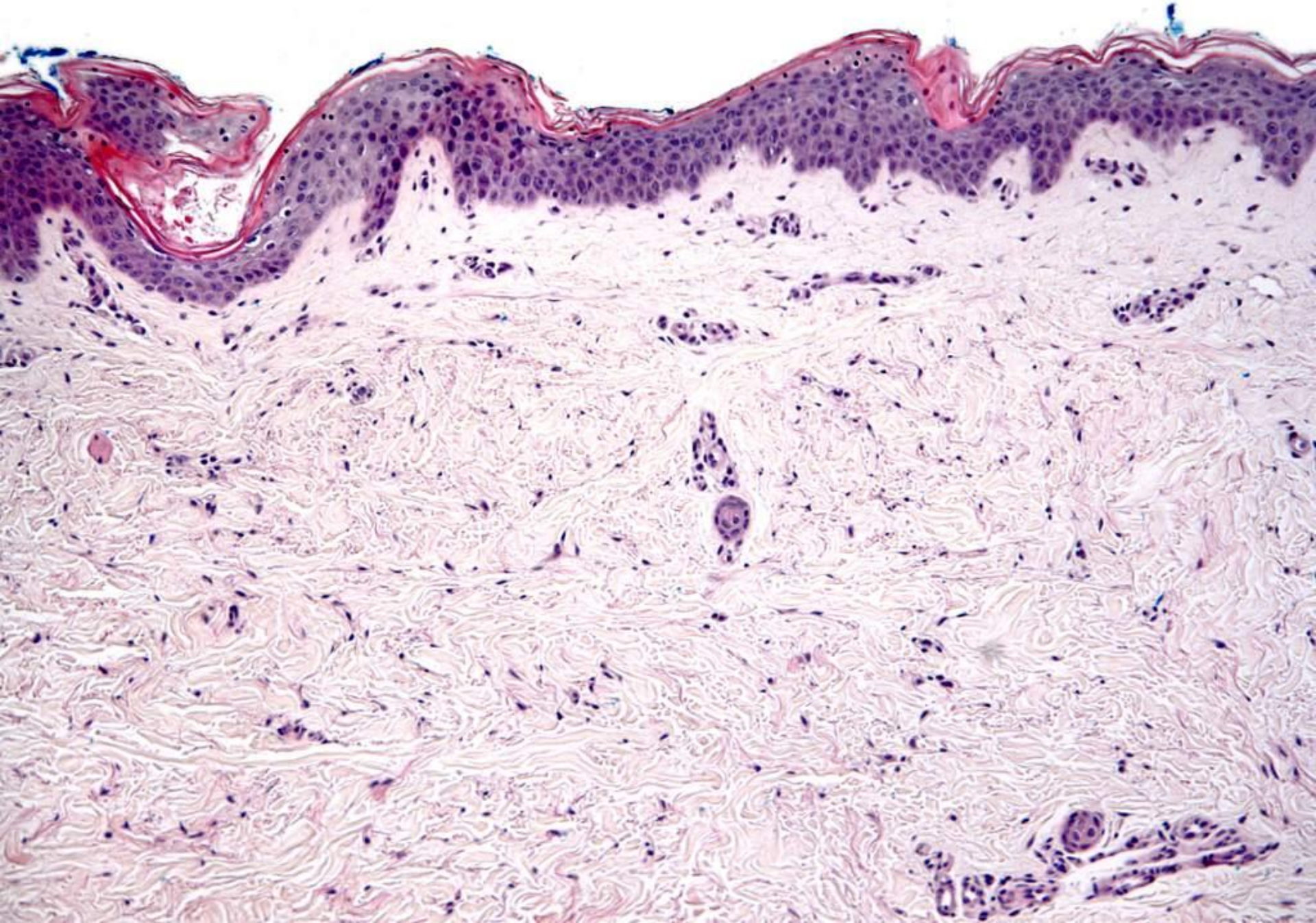


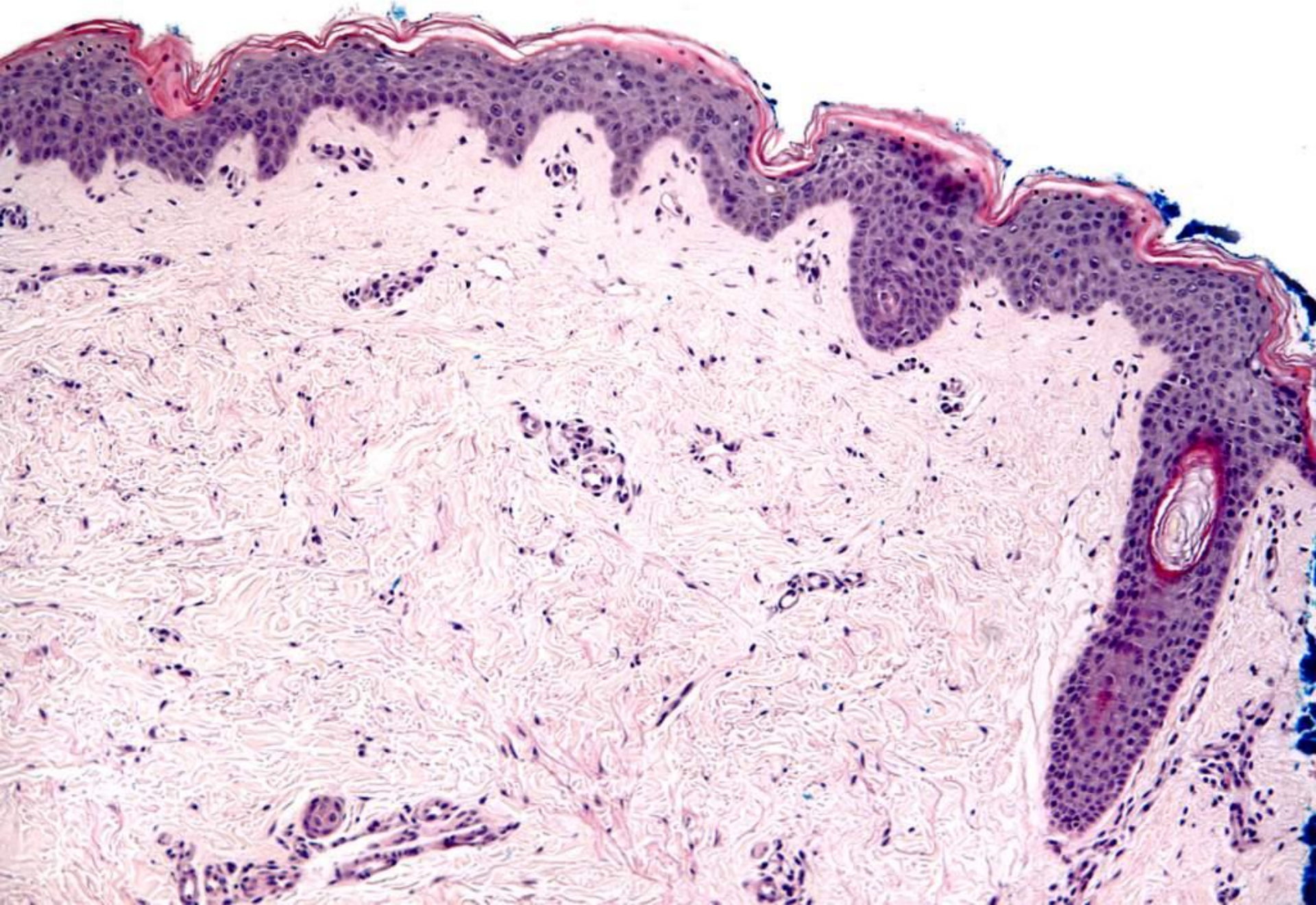


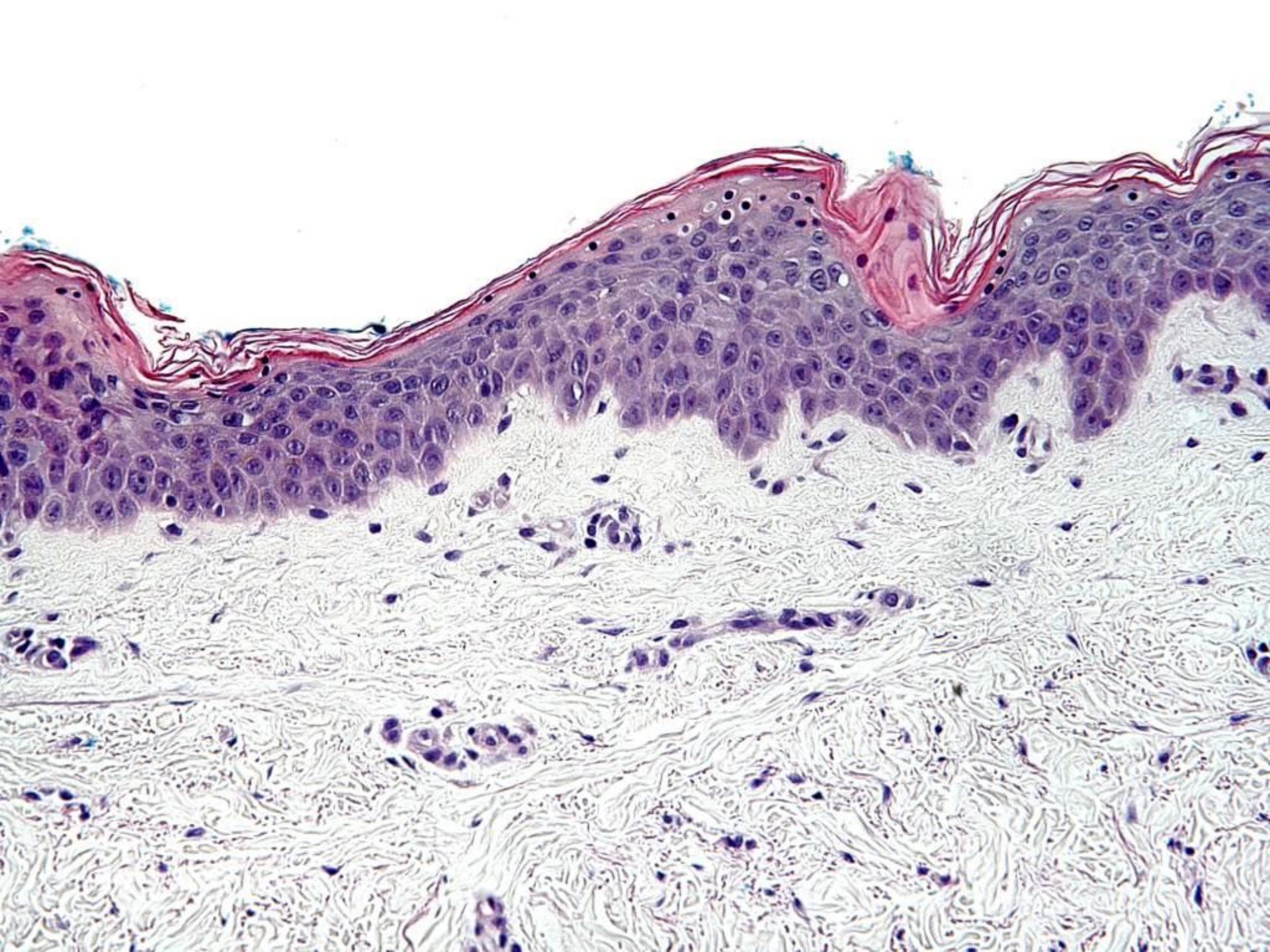












Nutritional Deficiency due to nonfunctional priopionic CoA carboxylase

- Patient has history of *propionic acidemia*
- Rare autosomal recessive metabolic disorder
- Causes accumulation of propionic acid
- Non functional propionyl CoA carboxylase, which converts propionyl CoA to methylmalonyl CoA

Propionic Acidemia/Aciduria

- Propionyl CoA carboxylase key step in converting certain AAs into sugar
- When blocked, increased levels of propionyl CoA accumulates, converted to propionic acid
- Accumulation of PA leads to organ damage, including brain, heart and liver
- Requires immediate treatment

Nutritional deficiency (necrolytic erythemas)

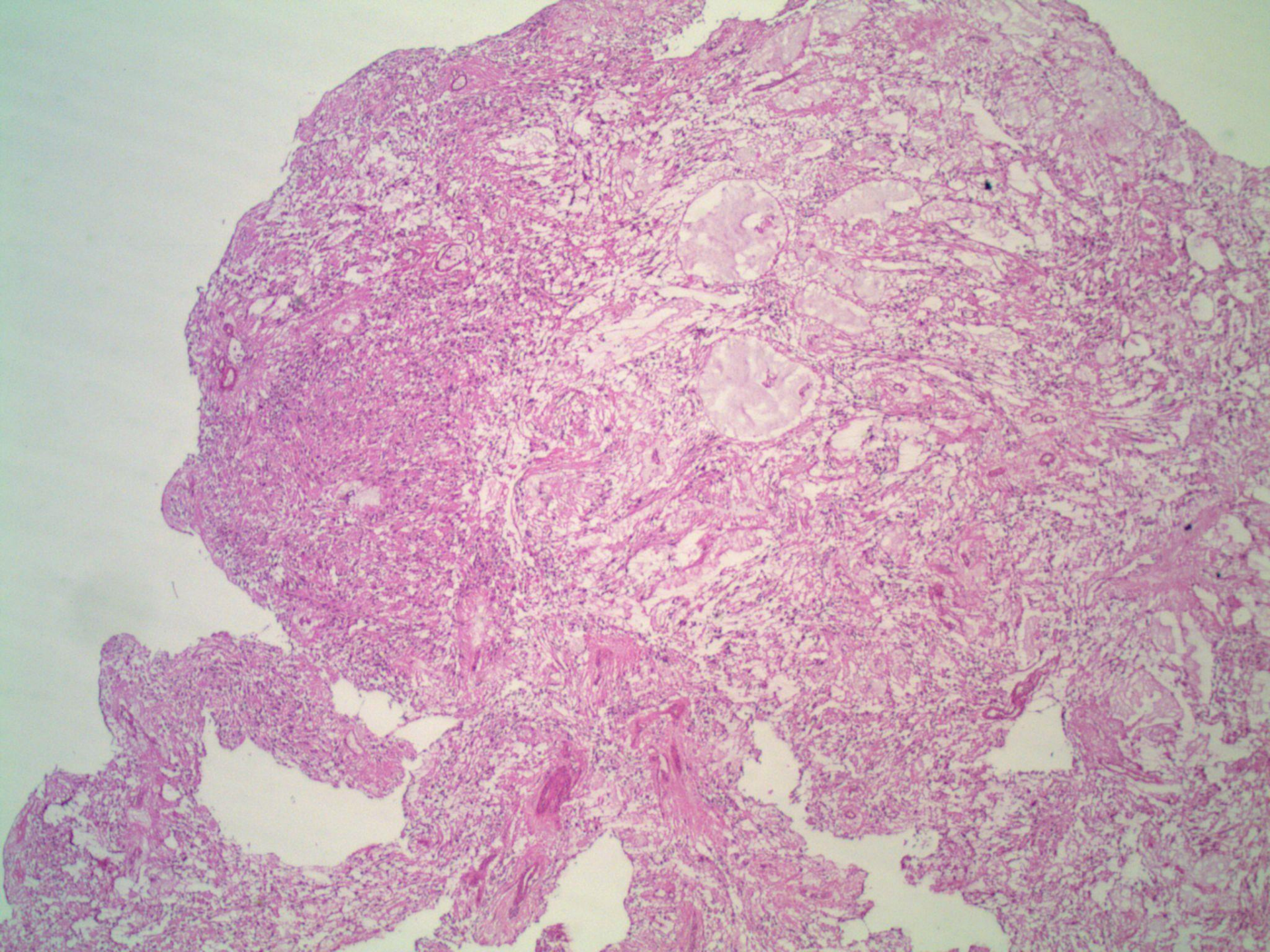
- Propionic acidemia can give rise to nutritional deficiency type rash
- Group of cutaneous diseases of metabolic origin
- Includes acrodermatitis enteropathica, glucagonoma syndrome, and necrolytic acral erythema

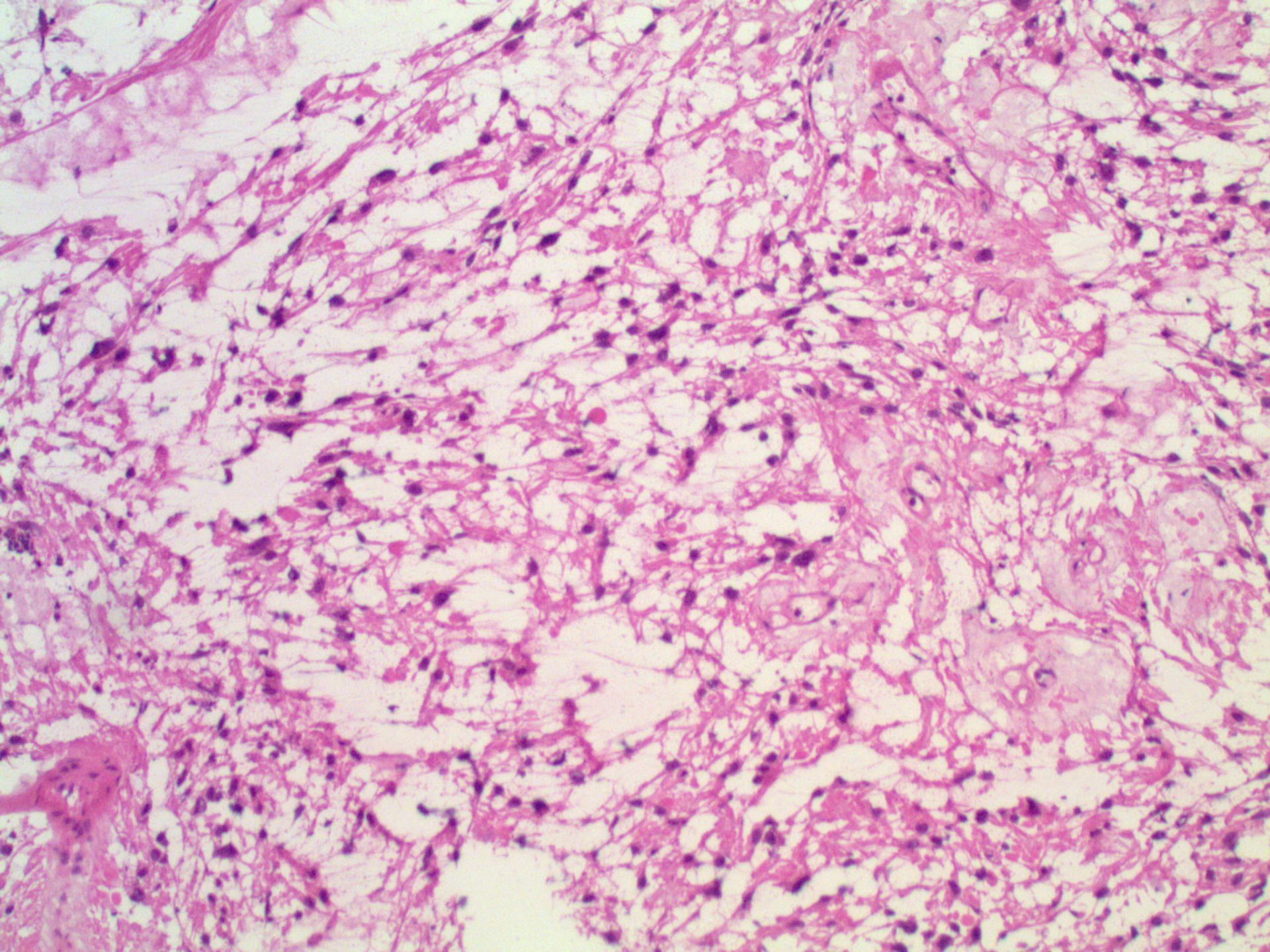
Nutritional deficiency (necrolytic erythemas)

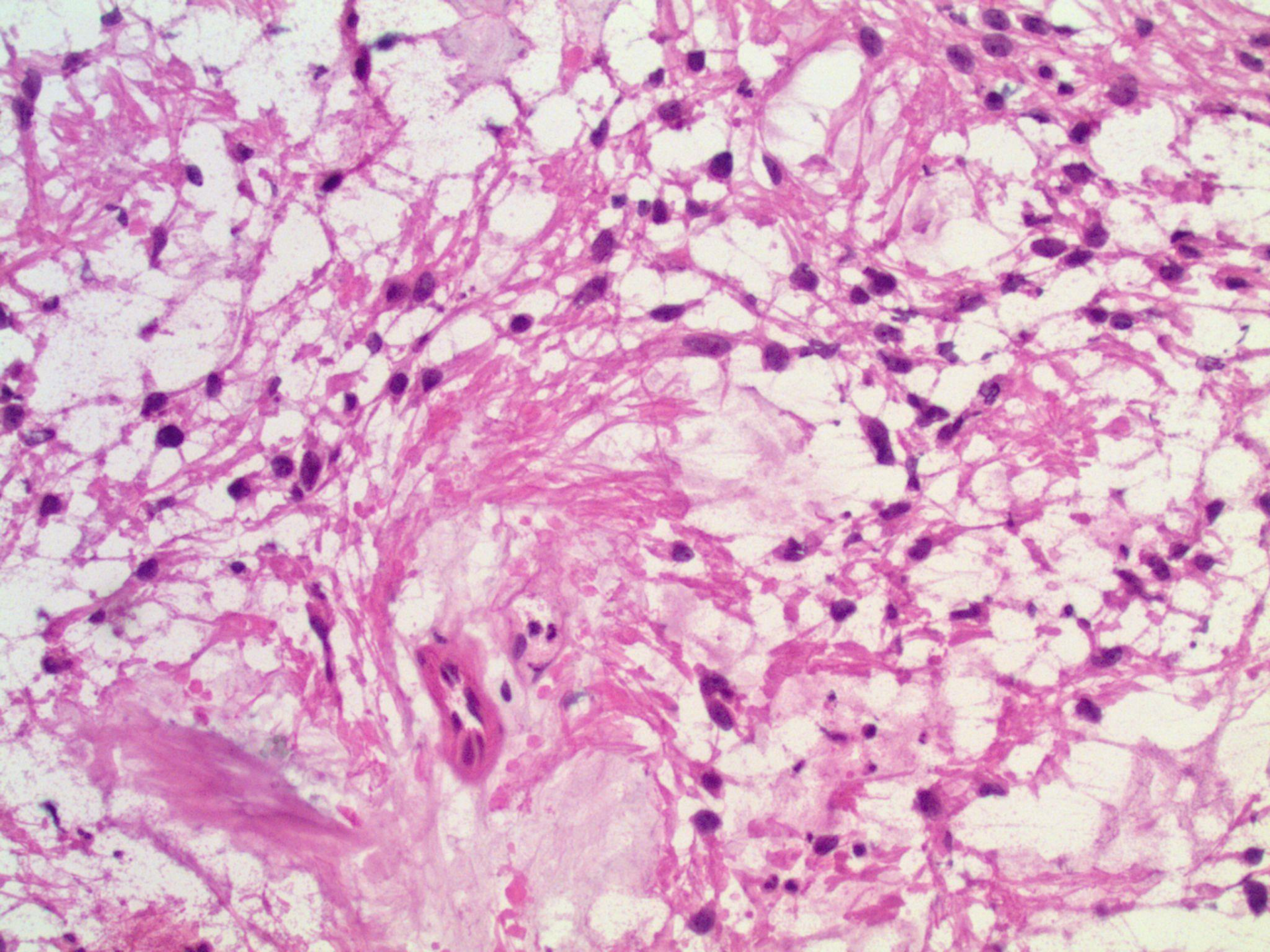
- On histopathology, there is confluent parakeratosis overlying an acanthotic epidermis with psoriasiform hyperplasia
- The granular layer is absent
- There is increasing uniform epidermal pallor involving the upper epidermis with pyknotic nuclei

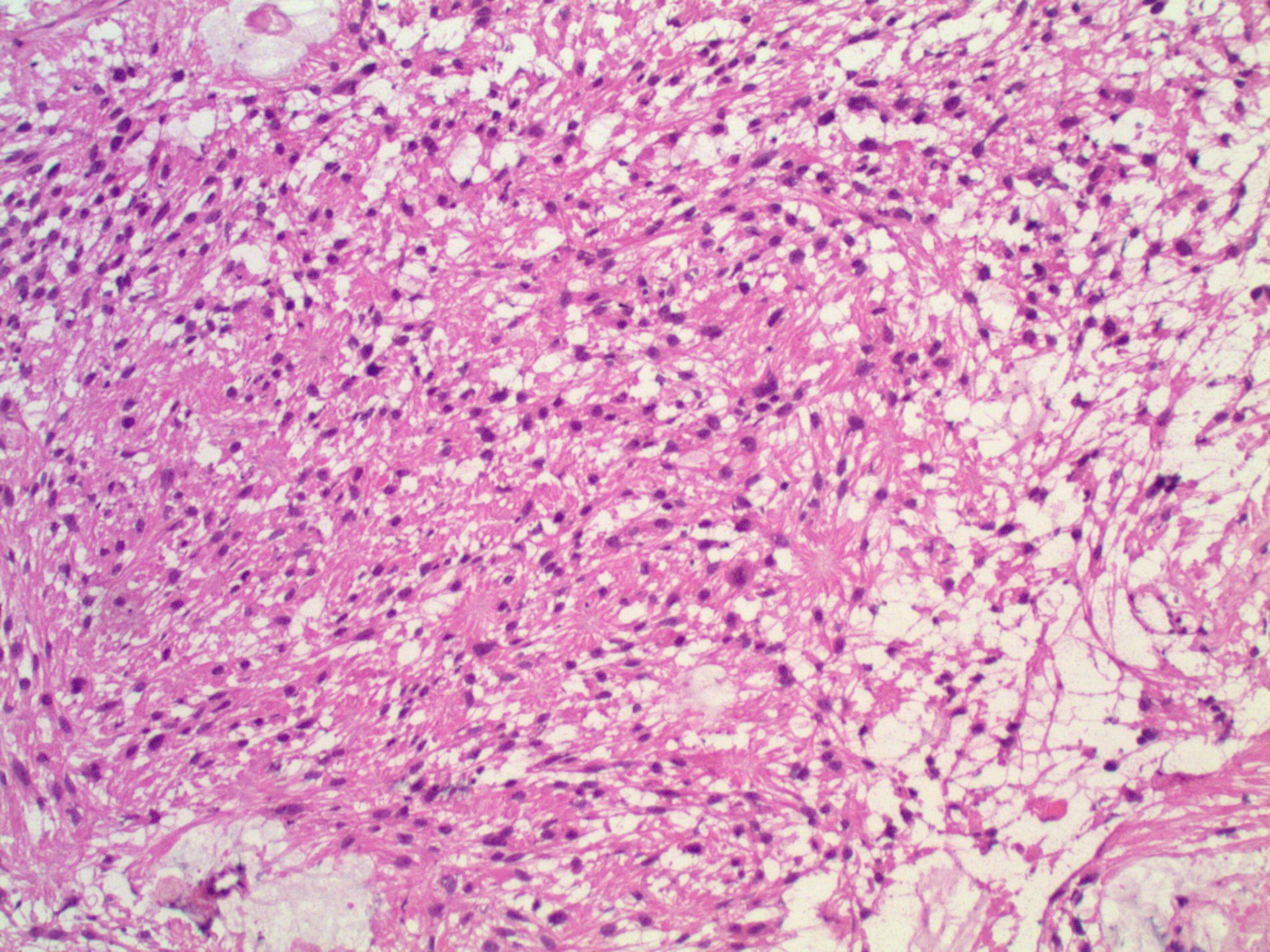
SB 5963
Ankur Sangoi; El Camino Hospital

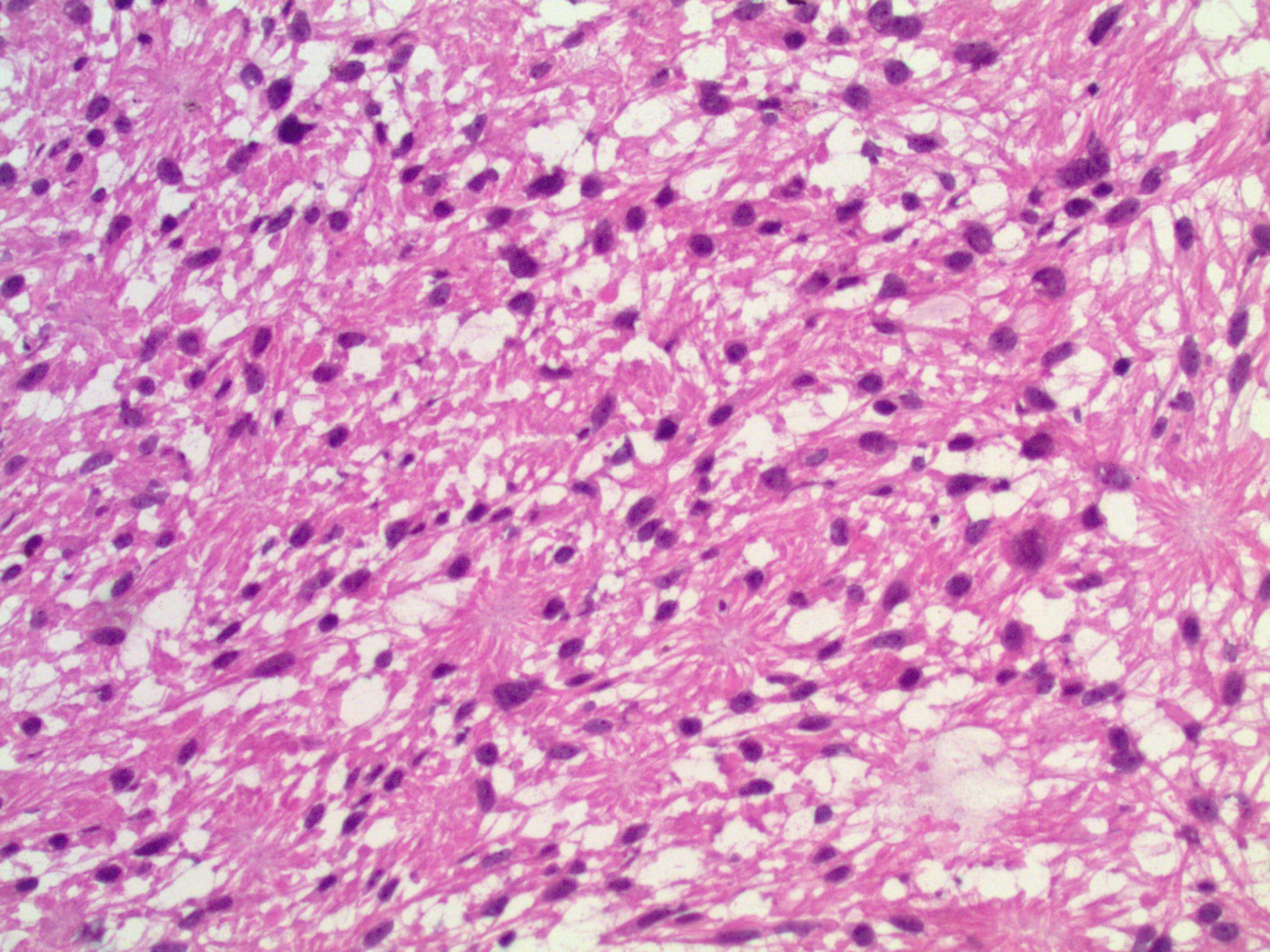
59-year-old man with lumbar spinal tumor. Frozen section/smear performed.

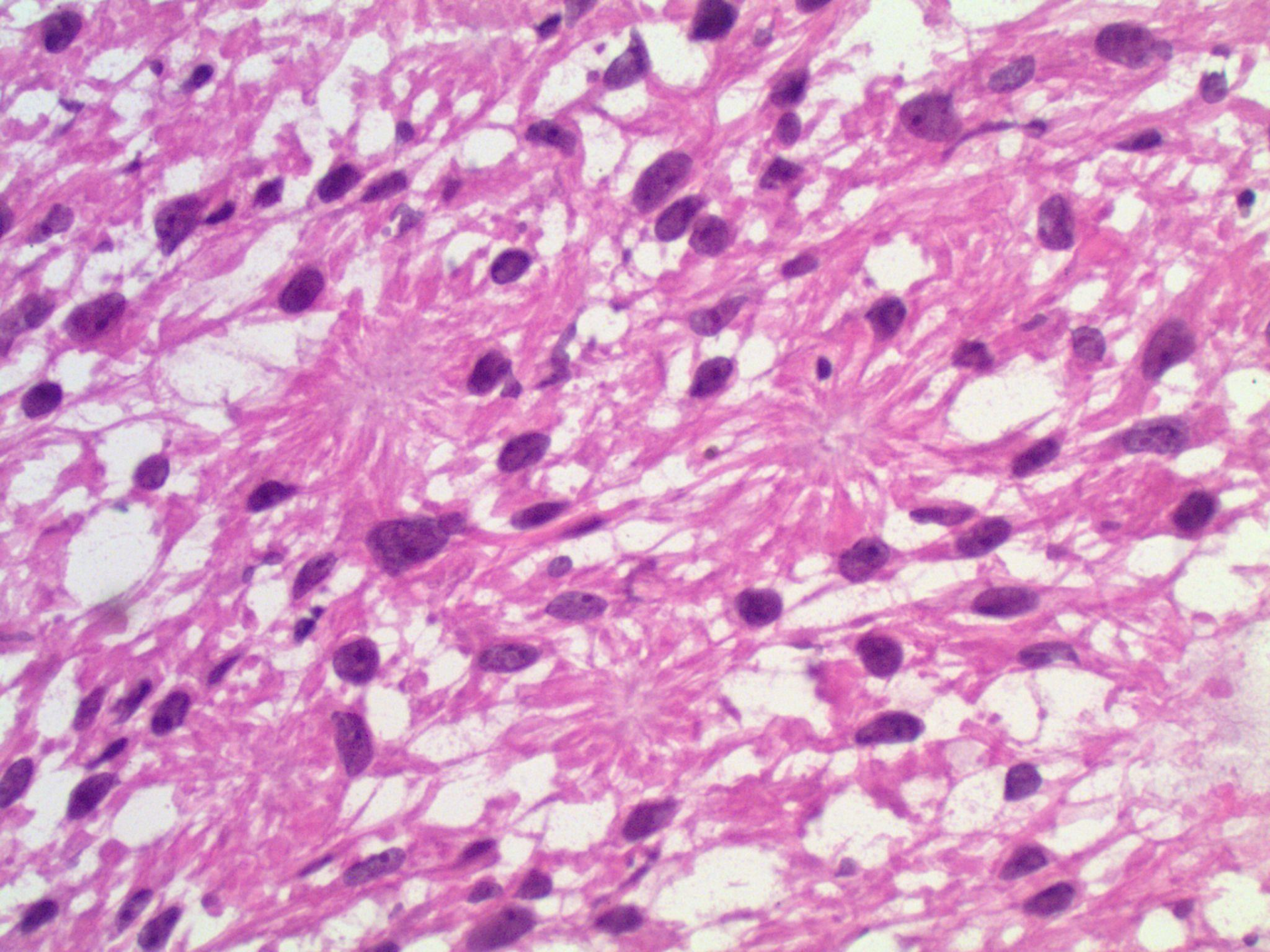


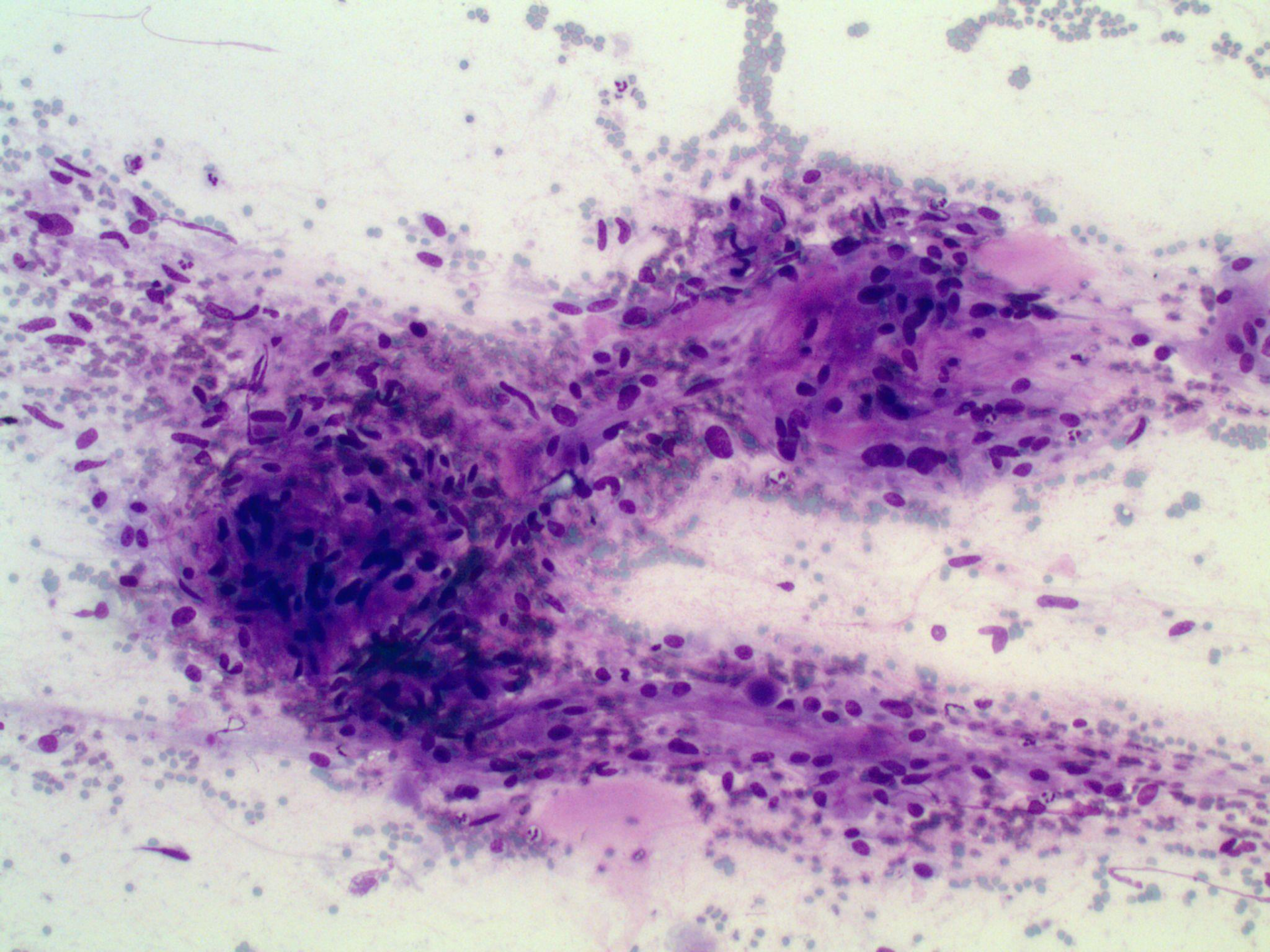


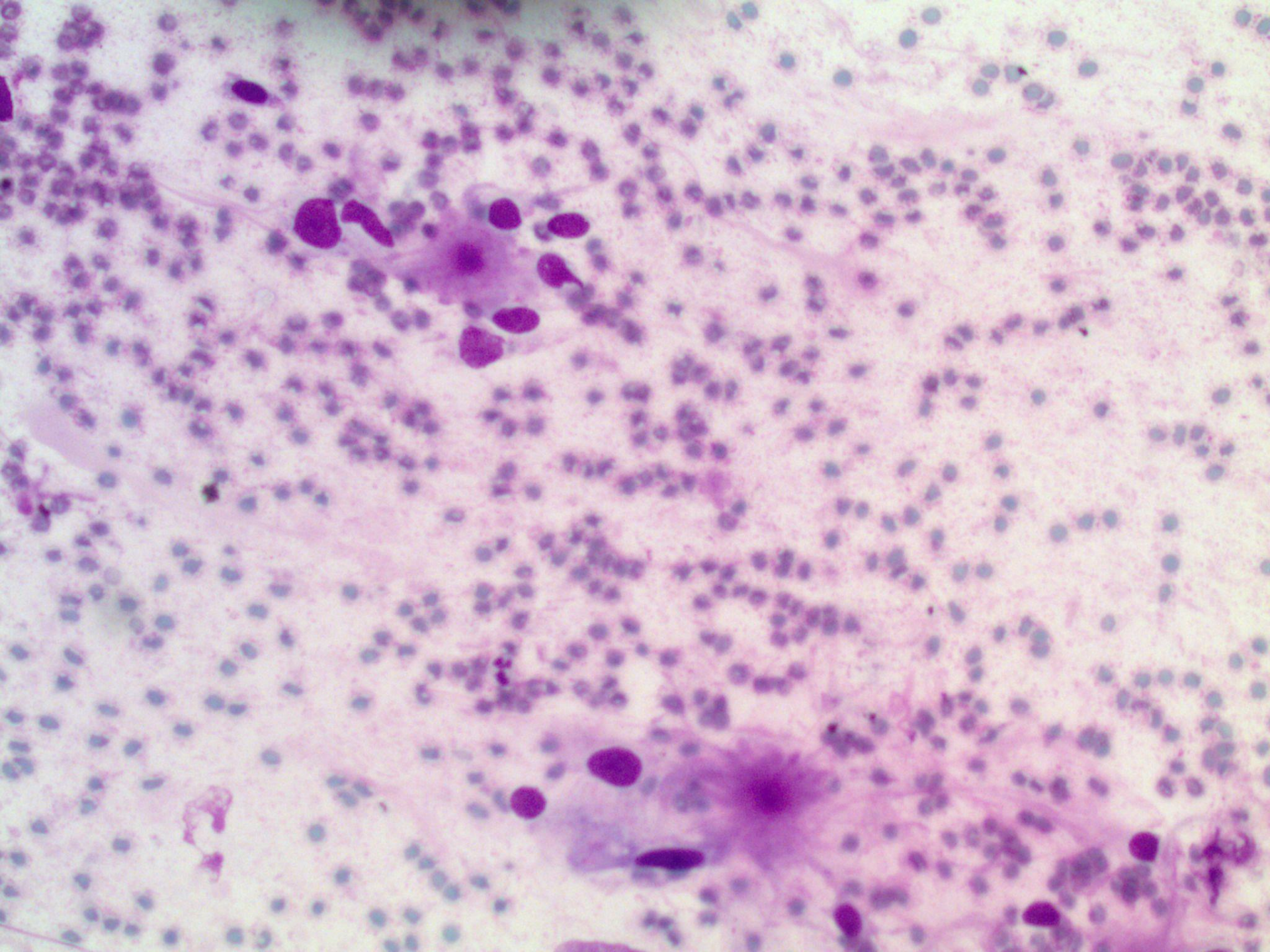


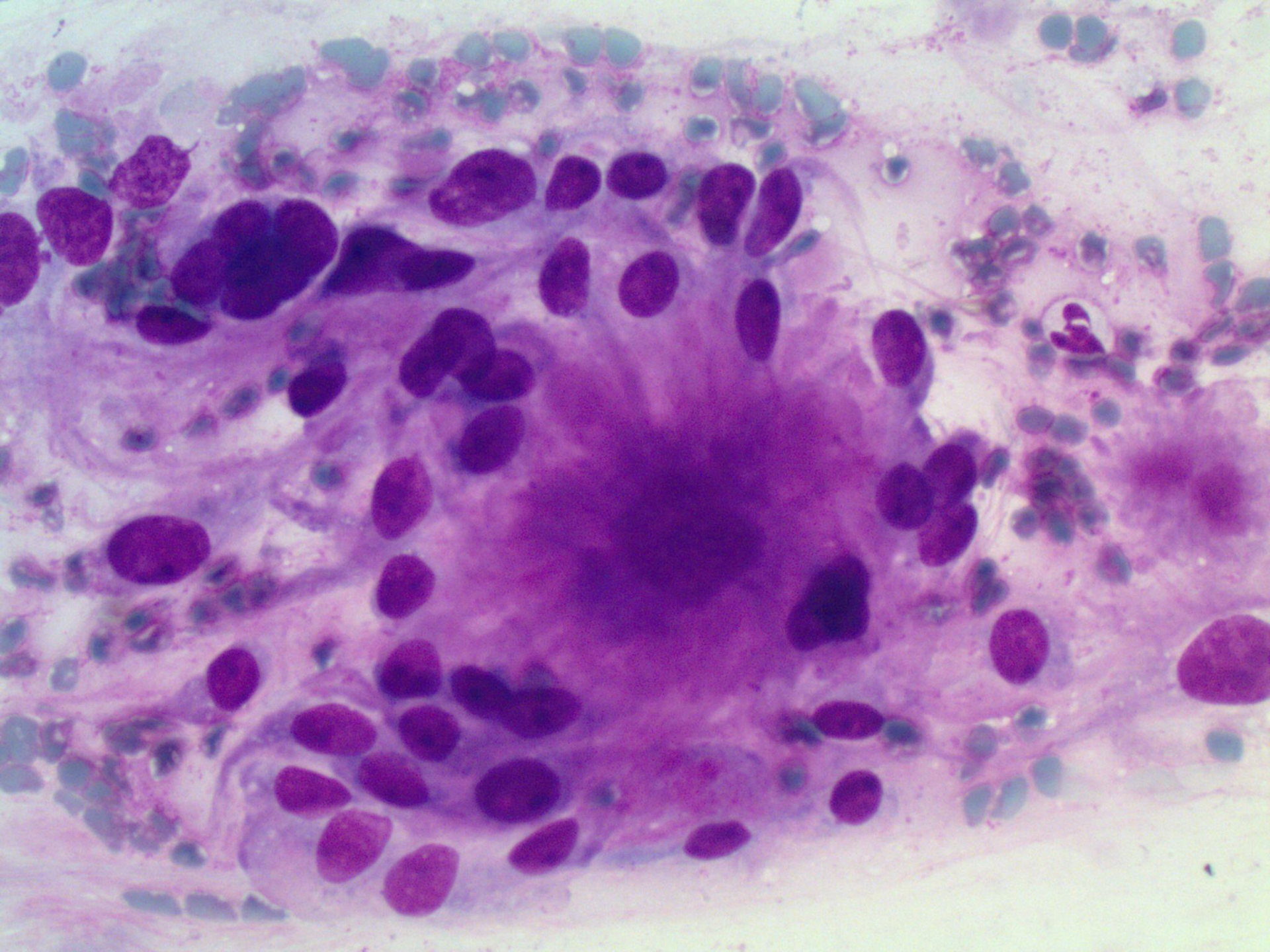


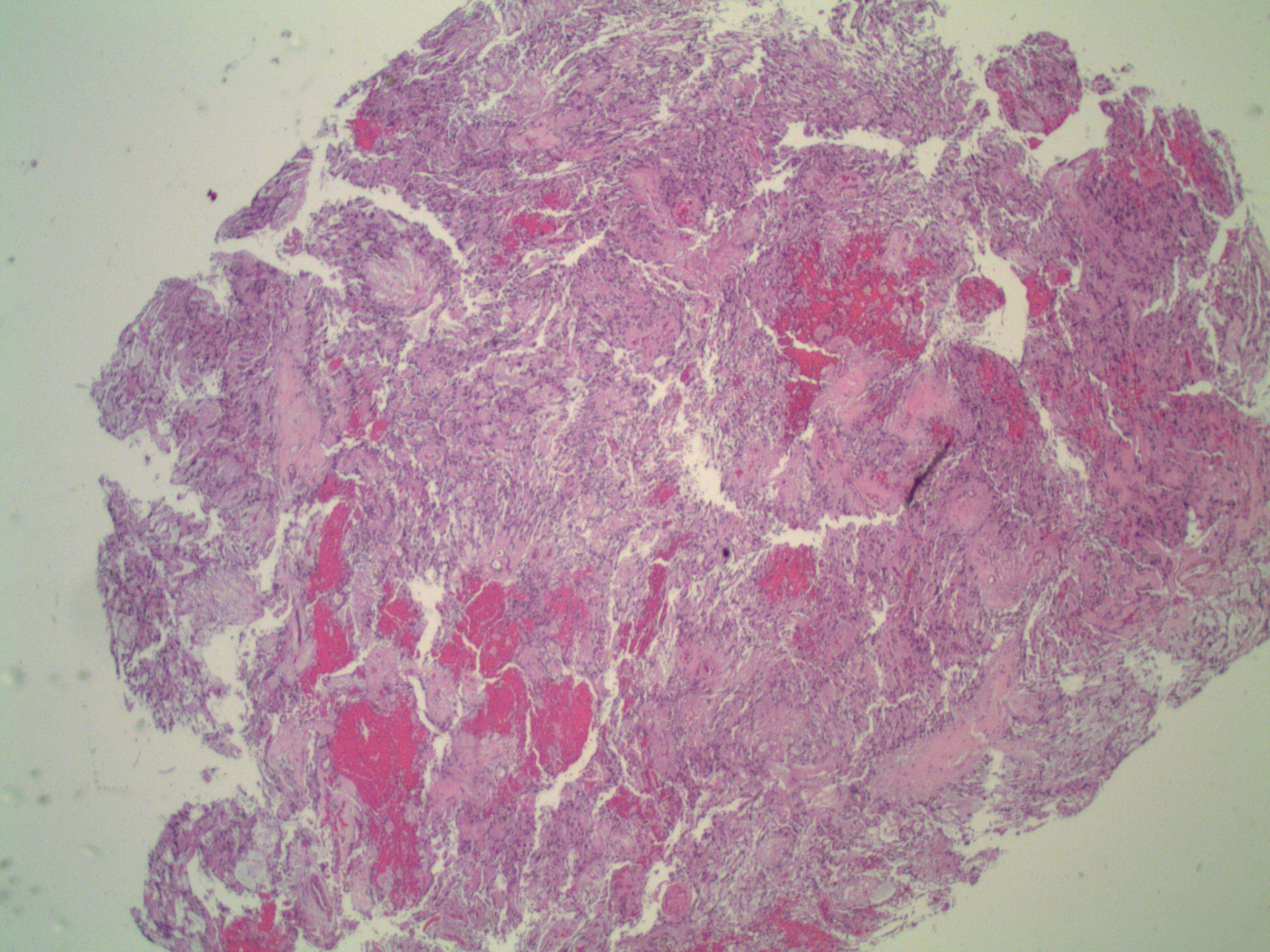


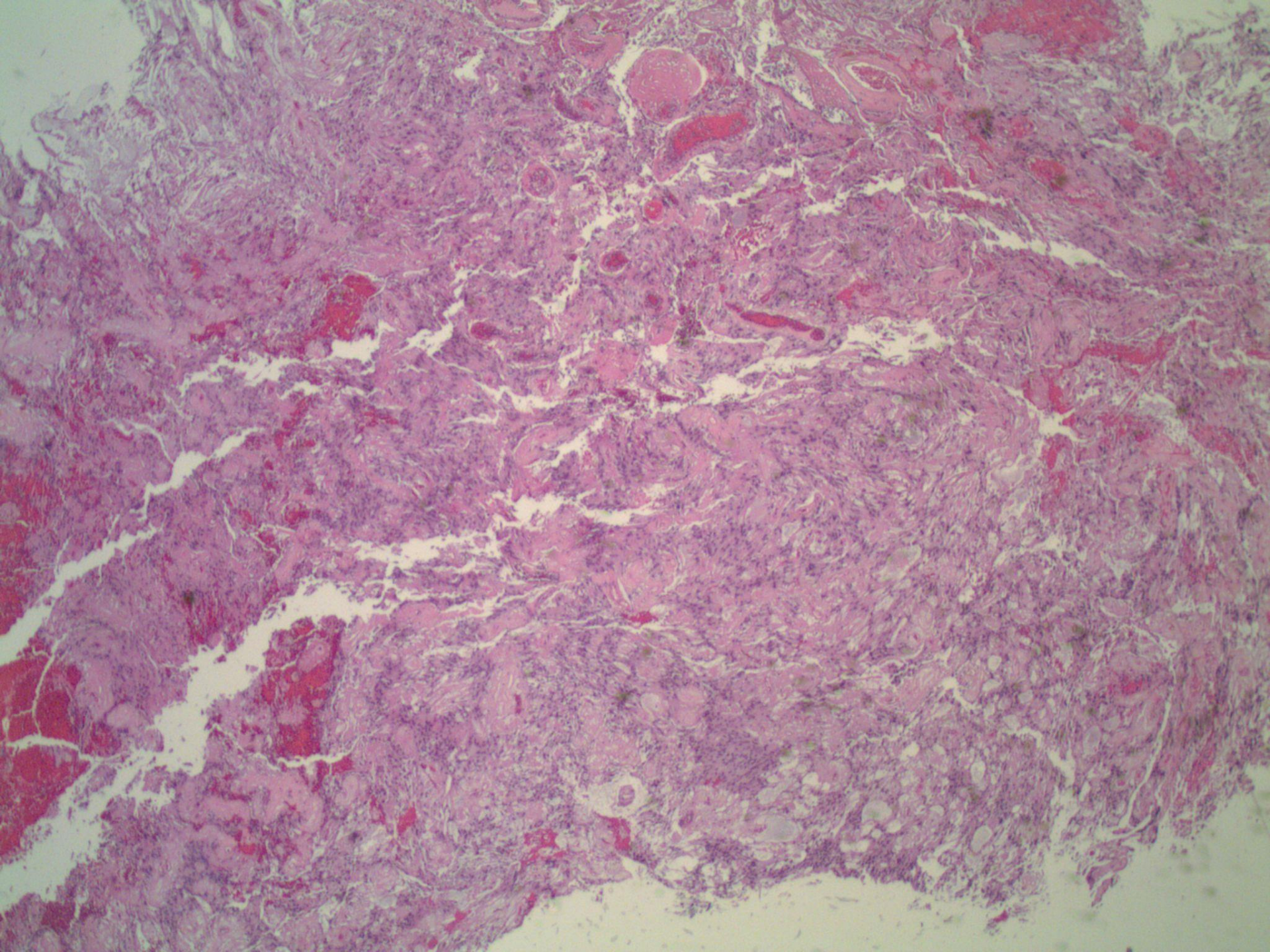


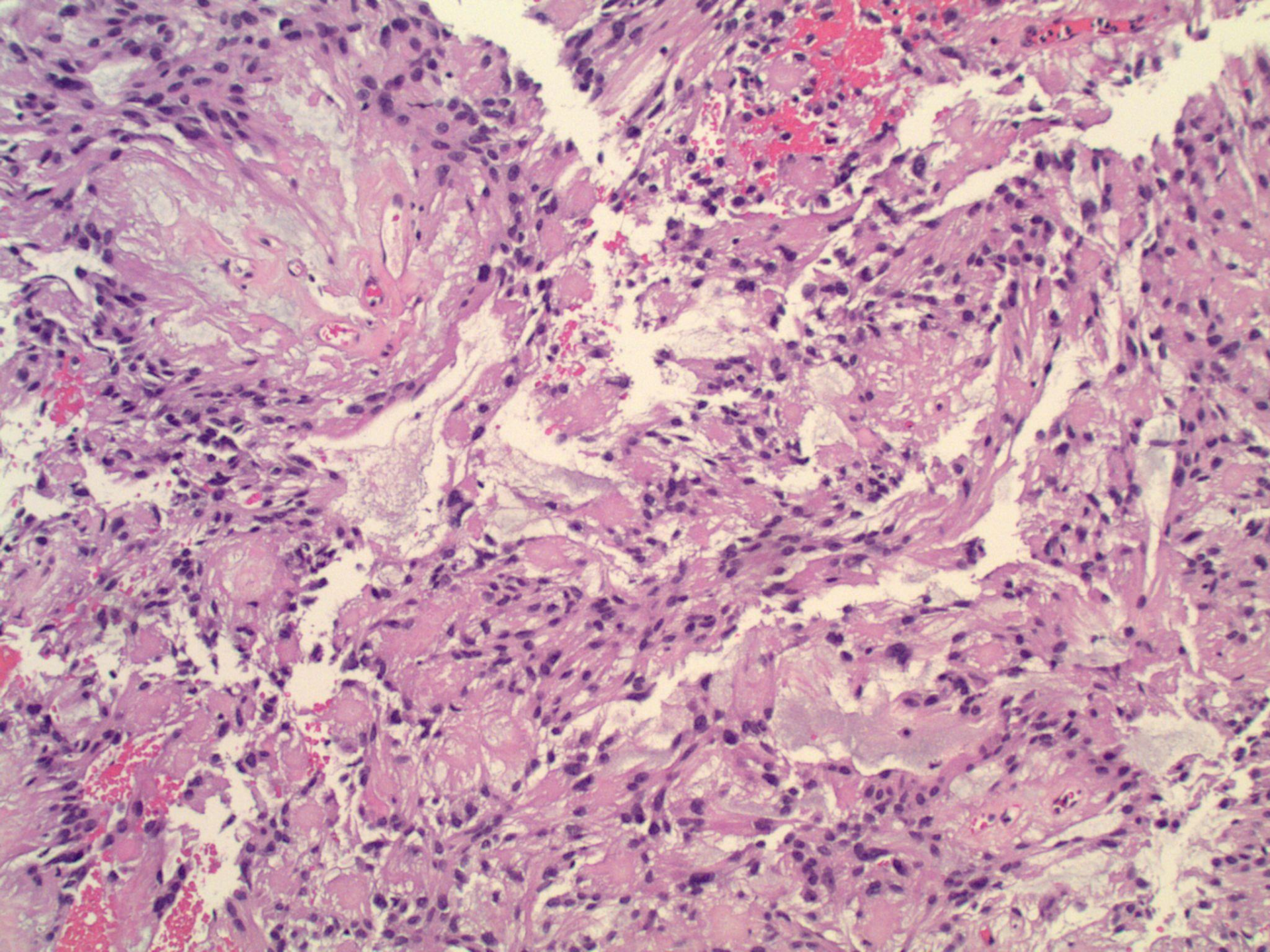


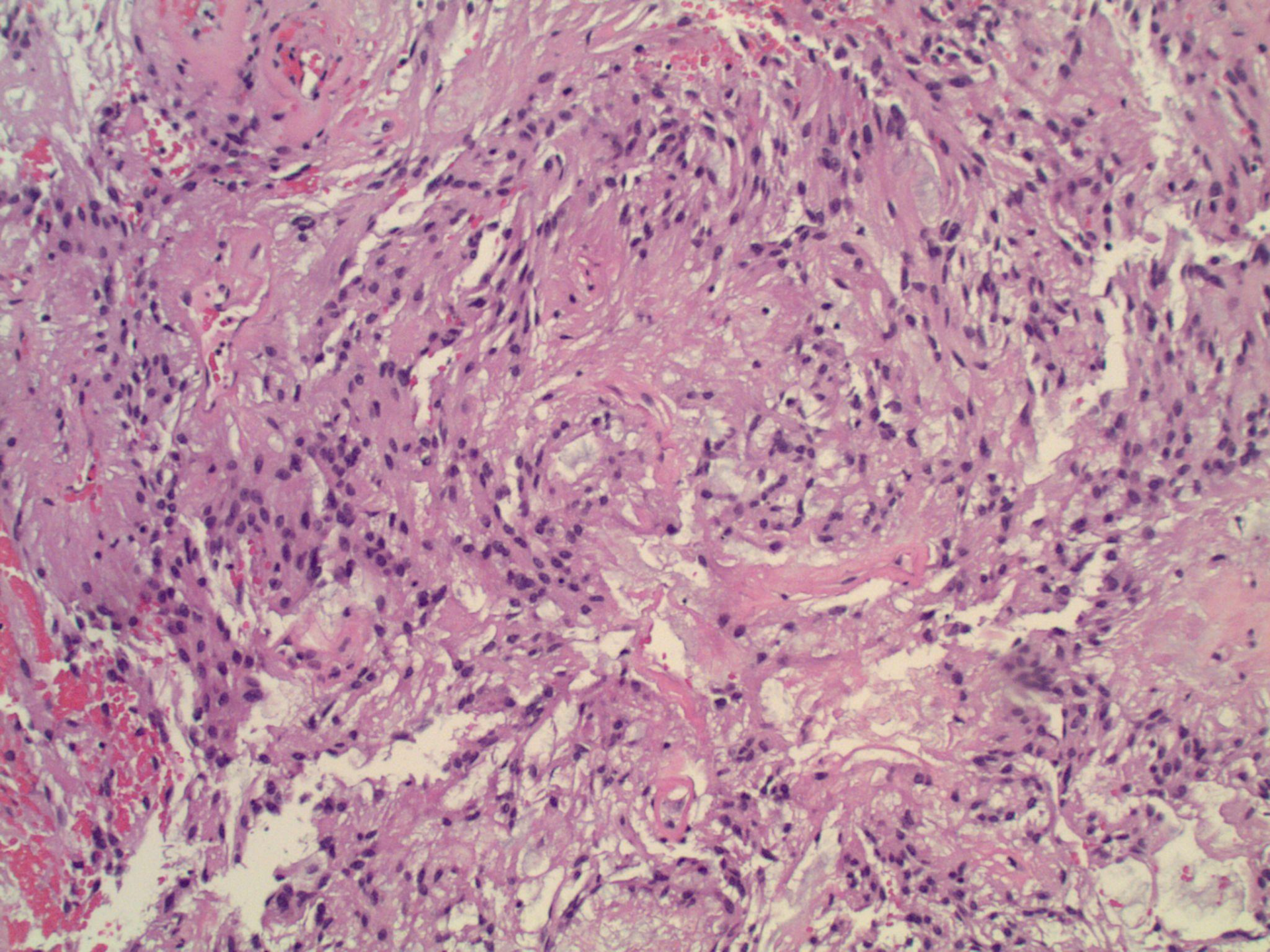


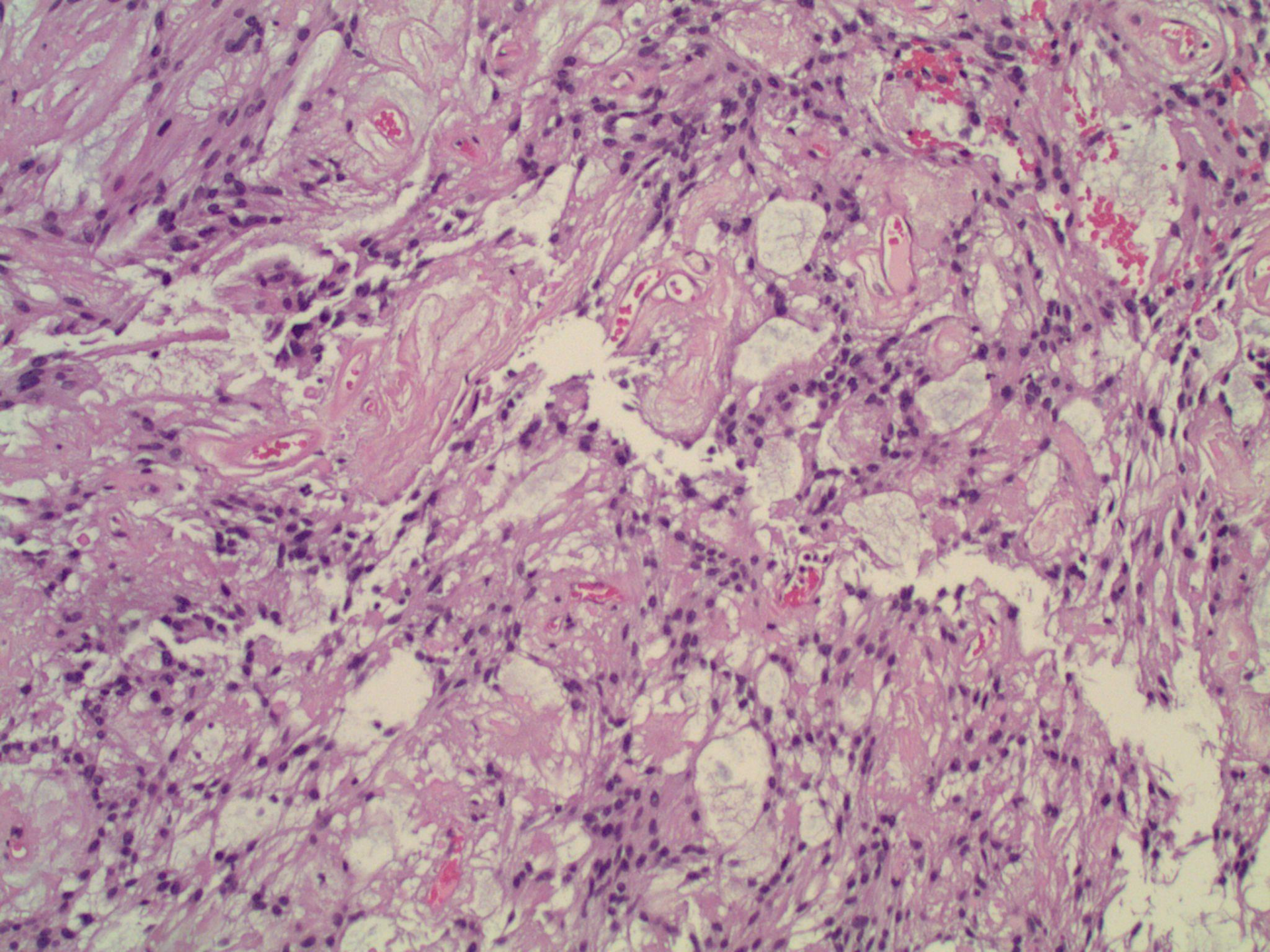


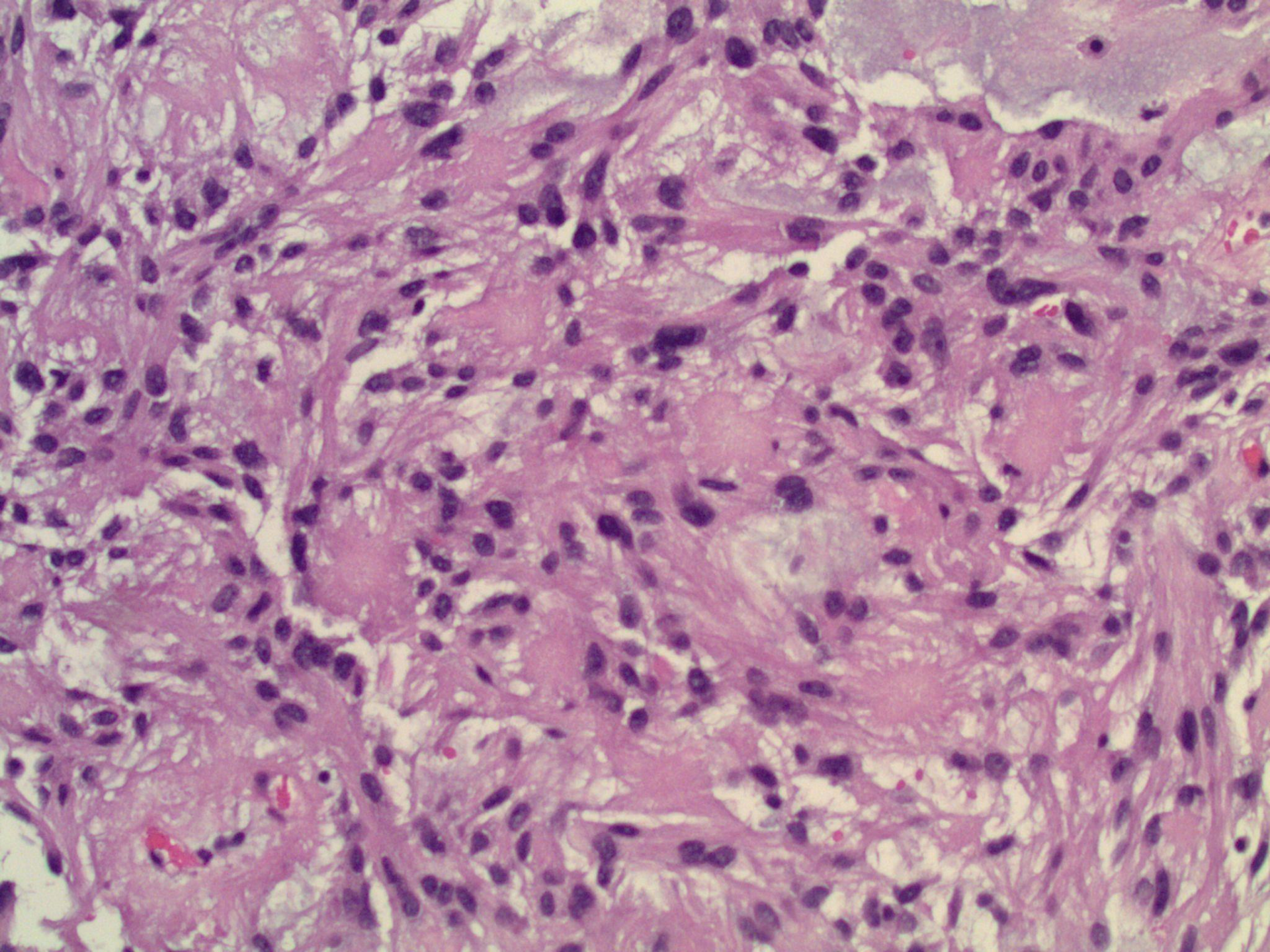


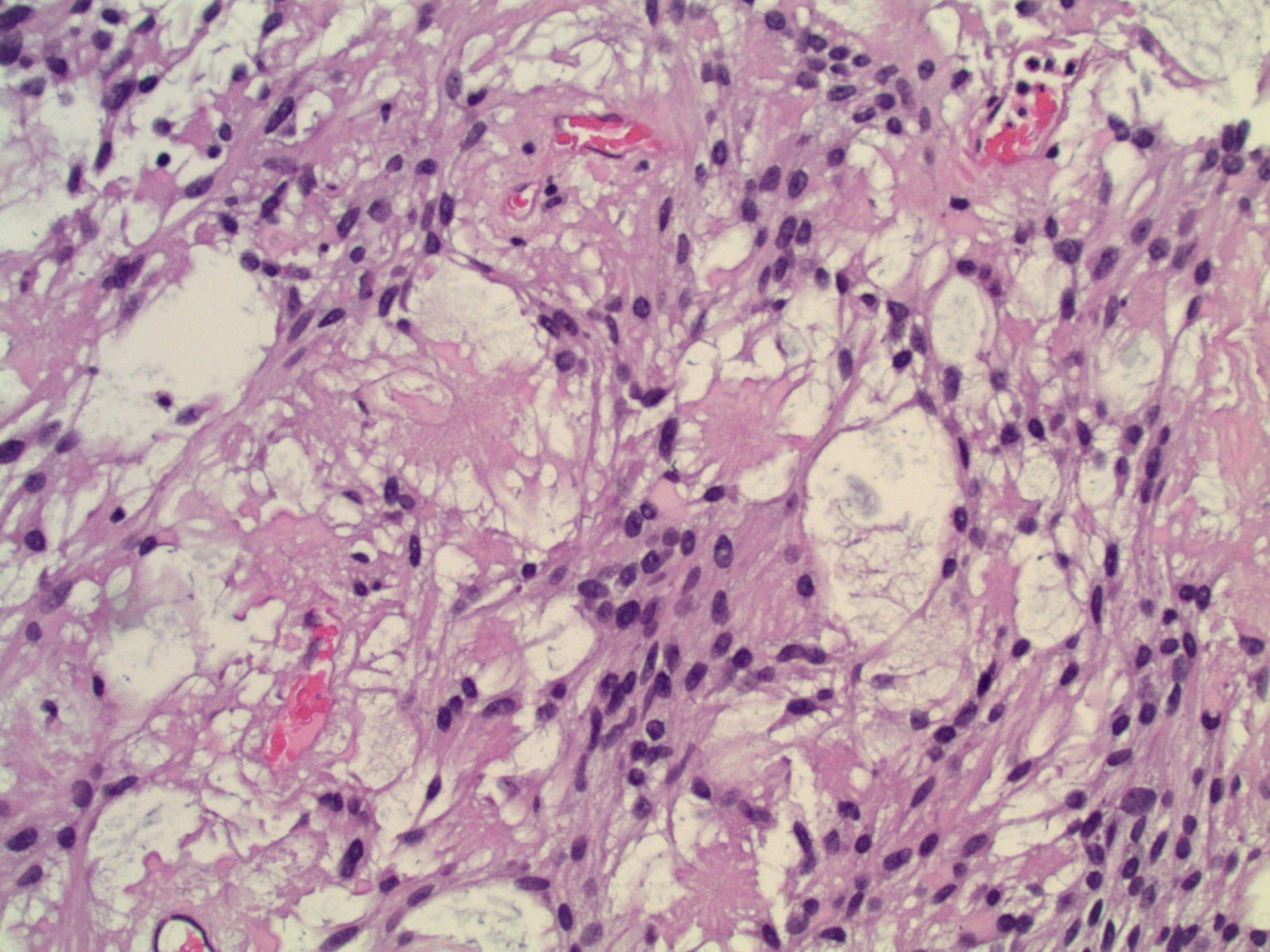






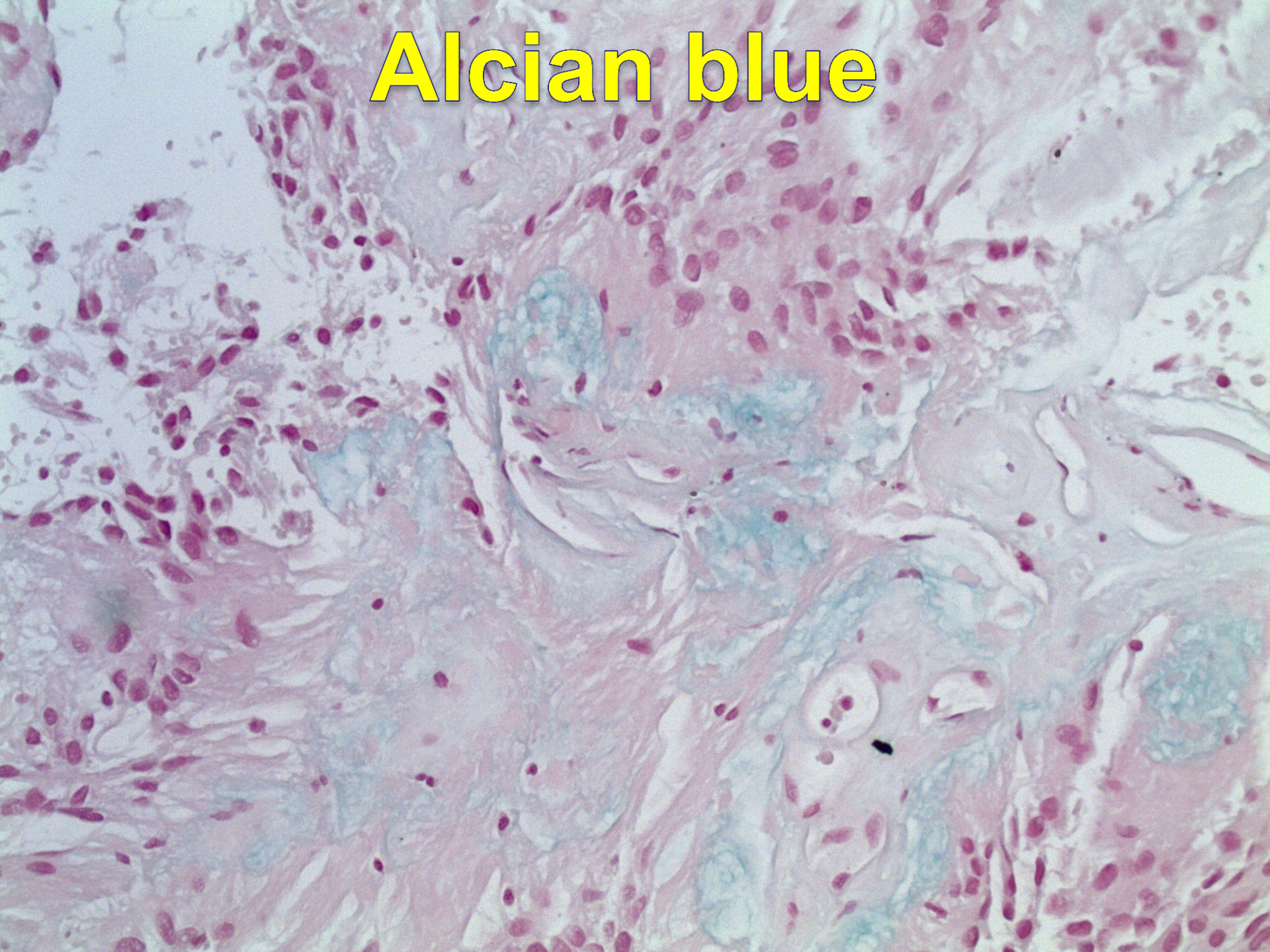


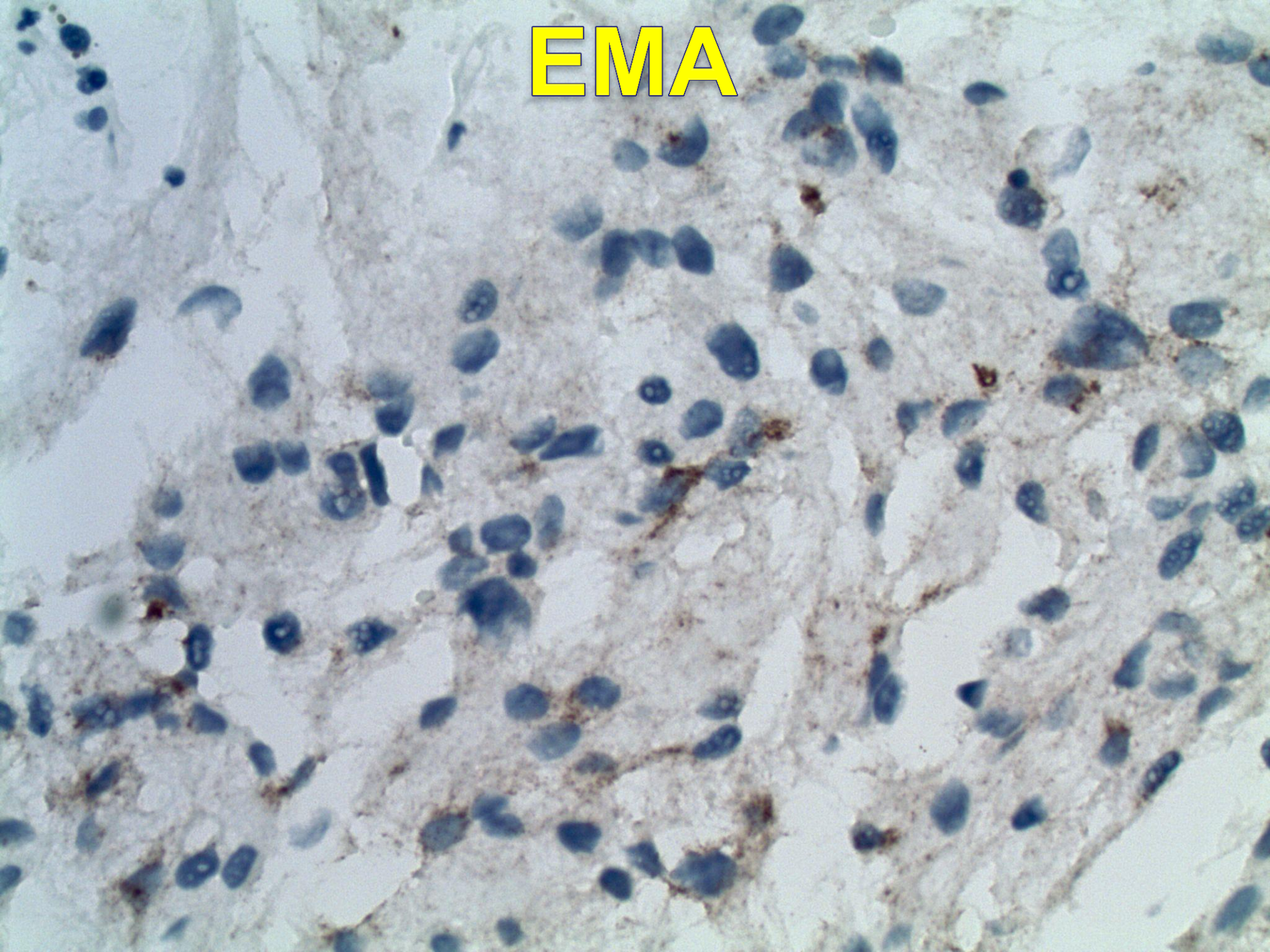




DIAGNOSIS

- Myxopapillary ependymoma
  - WHO grade 1 of 4


Alcian blue

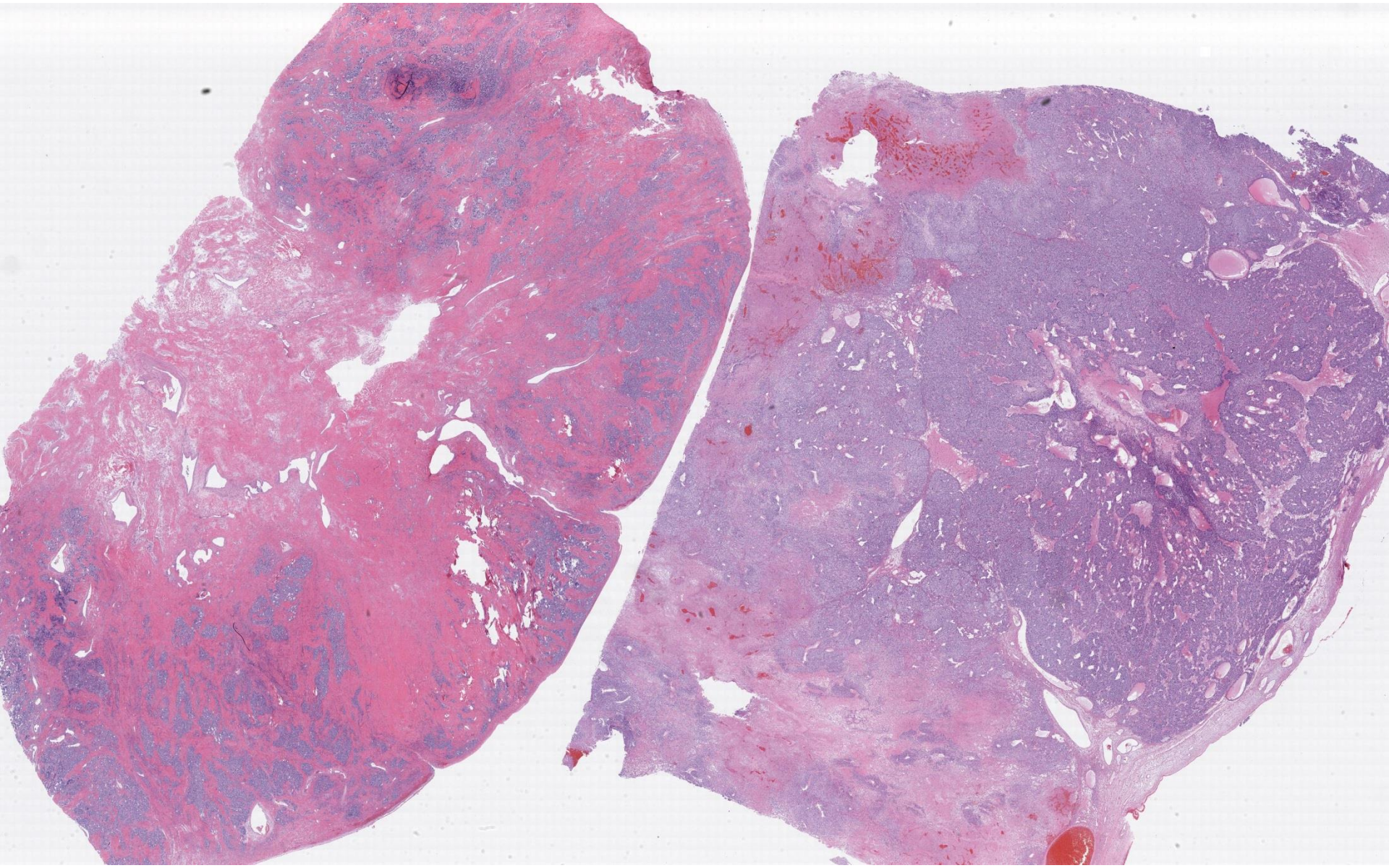

EMA

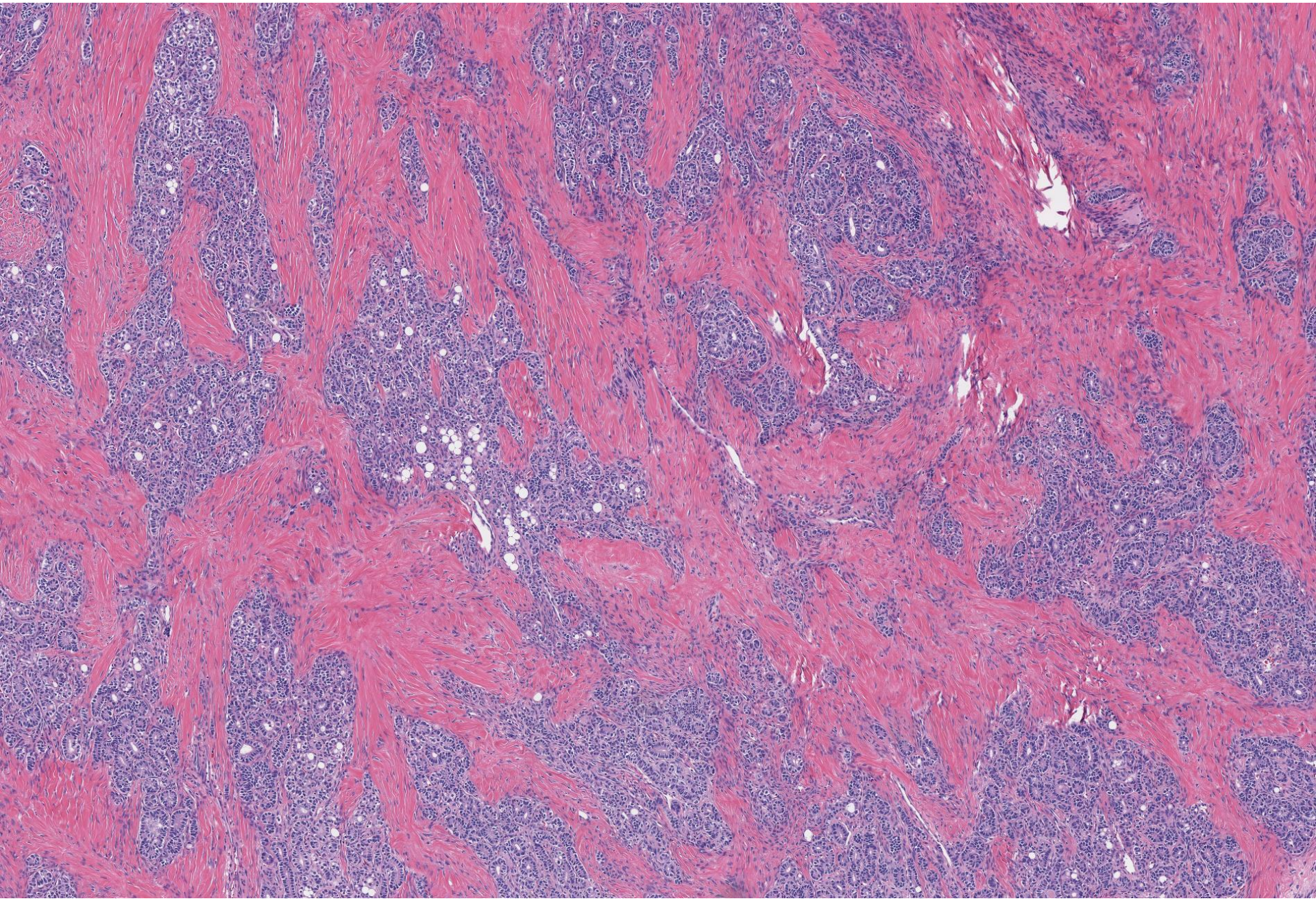
MYXOPAPILLARY EPENDYMOMA

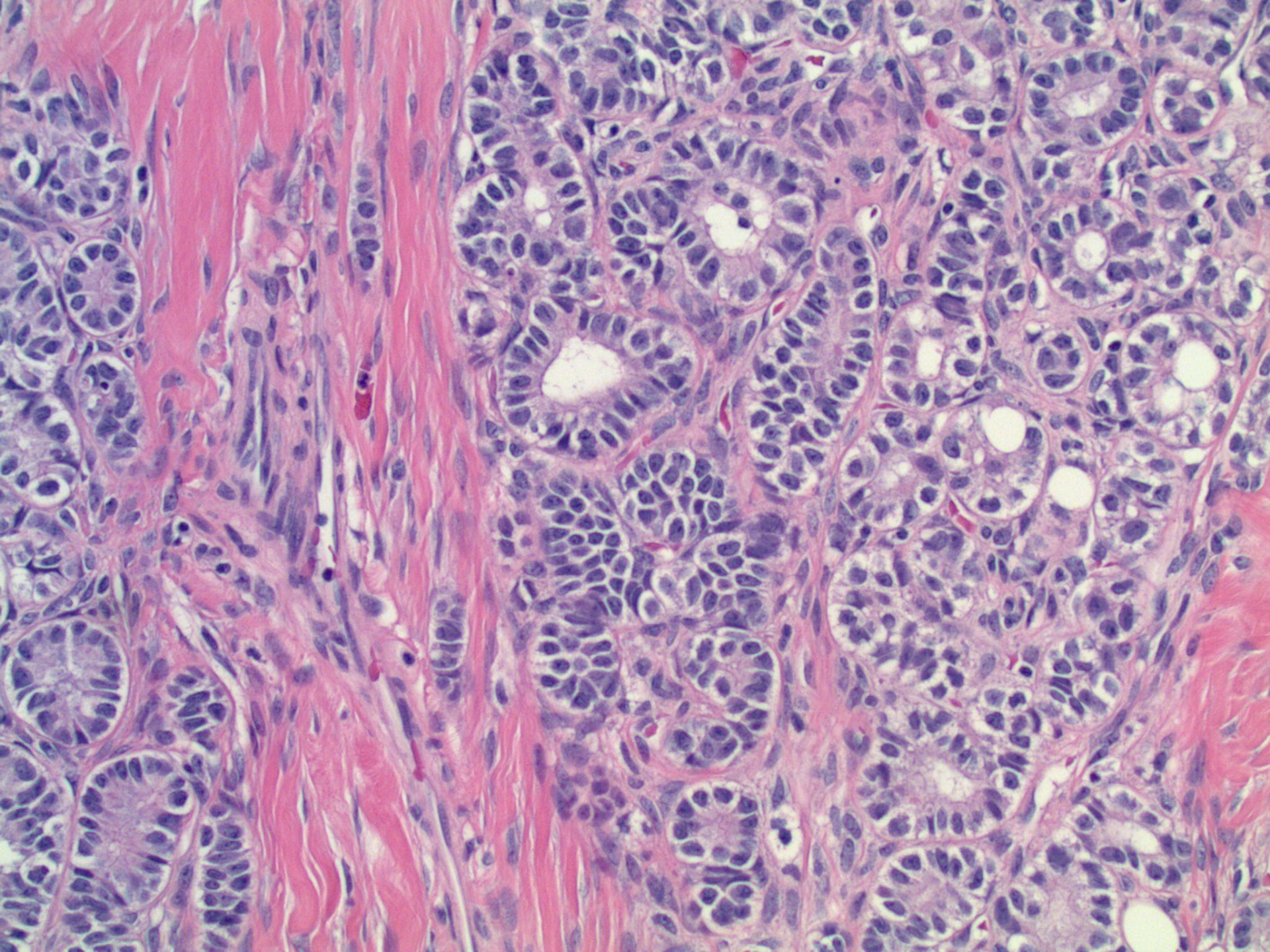
- 2/3 male, mean age 36 years
- Almost exclusively near conus medullaris, cauda equina, filum terminale of spinal cord
- Occasionally cervical-thoracic spine, intraventricular, brain parenchyma
- May arise as subcutaneous sacrococcygeal or presacral mass
- DDx
  - Carcinoma, chordoma, meningioma, myxoid chondrosarcoma, paraganglioma, schwannoma

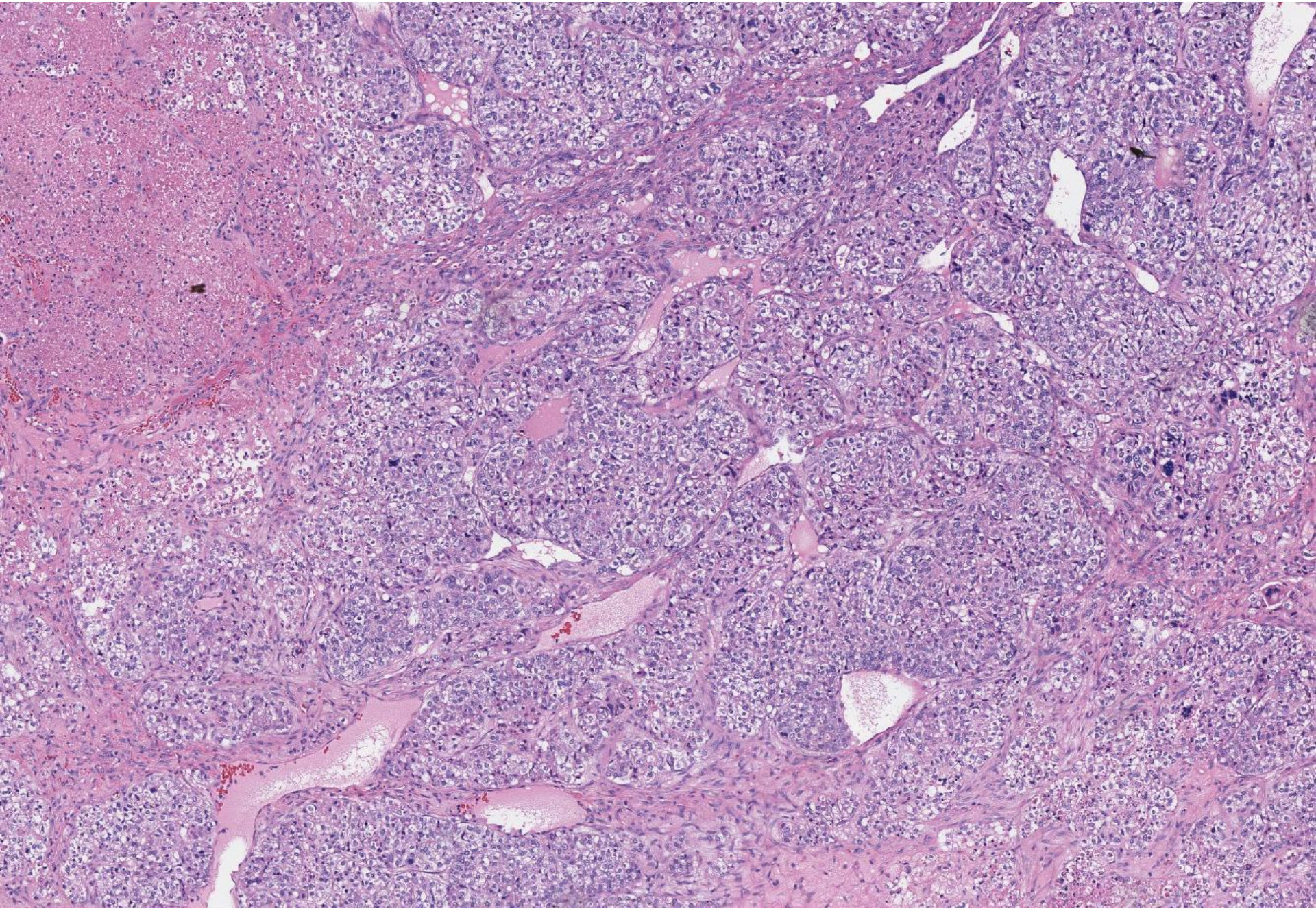
SB 5964
Mahendra Ranchod; Good Samaritan Hospital

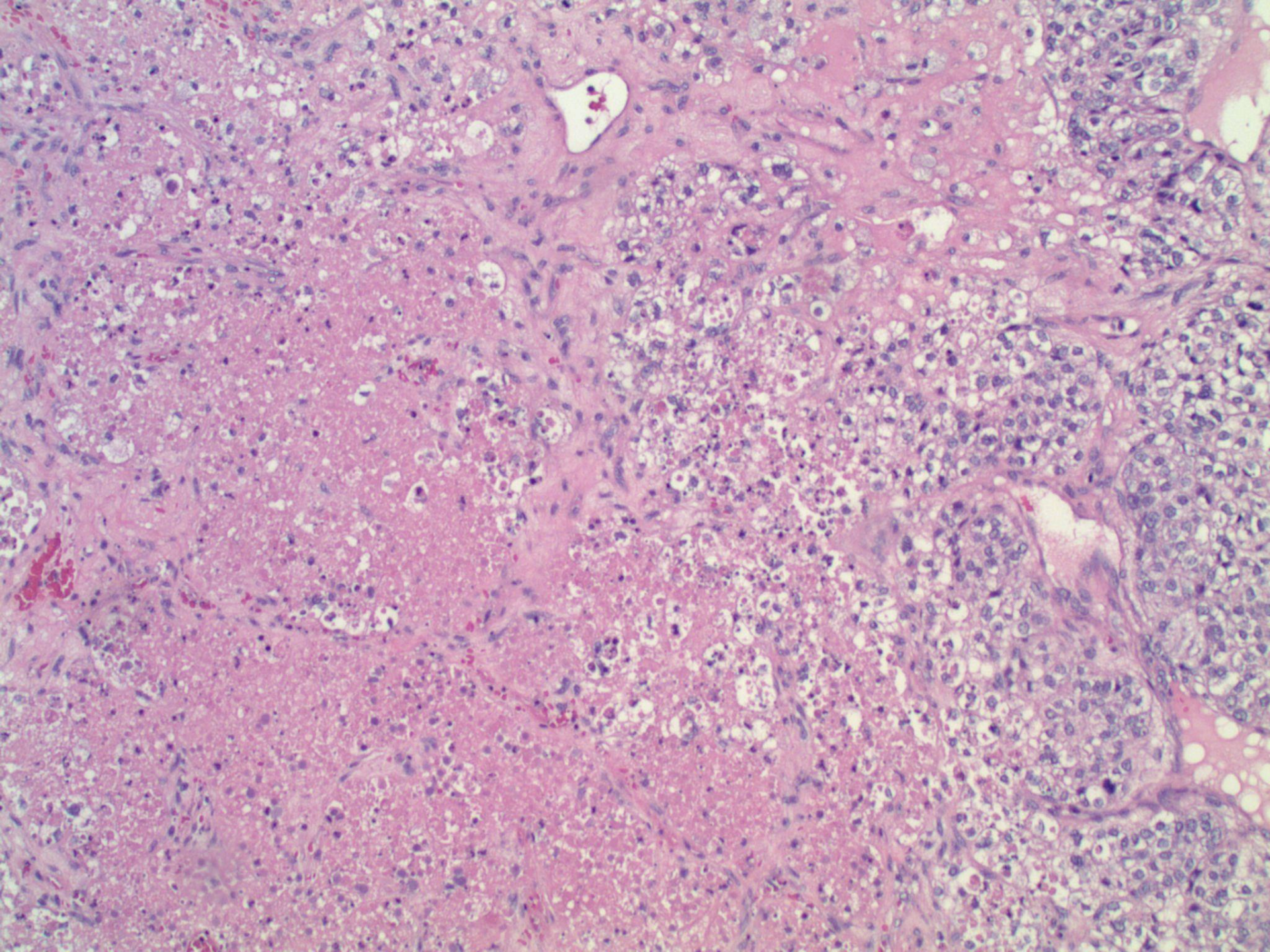
54-year-old woman with 22cm right ovarian mass.

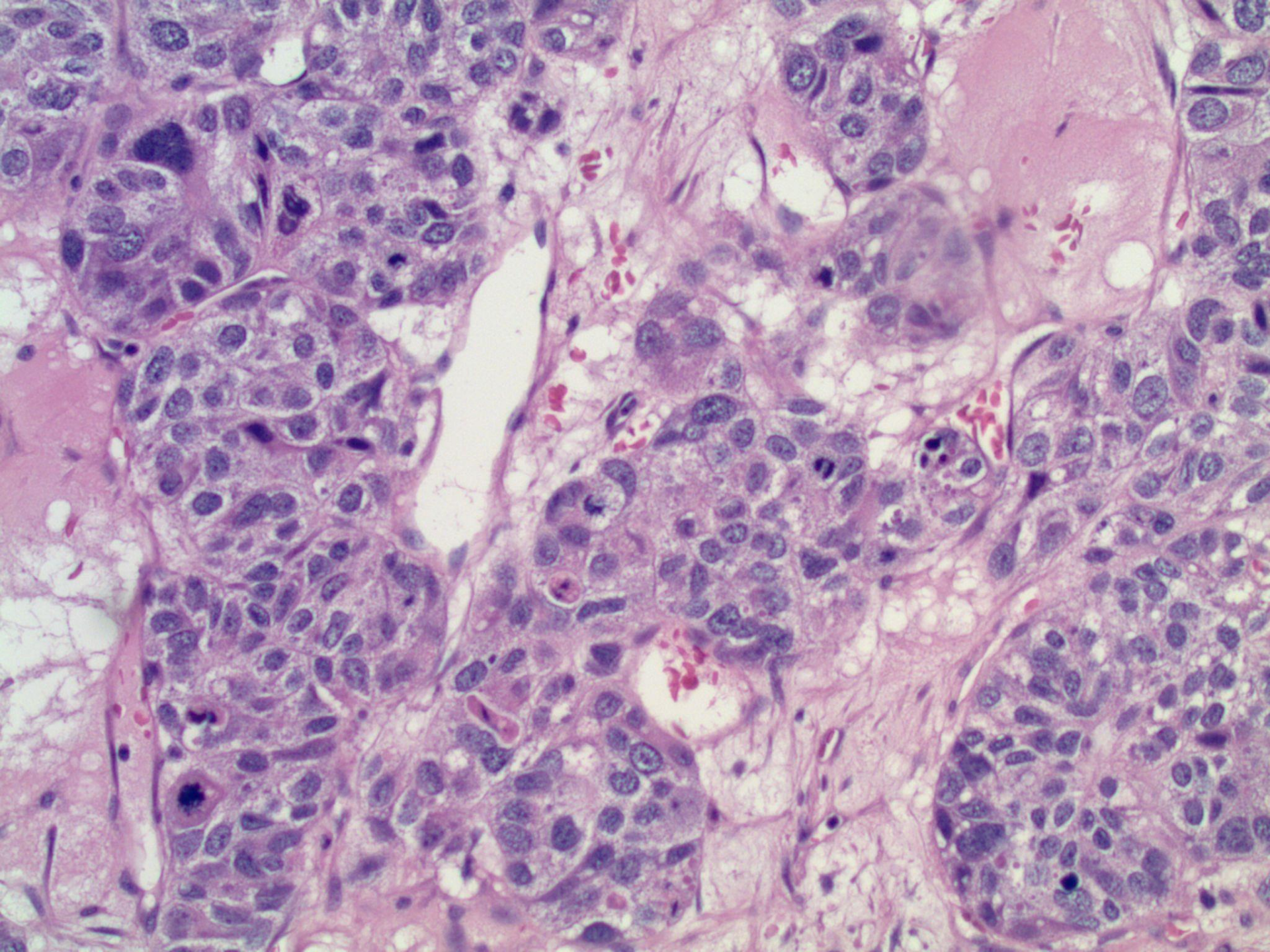


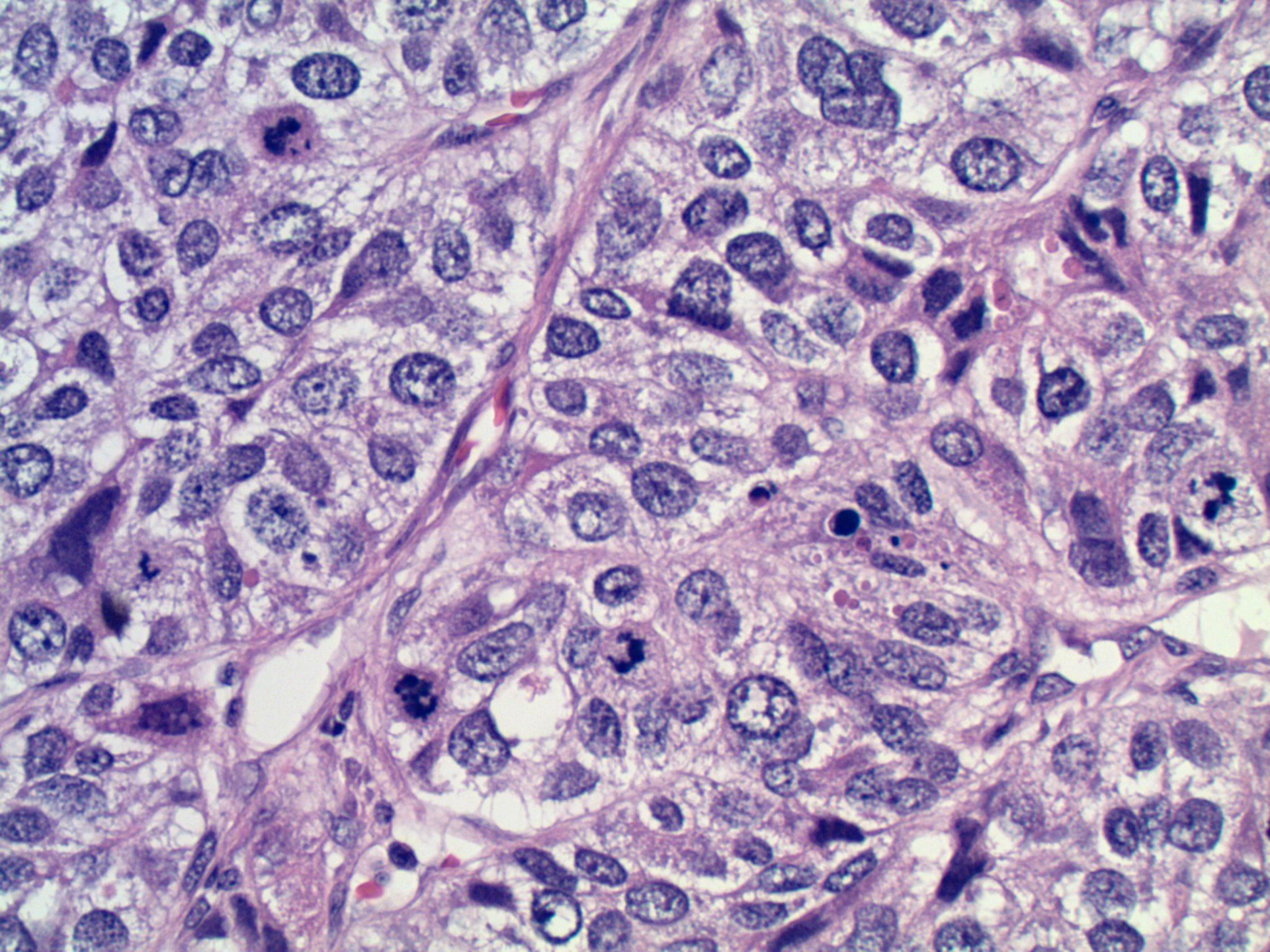


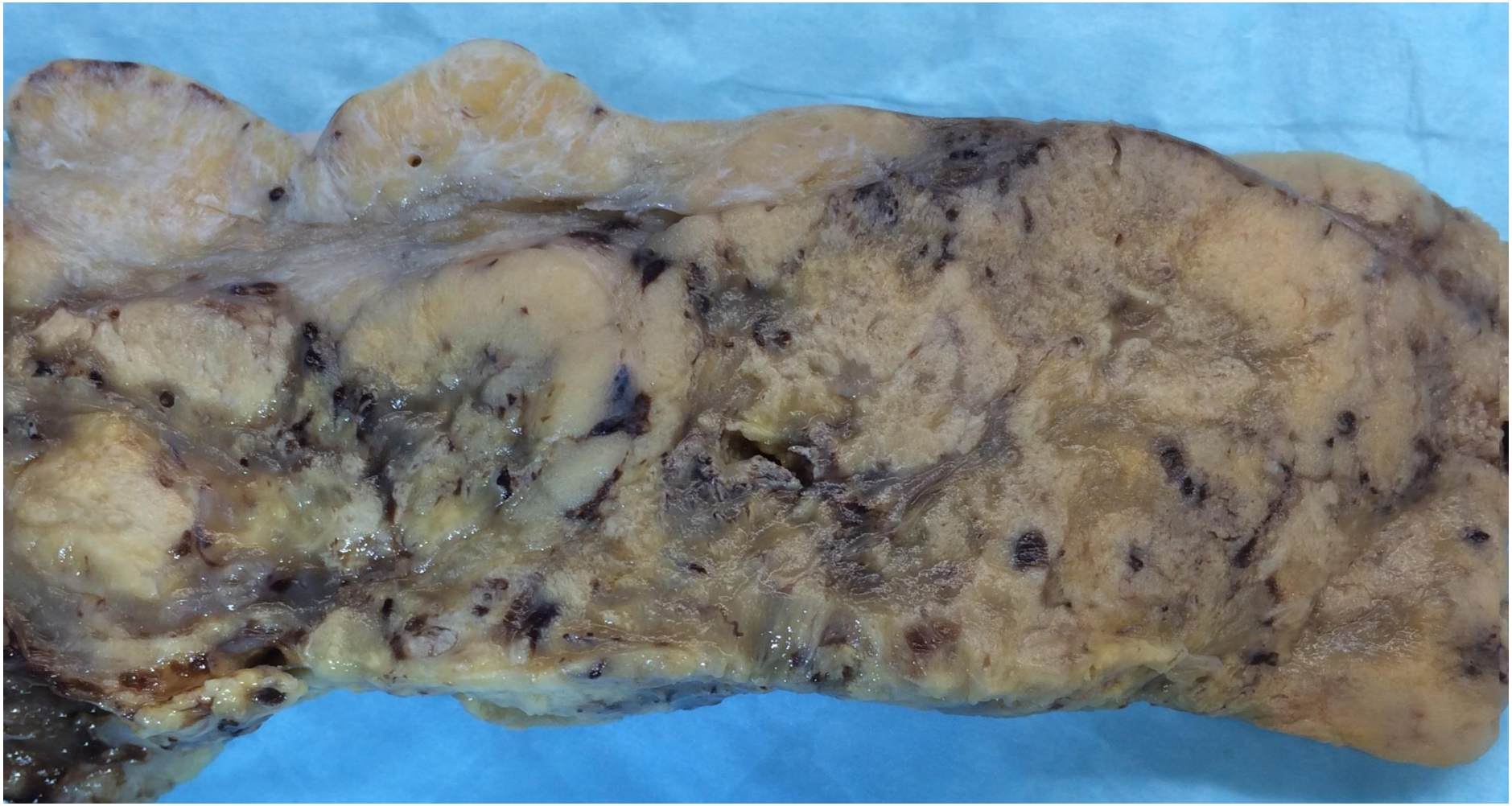












Sertoli Cell Tumors of Ovary

Oliva et al. Am J Surg Pathol 2005

54 cases

Stage 1	**44**
Stage 2	**1**
Stage 3	**3**
Not adequately staged	**6**

Sertoli Cell Tumors of Ovary

Immunohistochemical stains

AE1/3+CAM 5.2	65%
Inhibin	81%
CD99	86%
Calretinin	50%
Vimentin	94%
NSE	50%
SMA	22%

Sertoli Cell Tumors of Ovary
Differential Diagnosis

	Inhibin	EMA	Chro
Sertoli Cell	+	-	-
Endometrial CA	-	+	-
Carcinoid tumor	-	-	+

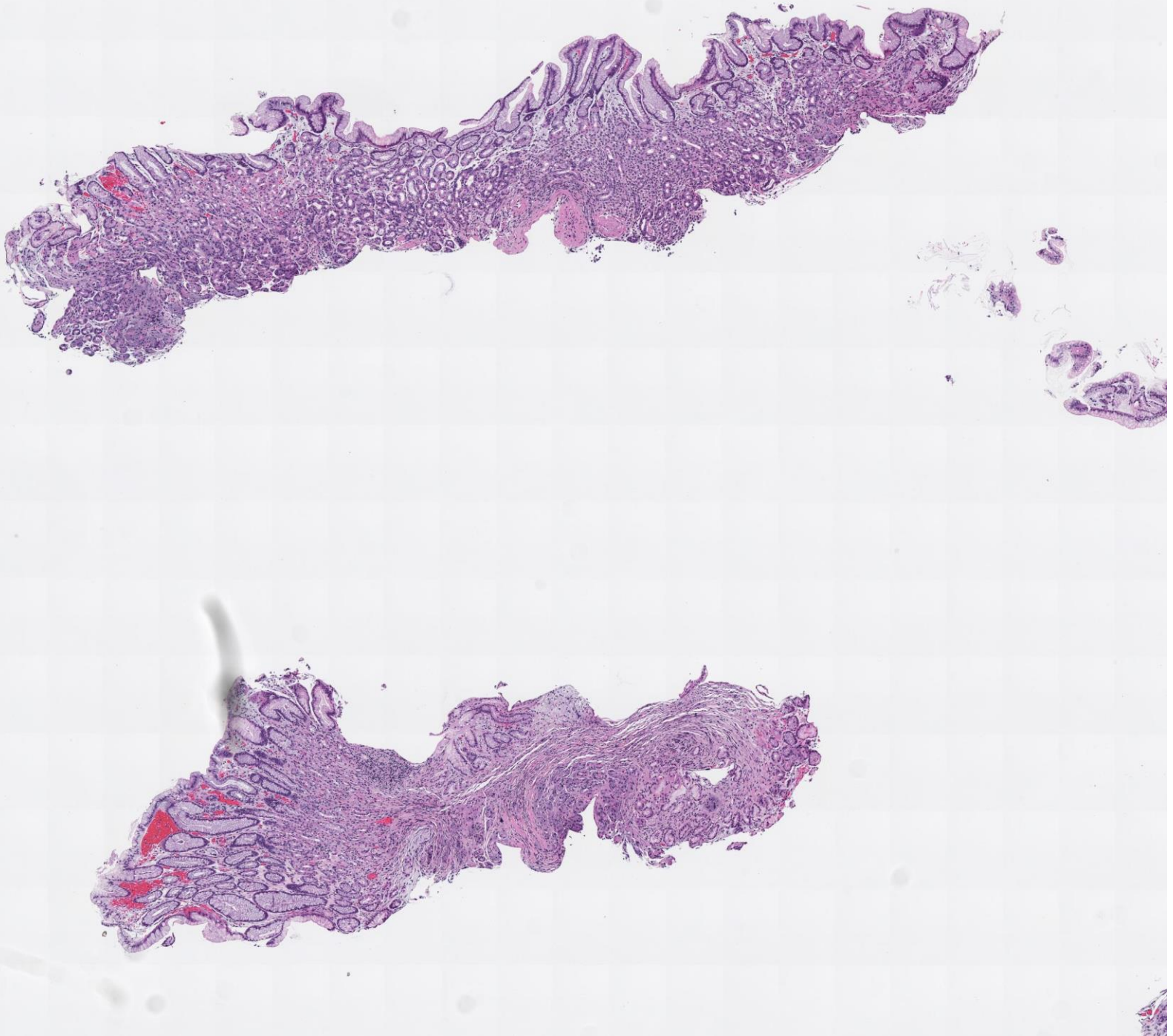
Sertoli Cell Tumors of Ovary

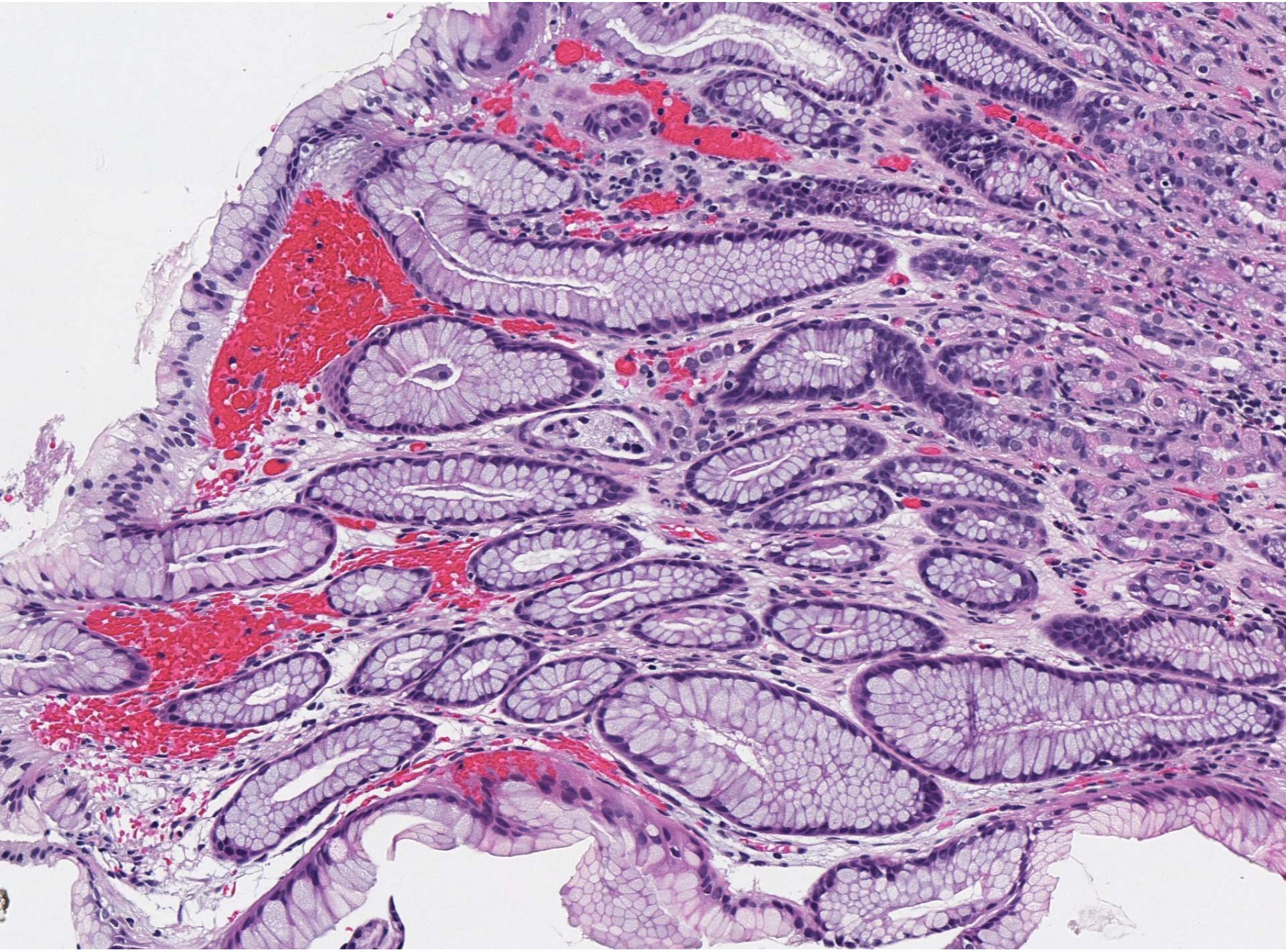
Criteria for malignancy

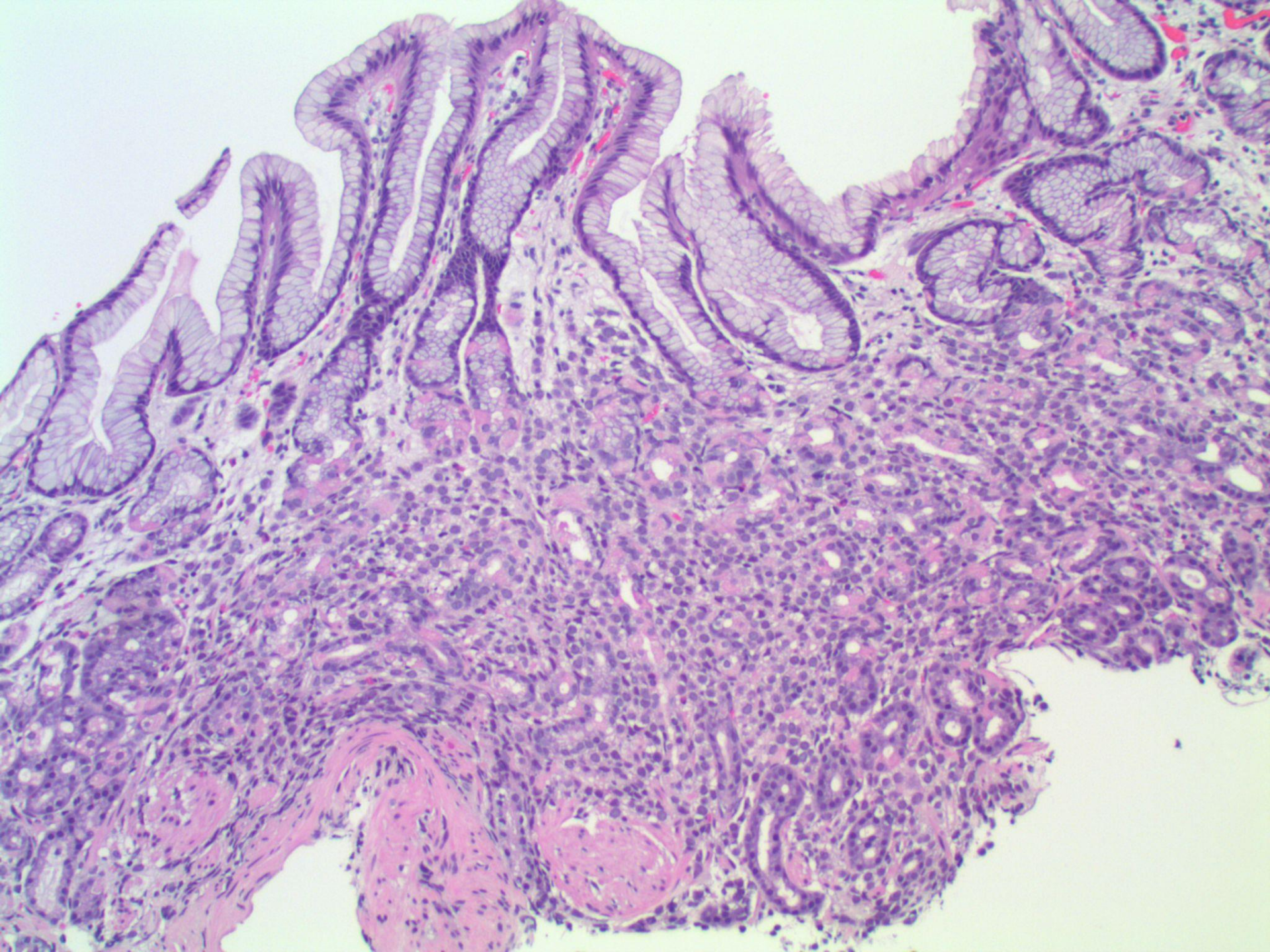
- Moderate to severe atypia
- > 5 mitoses/10HPF
- Necrosis (present in minority)

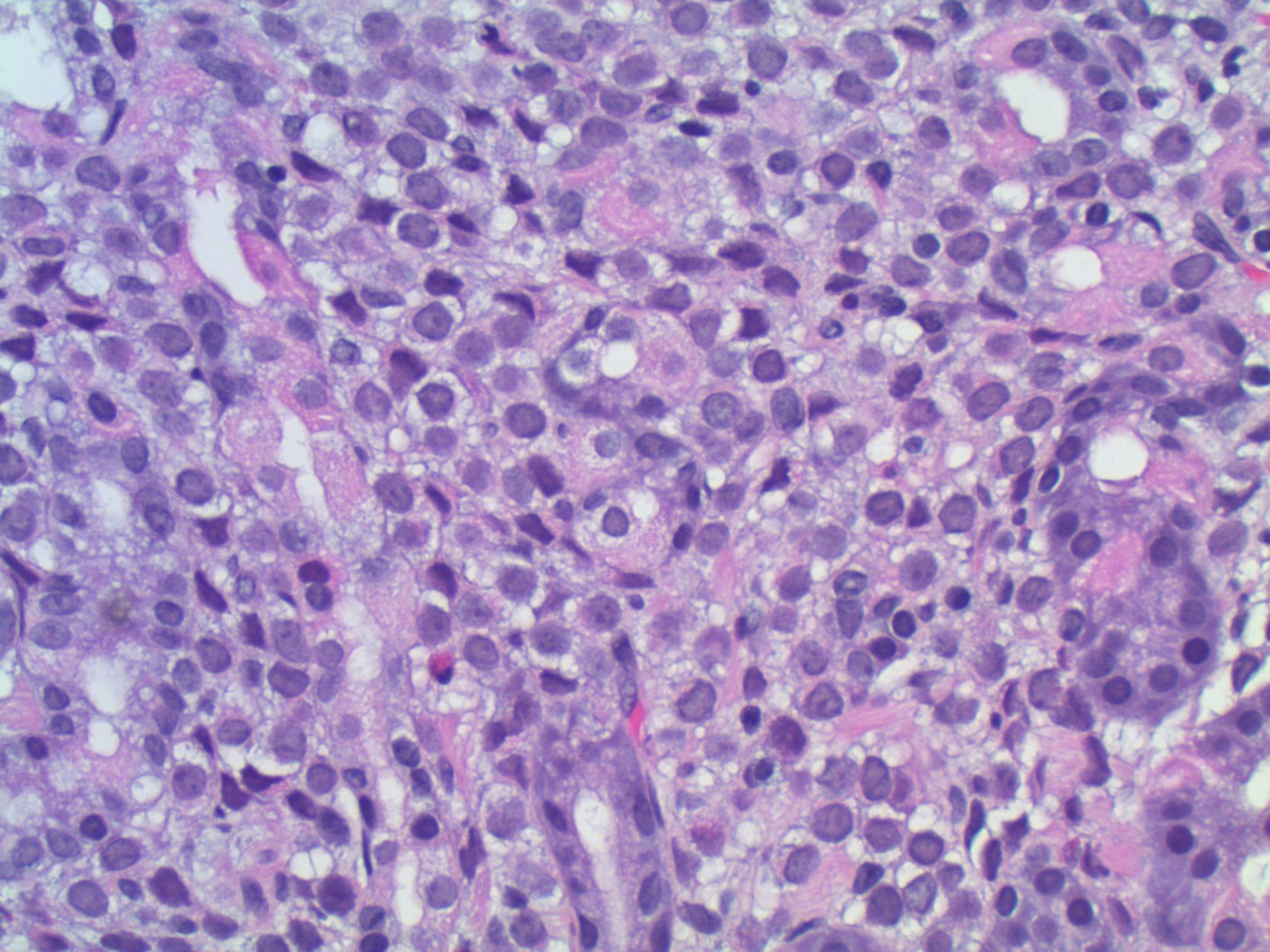
SB 5965
Ankur Sangoi; El Camino Hospital

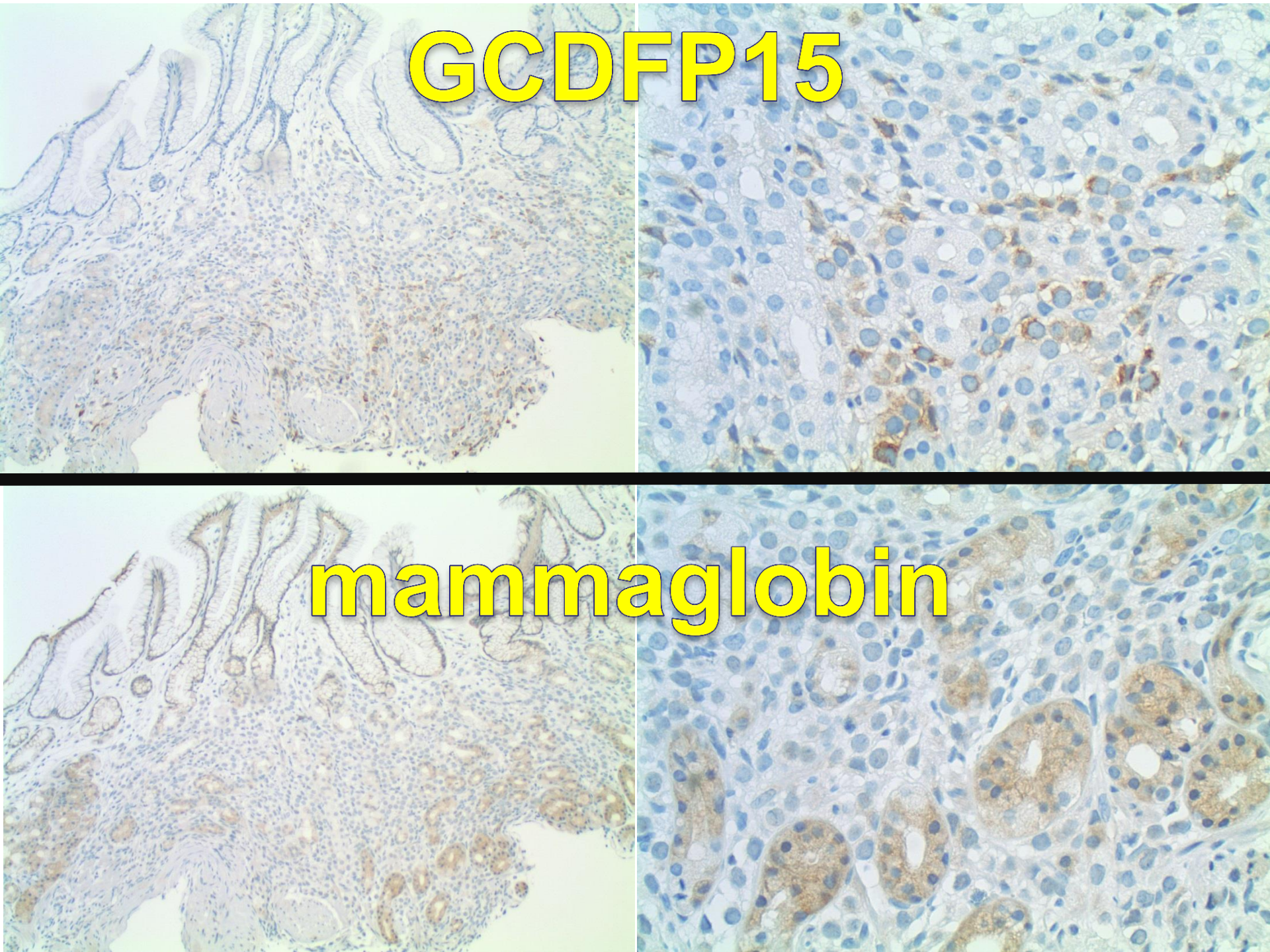
68-year-old woman with biopsy of gastric ulcer. Rule out H.pylori.

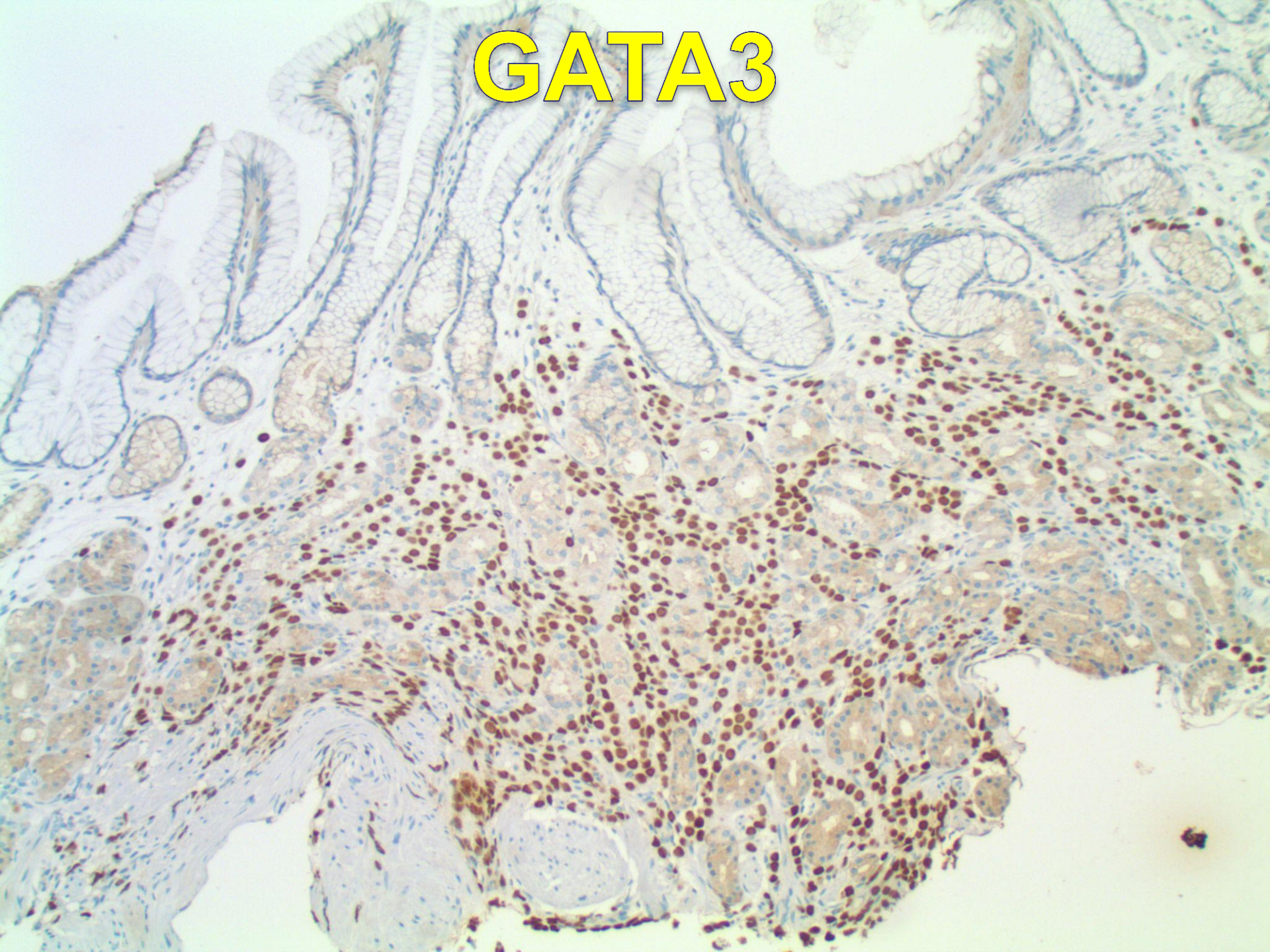


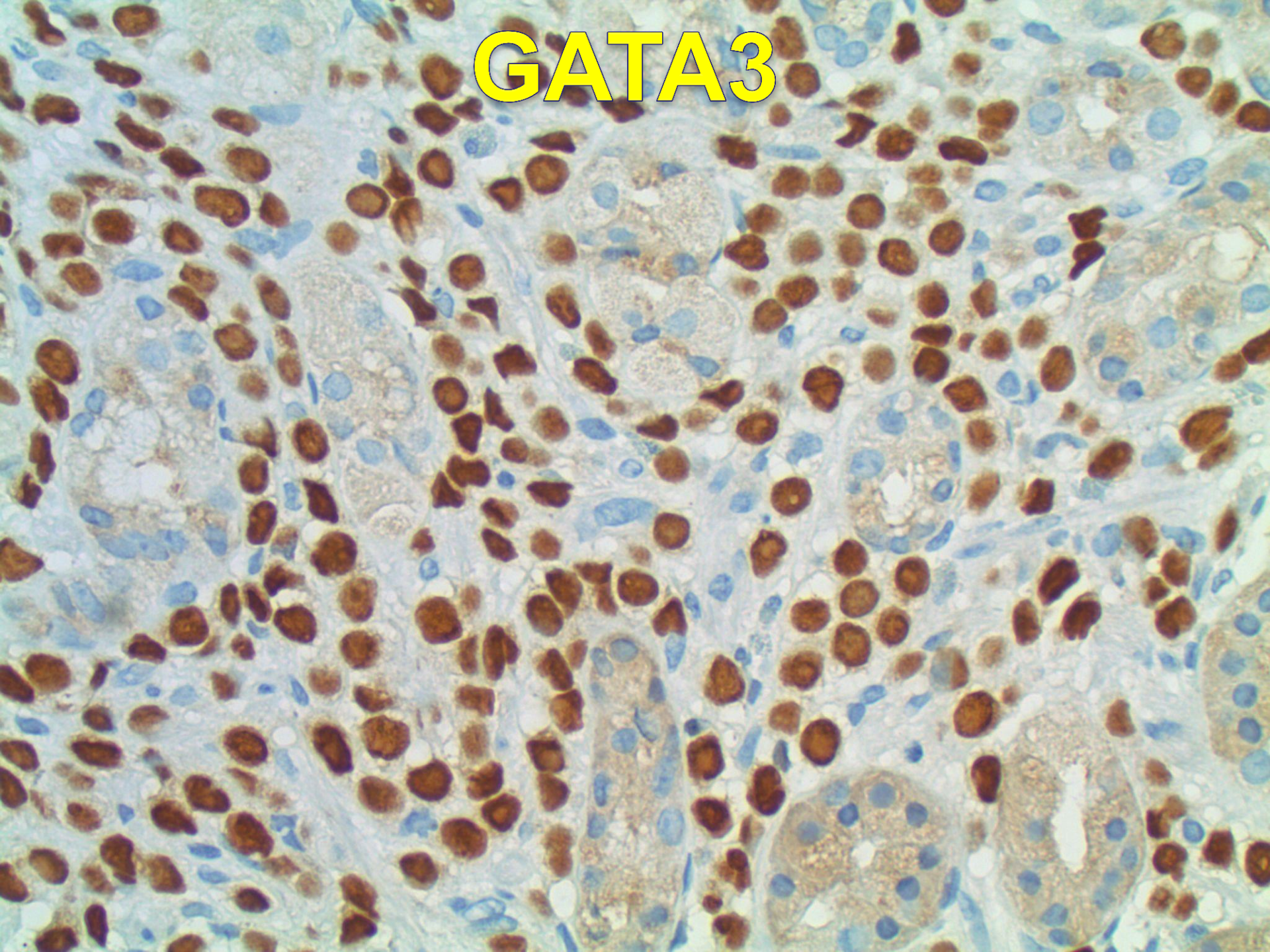







GCDFP15
mammaglobin


GATA3


GATA3

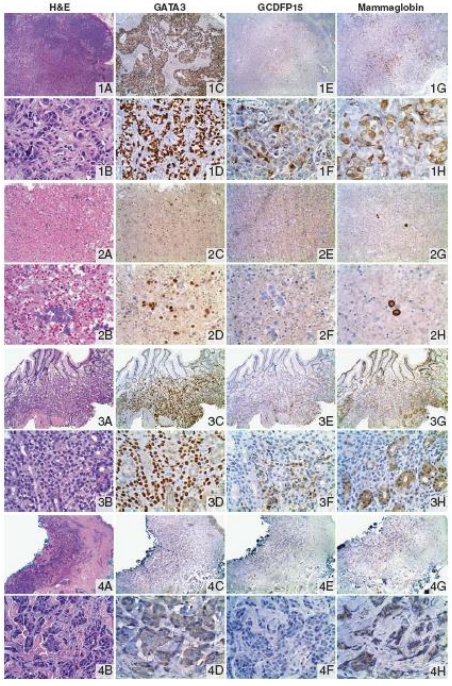
DIAGNOSIS

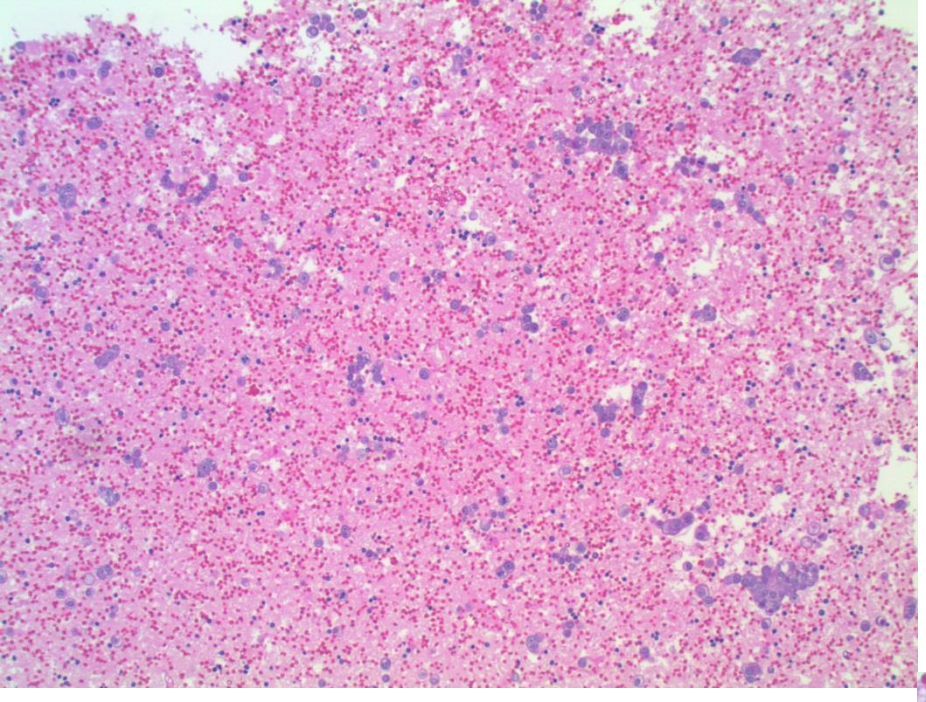
- Metastatic carcinoma
  - Consistent with breast origin (lobular ca)

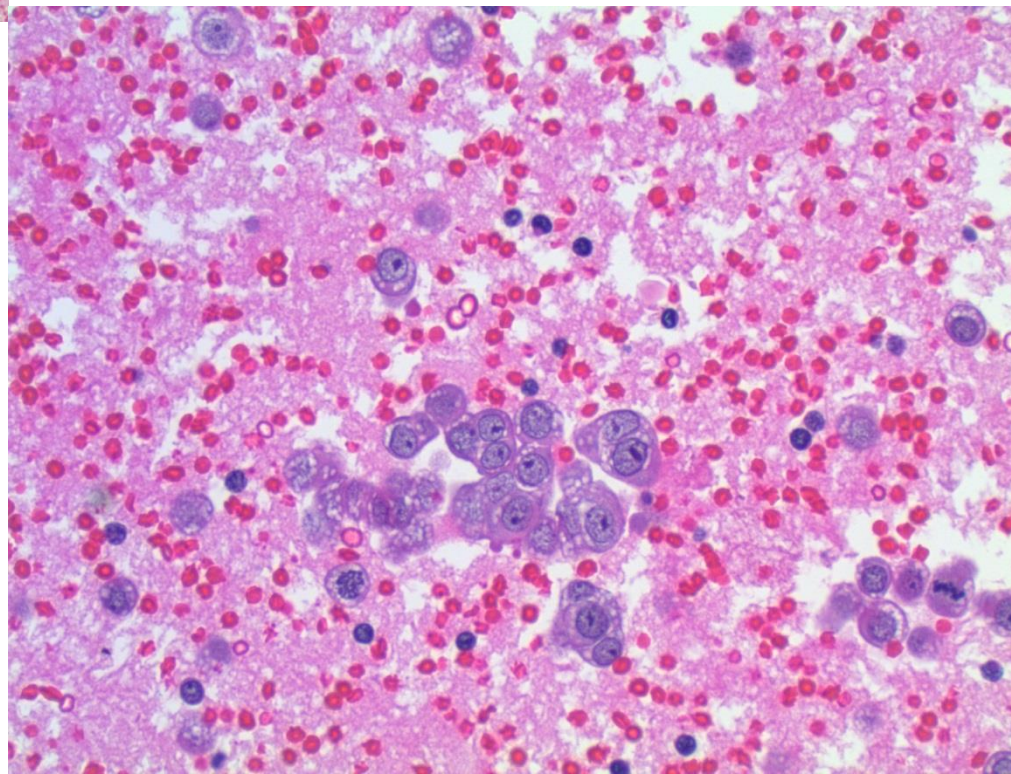
The Novel Marker GATA3 is Significantly More Sensitive Than Traditional Markers Mammaglobin and GCDFP15 for Identifying Breast Cancer in Surgical and Cytology Specimens of Metastatic and Matched Primary Tumors

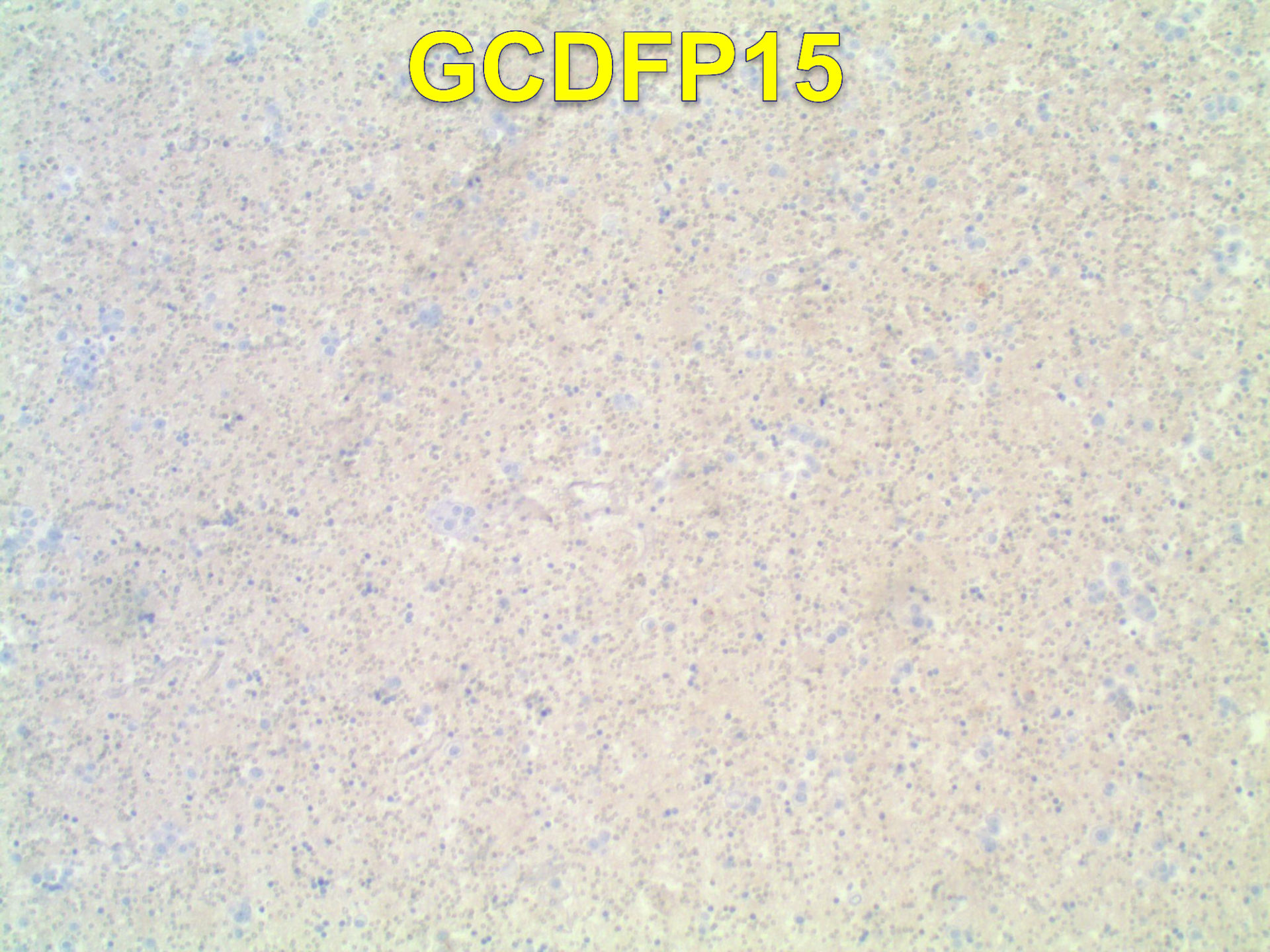
Ankur R. Sangoi, MD, Bijayee Shrestha, MD, PhD,* George Yang, MD,† Ourhay Mego, BS,† and Andrew H. Beck, MD, PhD‡*

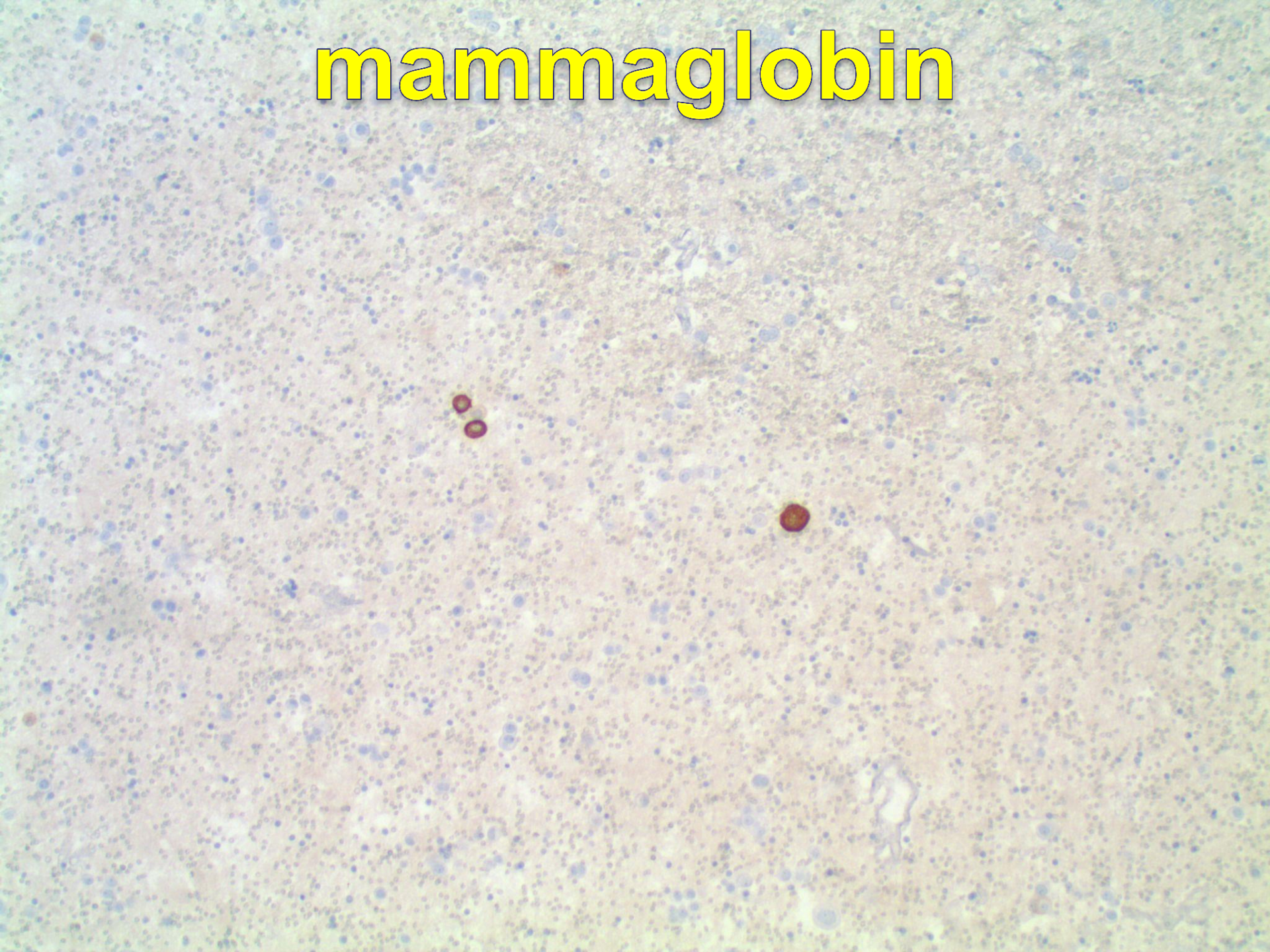
Appl Immunohistochem Mol Morphol 2015;

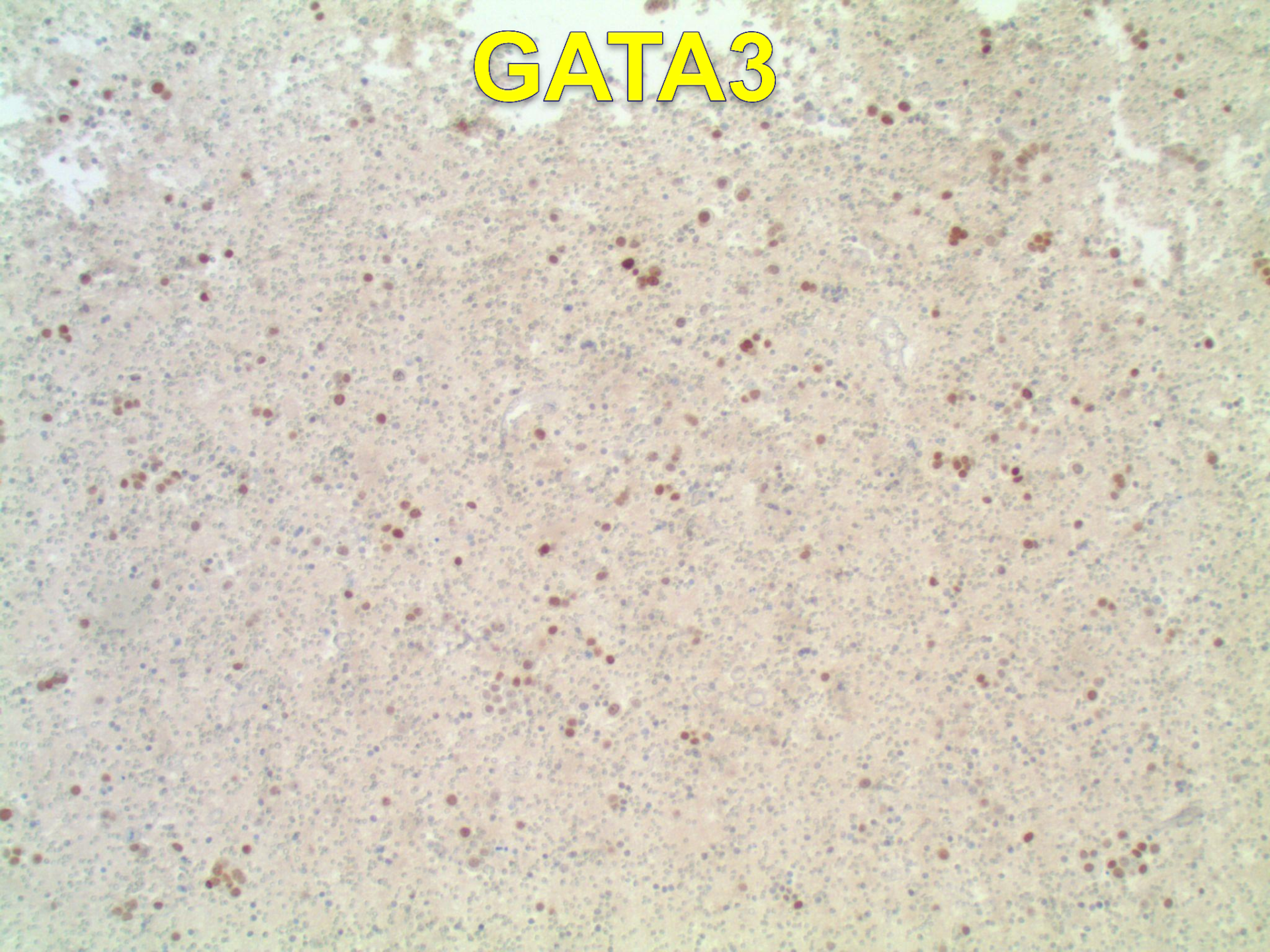







GCDFP15


mammaglobin


GATA3

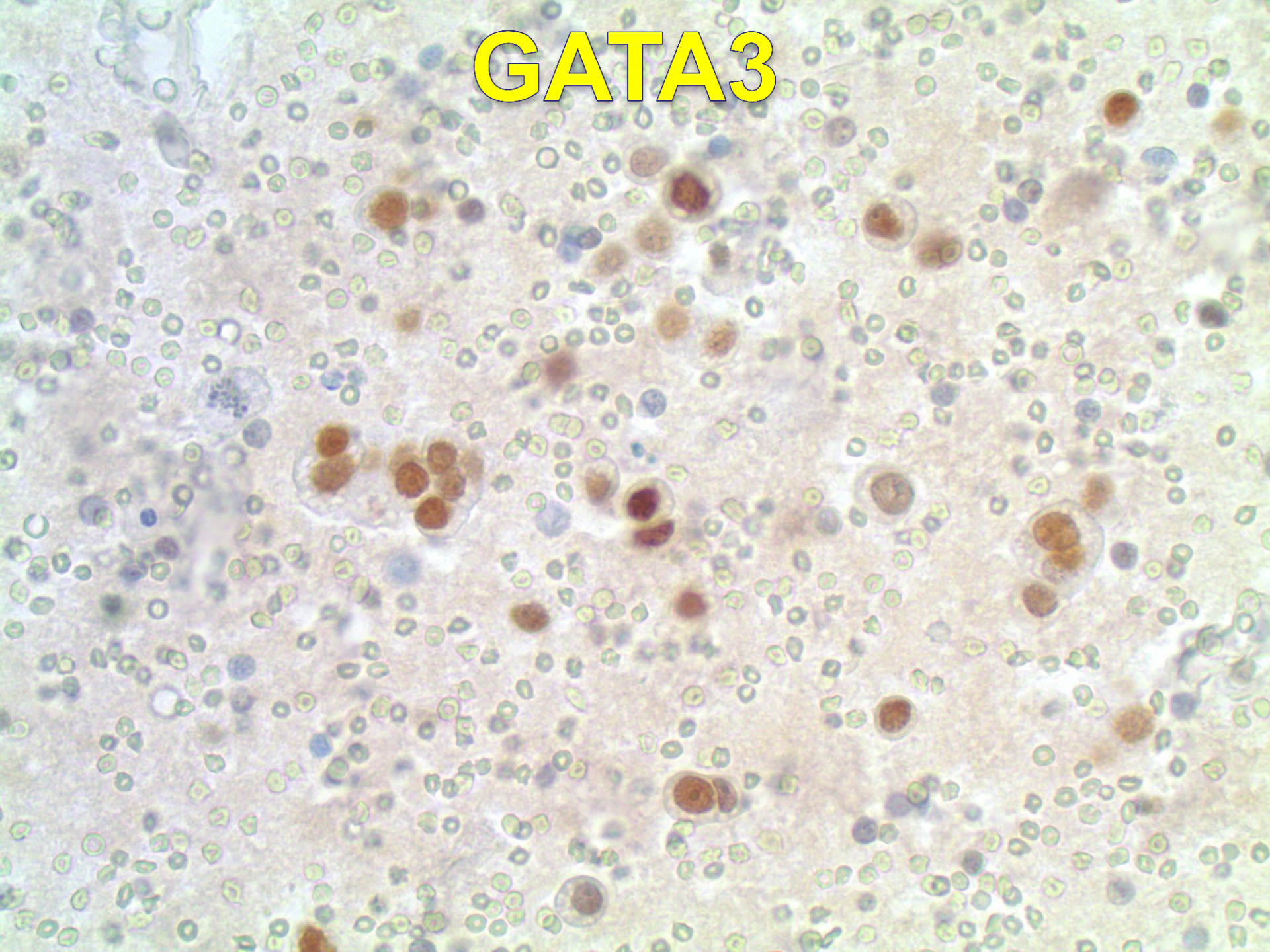
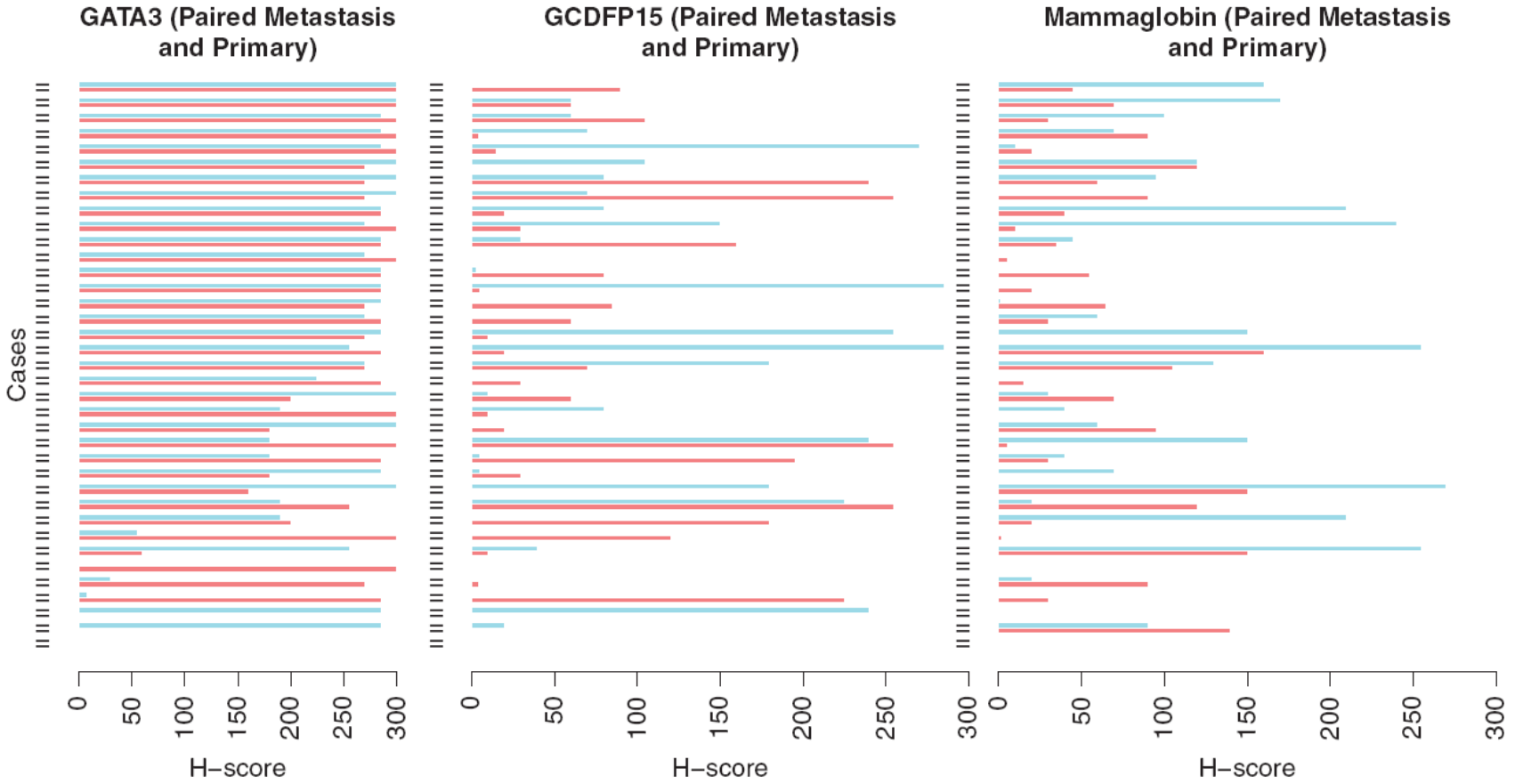

GATA3

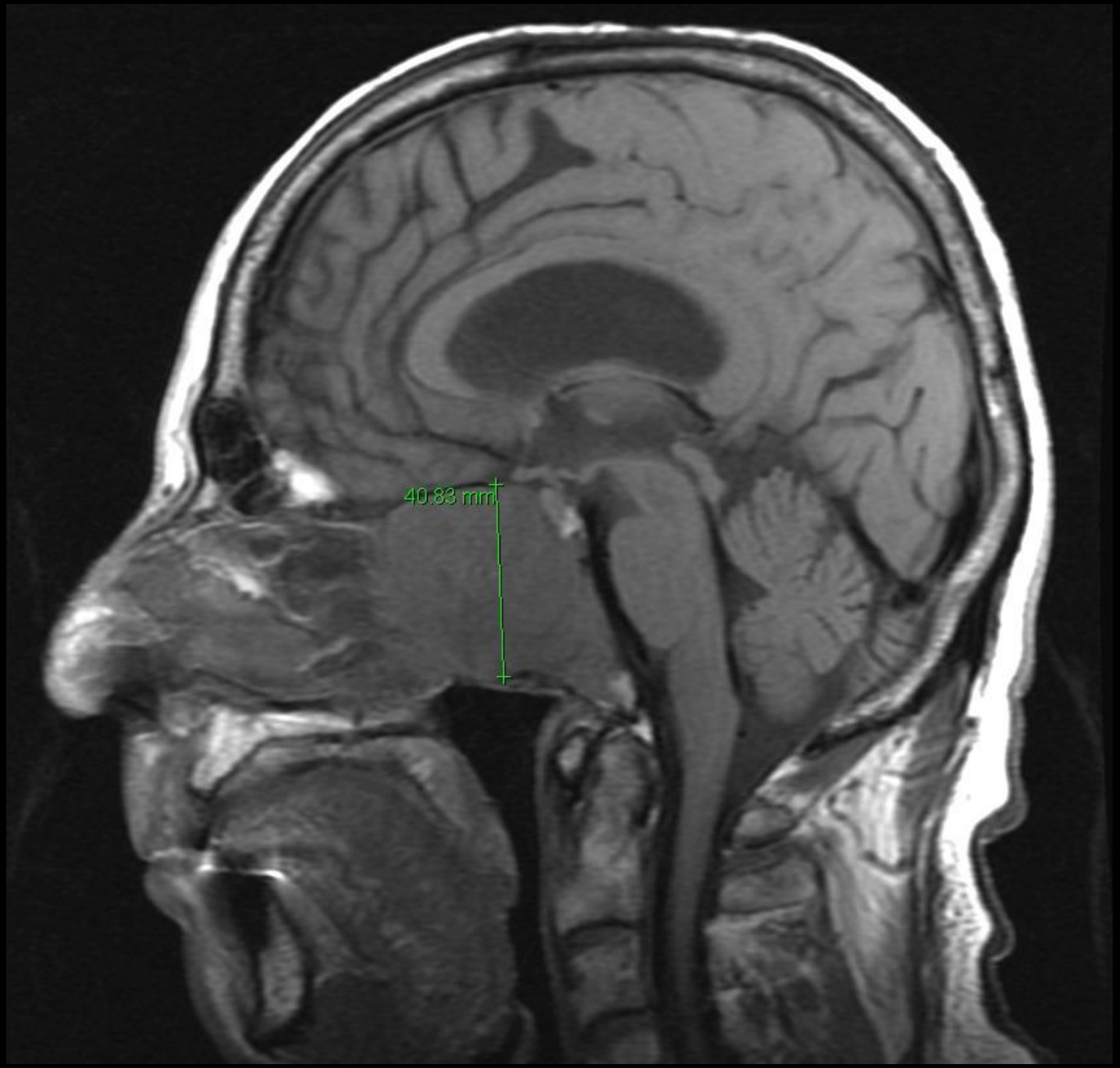
TABLE 1. Antibody Sensitivity With Minimum *H*-Score Cutoffs for a Positive Result in Metastatic (M) and Primary (P) Carcinomas

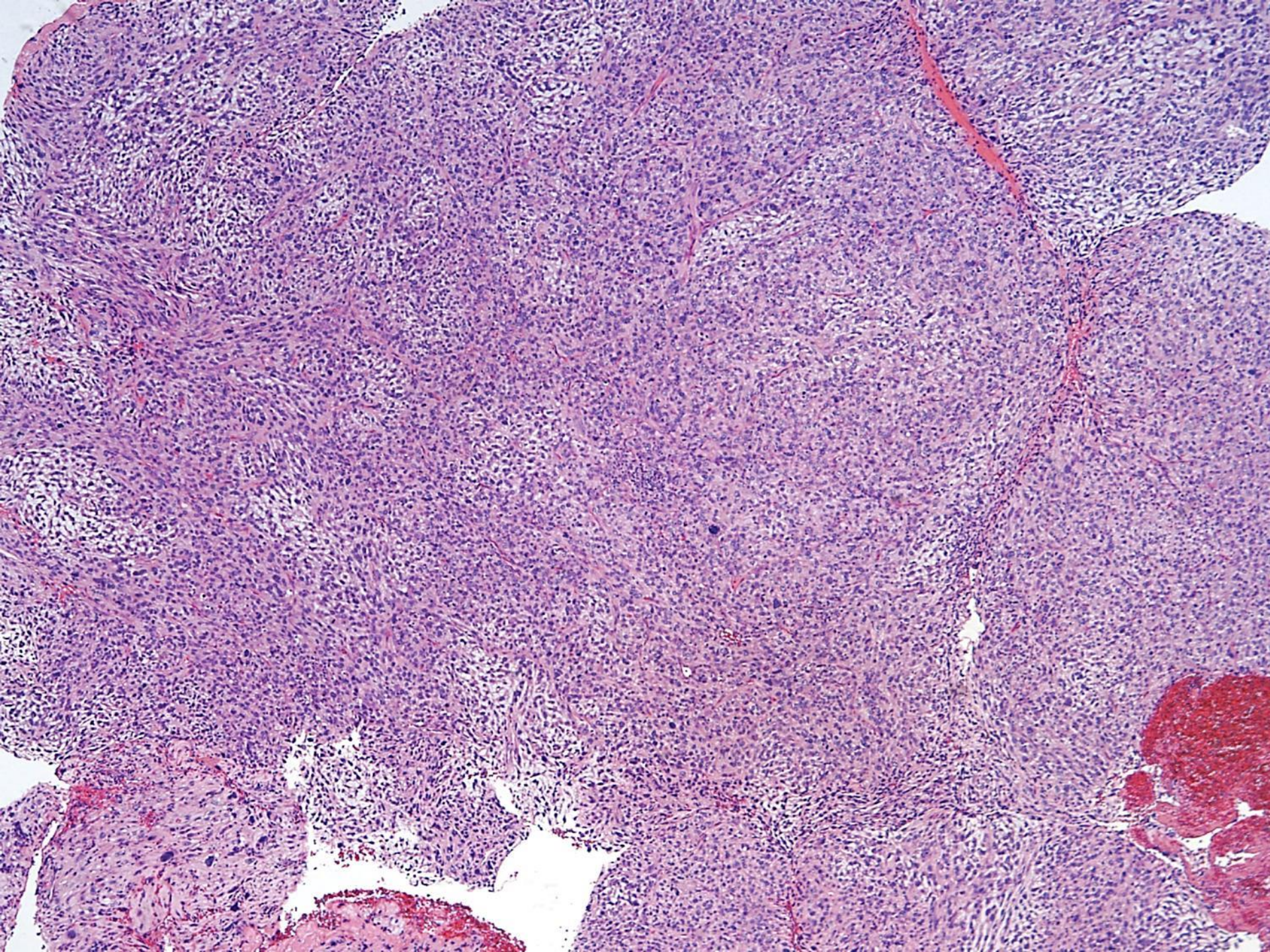
H-Score (0-300)	GATA3	GCDFP15	Mammaglobin
Any	M = 95%*, *P* = 94%	M = 65%, *P* = 83%	M = 78%, *P* = 89%
> 50	M = 93%*, *P* = 94%*	M = 37%, *P* = 50%	M = 47%, *P* = 48%
> 100	M = 90%*, *P* = 93%*	M = 25%, *P* = 33%	M = 27%, *P* = 22%
> 150	M = 86%*, *P* = 91%*	M = 21%, *P* = 24%	M = 19%, *P* = 7%
> 200	M = 73%*, *P* = 78%*	M = 18%, *P* = 17%	M = 9%, *P* = 4%
> 250	M = 66%*, *P* = 74%*	M = 14%, *P* = 11%	M = 6%, *P* = 0%

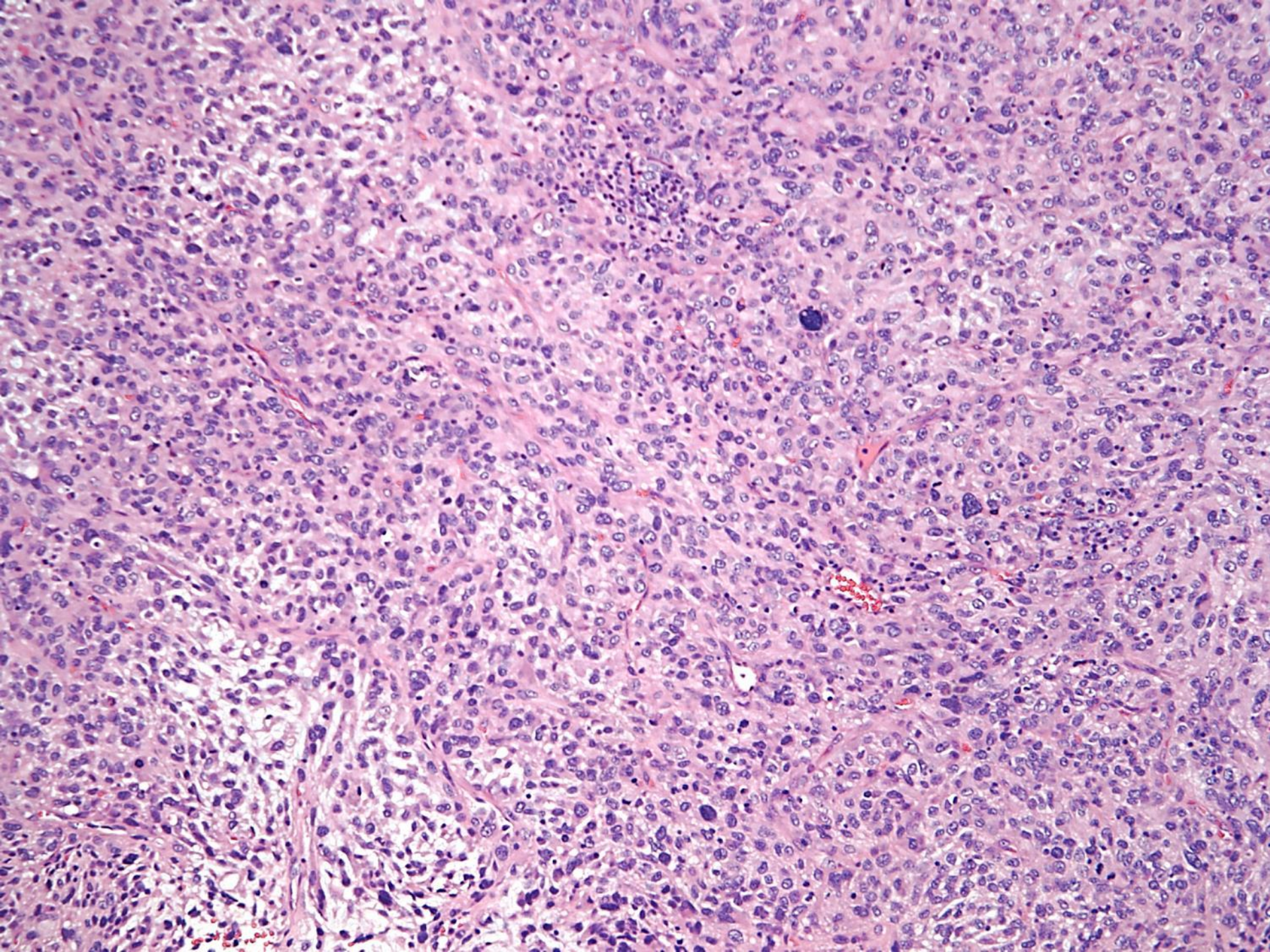


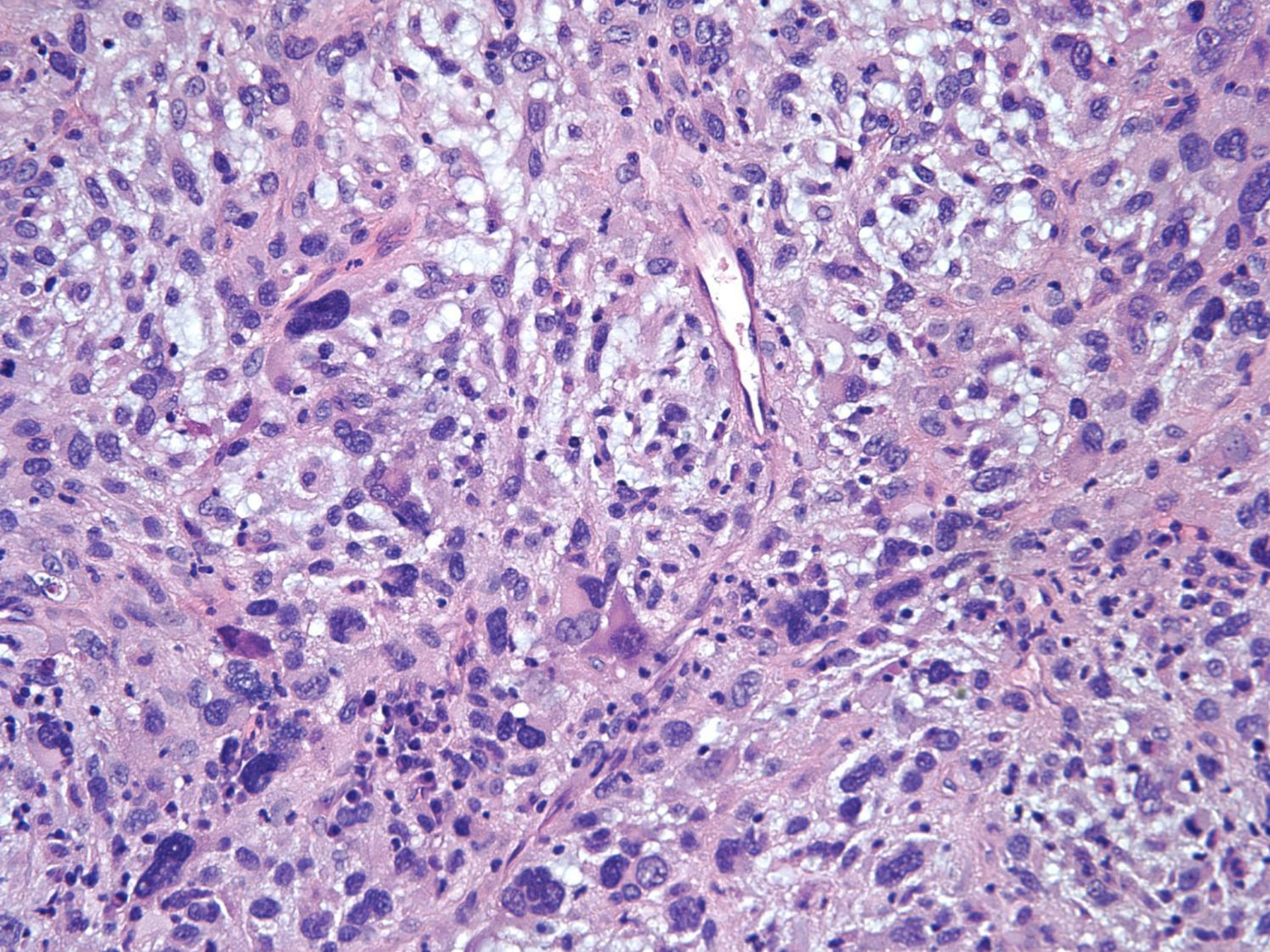
SB 5966
Allison Zemek/Hannes Vogel; Stanford

65-year-old man presents with headache, double vision, and right-sided hearing loss. He was found to have a 4.2cm clival mass extending to the sphenoid sinus on MRI.


40.83 mm

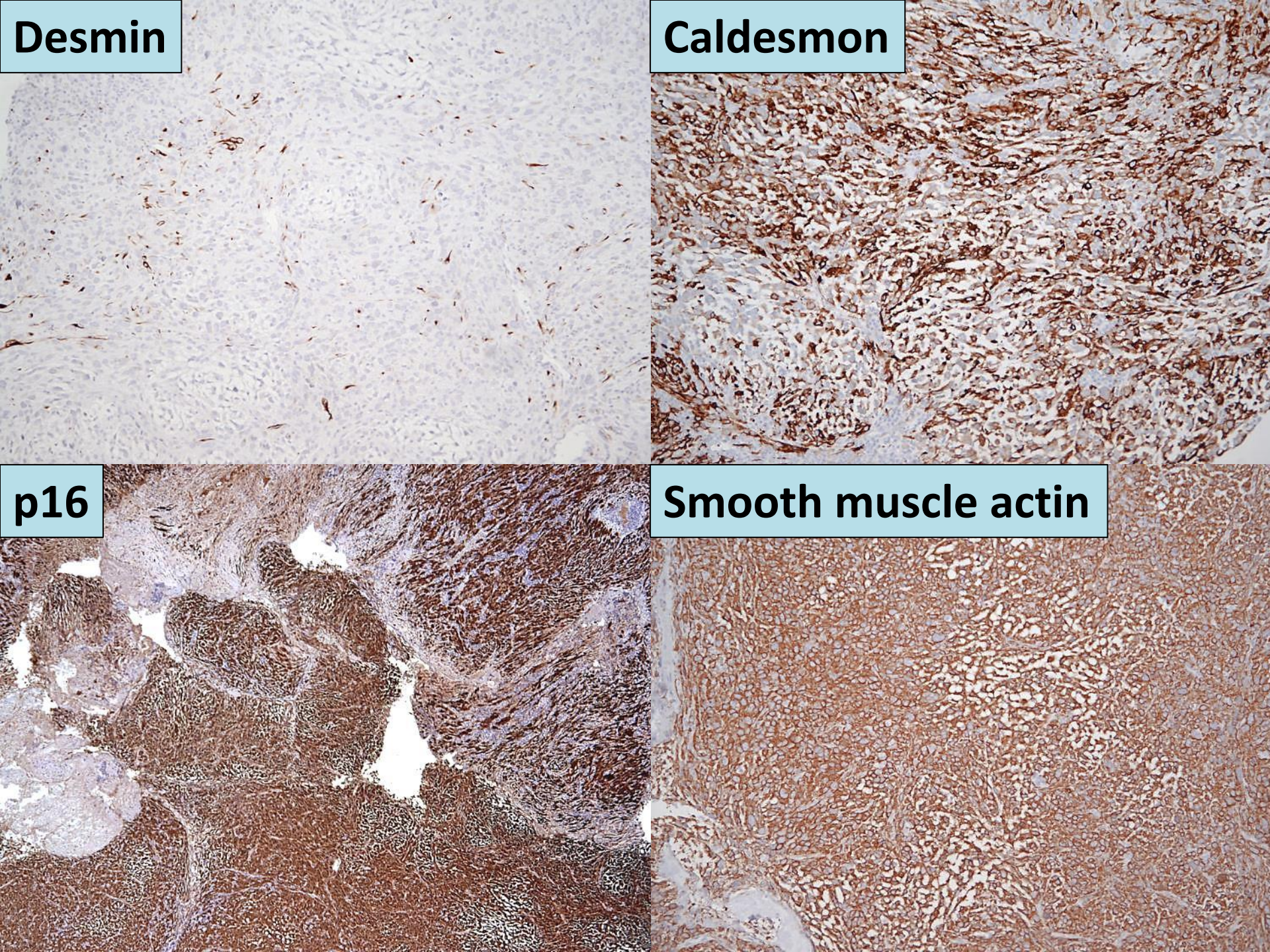






NEGATIVE:

Mixed cytokeratins (AE1/CAM5.2)
HMW cytokeratins (CK1,5, 10, 14)
CK5/6
p63
S100
Chromogranin
Synaptophysin
INI1 (intact)
ERG
CD30
CD34
Myogenin
Brachyury


Desmin
Caldesmon
p16
Smooth muscle actin

Sinonasal Leiomyosarcoma

Clinical features:

- Few reported cases
  - 5-10% soft tissue sarcomas in head and neck
  - 6-13% of those leiomyosarcoma
- <1% of non-epithelial tumors
- Peak in the 6th decade
- Nasal obstruction, discharge, swelling
- Blurry vision less common

Etiology:

- Prior history of radiation or chemotherapy

Sinonasal Leiomyosarcoma

Histopathologic features:

- Intersecting bundles of spindle cells
- Palisading, storiform, hypercellular
- Elongated, lobulated

Immunohistochemical features:

- **POS: Vimentin, Actin (SMA or SMMS), Desmin, h-caldesmon**
- **NEG: keratins, CD34, CD117, S100**

Differential Diagnosis

- Sinonasal hemagiopericytoma/SFT
- Peripheral nerve sheath tumor
- Fibrosarcoma
- Spindle cell carcinoma
- Melanoma

Sinonasal Leiomyosarcoma

Treatment:

- Chemotherapy and radiation

Prognosis:

- 1/2 of cases reported develop local recurrence
- 1/3 develop mets to lungs and liver
- Poor predictive factors: large size, mits, necrosis

Take home points:

- Tumor grade and histologic type crucial for prognosis
- Rhabdomyosarc most frequent, poorest prognosis
- Cytokeratins, LCA, S100, synapto, desmin, melanoma

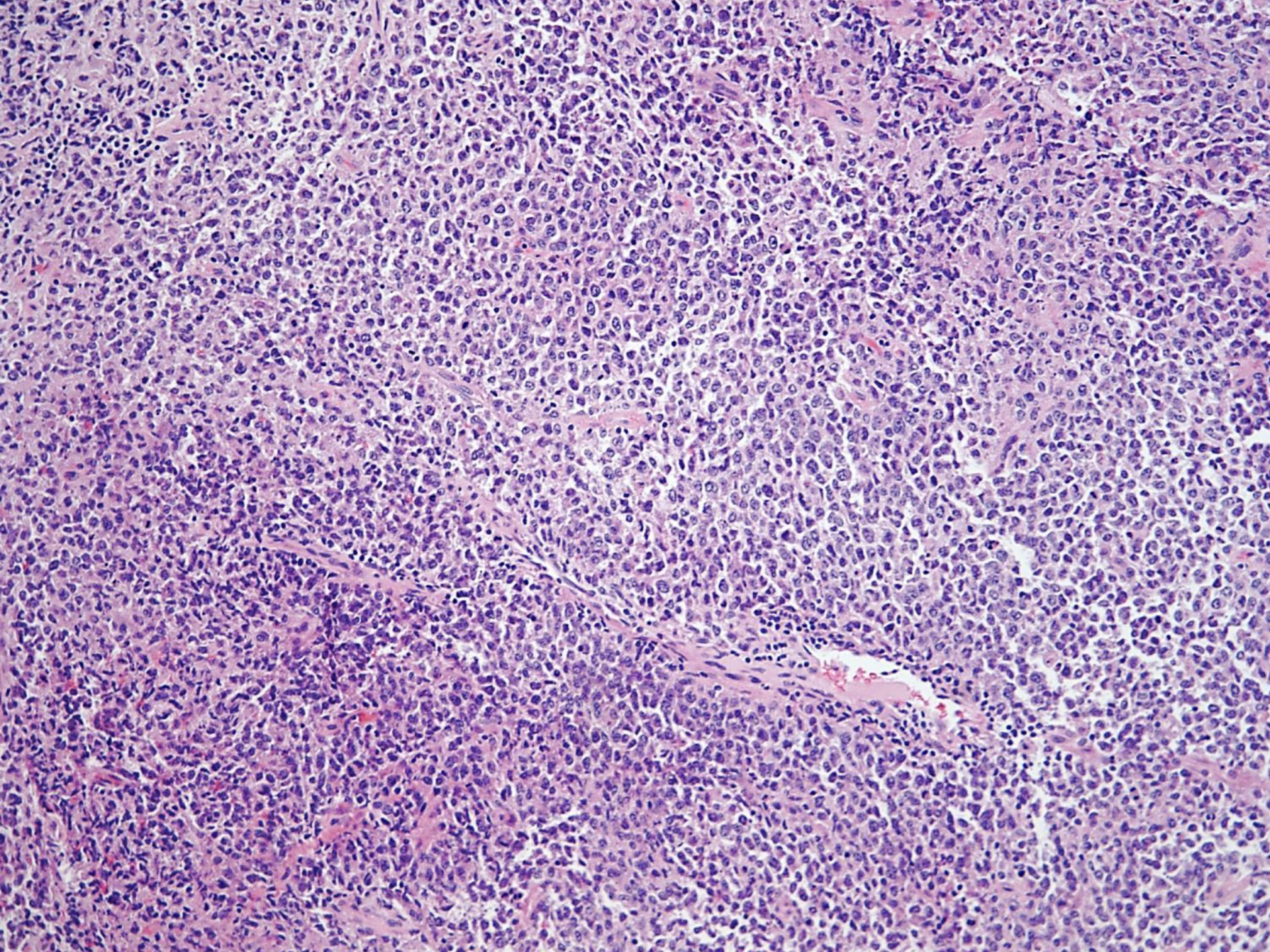
References

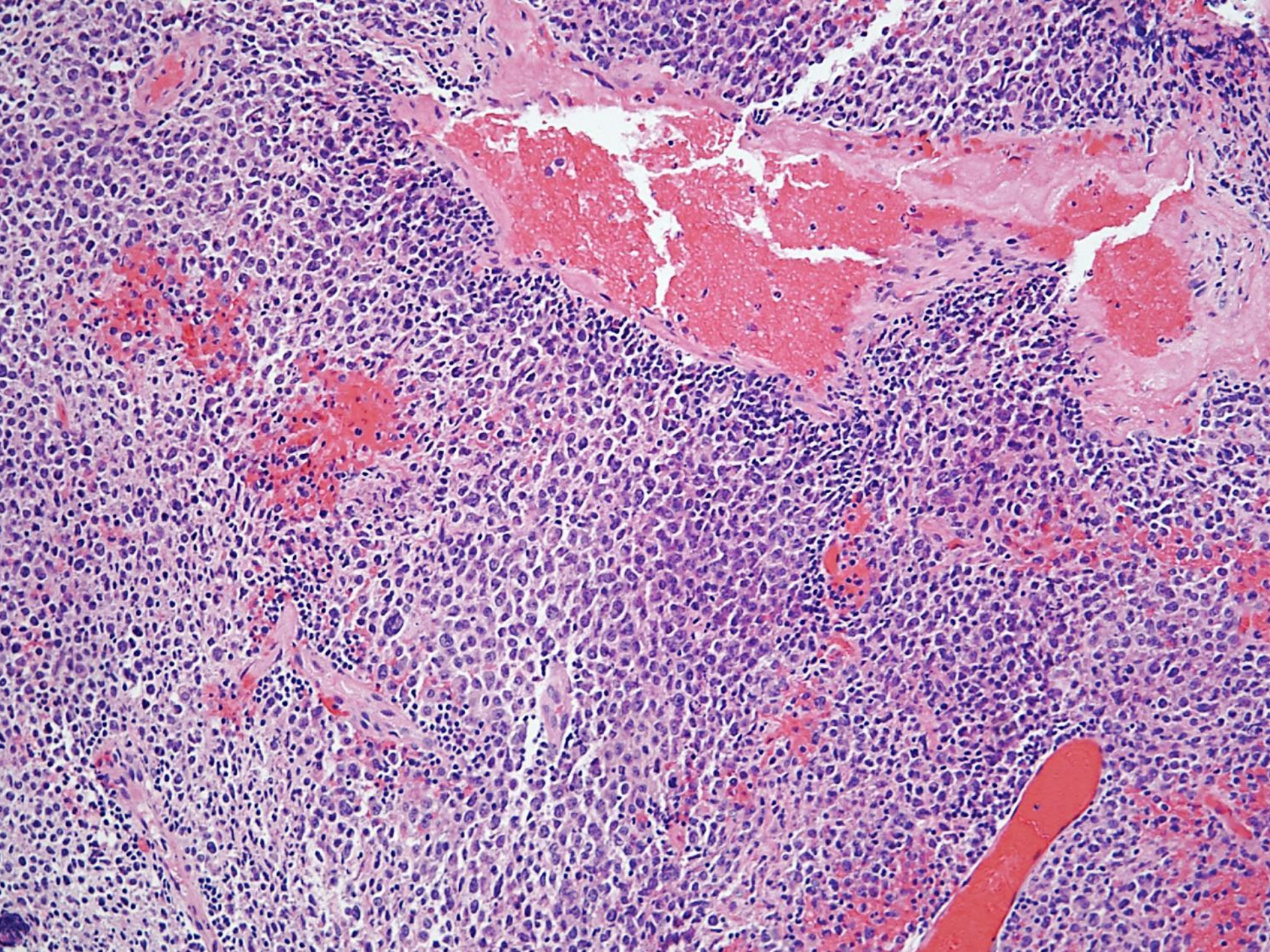
Szablewski, Vanessa, et al. "Adult sinonasal soft tissue sarcoma: Analysis of 48 cases from the French Sarcoma Group database." The Laryngoscope 125.3 (2015): 615-623.

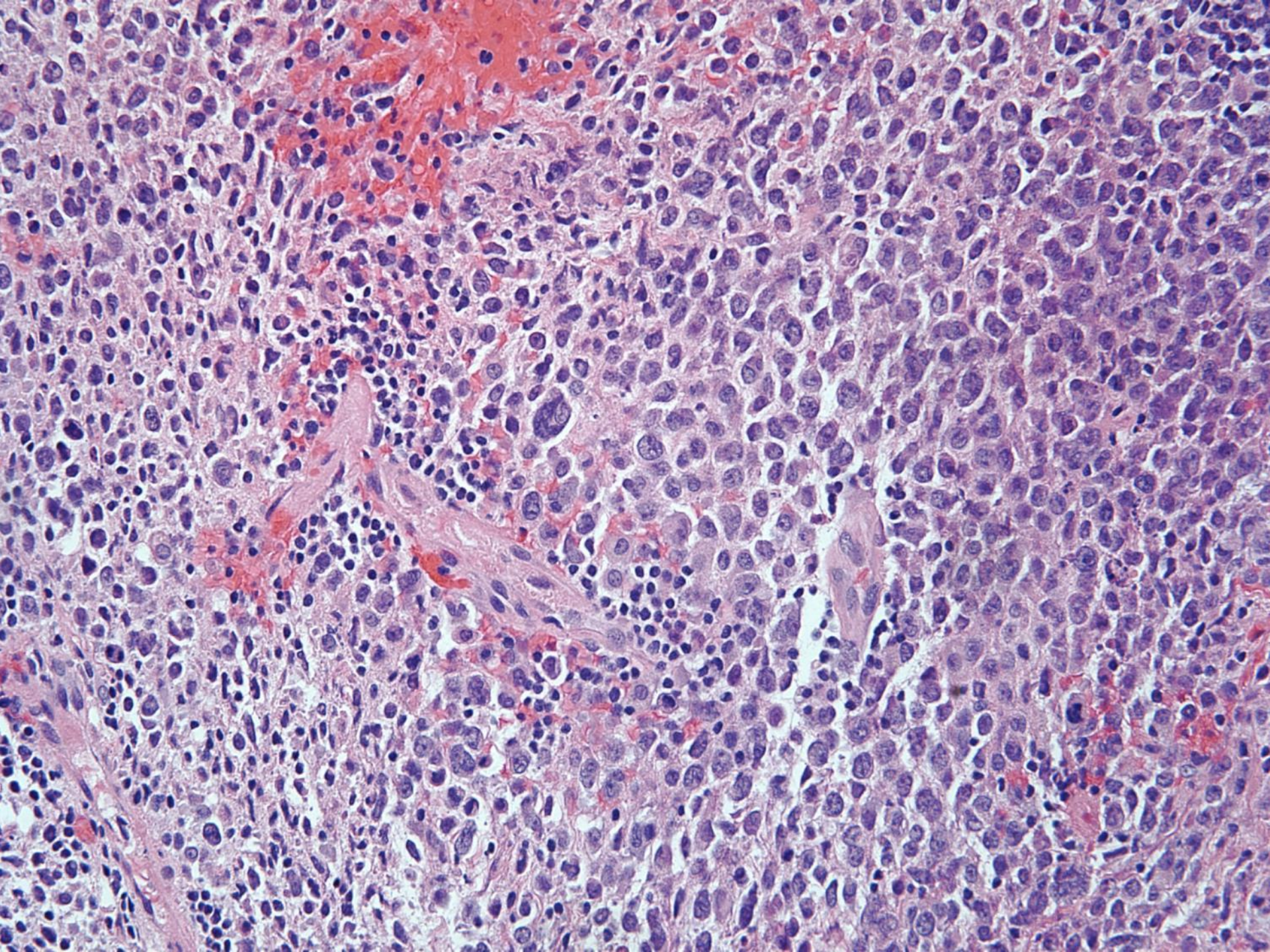
Barnes, Leon. Pathology and genetics of head and neck tumours. Vol. 9. IARC, 2005.

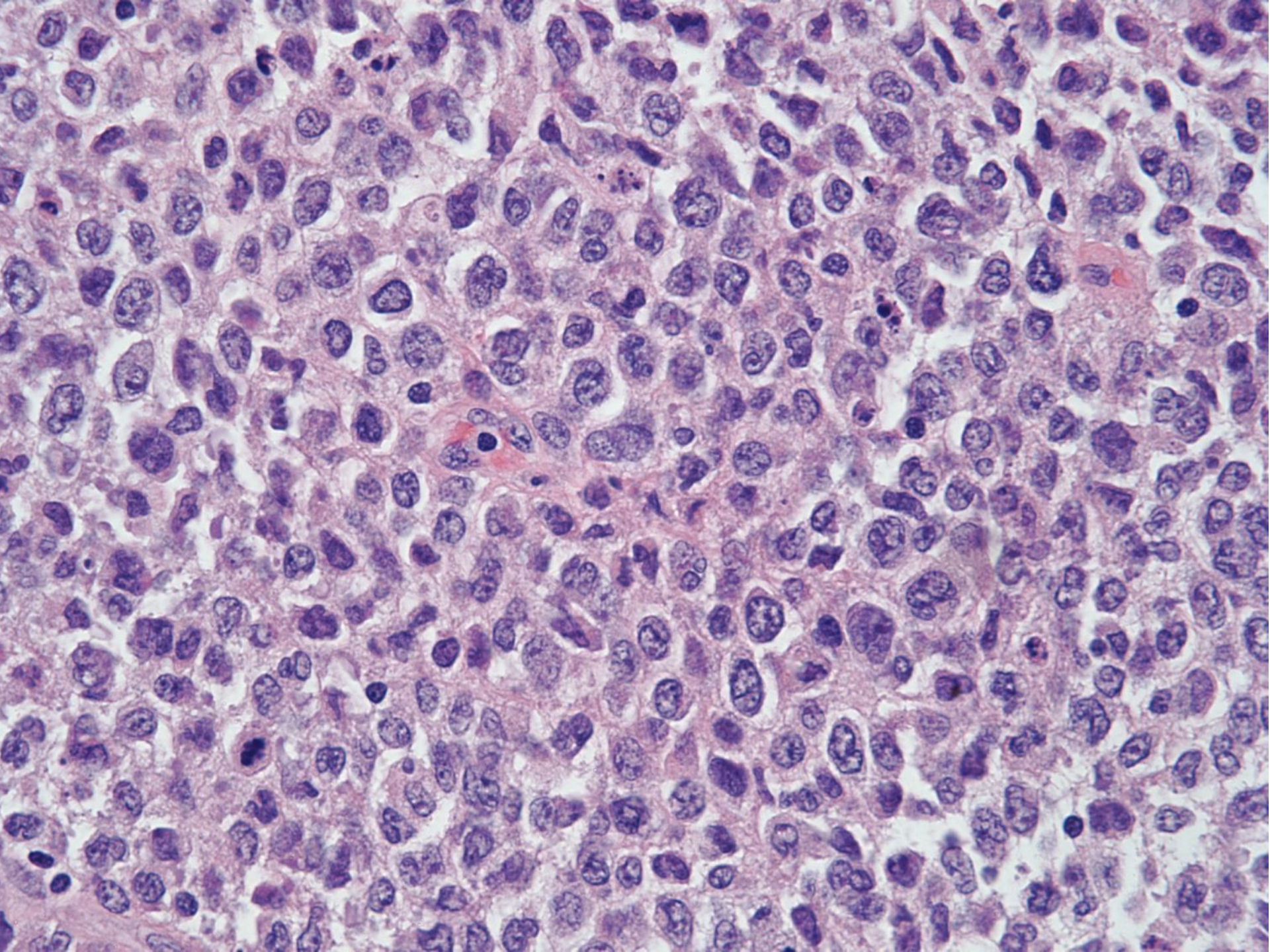
SB 5967
Allison Zemek/Hannes Vogel; Stanford

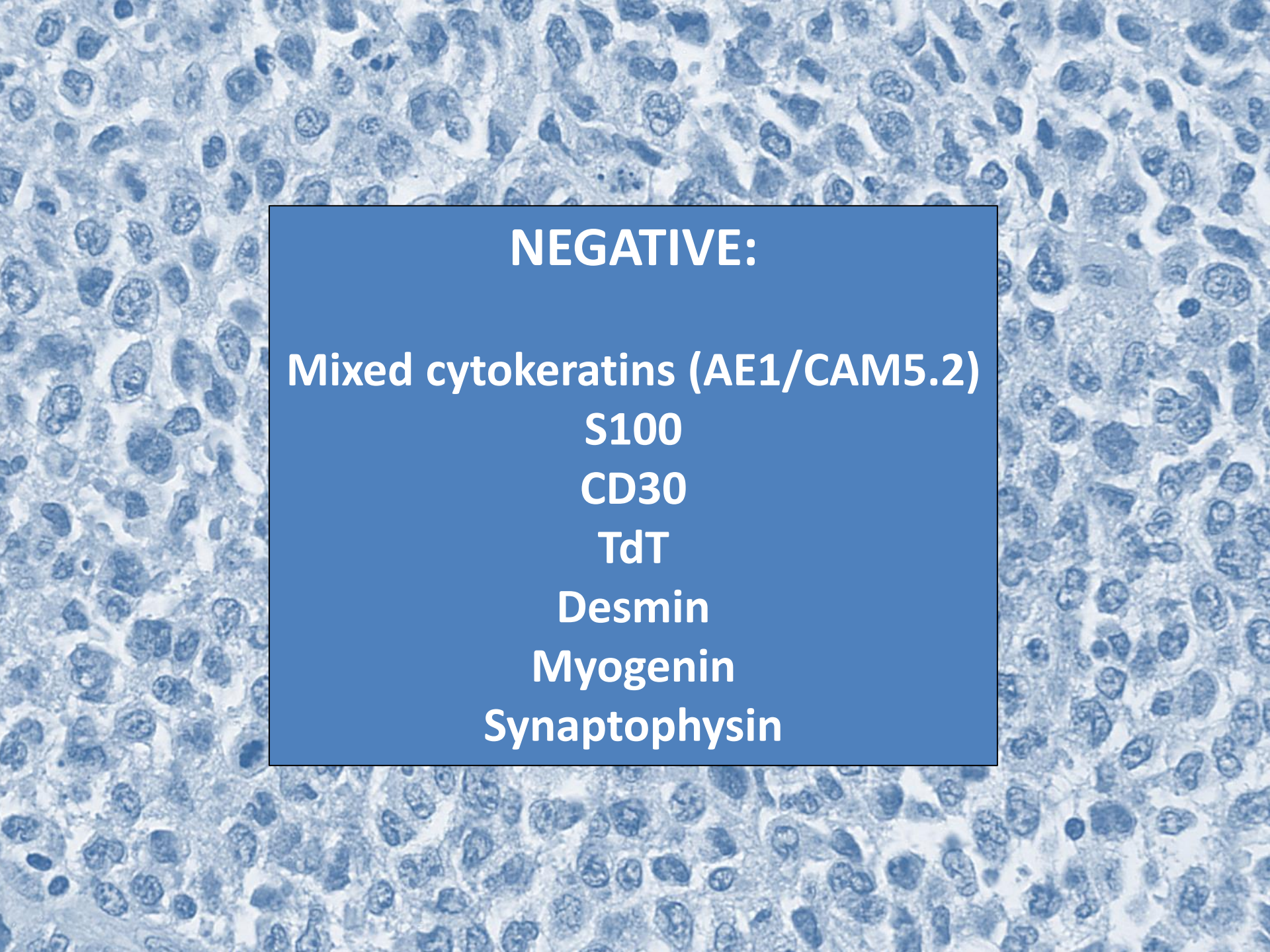
21-year-old man with neck tightness and onset of slurred speech. He was found to have skull base lesion involving right occipital condyle and right clivus.

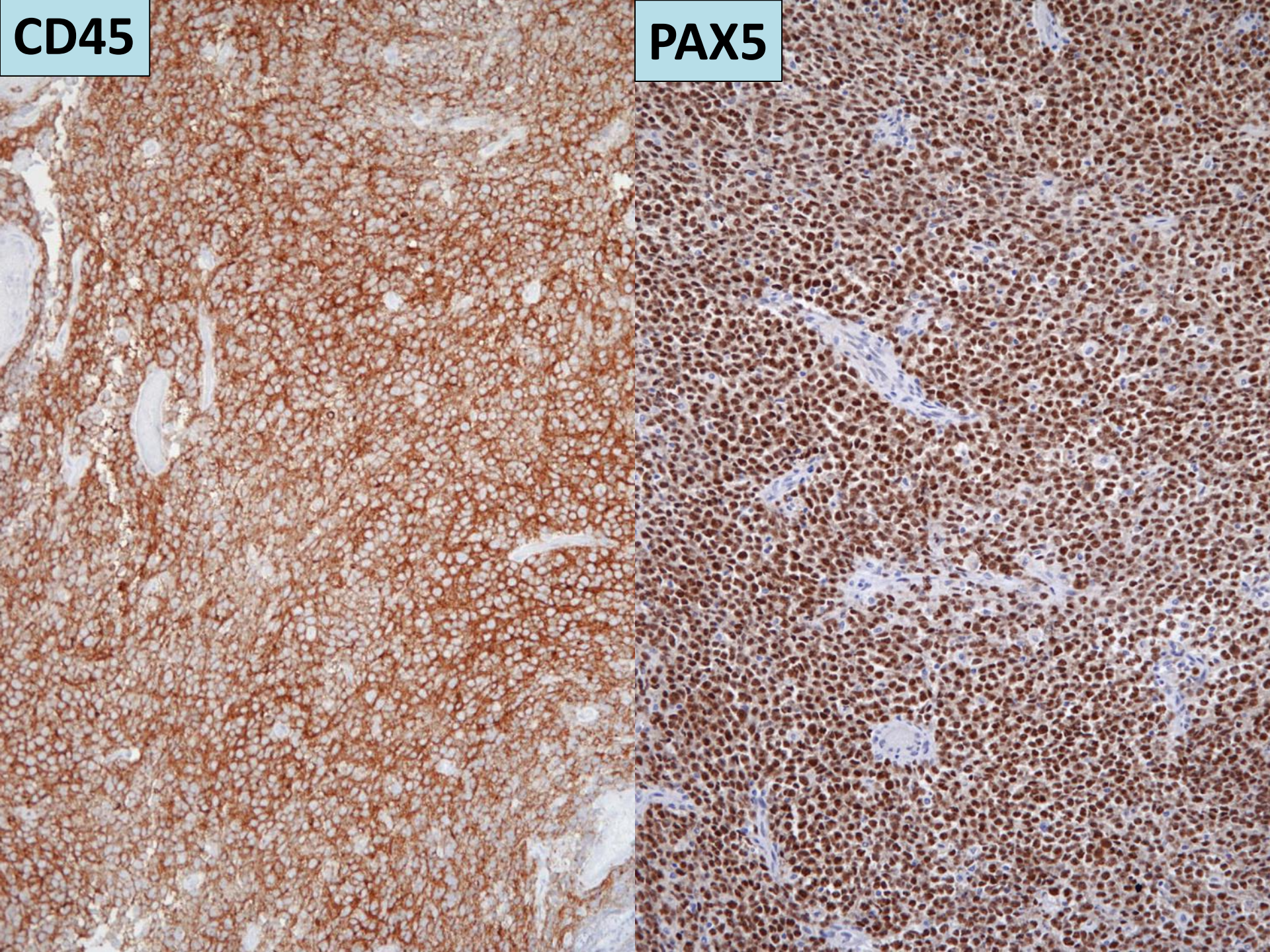









NEGATIVE:
Mixed cytokeratins (AE1/CAM5.2)
S100
CD30
TdT
Desmin
Myogenin
Synaptophysin


CD45
PAX5

Diffuse Large B-Cell Lymphoma

Clinical features:

- 25-30% of adult non-Hodgkin lymphomas
- Median age in 7th decade; also children, young adults
- Rapidly progressing

Pathogenesis:

- Usually primary, can progress from low grade
- Underlying immunodeficiency is a risk factor

Sites of Involvement:

- Up to 40% confined to extranodal sites
- Most common extranodal site is GI
- Few case reports of DLBCL involving clivus

Diffuse Large B-Cell Lymphoma

Histopathologic features:

- Diffuse proliferation of large lymphoid cells
  - Centroblastic variant
  - Immunoblastic variant
  - Anaplastic variant

Immunohistochemical features:

- Pan B-cell markers (CD19, CD20, CD22, CD79a)
- Surface and/or cytoplasmic Ig 50-75% of cases
- Germinal center like vs. non-germinal center like

Differential Diagnosis

- Metastatic carcinoma
- Clear cell sarcoma
- Ewing sarcoma
- Small cell carcinoma

Diffuse Large B-Cell Lymphoma

Treatment:

- Chemotherapy R-CHOP (and radiation)

Prognosis:

- Concordant BM involvement (10% 5 year survival)
- EBV+ worse clinical outcome

Take home points:

- Germinal center origin: CD10+ or BCL6+ and MUM1-
- Other prognostic markers controversial
- Consider lymphoma

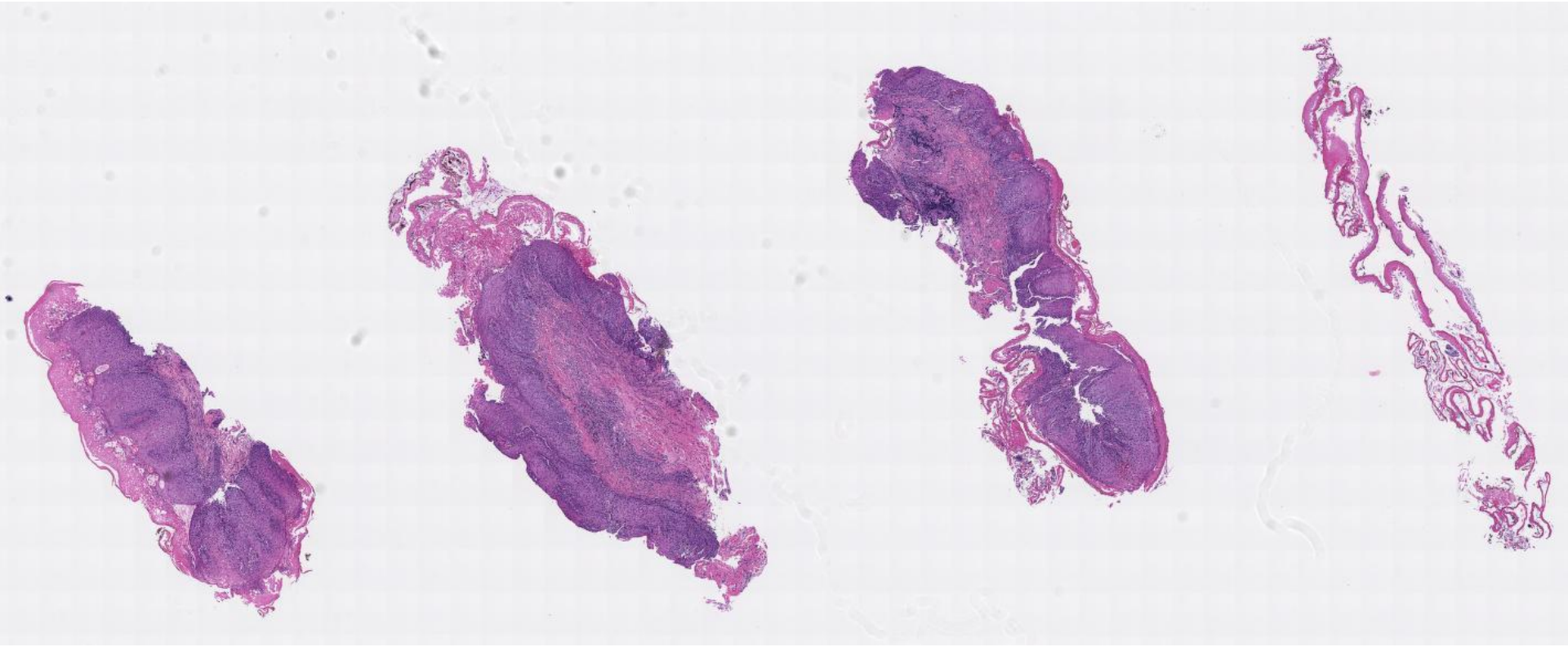
References

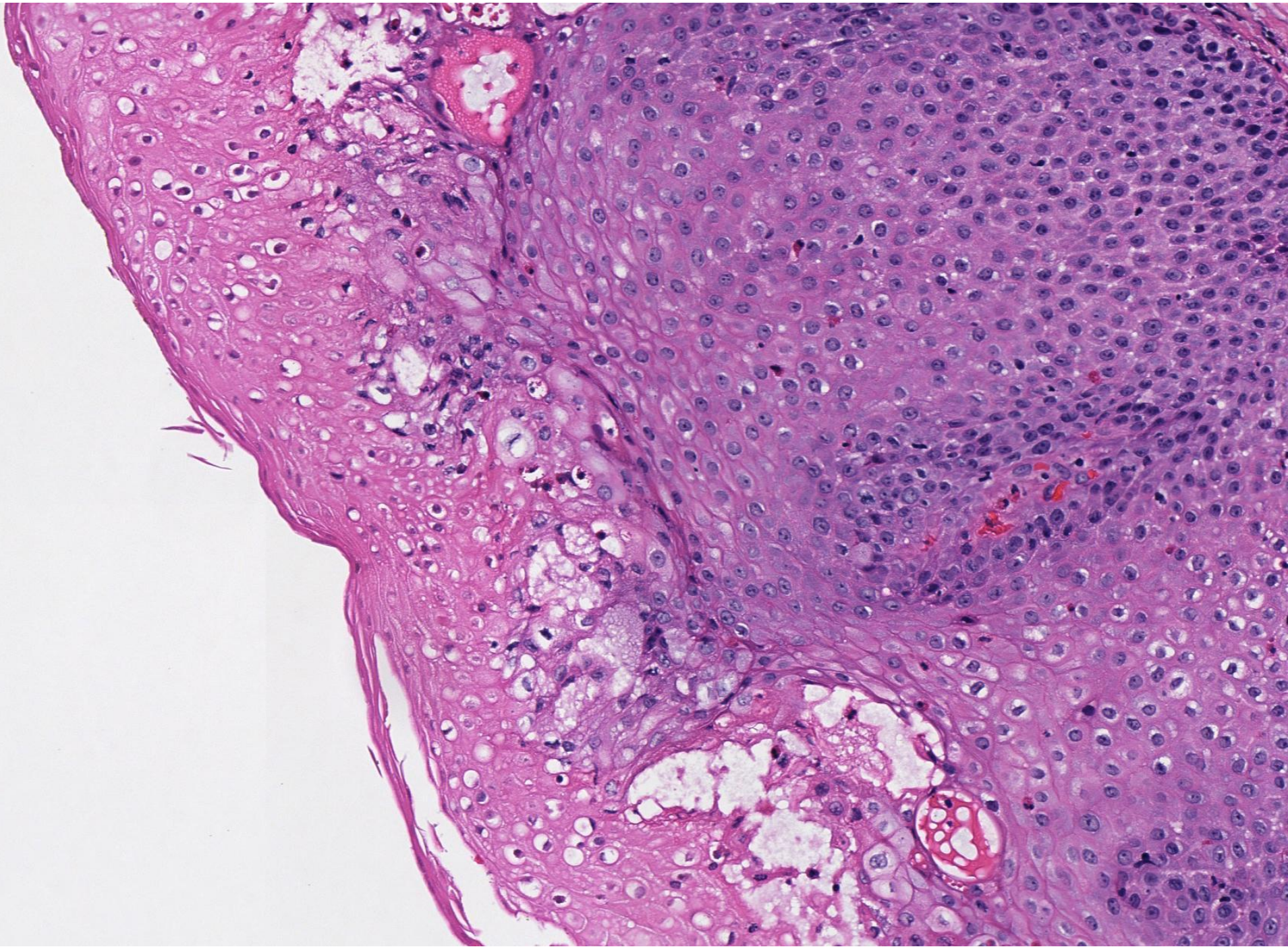
Tsai, Veling W., et al. "Primary B-cell lymphoma of the clivus: case report."Surgical neurology 58.3 (2002): 246-250.

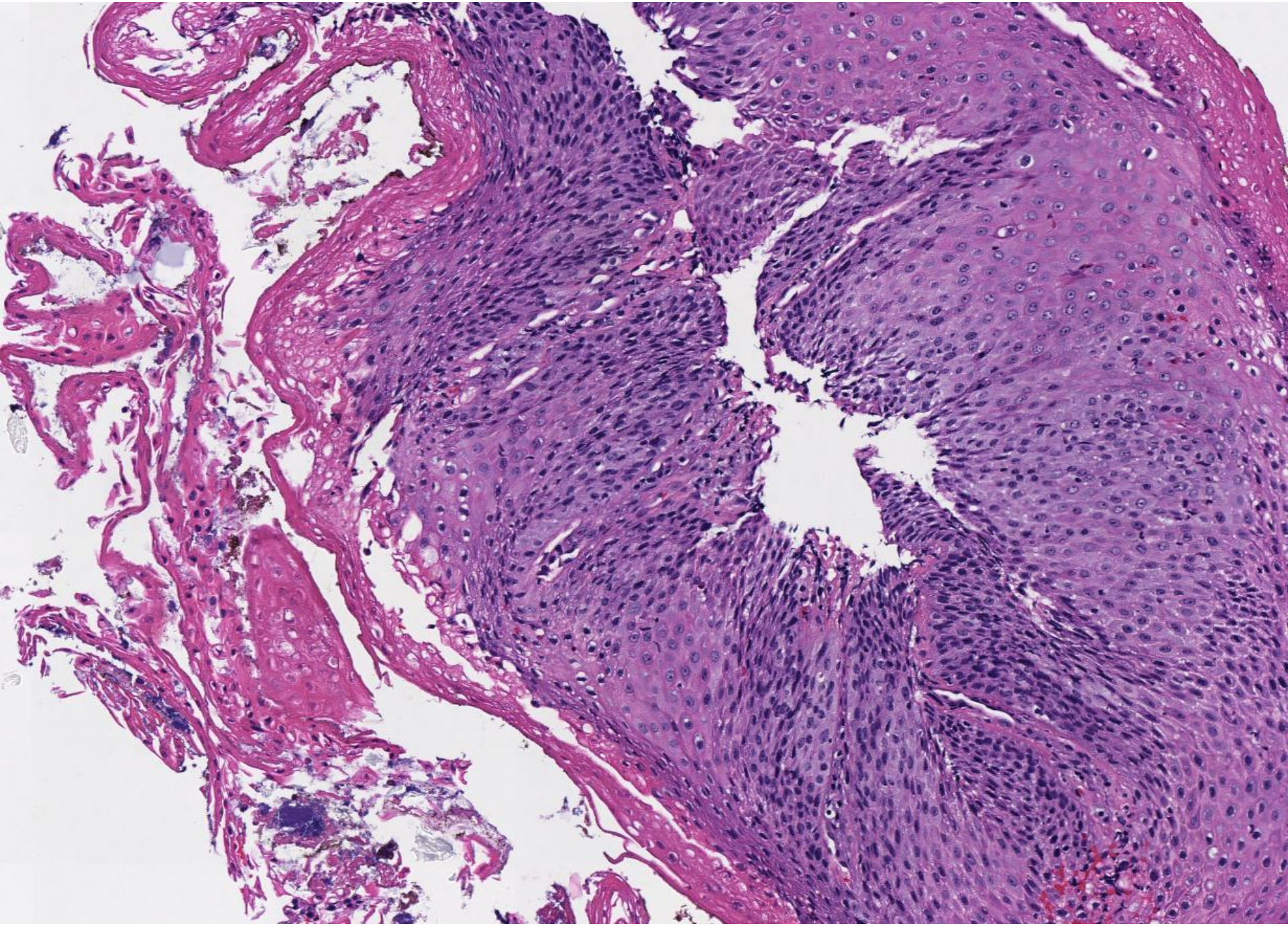
Swerdlow, Steven. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. IARC, 2008.

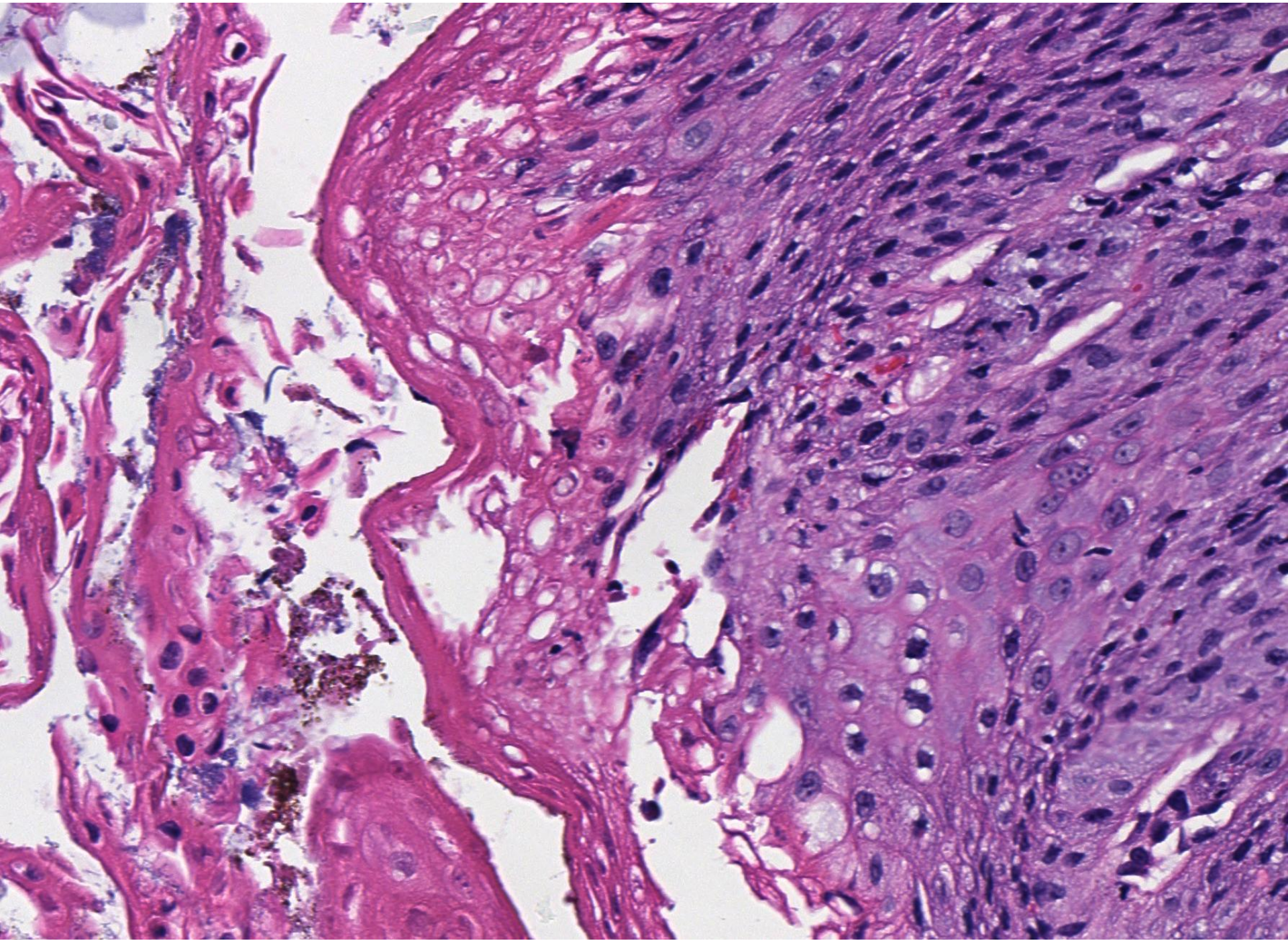
SB 5968
Ankur Sangoi; El Camino Hospital

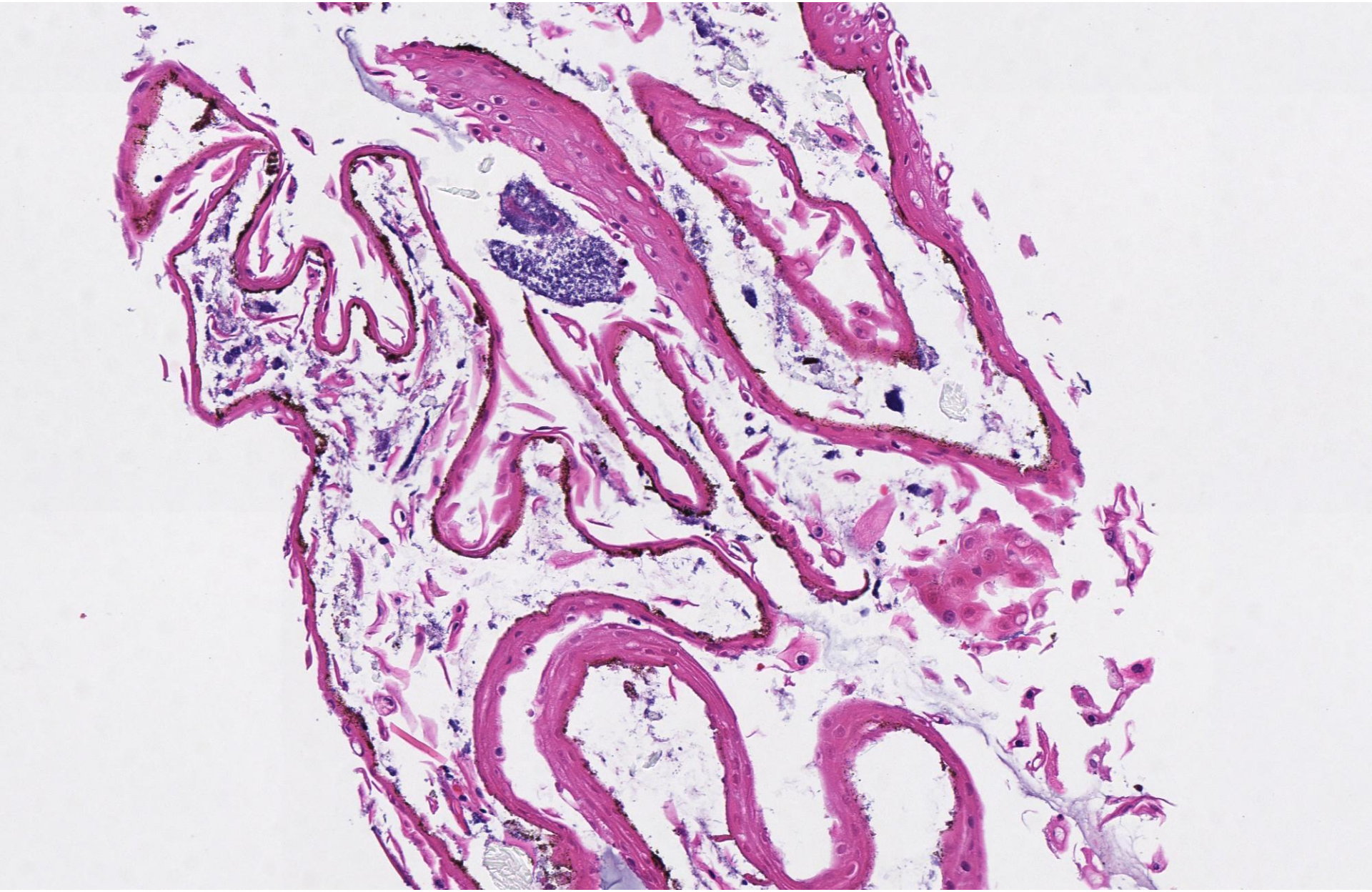
67-year-old man with biopsy of distal esophagus. Rule out ulcer vs Candida.

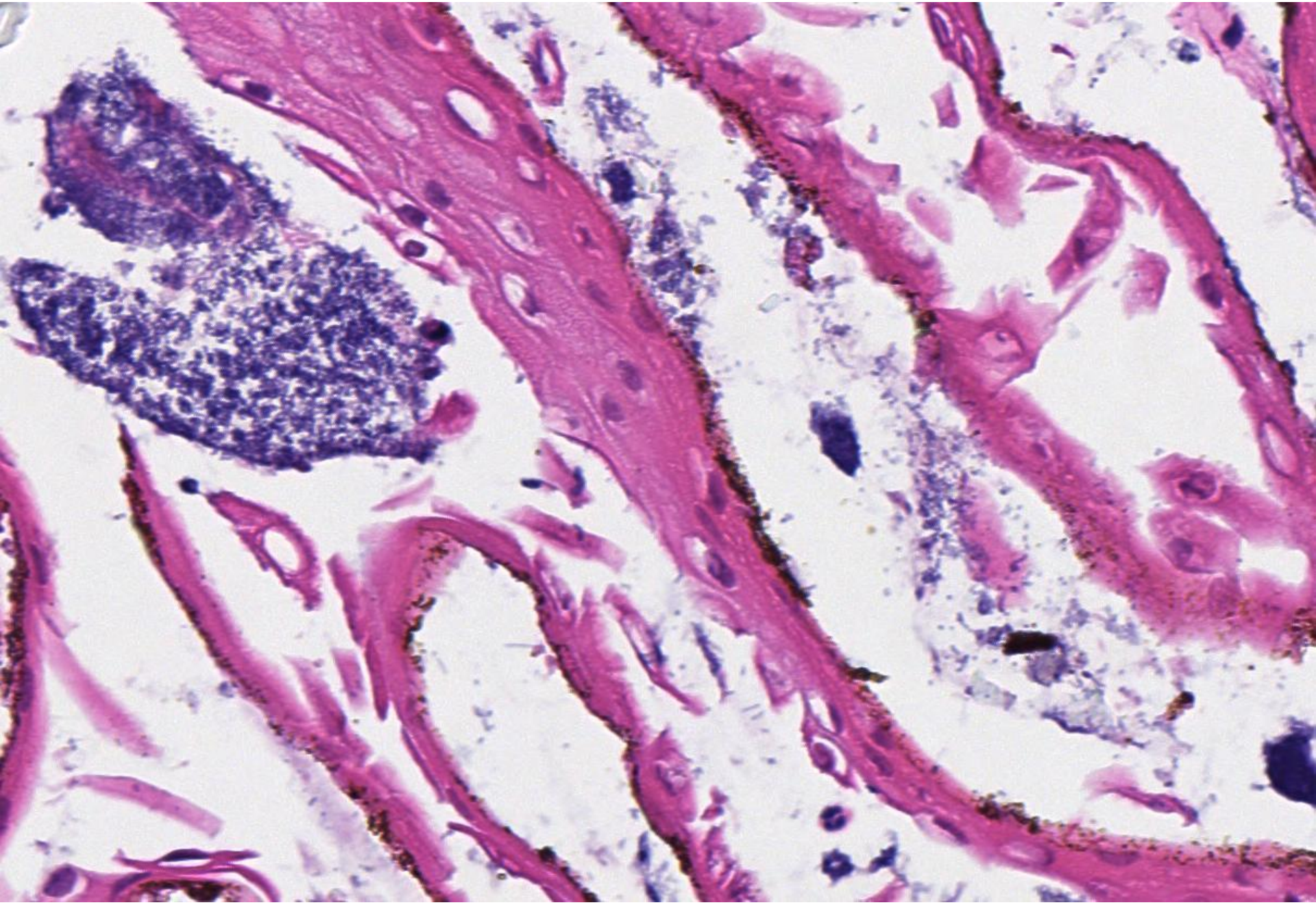










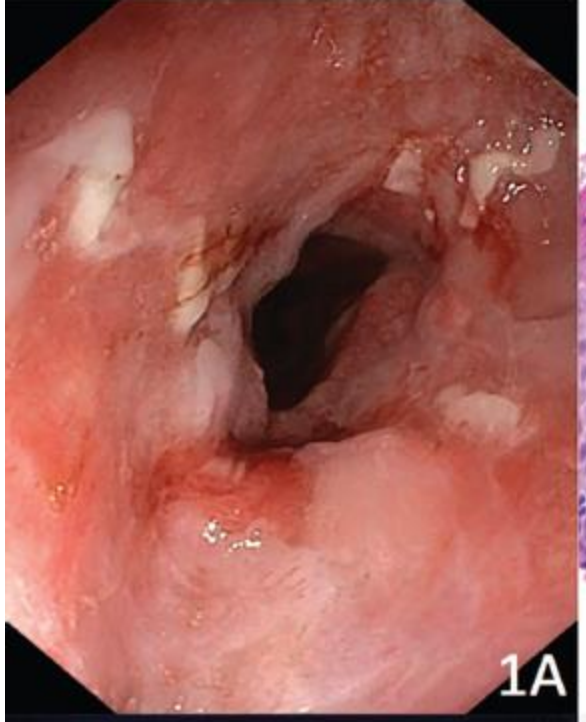


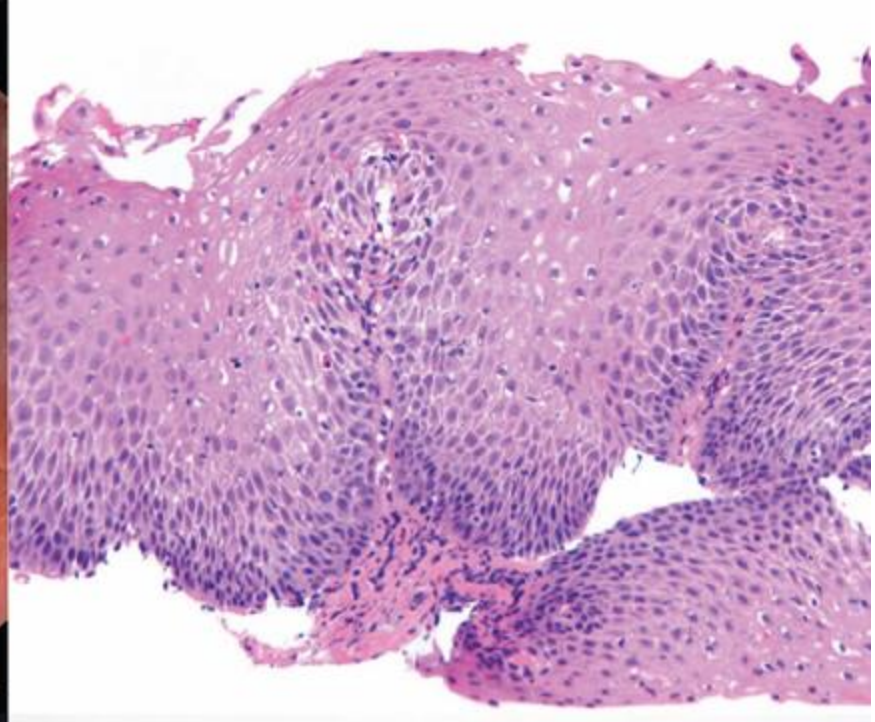
Dx: Sloughing esophagitis (“esophagitis dissecans superficialis”; EDS)

- In spite of its sometimes, dramatic presentation, EDS is a benign condition that resolves without lasting esophageal pathology

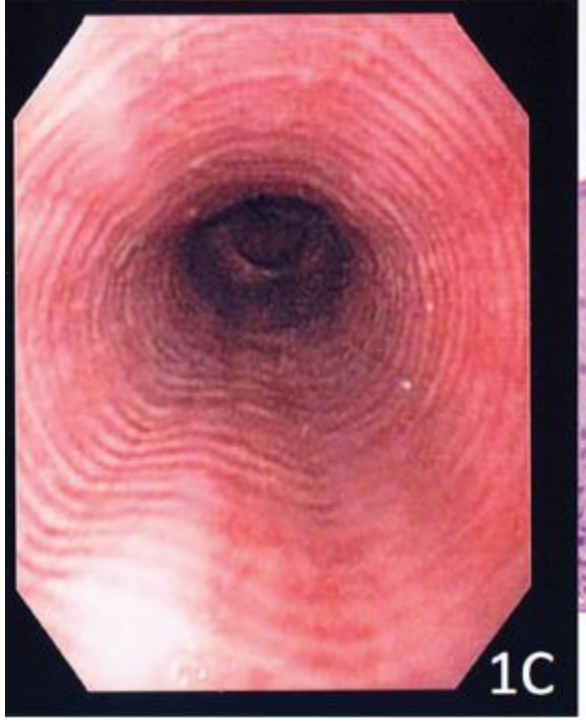
- Although an association with medications, skin conditions, heavy smoking, and physical trauma has been reported, the pathogenesis of EDS remains unexplained

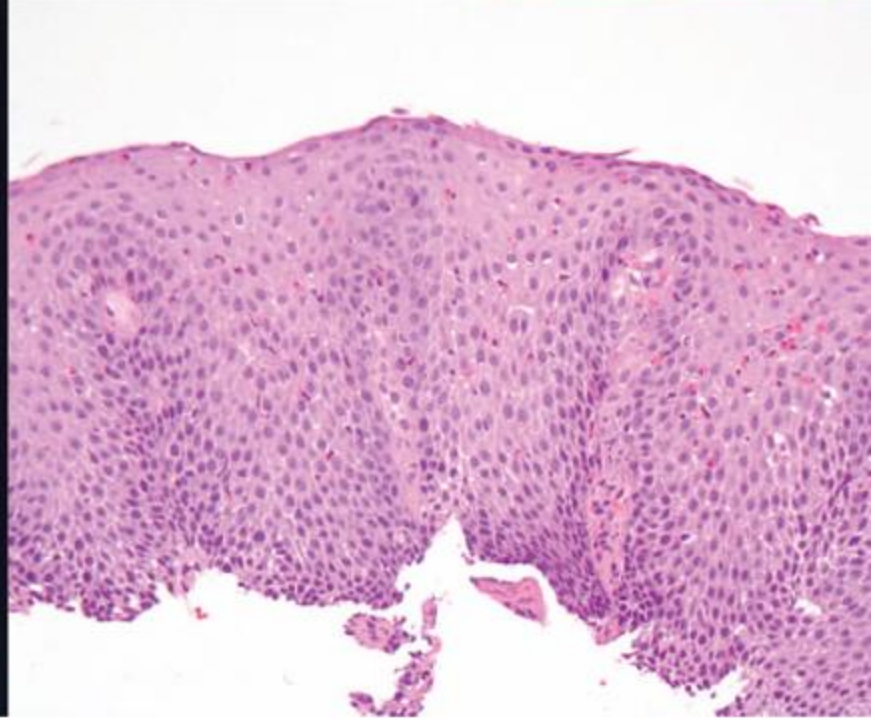
GERD



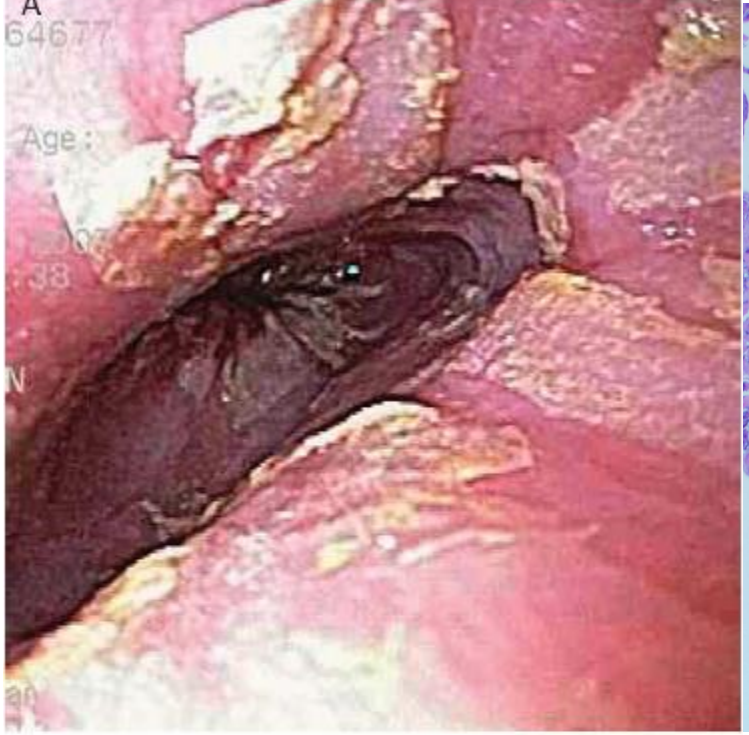


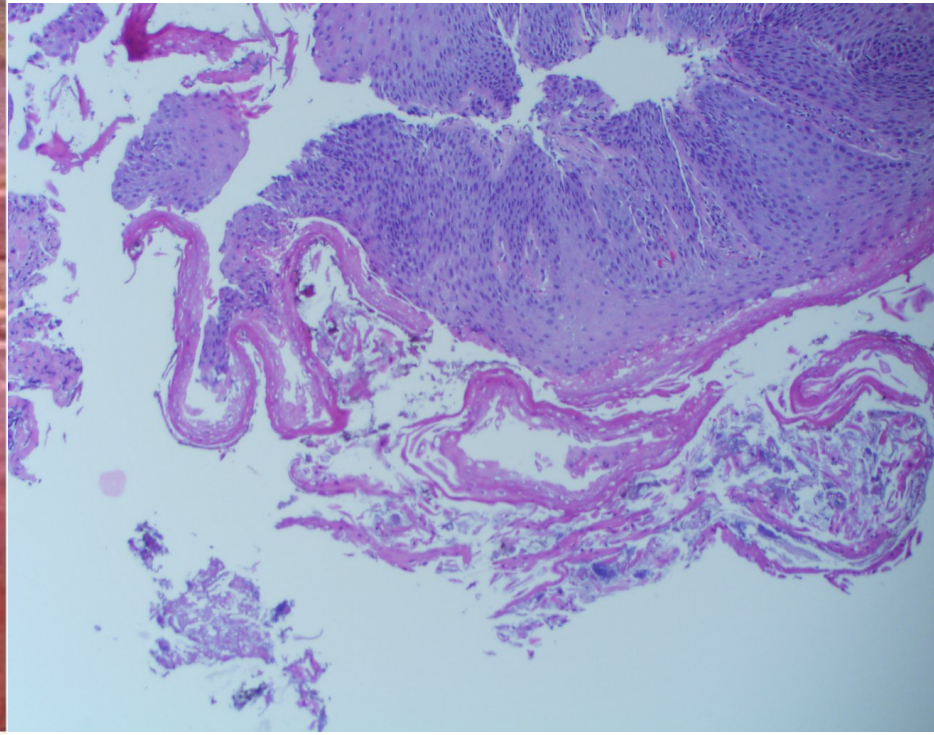
EE

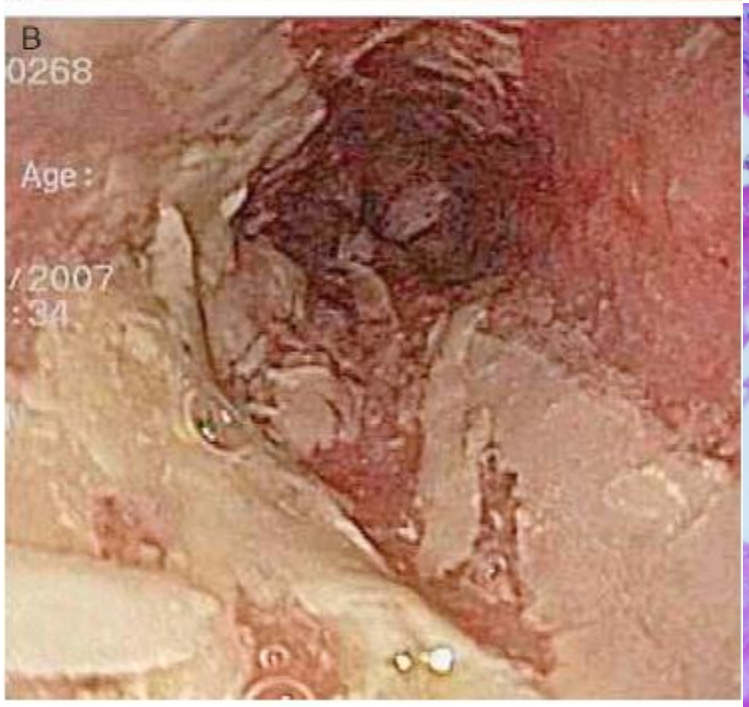


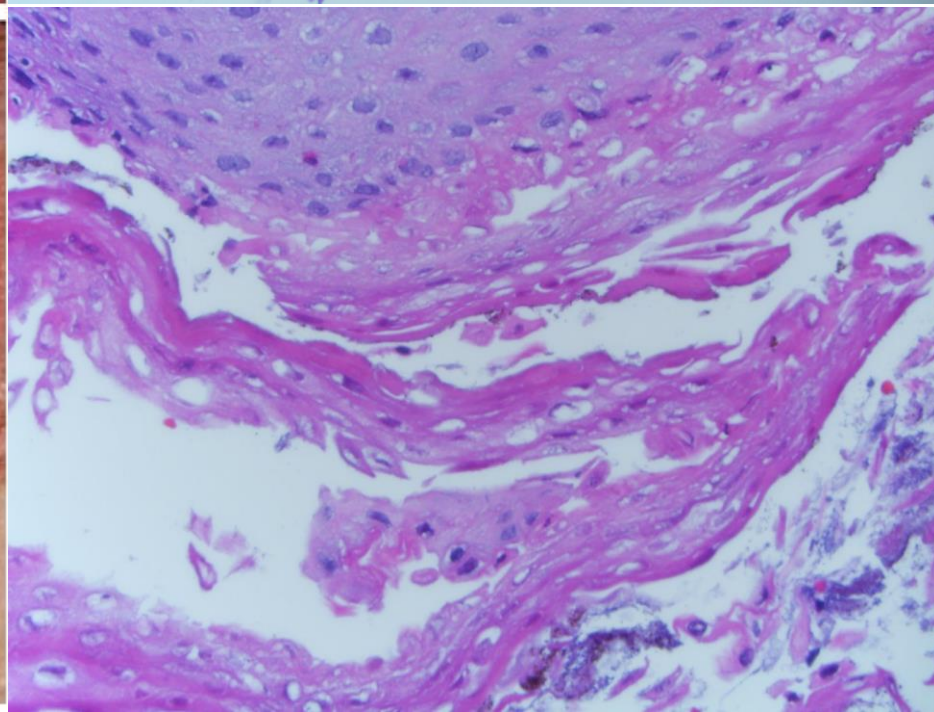


EDS









Esophagitis Dissecans Superficialis ("Sloughing esophagitis")

A Clinicopathologic Study of 12 Cases

Susanne W. Carmack, MD, Roopa Vemulapalli, MD,† Stuart J. Spechler, MD,† and Robert M. Genta, MD*†‡*

Am J Surg Pathol • Volume 33, Number 12, December 2009

Sloughing esophagitis is associated with chronic debilitation and medications that injure the esophageal mucosa

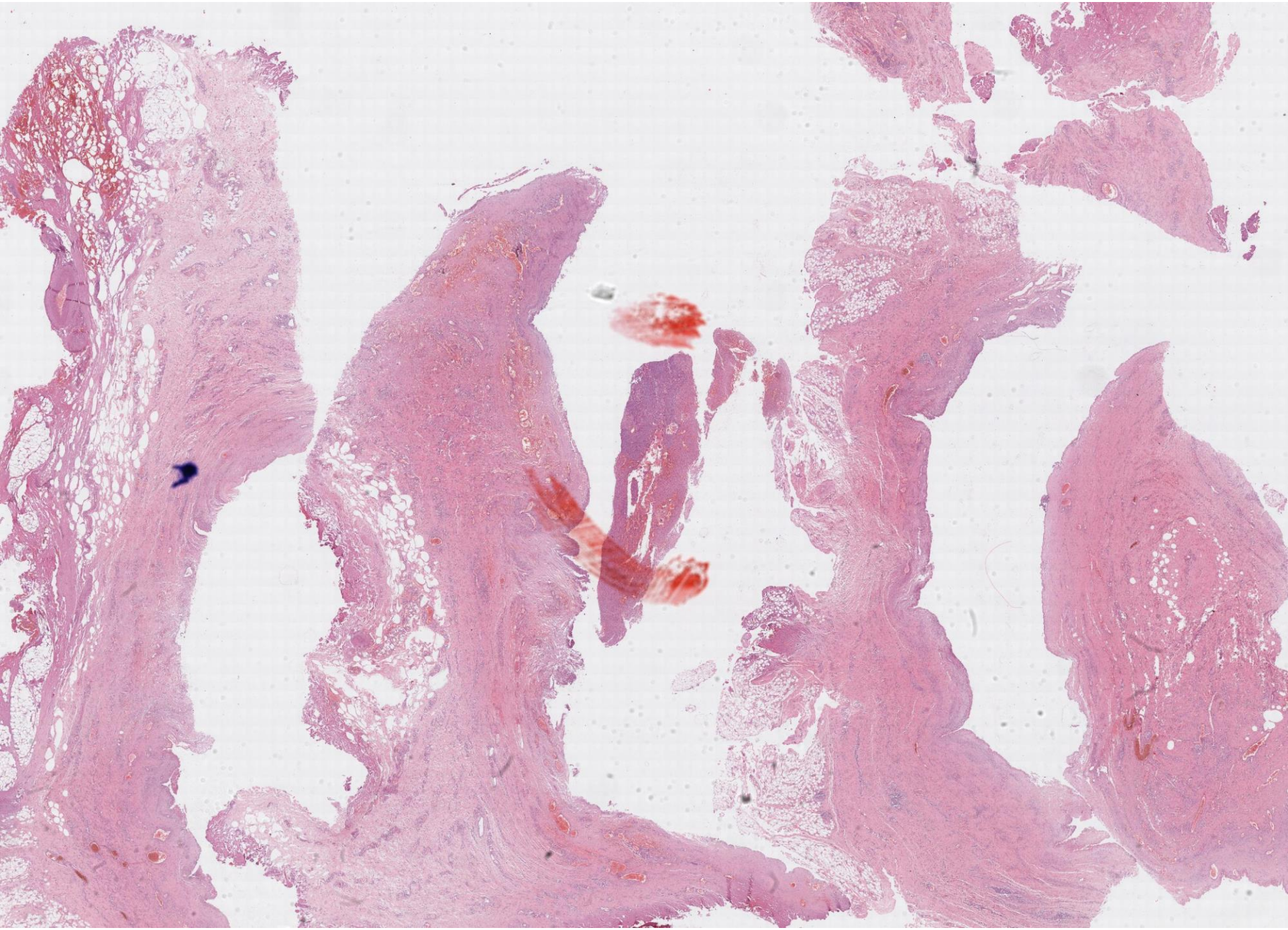
Julianne K Purdy, Henry D Appelman and Barbara J McKenna

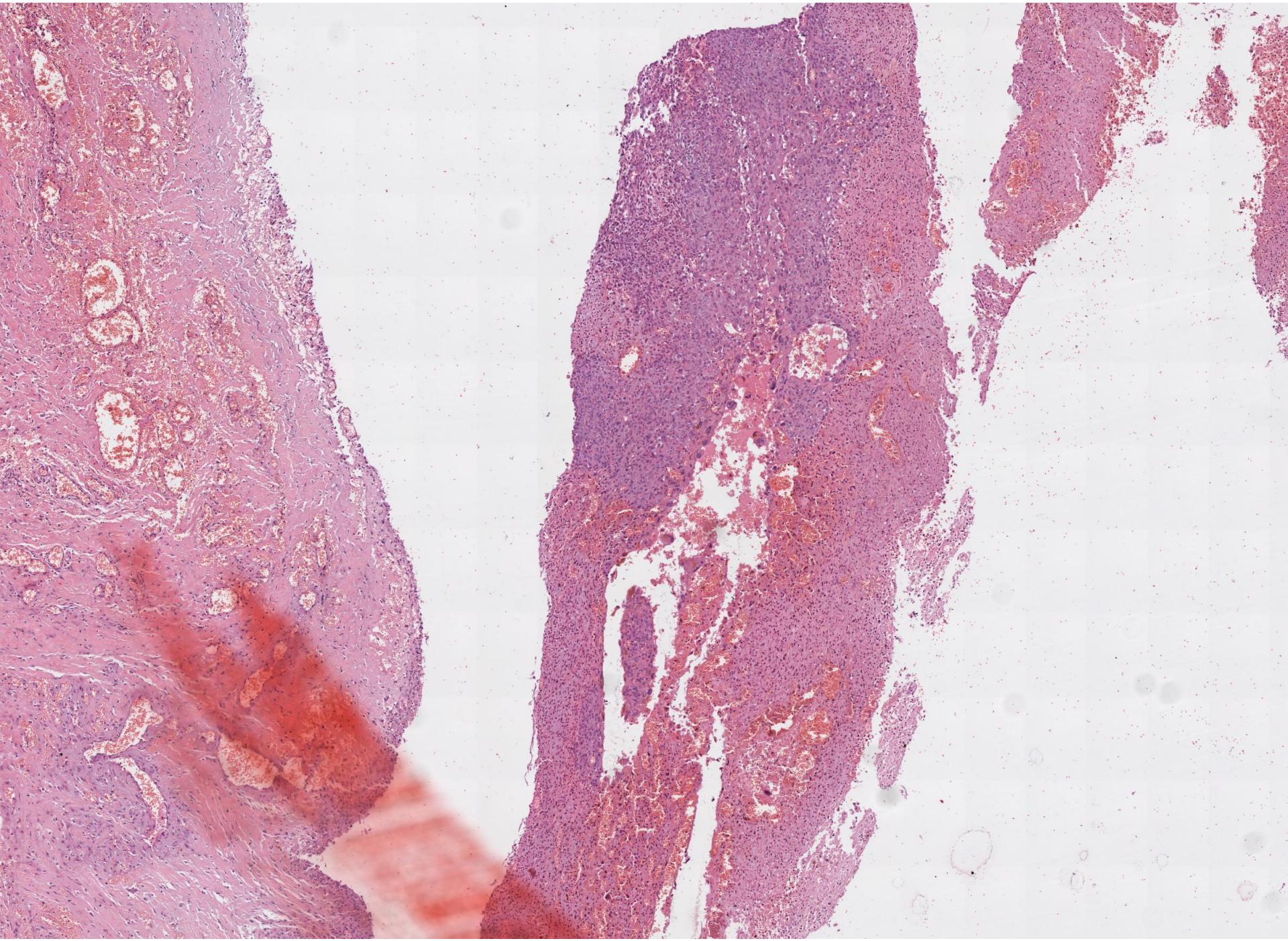
MODERN PATHOLOGY (2012), 1–9

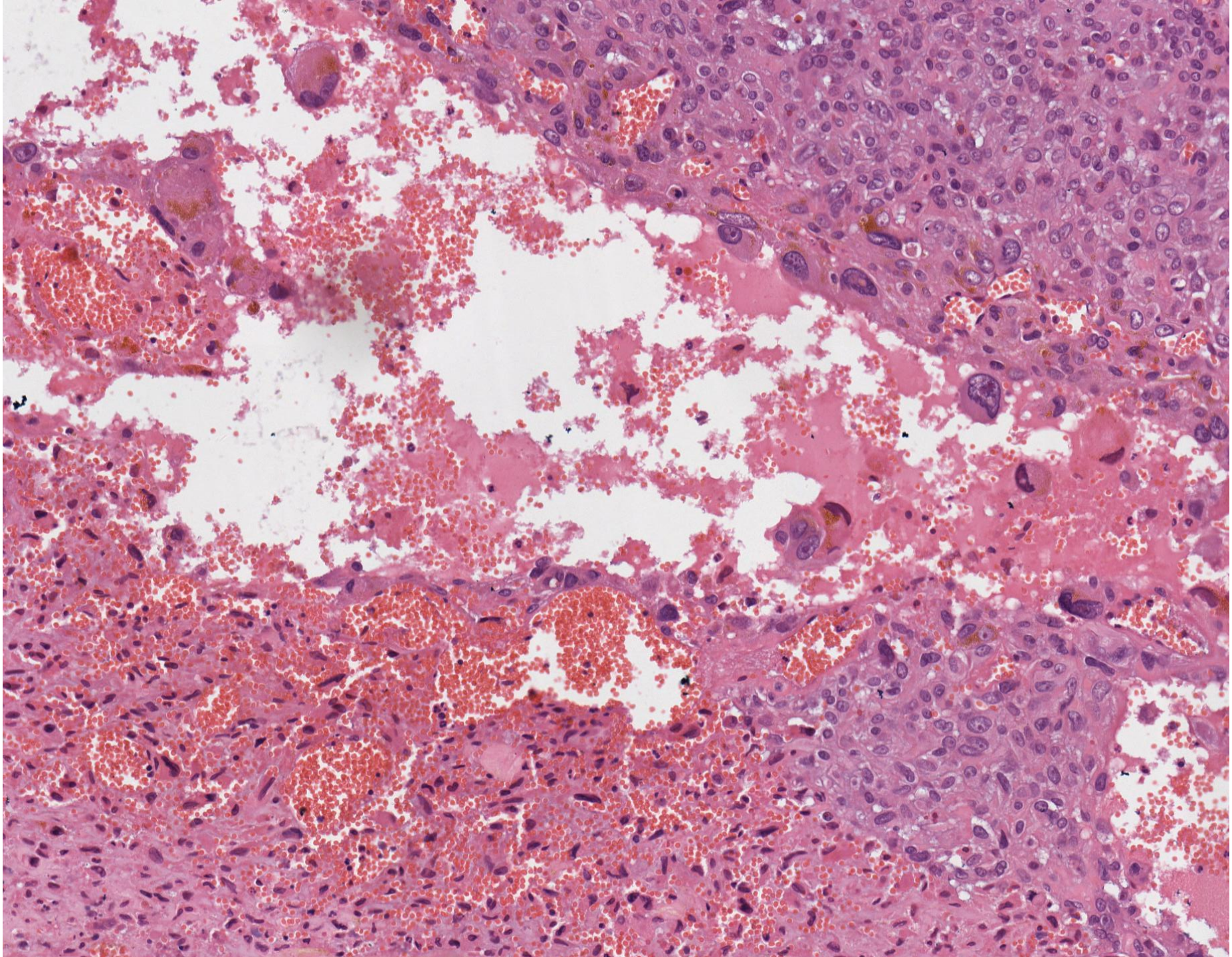
Pt	Age/Sex	Race	Indication for EGD	Social Habits	Esophageal Findings at EGD	Follow-up EGD
1	61 M	W	Dysphagia	Unknown	Diffuse erythema, patches of peeling mucosa mid to distal	Mild esophagitis
2	81 M	AA	Melena	75 pyr	Multiple patches of peeling mucosa	Resolution
3	77 M	AA	Weight loss	100 pyr, no alc	Distal 2 cm patch of peeling mucosa	
4	65 M	W	Dysphagia	120 pyr, remote alc	Grade 4 esophagitis	Resolution
5	60 M	AA	Melena	10 pyr, remote alc	Grade 3 esophagitis from mid to distal	Resolution
6	57 M	AA	Epigastric pain	40 pyr, heavy alc	Distal multiple patches of peeling mucosa	None
7	49 F	W	Heartburn	12 pyr, no alc	Mid to distal grade 3 esophagitis, achalasia	Resolution
8	65 M	W	Anemia	None	Mid to distal grade 4 esophagitis	None
9	80 M	W	IDA	60 pyr, current alc	Mid to distal grade 4 esophagitis	None
10	84 M	W	Melena	None	Sloughing of entire esophagus	None
11	63 M	W	Dysphagia	40 pyr, no alc	Multiple patches of peeling mucosa in mid to distal esophagus	None
12	84 M	W	Weight loss	50 pyr, no alc	Distal adherent yellow patches of peeling mucosa	None
Patients with histology compatible with EDS, but discordant endoscopic features						
1	57 M	H	Dysphagia	None	Esophageal dysmotility	—
2	84 M	AA	Dysphagia	None	Proximal, mid strictures	—
3	82 M	W	Dysphagia	45 pyr, no alc	Distal stricture with esophagitis	—
4	64 M	W	Dysphagia	None	Distal 1 cm stricture	—
5	62 M	W	Dysphagia	None	Distal 1 cm stricture	—
6	67 M	W	Dysphagia	None	Distal 1 cm stricture	—
7	61 M	W	Dysphagia	100 pyr, current alc	Distal grade 3 esophagitis, distal stricture, mid webs	—
8	51 M	AA	Dysphagia	80 pyr	White nummular lesions	—
9	60 M	W	Dysphagia	None	Mid 1 cm stricture, distal erosions	—

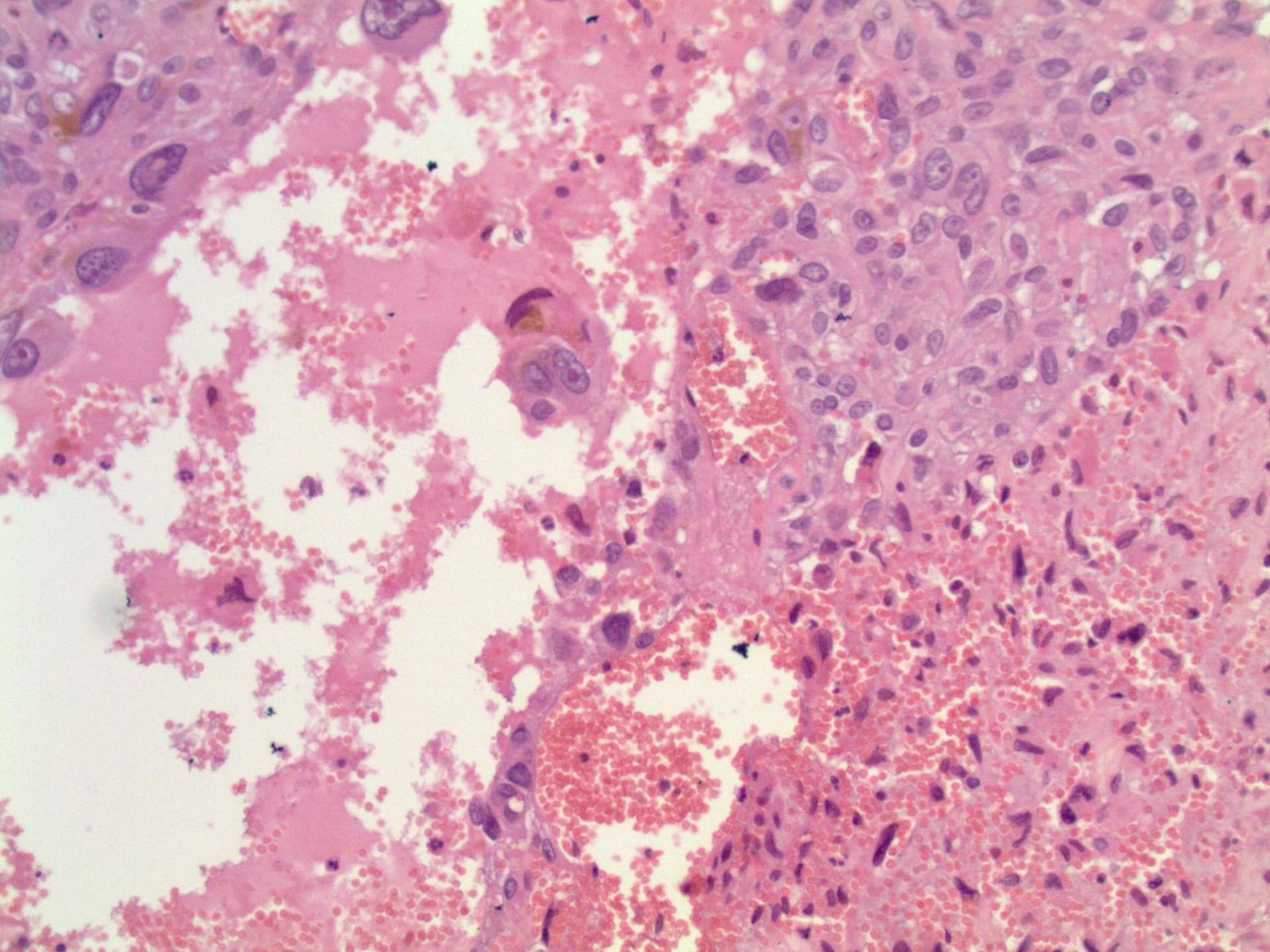
SB 5969
Nabeen Nayak; Sir Ganga Ram Hospital (New Delhi)

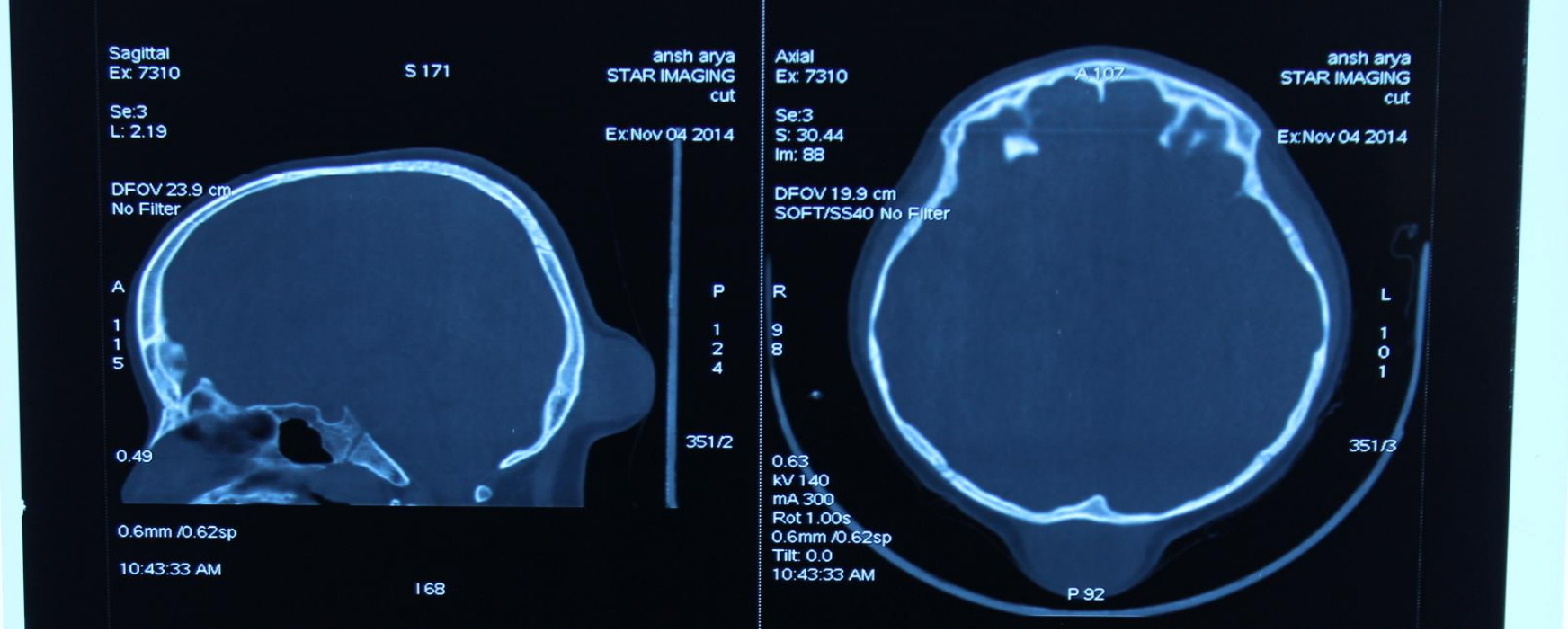
7-year-old boy with a soft painless swelling in the occipital area first noticed by the mother in July 2014 while bathing him. There was no definitive history of trauma and the swelling did not increase till 2 months later when it increased to about 1.5 times its original size without any pain. CT and MRI advised showed only a rounded soft tissue swelling with only a minimal scalloping of the underlying bone but no other changes. Mass was excised with a clinical diagnosis of sebaceous cyst.

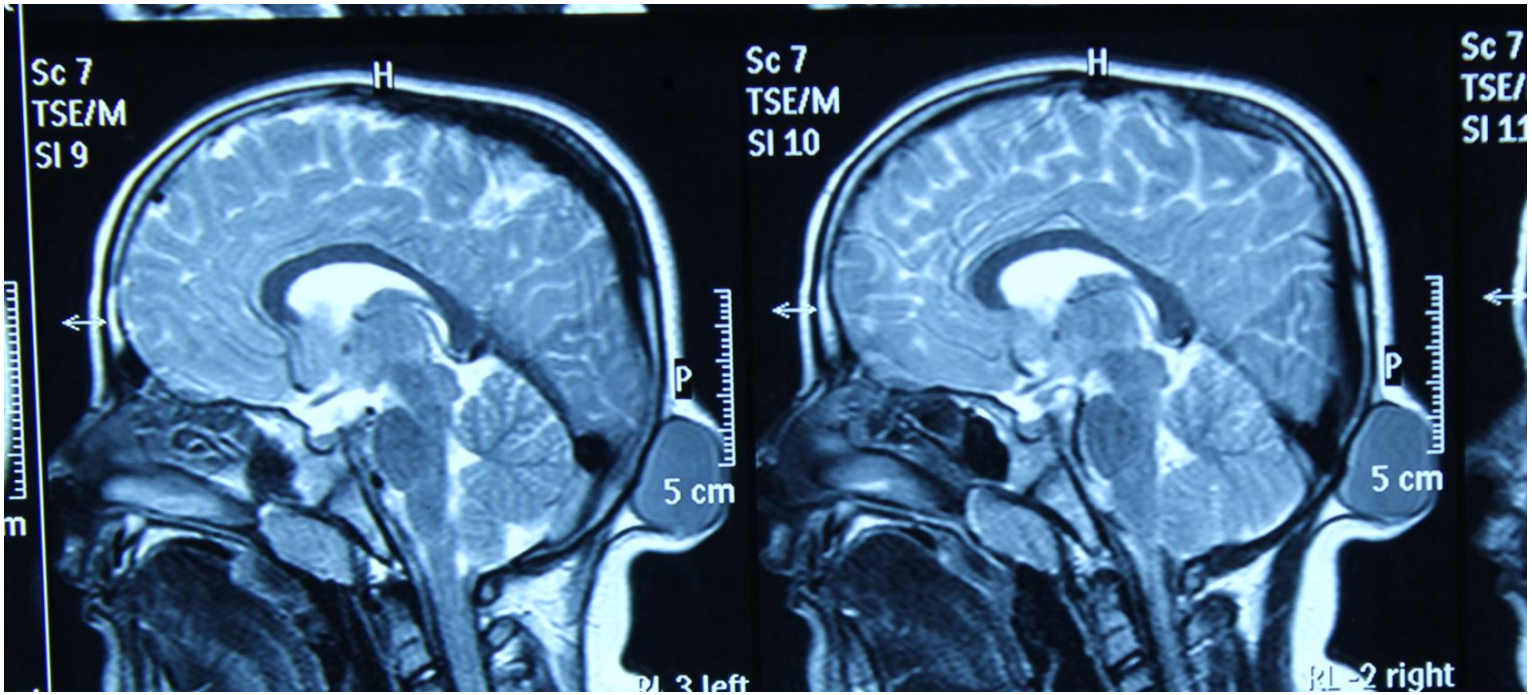




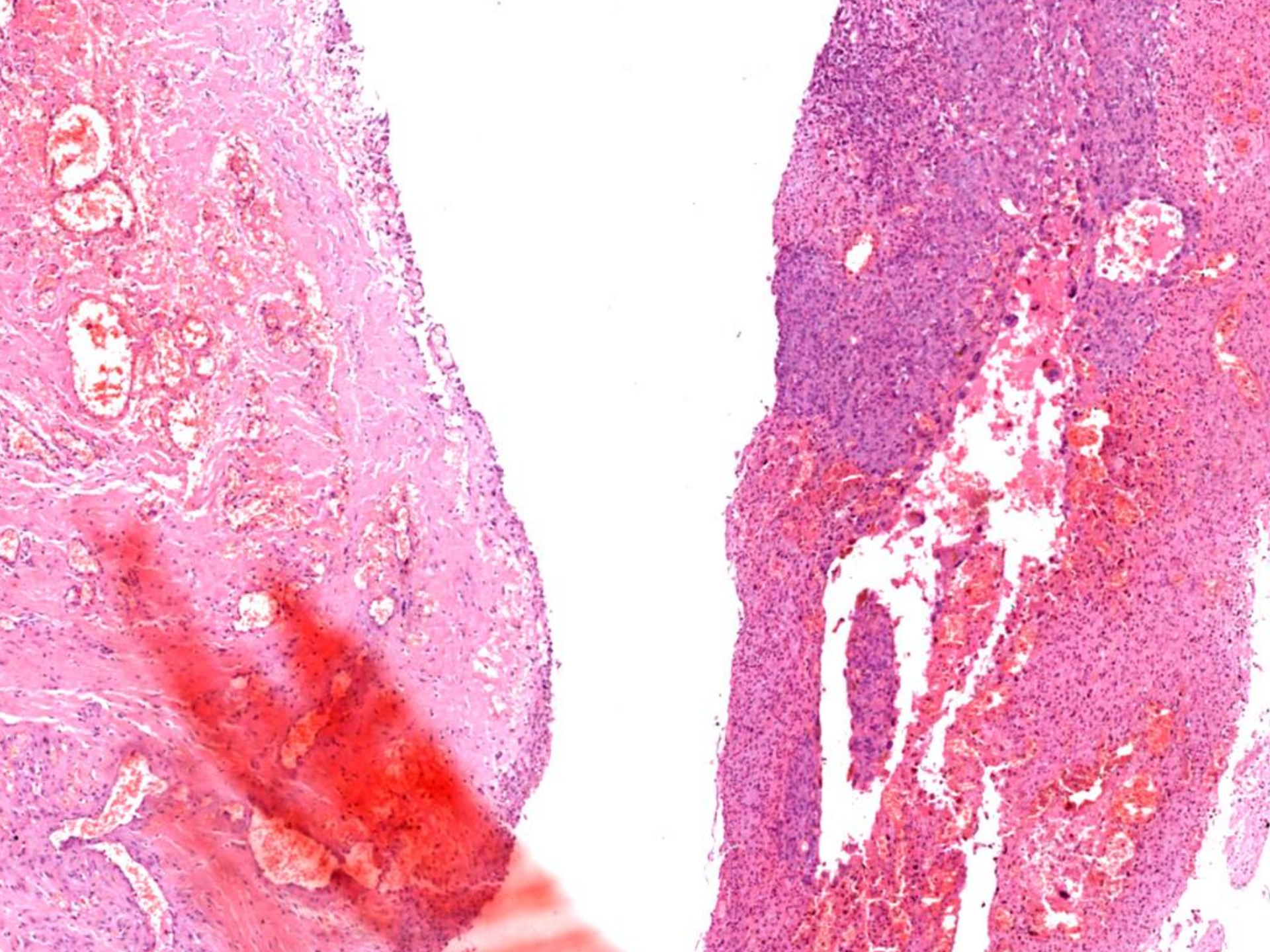


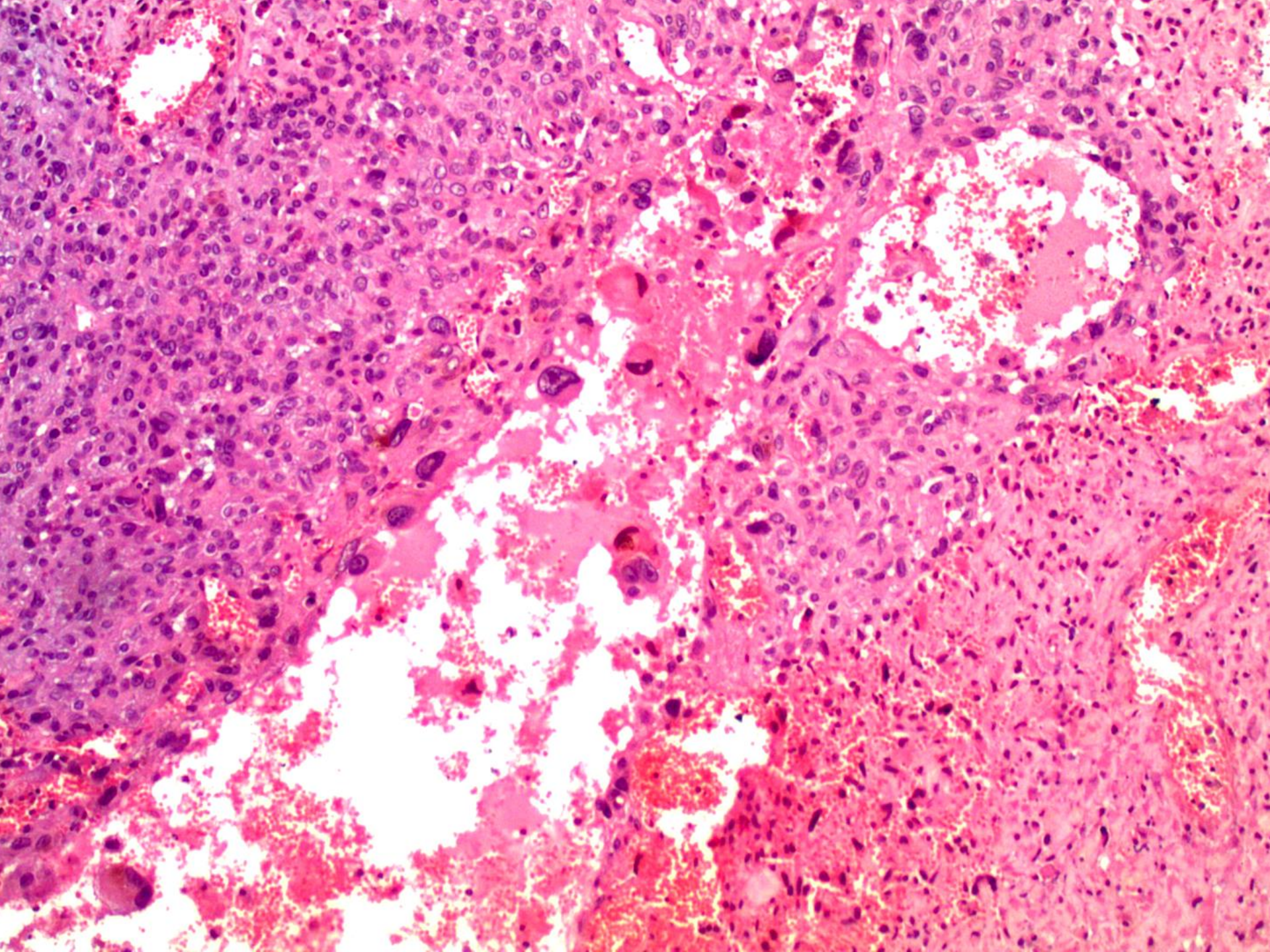


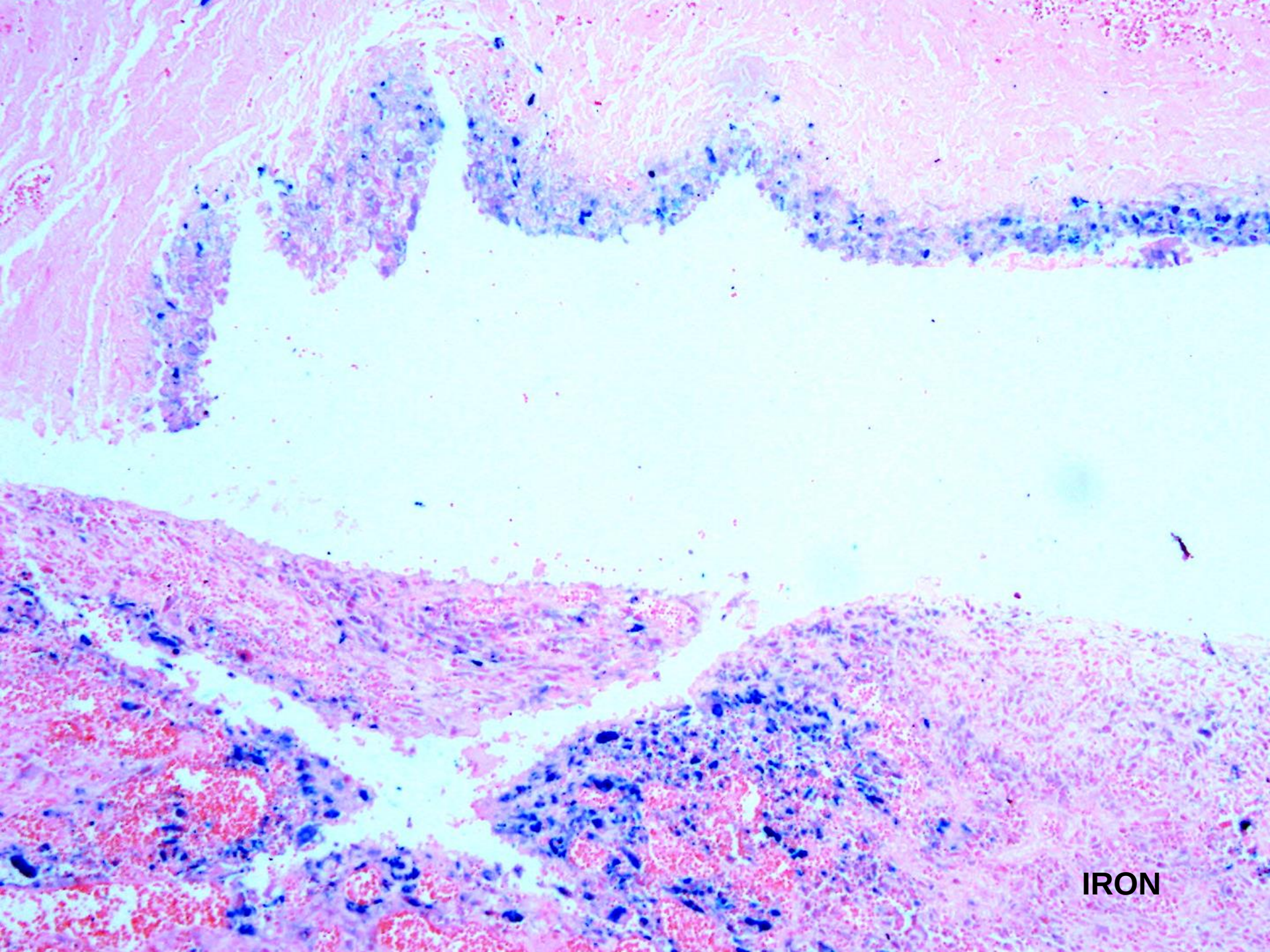

Sagittal
Ex: 7310
S 171
ansh arya
STAR IMAGING
cut
Se:3
L: 2.19
Ex:Nov 04 2014
DFOV 23.9 cm
No Filter
A
115
P
124
0.49
351/2
0.6mm /0.62sp
10:43:33 AM
I 68
Axial
Ex: 7310
A 107
ansh arya
STAR IMAGING
cut
Se:3
S: 30.44
Im: 88
Ex:Nov 04 2014
DFOV 19.9 cm
SOFT/SS40 No Filter
R
98
L
101
351/3
0.63
kV 140
mA 300
Rot 1.00s
0.6mm /0.62sp
Tilt: 0.0
10:43:33 AM
P 92

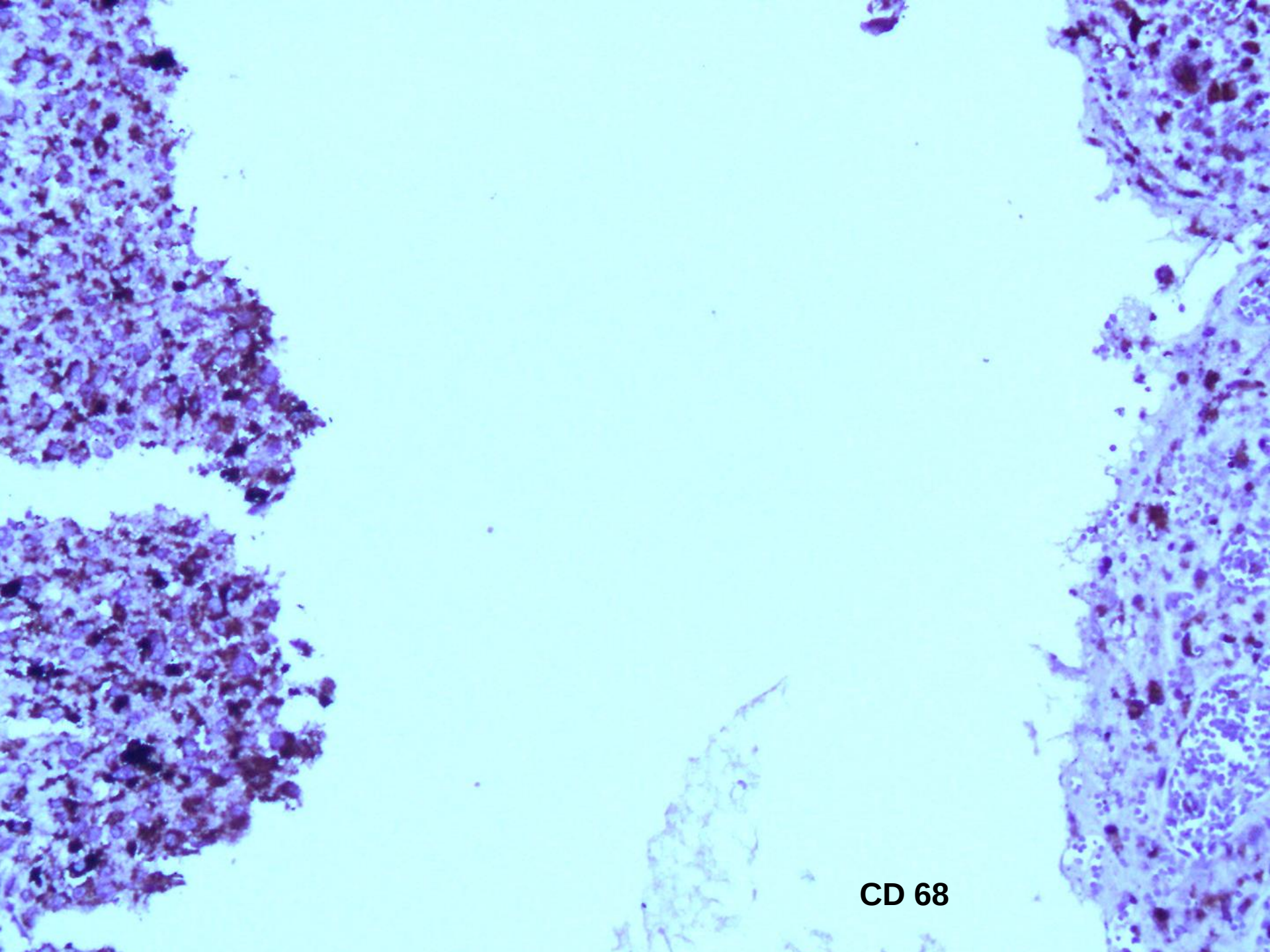

Sc 7
TSE/M
SI 9
H
P
5 cm
Sc 7
TSE/M
SI 10
H
P
5 cm

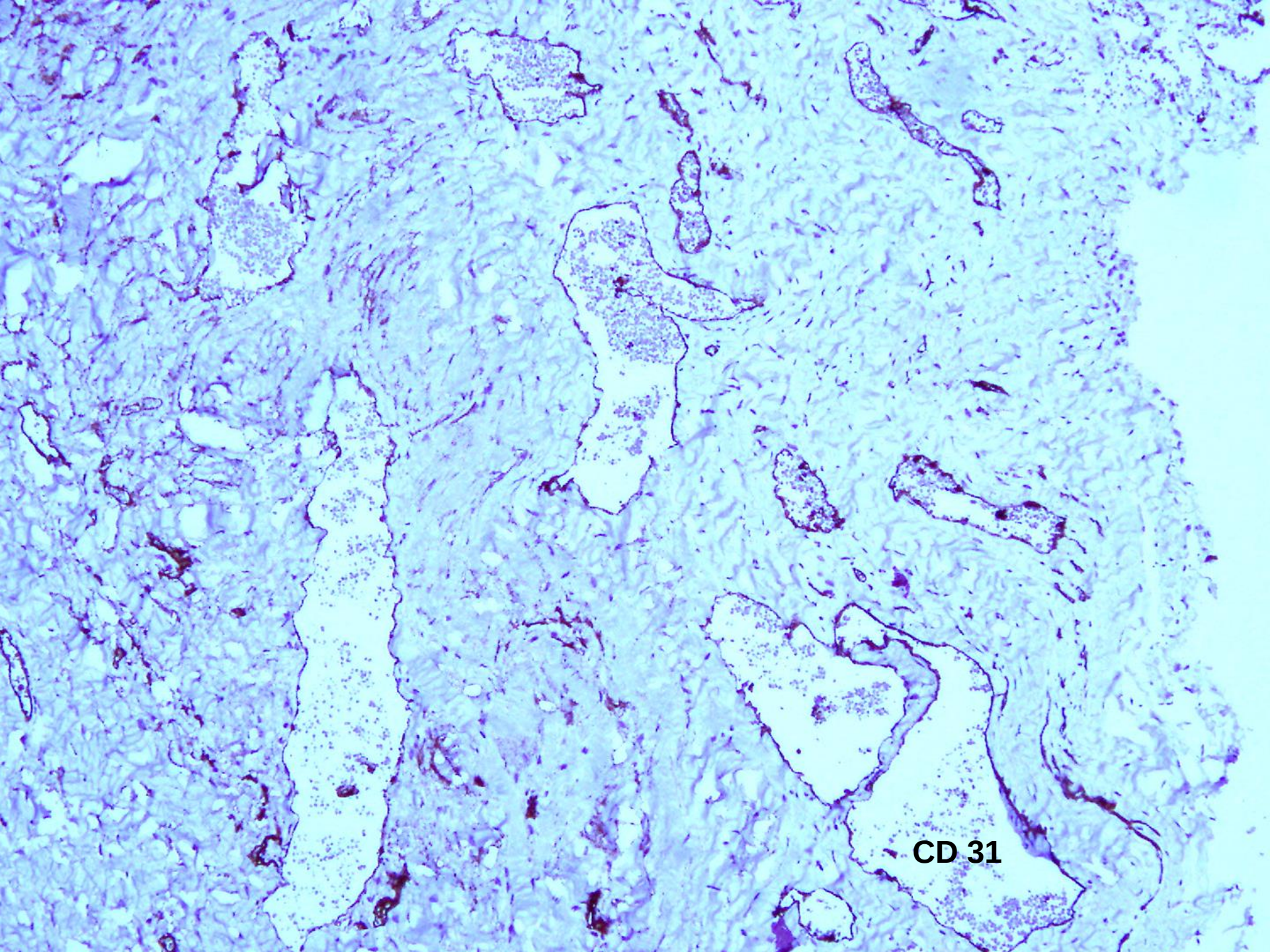
The **excised specimen** was an irregular, collapsed cystic tissue measuring 4X3 cm. The outer surface was unevenly rough. On cutting open it was mostly cystic with small amount of blood and a darkly congested inner lining. The wall varied from 0.5 to 0.7 cm. in thickness. Some thick fibrous strands were also present.






IRON


CD 68


CD 31

STAINS:

Iron stain - +ve intra- and extracellular

CD 68 - +ve in many mononuclear and some giant cells

CD 31 - +ve in vascular walls & patchily in aneurysmal spaces

-ve in cellular areas

Ki 67 - +ve only in few cells (approximately 2%)

SMA - +ve in several mononuclear cells

Multiple sections taken later revealed only two focal areas of fibromyxoid stroma with osteoid-like material but no calcified woven or lamellar bone was encountered.

DIAGNOSIS:

Consistent with **Aneurysmal bone cyst, soft tissue.**

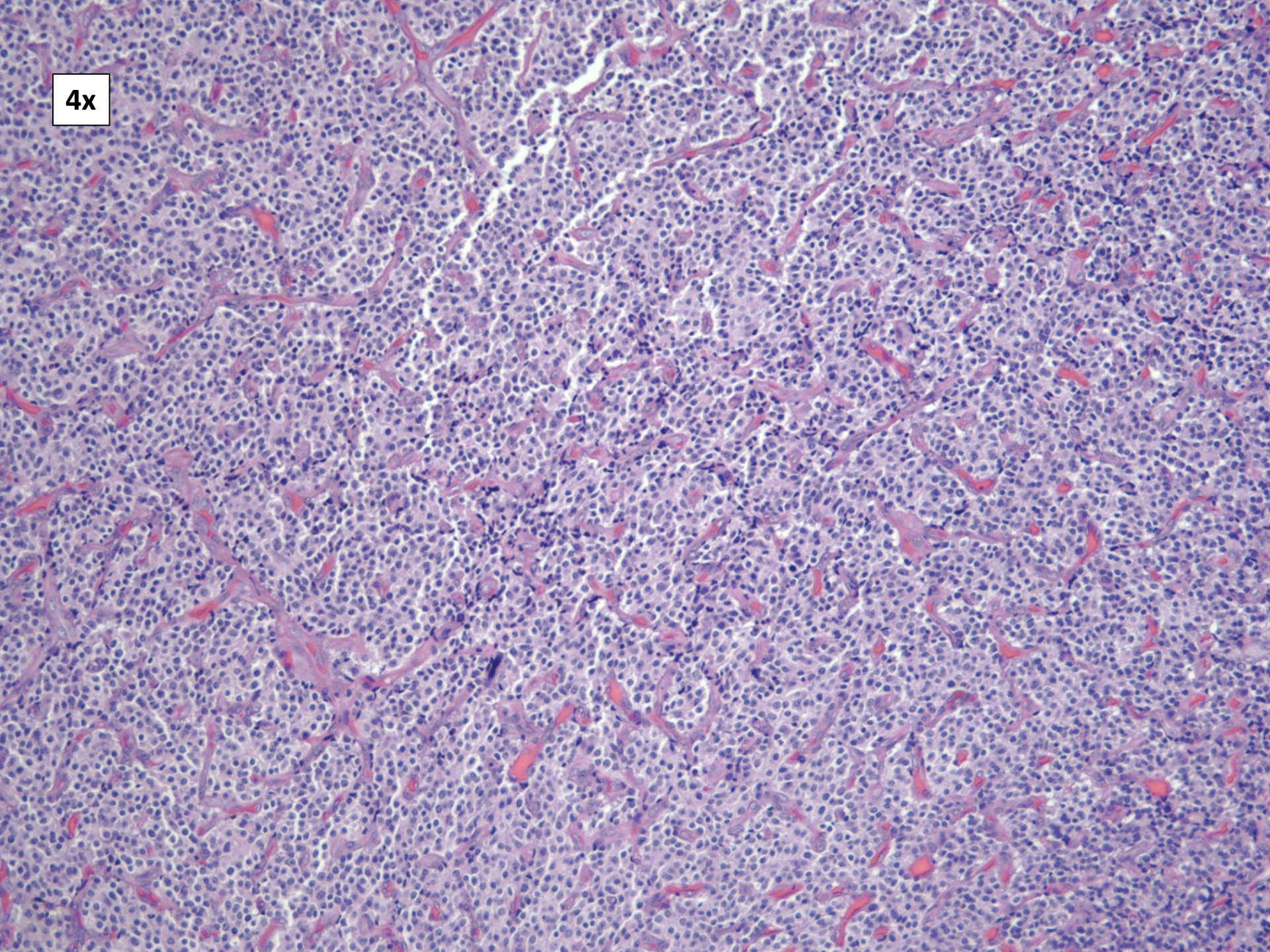
FOLLOW-UP:

A close follow-up was recommended.

Currently, 9 months after surgery the patient is normal and well. There has been no recurrence of the lesion.

SB 5970
Josh Segal/Hannes Vogel; Stanford

57-year-old man who presented with worsening headaches, ataxia, and weakness. Imaging revealed a 7 x 5 cm heterogeneously enhancing right temporoparietal intra-axial and extra-axial solid tumor with compression of midbrain and compression of the temporal horn of the temporal ventricular system.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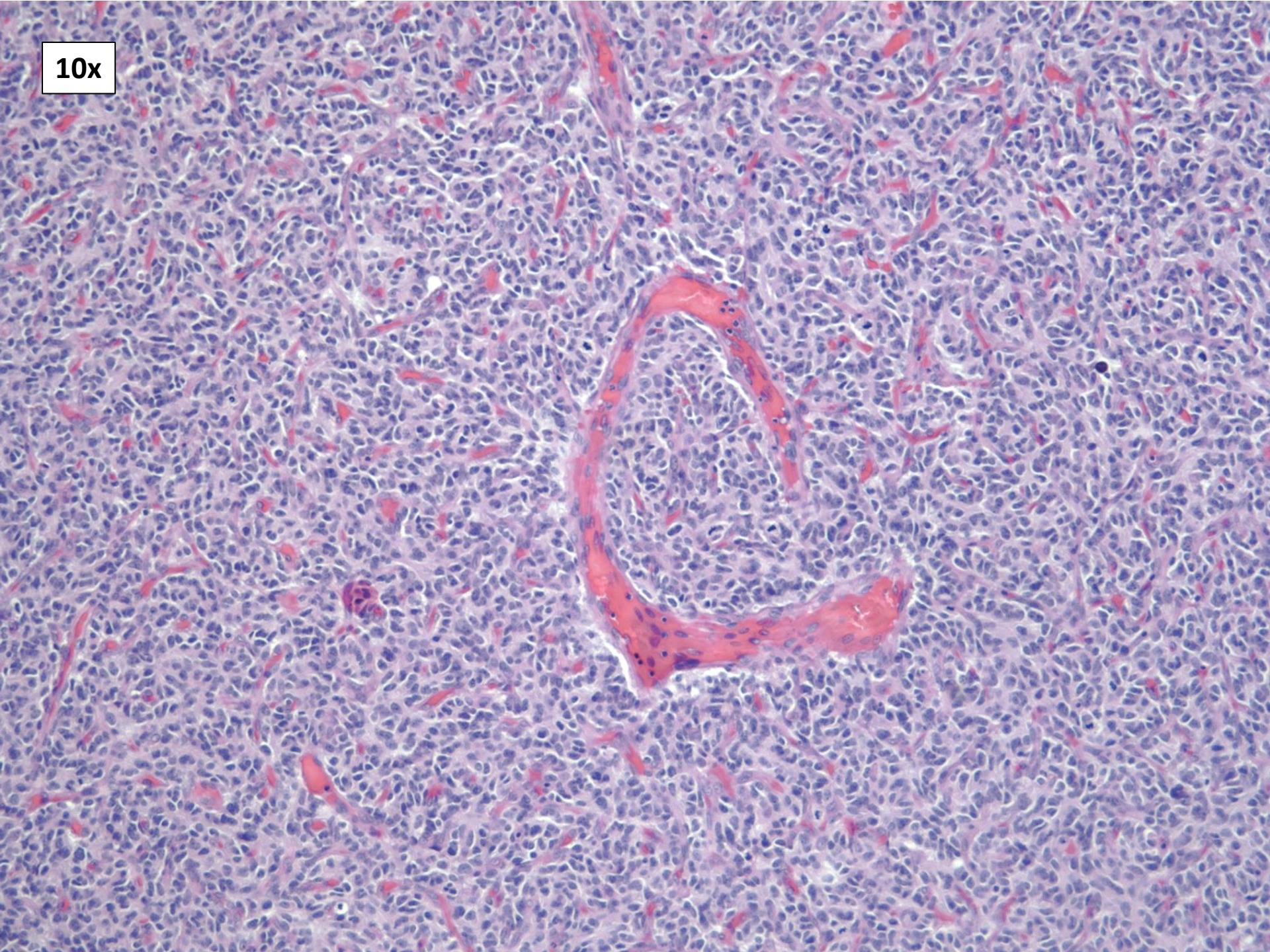
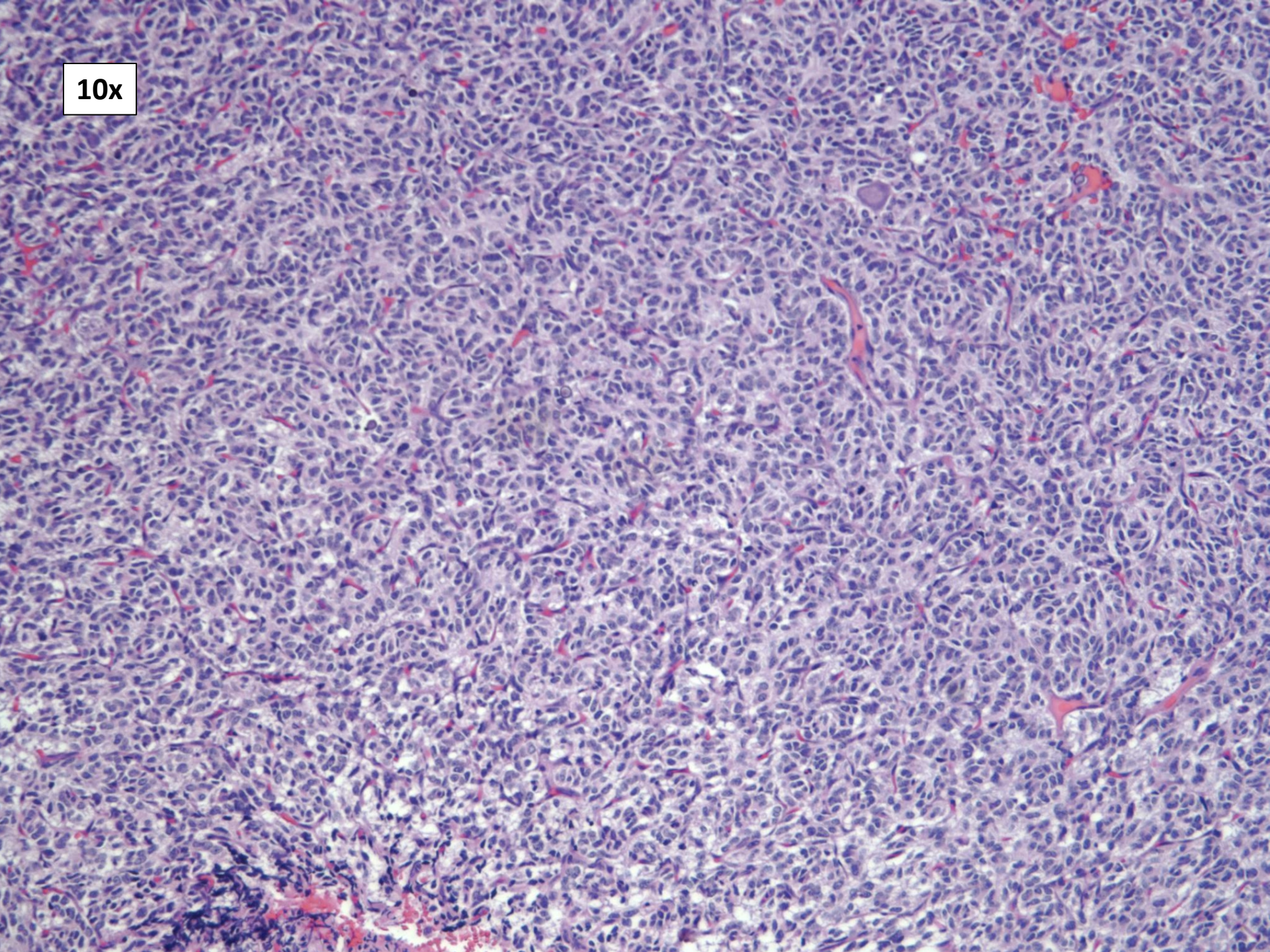

10x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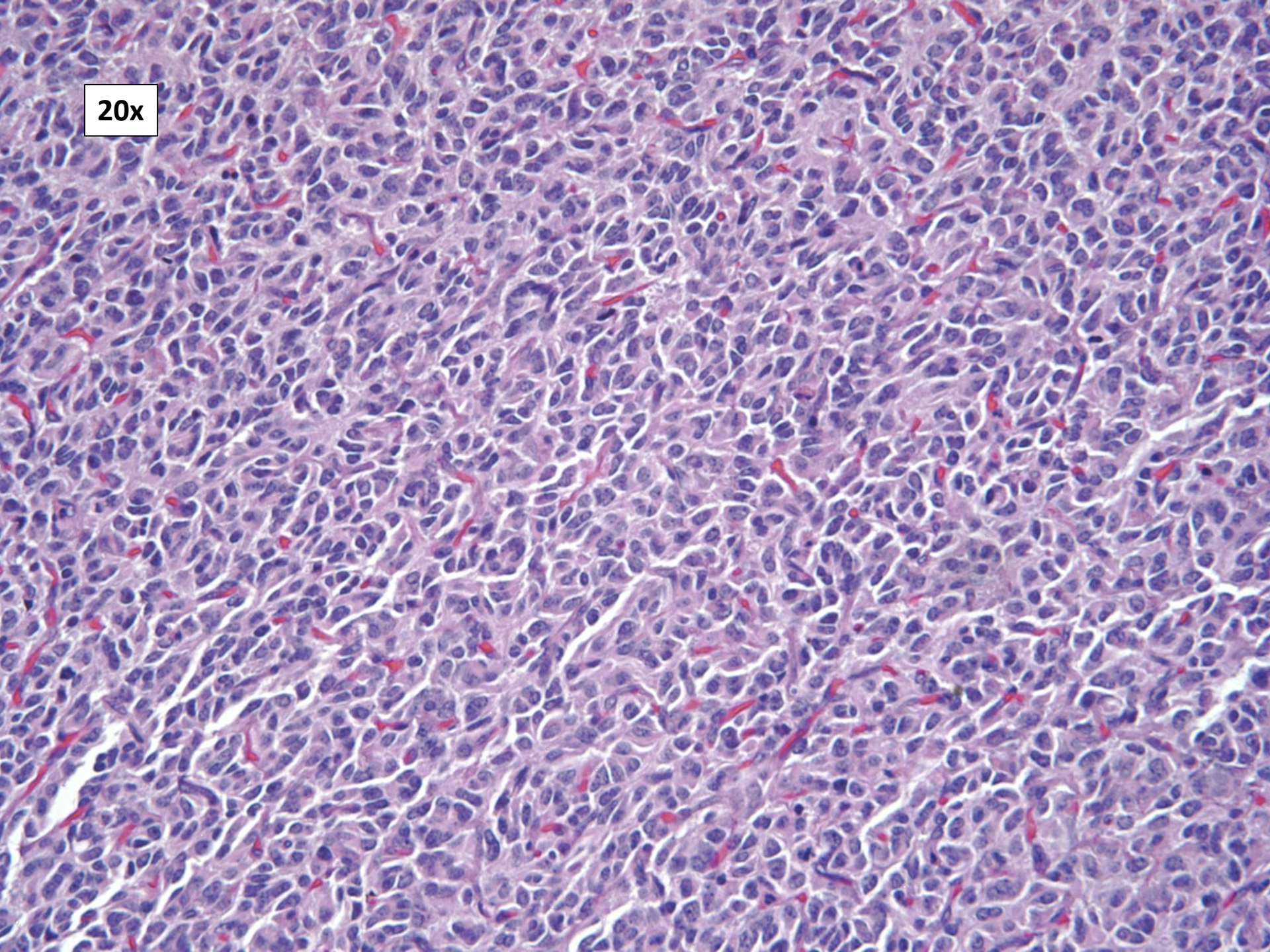
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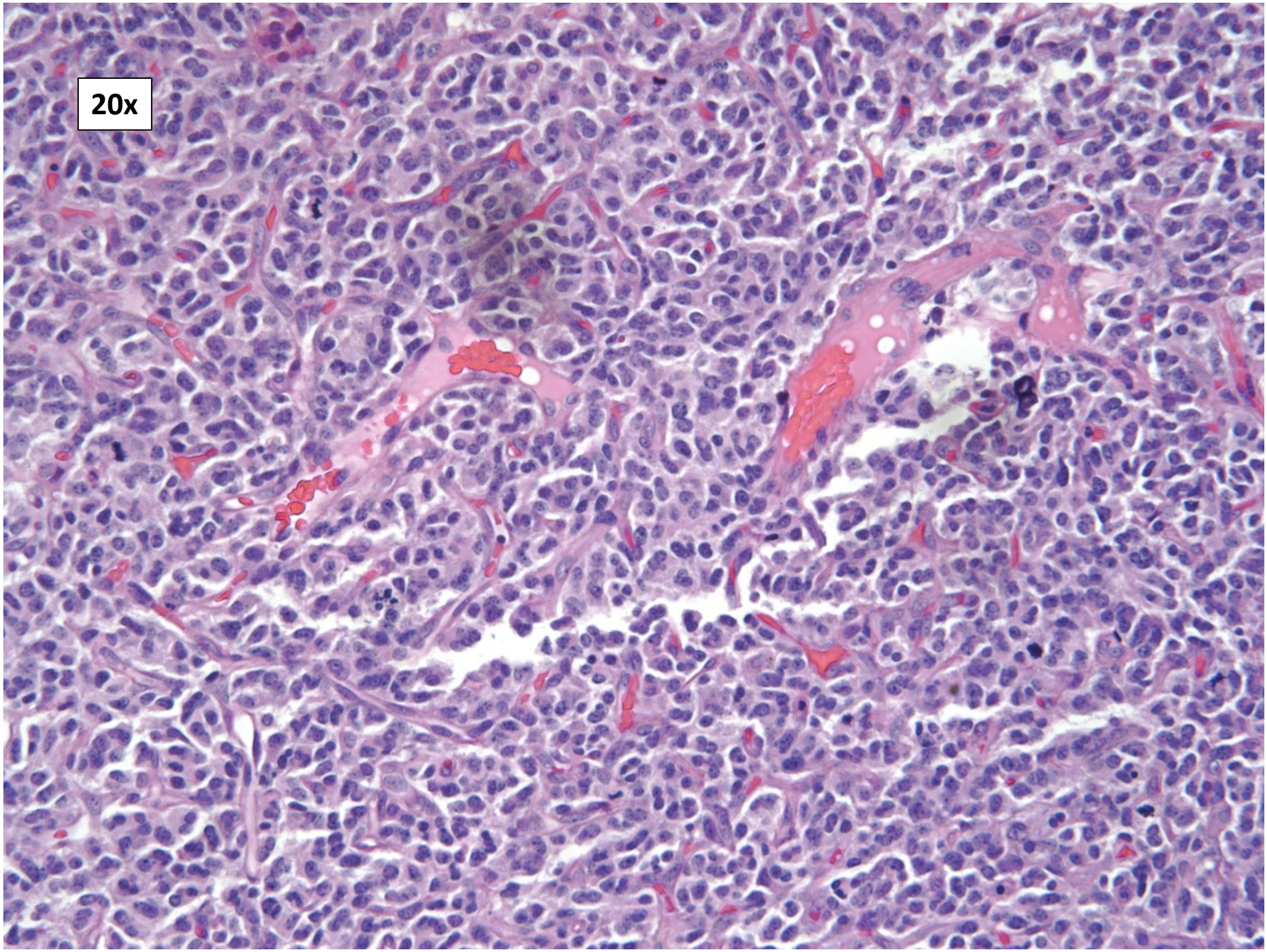
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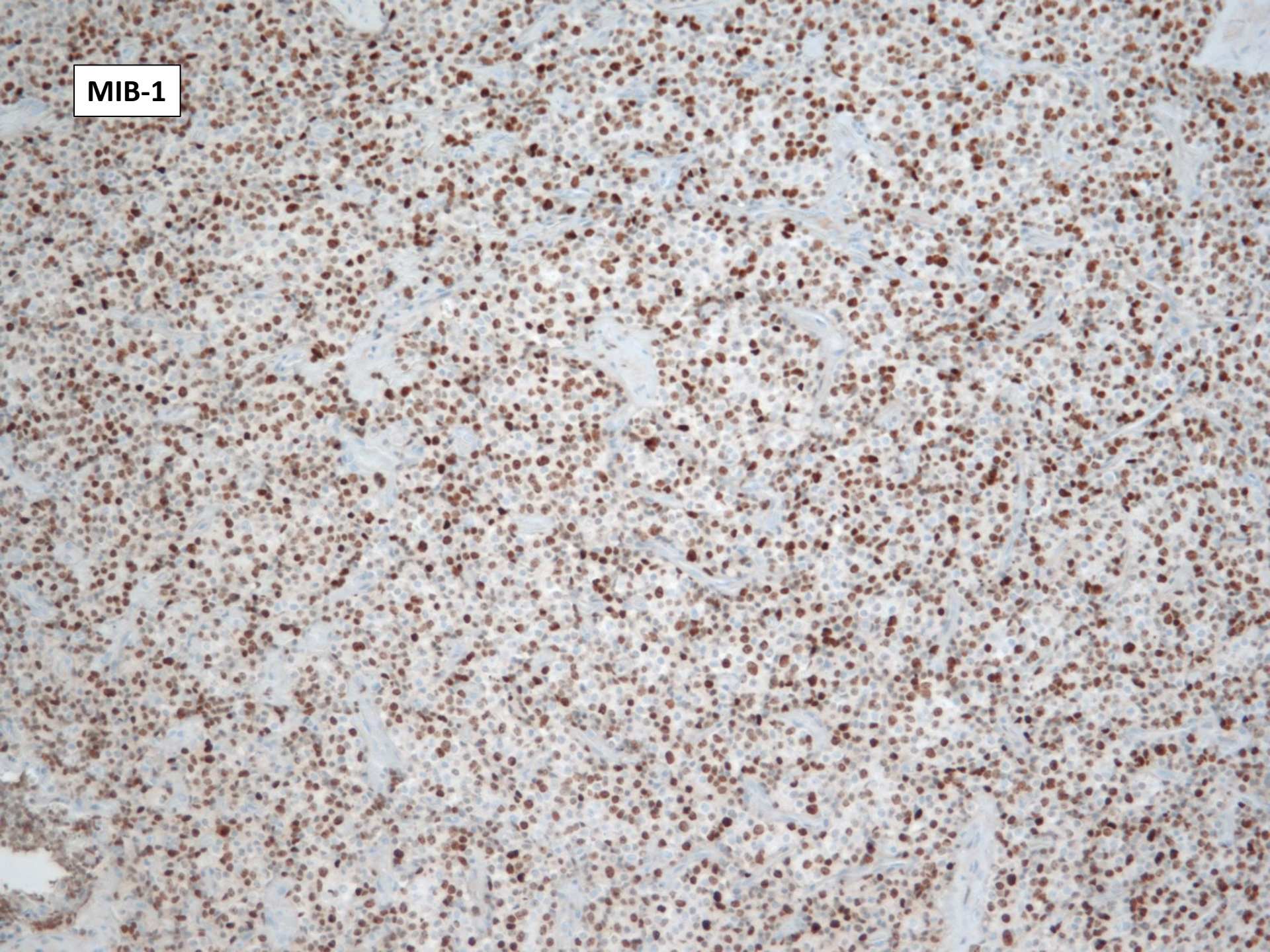
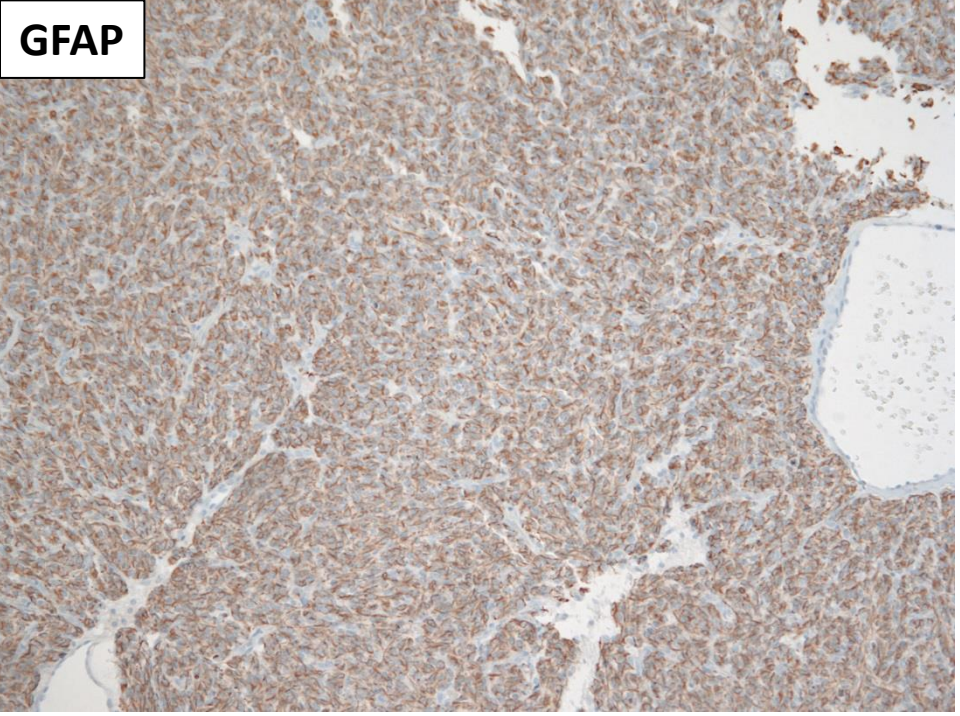
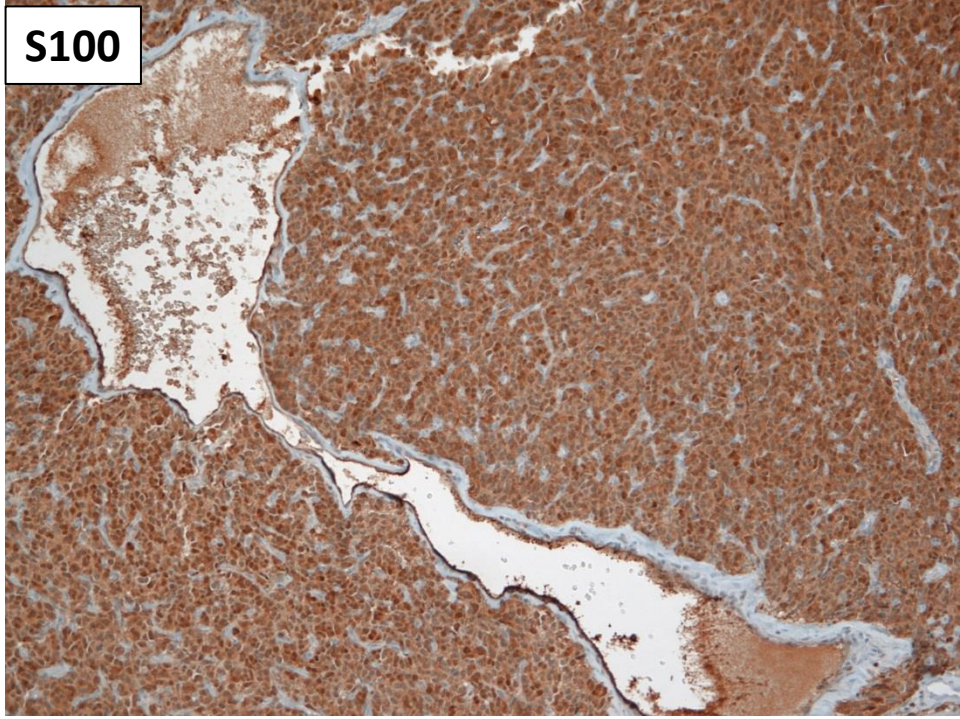
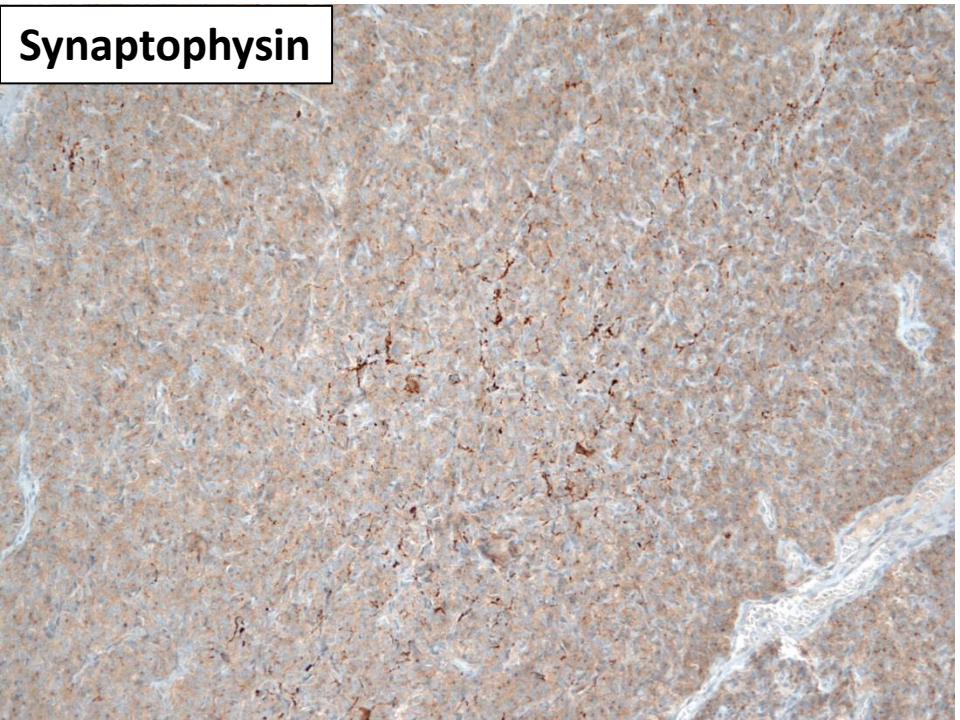
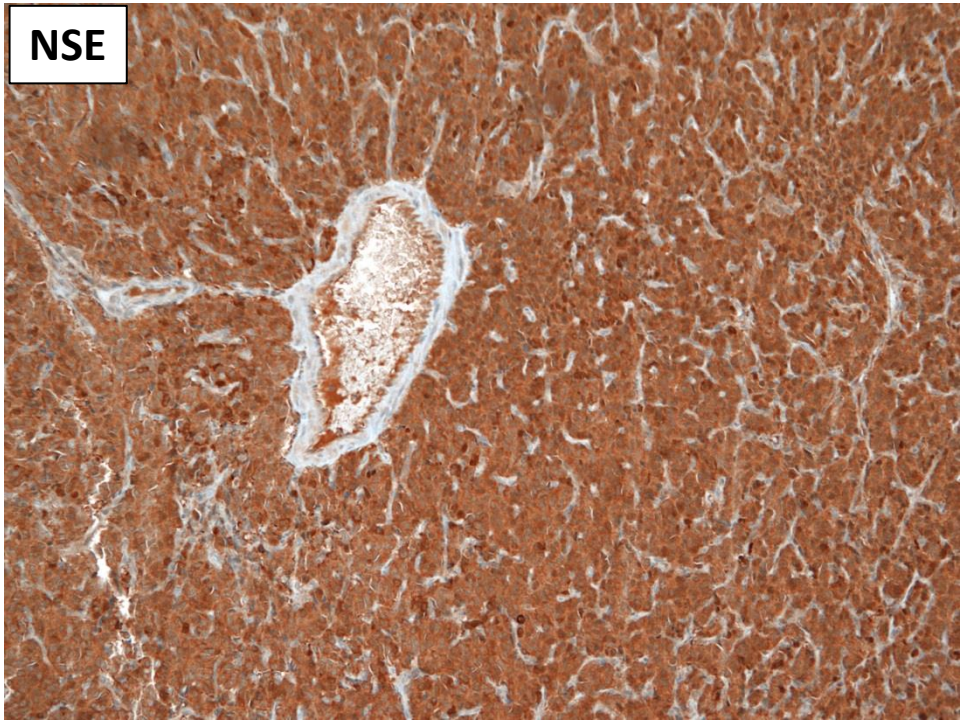

MIB-1


GFAP


S100


Synaptophysin


NSE

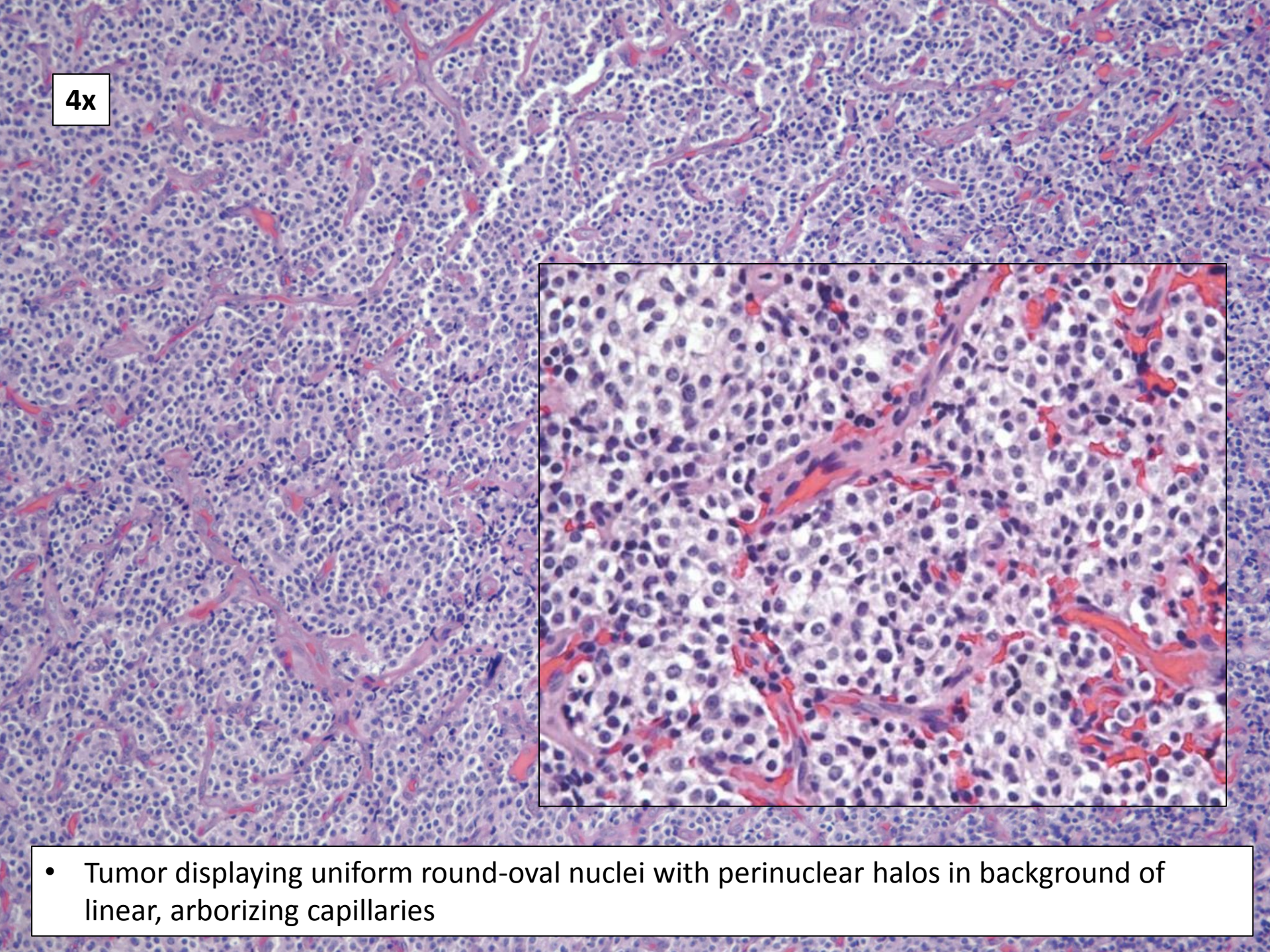
Ancillary Studies

- By report, 1p19q co-deletion was identified by fluorescence in situ hybridization studies (Knight Diagnostic Laboratories)

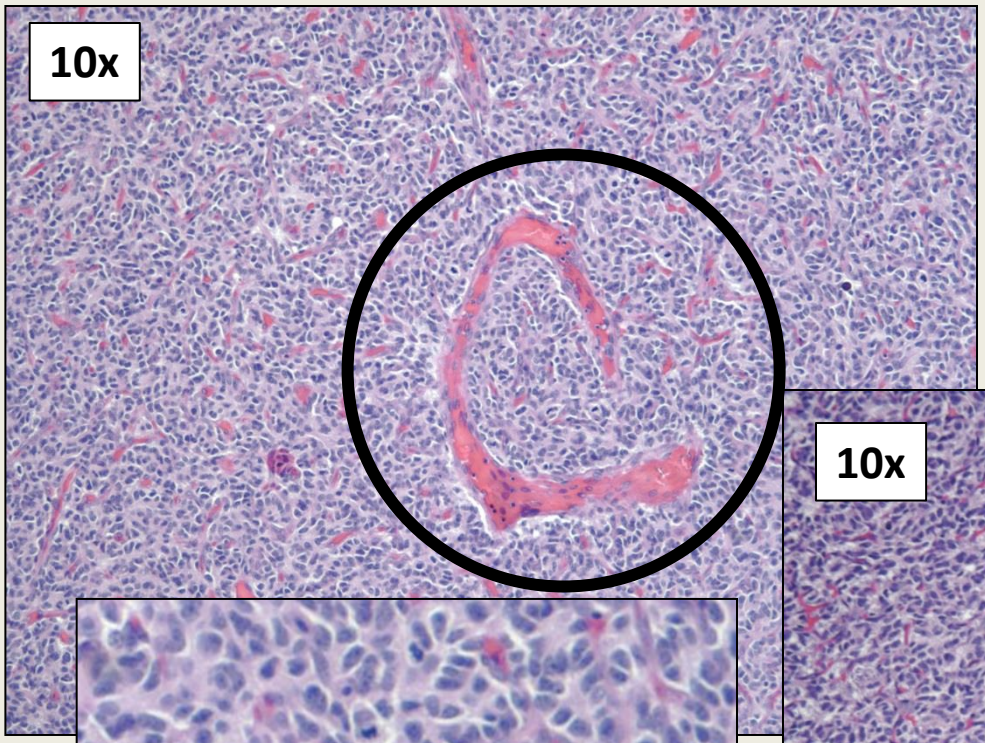
Clinical History

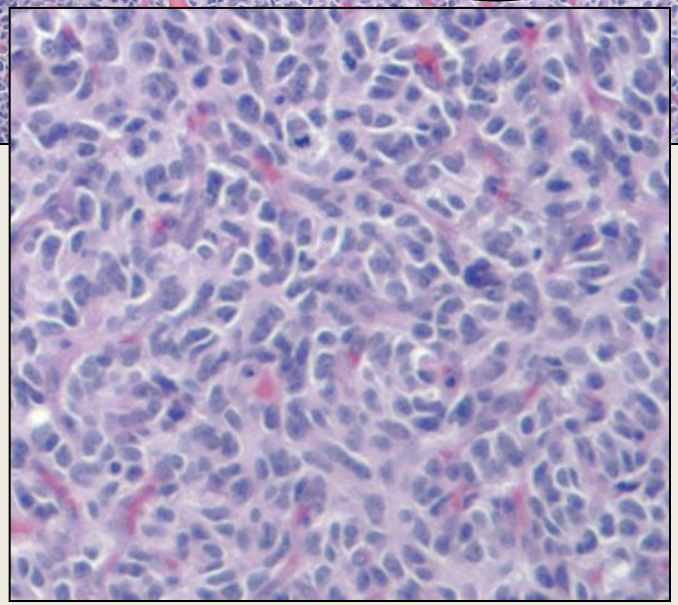
- The patient is a **57-year-old male** who presented with worsening headaches, ataxia, and weakness
  - Imaging revealed a **7 x 5 cm heterogeneously enhancing solid mass** within the right lateral ventricle, extending from the body of the ventricle into the atrium and occipital horn

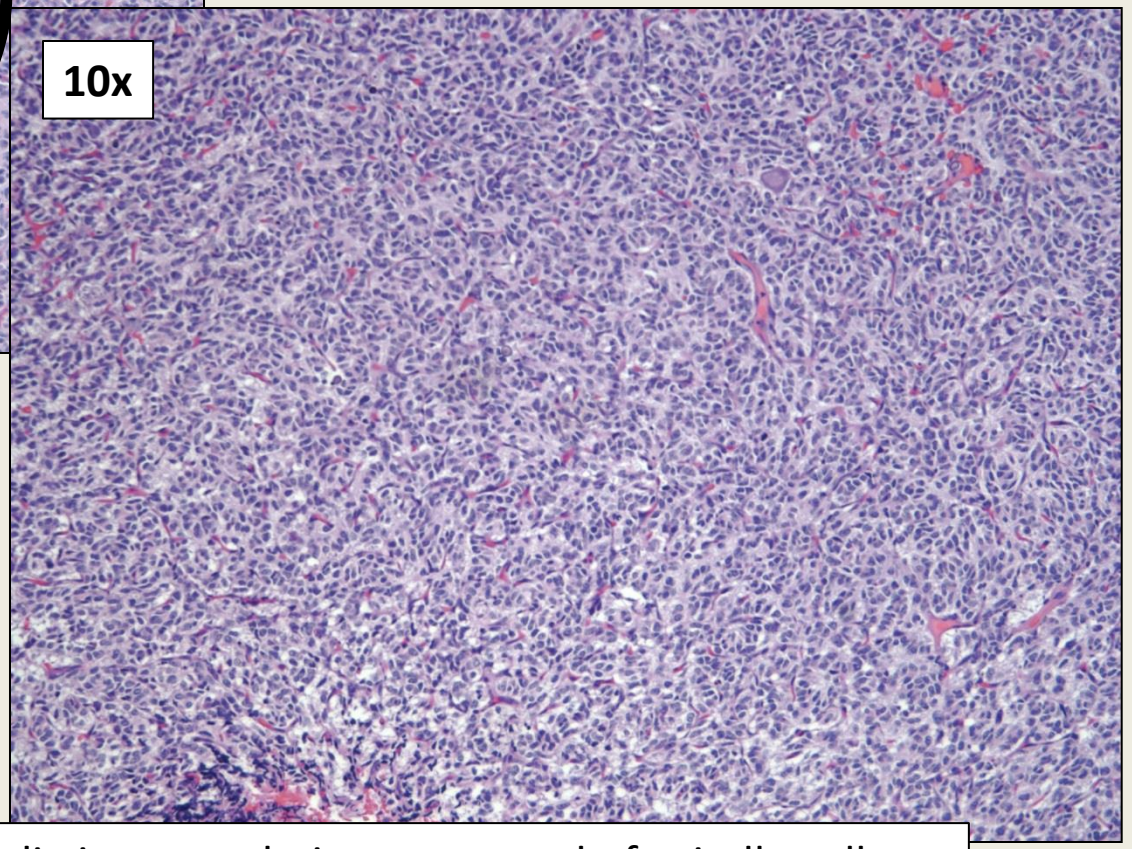
- An **intraventricular brain biopsy** was performed



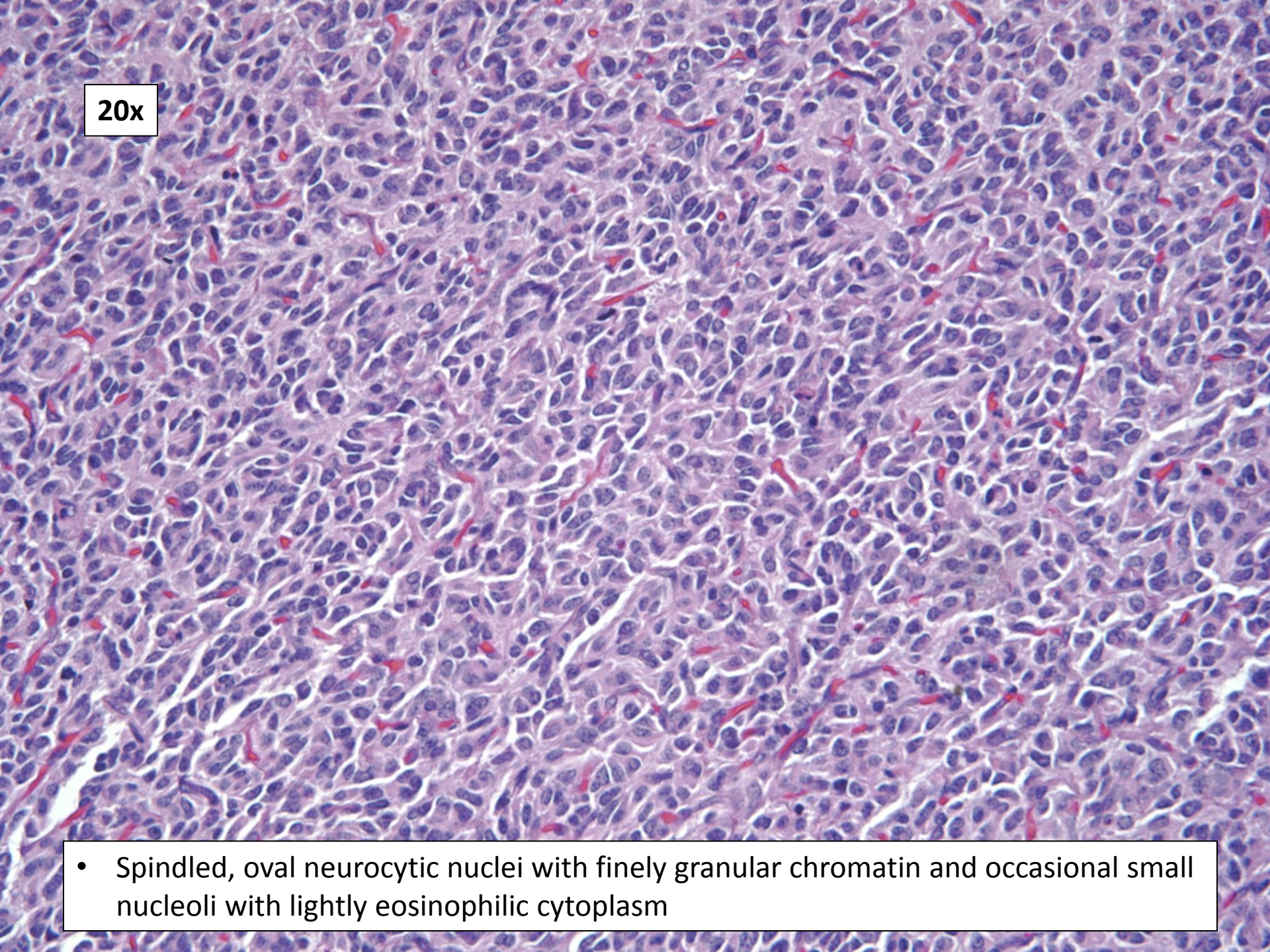
- Tumor displaying uniform round-oval nuclei with perinuclear halos in background of linear, arborizing capillaries



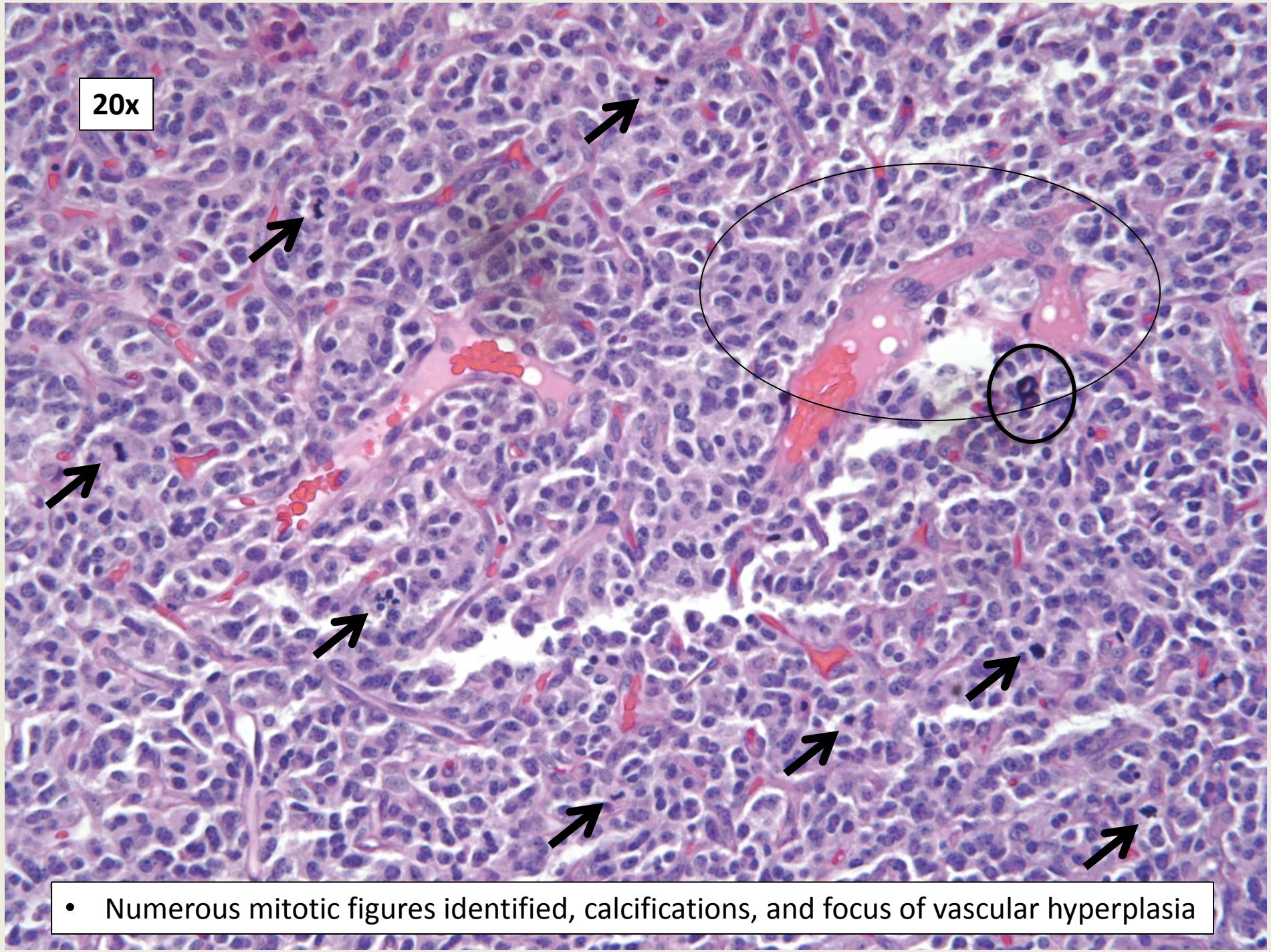




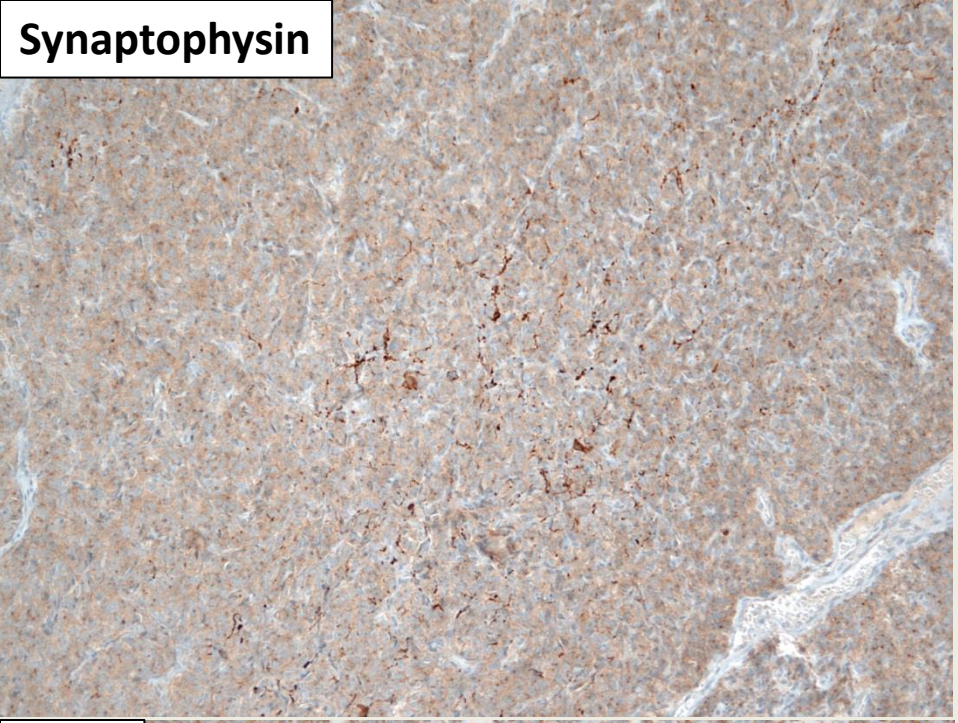
- Second morphologically distinct population composed of spindle cells with multinucleated forms and prominent mitotic figures and vascular hyperplasia

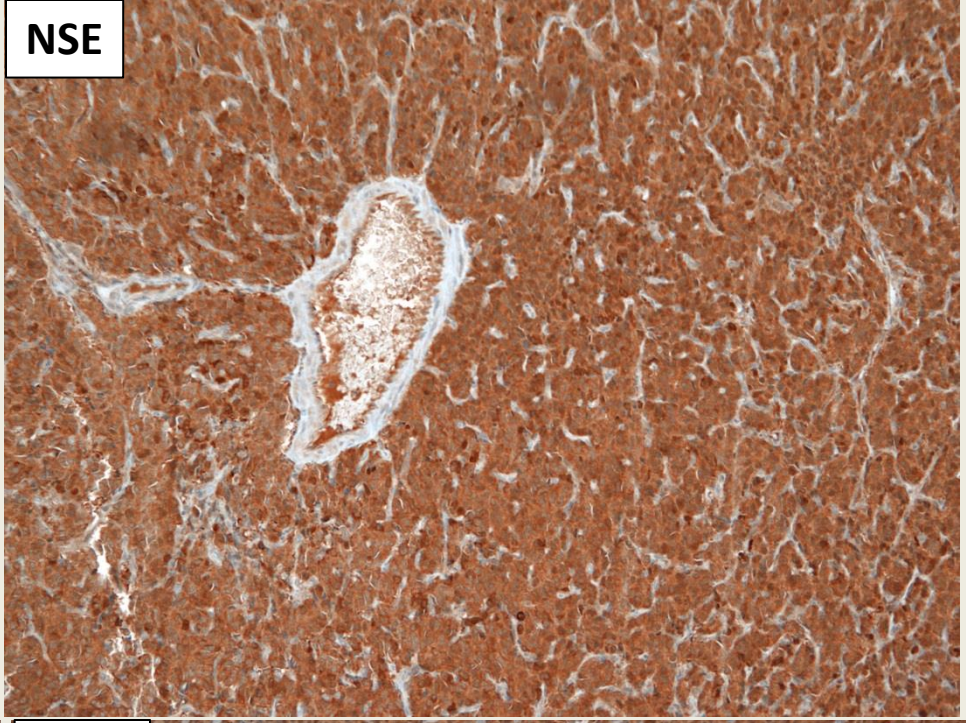


- Spindled, oval neurocytic nuclei with finely granular chromatin and occasional small nucleoli with lightly eosinophilic cytoplasm



- Numerous mitotic figures identified, calcifications, and focus of vascular hyperplasia


Synaptophysin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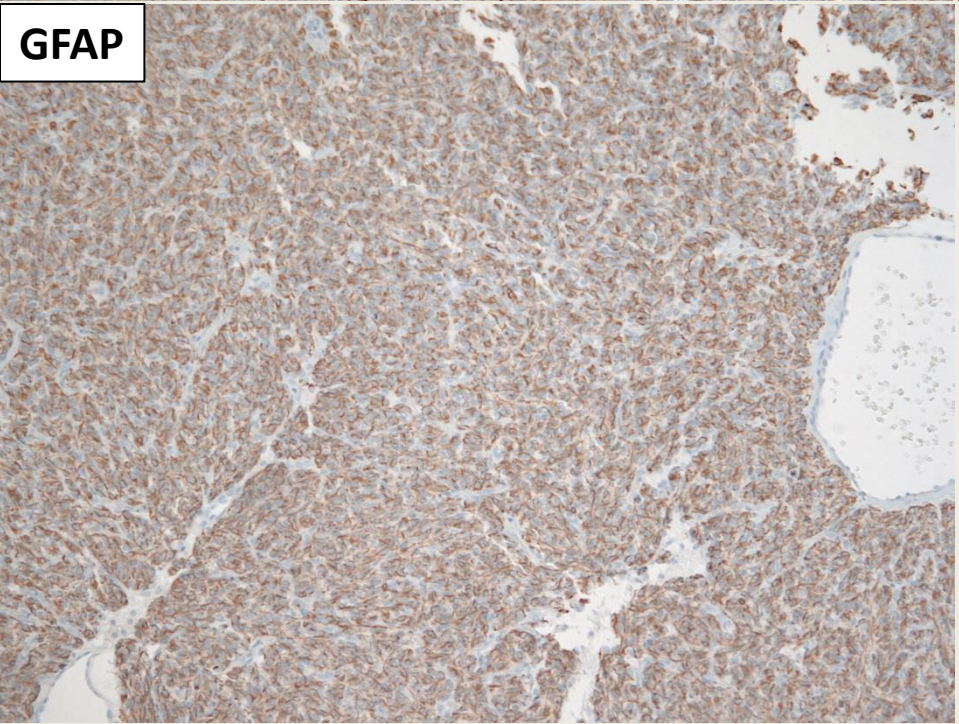
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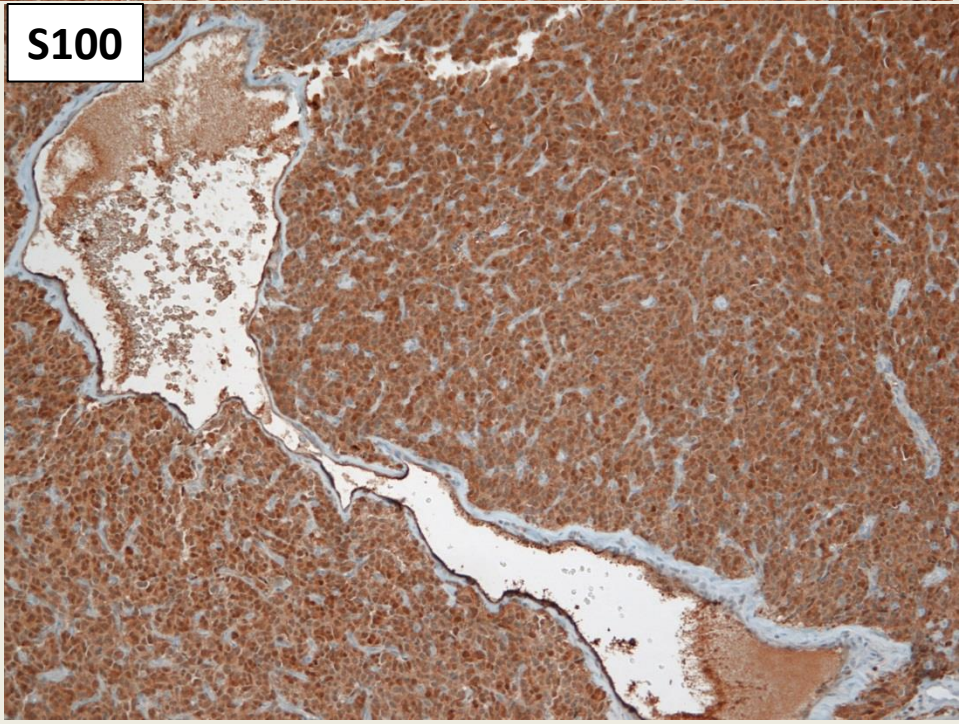
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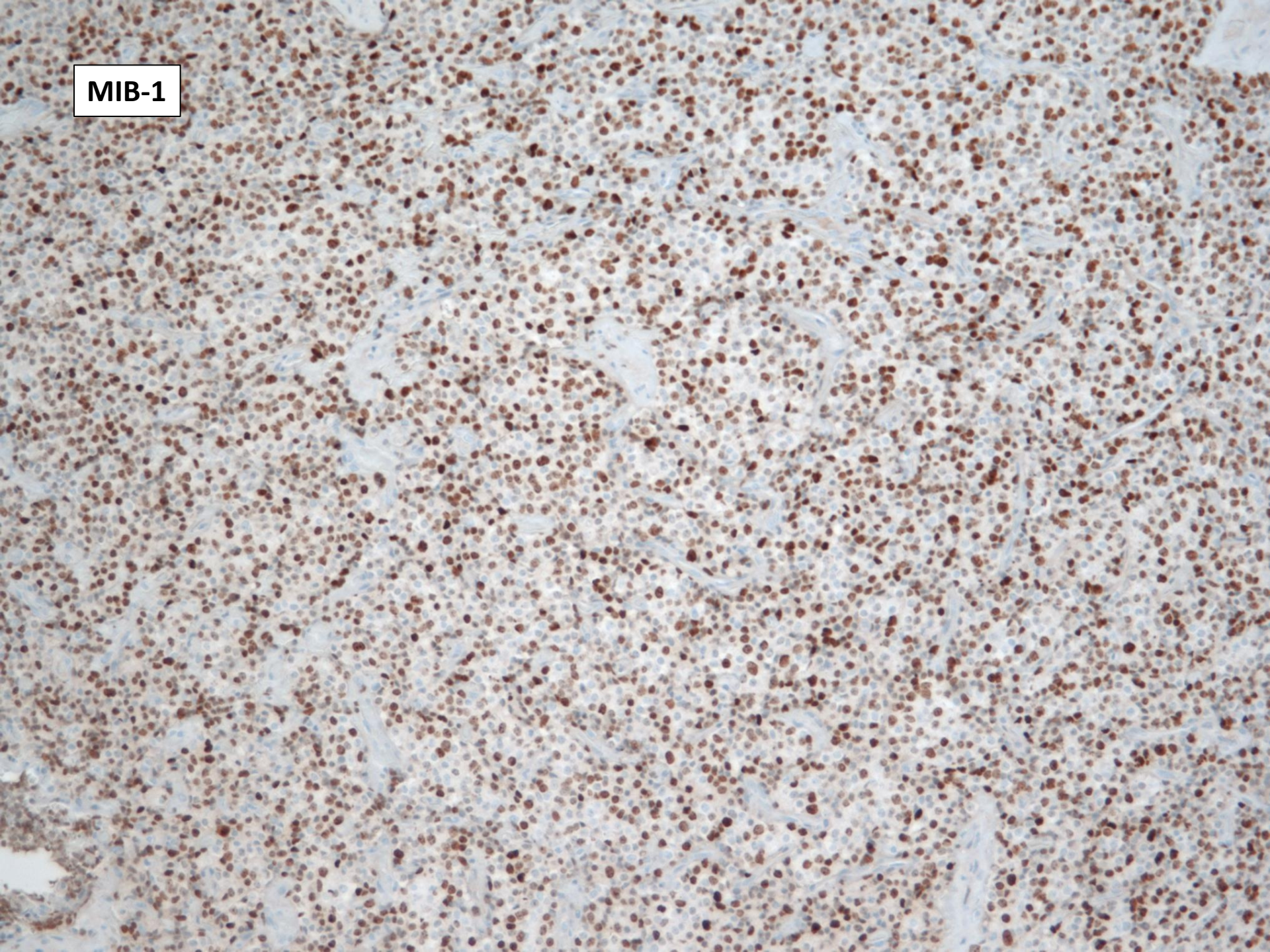

MIB-1

IHC Studies

- Lesional cells **positive** for **synpatophysin**, **neuron specific enolase**, S100, GFAP, CD56, and EMA
- Chromogranin equivocal
- MIB-1 (Ki67) immunostaining reveals **high proliferative index**
- Tumor cells **negative** for CD34, vimentin, desmin, actin, pancytokeratin, HMB45, Melan-A, CK7, TTF1, IDH1, and NeuN

Ancillary Studies

- By report, 1p19q co-deletion was identified by fluorescence in situ hybridization studies (Knight Diagnostic Laboratories)

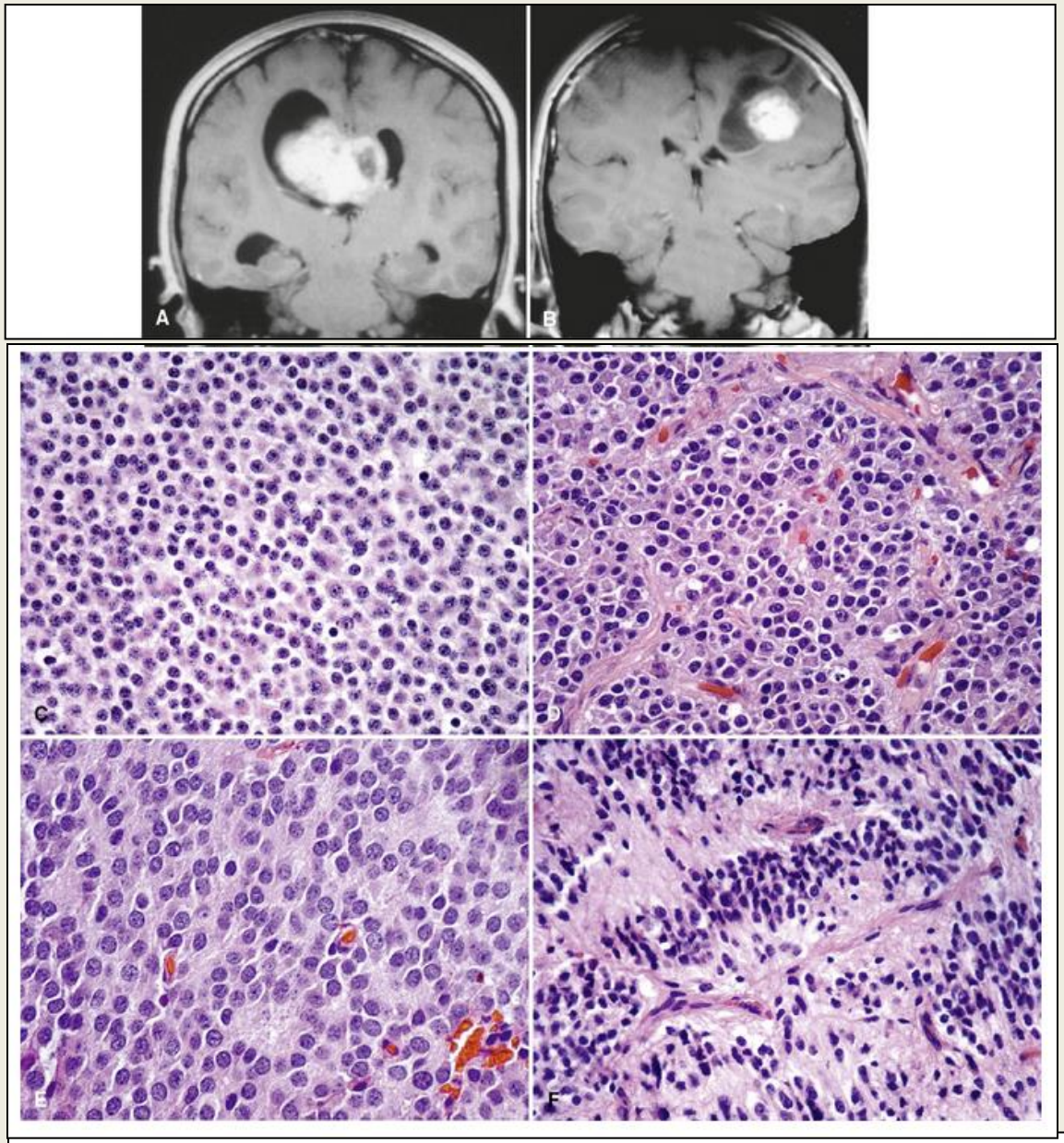
Central Neurocytoma (CN) – primary WHO grade II neoplasm of the CNS

- Well-demarcated, supratentorial, **intraventricular** neuronal tumors arising in the septum pellucidum and projecting into lateral ventricles, often in region **of foramen of Monro**
  - p/w signs of increased intracranial pressure 2/2 **obstructive hydrocephalus**

- CNs thought to **originate from mature neuronal cells** because of ultrastructural neuron-specific features like microtubules, neurofilaments, and synaptic junctions
  - Variably express both neuronal and glial markers on IHC study

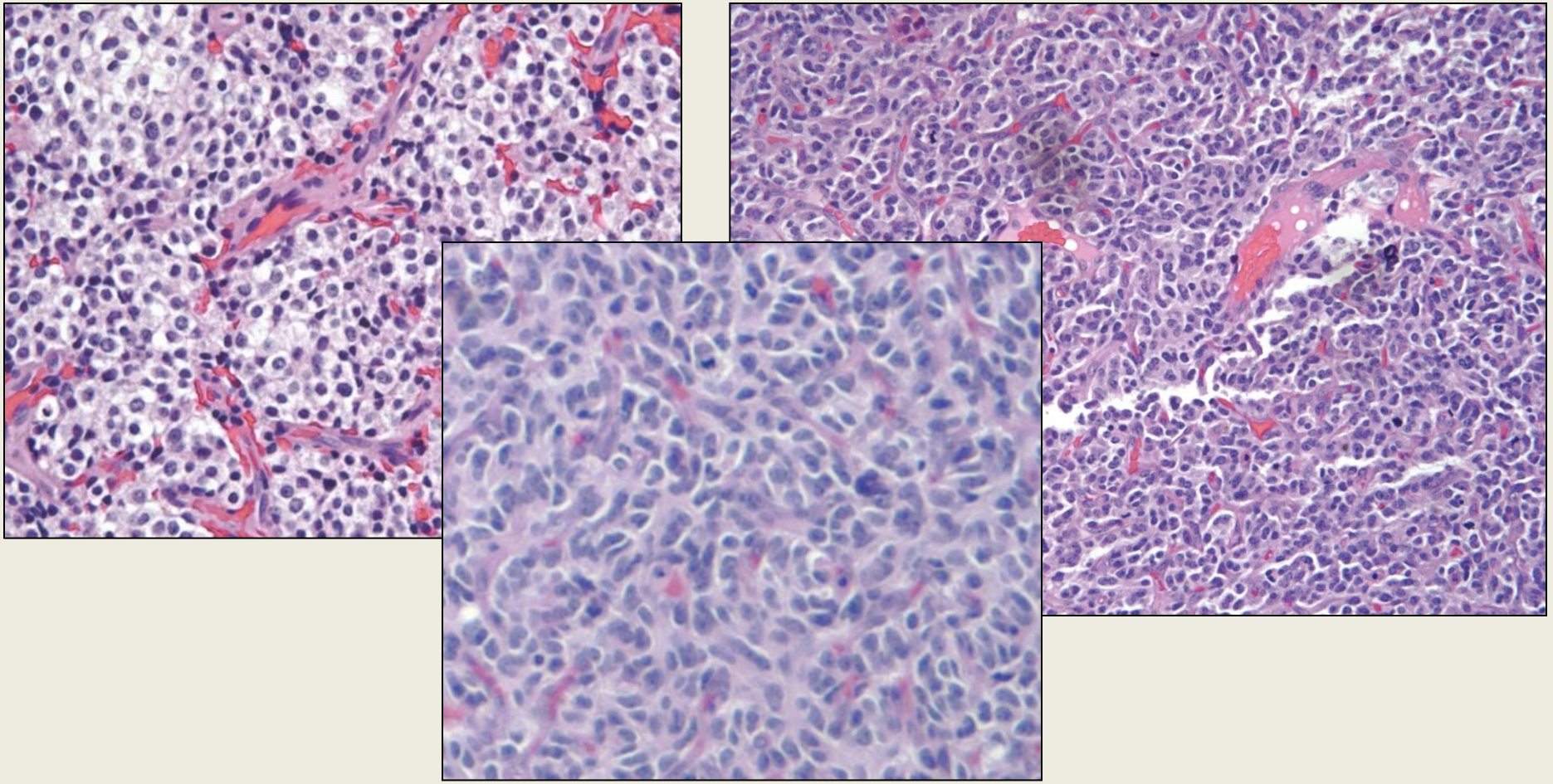
- Histologically similar tumors arising at other sites within brain parenchyma referred to as **extraventricular neurocytomas (EVN)**

CN - Radiologic Features and Histologic Appearance



- **Neuroimaging** demonstrates large, discrete intraventricular solitary lobulated mass
  - **Calcifications** often seen and micro- and macrocysts may give tumor **heterogeneous** appearance
- Histologically, densely packed small-medium sized round cells with scant eosinophilic cytoplasm present in sheets or clusters
  - Delicate **neuropil** background
- Round-oval cells with **perinuclear halos** imparts a “fried-egg” appearance
  - Mimic **oligodendroglioma** or clear cell **ependymoma**
- Rosettes (perivascular and neurocytic) may be seen

Perry, A., & Brat, D. J. (2010). *Practical surgical neuropathology: A diagnostic approach*. Philadelphia, PA: Churchill Livingstone/Elsevier.



- Unusual differentiation has been recorded
  - CN with lipomatous areas, melanocytic cells, rhabdomyomatous cells, spindle cell sarcoma like
- **EVN** exhibit wider morphologic spectrum with regard to cellularity and proliferation rates

Vemavarapu et al., Atypical central neurocytoma with sarcomatous differentiation. Arch Pathol Lab Med. 2014 Sep;138(9):1233-7.

Immunohistochemistry

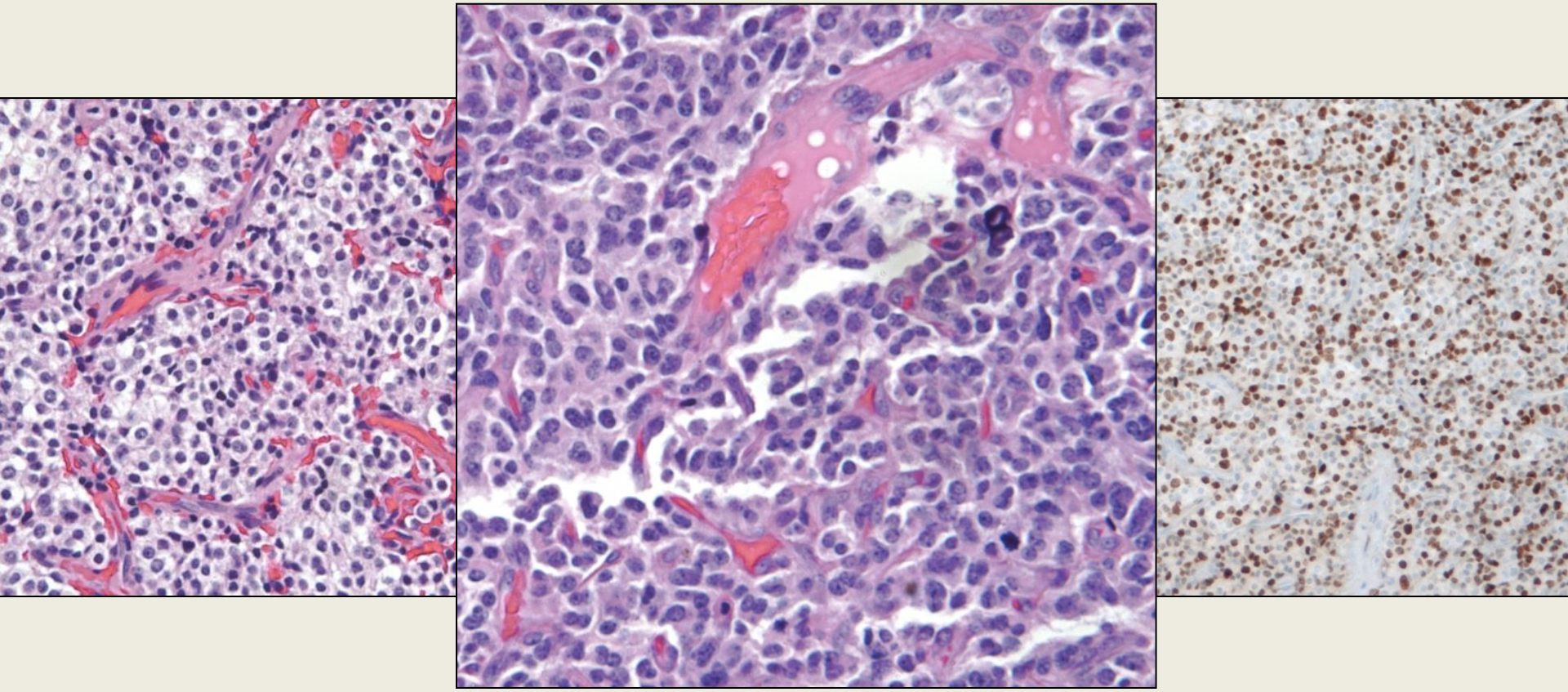
- Synaptophysin positive neurocytes and neuropil
- Neu-N variably positive
- Chromogranin-A negative except when ganglion-cell like morphology is present

- GFAP detected by some authors
  - May indicate bipotential cell of germinal matrix origin

Histologic Variants and Grading

- Most patients with CN have favorable clinical outcome
- Several studies noted that CNs with **brisk mitotic activity**, **microvascular proliferation**, and **necrosis** were indicative of aggressive behavior
  - **MIB-1** proliferation index has prognostic significance
- CN with MIB-1 index >3% show **higher rates of recurrence** and **tumor-related deaths**
- **Atypical central neurocytoma** – diagnosis for tumors with increased mitotic activity, vascular proliferation, and necrosis
  - Lower survival and worse local control at 5 years, compared to typical CN

DIAGNOSIS



- BRAIN, INTRAVENTRICULAR, EXCISION
  - ATYPICAL CENTRAL NEUROCYTOMA (SEE COMMENT)

Genetics

- Though there is histomorphologic similarity between **oligodendroglioma** and **CN**, the characteristic **1p/19q** codeletion seen in oligodendroglioma has not been shown to be associated with CN
  - rare examples of **EVN** have shown 1p/19q codeletion

- 1p19q co-deletion in oligodendrogliomas confers an **overall better prognosis** with better response to treatment
  - studies have shown that **EVNs associated with 1p19q loss may have increased risk for recurrence** and less favorable behavior

- There may be greater **overlap between oligodendrogliomas and neurocytoma** than previously thought
  - Whether these represent oligodendrogliomas with extensive neurocytic differentiation requires further study

Rodriguez FJ, Mota RA, Scheithauer BW, Giannini C, Blair H, New KC, Wu KJ, Dickson DW, Jenkins RB. Interphase cytogenetics for 1p19q and t(1;19)(q10;p10) may distinguish prognostically relevant subgroups in extraventricular neurocytoma. Brain Pathol. 2009 Oct;19(4):623-9.

Treatment and Prognosis

- CNs are low grade tumors behaving as a WHO grade II neoplasm
  - Tumor recurrence has been reported mainly in cases that were subtotally resected

- Gross total resection associated with better local tumor control and longer patient survival than subtotal resection
  - Subtotal resection – conventional external beam radiation therapy or focused radiosurgery advocated

- Atypical CN with a MIB-1 proliferation index >3% → worse prognosis with shorter disease-free interval
  - addition of radiation therapy improves local tumor control especially in setting of incomplete resection