Disclosures
Nov 5, 2018

Dr. Christine Louie has disclosed a financial relationship with Grail, Inc. (consultant), and Dr. Ankur Sangoi has disclosed financial relationships with Google (consultant). South Bay Pathology Society has determined that these relationships are not relevant to the clinical cases being presented.
The following planners and faculty had no financial relationships with commercial interests to disclose:

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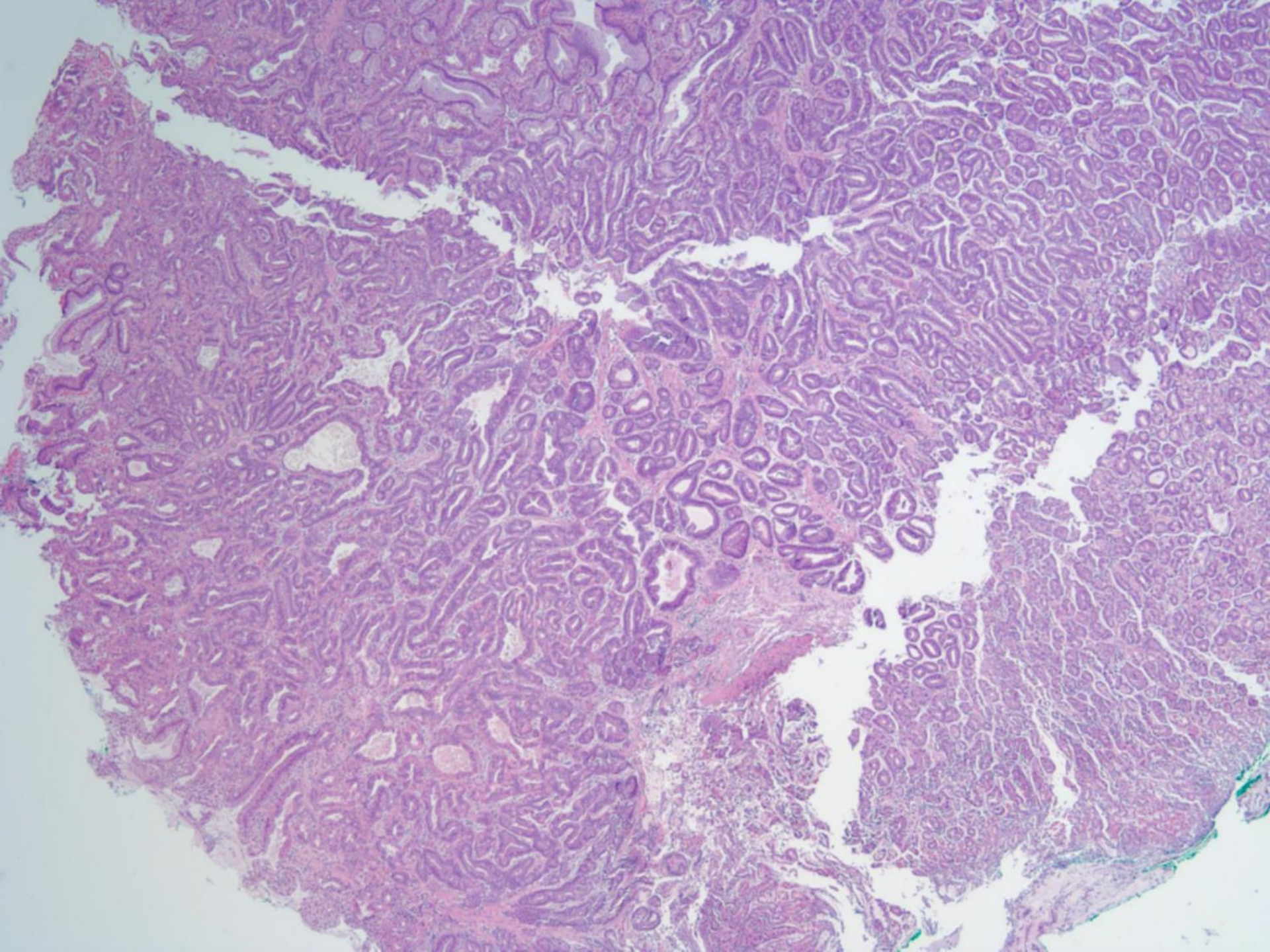
NOV 2018 DIAGNOSIS LIST

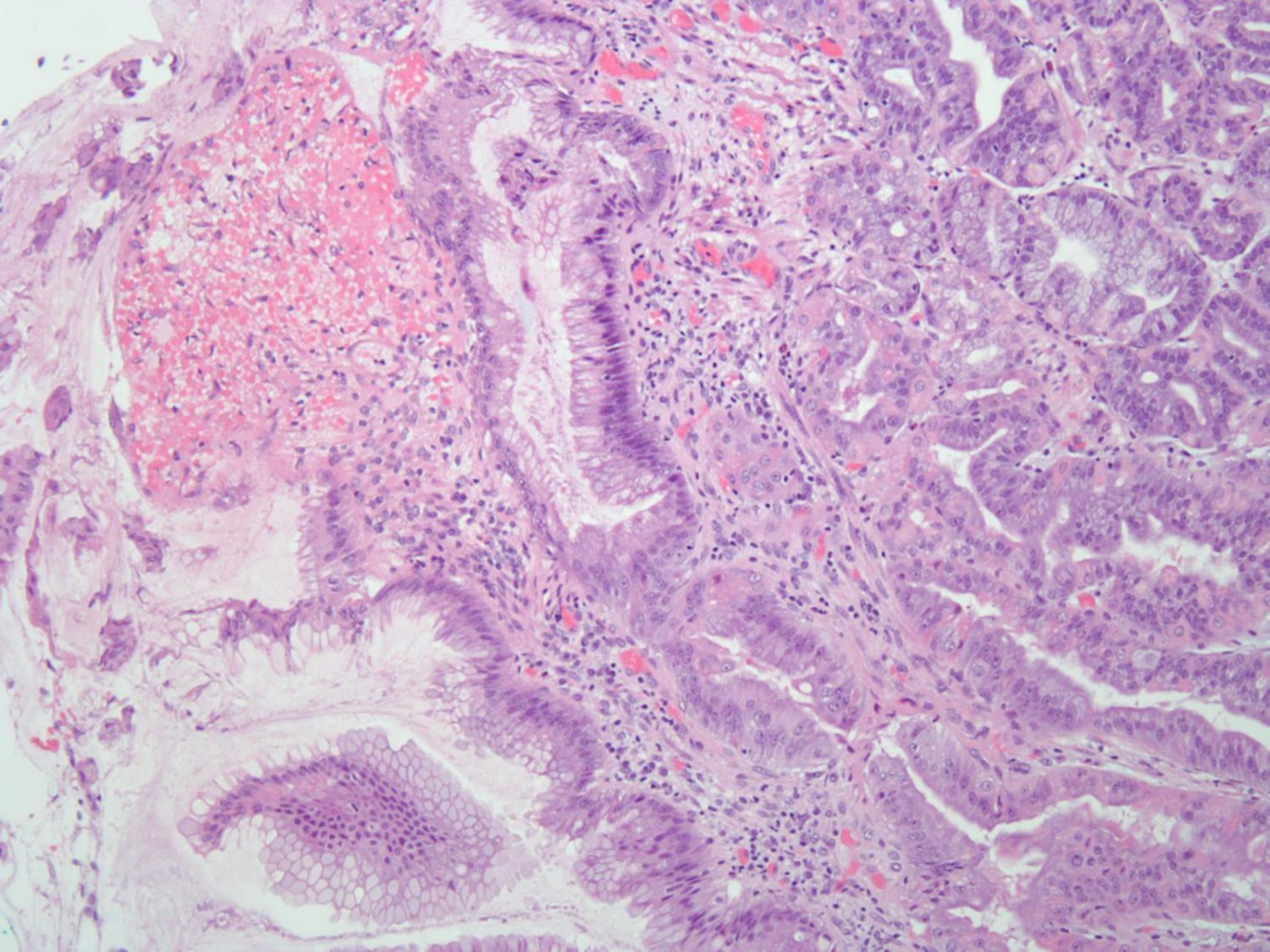
6321: gastric oxyntic polyp (stomach; GI pathology
6322: solitary xanthogranuloma (soft tissue; soft tissue pathology)
6323: meningothelial-like nodules (lung; neoplastic lung pathology)
6324: proctitis cystica profunda (anus; GI pathology)
6325: Adult granulosa cell tumor with luteinization (testis; GU pathology)
6326: consistent with goblet cell carcinoid (peritoneal cavity; GI pathology)
6327: leukemic non-nodal mantle cell lymphoma (liver; hematopathology)
6328: Cocciodiomycosis prostatitis (prostate; infectious disease pathology)
6329: systemic mastocytosis (large bowel; hematopathology)
6330: carcinosarcoma (gallbladder; GI pathology)

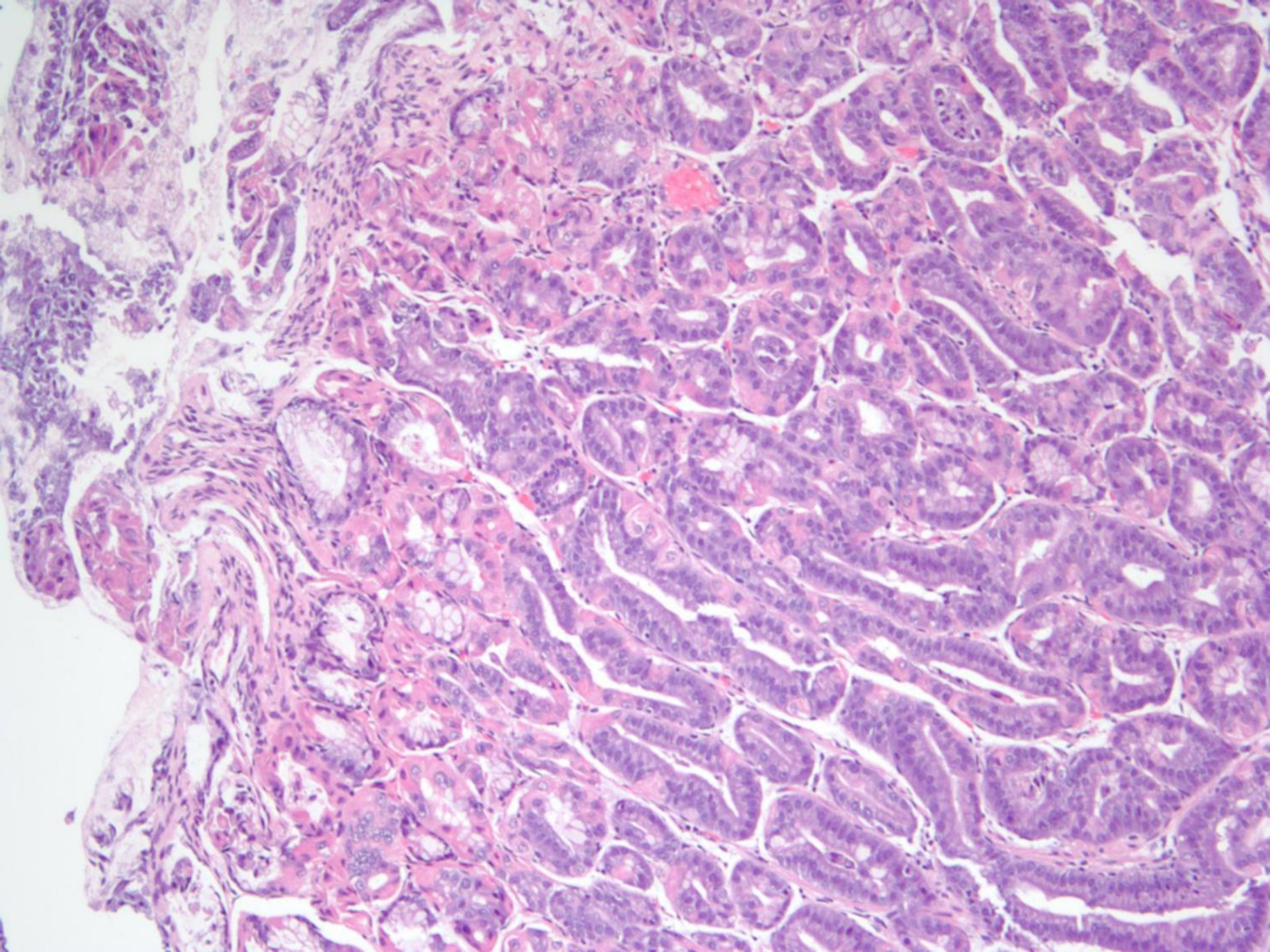
SB 6321

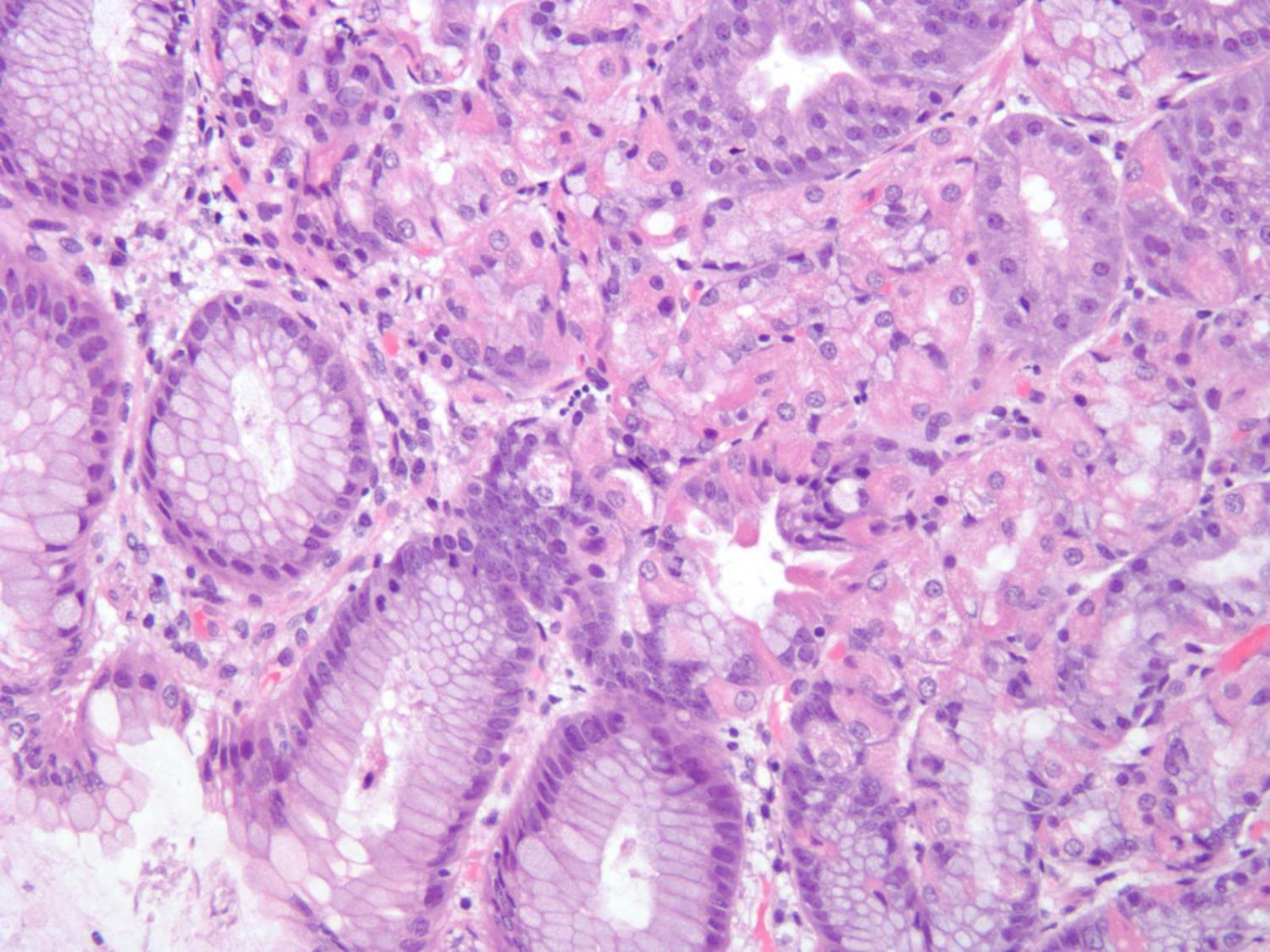
Charles Lombard; El Camino Hospital

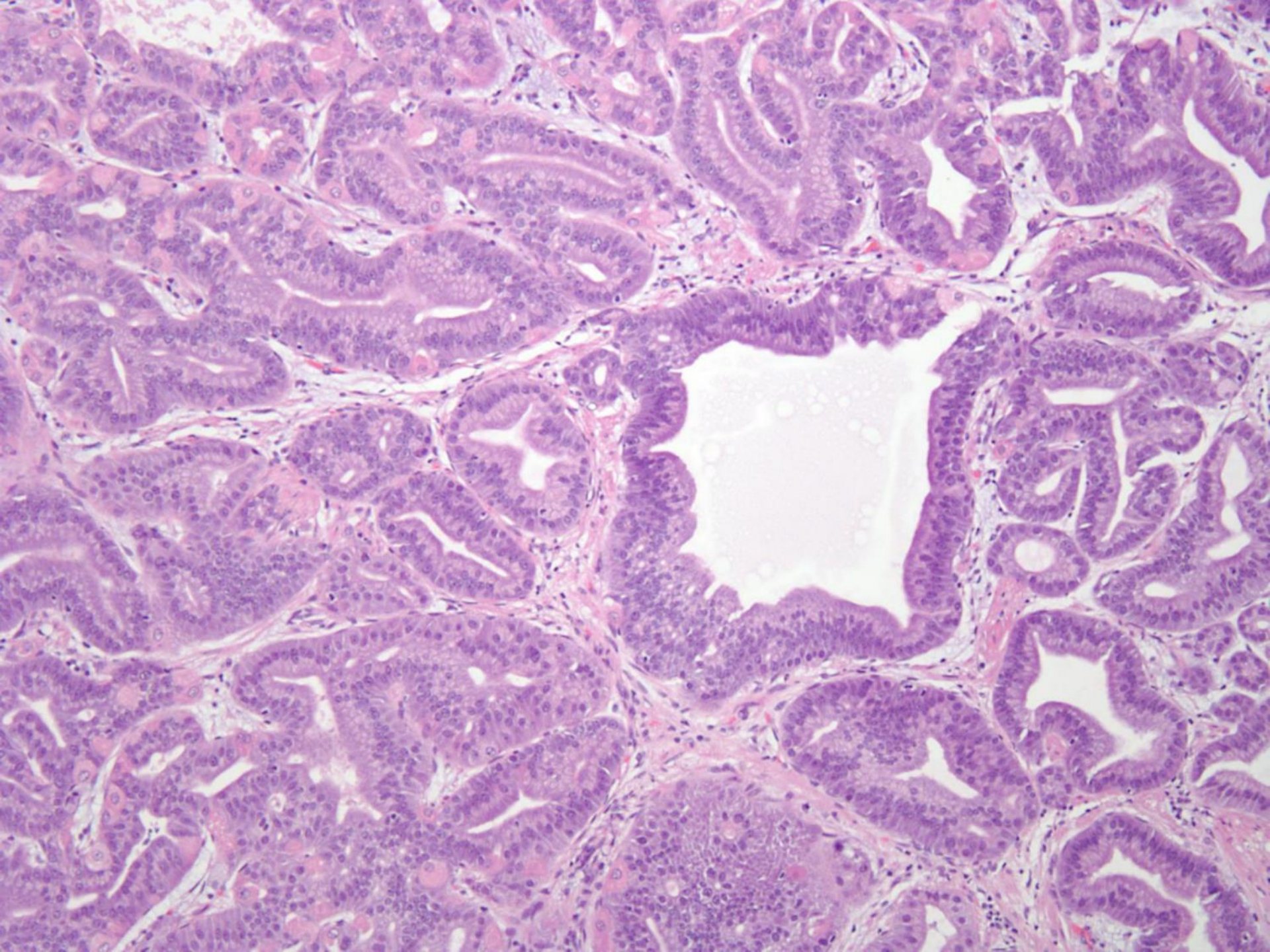
74-year-old female with gastric polyp snare.

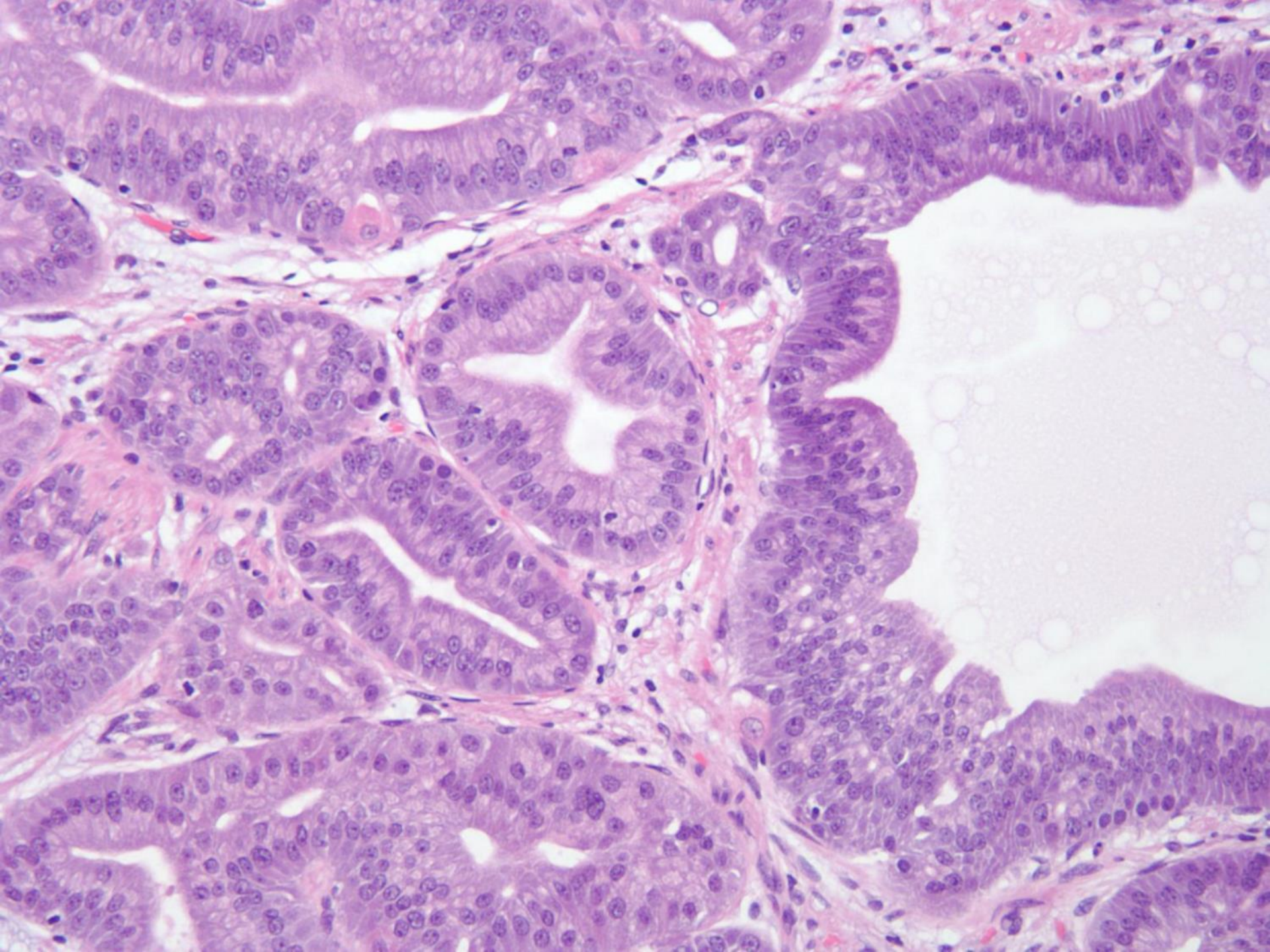


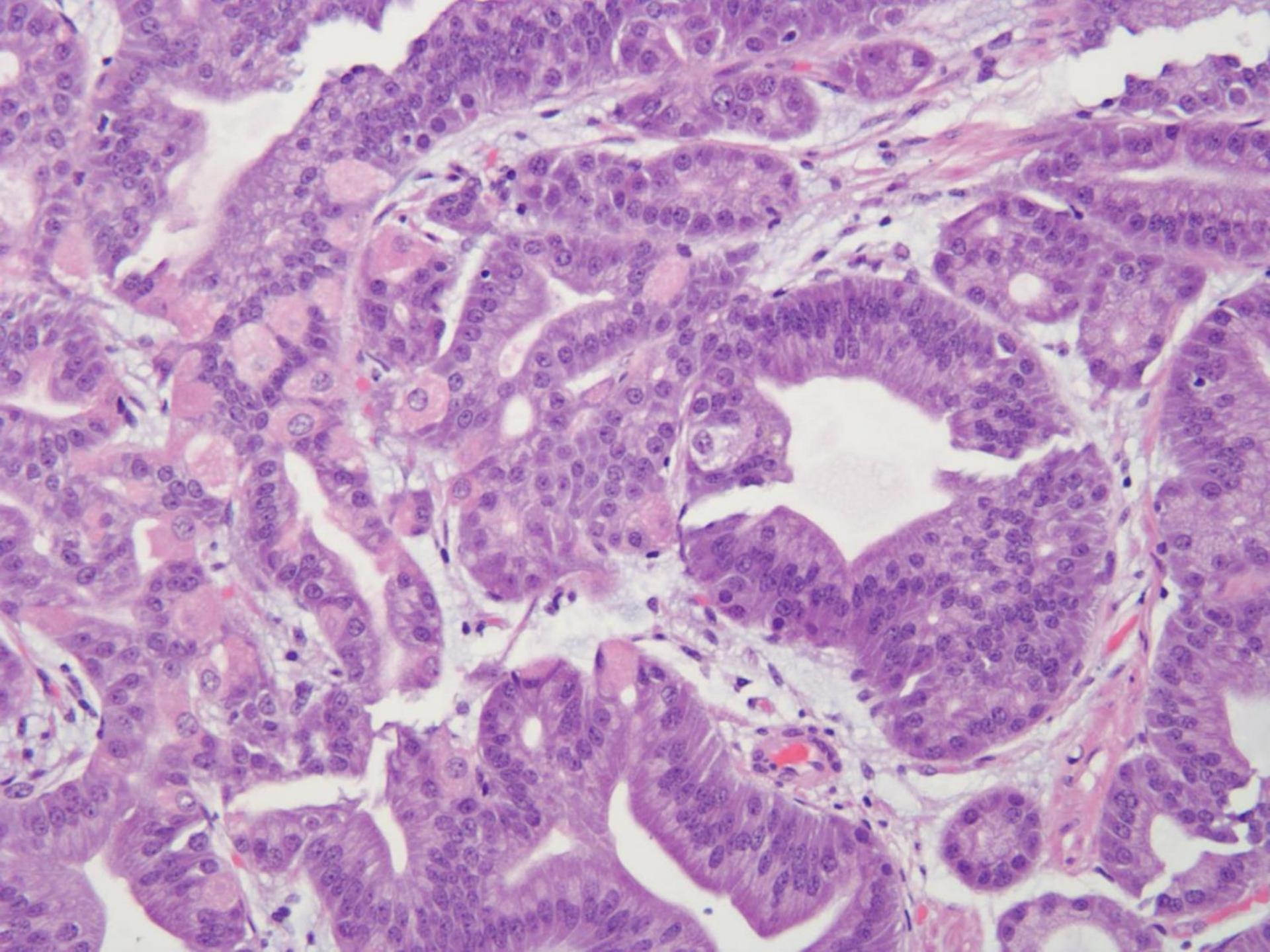












DIAGNOSIS?

Oxyntic Gland Polyp
Histologic features

- Always occur in oxyntic-type gastric mucosa
- Mixture of chief and oxyntic (parietal) cells
- Proliferation in “deeper” mucosa
- Variety of architectural patterns
  - Clustered/solid glands
  - Anastomosing cords
  - Dilated glands +/- infoldings
  - Pseudostratified epithelium
  - Cribriform areas
- Absence of true invasion/LVI
- Mild cytologic atypia
- Proliferation index low (< 2%)

Gastric Oxyntic Gland Polyp

- Rare lesions
- Upper third of stomach
  - 70% fundus; 30% cardia
  - Usually single
- 4-20 mm size
- No clinical progression of disease
- ??? Precursor lesion for chief cell predominant adenocarcinoma
  - There are more chief cells in these polyps than oxynitic cells

DDX of Oxnytic gland polyp

- Originally described as variant of fundic gland polyp, however, microcyst formation is not a common finding in most oxyntic gland polyps.
- Variant gastric adenocarcinoma of fundic gland type/chief cell predominant type
  - OGP: Lacks atypia, desmoplasia, true invasion
- Neuroendocrine tumor
  - OGP: Lack chromogranin/synaptophysin/typical nuclear features of neuroendocrine tumor

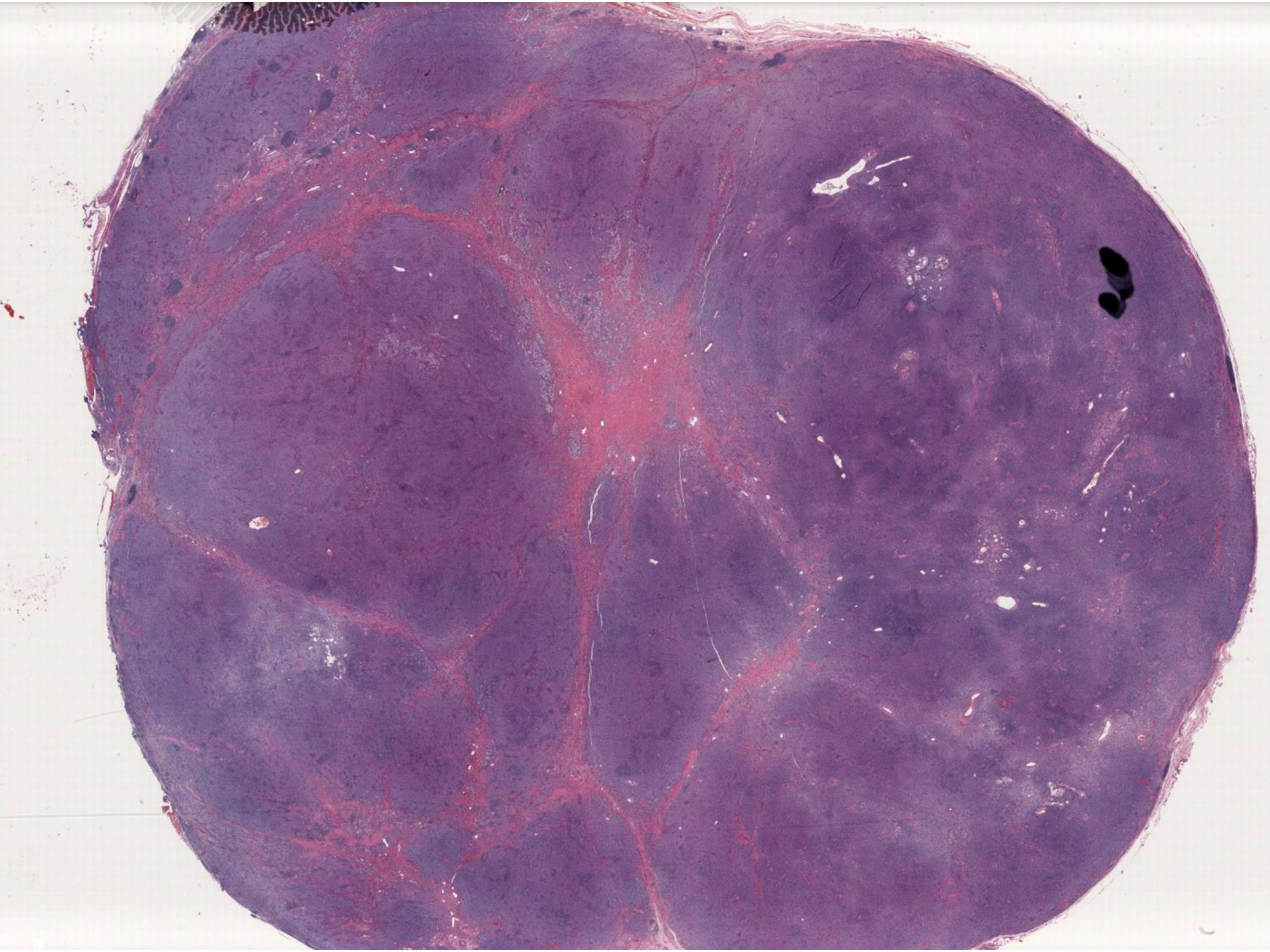
References

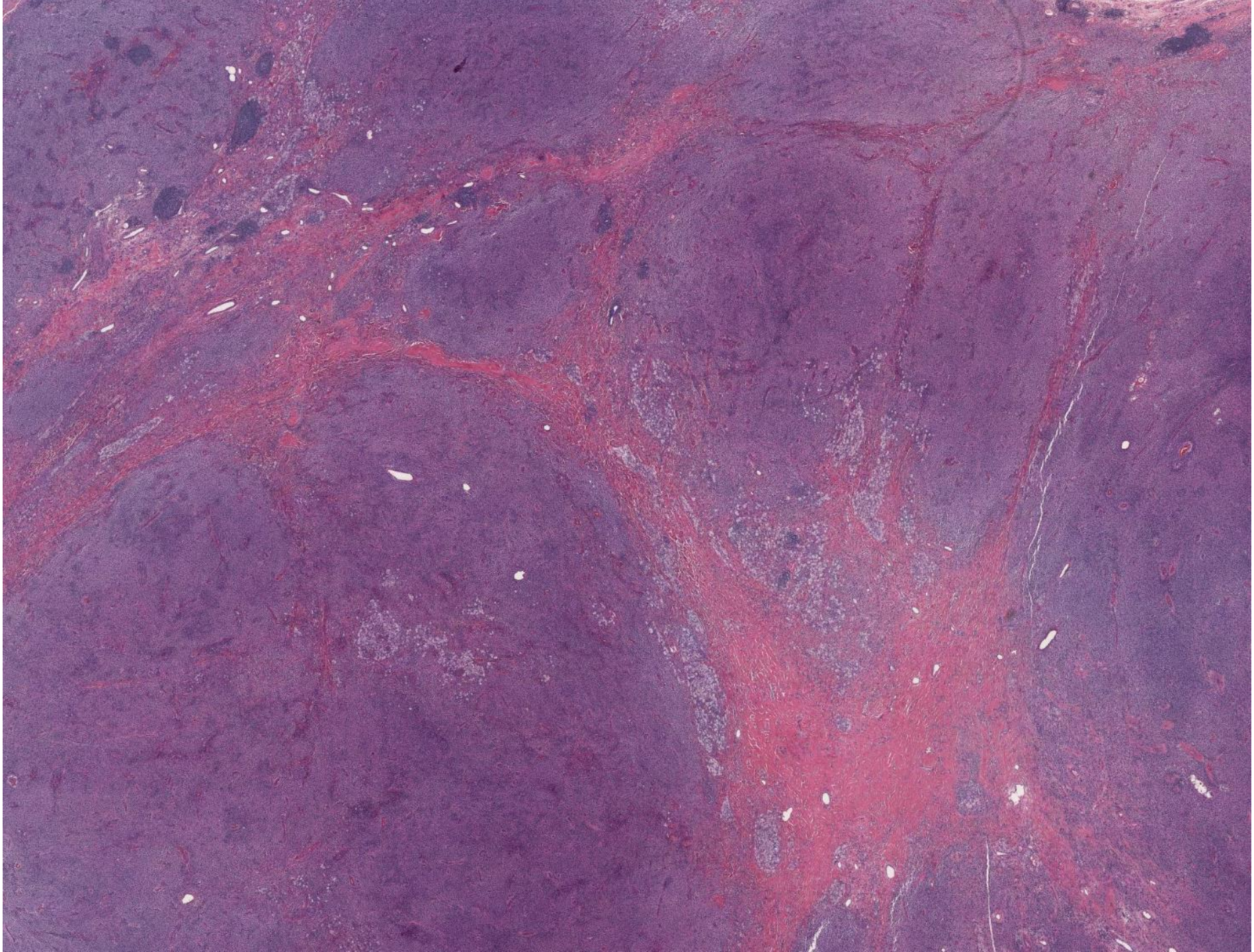
- Singhi et al: “Gastric adenocarcinoma with chief-cell differentiation: A proposal for reclassification as oxyntic gland polyp/adenoma”. AJSP 2012; 36: 1030-5.
- Chan et al: “Chief cell predominant gastric polyps”. Histopathology 2016; 68: 825-33.

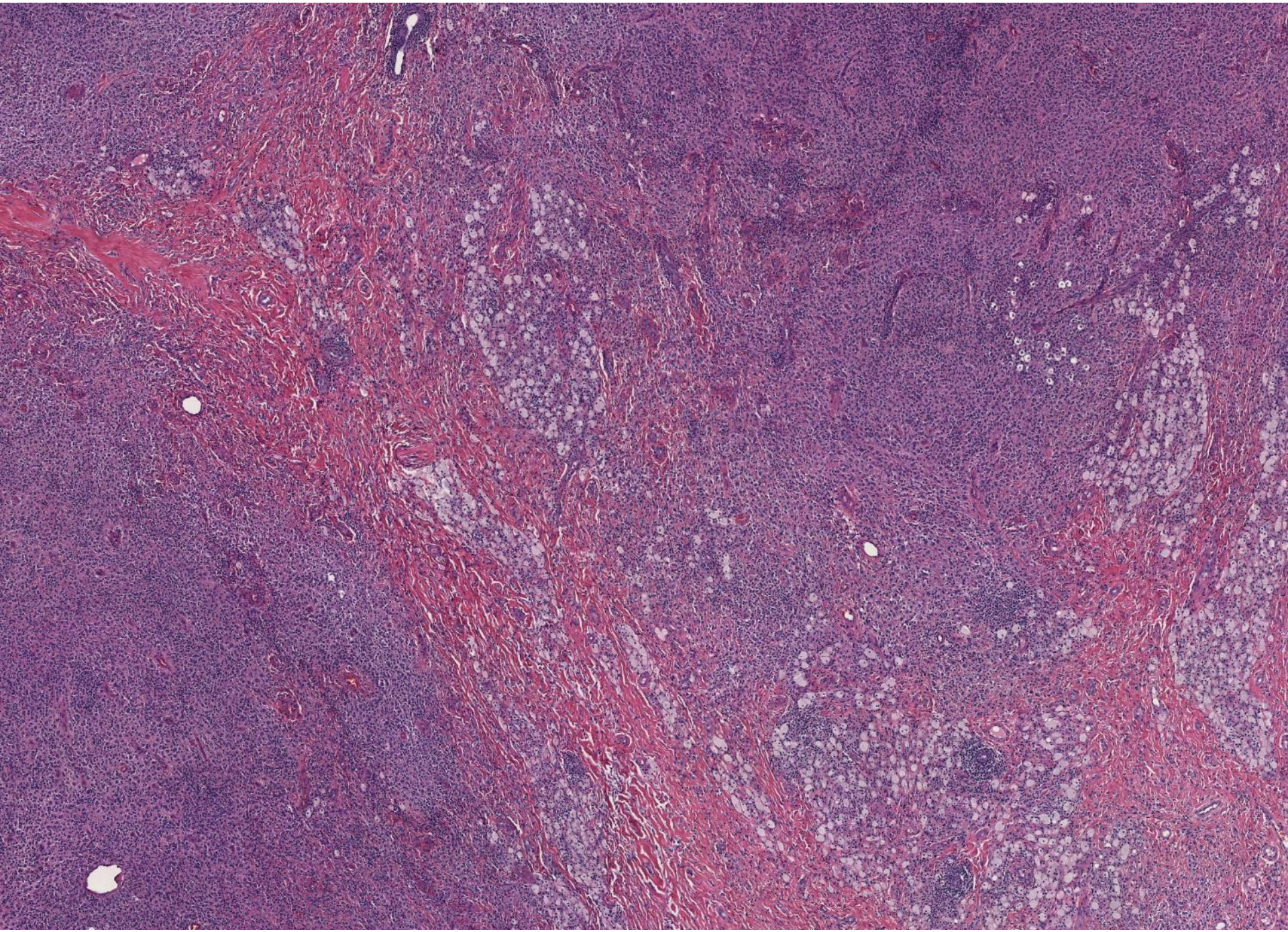
SB 6322
(scanned slide available)

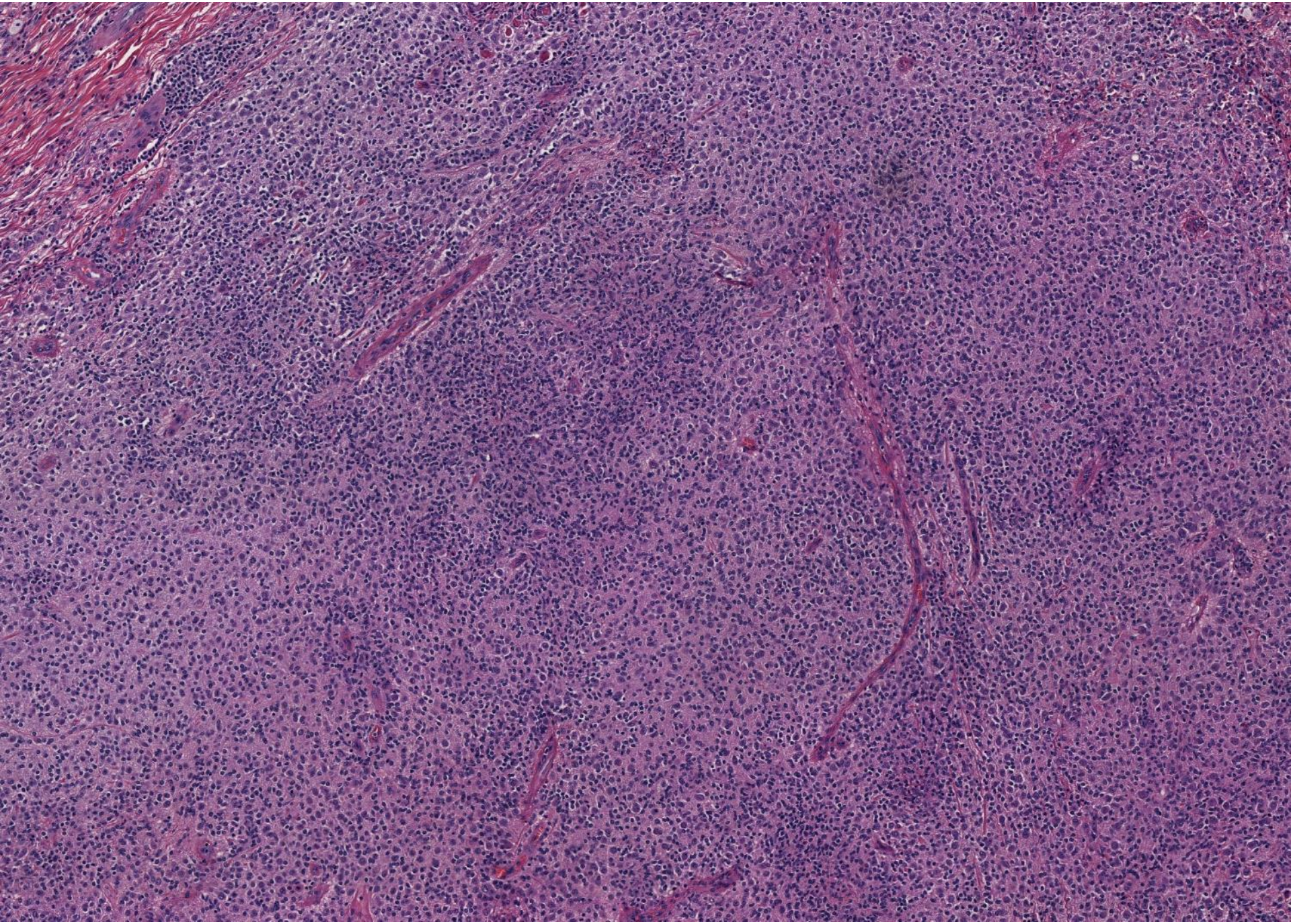
Mahendra Ranchod; Good Samaritan Hospital

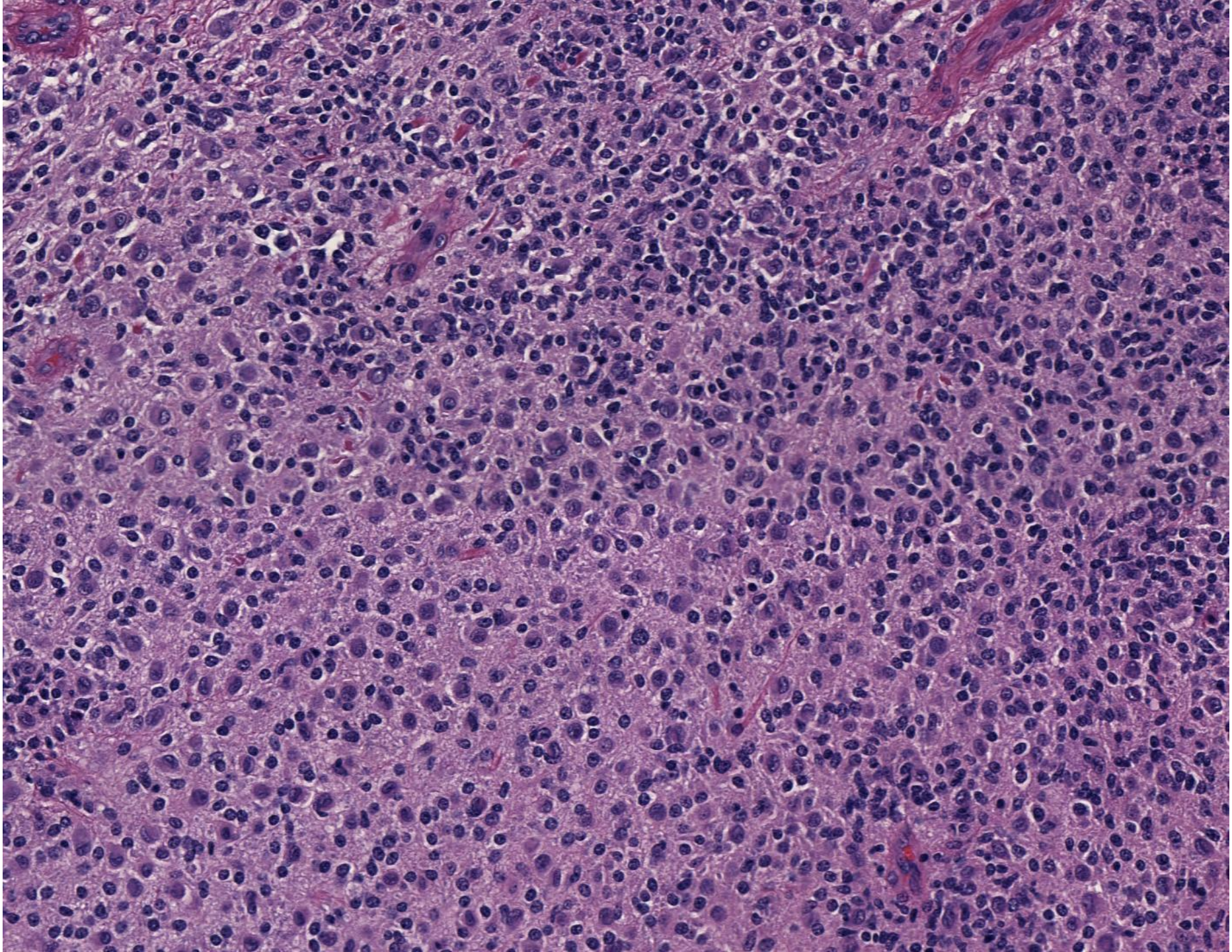
67-year-old female with 4.5cm subcutaneous arm mass.

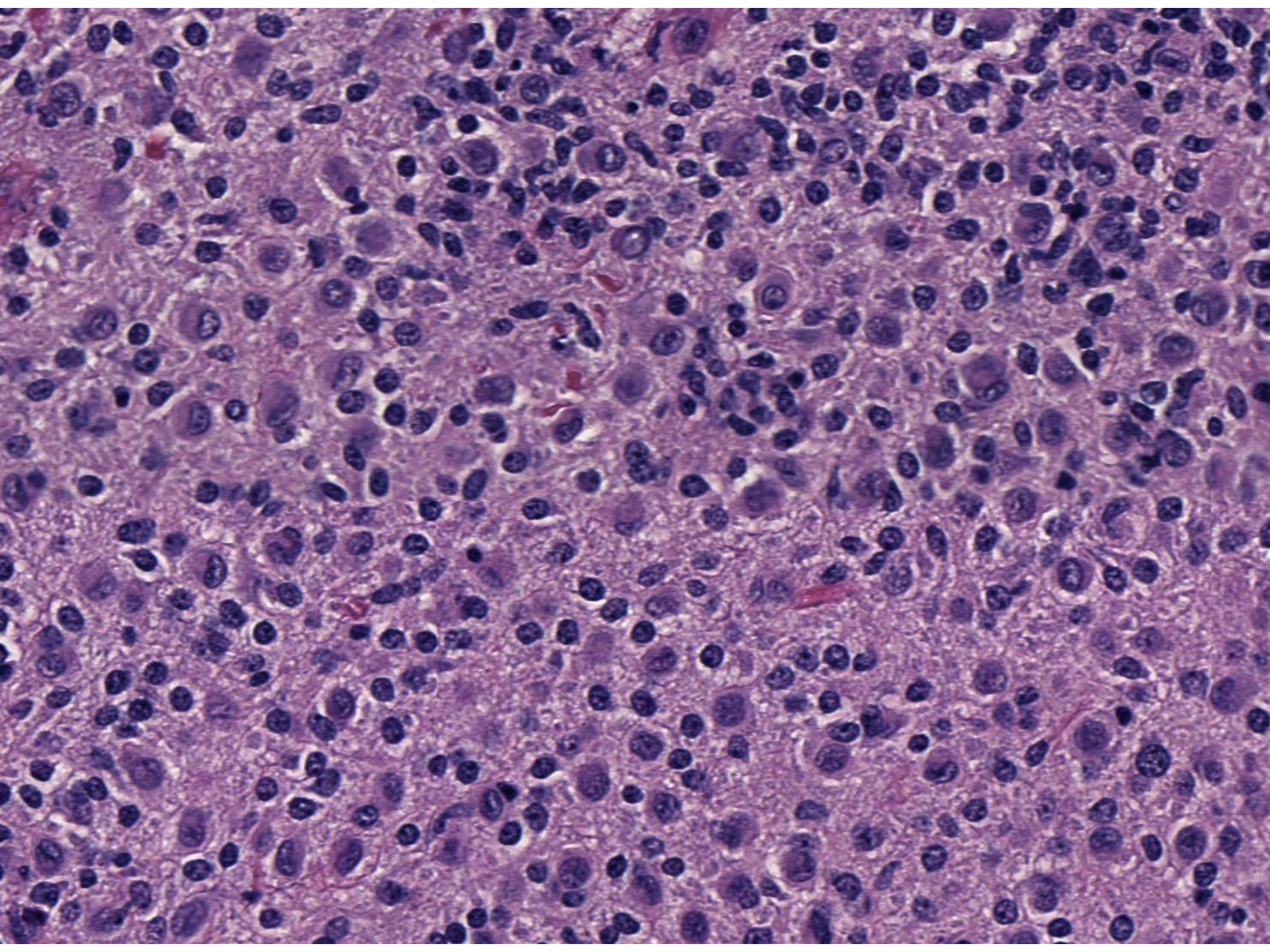


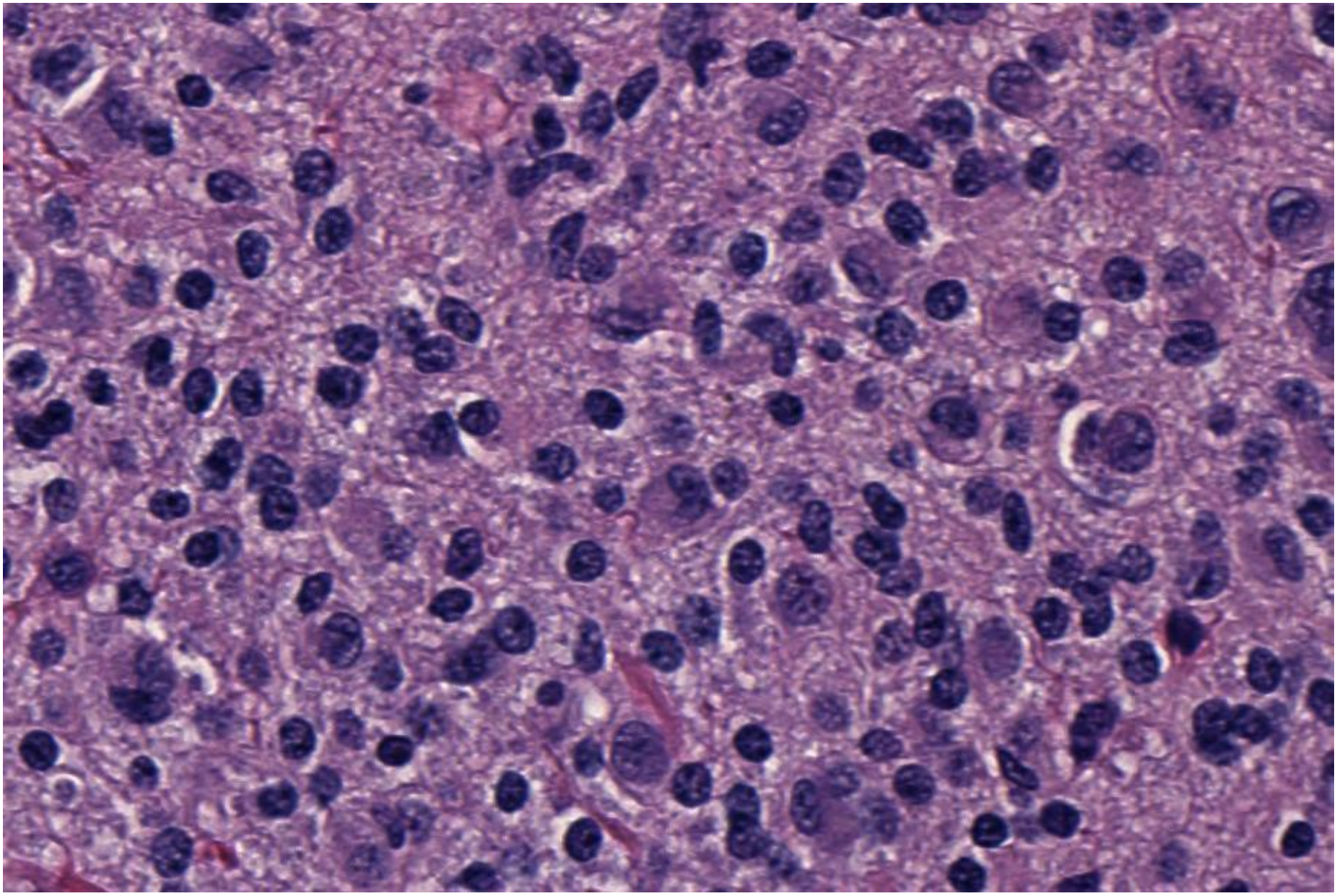


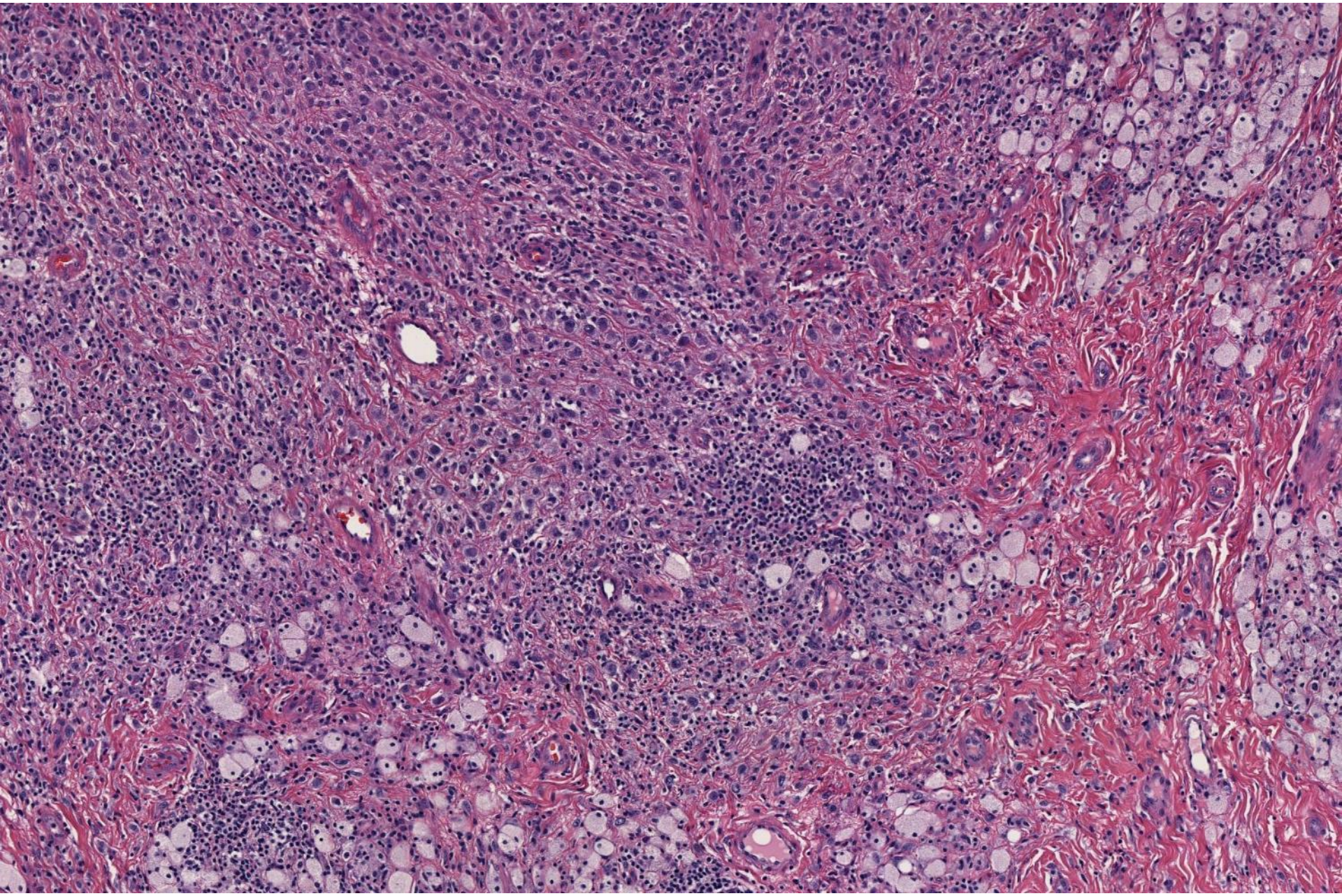


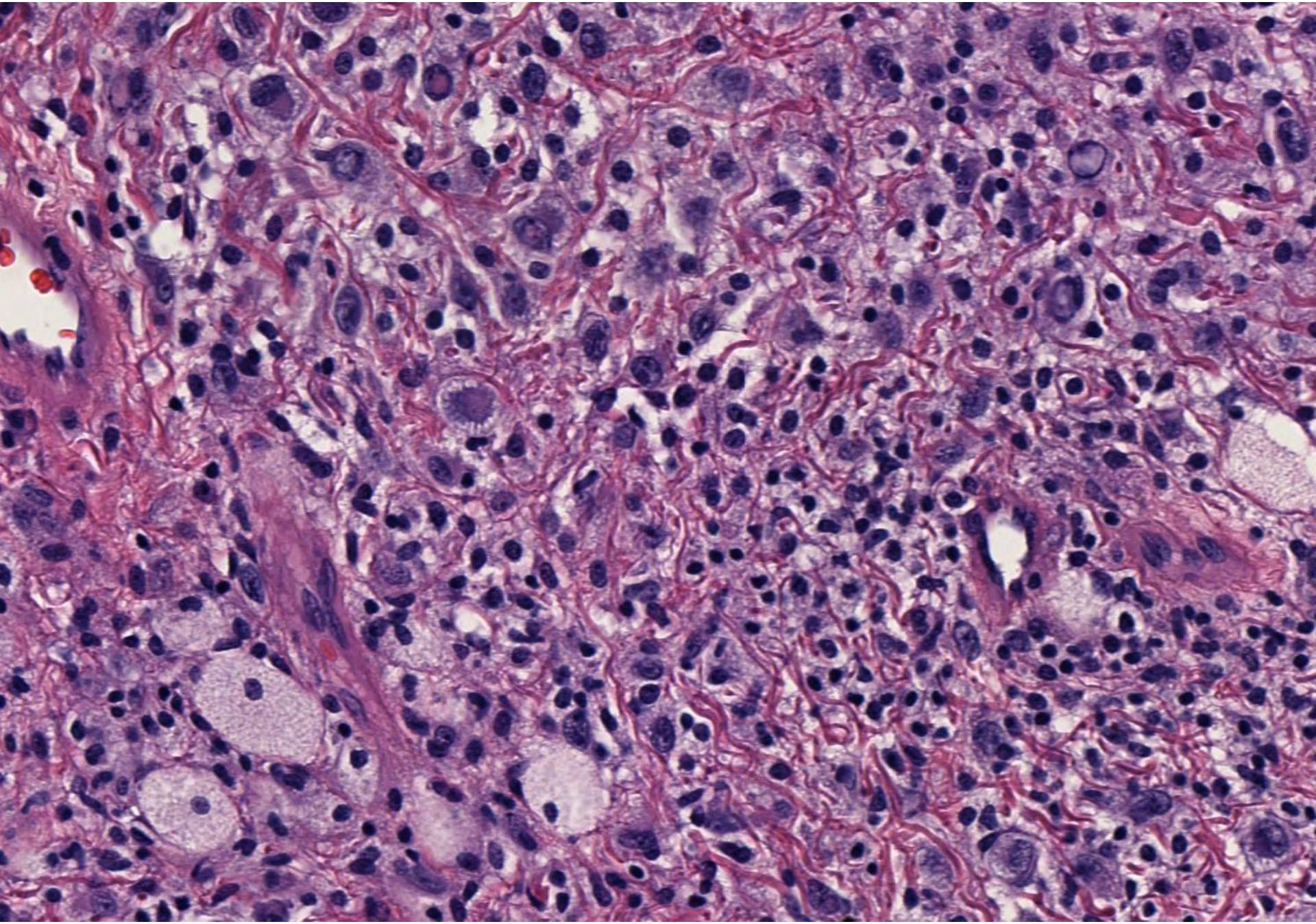












DIAGNOSIS?

Xanthogranuloma

- Uncommon in adults
- Occurs in soft tissue
- Almost always solitary
- Usually cured by surgical resection
- Local recurrence infrequent
- Related to more common JXG

Juvenile Xanthogranuloma

Kiel Pediatric study of 129 cases, 2005

- **Median age 5 months (birth-244 months)**
- **80% solitary, cutaneous**
- **15% solitary subcutaneous or deep soft tissue**
- **<5% systemic**
- **83% cured by surgical resection**
- **10% recur locally**
- **7% develop additional lesions**
- **Death infrequent. Occurs with systemic disease.**

Xanthogranuloma
(adult and pediatric)

- Histology variable
- Histiocytes dominant
- Lipidization variable and may be scanty
- Multinucleated histiocytes variable
- Lymphocytes, plasma cells and eosinophils
- Fibrosis with lobular or storiform pattern
- Mitoses infrequent

Xanthogranuloma
(adult and pediatric)

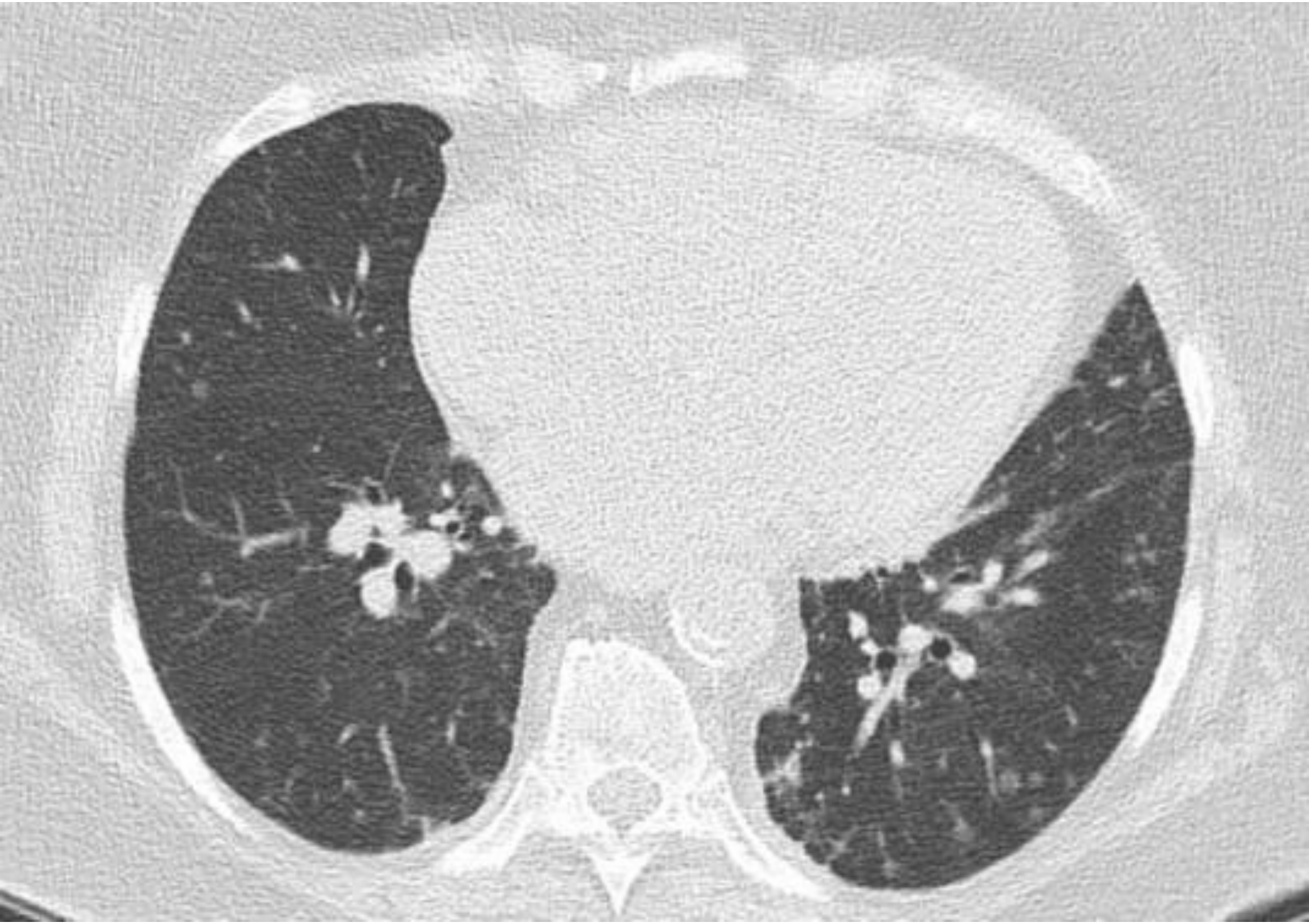
- **Positive stains**
  - **CD 68**
  - **alpha-1 anti-trypsin**
  - **CD31**
  - **Factor XIIIa**

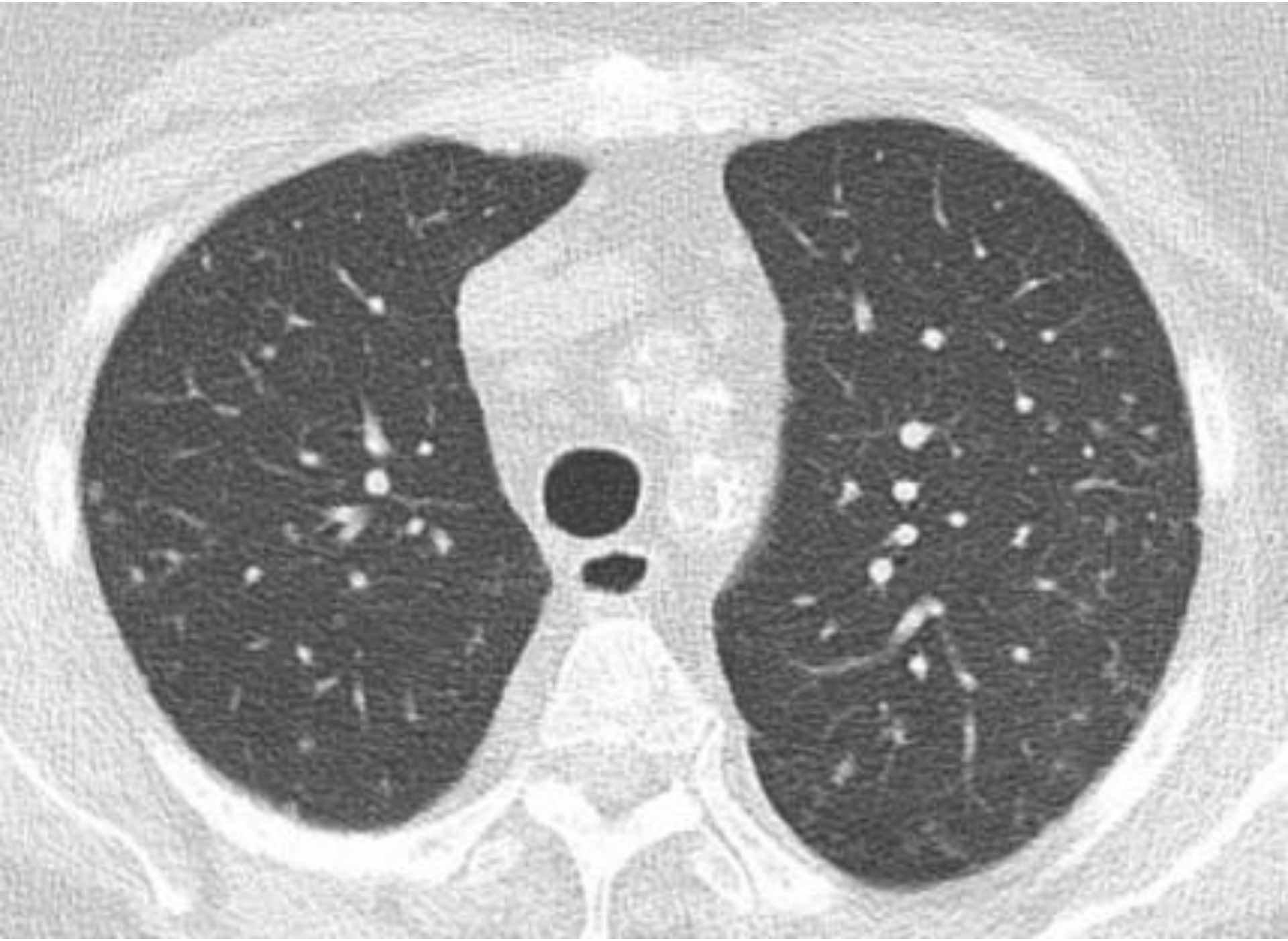
- **Negative stains**
  - **S100**
  - **CD1a**

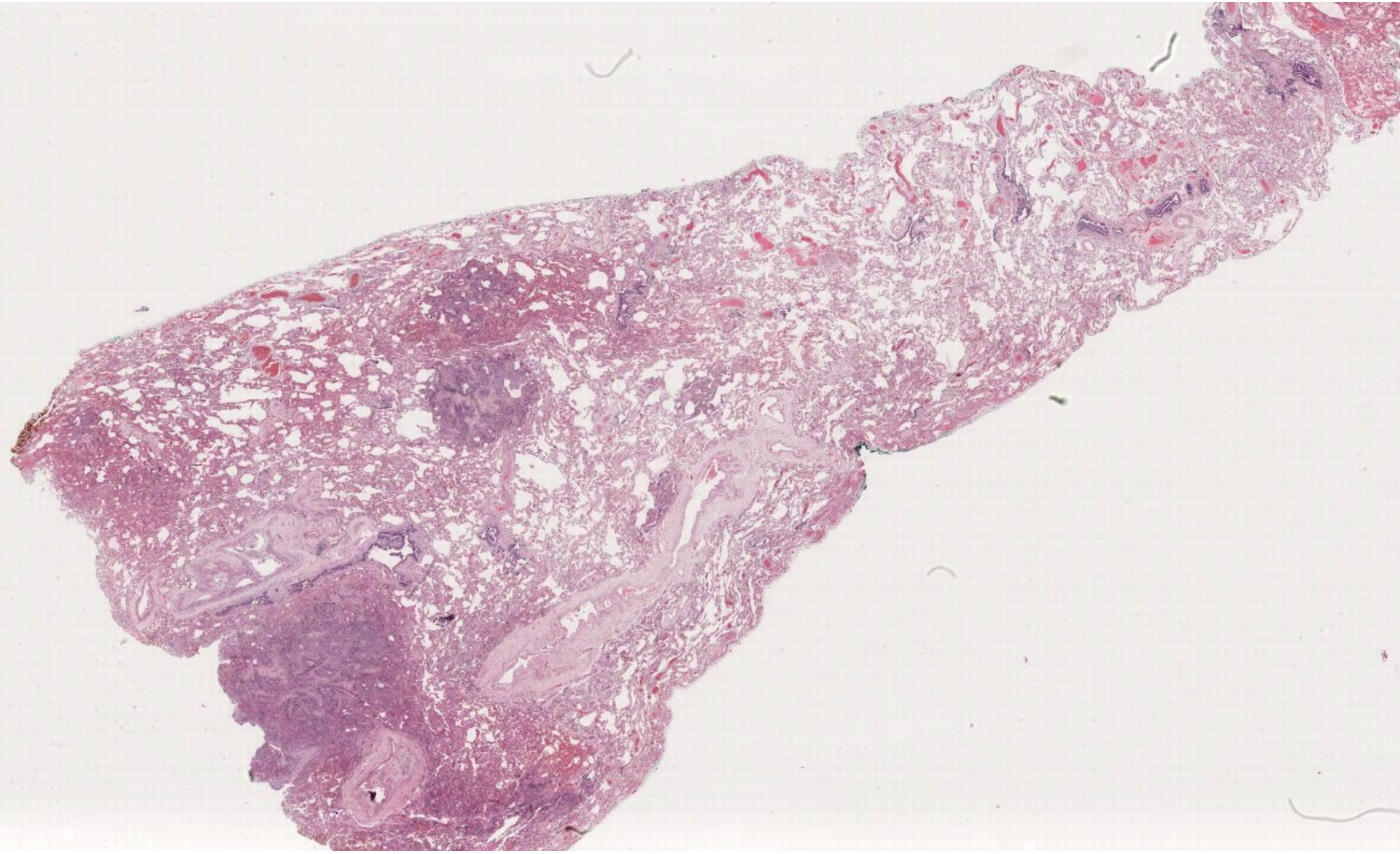
SB 6323
(scanned slide available)

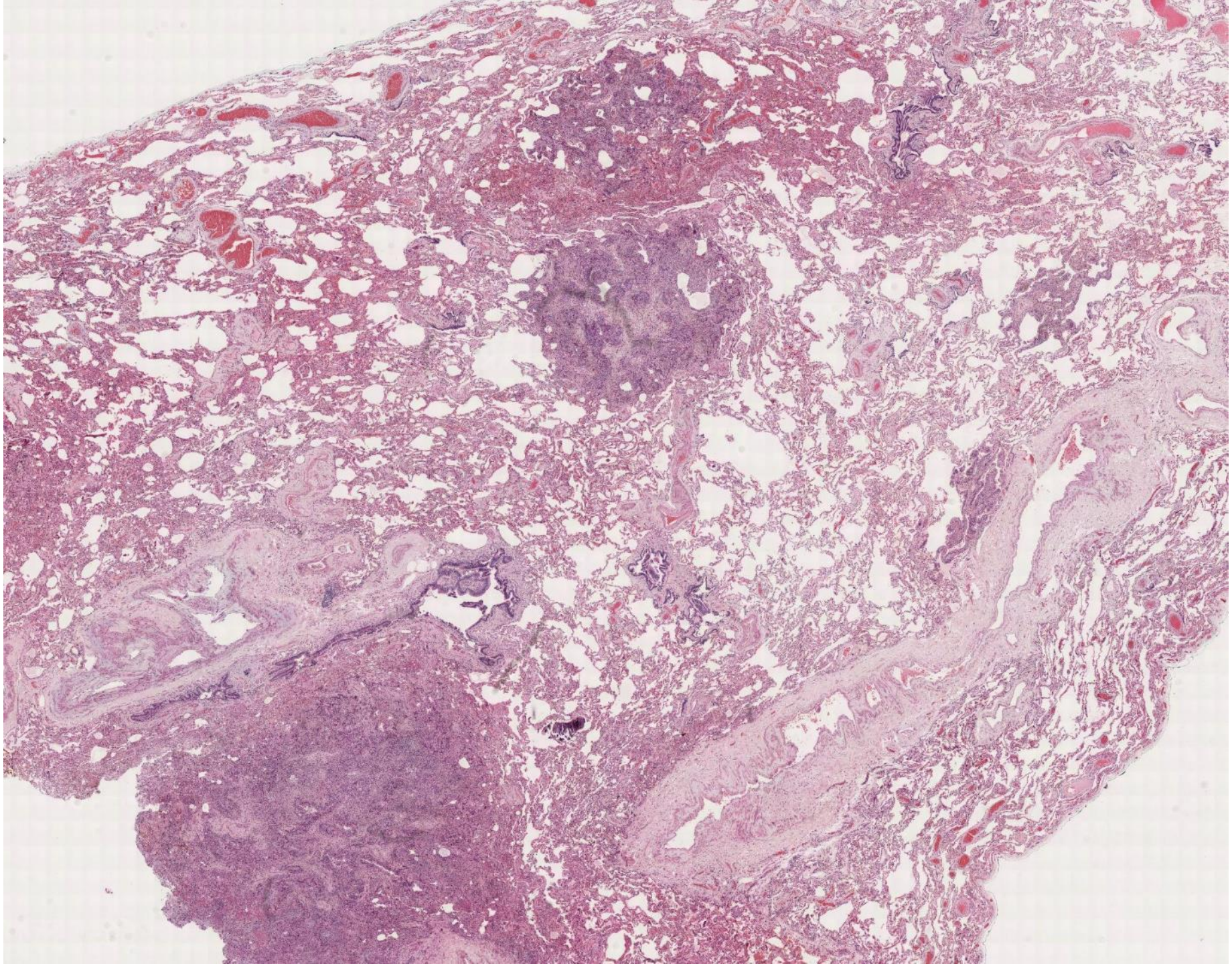
Charles Lombard; El Camino Hospital

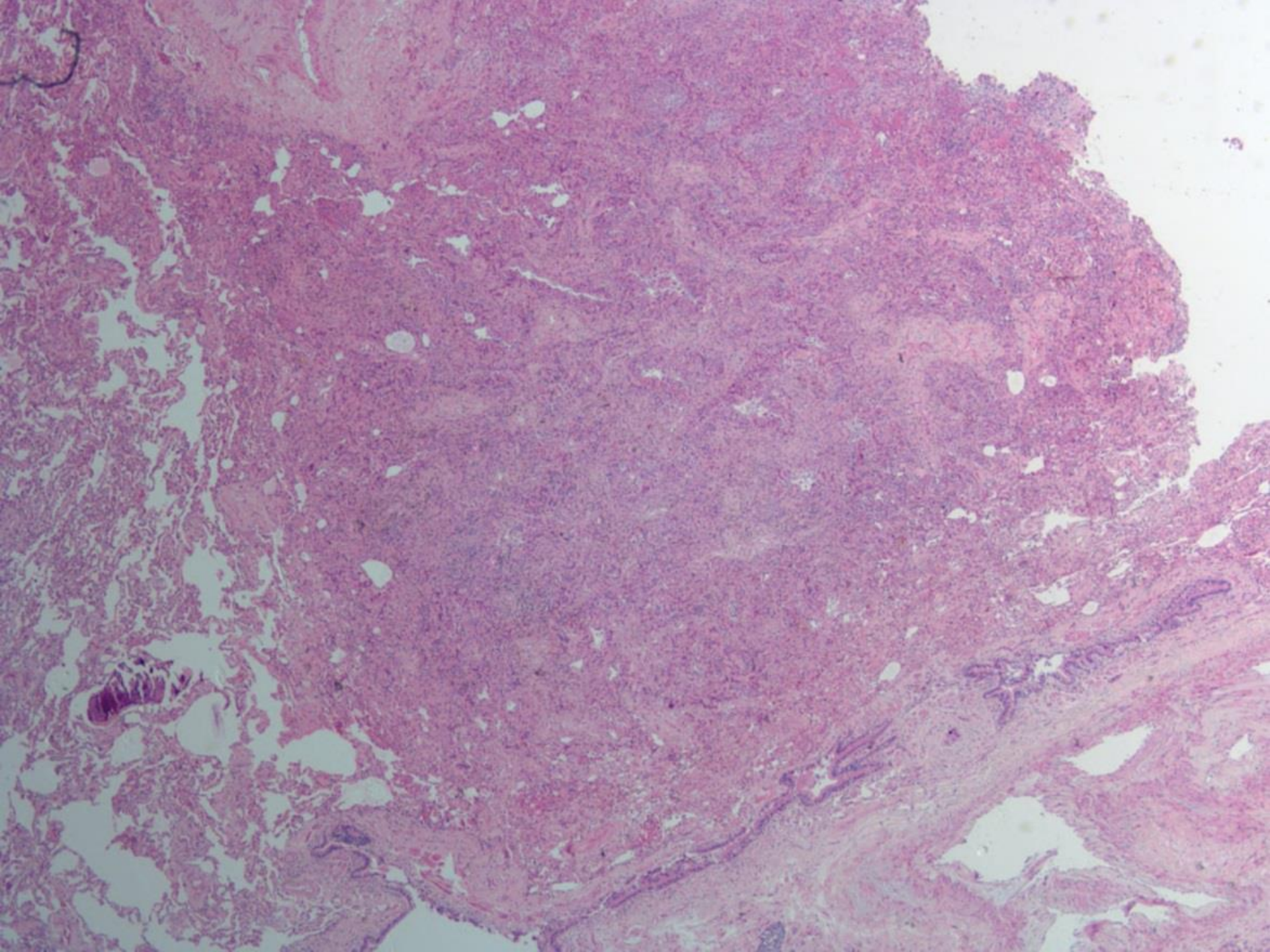
78-year-old female with miliary nodules in lung, clinically silent.

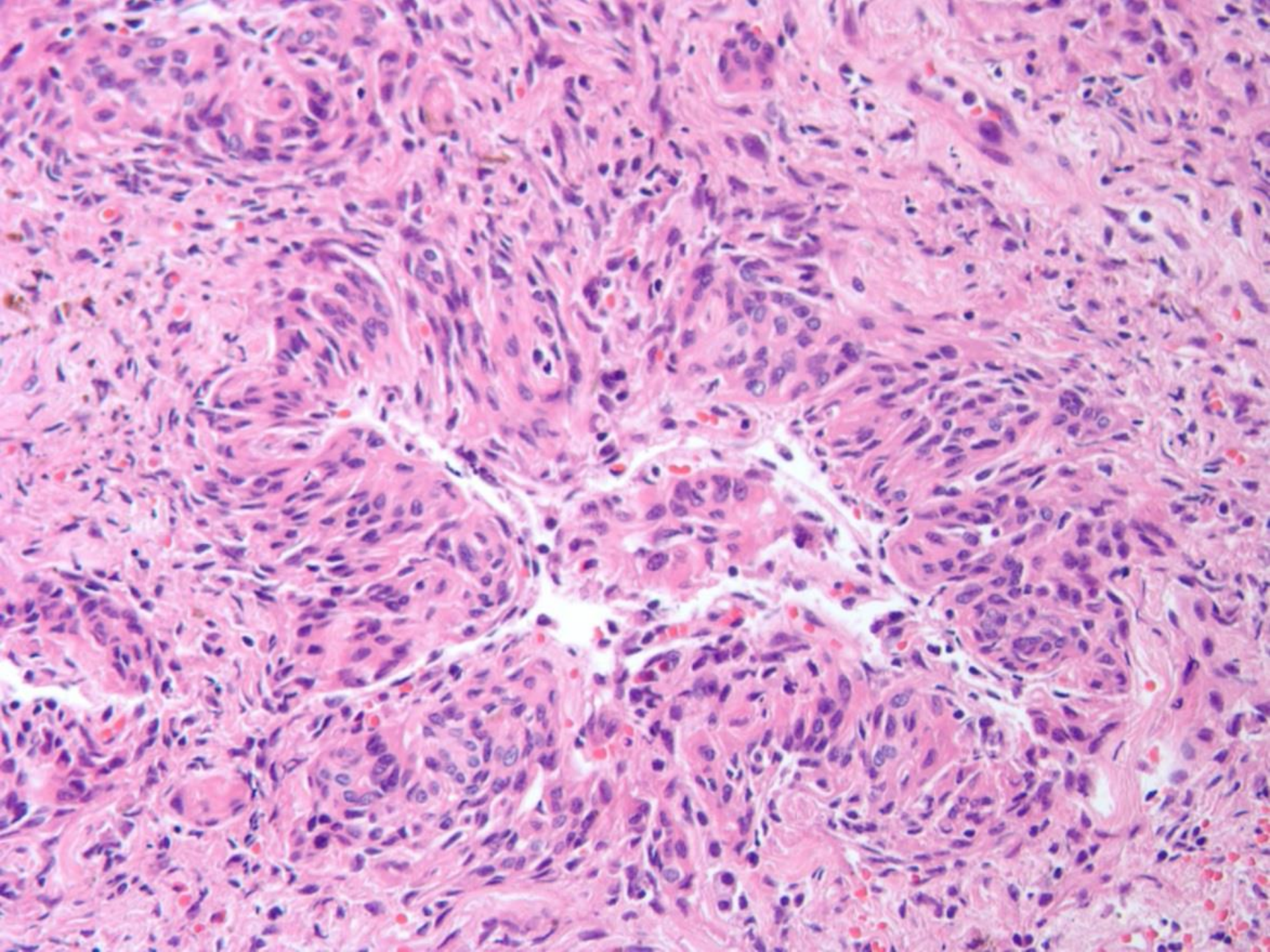


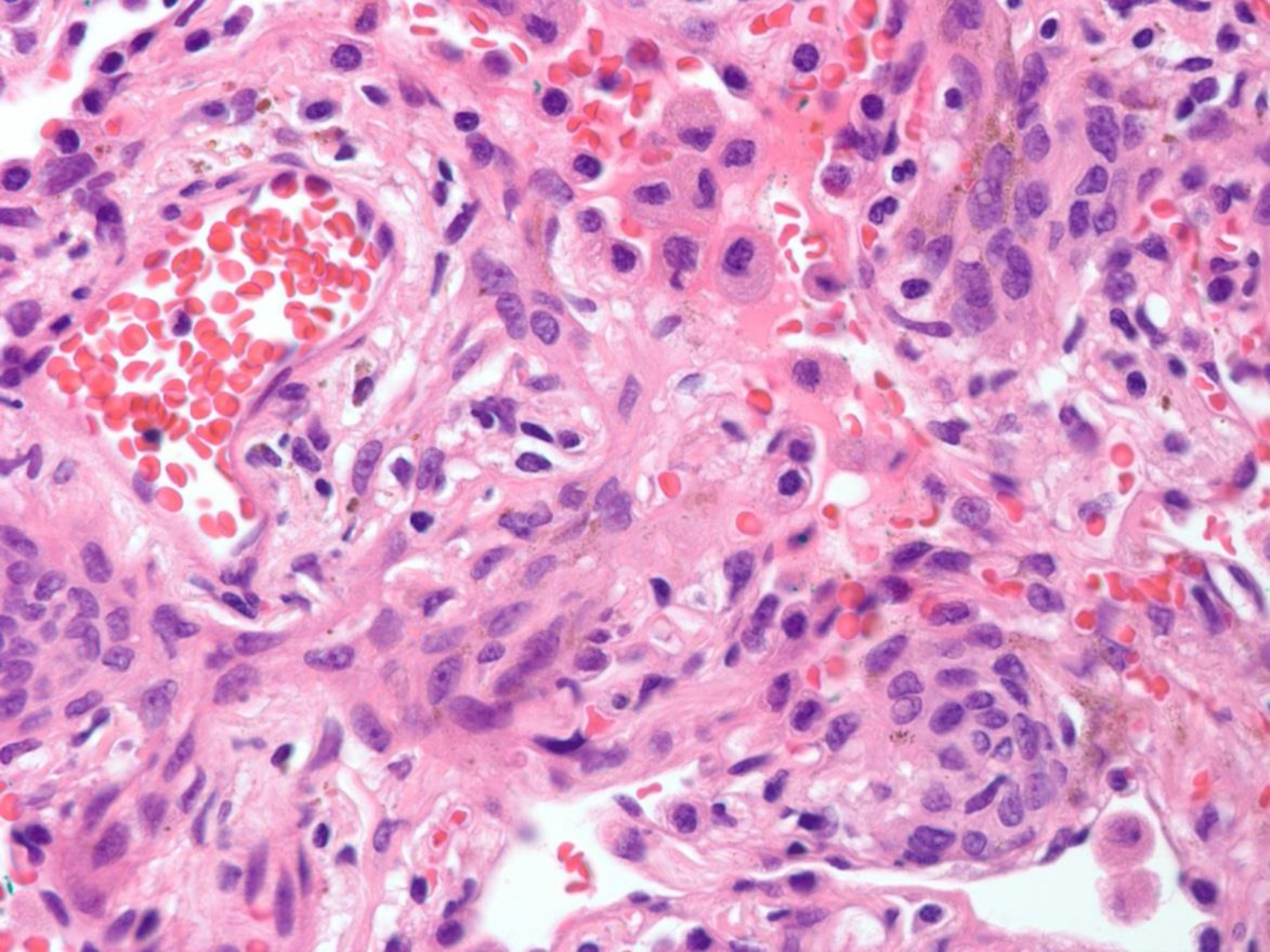


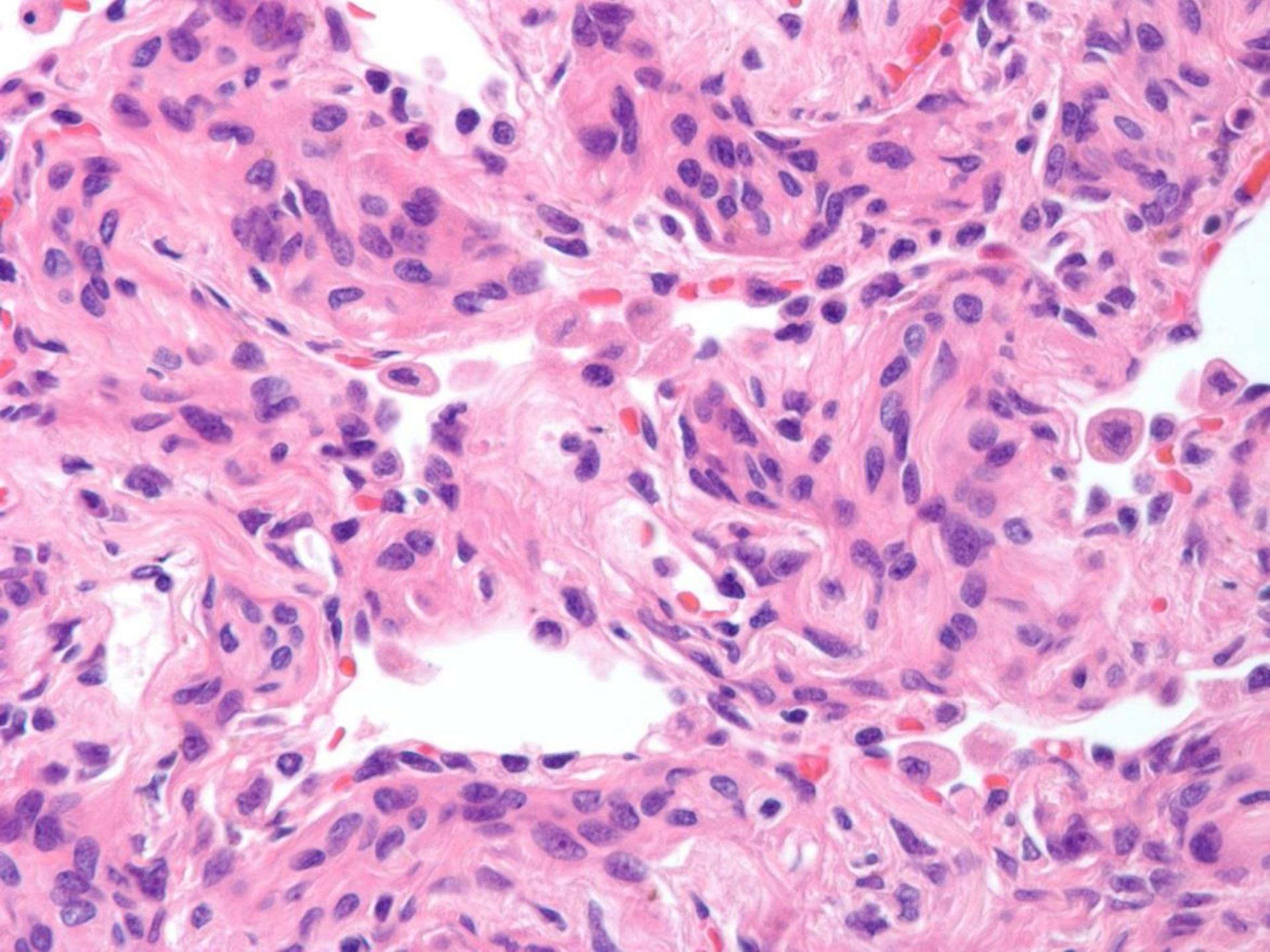




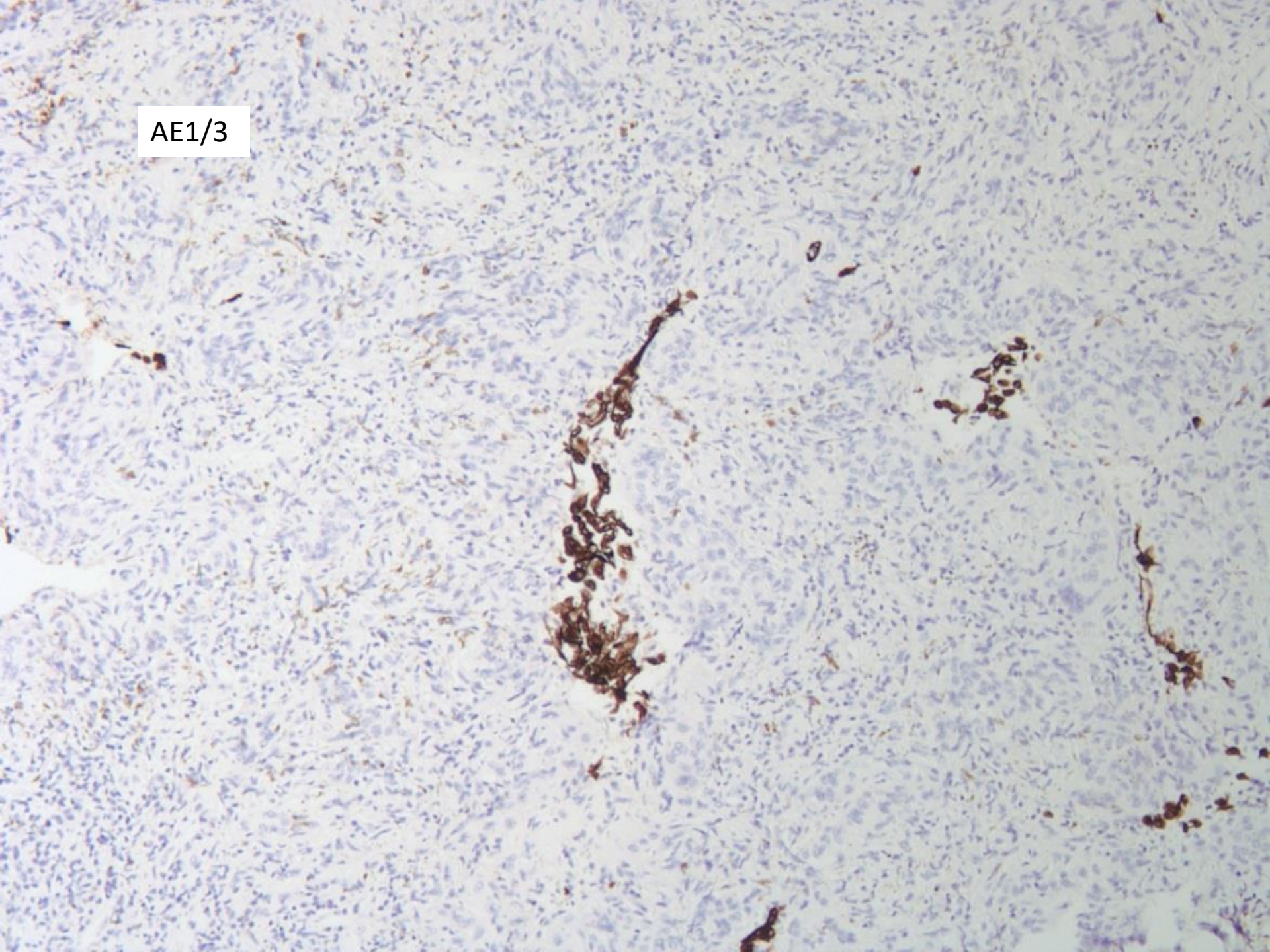


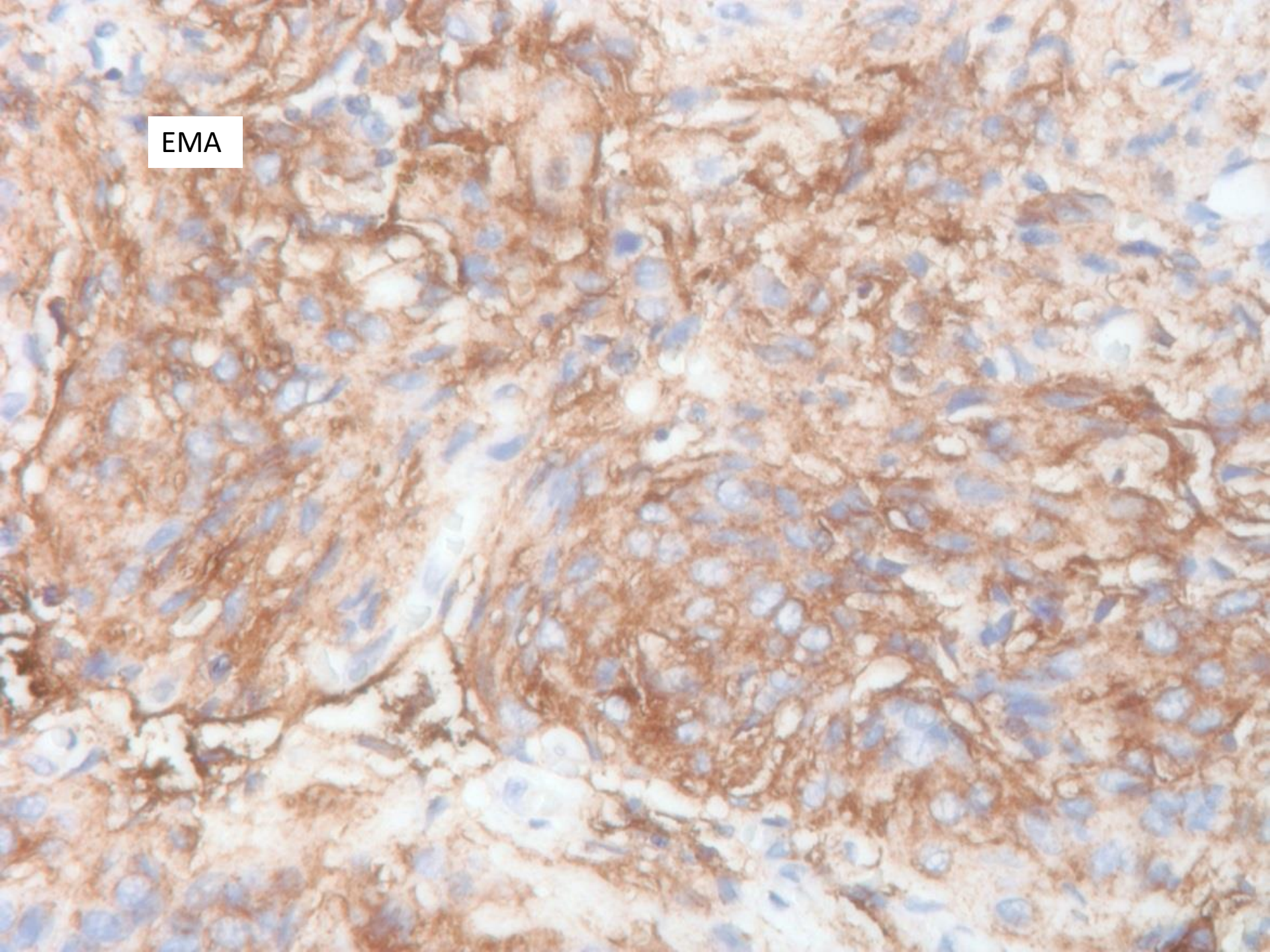






DIAGNOSIS?


AE1/3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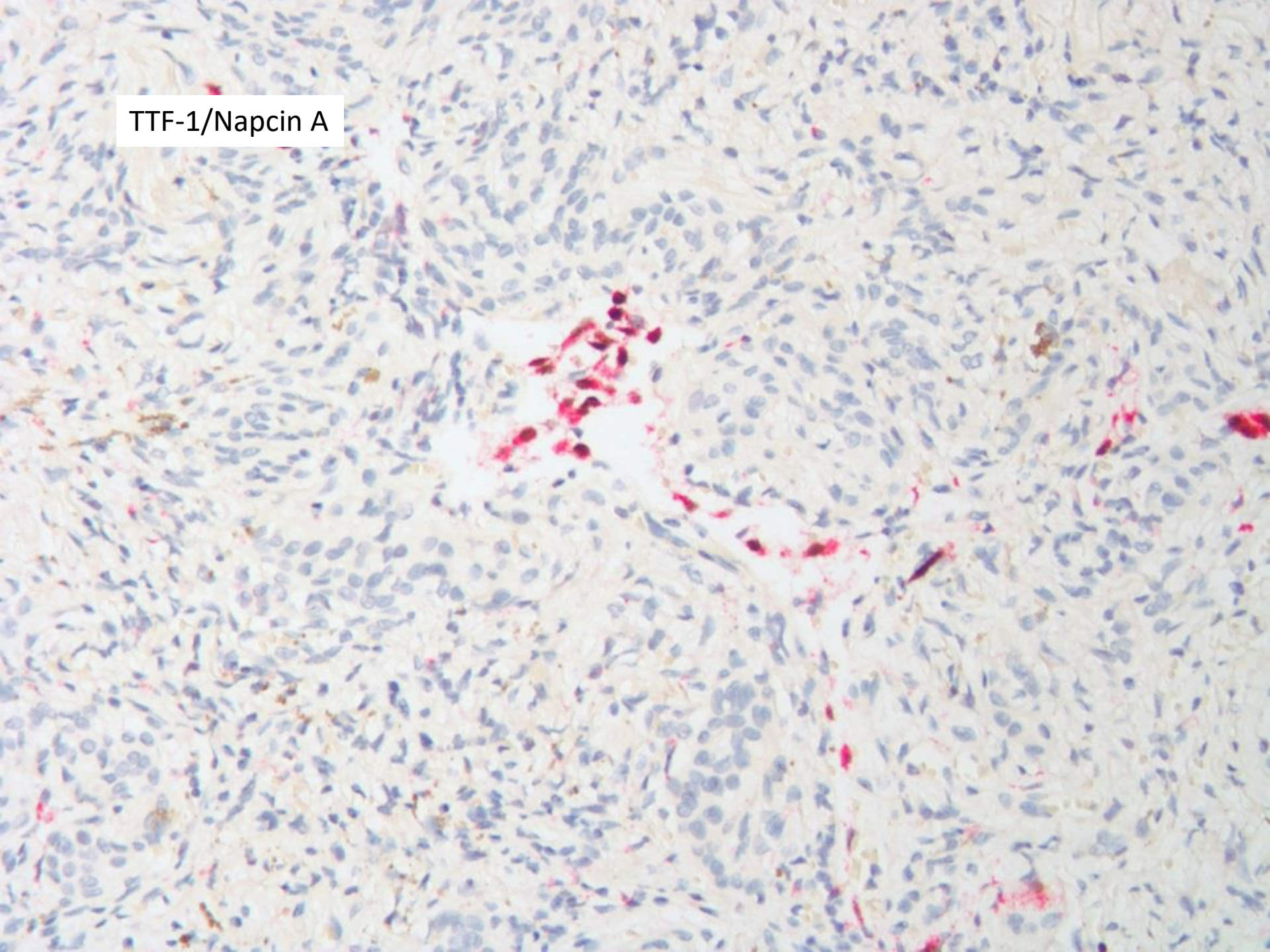
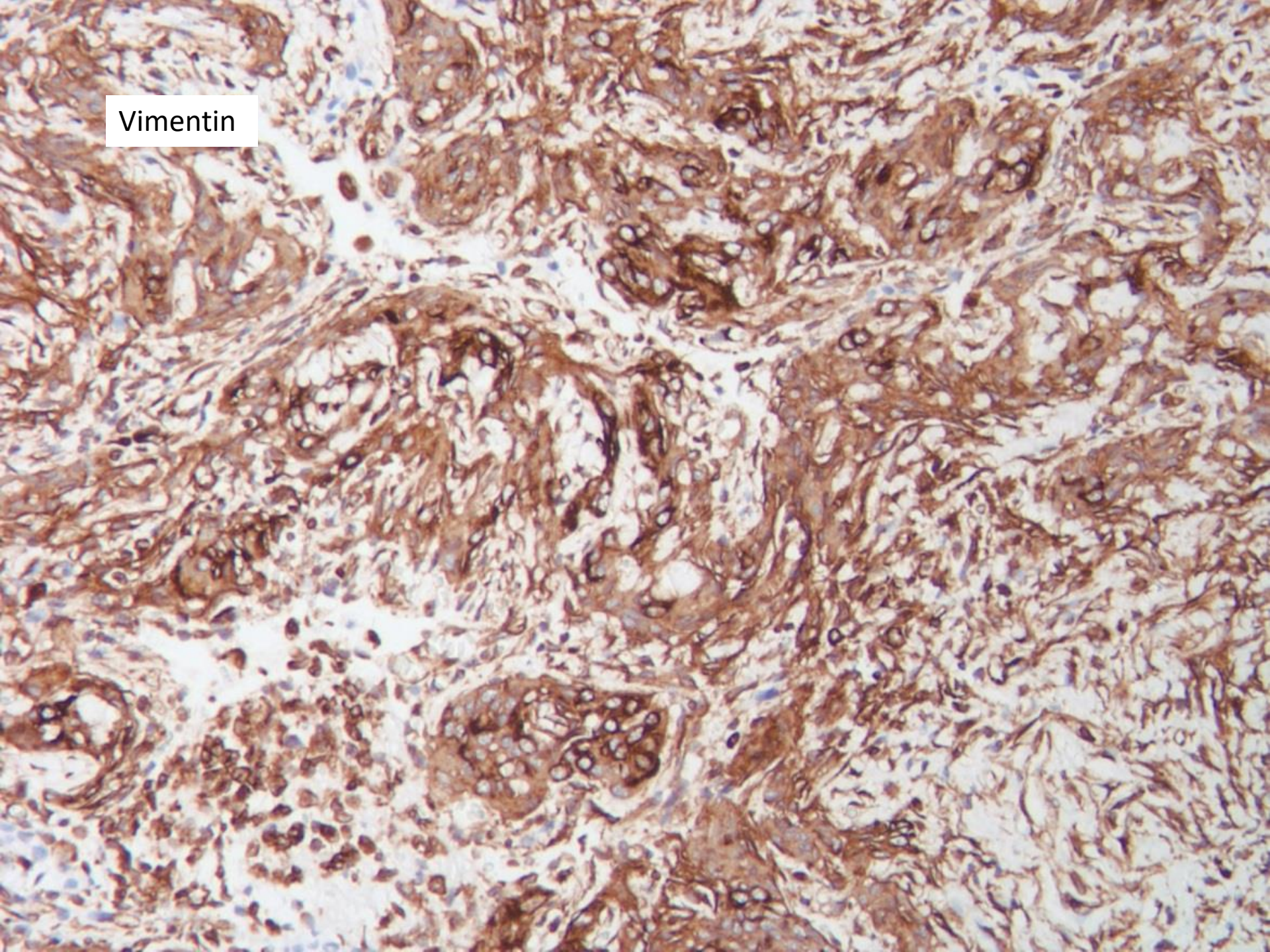
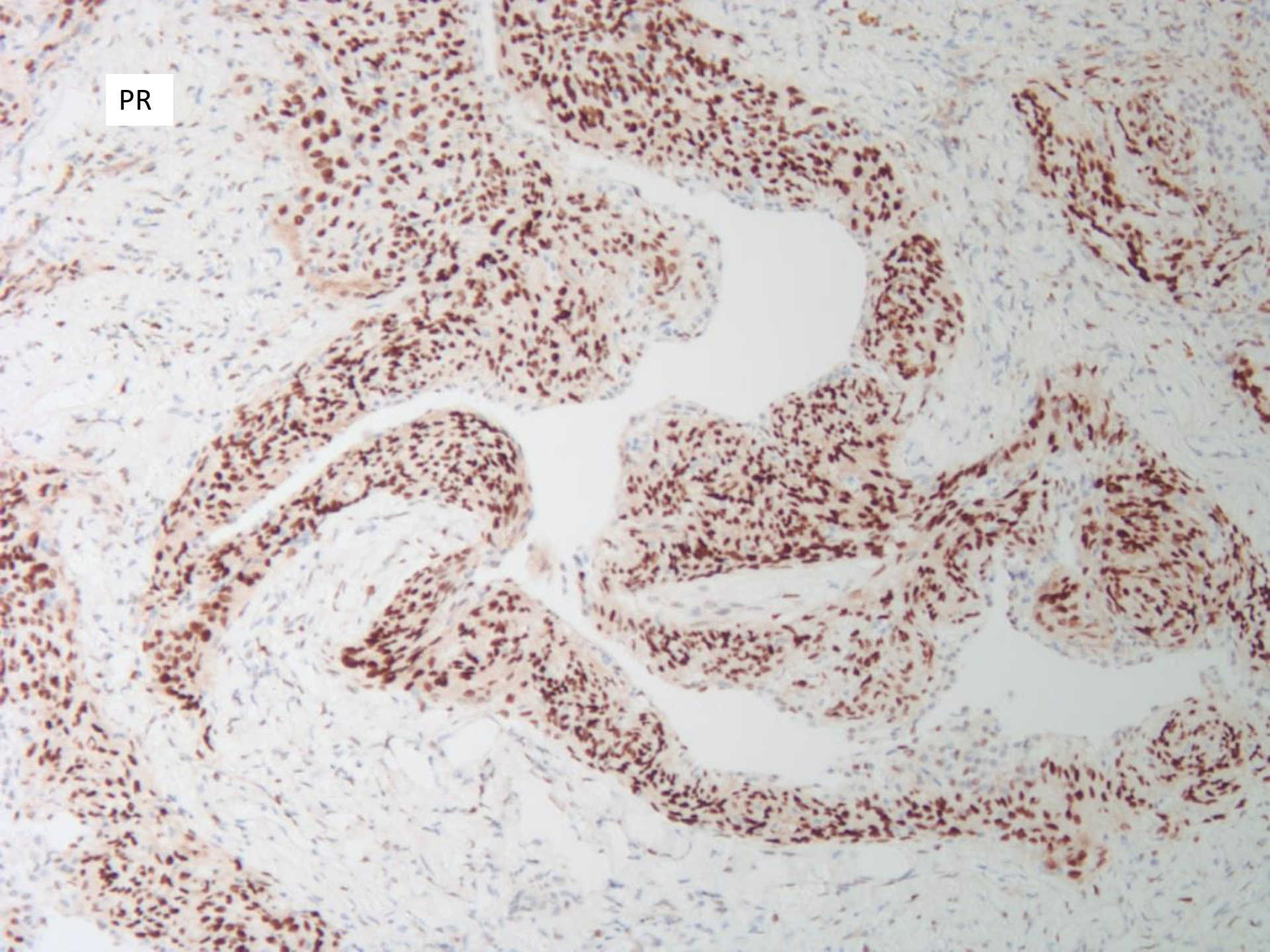
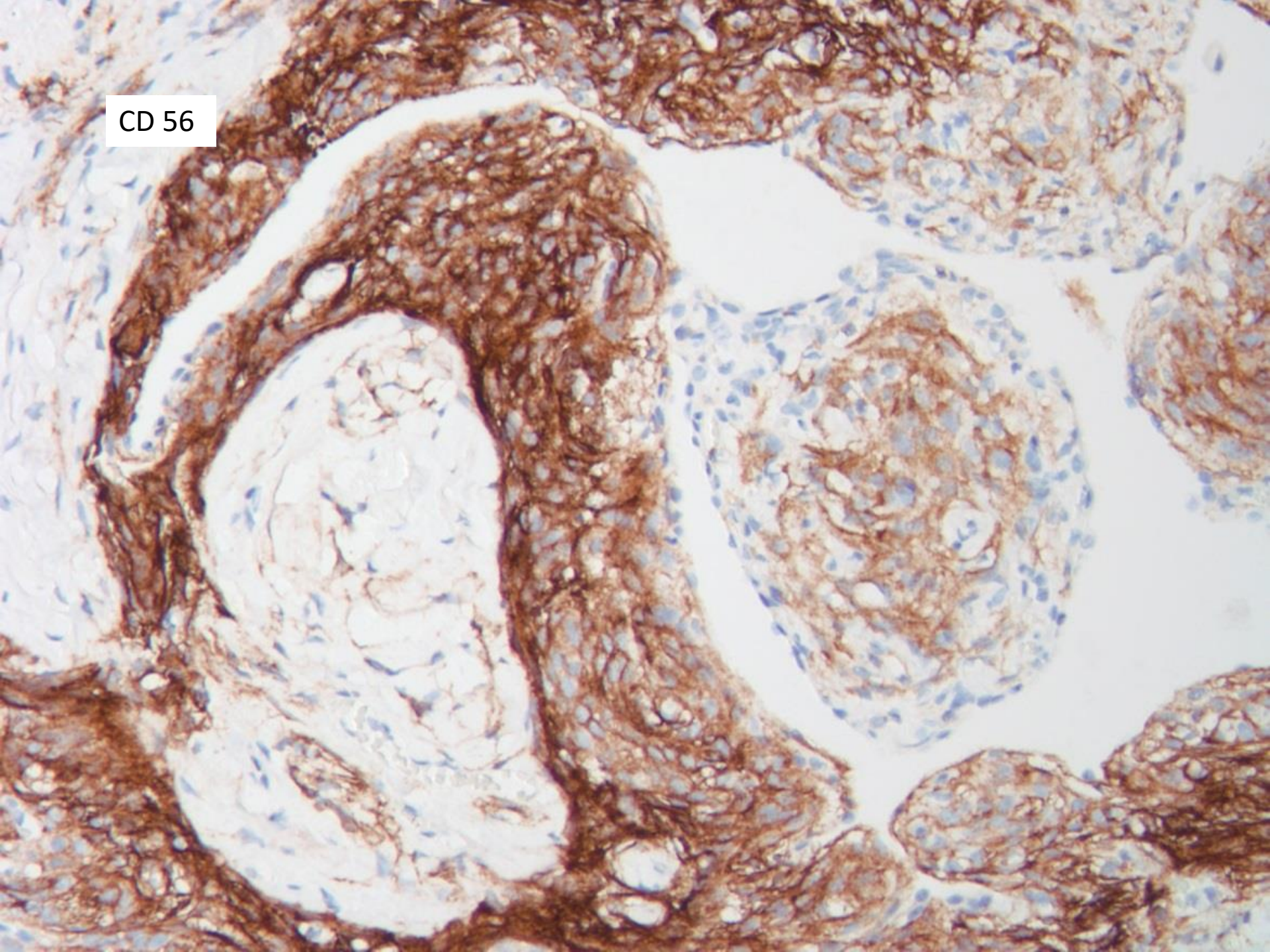

TTF-1/Napcin A


Vimentin


PR


CD 56

Pulmonary meningothelial-like nodules

- Originally described by D. Korn, K. Bensch, A. Liebow, and B. Castleman as “chemodectoma”
  - Based on similarity to carotid body tumors
  - Relationship to vessels
- Gaffey , Mills, and Askin in 1988 recognized similarity to meningothelial cells and proposed current terminology
  - IHC
  - EM
  - Lack of NE differentiation
- Lesions are not clonal by X-linked polymorphism studies
  - Probably a reactive condition; not a true neoplasm

Pulmonary meningothelial-like nodules: associations

- Very common
  - 13% of OLBx
  - 48% of lobectomies
  - Most frequent in 6th decade
  - F>M
- Associations
  - Thromboembolic disease
  - RB-ILD/other CISLD
  - CHF
  - Pulmonary carcinoma
- They are not found in infants and children

Pulmonary meningothelial-like nodules: DDX

- Spindle cell carcinoid
- Sclerosing pneumocytoma
- Metastatic meningioma
- Metastatic sarcoma
- Primary pulmonary meningioma
- SFT
- Spindle cell mesothelioma
- Spindle cell thymoma

Pulmonary meningothelial-like nodules: IHC

- EMA, CD56, PR, Vimentin: Positive
- Synaptophysin, Chromogranin: Negative
- Keratin: Negative
- TTF-1: Negative
- CEA: Negative
- Ki-67: Low

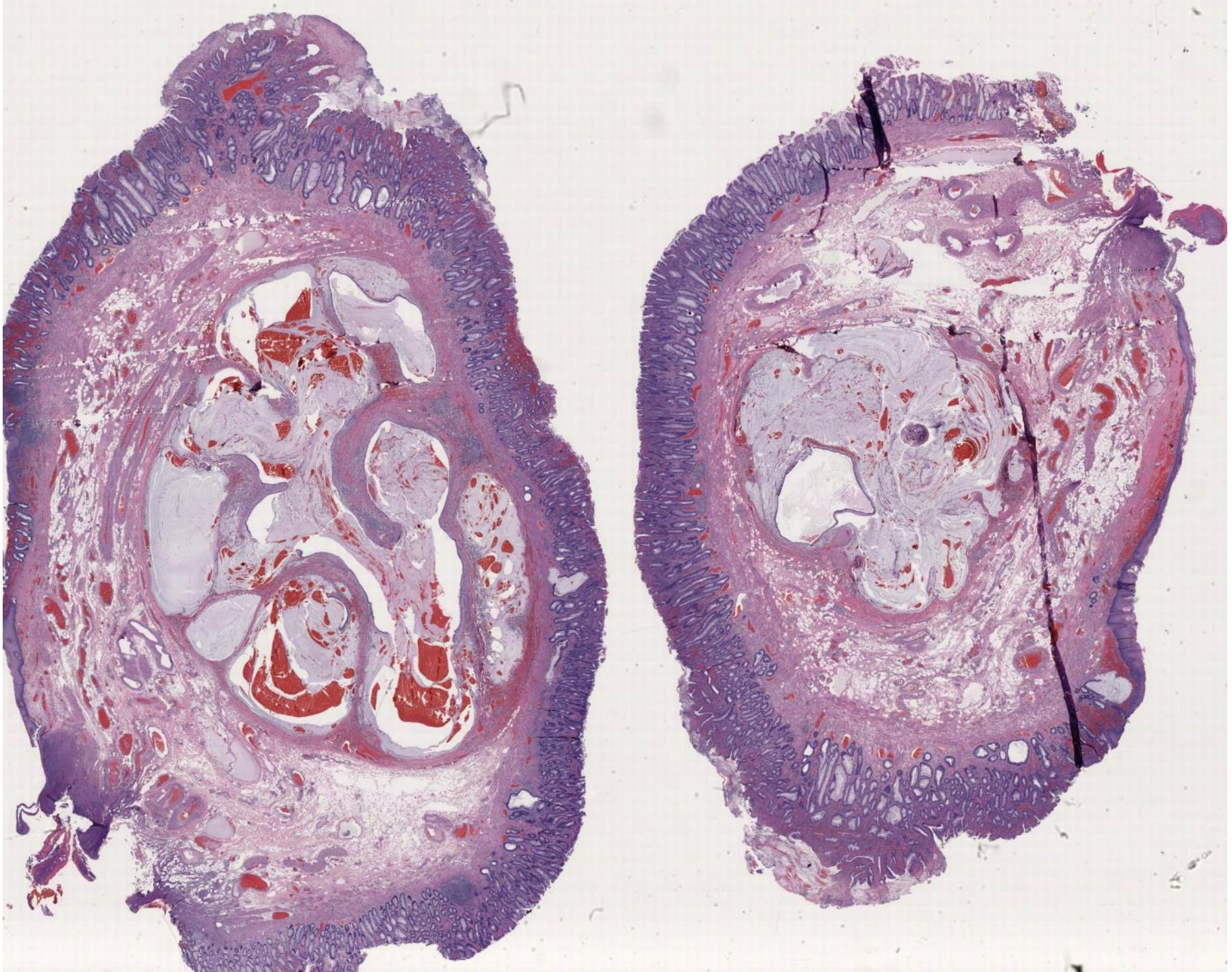
References

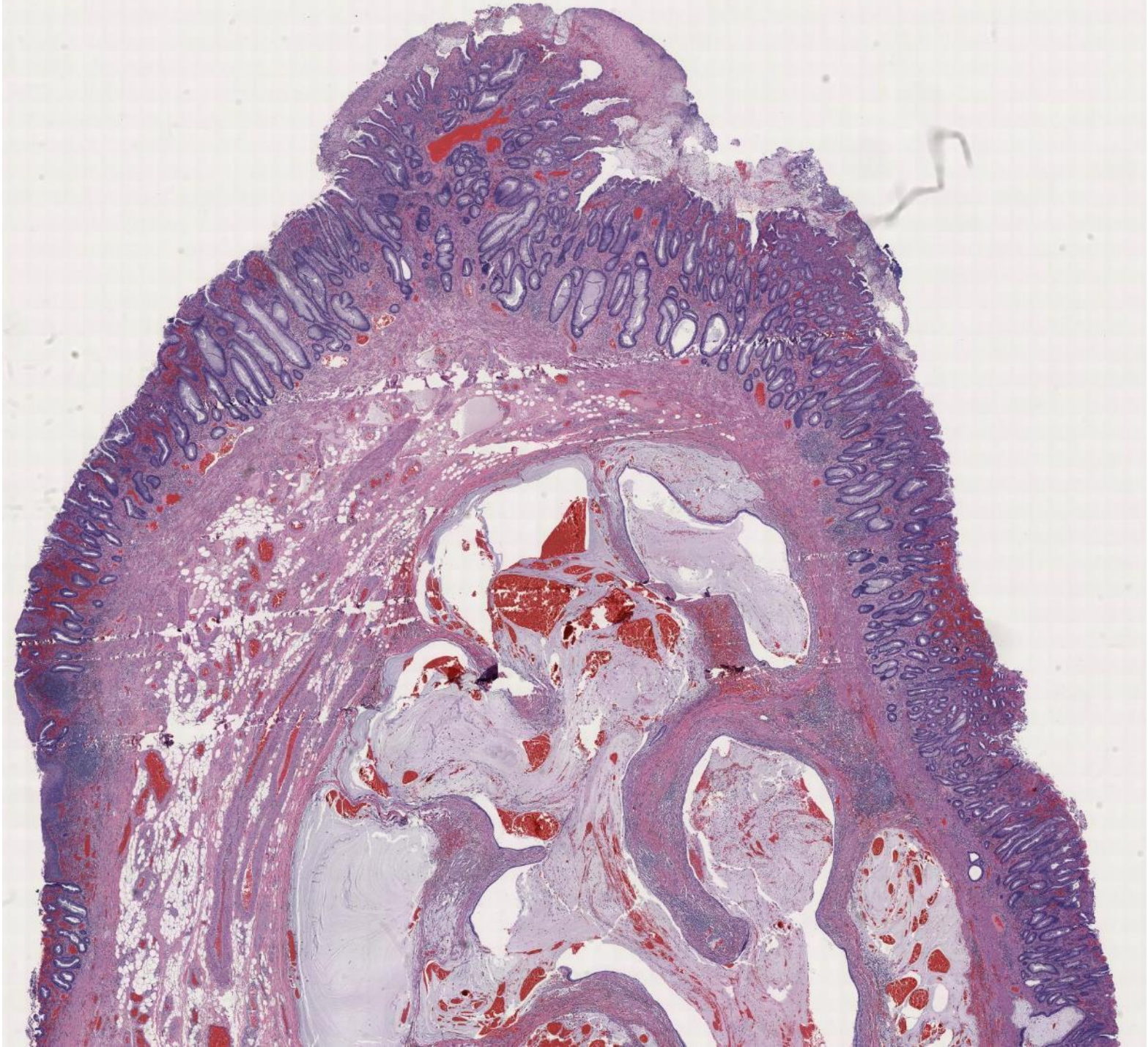
- Katzenstein et al: Pulmonary meningothelial-like nodules:new insights into a common but poorly understood entity. AJSP 2009; 33 (4): 487-95.
- Lee et al: Pulmonary meningothelial-like nodules simulating hematogenous lung metastasis: Occasionally report. Tuberculosis and Respiratory Diseases 2013; 75: 67-70.

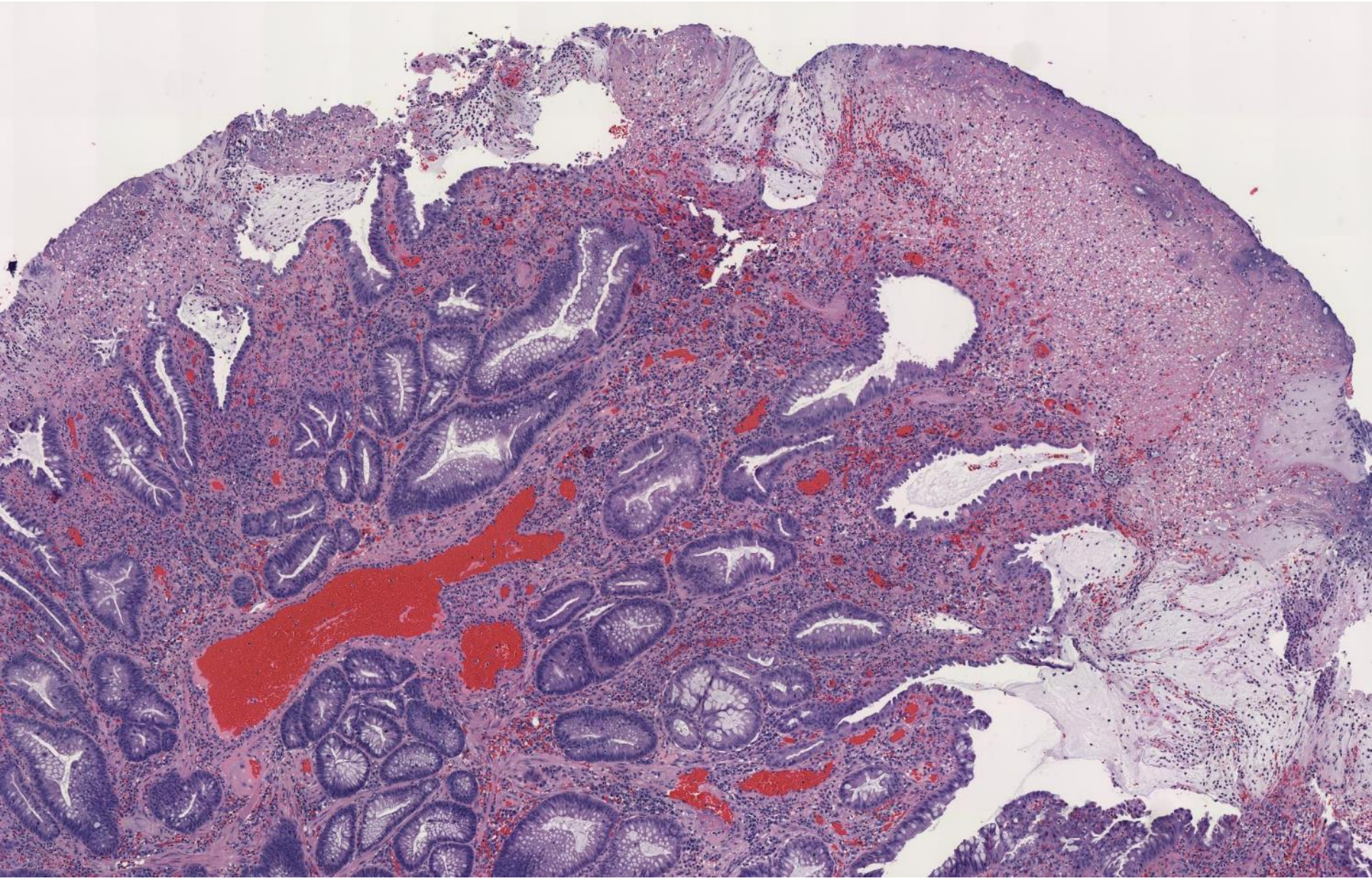
SB 6324
(scanned slide available)

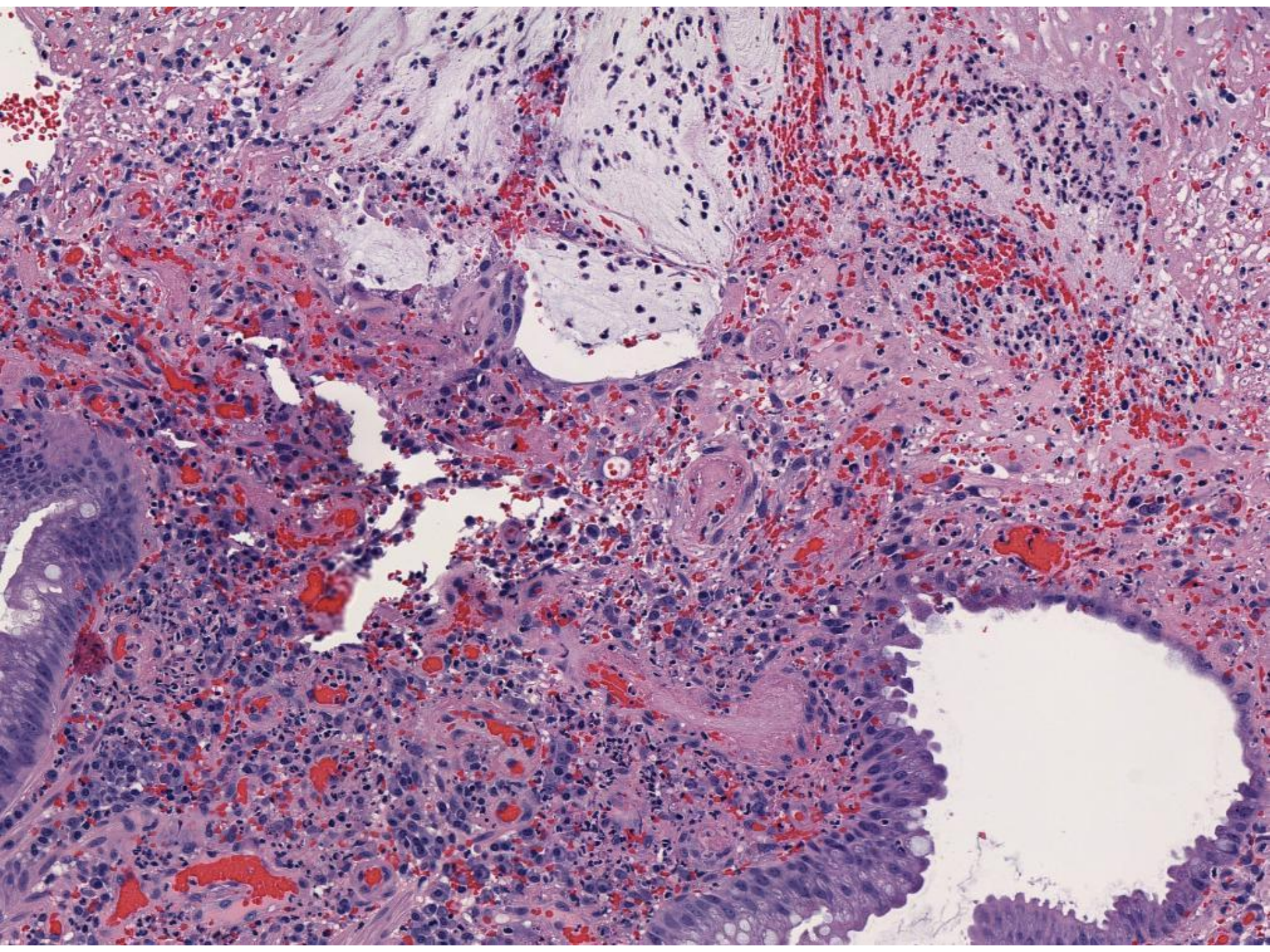
Mahendra Ranchod; Good Samaritan Hospital

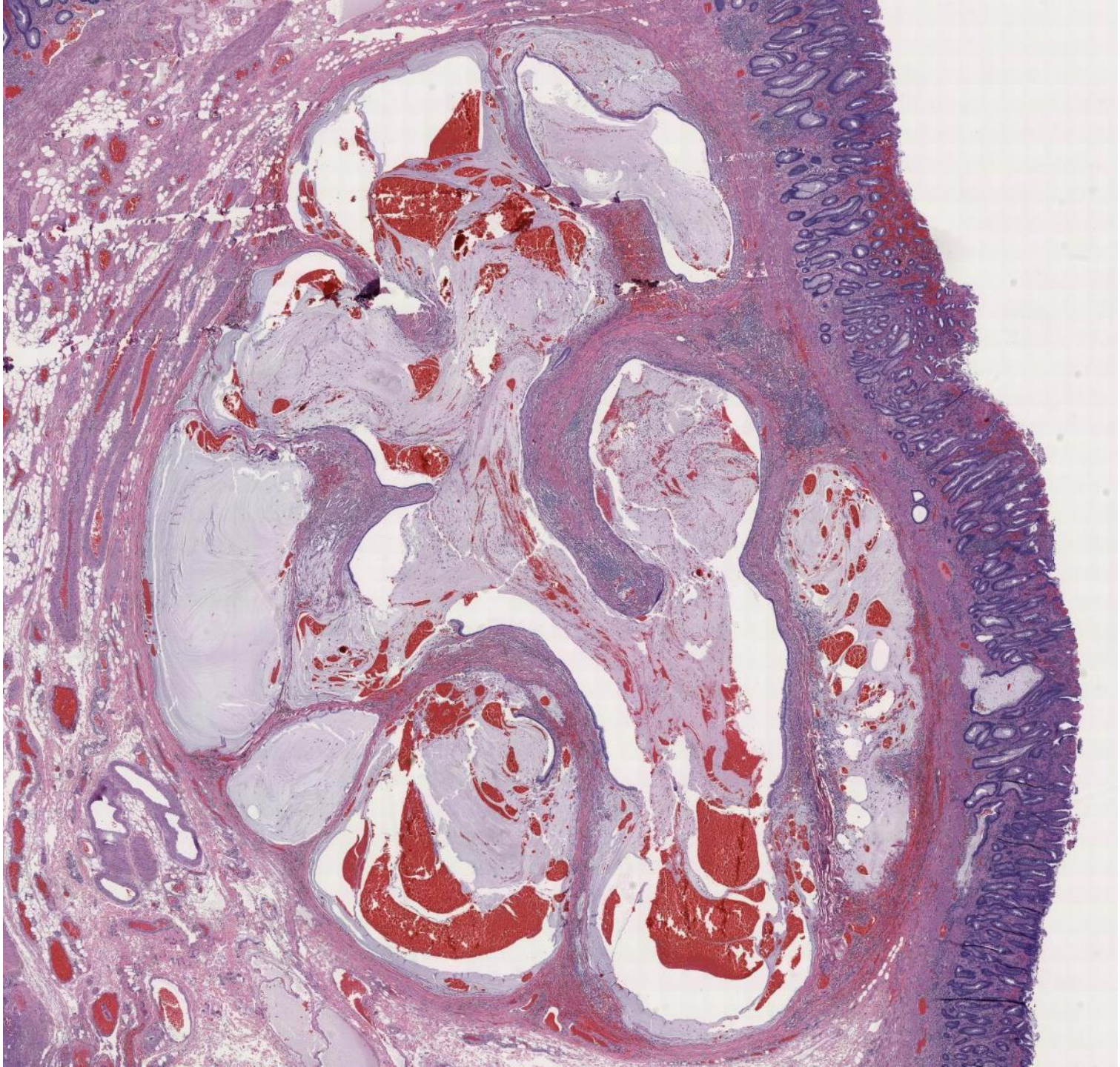
48-year-old male with 2cm mass in upper anal canal at time of hemorrhoidectomy.

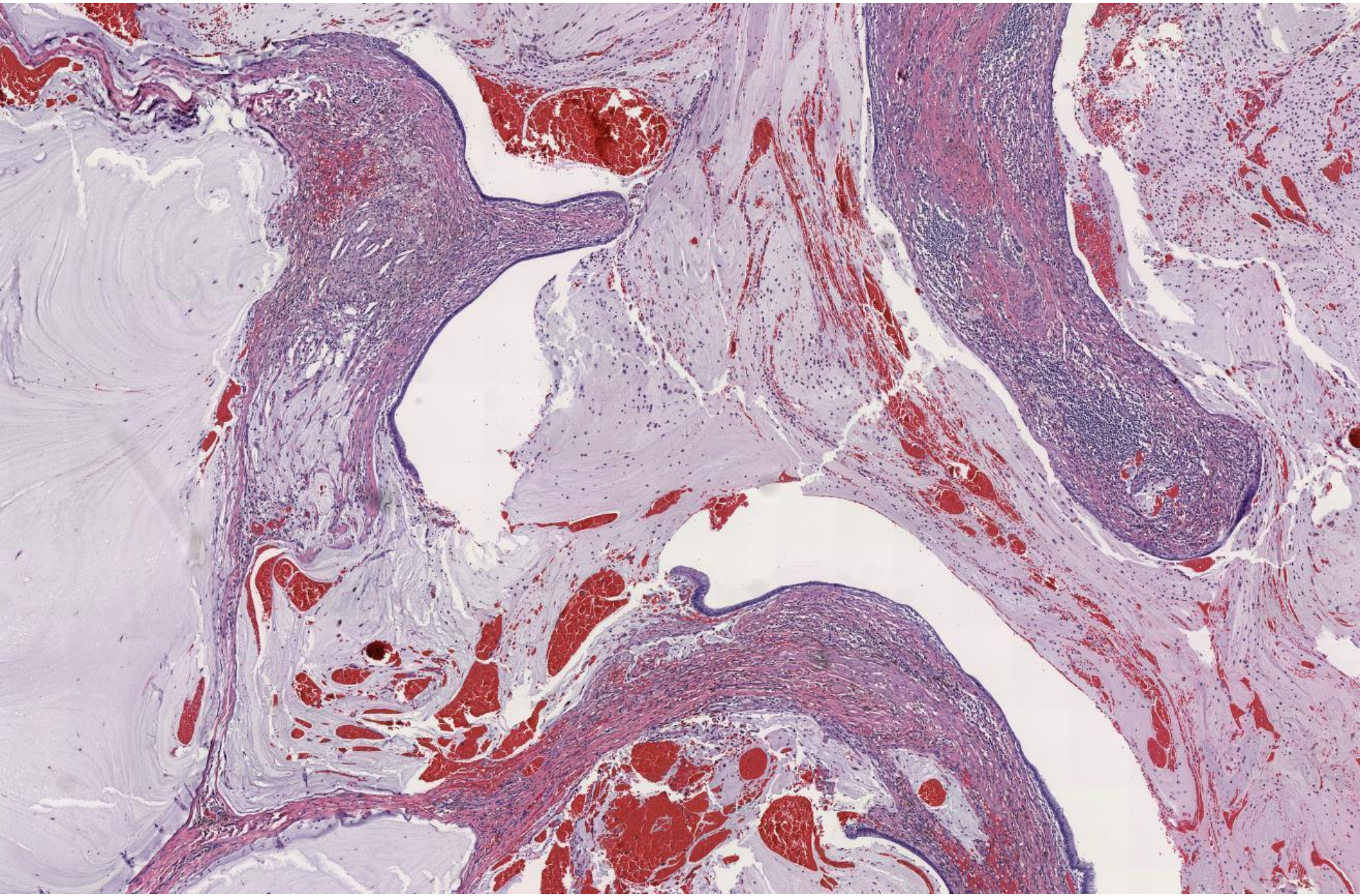


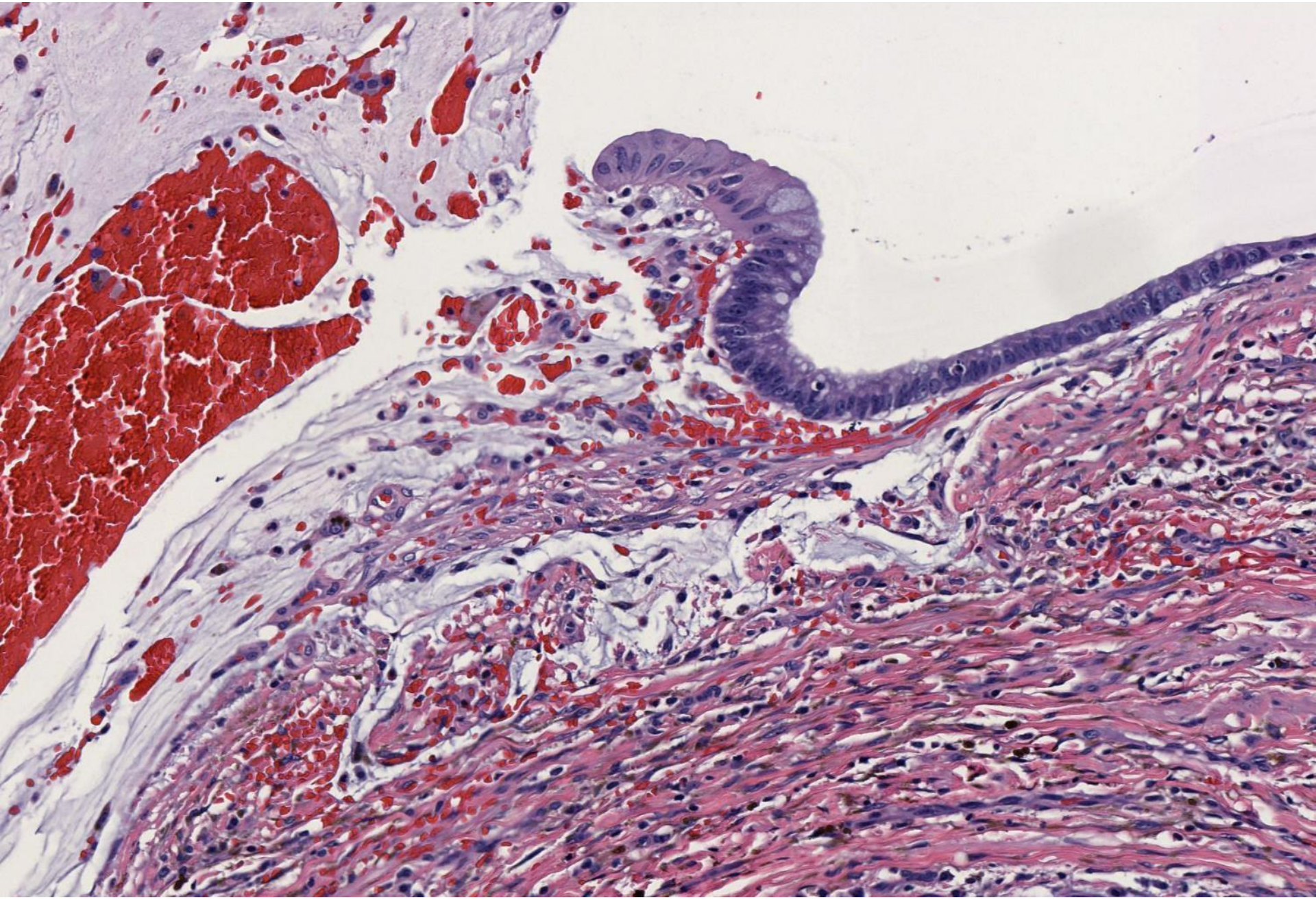


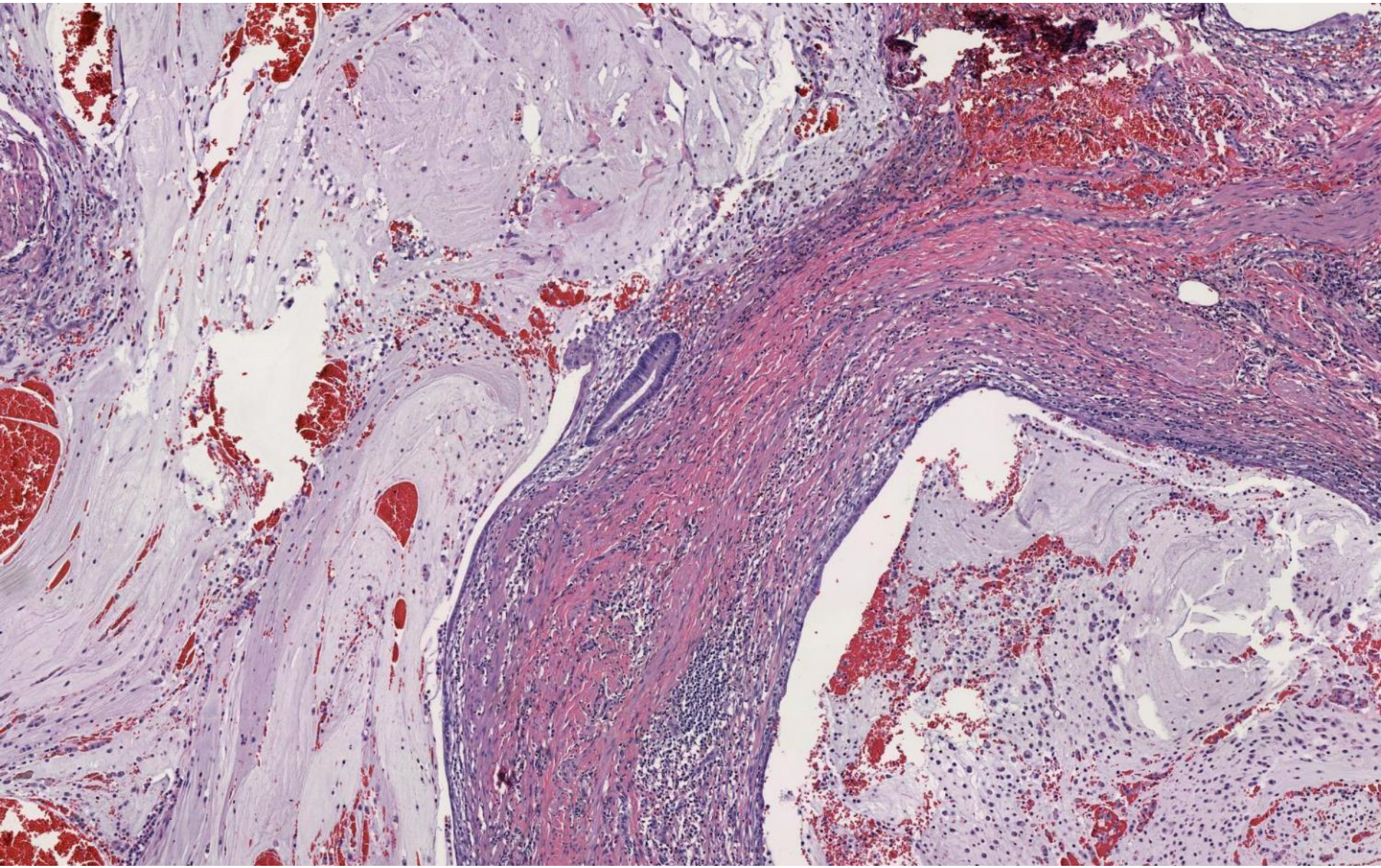


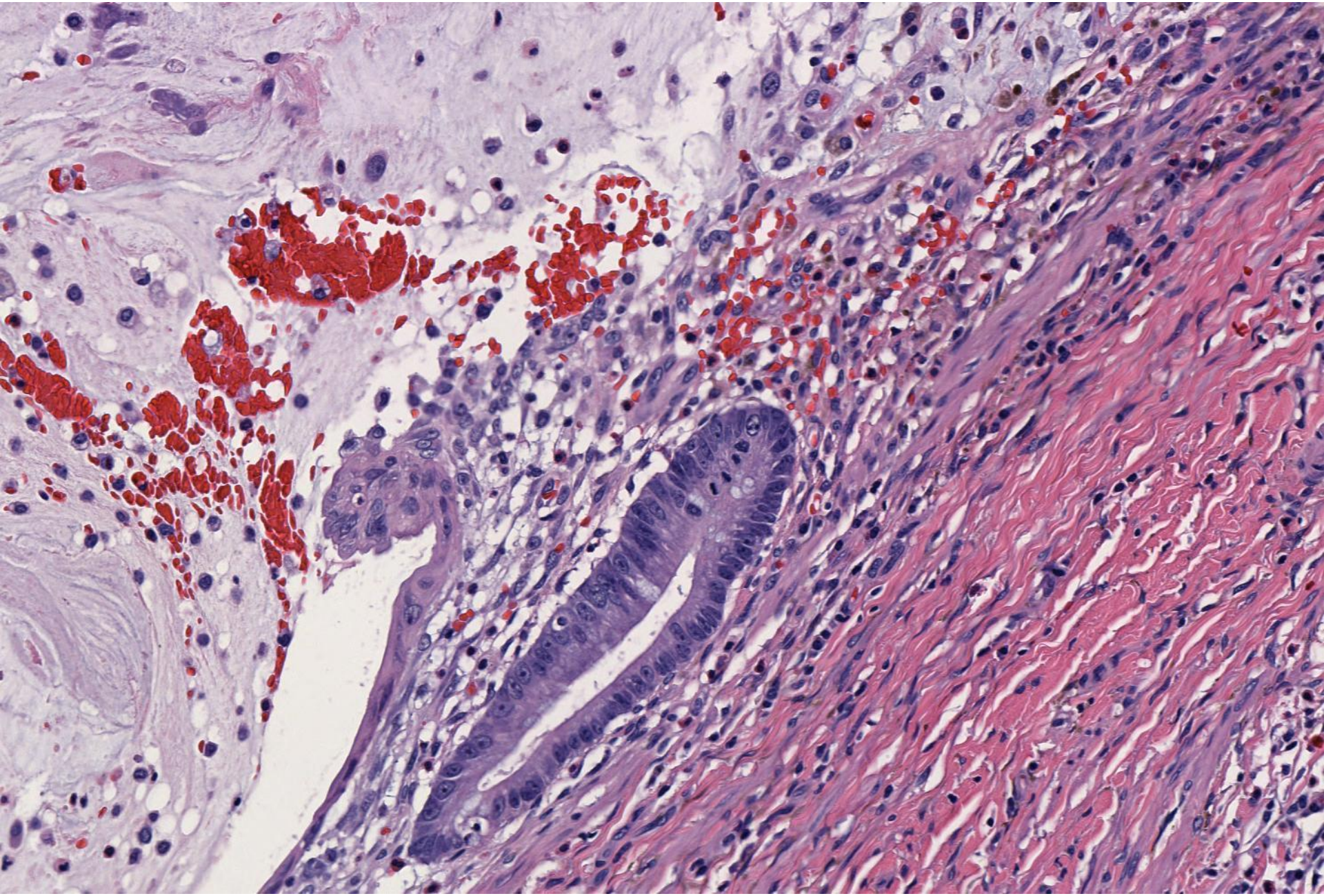












DIAGNOSIS?

Proctitis Cystica Profunda

- Displacement of glandular epithelium into deep layers of rectum
- Usually associated with prolapse
- Polypoid mass mistaken for invasive adenocarcinoma

Etiology of Cystica Profunda

(Gastritis cystica polyposa, enteritis cystica polyposa, colitis cystica profunda)

- **Mechanical**
  - **Rectal prolapse**
- **Traumatic**
  - **Surgical anastomosis**
- **Inflammatory**
  - **U.C., Crohn's disease, Infection**
- **Ischemia**
- **Radiation**

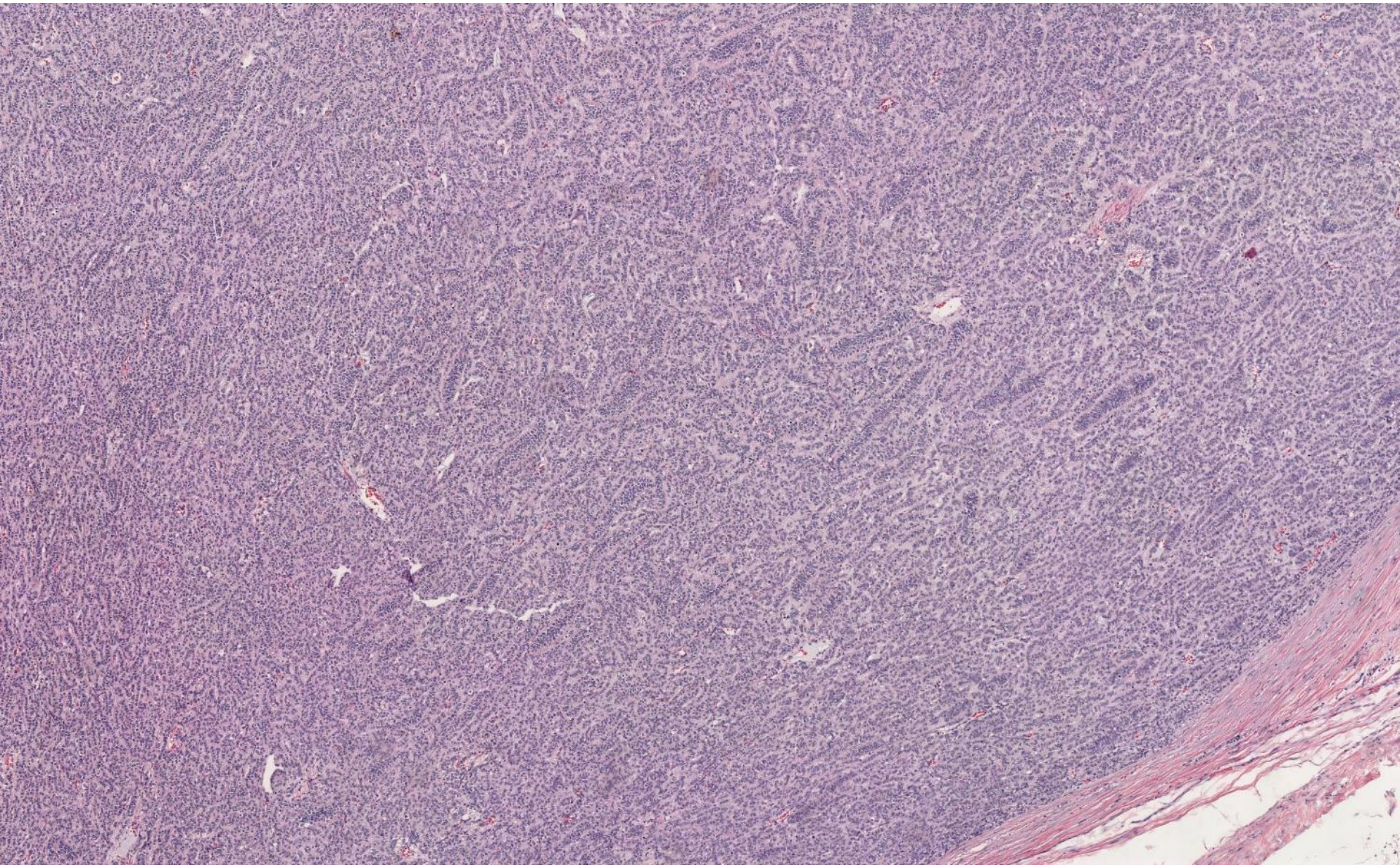
Clues to Diagnosis of Cystica Profunda

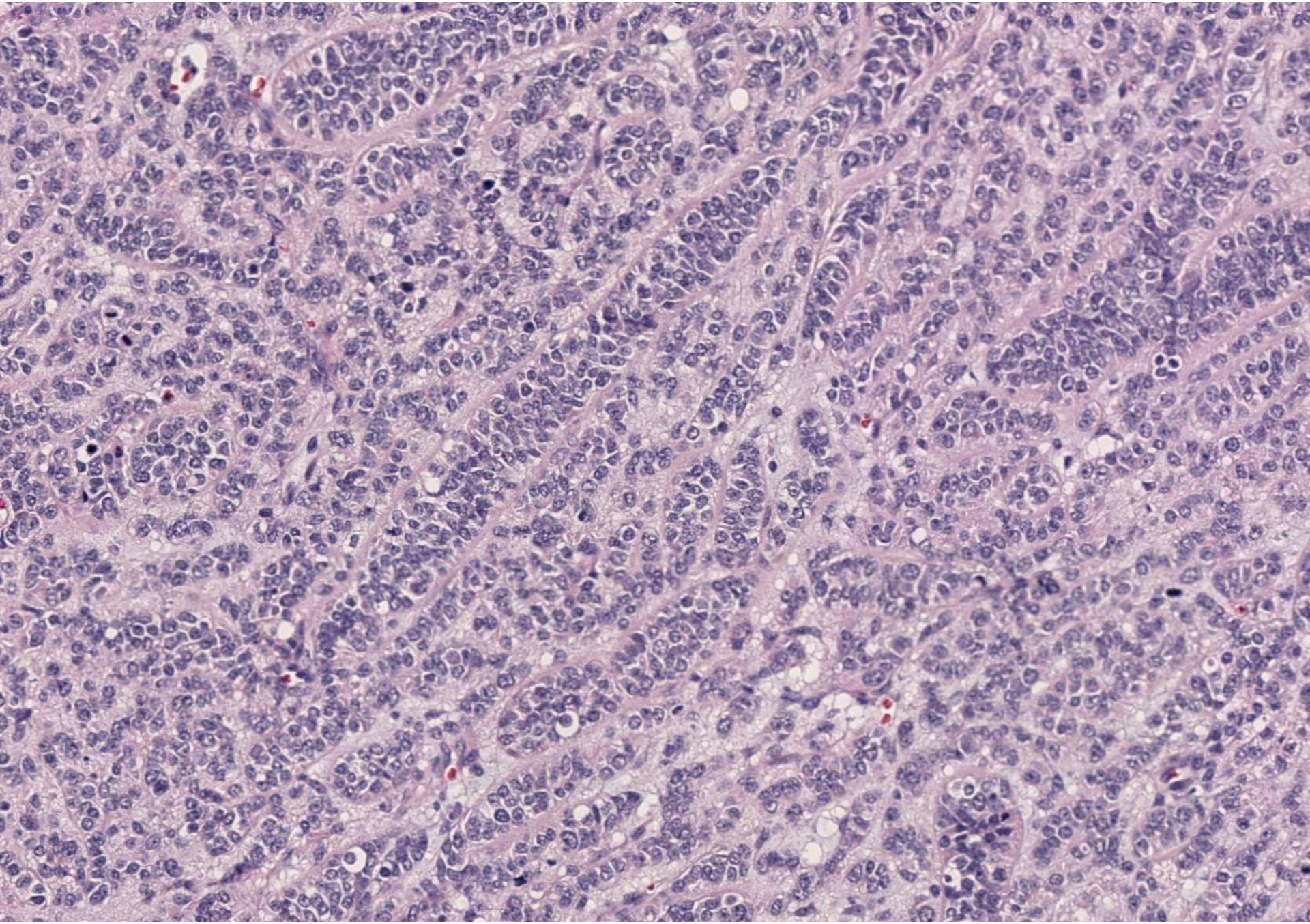
- Clinical history
- Glandular displacement without cytologic atypia
- Rounded contours
- Lamina propria, hemosiderin etc.
- Single layer of columnar cells around mucin pools, continuous or discontinuous
- Epithelial cells around mucin pools, not floating in mucin
- Associated changes (prolapse, anastomosis, but be cautious with U.C. and Crohn's).

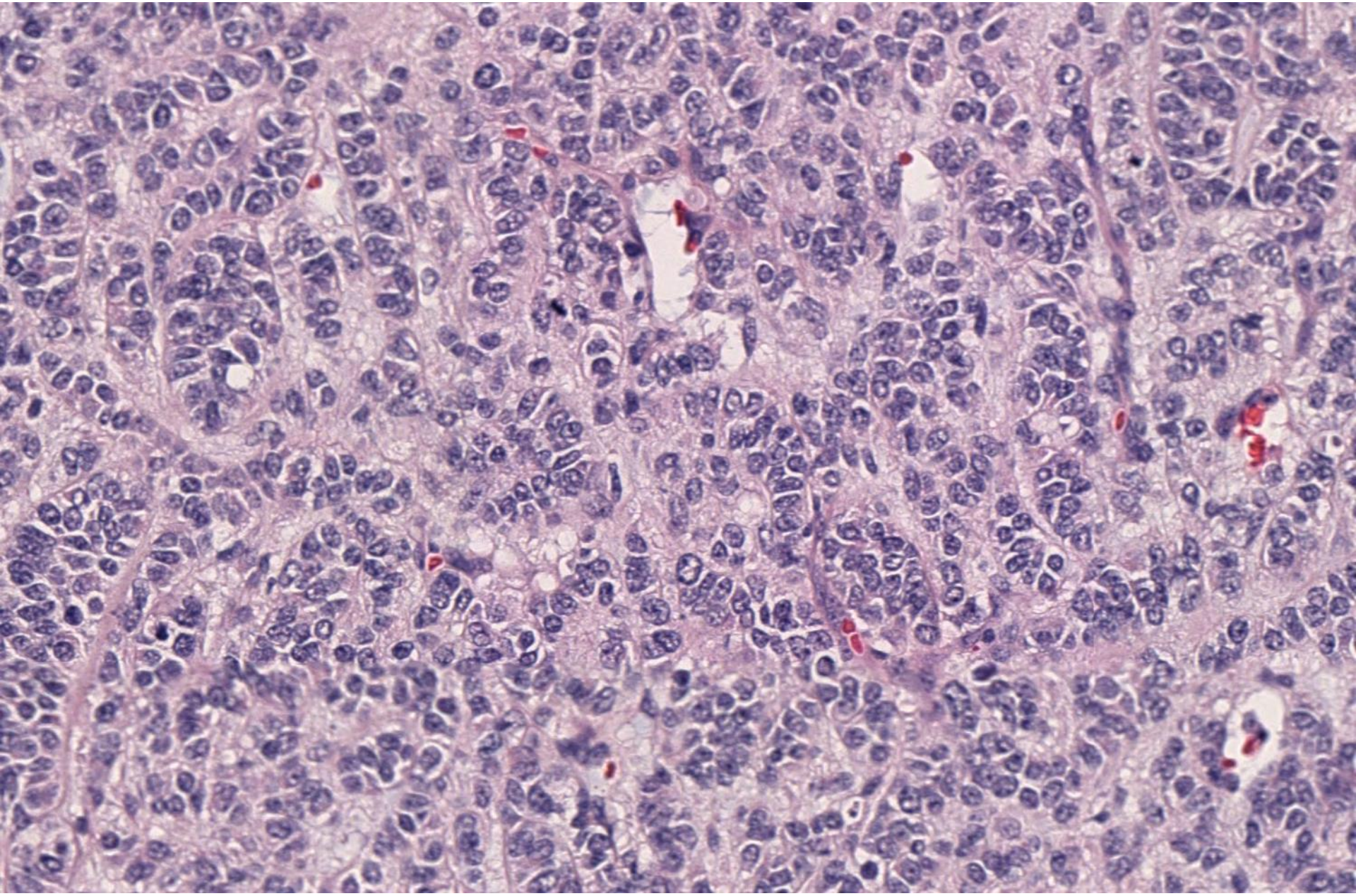
SB 6325
(scanned slide available)

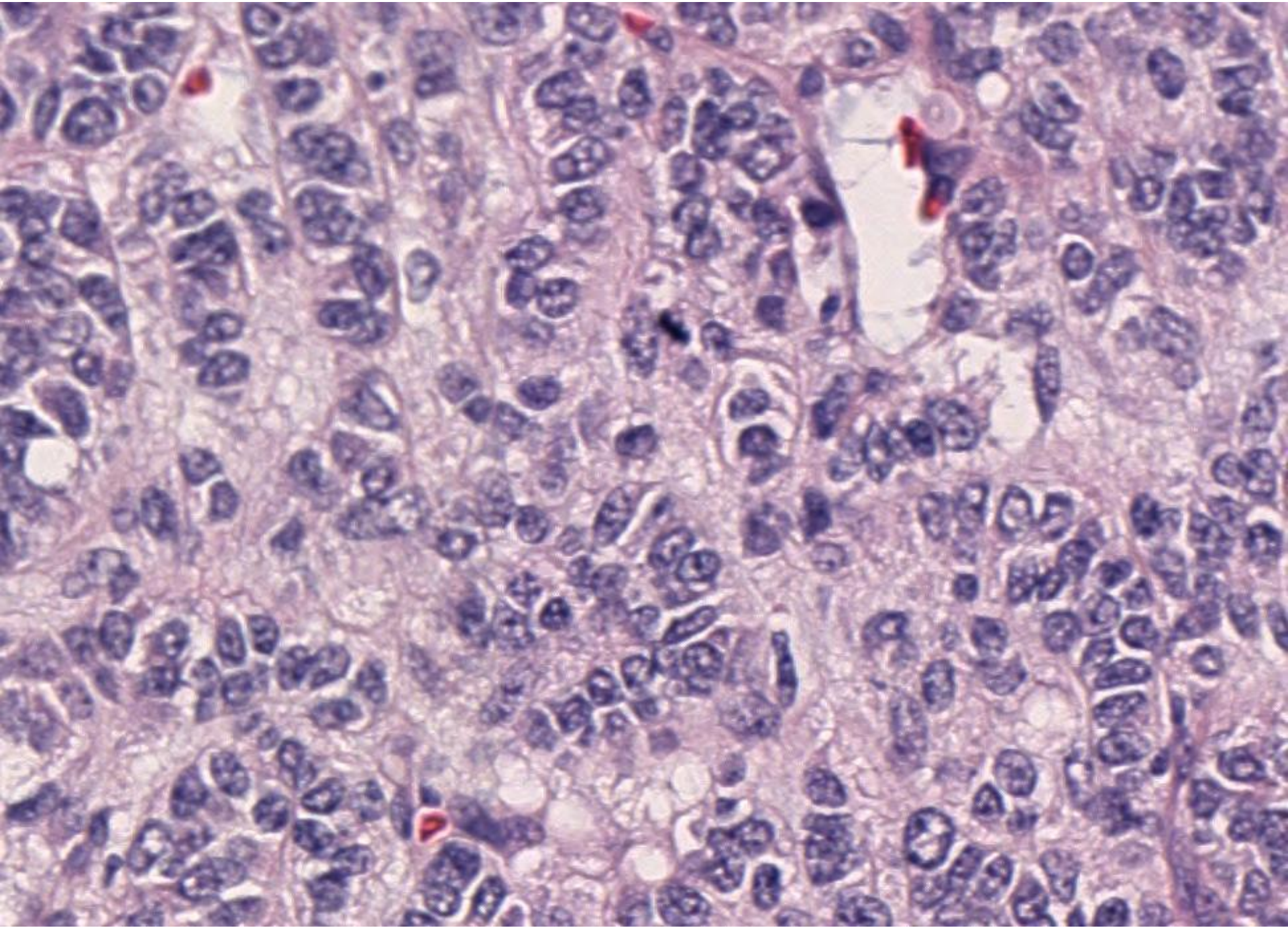
Sunny Kao; Stanford

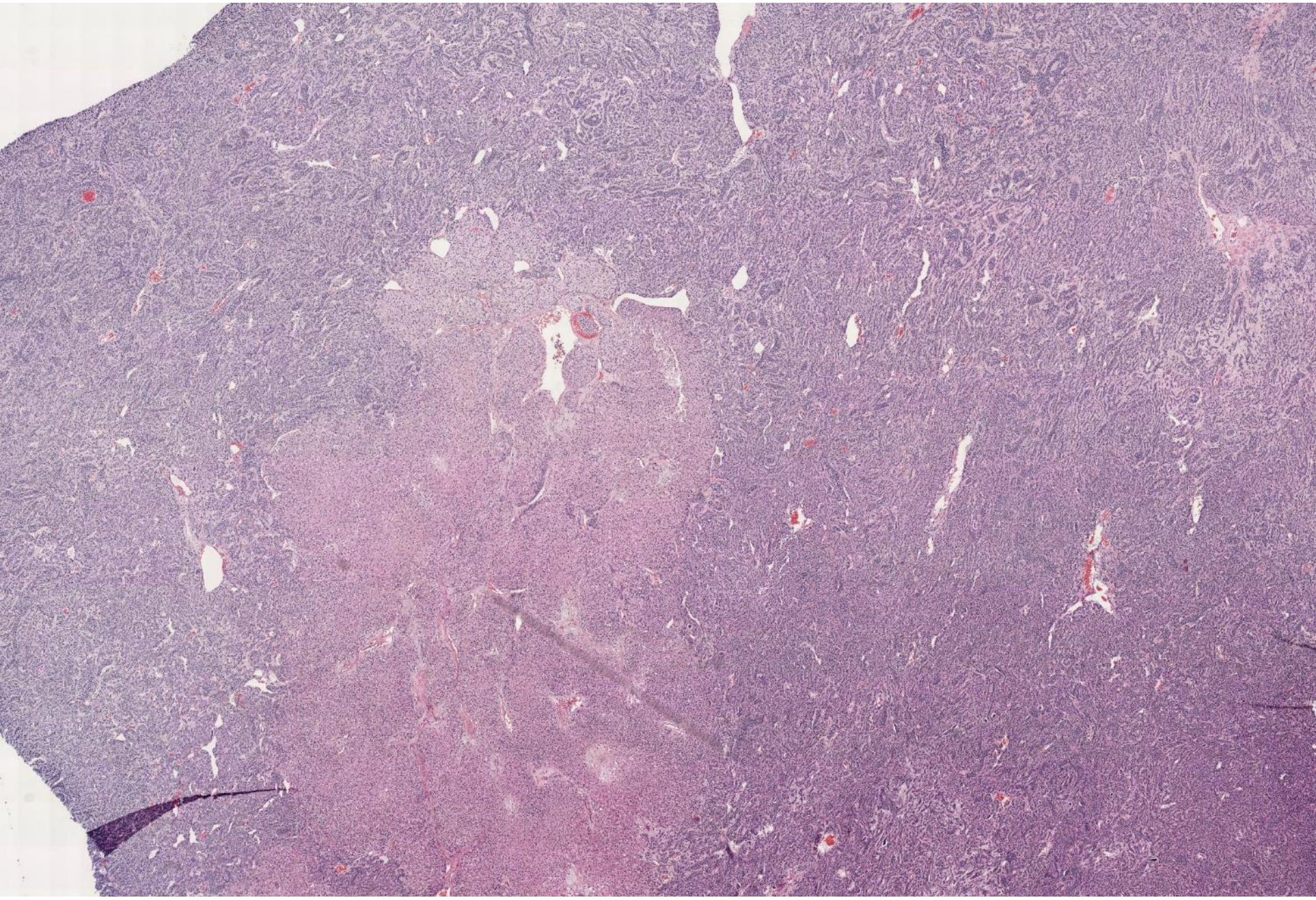
65-year-old male with left testicular mass and normal serum tumor markers.

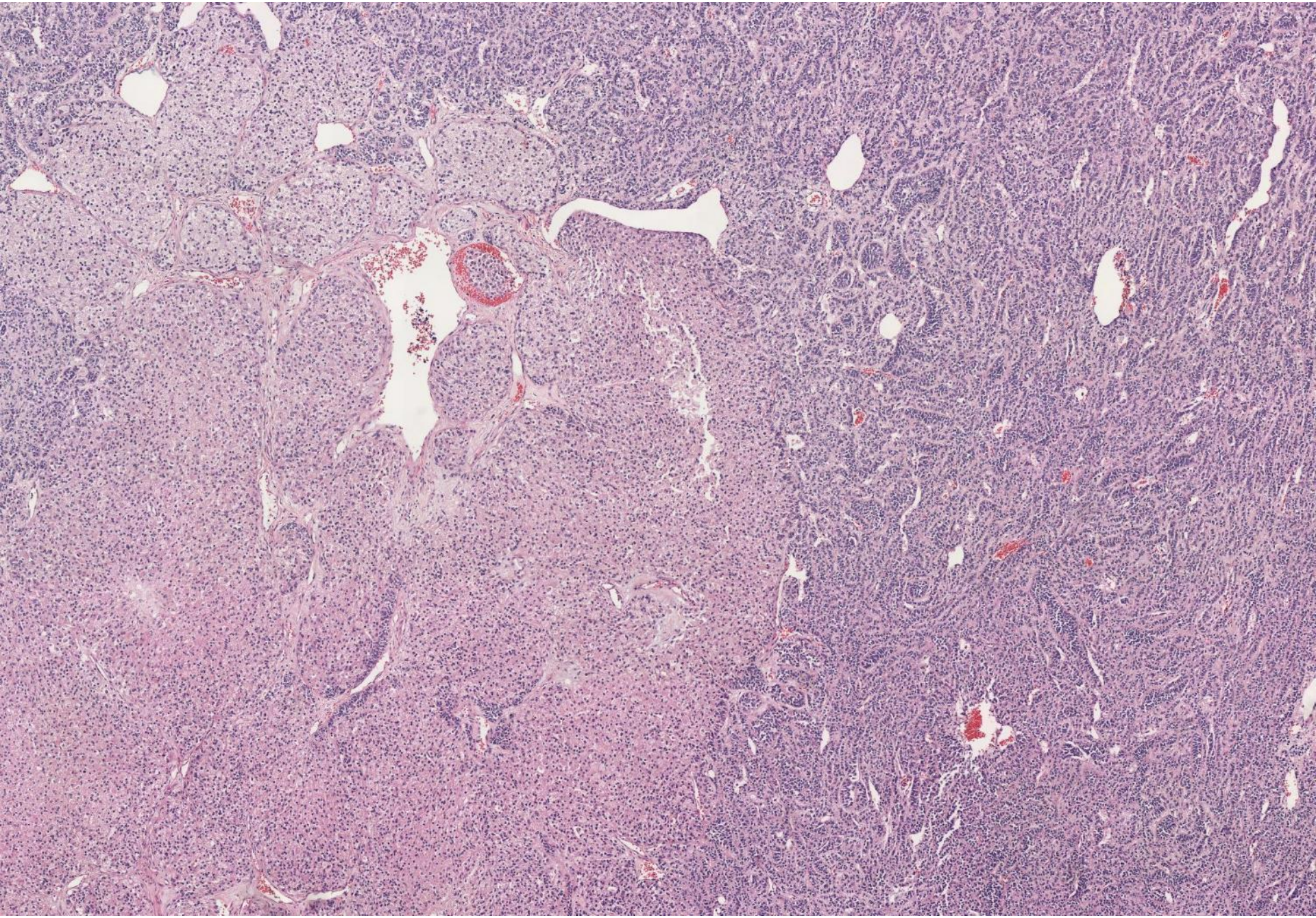


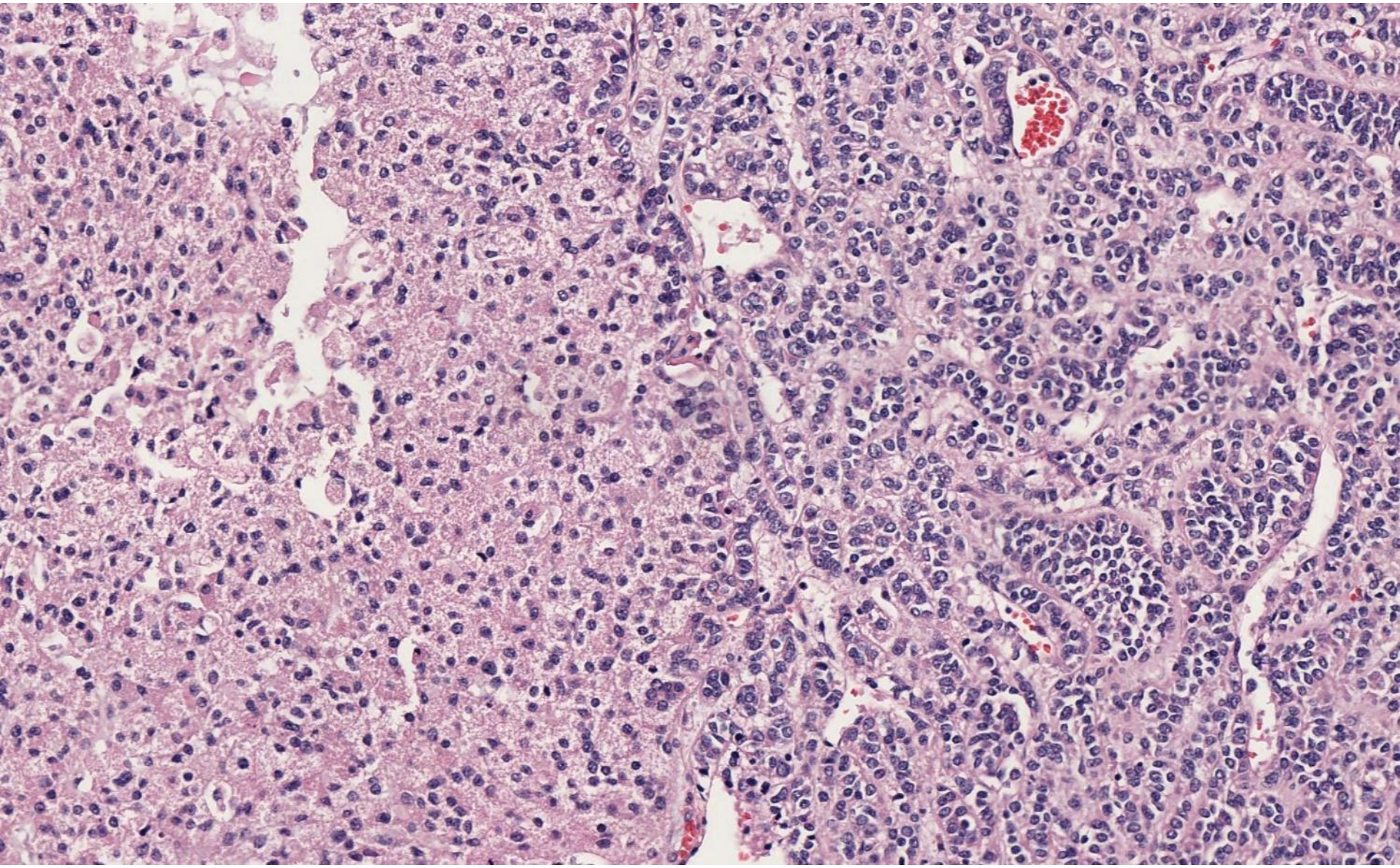


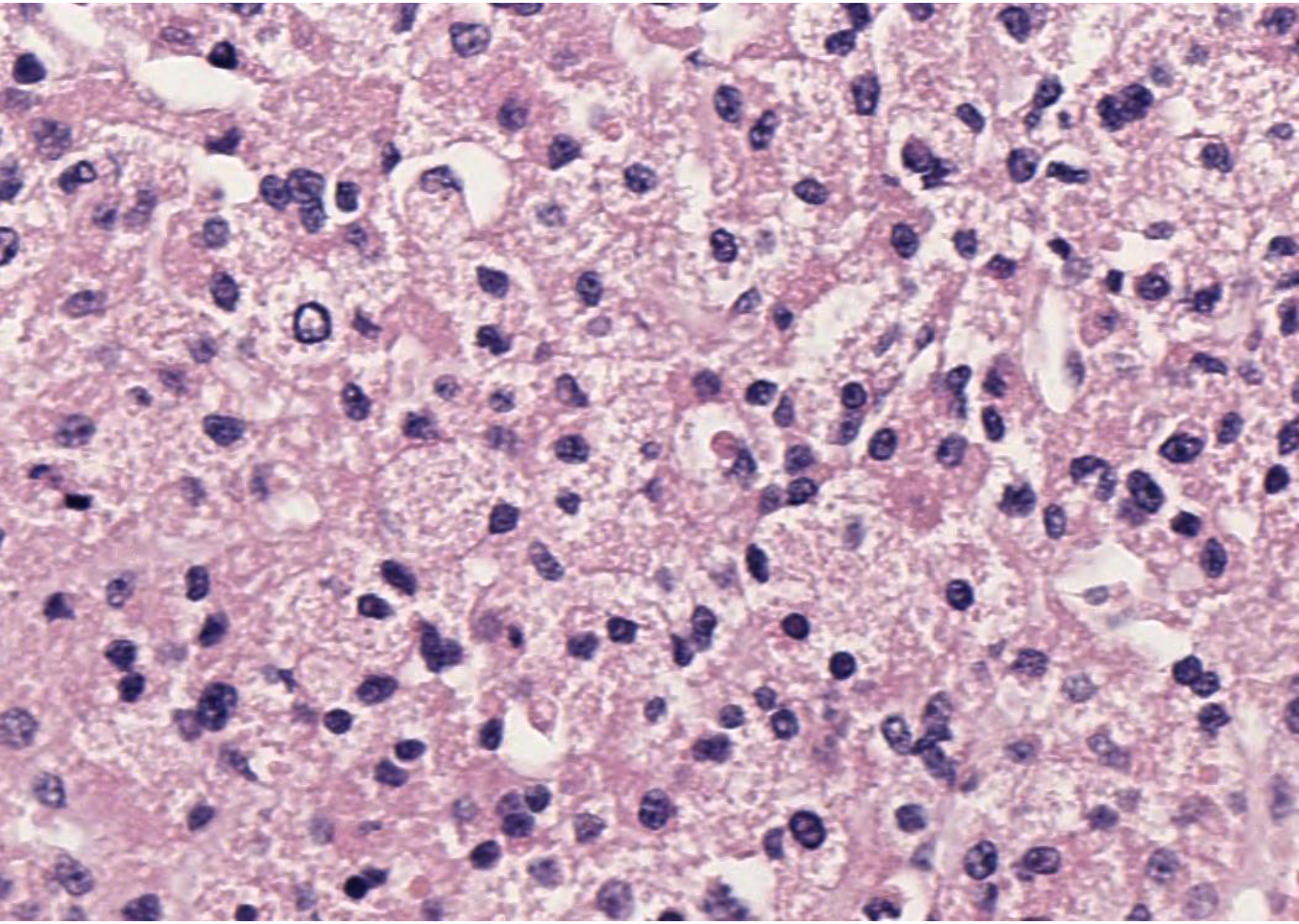


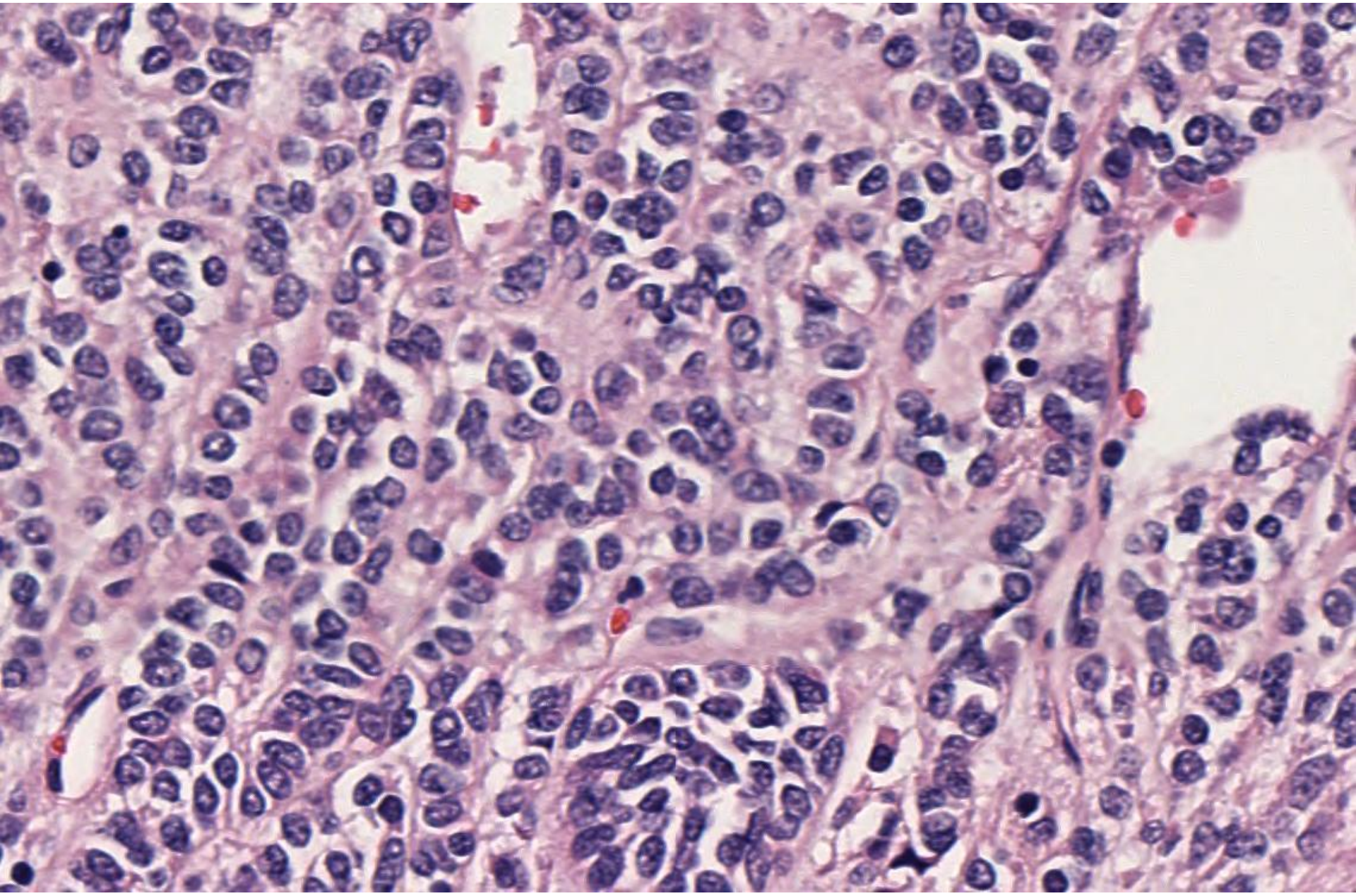










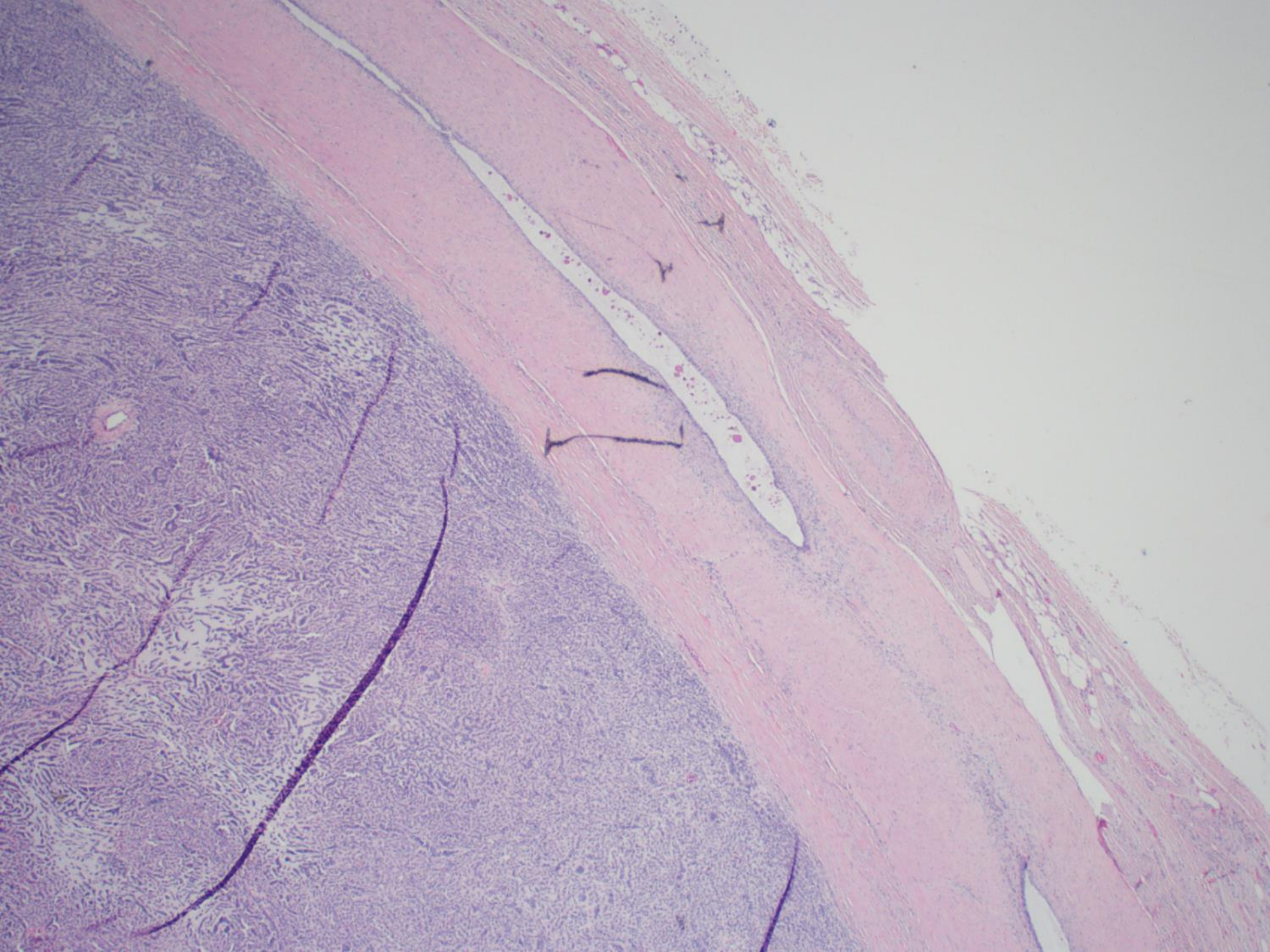


DIAGNOSIS?

SB 6325

65 year-old male with left testicular mass and noremal serum tumor markers

Sunny Kao; Stanford



DDx

- **Germ cell tumor (YST?)**
- **Sex cord stromal tumor (Sertoli cell tumor, granulosa cell tumor, etc.)**
- **Metastasis (well-differentiated neuroendocrine tumor, carcinoma, etc.)**

Adult granulosa cell tumor

- **Rarely encountered in the male**
- **Morphology identical to the GYN counterpart**
- **Acquired *FOXL2* mutations identified in a subset, and may be positive for FOXL2 IHC**

Malignant features

- **Infiltrative borders**
- **LVI**
- **Size > 4**
- **(Necrosis)**
- **(Atypia)**
- **(Elevated mitotic rate)**

Our patient's tumor

- **Invasion of spermatic cord and cord margin**
- **Extensive LVI**
- **Rete testis invasion**

- ***Follow-up*: Received chemotherapy and developed large retroperitoneal mass. Presumed metastatic tumor and no biopsy. Obstructing left kidney with hydronephrosis.**

References

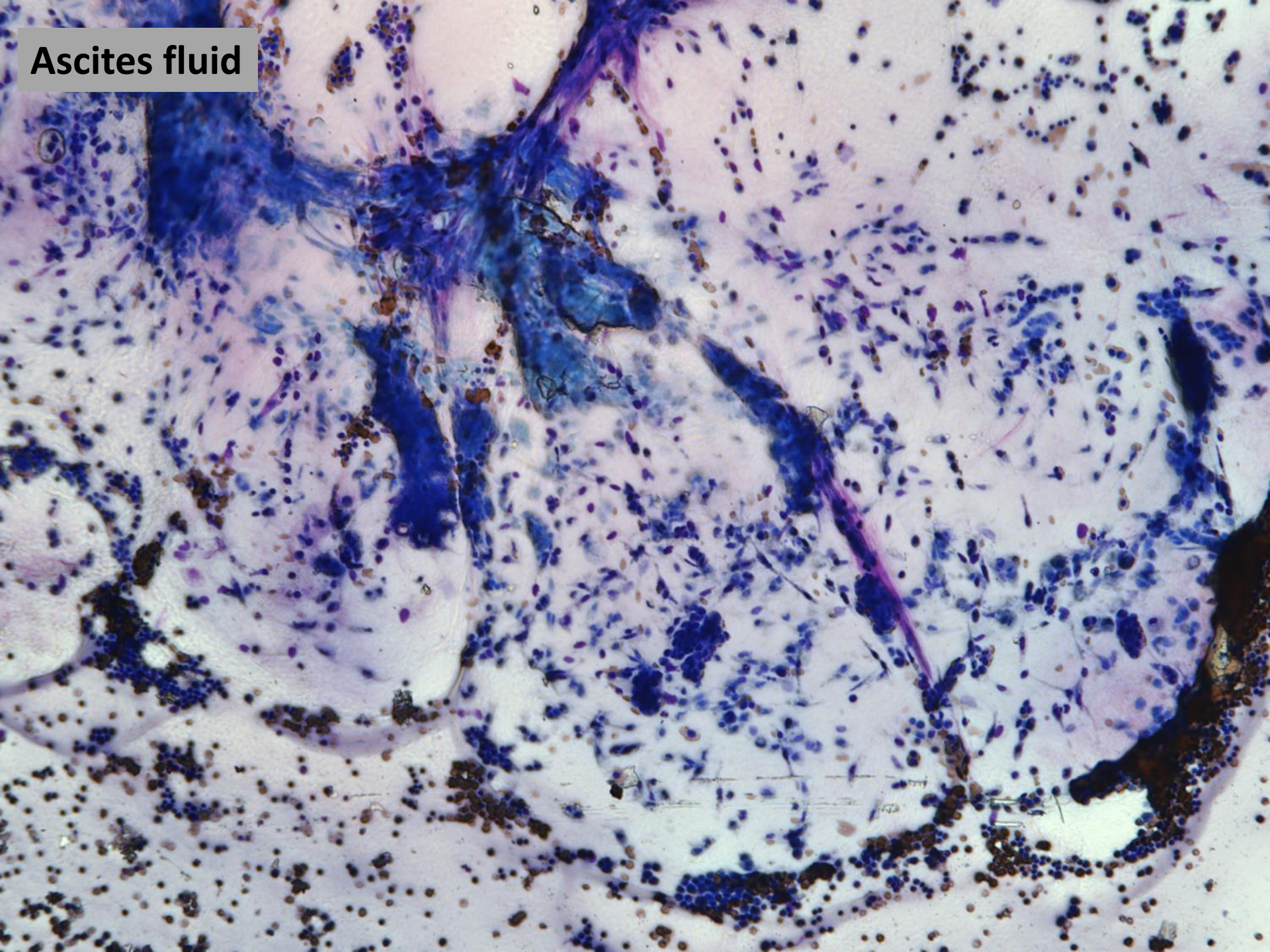
- Hanson JA, Ambaye AB. Adult testicular granulosa cell tumor. Arch Pathol Lab Med 2011;135:4.

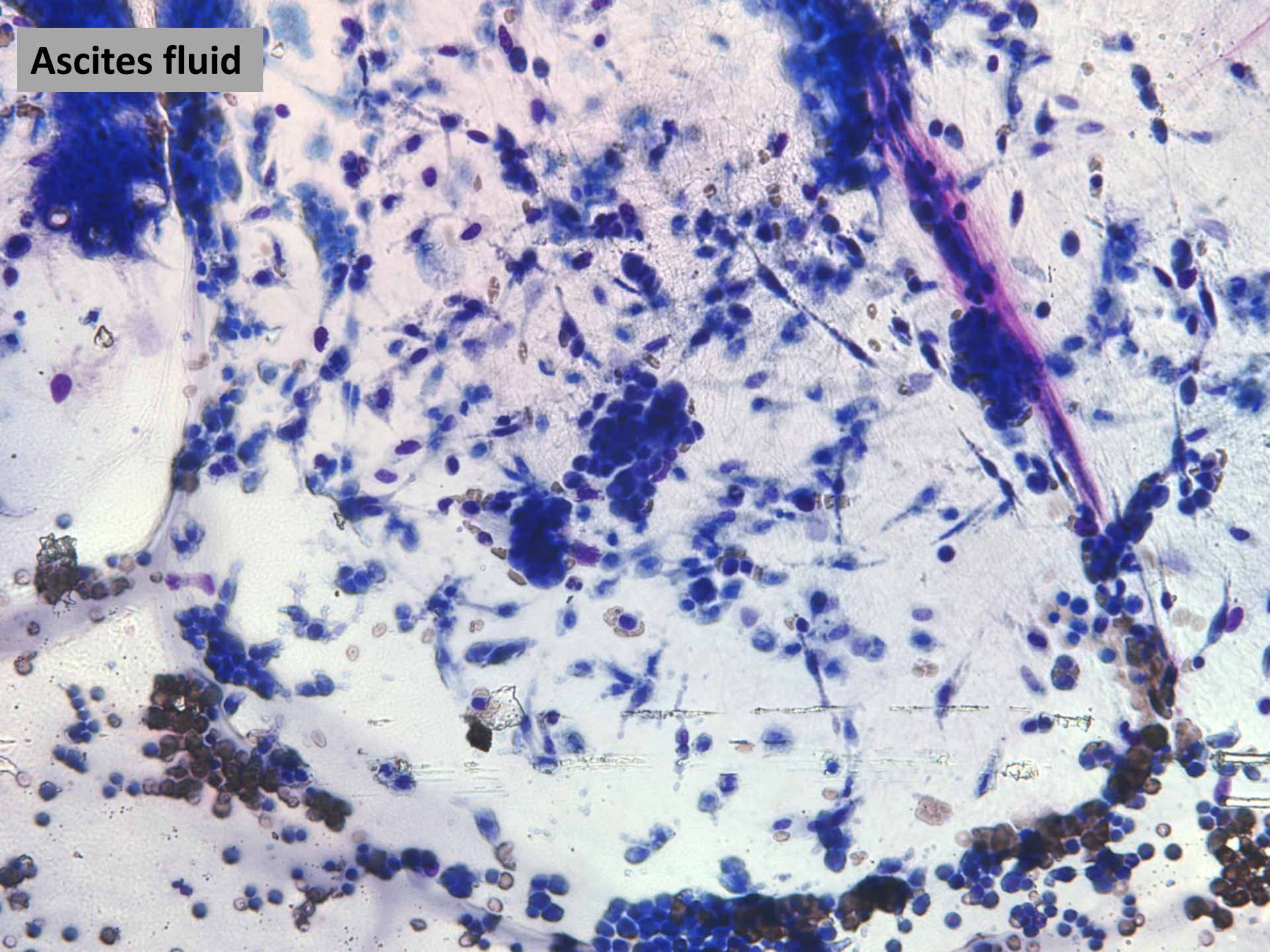
- Cornejo KM, Young RH. Adult granulosa cell tumorsof the testis: a report of 32 cases. Am J Surg Pathol 2014;38(9):1242–50.

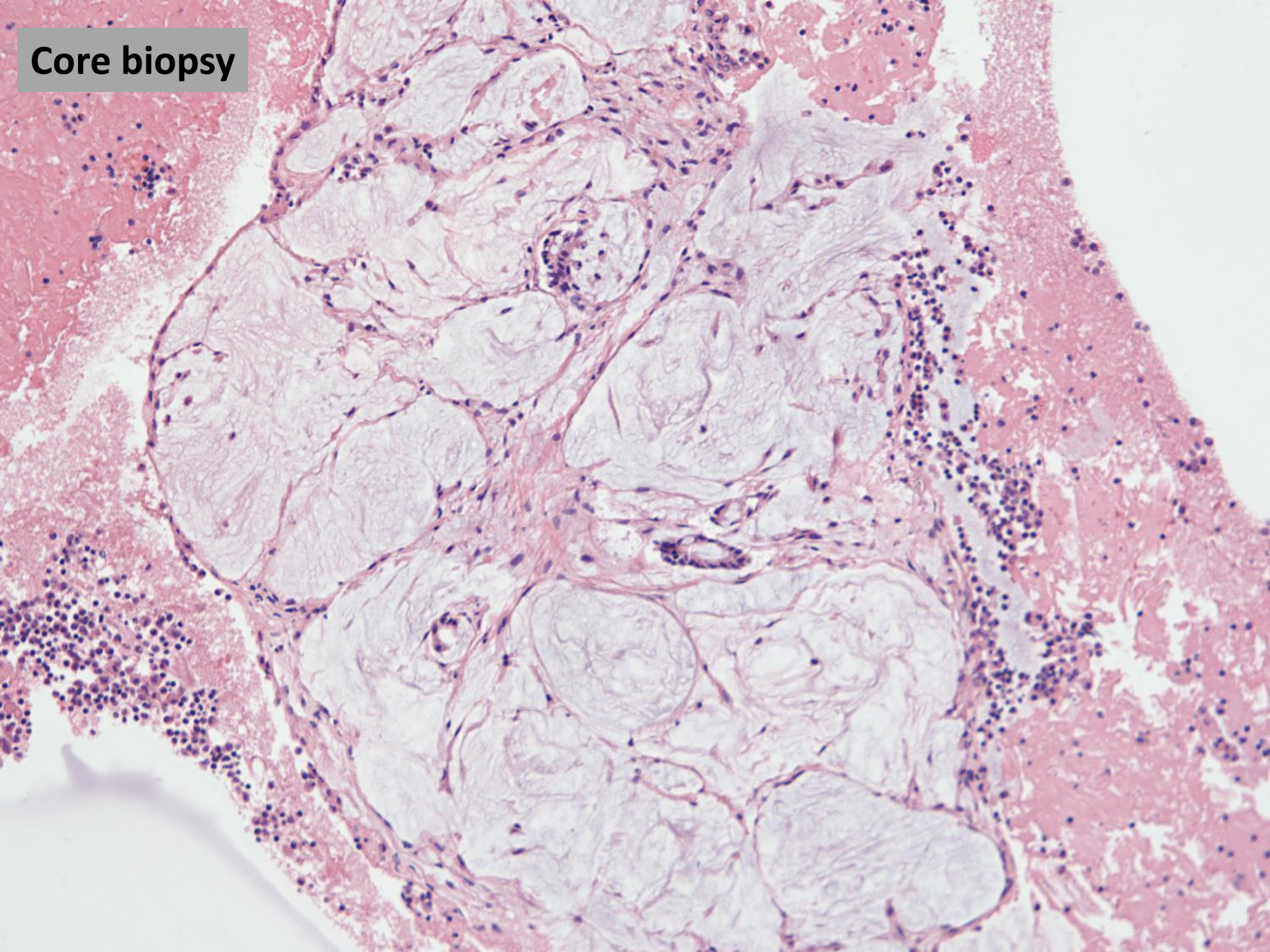
SB 6326

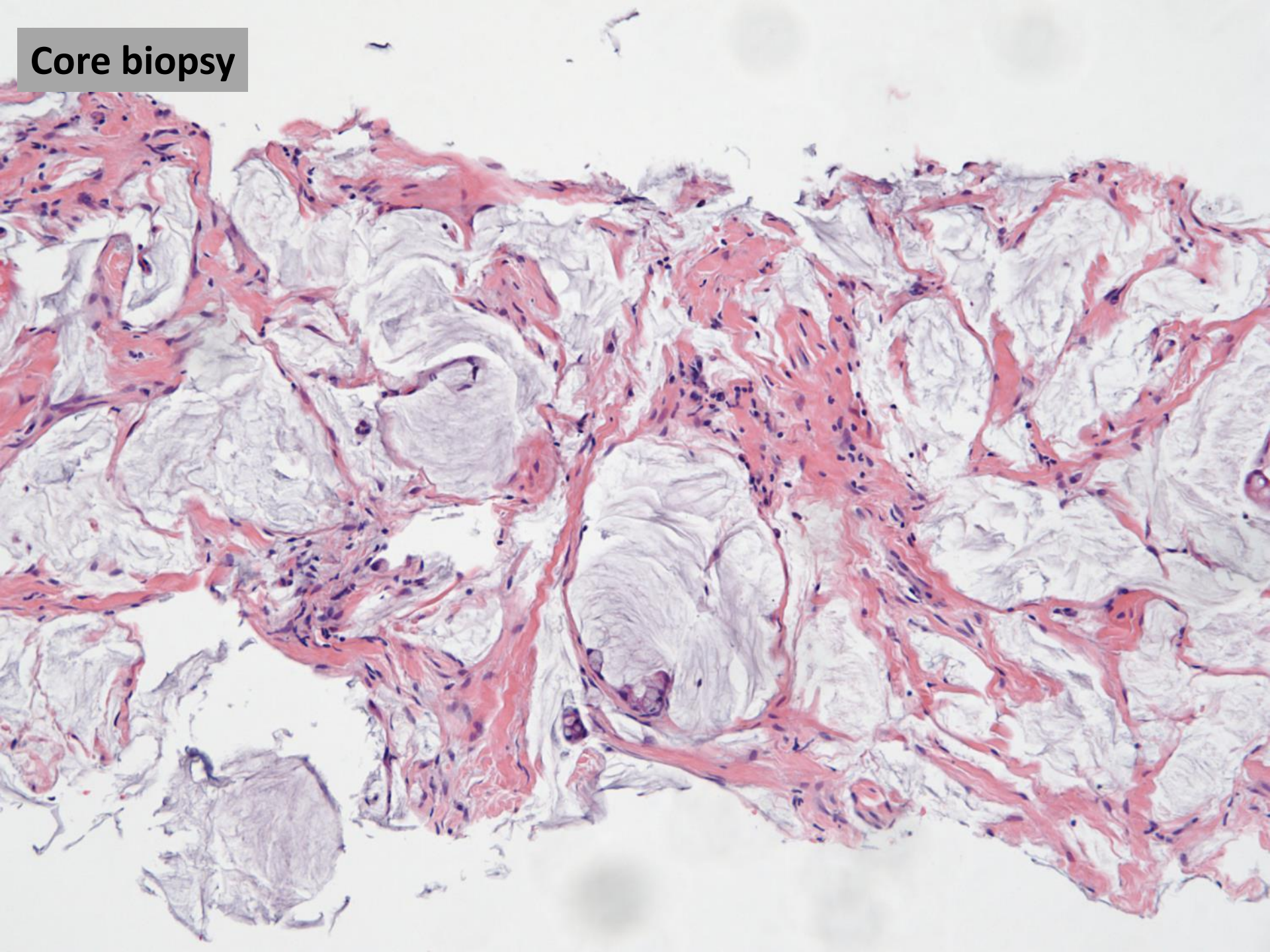
Erna Forgo/Christine Louie; Palo Alto VA

63-year-old male with h/o abdominal surgery 20 years ago for carcinoid tumor, now presenting with abdominal pain, nausea, and vomiting. Ascites fluid and core biopsy of abdominal mass submitted.


Ascites fluid


Ascites fluid


Core biopsy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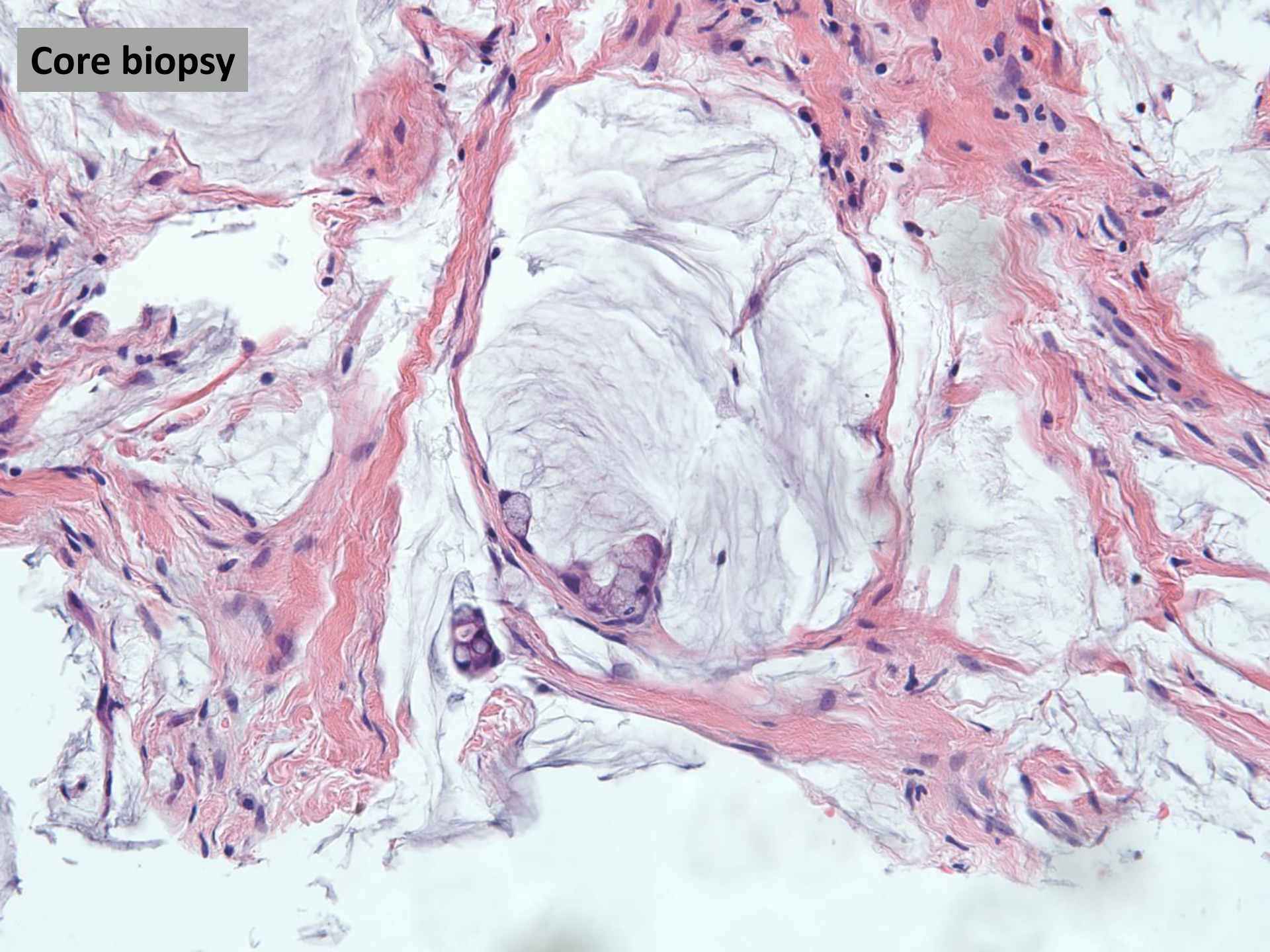
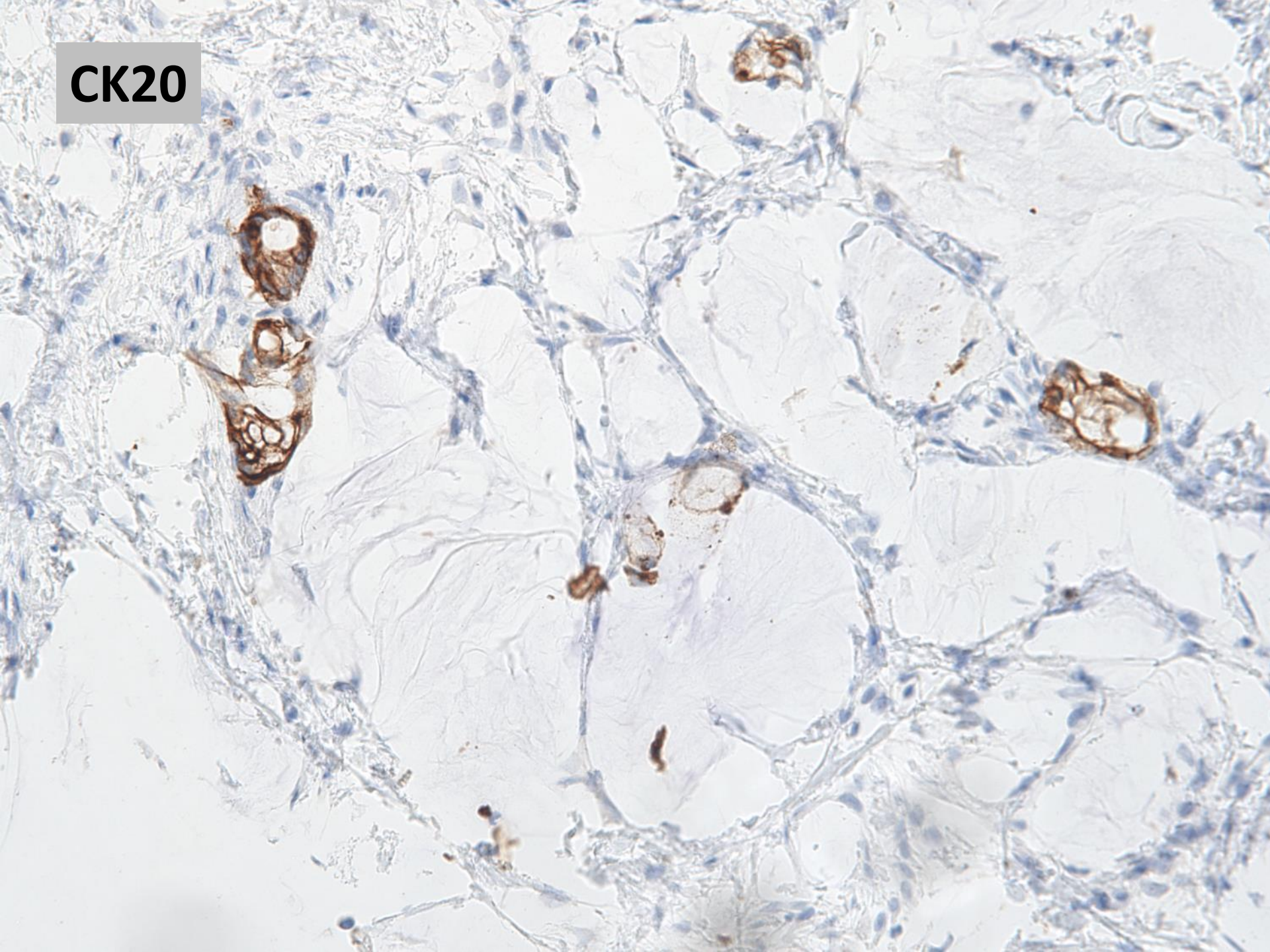

Core biopsy

DIAGNOSIS?


CK20

Additional Immunostains

CDX2 – positive

CD56 – negative

MLH1, MSH2, MSH6, PMS2 – intact expression

Differential Diagnosis

- Low-grade appendiceal mucinous neoplasm
- Metastatic goblet cell carcinoid (due to history)
- Goblet cell adenocarcinoma
- Metastatic mucinous carcinoma of stomach
- Metastatic mucinous carcinoma of colon

Prior Appendectomy in 1998

- By report, a goblet cell carcinoid "infiltrating through the submucosa and muscularis" of the appendix was present

Chin Med J (Engl). 2014;127(3):591-2.

Late recurrence and metastasis of an appendiceal goblet cell carcinoid 24 years after appendectomy.

Tang M[1], Ai B[1], Ding L[1], Du J[2], Cheng G[1], Zhang Y[3].

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2 Department of Pathology, Beijing Hospital of the Ministry of Health, Beijing 100730, China.
3 Department of Oncology, Beijing Hospital of the Ministry of Health, Beijing 100730, China. Email: zhyq95@163.com.

PMID: 24451973

Diagnosis

Ascitic fluid, ultrasound-guided paracentesis

-- **Involved by mucinous neoplasm**

Left upper quadrant abdominal mass, image-guided core biopsy

-- **Mucinous neoplasm, most consistent with recurrent/metastatic goblet cell carcinoid**

Goblet Cell Carcinoid (GCC)

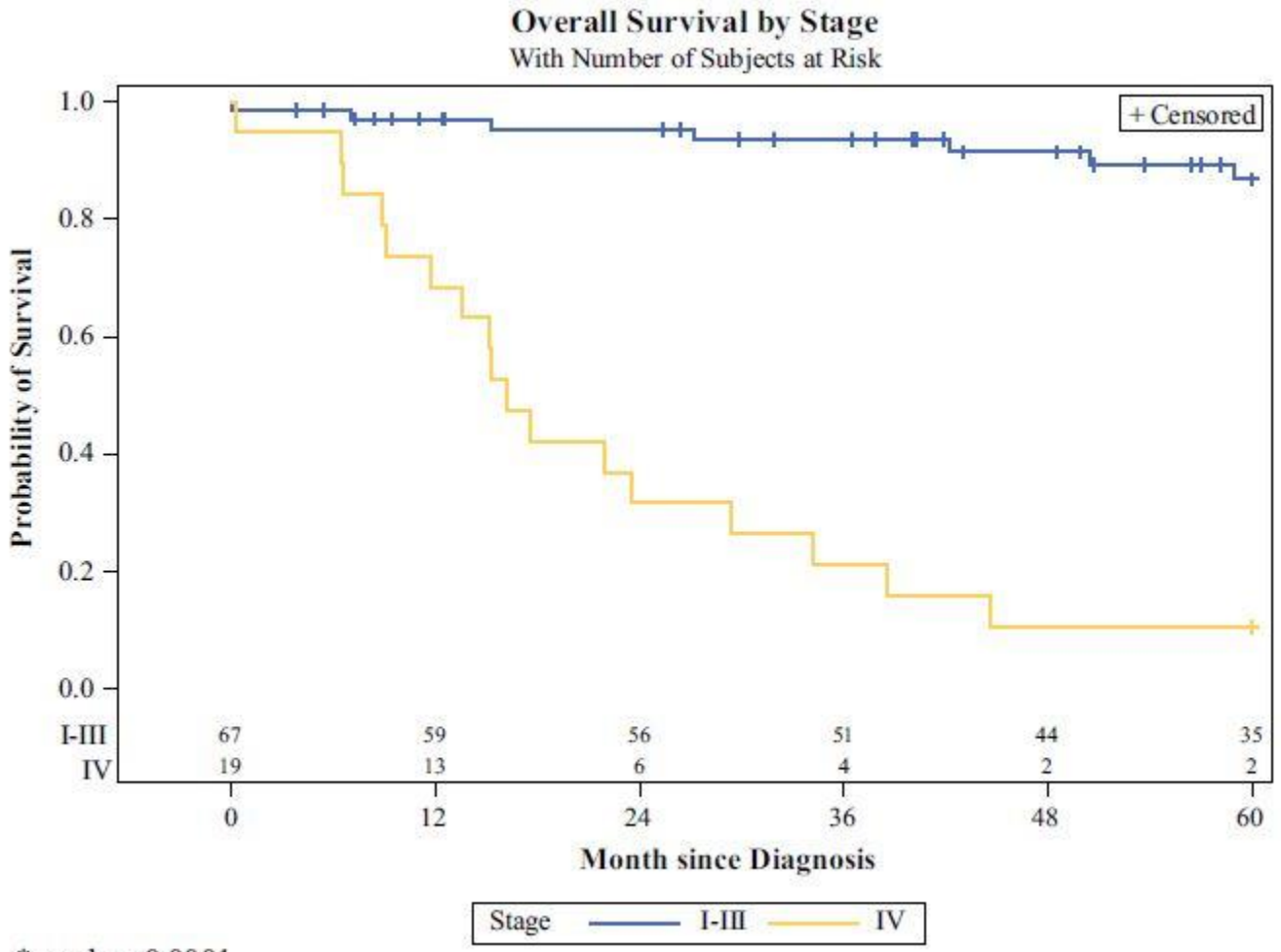
- Proliferation of mucin-producing cells with features of both neuroendocrine and glandular differentiation

- Goblet cell adenocarcinoma (~~AdGCC~~):
  - Aggressive tumor in which unequivocal adenocarcinoma is found in conjunction with (and presumably arising from) goblet cell carcinoid

Am J Surg Pathol. 2018 Jul;42(7):898-910

Clinical Concerns

- GCC more aggressive than conventional NET (carcinoid)
- Goblet cell adenocarcinoma behaves like conventional adenocarcinoma
- Some suggest regional resection even for localized tumors
- Presentation: acute appendicitis, perforation



Ann Surg Oncol. 2018 Aug;25(8):2391-2399

Prognostic Implication of Perforation in Classical Appendiceal Carcinoid/NET

TABLE 1 Studies mentioning perforation associated with classical carcinoid of Appendix

Carcinoids	*N* total	Study design	Single/ multicenter	*N* perforations (%)	Mean follow-up (months)	Overall survival (%)	DOD	Survival in perforated appendix (%)	DOD in perforated appendix
Barreto et al.[24]	8	Retrospective	Single	2 (25)	NA	NA	NA	NA	NA
Boxberger et al.[15]	238	Prospective	Multi	54 (25)	35	100	0	100	0
Bucher et al.[18]	39	Retrospective	Single	8 (21)	67	95	1	NA	NA
Corpron et al.[19]	22	Retrospective	Single	2 (9)	120	95	0	NA	NA
Dall'Igna et al.[21]	14	Retrospective	Multi	2 (14)	75	100	0	100	0
Doede et al.[25]	8	Retrospective	Single	1 (13)	80	100	0	100	0
Gouzi et al.[16a]	181	Retrospective	Multi	18 (10)	60[b]	94	2	NA	NA
Hatzipantelis et al.[22]	19	Retrospective	Single	1 (5)	45	100	0	100	0
Kulkarni and Sergi[27]	7	Retrospective	Single	1 (14)	53	100	0	100	0
Mathur et al.[17]	1	–	–	1	6	100	0	100	0
Oeconomopoulos[28]	3	Retrospective	Single	2 (67)	NA	NA	NA	NA	NA
Parkes et al.[20]	40	Retrospective	Multi	5 (8)	18[b]	97	0	NA	NA
Pelizzo et al.[26]	10	Retrospective	Single	2 (20)	36	100	0	100	0
Prommegger et al.[23]	36	Retrospective	Multi	2 (6)	120	100	0	100	0
Stuhldreier et al.[30]	1	–	–	1	2	100	0	100	0
Volpe et al.[29]	1	–	–	1	6	100	0	100	0
Total	628			103			3		0
Mean				16 %	50	98.7 %		100 %	

DOD death due to disease, *NA* not applicable

[a] Perforation in goblet cell not seperately described (seven cases), survival given for classical carcinoids

[b] Median

Ann Surg Oncol. 2015 Mar;22(3):959-65

Prognostic Implication of Perforation in GCC

TABLE 2 Studies mentioning perforation associated with goblet cell carcinoid of Appendix

Goblet cell carcinoids	*N* total	Study design	Single/ multicenter	*N* perforations (%)	Mean follow-up (months)	Overall survival (%)	DOD	Survival in perforated appendix (%)	DOD in perforated appendix
Butler et al.[35]	9	Retrospective	Multi	NA	30	56	4	NA	NA
Gordon et al.[37]	1	–	–	1	NA	NA	NA	NA	NA
Kanthan et al.[32]	7	Retrospective	Single	3 (43)	62	57	3	33	1
Klein[36]	3	Retrospective	Single	2 (67)	33	100	0	100	0
Lee et al.[34]	27	Retrospective	Multi	2 (7)	NA	71	8	NA	NA
Stancu et al.[31]	16	Retrospective	Single	7 (70)[a]	24	88	2	100	0[b]
Toumpanakis et al.[33]	15	Retrospective	Single	3 (20)	30	80	3	67	1
Total	78			18			16		2
Mean				20 %	37	75 %		75 %	

DOD death due to disease, *NA* not applicable

[a] In six patients, no data regarding clinical presentation was available

[b] Five were lost to follow-up

Ann Surg Oncol. 2015 Mar;22(3):959-65

New terminology → ~~AdGCC~~

- Goblet cell carcinoid tumor range from indolent to highly aggressive, depending on tumor grade
- Current grading systems for these tumors are based on identifying an adenocarcinoma arising in the setting of a goblet cell carcinoid tumor, which distinguishes this tumor from other GI tract adenocarcinomas
- Proposal: classification as goblet cell adenocarcinomas and graded similar to colorectal adenocarcinoma grading

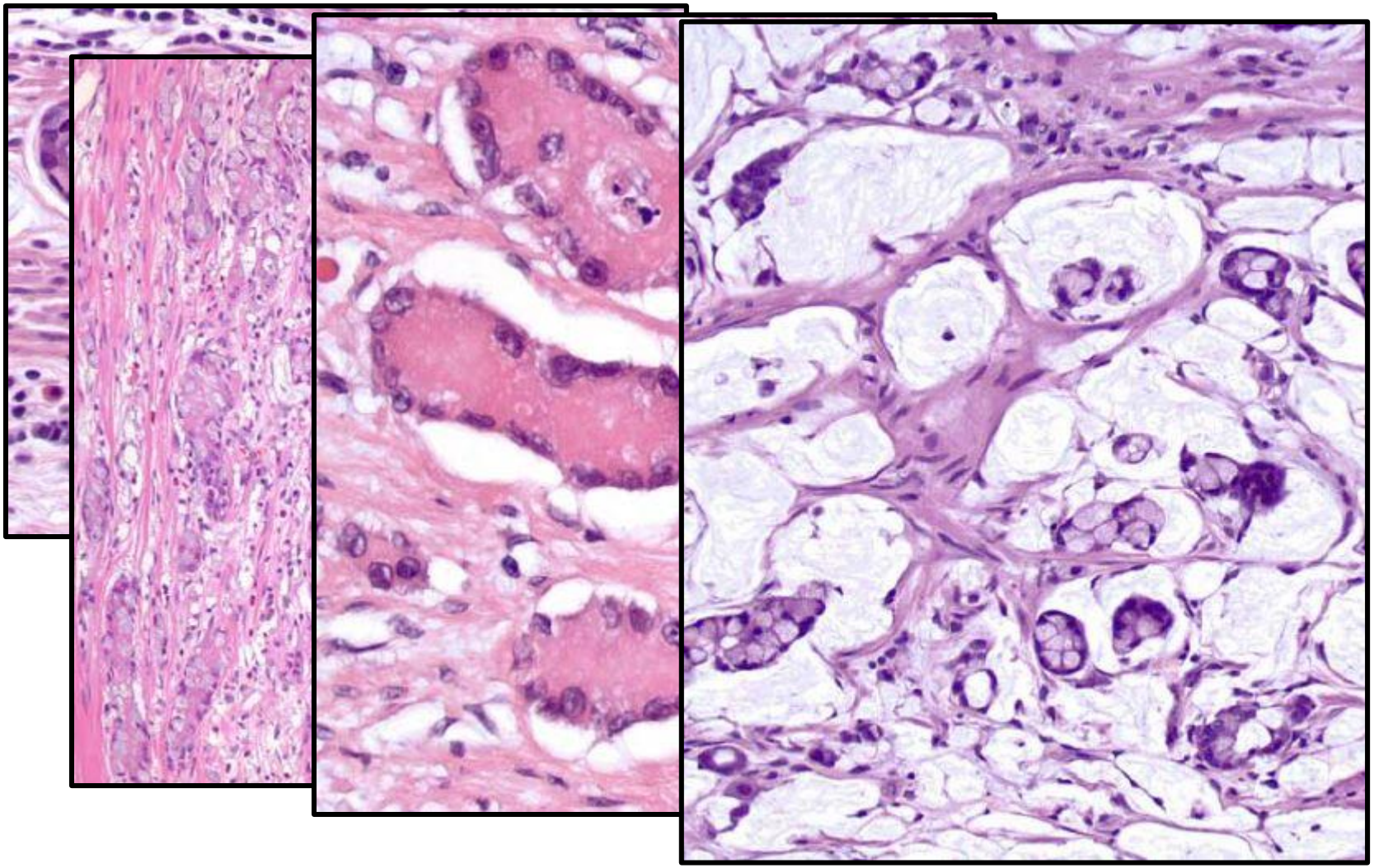
Am J Surg Pathol. 2018 Jul;42(7):898-910

Low-grade Histologic Feature	Common High-grade Histologic Features
Tubular growth with round to oval discrete tumor clusters comprising a mixture of goblet cells, cuboidal cells, and Paneth-like cells, with or without lumens	Single cells, including nonmucinous single cells and signet ring-like cells, often admixed with abortive tubules
Simple trabecular growth consistent with tubules sectioned longitudinally	Single file growth or sheets of tumor cells, often admixed with abortive tubules
Limited tubule fusion or crowding	Fusion of goblet cell clusters to form anastomosing complex growth of goblet cell clusters or tubules
Mucin pools with discrete tubules or clusters, including ectatic tubules	Very large aggregates of goblet cells or drifts of goblet cells in extracellular mucin
Tubular nonmucinous glands including oncocytic tubules	Mucin-poor tumor cells in nests or clusters with high N:C ratio and jagged outlines Glands lined by cuboidal or columnar cells with high cytologic grade that resemble conventional adenocarcinoma Glands floating in mucin lined by columnar cells with high cytologic grade

Grade 1 (low-grade) tumors consist of <75% low-grade features and < 25% high-grade features. Grade 2 (intermediate-grade) tumors consist of 50% to 75% low-grade features, with the balance being any combination of high-grade features. Grade 3 (high-grade) tumors have < 50% low-grade components, with the balance being any combination of high-grade features.

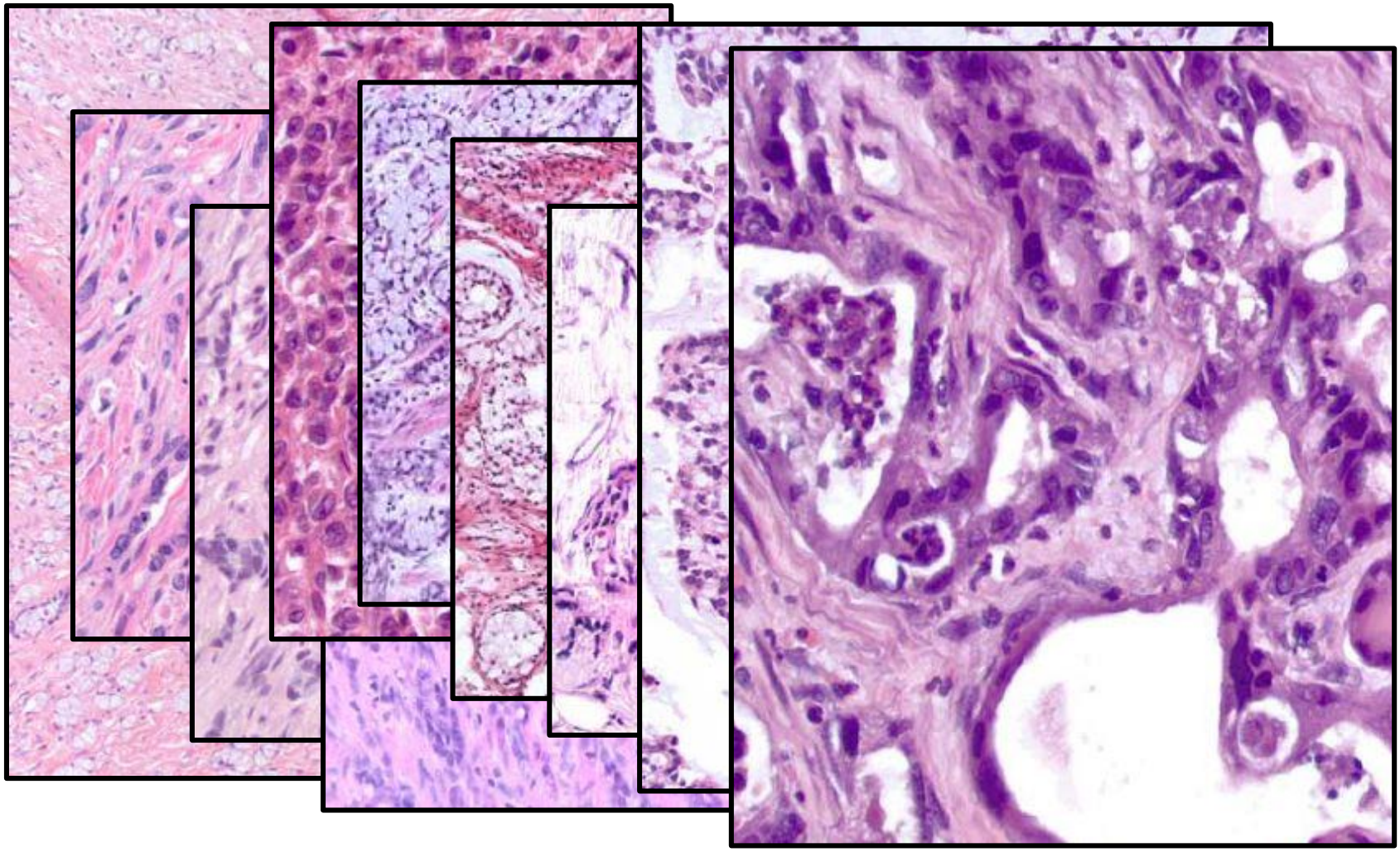
Am J Surg Pathol. 2018 Jul;42(7):898-910

Low-grade goblet cell adenocarcinoma



Am J Surg Pathol. 2018 Jul;42(7):898-910

High-grade goblet cell adenocarcinoma



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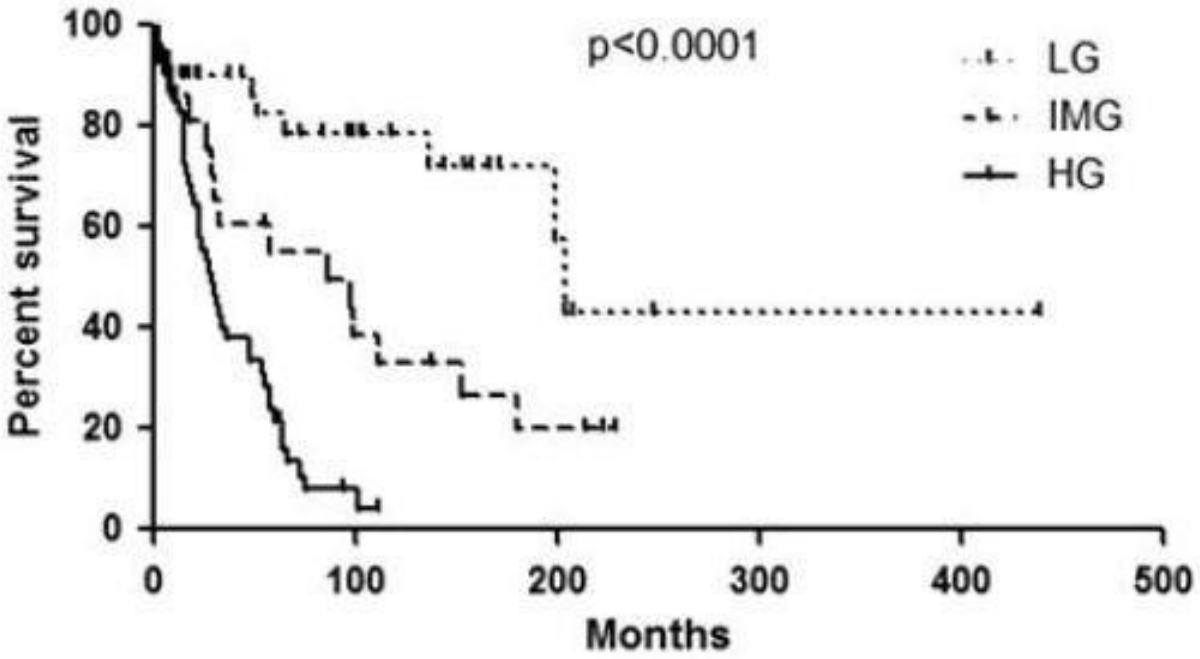
Histologic grade correlates with OS



	Median survival (month)	5 year survival (%)	10 year survival (%)
LG (n=42)	204	82	78
IMG (n=22)	86	55	33
HG (n=56)	29	22	4

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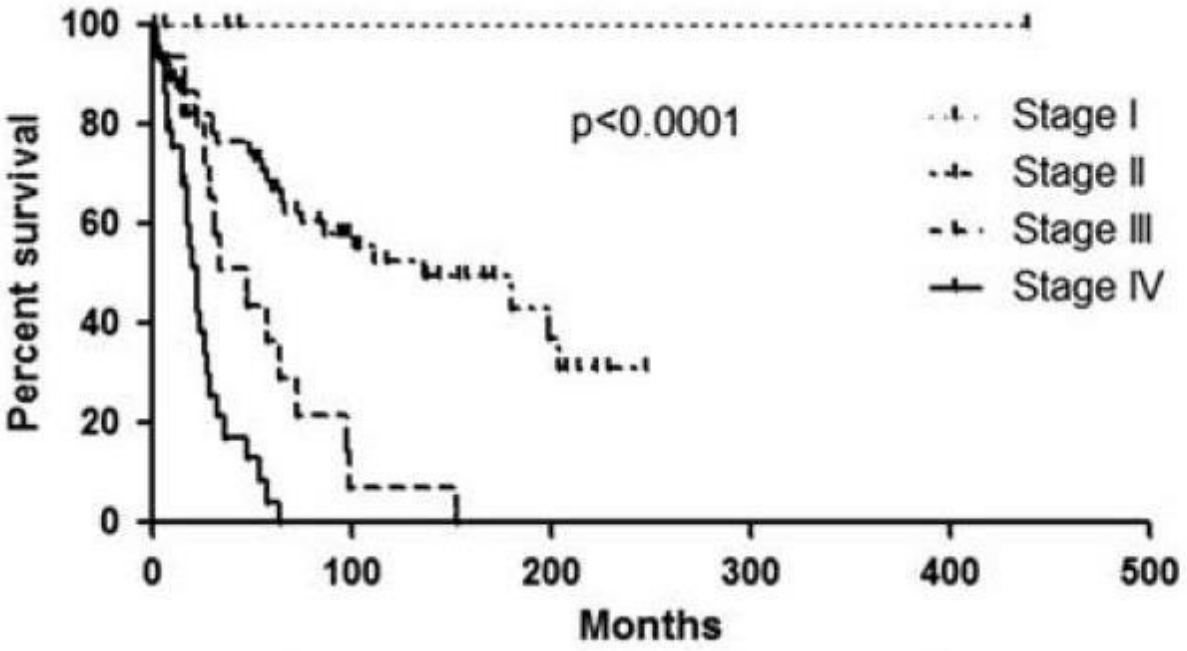
Tumor stage correlates with OS



	Median survival (month)	5 year survival (%)	10 year survival (%)
Stage I (n=5)	n/a	100	100
Stage II (n=69)	136	67	43
Stage III (n=16)	48	36	0
Stage IV (n=30)	22	4.2	0

Am J Surg Pathol. 2018 Jul;42(7):898-910

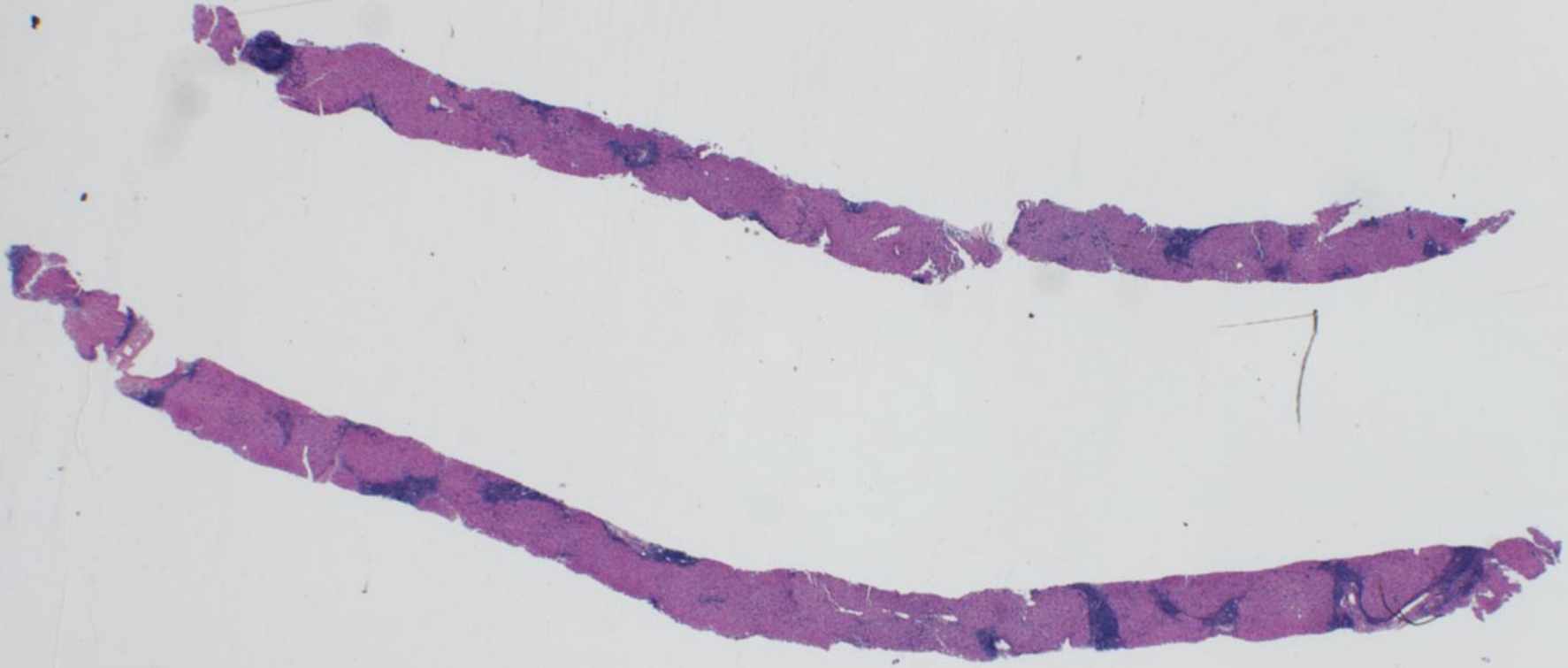
Take Home Points

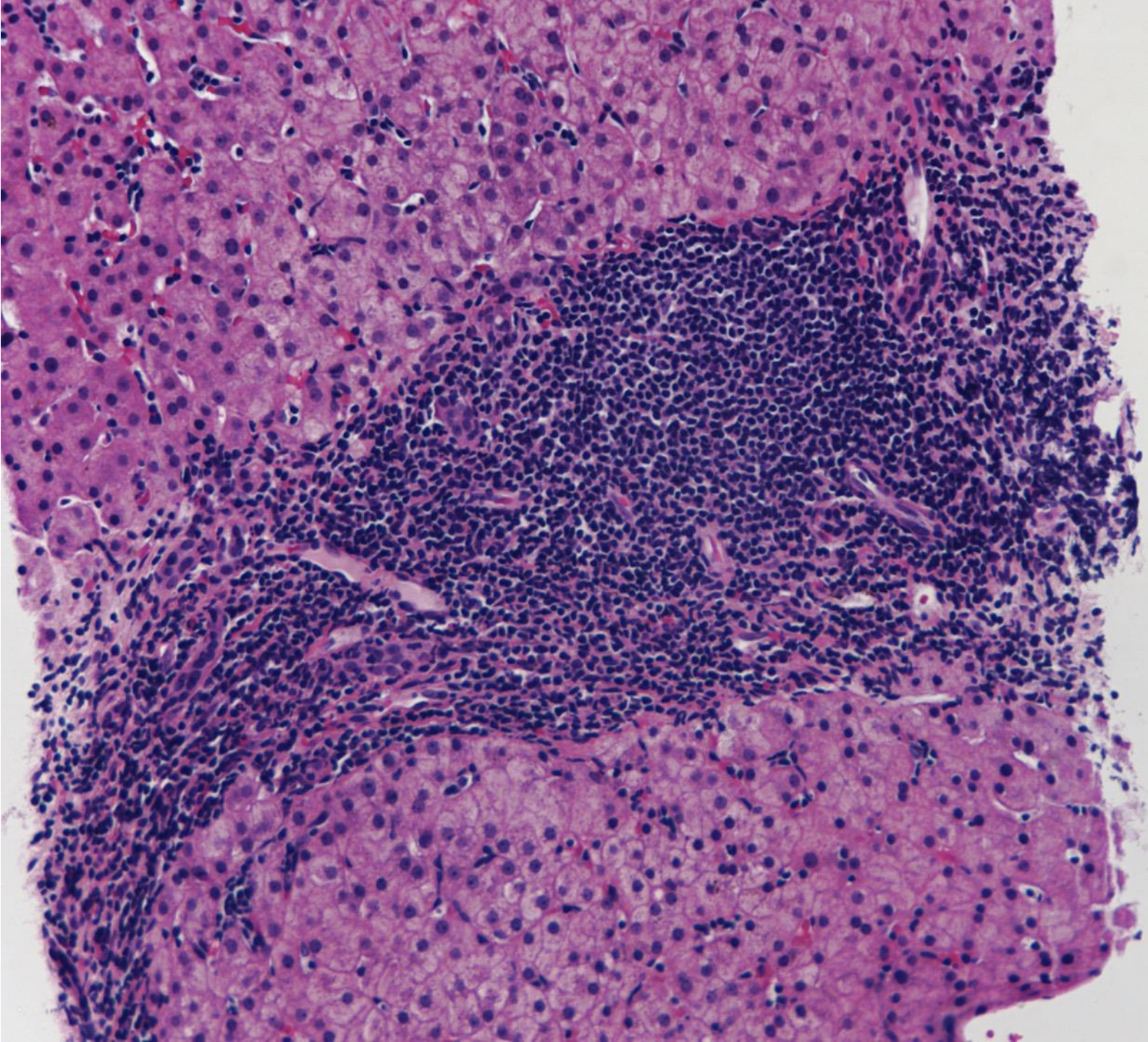
- GCC is more aggressive than conventional NET (carcinoid) with different genomic profile
- Aggressive features must be carefully sought
- GCC/Goblet cell adenocarcinoma must be considered when evaluating disseminated mucinous/signet ring carcinomas
- Careful evaluation of appendiceal margin and extent of infiltration through appendiceal wall is important for stage and prognosis
- Goblet cell adenocarcinoma (~~AdGCC~~) is the new terminology

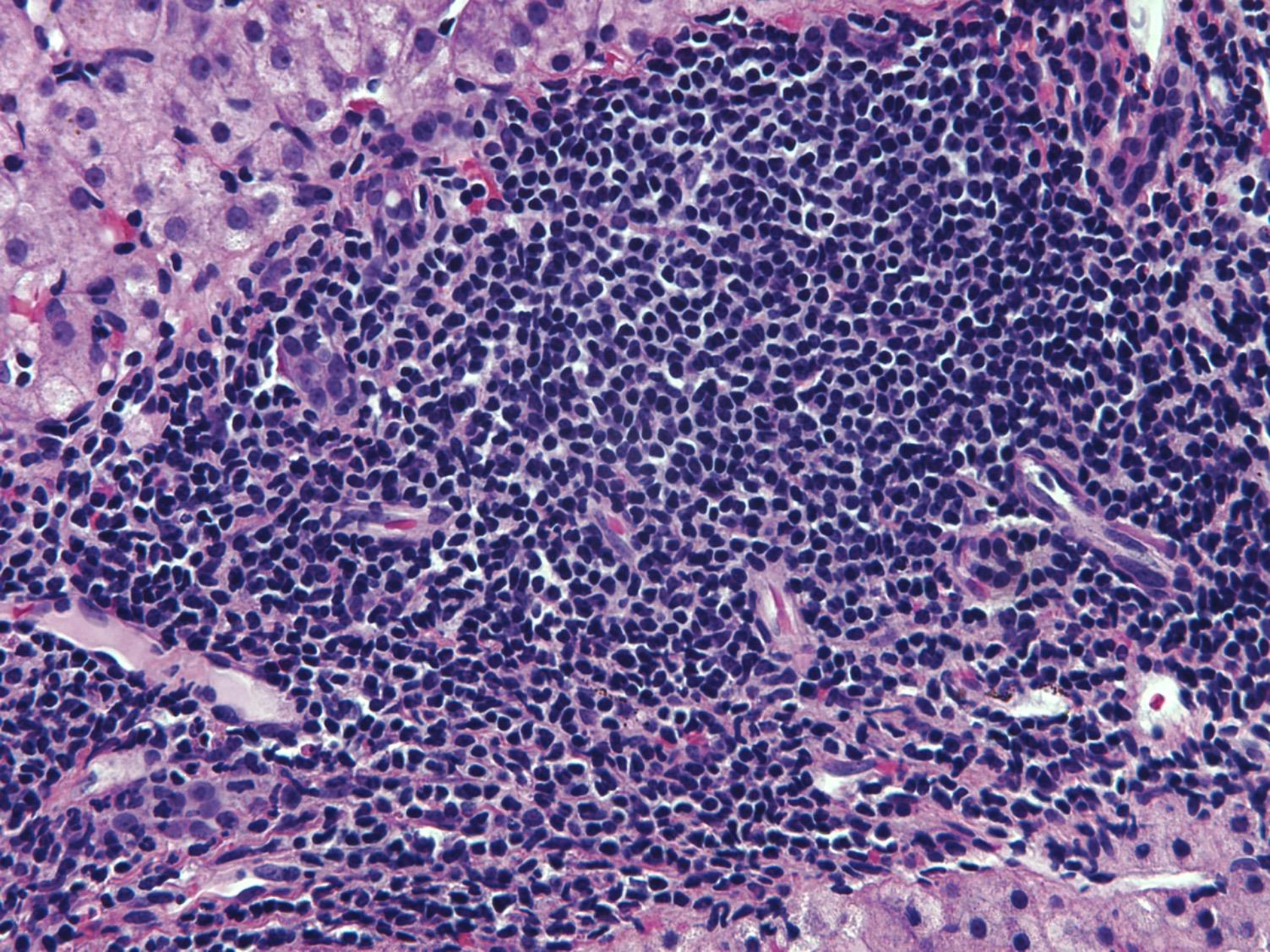
SB 6327

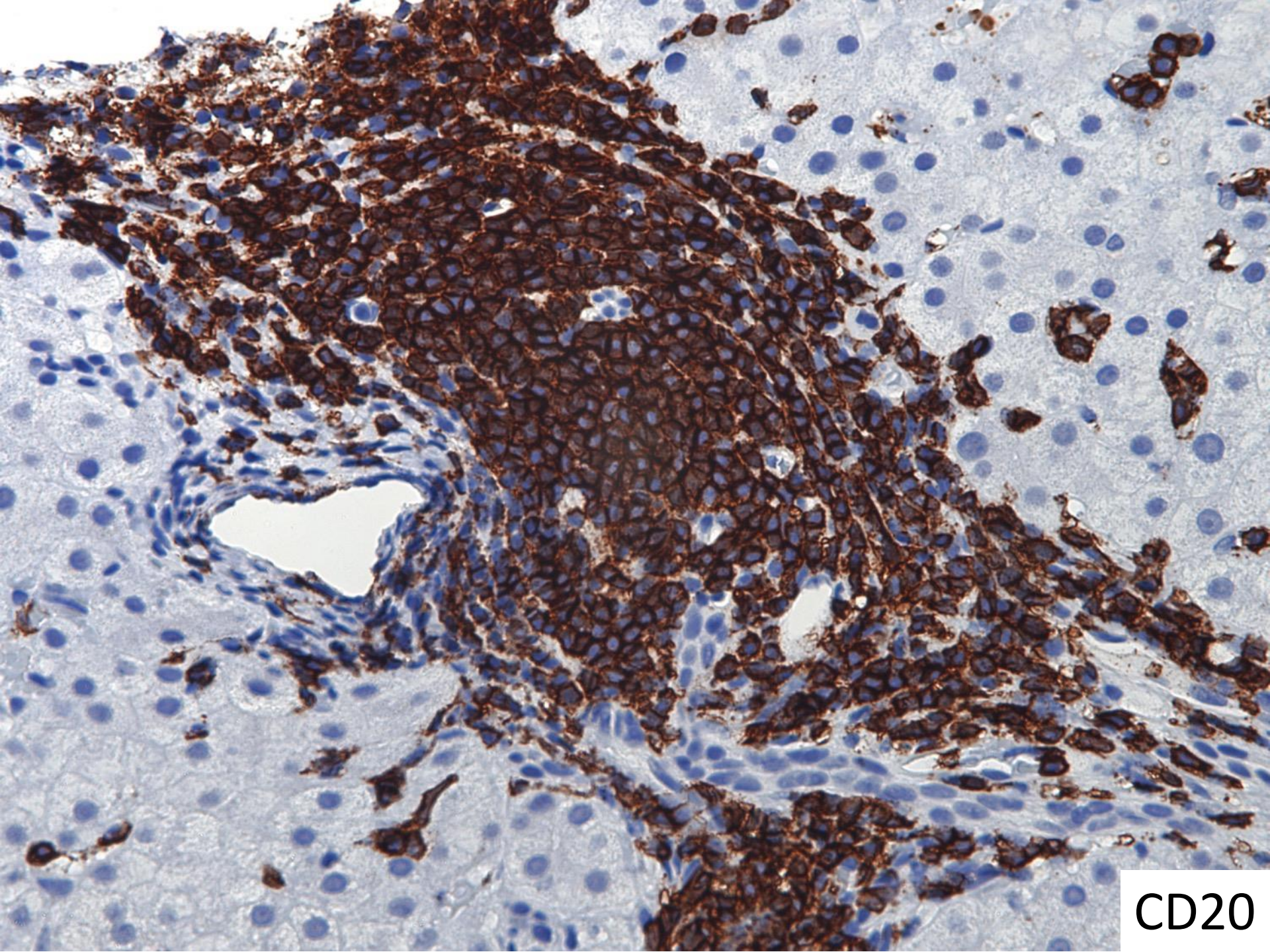
Joshua Menke/Bob Ohgami; Stanford

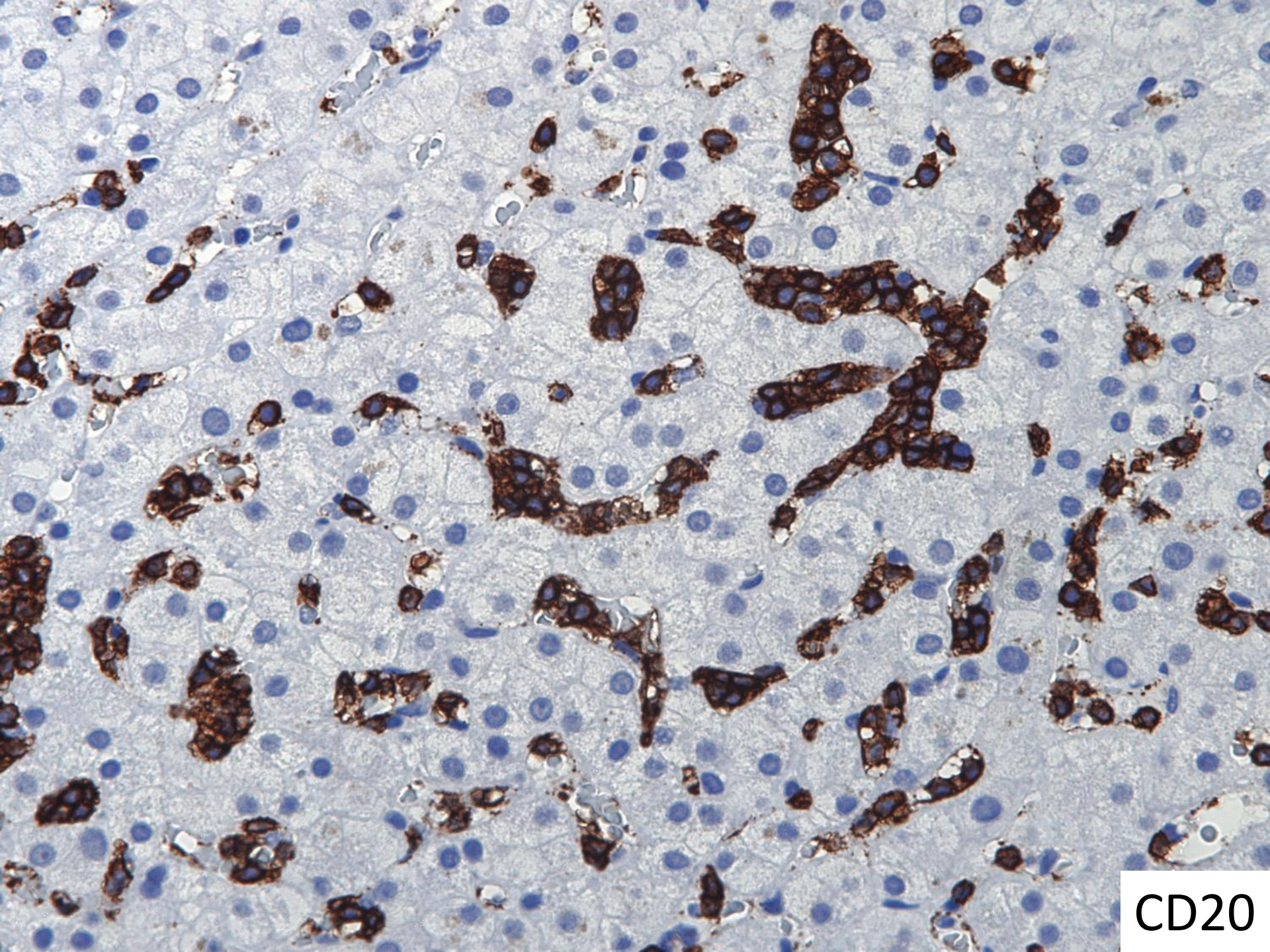
81-year-old male with h/o B-cell lymphoma involving bone marrow, who presents with liver masses. No reported lymphadenopathy.

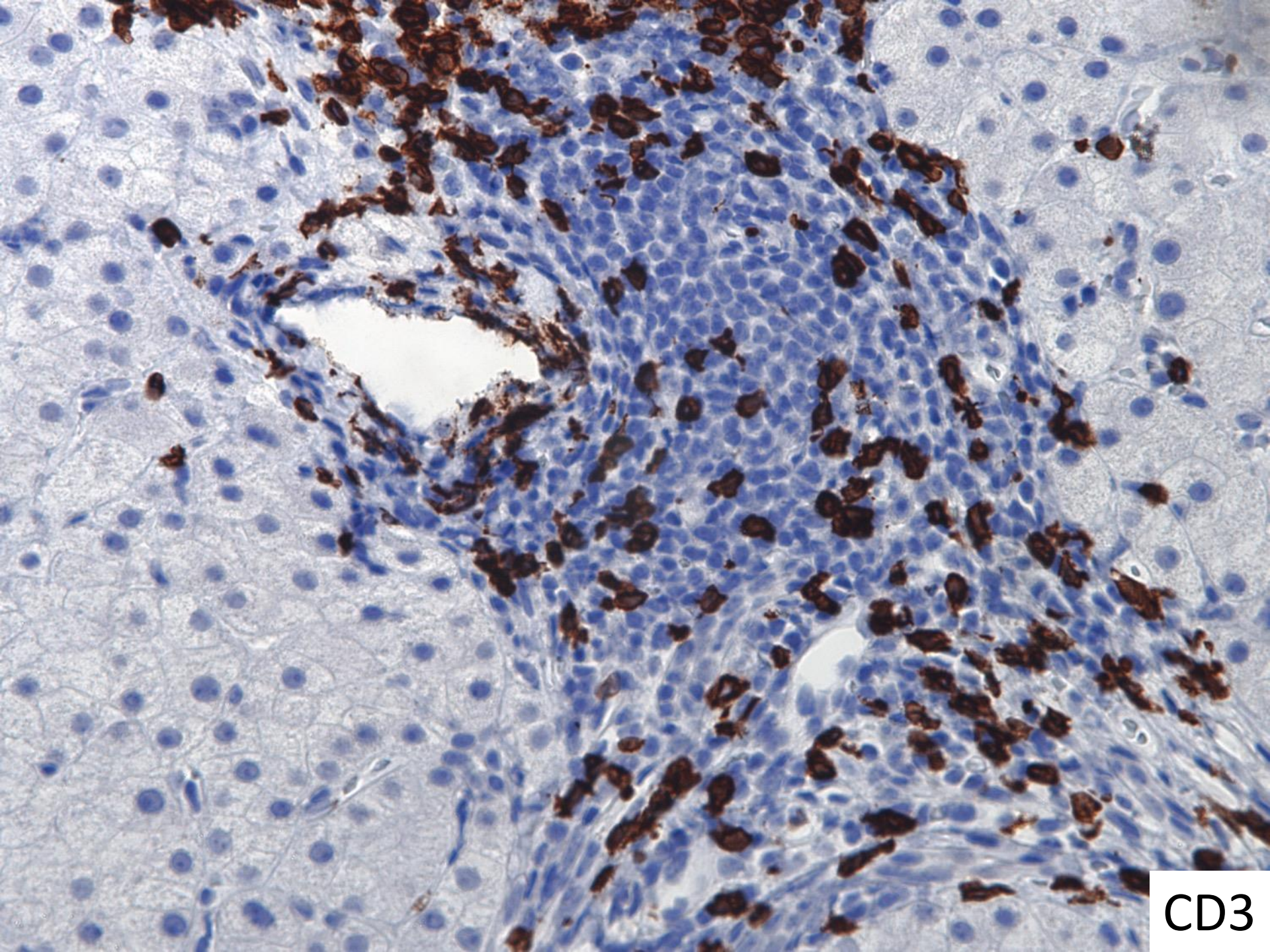


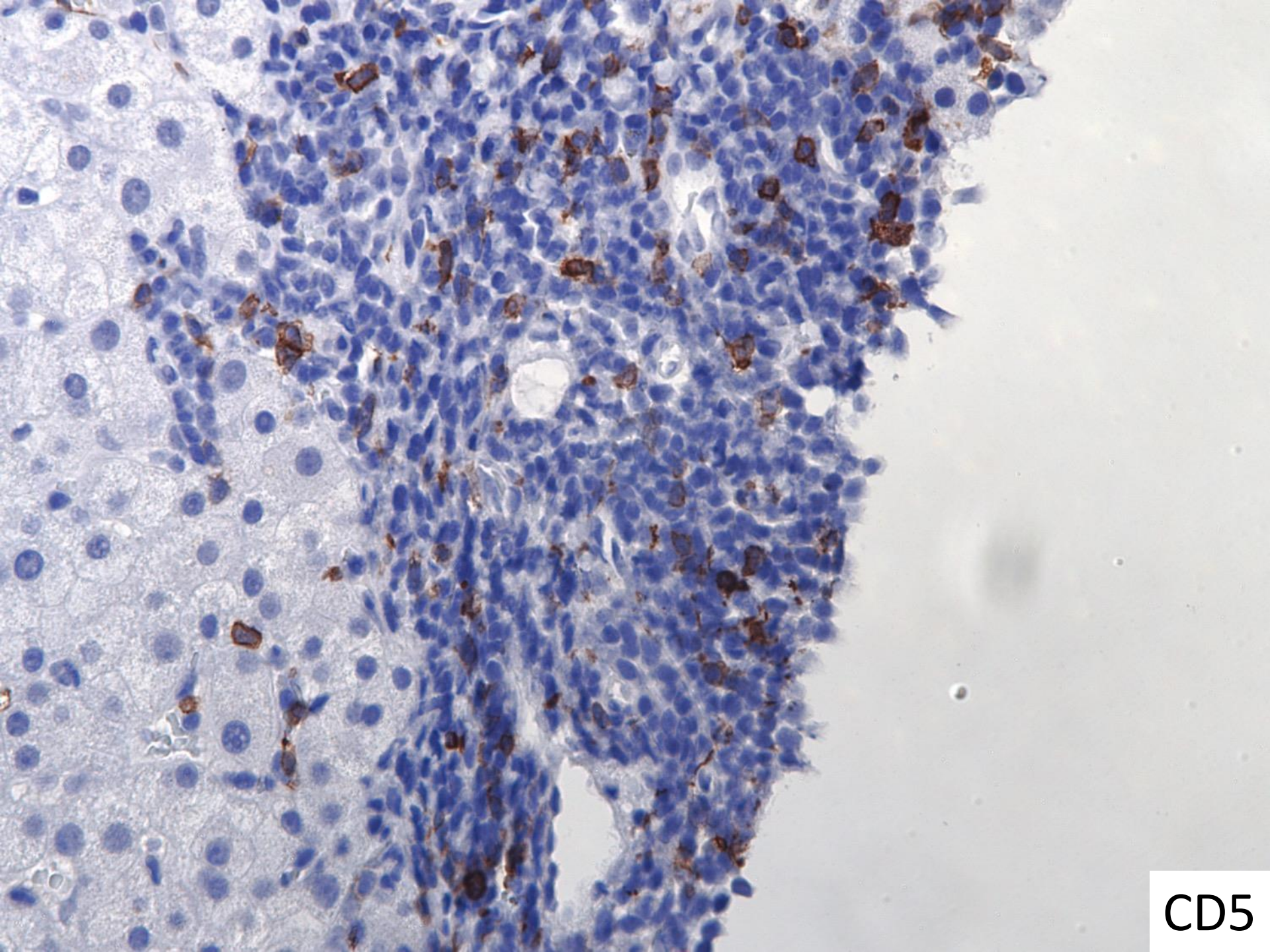





CD20


CD20


CD3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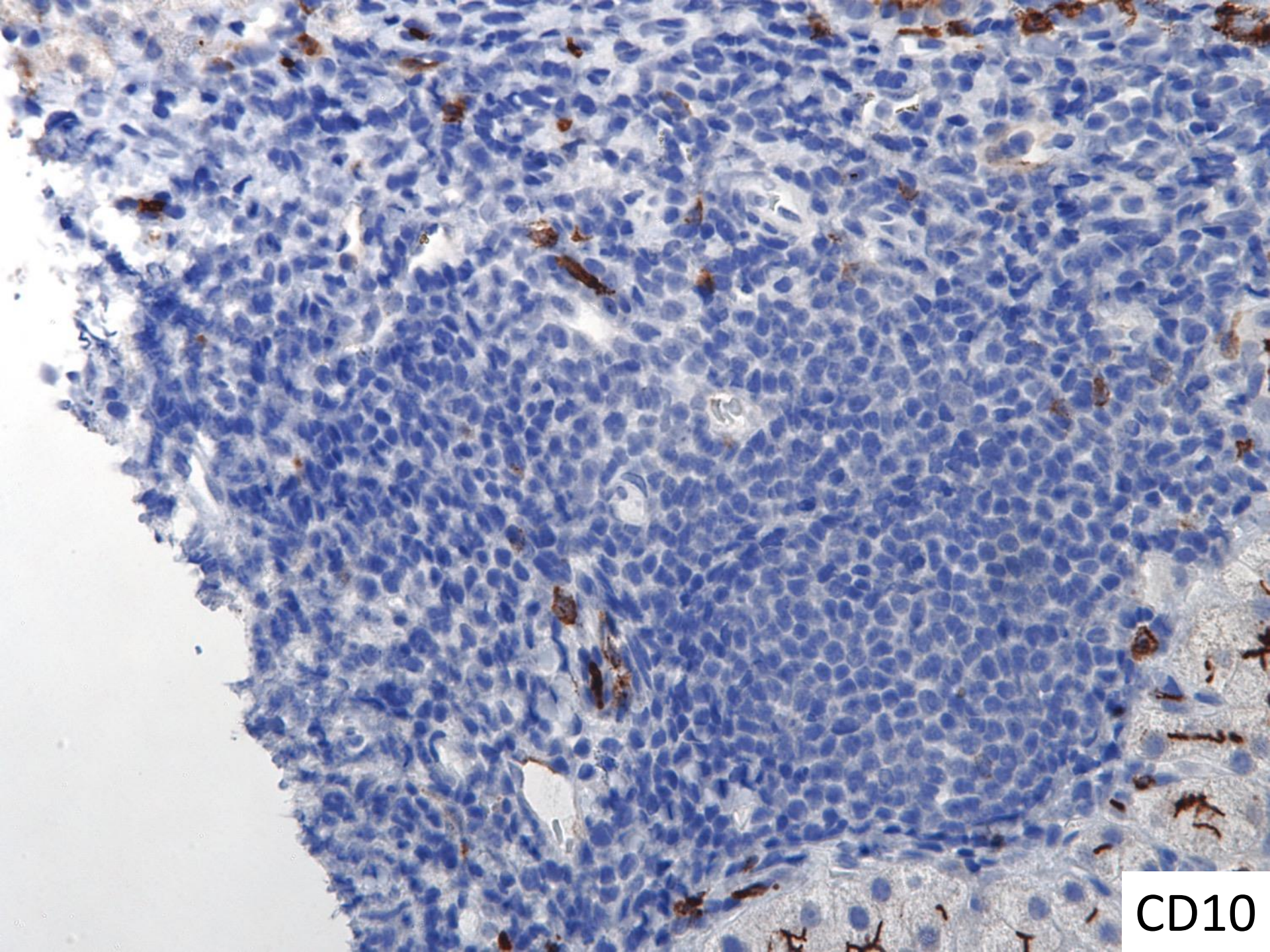
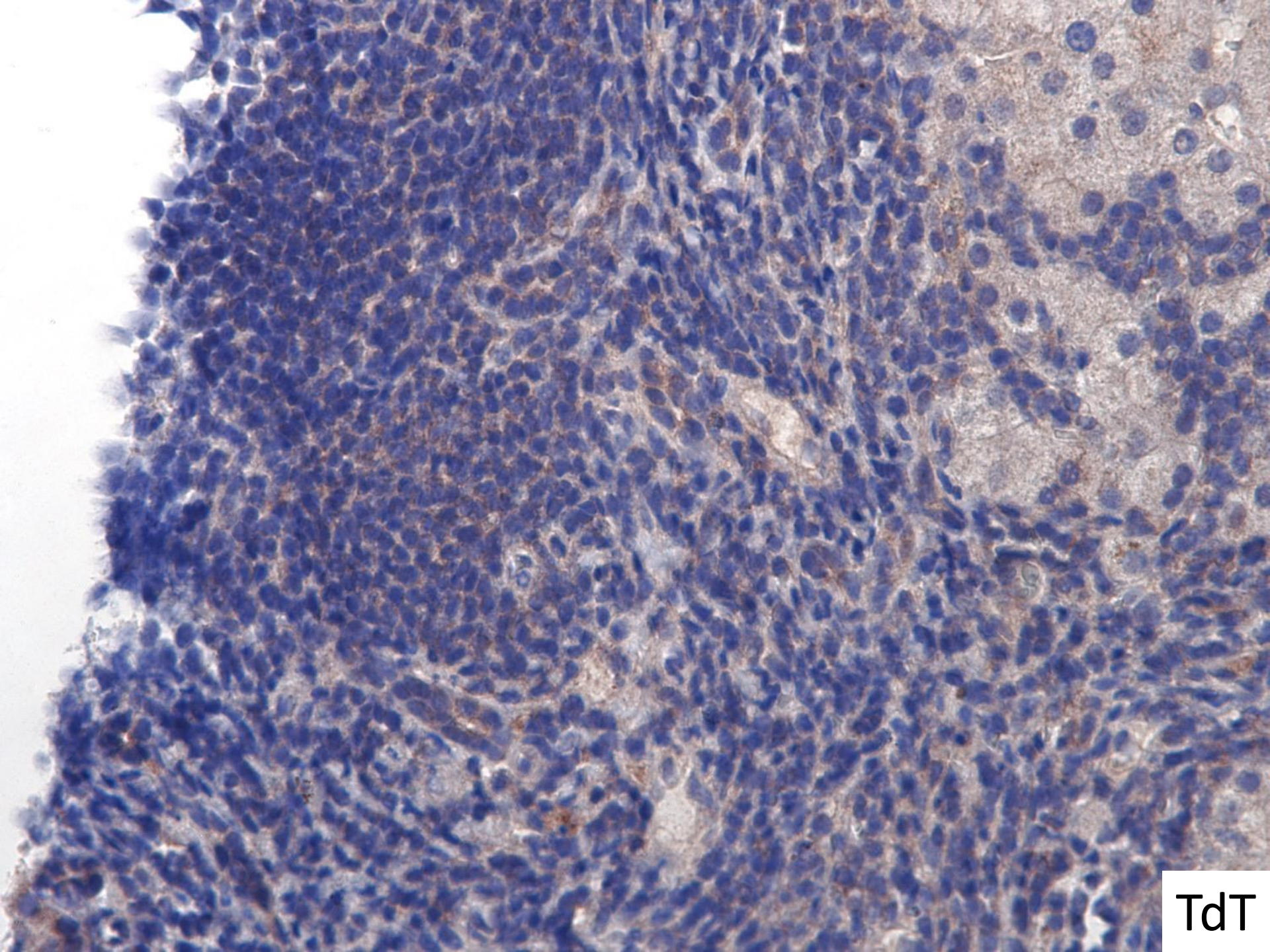
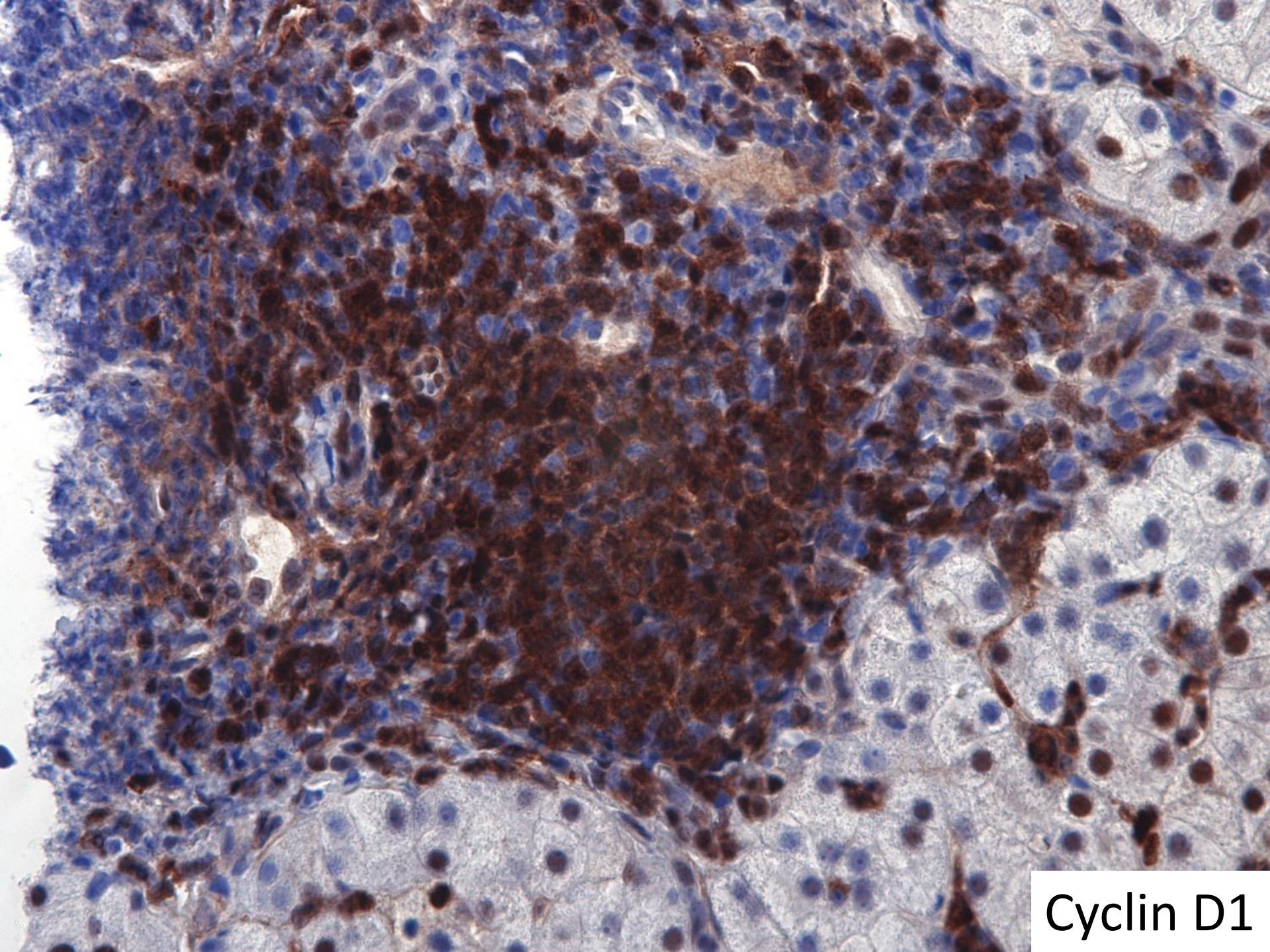
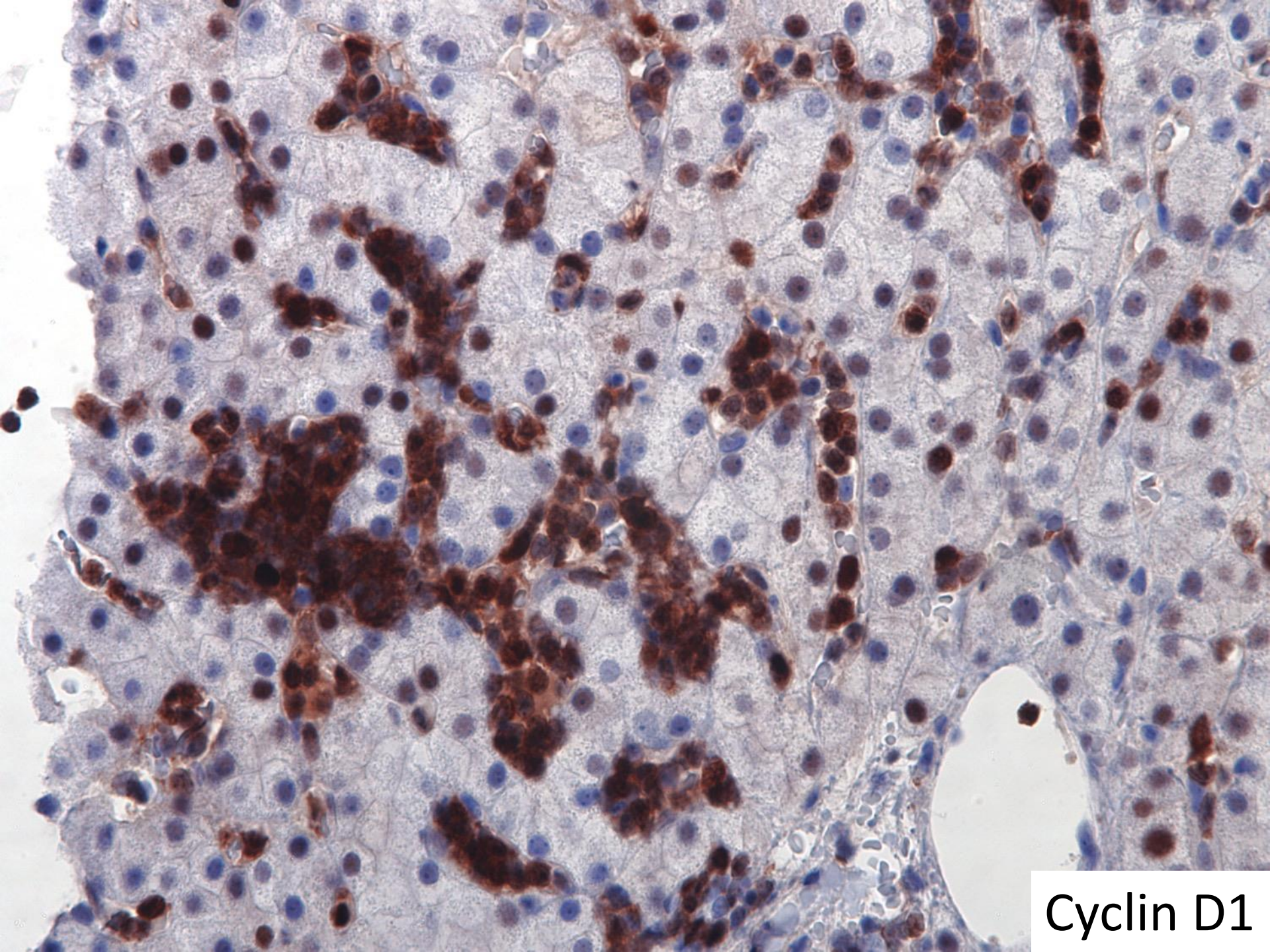

CD10


TdT


Cyclin D1


Cyclin D1

DIAGNOSIS?

South Bay Case

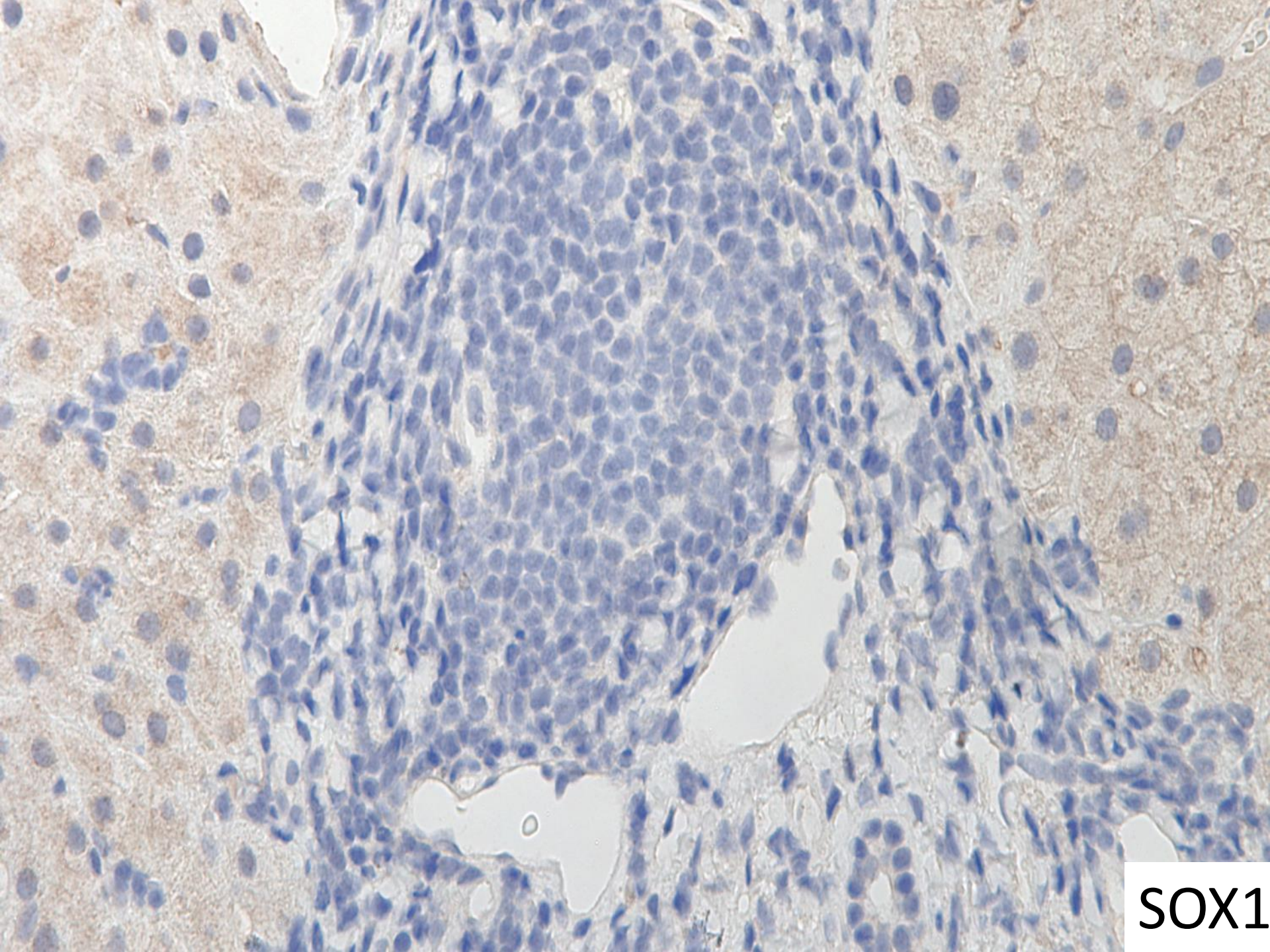
Joshua Menke

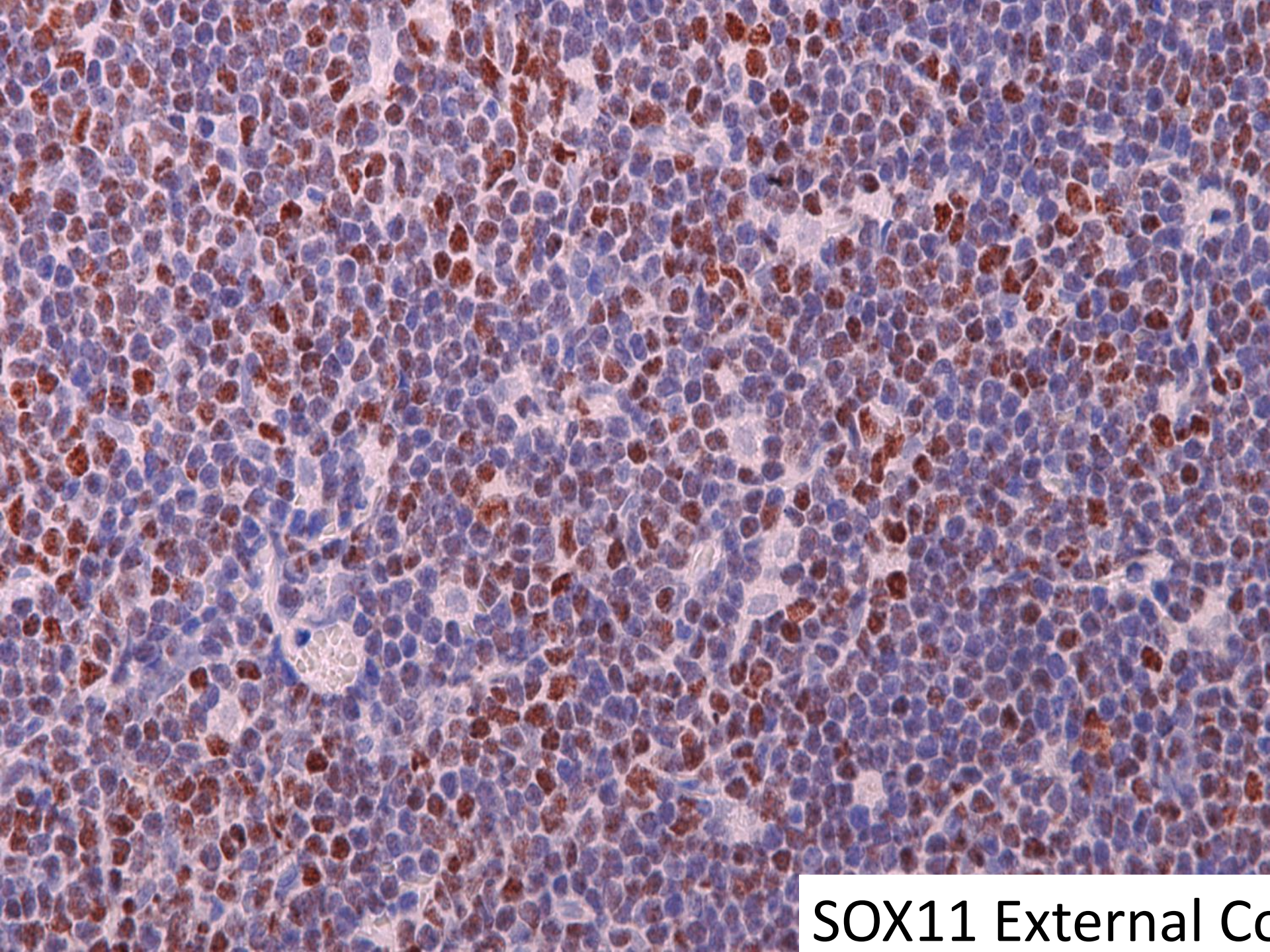
Raheem Peerani

Bob Ohgami

Differential diagnosis

- Chronic portal tract inflammation
- B-cell lymphoma
  - Mantle cell lymphoma
  - Hairy cell leukemia
  - Marginal zone lymphoma
  - Lymphoplasmacytic lymphoma
  - Chronic lymphocytic leukemia and others
- B lymphoblastic leukemia


SOX1


SOX11 External Co

Additional markers

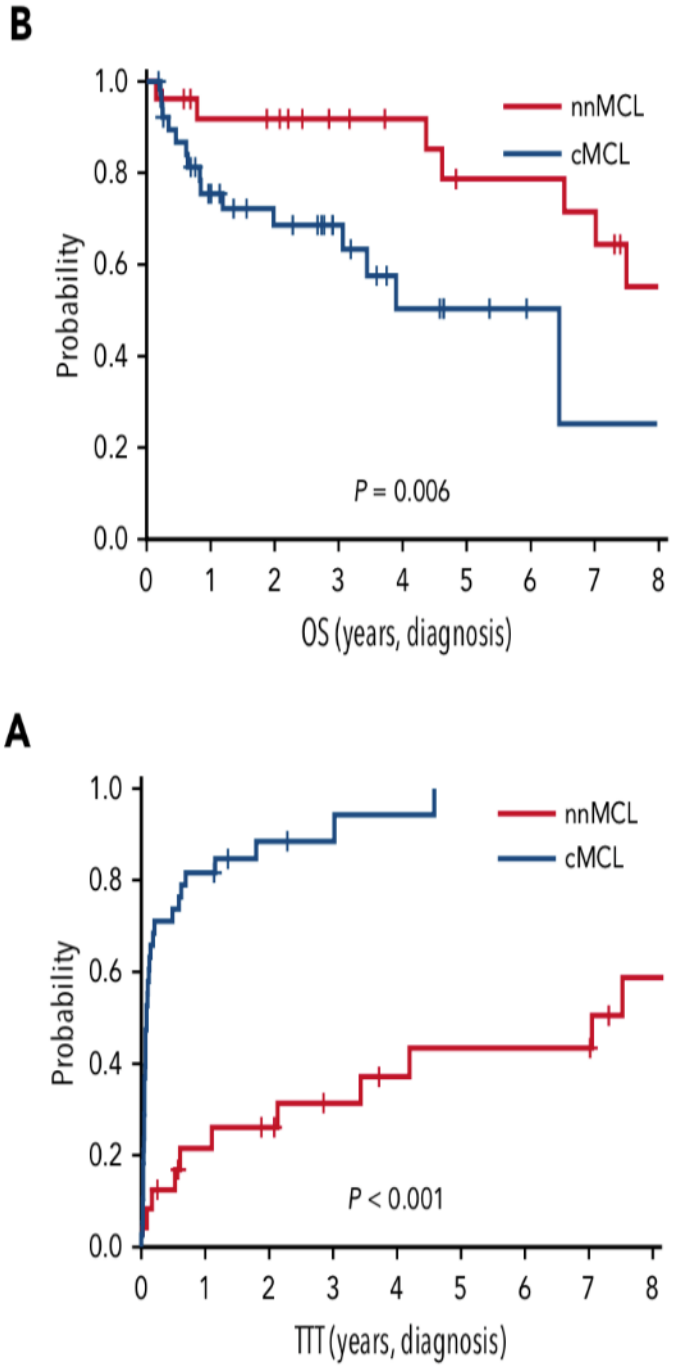
- CD123 and Annexin A1 immunostains are negative
- CD25 and CD103 negative by flow cytometry
- Ki-67 proliferation index is 5%

Additional studies

- **CCND1/IGH or t(11;14) fusion was detected** by FISH
- By report, *BRAF V600E* was negative by immunohistochemistry and *BRAF* mutation was not identified by PCR
- By report, HFE genotype was negative
- Normal sequencing study was obtained by NGS including a negative mutational study for *MYD88*

Diagnosis: Leukemic non-nodal mantle cell lymphoma

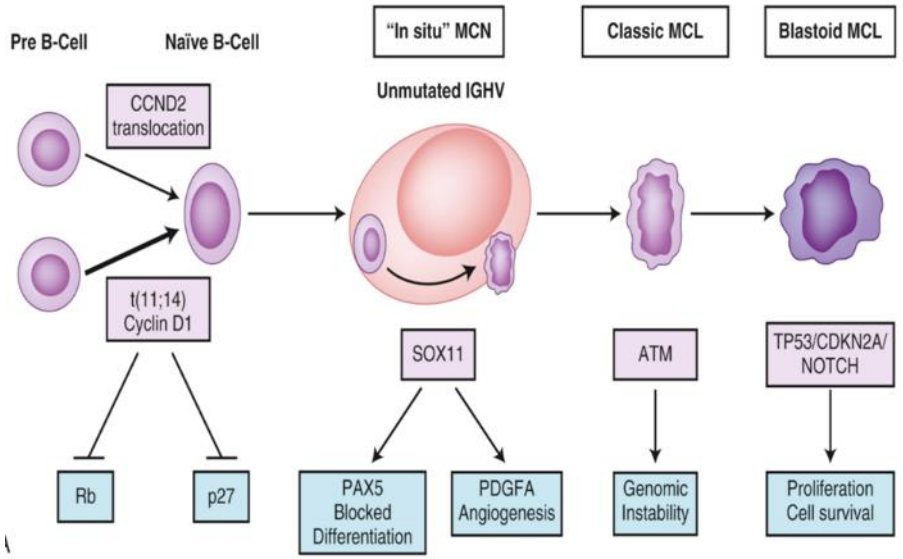
- Rare, under recognized subset of mantle cell lymphoma (MCL) now in WHO classification
- Characterized by involvement of peripheral blood, bone marrow, and sometimes spleen; little to no lymphadenopathy; and indolent clinical course that may not require therapy (at least initially)
- Similar immunophenotype to conventional MCL, but **SOX11 negative**, Ki-67 low (2%), CD200 positive, CD5 negative in 30%



Cristina Royo, et al. Leukemia. 2014.
Guillem Clot, et al. Blood. 2018.

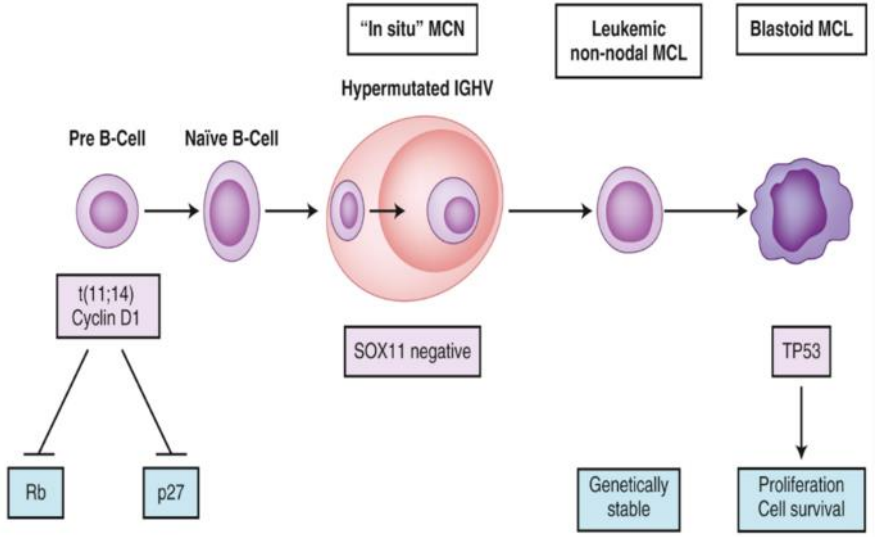
Two genetic subtypes of MCL

Conventional MCL



- Unmutated *IGHV*
- Complex karyotype
- Increased SOX11 expression
- Mutations in *ATM*, *CDKN2A*, chromatin-modifier genes (*MLL2, WHSC1,* and *MEF2B*), *TP53*

Leukemic non-nodal MCL



- Hypermutated *IGHV*
- Noncomplex karyotype
- Decreased SOX11 expression
- Activating *TLR2* mutations and *TP53*

Elaine Jaffe, et al. Hematopathology. 2016

Conclusions

- Leukemic non-nodal MCL is more indolent with a longer time to treat compared to conventional MCL
- Leukemic and bone marrow presentations of MCL are not necessarily associated with a worse prognosis
- Correlation with clinical presentation and SOX11 immunostain are important to identify different MCL subsets
- Leukemic non-nodal MCL and conventional MCL show different genetic pathways with a common mechanism of progression (i.e. *TP53* mutation)
  - Various gene signatures can reliably distinguish the two MCL subtypes

References

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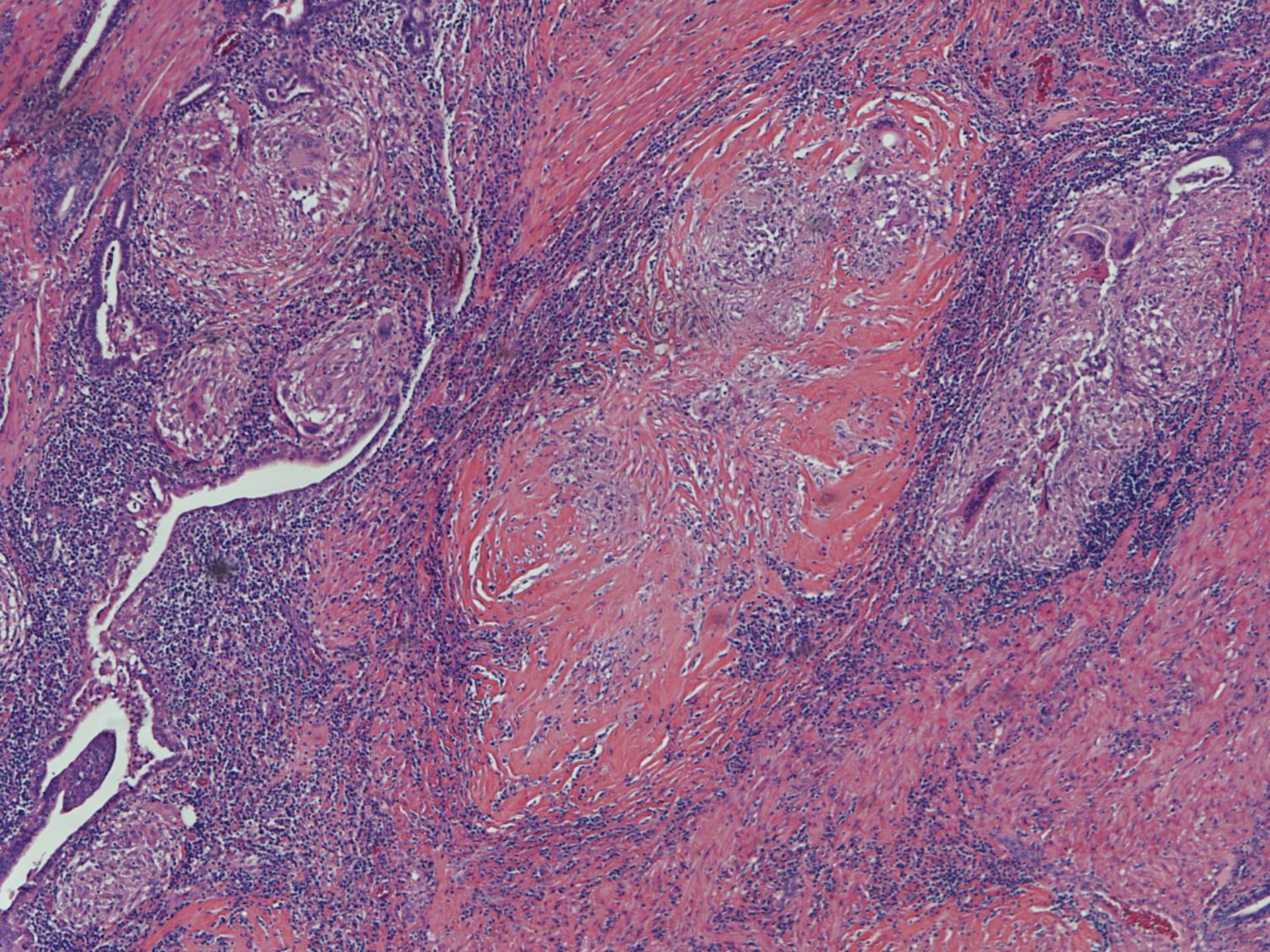
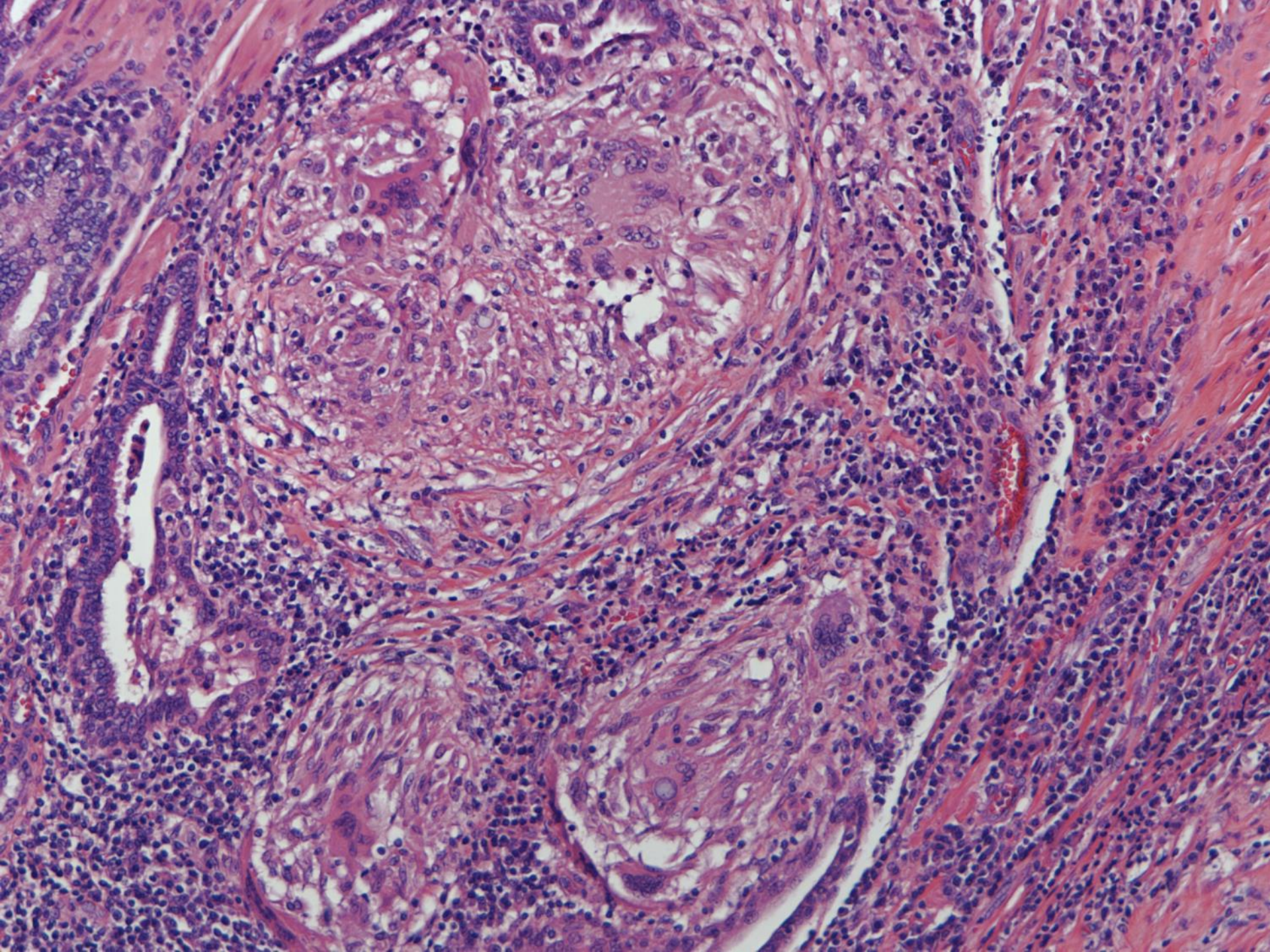
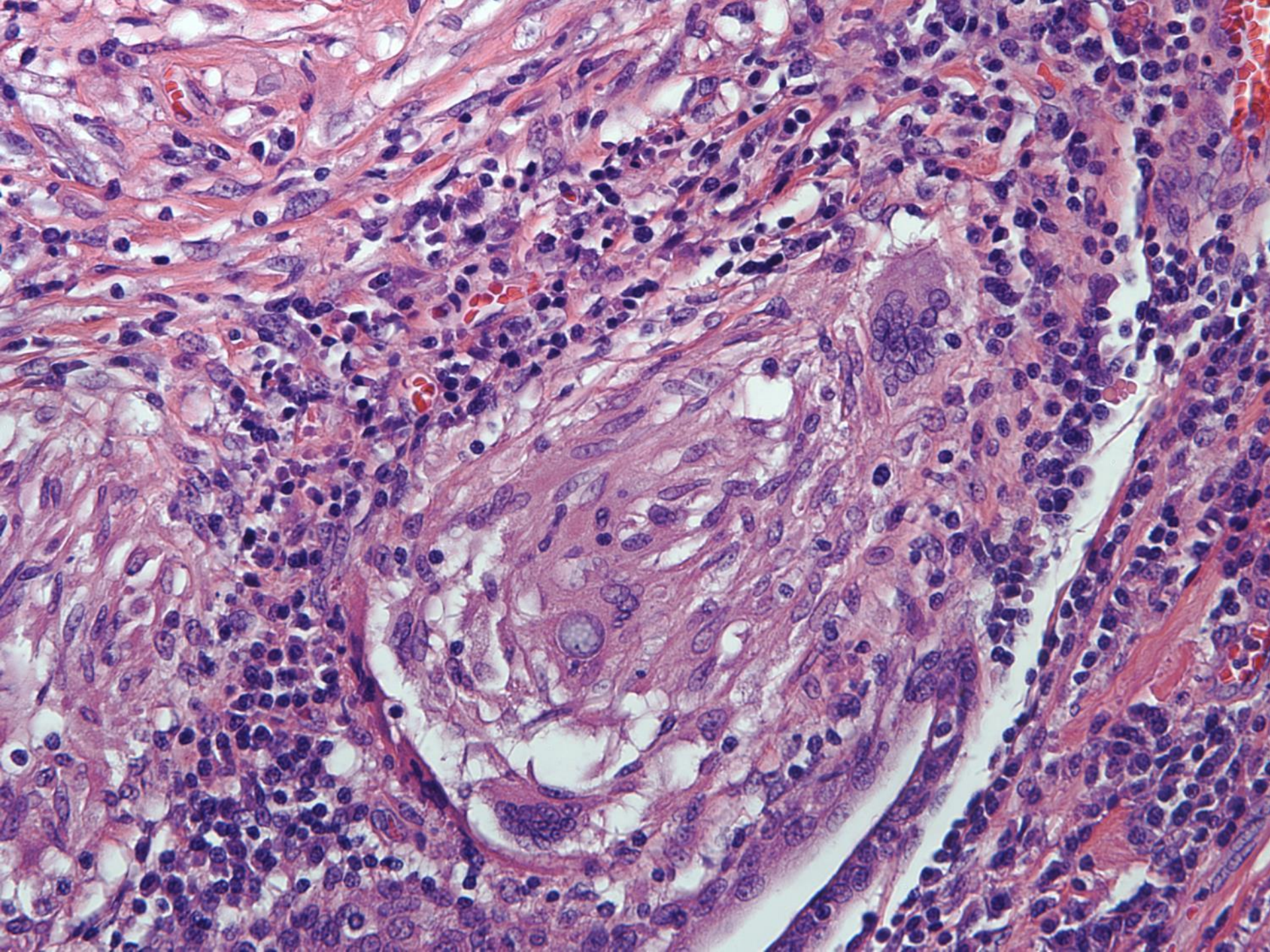
SB 6328

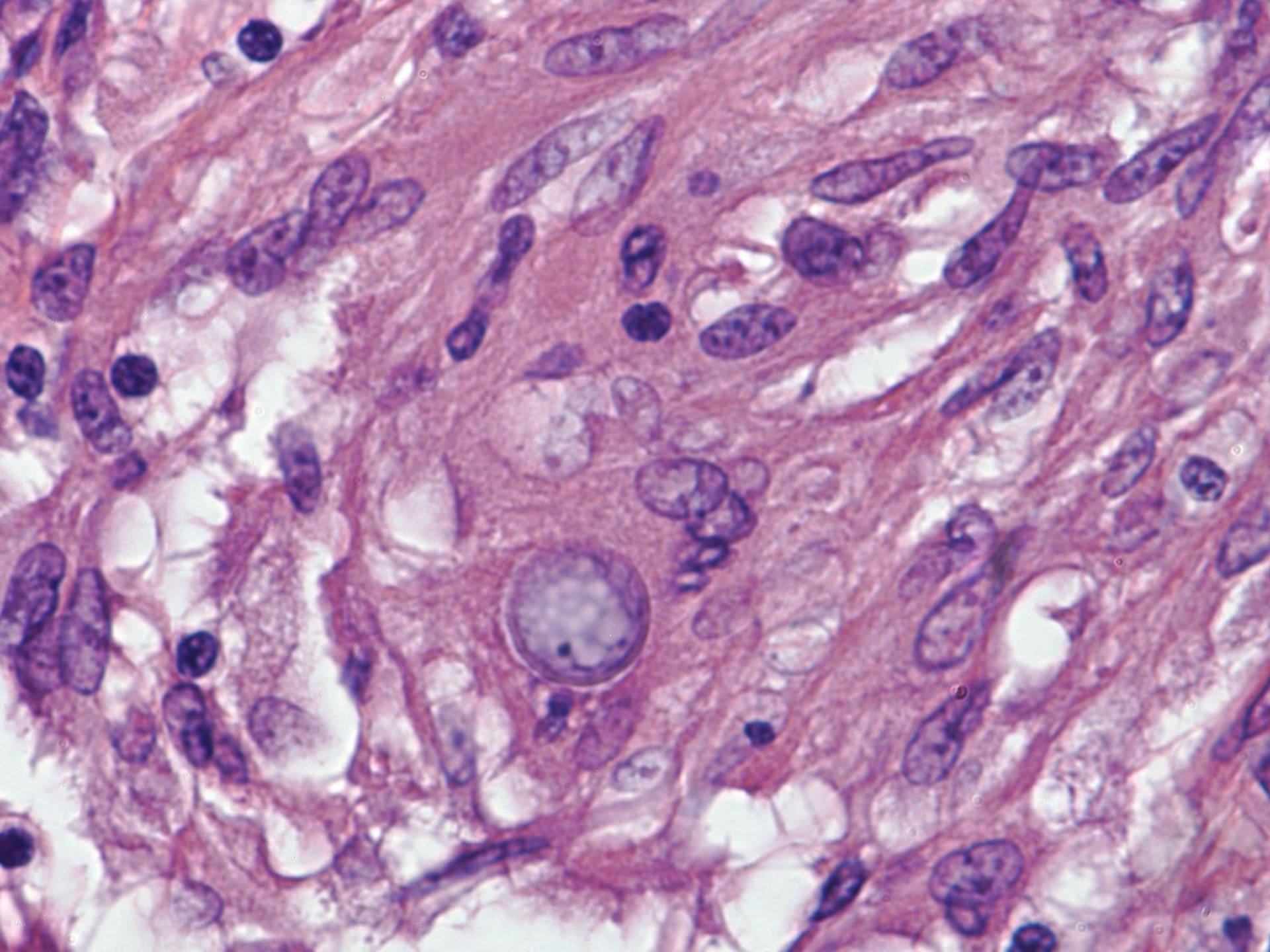
Atif Saleem/Megan Troxell; Stanford

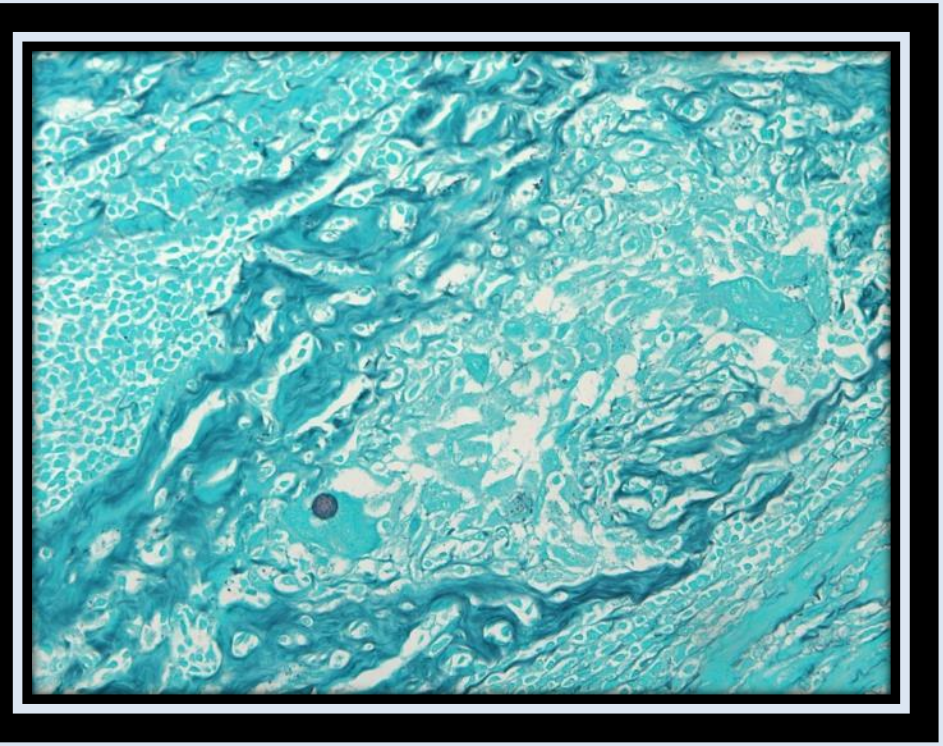
53-year-old male who resides in Midwest with biopsy-proven 3+3 prostatic adenocarcinoma and BPH, presents for radical prostatectomy.

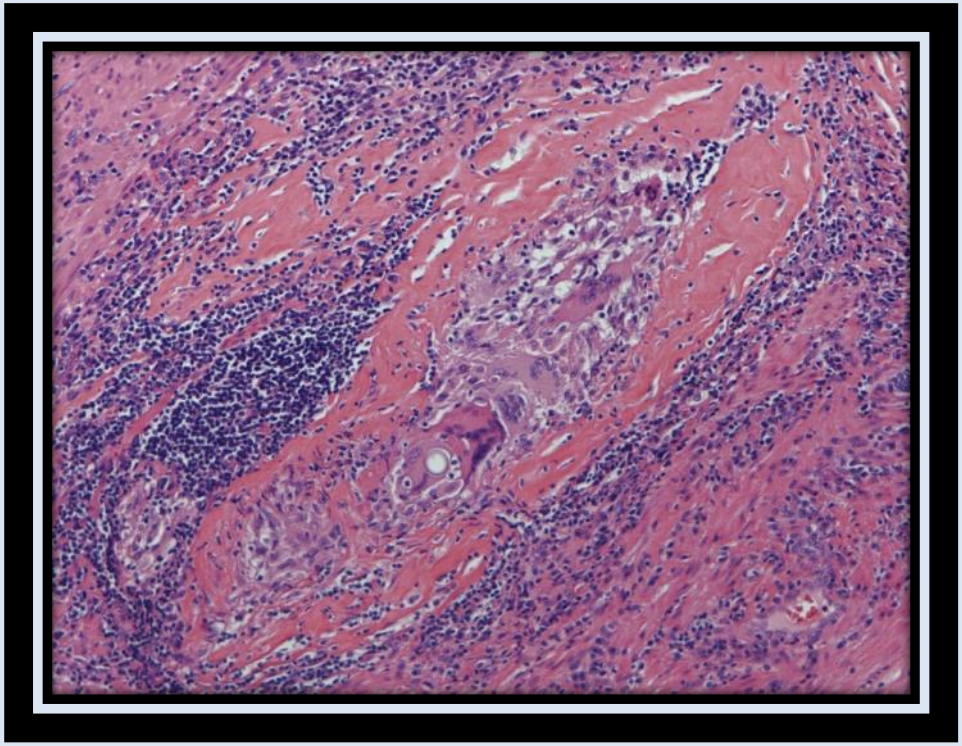


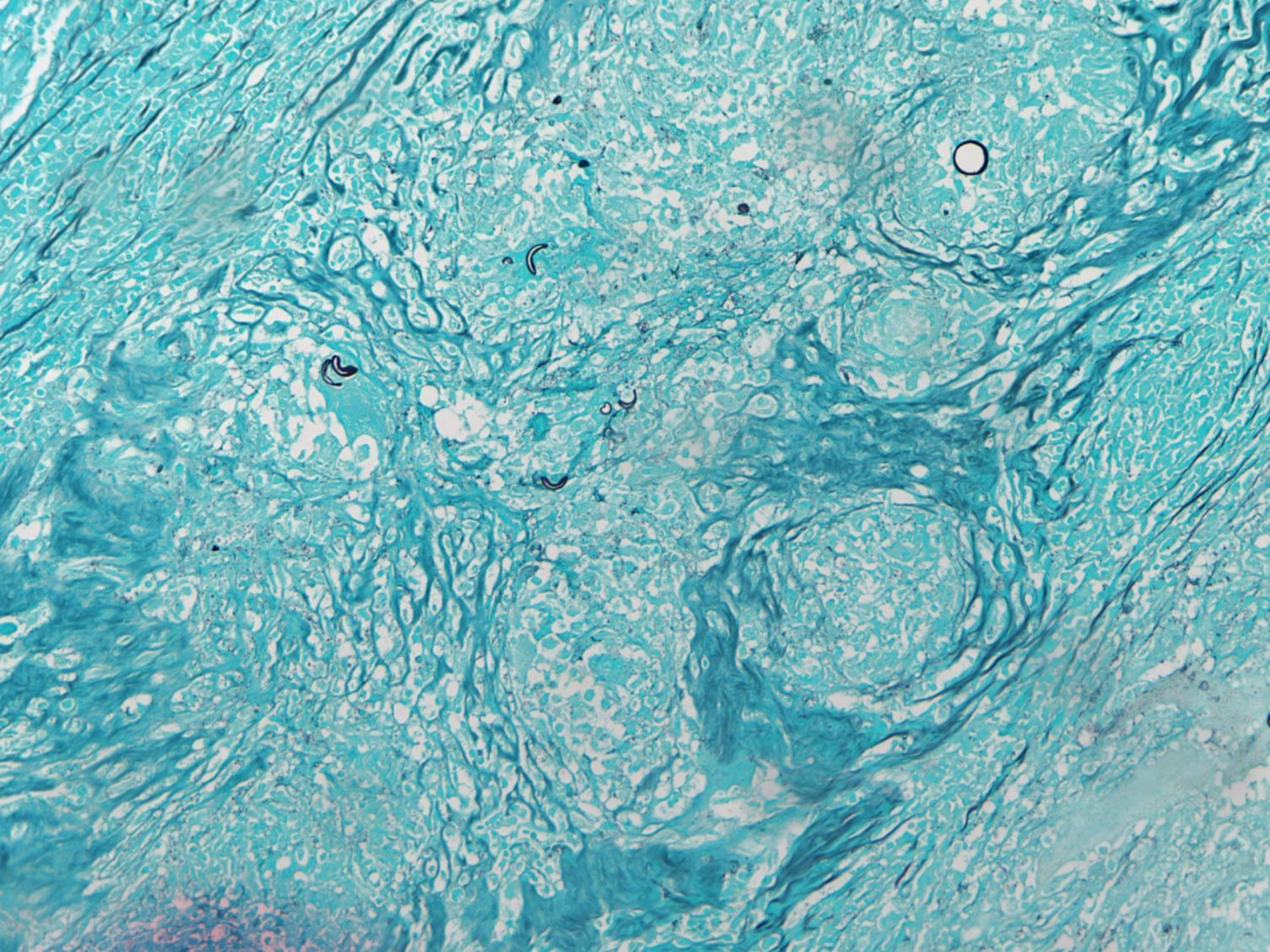








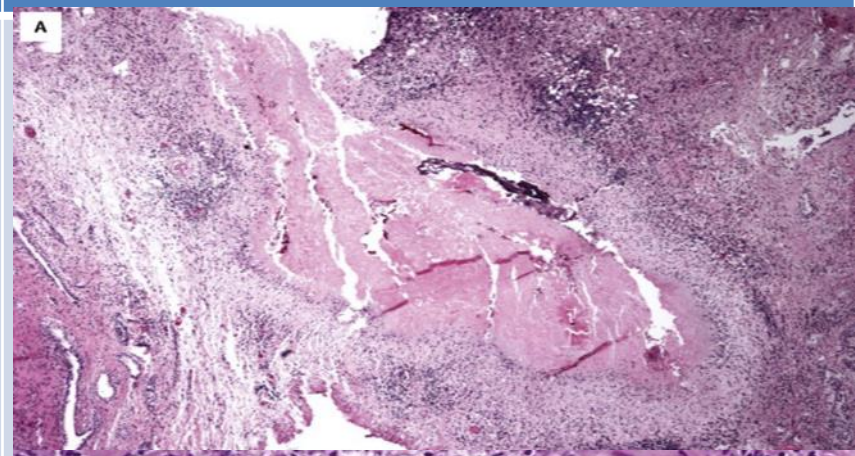
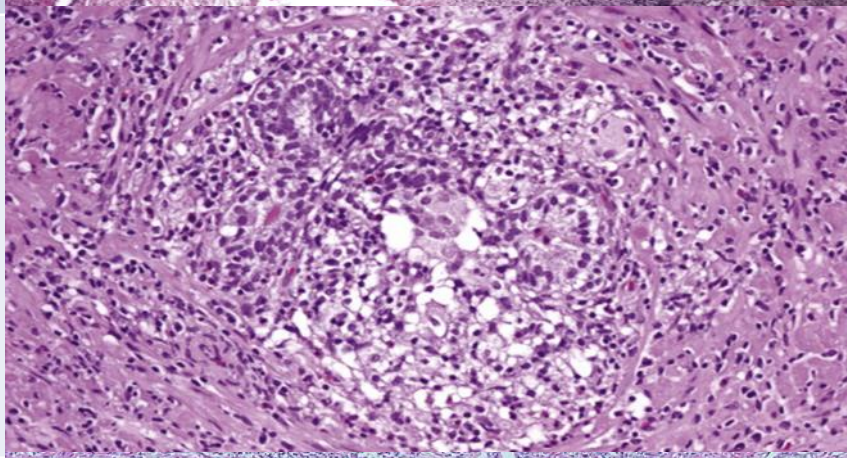
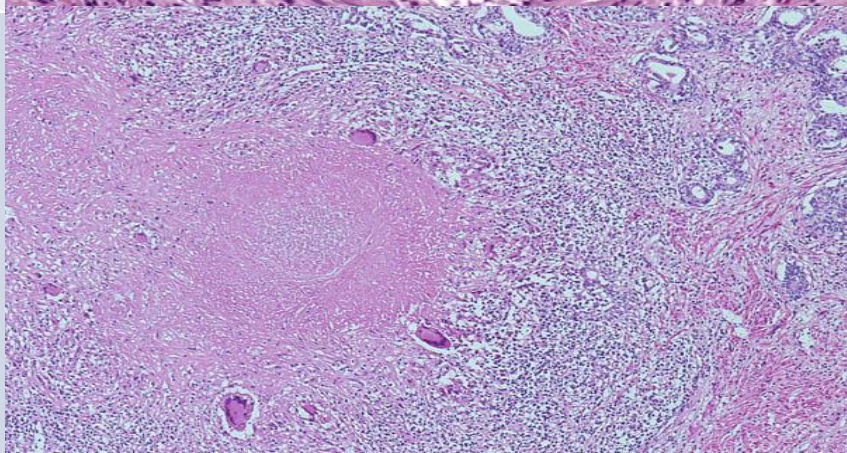




DIAGNOSIS?

Clinical Presentation

- 53-year old male with **prostatic adenocarcinoma** in 2/2018 (Gleason 3+3, 3/12 cores)
- PMH: **Epididymitis** (in college and in 2013), pneumonia (2008-2009)
- SH: Exercises regularly (triathlons in **Arizona** and other locations)
- Labs: PSA 5.1 ng/mL
- Imaging: MRI Prostate showed 2 PI-RADS 4 lesions in addition to "**heterogeneous T2 signal abnormality**, may relate to prior prostatitis"
- Plan: Radical prostatectomy

Differential Diagnosis	Features	Microscopic
Postbiopsy granuloma	-Irregularly shaped -Can have central fibrinoid necrosis -Can be seen 9 days – 52 months after TURP	
Nonspecific granulomatous prostatitis	-Central necrosis usually absent -Typically shows ruptured acini	
Infectious granulomatous prostatitis	-Granulomas with or without necrosis -Dense associated inflammatory infiltrate	

Whittier, Susan. *Coccidioides.* Expertpath, 2018

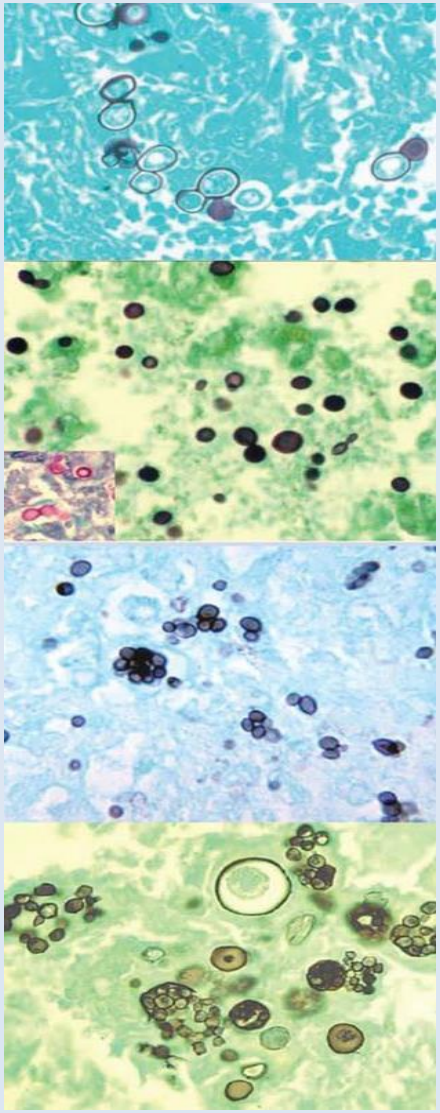
Fungal Prostatitis

– *Blastomyces dermatitidis*

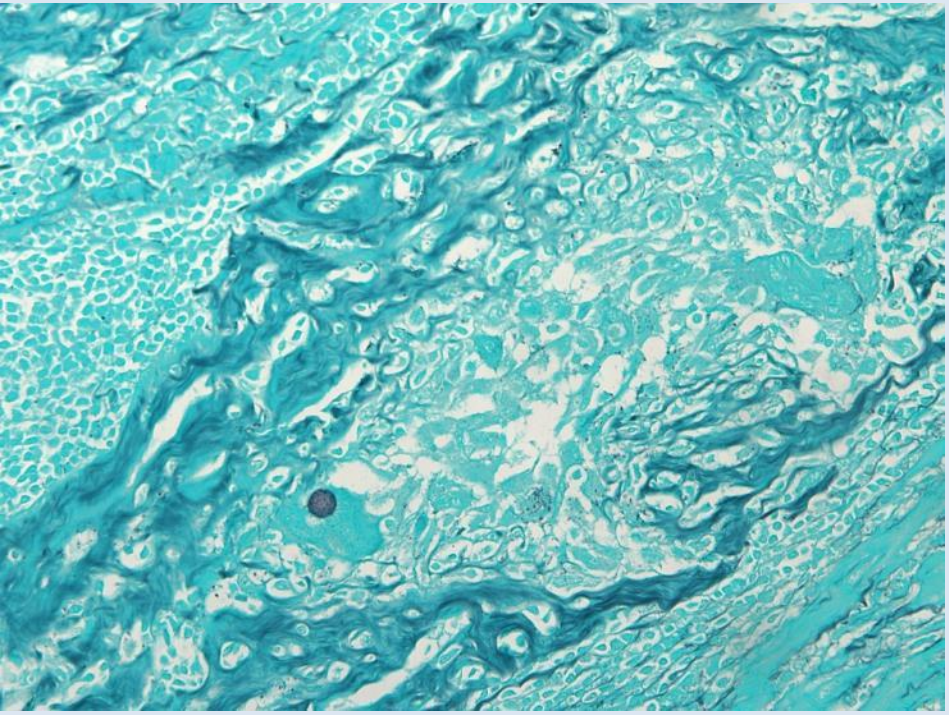
– *Cryptococcus spp.*

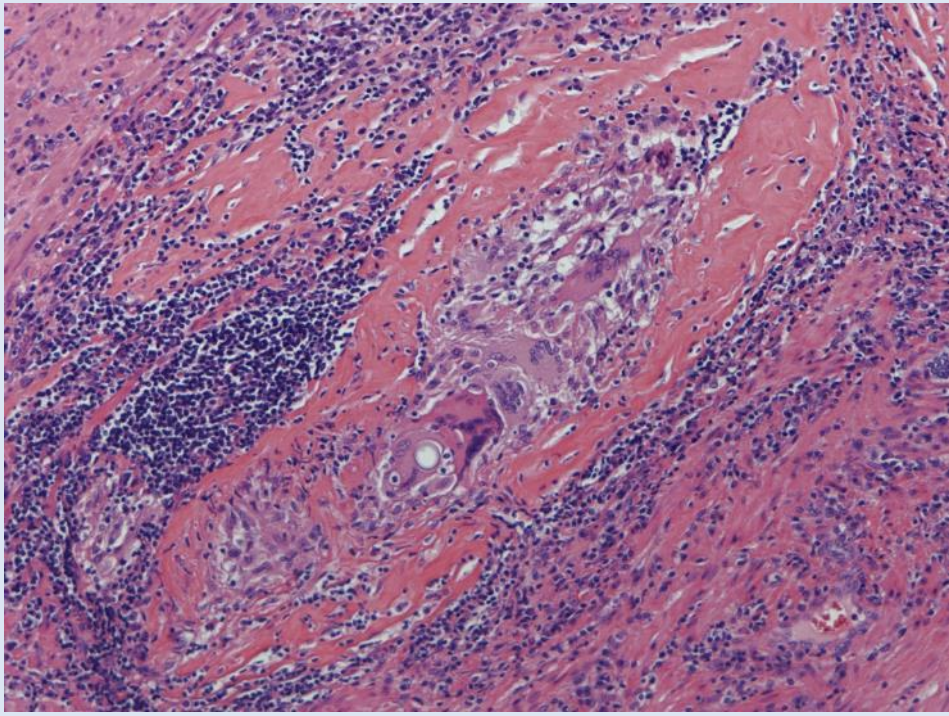
– *Histoplasma capsulatum*

– *Coccidioides spp.*



Armstrong, David et al. (2016). Diagnostic Microbiology of the Immunocompromised Host: Skin and Soft Tissue Infection.





Final Diagnosis

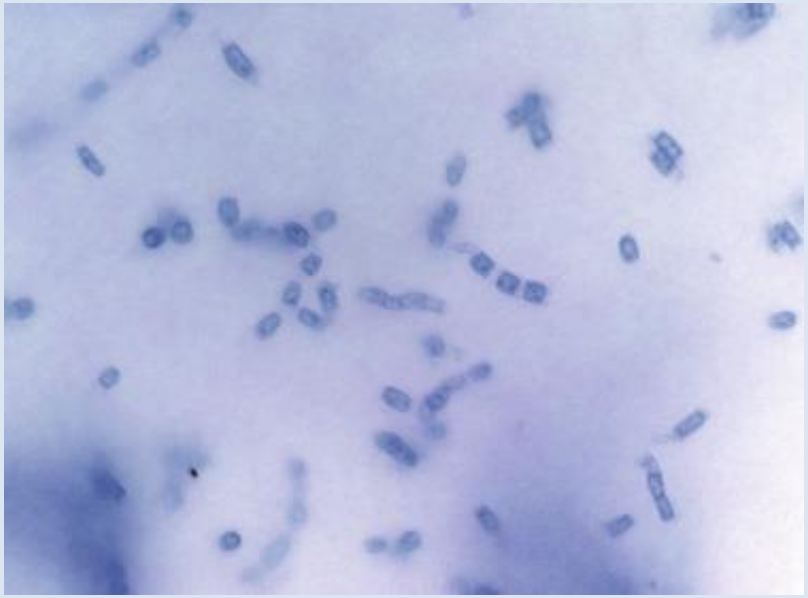
PROSTATE, ROBOTIC ASSISTED PROSTATECTOMY

-- PROSTATE ADENOCARCINOMA, GLEASON SCORE 3 + 3 = 6 (GRADE GROUP 1)

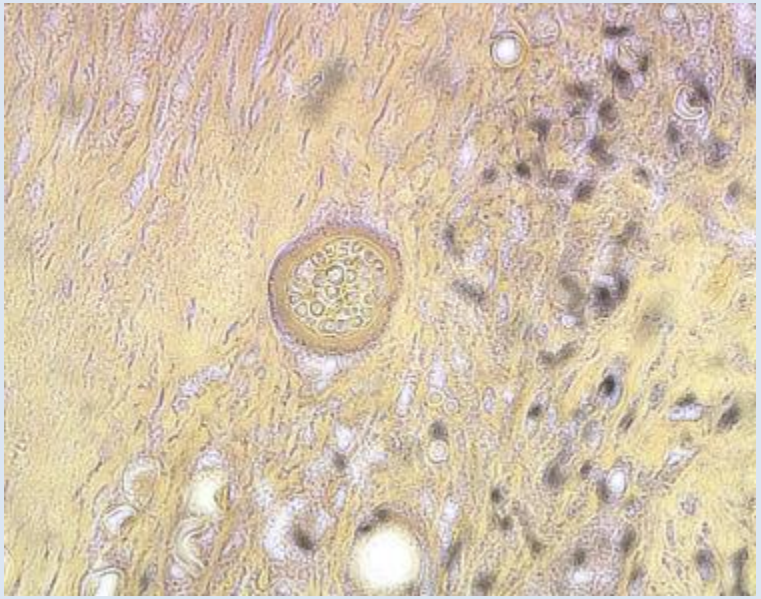
-- NECROTIZING GRANULOMATOUS PROSTATITIS, FAVOR COCCIDIOMYCOSIS PROSTATITIS

Coccidioides Morphology

- *Coccidioides immitis and C. posadasii* (virtually indistinguishable) = dimorphic fungus



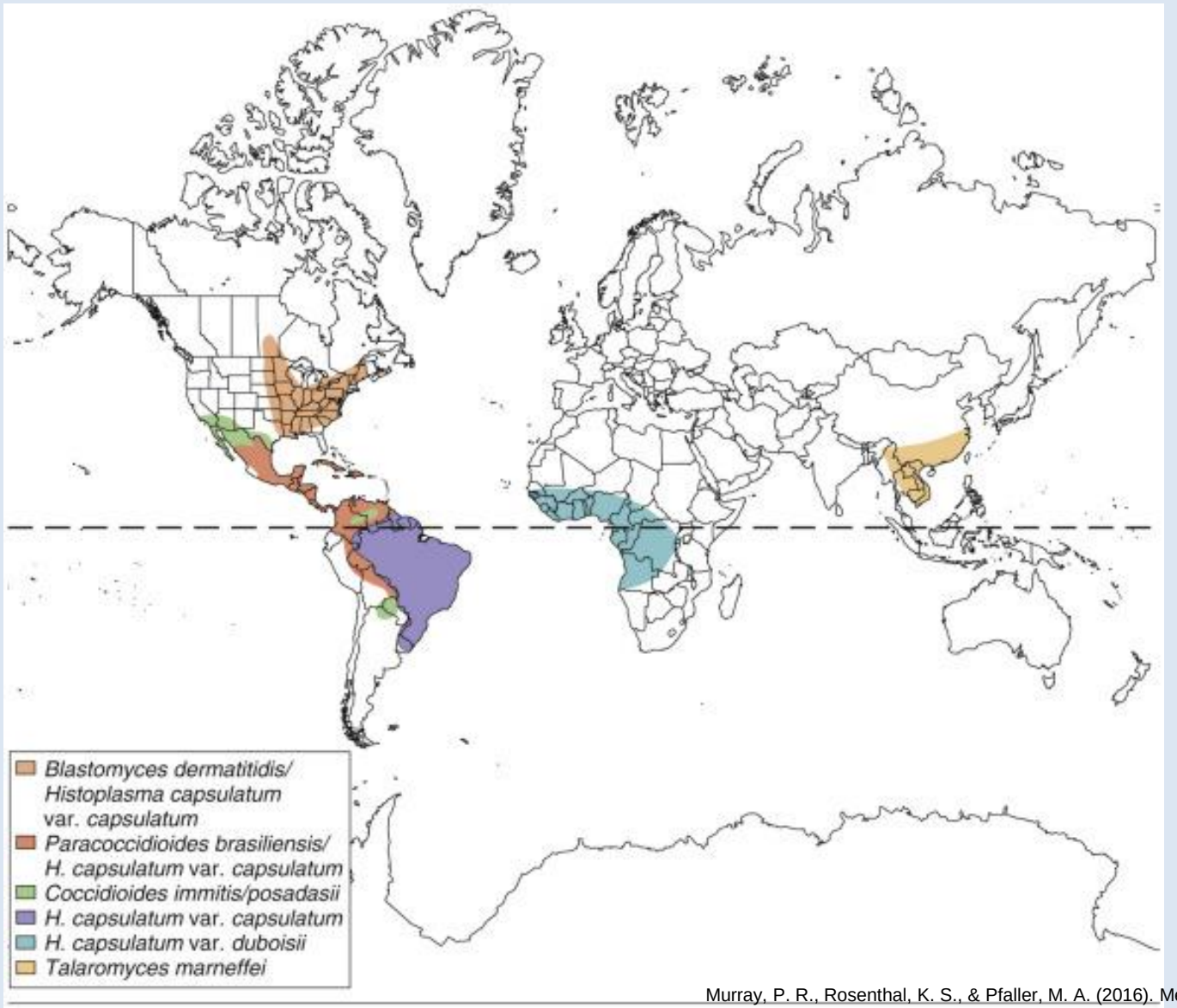
Mold phase: hyaline arthroconidia alternate with disjunctor cells



Spherule filled with endospores

Murray, P. R., Rosenthal, K. S., & Pfaller, M. A. (2016). Medical microbiology.

Coccidioides Epidemiology



Murray, P. R., Rosenthal, K. S., & Pfaller, M. A. (2016). Medical microbiology.

Coccidioides Clinical Features

- Primary coccidiomycosis: asymptomatic pulmonary disease (~60%), flulike illness, allergic reactions (i.e., erythema nodosum)
  - Usually resolves without therapy
- Secondary coccidiomycosis: pulmonary nodules, cavitary disease
  - Dissemination follows in ~1% (mortality exceeds 90% without treatment)

TABLE

Table 64-3

Risk Factors for Disseminated Coccidioidomycosis

Risk Factor	Highest Risk
Age	Infants and elderly
Sex	Male
Genetics	Filipino > African American > Native American > Hispanic > Asian
Serum CF antibody titer	>1 : 32
Pregnancy	Late pregnancy and postpartum
Skin test	Negative
Depressed cell-mediated immunity	Malignancy, chemotherapy, steroid treatment, HIV infection

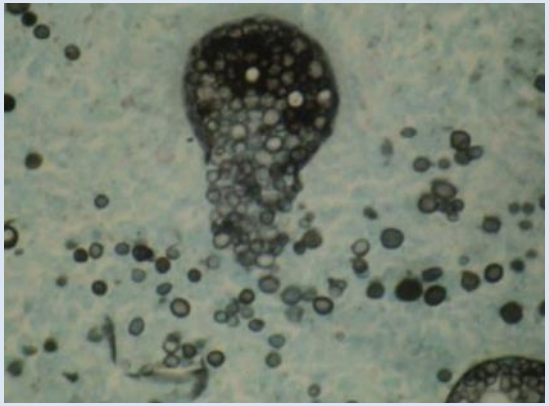
CF, Complement fixation; *HIV,* human immunodeficiency virus.

From Cohen J, Powderly WG, Opal SM: *Infectious diseases,* ed 3, Philadelphia, 2010, Mosby.

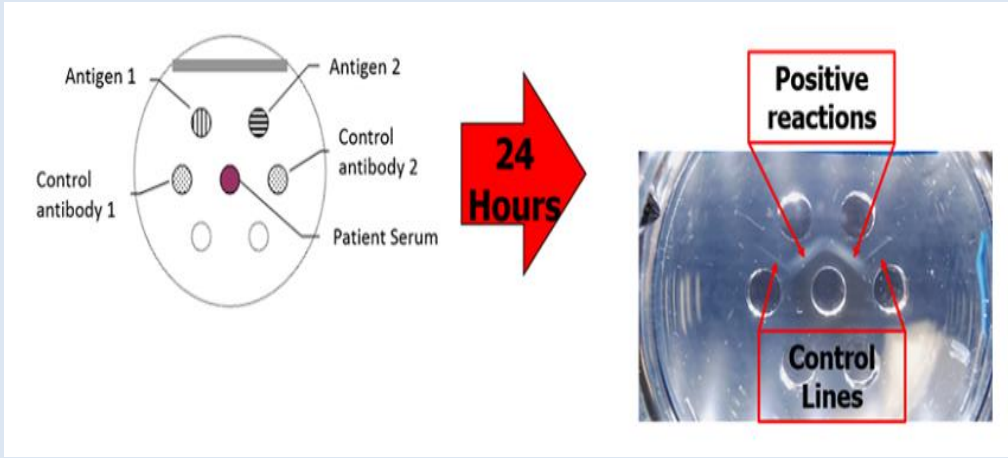
Murray, P. R., Rosenthal, K. S., & Pfaller, M. A. (2016). Medical microbiology.

Coccidioides Diagnosis

- Microscopic evaluation: endosporulating spherules sufficient for diagnosis
- Culture: less preferred (highly infectious), colonies develop within 3-5 days
- Serology: EIA, exoantigen immunodiffusion test, latex test, complement fixation, tube precipitin
- Fungal ID by sequencing



Spherules of *Coccidioides* demonstrating release of endospores



Immunodiffusion test

Murray, P. R., Rosenthal, K. S., & Pfaller, M. A. (2016). Medical microbiology.

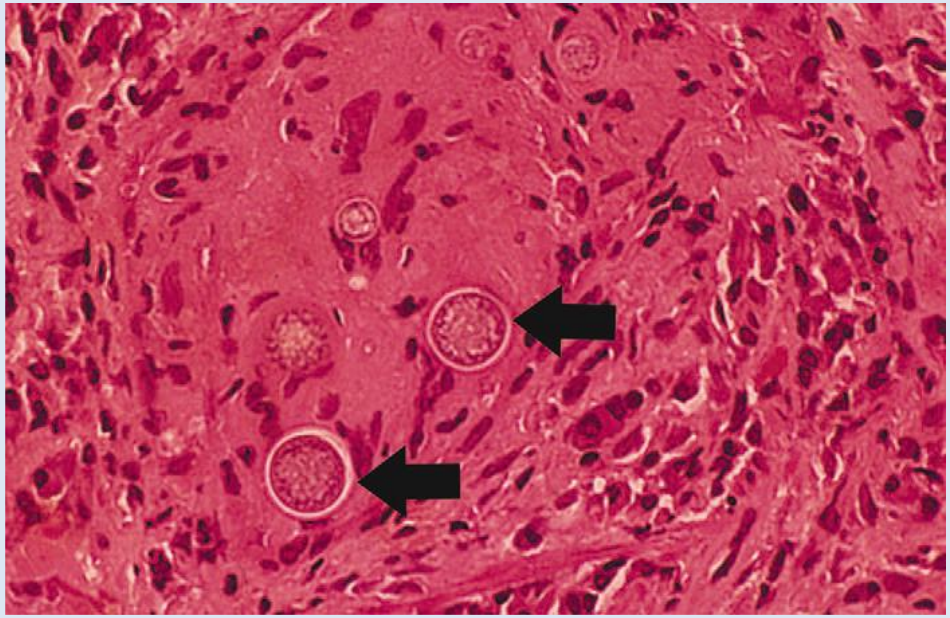
Treatment

- **Most immunocompetent patients with primary coccidiomycosis do not require antifungal therapy**
- Antifungal therapy for those with severe disease or at risk of dissemination or complications
- Late pregnancy/postpartum: amphotericin B
- Immunocompromised: amphotericin B followed by an azole x 1 year
- Chronic cavitary pneumonia: azole x 1 year
- Meningeal coccidiomycosis: azole indefinitely

Kauffman, C.A., et al. (2018). Primary coccidioidal infection. *UptoDate.*

Coccidiomycosis prostatitis

- Epidemiology: Incidence 0.1%, history of primary pulmonary infection
- Symptoms: obstructive symptoms, many asymptomatic
- Diagnosis: Microscopy
- Treatment: If diagnosed by biopsy, monitor; **if diagnosed on TURP or prostatectomy, then antifungal therapy**



Sohail, Muhammad R., et al. *The Journal of urology* 173.6 (2005).; Yurkanin, J. Paul et al. *Journal of Infection* 52.1 (2006).

Follow Up

- The patient was experiencing night sweats post-operatively for which he was given fluconazole 800 mg per day and is now improving (plan to retest complement fixation in 1-2 months)

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11. Gomez CA, Budvytiene I, Zemek AJ, Banaei N. Performance of Targeted Fungal Sequencing for Culture-Independent Diagnosis of Invasive Fungal Disease. Clin Infect Dis. 2017 Nov 29;65(12):2035-2041.

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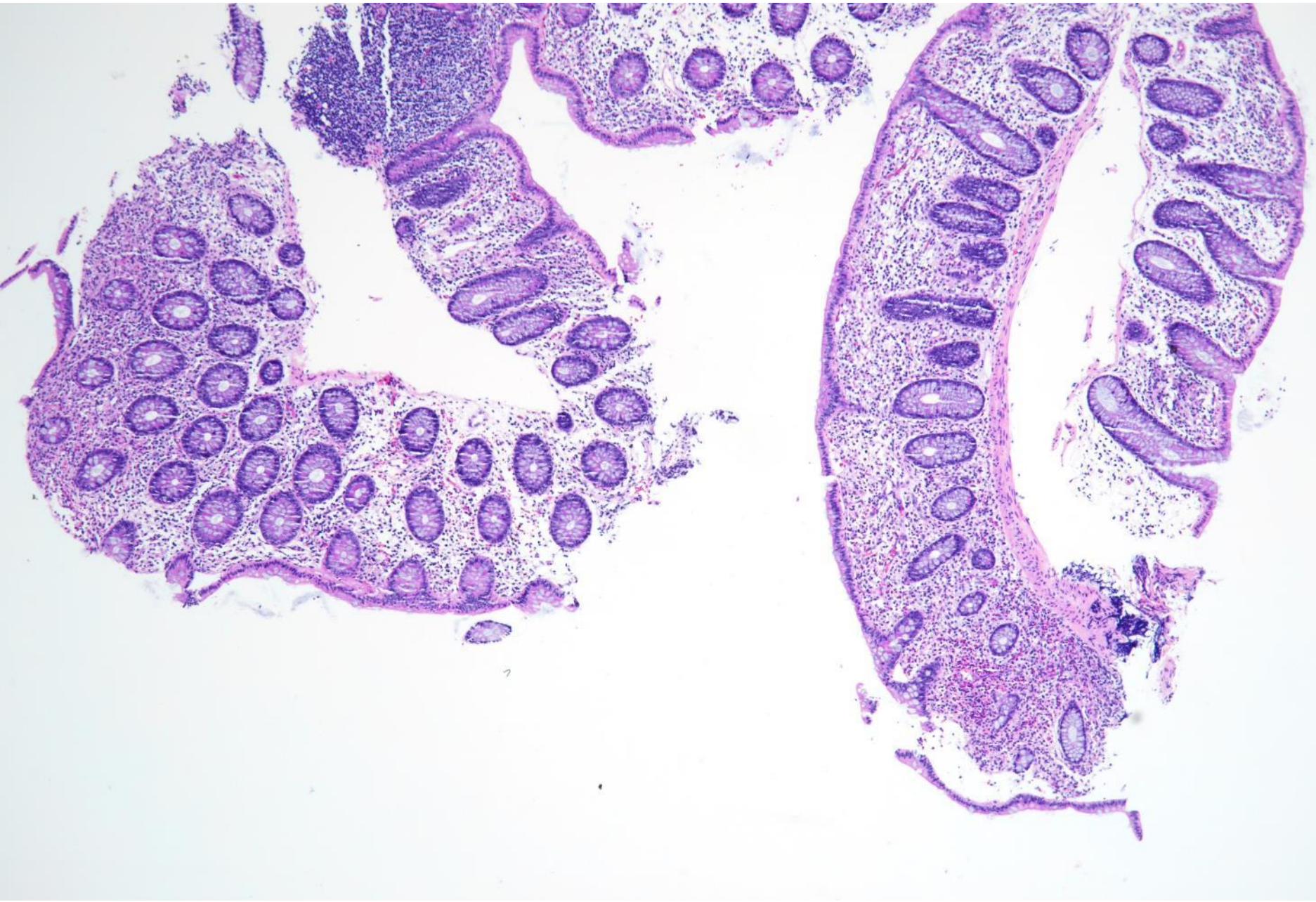
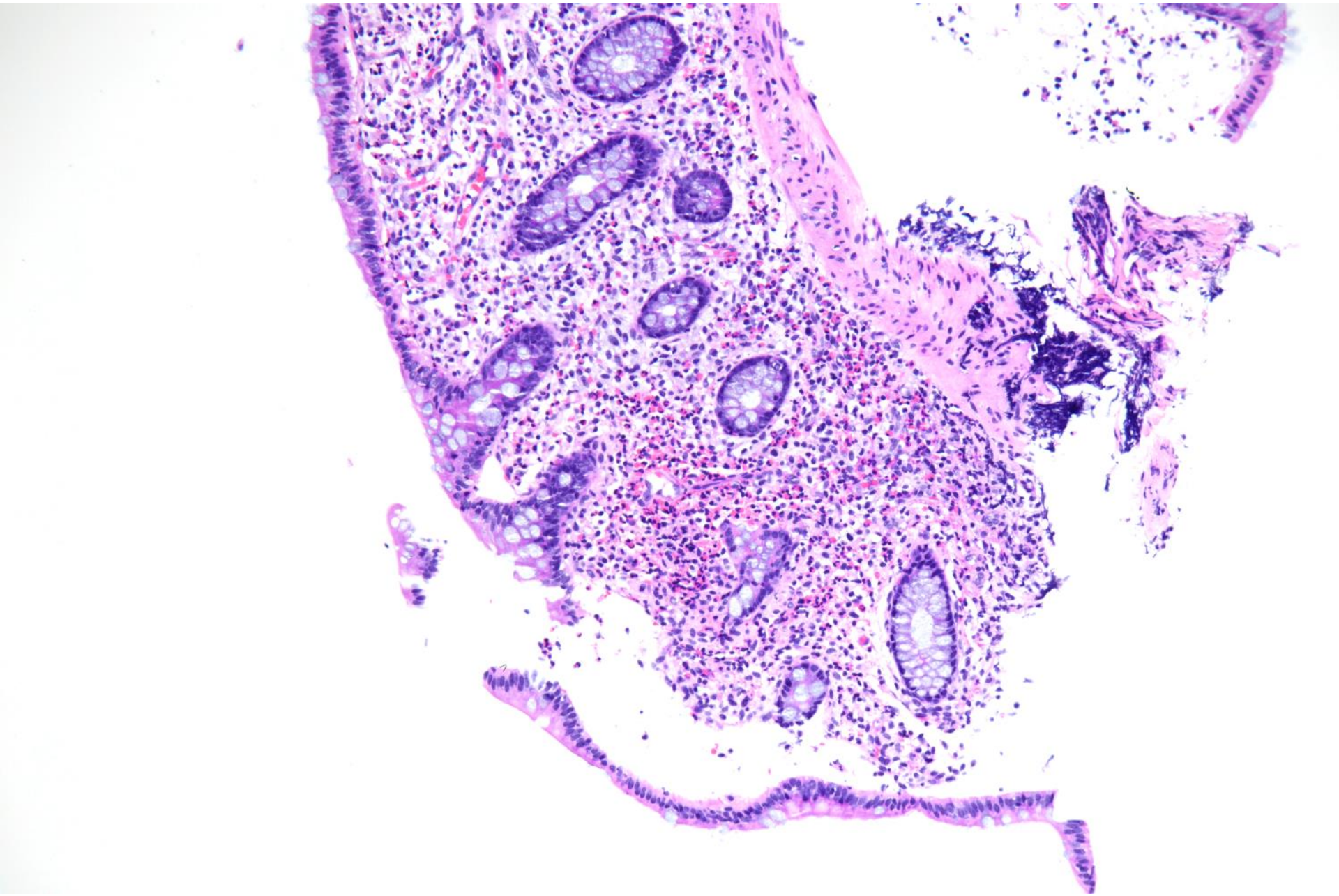
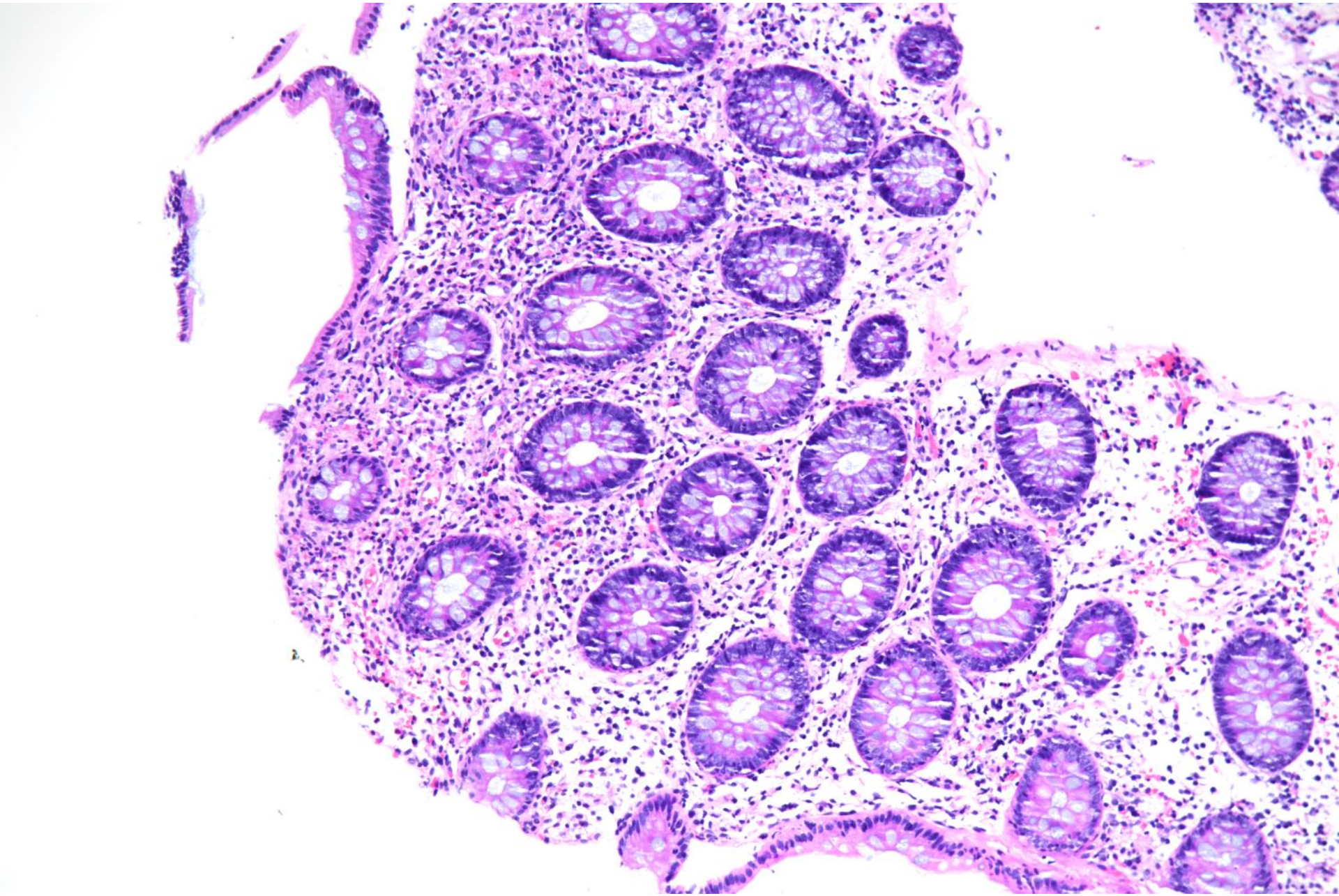
SB 6329

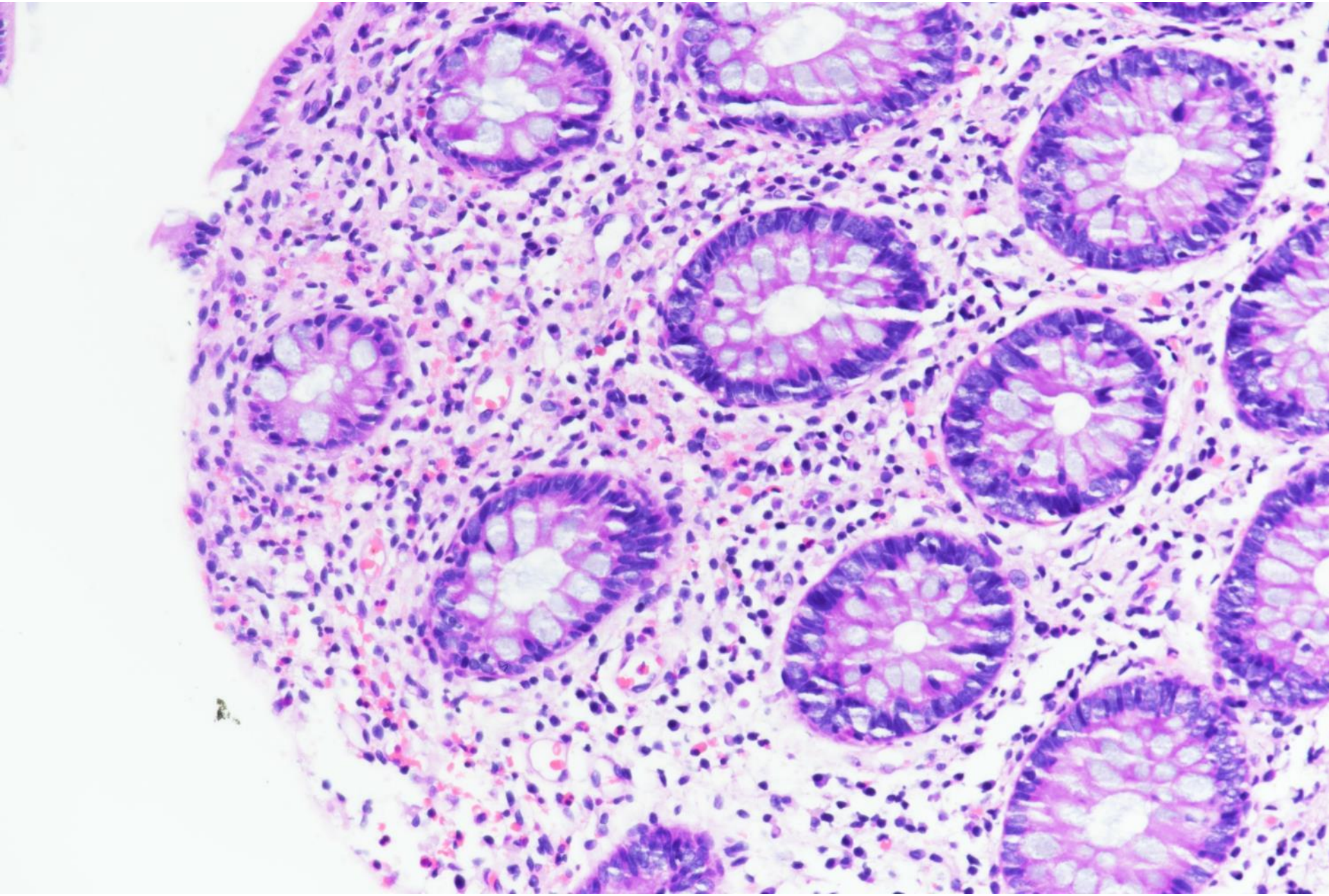
Marietya Law/Linlin Wang; UCSF

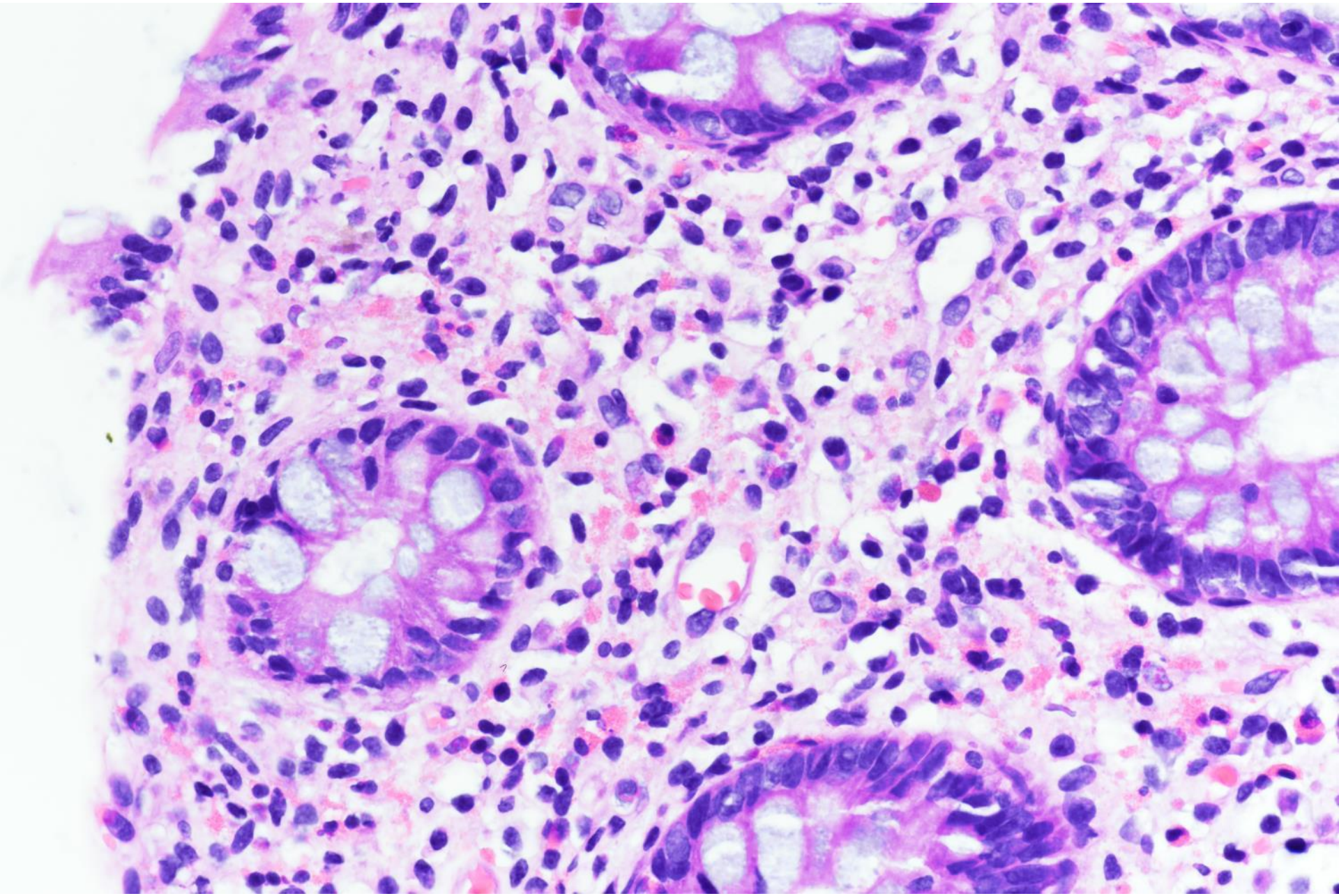
35-year-old female with cramping, bloating, and diarrhea.

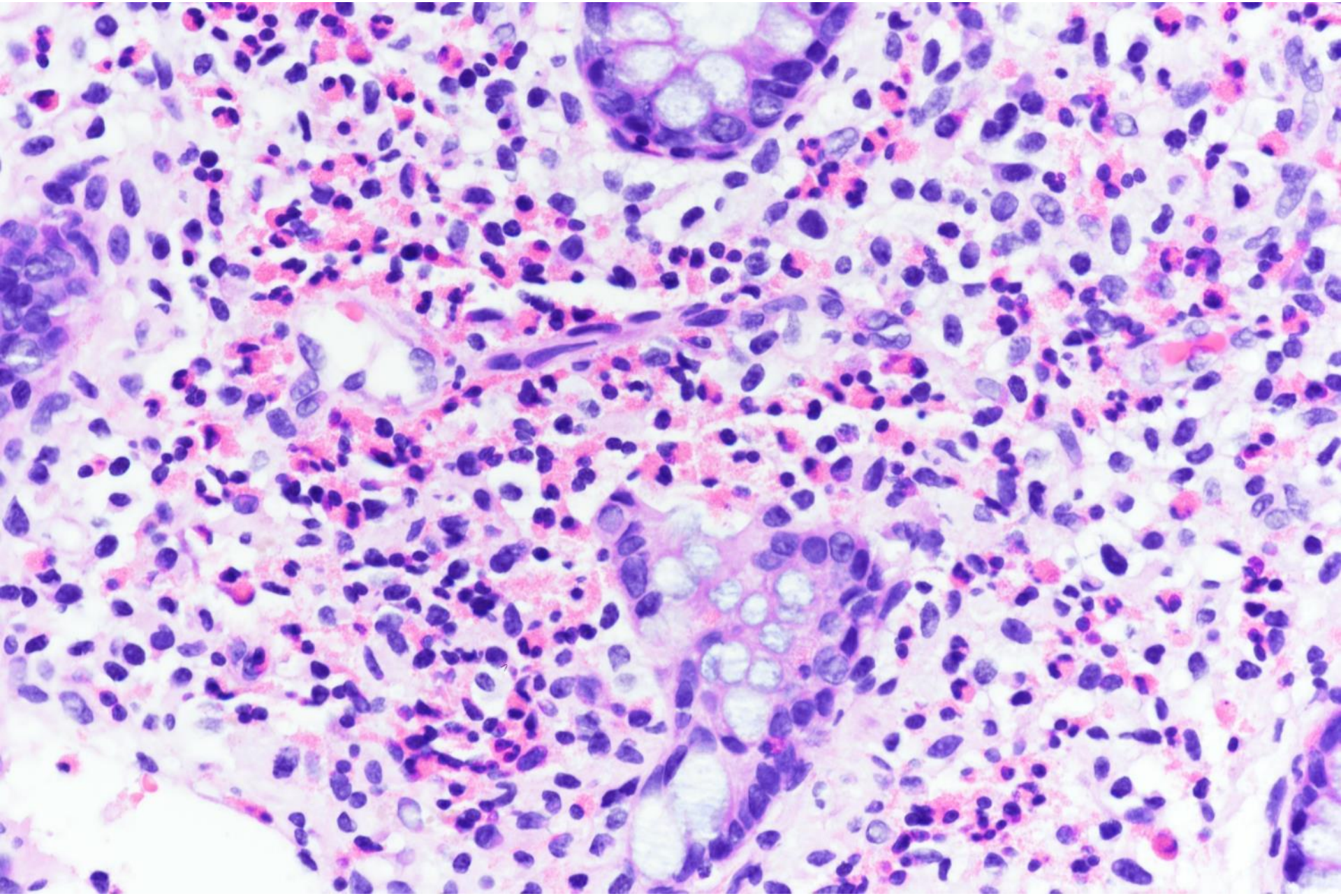


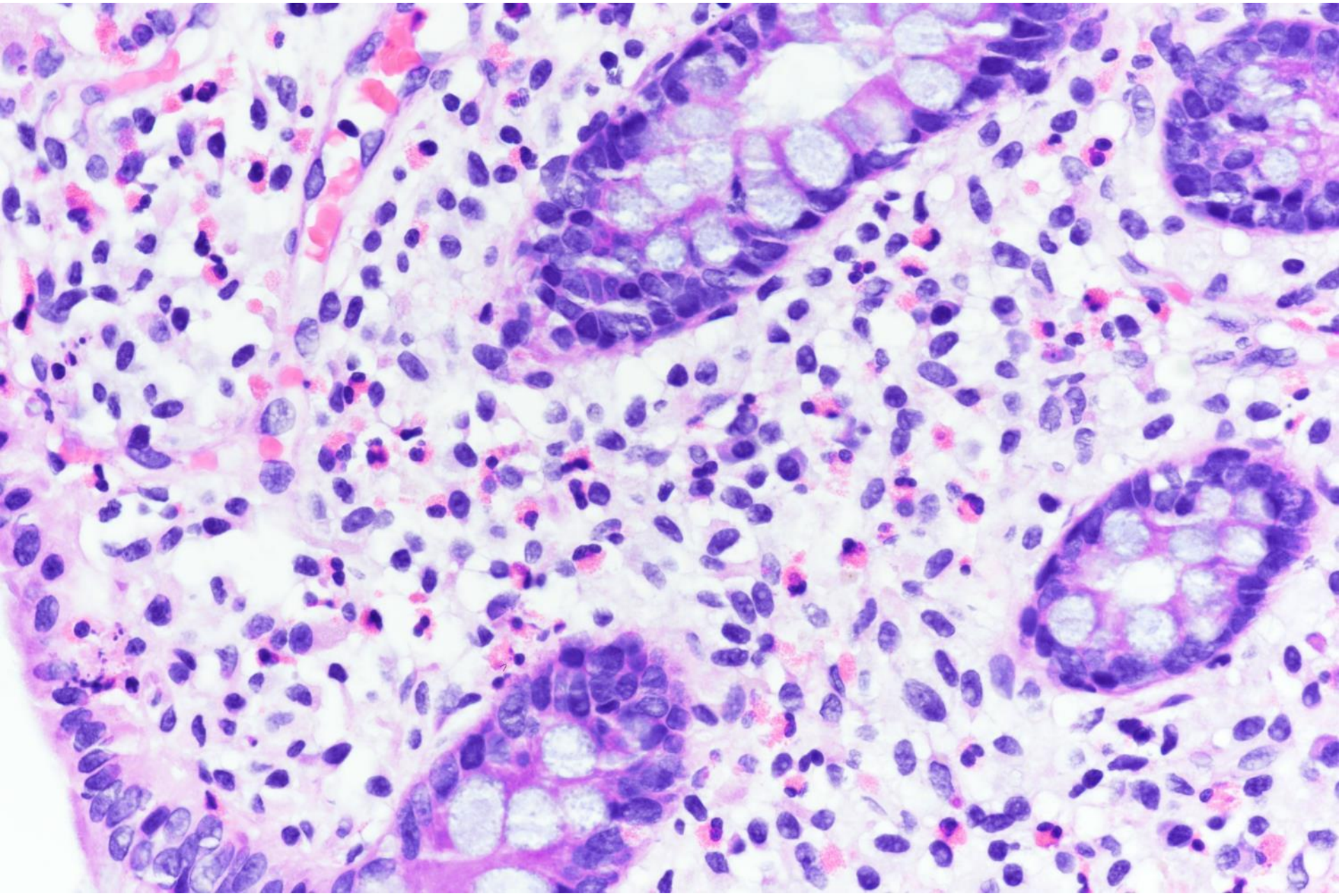












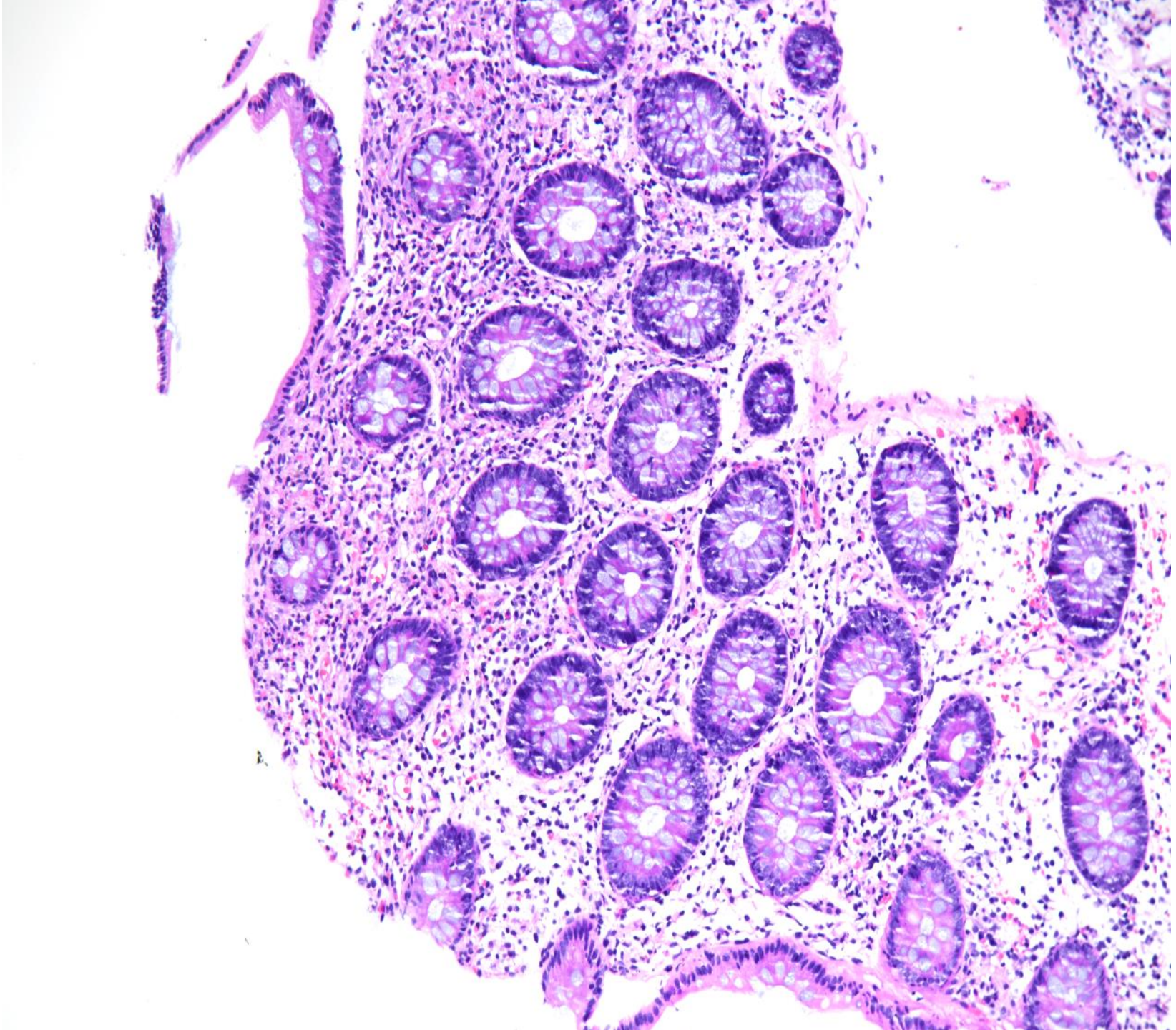
DIAGNOSIS?

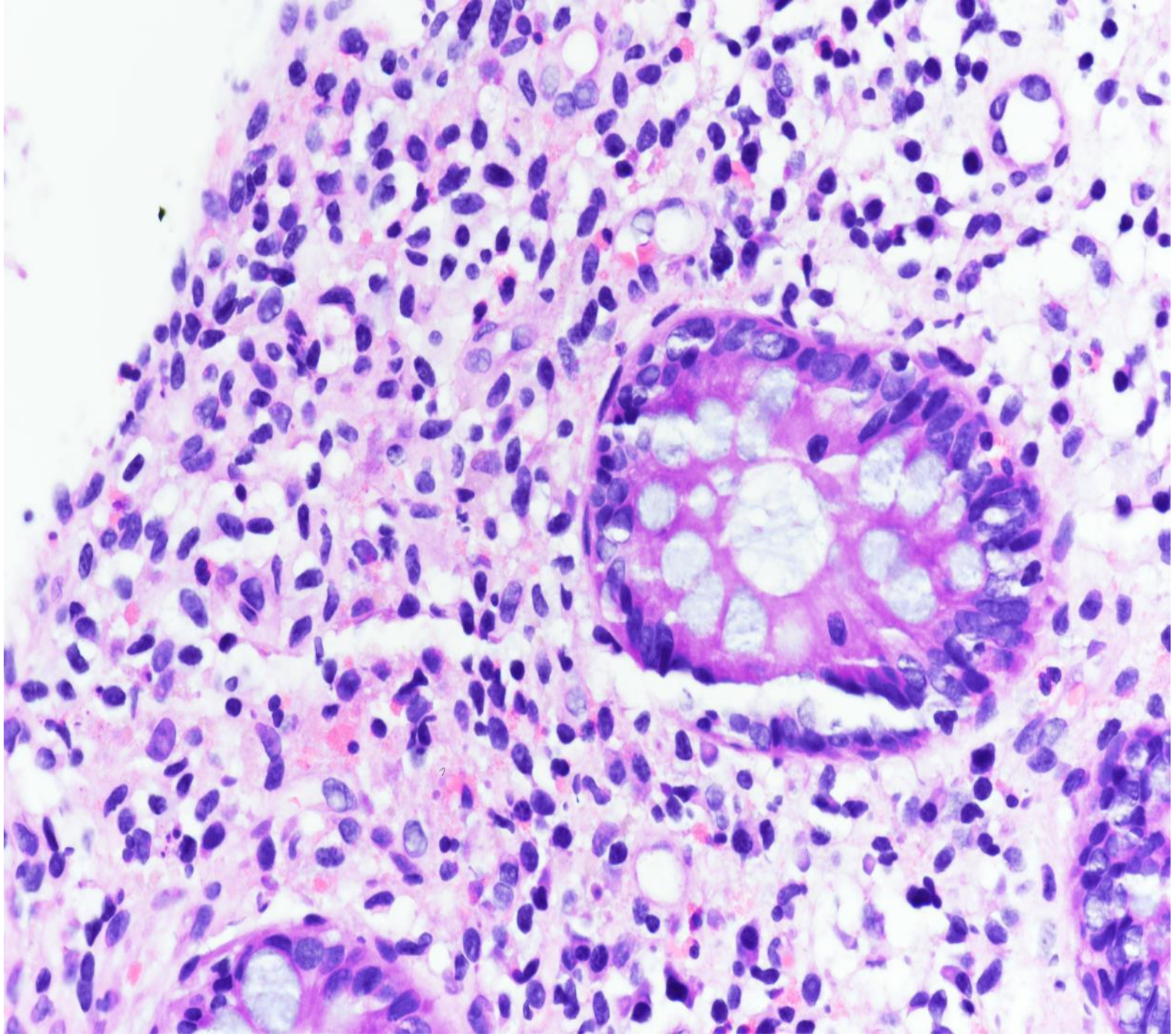
South Bay Meeting

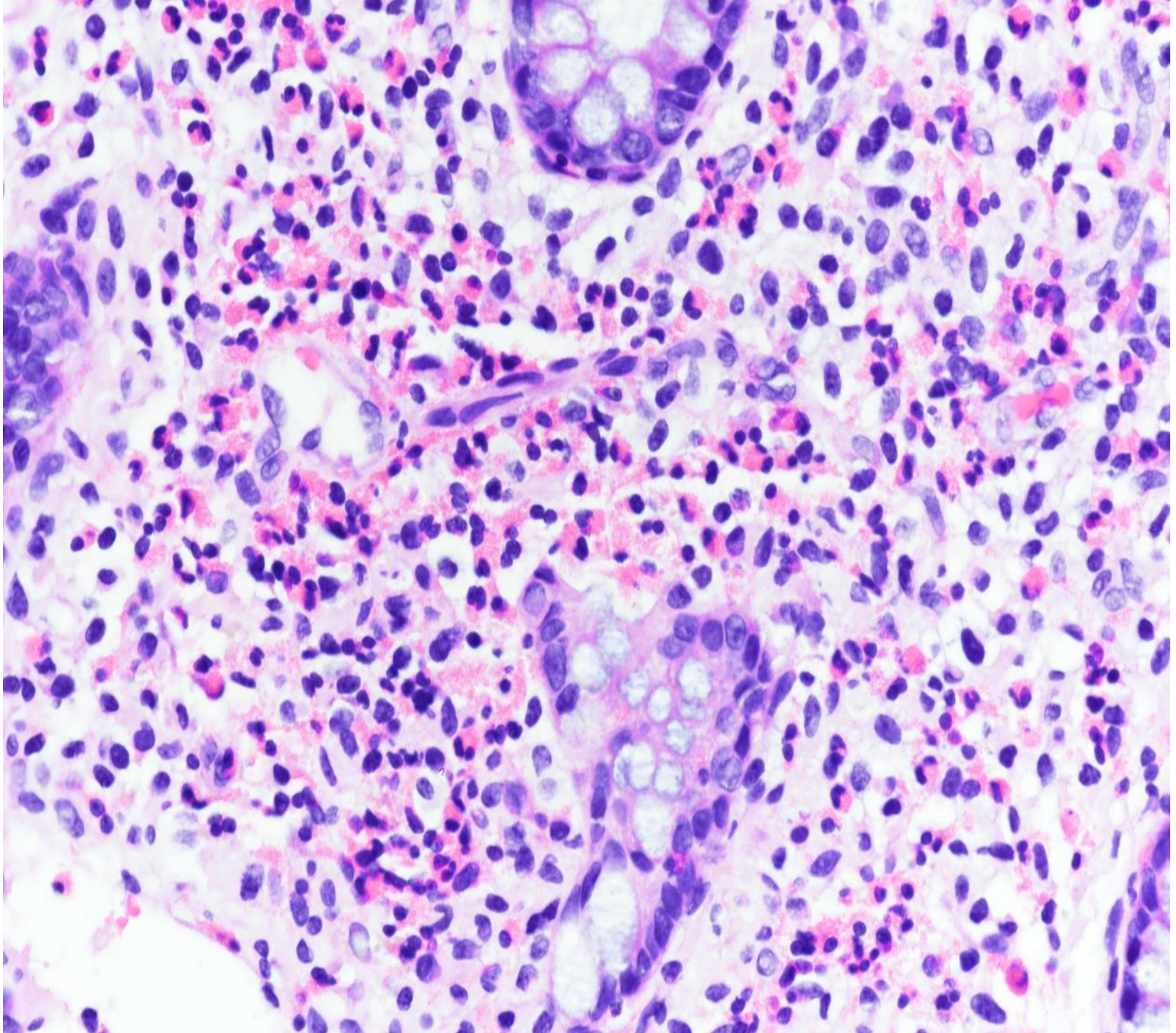
November 5th, 2018

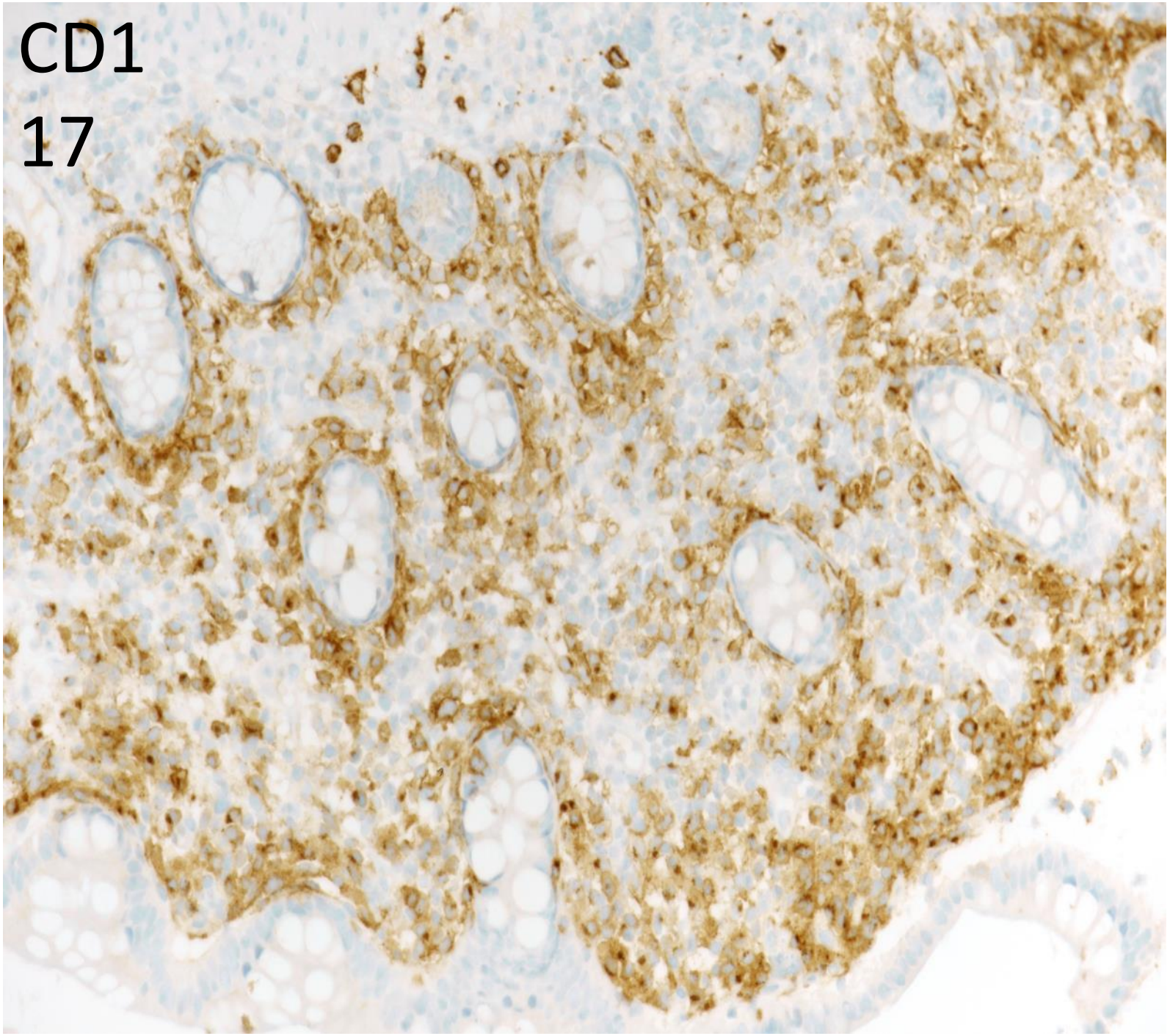
Marietya I. S. Lauw, MD

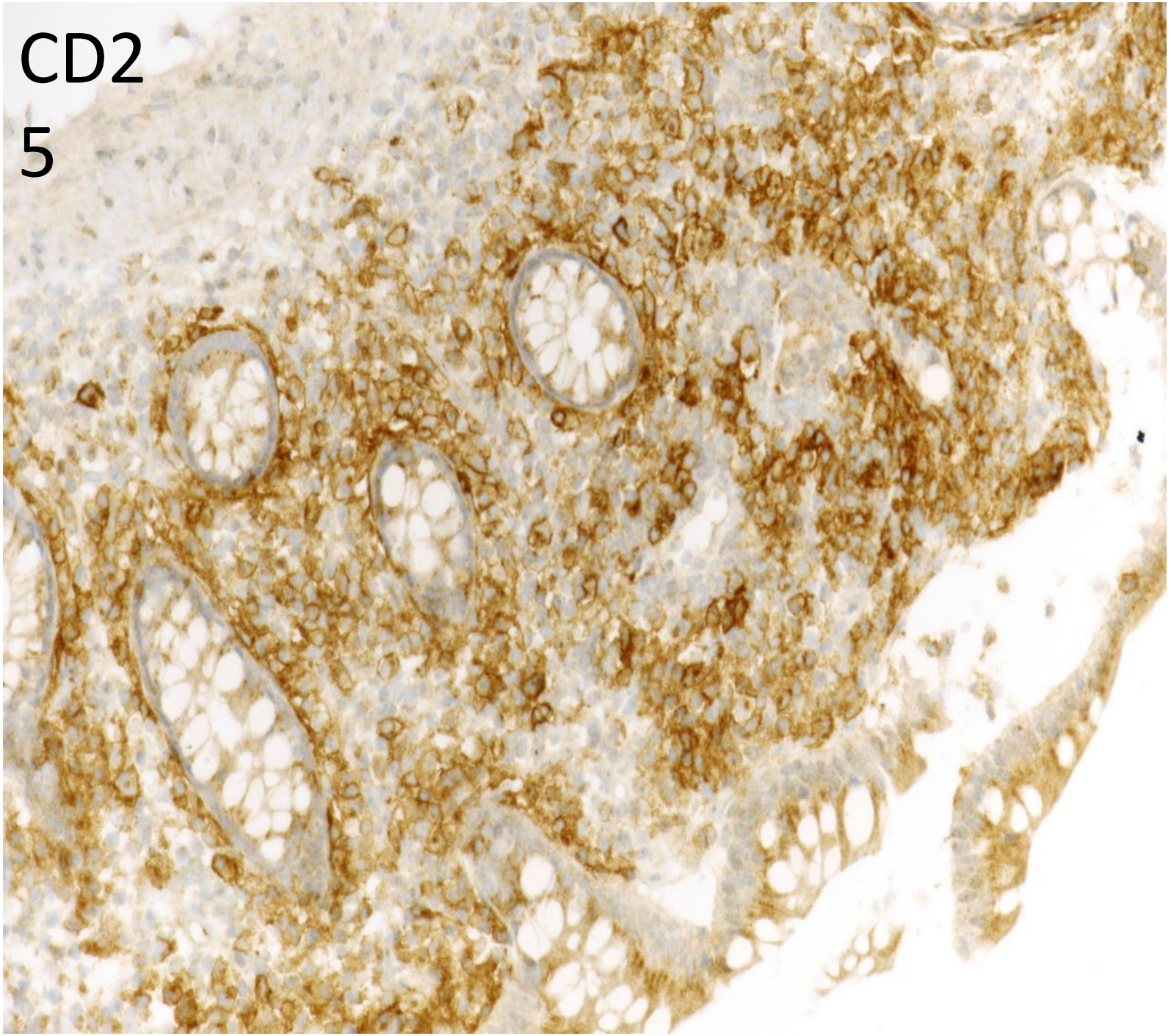
University of California San Francisco








CD1
17


CD2
5

Molecular Study

- Positive for p.D816V c.2447A>T mutation in *KIT* exon 17 in peripheral blood

2017 WHO Criteria for Systemic Mastocytosis

- **Major criterion + at least 1 minor criterion OR ≥3 minor criteria**
- **Major criterion**

  Multifocal dense infiltrates of mast cells (≥15 mast cells in aggregates) detected in sections of bone marrow and/or other extracutaneous organ(s)

- **Minor criteria**

  1. In biopsy sections of bone marrow or other extracutaneous organs,

     >25% of the mast cells in the infiltrate are spindle-shaped or have atypical morphology or

     >25% of all mast cells in bone marrow aspirate smears are immature or atypical

  2. Detection of an activating point mutation at codon 816 of KIT in the bone marrow, blood or another extracutaneous organ

  3. Mast cells in bone marrow, blood or another extracutaneous organ express CD25, with or without CD2, in addition to normal mast cell markers

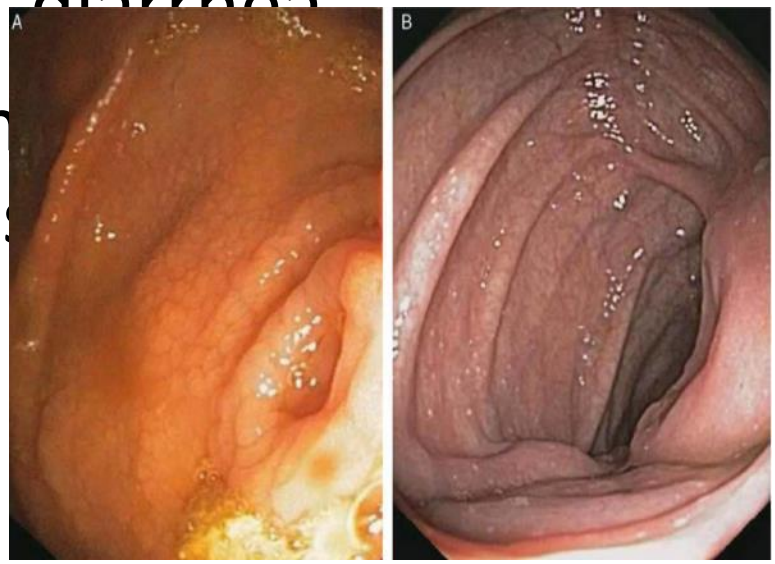
  4. Serum total tryptase is persistently >20 ng/mL, unless there is an associated myeloid neoplasm, in which case this parameter is not valid

Revised criterion from 2008 WHO

Systemic Mastocytosis Involving GI Tract

- Gastrointestinal involvement by SM is seen in 70% to 80% of SM
- Symptoms related to GI involvement are often nonspecific:

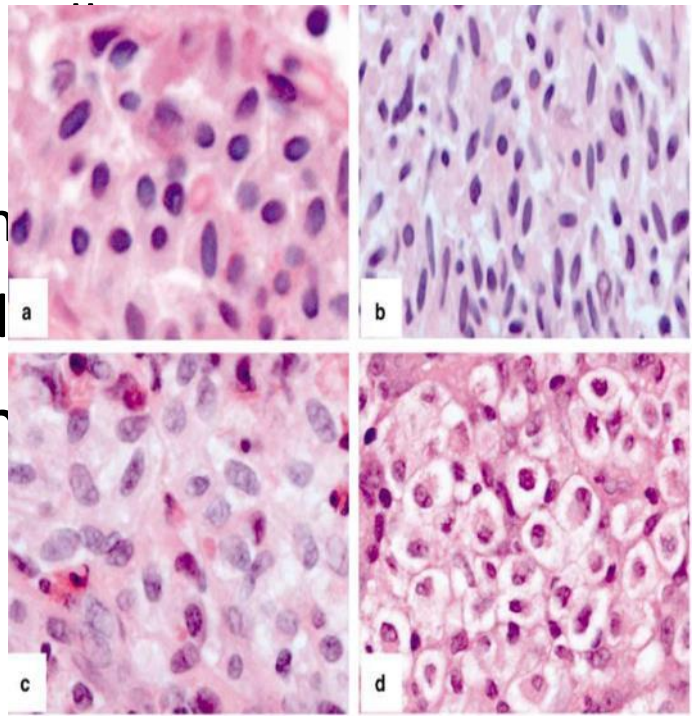
  abdominal pain or diarrhea
- Endoscopic findings: n
  erythema, loss of fold



Behdad A et al. Arch Pathol Lab Med. 2013;137(9):1220-3
Kirsch R et al. Mod Pathol. 2008;

Histologic Features of SM in GI Tract

- Mast cell infiltration of the lamina propria
  - Small round cells resembling normal mast
  - Elongated or spindle-shaped cells
  - Plump or fusiform cells with pale eosinoph
  - Large, round cells with abundant pale to cl
- Marked eosinophilic infiltrate, wh obscure the mast cell infiltrate
- Mucosal architectural distortion



Behdad A et al. Arch Pathol Lab Med. 2013;137(9):1220-3
Kirsch R et al. Mod Pathol. 2008; 21(12):150
16

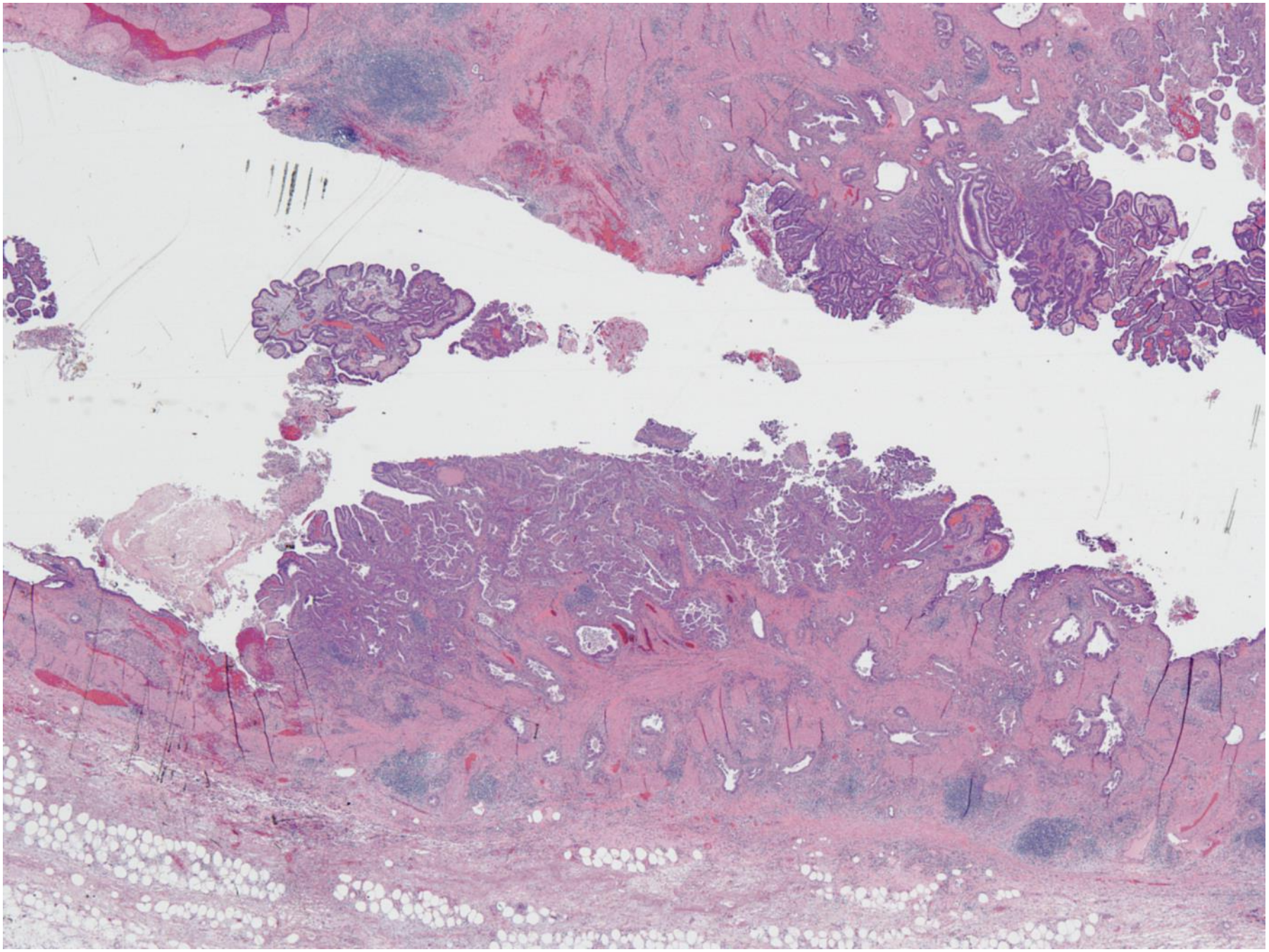
Take Home Messages

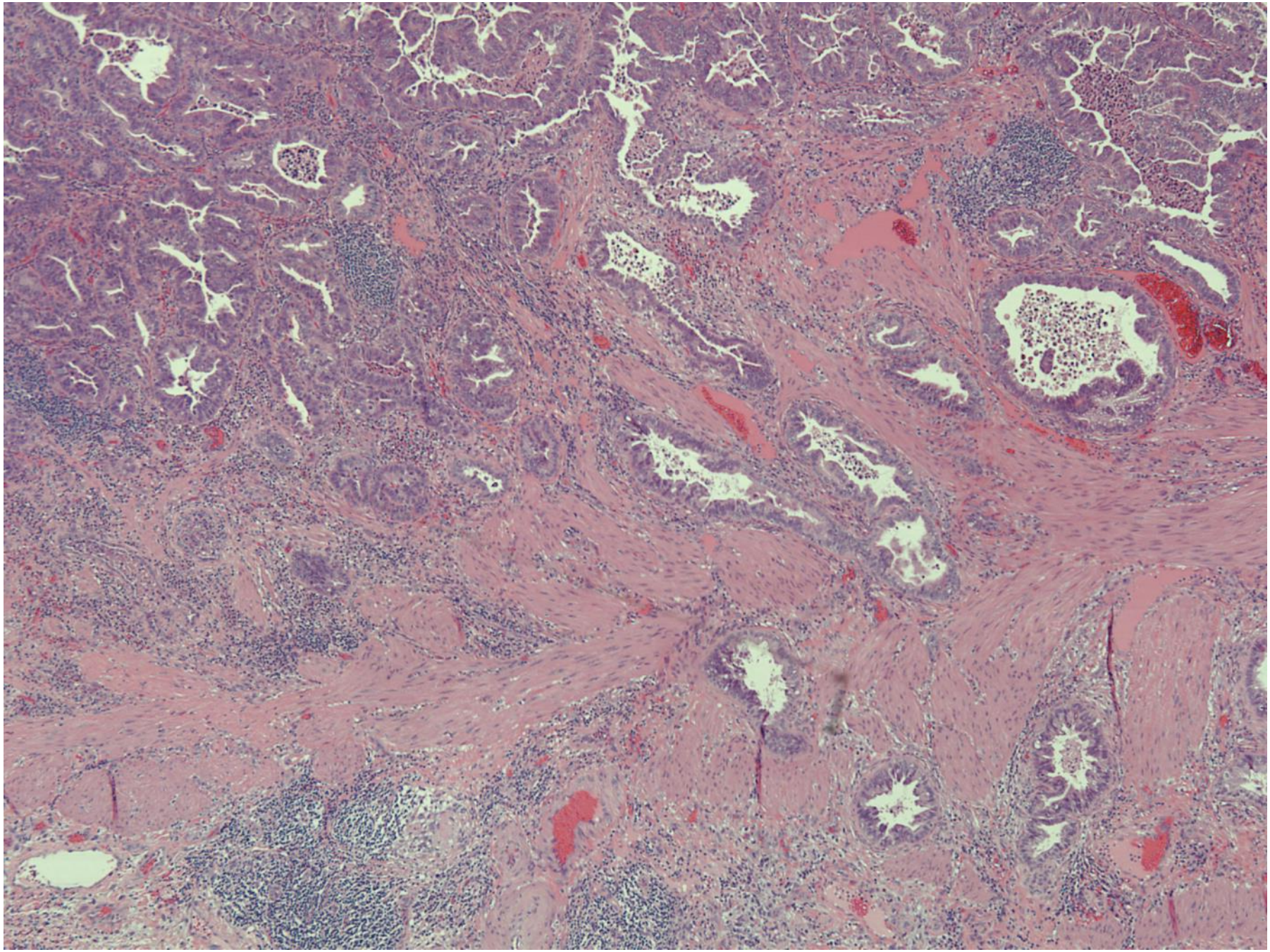
- SM in GI tract is characterized by a spectrum of findings that may be mistaken for eosinophilic colitis, histiocytic infiltrates or inflammatory bowel disease.
- High index of suspicion in GI biopsies with these features, especially in patient with prolonged, unexplained symptoms.
- CD117, CD25 immunostains and *Kit* mutation analysis can be helpful.

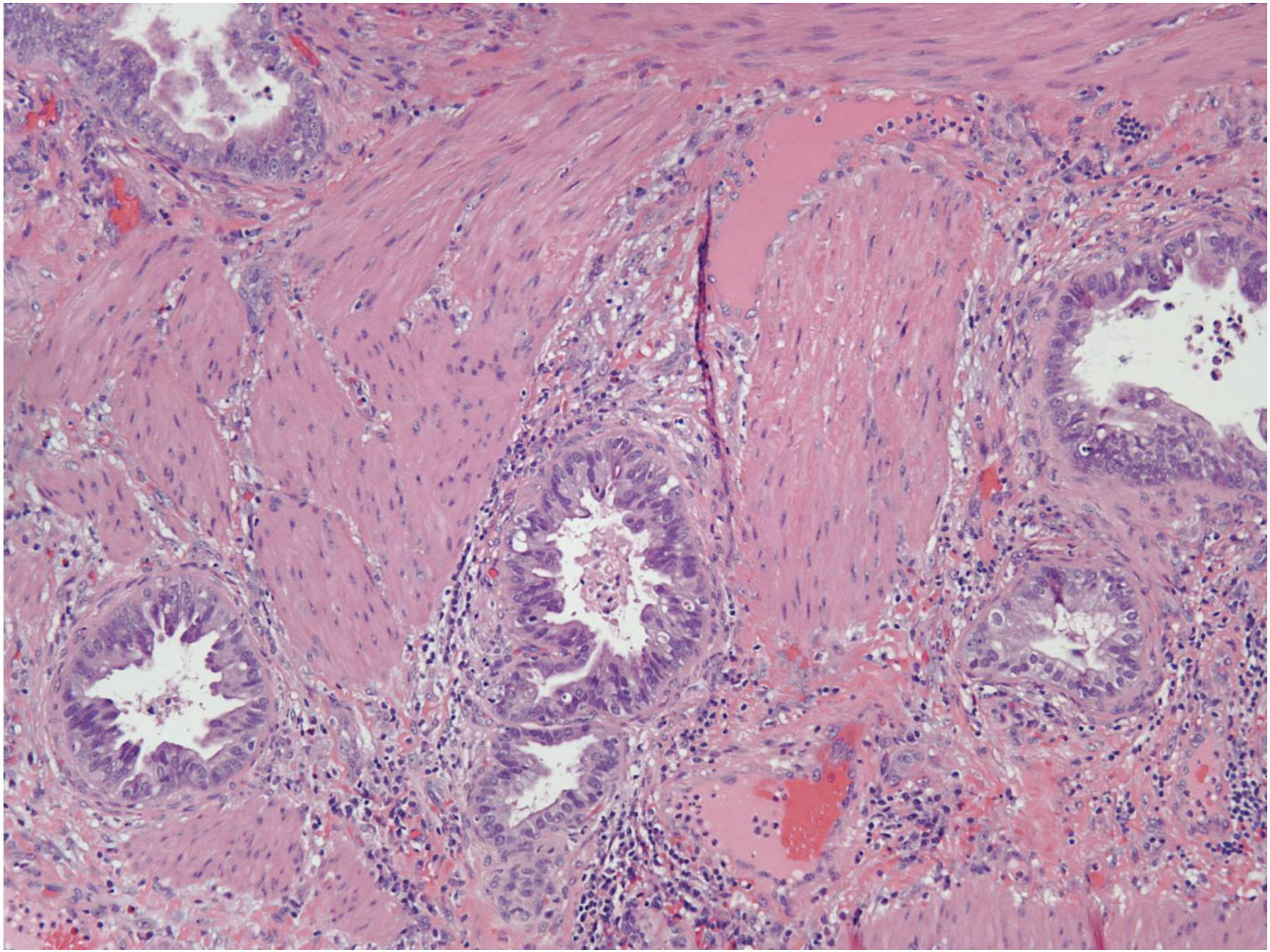
SB 6330

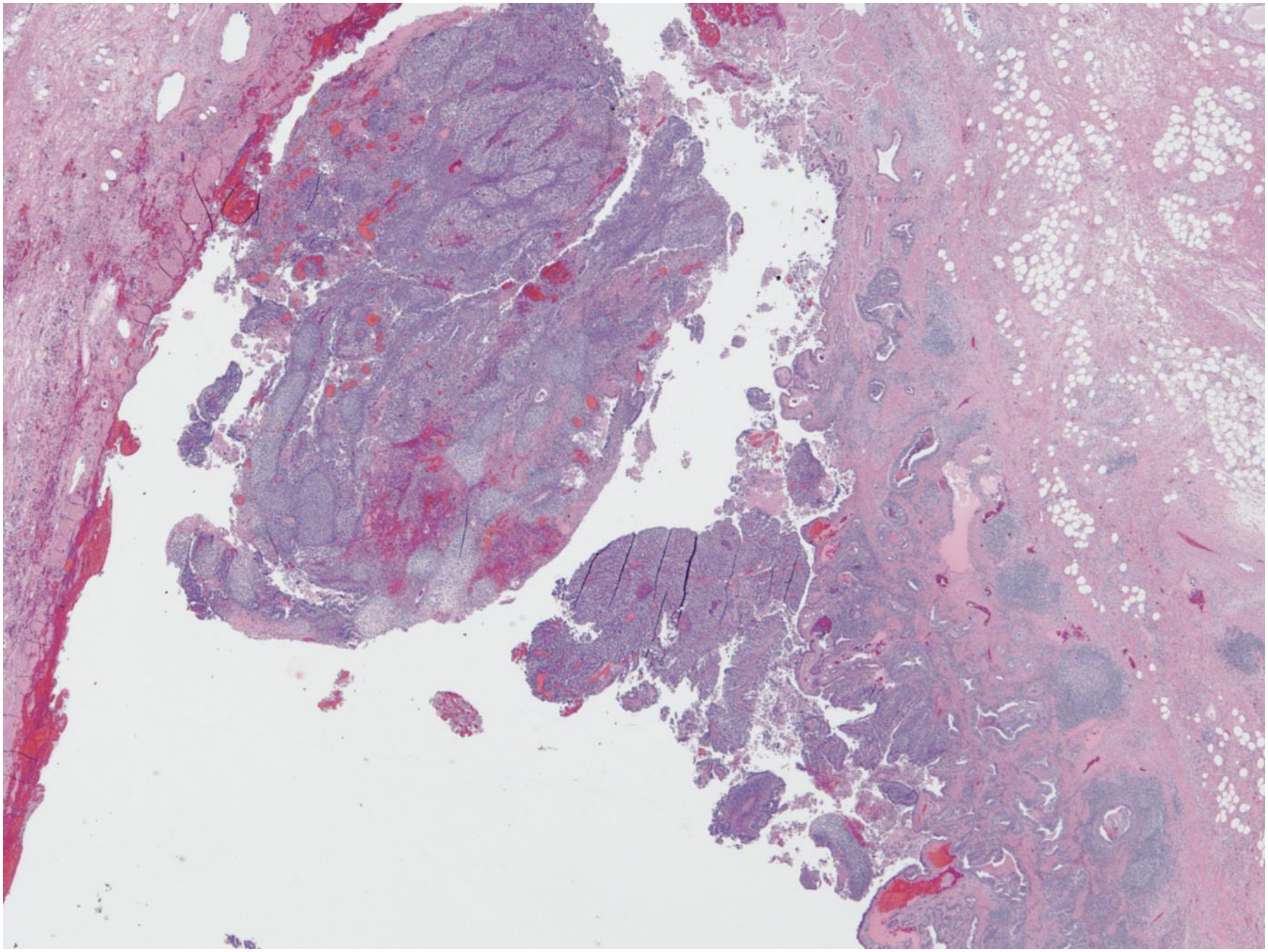
Hannah Wang/David Bingham; Stanford

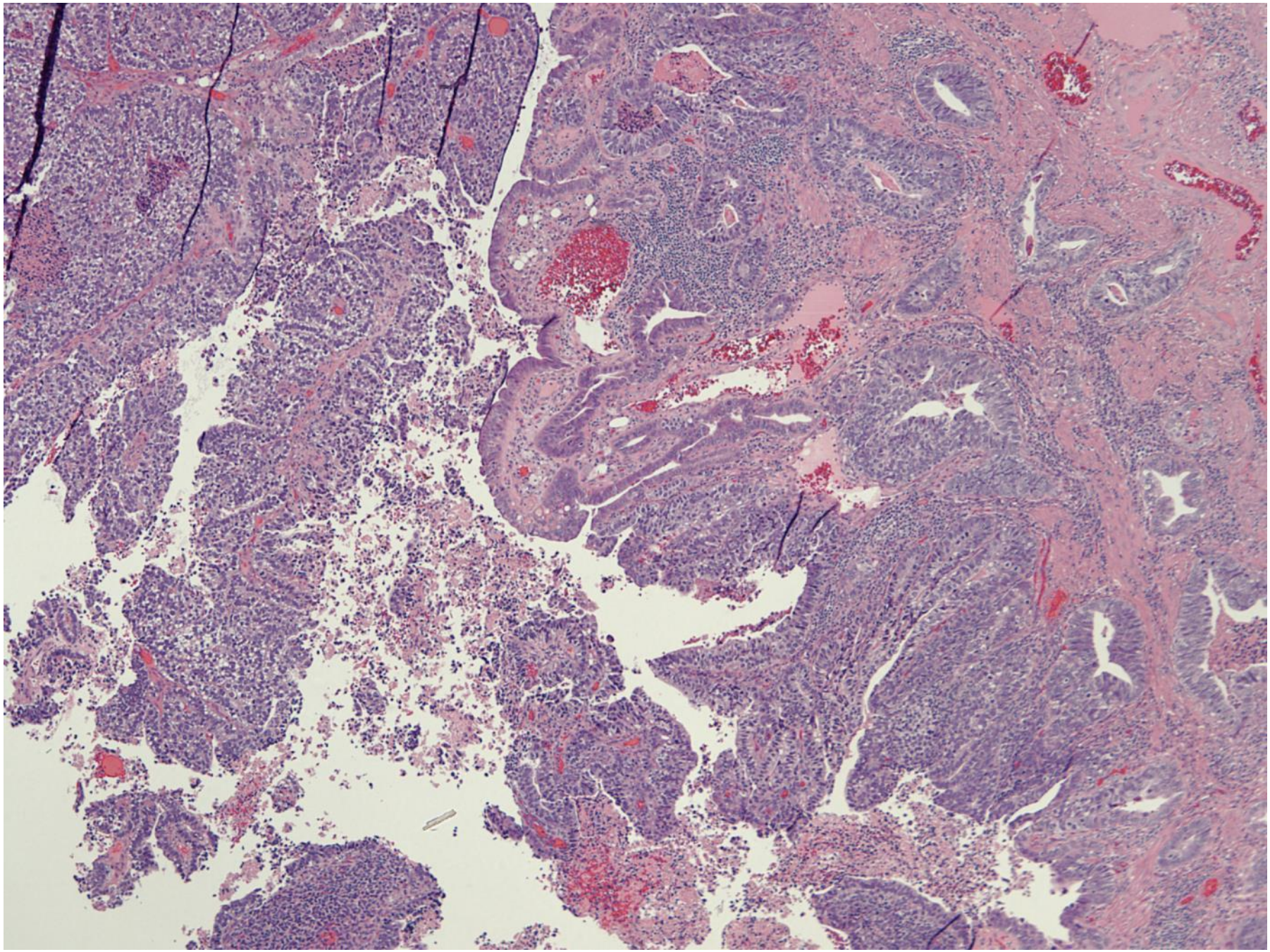
70-year-old male with acute severe postprandial RUQ pain. Imaging revealed 5cm fungating mass in proximal body of gallbladder.

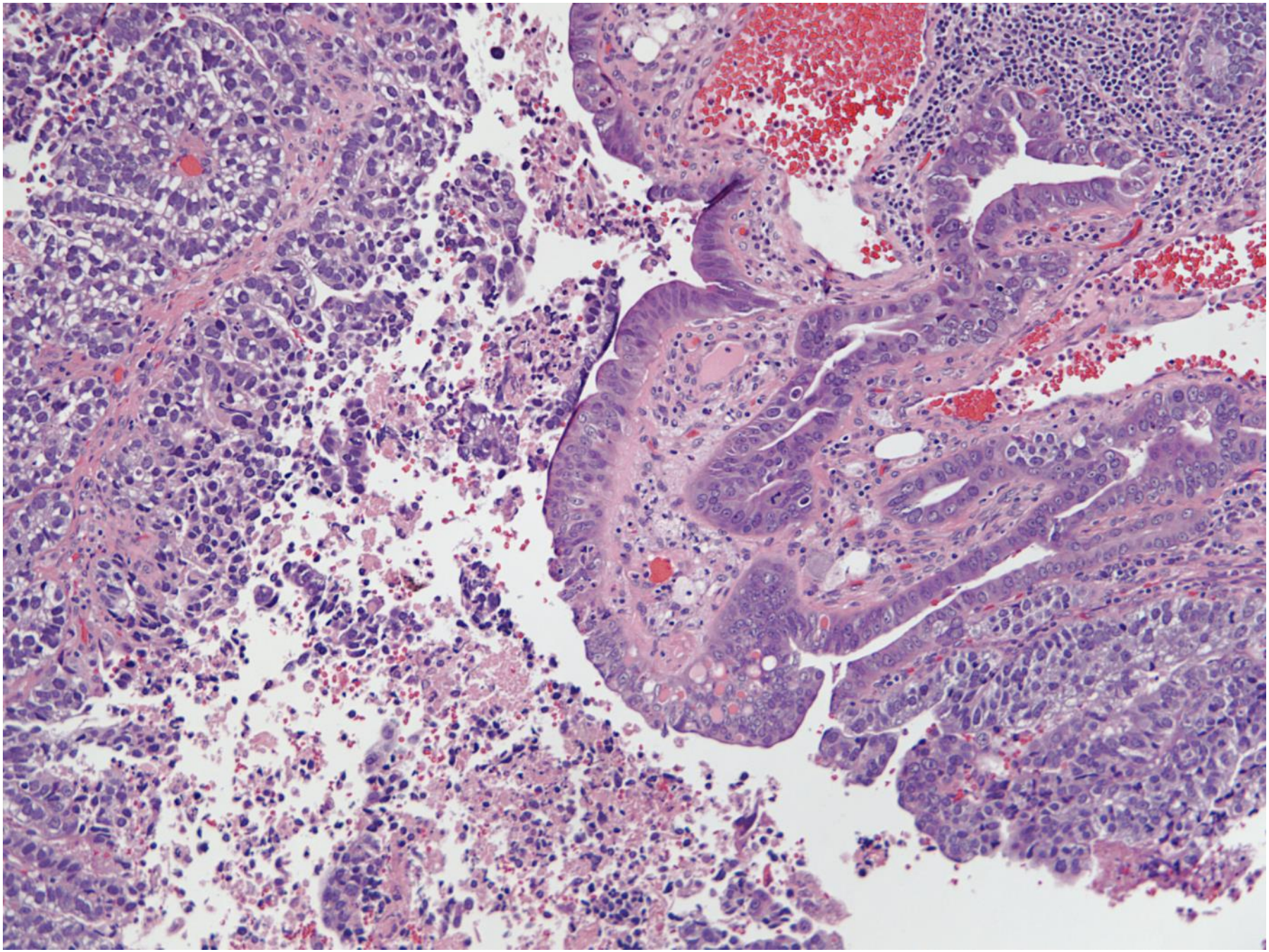


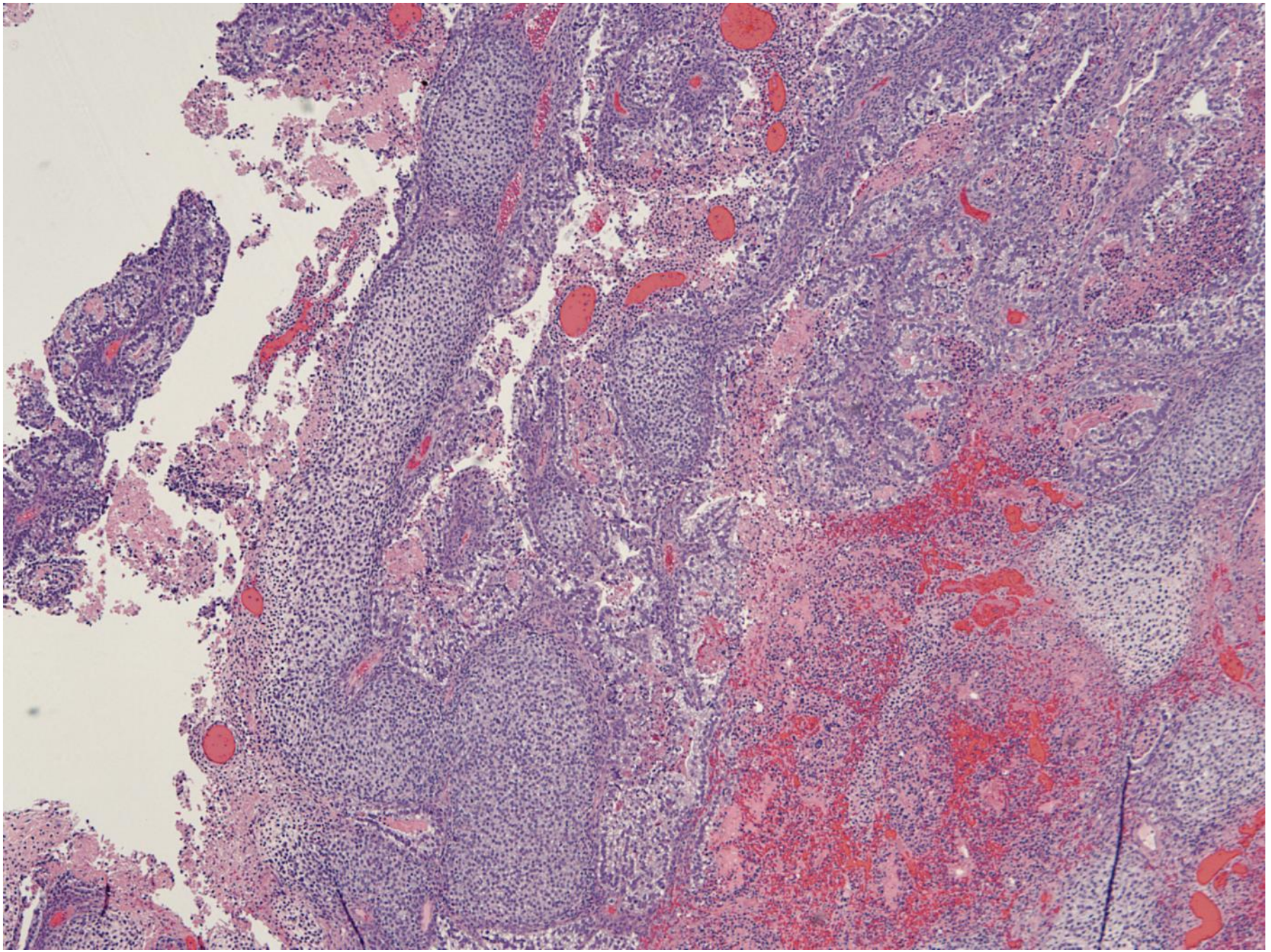


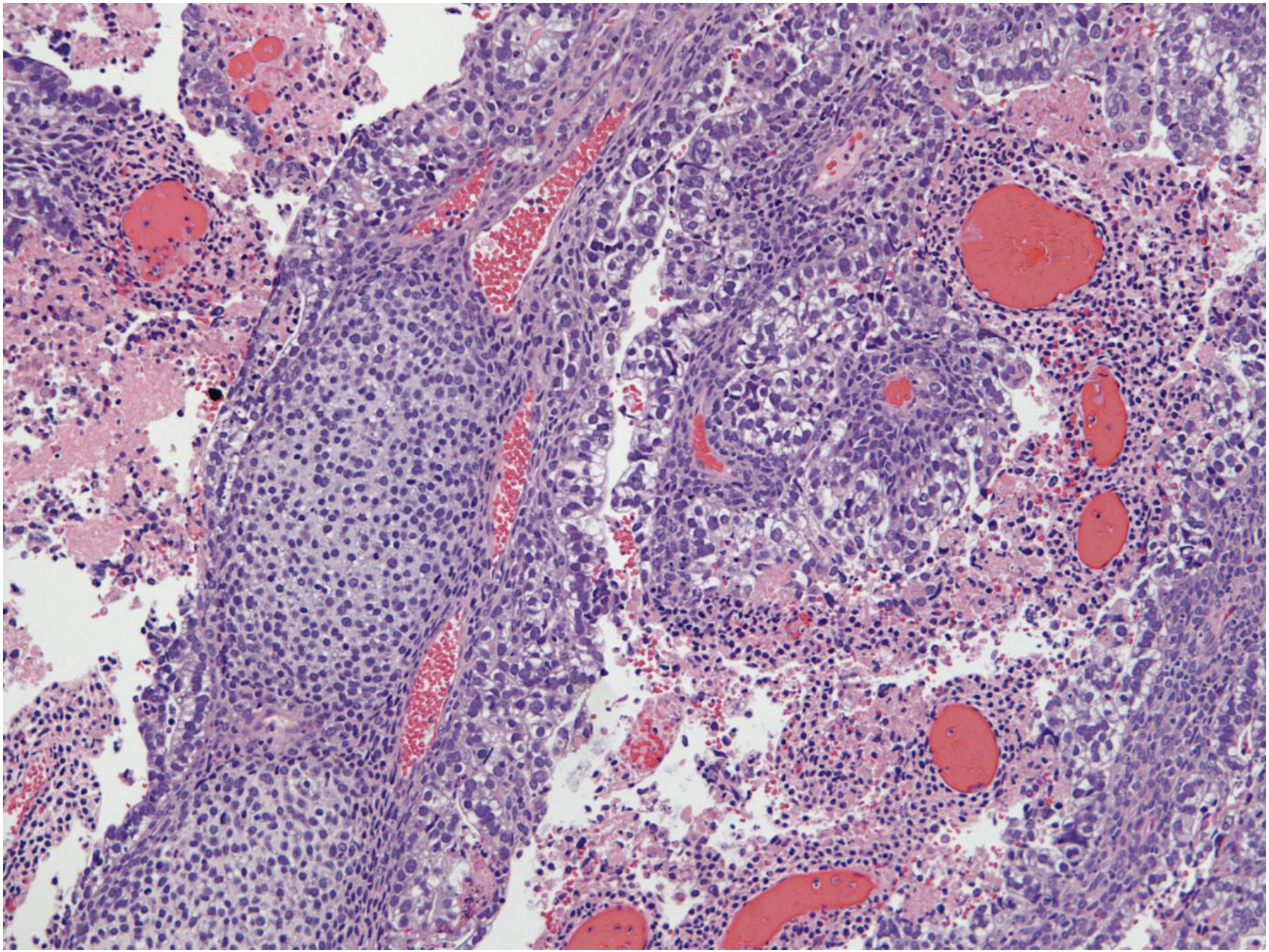


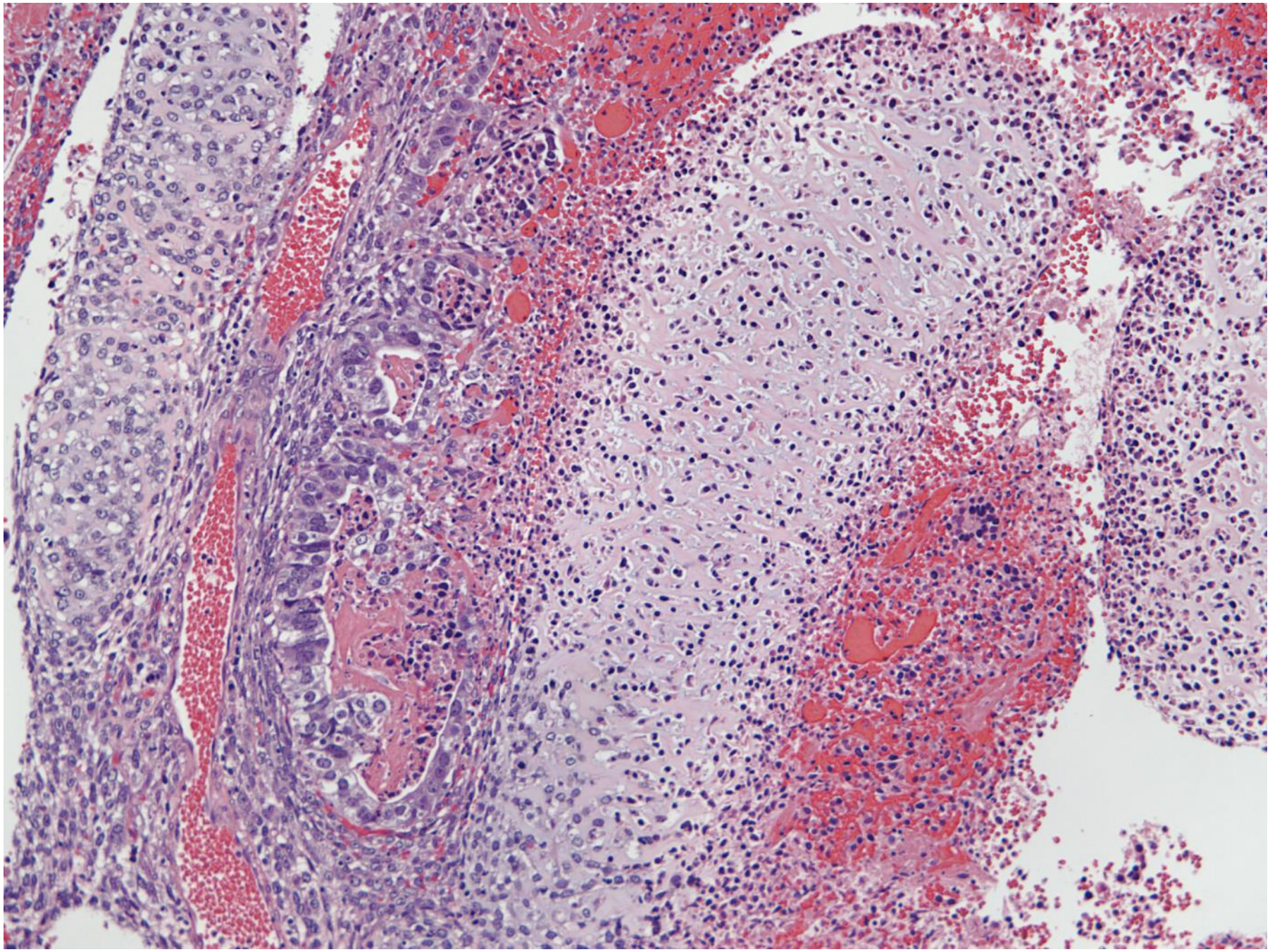












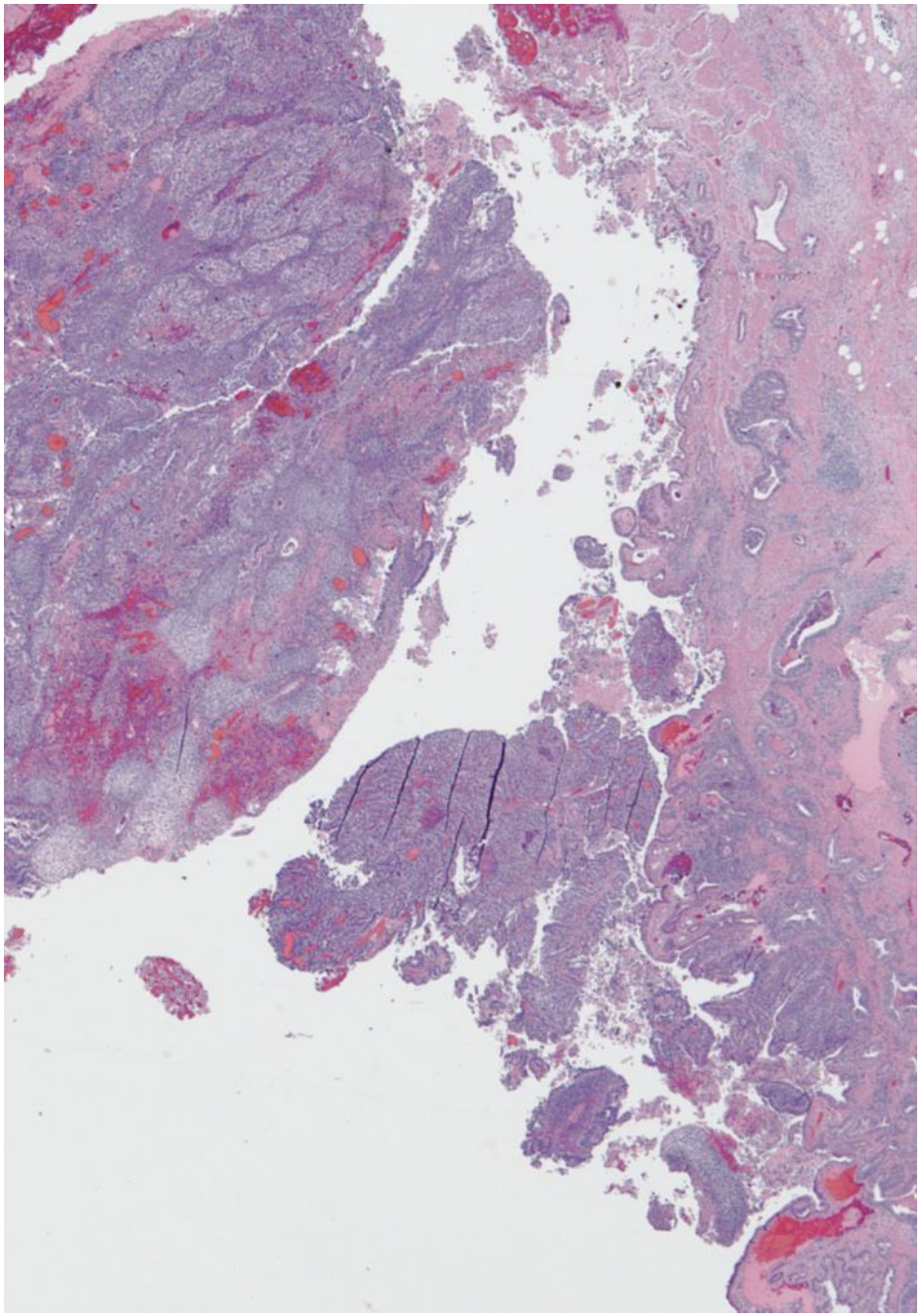
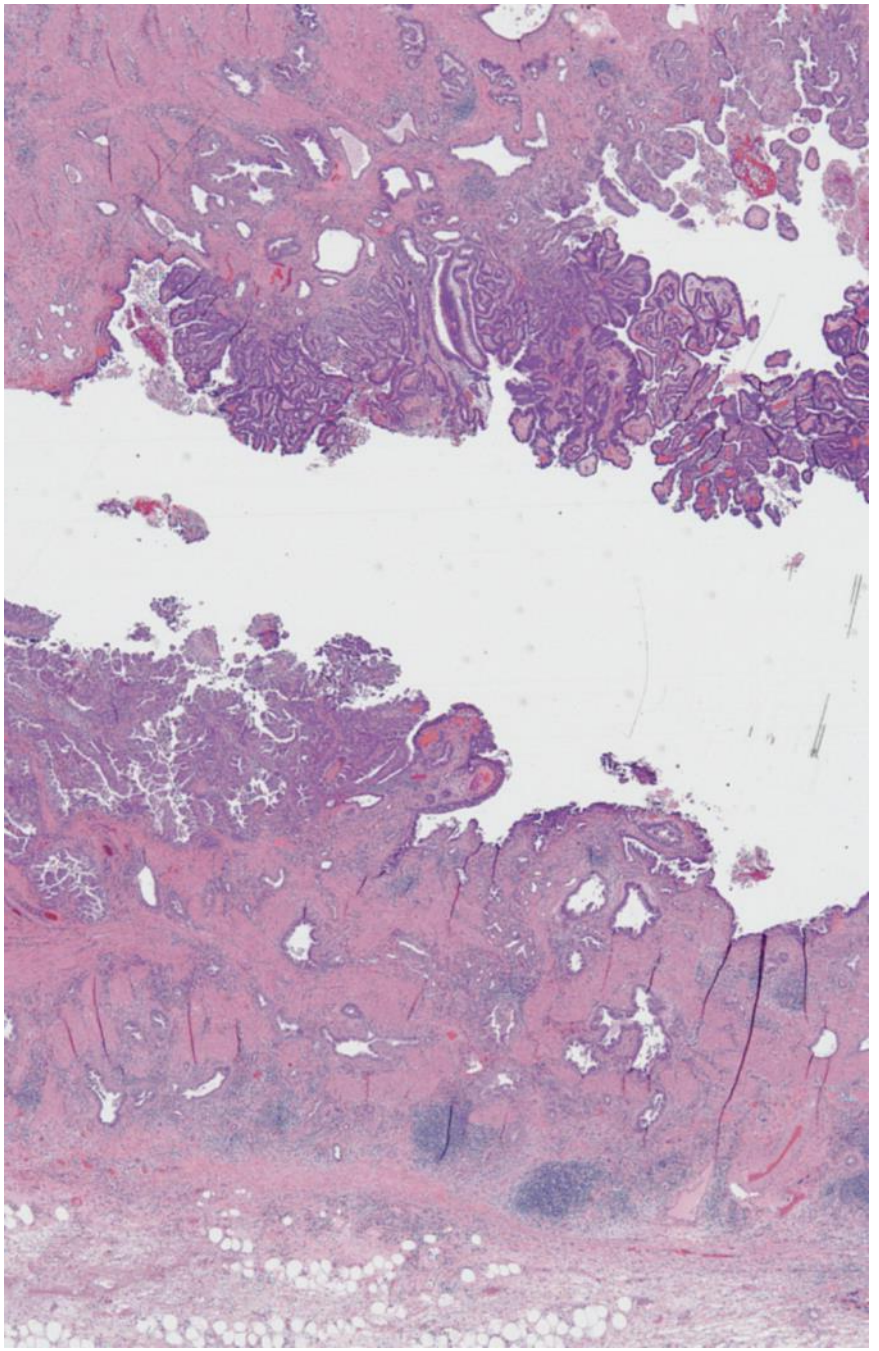
DIAGNOSIS?

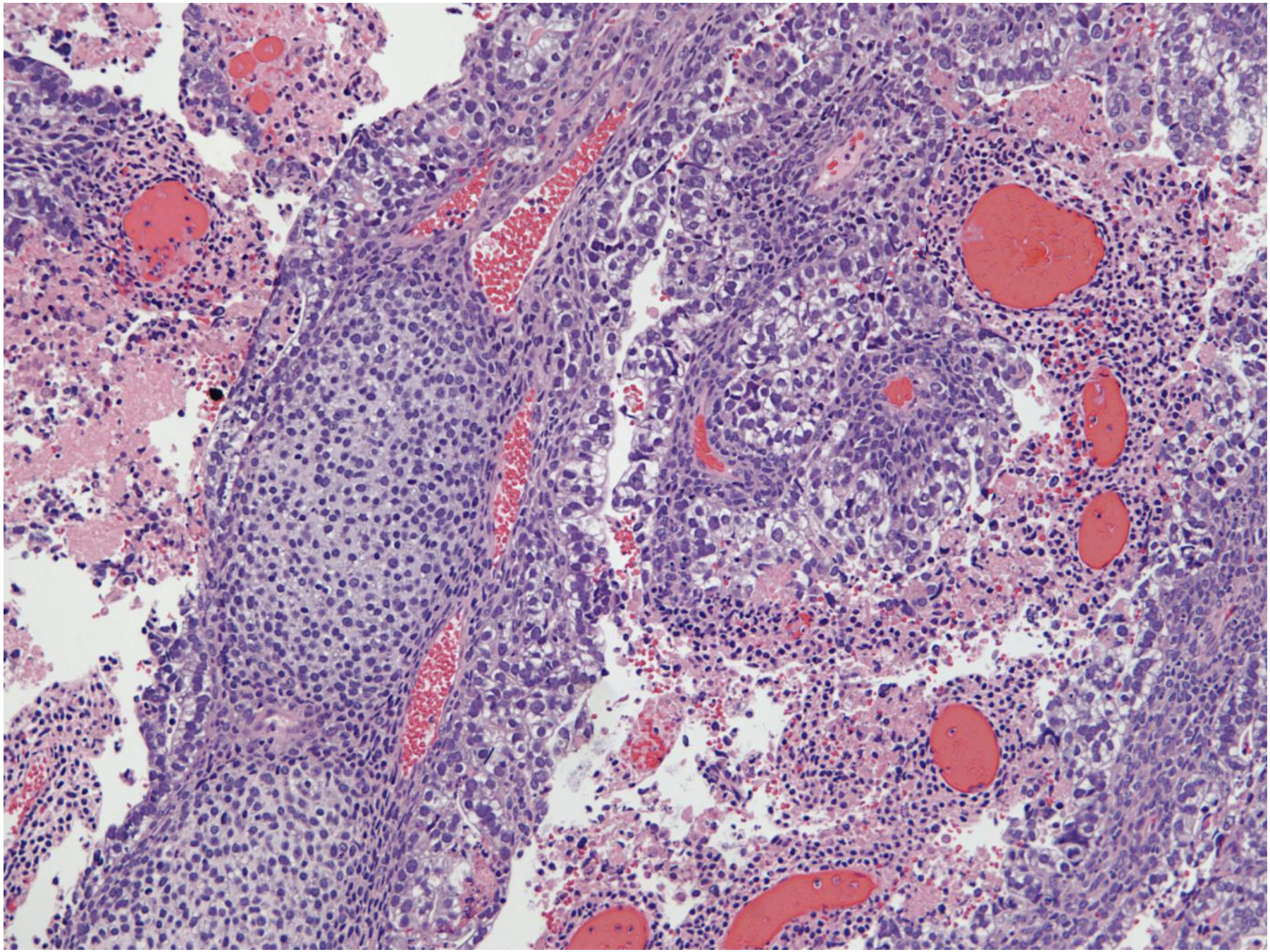
Diagnosis

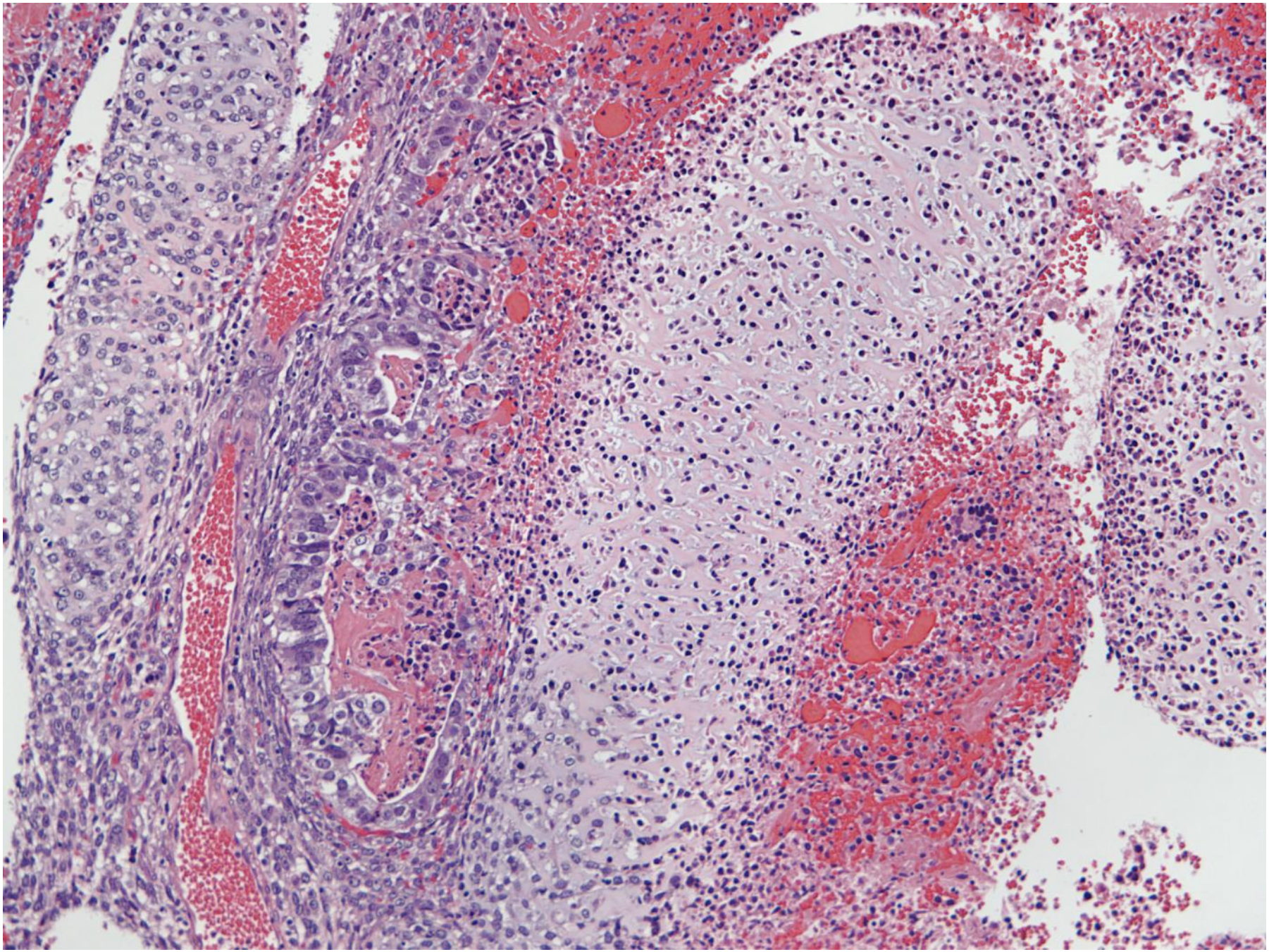
Carcinosarcoma, arising within intracholecystic papillary-tubular neoplasm (ICPN)

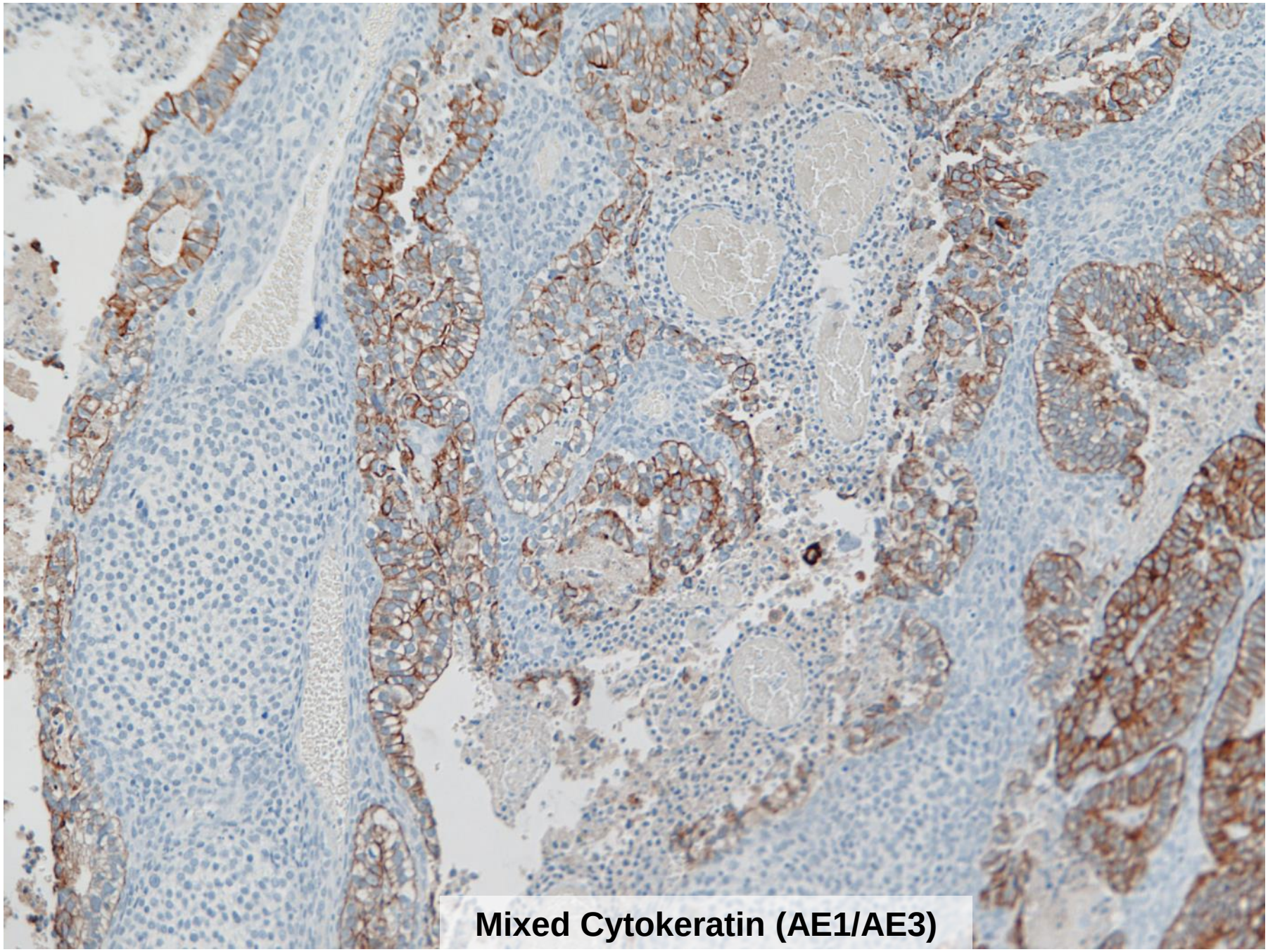
Invasive into perimuscular connective tissue on hepatic side without liver involvement (pT2b)

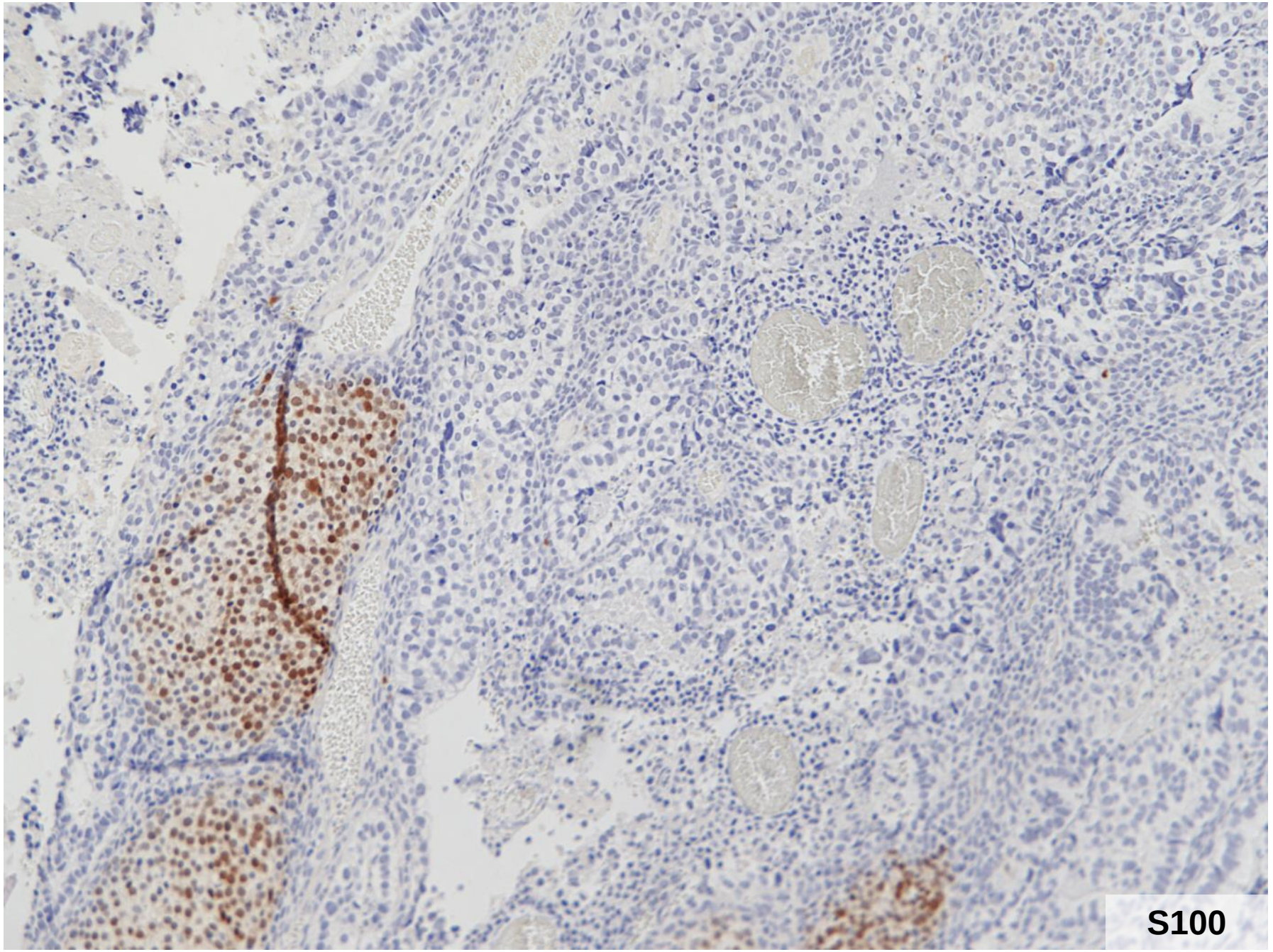
Nineteen negative hepatoduodenal lymph nodes (pN0)






Mixed Cytokeratin (AE1/AE3)


S100

Carcinosarcoma of the Gallbladder

Rare malignant neoplasm in this site (<1%)

Many have a papillary component grossly

Unknown whether this represents collision tumor, dedifferentiation, or origin from single pluripotent stem cell

Largest study by Okabayashi et al. 2009 (n=36)

- Sex: 2.6:1 (M:F)
- Mean age: 67.7 (range 45-90)
- Mean size: 8.4 cm (range 2.5 to 16 cm)
- No specific radiographic findings

Okabayashi T et al. Surgical outcome of carcinosarcoma of the gallbladder: A review. World J Gastroenterol. 2009 Oct 21; 15(39): 4877-4882

Carcinosarcoma of the Gallbladder

Malignant epithelial and mesenchymal components

Epithelial: Adenocarcinoma most common, then squamous

Mesenchymal:

Table 2. Mesenchymal cell characteristics of carcinosarcoma of the gallbladder: a review of the literature[6–45]

	Mesenchymal elements			
	Chondro-sarcoma	Osteo-sarcoma	Rhabdomyo-sarcoma	Spindle-cell carcinoma
Number of cases[a]	18	9	5	29
Age (mean; years)	70.3	64.4	64.3	68.5
Sex (M/F)	5/13	2/7	1/4	5/24
Median postoperative survival (months)[b]	4	4	NC	6

NC, Median survival could not be calculated
[a]Repetition exists
[b]Restricted to cases mentioned in the follow-up data

Ajiki T et al. *Carcinosarcoma of the gallbladder with chondroid differentiation.* J Gastroenterol. 2002;37(11):966-71.

Table 2 Clinical characteristics after surgical resection for carcinosarcoma of the gall bladder

Characteristics	*n*	Survival rate (%)			Median survival in months (range)	*P* value
		1 yr	2 yr	3 yr		
Overall	36	37.2	31.0	31.0	7.0 (4.4-9.6)	
Age (yr)						
< 65	14	37.7	18.9	18.9	5.0 (0.3-9.7)	0.887
> 65	22	36.7	36.7	36.7	7.0 (4.2-9.8)	
Gender						
Male	10	36.0	24.0	24.0	6.0 (0.3-13.7)	0.877
Female	26	37.5	37.5	37.5	6.0 (3.3-8.7)	
Palpable mass						
Present	14	48.0	48.0	48.0	7.0	0.853
Absent	11	47.6	23.8	23.8	8.0 (0.0-16.9)	
Stone						
Present	10	40.0	-	-	7.0 (3.2-10.8)	0.937
Absent	20	42.1	33.7	33.7	7.0 (3.4-10.6)	
Size of the tumor (cm)						
< 5	8	60.0	60.0	60.0	-	0.361
> 5	21	36.6	24.4	24.4	7.0 (5.1-8.9)	
Si or organ invasion						
Present	18	9.2	0.0	0.0	4.0 (2.2-5.8)	0.001
Absent	10	88.9	88.9	88.9	-	
Scc component						
Present	8	28.6	14.3	-	4.0 (1.4-6.6)	0.291
Absent	16	31.2	31.2	31.2	7.0 (4.8-9.2)	
Stage						
II	10	87.5	87.5	87.5	-	0.001
III or IVa	18	13.8	0.0	0.0	4.0 (2.2-5.8)	
Changing trends						
1970-1989	12	45.5	30.3	-	4.0 (0.0-12.9)	0.920
1990-1999	10	44.4	44.4	-	7.0 (4.1-9.9)	
2000-2009	14	20.8	20.8	20.8	7.0 (4.8-9.2)	

Scc: Squamous cell carcinoma; Si: Serosal invasion; Stage: Classification according to International Union Against Cancer (UICC).

- Survival data for gallbladder adenocarcinoma is similarly dismal and stratifies similarly by stage
- Unknown whether adjuvant chemotherapy or radiation is effective
- Reports of local recurrence, liver metastases, and peritoneal dissemination of either component

Okabayashi T et al. Surgical outcome of carcinosarcoma of the gallbladder: A review. World J Gastroenterol. 2009 Oct 21; 15(39): 4877-4882

Patient Follow-up

Planned treatment with 4 weeks of chemotherapy (gemcitabine/xeloda) followed by 6 weeks radiation

At 4-week postoperative visit, CT with contrast showed:

1. Status post partial hepatectomy and cholecystectomy for patient's gallbladder cancer. Complex fluid in the resection bed noted. No definite evidence of residual disease.

2. 1.1 cm x 0.8 cm nodule in the gallbladder fossa/periportal region, either a lymph node or post-surgical changes. Attention on follow-up.