Disclosures
November 7, 2016

Dr. Keith Duncan has disclosed that he receives an hourly fee for slide review from Abbvie Biotherapeutics and Oxford Biotherapeutics. The planners have determined that this financial relationship is not relevant to the case being presented and does not present a conflict of interest.

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

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SB 6101

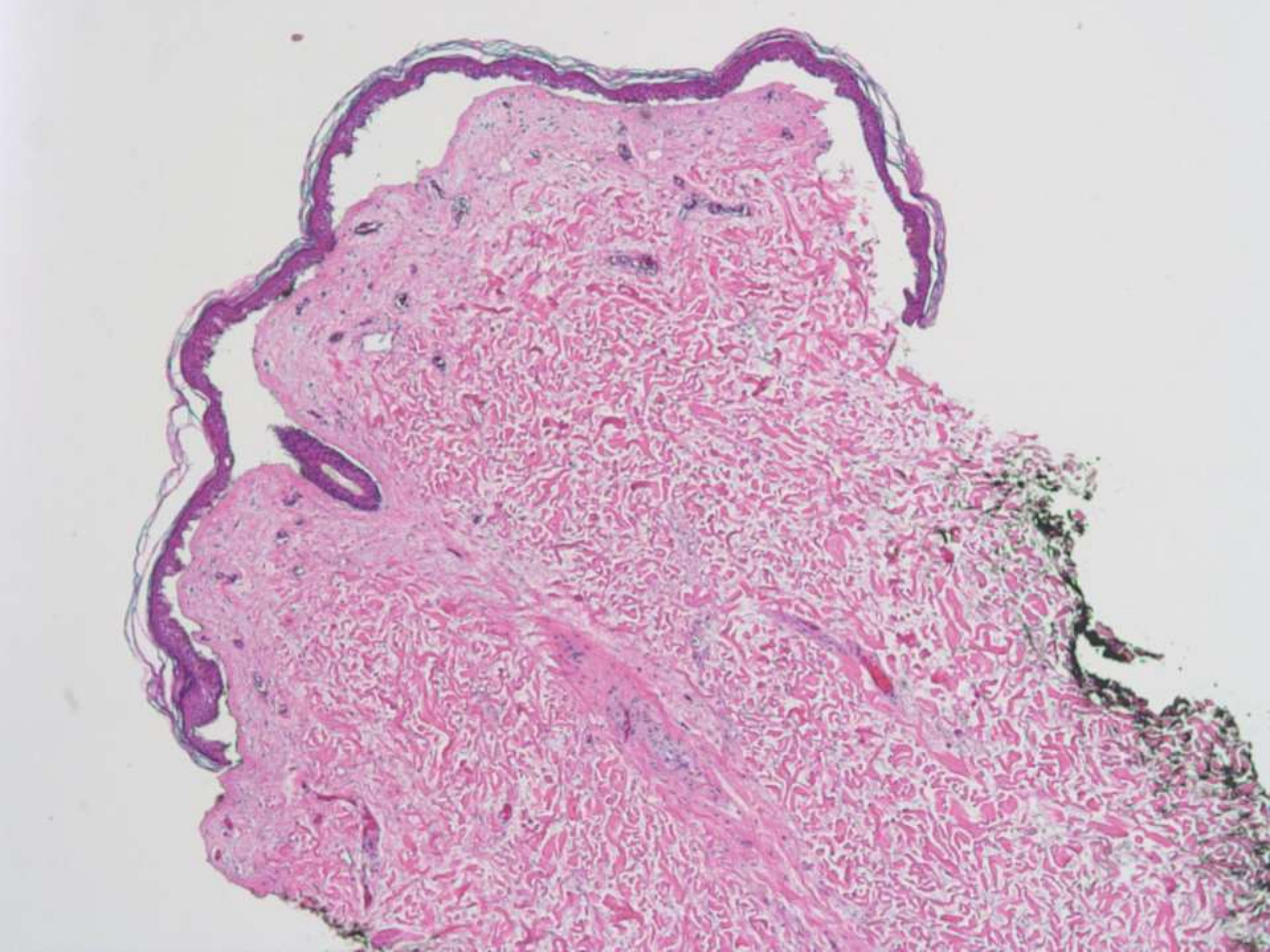
Charles Lombard; El Camino Hospital

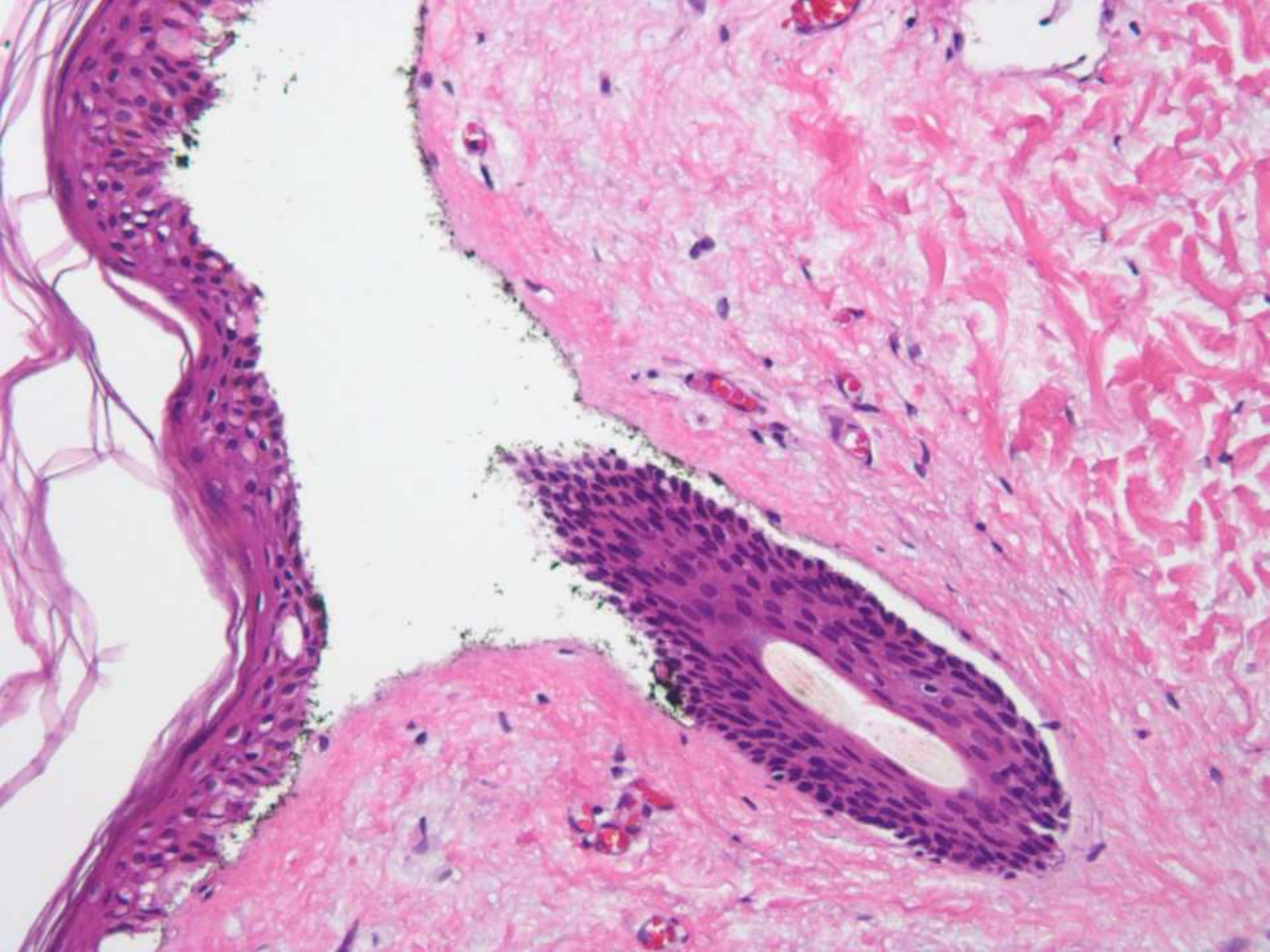
71-year-old female with 1 day onset respiratory failure/DIC, D dimer=69K. Has retiform purpura 30% total body surface area with numerous flaccid bullae without ocular, nasal, perianal, and genital erosion. Favor skin necrosis secondary to DIC ddx

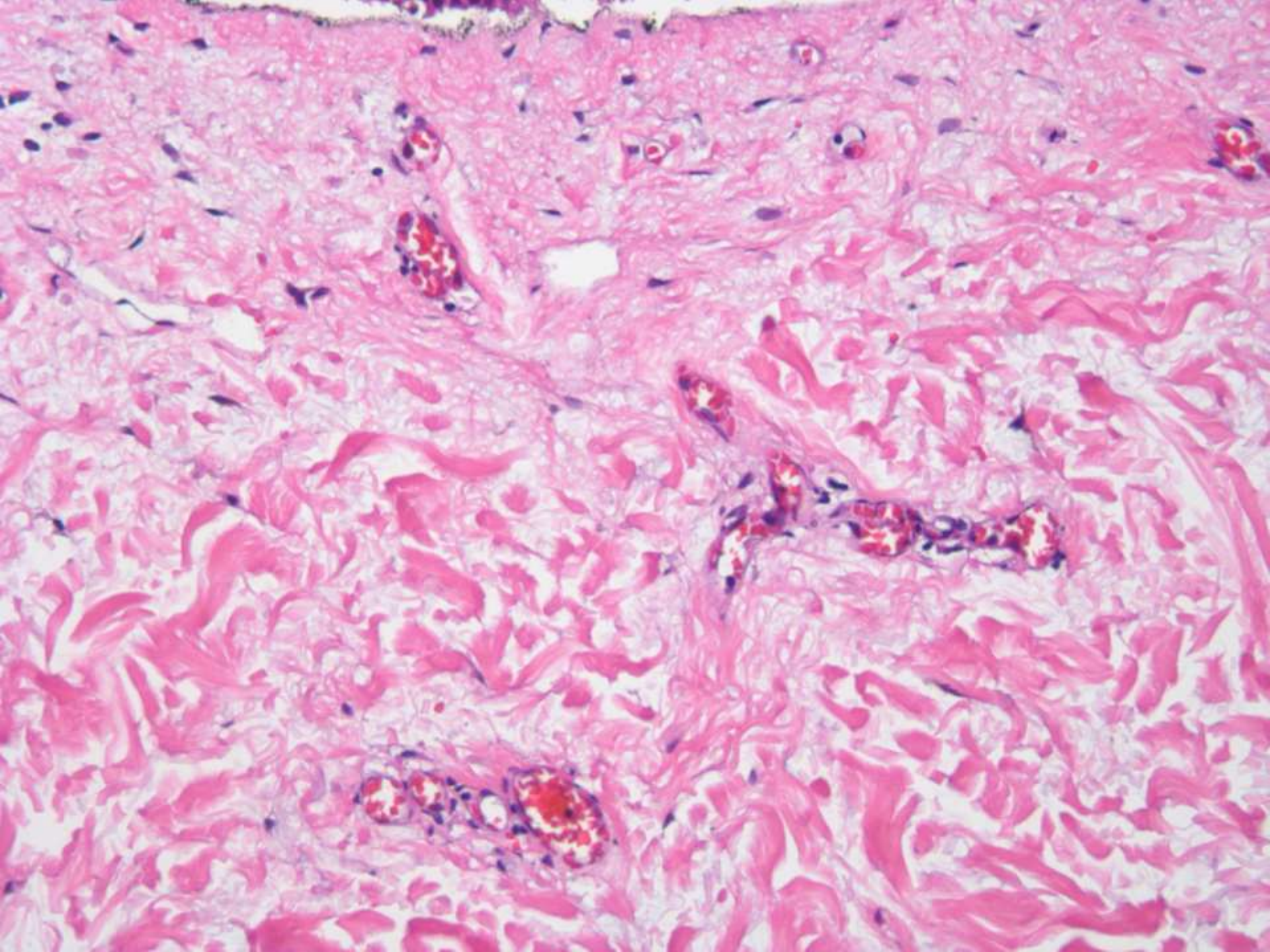
primary bullous disorder, SJS/TEN.

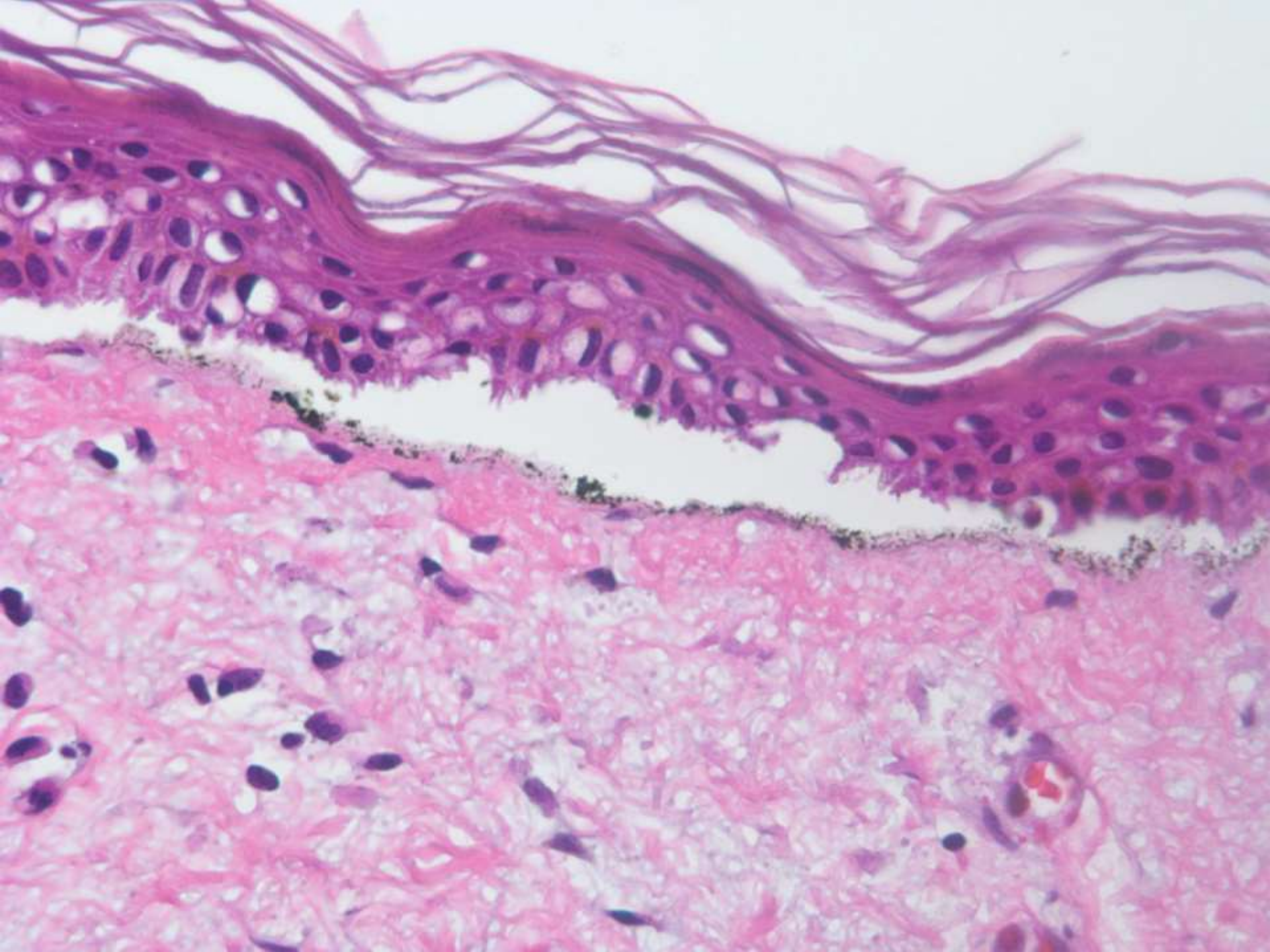
71 yo F

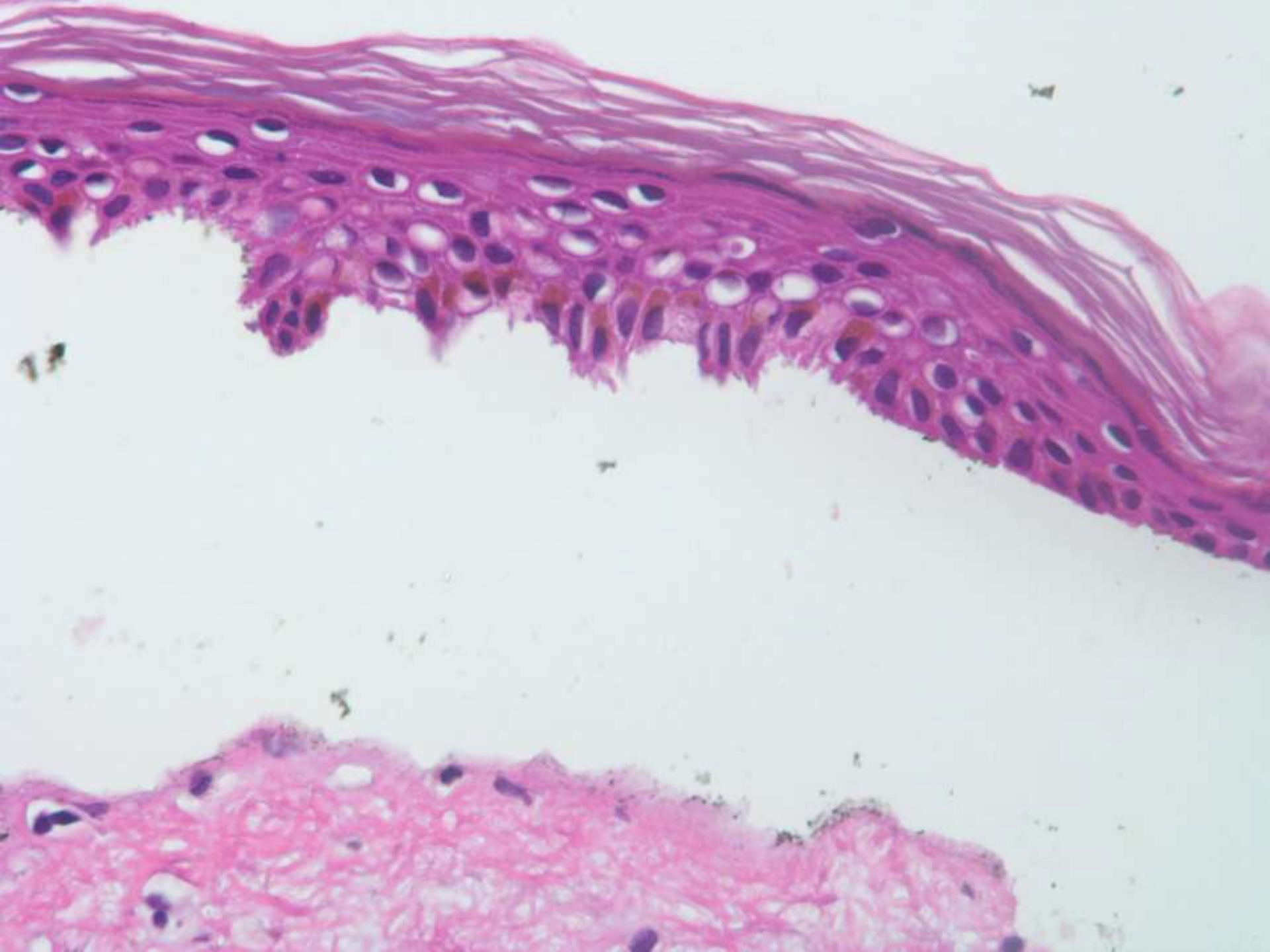
- Acute respiratory failure
- DIC
  - D-dimer: 69,000
  - Hyperthermia/Rhabdomyolysis
- Retiform purpura 30% BSA with numerous flaccid bullae
  - Arms, legs (ankle to groins), abdomen
  - No mucosal lesions
- Clinical DDX:
  - SJS/TEN
  - Primary bullous skin disease
  - Cutaneous necrosis due to DIC
- Abdominal wall biopsy
  - IF Negative

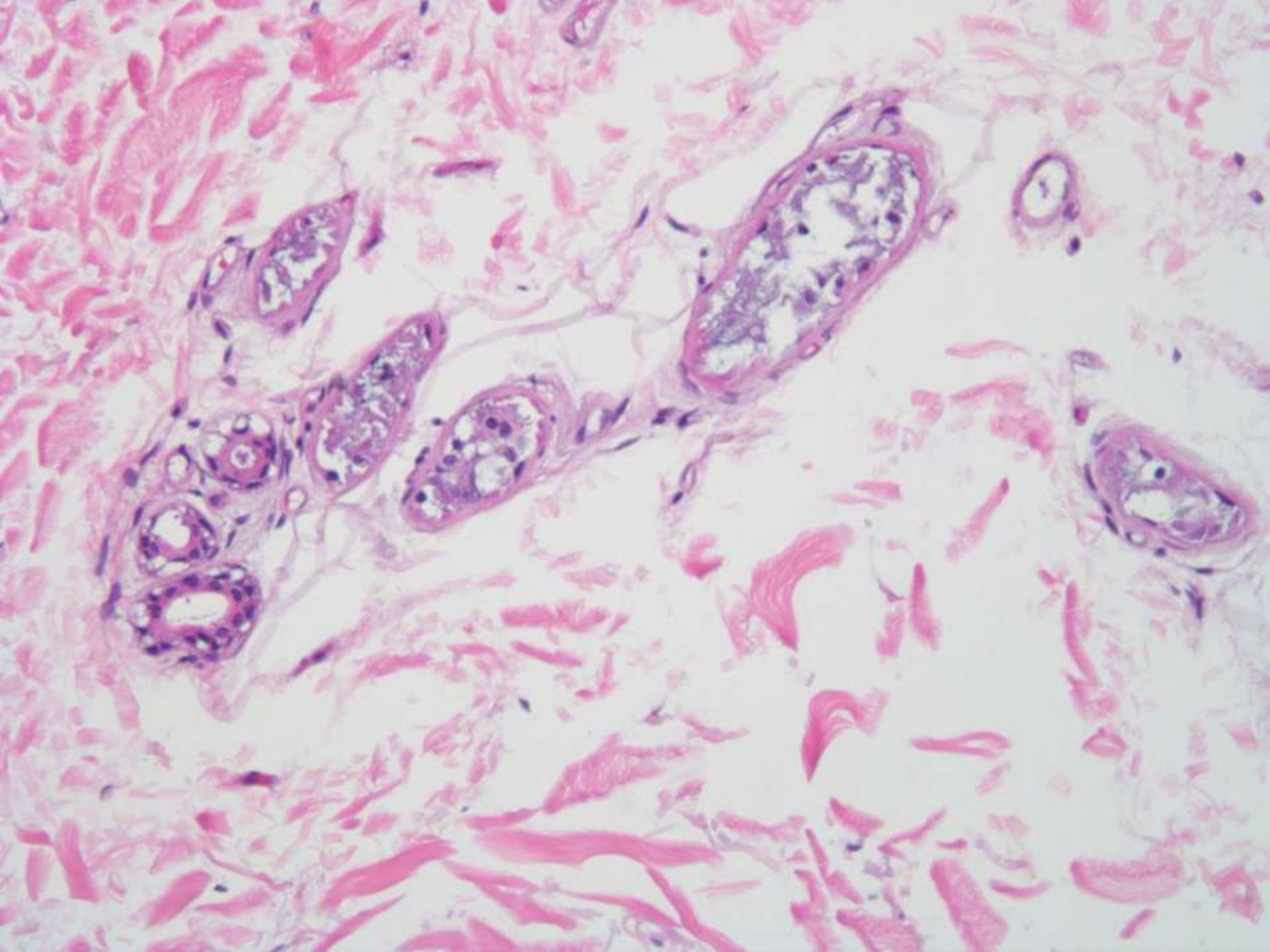


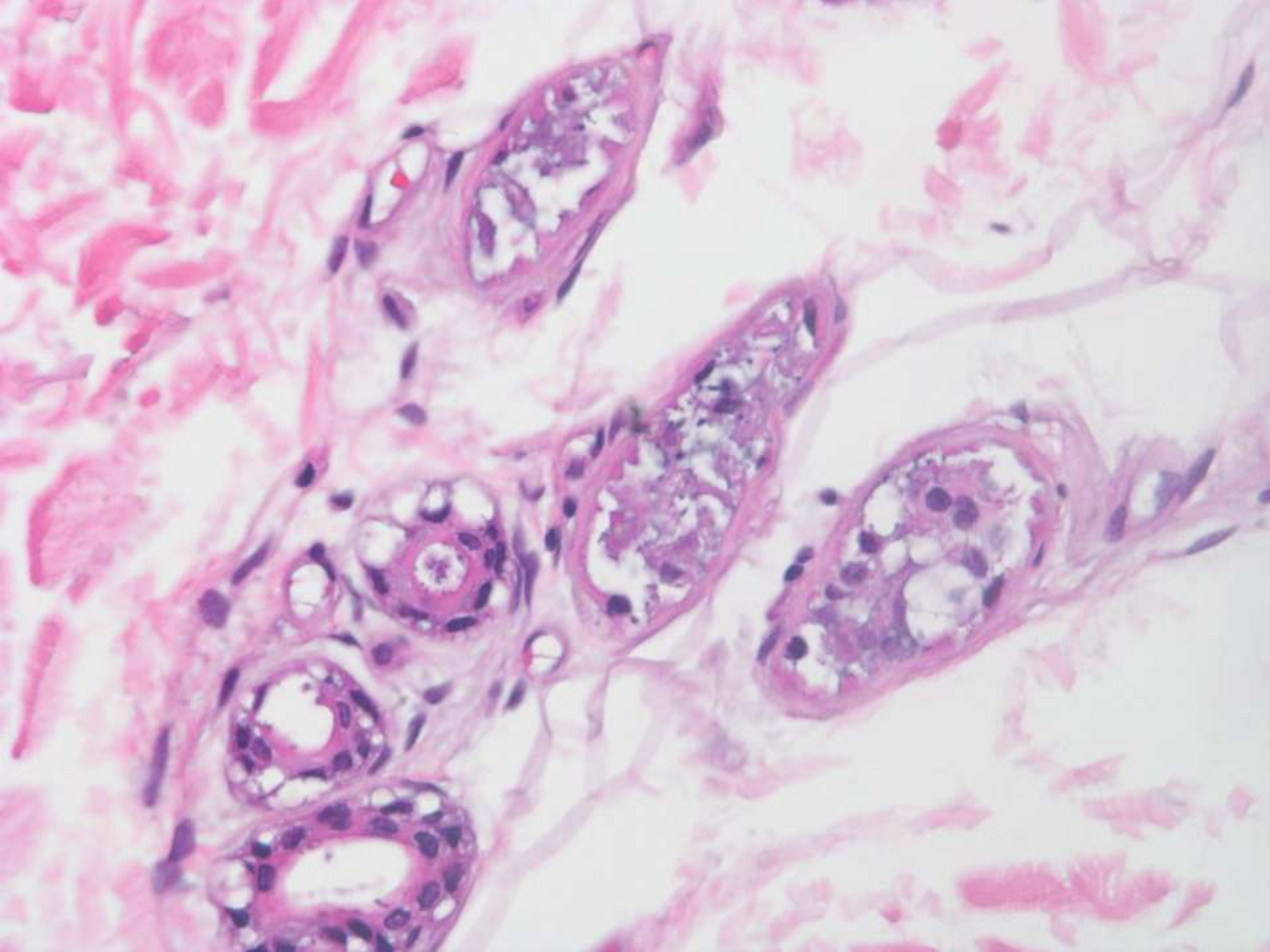












DIAGNOSIS?

“Coma” blister
Non-inflammatory subepidermal split with underlying early eccrine gland necrosis

Coma blisters

- Self-limited skin lesions that occur at sites of pressure
- Commonly associated with medication overdose (barbiturates)
- Also seen in comatose patients with medical/neurologic conditions
- Also seen in non-comatose patient's with respiratory failure (both pressure and non-pressure bearing sites)

Pathology

- Pauci- inflammatory subepidermal blister
- No inflammatory infiltrate in underlying dermis
- DIF : negative
- Absence of vascular thrombosis/vasculitis
- Underlying eccrine glands show degeneration/necrosis
- DDX includes: celll poor autoimmune disease, SJS/TEN, Vasculitis/vasculopathy

Pathogenesis

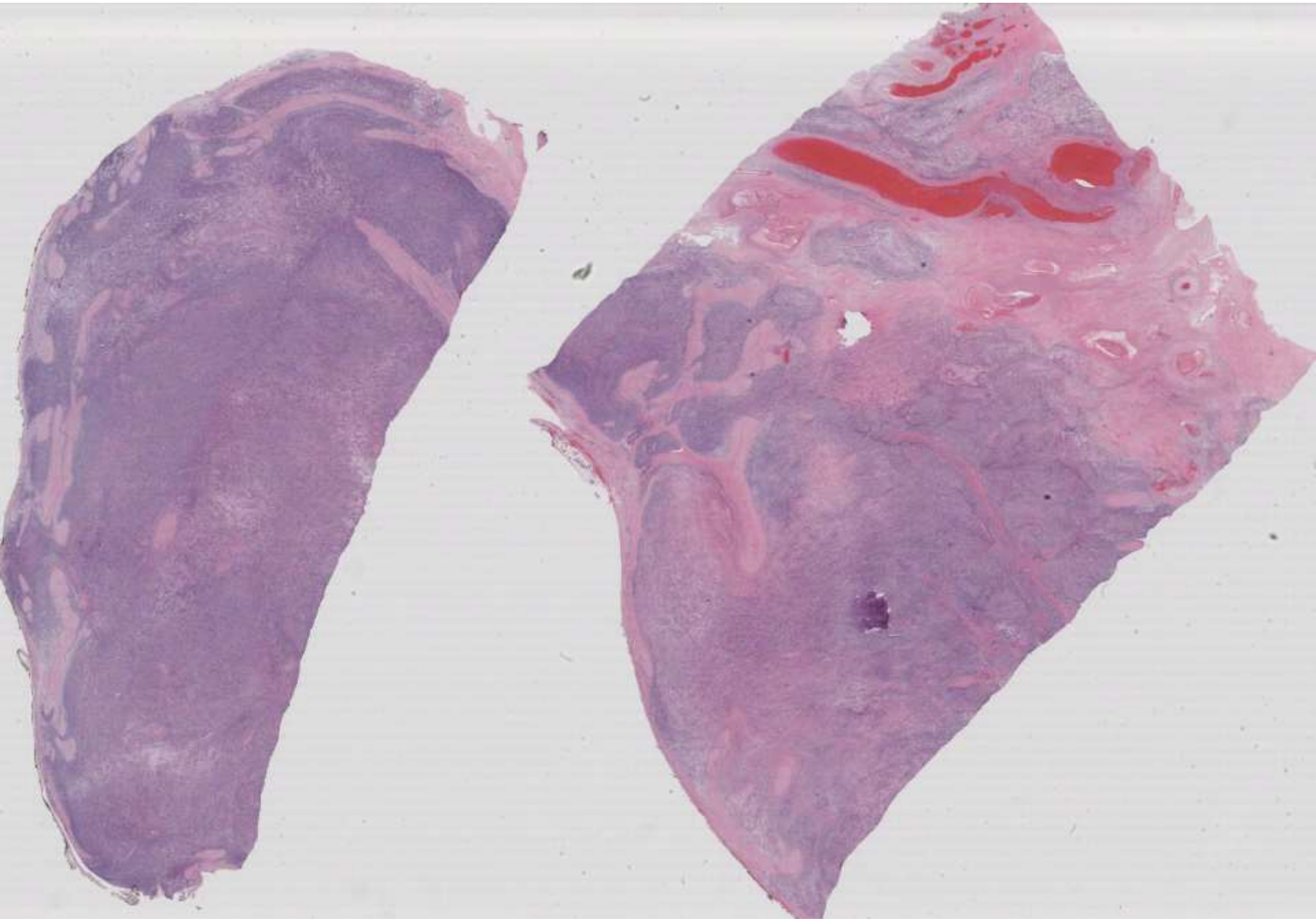
- Thought to be related to hypoxia and/or toxic effects of drugs on the skin and eccrine glands.

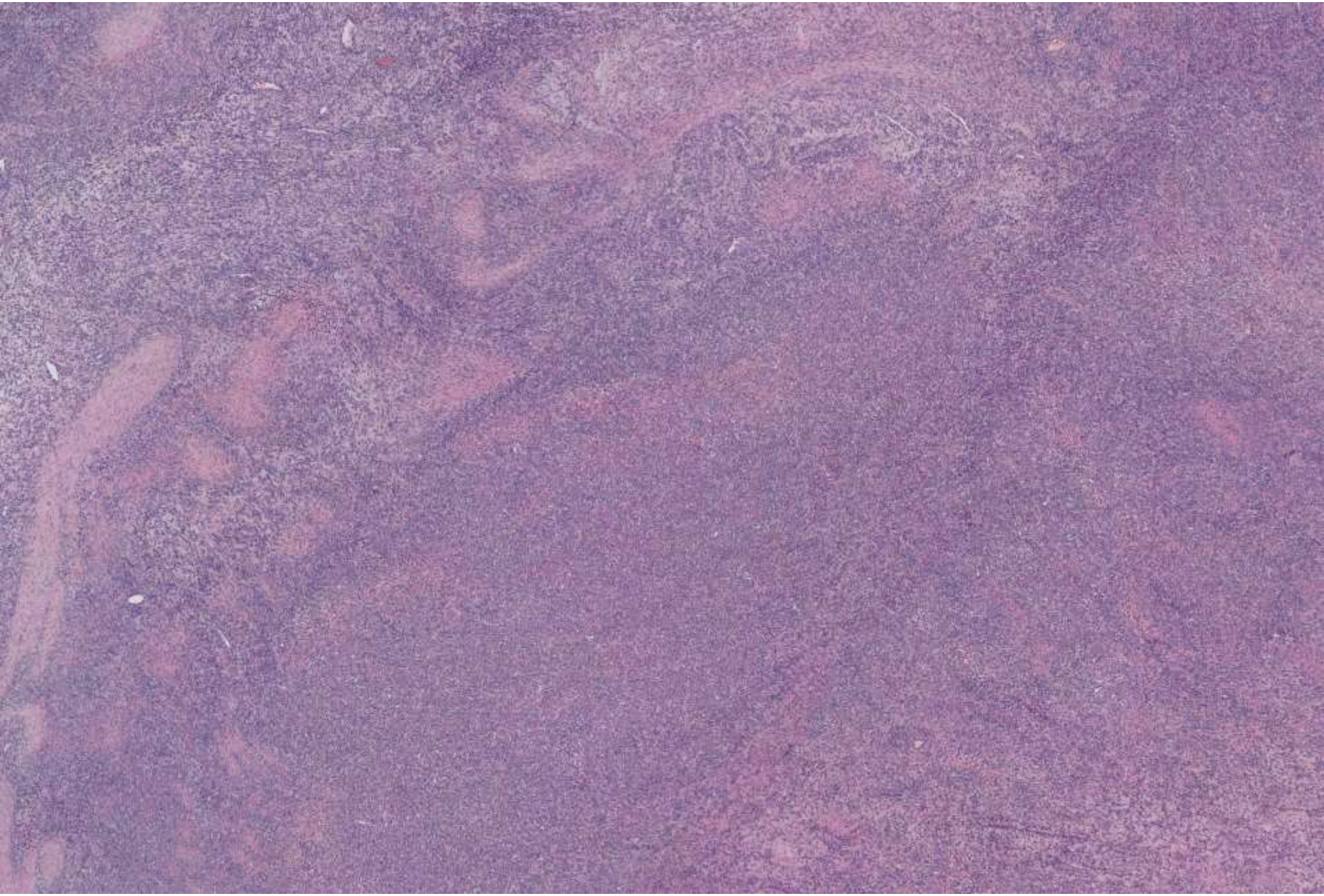
- F/U: Pt died shortly after bx.

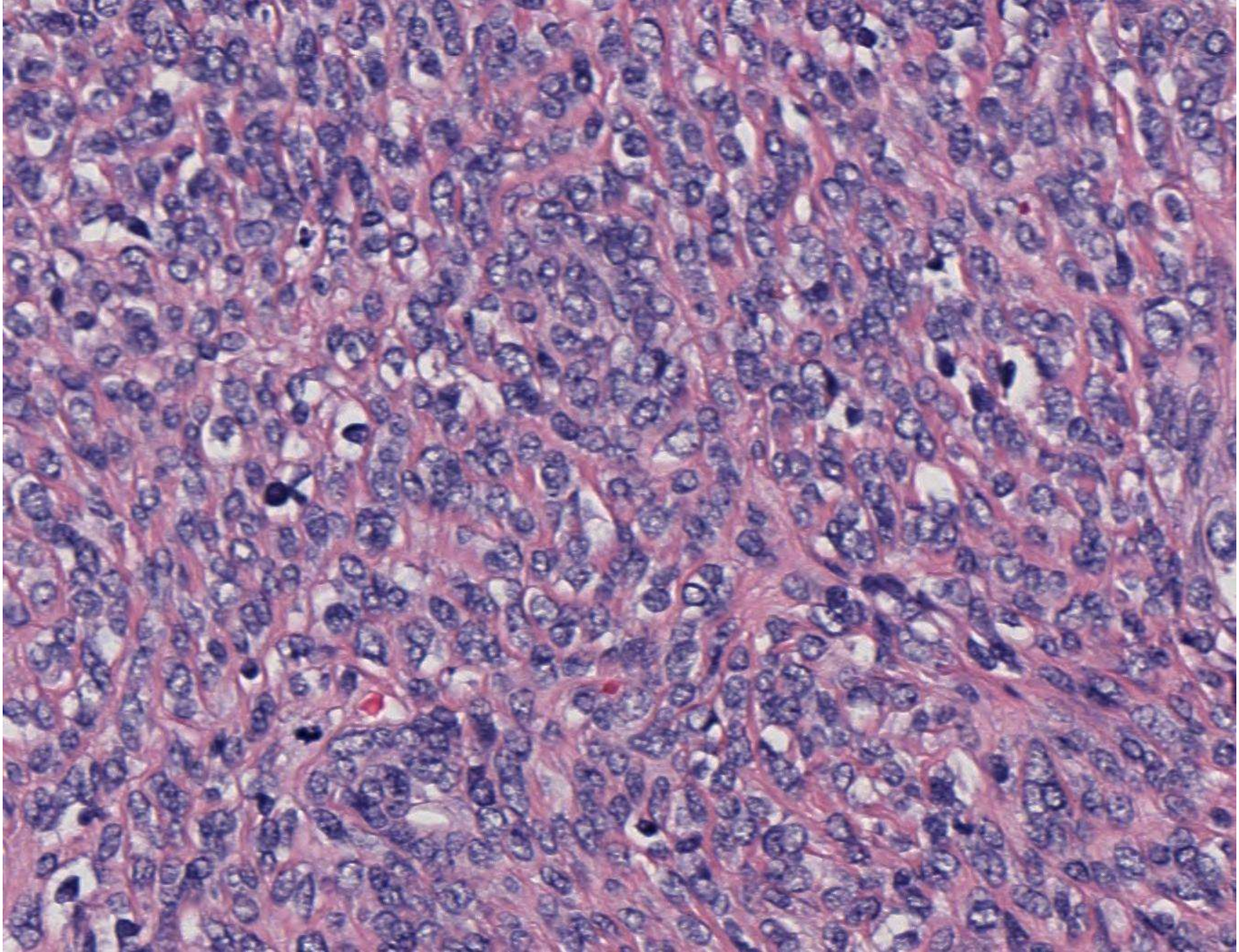
SB 6102
(scanned slide available)

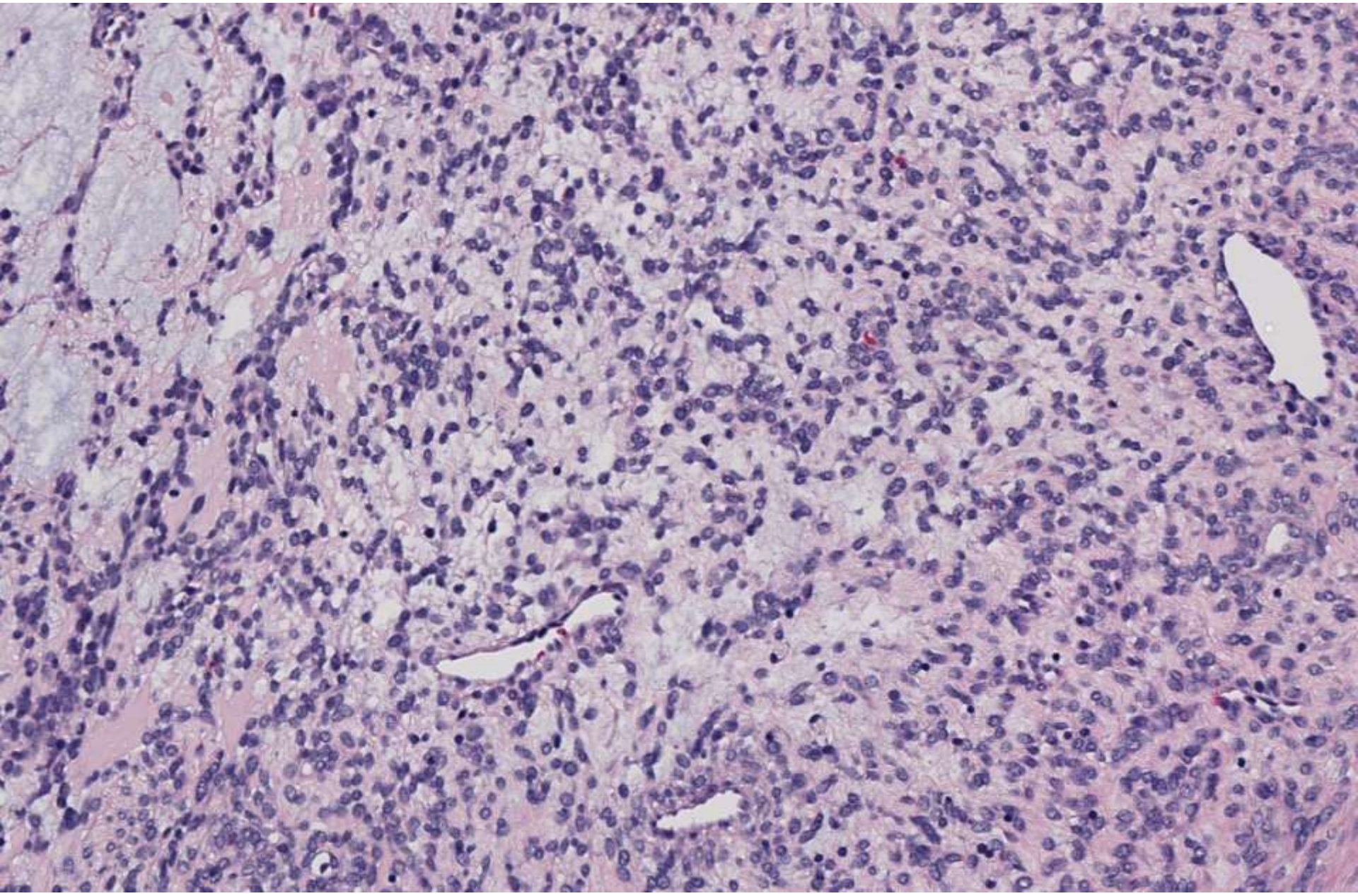
Keith Duncan; Mills-Peninsula

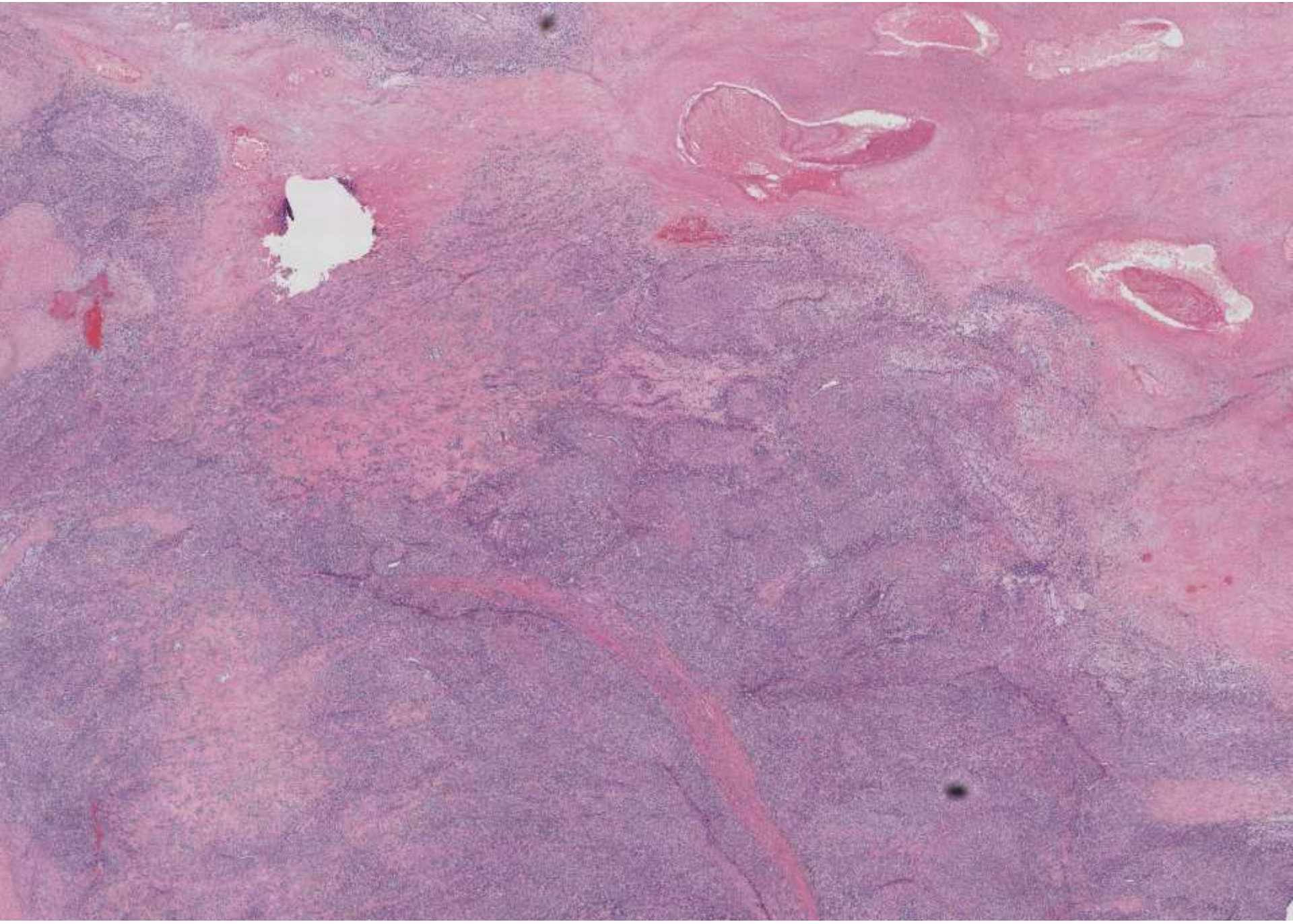
75-year-old female with “multinodular goiter”, recurrent nerve palsy, and 11cm tan white firm mass thought to have originated from inferior thyroid.

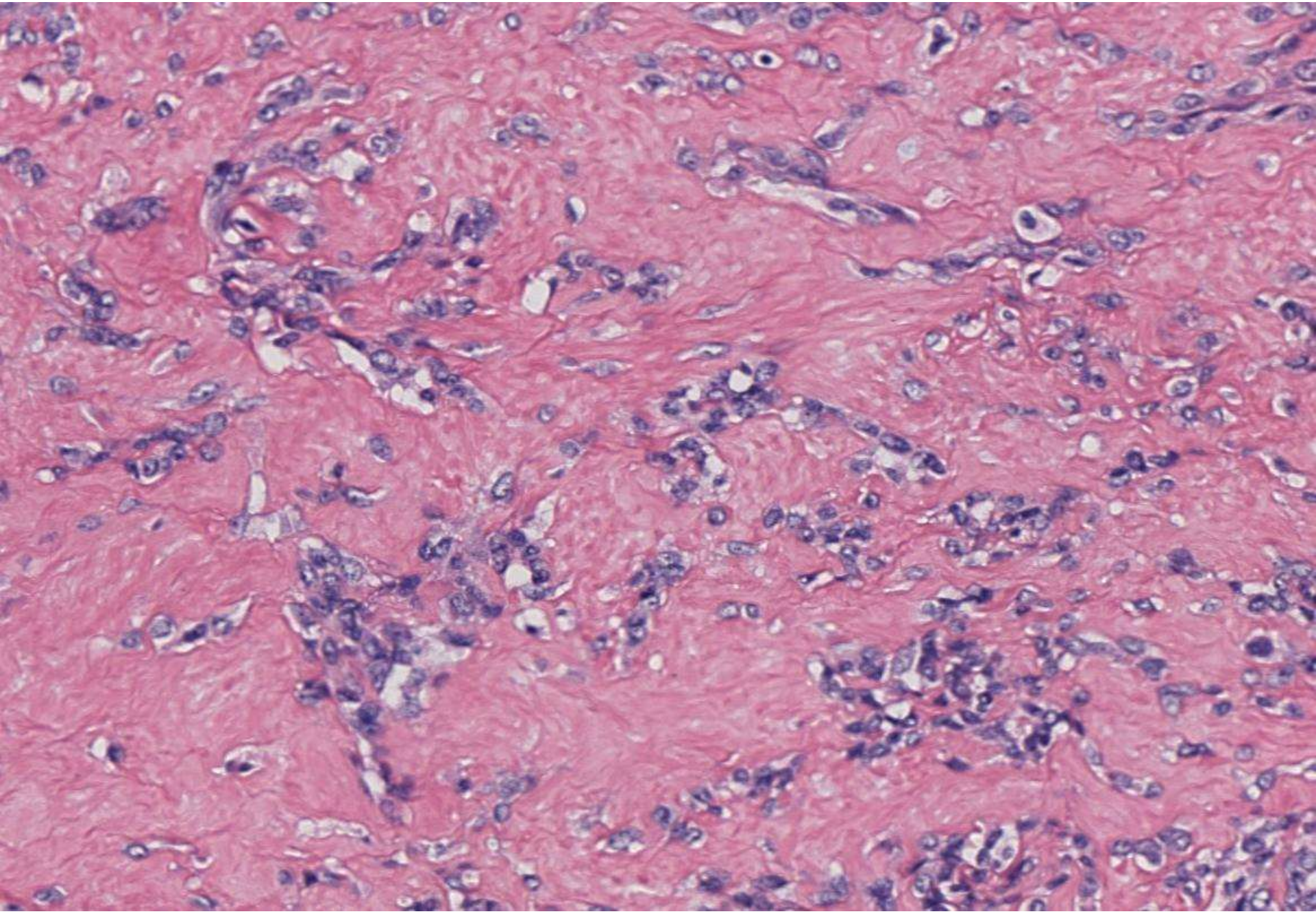


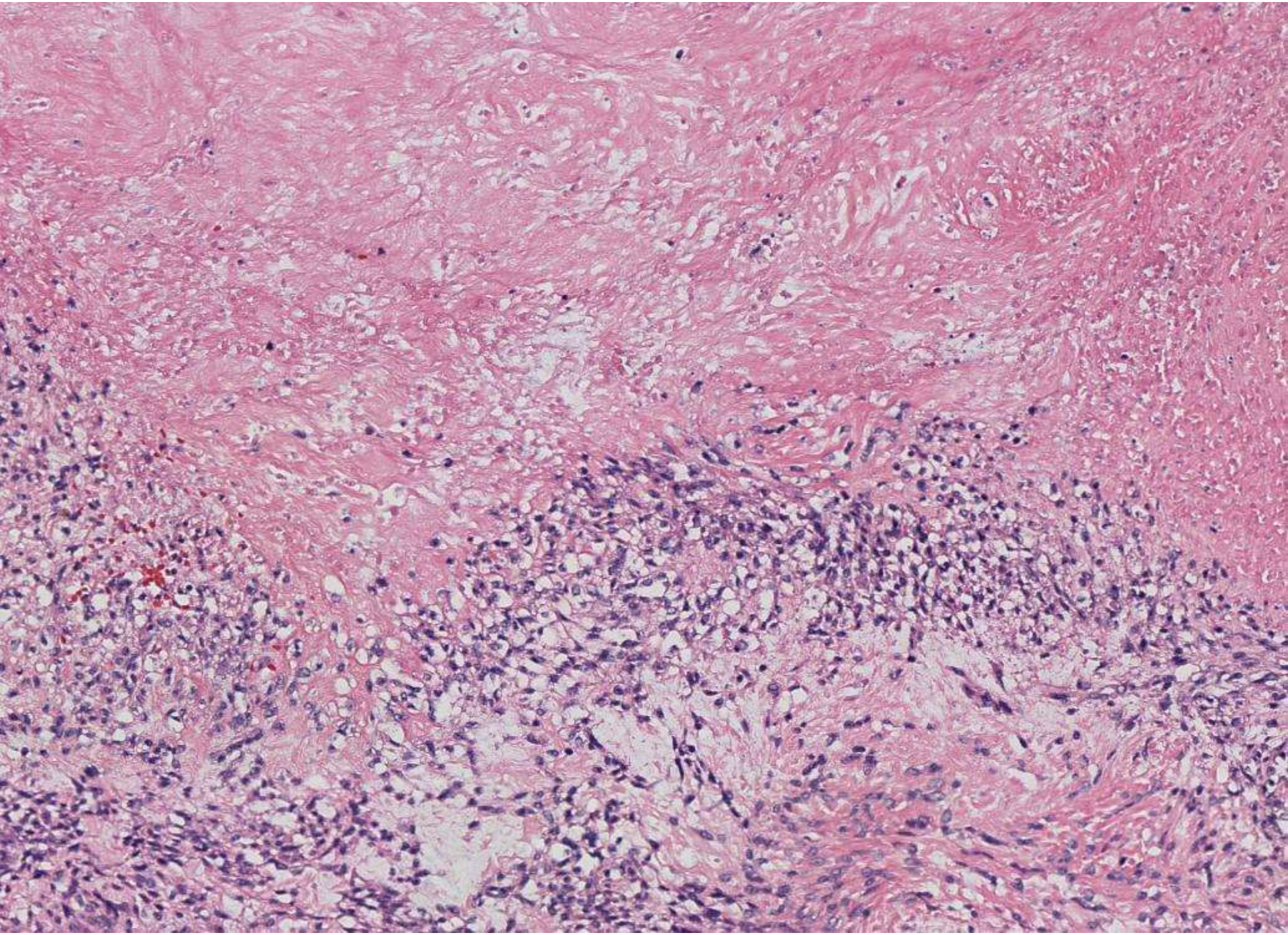


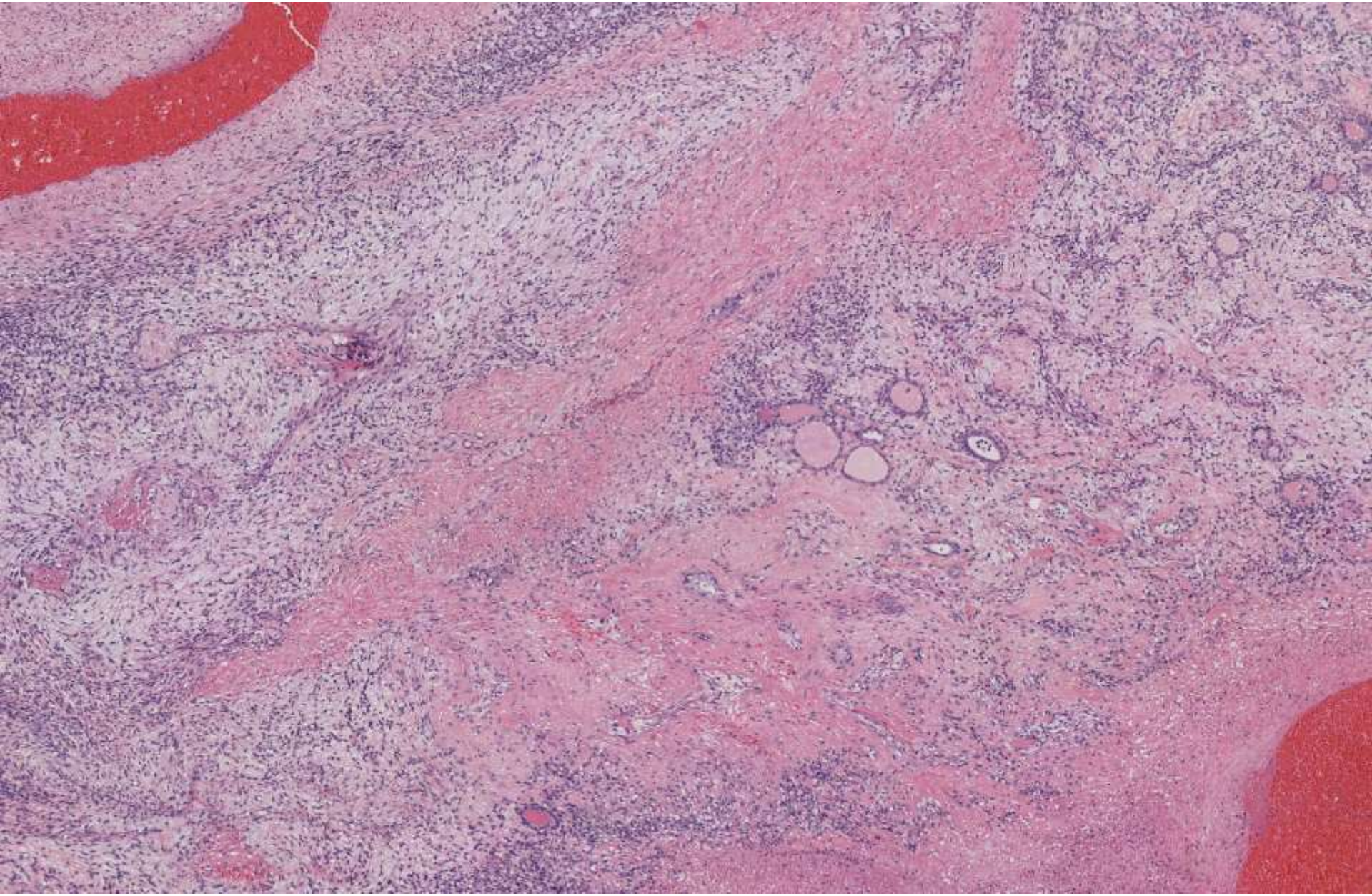


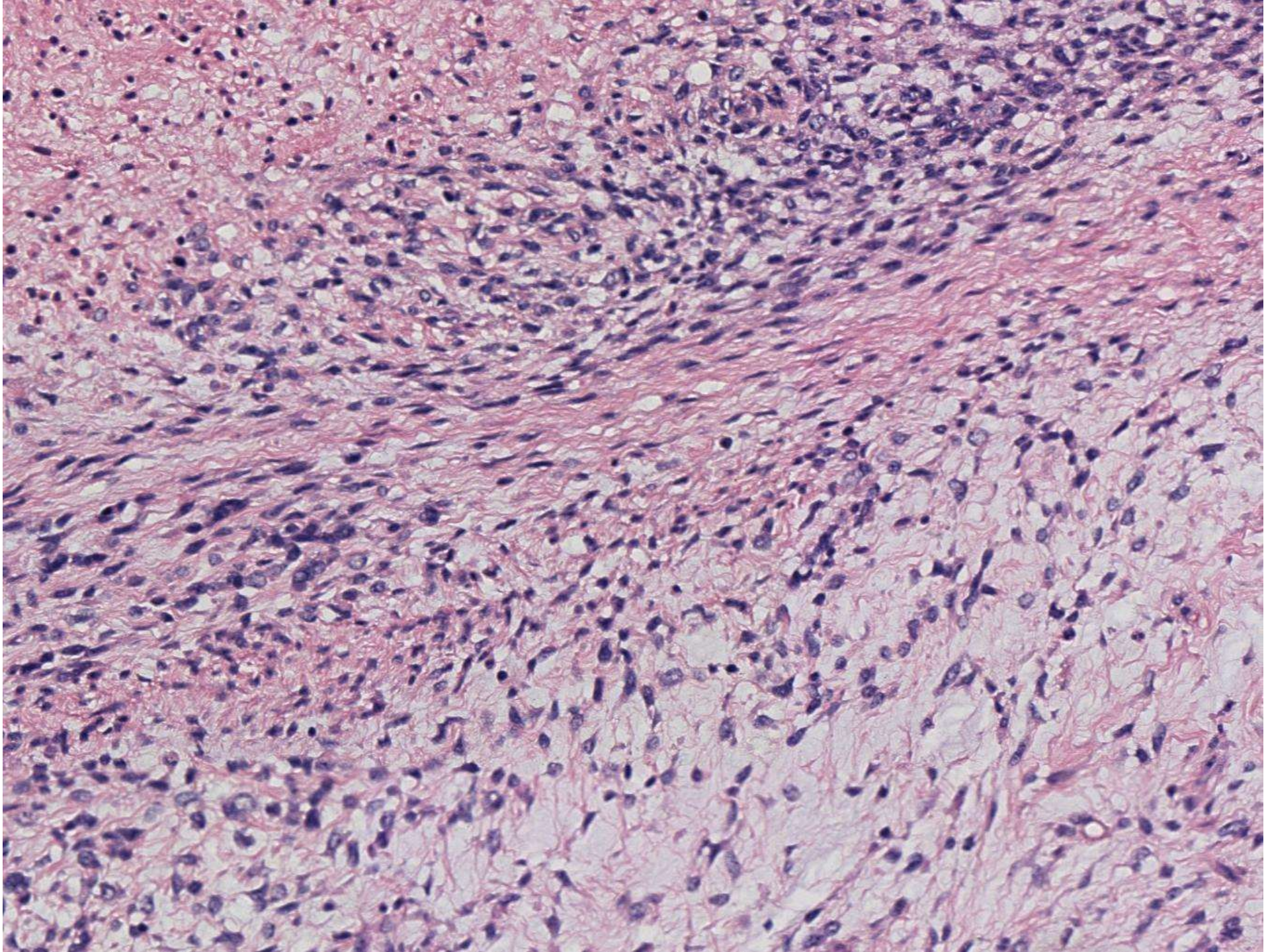












DIAGNOSIS?

SB 6102

SURGEON (AND MRI) ORIGINALLY THOUGHT TUMOR WAS ARISING FROM THYROID (13 CM IN GREATEST DIMENSION):

DIFF DX: BIPHASIC TUMORS:
SYNOVIAL SARCOMA
SARCOMATOID CARCINOMA OR MESOTHELIOMA
SETTLE (SPINDLED EPITHELIAL TUMOR OF THMIC LIKE DIFFERNTATION)
CASTLE (CARCINOMA SHOWING THYMIC LIKE DIFFERENTIATIOIN)

HOWEVER, EPITHELIAL COMPONENT PROVED TO BE ENTRAPPED THYROID GLANDS

SB 6102

EPITHELIAL COMPONENT CK7, CK19, TTF-1 AND THYROGLOBULIN POSITIVE

SPINDLED ZONES: VIMENTIN AND BCL-2 POSITIVE
NEGATIVE STAINS: CD10, CD34, DESMIN, Mel-A, WT-1 and S100--
ALSO NEGATIVE, EMA, CK5, CD5 AND P63

TRANSLOCATION STUDY FOR X, 18 (SYT/SSX)
SYNOVIAL SARCOMA WAS NEGATIVE

SB6102

REFERRED TO STANFORD:

STRONG DIFFUSE NUCLEAR STAINING FOR STAT-6 SURROGATE MARKER FOR THE NAB2-STAT6 TRANSLOCATION

STAT-6 NEGATIVE IN SYNOVIAL SARCOMAS AND SARCOMATOID MESOTHELIOMAS

CONCLUSION: MALIGNANT SOLITARY FIRBROUS TUMOR

MALIGNANT SOLITARY FIBROUS TUMOR

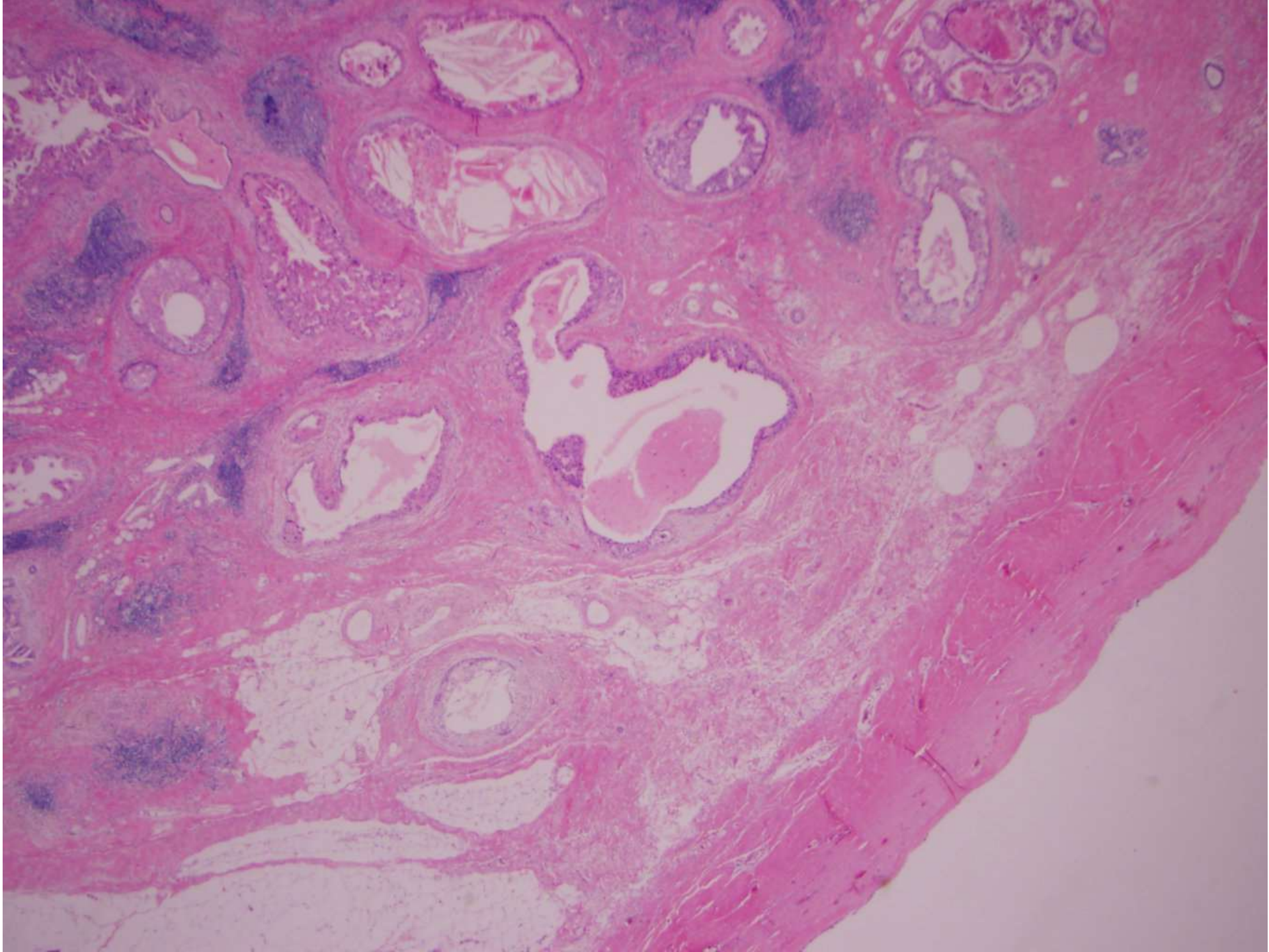
HIGH RISK FEATURES:
LARGE SIZE, CELLULAR FOCI WITH INCREASED ATYPIA, HIGH MITOTIC ACTIVITY, DIFFUSELY INFILTRATIVE BORDER AND TUMOR CELL NECROSIS
ASSOCIATED WITH RECURRENCE AND METASTASES

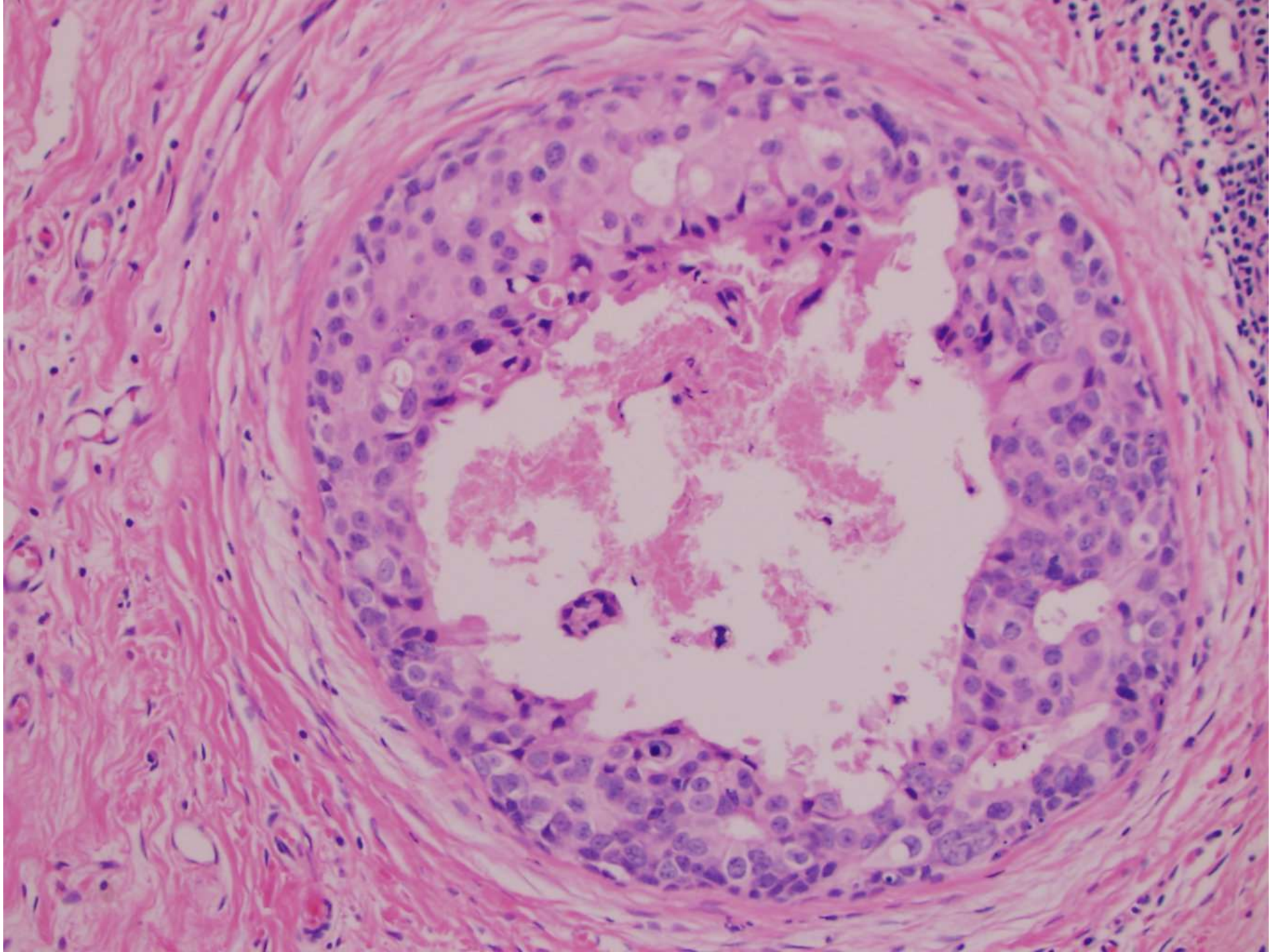
HISTORY OF PLEURAL SOLITARY FIBROUS TUMOR 1995- 20 X 15 X18 CM PLEURAL MASS ? MET FROM THAT LESION?

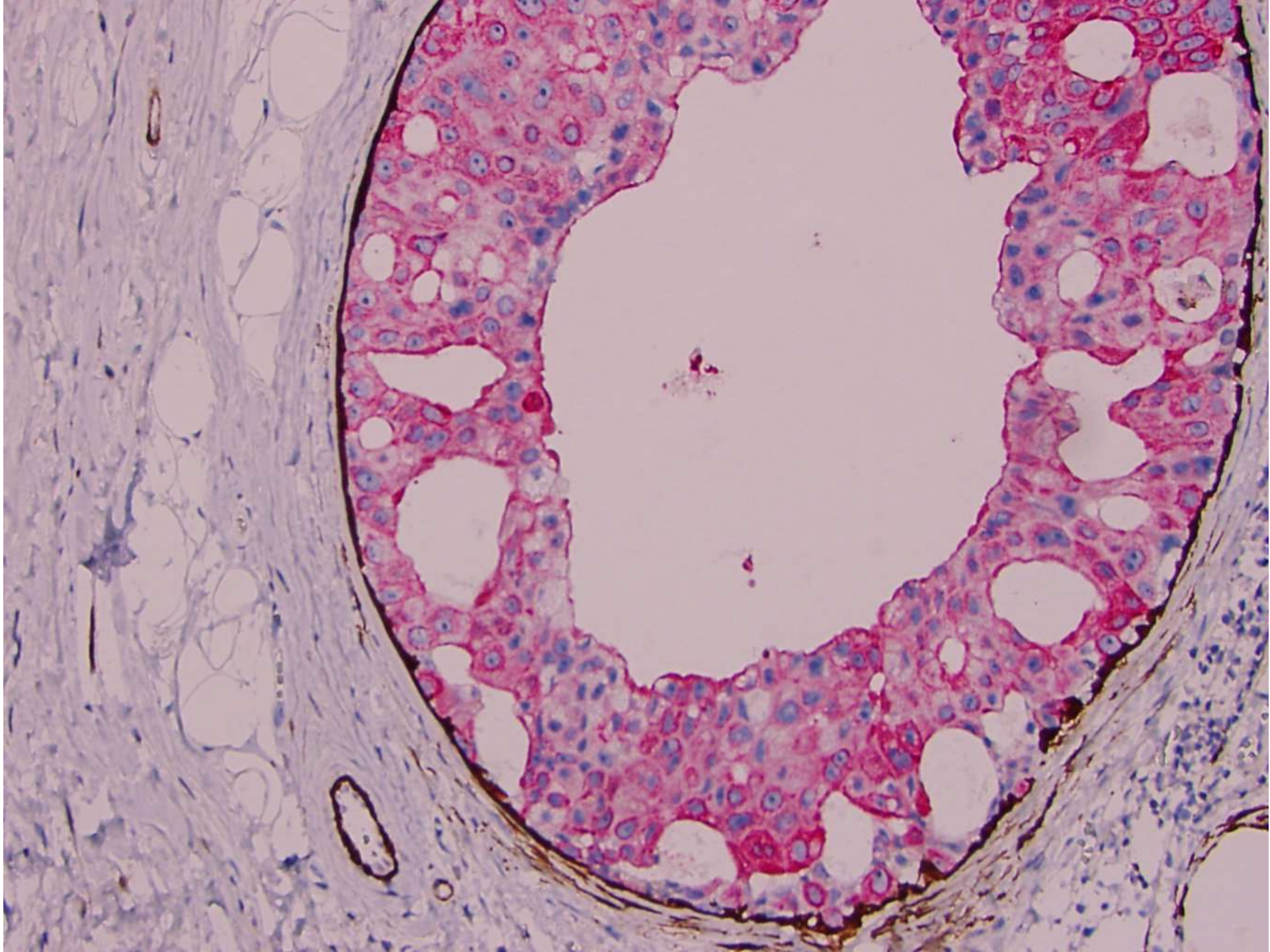
SB 6103

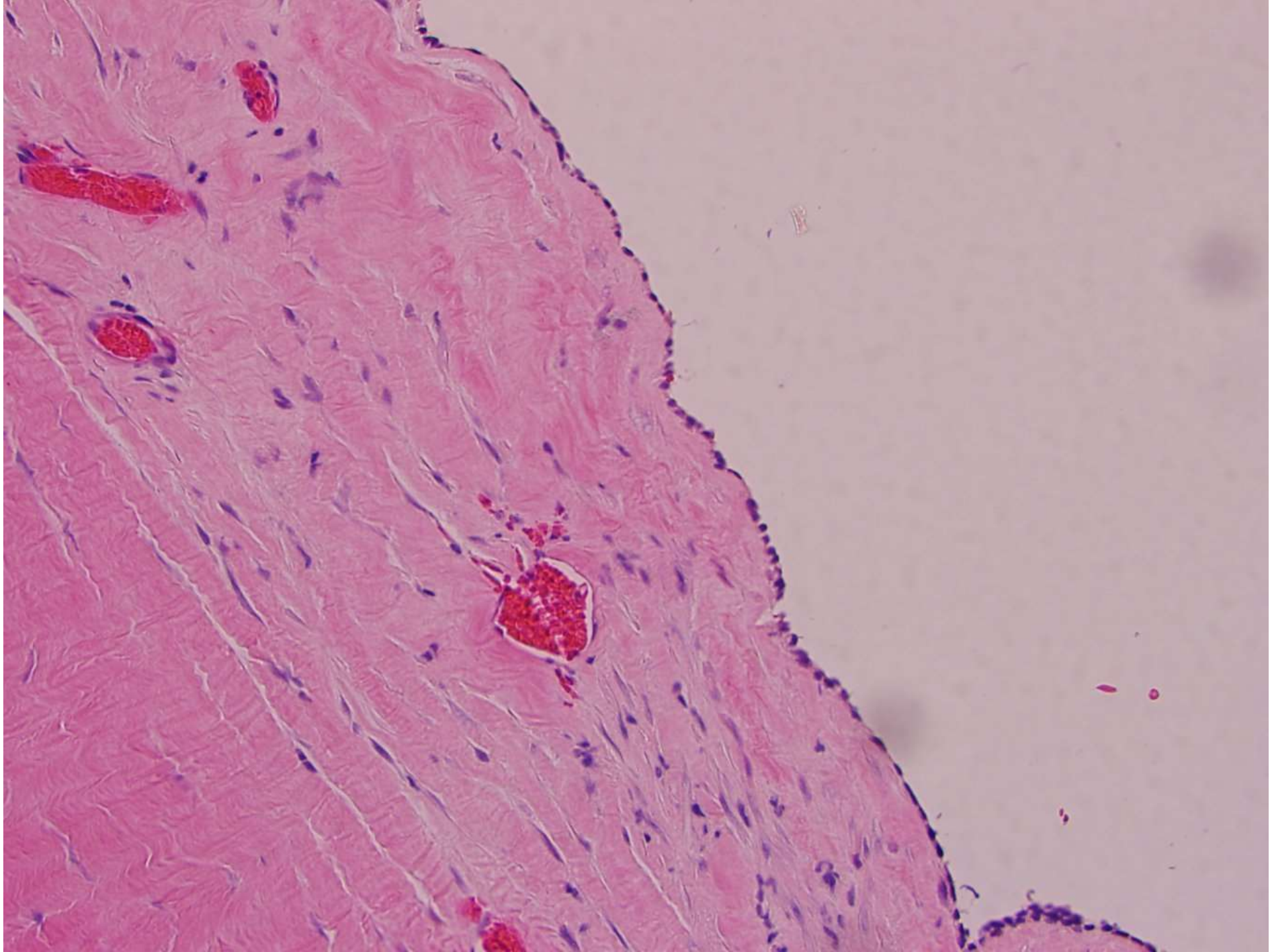
Greg Rumore; Kaiser Walnut Creek

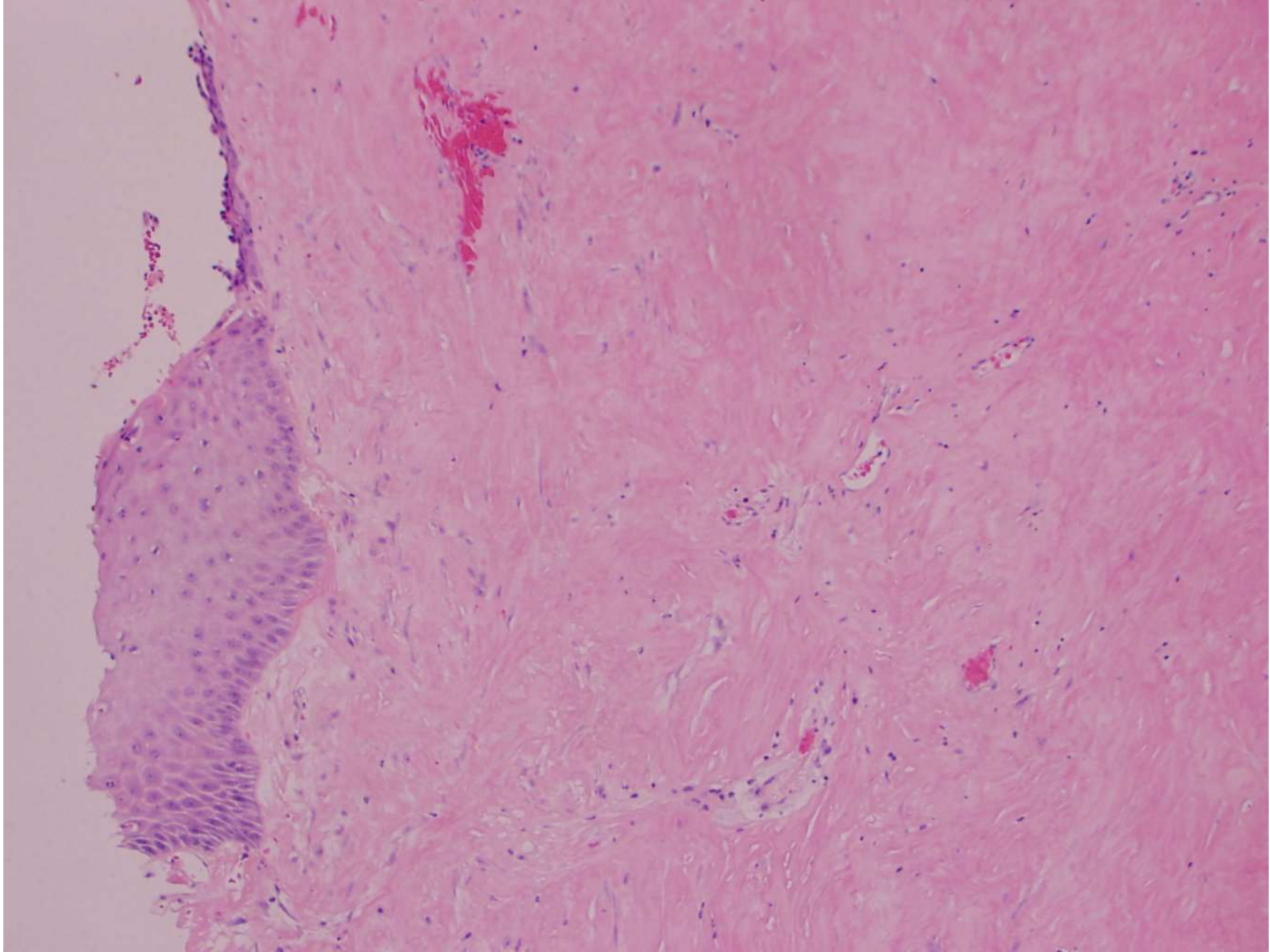
54-year-old woman status post breast augmentation in 2000. Developed capsular contraction and pain in breast necessitating implant replacement in 2008. Now with nipple discharge and continued pain. Underwent bilateral mastectomy.

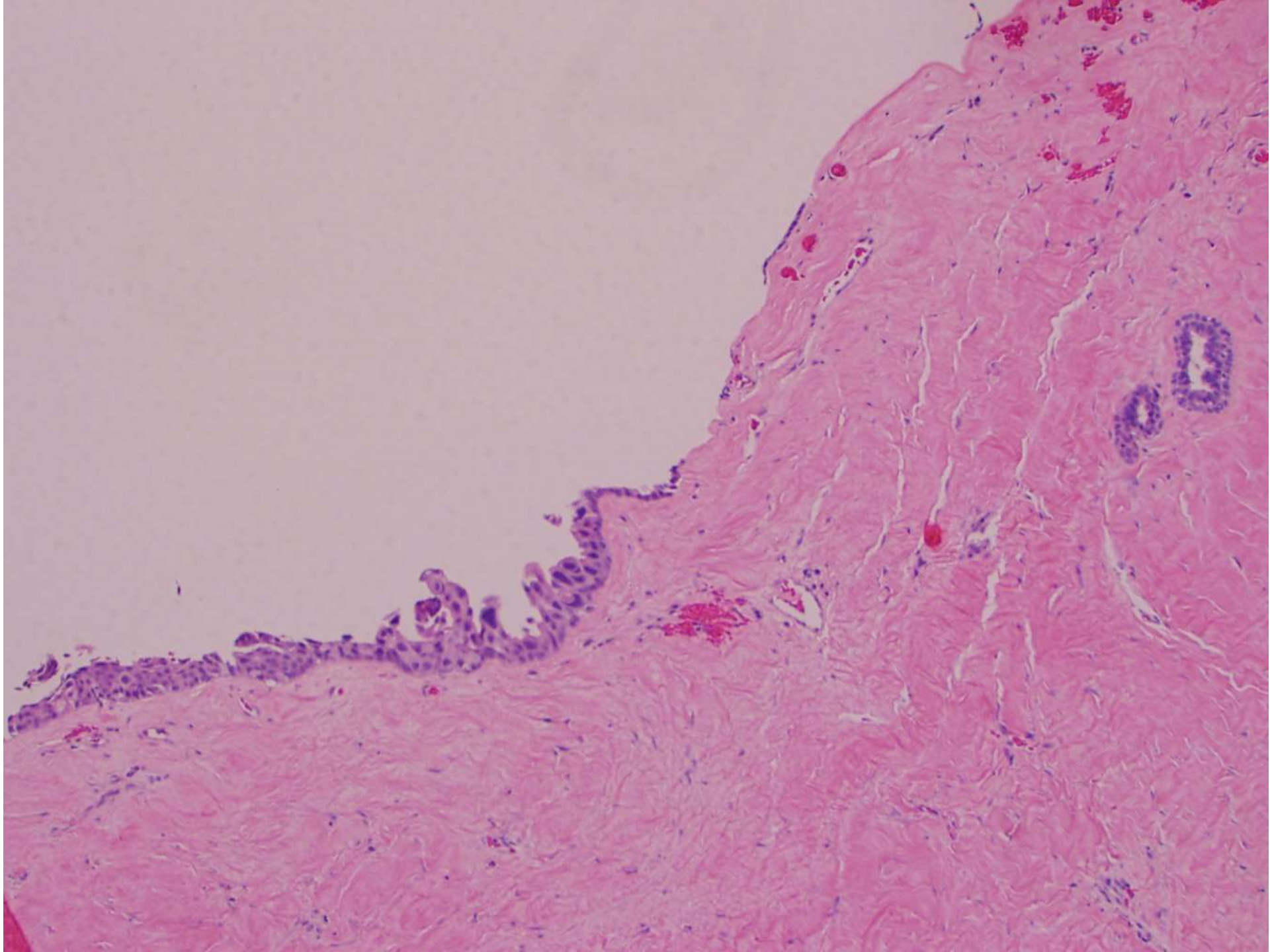


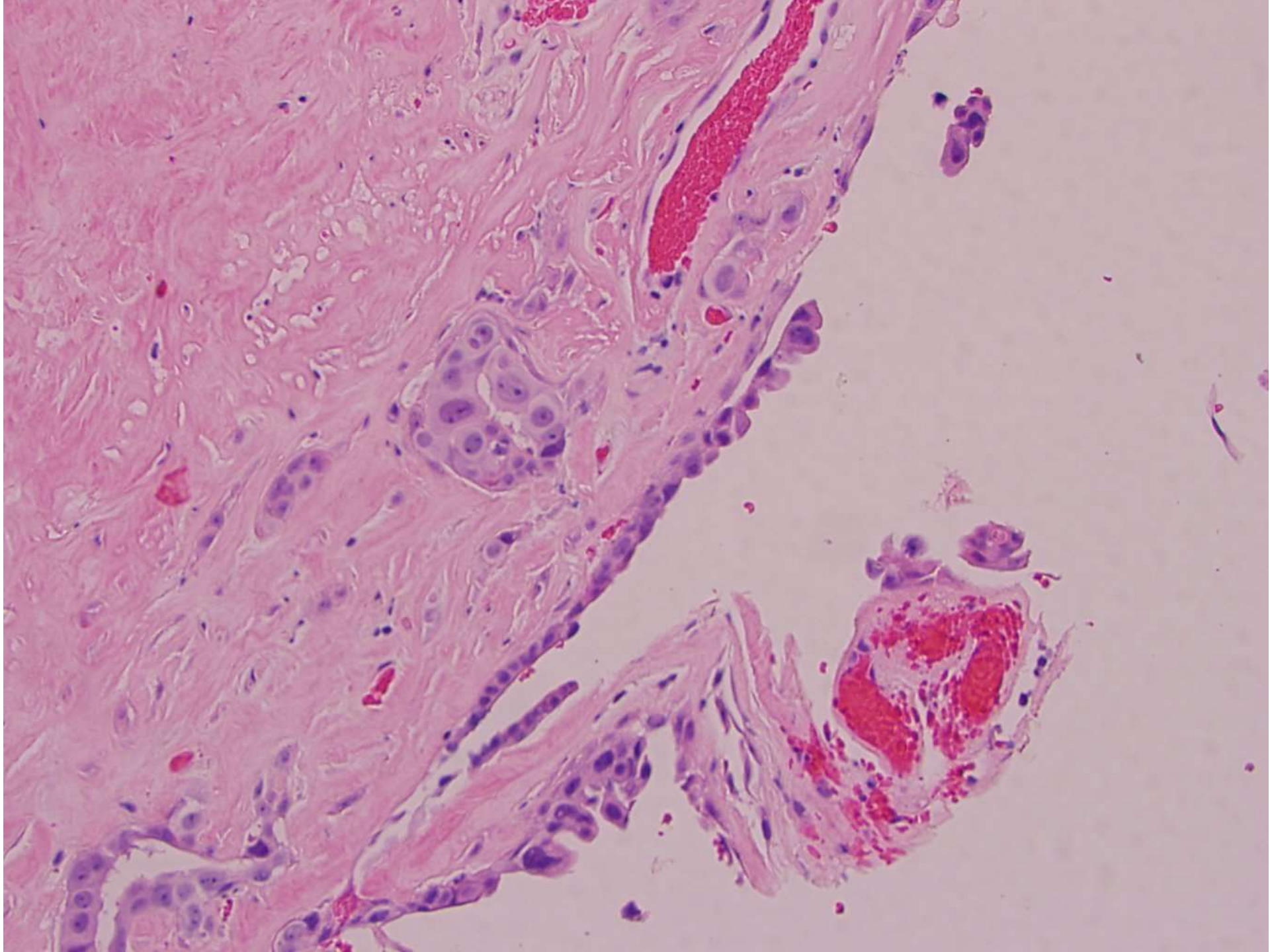


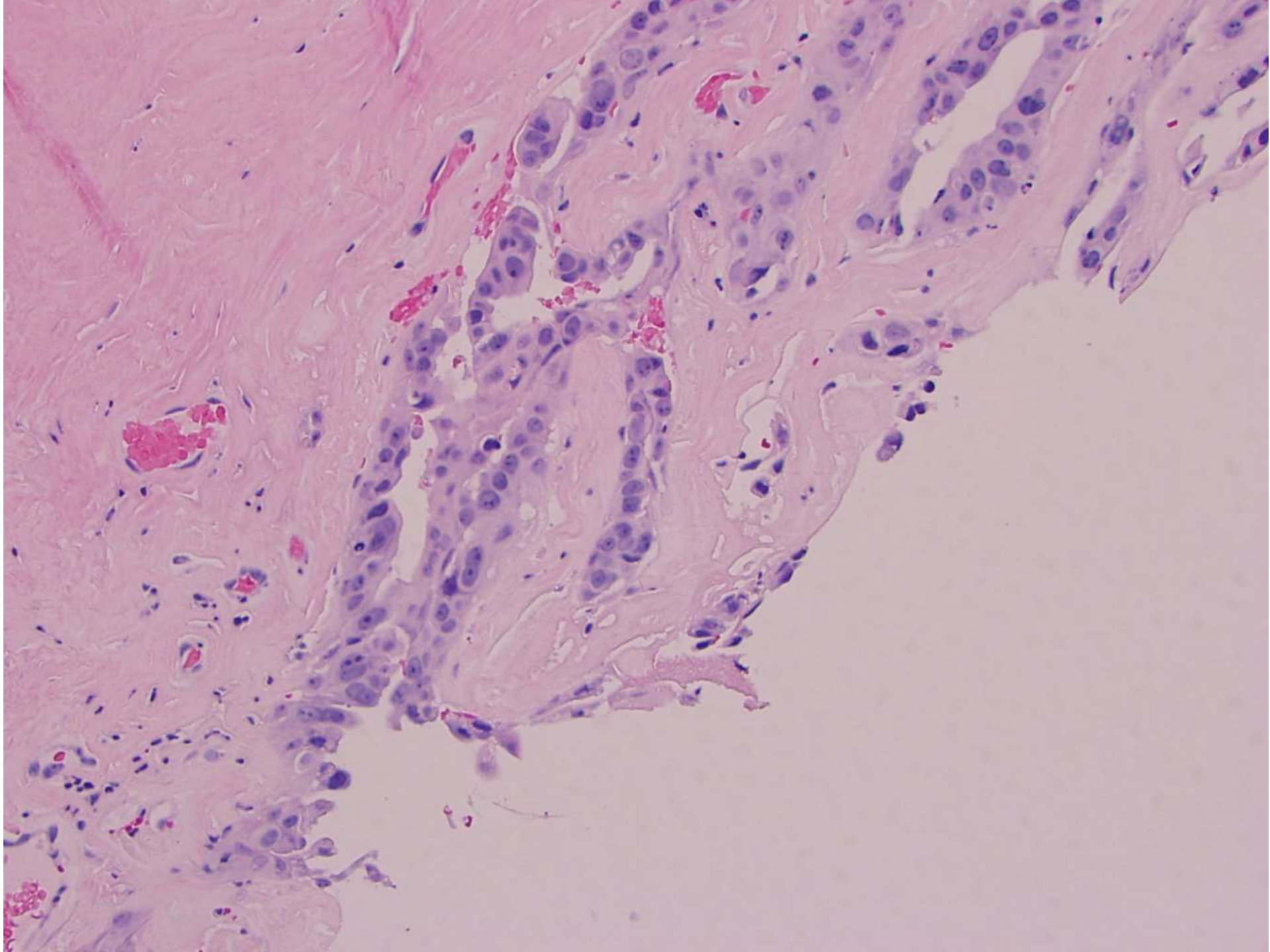


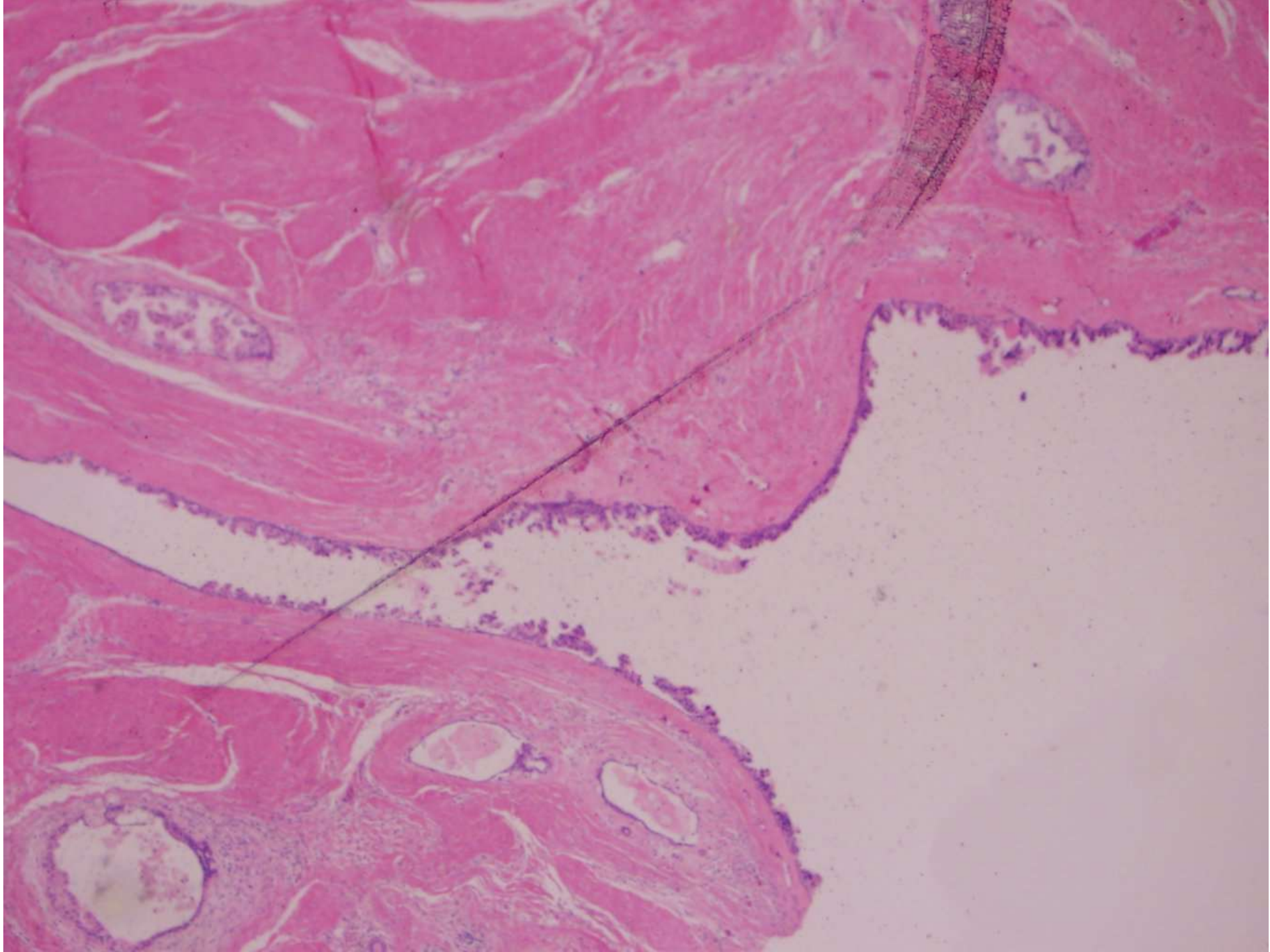


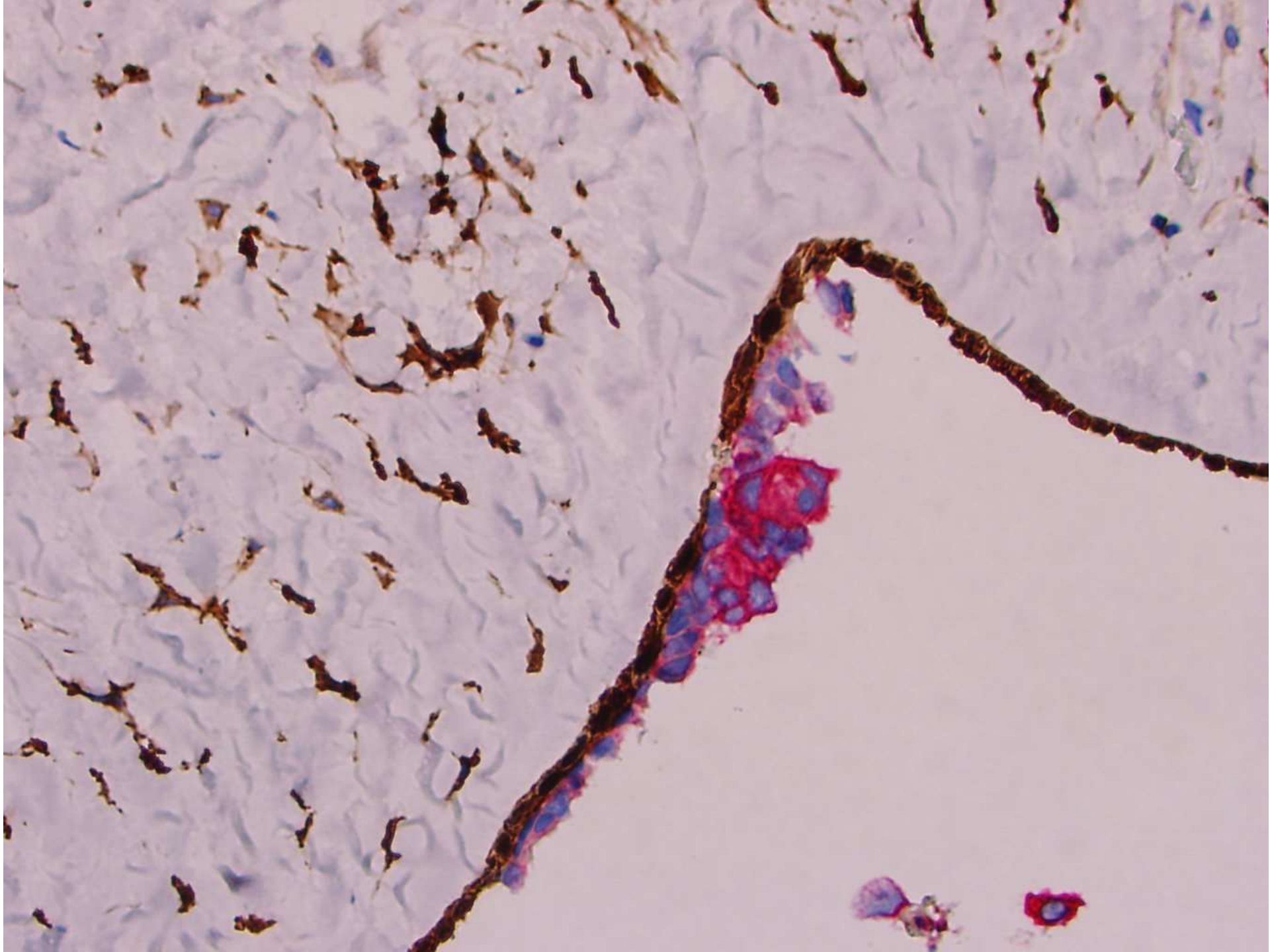


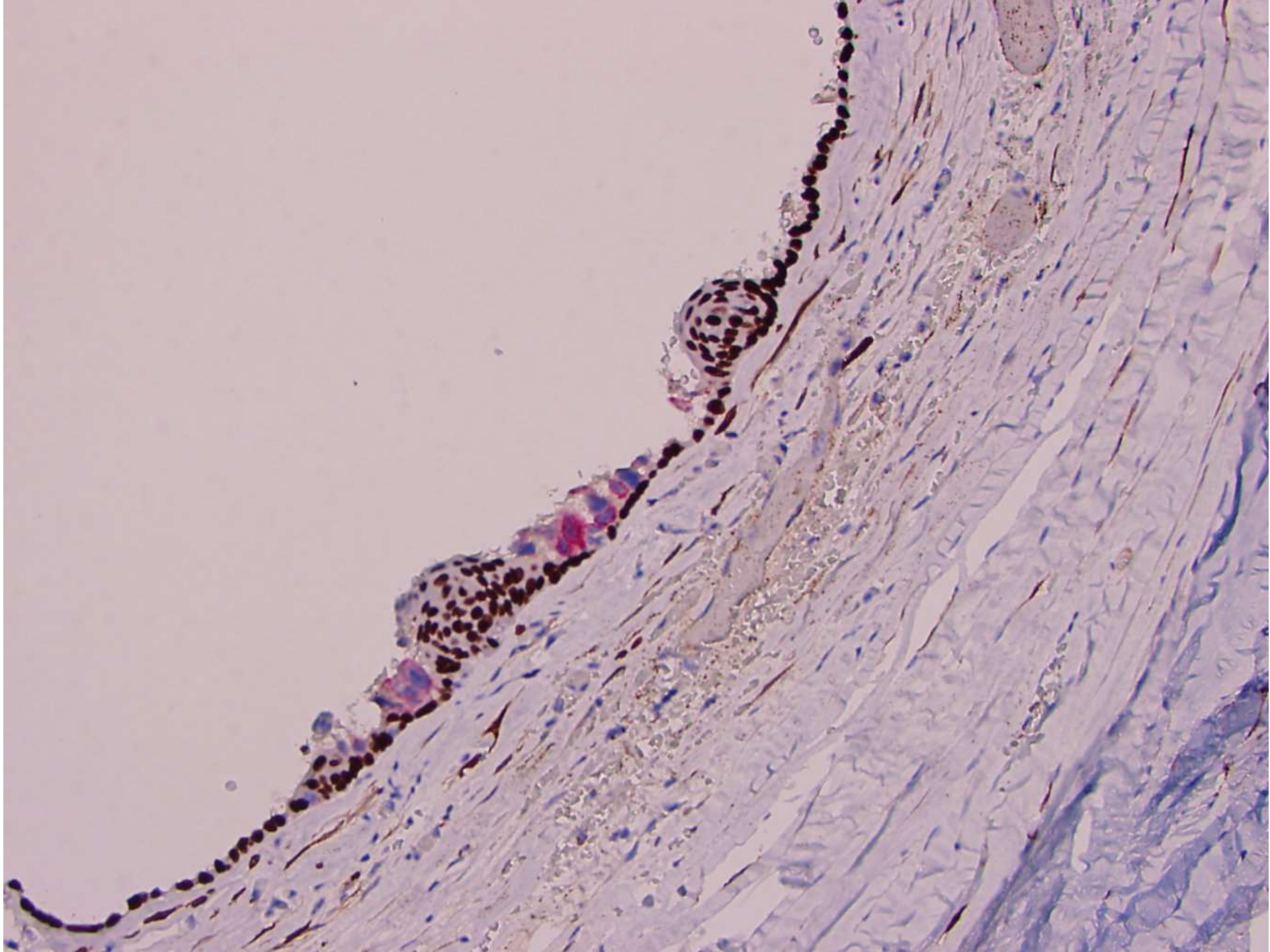


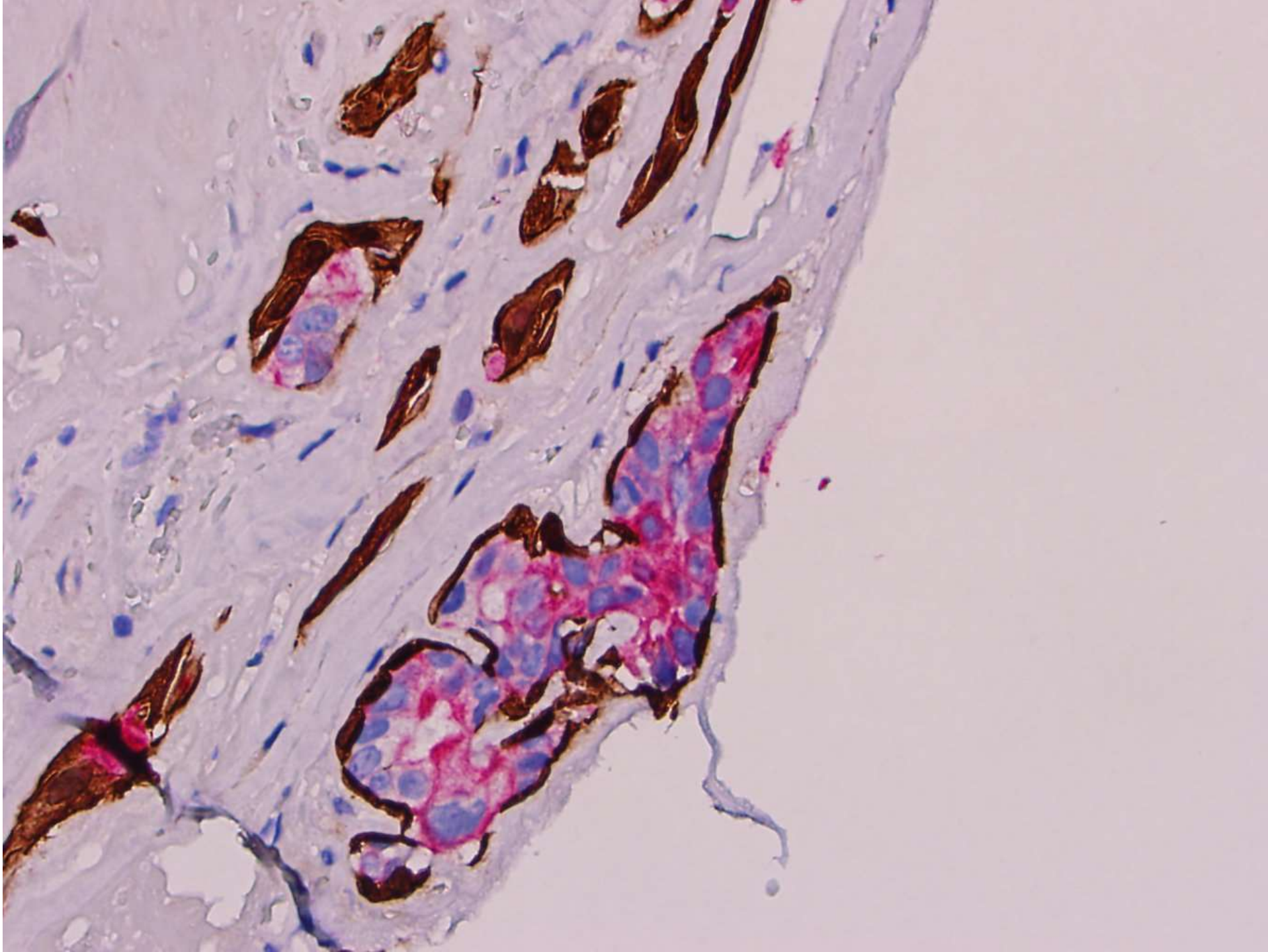












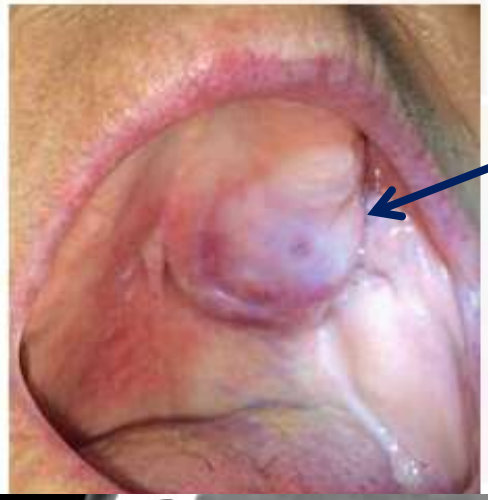
DIAGNOSIS?

Dx:DCIS involving implant capsule

SB 6104

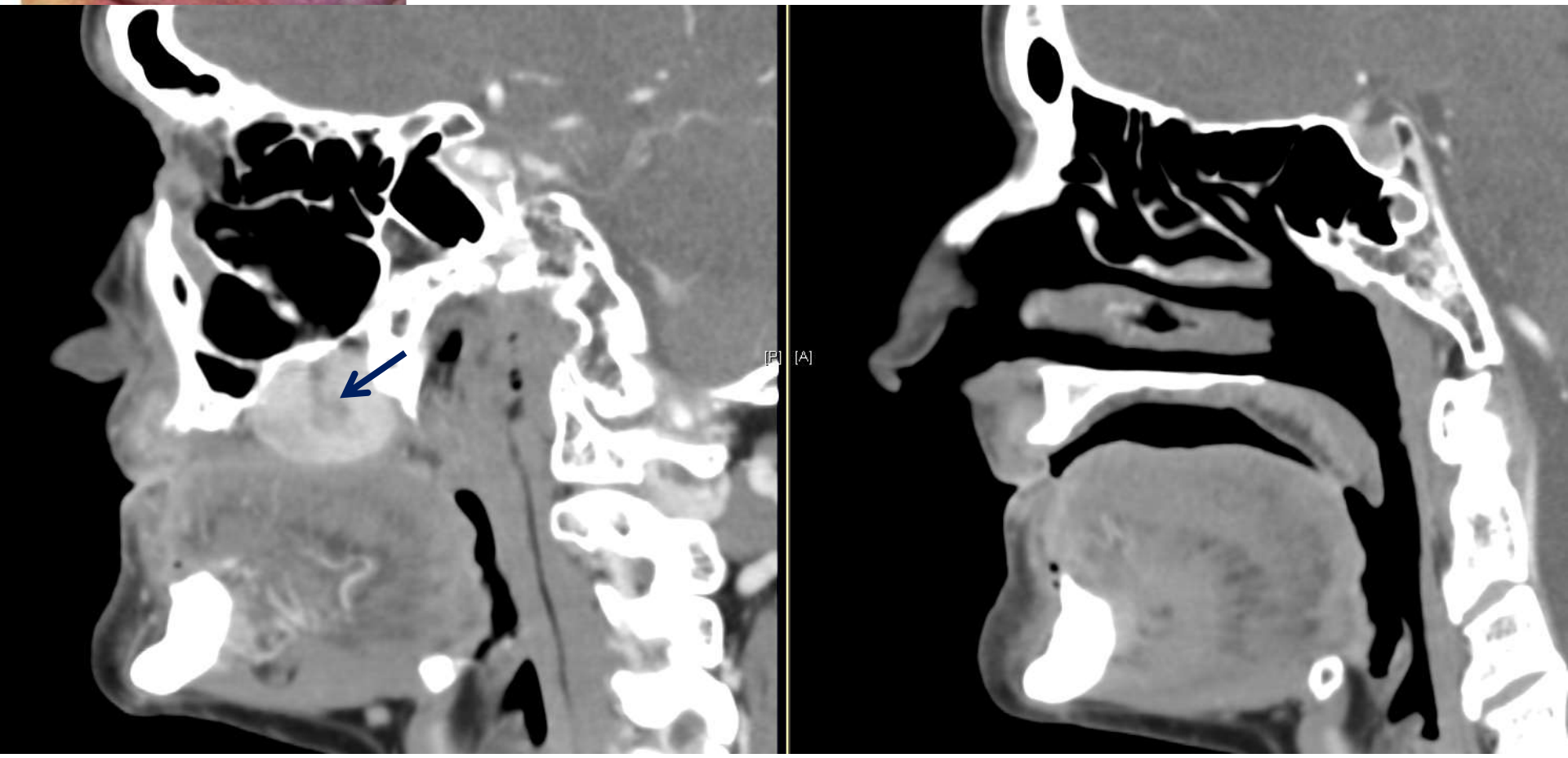
Allison Zemek/John Higgins; Stanford

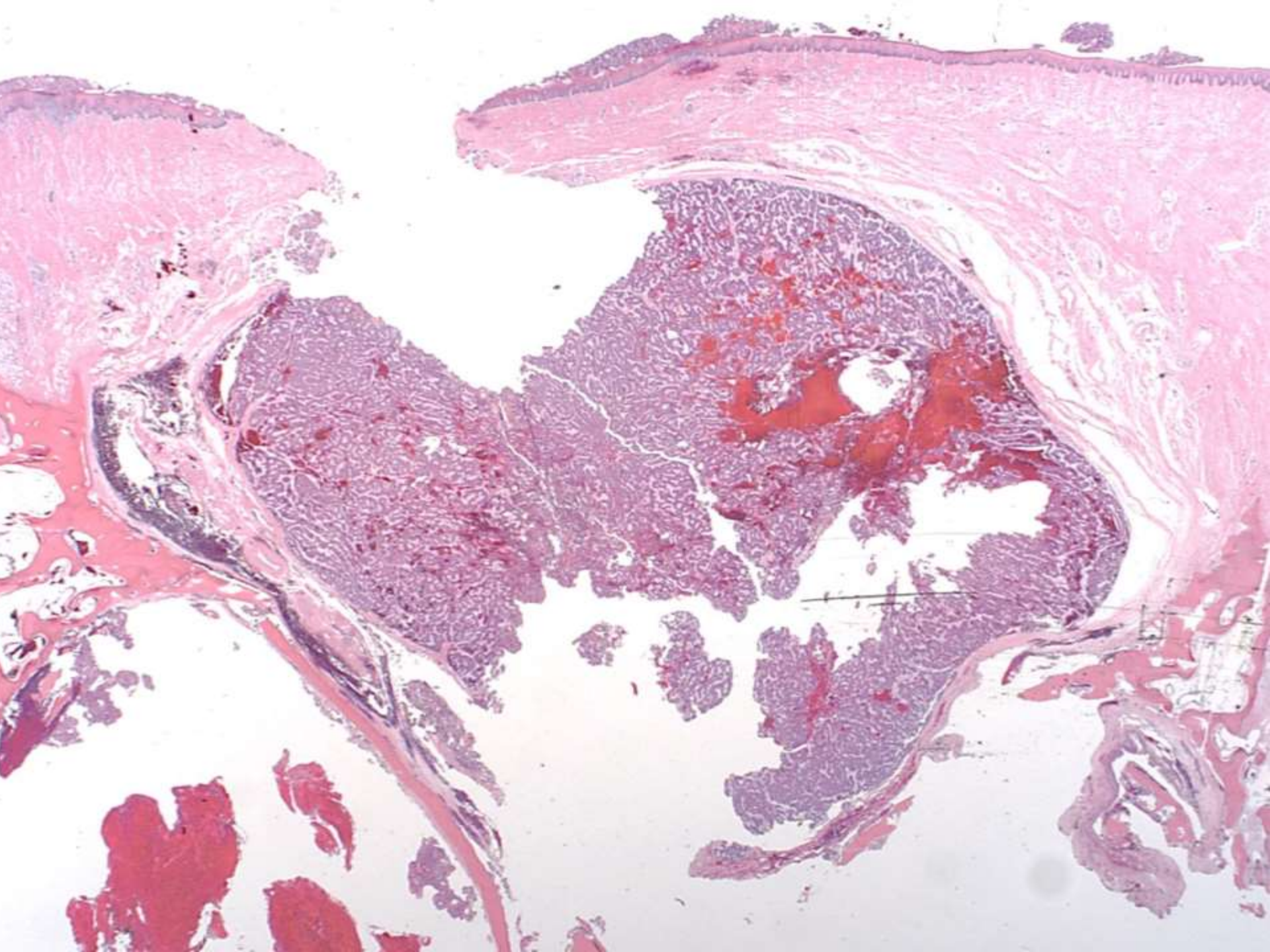
66-year-old female with left palate mass with evidence of deep extension on the CT scan, extending to the posterolateral border of the palate and pterygopalatine fossa.

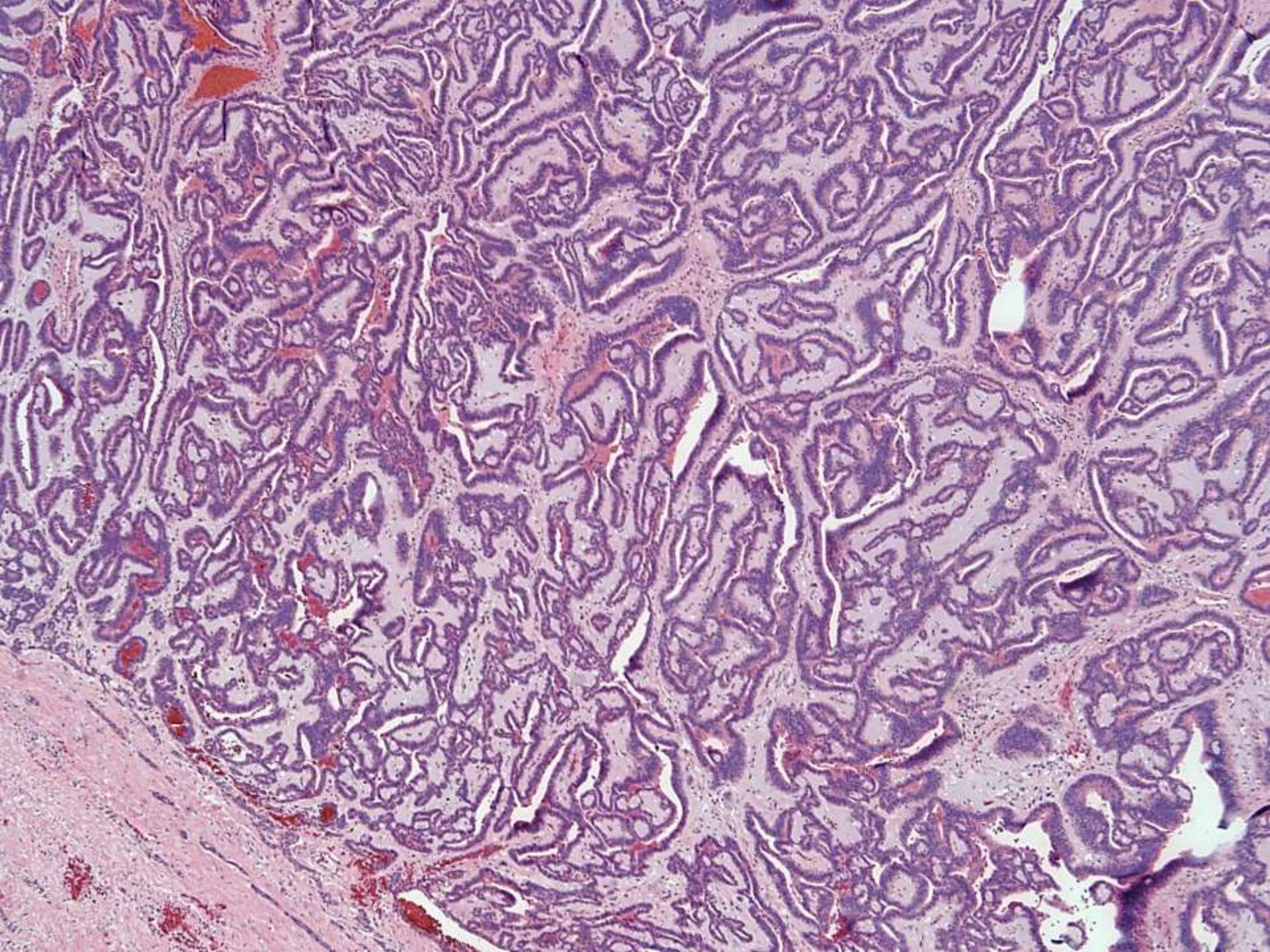


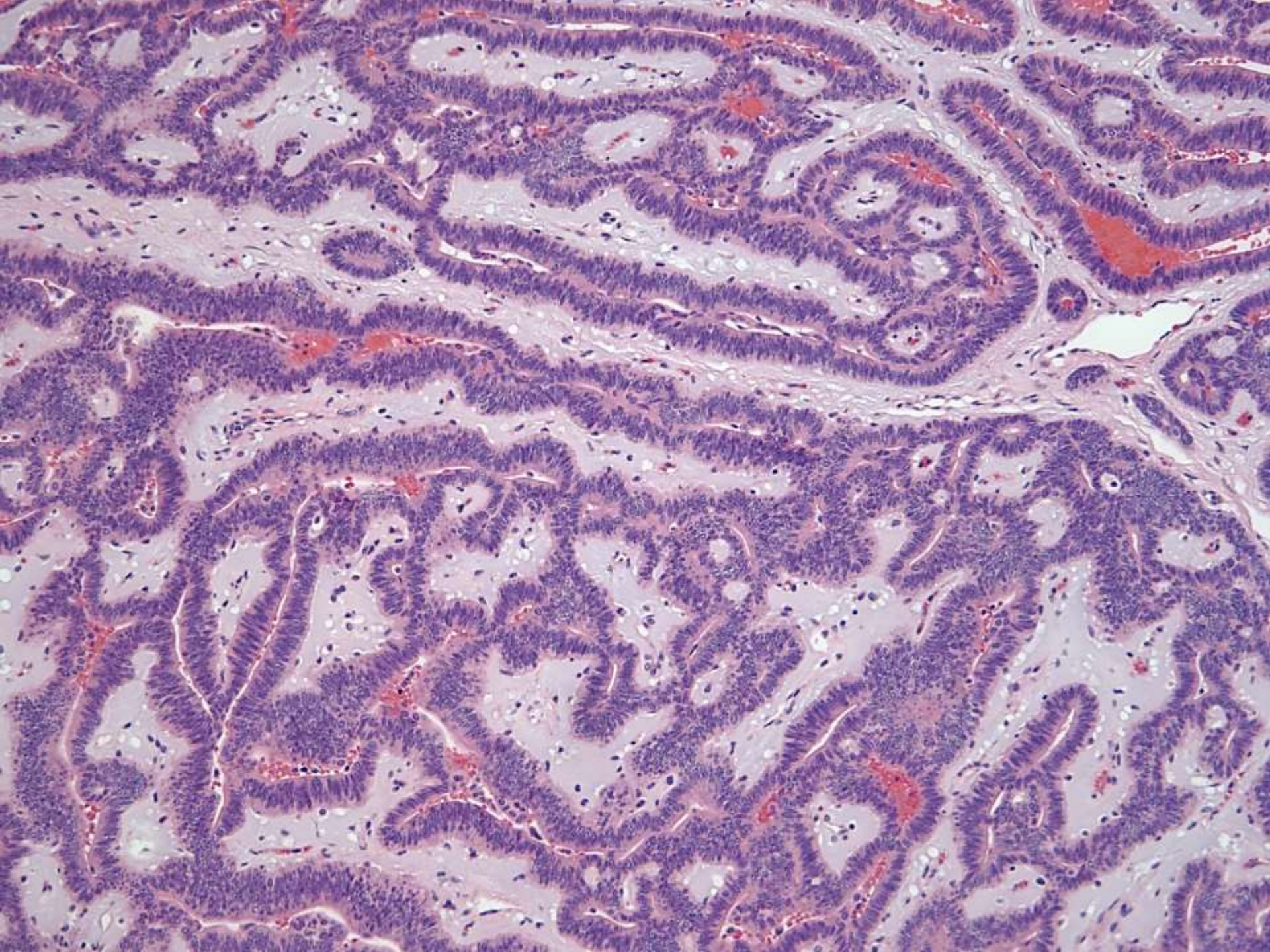
Left palate mass

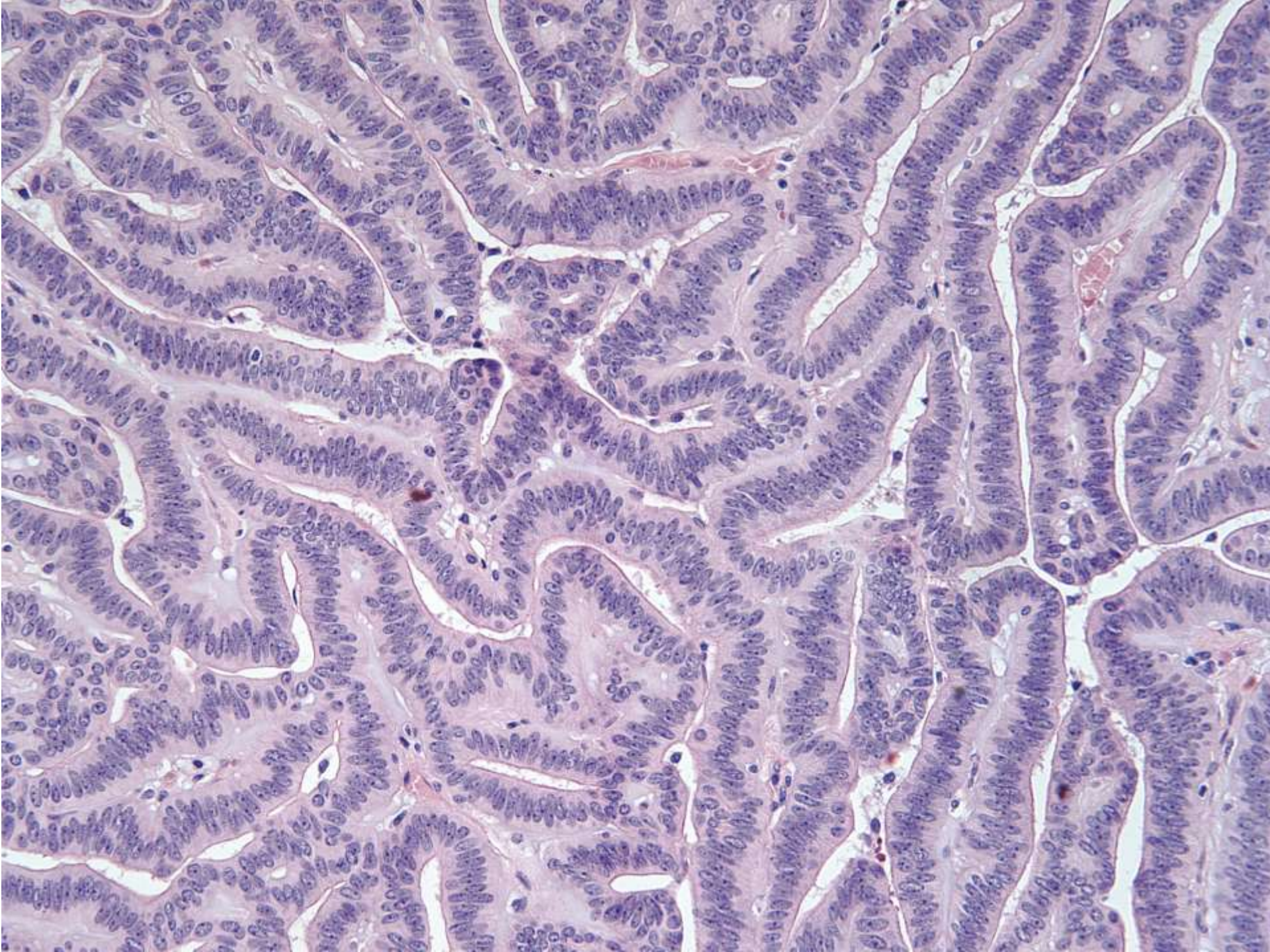
CT face with contrast:
2.8 cm lobular submucosal mass of left paramedian palate











DIAGNOSIS?

Canalicular Adenoma

Clinical features:

- Mean age 65y, slight female predominance
- Primarily oral (upper lip 74%, buccal 12%, palate)
- Rarely major salivary glands
- Small, non-ulcerating, painless, slow-growing mass

Canalicular Adenoma

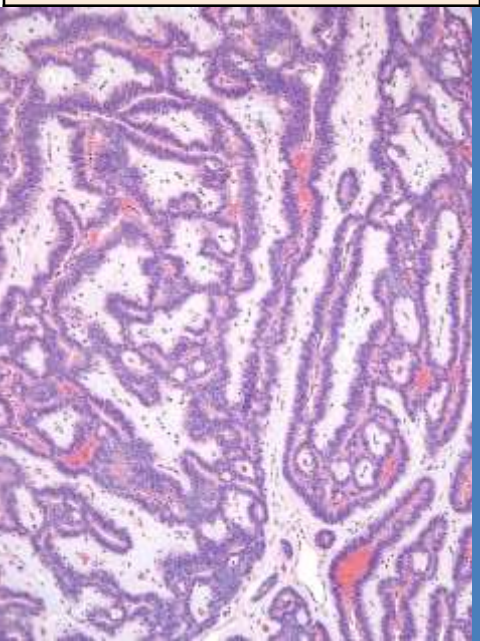
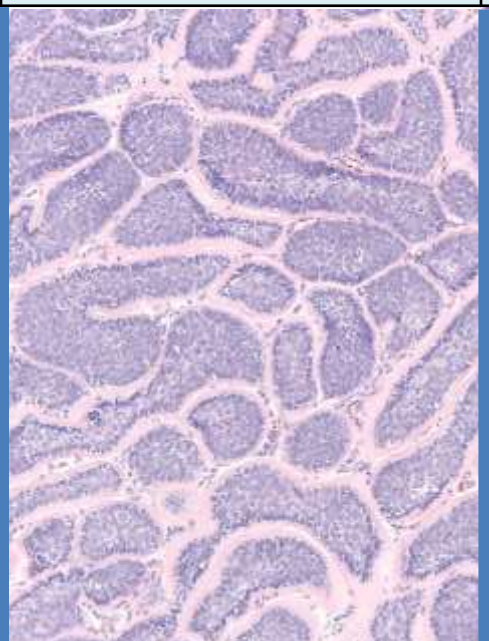
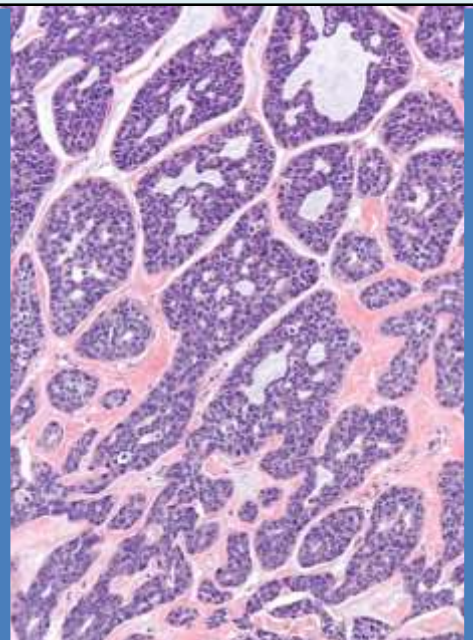
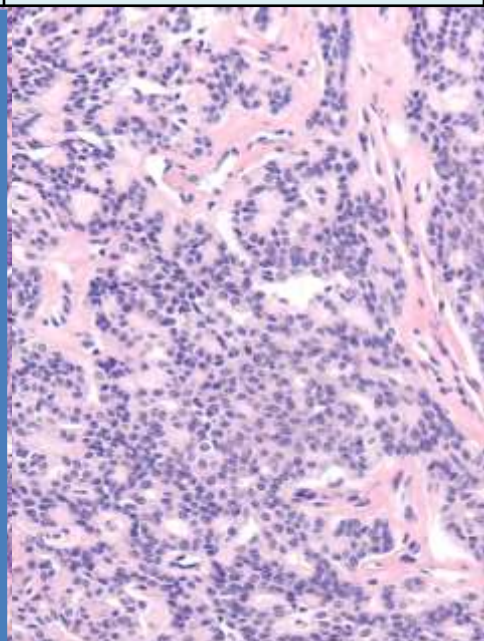
Histopathologic features:

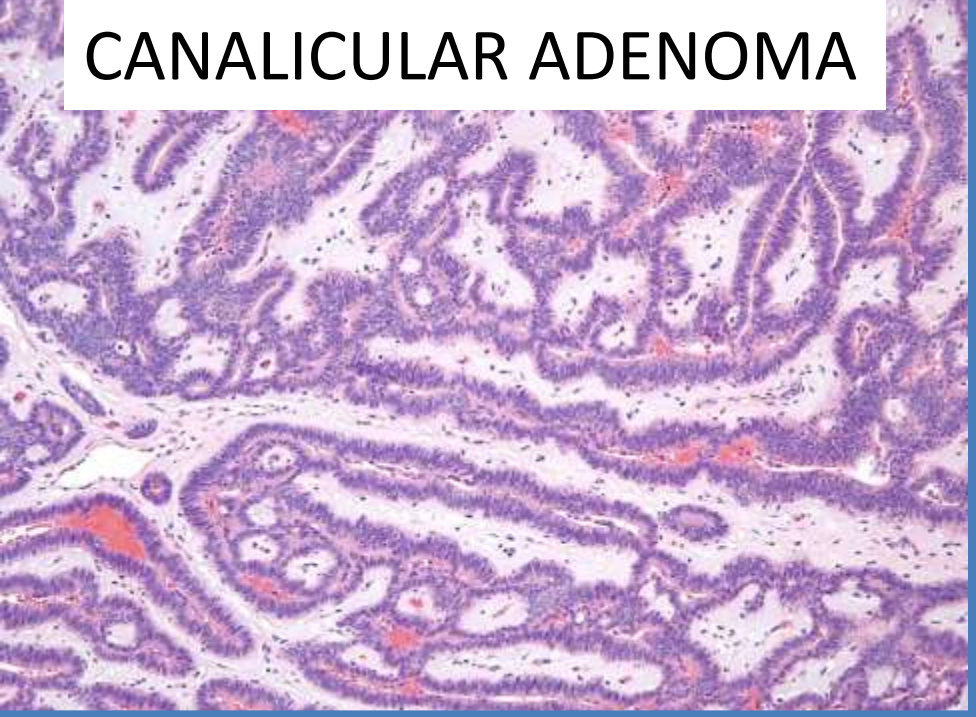
- Well circumscribed
- Bilayered strands of cuboidal/columnar cells
- Bland oval nuclei, no mitoses
- Edematous stroma with capillaries

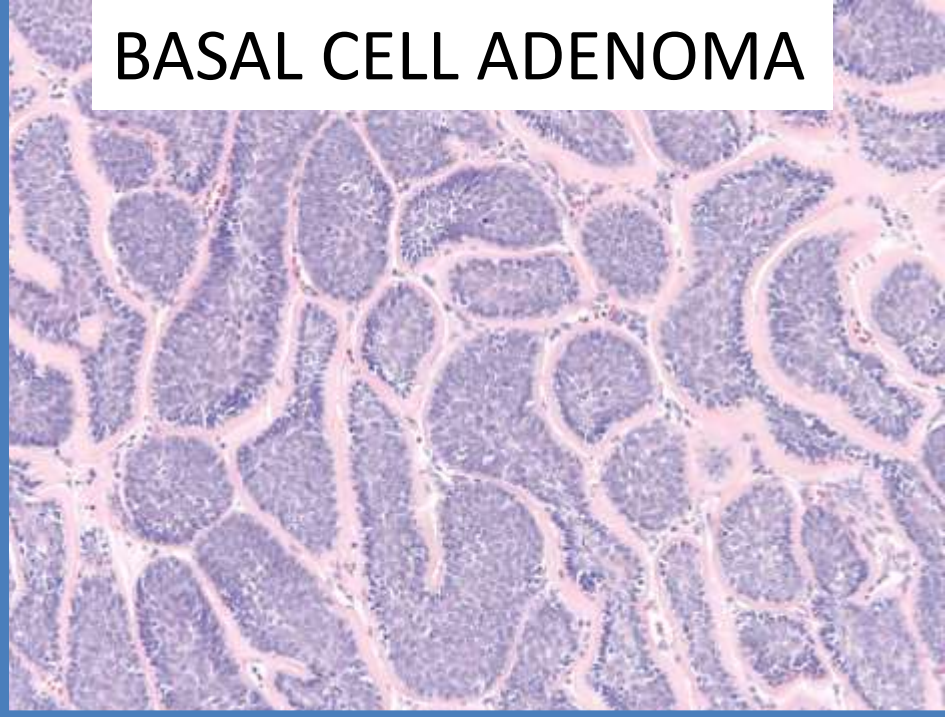
Immunohistochemical features:

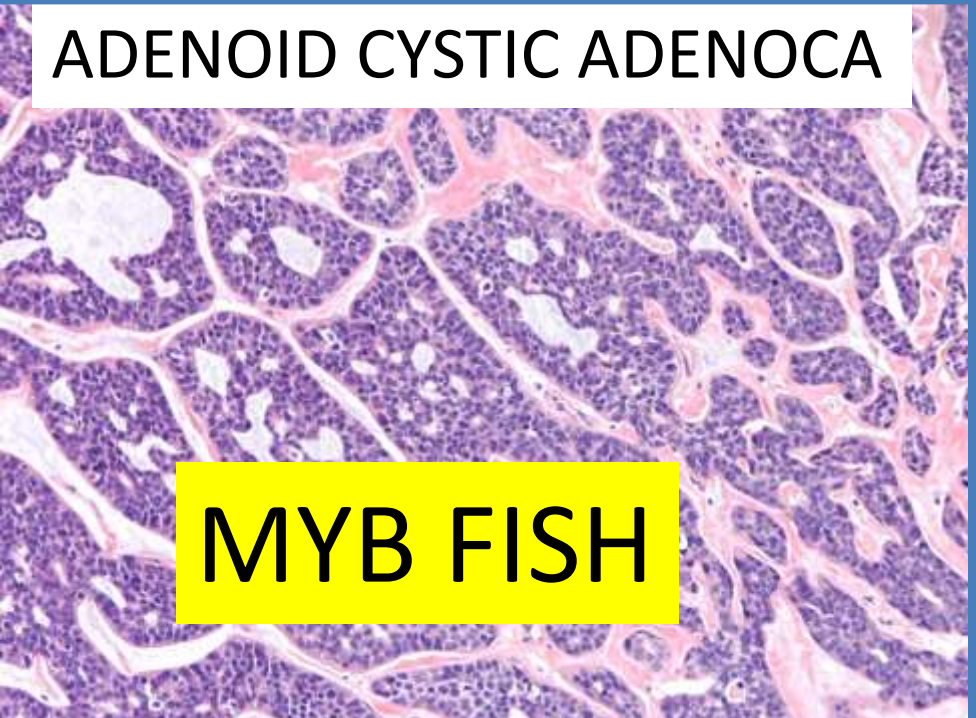
- Not generally necessary
- Absence of myoepithelial/basal cell component

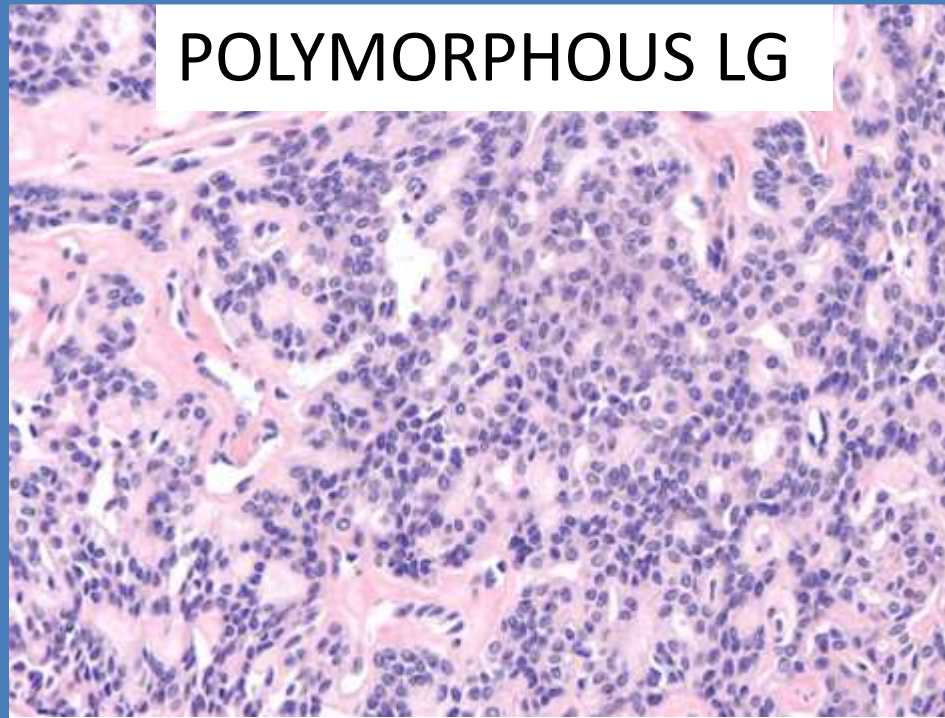
Canalicular Adenoma	Basal Cell Adenoma	Adenoid Cystic Carcinoma	Pleomorphous LG Adenoca
Minor salivary 1% of all tumors Recurrence rare	Parotid gland 2% of all tumors Membranous*	50% minor gland 10% of all malig	60% palate 25% of malg oral 10-20% recur
Bilayered cells Loose stroma CK, S100, GFAP+	Palisading cells Hyaline stroma p63, SMA, MSA	Cribriform Pseudocyts PAS, CD117, p63	LG cells Varied patterns CK, S100, vim


CANALICULAR ADENOMA


BASAL CELL ADENOMA


ADENOID CYSTIC ADENOCA
MYB FISH


POLYMORPHOUS LG

Canalicular Adenoma

Treatment:

- Local surgical resection with negative margins

Prognosis:

- Recurrence is rare
- Multiple nodules or erosion into bone is rare

Follow up:

- No evidence of recurrence after 1.5 years

References

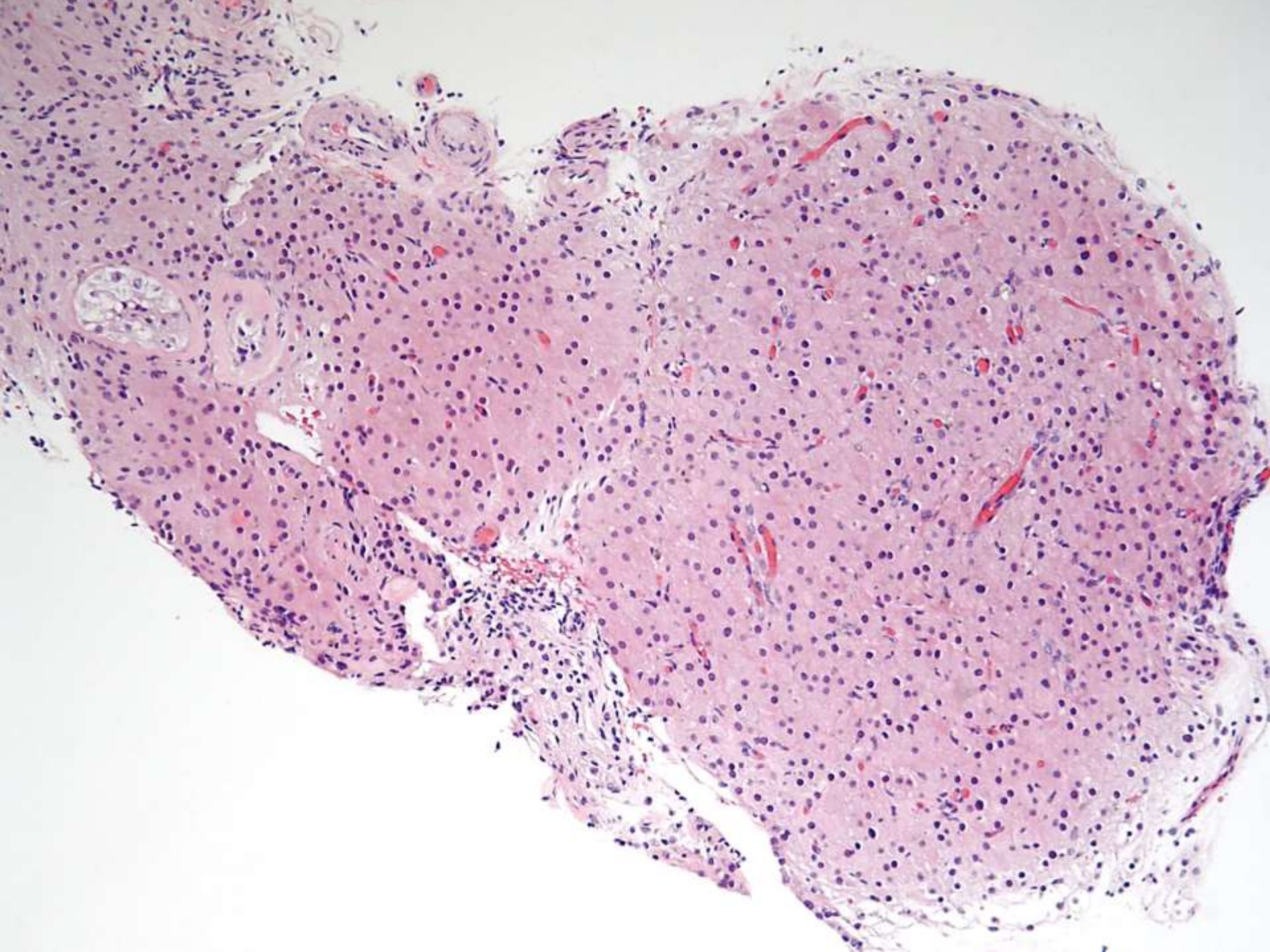
Thompson. Head and Neck Pathology.

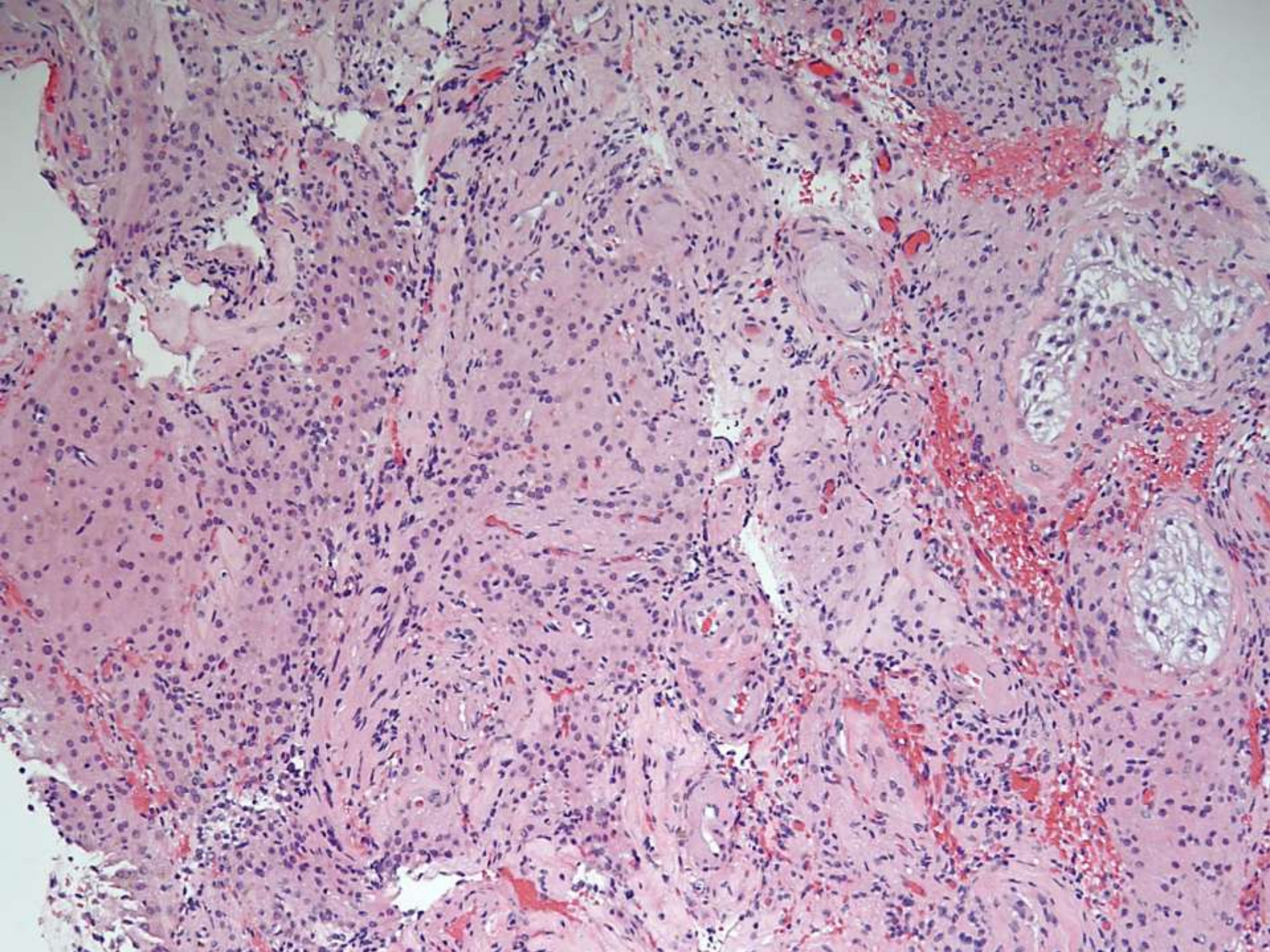
Fletcher. Diagnostic Histopathology of Tumors.

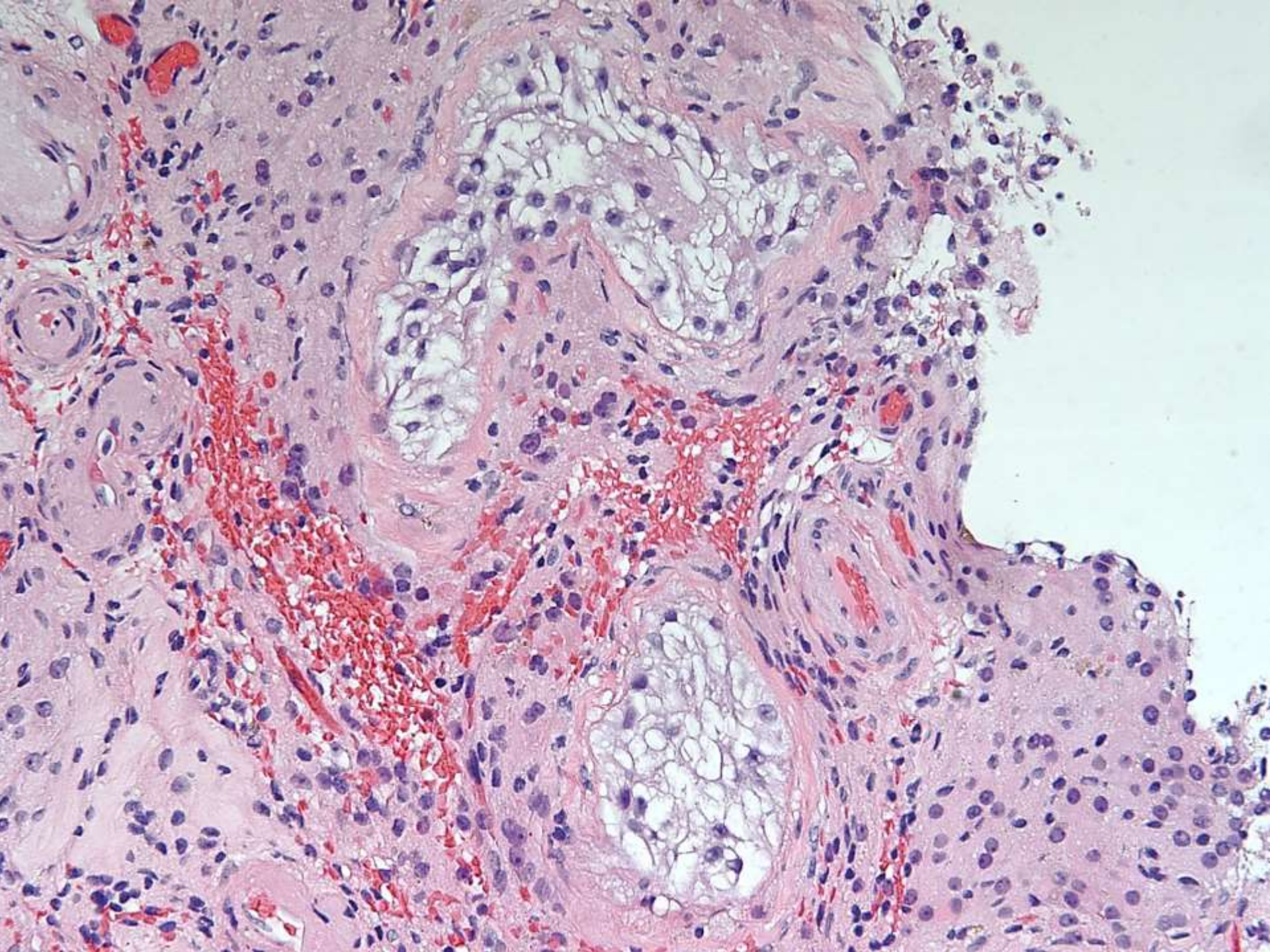
SB 6105

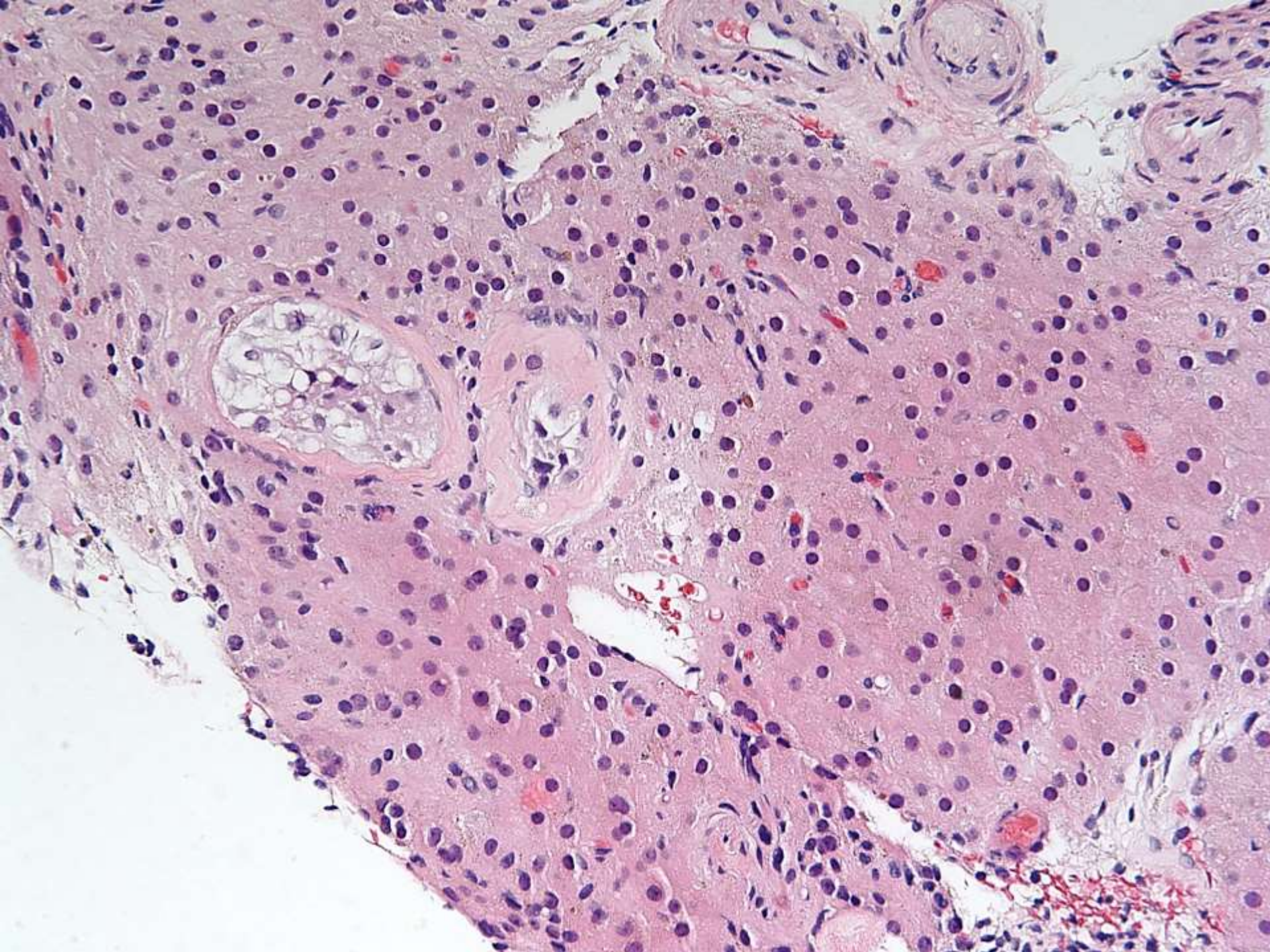
Allison Zemek/John Higgins; Stanford

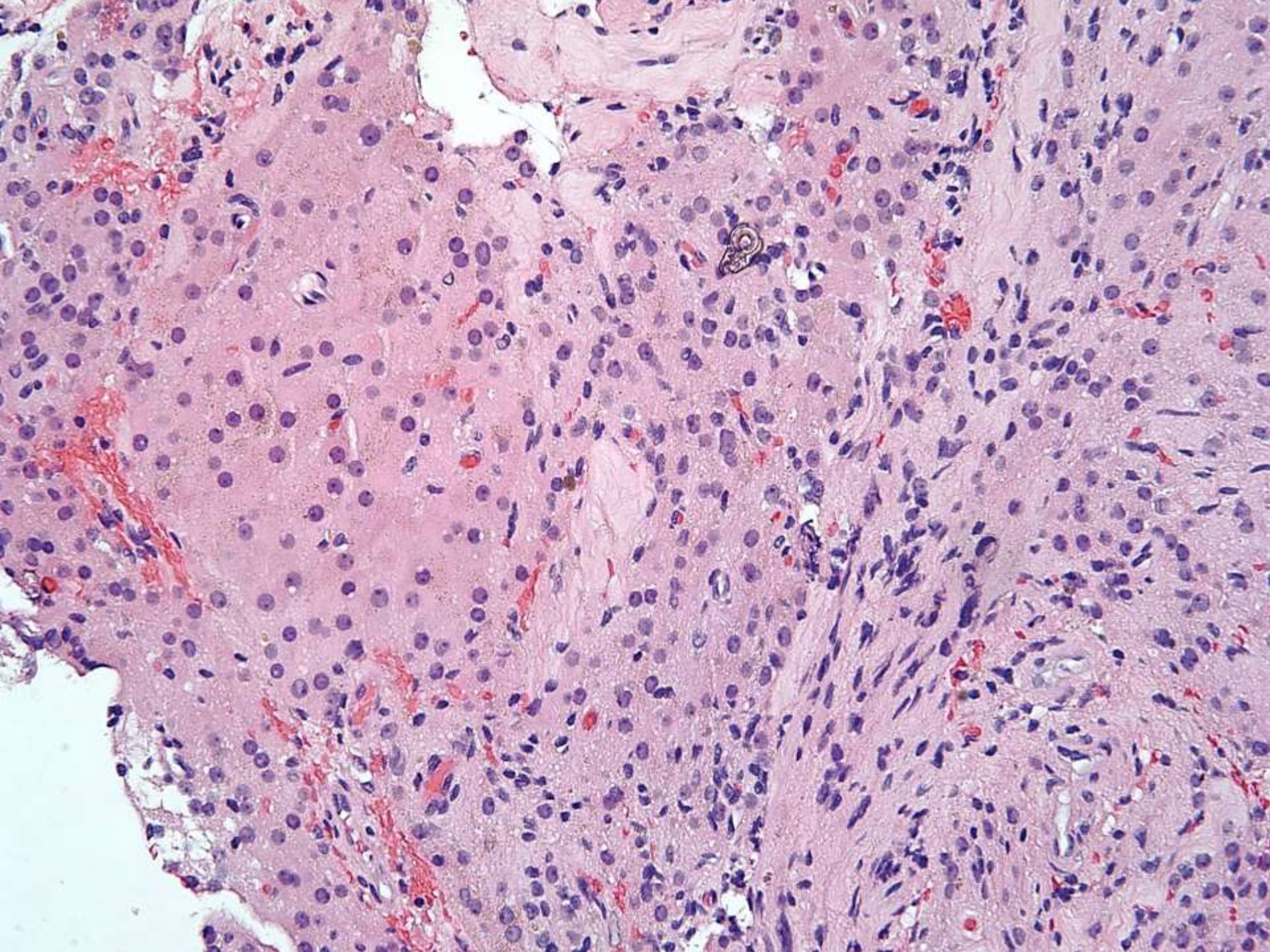
42-year-old man with azoospermia and elevated gonadotropins.











DIAGNOSIS?

Klinefelter Syndrome

Clinical features:

- Described in 1942 by Dr. Klinefelter
- Reduced body hair, gynecomastia, small testes, azoospermia, increased FSH/LH
- Only 25% are diagnosed

Pathogenesis:

- 47, XXY
- 48,XXXY and 46,XY/46,XXY mosaicism
- 46, XX (translocation of testis-determining factor)

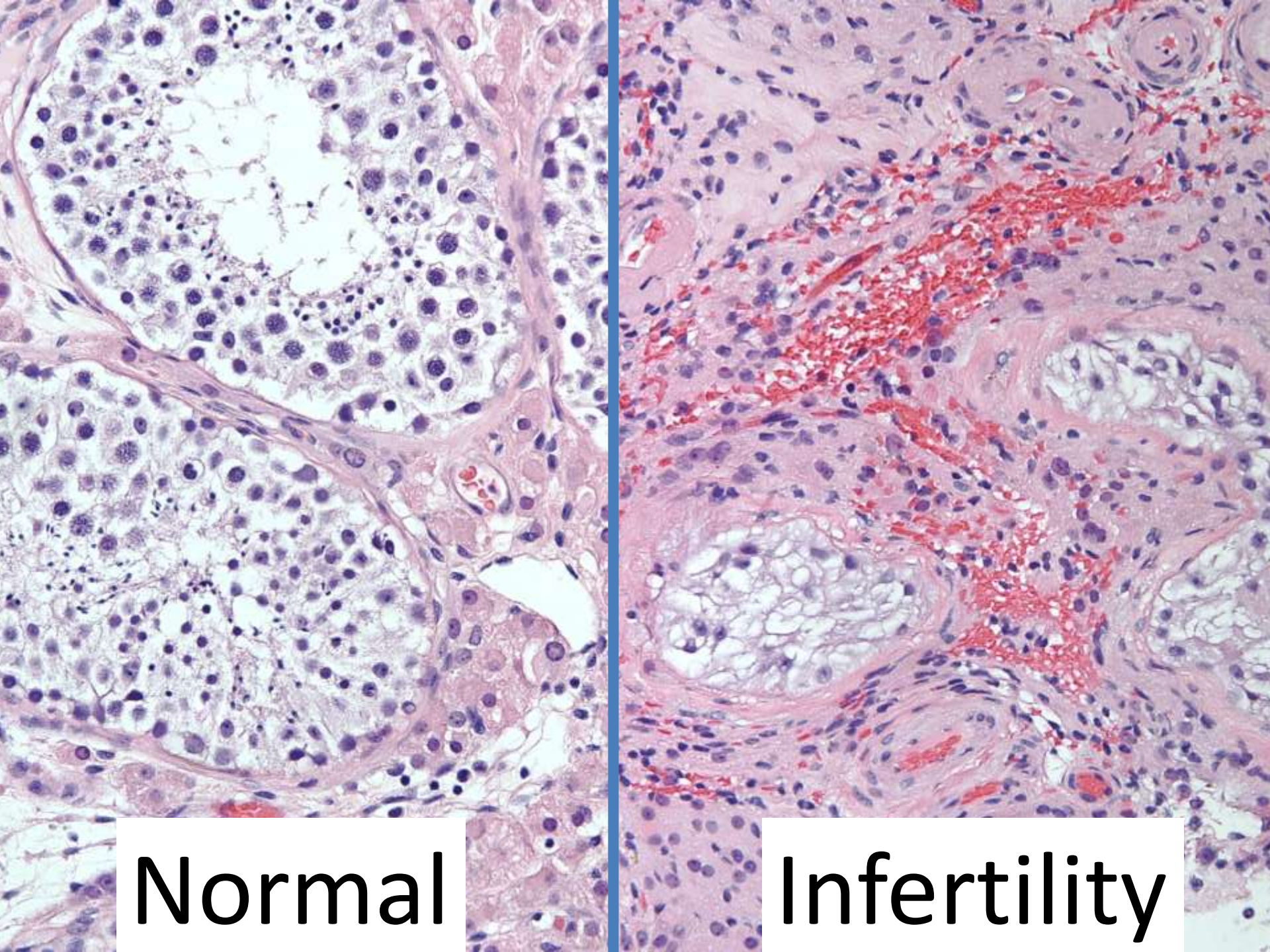
Klinefelter Syndrome

Histopathologic features of male infertility:

- Nodules of Leydig cells (esp in Klinefelter)
- Normal-reduced tubule size, atrophic
- Fibrotic interstitium
- 1% have malignant intratubular germ cells

Klinefelter syndrome

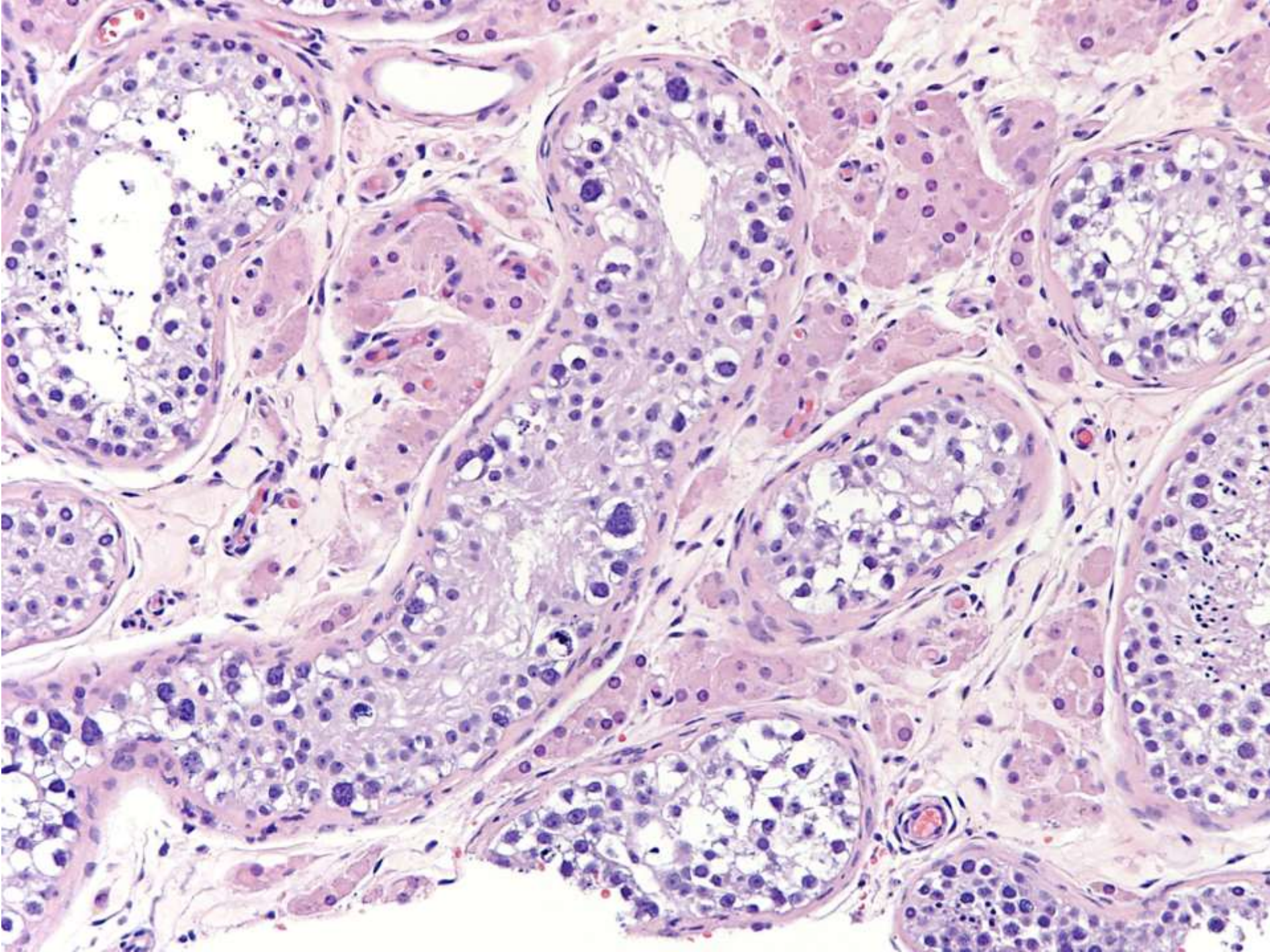
- Can be normal at birth
- Tubules may be lined by only Sertoli cells
- Marked tubular atrophy, sclerosis, Leydig cell nodules


Normal
Infertility

Malignancy risk in KS patiets

Davis et al. **Advances in the Interdisciplinary Care of Children with Klinefelter Syndrome.** Advances in Pediatrics 63 (2016) 15–46

- Malignant intratubular germ cells (1%)
- Breast cancer (3-7%)
- Extragonadal germ cell tumors (0.1%)
- Non-hodgkin lymphoma (+/-)



Klinefelter Syndrome

Treatment:

- Up to 50% of KS are infertile, but ~50% successful ART
- Microdissection of testis
- Exogenous testosterone, genetic counseling

Prognosis:

- Variable, psychosocial impairment
- Other morbidities chronic bronchitis, bronchiectasis, emphysema, varicose veins, SLE, diabetes

References

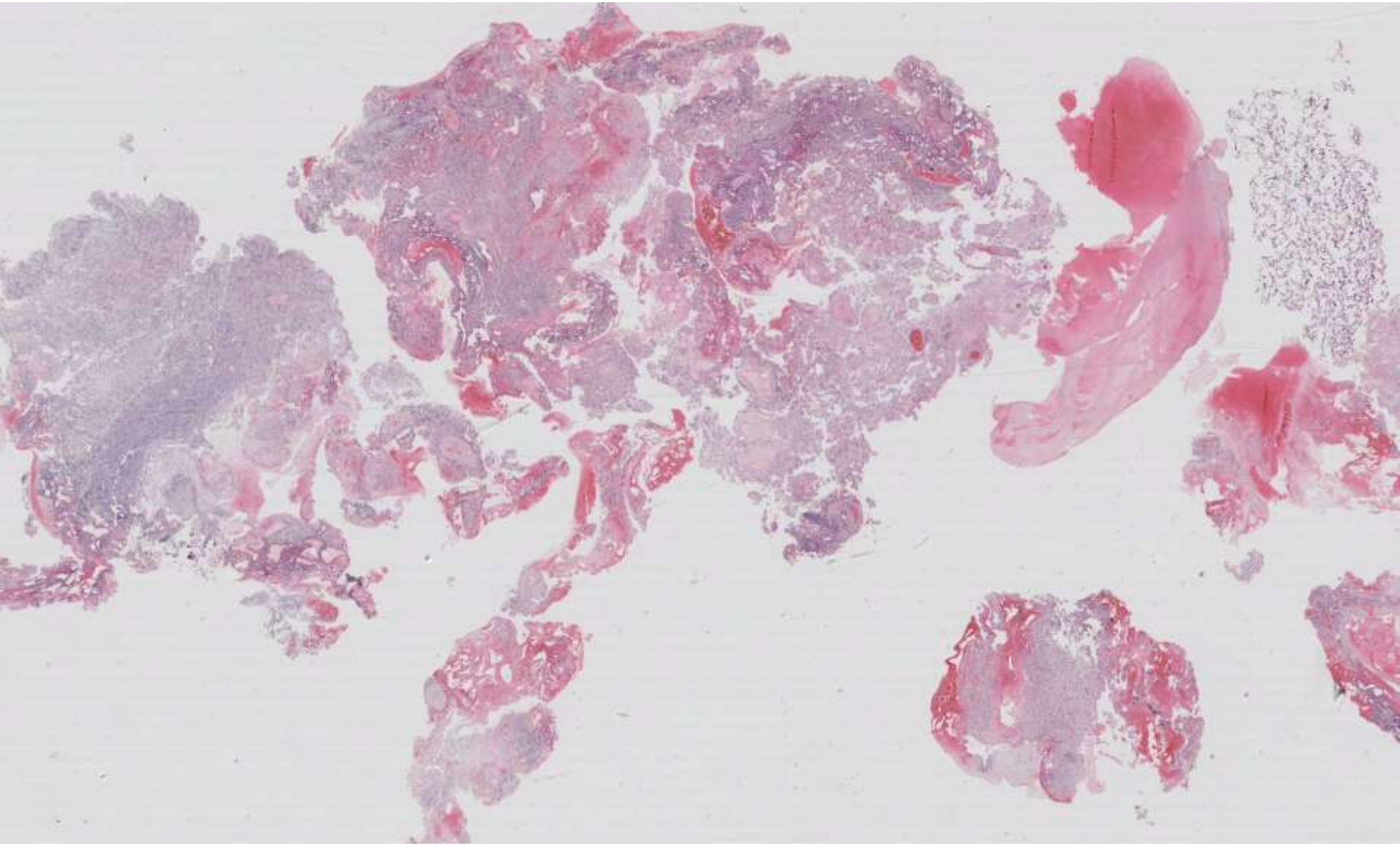
Davis et al. Advances in the Interdisciplinary Care of Children with Klinefelter Syndrome. Advances in Pediatrics 63 (2016) 15–46

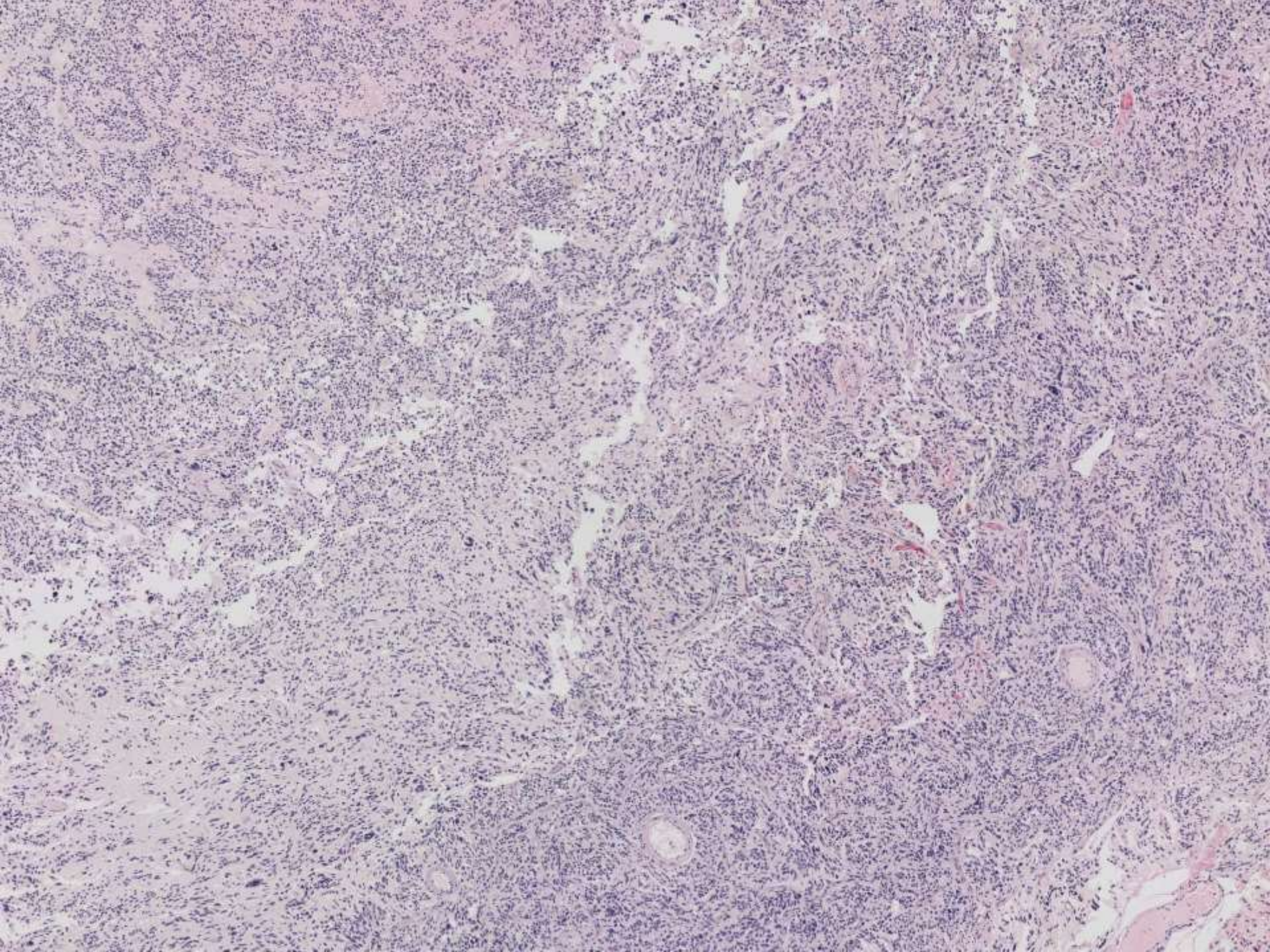
Genitourinary Pathology: Foundations in Diagnostic Pathology, Second Edition.

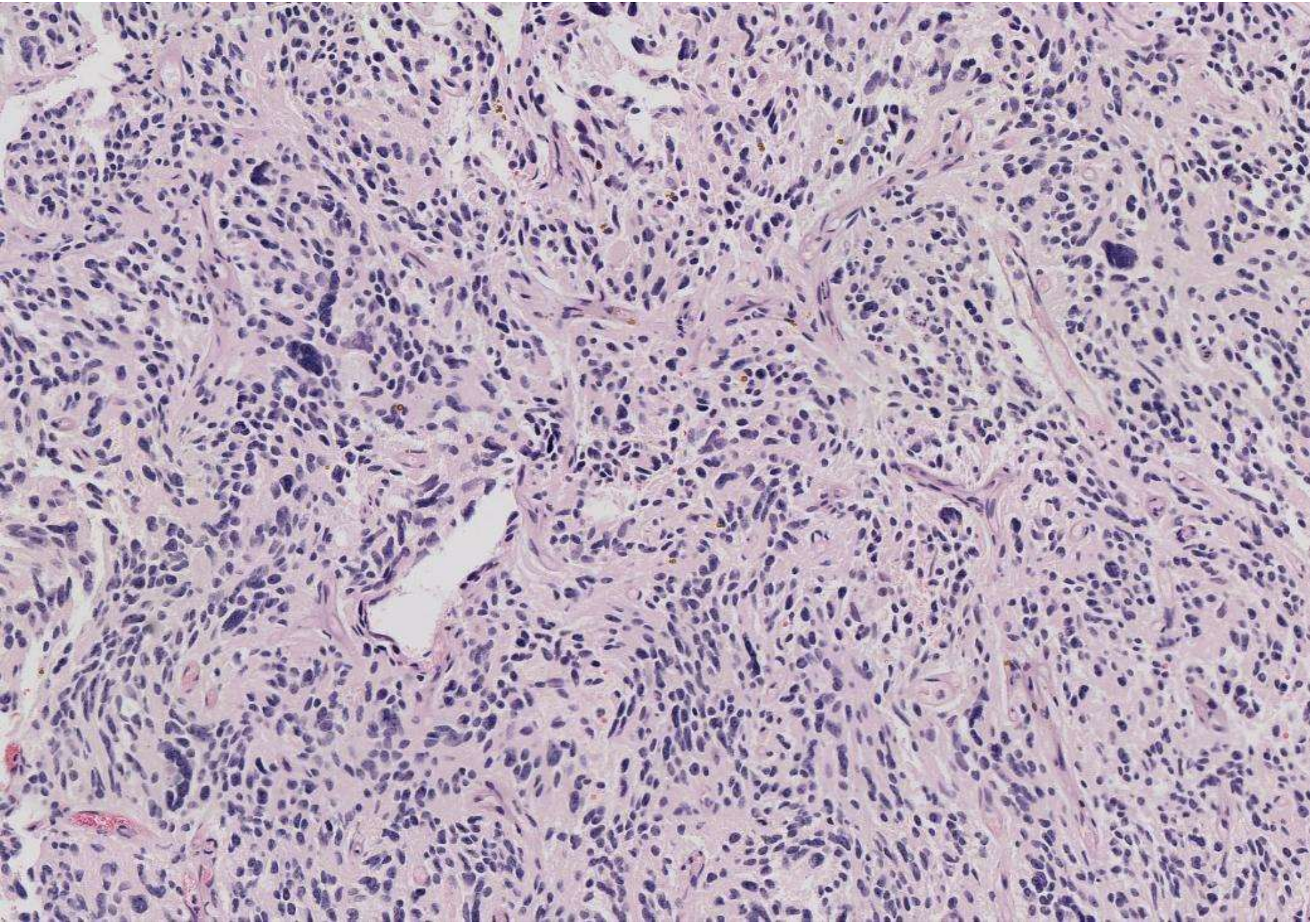
SB 6106 (scanned slide available)

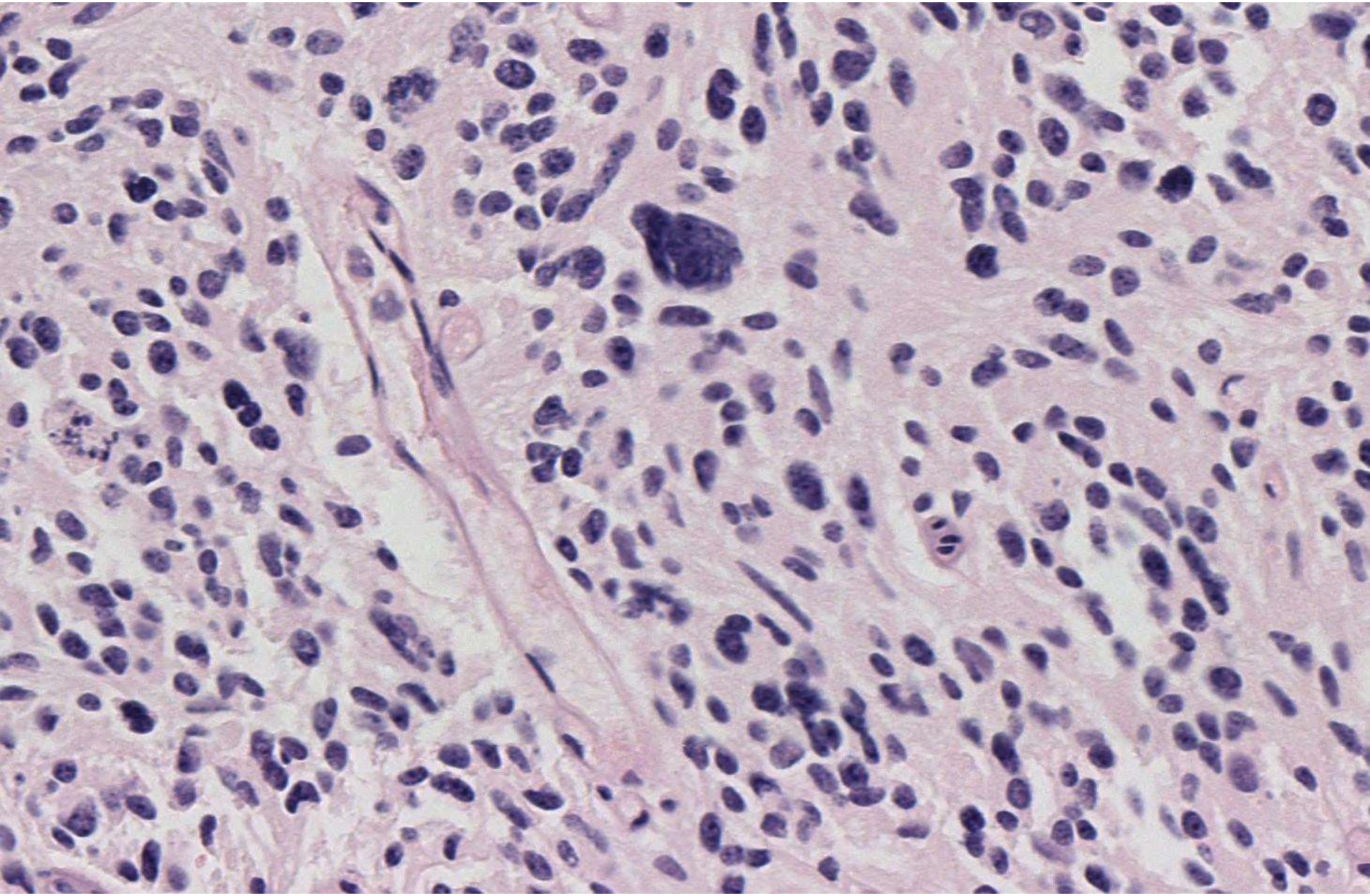
David Levin; Washington Hospital

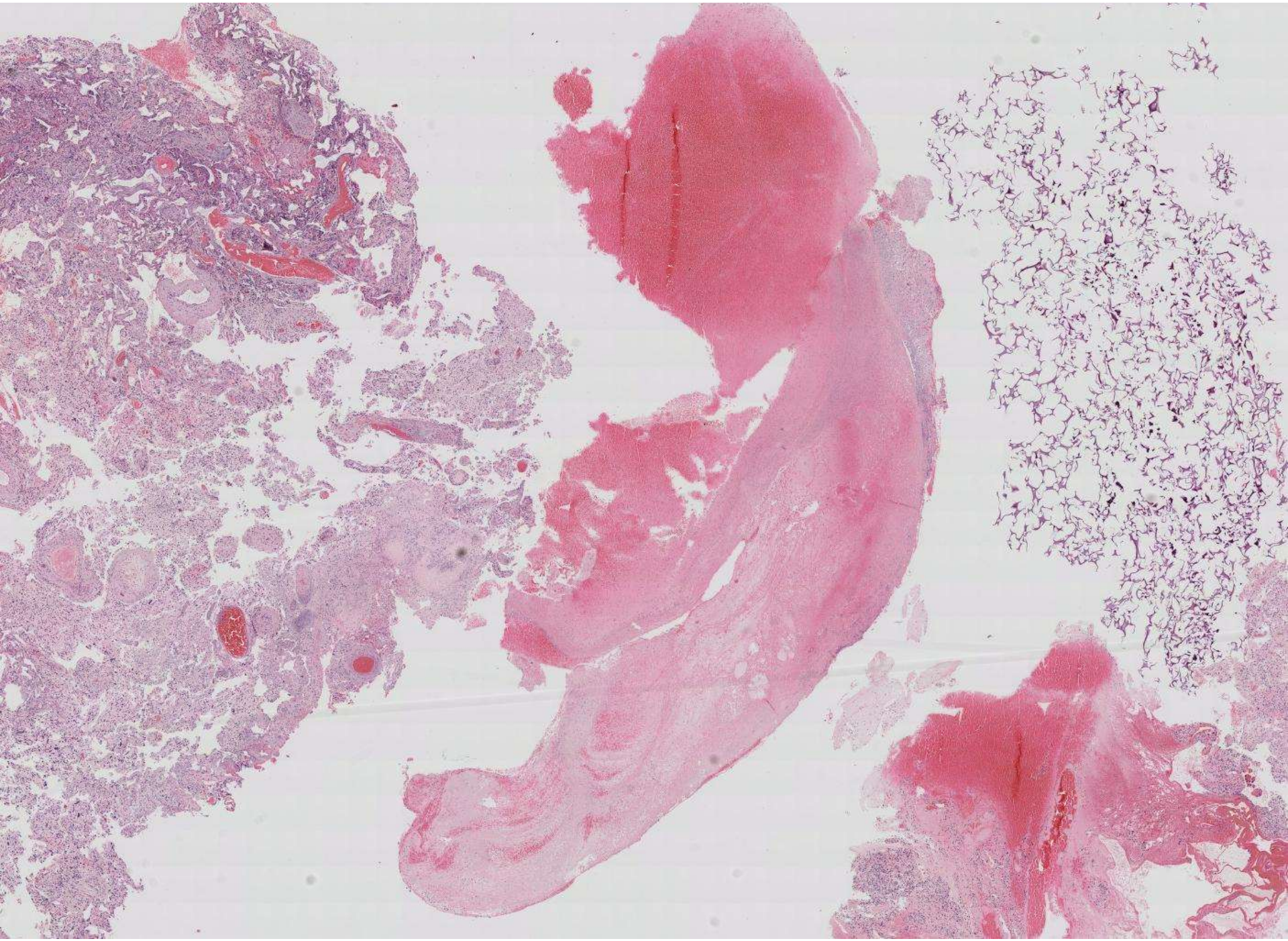
Posterior fossa brain tumor. Gradual onset of symptoms over the past year, MRI shows a midline cerebellar lesion occupying most of vermis. Pre-op DDx includes AVM with evolving seroma and hemangioblastoma.

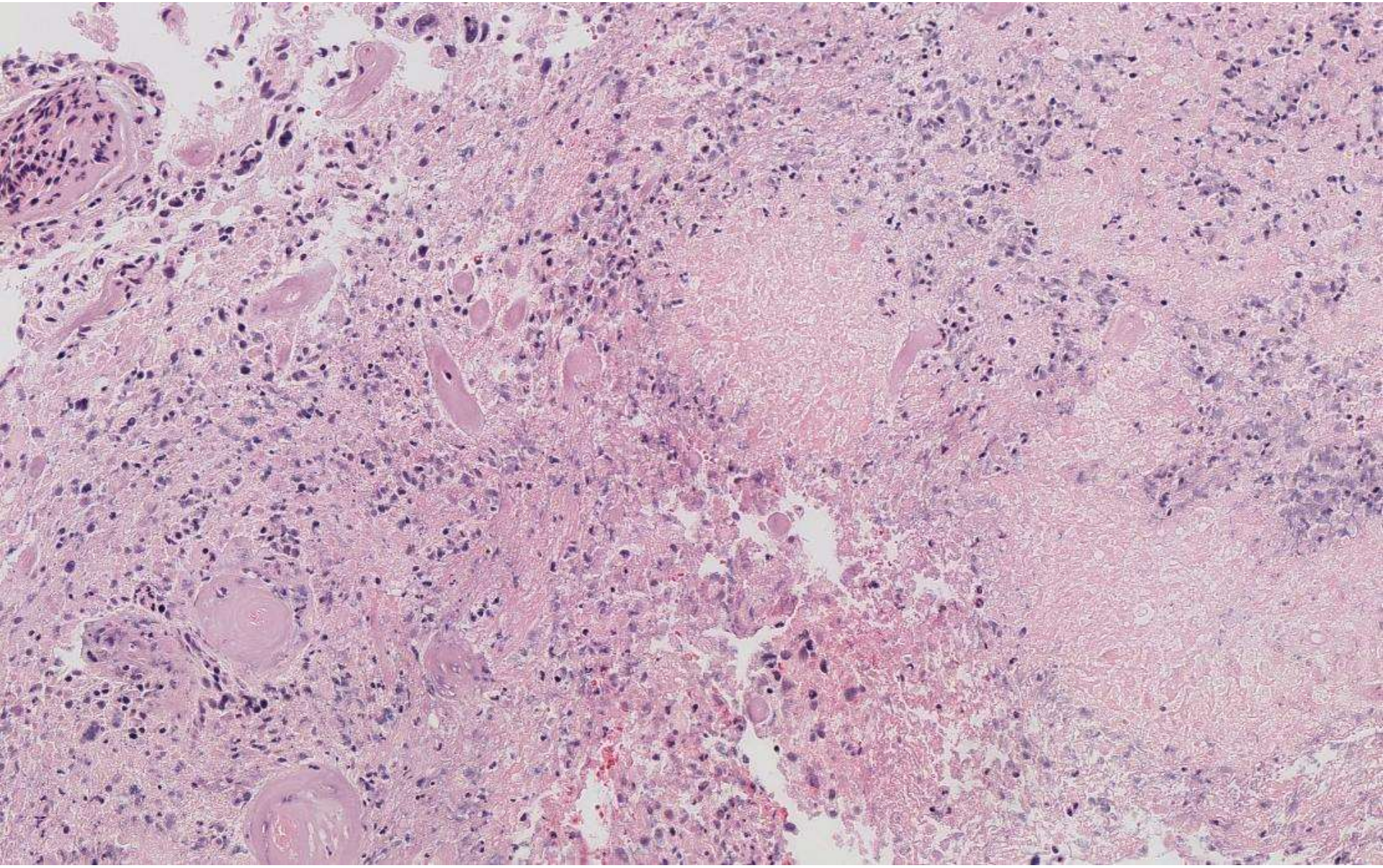


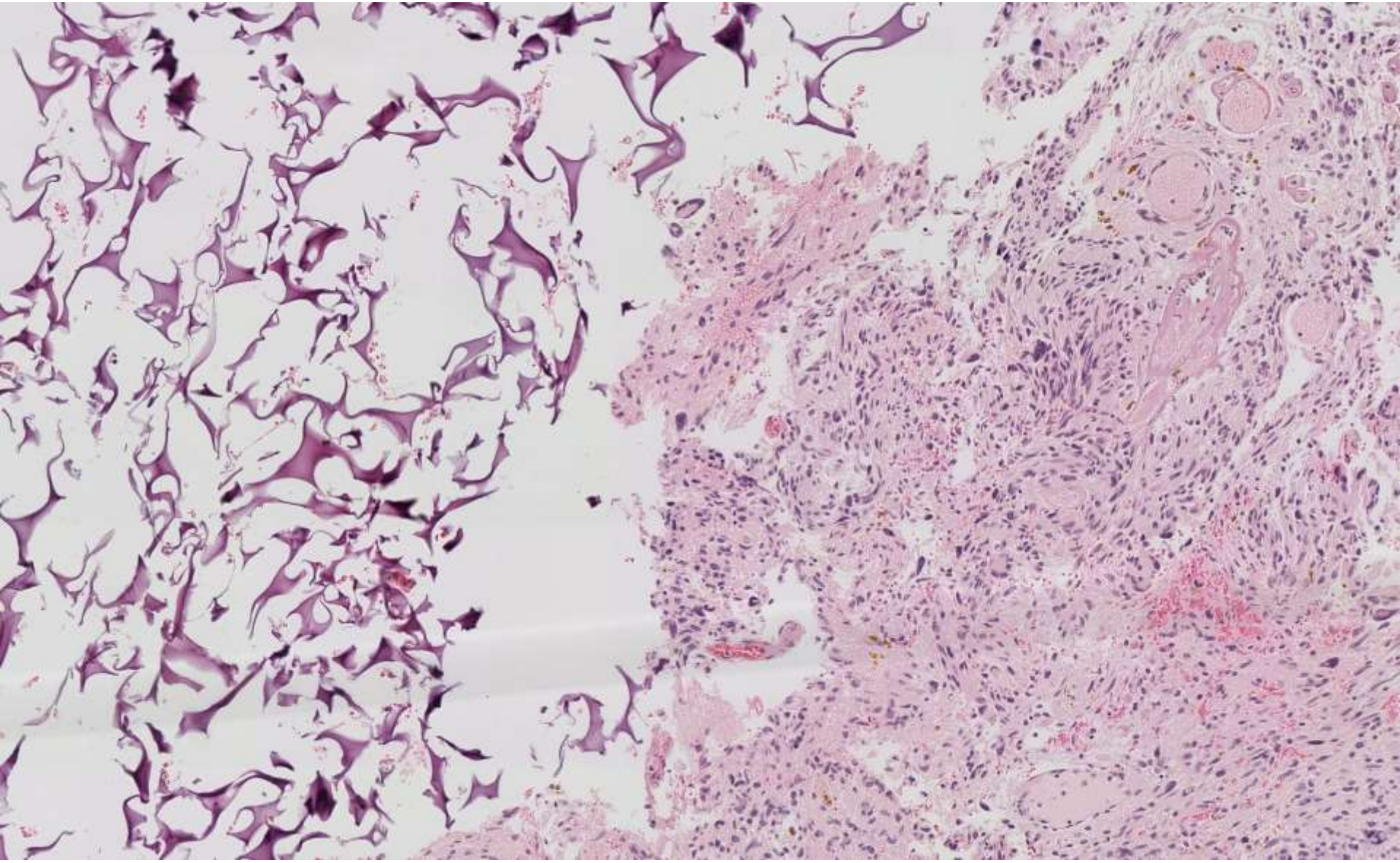


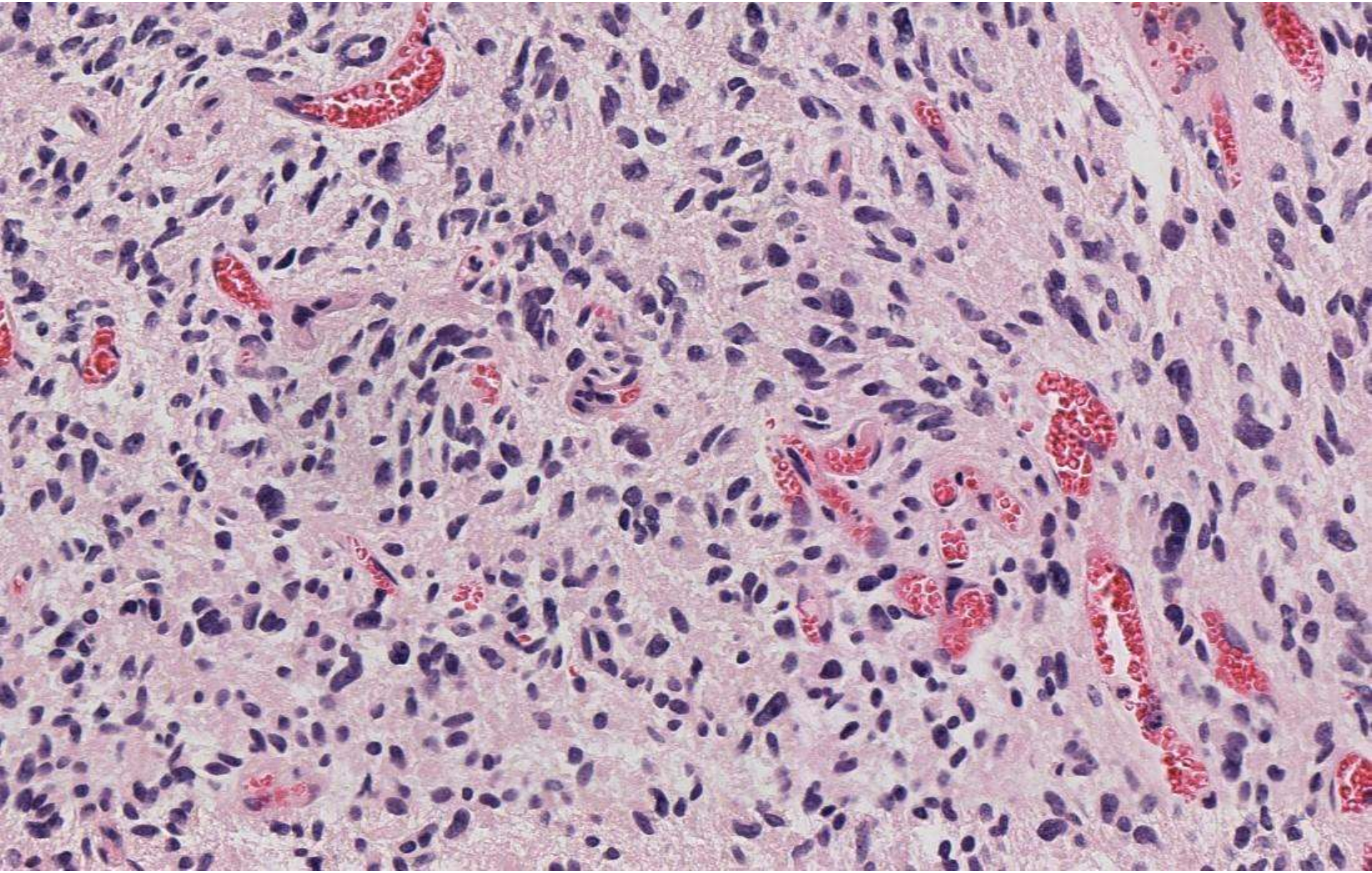


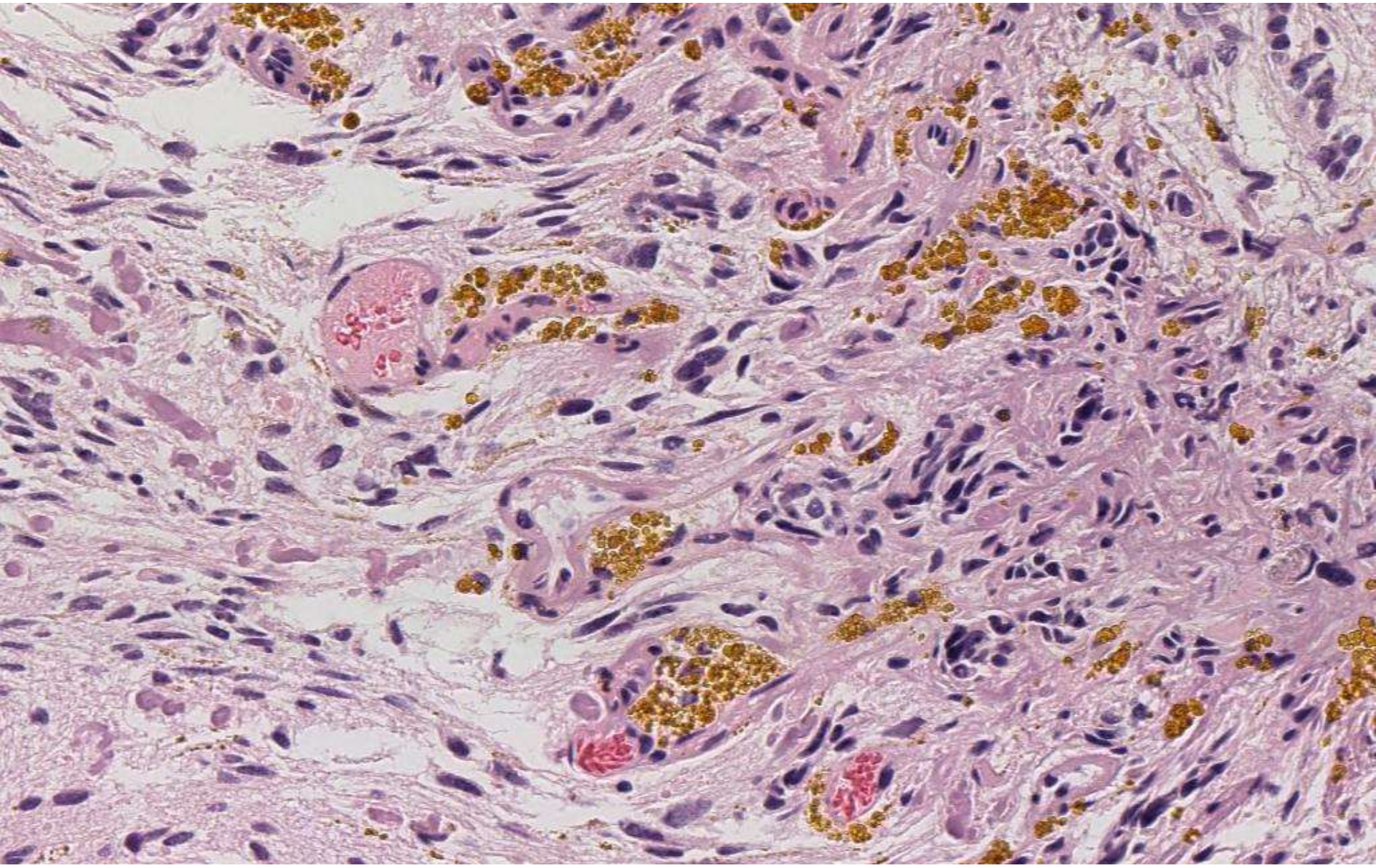












DIAGNOSIS?

LOW GRADE GLIOMA, FAVOR PILOCYTIC ASTROCYTOMA

- The pt is status post pre-op embolization 1 week prior to resection
- Microvascular proliferation
- No mitotic figures
- Ki-67 1-3% - Low proliferation rate
- Rosenthal fibers
- Positive for GFAP, S100
- Negative for AE1/AE3, EMA, Inhibin, CD10
- FISH neg for BRAF V600E mutation

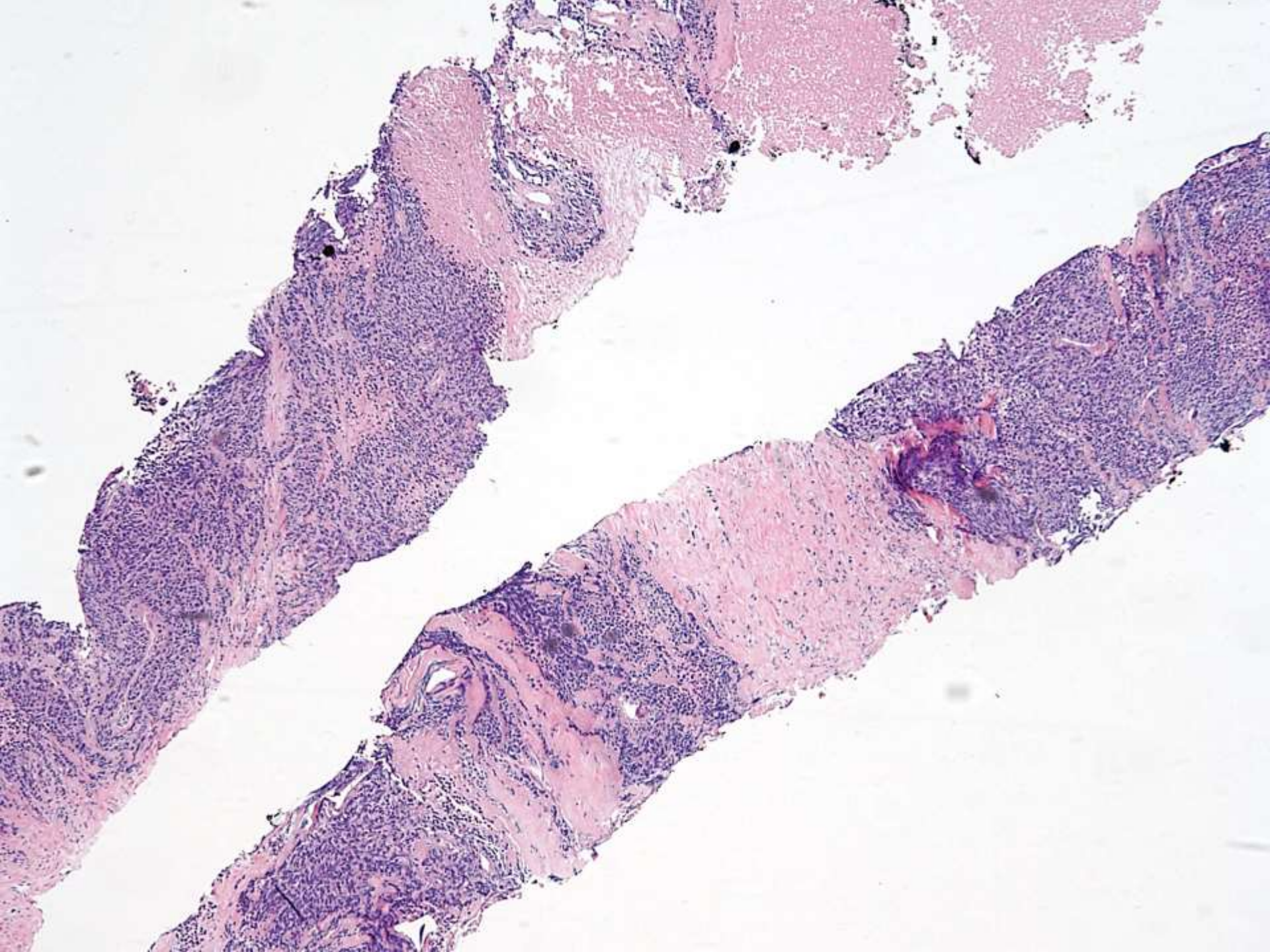
LOW GRADE GLIOMA, FAVOR PILOCYTIC ASTROCYTOMA

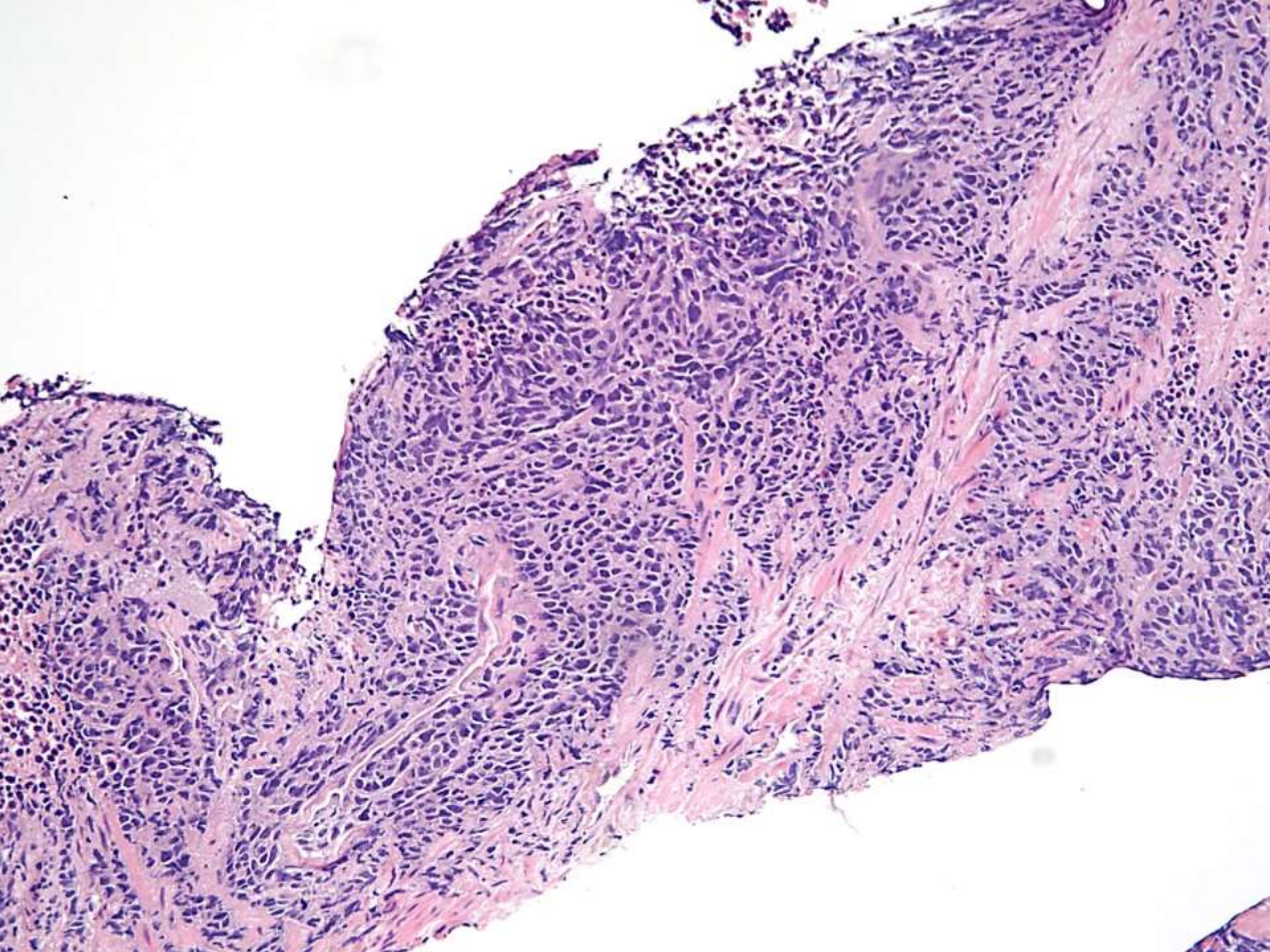
- PA can have necrosis (without palisading), vascular proliferation and pleomorphic cells
- No gender predilection
- First two decades of life
- 0.8 per 100,000
- 21% of CNS tumors in pts 0-14yr
- 16% of CNS tumors in pts 15-19yr
- “Relatively Few in pts over 50yr” (who 2007)

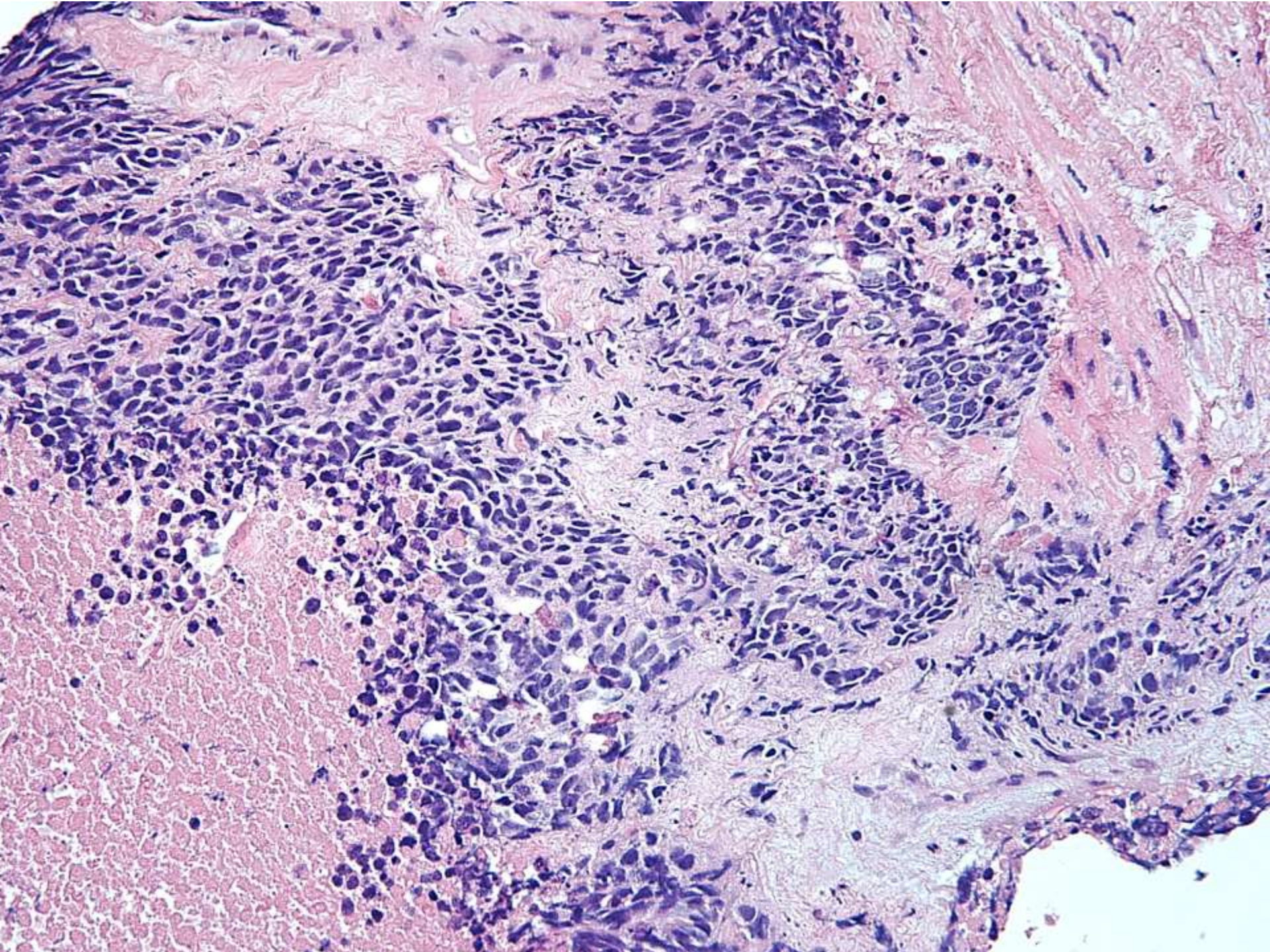
- “Adult pilocytic astrocytomas: clinical features and molecular analysis” Theeler et.al. (at Walter Reed Hospital) Neuro-Oncology 2014
  - 127 adult PAs
  - The majority of adult PAs are supratentorial
  - Recurrencewas seen in 42% of cases, and 13% of patients died during follow-up (60mo)
  - Adjuvant radiotherapy following surgical resectionwas associated with a statistically significant decrease in progression-free survival
  - No BRAF V600E mutations (0 of 40 tested)

SB 6107

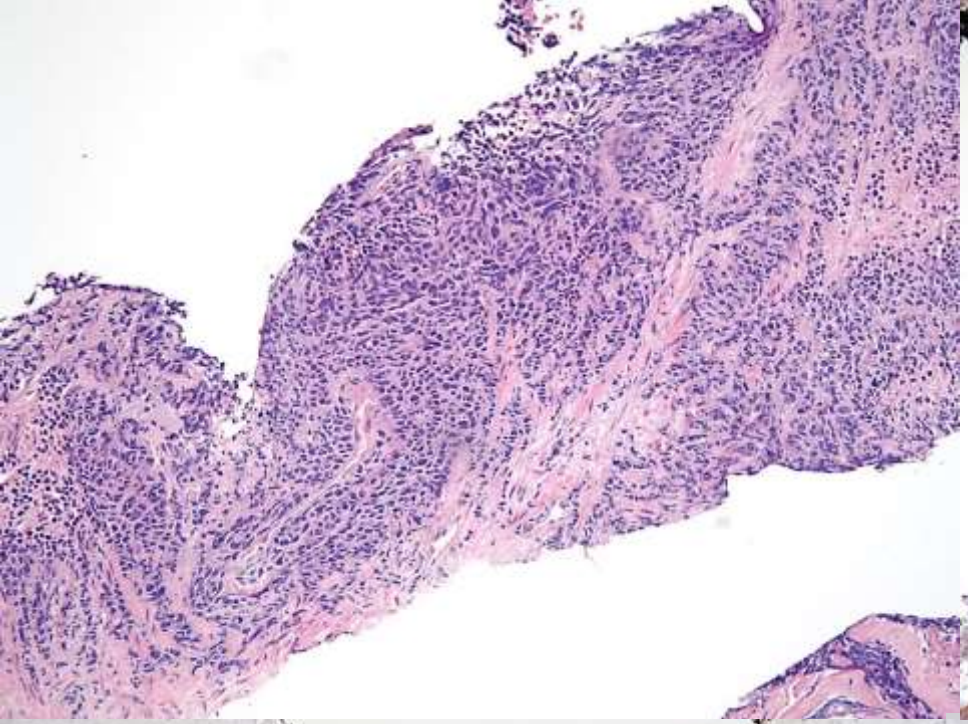
Allison Zemek/John Higgins; Stanford
78 year-old mane with history of prostate cancer treated with radiation in 1997. Now with a low PSA (0.4) but greatly enlarged prostate on noncontrast CT that has grown markedly over a short time.

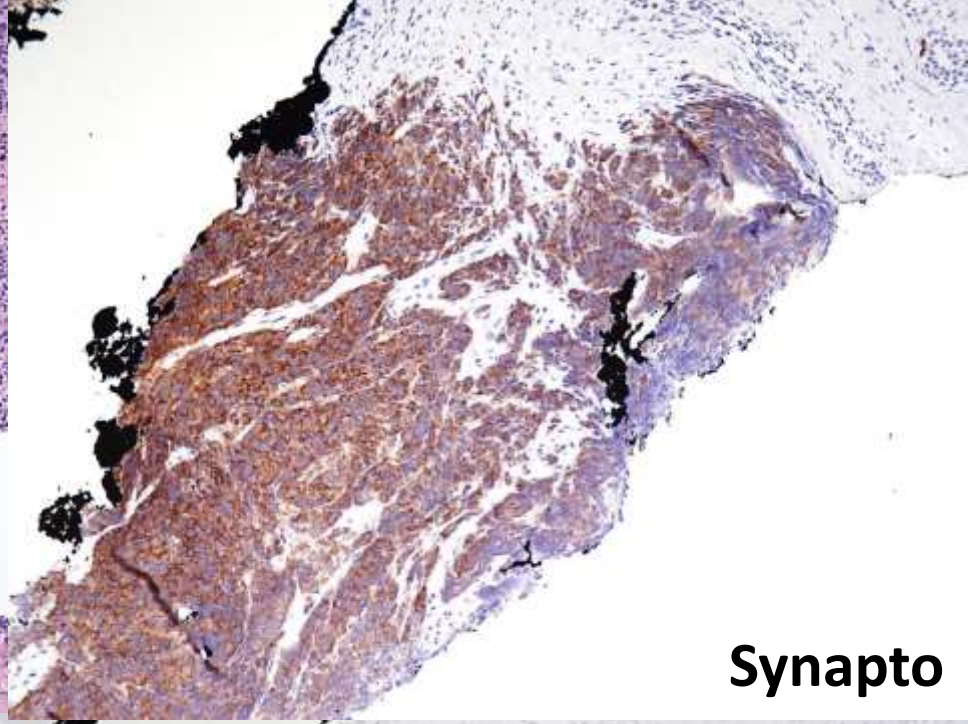


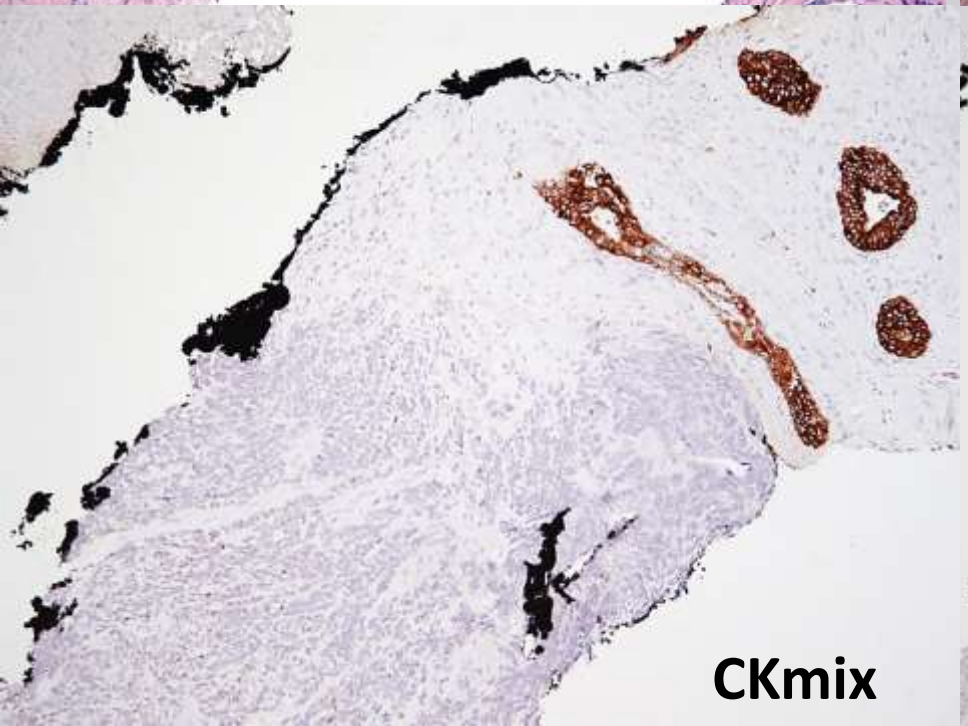


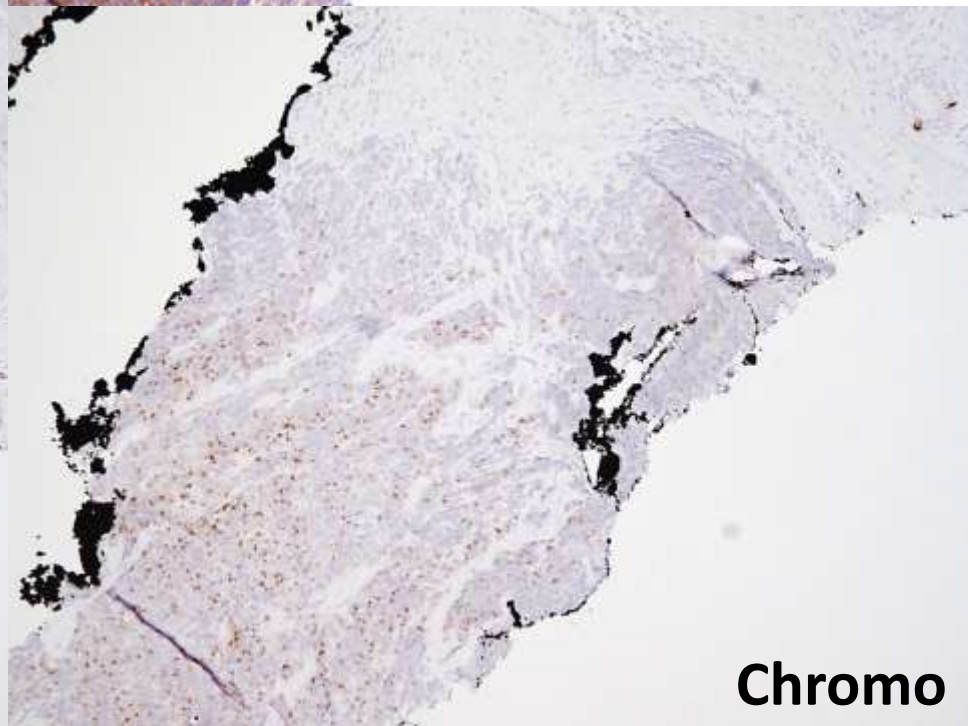


DIAGNOSIS?




Synapto


CKmix


Chromo

Small Cell Neuroendocrine Carcinoma

Clinical features:

- Median 67 years
- Rare cases with paraneoplastic syndromes
- Some with history of conventional

Pathogenesis:

- Neuroendocrine cells within glandular and ductal epithelium
- Indistinguishable on H&E or show Paneth cell-like change
- Cell of origin disputed

Small Cell Neuroendocrine Carcinoma

Histopathologic features:

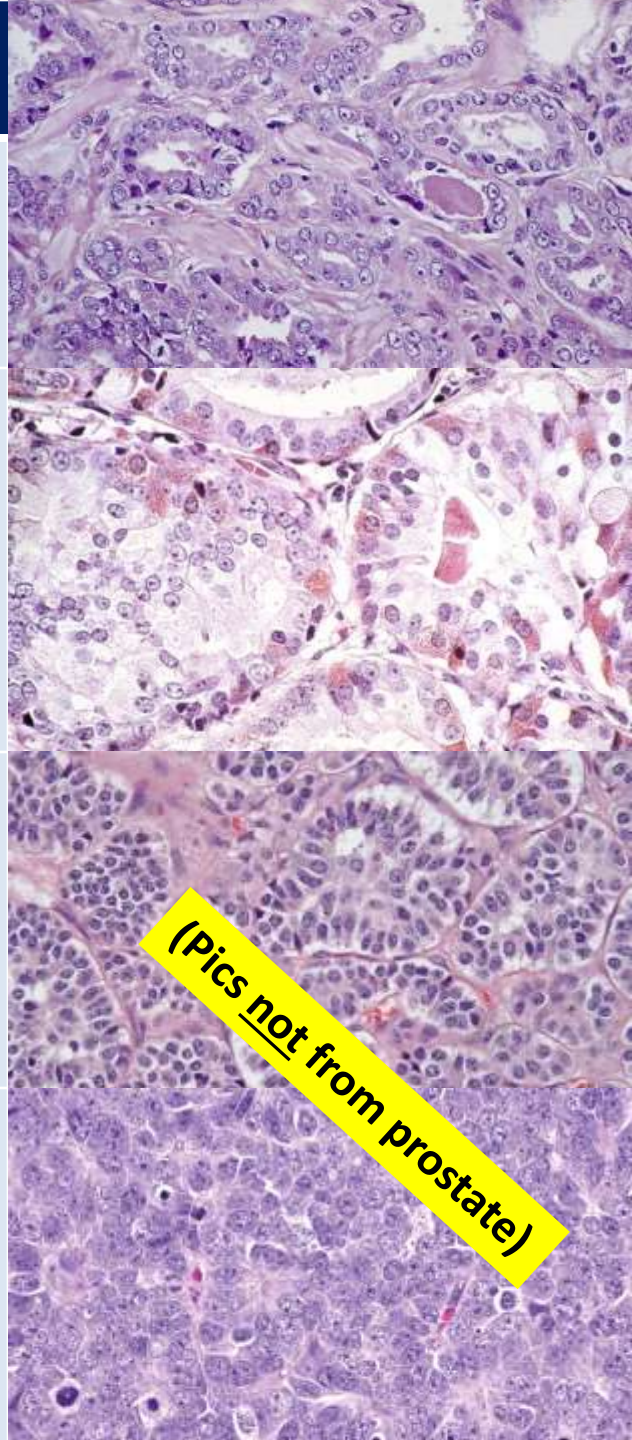
- Identical to SCNEC in lung, no Gleason score
- 50-60% are pure
- 40-50% have admixed acinar adenoca, abrupt transition

Immunohistochemical features:

- 90% synapto/chromo +
- 25% focal PSA, p63+
- 35% HMWCK+
- >50% TTF1+
- AR generally negative
- CD44 reported 100% prostatic

GU WHO 2016, other neuroendocrine tumors

Neuroendocrine cells in **usual** prostate adenocarcinoma	• 10-100% • Neuroendocrine IHC **not recommended** for general
Adenocarcinoma with **Paneth-cell** like neuroendocrine differentiation	• Eosinophilic granules positive by IHC • Can be **pattern 5**, but do not behave like high-grade
Well-differentiated neuroendocrine tumor	• Extremely rare • Tend to be locally advanced, but favorable
Large cell neuroendocrine	• Extremely rare • Acinar high grade adeno



Small Cell Neuroendocrine Carcinoma

Treatment:

- Treated aggressively (chemo/rad)

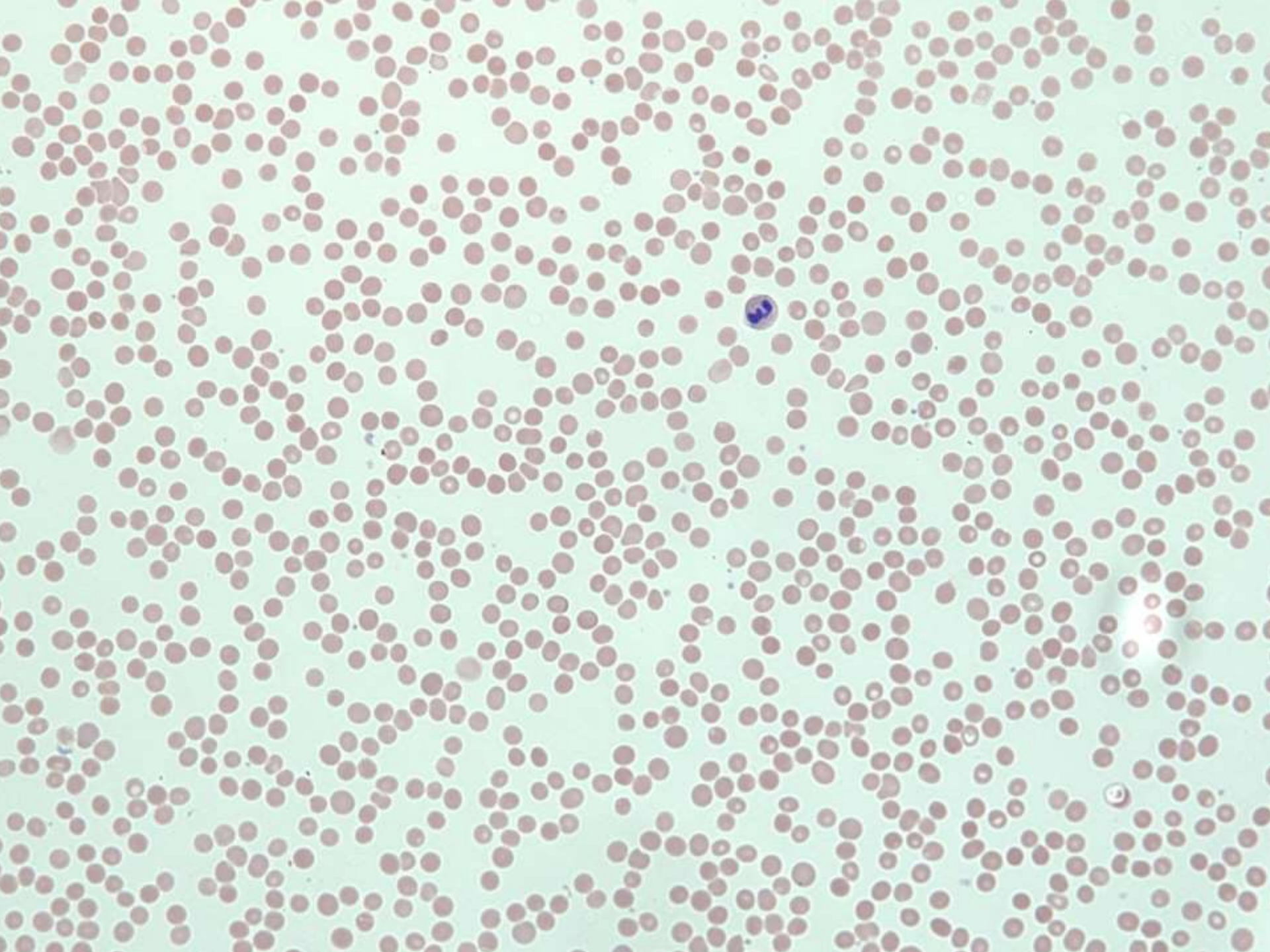
Prognosis:

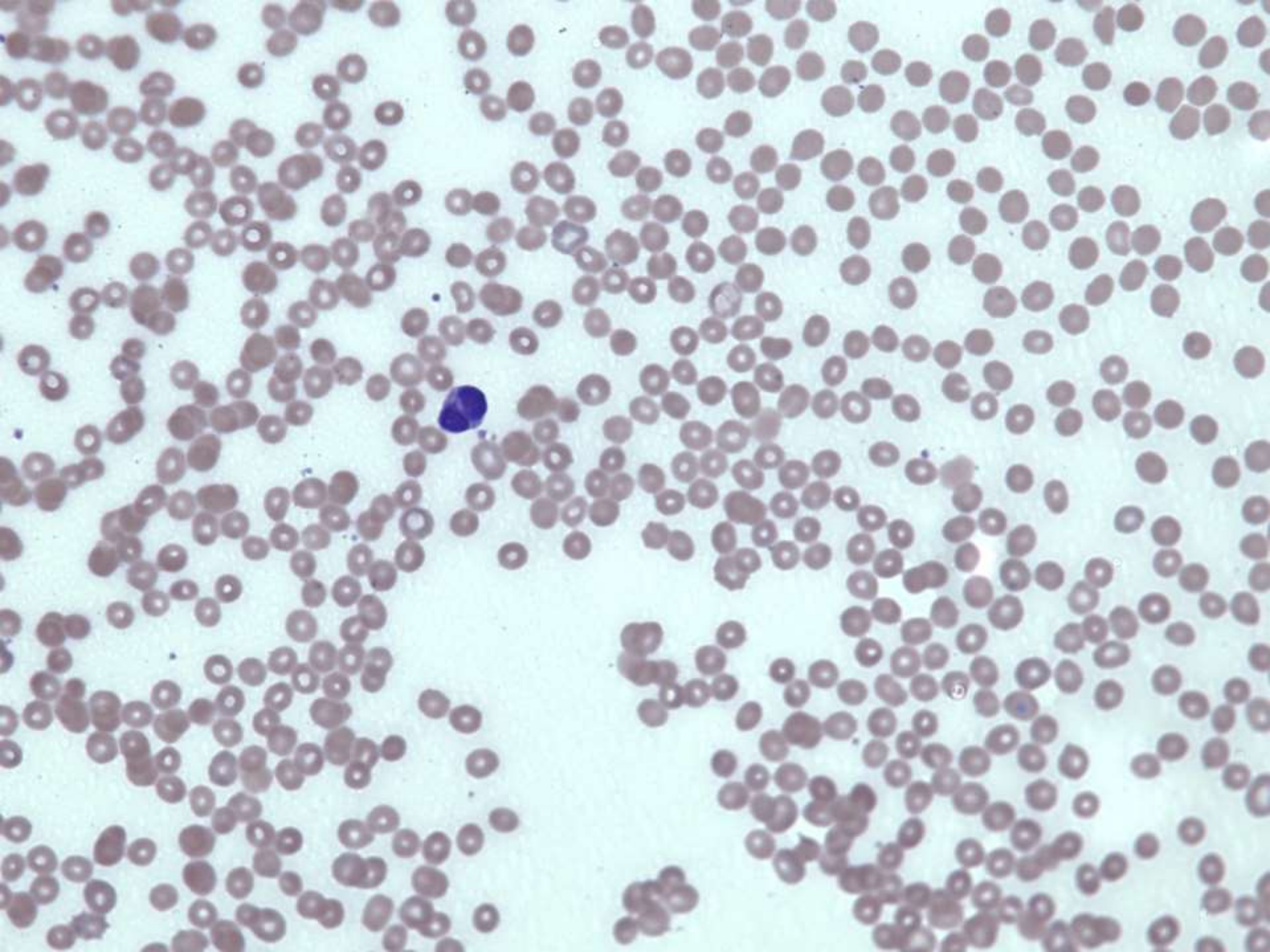
- Poor
- Median survival 19 mo
- 60% present with metastatic disease
- If progressing from usual adeno, median is 7 mo

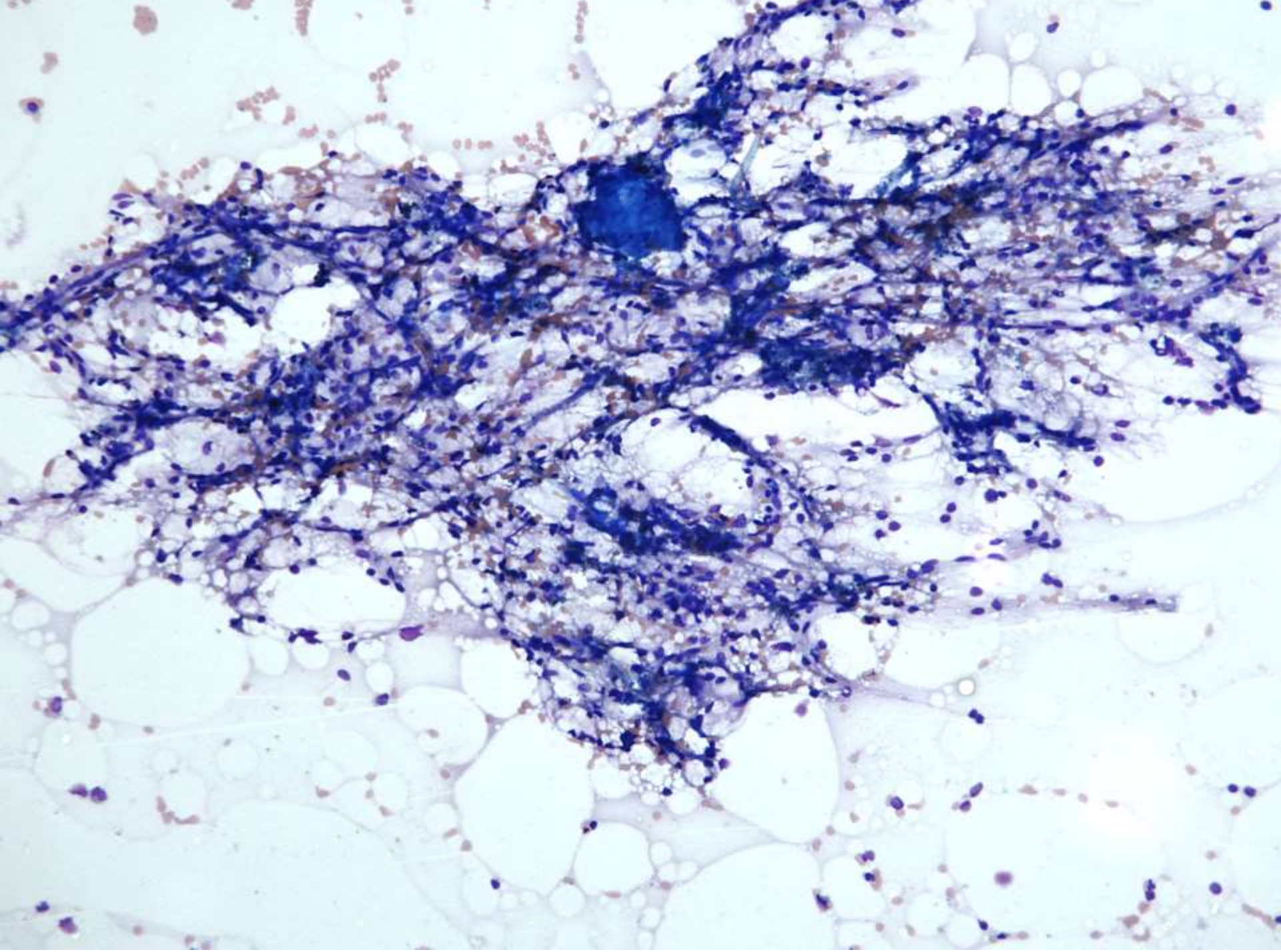
SB 6108

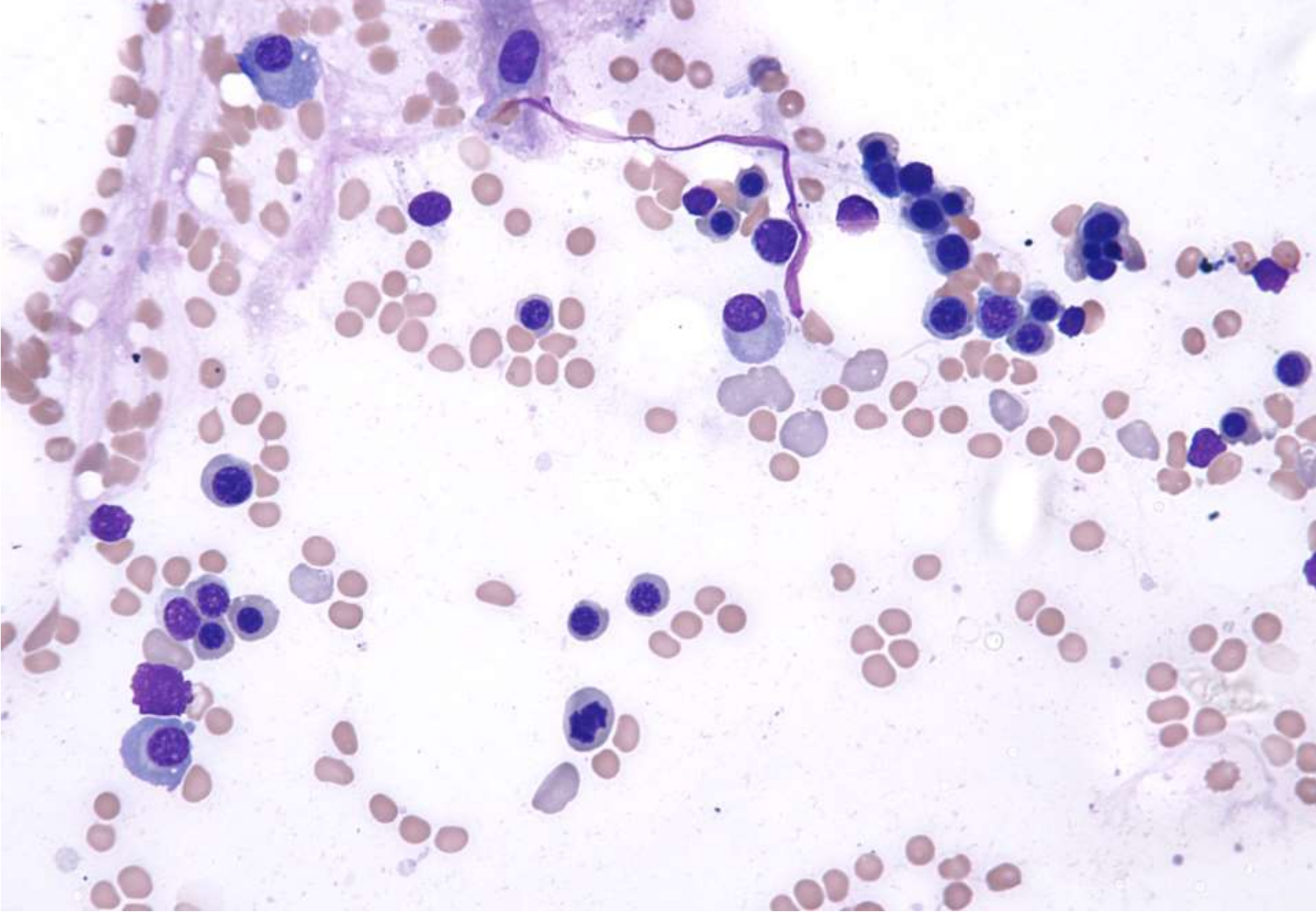
Jenny Hoffmann/Dean Fong; Stanford/Palo Alto VA

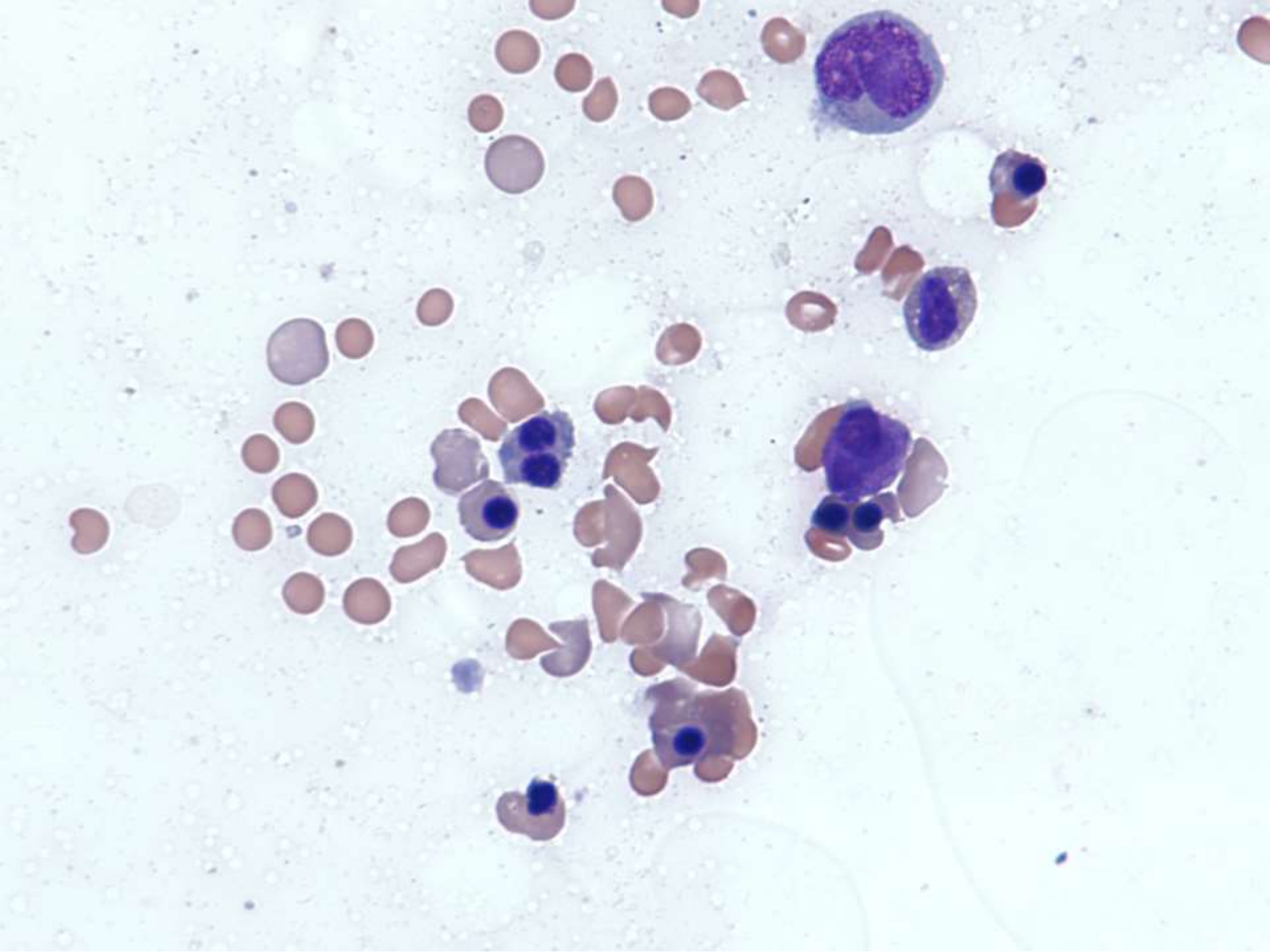
69-year-old man with history of prostate cancer s/p XRT, with new onset pancytopenia. A bone marrow biopsy was performed.

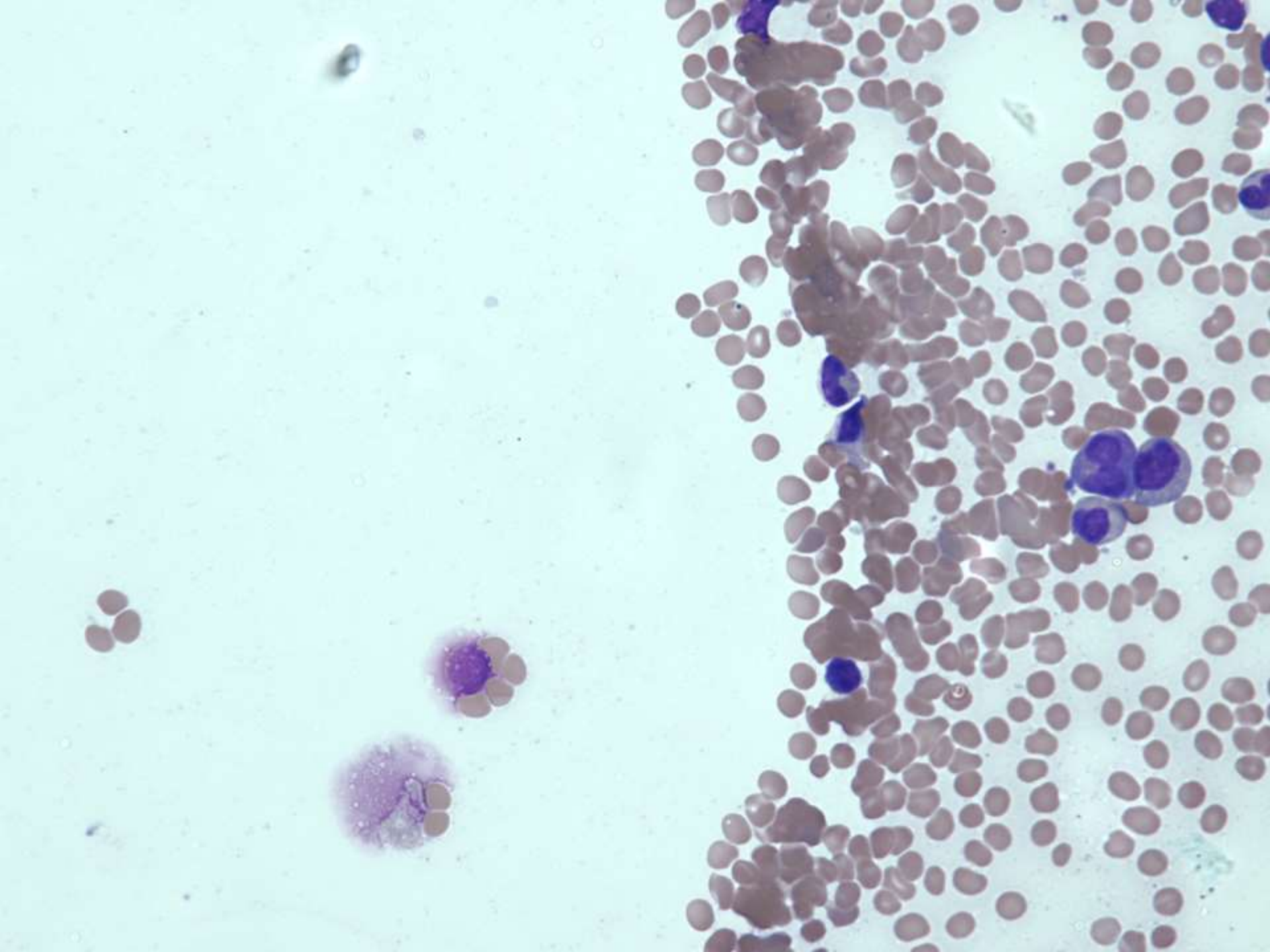


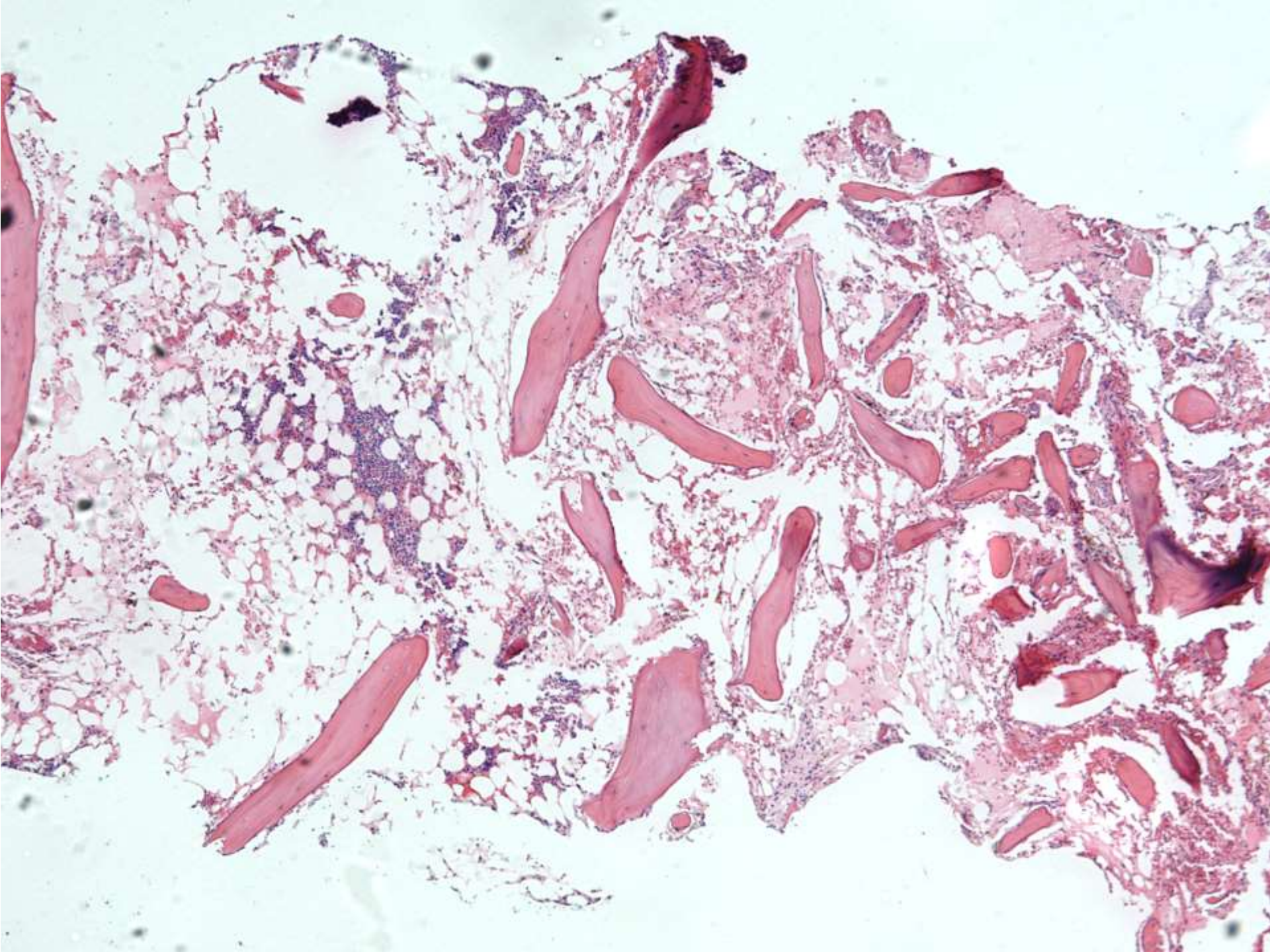


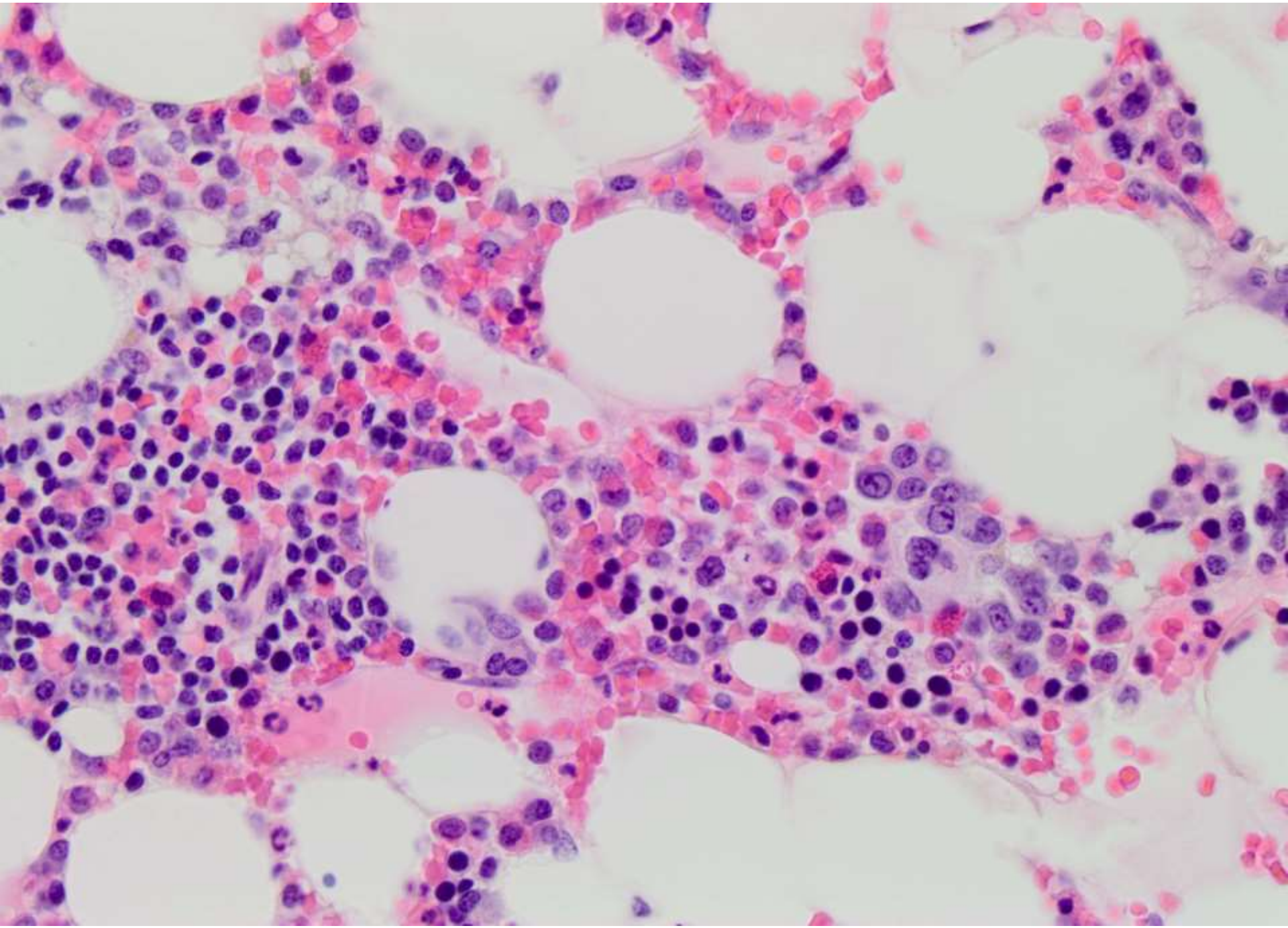




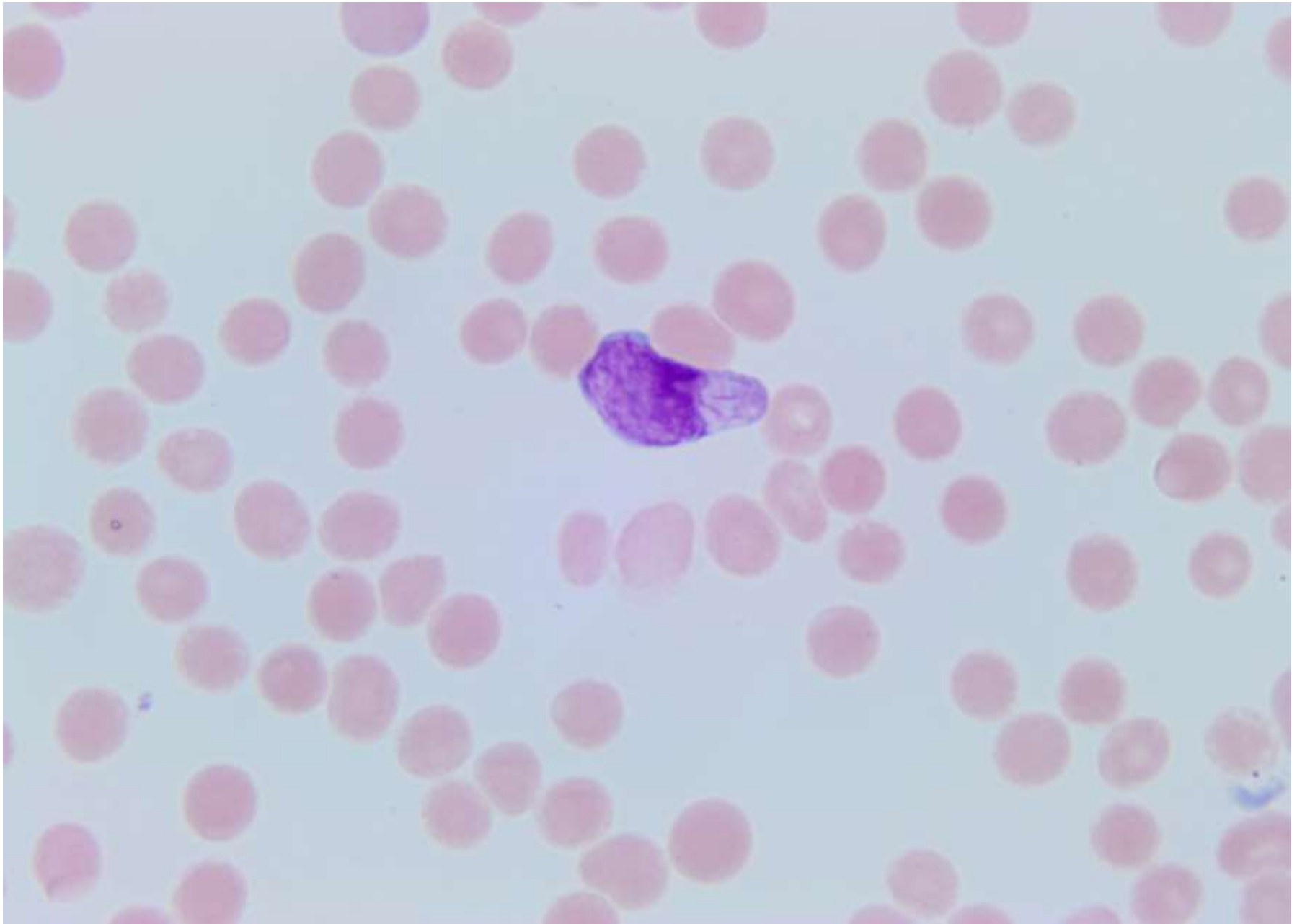


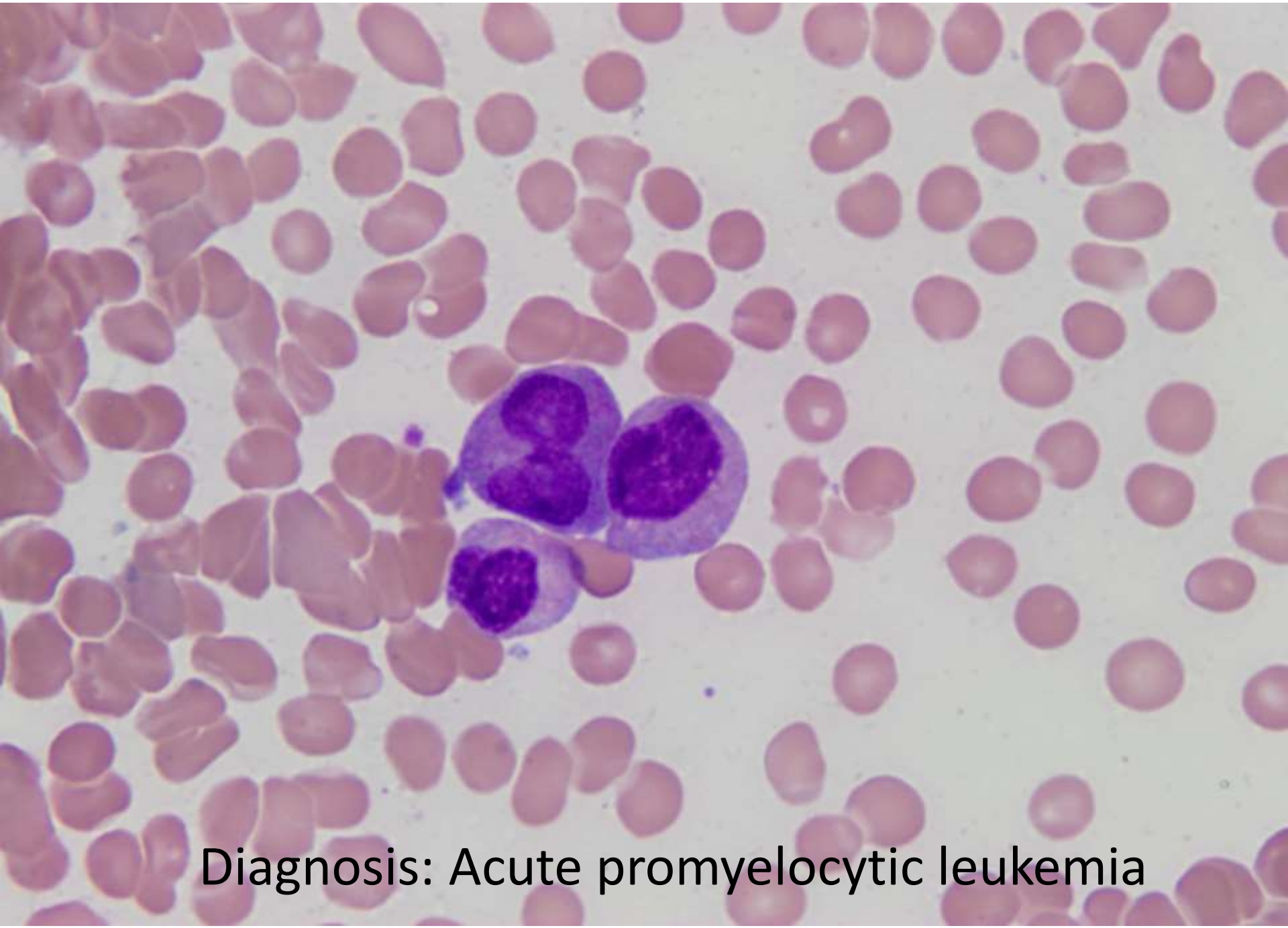






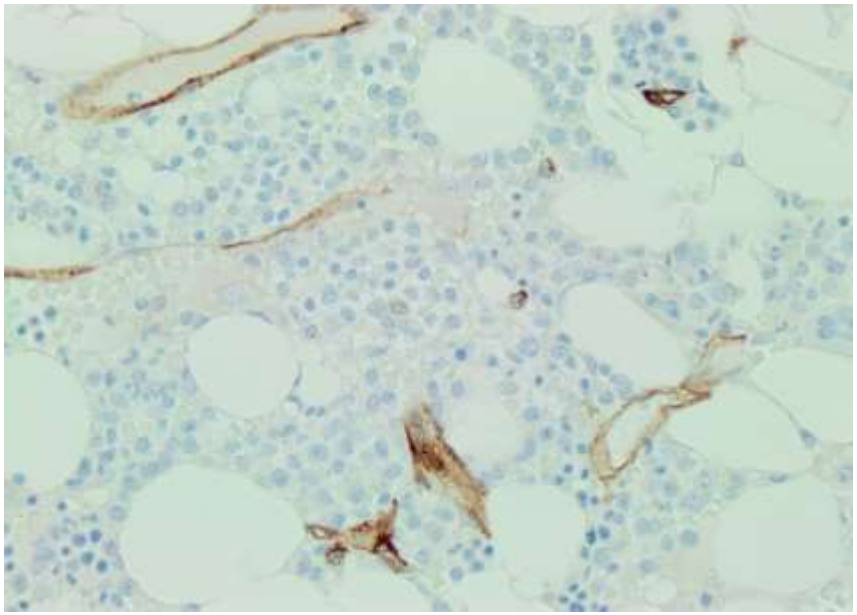
DIAGNOSIS?



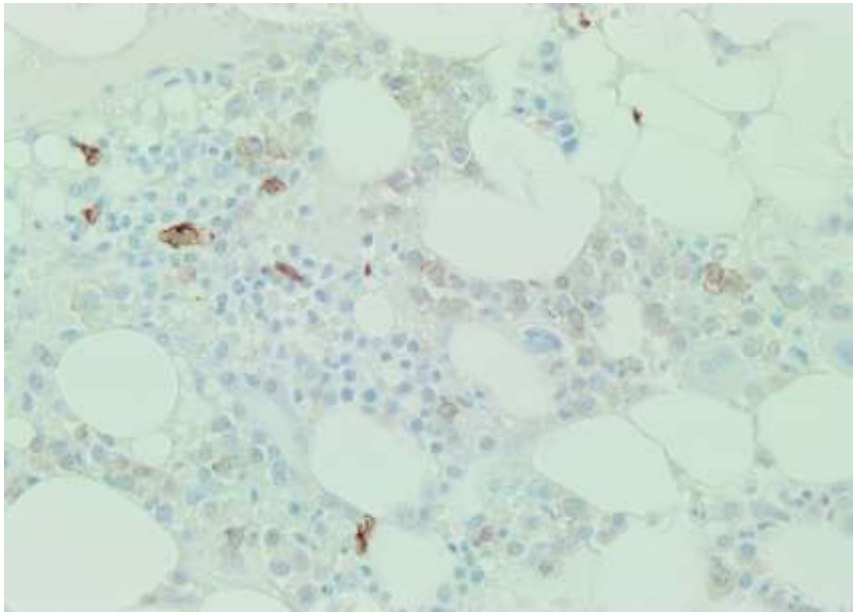

Diagnosis: Acute promyelocytic leukemia

Immunohistochemistry

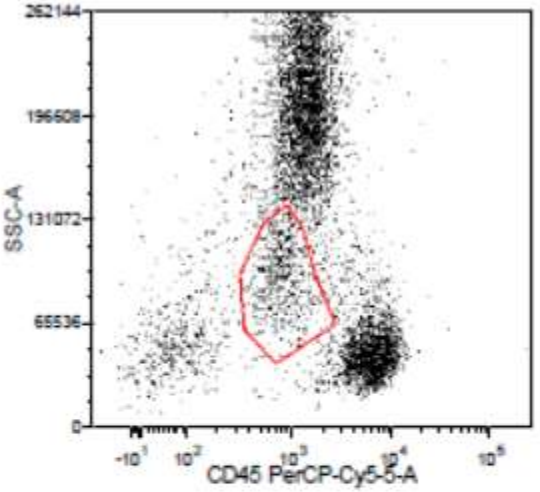
CD34

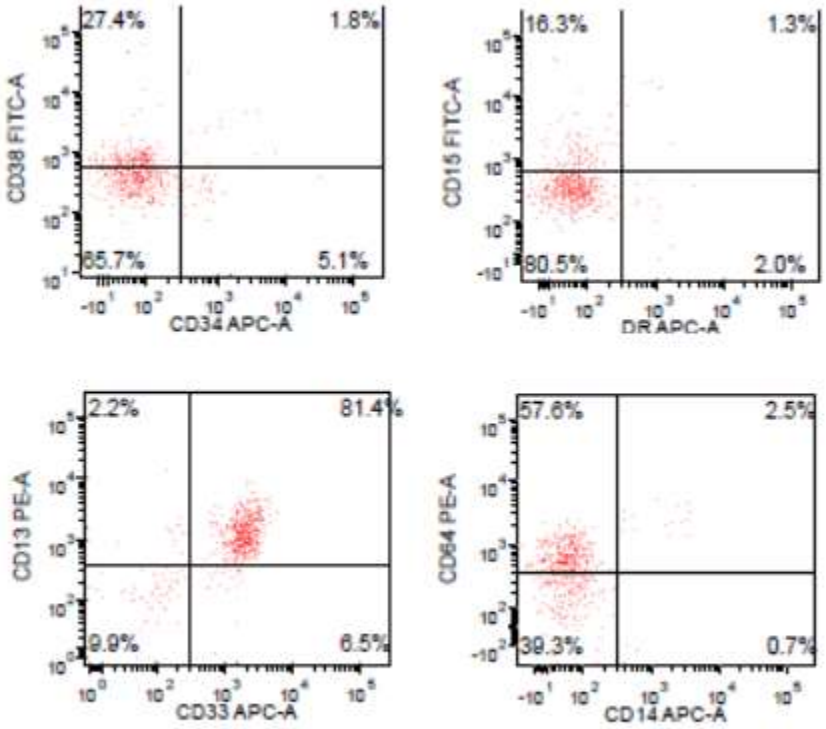


CD117



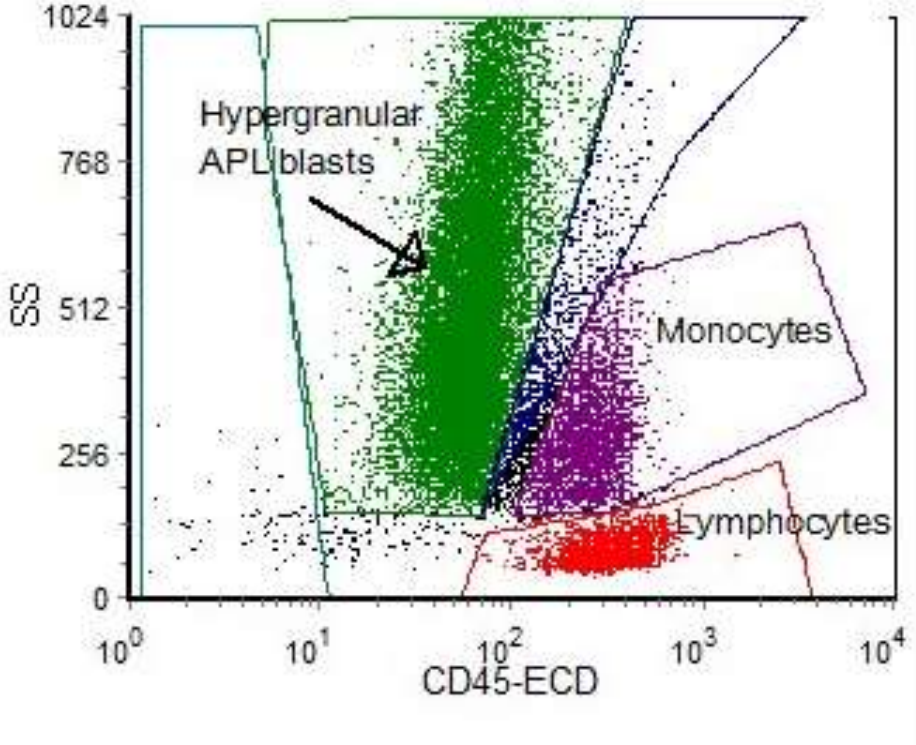
Flow Cytometry

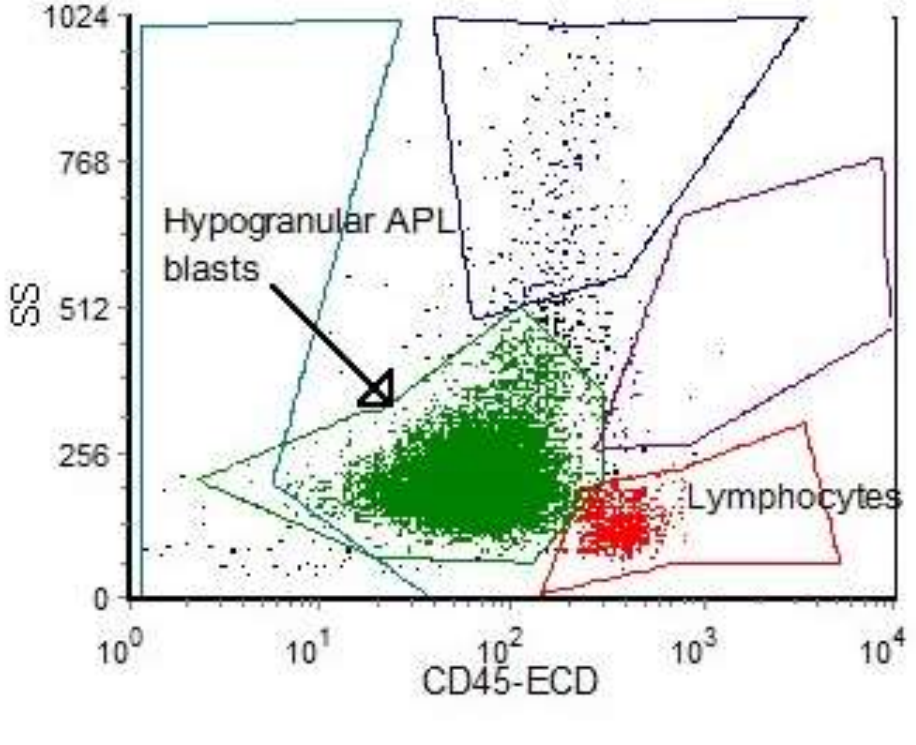




- Abnormal blast population:
  - 8%

Gating on APL blasts/blast equivalents

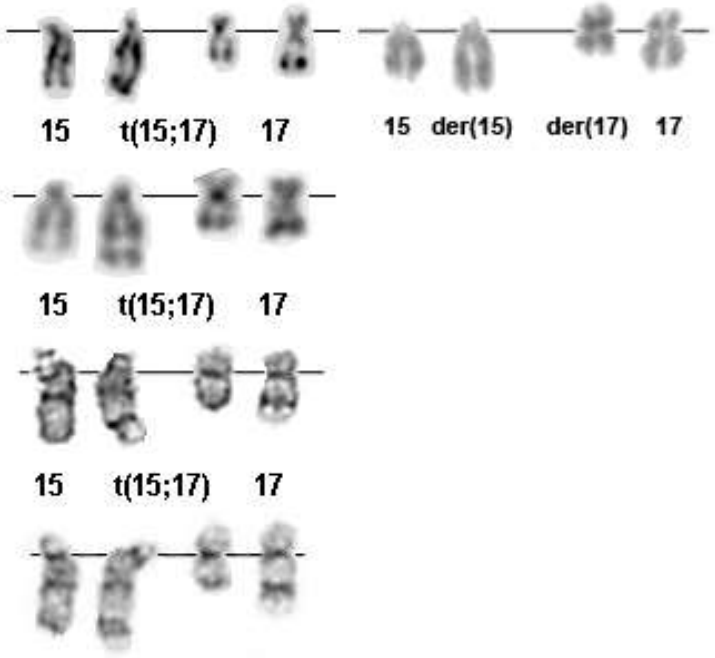


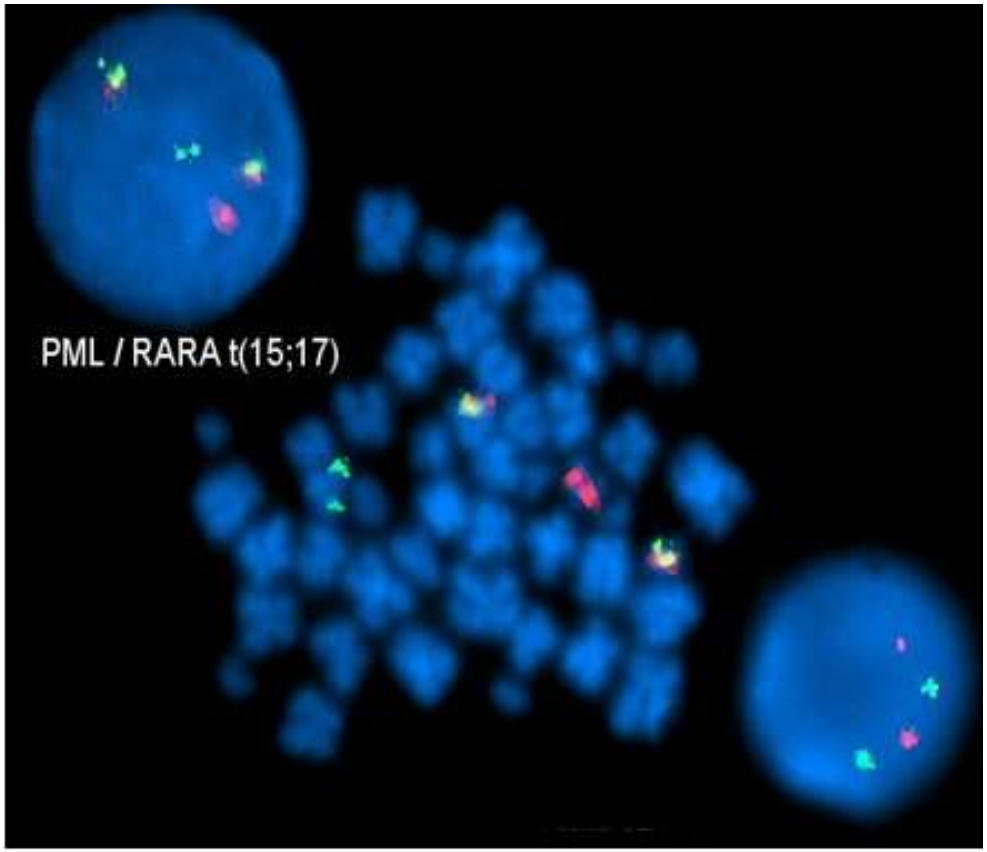


Marker or parameter	APL hypergranular	APL hypogranular
SSC	markedly increased	decreased (blast region)
CD2	23% (dim)	90% (dim to mod)
CD4	27% (dim)	50% (dim)
CD11b	0% (occassional subset)	0%
CD11c	6% (dim)	0%
CD13	0%	100% (dim to mod)
CD14	0%	0%
CD16	0%	0%
CD19	0%	0%
CD33	100% (mod to bright)	100% (bright)
CD34	2% (occassional subset)	75%
CD45	100% (moderate)	100% (moderate)
CD56	15%	20%
CD64	70% (dim)	90% (dim)
CD117	100% (moderate)	100% (moderate)
HLA Dr	0%	0%

FISH and Cytogenetics

- 46XY,t(15;17)(q24;q21)[12] / 46,XY[8]
- t(15;17) PML/RARA





Therapy-related APL (t-APL)?

- Despite presence of recurrent genetic abnormalities, patient w/ history of cytotoxic chemotherapy or radiation still considered to have t-AML[1]
- Prognosis of t-APL not entirely clear – data is mixed
  - Reports of similar or better compared to other types of t-AML[2-3]
  - Reports of similar or worse than patients w/ patients with de novo APL[2, 4-6]

References

1) Vardiman JW, Arber DA, Brunning RD, et al. Therapy-related myeloid neoplasms. In: Swerdlow SH, Campo E, Harris NL, et al., editors. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4. Lyon, France: IARC Press; 2008.

2) Andersen MK, Larson RA, Mauritzson N, et al. Balanced chromosome abnormalities inv(16) and t(15;17) in therapy-related myelodysplastic syndromes and acute leukemia: report from an international workshop. *Genes Chromosomes Cancer*. 2002;33:395–400.

3) Pollicardo N, O'Brien S, Estey EH, et al. Secondary acute promyelocytic leukemia: characteristics and prognosis of 14 patients from a single institution. *Leukemia.* 1996;10:27–31.

4) Beaumont M, Sanz M, Carli PM, et al. Therapy-related acute promyelocytic leukemia. *J Clin Oncol.* 2003;21:2123–2137.

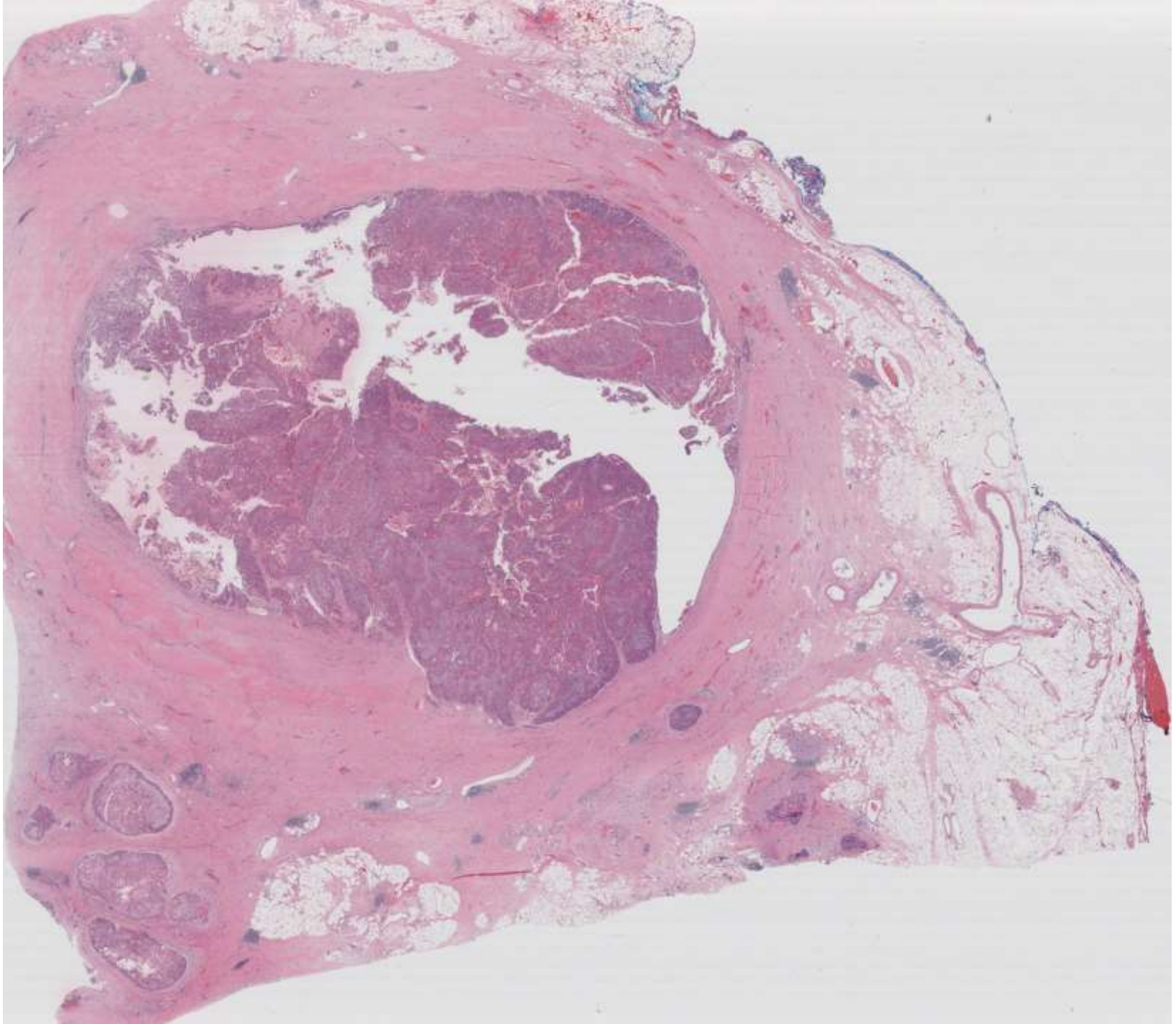
5) Detourmignies L, Castaigne S, Stoppa AM, et al. Therapy-related acute promyelocytic leukemia: a report on 16 cases. *J Clin Oncol.* 1992;10:1430–1435

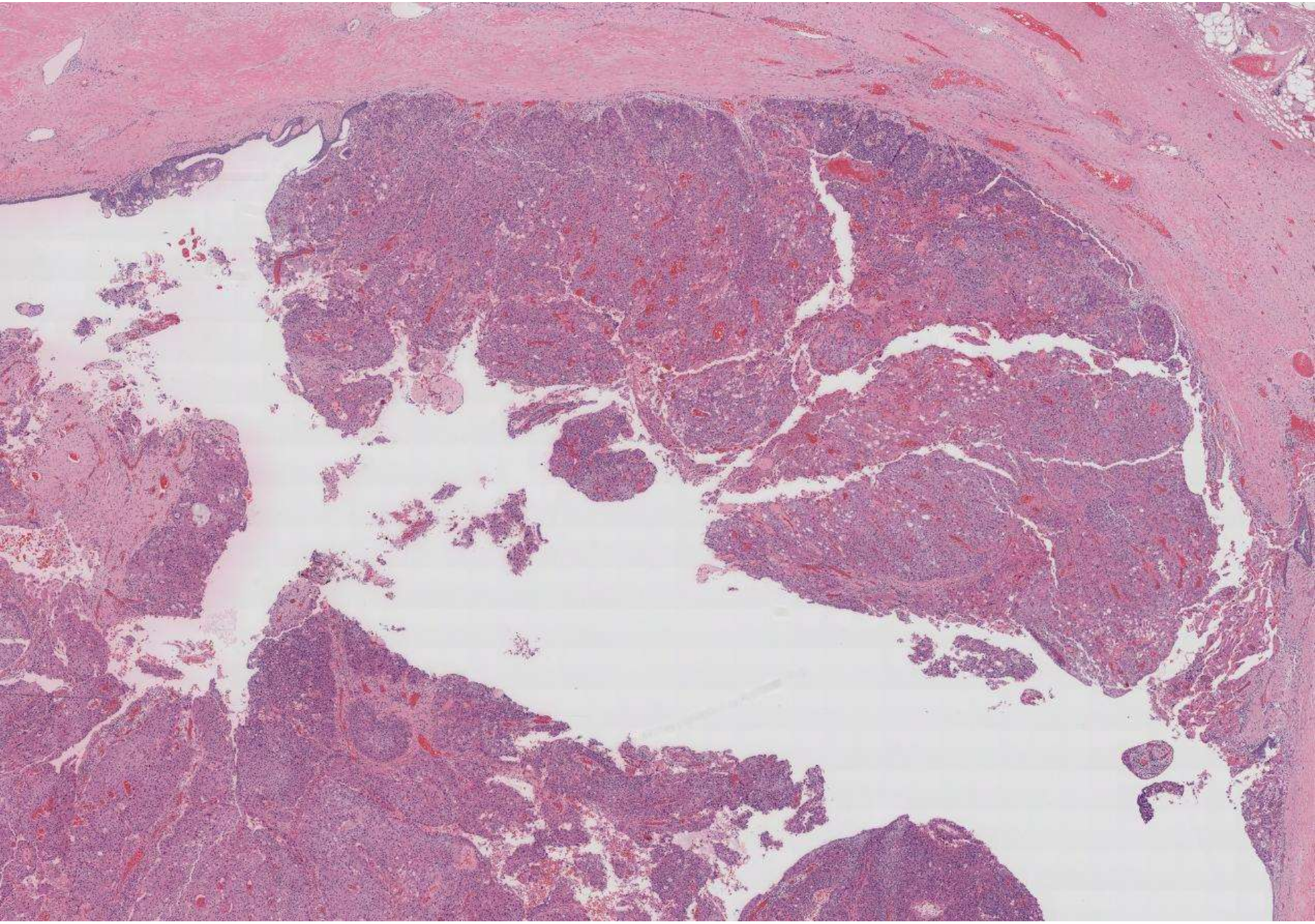
6) Duffield AS, Aoki J, Levis M et al. Clinical and pathologic features of secondary acute promyelocytic leukemia. *Am J Clin Pathol.* 2012;137(3):395-402.

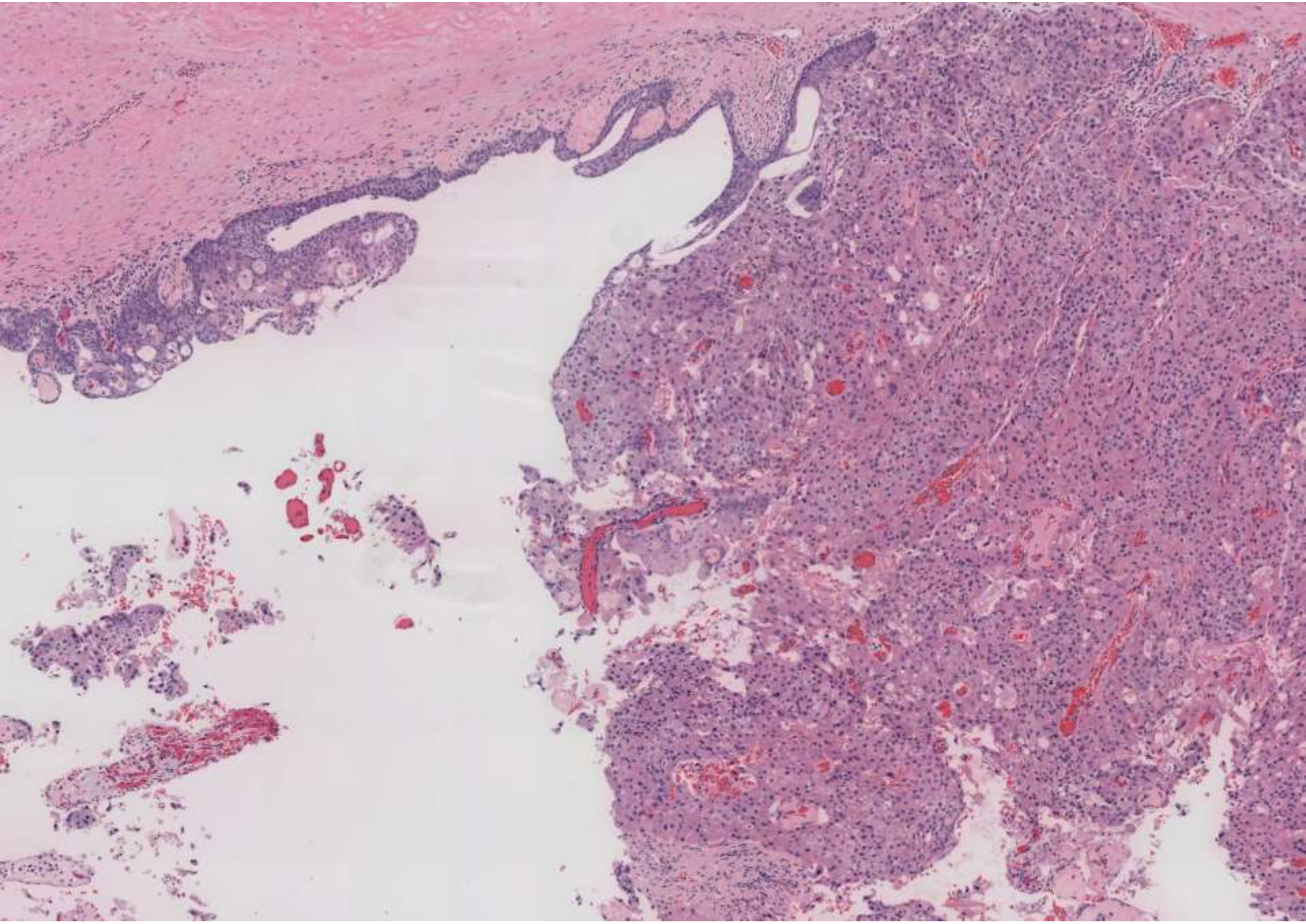
SB 6098 (Case from Oct 2016; scanned slide available)

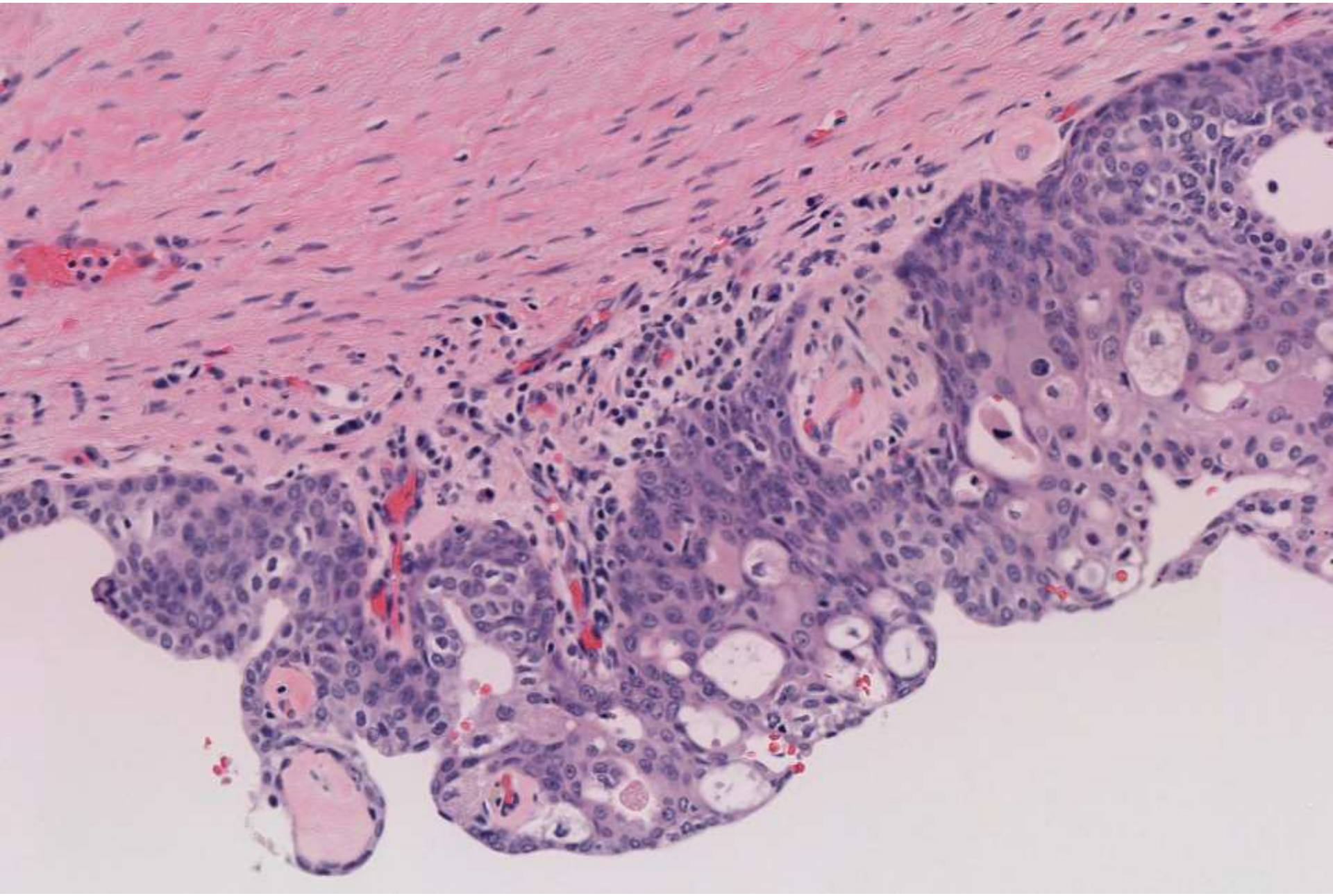
James Mathews; Kaiser San Francisco

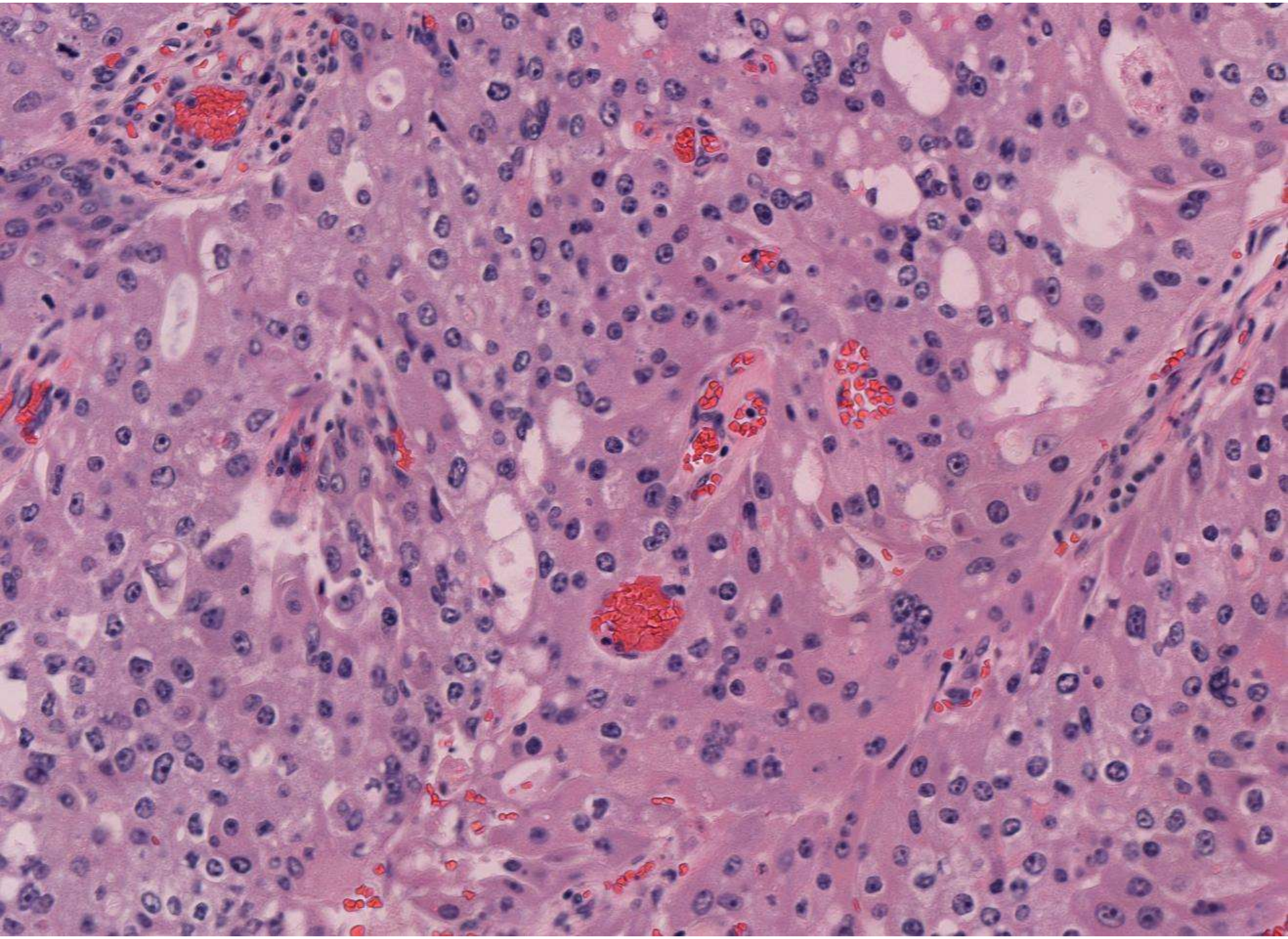
59-year-old man with chronic pancreatitis found to have a 3.7cm pancreatic head mass.

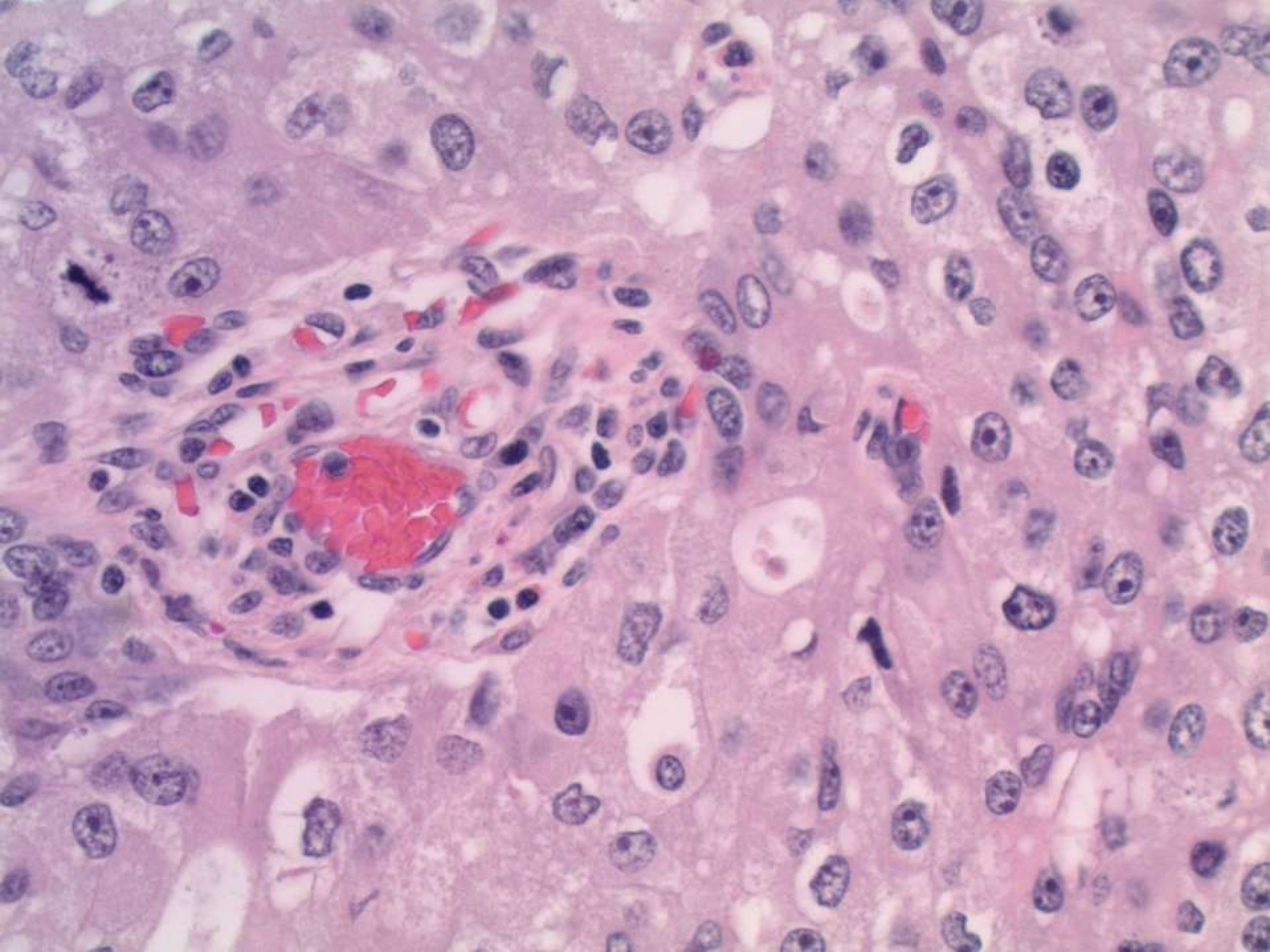


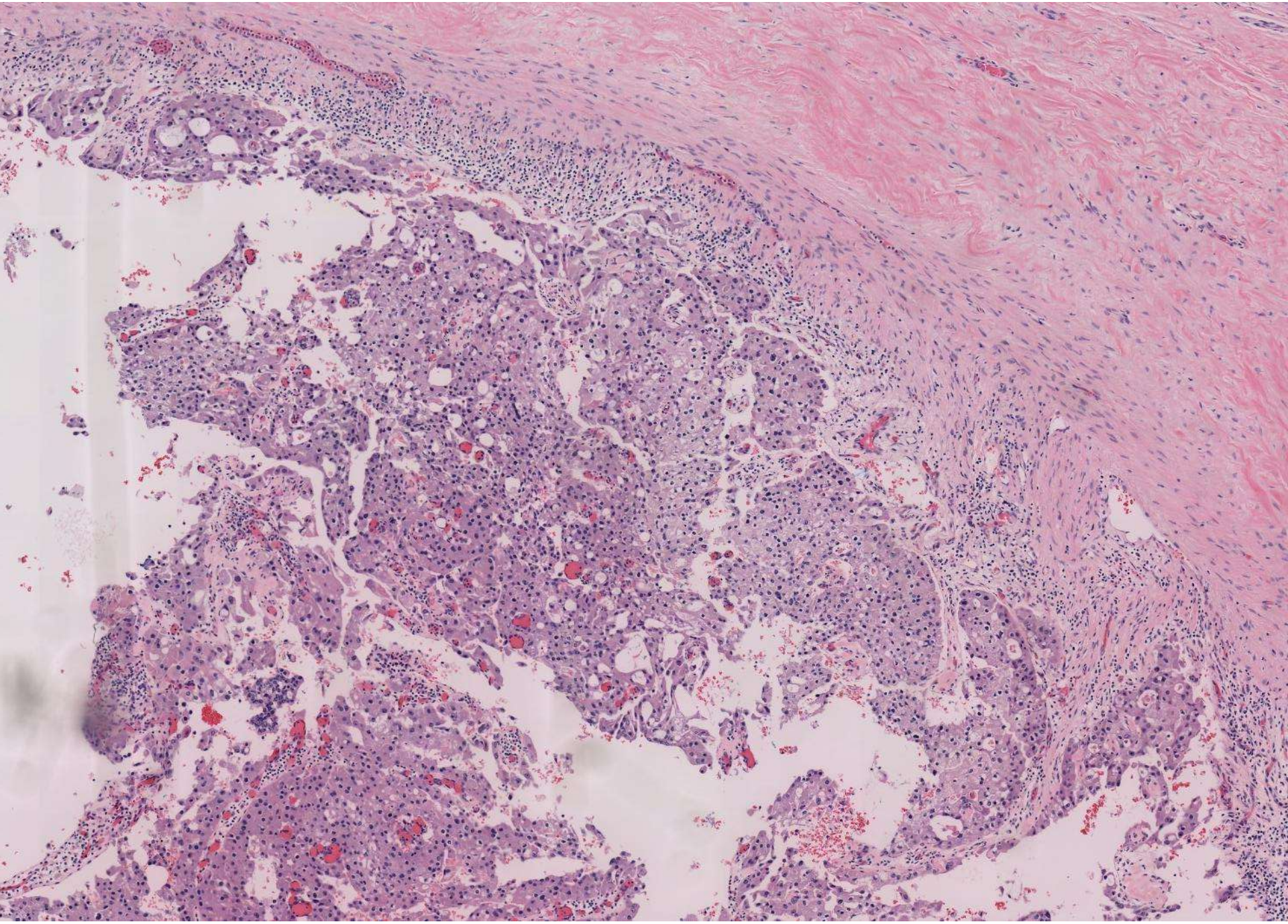


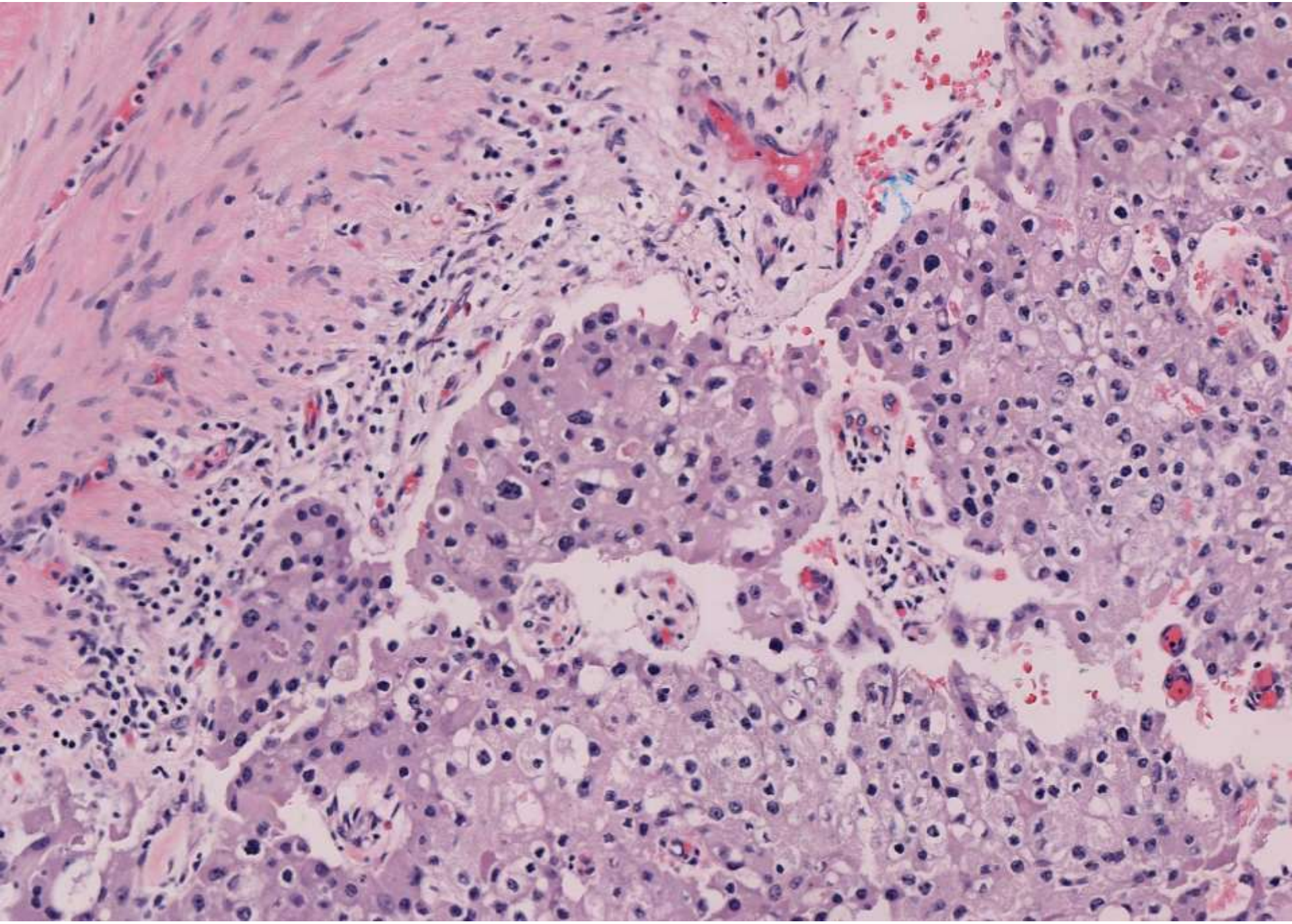


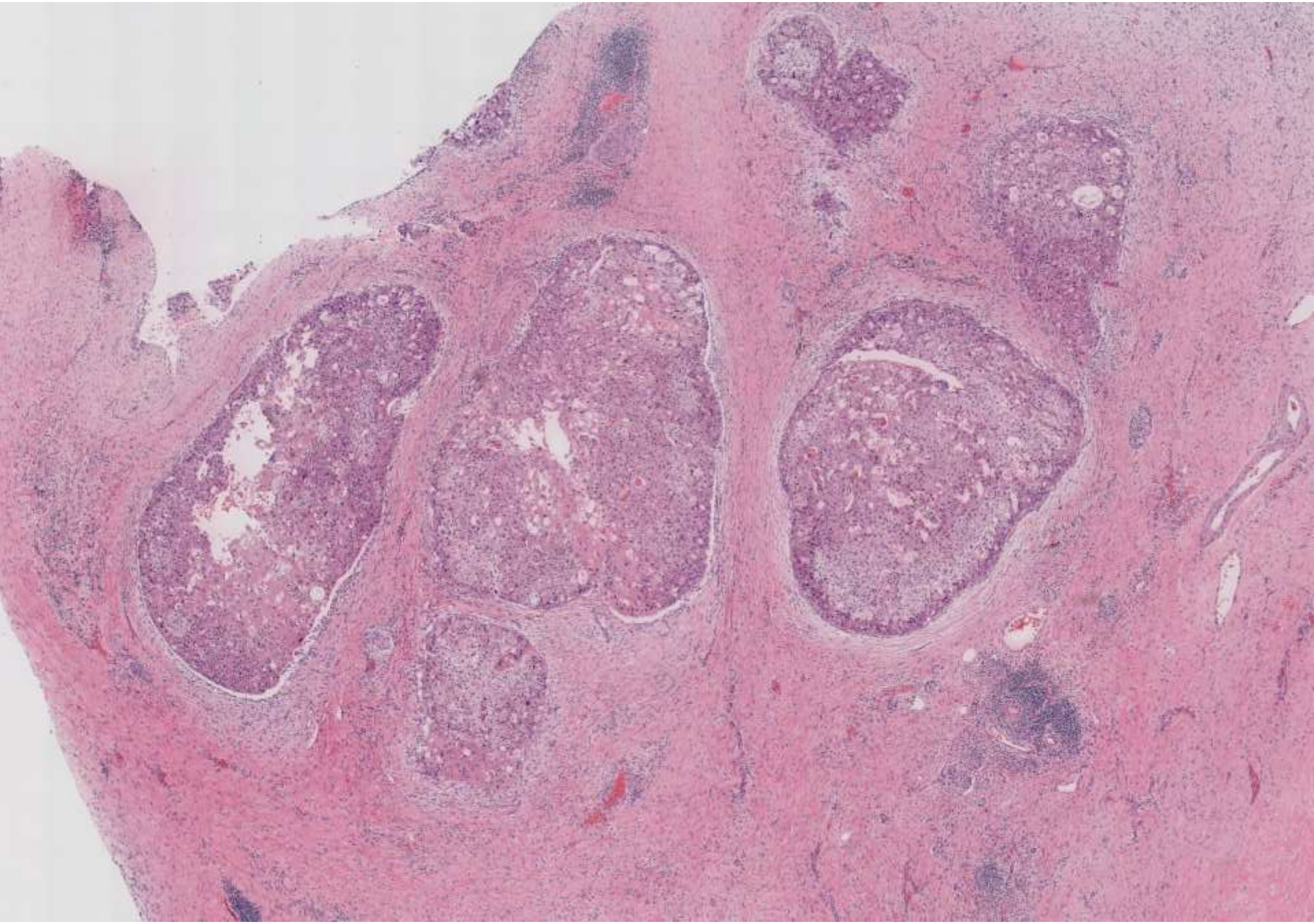


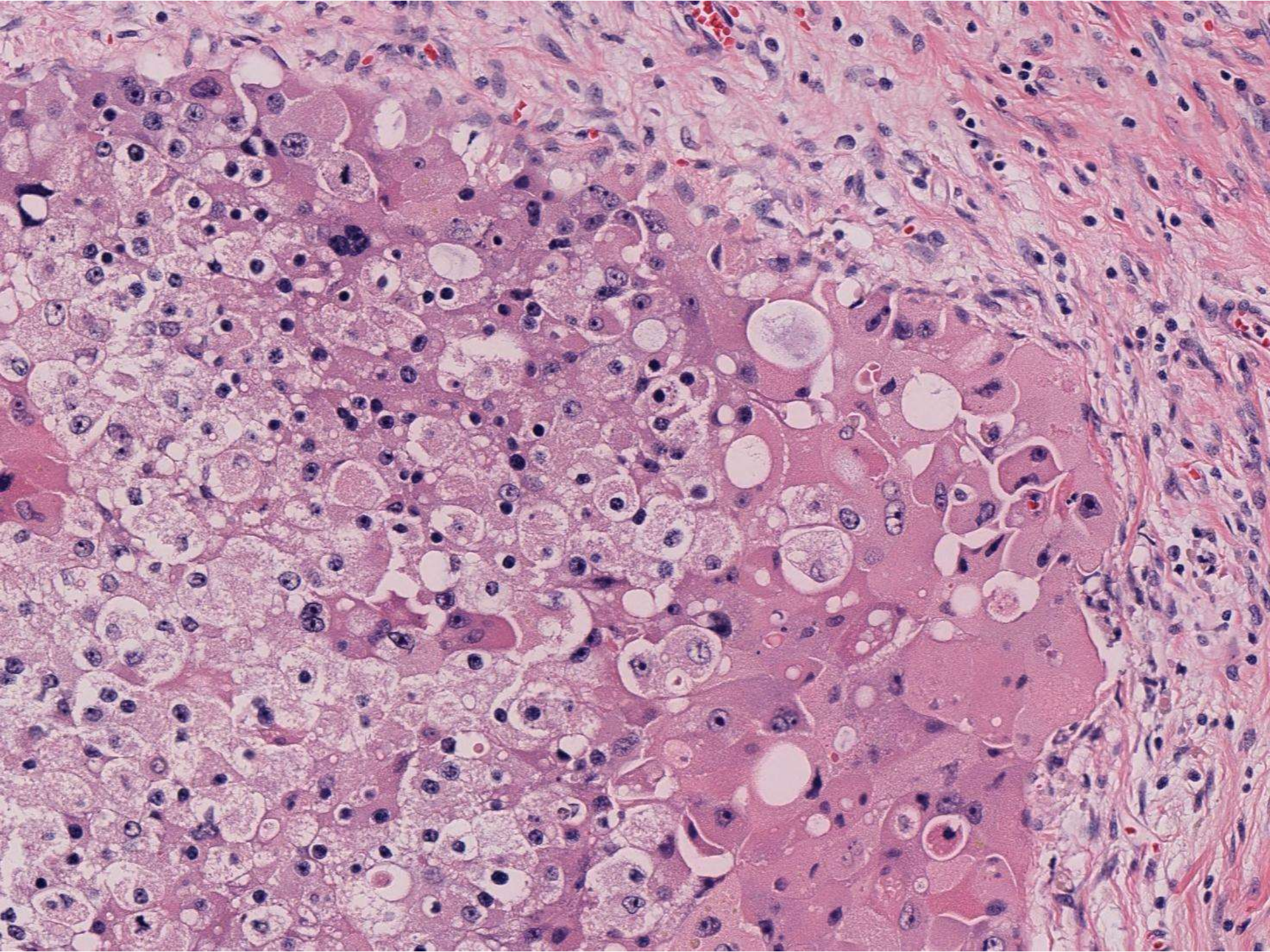










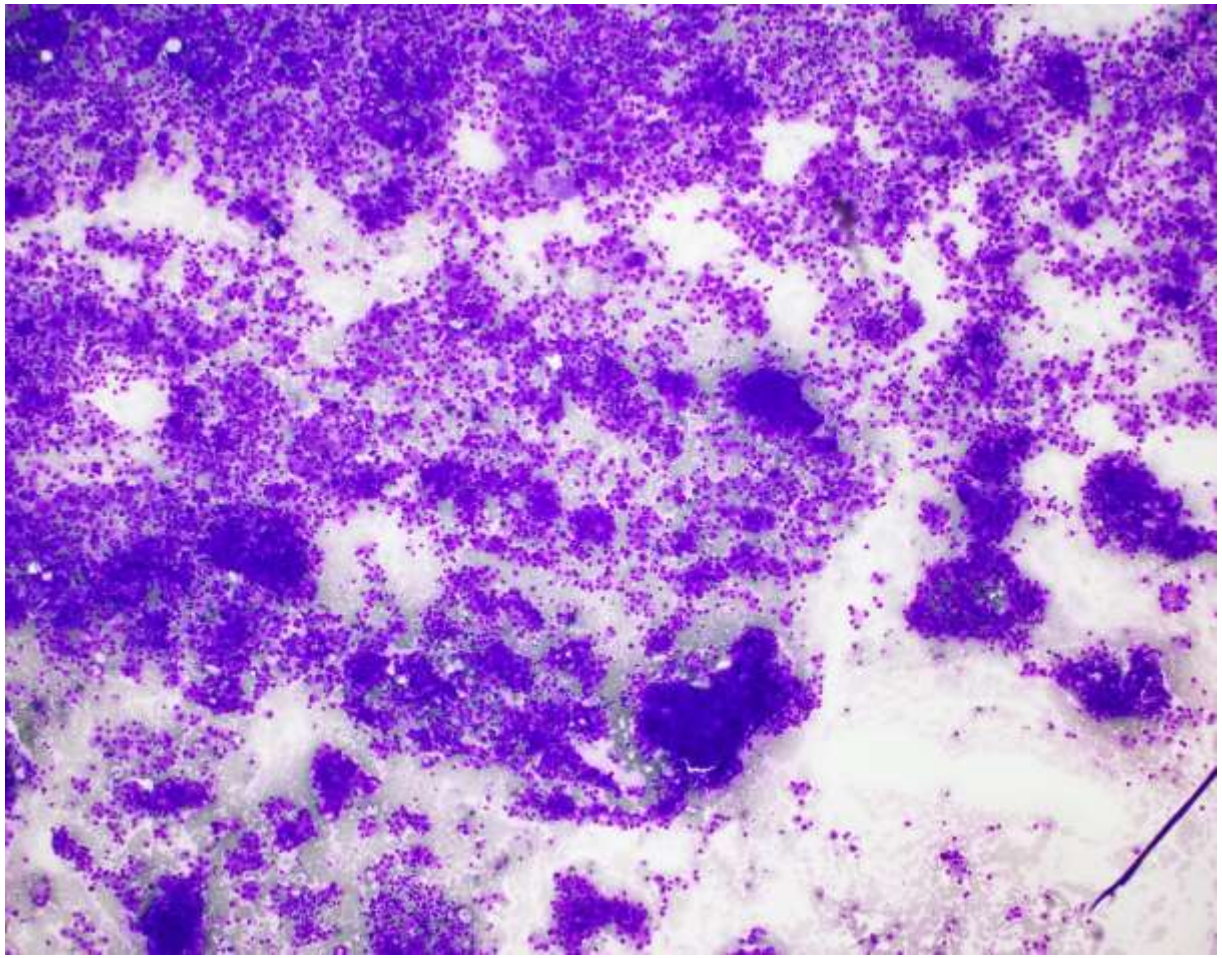


DIAGNOSIS?

Invasive oncocytic carcinoma arising in association with an Intraductal Oncocytic Papillary Neoplasm of the Pancreas

59 year old man with jaundice and itching. He was found to have a mass in the head of the pancreas.

FNA



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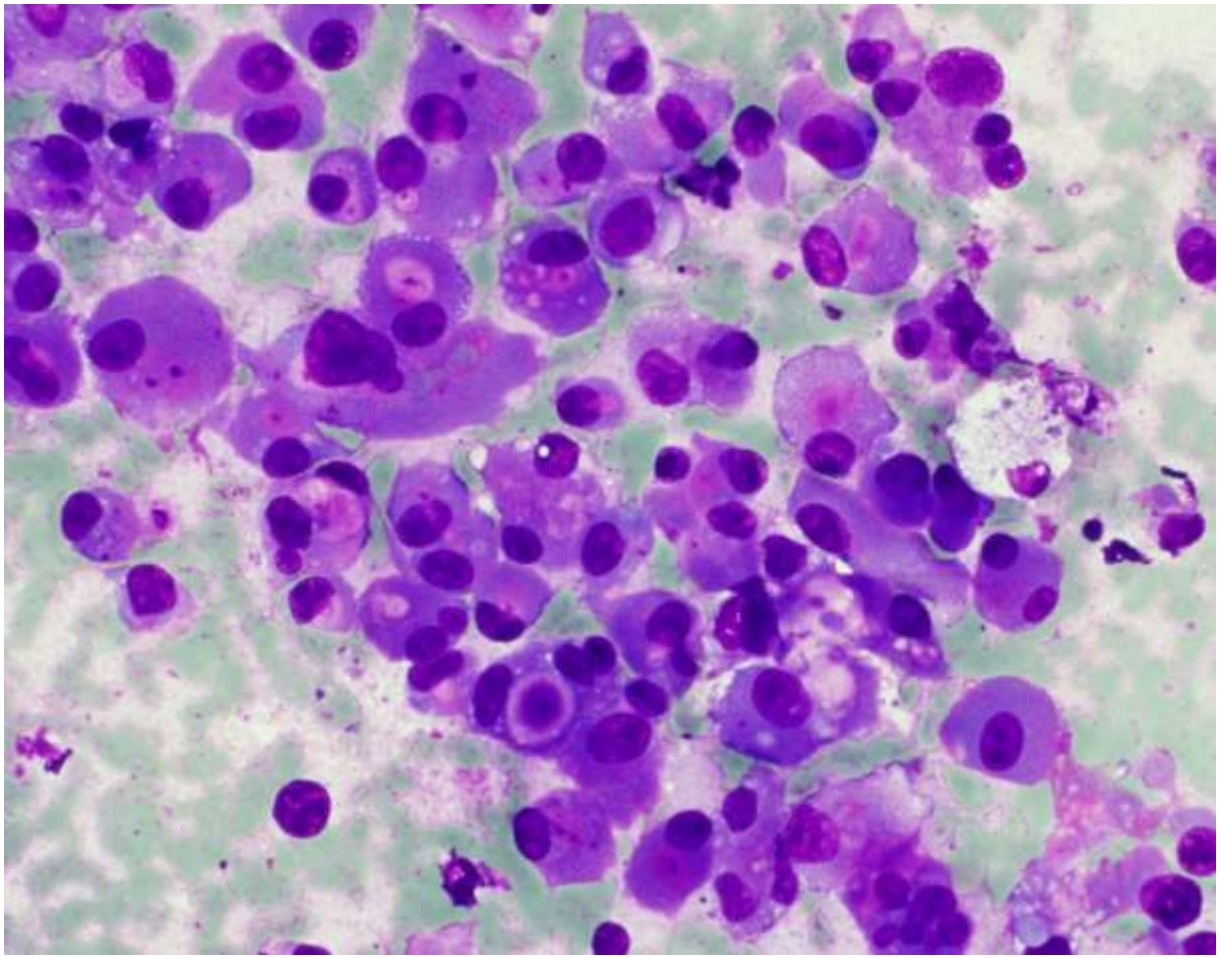

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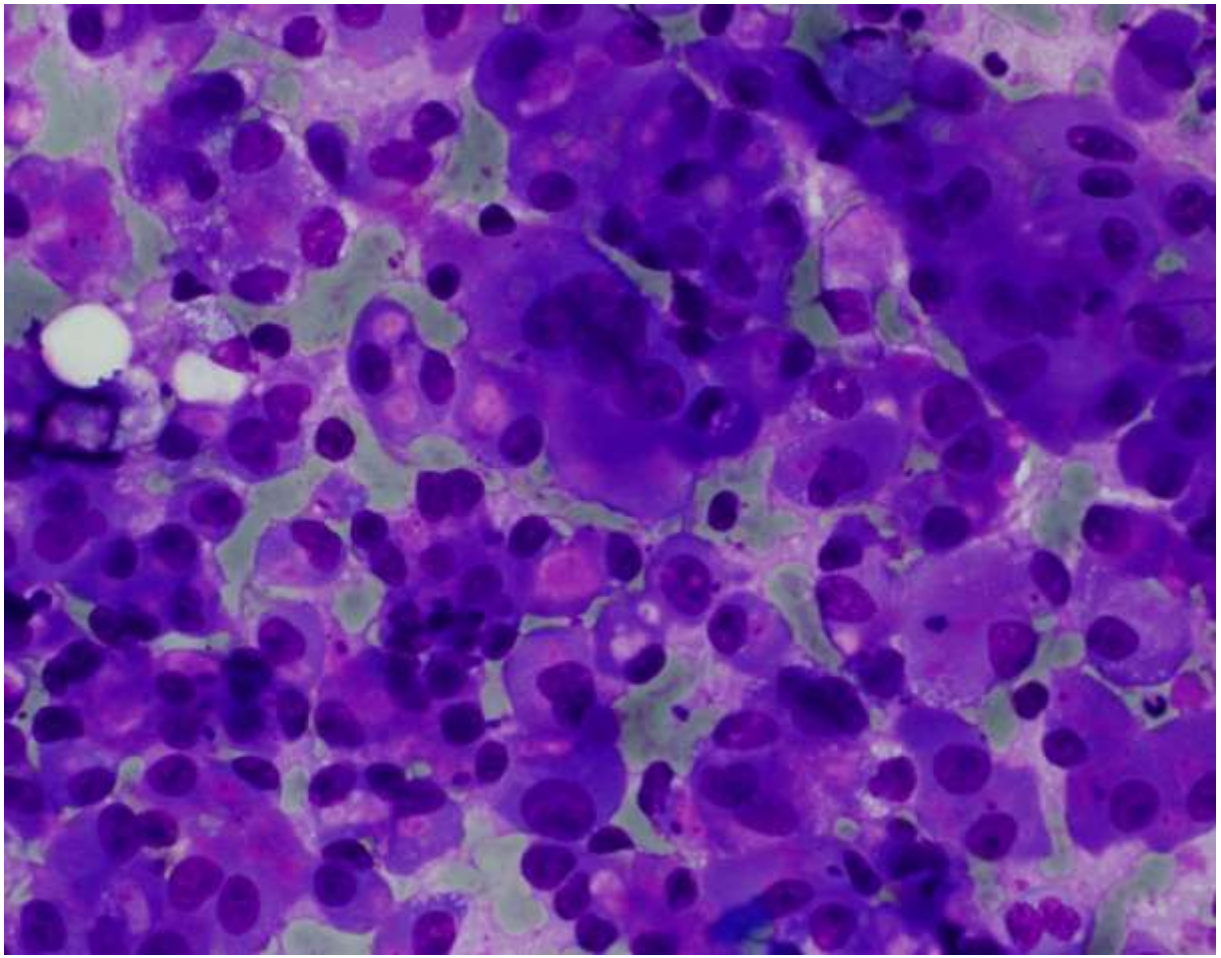
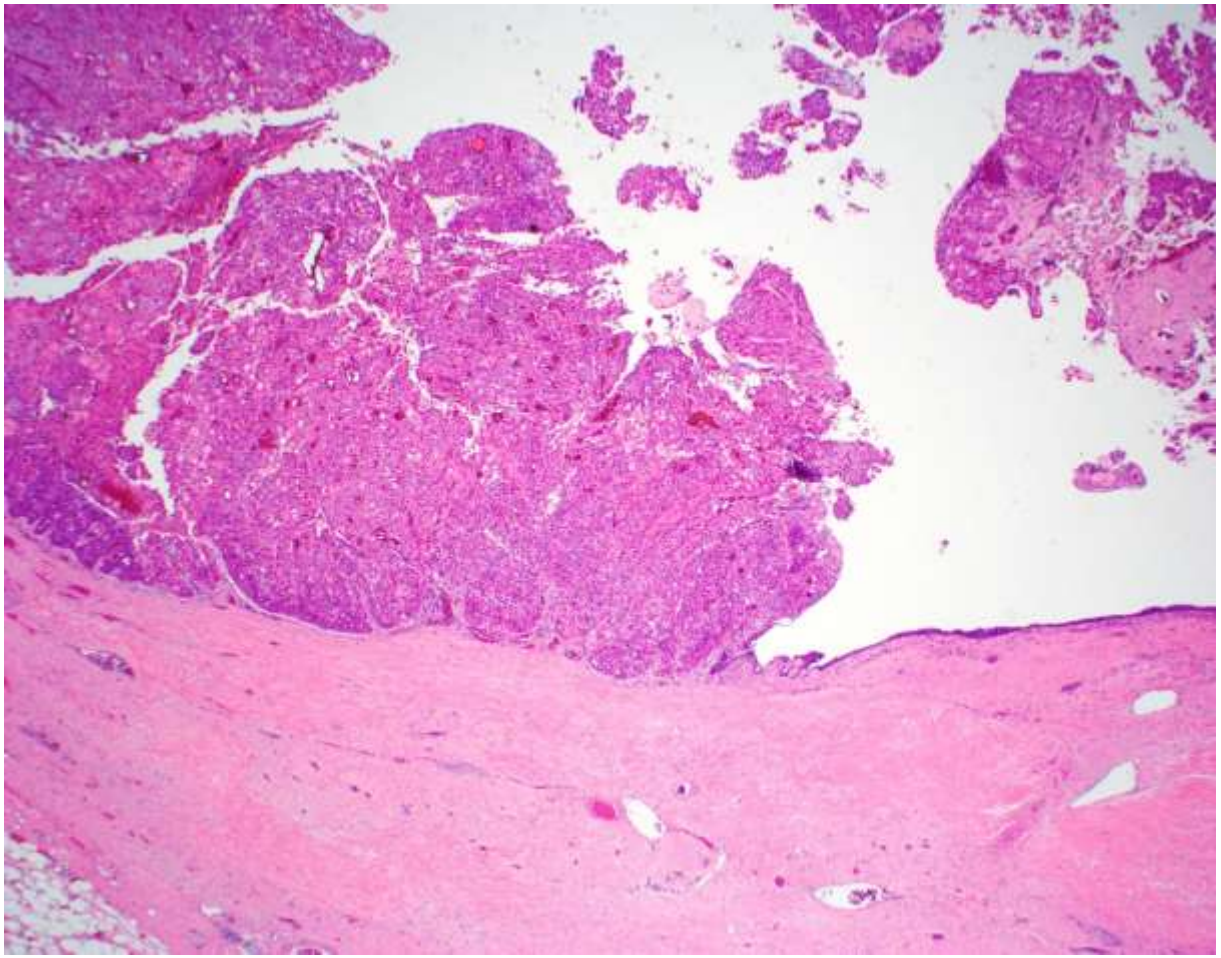
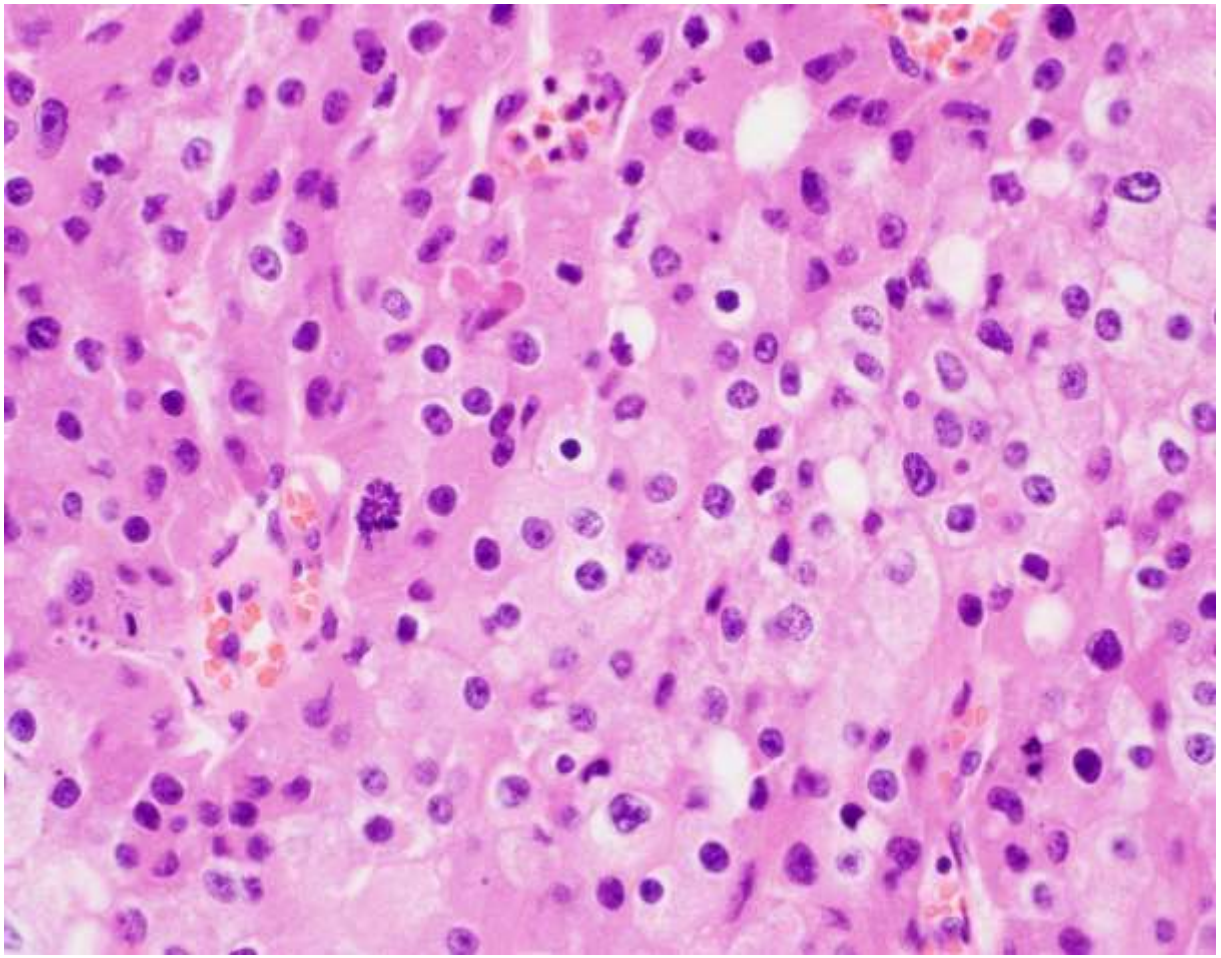


Histology



Histology



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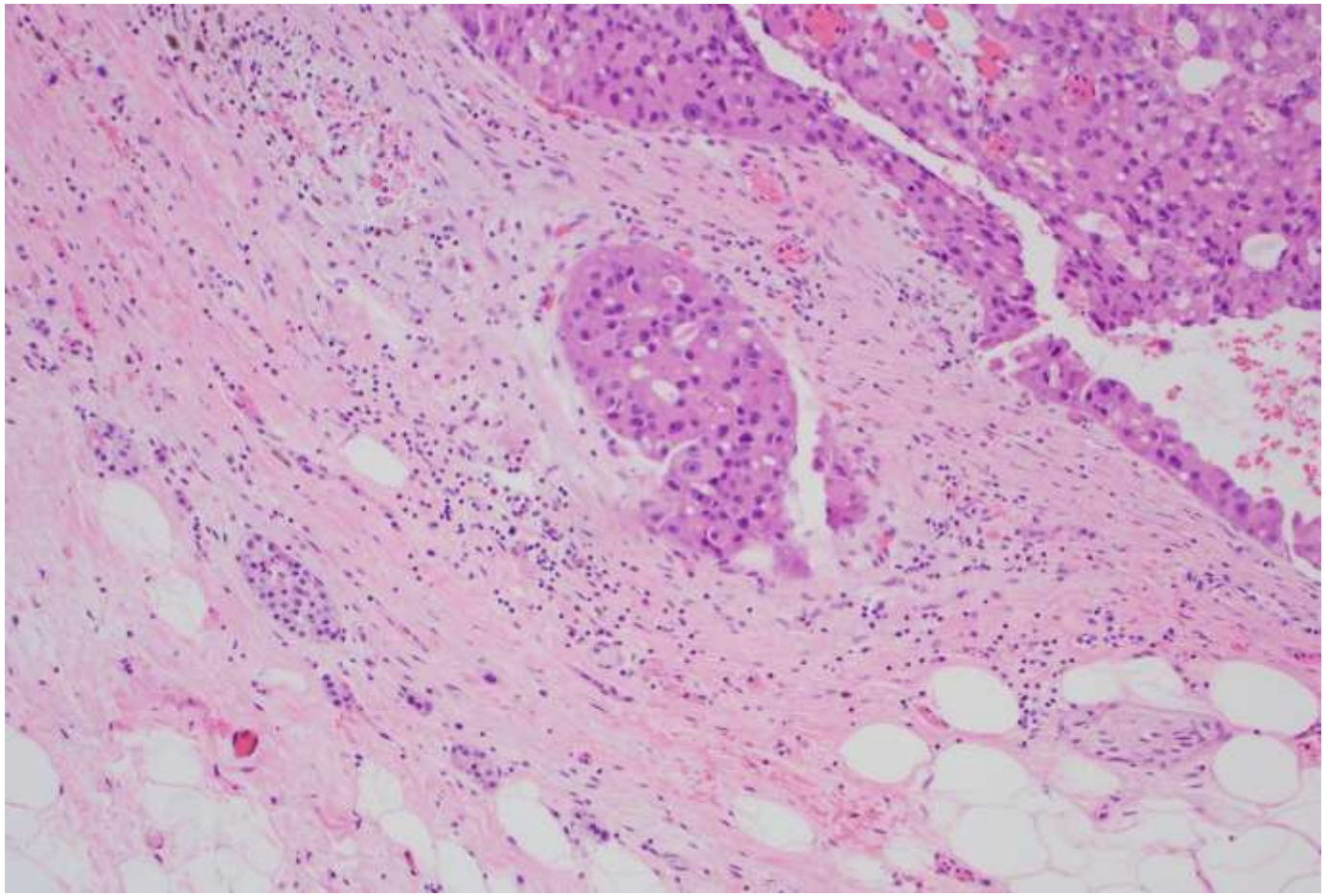
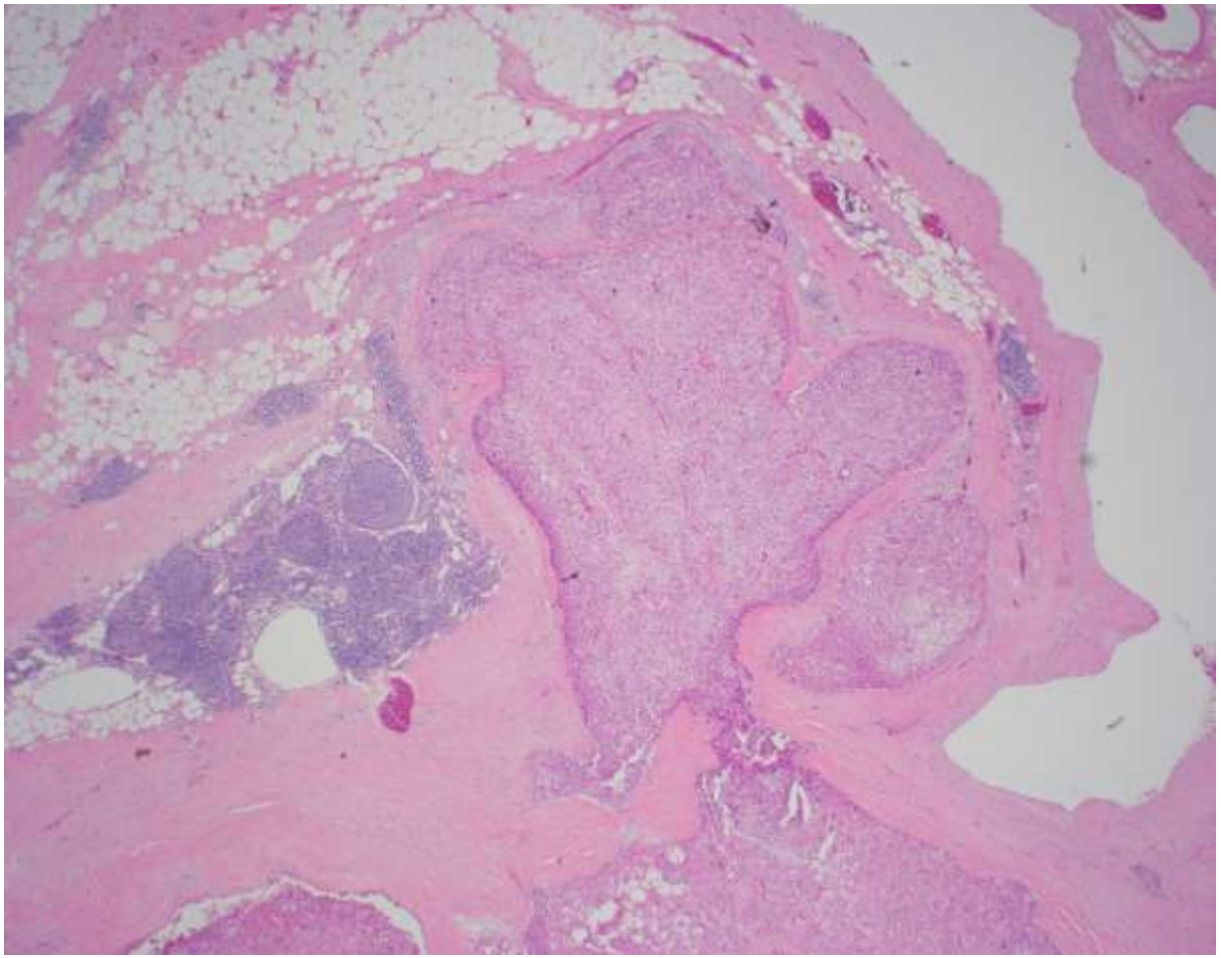


Histology



Differential diagnosis

- Intraductal oncocytic papillary neoplasm
- Neuroendocrine tumor
- Acinar cell carcinoma

Staining Pattern

Positive stains

- Pancytokeratin
- Heppar-1
- EMA (rare cells)
- Mucicarmine (intracytoplasmic vacuoles)

Negative stains

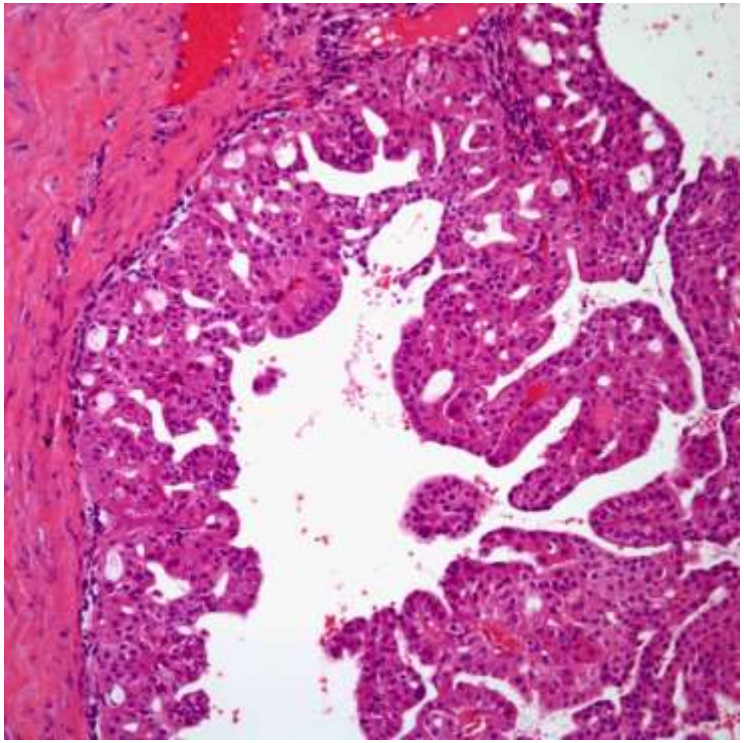
- Synaptophysin/Chromogranin
- CK7/CK20
- PAS
- CD117

Diagnosis

- Intraductal oncocytic papillary neoplasm with associated invasive oncocytic carcinoma

Intraductal Oncocytic Papillary Neoplasm (IOPN)

- Papillary growth with arborizing
  - Papillae may fuse producing a solid pattern
- Oncocytic cells with large nuclei and prominent nucleoli
- Mucin containing intraepithelial lumina
- Associated invasive carcinomas may maintain oncocytic features or have a mucinous appearance



http://www.cancernetwork.com

Clinicopathologic correlations

- Of 400 cases of IPMN, 18 cases were IOPN (4.5%)
- Male predominance
- Tend to involve the main pancreatic duct
- Frequently associated with invasive carcinoma (61%) and high-grade dysplasia
- 10 year recurrence rate: 46%
- Recurrences up to 11 years
- At a median follow-up of 7 years, no patients had died of disease

Marchegiani, et al. J Am Coll Surg. 2015 May;220(5):839-44.

Clinicopathologic correlations

- Eleven patients
- Mean age 62
- Slight male predominance (6 vs. 5)
- 9 cases intraductal, 1 case with microinvasion, 1 case with widespread invasion
- 7 patients alive and free of disease (1 year mean follow-up), 4 patients died with no evidence of disease, 1 patient had recurrence

Adsay, Et l. Am J Surg Pathol. 1996 Aug;20(8):980-94.

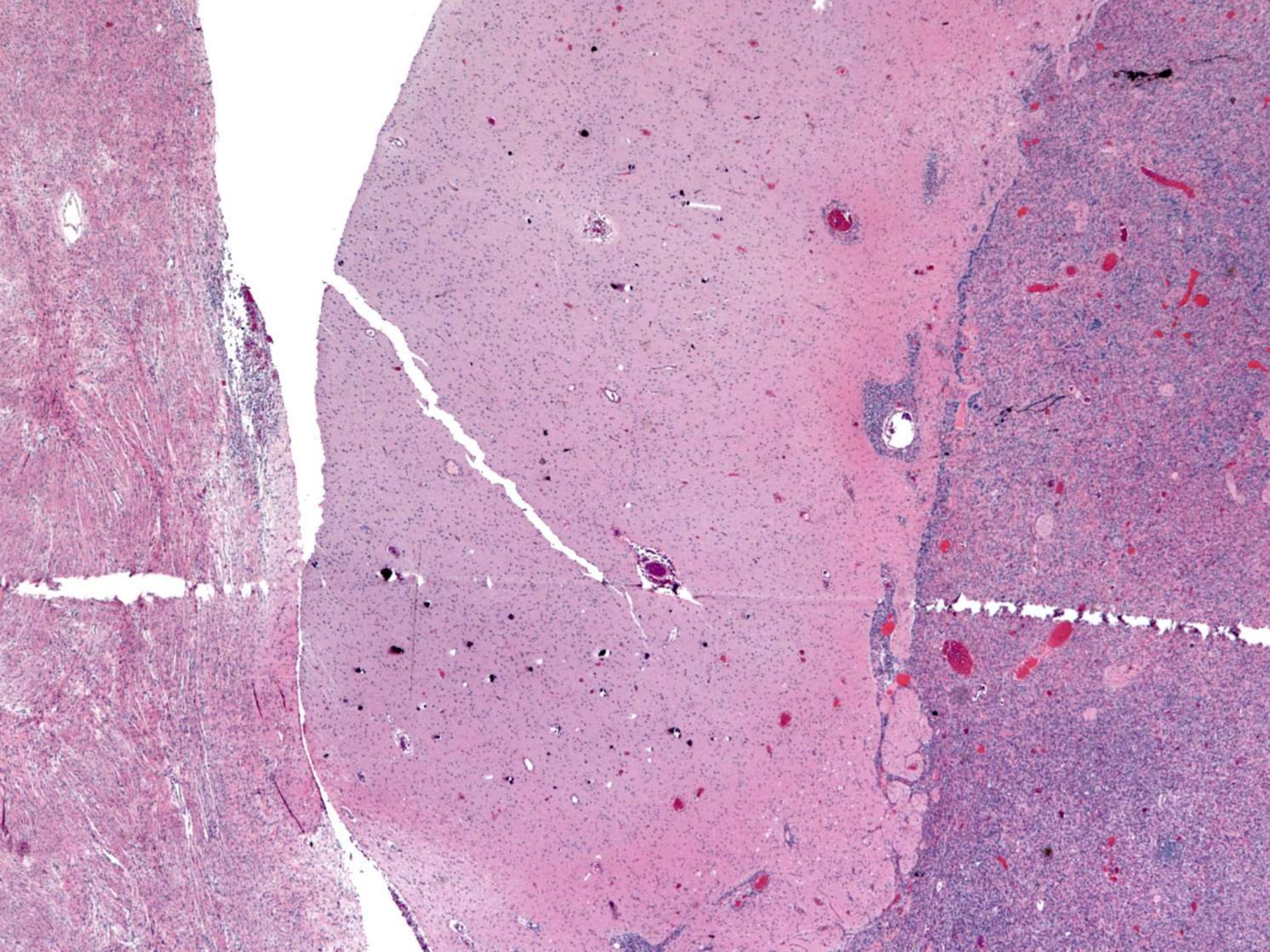
References

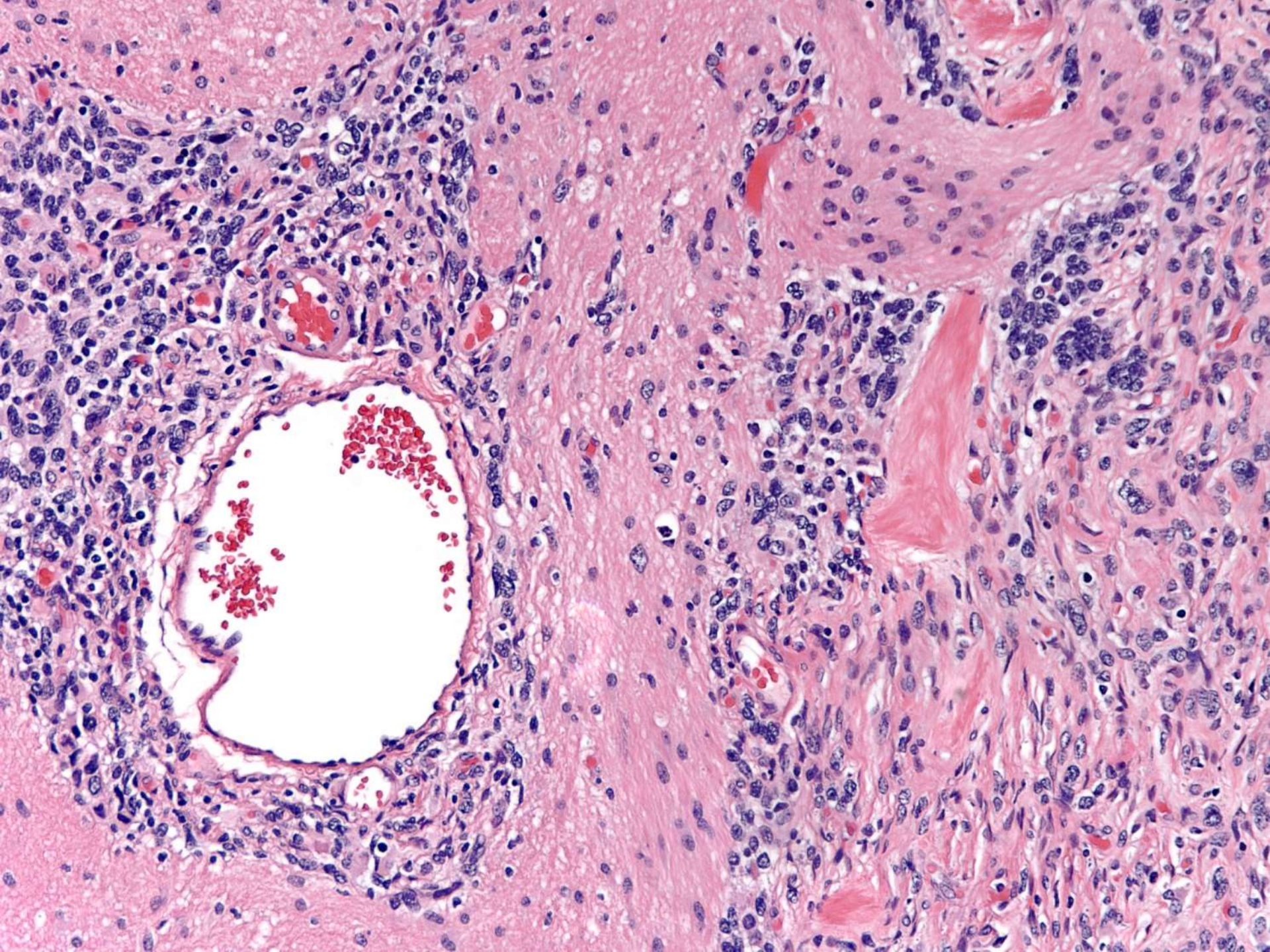
- Adsay NV, Adair CF, Heffess CS, Klimstra DS. Intraductal oncocytic papillary neoplasms of the pancreas. Am J Surg Pathol. 1996 Aug;20(8):980-94.
- Bosman FT, Carneiro F, Hruban RH, Thiese ND (Eds). WHO Classifiication of Tumors of the Digestive System, IARC, Lyon 2010.
- Marchegiani G, Mino-Kenudson M, Ferrone CR, Warshaw AL, Lillemoe KD, Fernández-del Castillo C.
- Robert Odze and John Goldblum. Surgical Pathology of the GI Tract, Liver, Biliary Tract and Pancreas, Third Edition.

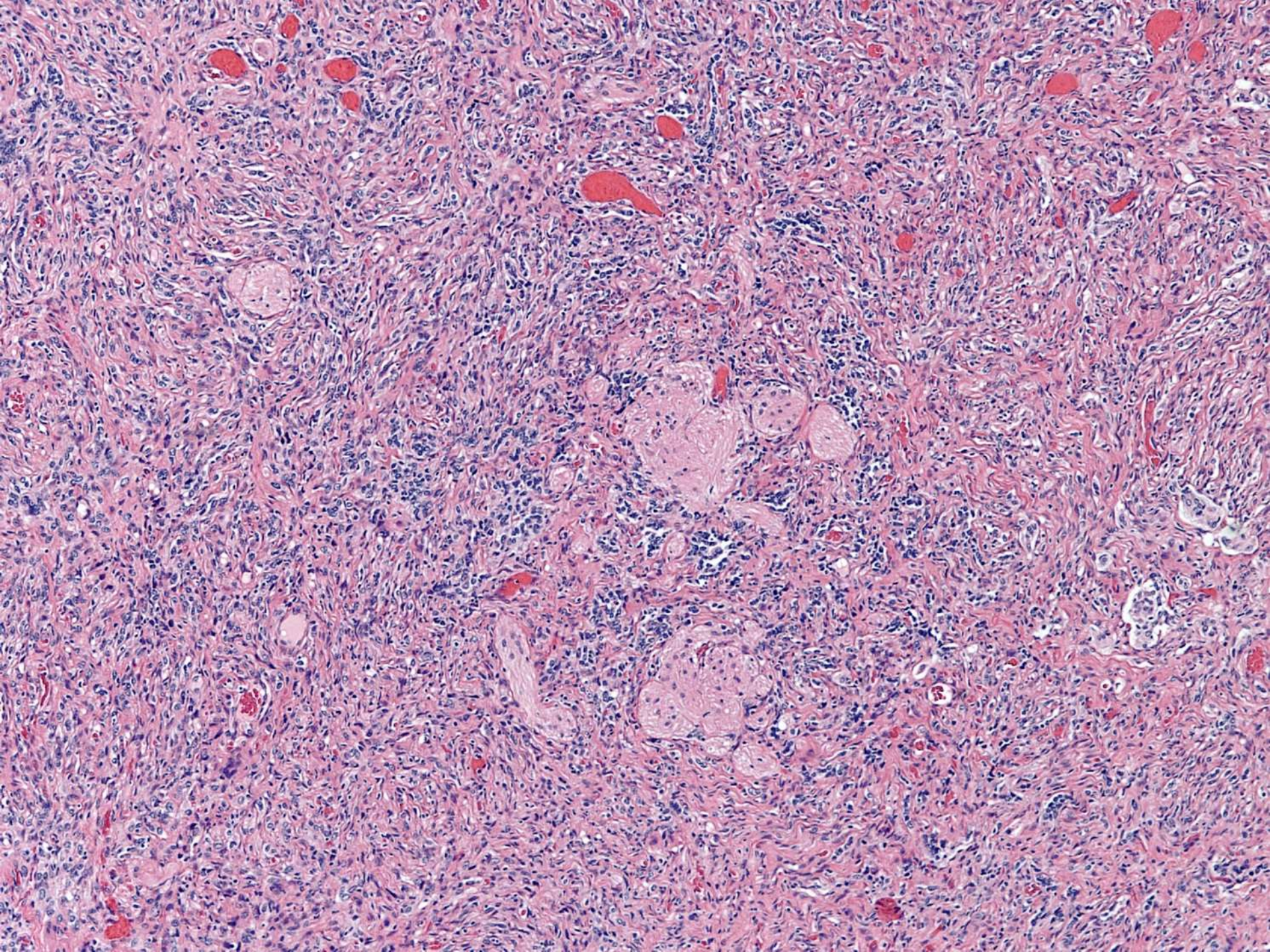
SB 6110

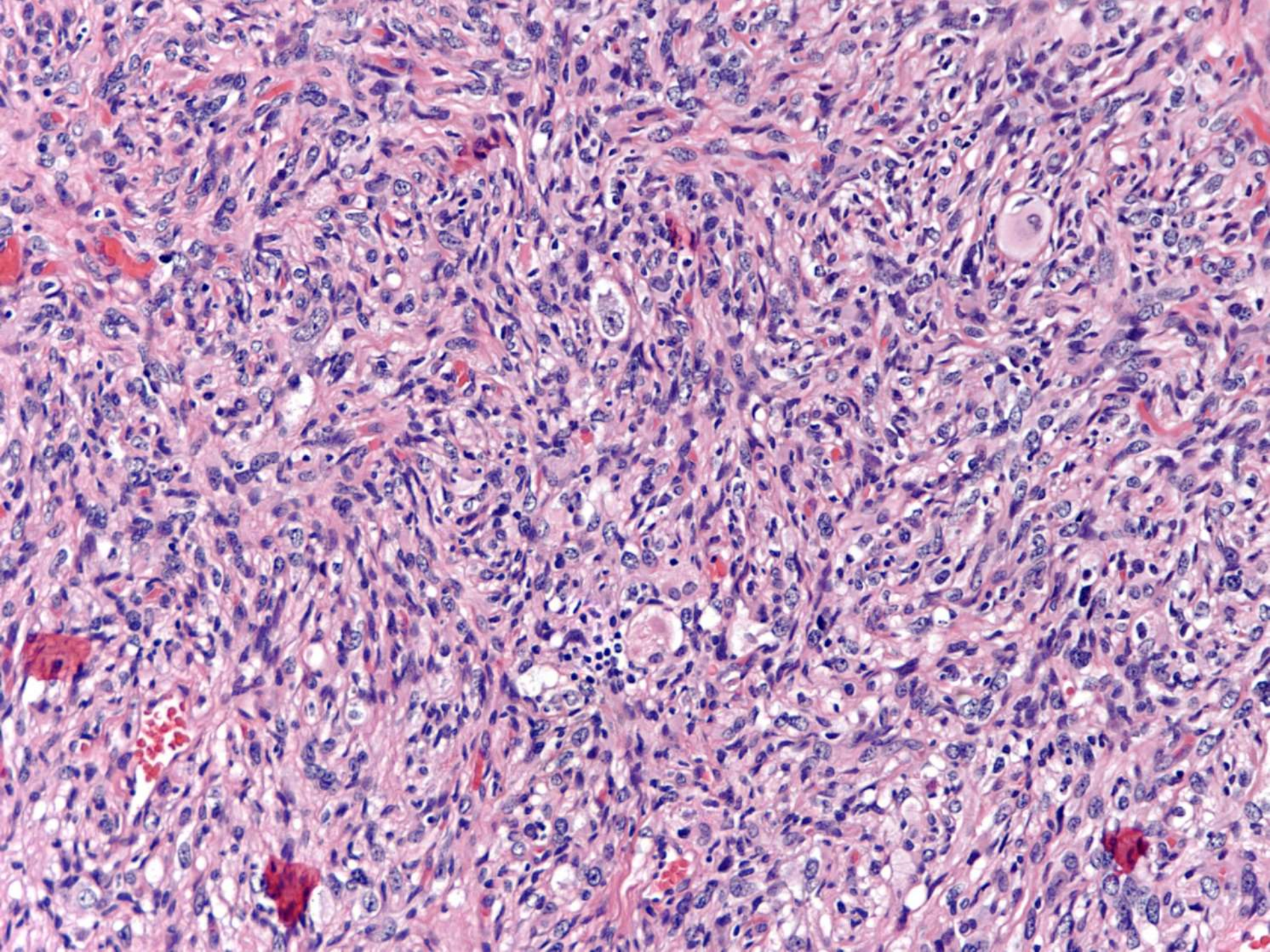
Peyman Samghabadi/Hannes Vogel; Stanford

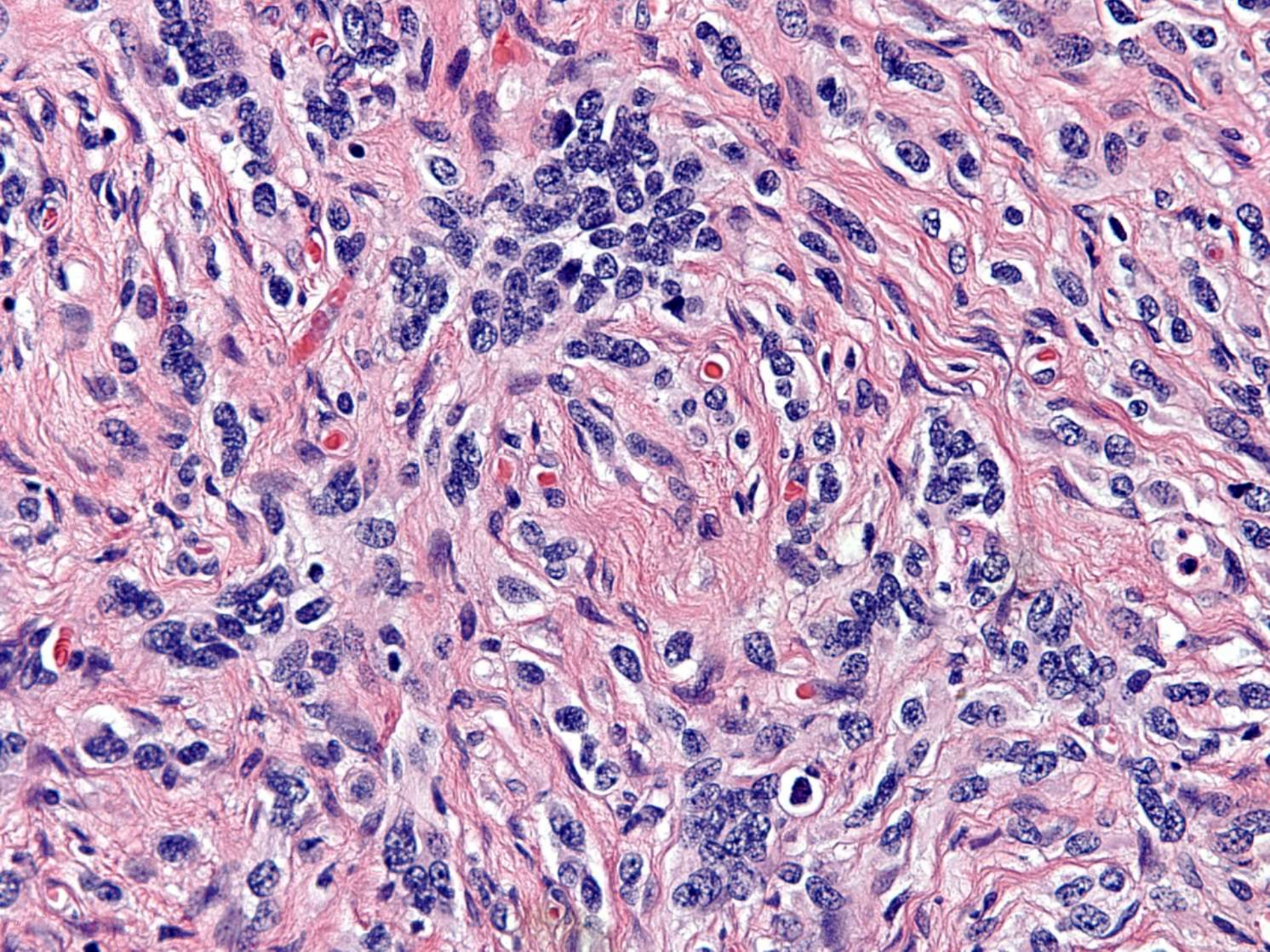
22-month-old-male with a three week history of headache and emesis. MRI reveals a left frontoparietal well circumscribed mass (3.7 cm) with contrast enhancement, extending to the dura. It is surrounded by a large cystic component (~ 8 cm) containing multiple locules and fluid levels.

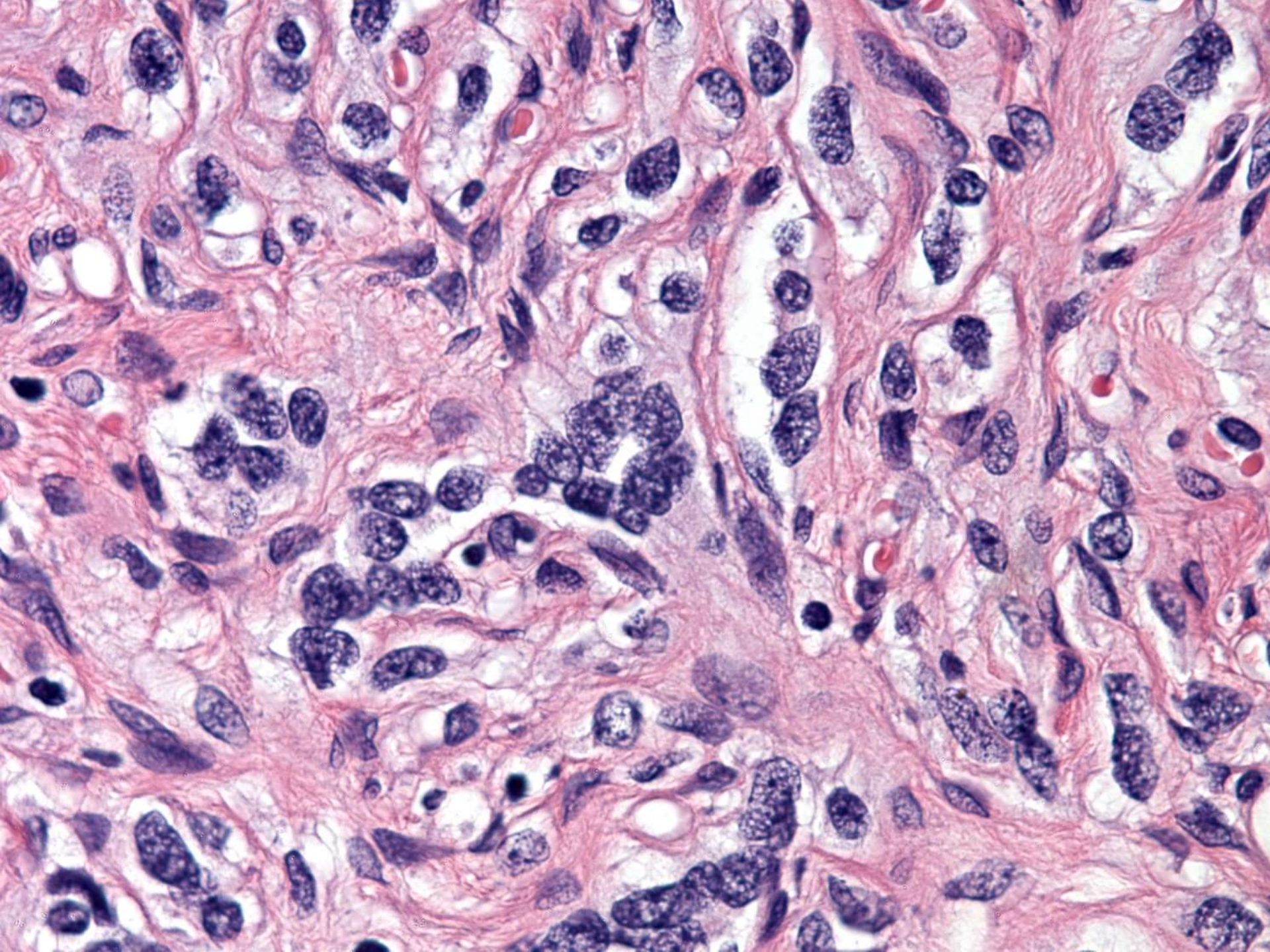


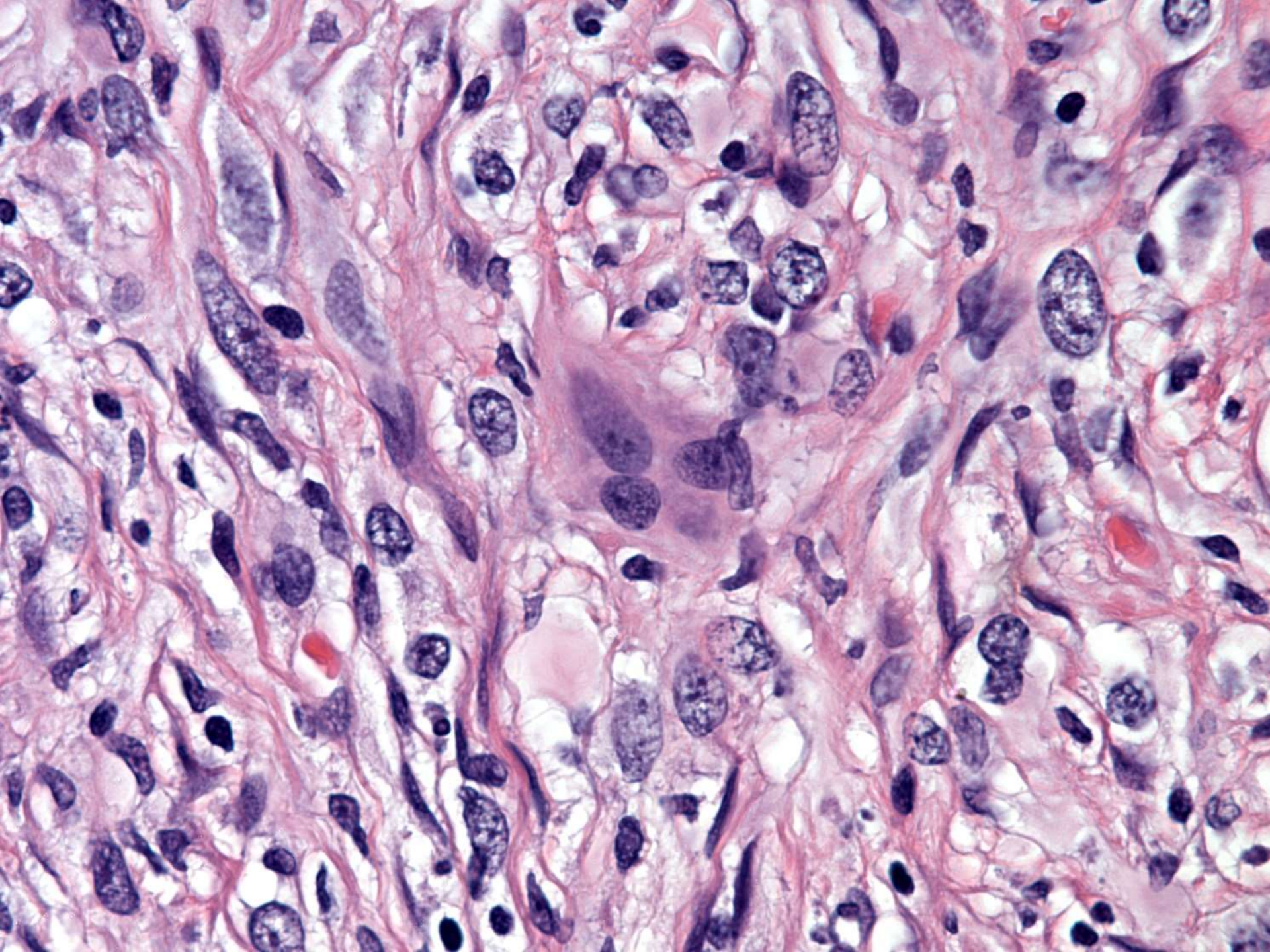


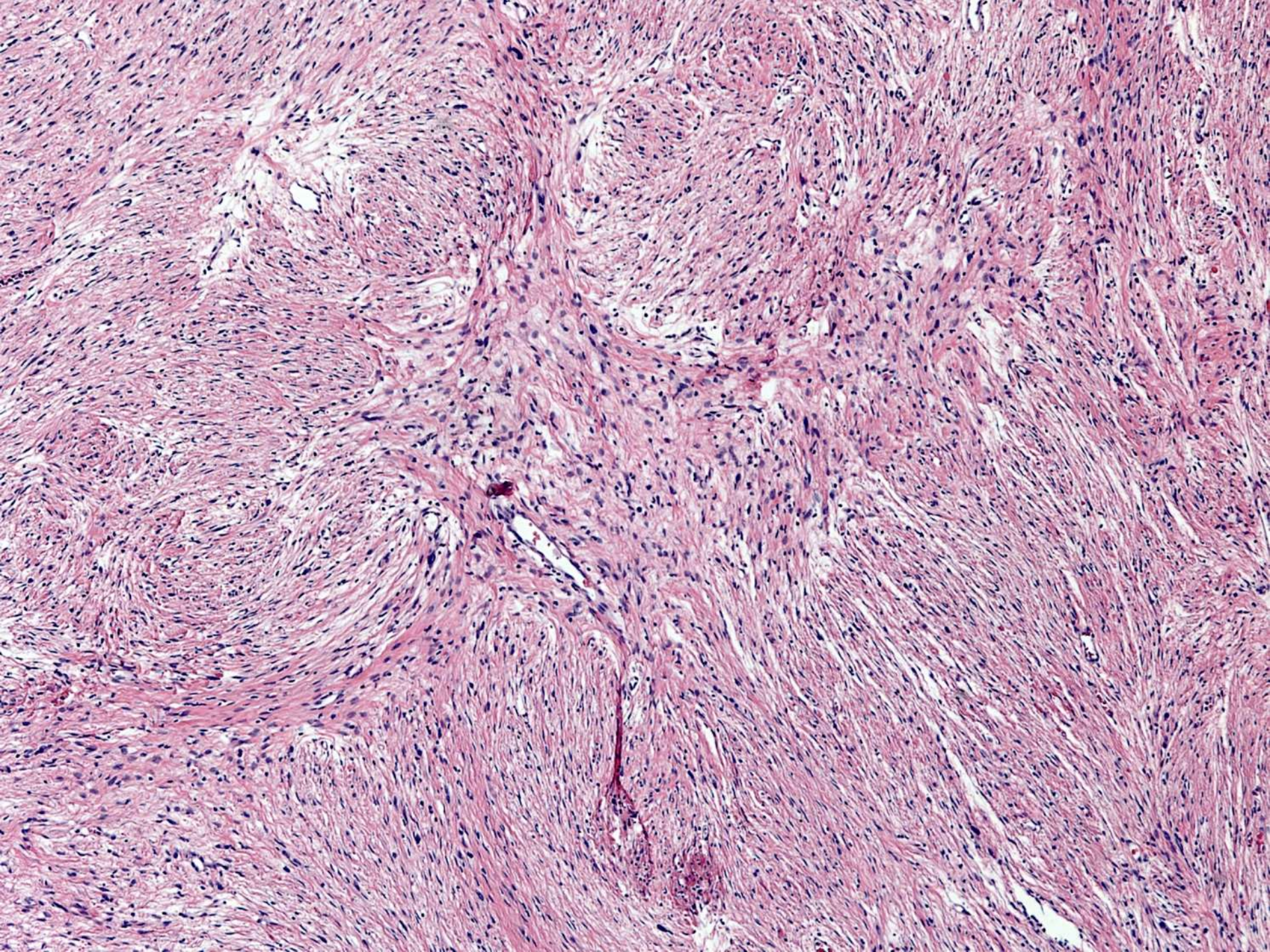


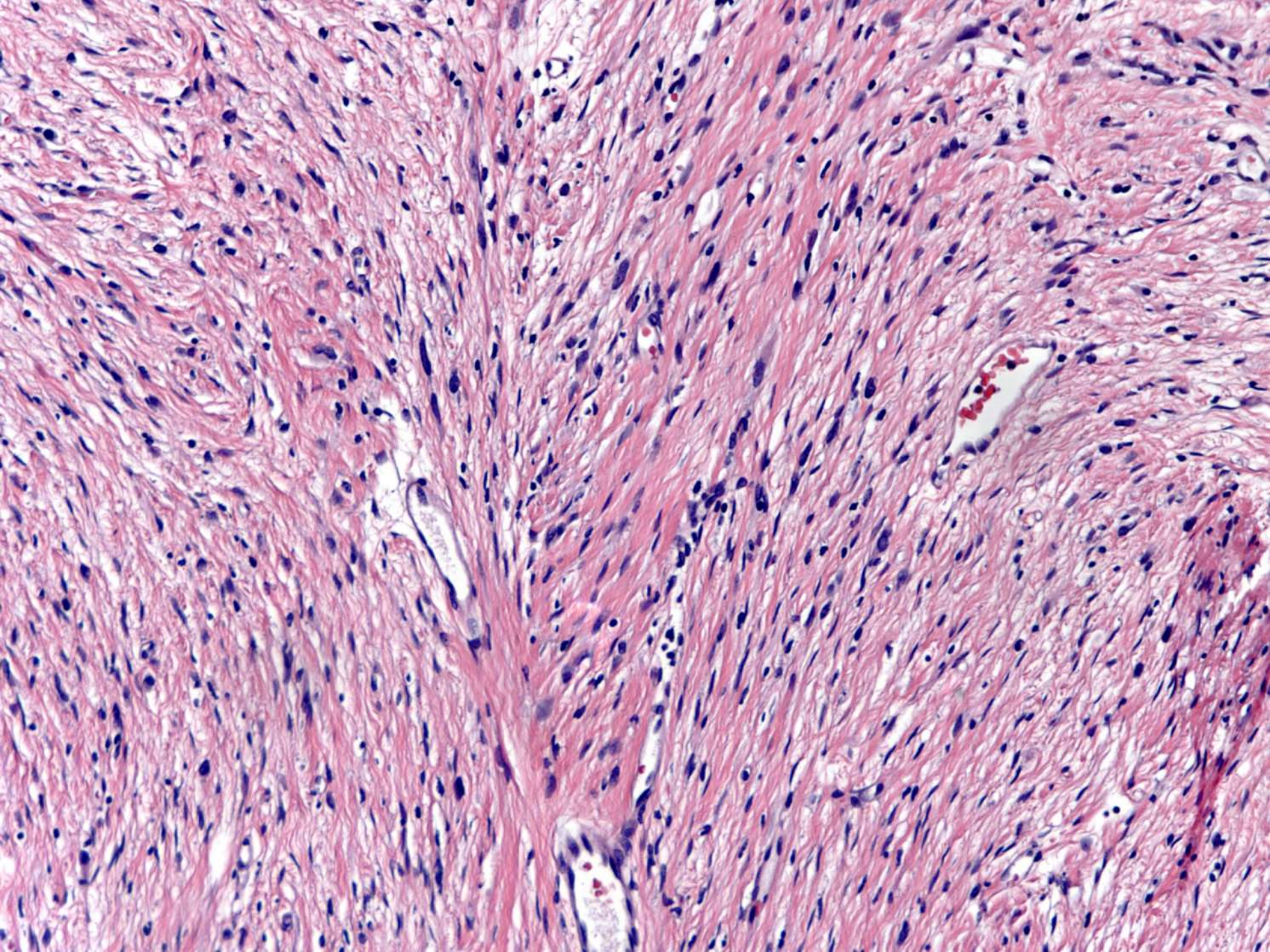


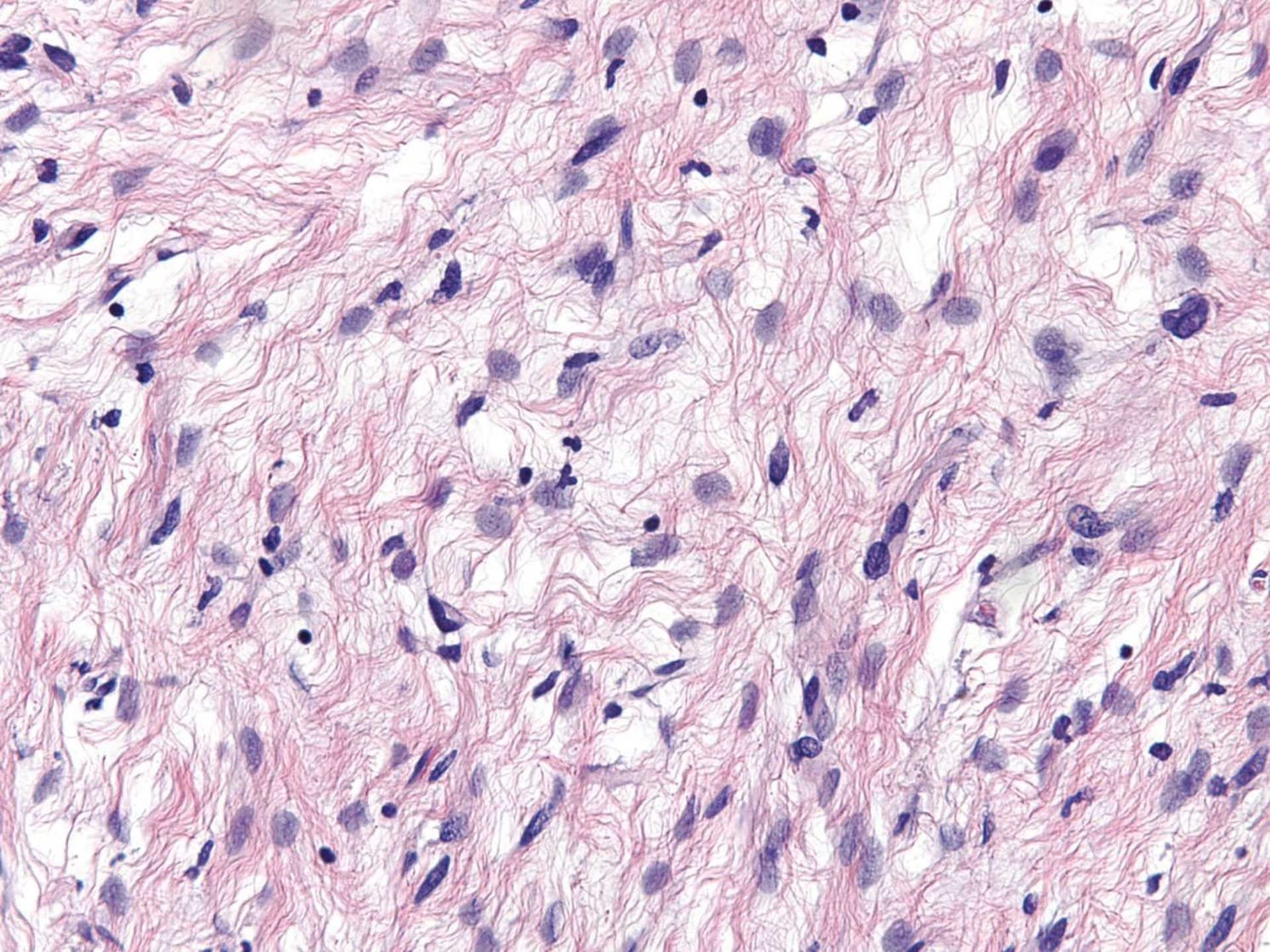


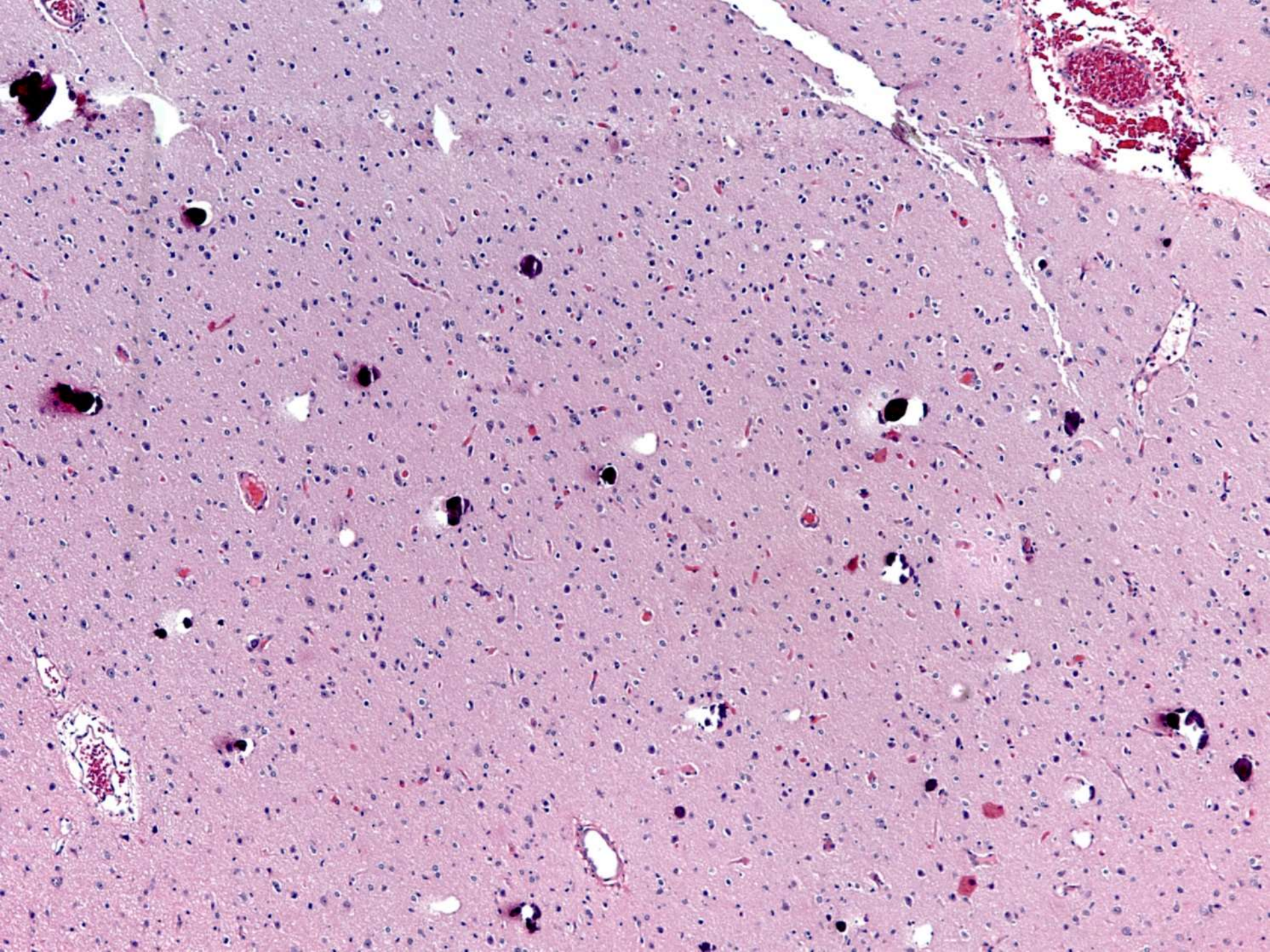






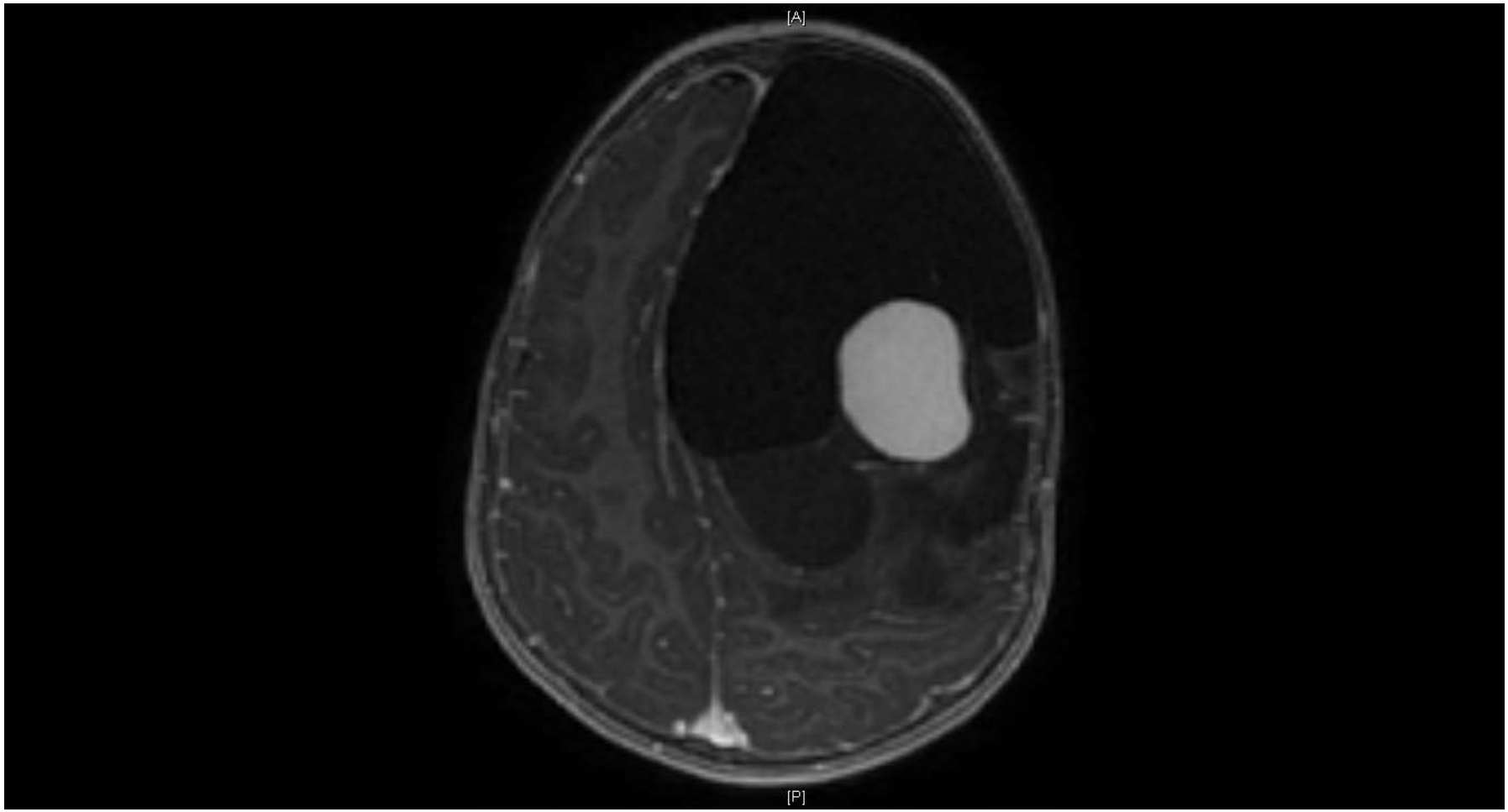


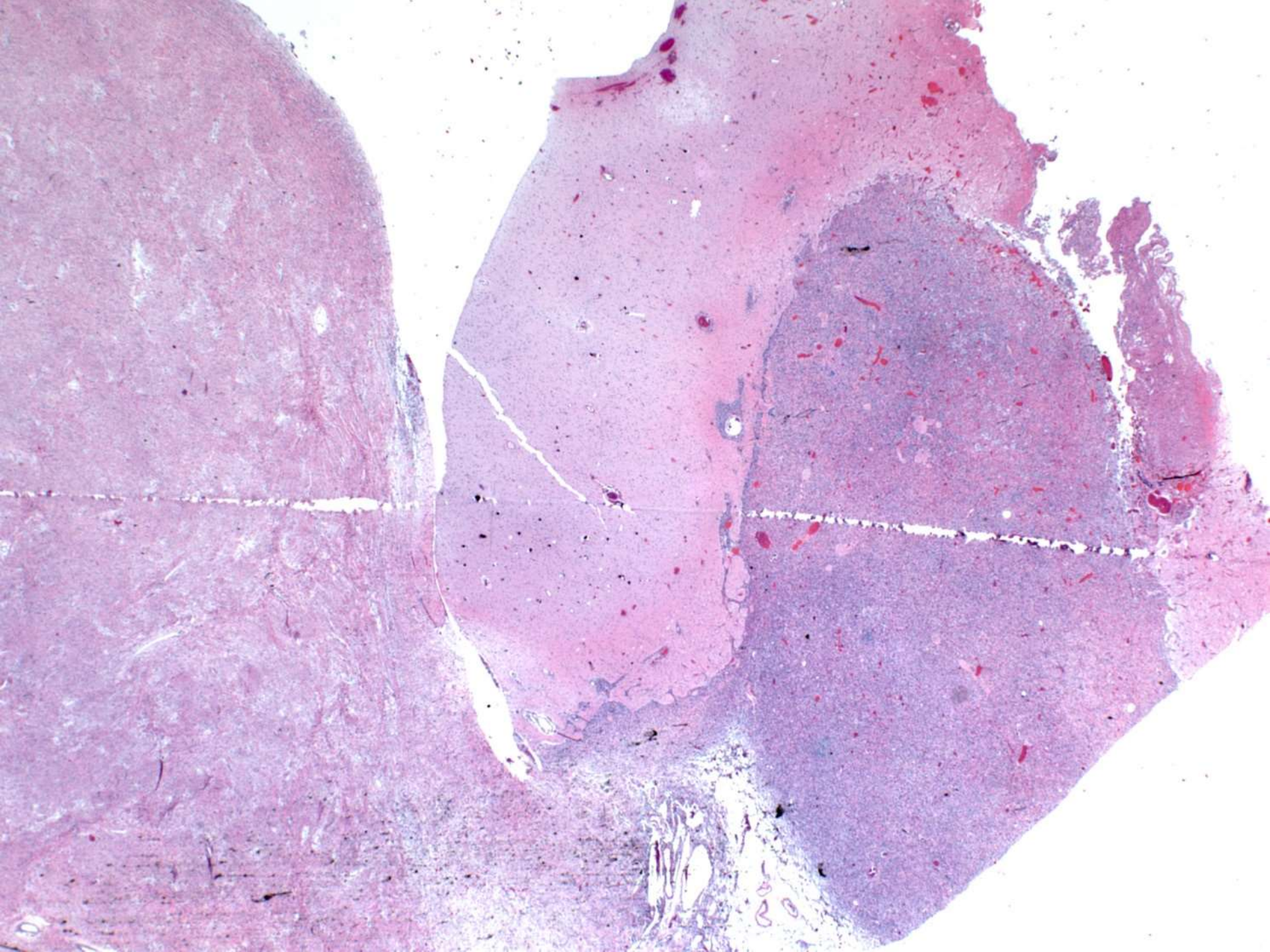


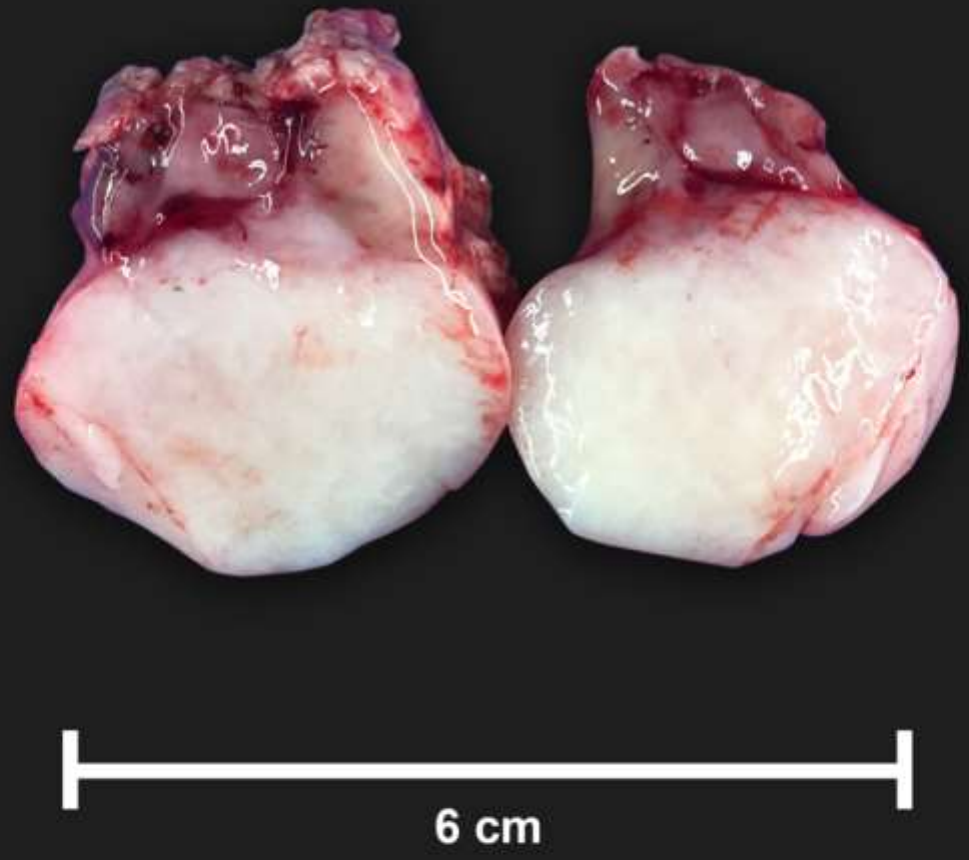


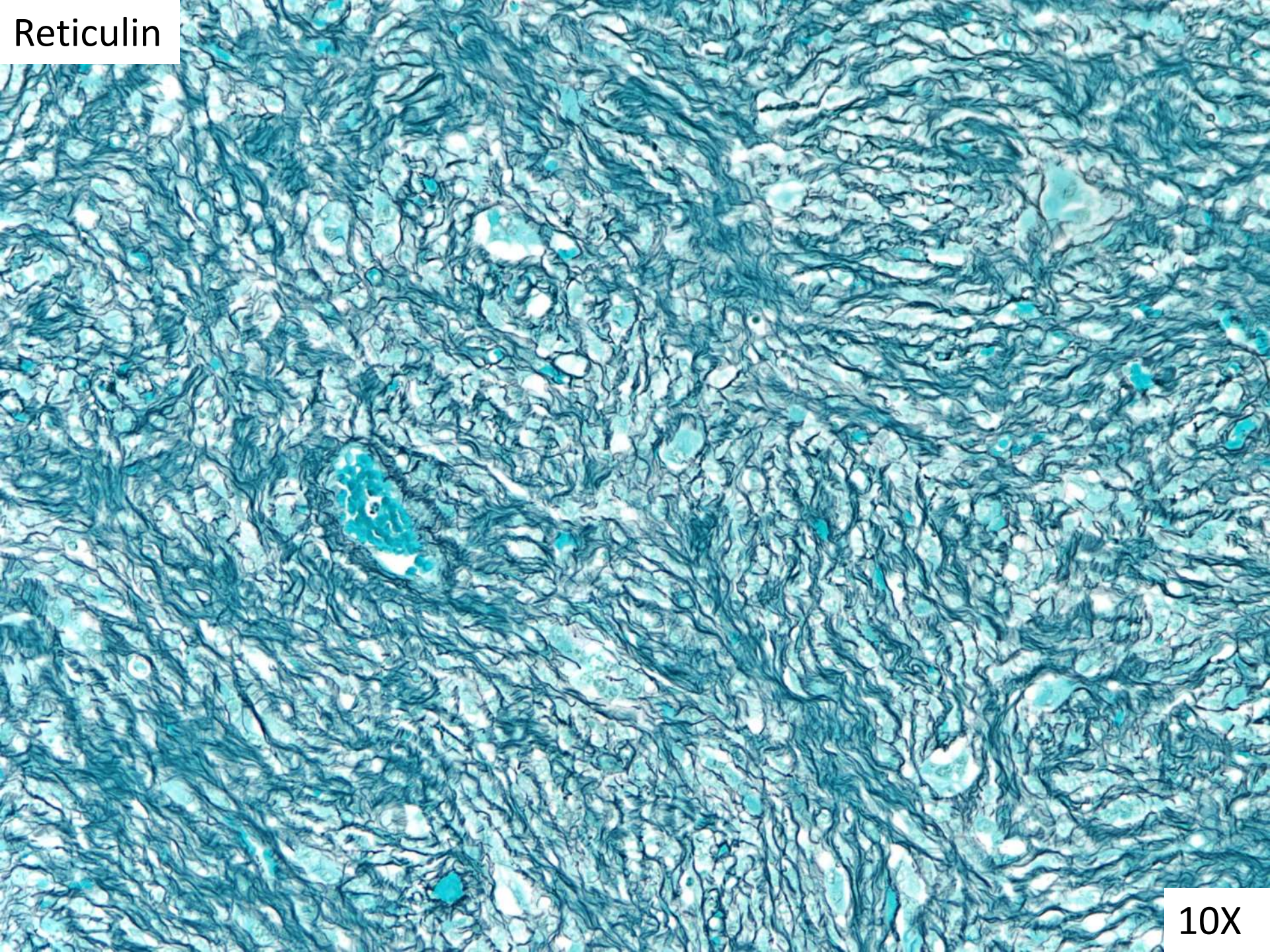
DIAGNOSIS?

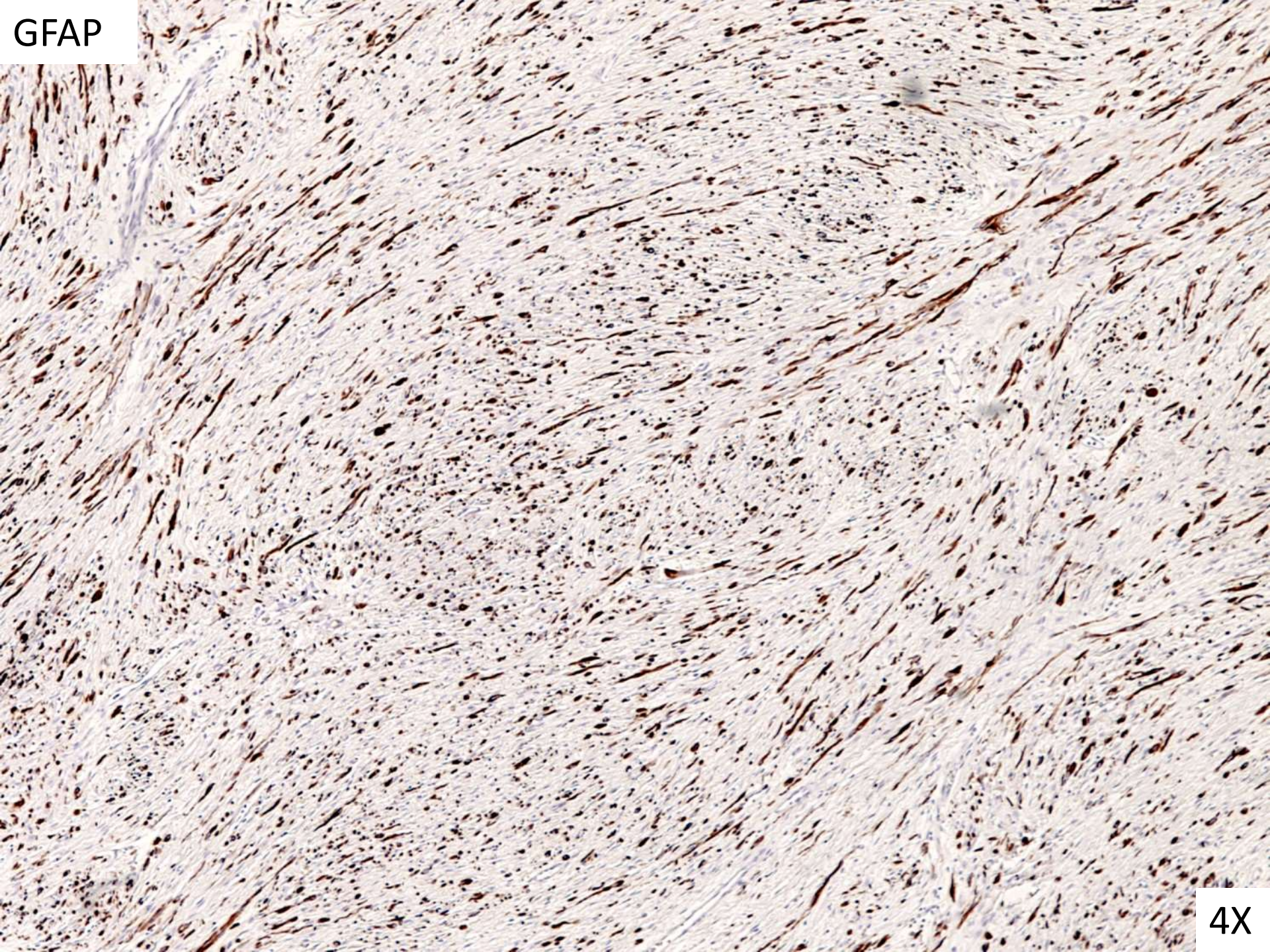
T1 Post Contrast Axial MR

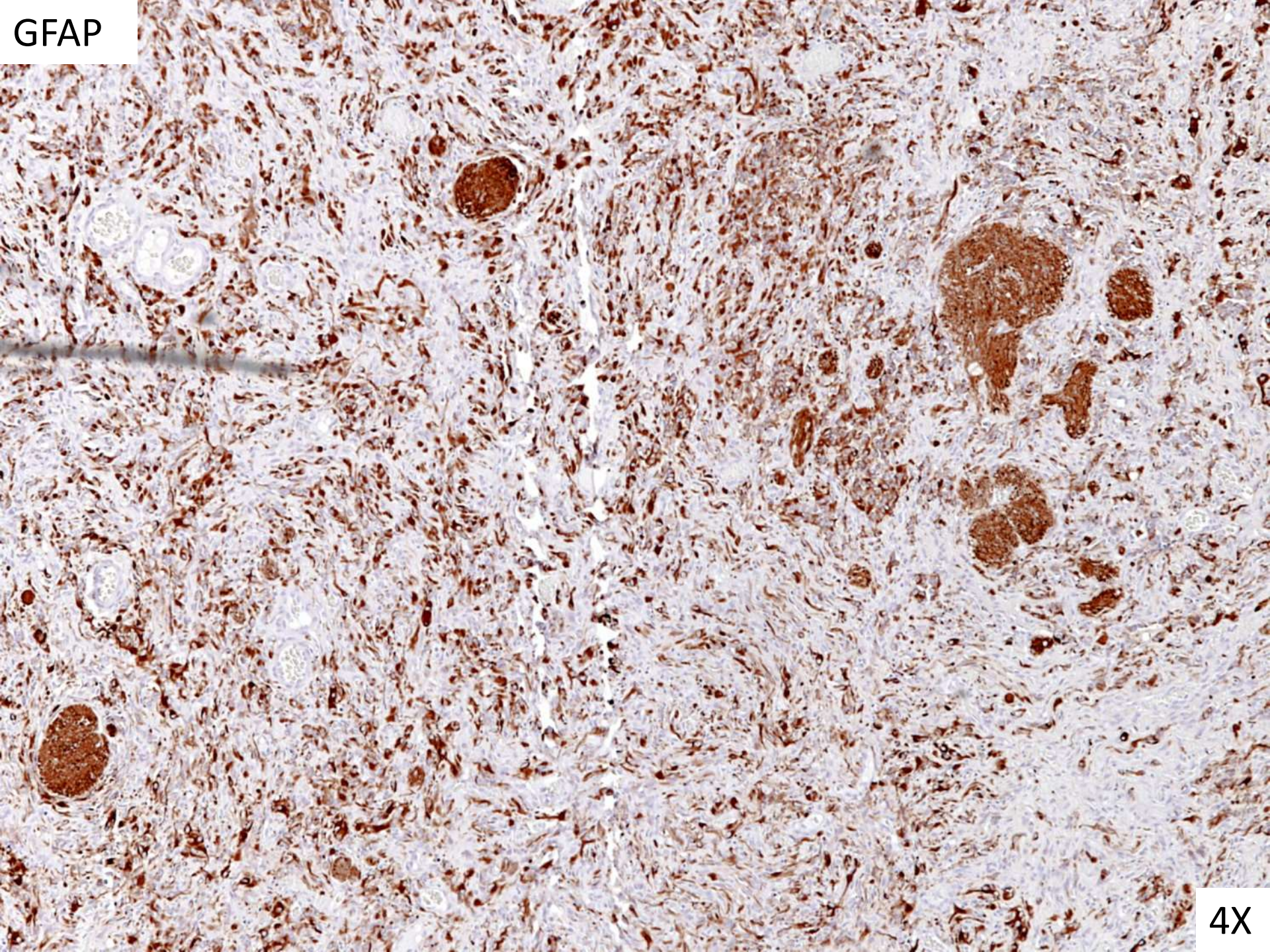


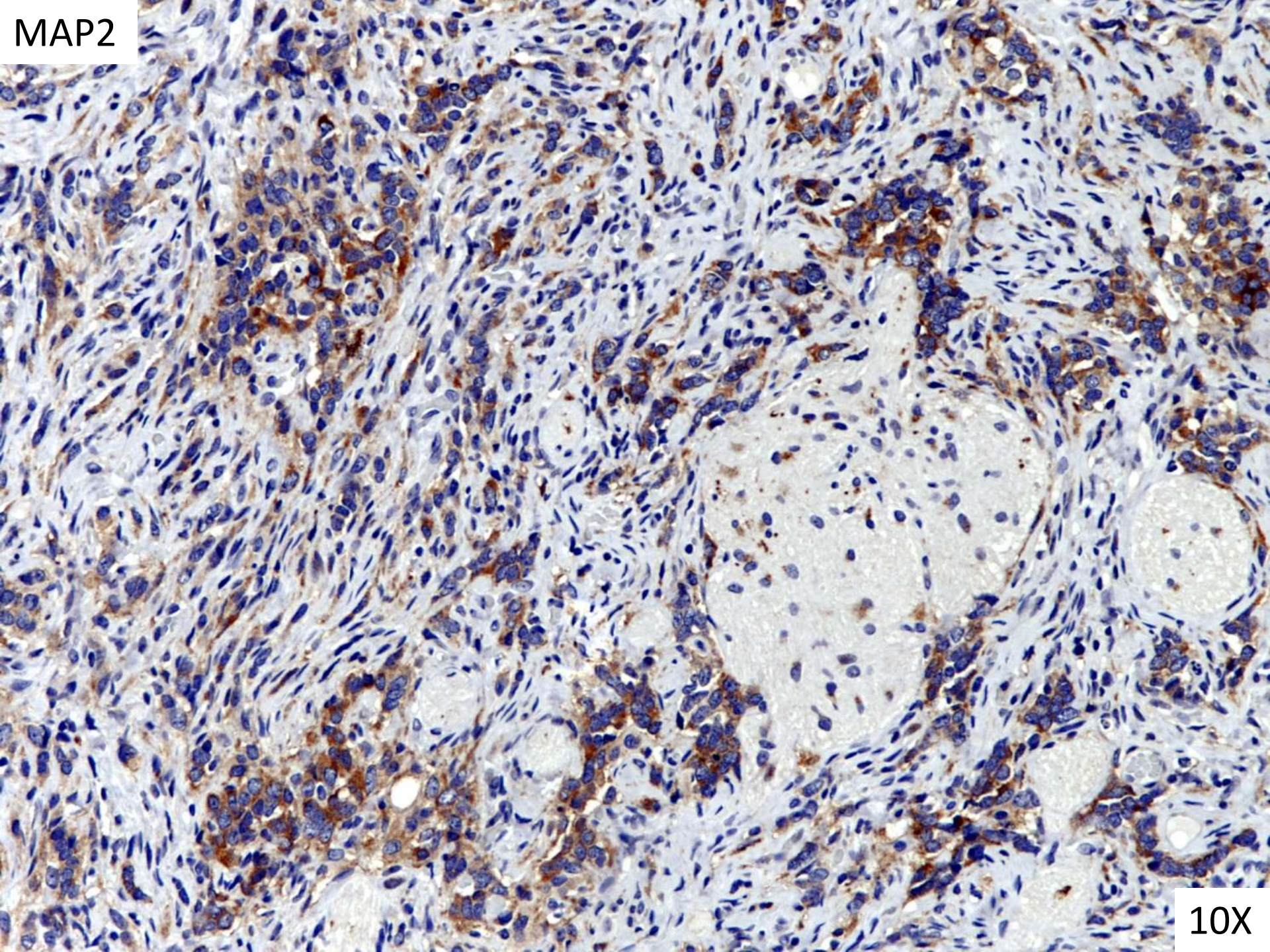


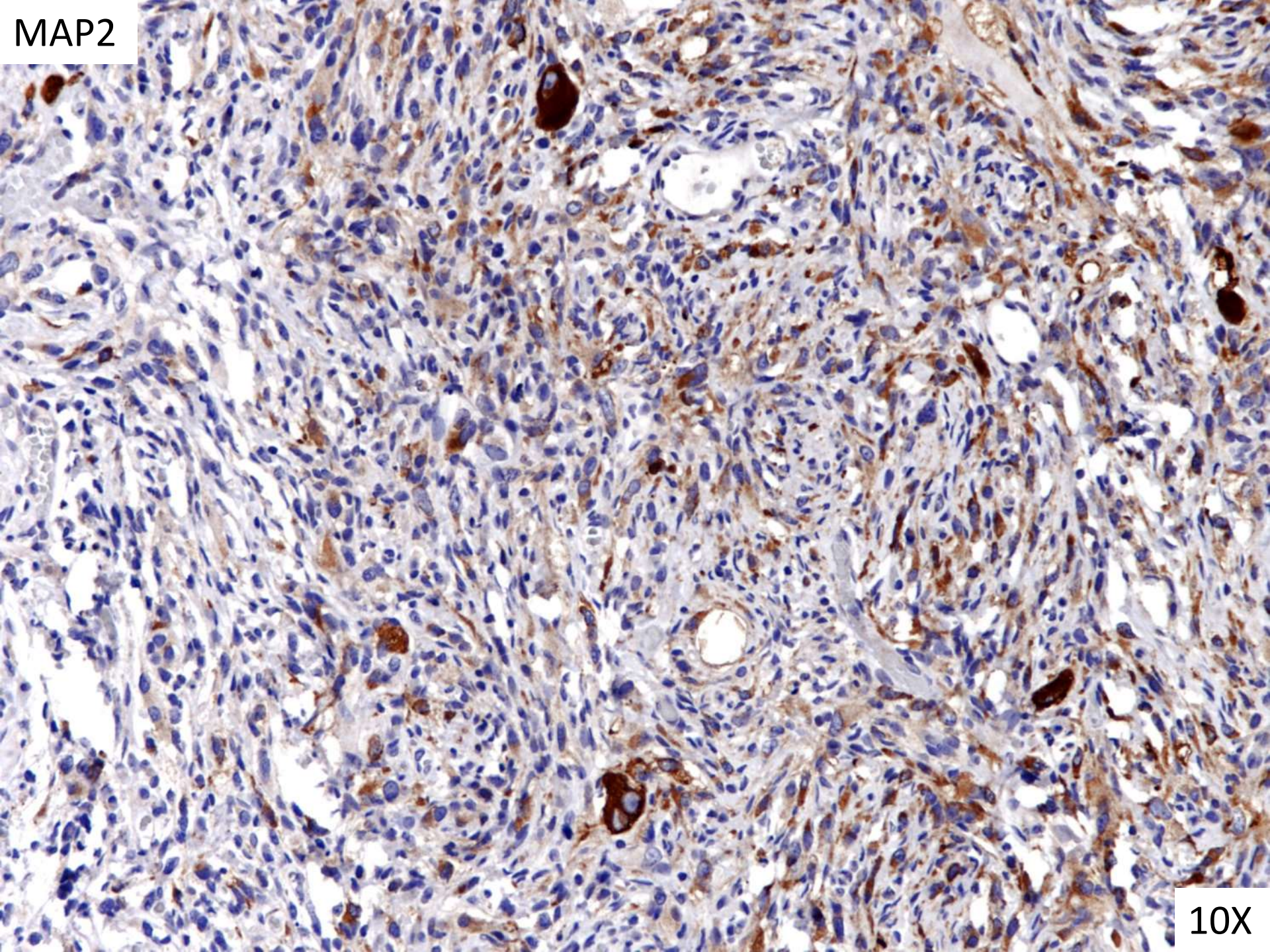

6 cm

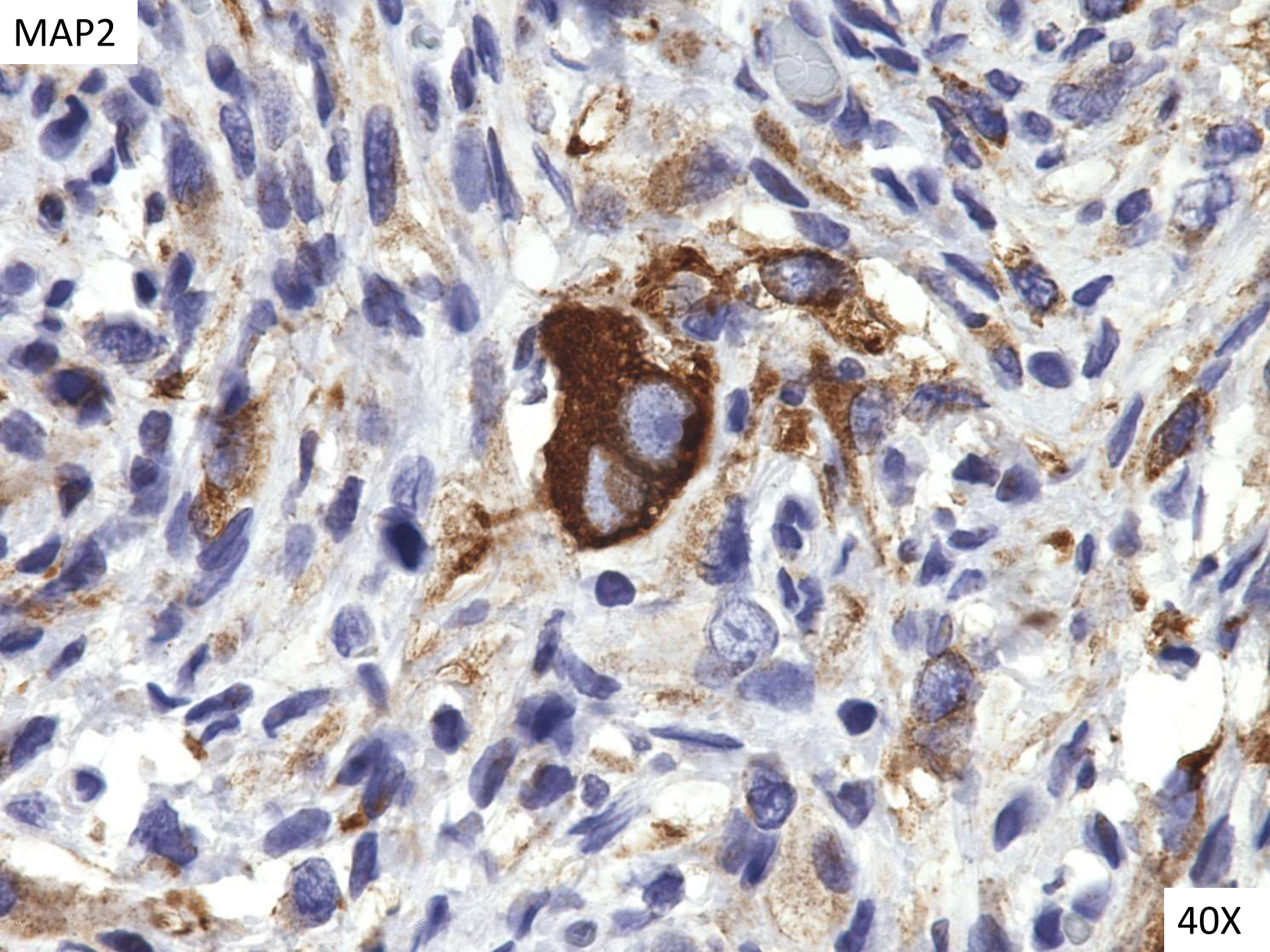

Reticulin
10X


GFAP
4X


GFAP
4X


MAP2
10X


MAP2
10X


MAP2
40X

DIAGNOSIS

DESMOPLASTIC INFANTILE GANGLIOGLIOMA, WHO GRADE I

Epidemiology

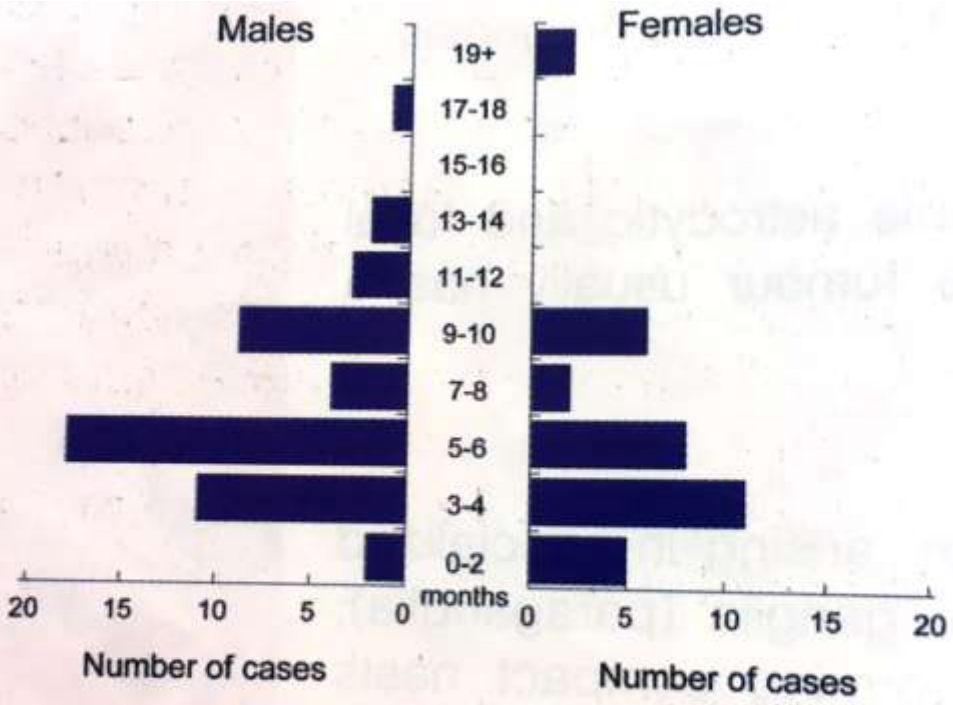


Fig. 6.01 Age (months) and sex distribution of desmoplastic infantile astrocytoma and ganglioglioma, based on 84 published cases.

Clinical Features

- Rapidly increasing head circumference
- Bulging fontanelle
- Hypertonus
- Forced downward deviation of the eyes (Parinaud syndrome)

IMMUNOPHENOTYPE

Astrocytes (fibroblast-like)	Neuronal (variable)	Primitive Neuroepithelium
GFAP (most)	GFAP (variable)	GFAP (variable)
SMA (uncommon)	Class III β-Tubulin	Class III β-Tubulin
Vimentin	Synaptophysin	Synaptophysin
	Neurofilament (Heavy)	Desmin (uncommon)
	MAP2	MAP2