Disclosures
March 13, 2017

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

Presenters:

Oscar Silva, MD, PhD
Megan Troxell, MD, PhD
Erna Forgo, MD
Dita Gratzinger, MD, PhD
Balaram Puligandla, MD
Keith Duncan, MD, PhD
Allison Zemek, MD
Gerry Berry, MD
Peyman Samghabadi, MD
Donald Born, MD
Hannes Vogel, MD
Jonathan Lavezo, MD
Bart Singer, MD
Kimberly Allison, MD
Sunny Kao, MD

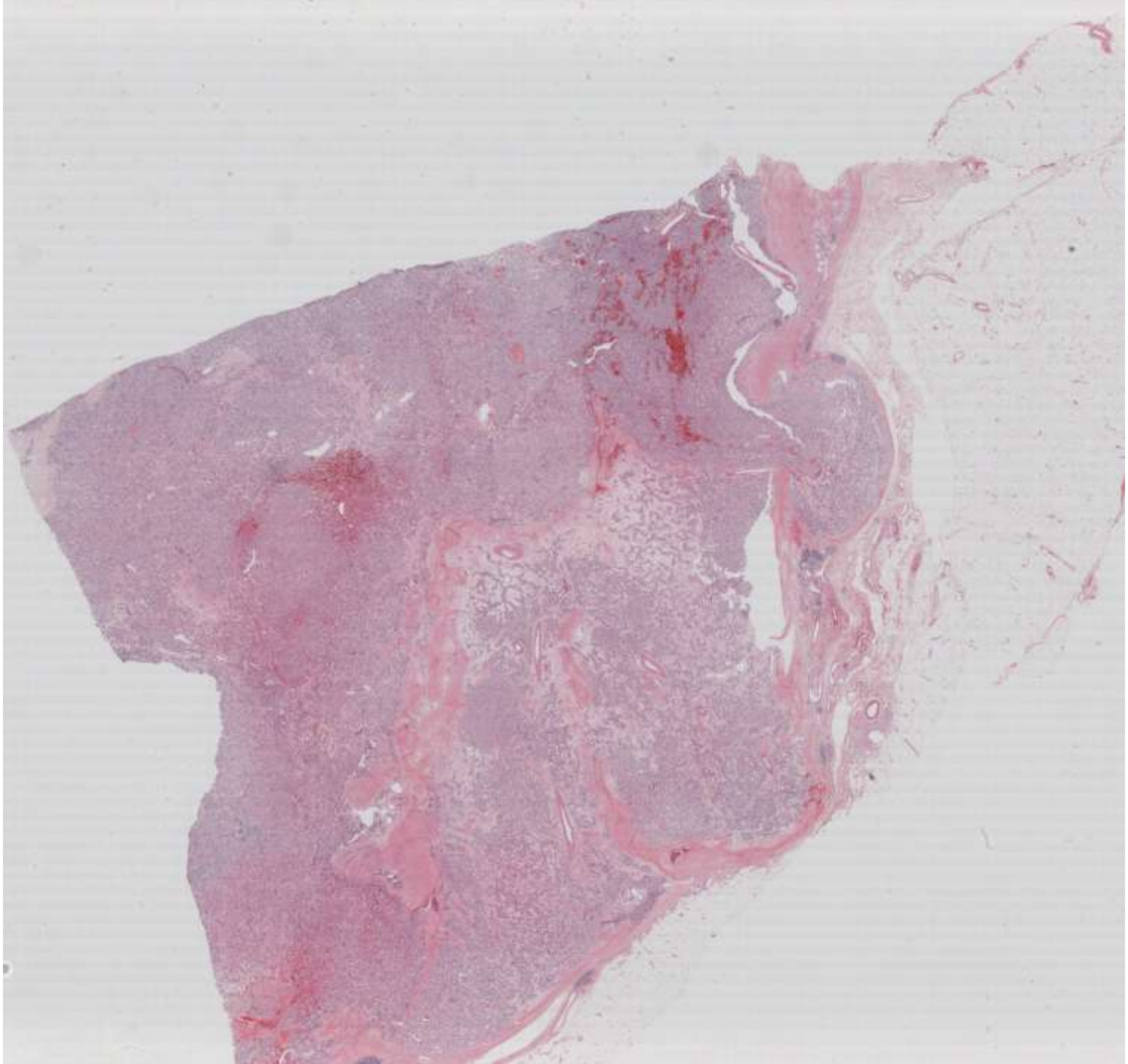
Activity Planners/Moderator:

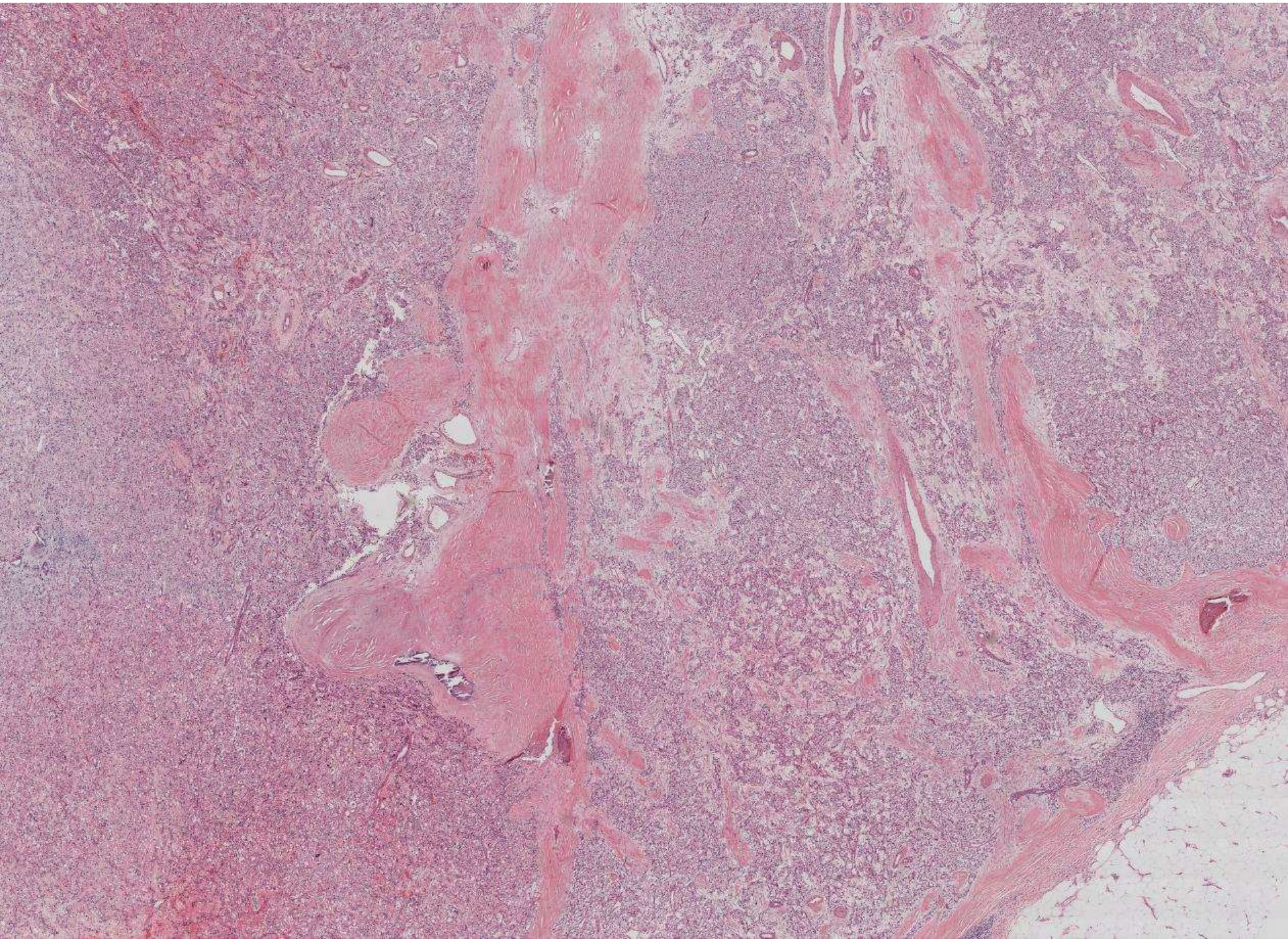
Kristin Jensen, MD
Ankur Sangoi, MD

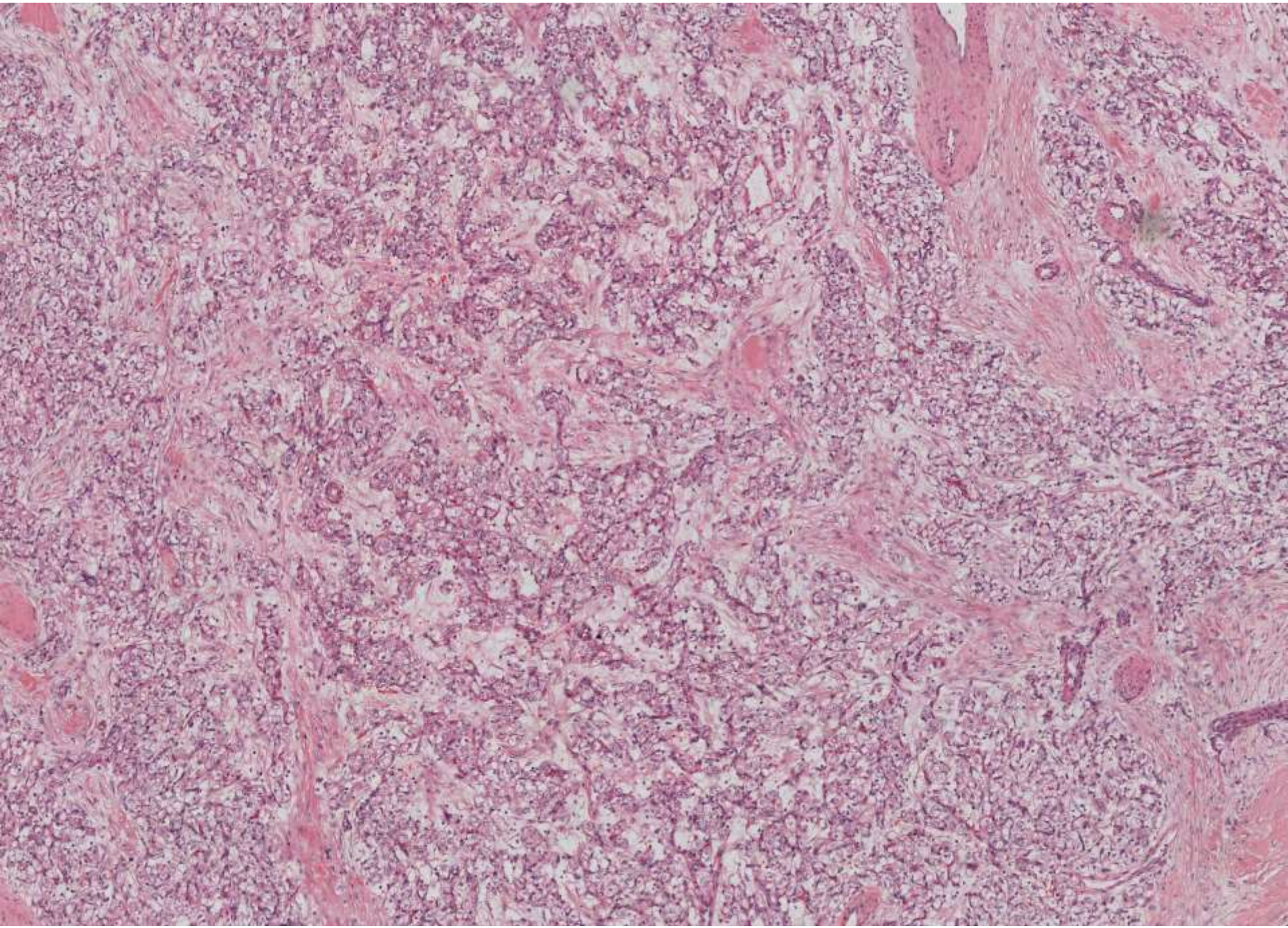
SB 6141
[scanned slide available]

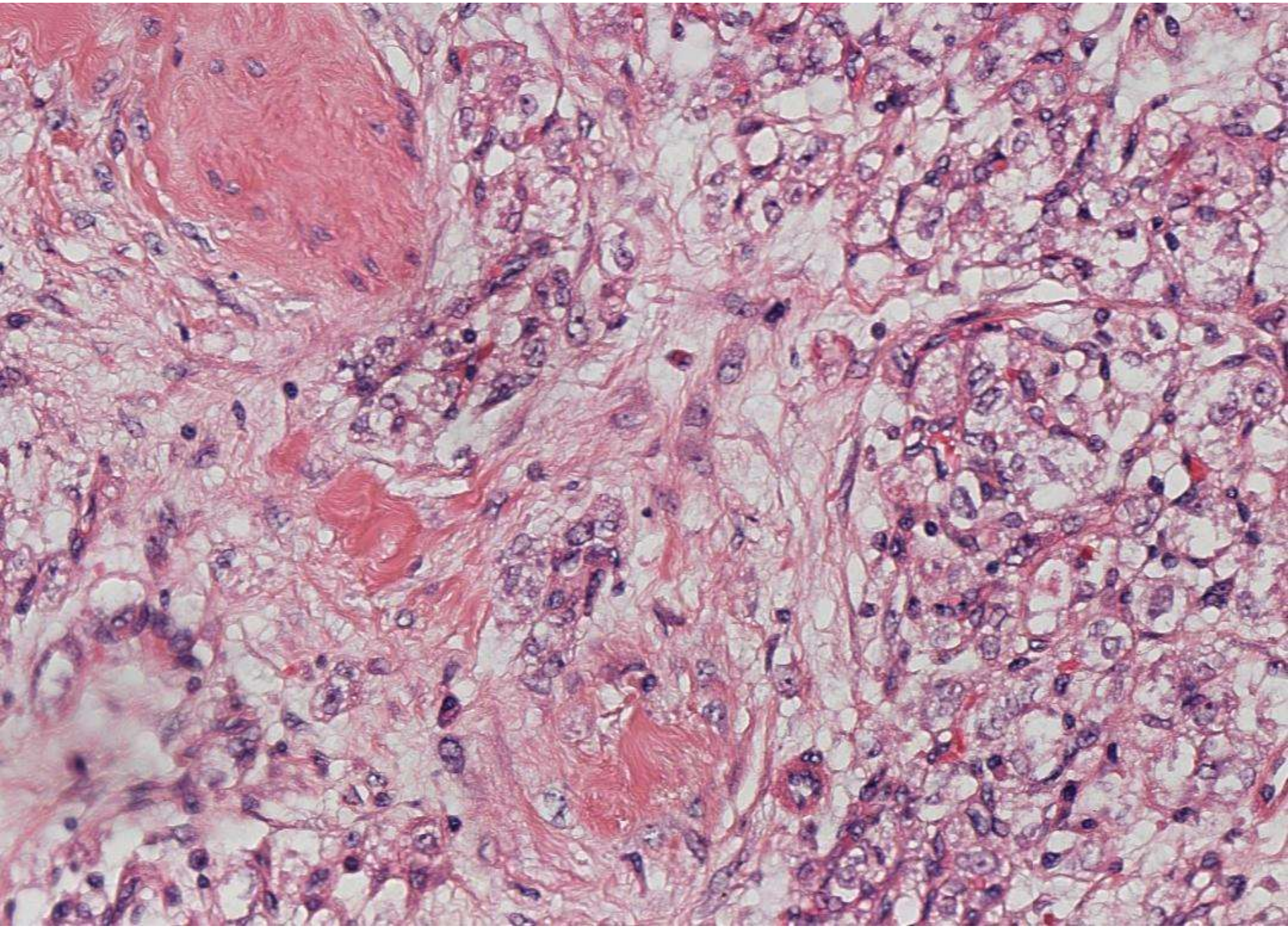
Oscar Silva/Megan Troxell; Stanford

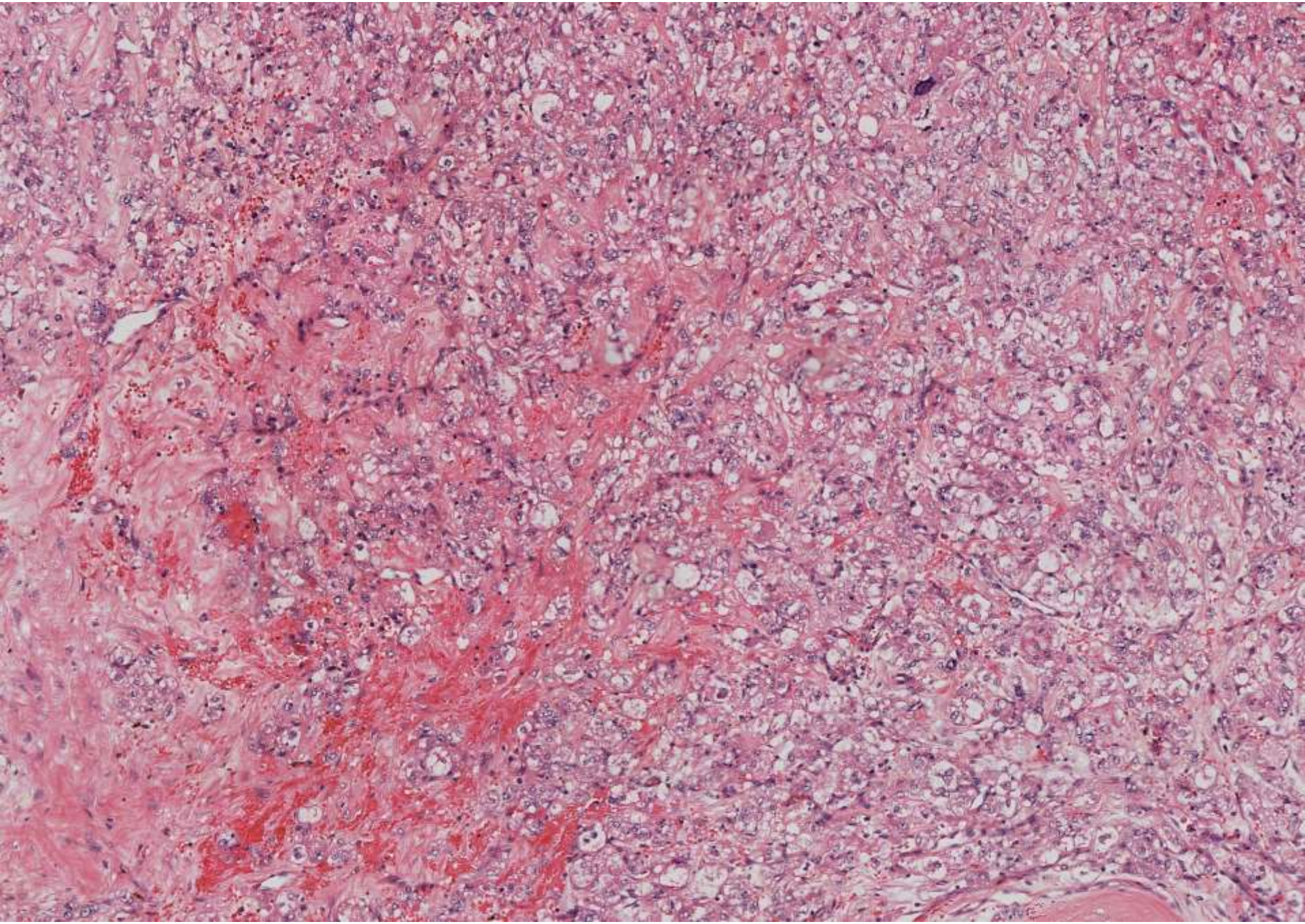
54-year-old F with left kidney mass, mid lower pole, 5.5cm.

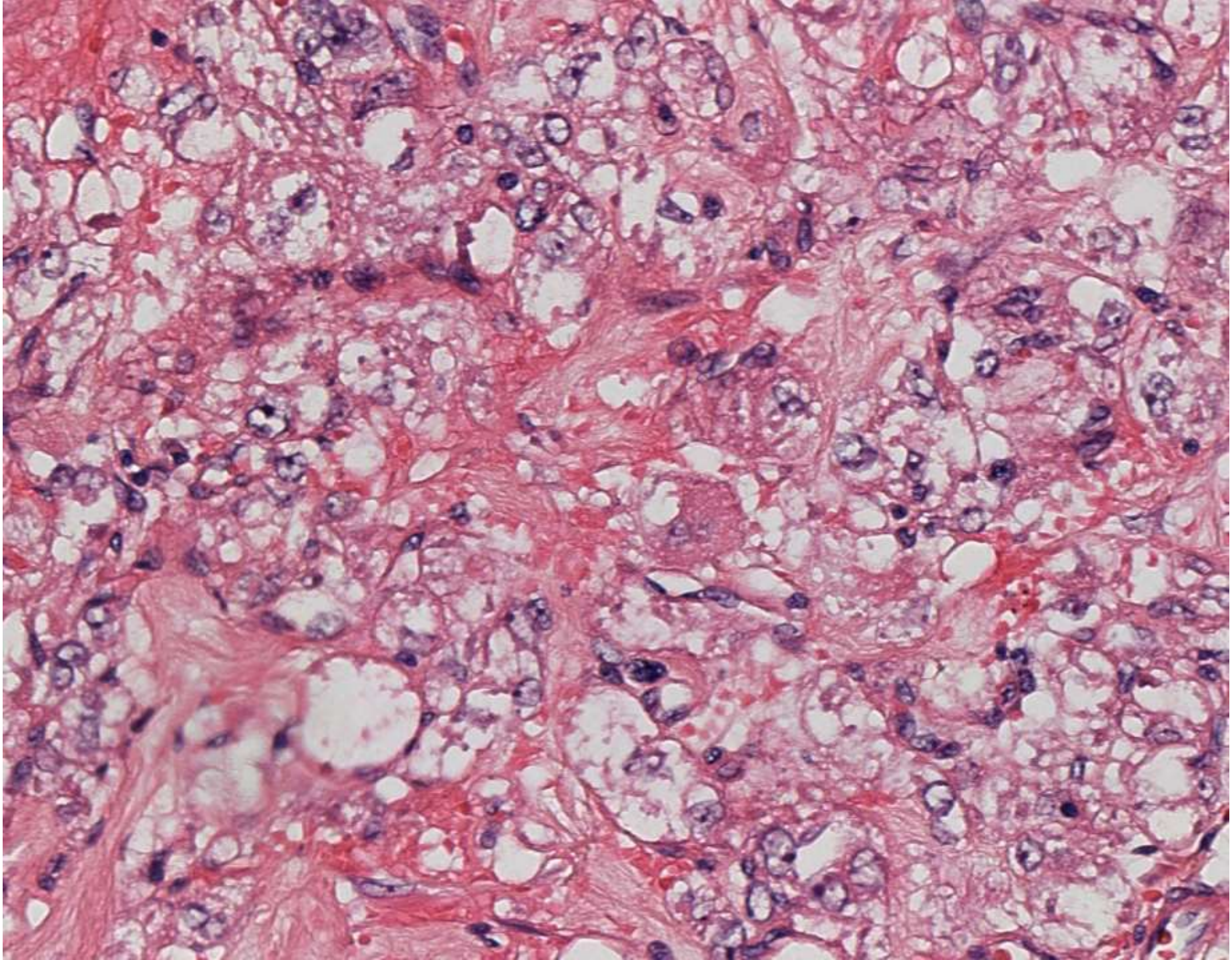


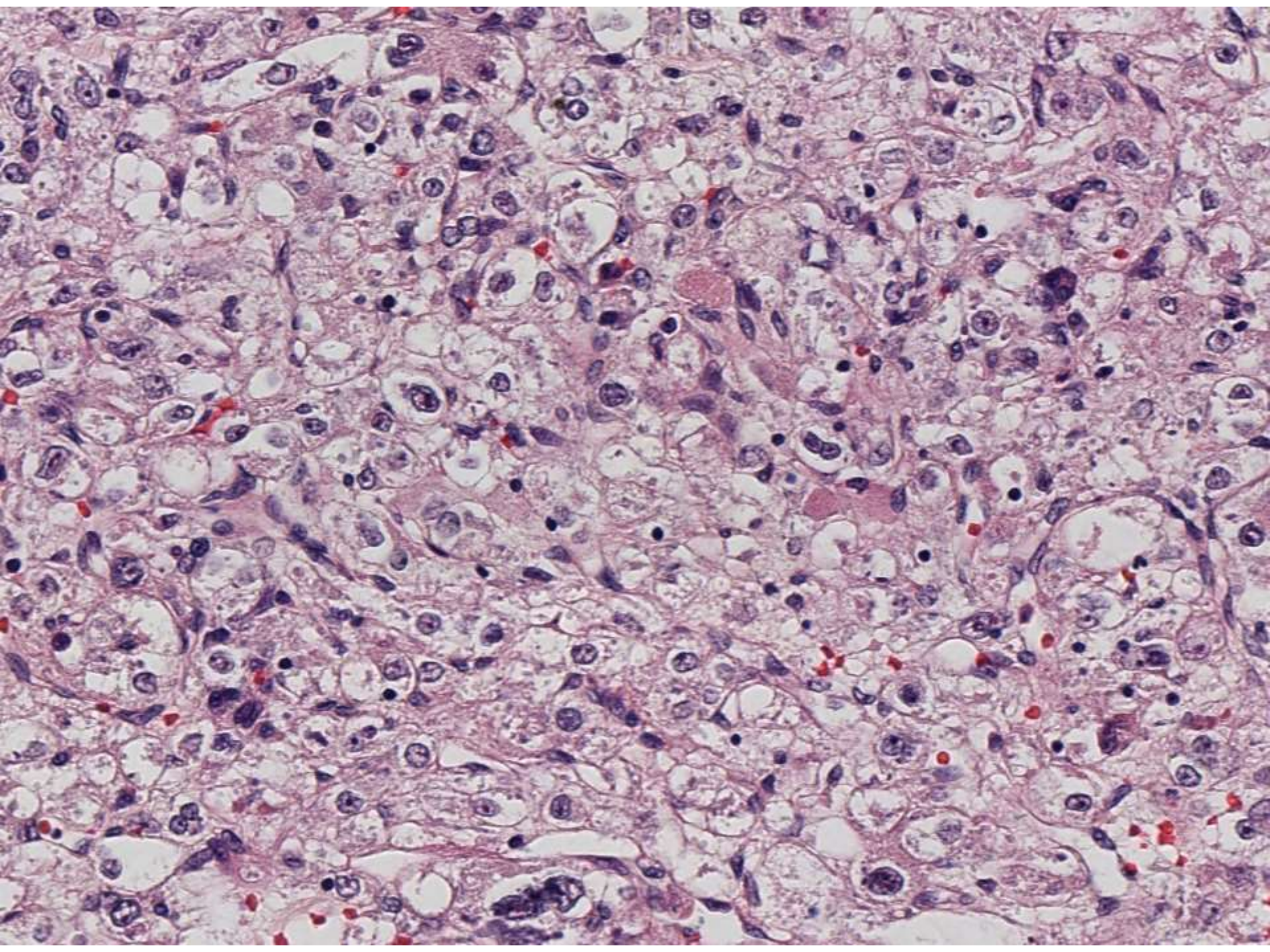


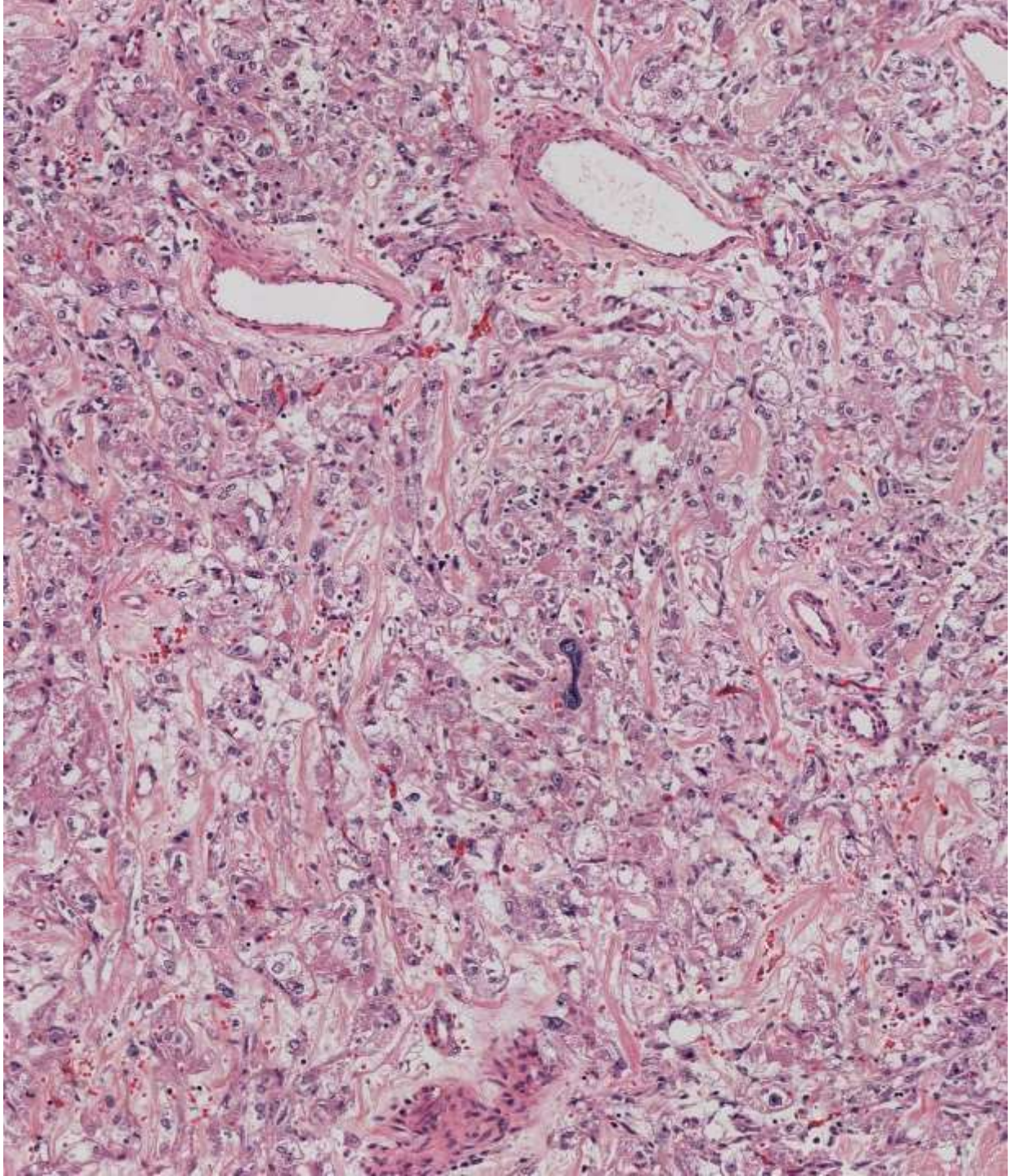


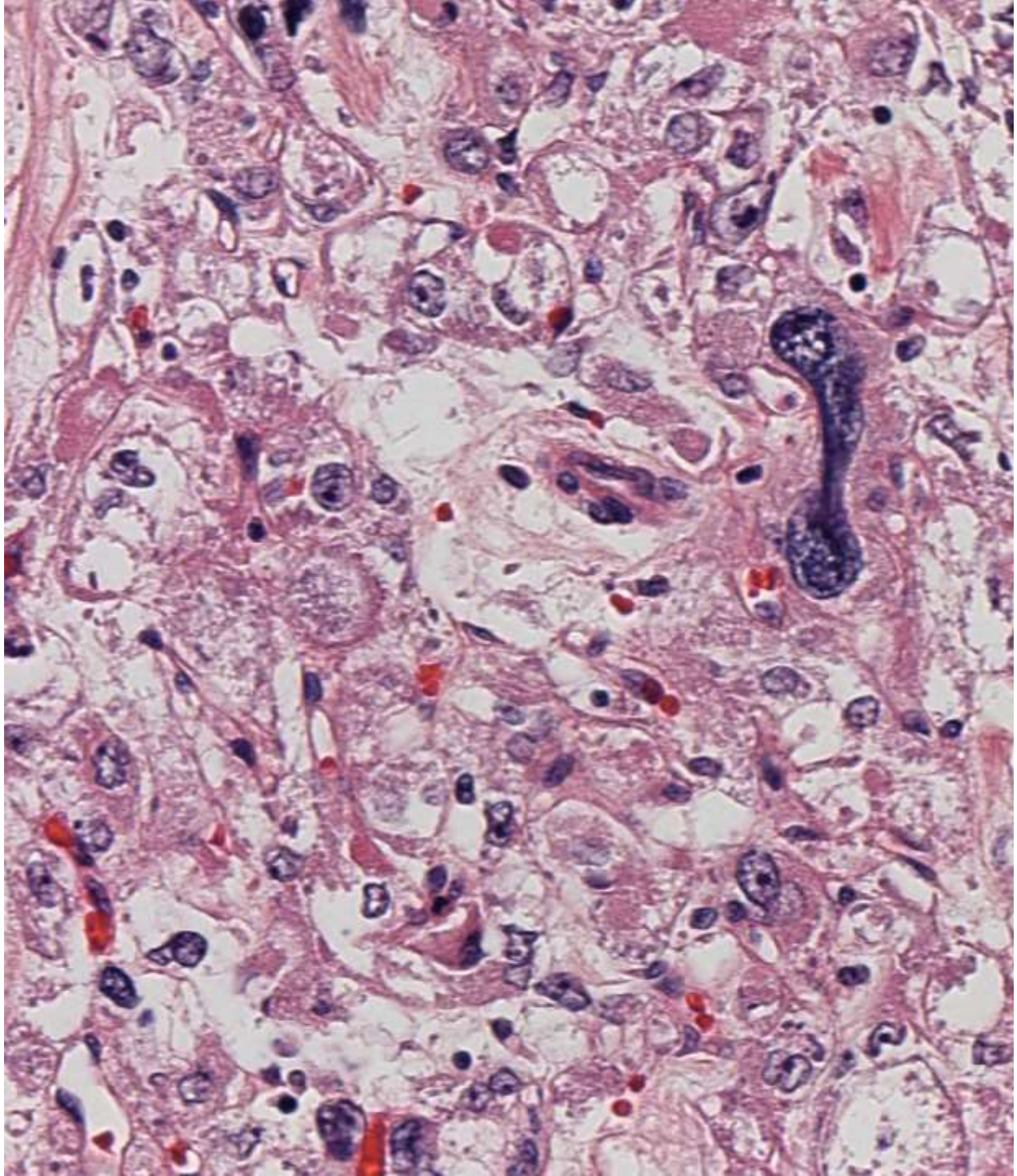






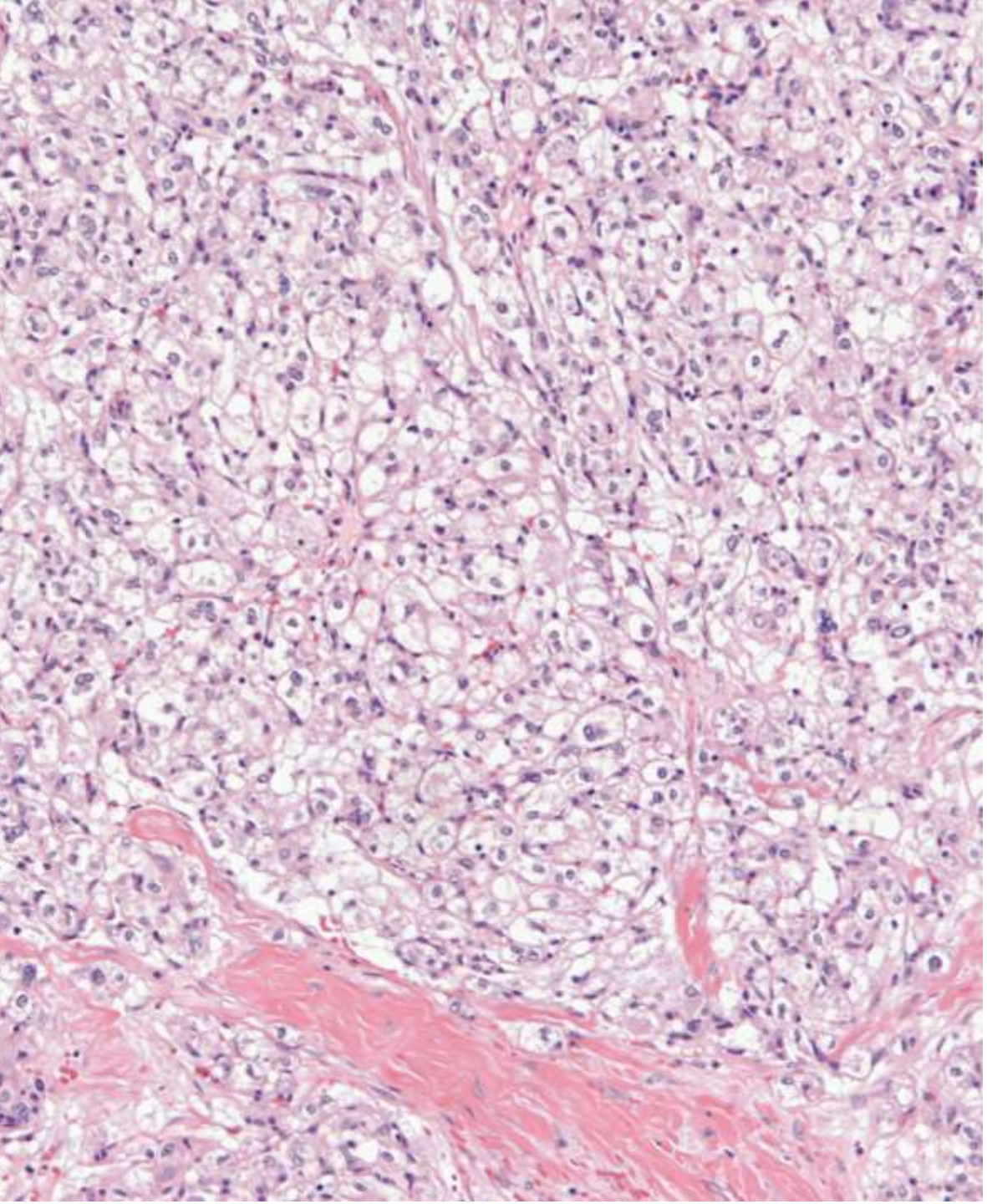


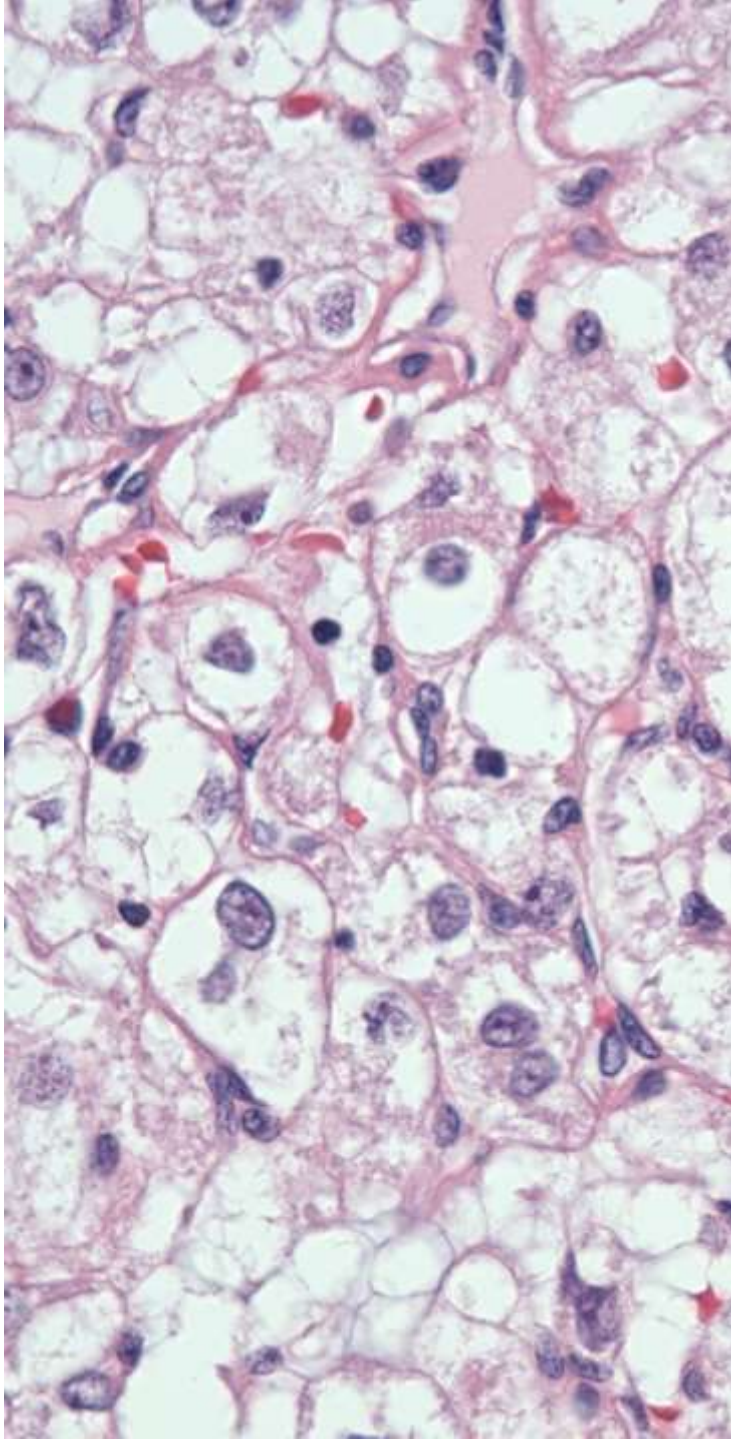


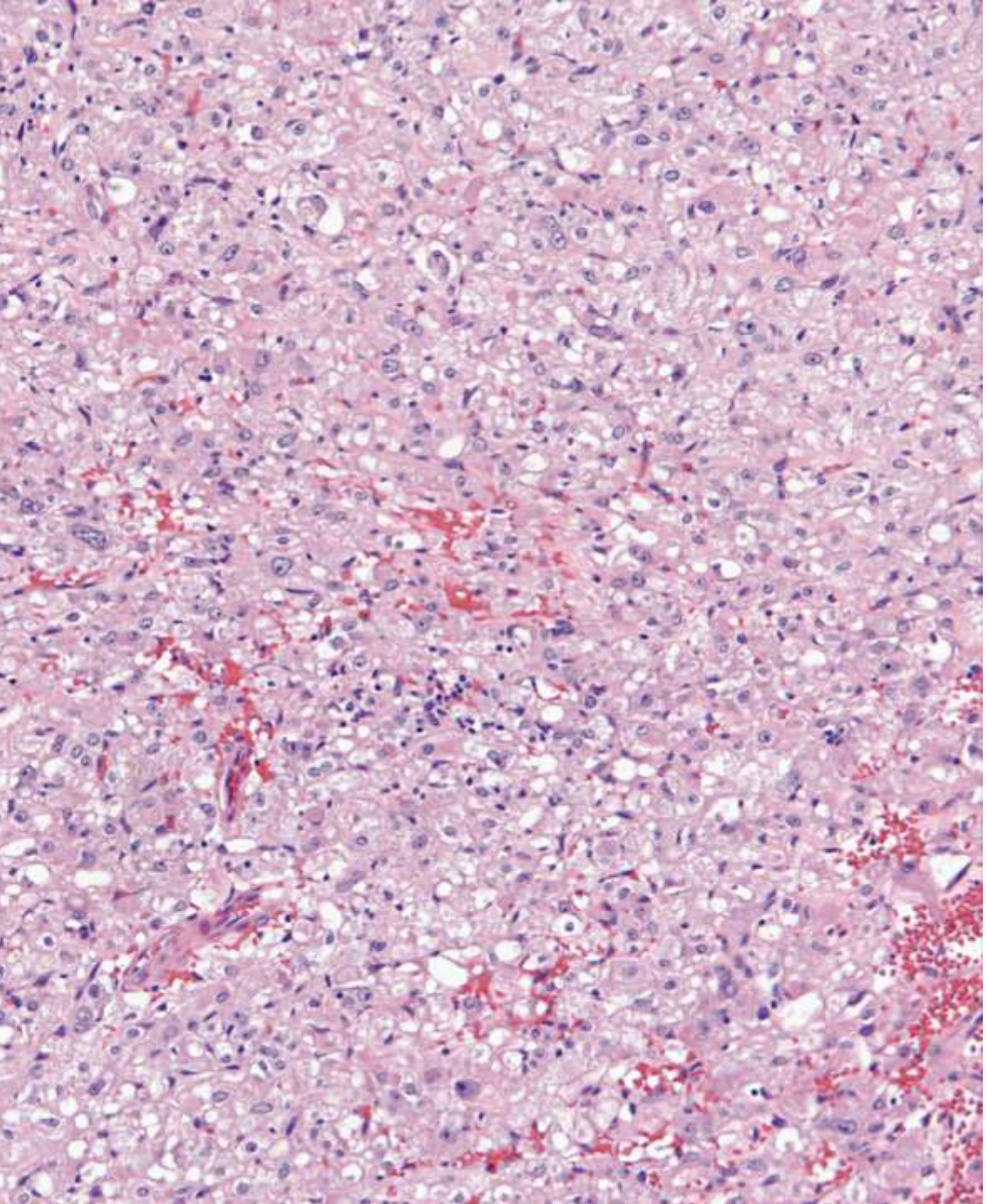
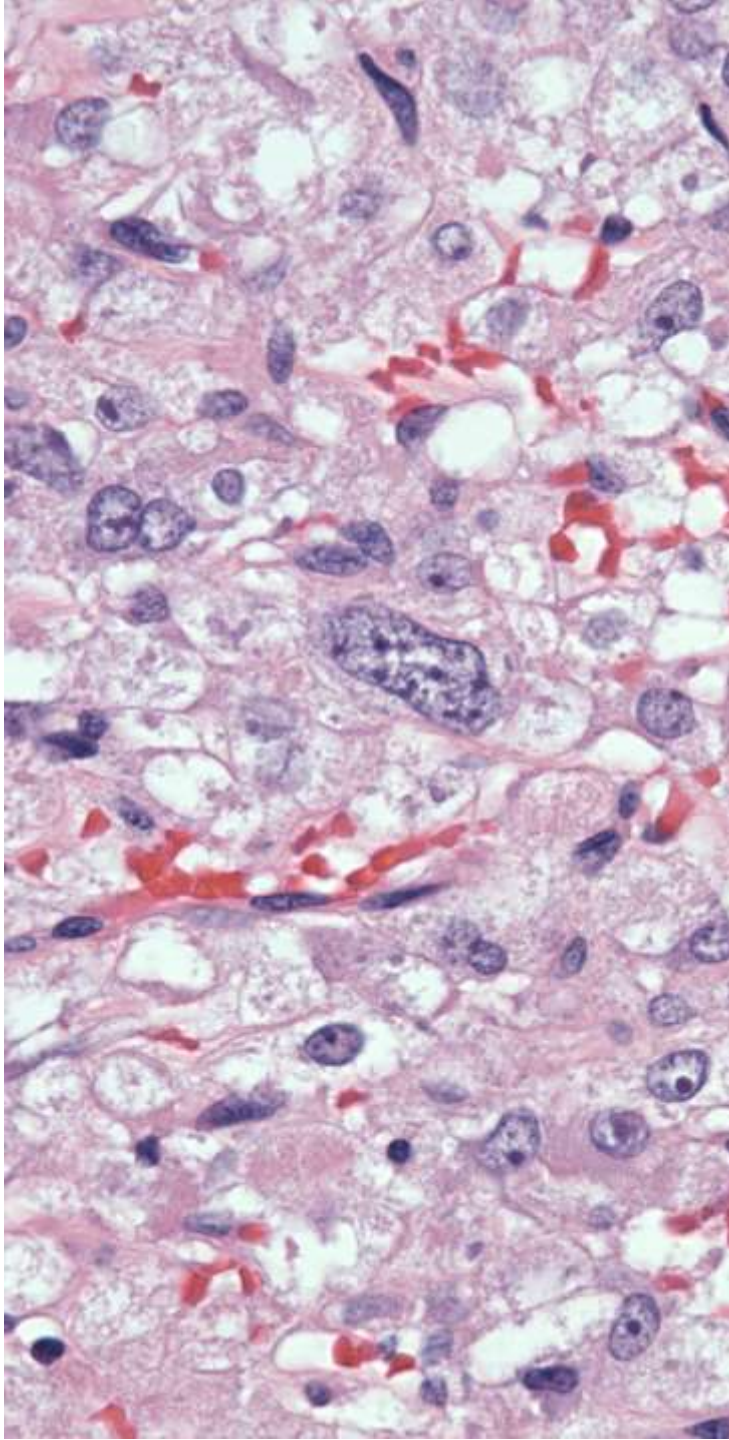


DIAGNOSIS?

History: 53 year old female with 6.2 x 6.1 cm left kidney mass





Differential Diagnosis

Clear Cell RCC

Chromophobe RCC

RCC variant (sarcomatoid, MiT family, SDHB)

Epithelioid Angiomyolipoma (eAML)

Melanoma

IHC

CAIX (Clear Cell RCC)
CD117 (Chromophobe RCC)
Racemase (Papillary RCC)
SDHB (SDHB-deficient RCC)
PAX8 (Renal)
CKMIX (Epithelial)
S100 (Melanoma)
HMB-45 (eAML)
Smooth Muscle Actin (eAML)
Melan A (eAML)

IHC

CAIX (Clear Cell RCC)
CD117 (Chromophobe RCC)
Racemase (Papillary RCC)
SDHB (SDHB-deficient RCC)
PAX8 (Renal)
CKMIX (Epithelial)
S100 (Melanoma)
HMB-45 (eAML) - dim
Smooth Muscle Actin (eAML)
Melan A (eAML) - dim

Diagnosis:

MOST COMPATIBLE WITH EPITHELIOID ANGIOMYOLIOMA

Renal Angiomyolipoma

Most common type of PEComa

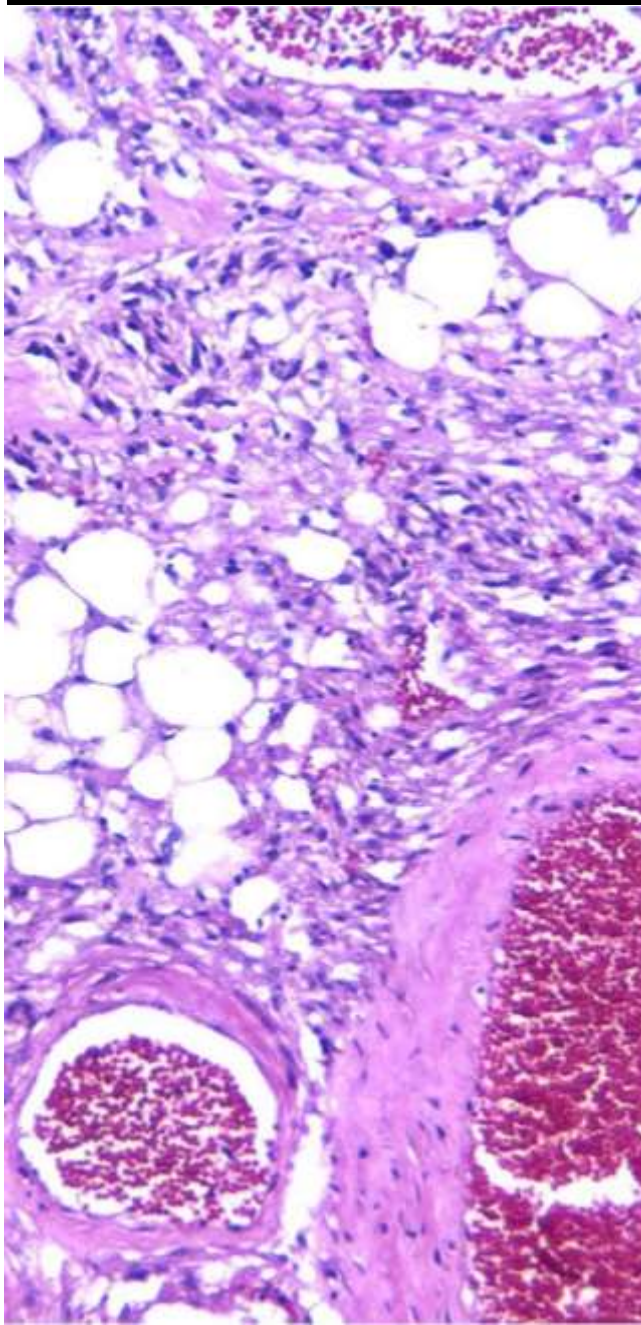
Two major types: classic and epithelioid (7%)

Classic AMLs usually benign, eAMLs are more frequently malignant (local recurrence or metastasis)

Clinicopathologic features of eAMLs associated with malignancy

1. Necrosis
2. Tumor size >7cm
3. Extra-renal extension or renal vein involvement
4. Carcinoma-like growth pattern
5. Association with TSC complex

Classic Angiomyolipoma



Renal Angiomyolipoma

Associated with tuberous sclerosis complex (TSC) gene alterations (both germline and sporadic)

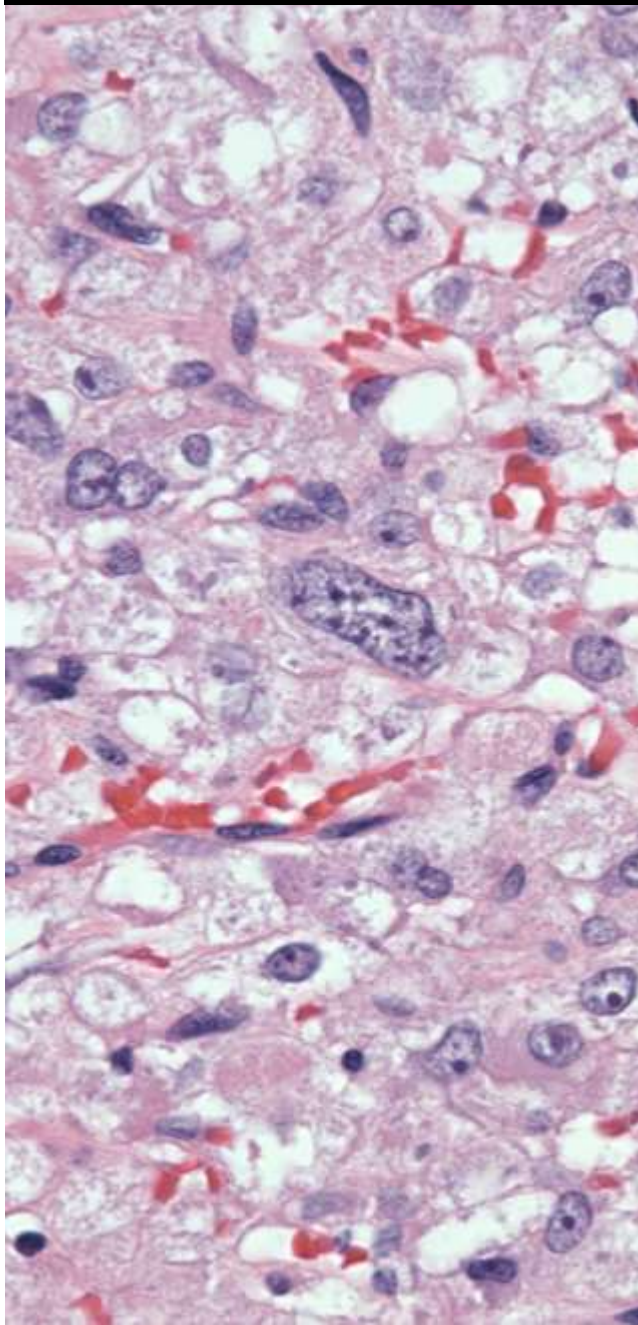
- TSC1/TSC2 inhibit mTOR signaling
- mTOR inhibitors as targeted therapy

TFE3 gene rearrangements found in ~20% of PEComas with 3 cases of TFE3 gene rearranged renal AMLs described

- Clinically important because may be non-responsive to mTOR inhibitors
- MET inhibitors as possible targeted therapy (phase II ASPS)

TSC1/TSC2 mutations and TFE3 gene rearrangements appear to be mutually exclusive

Epithelioid Angiomyolipoma



TFE3 Gene Rearrangement

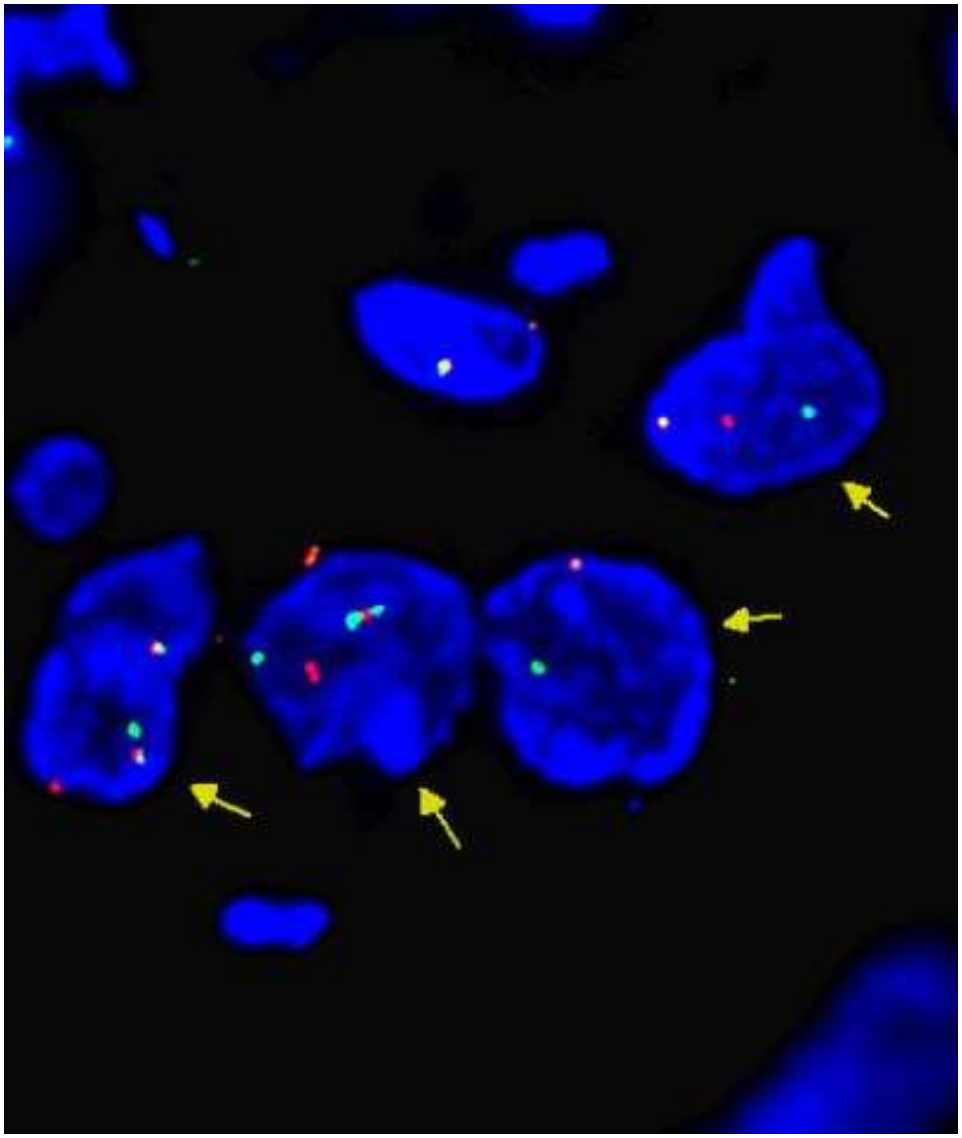
FISH break apart probe for TFE3 gene

OUR CASE: TFE3-rearranged

2/3 prior renal TFE3-rearranged eAMLs showed SFPQ-PSF fusion partner

(our case: partner unknown)

TFE3-PSF seen in other PEComas and MiT RCCs



TFE3 REARRANGED RENAL eAML FOLLOW-UP

Our patient had a CT scan performed on 12/14/16 which was negative for recurrent disease, follow-up scanned scheduled for 6 months

Long-term follow-up is indicated following resection of epithelioid AMLs with features suggesting malignant transformation since metastatic disease may become evidence years later

REFERENCES

Kryvenko ON, Jora M, Argani P, Epstein JI. Diagnostic Approach to Eosinophilic Renal Neoplasms. Arch Pathol Lab Med. 2014; 138: 1531-1541

Nese N, et al. Pure epitheloid PEComas (so called epitheloid angiomyolipoma) of the kidney: A clinicopathologic study of 41 cases: detailed assessment of morphology and risk stratification. American Journal of Surgical Pathology. 2011; 35(2): 161-176

Argani P, et al. A Distinctive Subset of PEComas Harbors TFE3 Gene Fusions. American Journal of Surgical Pathology. 2010; 34: 1395-1406

Ohe C, et al. A renal epithelioid angiomyolipoma/perivascular epithelioid cell tumor with TFE3 gene break visualized by FISH. Med Mol Morphol. 2012; 45: 234-237

Thway K and Fisher C. PEComa: morphology and genetics of a complex tumor family. Annals of Diagnostic Pathology. 2015: 19: 359-368

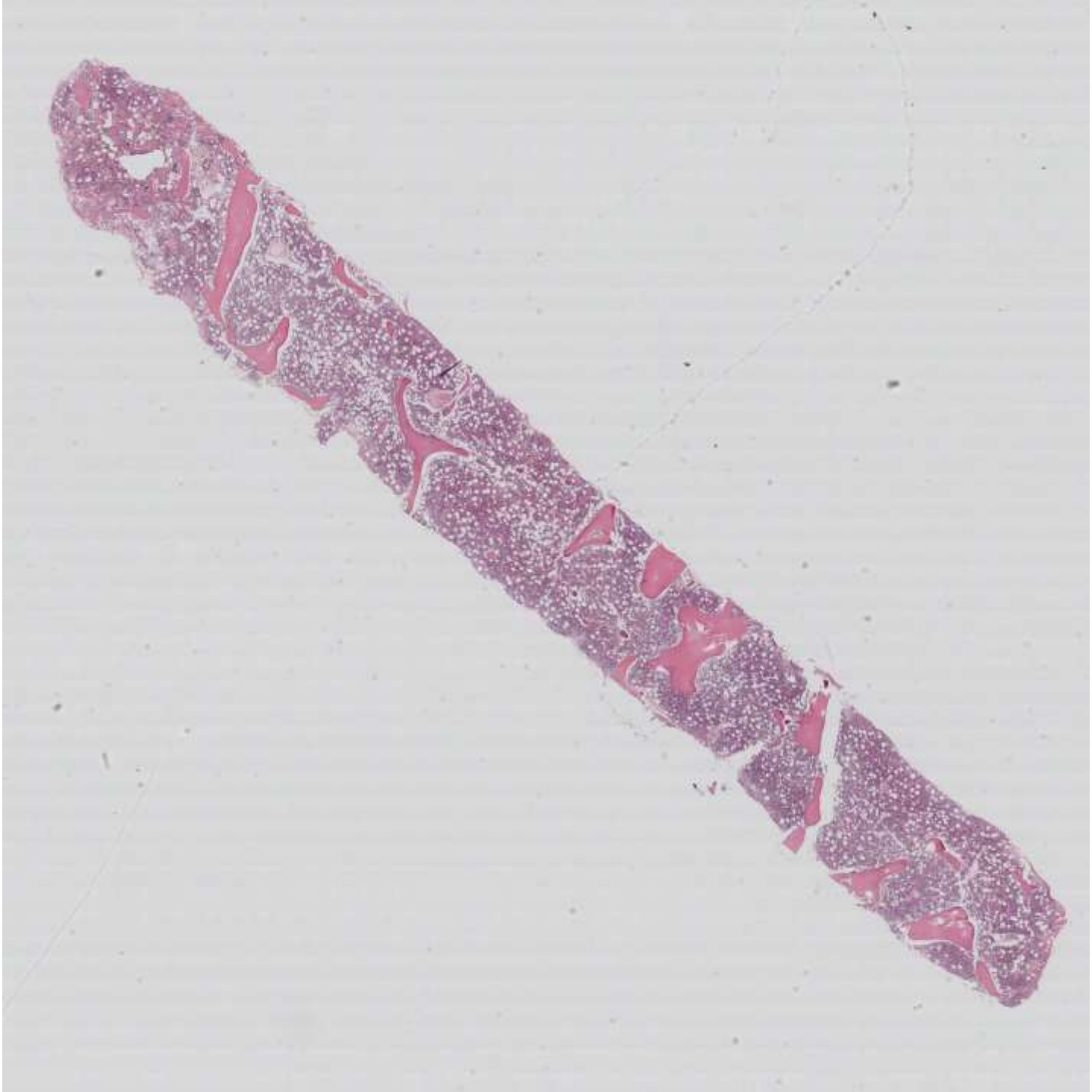
Agaran N, et al. Dichotomy of Genetic Abnormalities in PEComas With Therapeutic Implications. American Journal of Surgical Pathology. 2015; 39: 813-825.

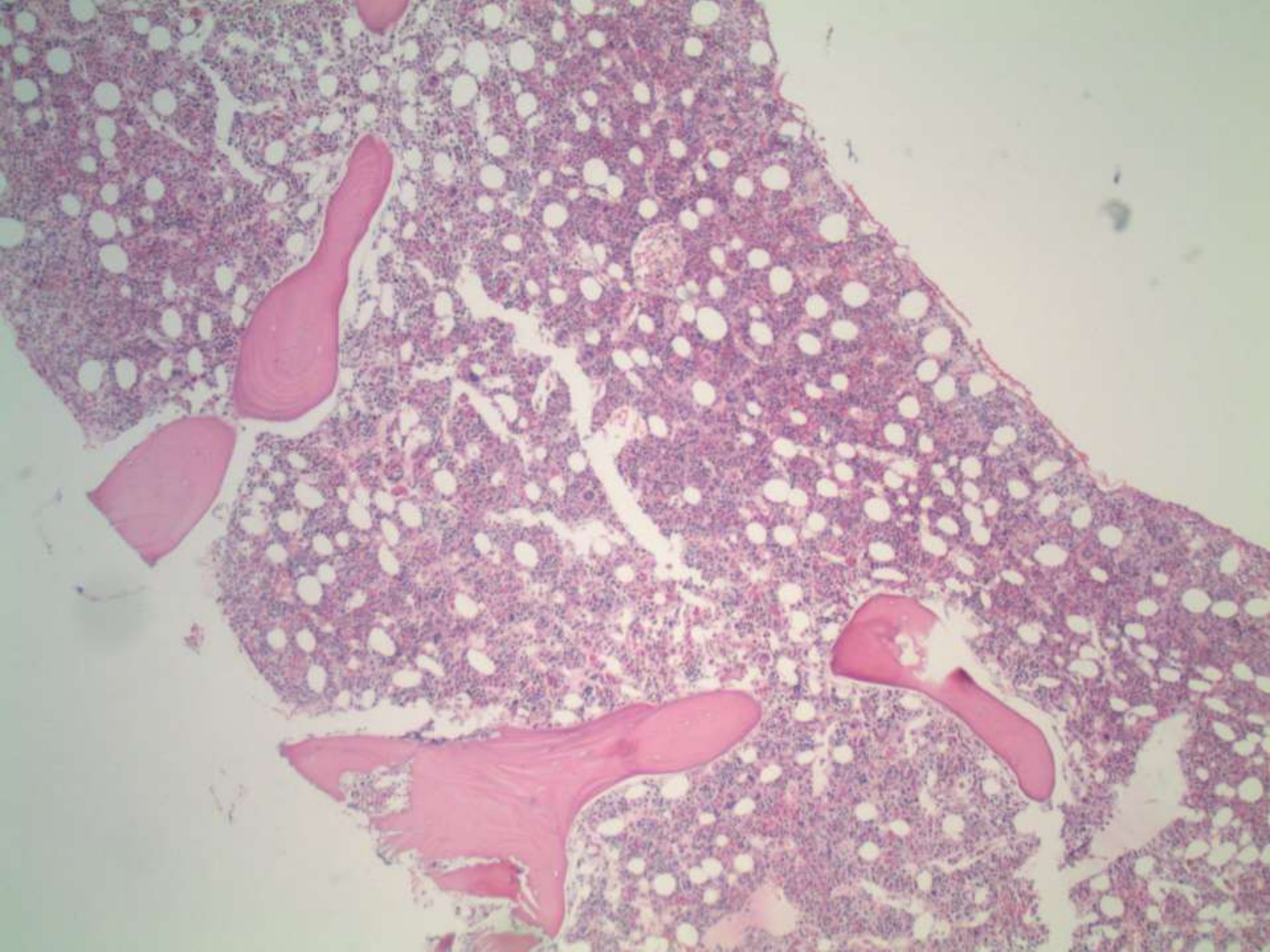
Argani P, et al. TFE3-Fusion Variant Analysis Defines Specific Clinicopathologic Associations Among Xp11 Translocation Cancers. American Journal of Surgical Pathology. 2016; 40: 723-737.

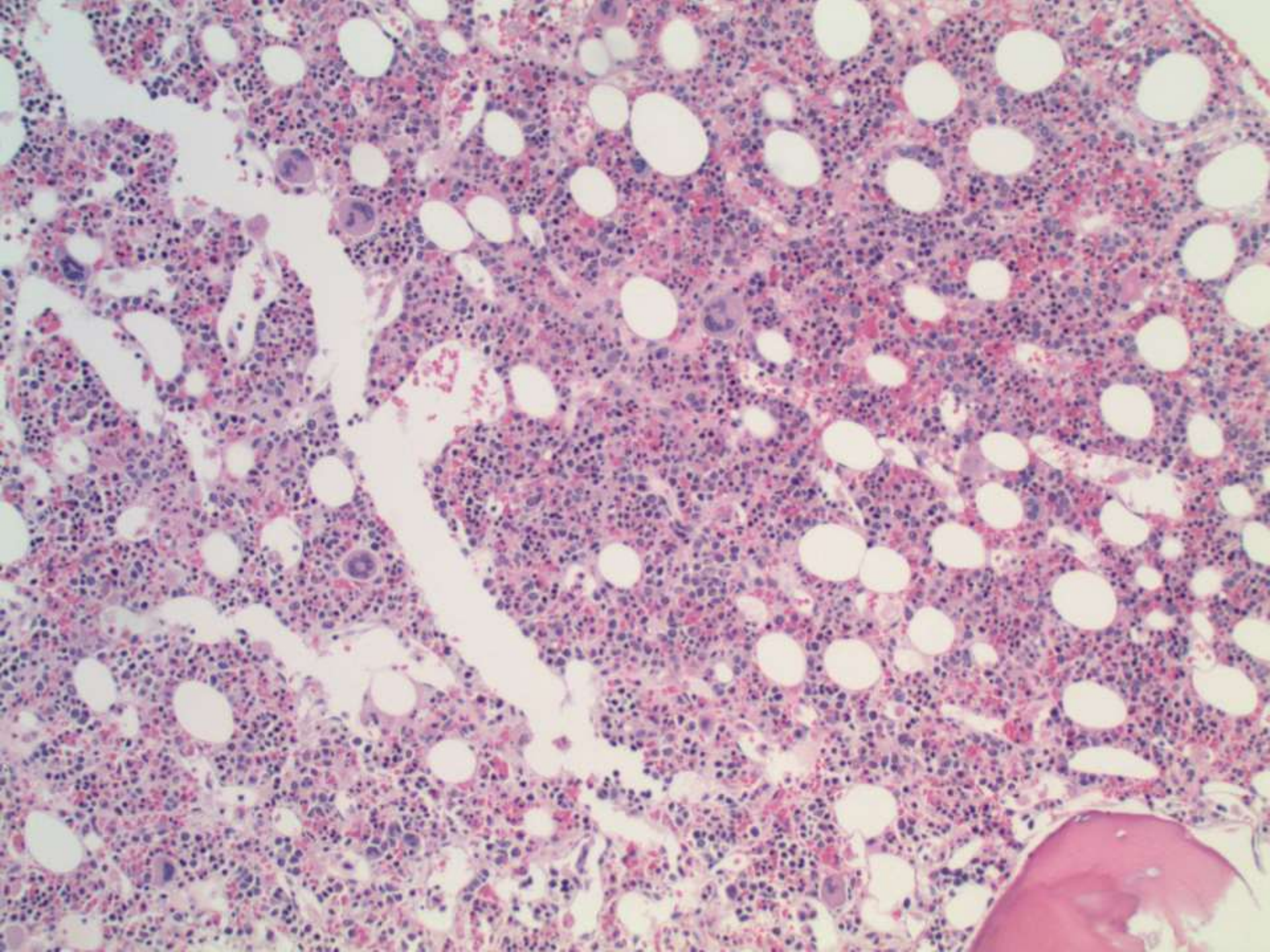
SB 6142
[scanned slide available]

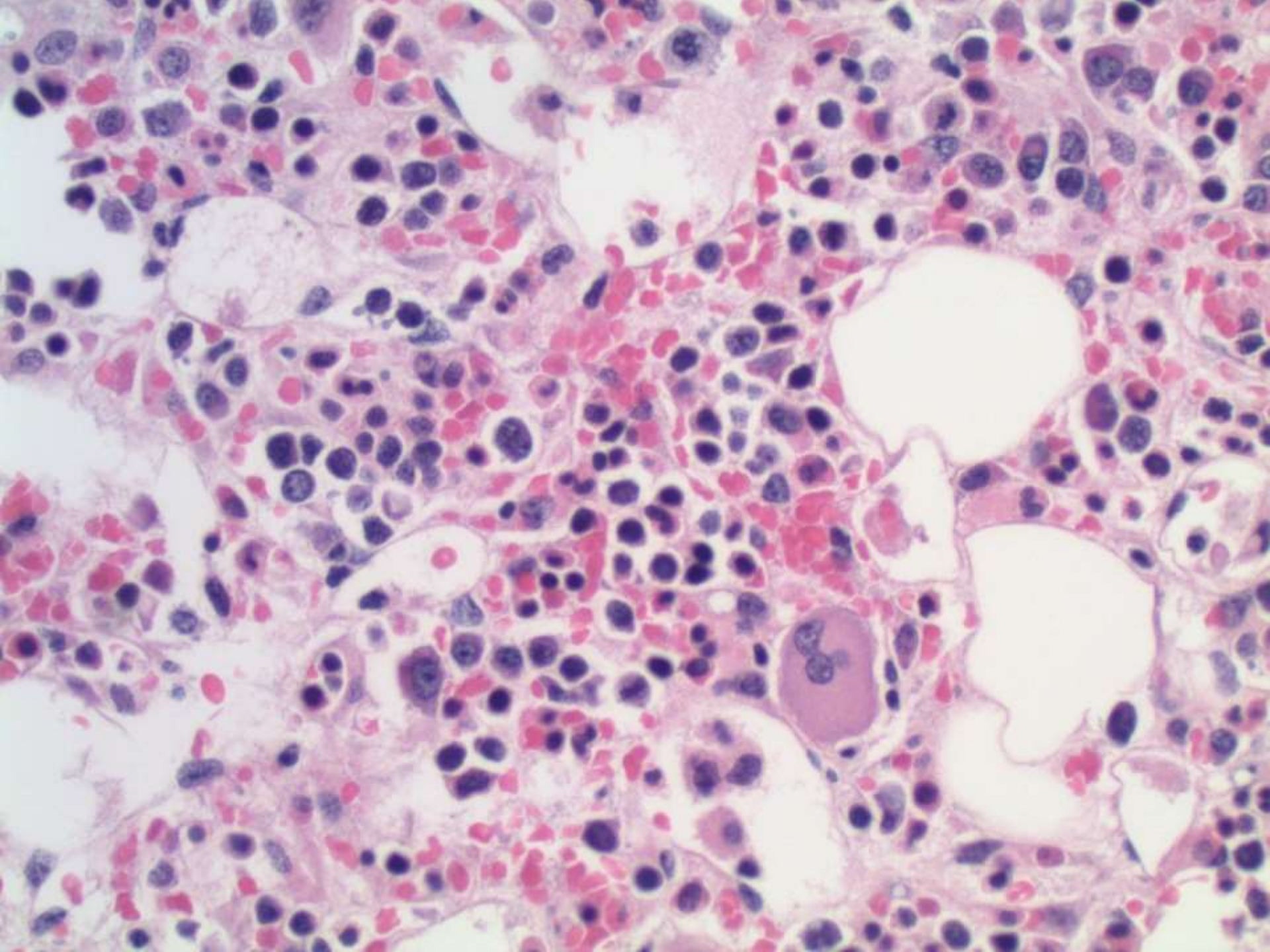
Erna Forgo/Dita Gratzinger; Stanford

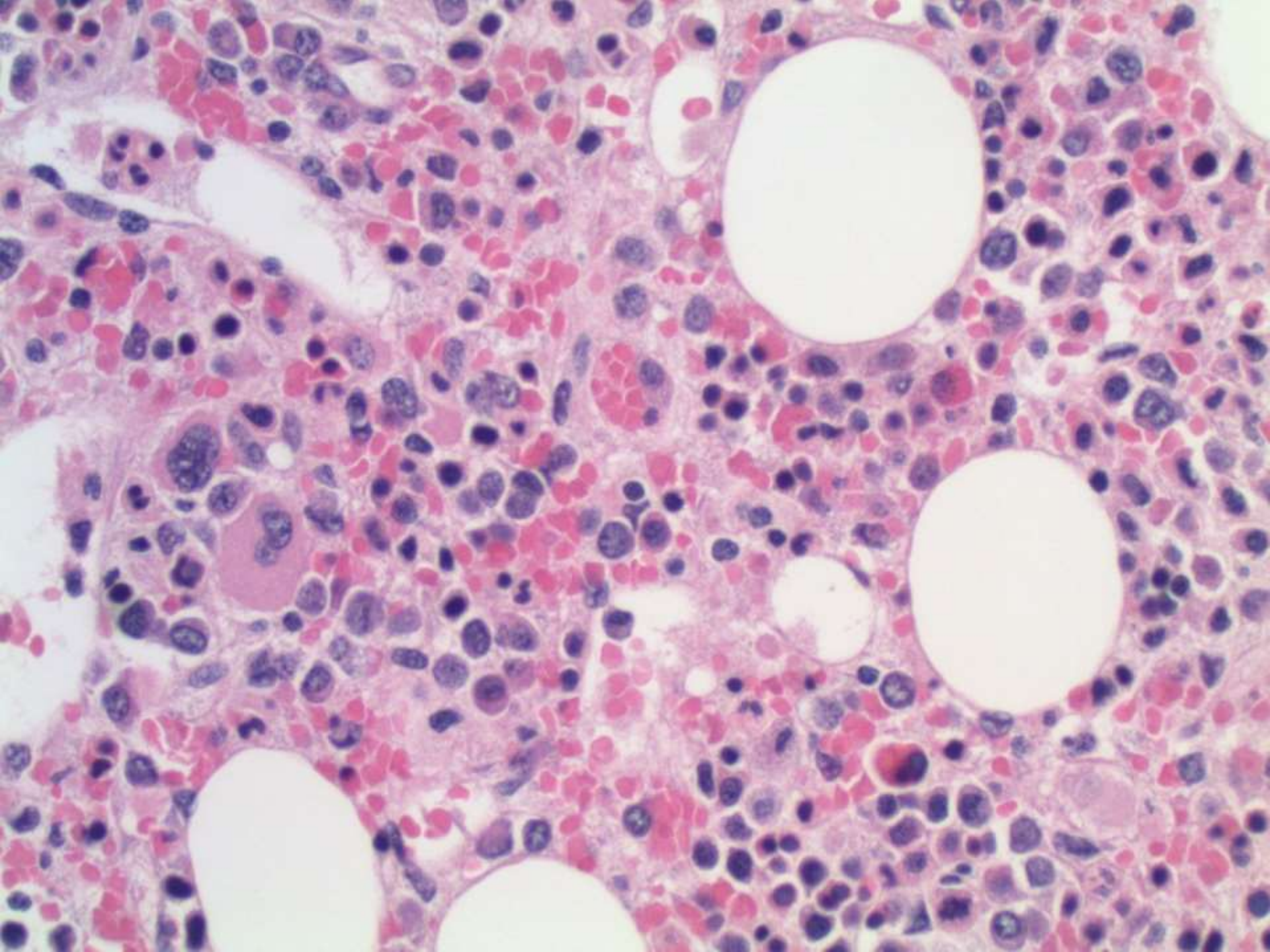
46-year-old F with remote history of solid malignancy of unknown type, now with cytopenia. Bone marrow core biopsy submitted.

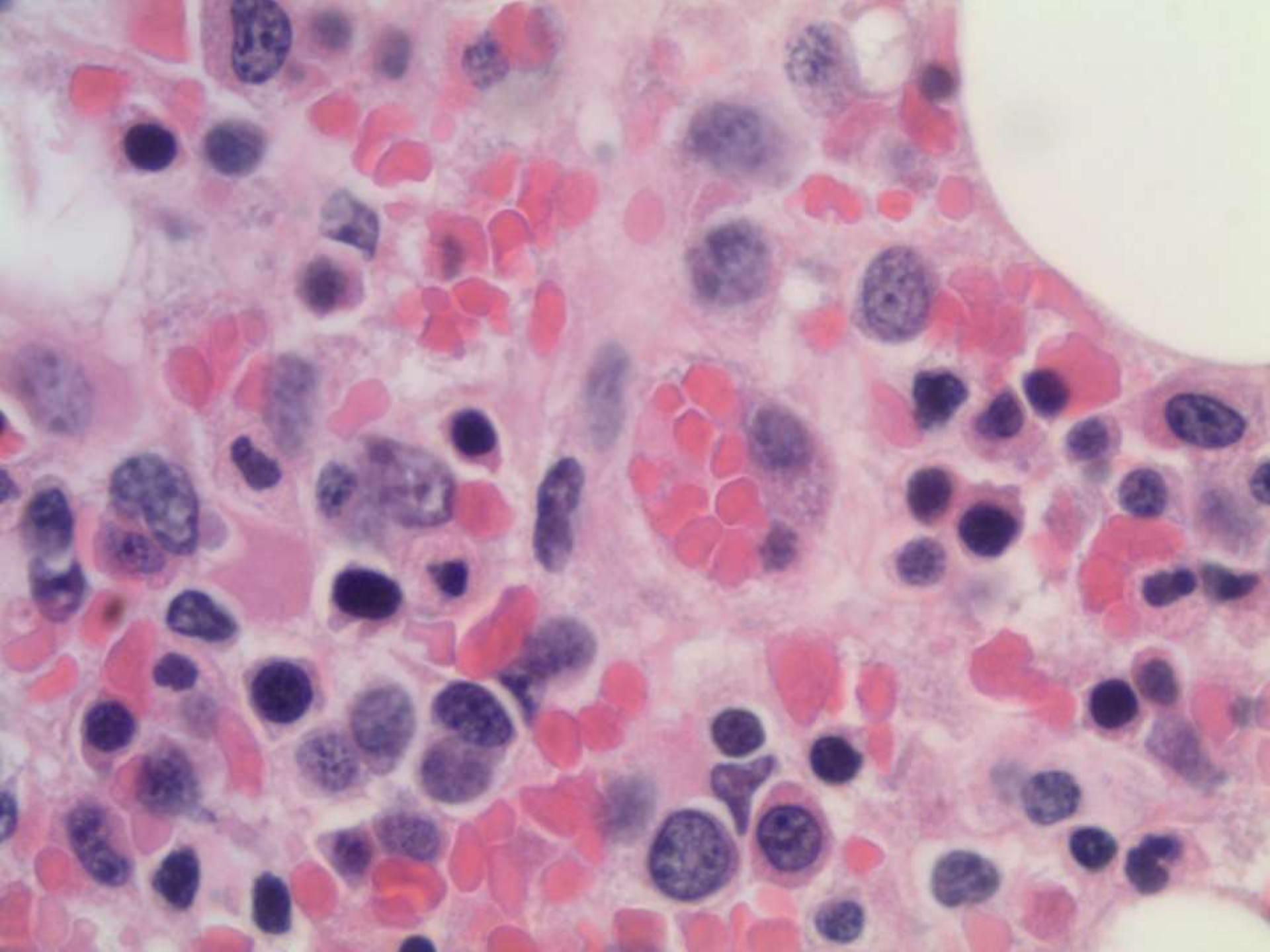




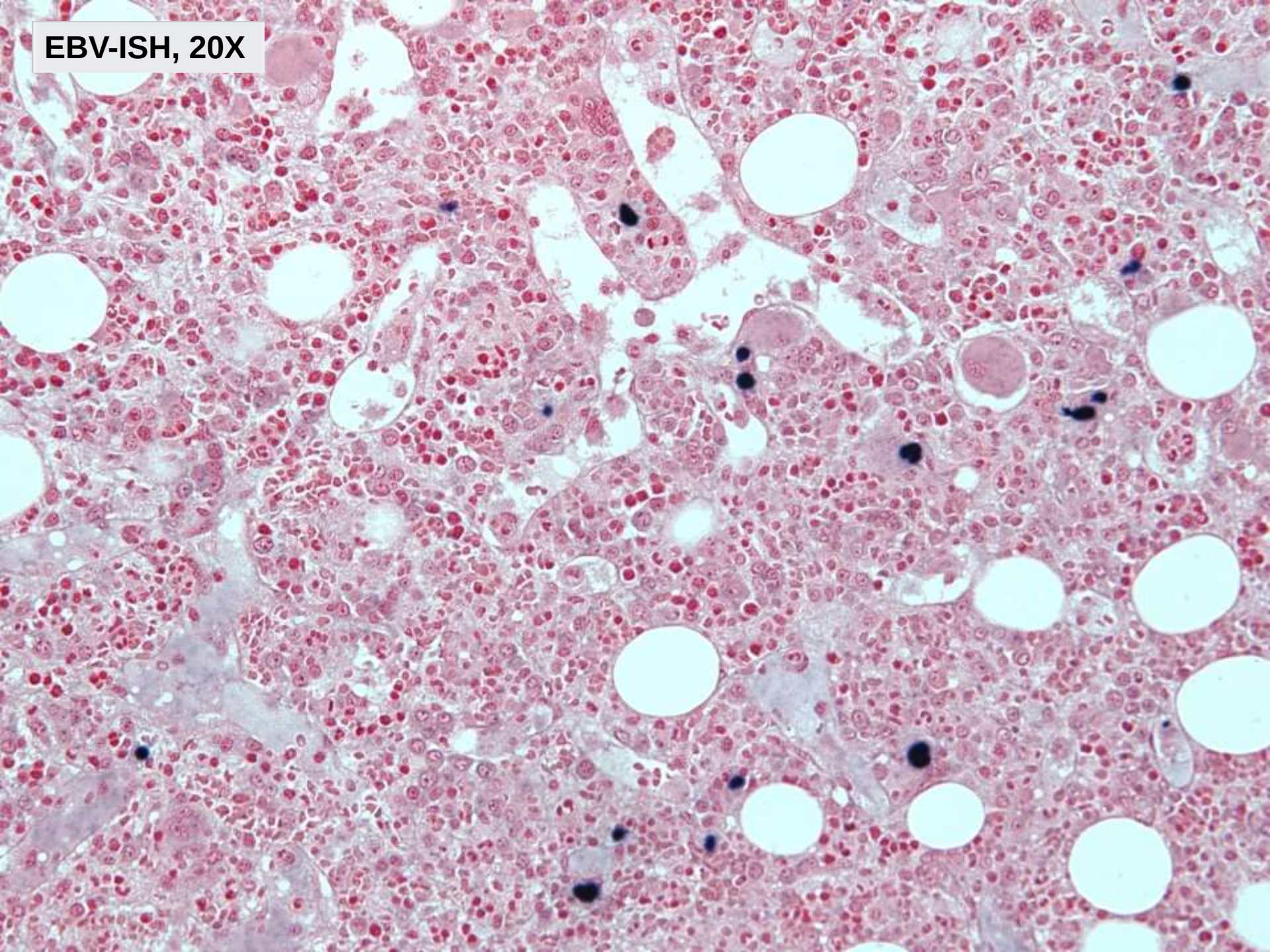








DIAGNOSIS?


EBV-ISH, 20X

EBV-Associated Hemophagocytic Histiocytosis (HH)

- Bone marrow aspirate and biopsy results:
  - Florid hemophagocytic histiocytosis, dyspoiesis and an increase in EBV positive lymphocytes
    - “EBV-associated hemophagocytic histiocytosis”

- Multilineage dysplasia, a frequent confounder in the setting of HH, raises the concern for a myeloid neoplasm
- Prominent intrasinusoidal histiocytosis raises the concern for malignancy

Clinical History

- 46 year old female with history of "jaw cancer" 22 years ago status post surgery (right lower jaw resection), chemotherapy, radiation therapy, and bone marrow transplant (no details available)
- She presents with 1 week history of generalized weakness, back and abdominal pain, fevers to 104°F and 15 lb weight loss
- She progressed to dysphagia, cough and difficulty breathing

Clinical History cont'd

- She presented to her PCP and was found to have:
  - pancytopenia (WBC1.9, Plt 7)
  - acute kidney injury (Cr 4.3)
  - acute liver injury (transaminases in 700s, INR 1.3)
  - widespread presumed metastatic cancer to liver, lung, spleen, kidney and mesentery based on CT imaging studies
- Transferred to Stanford (7/27/2016)
  - Sepsis
  - Severe thrombocytopenia + DIC (Fibrinogen: 146, PT: 19.4, INR: 1.7, PTT: 54.8 , TT: 19.8)
  - Ferritin: 24,000

Hemophagocytic Histiocytosis

- Cytokine dysfunction, resulting in overwhelming activation of T lymphocytes and macrophages
  - Leads to systemic symptoms and organ damage
- Clinical and laboratory criteria (5 out of 8 criteria)
  - **Fever**
  - **Cytopenias**
  - **Splenomegaly**
  - Hypertriglyceridemia &/or **hypofibrinogenemia**
  - **Serum ferritin > 500 µg/L**
  - **Hemophagocytosis**
  - Low or absent NK-cell activity
  - Soluble CD25 (sIL-2 receptor) > 2,400 U/mL

Etiology/Pathogenesis

- **Inherited genetic defects**:
  - Result in depressed functional cytotoxicity of natural killer (NK) cells and cytotoxic T cells
  - Perforin (*PRF1*) mutation
  - Chediak-Higashi syndrome (*LYST* gene defect)
  - X-linked lymphoproliferative disease (XLP)
- **Acquired/secondary defects**:
  - Viruses: **EBV**, CMV, Parvovirus B19, Herpes, measles, HHV8, HIV
  - Bacteria, parasites, fungi
  - Autoimmune disorders: SLE, RA
  - Malignancies: **NK/T-cell lymphoma**, AML, MDS, T/B-cell ALL, carcinoma

Patient Follow-Up

- Right submandibular lymph node (7/29/2016)
  - **EBV** positive lymphoproliferation
- Mesenteric Mass (8/25/2016)
  - Most consistent with **extranodal NK/T-cell lymphoma**, nasal type
  - Predominantly T cells by Flow Cytometry
- Currently undergoing preparatory regimen for non-myeloablative allogeneic stem cell transplant on 3/3/2017

Viral Etiology of Secondary HH in Chinese Population

- 54 Chinese patients fulfilled criteria for secondary HH
- 24/50 had viremia
- EBV was the most common virus
- Severe SHH patients with EBV-viremia:
  - Significantly high levels of ferritin, lactate dehydrogenase, AST, ALT
- Positively relationships existed between EBV DNA titers and levels of AST and ALT ($P<0.05$)
- The prognosis of SHH patients with EBV viremia was worse
- EBV is the major pathogen in virus-associated SHH
  - EBV load influence disease development in SHH

Chen J et al. *Journal of Medical Virology*, 2016

Extranodal NK/T Cell Lymphoma (ENKTL) Across Ethnic Groups

- Aggressive extranodal non-Hodgkin lymphoma most commonly occurring in East Asia and Latin America
- Increasing incidence in the United States
  - Incidence of ENKTL is higher in Asian Pacific Islanders and non-white Hispanics
  - Outcomes may be worse in non-whites
- Universal association of ENKTL with EBV across all ethnic groups suggests a common pathogenesis

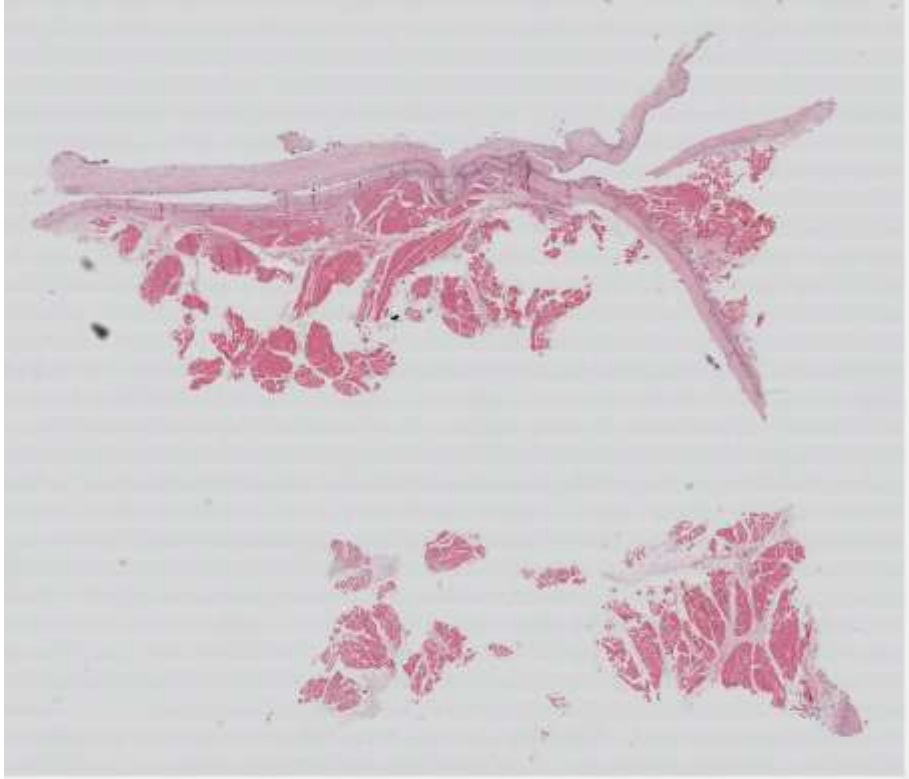
Haverkos B et al. *Curr Hematol Malig Rep*, 2016

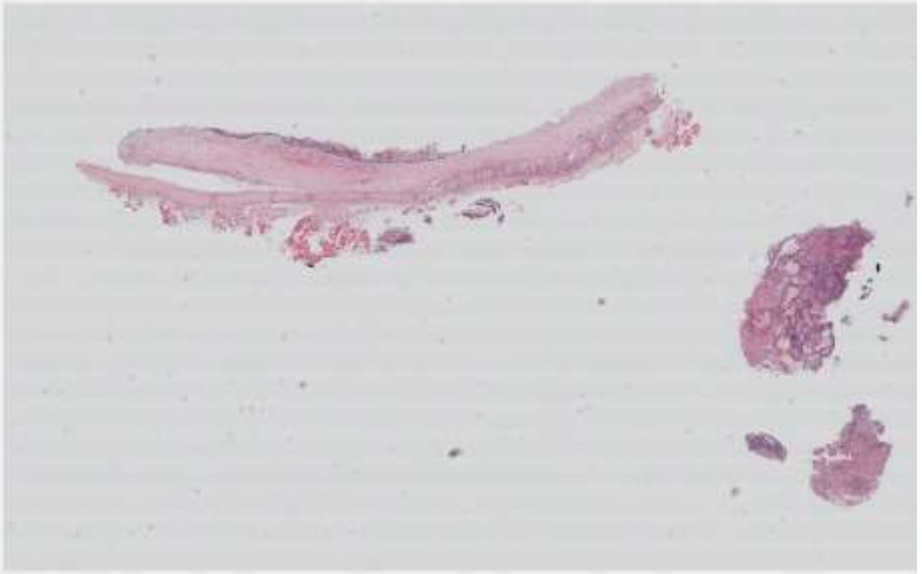
THANK YOU!

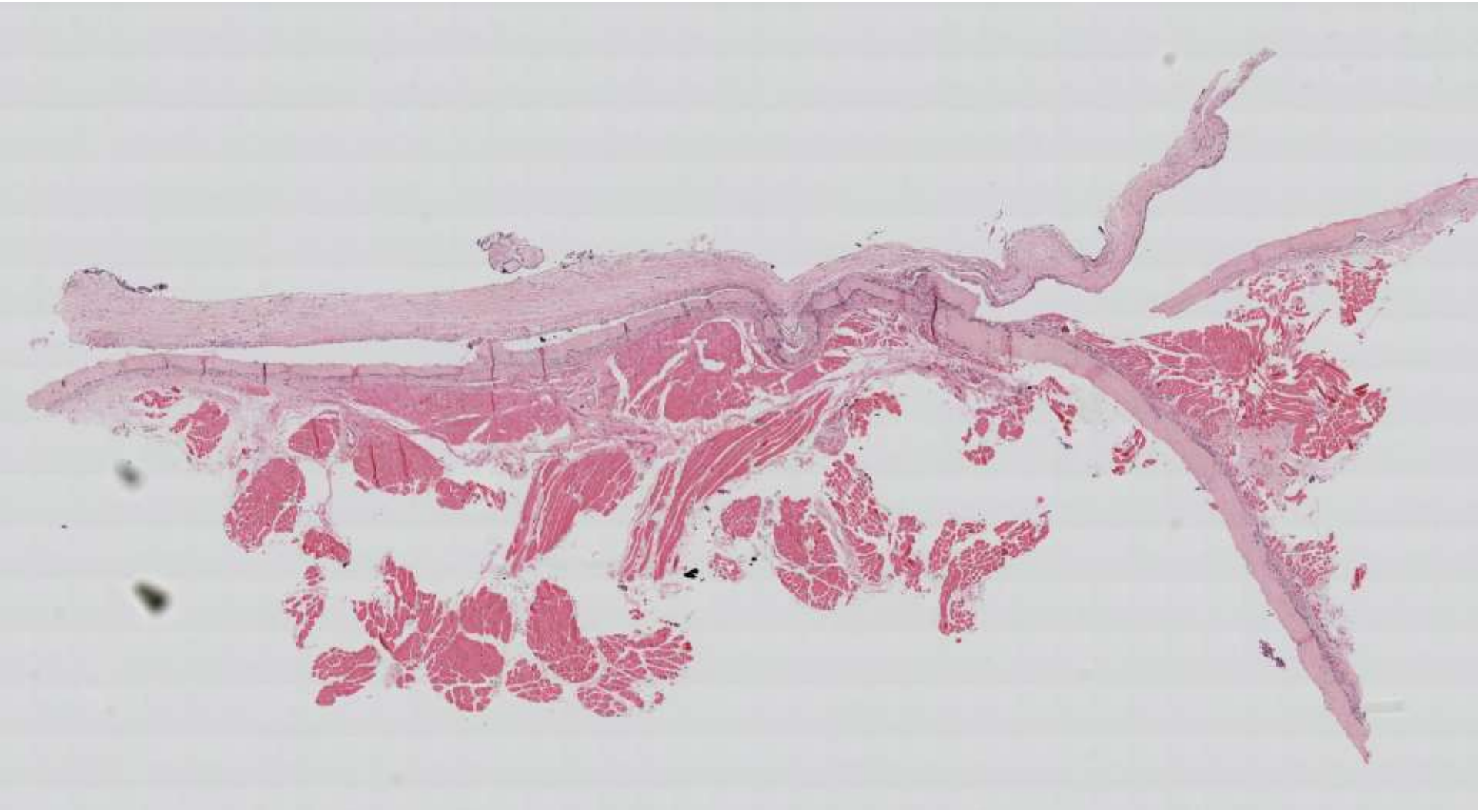
SB 6143
[scanned slide available]

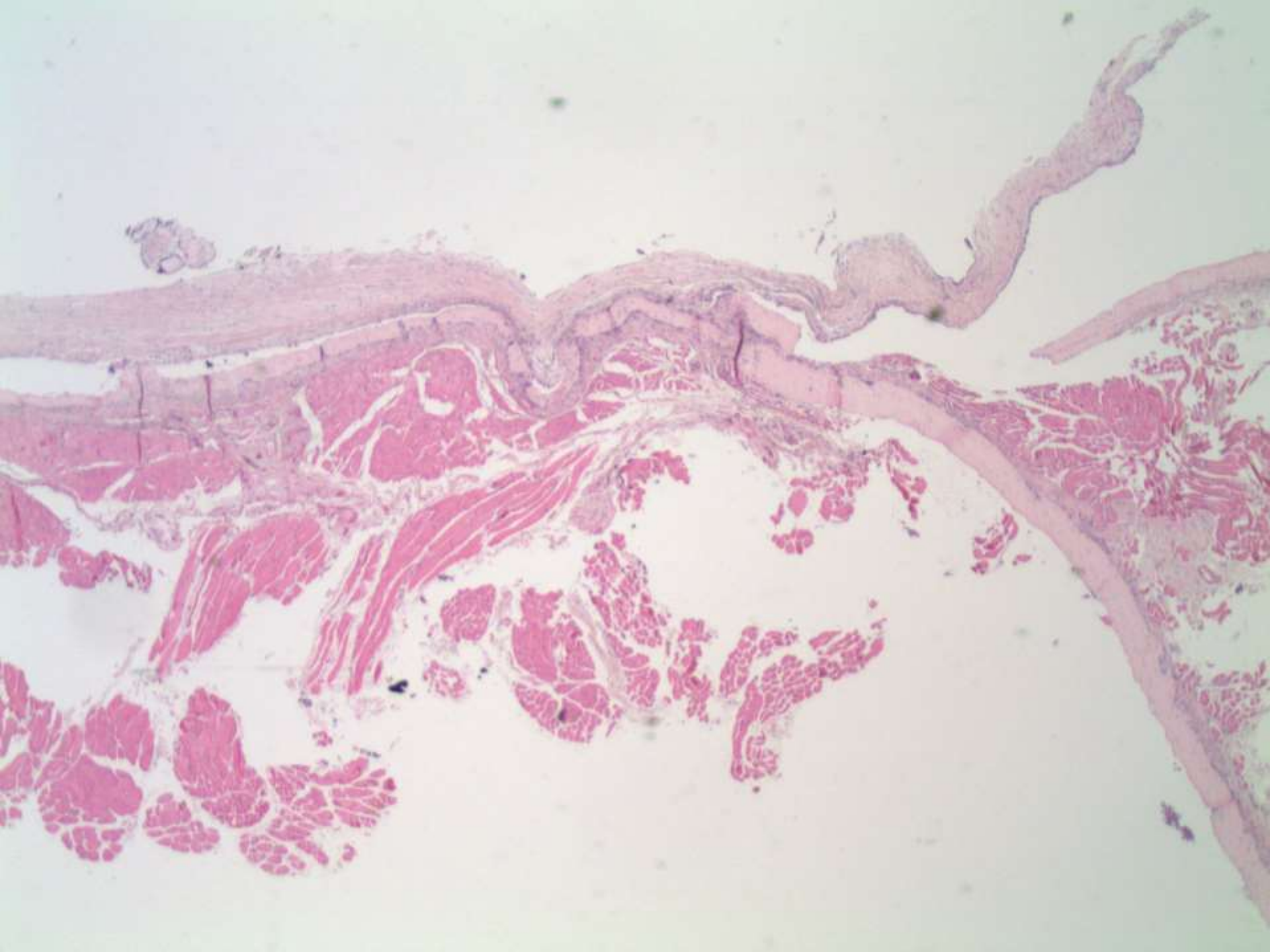
Balaram Puligandla; Kaiser Oakland

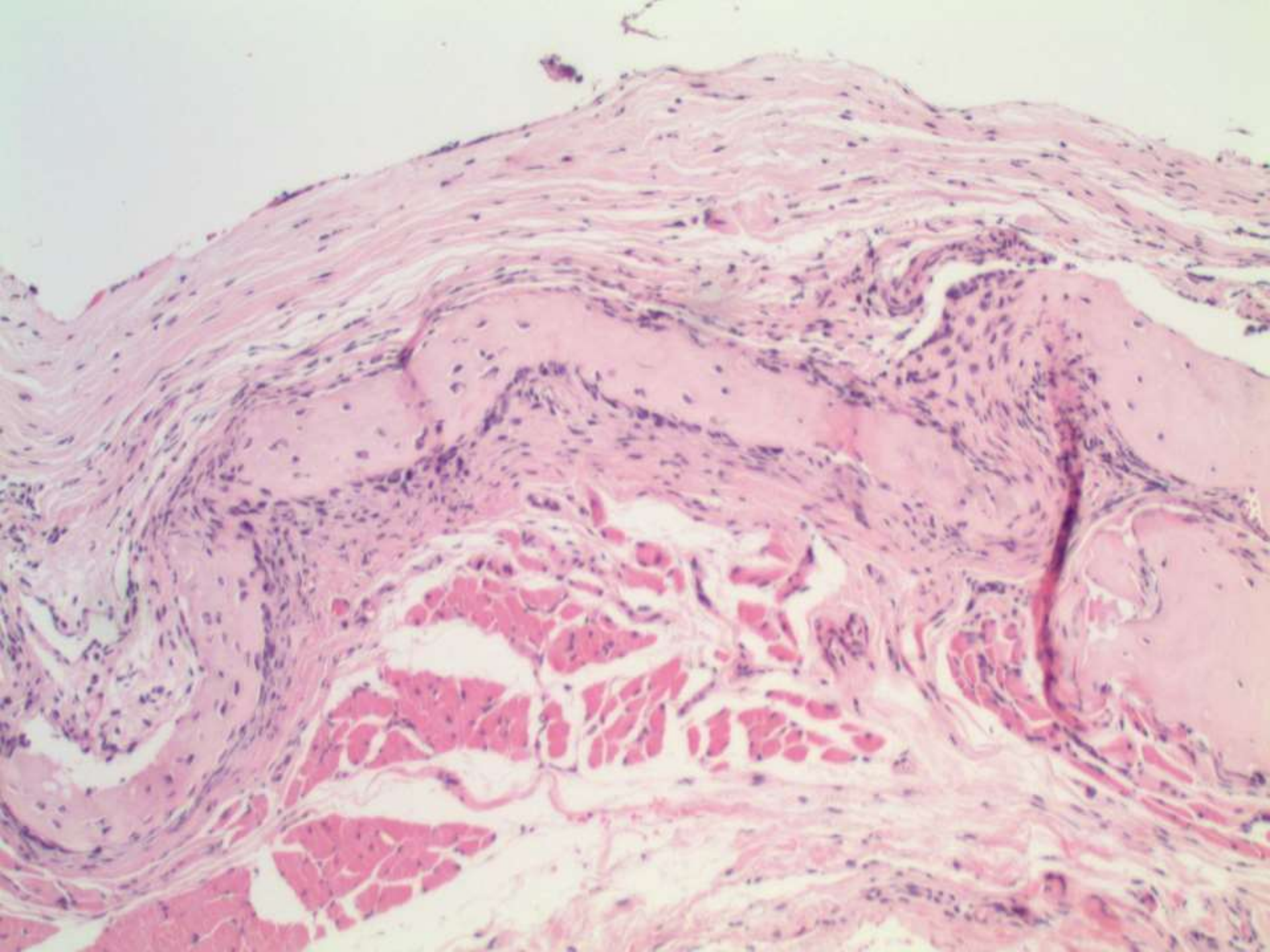
44-year-old M with lesion of anterior mandible that appears unicystic. Straw color fluid aspirated from cyst. Thin walled lesion. DDx: dentigerous cyst, KOT.

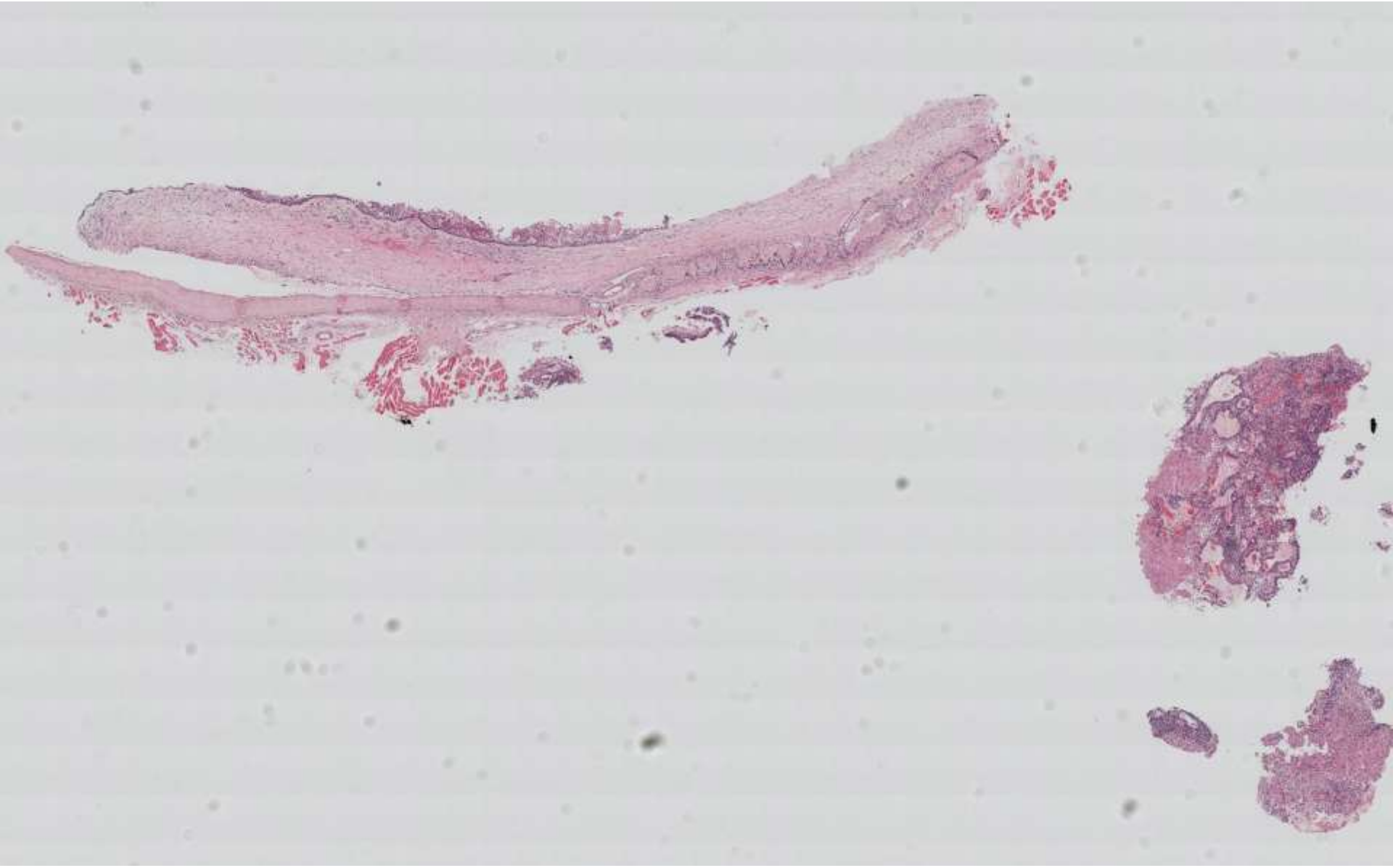


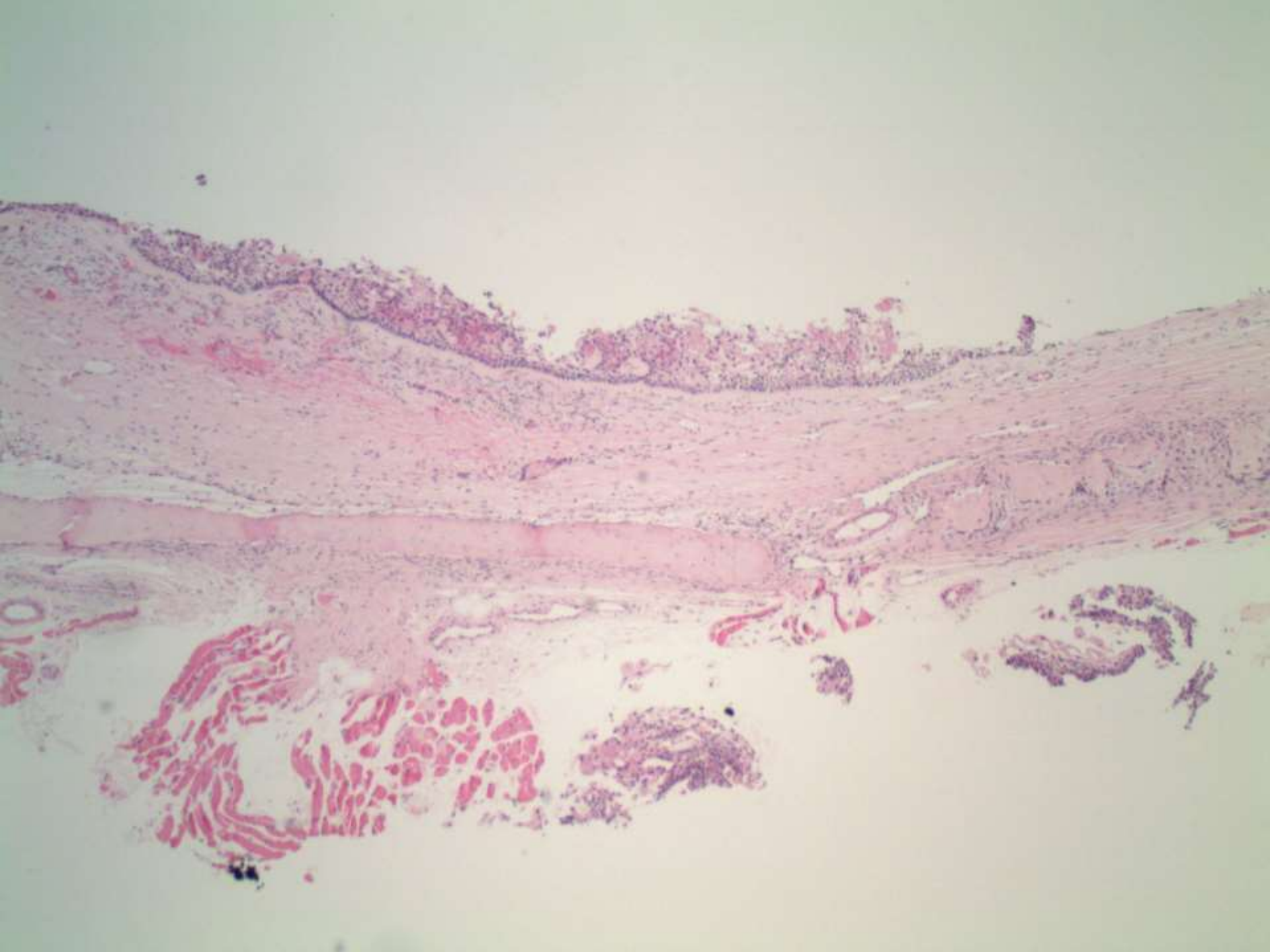


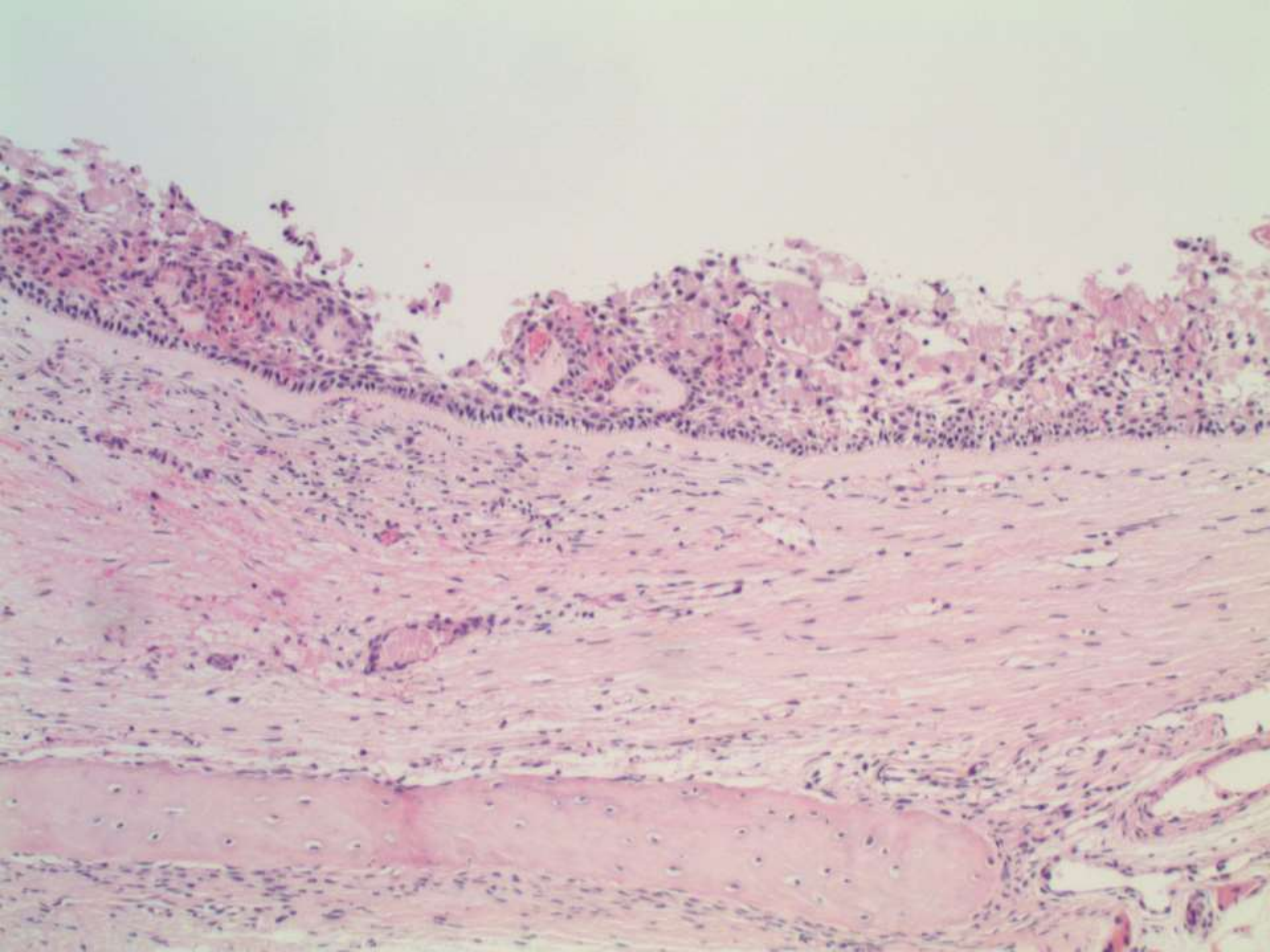


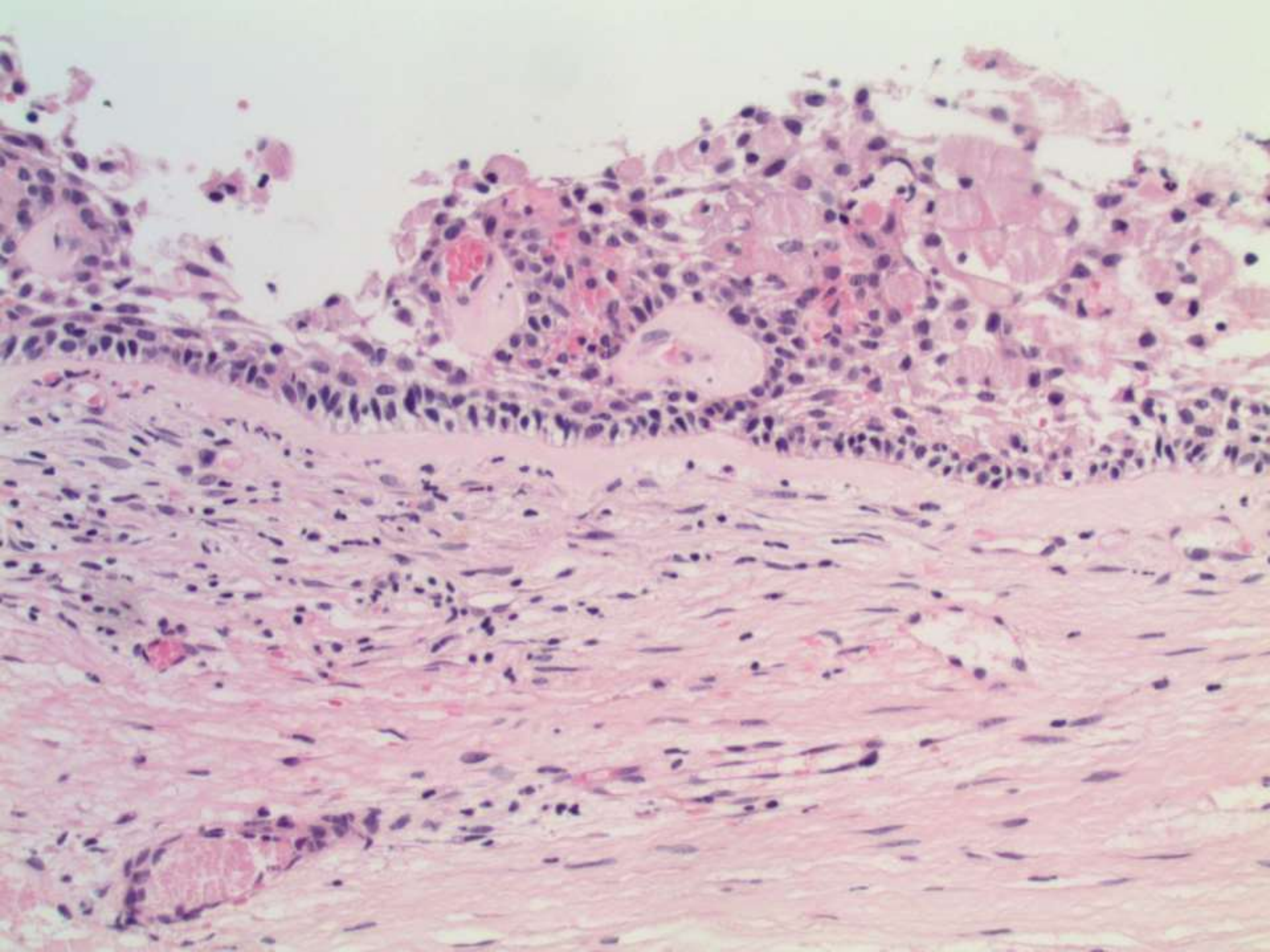


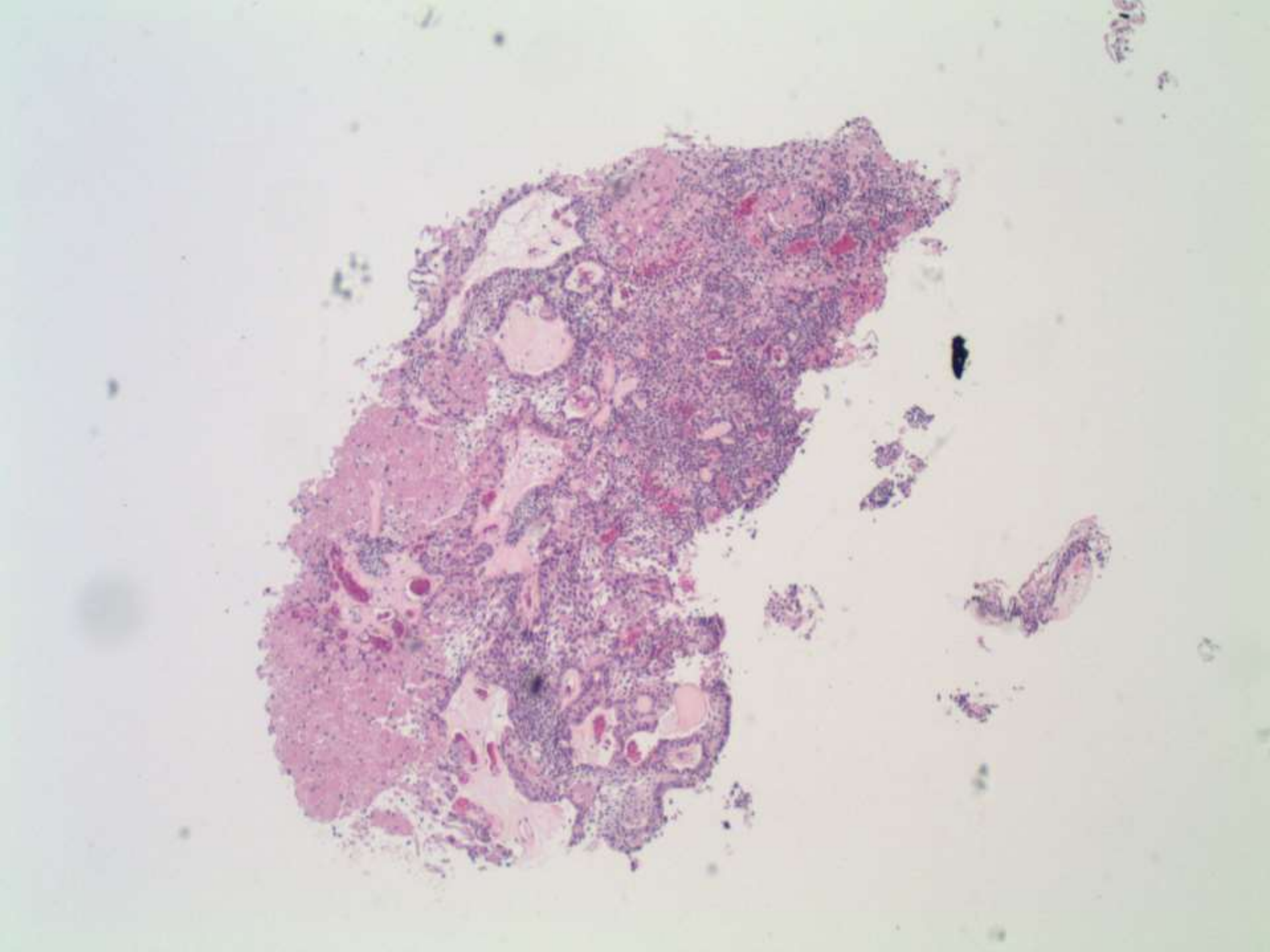


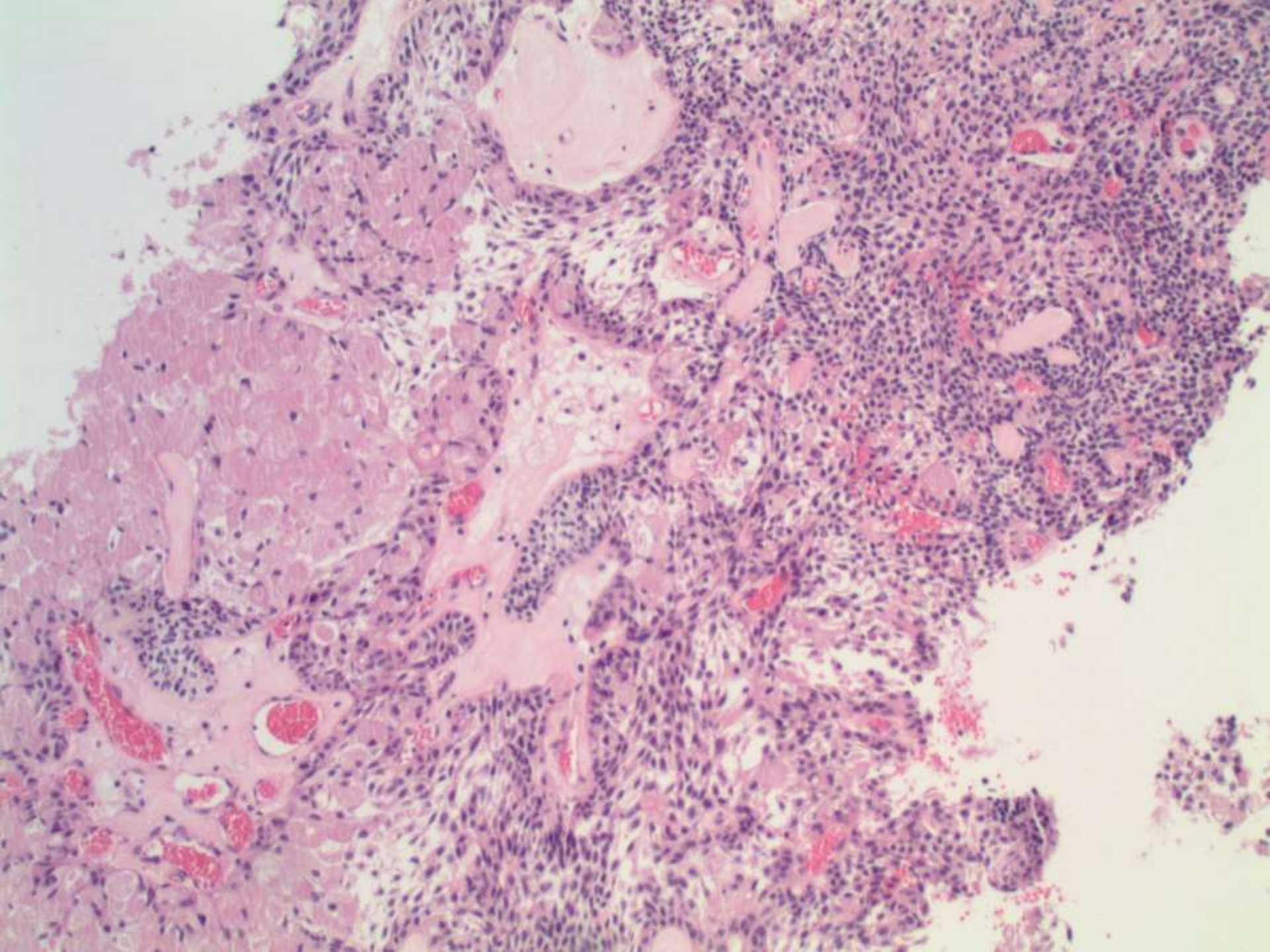


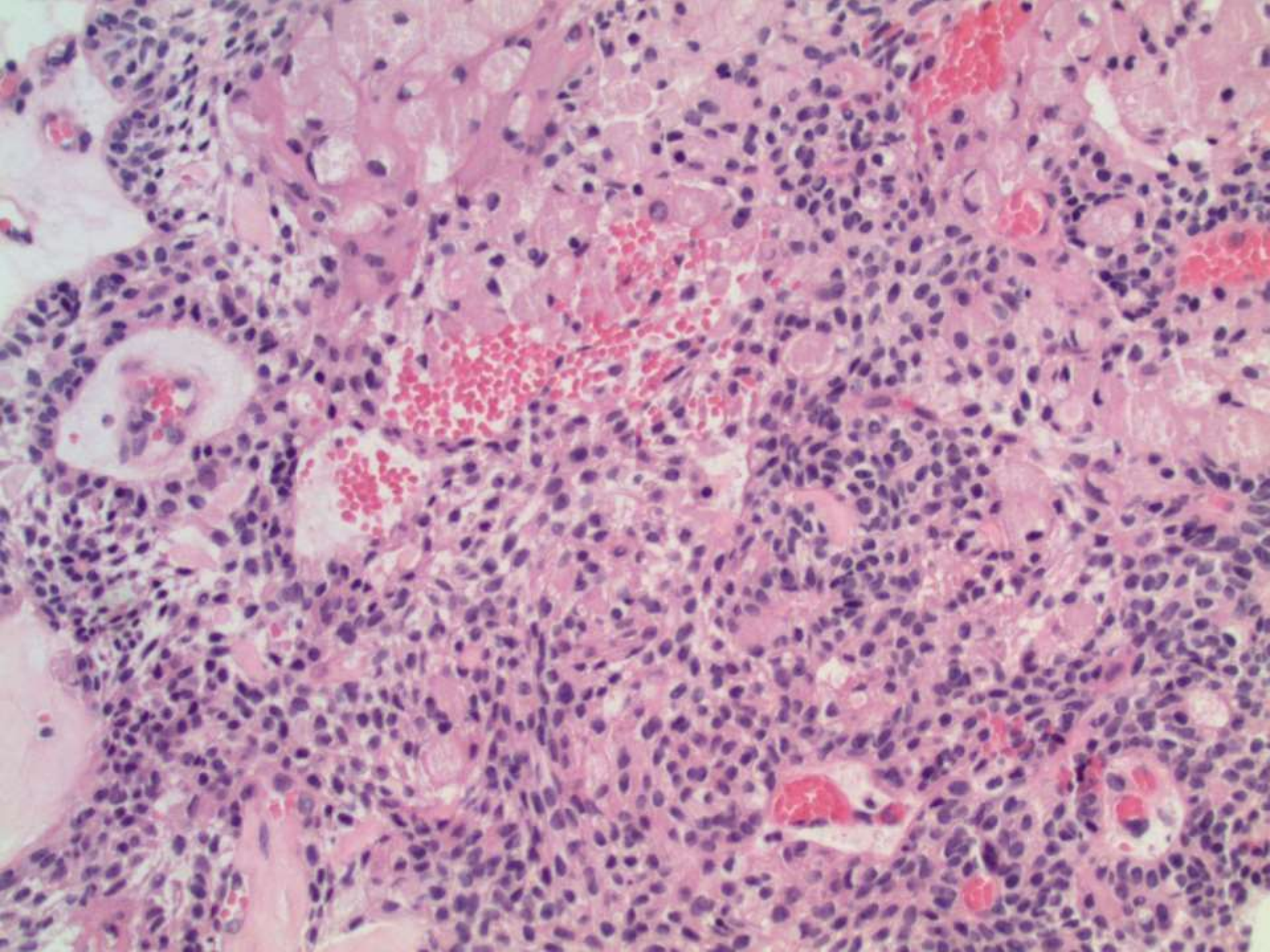












DIAGNOSIS?

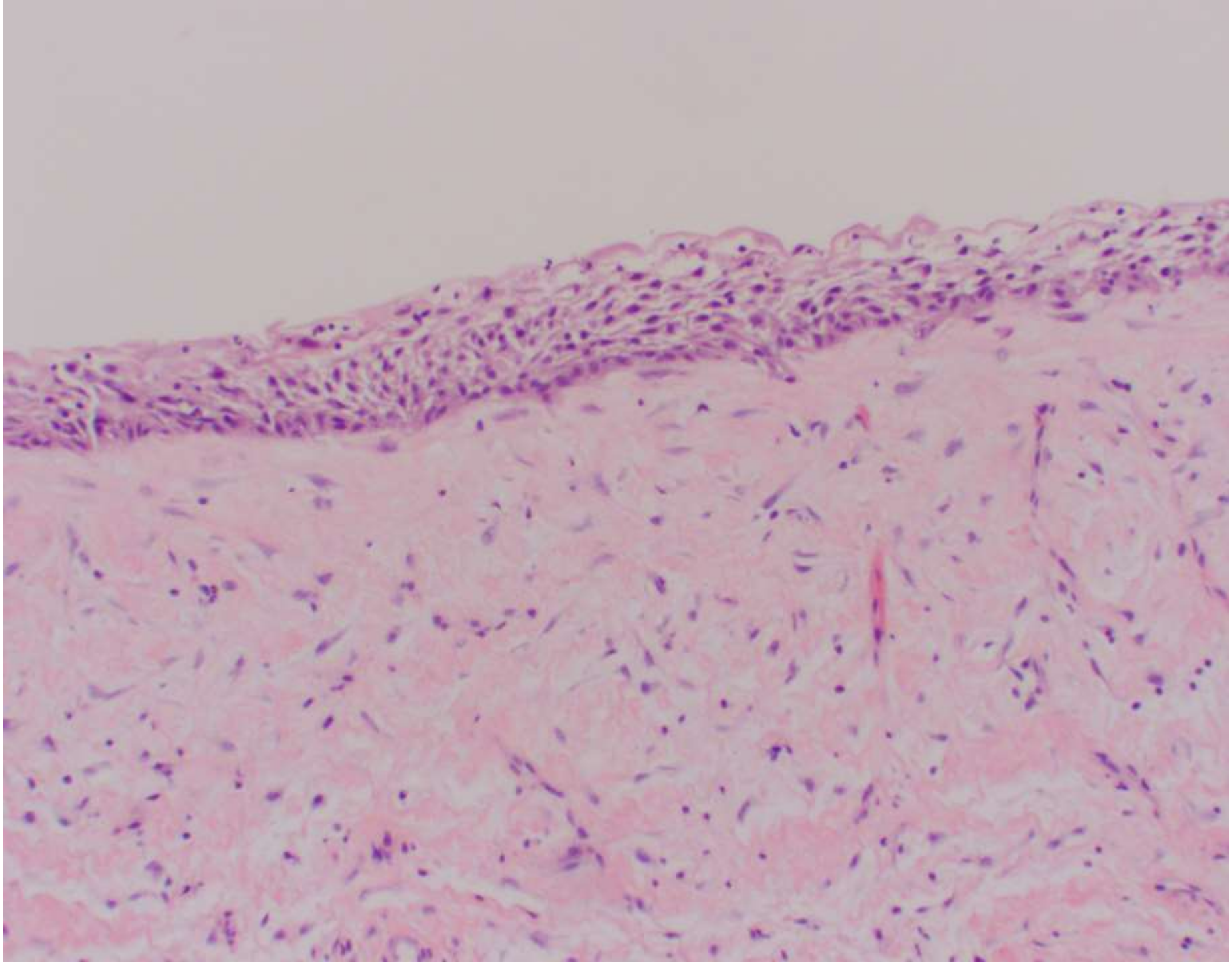
Cystic Ameloblastoma With Granular Cell Changes

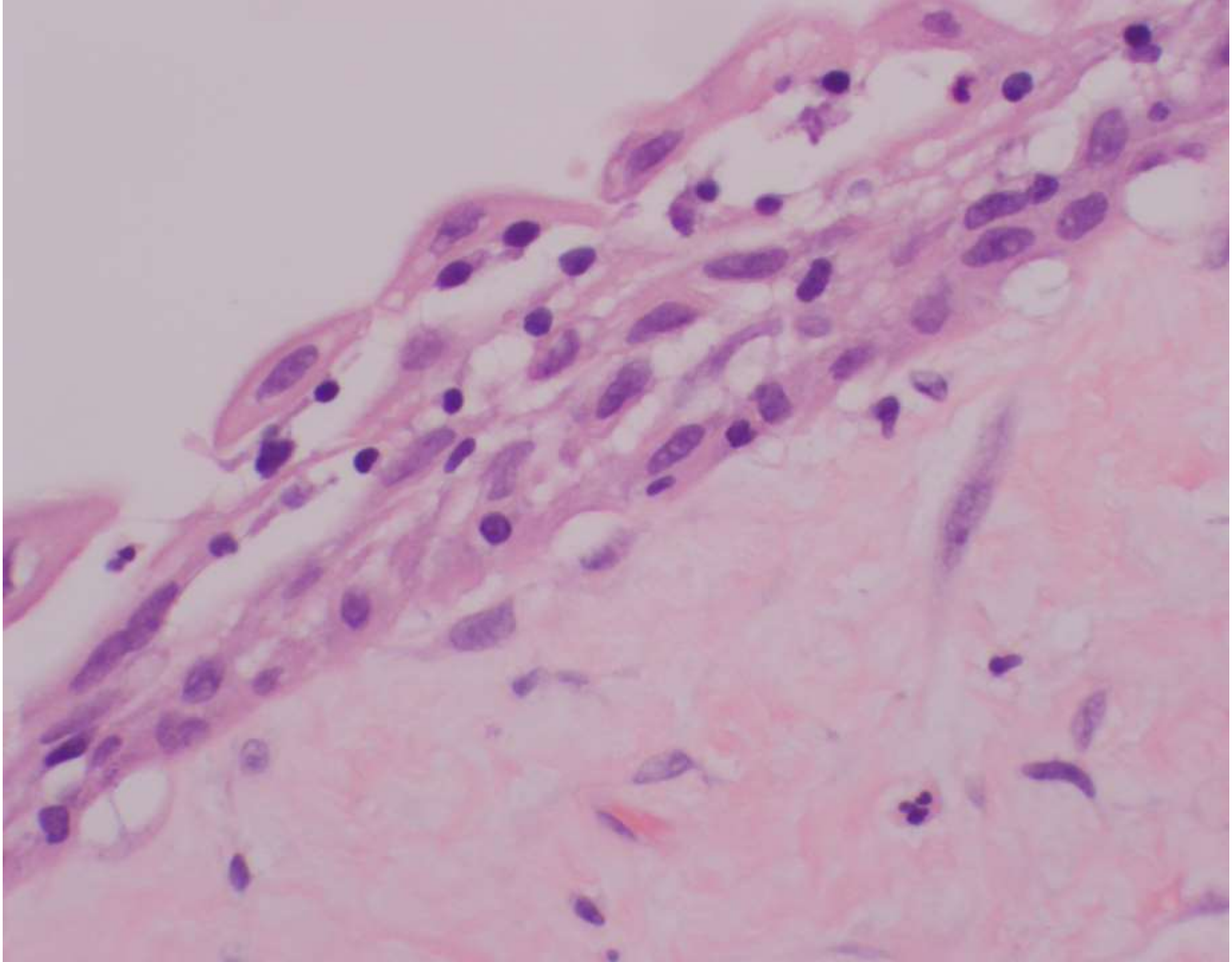
Cystic Ameloblastoma

- 5-15% of all ameloblastomas
- Typically seen in a younger age group
- Radiographically indistinguishable from other odontogenic cysts
- Can be multiloculated
- 25% show cortical perforation
- Easily missed if not familiar with the histopathologic features

Histopathologic Features

- Basal Palisading
- Thin, non-keratinizing epithelium
- Spongiosis





Why We Should Not Miss This Dx

- Ameloblastomas have a high recurrence rate following curettage (20%-90%)
- Lower for cystic vs solid and can occur many years after initial surgery
- Excision recommended

Granular Cell Changes

- Can be seen other odontogenic tumors
- Due to increased lysosomes
- ? Degenerative process
- Does not otherwise affect prognosis

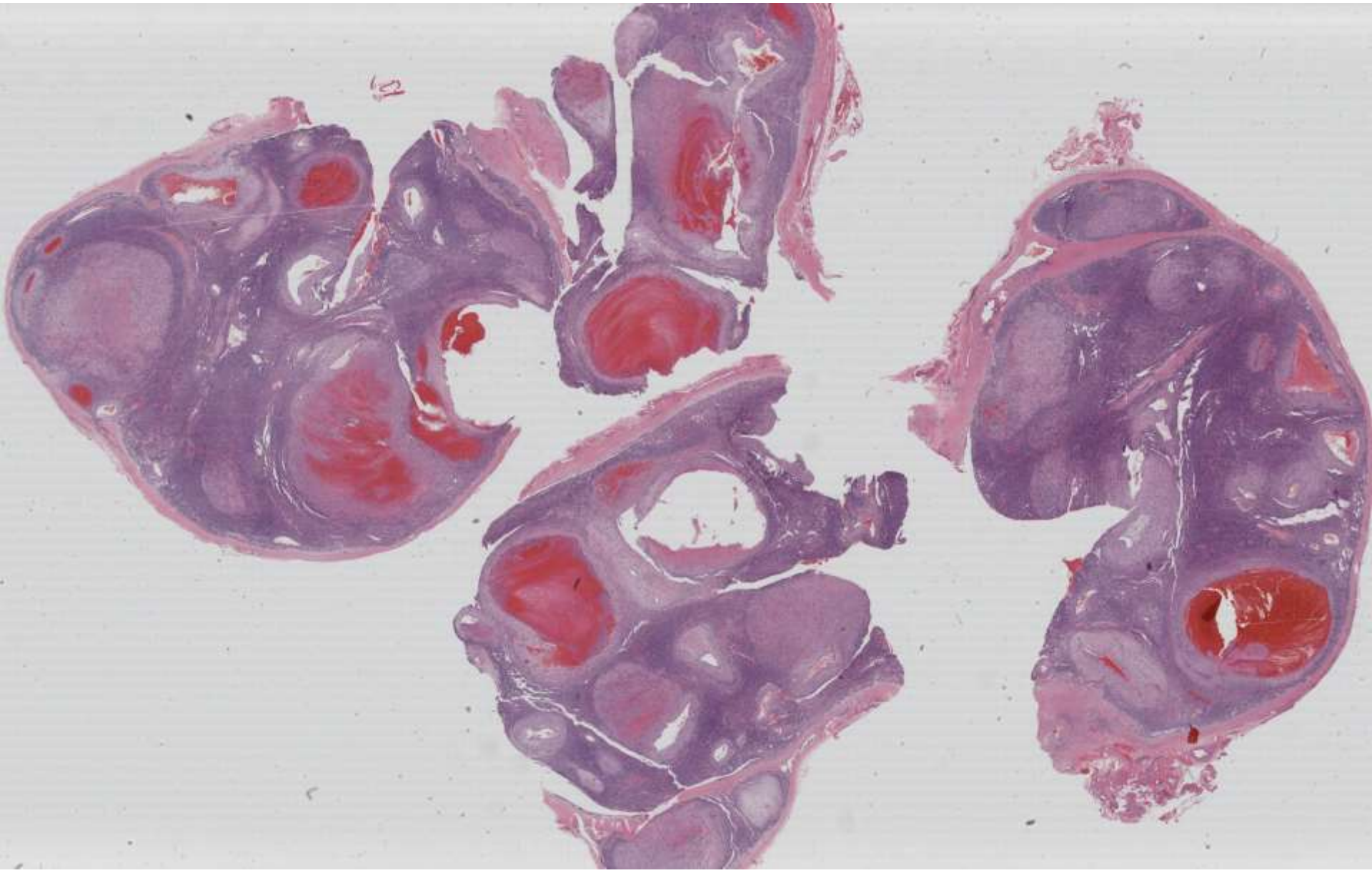
Take Home Message

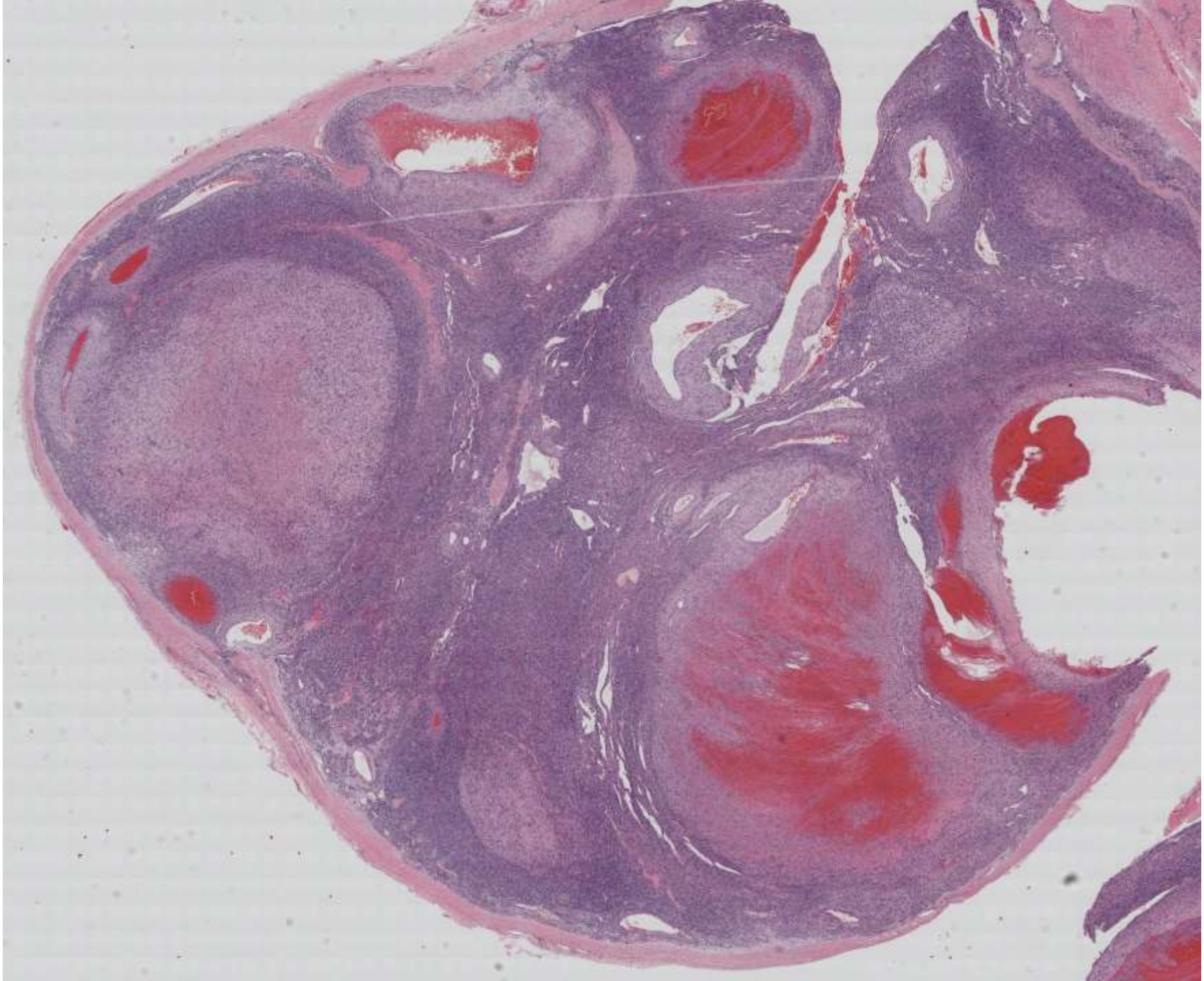
- In any odontogenic cyst look for the thin, spongiotic epithelium before diagnosing a dentigerous cyst.

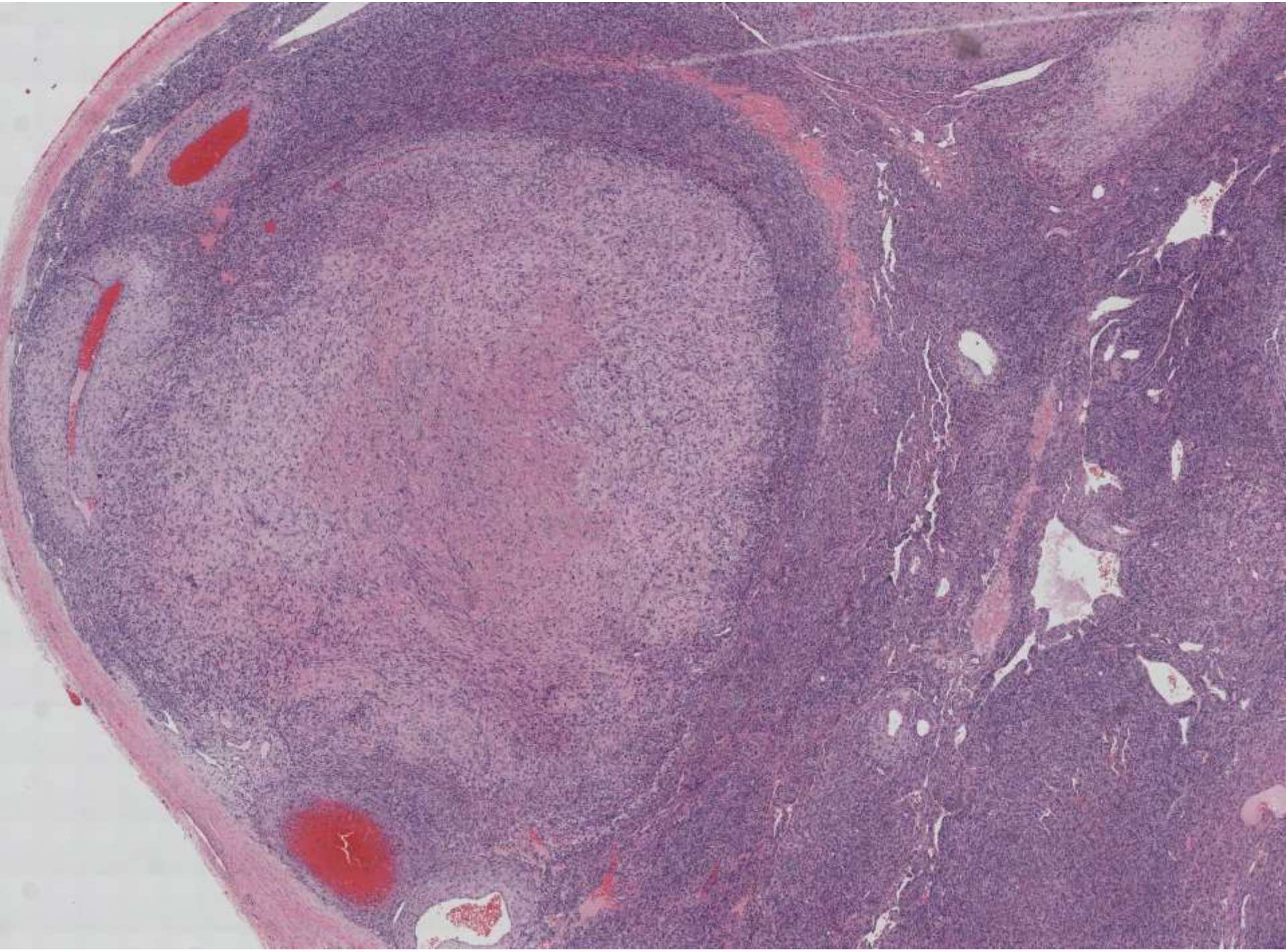
SB 6144

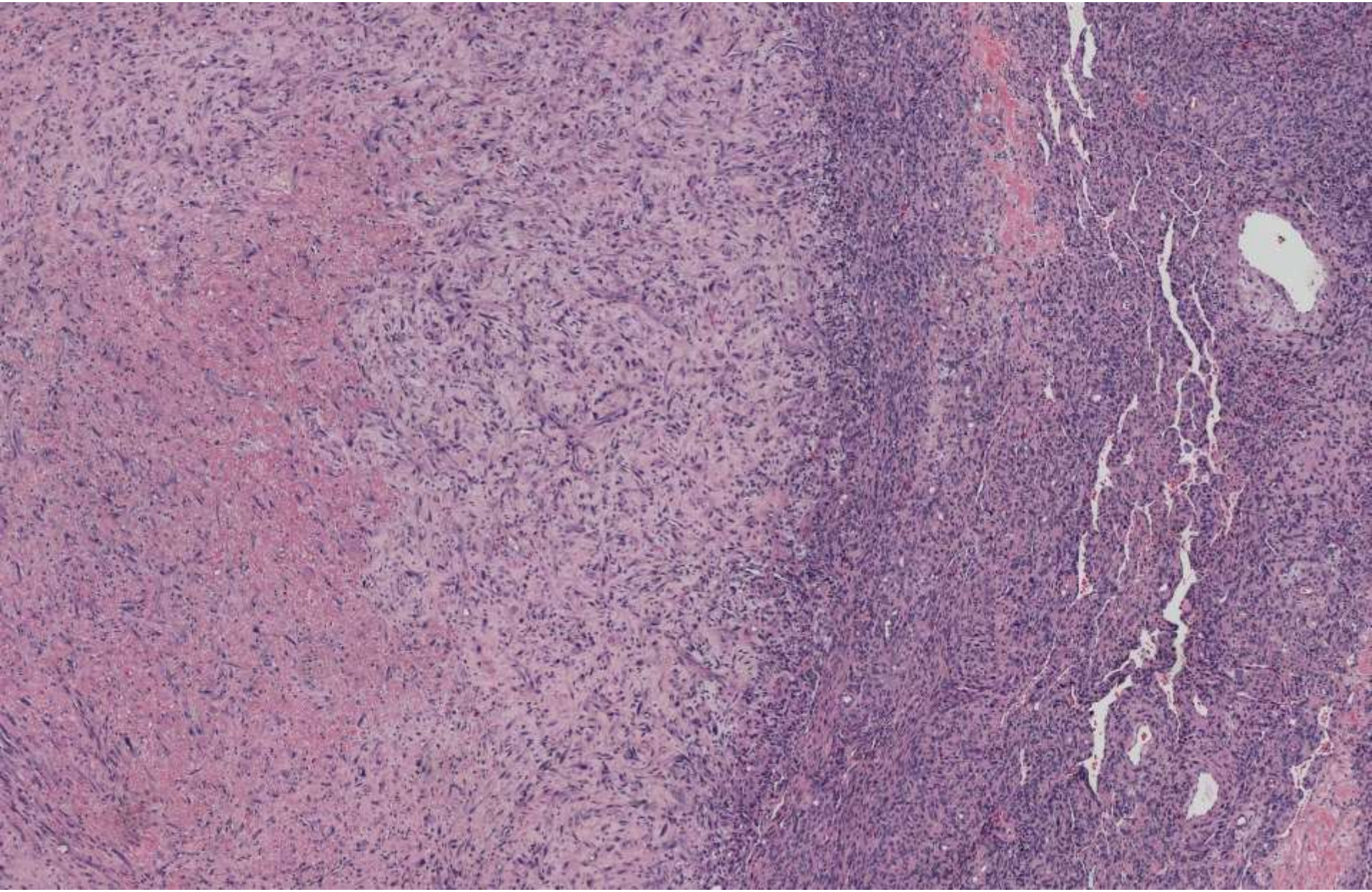
Keith Duncan; Mills-Peninsula

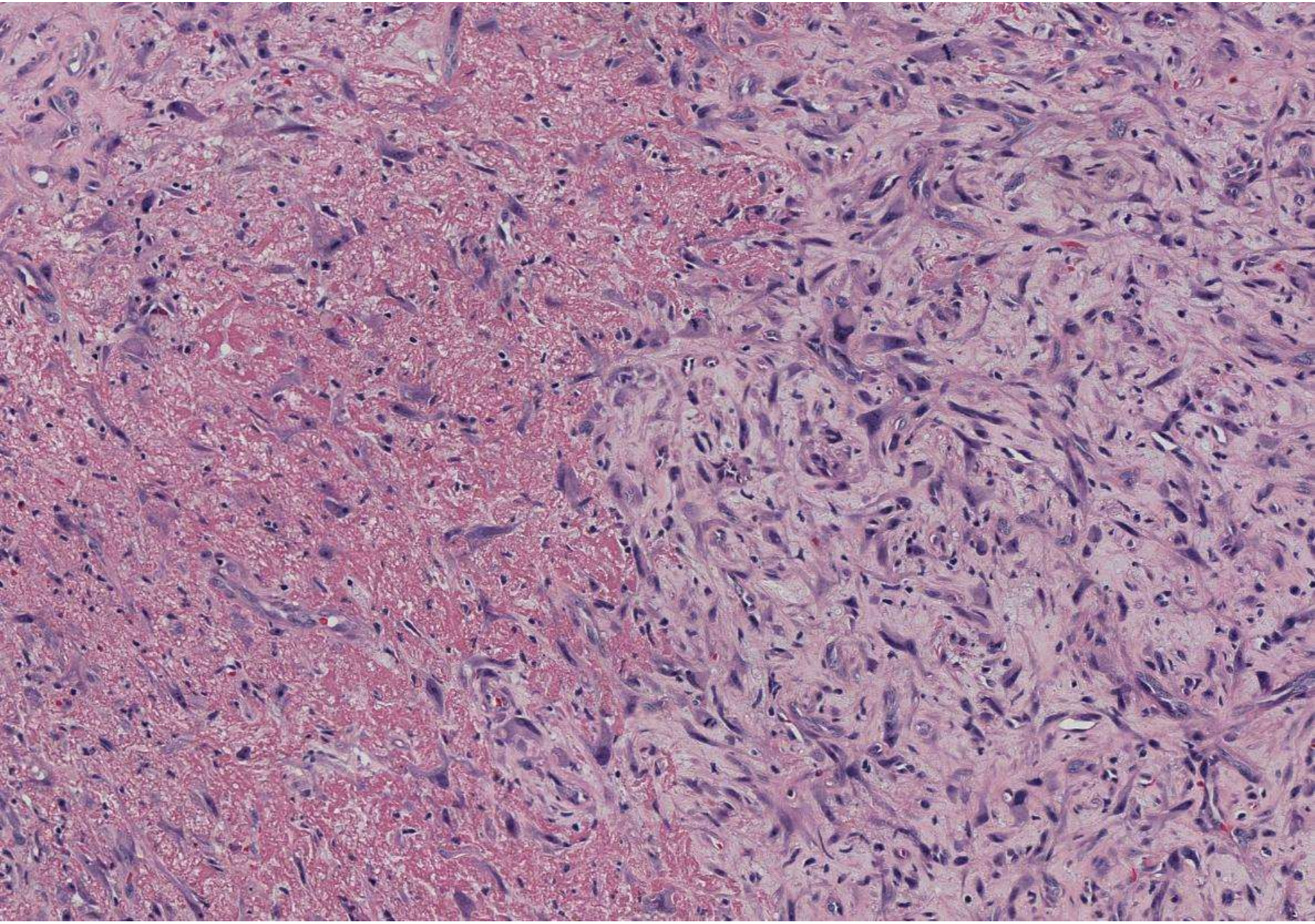
89-year-old M with pulsating radial artery aneurysm.

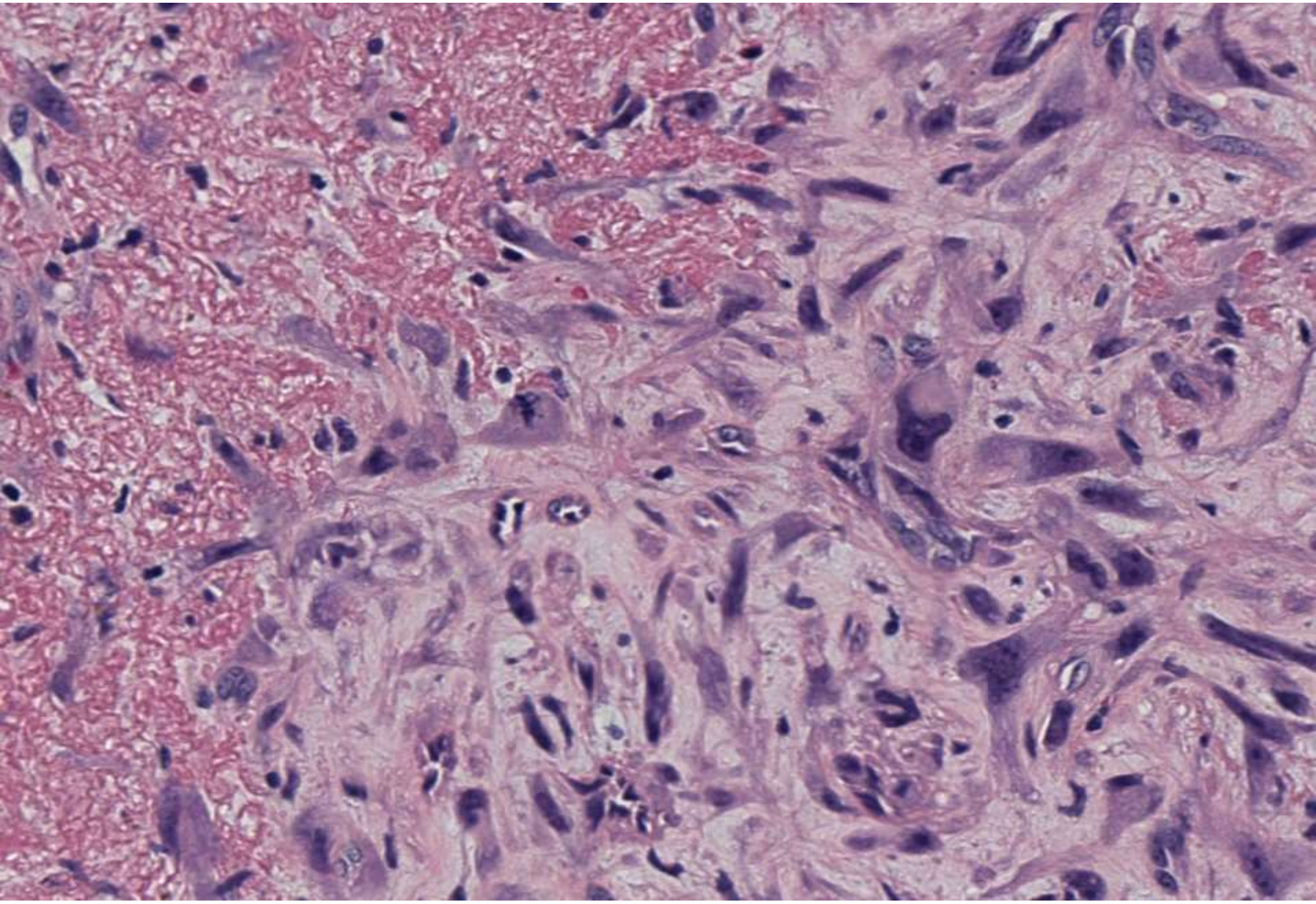


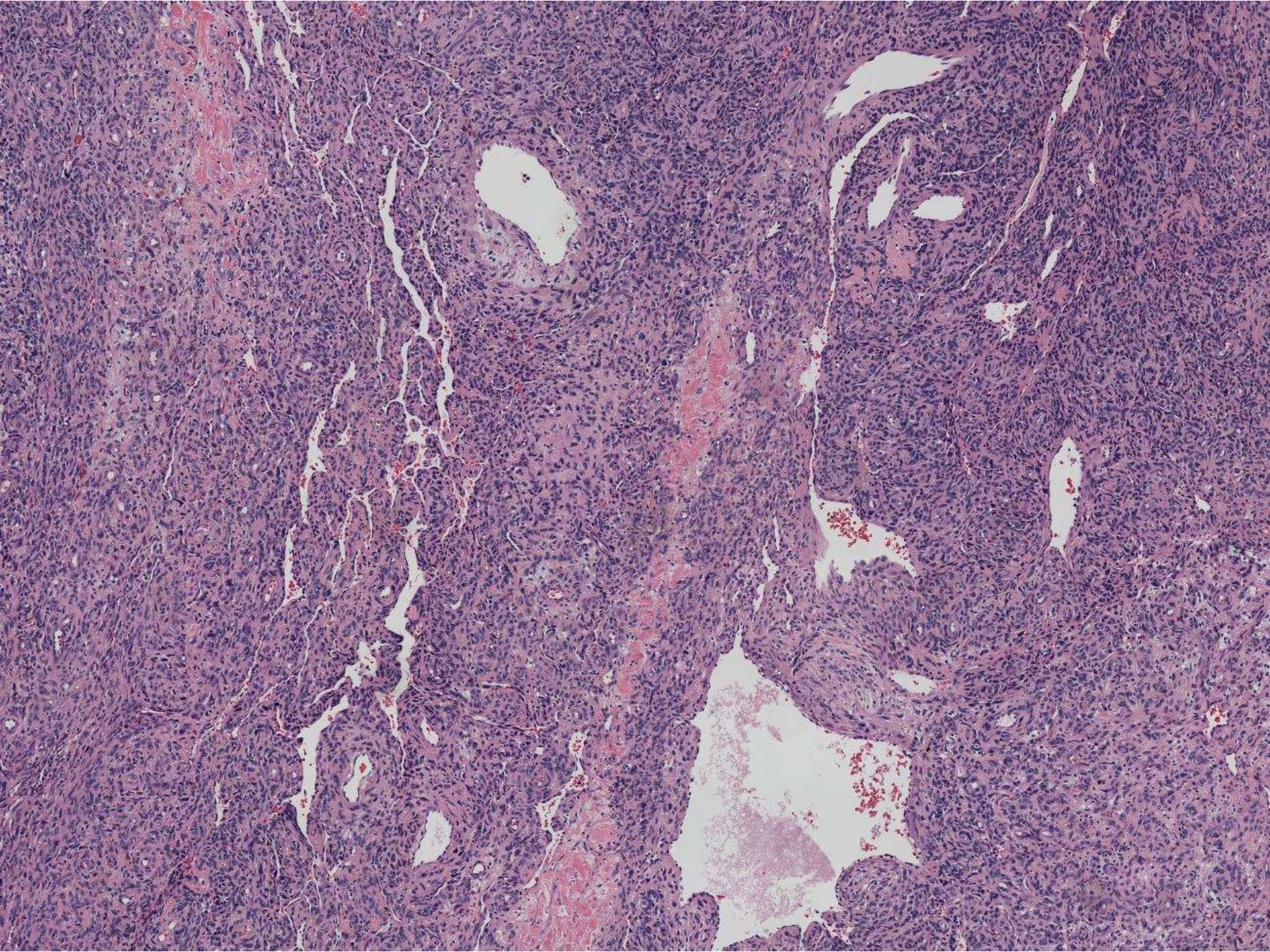


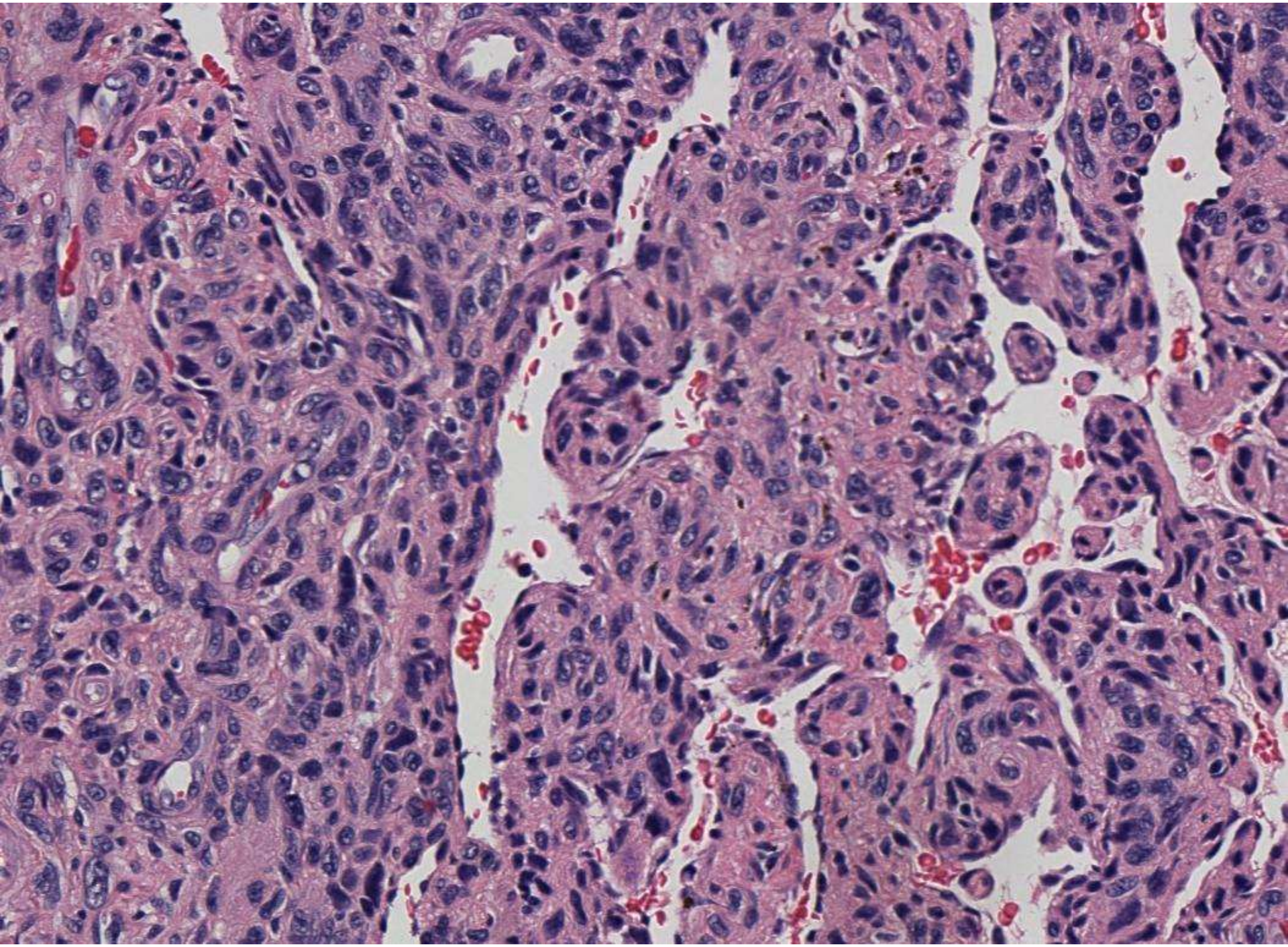












DIAGNOSIS?

MALIGNANT MYOEPITHELIOMA

- AKA MYOEPITHELIOMA CARCINOMA
- Rare tumor composed of cytologically malignant myoepithelial cells with mitotic activity
- Median age 60 years
- 2/5 yr survival 88%/55%

MALIGNANT MYOEPITHELIOMA

- Infiltrating spindle cells with fibrillar eosinophilic cytoplasm
- Infiltrative growth pattern most frequently with thin anastomosing cords of tumor cells associated with an intimately admixed reactive spindle cell stroma

- Arises from myoepithelial cells of ductules
-
- Mitotic figures common, but may be less than 4/10 HPF
- May have clear cells due to glycogen, +/-necrosis

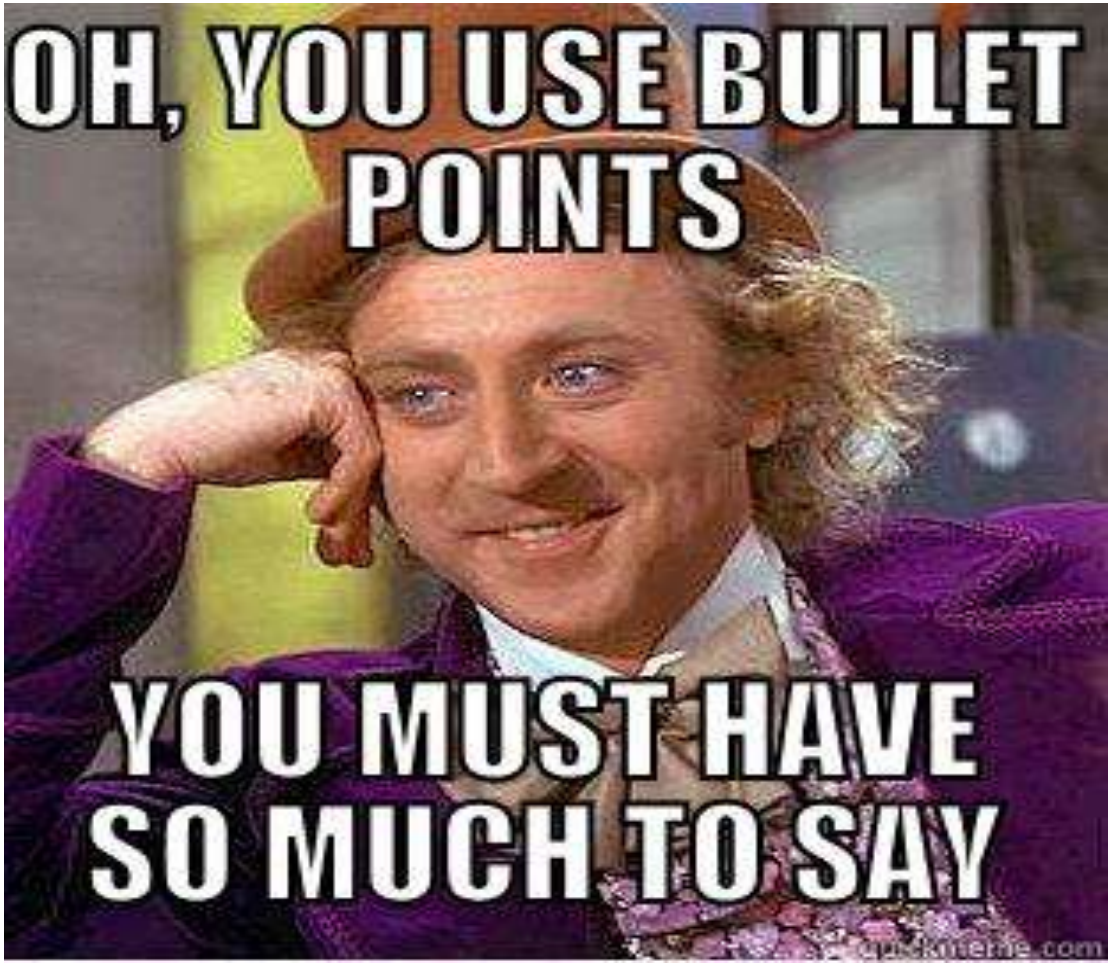
MYOEPITHELIOMA
IPOX

- **POSITIVE STAINS**
- **MYOEPITHELIAL MARKERS: SMOOTH MUSCLE ACTIN, S100 AND P63**
- **ALSO CD10, CYTOKERATIN, VIMENTIN**

- **REACTIVE STROMA: WEAK POSITIVITY FOR CALPONIN, S100 AND SMOOTH MUSCLE ACTIN**

MYOEPITHELIOMA
DIFF DX

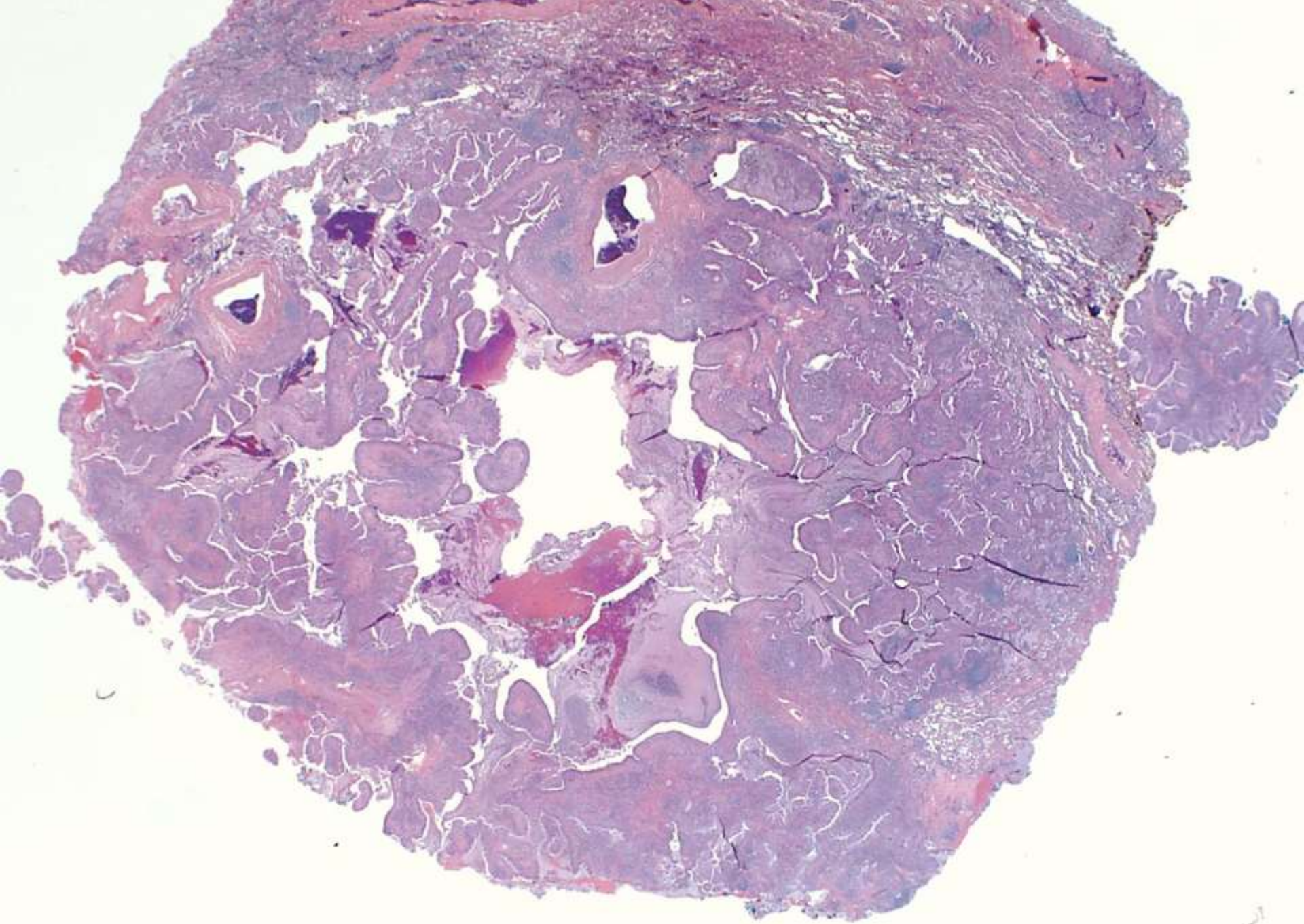
- Fibromatosis: no dominant nodule
- Myofibroblastic lesions: usually no dominant nodule, keratin negative
- Spindle cell carcinoma: negative for myoepithelial markers

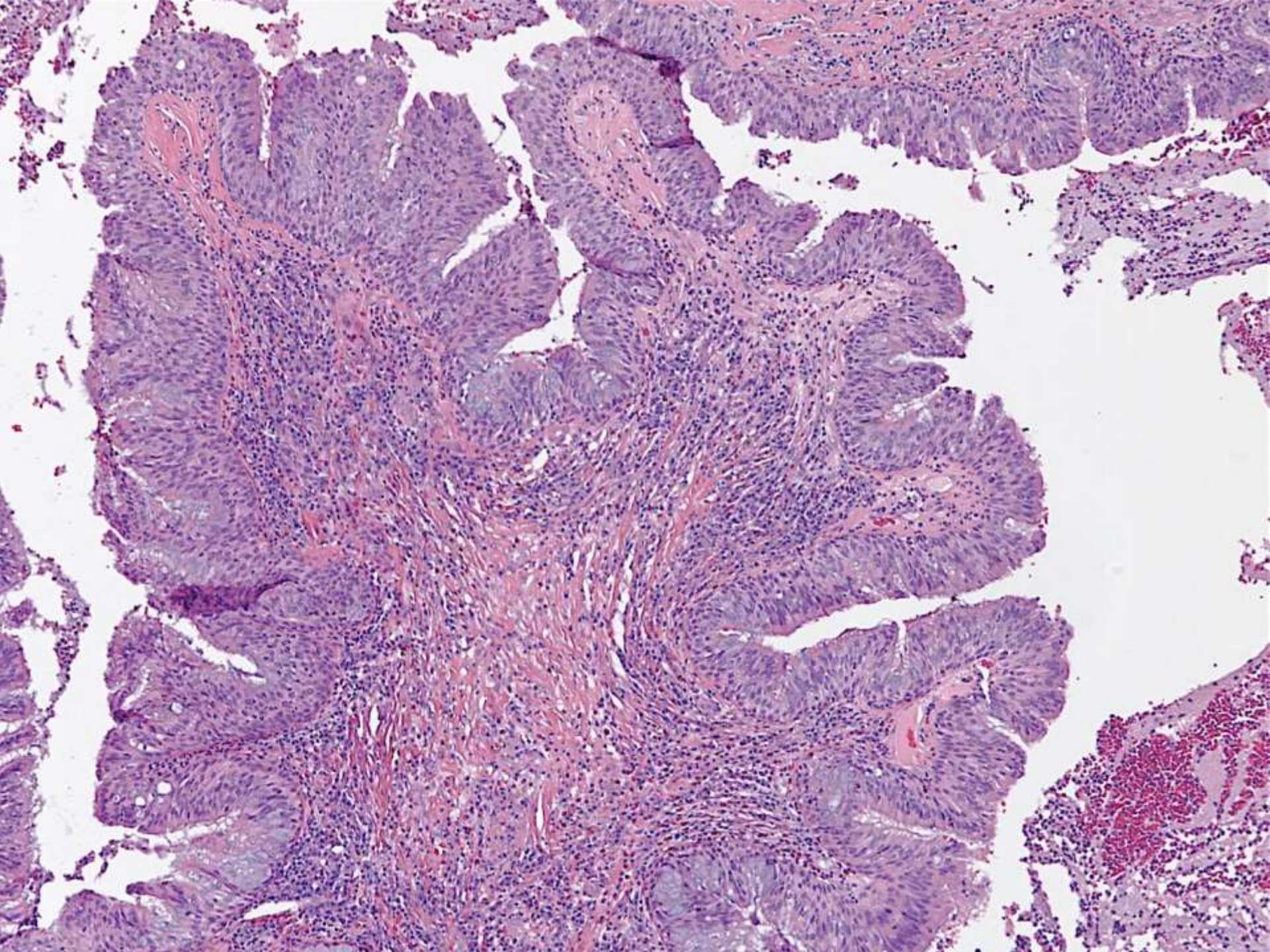

OH, YOU USE BULLET POINTS
YOU MUST HAVE SO MUCH TO SAY

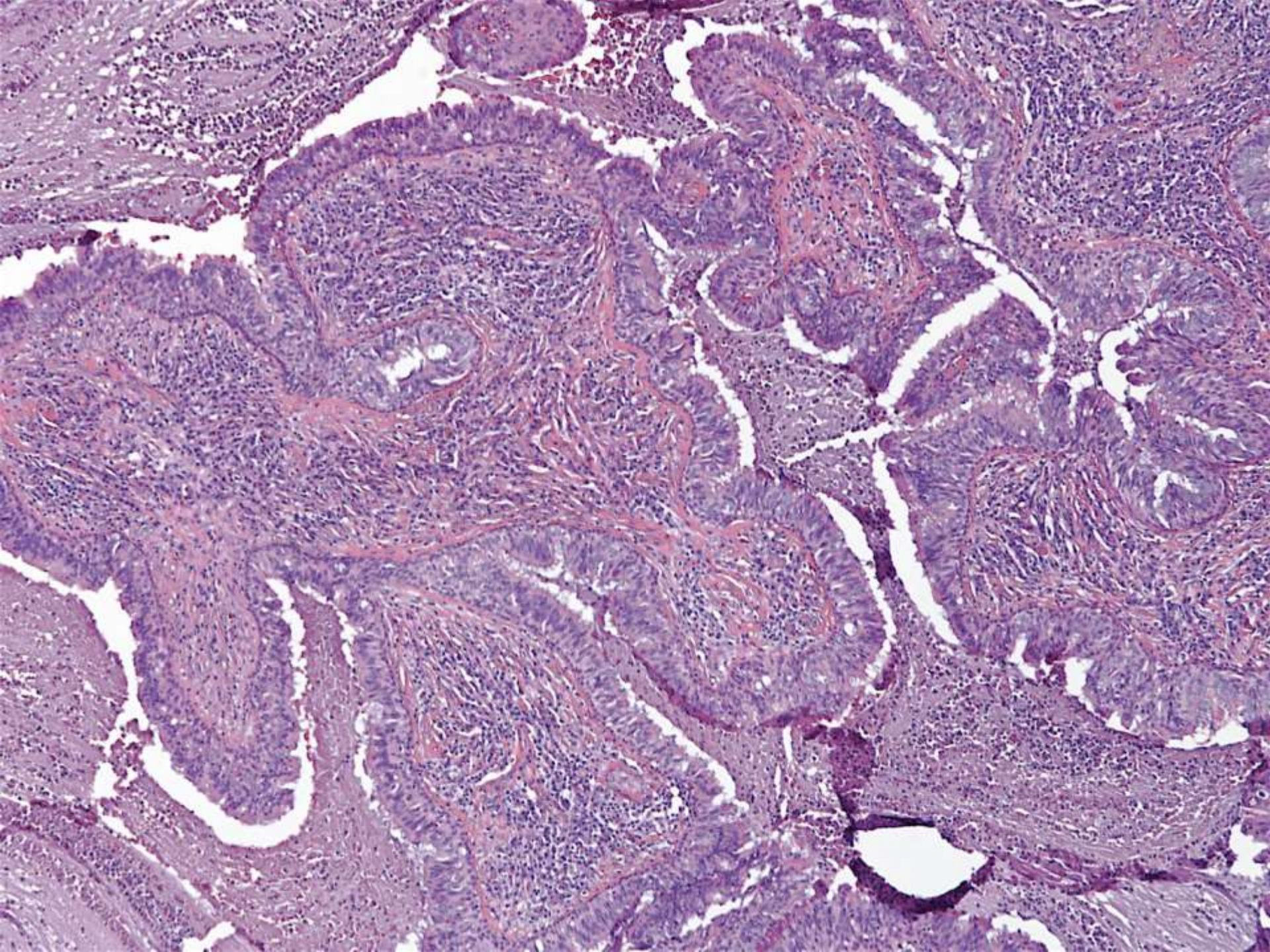
SB 6145

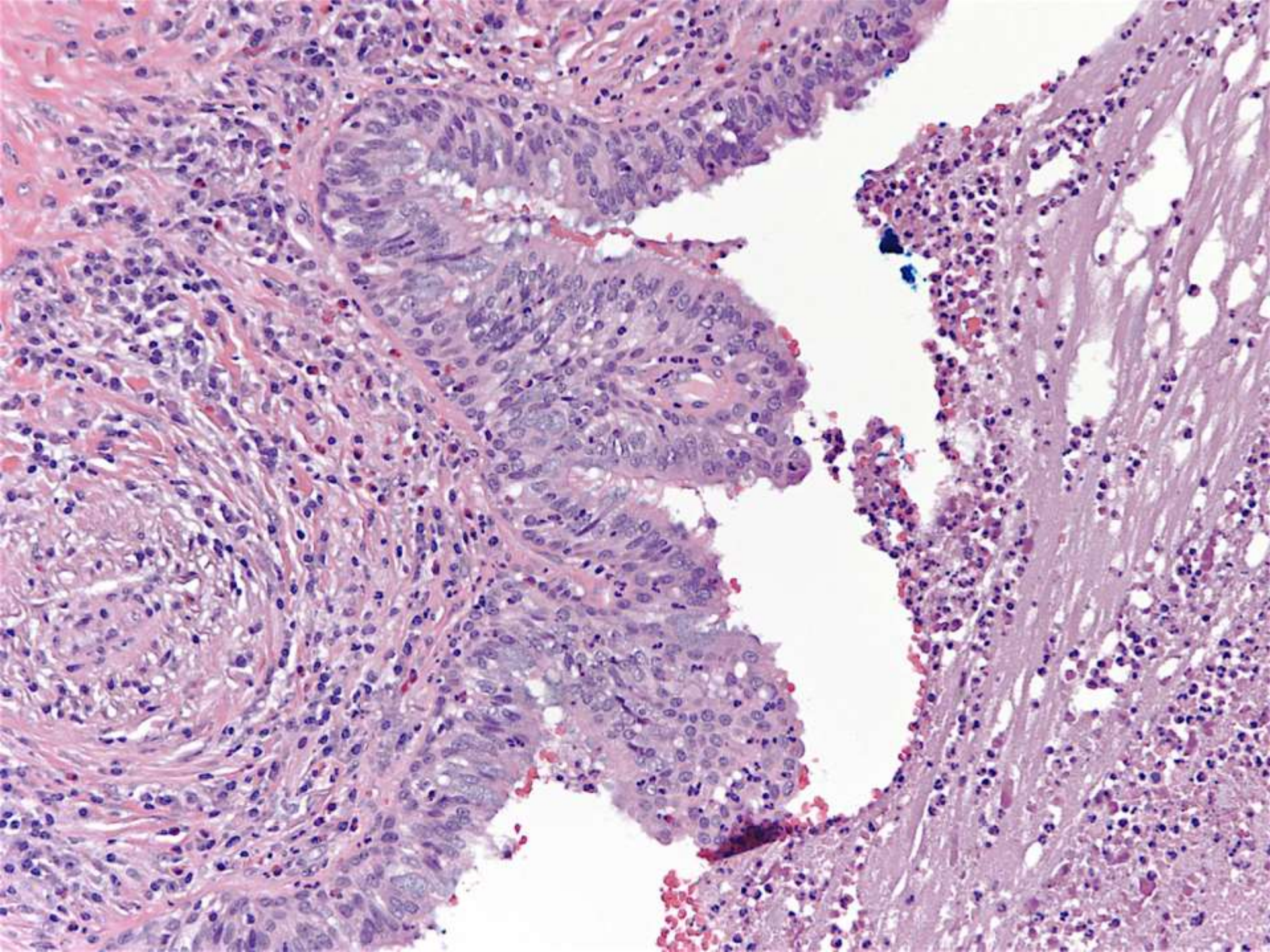
Allison Zemek/Gerald Berry; Stanford

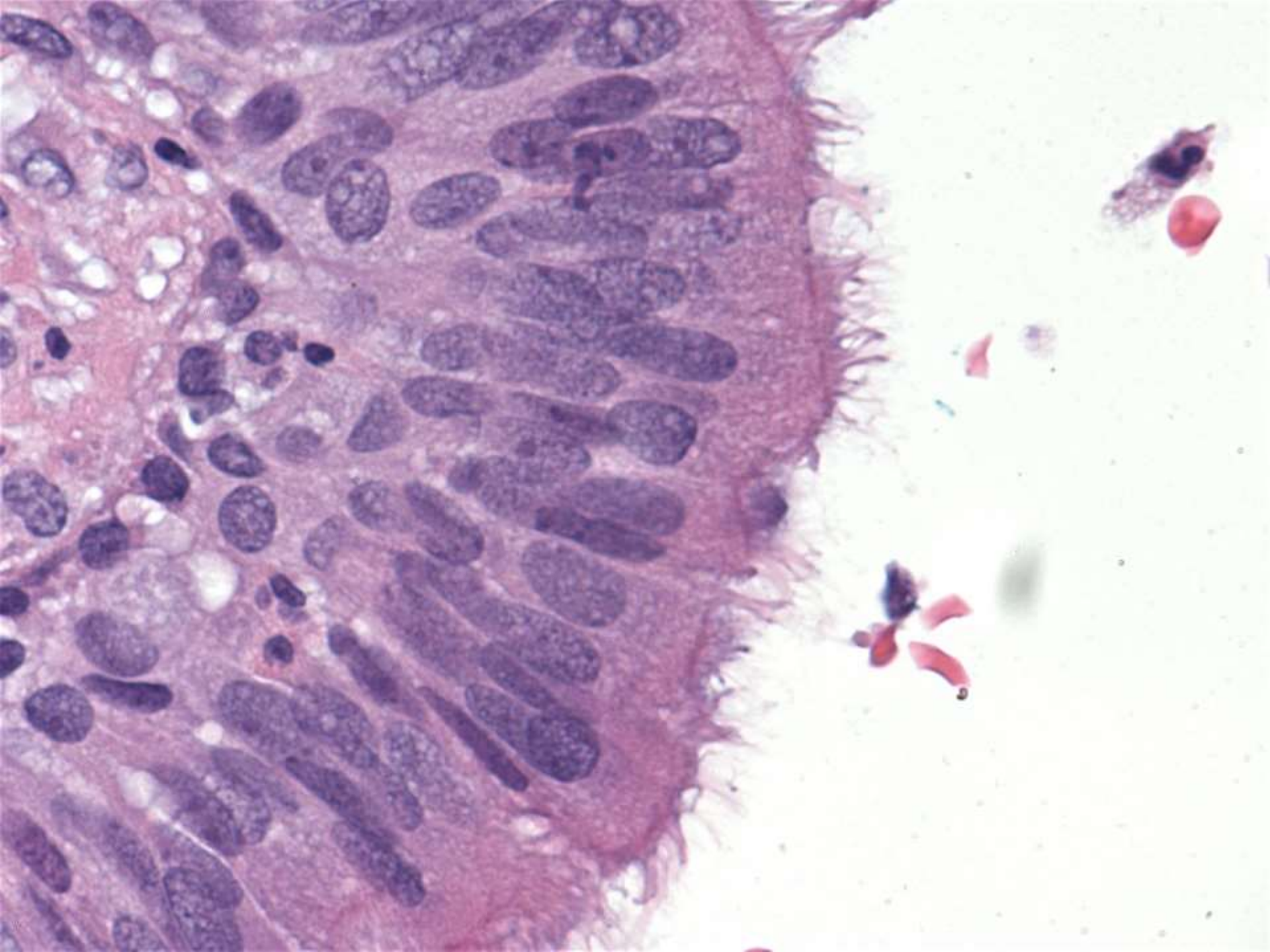
63-year-old F with history of bronchiectasis, found to have 2.8cm nodule in left lower lobe. Lobectomy specimen submitted.











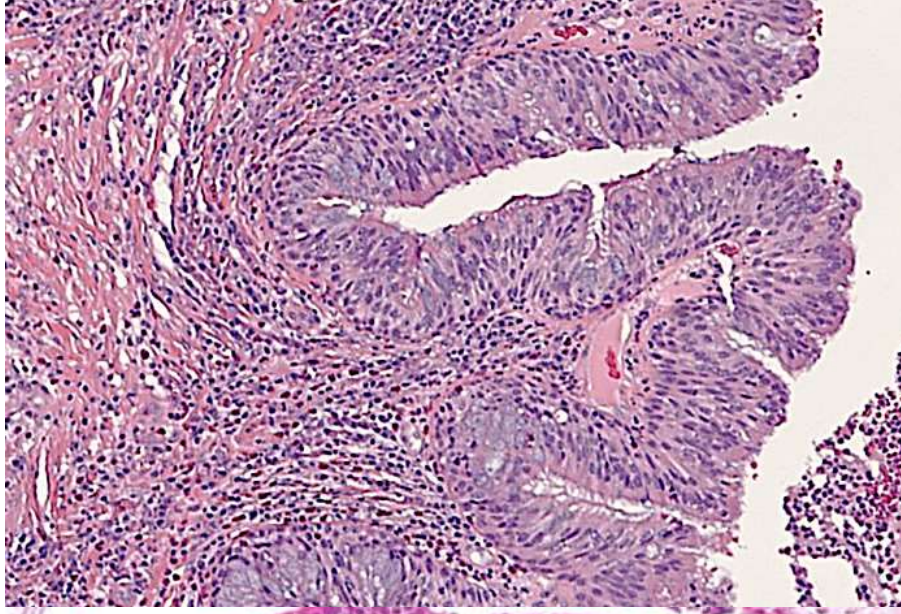
DIAGNOSIS?

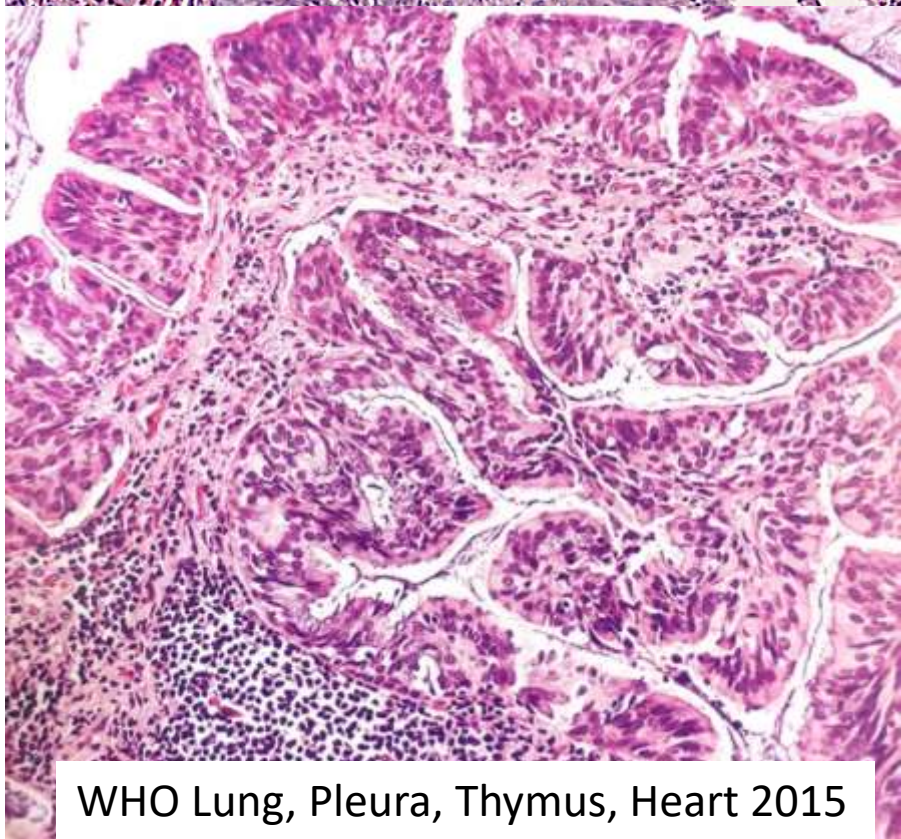
Glandular papilloma

- Synonym
  - Columnar cell papilloma
- Epidemiology
  - Rare
  - M:F = 1:1
  - 6^{th}-7^{th} decade
- Clinical features
  - Obstruction
  - Usually central

Glandular papilloma

- Synonym
  - Columnar cell papilloma
- Epidemiology
  - Rare
  - M:F = 1:1
  - 6^{th}-7^{th} decade
- Clinical features
  - Obstruction
  - Usually central



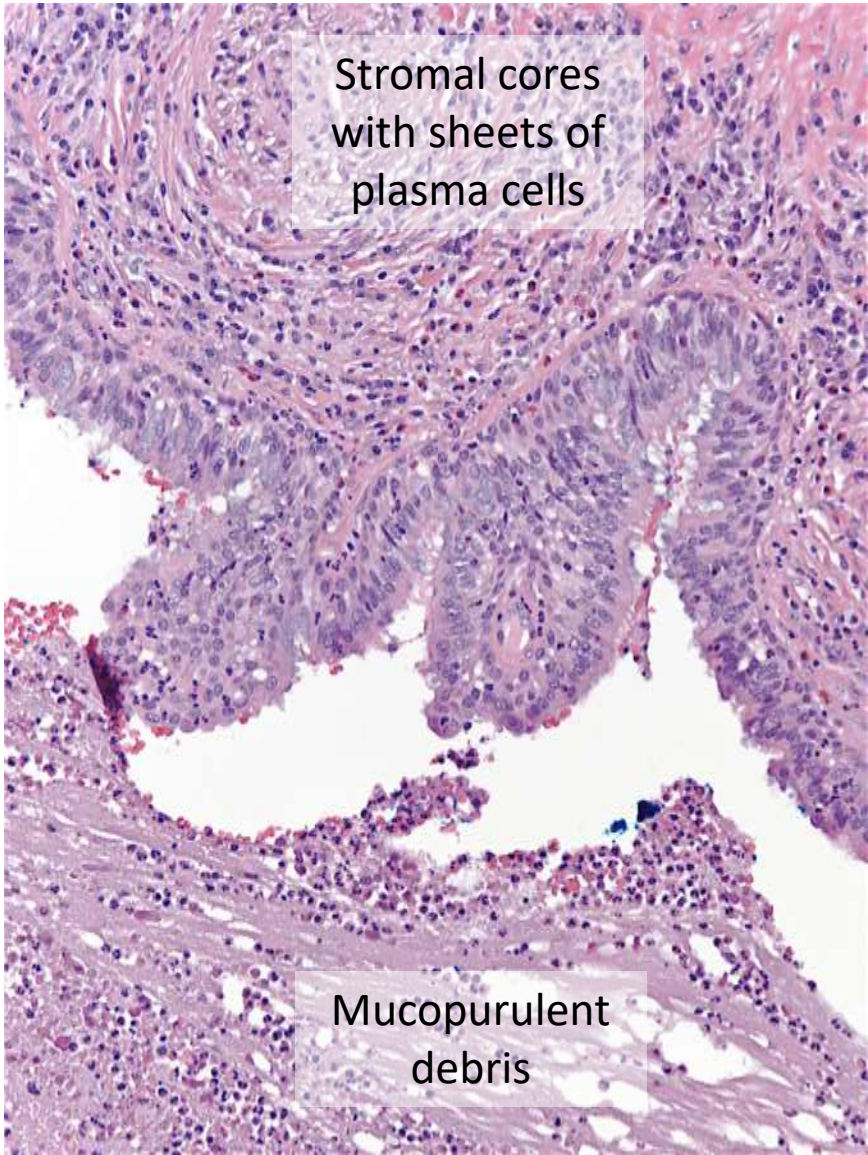


WHO Lung, Pleura, Thymus, Heart 2015

Glandular papilloma

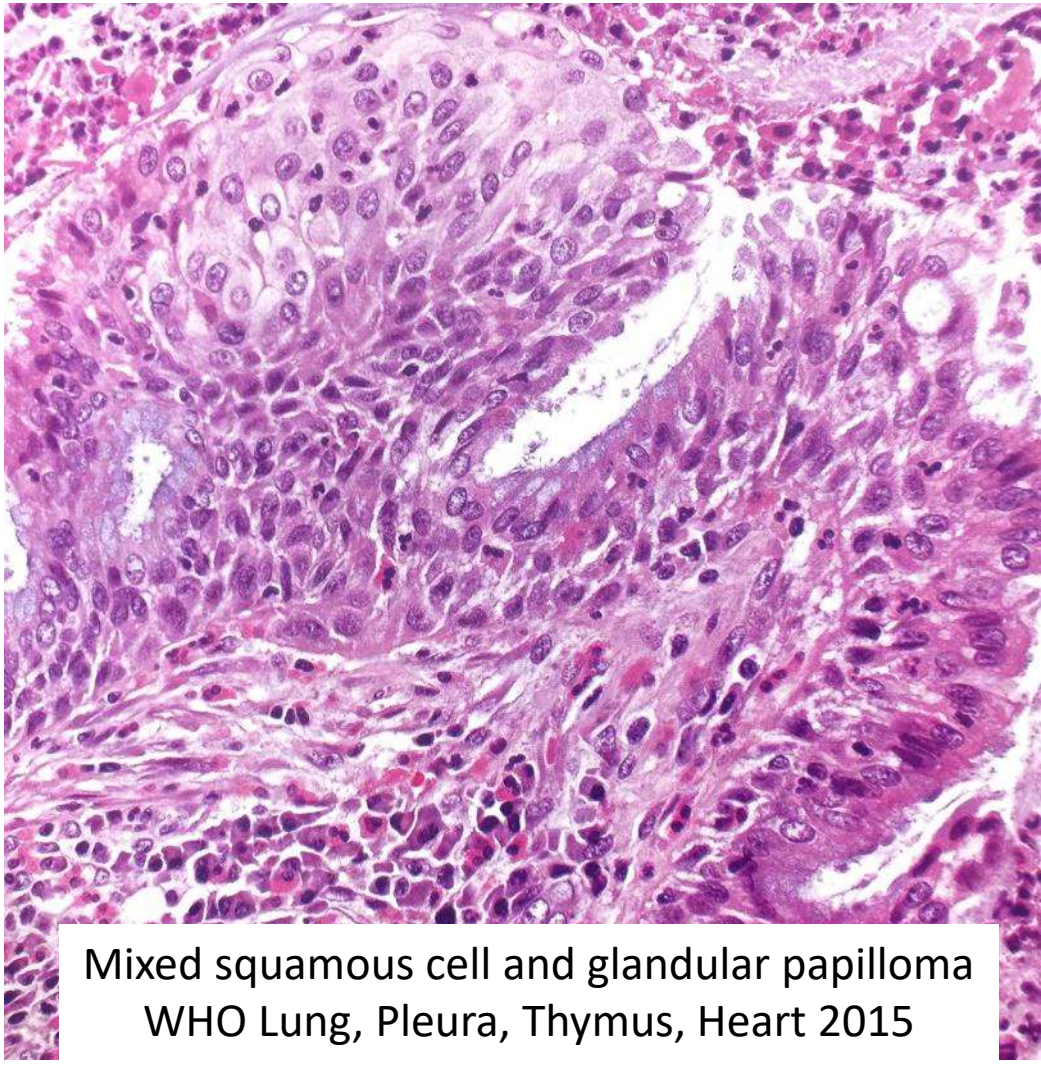
- Gross
  - 0.7-4.0 cm
  - Papillary fronds

- Histology
  - Broad epithelial-lined
  - Vascular stromal cores
  - Absent nuclear atypia, mitosis, necrosis



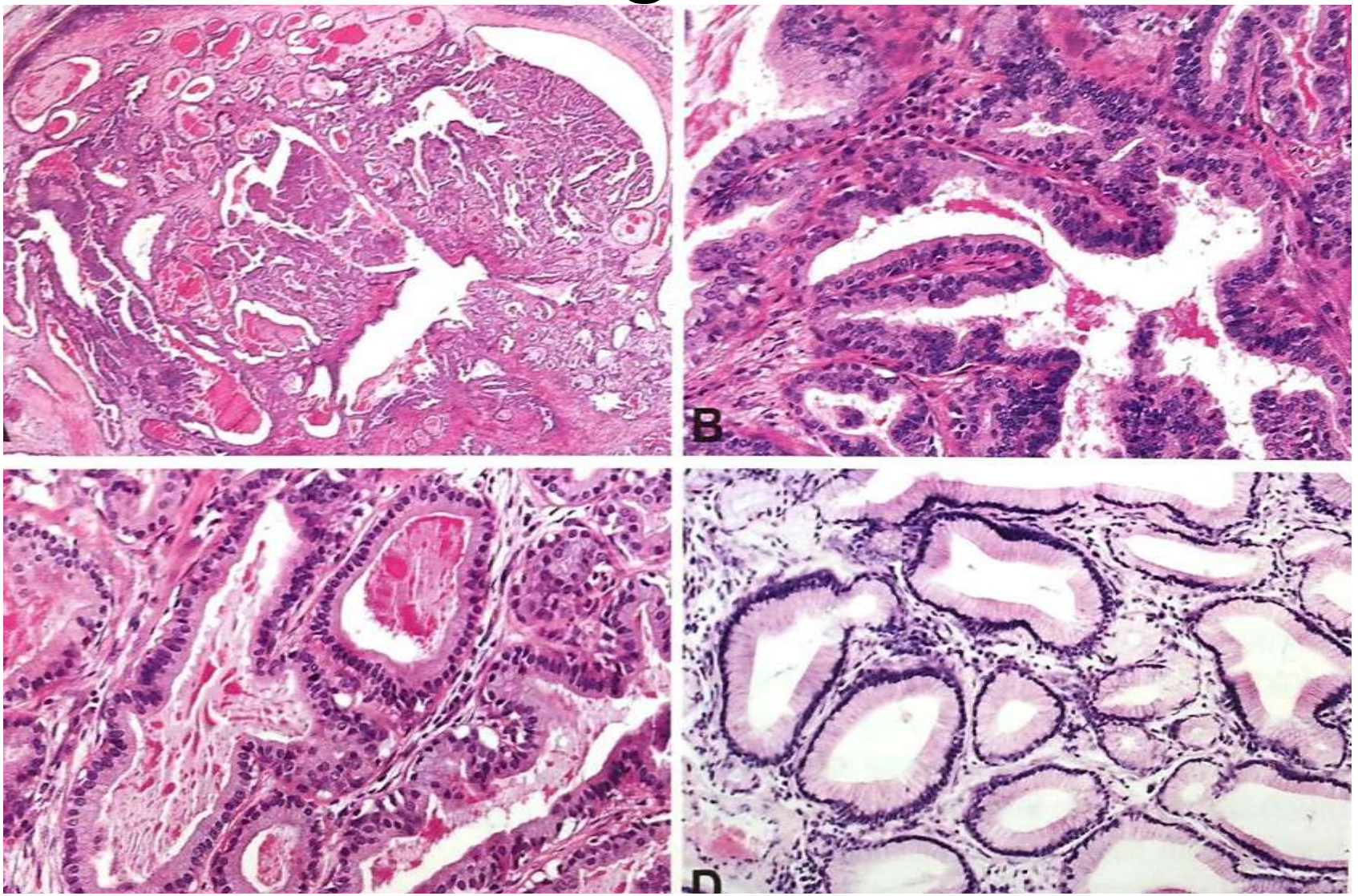
Glandular papilloma

- Differential diagnosis
  - Mixed
  - Mucous gland adenoma
  - Adenocarcinoma
- Potential pitfalls
  - Frozen section
  - Incidental



Mixed squamous cell and glandular papilloma
WHO Lung, Pleura, Thymus, Heart 2015

DDx: mucous gland adenoma



WHO Lung, Pleura, Thymus, Heart 2015

Glandular papilloma

- Prognosis
  - Complete excision
  - No malignant transformation

- Take home points
  - Rare benign lesion
  - Look for squamous differentiation
  - Potential pitfall at frozen section

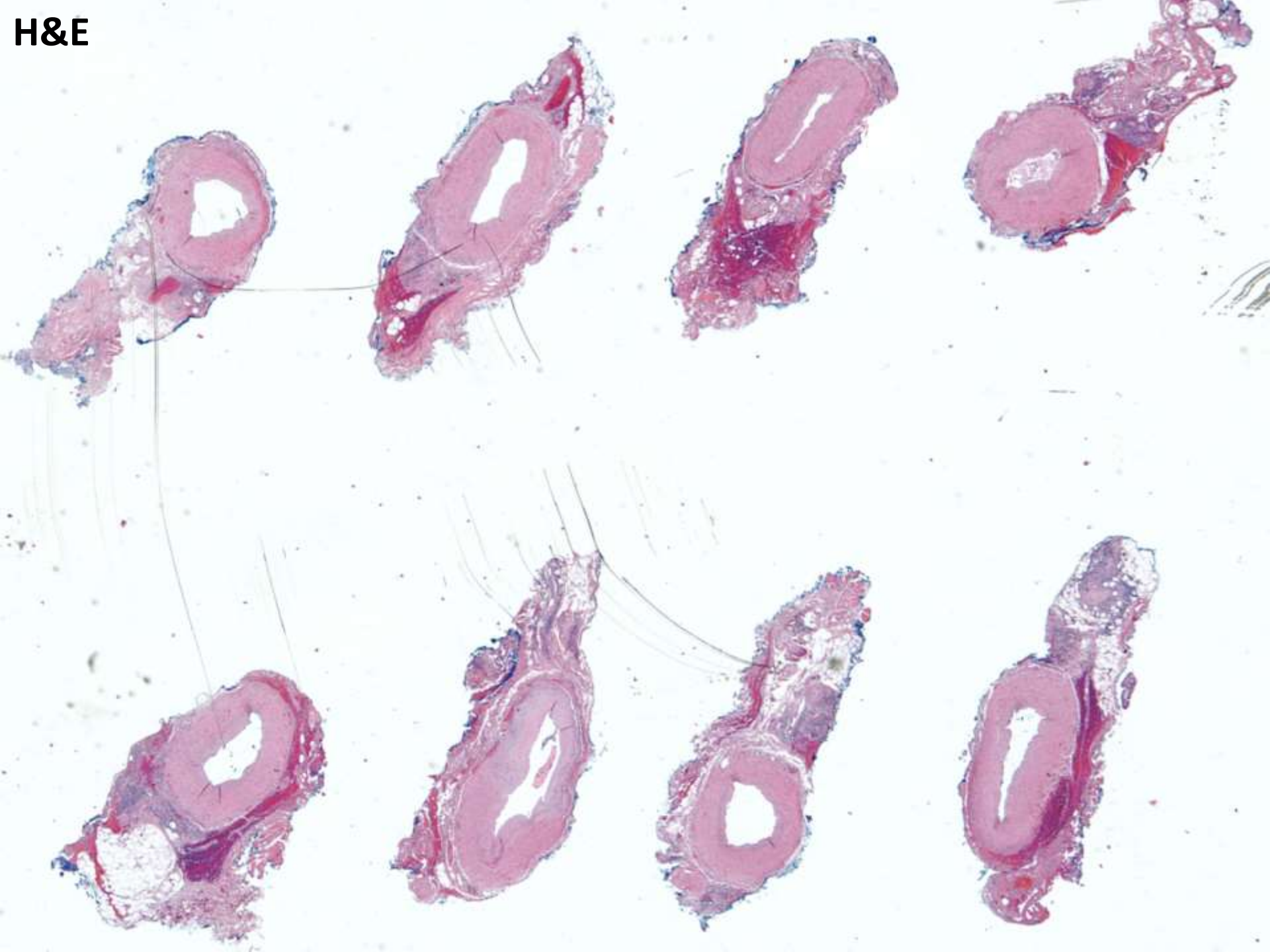
References

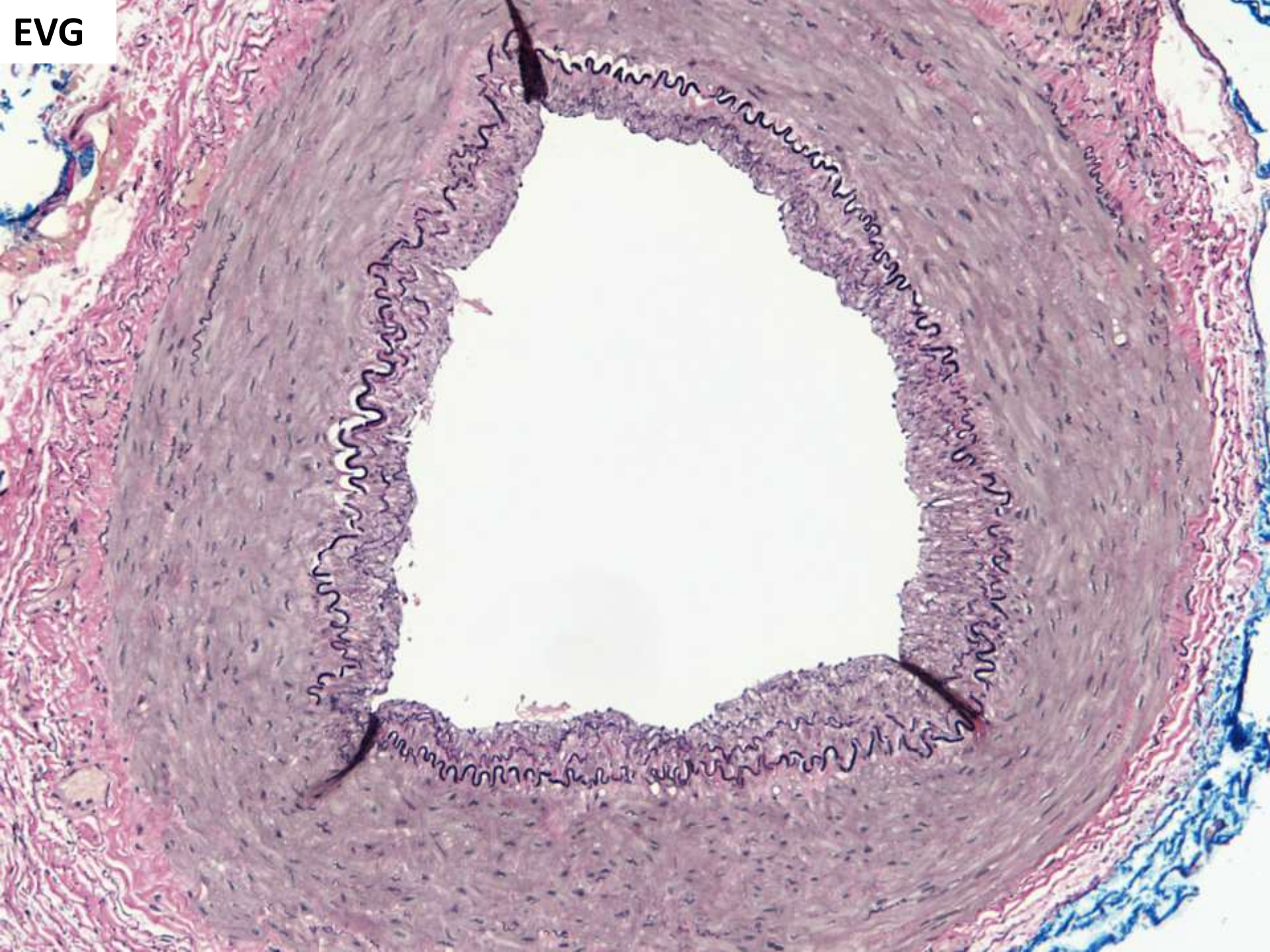
- WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart. Fourth edition. 2015
- Aida et al. Solitary peripheral ciliated glandular papillomas of the lung: a report of 3 cases. Am J Surg Pathol. 32:1489-94
- Emerson et al. Solitary peripheral pulmonary papilloma evaluation on frozen section: a potential pitfall for the pathologist. Pathol Res Pract. 208:726-9

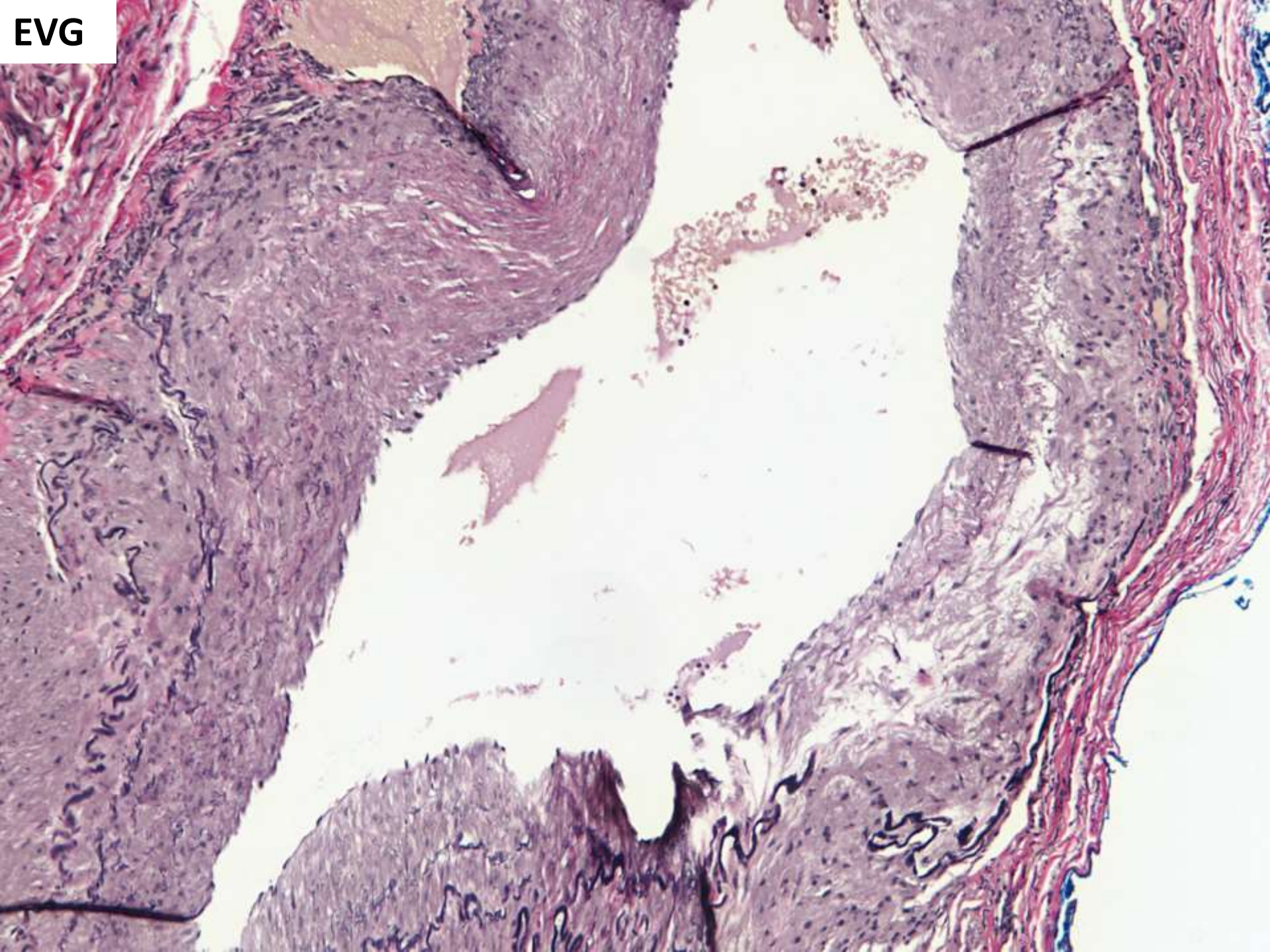
SB 6146

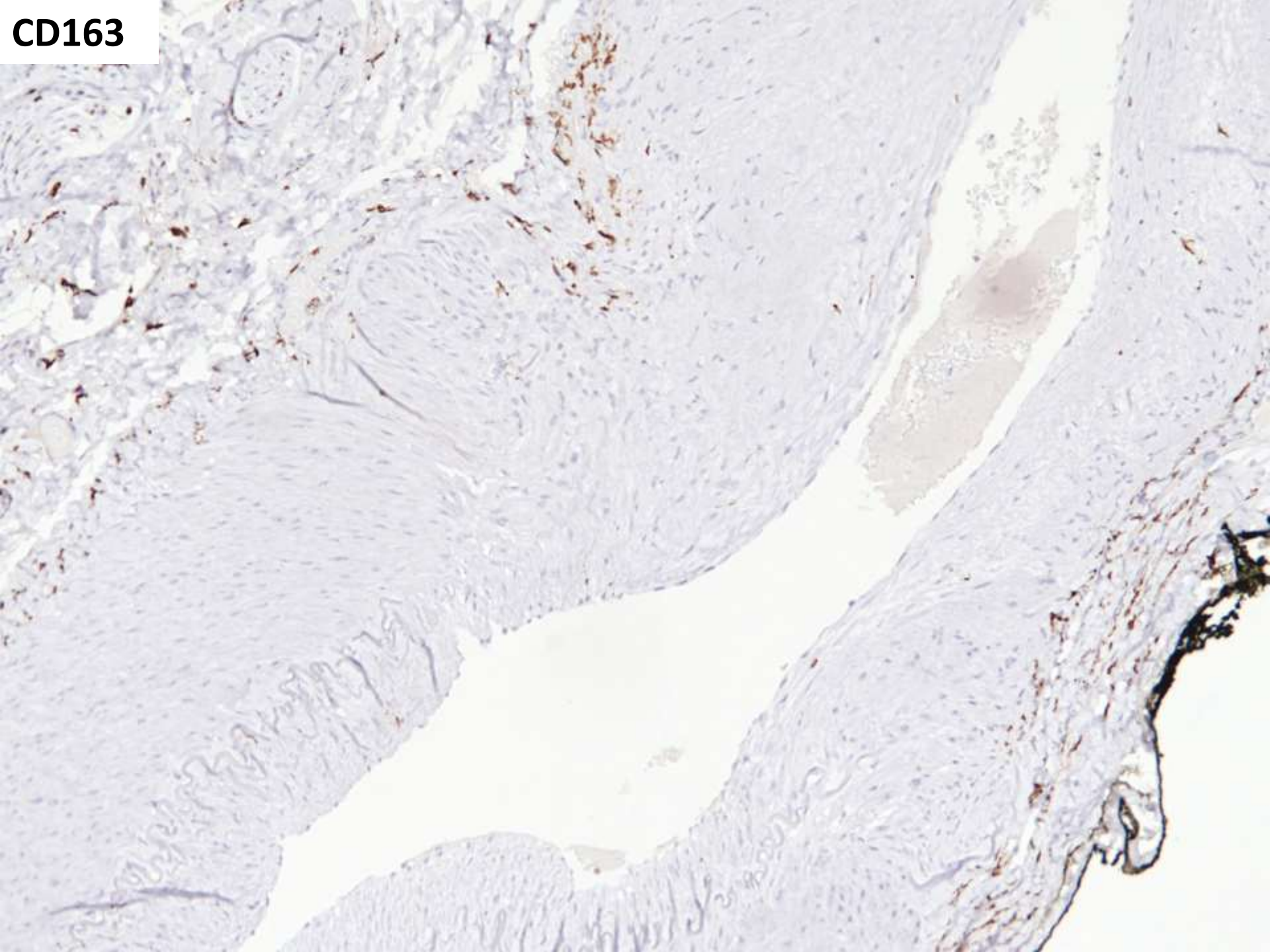
Peyman Samghabadi/Donald Born/Hannes Vogel; Stanford

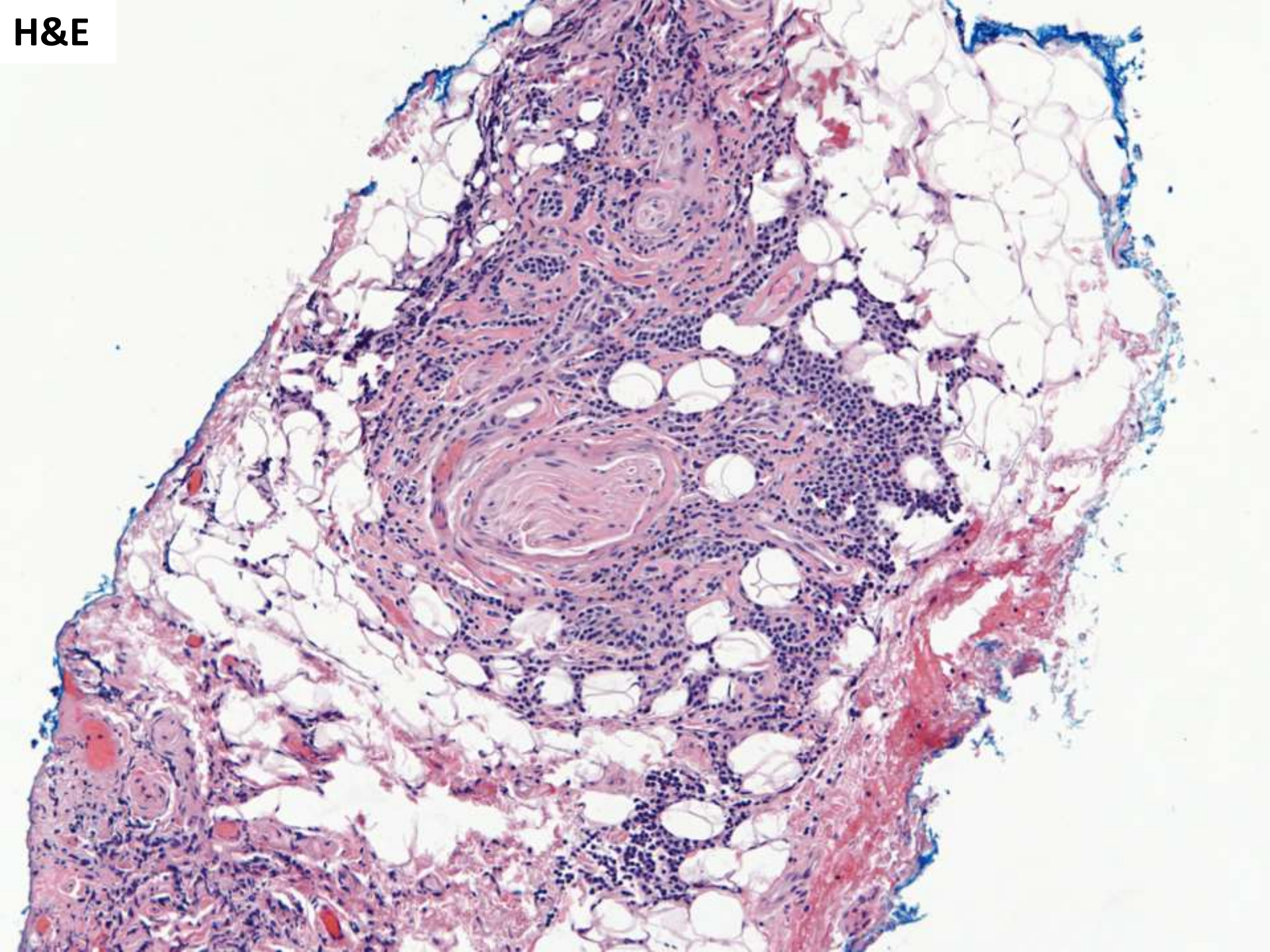
74-year-old M with diagnosis of giant cell arteritis (2012) and low grade B-cell lymphoma (2010) s/p chemo in remission since 2013. He now presents with headache, pain near his TMJ, and ESR of 60 (111 in 2012). He does not respond to prednisone therapy and is referred for temporal artery biopsy.

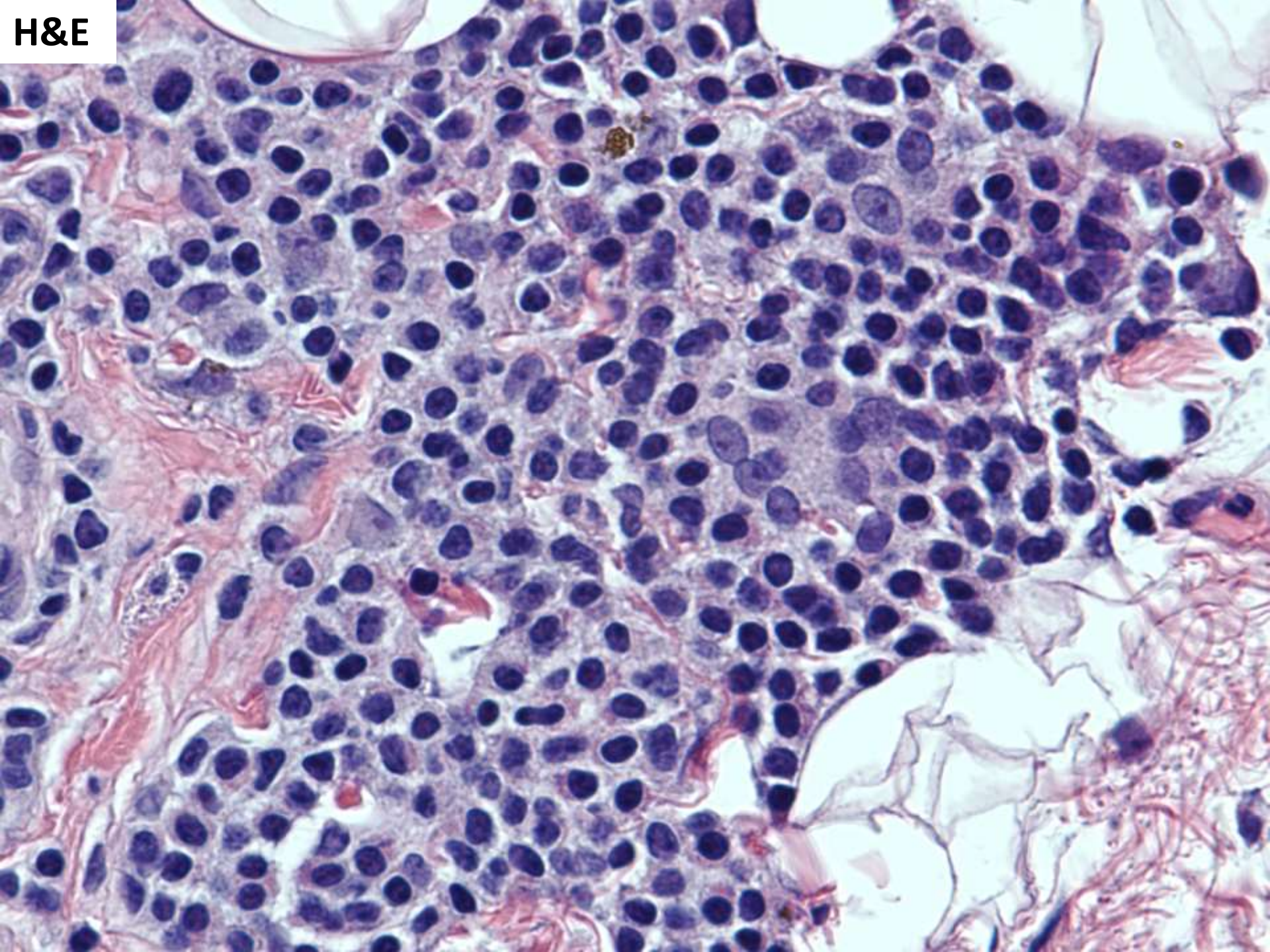

H&E


EVG

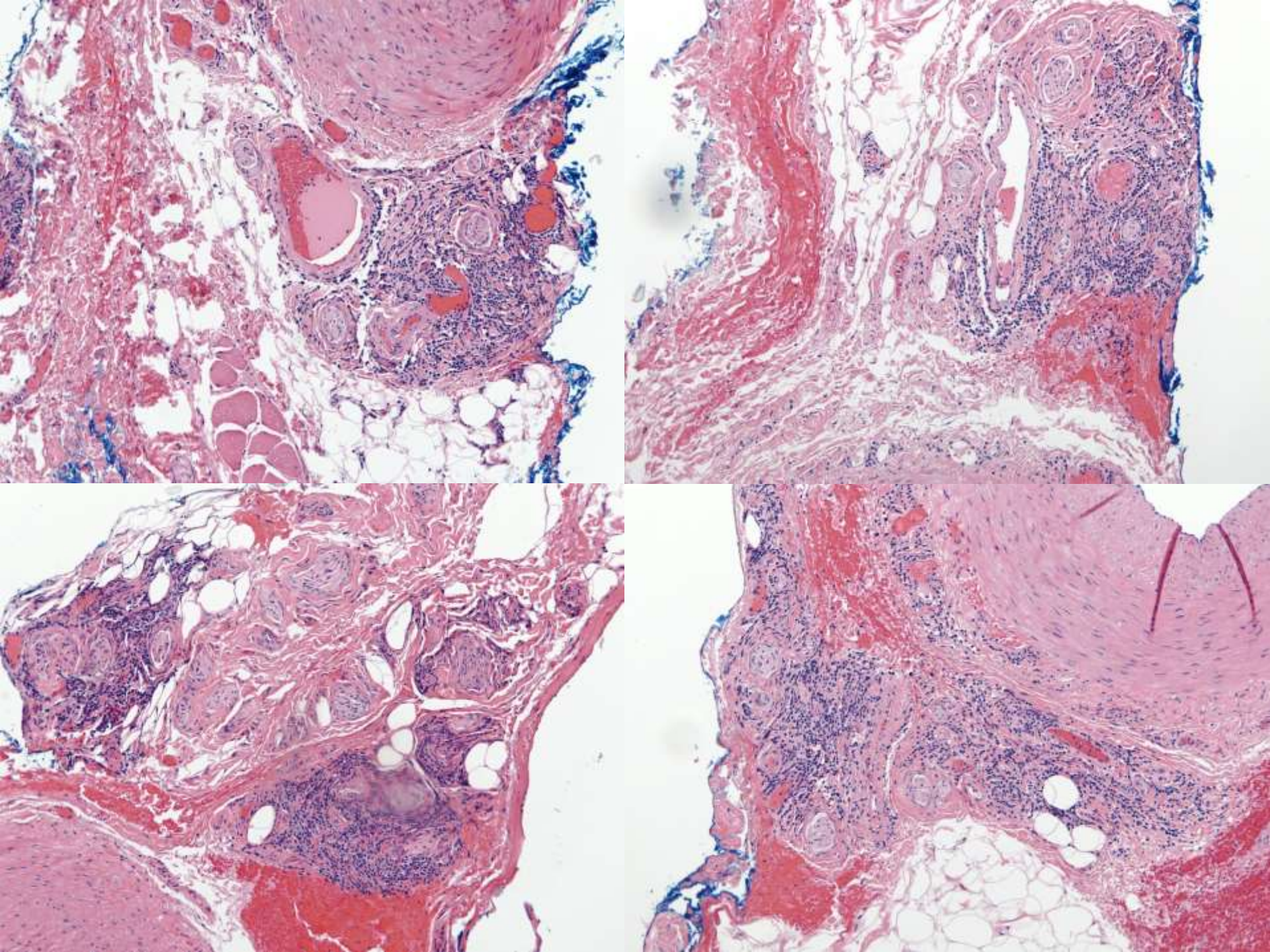

EVG

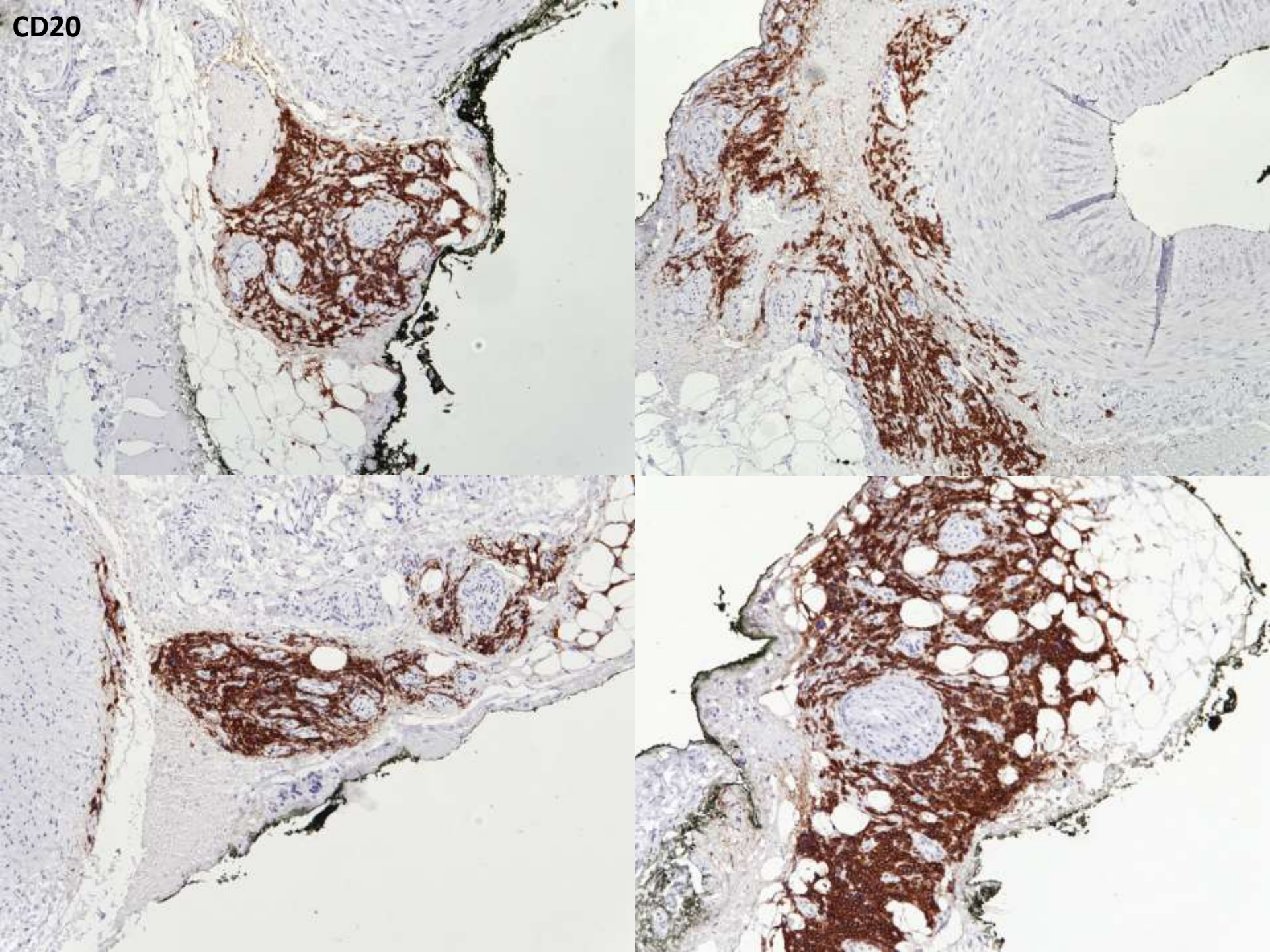

CD163

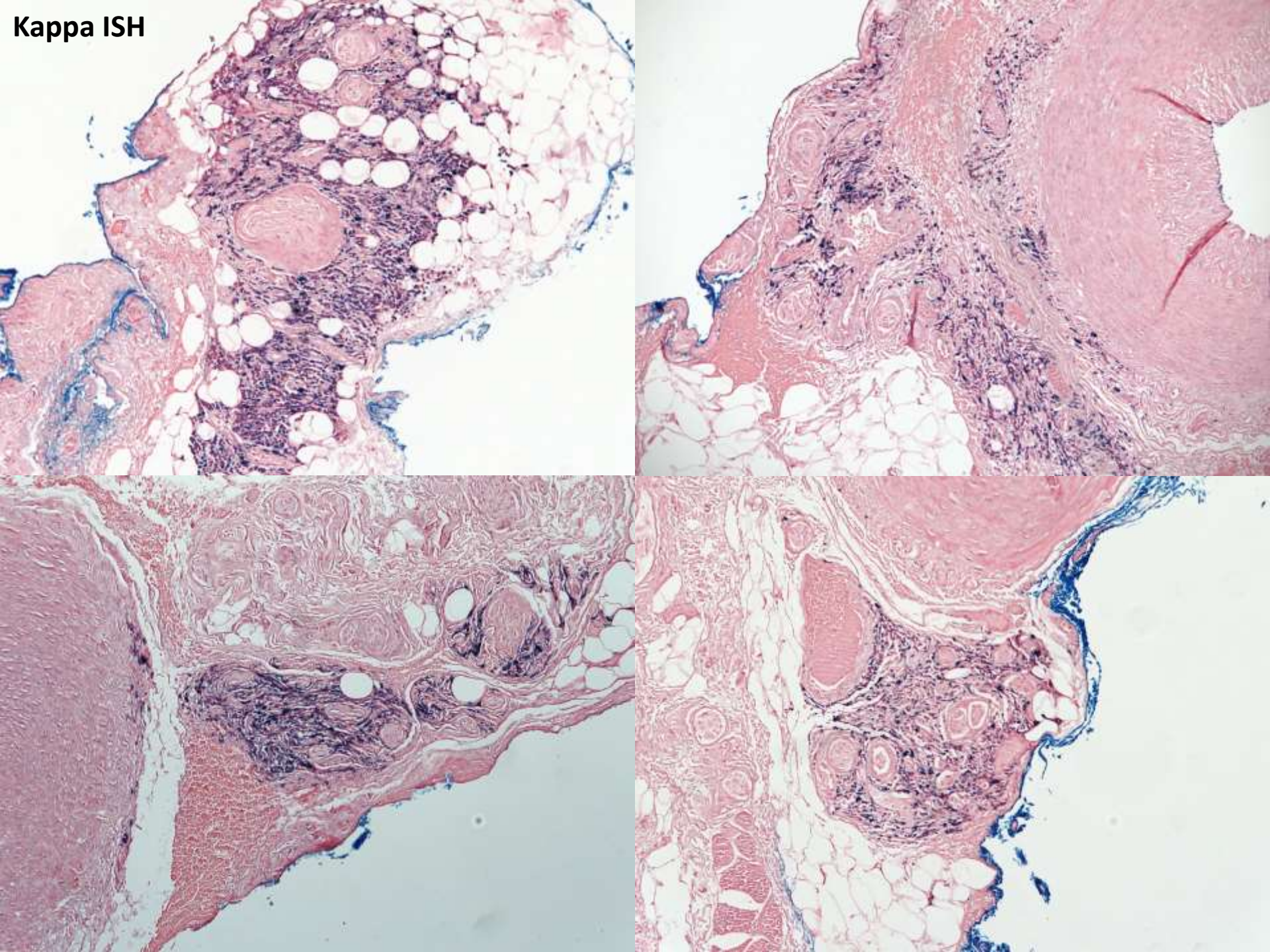

H&E


H&E

DIAGNOSIS?




CD20


Kappa ISH

Further Ancillary Studies

- IgM+, IgG-, IgA-
- MYD88 mutant (Leu265Pro)

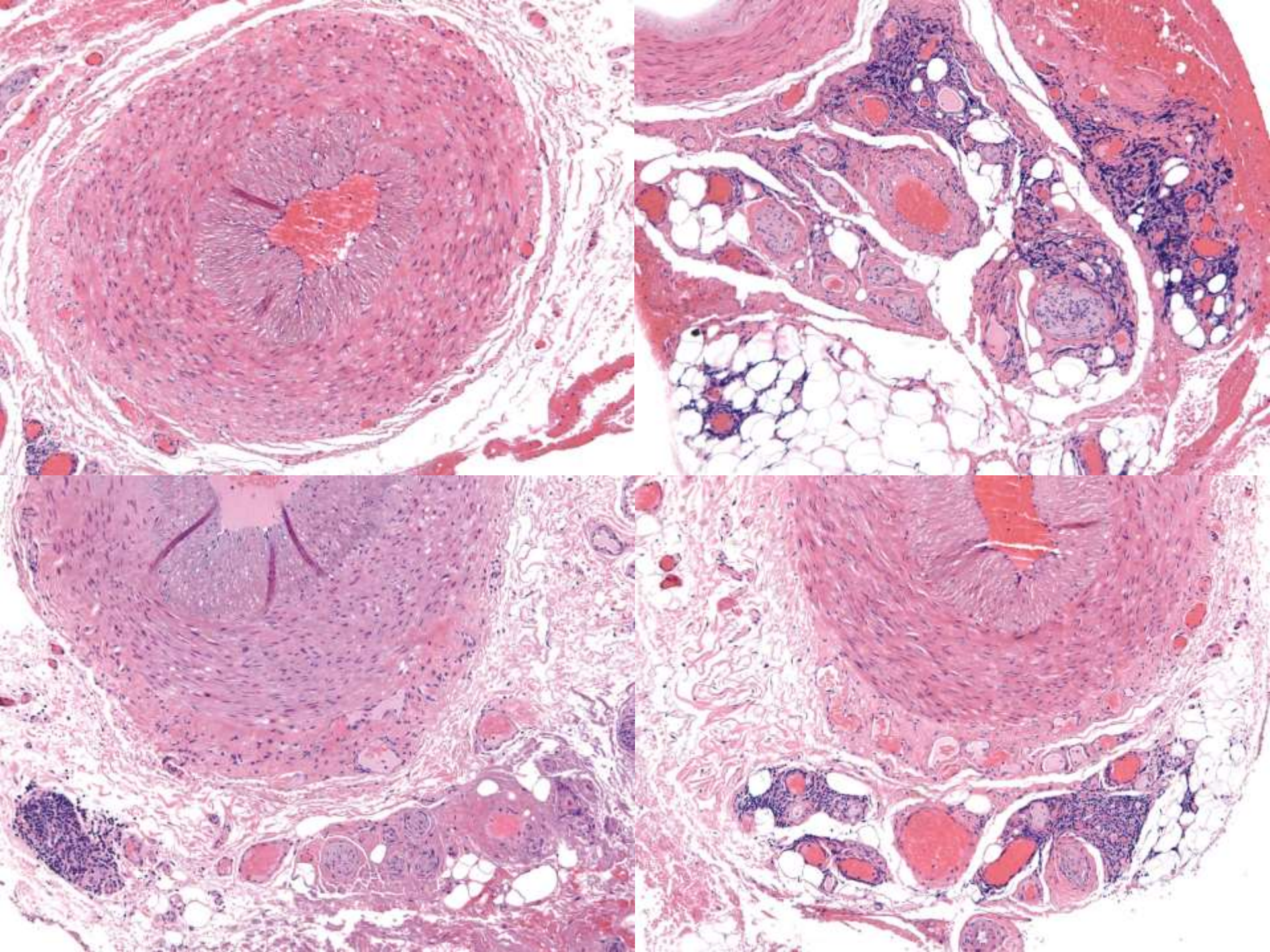
TEMPORAL ARTERY, RIGHT, BIOPSY

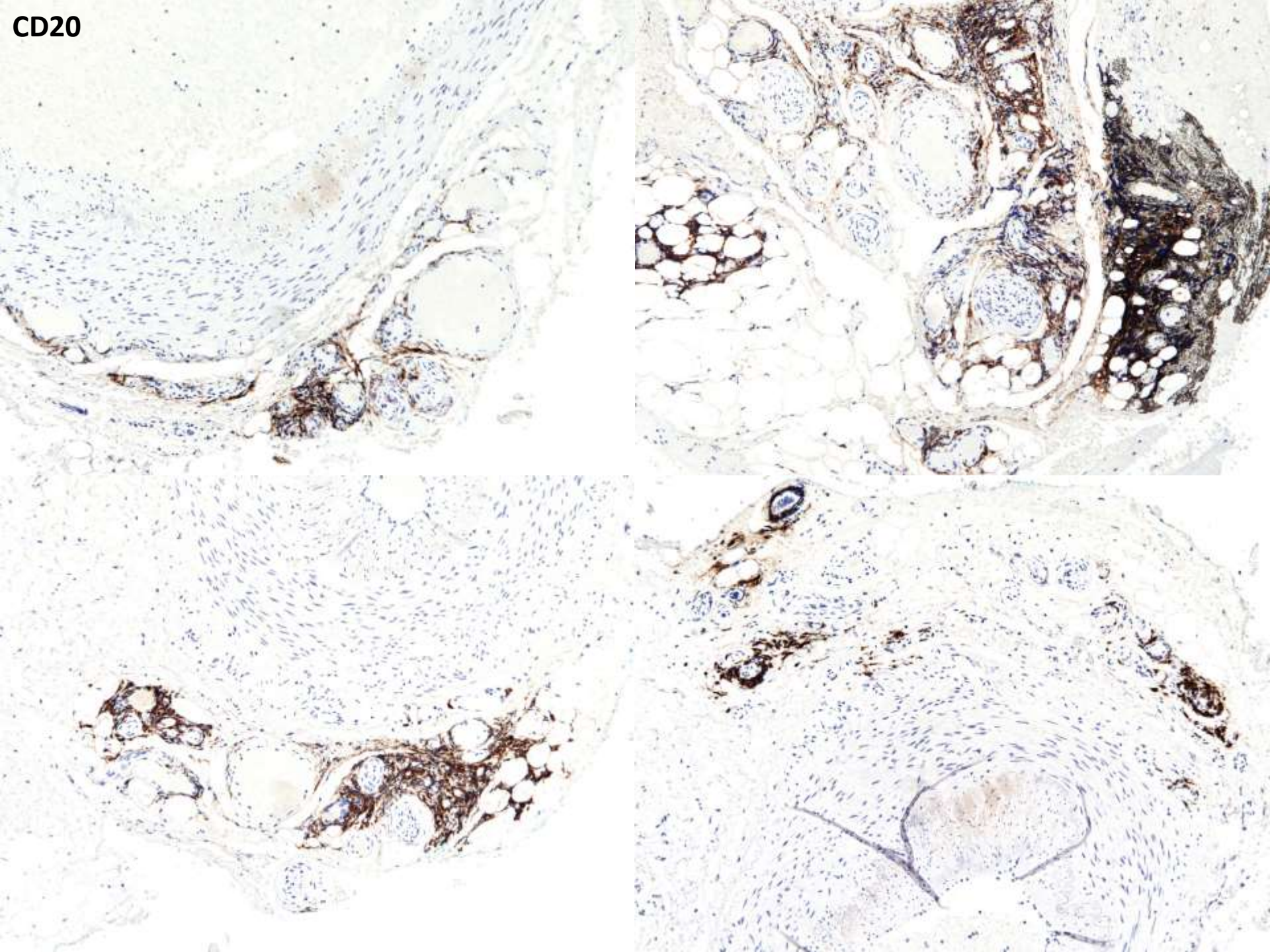
-- **CONSISTENT WITH GIANT CELL ARTERITIS**

-- **LOW GRADE B-CELL LYMPHOMA, CONSISTENT WITH LYMPHOPLASMACYTIC LYMPHOMA**

From the dungeons of Care Everywhere…

- 2010: LN bx→ Low Grade B Cell Lymphoma (IgM+, IgG-, ddx LPL, MZL, etc)
  - IgM 450, night sweats, anemia
  - Dx: Stage IA IgM kappa lymphoplasmacytoid lymphoma, no rx given
- 2012: Symptoms of GCA, biopsy reveals **adventitial lymphocytic infiltrates**
  - Symptoms resolve with steroids + Mtx




CD20

From the dungeons of Care Everywhere…

- 2013: Marrow bx shows 70-80% involvement by LPL
  - Started on Rituxan/Bendamustine
- 2016: GCA symptoms recur after removal of immunosuppression → current biopsy

Case Report

Syndrome of Temporal Arteritis with Perivascular Infiltration by Malignant Cells in a Patient with Follicular Small Cleaved Cell Lymphoma

ELLA WEBSTER, LOURDES C. CORMAN, and RAUL C. BRAYLAN

Abstract. **A patient with follicular small cleaved cell lymphoma presented with Sjögren's syndrome and symptoms of polymyalgia rheumatica and temporal arteritis. Biopsy of the temporal artery showed an extensive perivascular infiltrate by malignant cells without evidence of giant cells.** *(J Rheumatol 1986;* **13:1163-1166)**

Key Indexing Terms:
LYMPHOMA SJÖGREN'S SYNDROME POLYMYALGIA RHEUMATICA
TEMPORAL ARTERITIS PERIVASCULAR/PERIARTERIAL INFILTRATE

We report a patient with follicular small cleaved cell lymphoma who developed Sjögren's syndrome, polymyalgia rheumatica (PMR) and a temporal arteritis syndrome. The symptoms of PMR were responsive only to daily doses of prednisone of 40 mg or more, and the symptoms of arteritis developed at a time of dissemination of the underlying lymphoma. Biopsy of the temporal artery showed extensive peri

was given with marked symptomatic improvement. In Octo
ing one of several unsuccessful attempts to reduce the dose
she developed swelling of her eyes and face and nasal dry
was 50 mm/h, the RF titer was now 1:5120, a serum antinu
(ANA) was negative and muscle enzymes were normal. Bi
salivary glands showed lymphocytic infiltration and ductal c
tent with Sjogrën's syndrome (Figure 2), but antibodies to
antigens were negative. In January 1984, a one-month cours

Lymphomatous Perivascular Infiltration Involving the Temporal Artery

To the Editor:

Temporal or giant cell arteritis is a granulomatous vasculitis whose clinical manifestations include painful, swollen temporal arteries, headache, fatigue, jaw claudication, and loss of vision. We describe a patient who presented with signs suggesting temporal arteritis, but whose biopsy showed extensive perivascular infiltration by neoplastic, small lymphoid cells in keeping with small lymphocytic lymphoma. Other diseases that may resemble temporal arteritis are discussed, including the lymphoproliferative disorders, amyloidosis, and other forms of vasculitis.

A 59-year-old white businessman had been followed since 1984 for an IgM kappa monoclonal gammopathy (macroglobulinemia). He initially presented with asymptomatic splenomegaly. A bone marrow biopsy revealed normocellular marrow and presence of multifocal aggregates of small lymphoid cells, with some plasmacytoid differentiation, consistent with lymphomatous infiltration. Serum immunoglobulin levels were as follows: IgA 61 mg %, IgG 400 mg %, and IgM 2650 mg %. Urine immunoelectrophoresis revealed no protein. He received no treatment for this disorder. A tumor was removed from his upper lip in 1990. The histopathology demonstrated a small lymphocytic lymphoma. He was referred in 1994 for evaluation of possible temporal arteritis.

He gave a 4 week history of tenderness and swelling in the region of his left temporal artery. He had no change in vision, facial claudication, or headache. He had no history of fever, articular pain, weight loss, or fatigue. Examination showed tenderness and swelling in the region of the left temporal artery, with preservation of a pulse, and moderate splenomegaly. The hemoglobin, white blood cell count, and sedimentation rate were normal.

Figure 1. Dense lymphomatous infiltrate surrounding temporal artery. Arrow shows perivascular inflammation adjacent to vessel wall (hematoxylin and eosin, original magnification × 400).

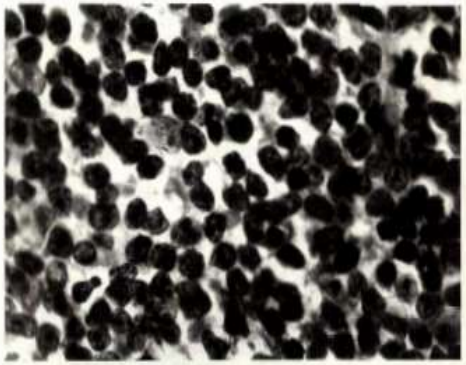


Figure 2. Diffuse proliferation of monomorphous small lymphocytes (hematoxylin and eosin, original magnification × 1000).

ELSEVIER

Cardiovascular Pathology 20 (2011) 244–246

CARDIOVASCULAR PATHOLOGY

Case Report

Perivascular mantle cell lymphoma affecting a temporal artery—a highly unusual cause of temporal headache

Imran Masood[a], Ben While[a], Hardeep S. Mudhar[b,*]

[a]*Department of Ophthalmology, Royal Hallamshire Hospital, Glossop Rd, Sheffield, S10 2JF England, UK*
[b]*Department of Histopathology, Royal Hallamshire Hospital, Glossop Rd, Sheffield, S10 2JF England, UK*

Received 15 January 2010; received in revised form 31 March 2010; accepted 6 May 2010

Abstract

Introduction: Temporal artery biopsy is a widely performed procedure for clinically suspected temporal arteritis. We the report the case of a 79-year-old male with mantle cell non-Hodgkin's lymphoma previously treated with chemotherapy under follow-up with right-sided orbital recurrence, who developed right temporal headache, tenderness, and visual symptoms in the right eye. His symptoms were unresponsive to steroid treatment and he underwent a temporal artery biopsy. **Methods:** The temporal artery was fixed in standard 10% buffered formalin, processed to paraffin wax, 4 micron sections cut through the entire artery and stained with standard haematoxylin and eosin. Some sections were exposed to CD20, CD5, and cyclin D1 immunohistochemistry. **Results:** Histology showed a perivascular, nodular lymphoid infiltrate composed of small centrocyte-type lymphocytes around the main artery and identical lymphocytes within the wall of a main artery branch. Additionally, the lymphocytes were located around a peripheral nerve in the peri-artery connective soft tissues. These lymphocytes were positive for CD5, CD20, and cyclin D1 indicating a diagnosis of peri-neural, peri-vascular mantle cell non-Hodgkin's lymphoma of identical appearance to that in the index biopsy. **Conclusion:** This report describes a highly unusual histological and clinical scenario of peri-temporal artery Mantle cell lymphoma causing temporal headache from peripheral nerve and artery side branch involvement by the lymphoma immediately adjacent to the temporal artery. We propose that involvement of a temporal artery by lymphoma be considered in the differential diagnosis, in patients with an established diagnosis of lymphoma, if presenting with "temporal arteritis" type headache symptoms. © 2011 Elsevier Inc. All rights reserved.

Keywords: Temporal arteritis; Lymphoma; Peri-neural; Mantle cell lymphoma; Temporal artery

Case Report

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

Otolaryngology–Head and Neck Surgery
2015, Vol. 152(1) 187–188
© American Academy of Otolaryngology–Head and Neck Surgery Foundation 2014
Reprints and permission:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/0194599814555856
http://otojournal.org

SAGE

Perivascular Marginal Zone Lymphoma Mimicking Temporal Arteritis

Maximilian Linxweiler, MD[1], Andrea Hasenfus, MD[2], Gregor Wolf, MD[1], and Bernhard Schick, MD[1]

No sponsorships or competing interests have been disclosed for this article.

Keywords
marginal zone lymphoma, giant cell arteritis, temporal artery biopsy, halo sign

Received May 12, 2014; revised September 8, 2014; accepted September 26, 2014.

Giant cell arteritis (GCA) is the most common form of primary systemic vasculitis, and it mainly affects large- and medium-sized vessels in elderly people. Its clinical symptoms include temporal headaches, jaw claudication, a thickened temporal artery, and in severe conditions, visual disturbance and stroke as a consequence of inflammatory vascular obliteration.[1] However, similar symptoms can be caused by other diseases as well, such as granulomatosis with polyangiitis (Wegener's granulomatosis) and vessel-infiltrating malignancies.[2] In this article, we present the first report of a perivascular marginal zone lymphoma that affected the temporal artery and manifested the typical clinical symptoms and sonographic findings of GCA. The scientific use of the patient's tissue and clinical data was approved by the Saarland Medical Association ethics review committee.

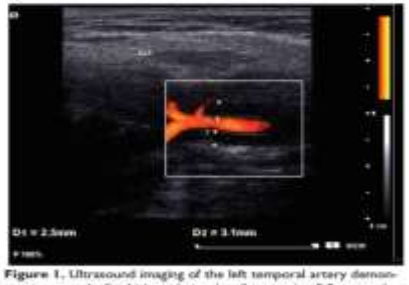


Figure 1. Ultrasound imaging of the left temporal artery demonstrating a markedly thickened vessel wall measuring 2.5 mm and 3.1 mm.

Considering temporal arteritis, infectious disease, and neoplasm as differential diagnoses, we decided to perform a biopsy through transparotideal partial resectioning of the left temporal artery. Intraoperatively, the vessel appeared markedly thickened with palpable induration. The histomorphological analysis of the resected tissue, which was macro-

ARTHRITIS & RHEUMATISM
Vol. 64, No. 2, February 2012, pp 549–556
DOI 10.1002/art.33362

Small-Vessel Vasculitis Surrounding an Uninflamed Temporal Artery and Isolated Vasa Vasorum Vasculitis of the Temporal Artery

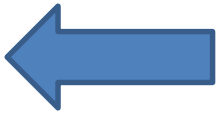
Two Subsets of Giant Cell Arteritis

Giovanna Restuccia, Alberto Cavazza, Luigi Boiardi, Nicolò Pipitone, PierLuigi Macchioni, GianLuigi Bajocchi, Maria Grazia Catanoso, Francesco Muratore, Alessandra Ghinoi, Luca Magnani, Luca Cimino, and Carlo Salvarani

Objective. **To evaluate the frequency and clinical characteristics of periadventitial small-vessel vasculitis (SVV) and isolated vasa vasorum vasculitis (VVV).**

Methods. **We identified 455 temporal artery biopsies performed in residents of Reggio Emilia, Italy between 1986 and 2003. Slides of temporal artery biopsy specimens were reviewed by a pathologist who was blinded with regard to clinical data. SVV was defined as inflammation of the small vessels external to the temporal artery adventitia, and VVV was defined as isolated inflammation of temporal artery vasa vasorum. Medical records of patients with SVV and/or VVV were reviewed, initial and cumulative doses prednisone were significantly lower and the frequency of peripheral synovitis was higher in the patients with SVV, and the frequency of cranial ischemic events was similar in the 2 groups. In contrast, the clinical characteristics and erythrocyte sedimentation rate at diagnosis of patients with isolated VVV were similar to those of patients with classic GCA.**

Conclusion. **Our findings indicate that isolated VVV and SVV should be considered part of the histopathologic spectrum of GCA.**



Giant cell arteritis (GCA) is a vasculitis that

Medicine

OBSERVATIONAL STUDY

OPEN

Description and Validation of Histological Patterns and Proposal of a Dynamic Model of Inflammatory Infiltration in Giant-cell Arteritis

José Hernández-Rodríguez, MD, PhD, Giuseppe Murgia, MD, Irama Villar, MD, Elías Campo, MD, PhD, Sarah L. Mackie, BM, BCh, PhD, Aruna Chakrabarty, MD, Elizabeth M.A. Hensor, BSc, PhD, Ann W. Morgan, MBChB, FRCP, PhD, Carme Font, MD, PhD, Sergio Prieto-González, MD, Georgina Espigol-Frigolé, MD, PhD, Josep M. Grau, Md, PhD, and Maria C. Cid, MD, PhD

Abstract: The extent of inflammatory infiltrates in arteries from patients with giant-cell arteritis (GCA) have been described using different terms and definitions. Studies investigating the relationship between GCA histological features and clinical manifestations have produced controversial results. The aims of this study were to characterize and validate histological patterns in temporal artery biopsies (TABs) from GCA patients, to explore additional histological features, including the coexistence of different patterns, and also to investigate the relationship of the inflammatory patterns with clinical and laboratory features.

We performed histological examination of TAB from patients with GCA consecutively diagnosed between 1992 and 2012. Patterns of inflammation were defined according to the extent and distribution of inflammatory infiltrates within the artery. Clinical and laboratory variables were recorded. Two external investigators underwent a focused, one-day training session and then independently scored 77 cases. Quadratic-weighted kappa was calculated.

TAB from 285 patients (200 female/85 male) were evaluated. Four histological inflammatory patterns were distinguished: 1 – adventitial (n = 16); 2 – adventitial invasive: adventitial involvement with some extension to the muscular layer (n = 21); 3 – concentric bilayer: adventitial and intimal involvement with media layer preservation (n = 52); and 4 – panarteritic (n = 196). Skip lesions were observed in 10% and coexistence of various patterns in 43%. Raw agreement of each external scorer with the gold-standard was 82% and 77% (55% and 46% agreement expected from chance); kappa = 0.82 (95% confidence interval [CI] 0.70–0.95) and 0.79 (95% CI 0.68–0.91). Although abnormalities on temporal artery palpation and the presence of jaw claudication and scalp tenderness tended to occur more frequently in patients with arteries depicting more extensive inflammation, no stat-

Main Histological Patterns Involving the Temporal Artery in GCA

According to the distribution of inflammatory infiltrates through the artery wall, 4 main histological patterns were differentiated as follows (Fig. 1):

(1) Adventitial pattern: when inflammatory cells were restricted to the adventitia, with preservation of media and intima layers (n = 16 biopsies; 5.6%).
(2) Adventitial invasive pattern: when adventitial infiltration was followed by local invasion of the muscular layer, with integrity of the intima (n = 21 biopsies; 7.3%).
(3) Concentric bilayer pattern: when inflammatory cells were infiltrating the adventitia and the intima (or the intima/media junction), with a preserved media (n = 52 biopsies; 18.2%).
(4) Panarteritic pattern: when the inflammatory infiltrates were distributed through the 3 arterial layers (n = 196 biopsies; 68.8%).

Take home points…

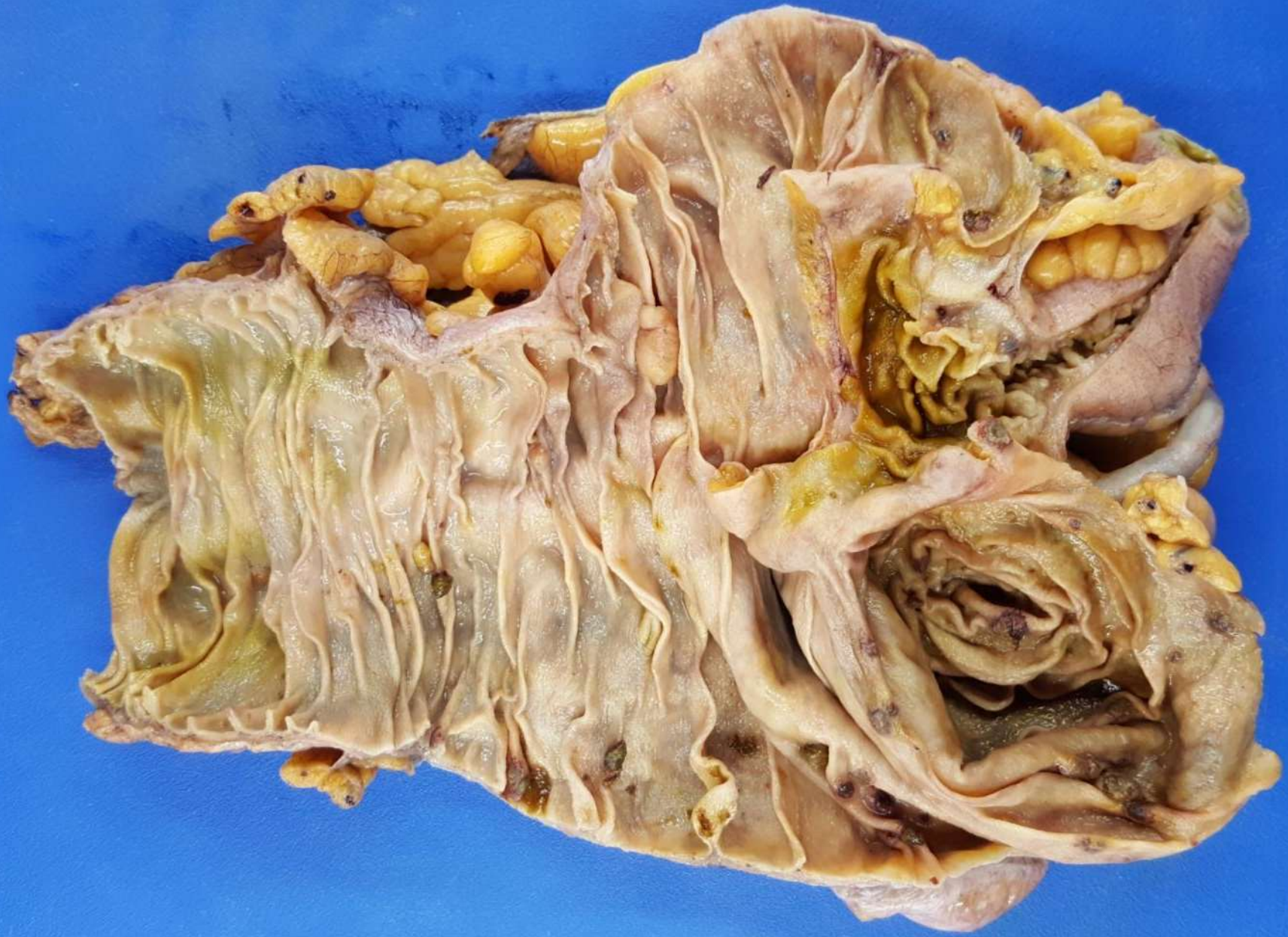
- HISTORY!

- While rare, lymphoma is an important ddx in GCA, particularly in cases with periadventitial/adventitial infiltrates only

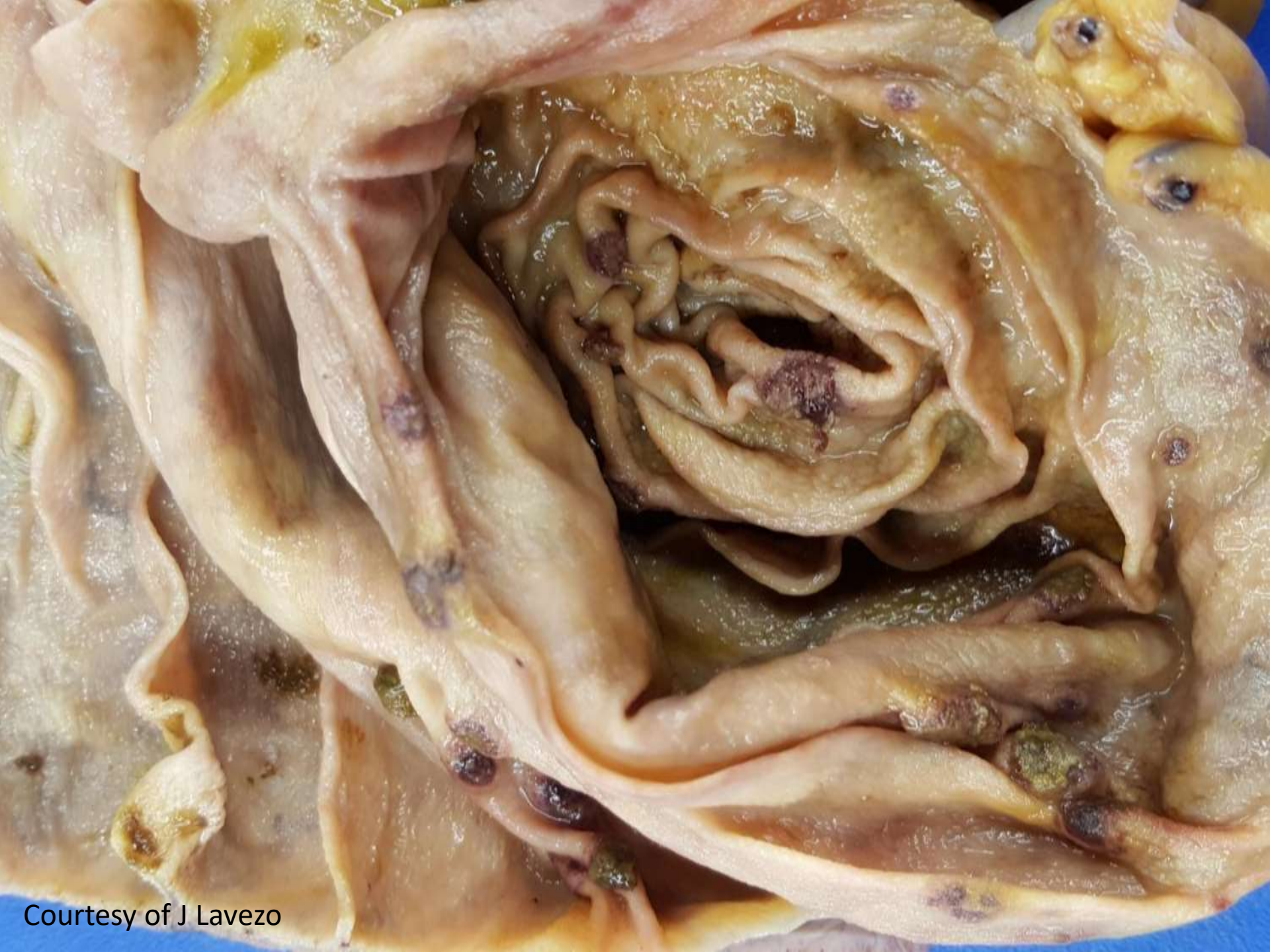
SB 6147

Jonathan Lavezo/Allison Zemek/Gerald Berry; Stanford

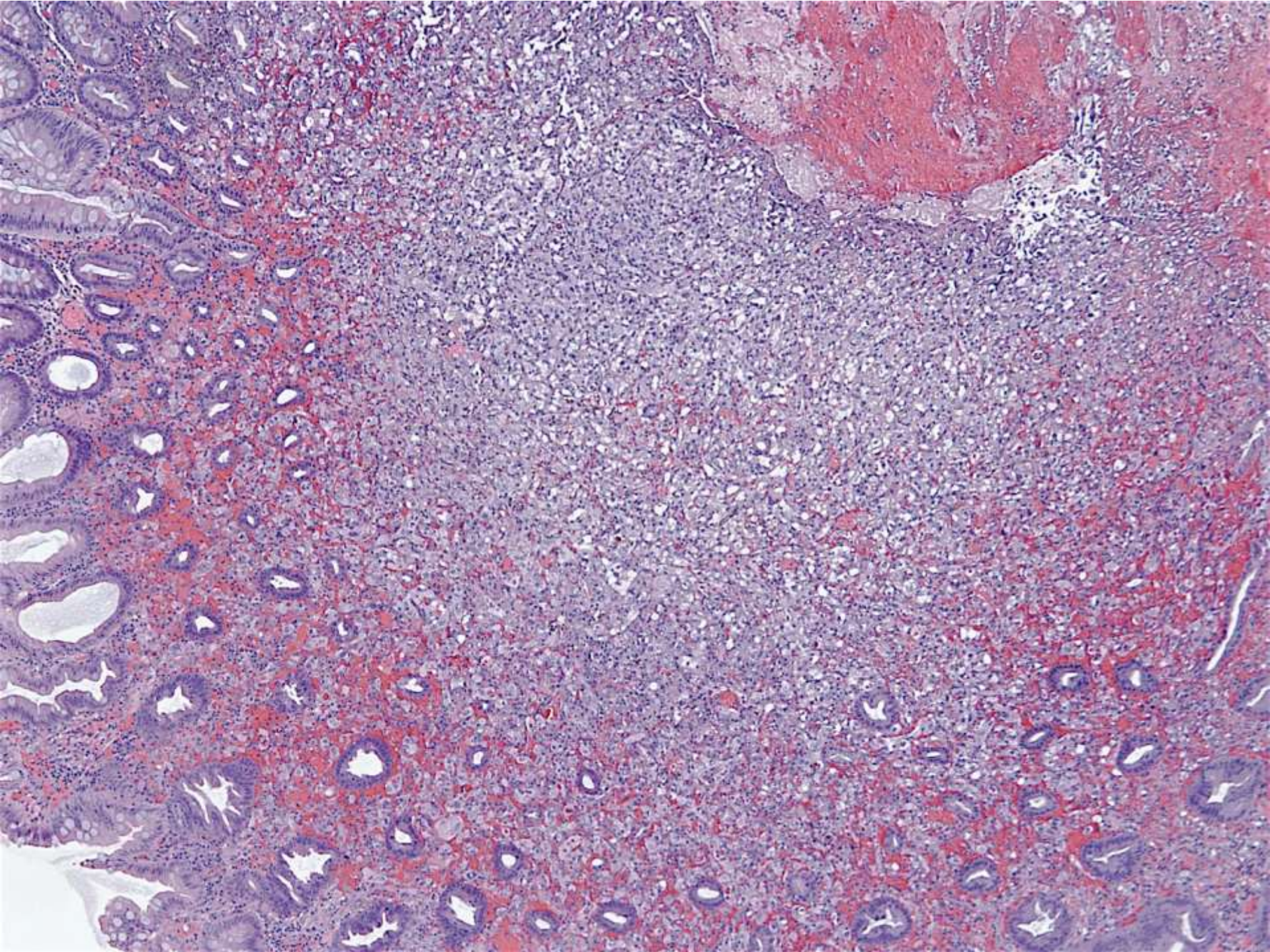
78-year-old M with acute GI bleeding, history of melena, severe blood loss anemia. Found to have multiple nodular/erosive lesions in cecum and proximal colon.

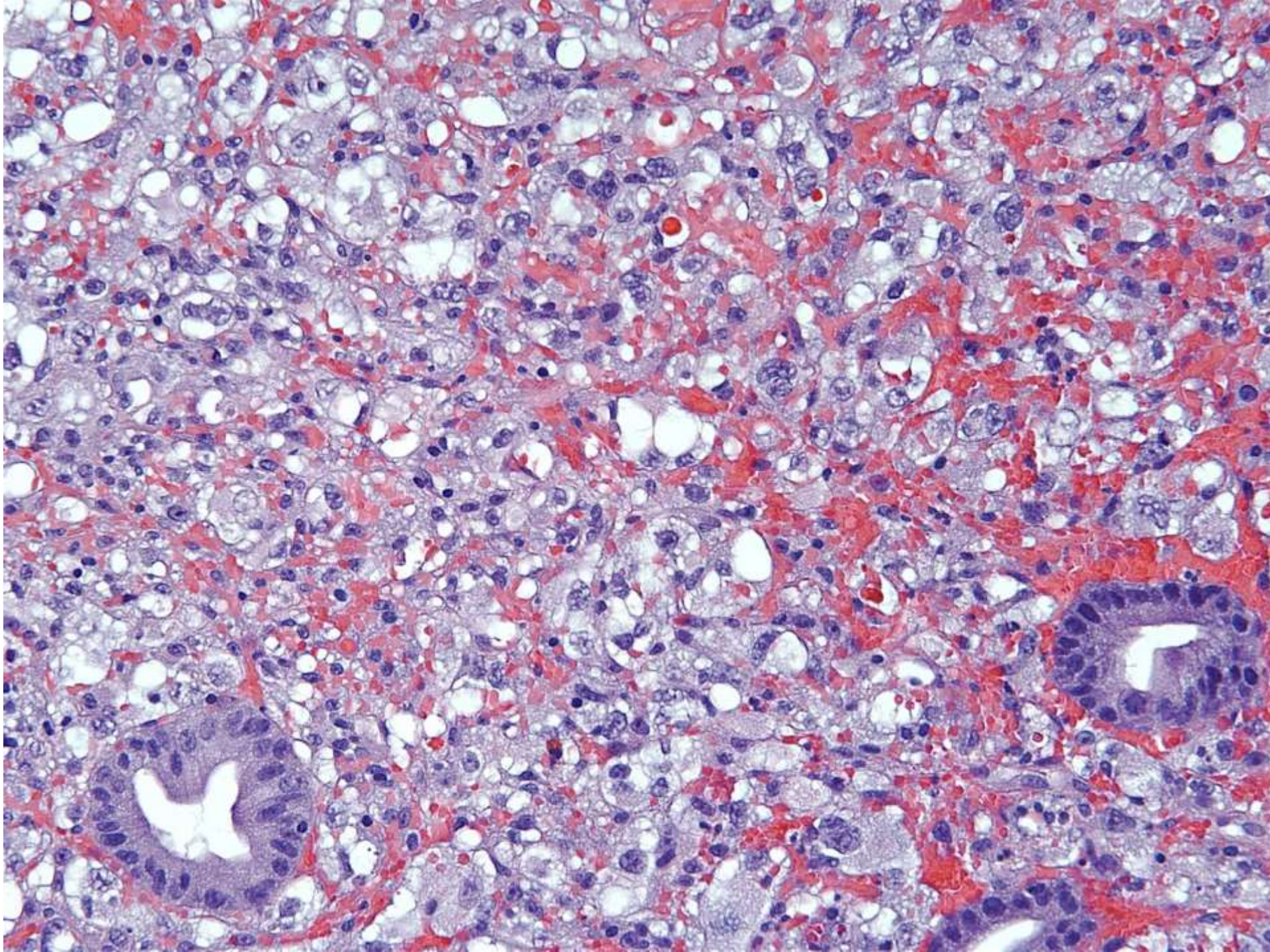


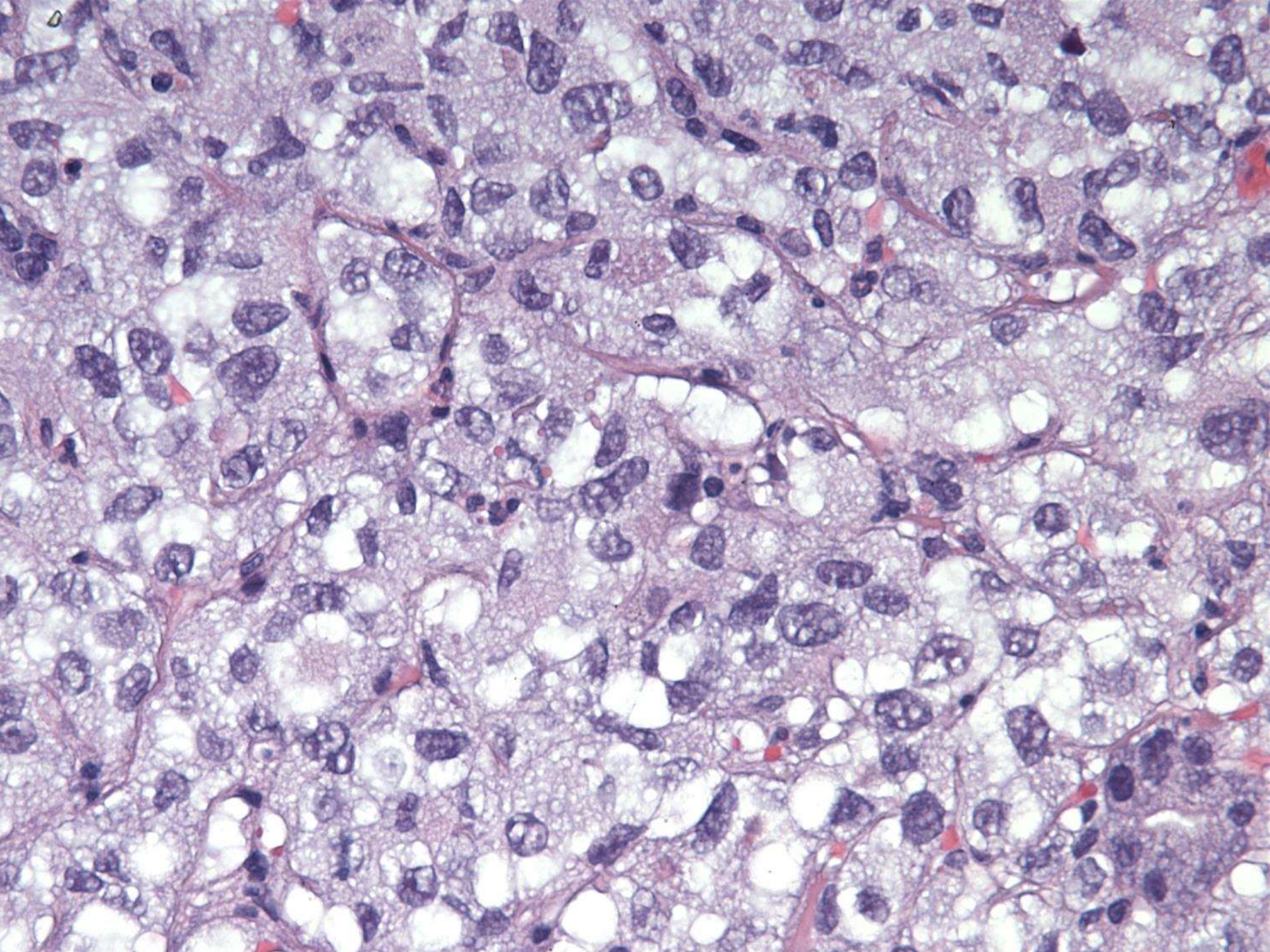
Courtesy of J Lavezo

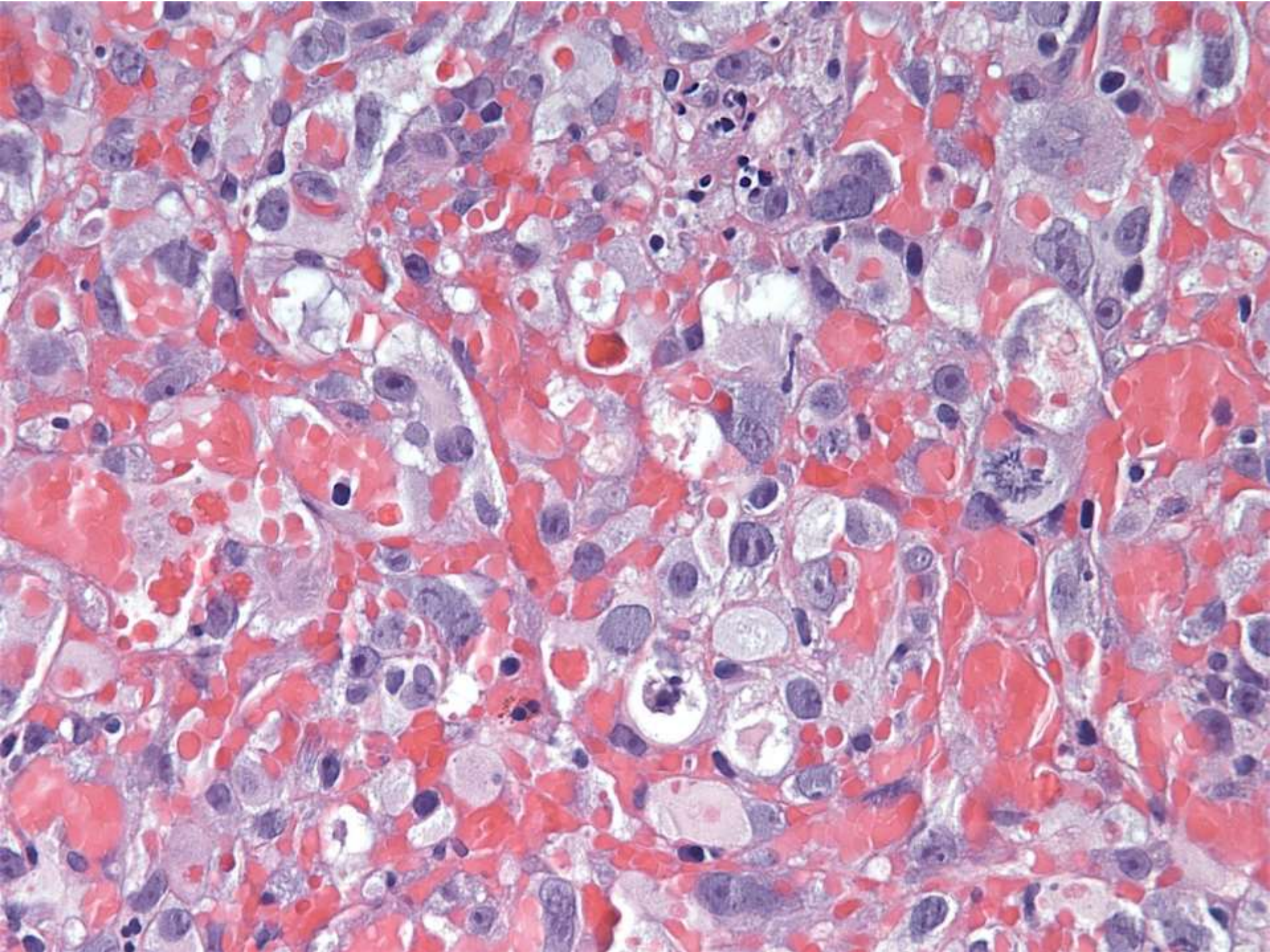


Courtesy of J Lavezo

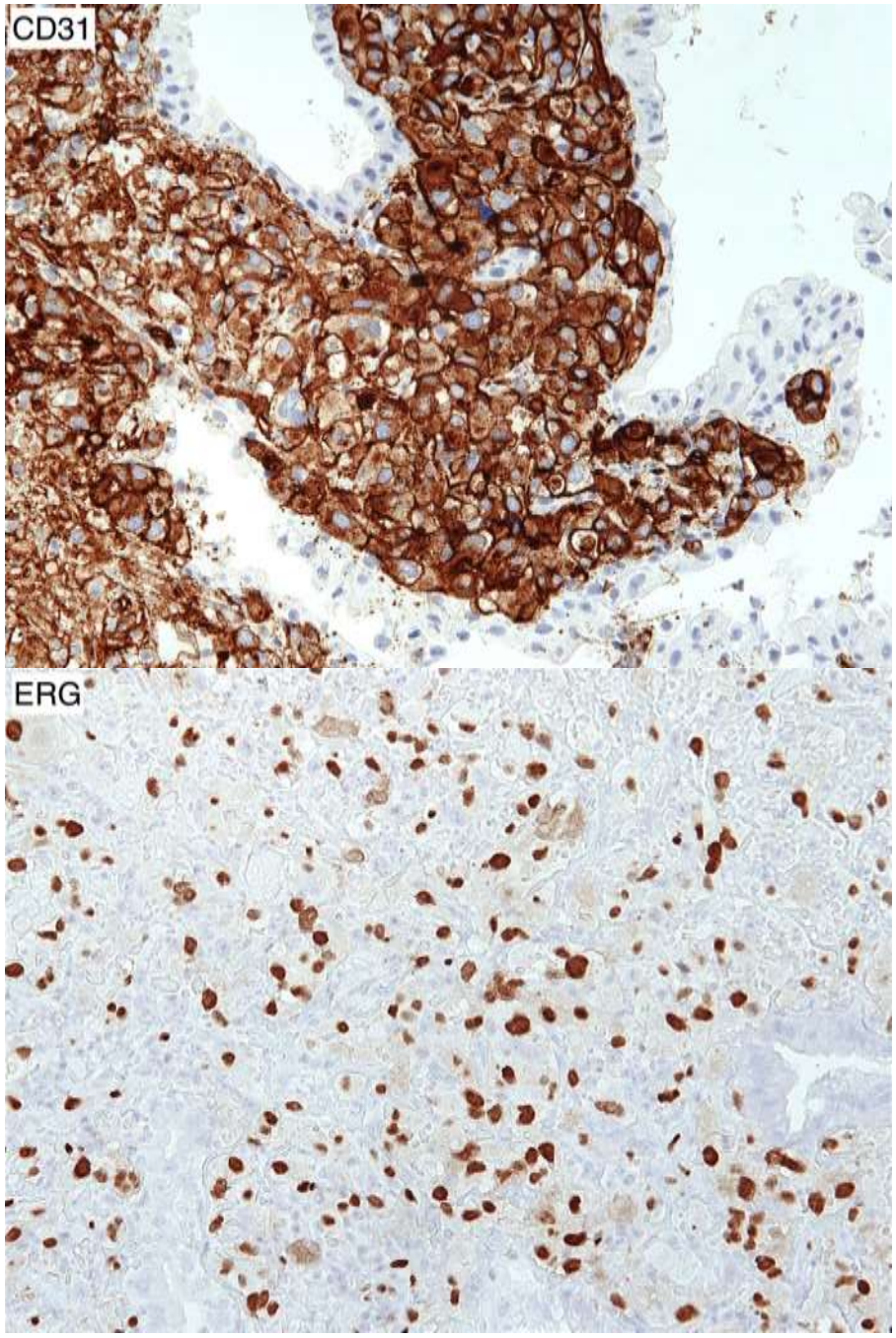






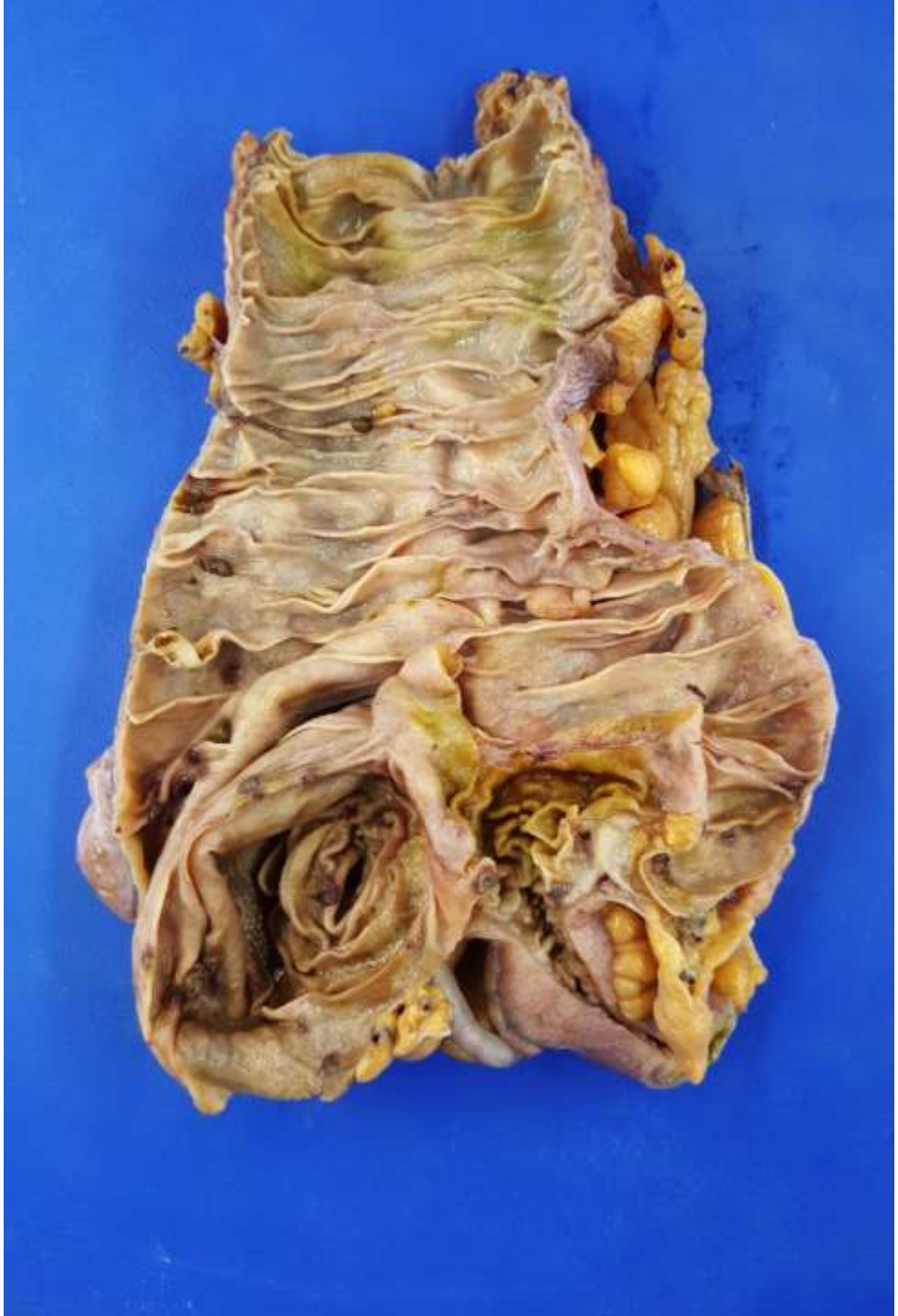


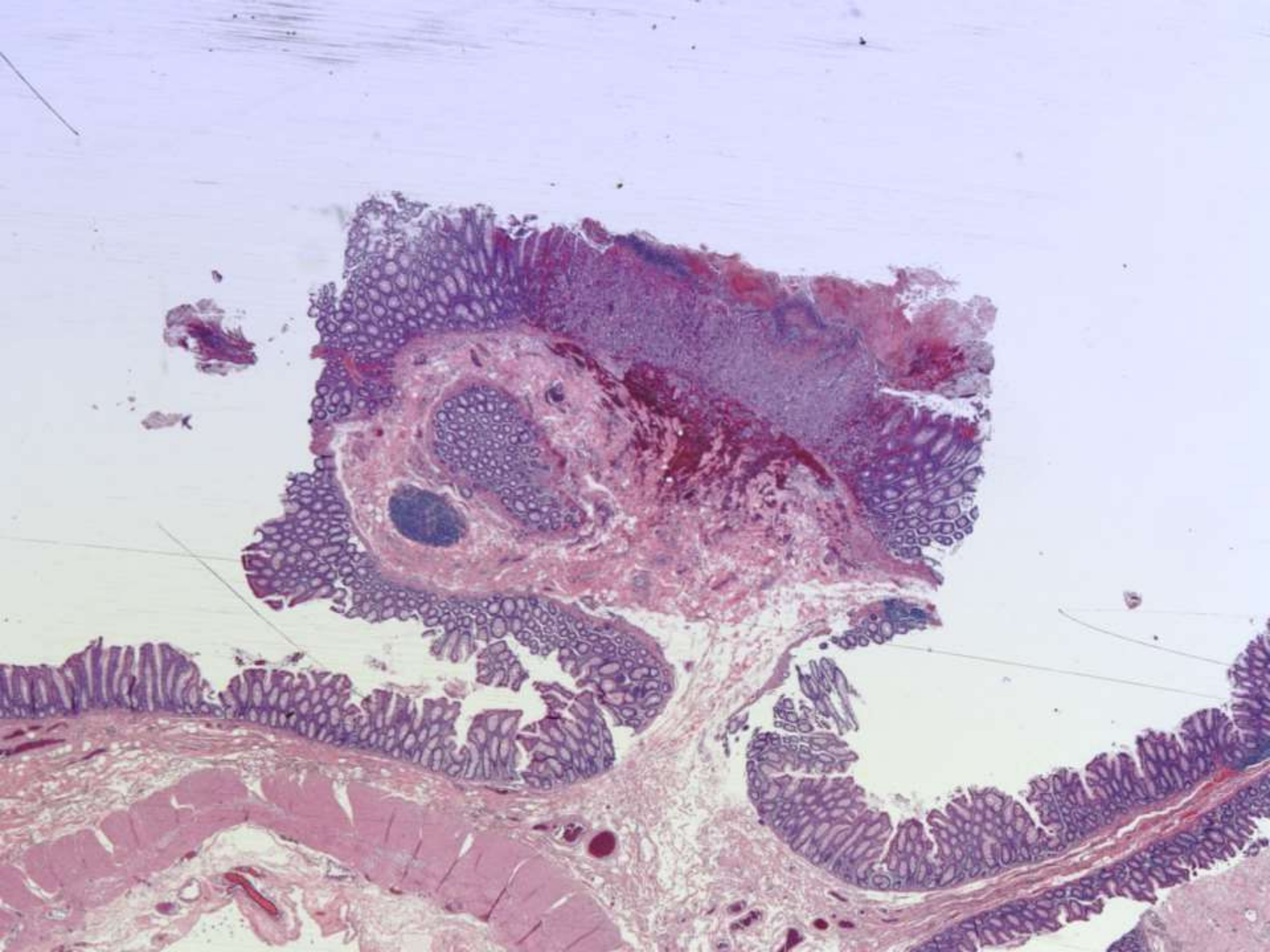
DIAGNOSIS?

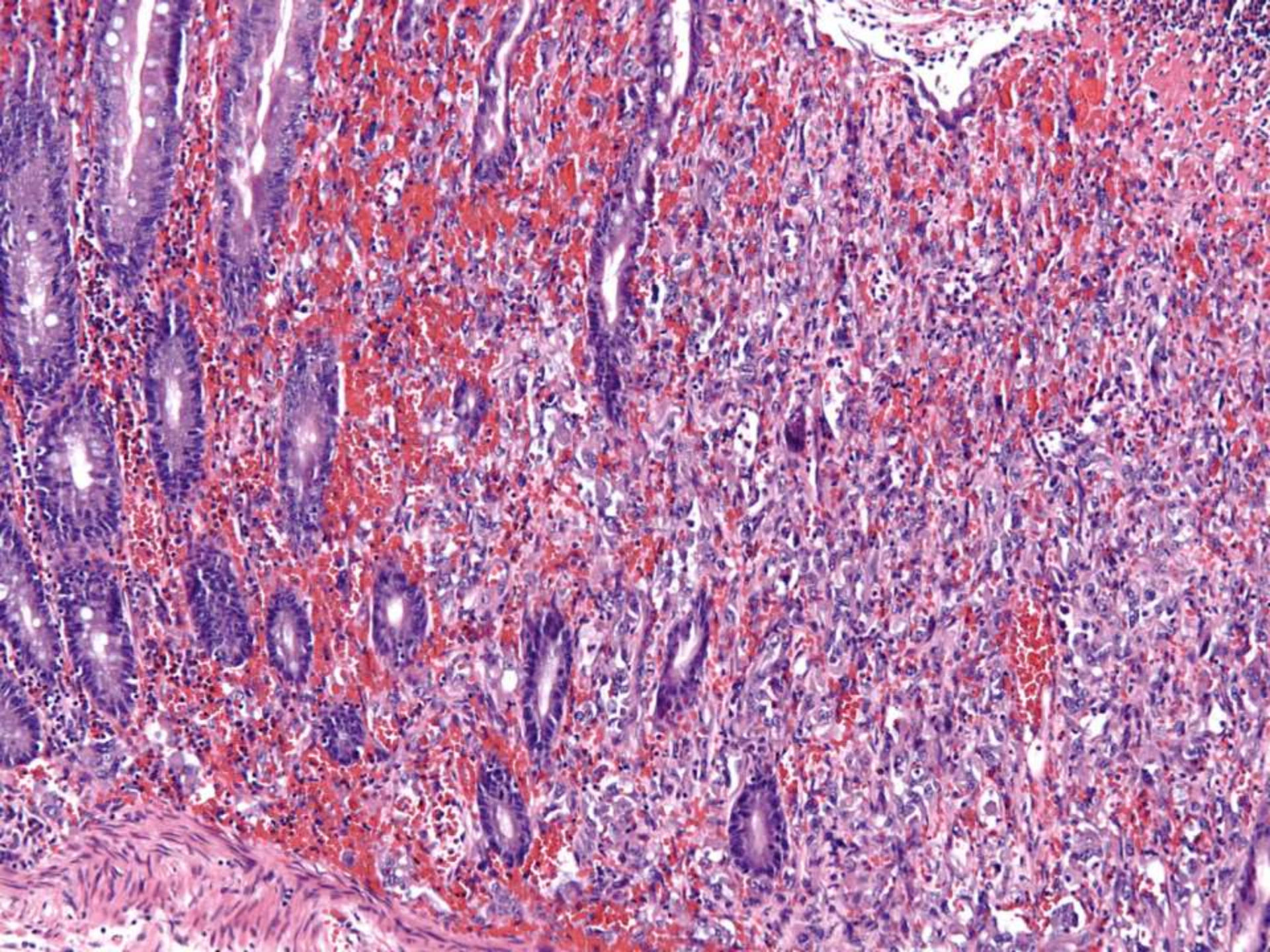


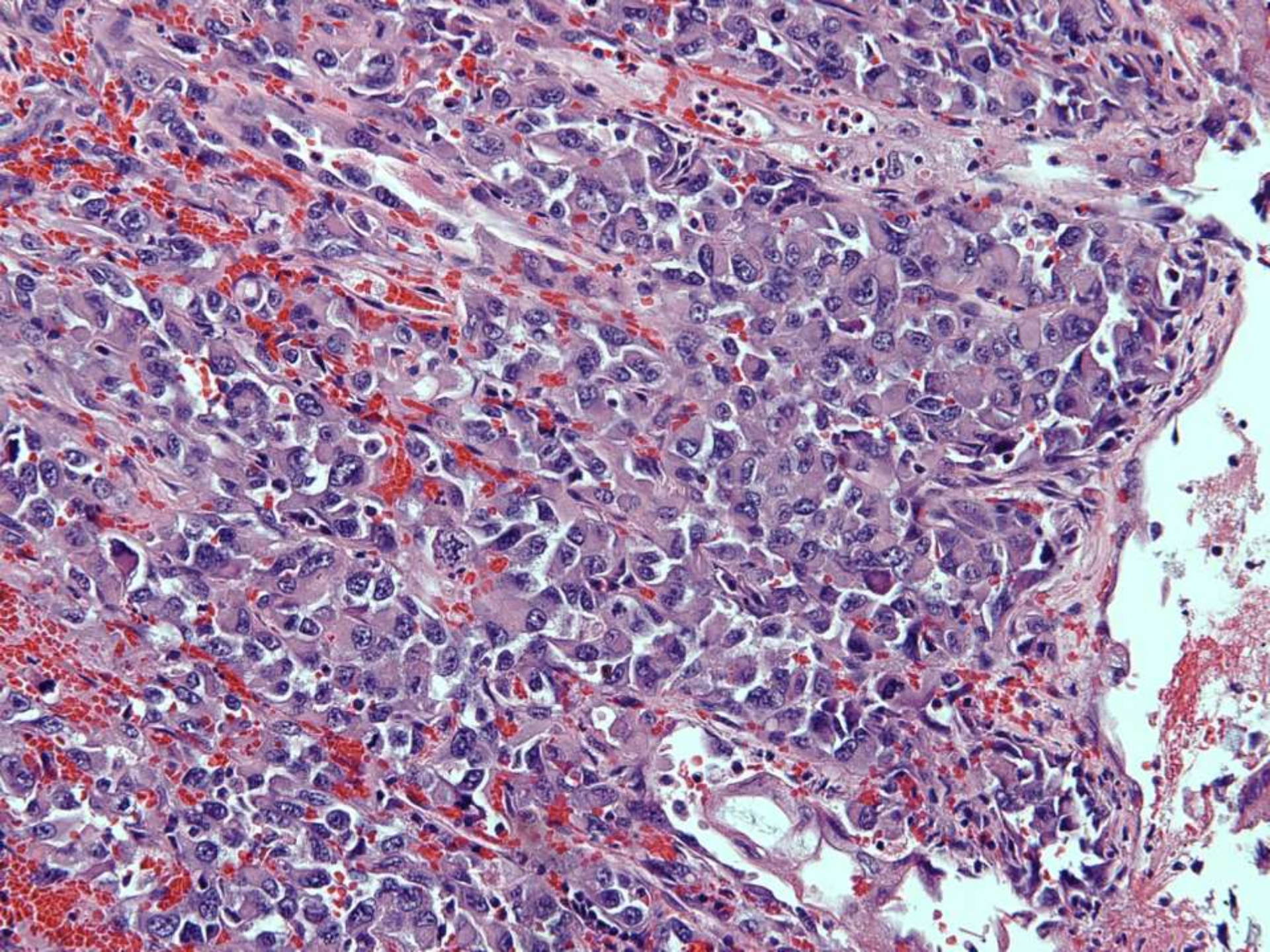
Negative

- S100
- HMB45
- AE1/AE3
- HHV8
- SF-1
- PAX8
- CD45
- CD30
- CD68
- CD117
- SALL4
- INI1 - retained









Take Home Points

- Extremely rare with poor prognosis
- Associations:
  - Prior Radiotherapy/chemotherapy, radiation exposure, vinyl chloride exposure, lymphedema
  - Reported associations with vascular grafts and chronic inflammatory
- Cytokeratin expression can be seen in poorly differentiated angiosarcomas with epithelioid cytomorphology
- DDX: Poorly Differentiated Carcinoma, Malignant Melanoma, Epithelioid Sarcoma, Epithelioid MPNST

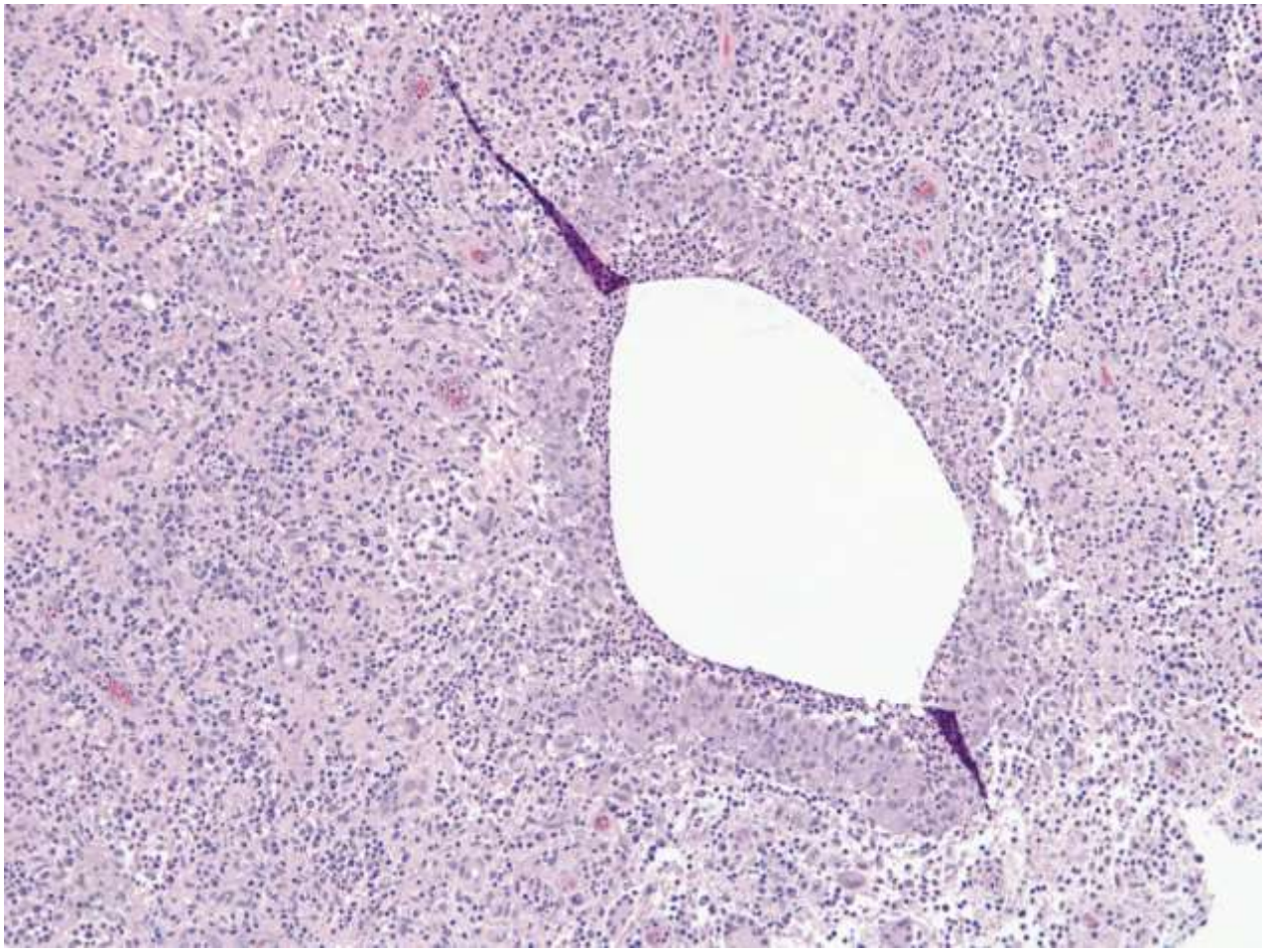
References

- Allison, K H Et Al. Angiosarcoma Involving the Gastrointestinal Tract: A series of primary and metastatic cases. *Am J Surg Path*: 28.3; March 2004
- Milite, D Et AL. Aortic Epithelioid Angiosarcoma after Endovascular Aneurysm Repair. *Annals of Vas Surg*; 35: 207.e17-207.e21 Aug 2016

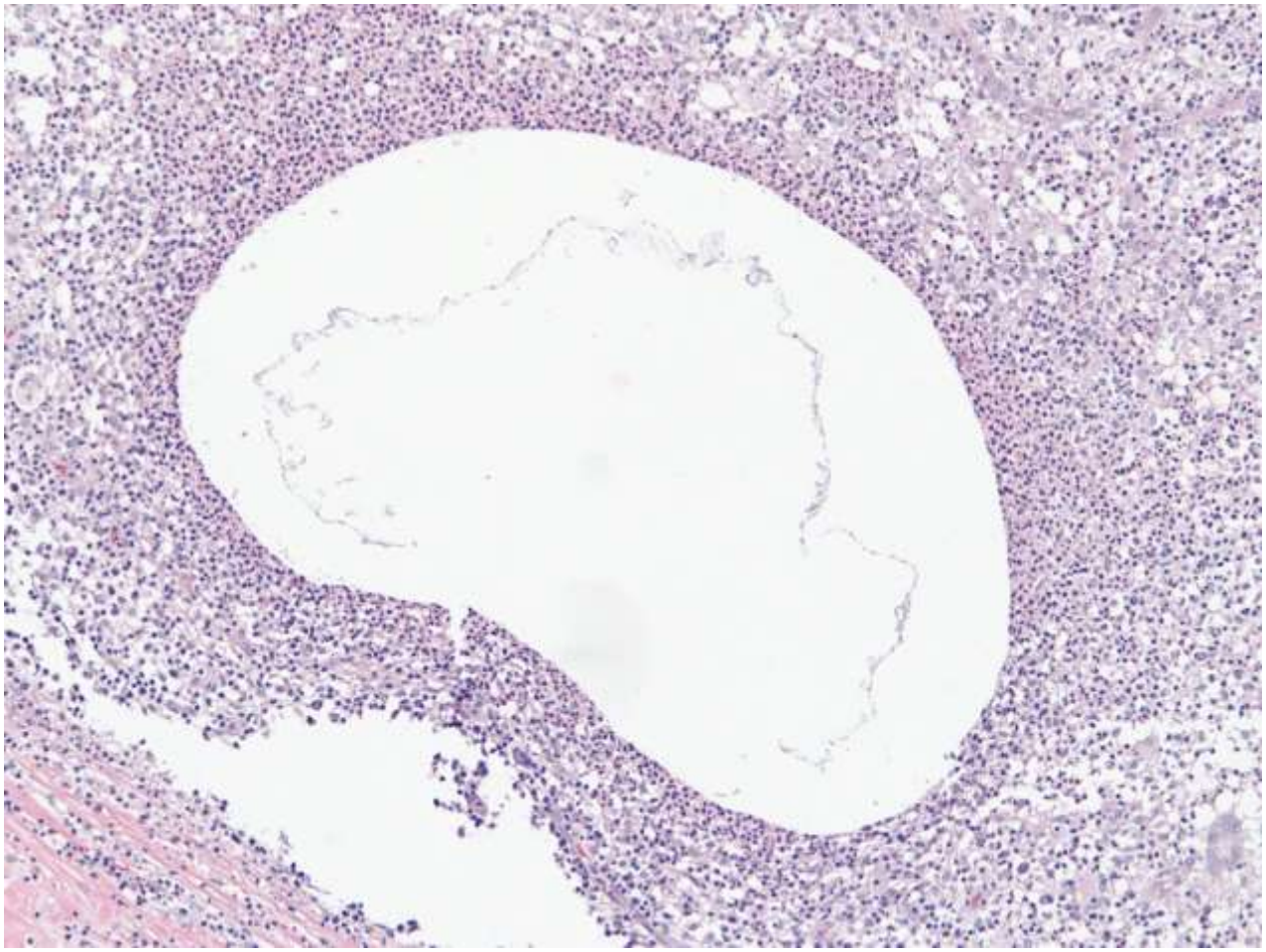
SB 6148

Bart Singer/Kimberly Allison; Stanford

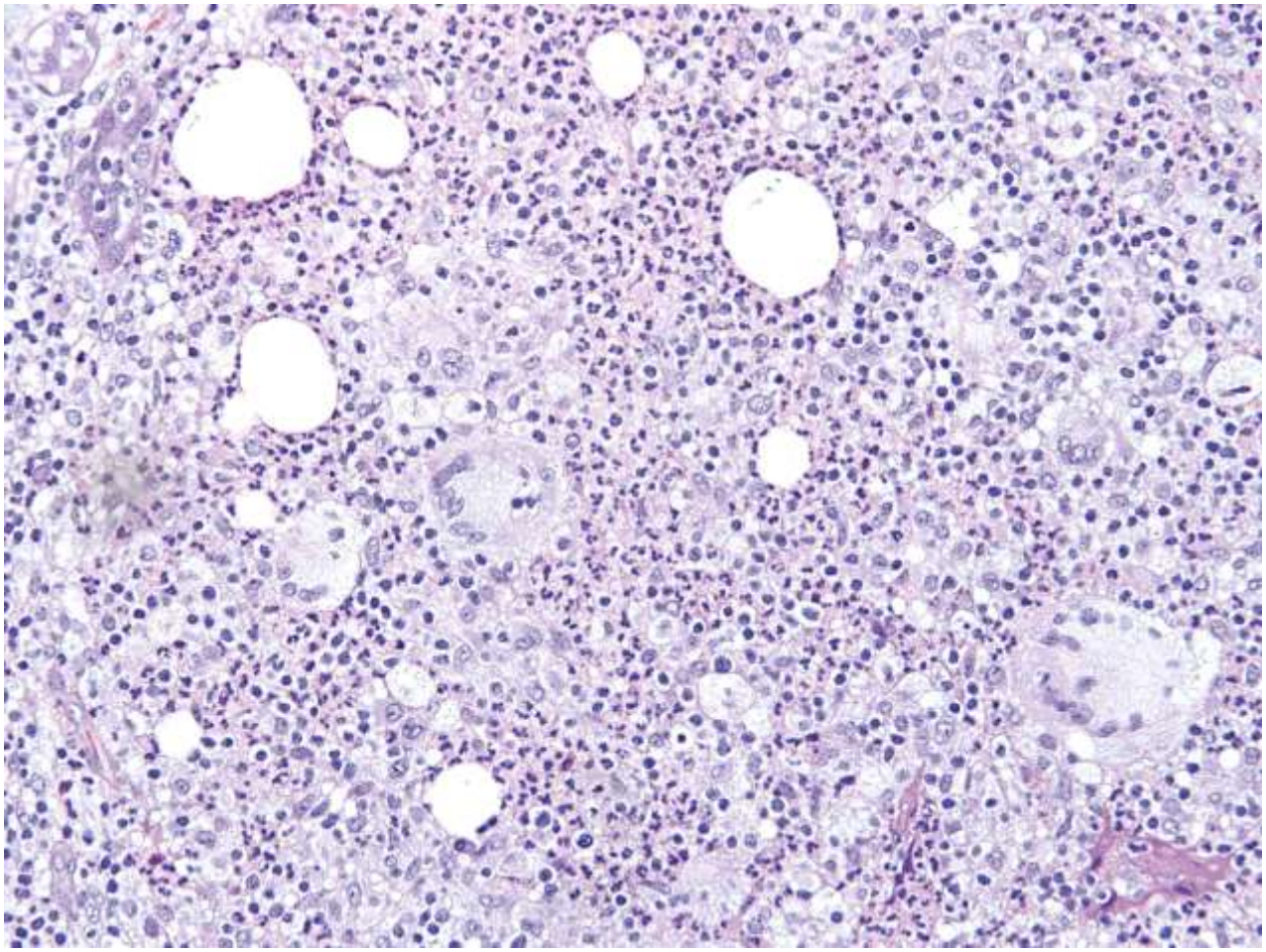
36-year-old F with 3 month history of right breast pain, swelling, erythema, and fever. Had I&D which expressed small amount of purulent drainage. Multiple courses of antiobiotic therapy with no improvement. She now undergoes a right breast biopsy and debridement.



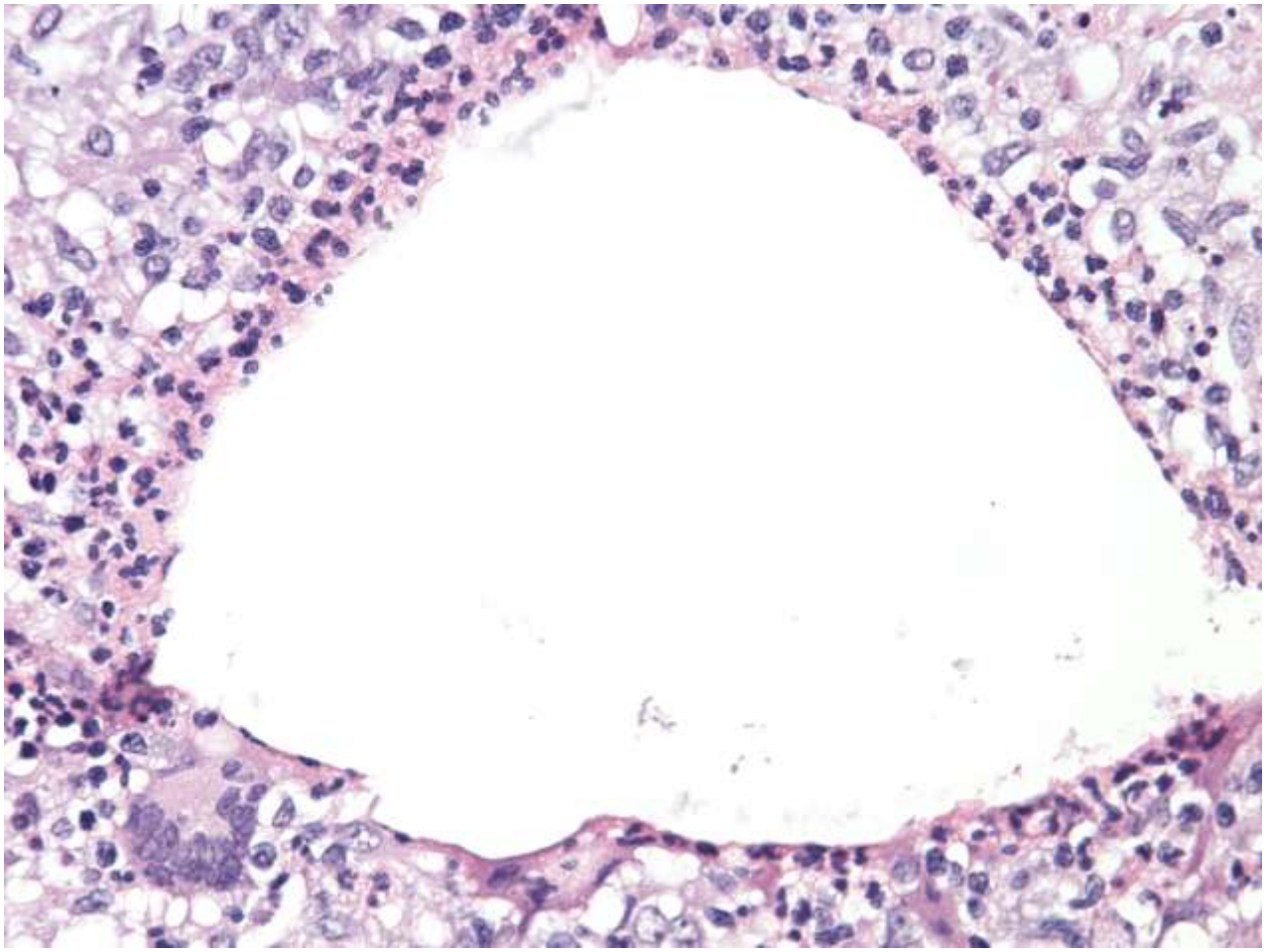
10 x



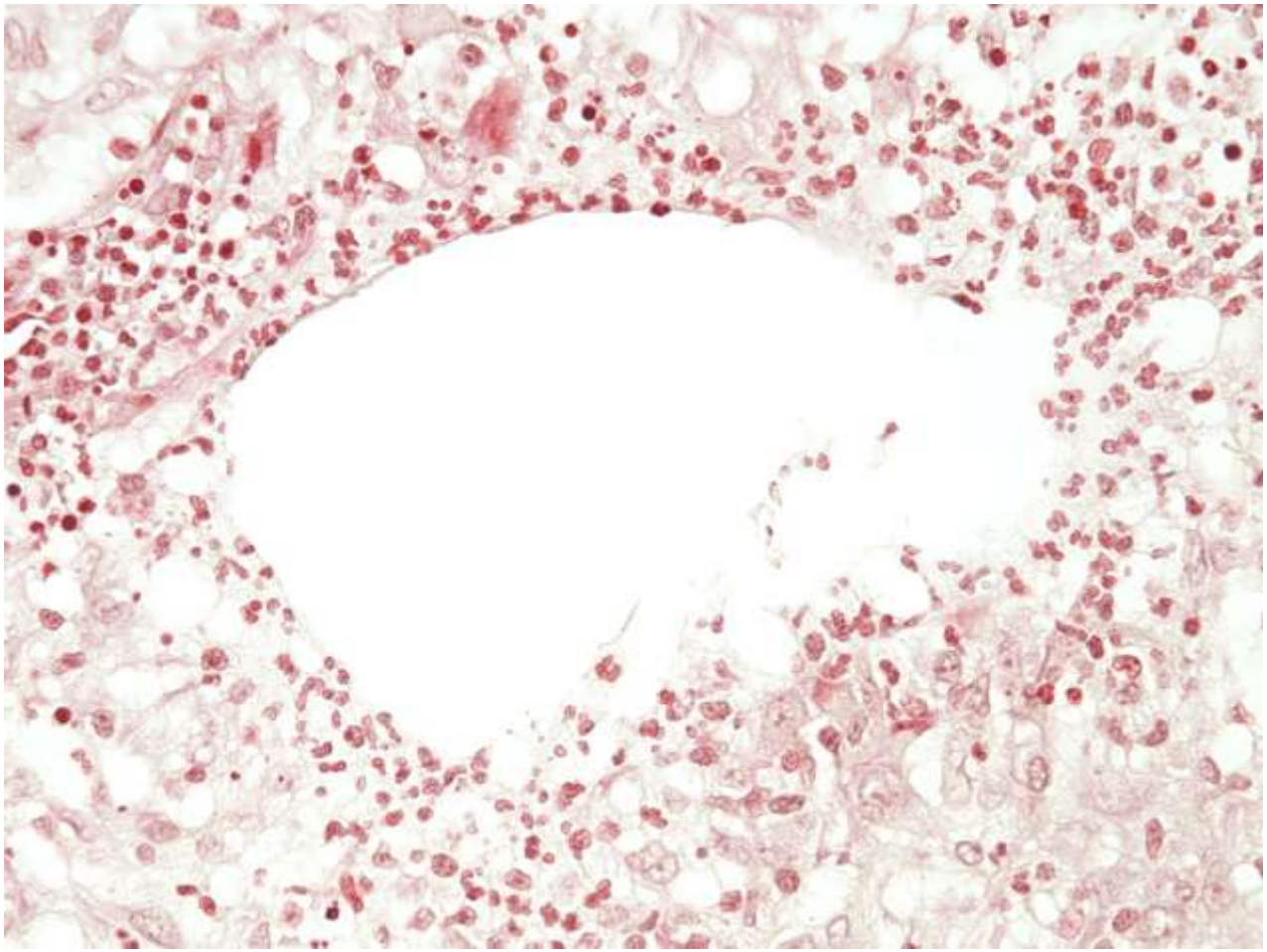
10 x



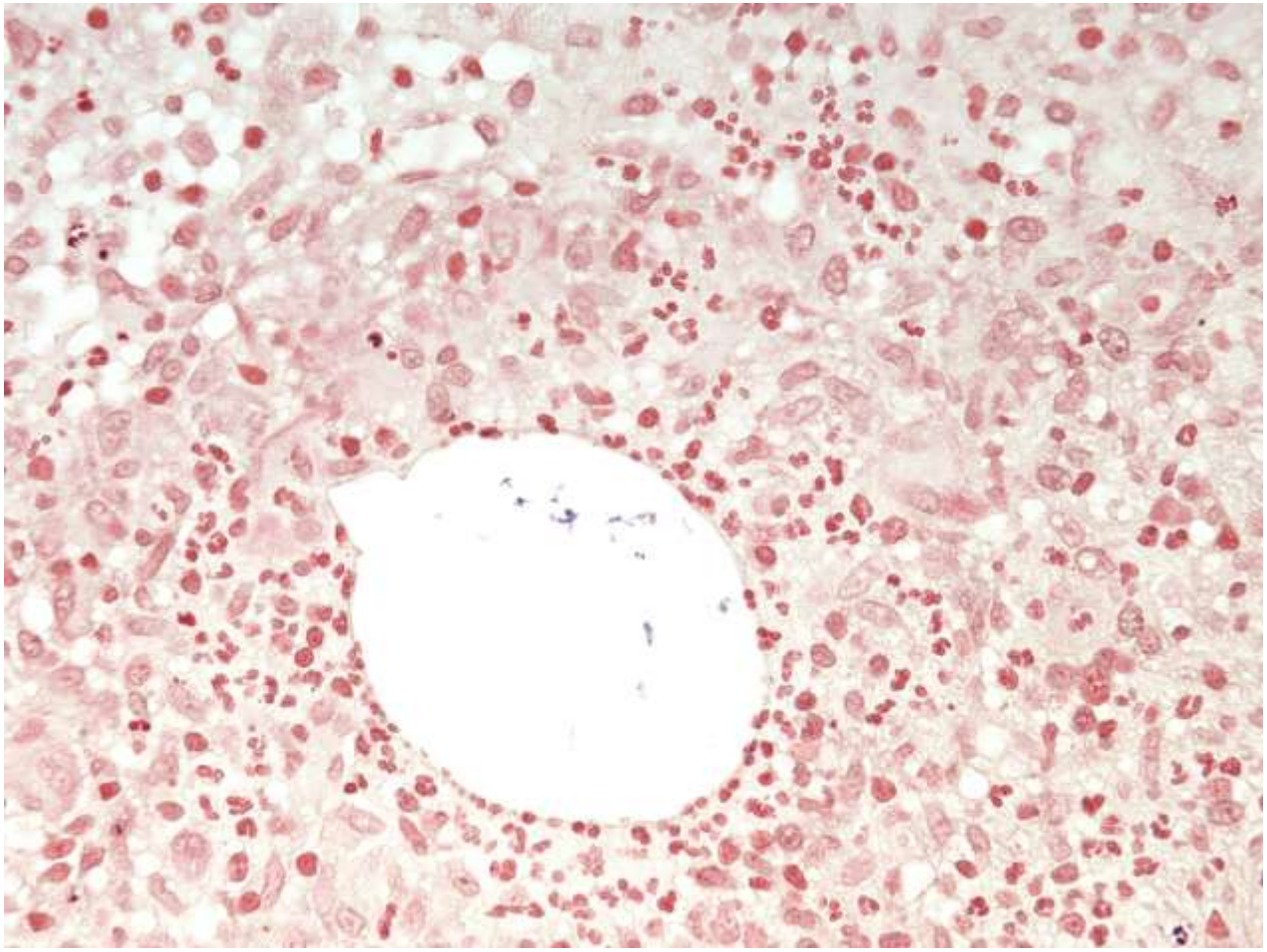
20 x



40 x



Gram stain, 40 x



Gram stain, 40 x

DIAGNOSIS?

Cystic Neutrophilic Granulomatous Mastitis

Bart Singer
Clinical Fellow, Breast Pathology
Stanford

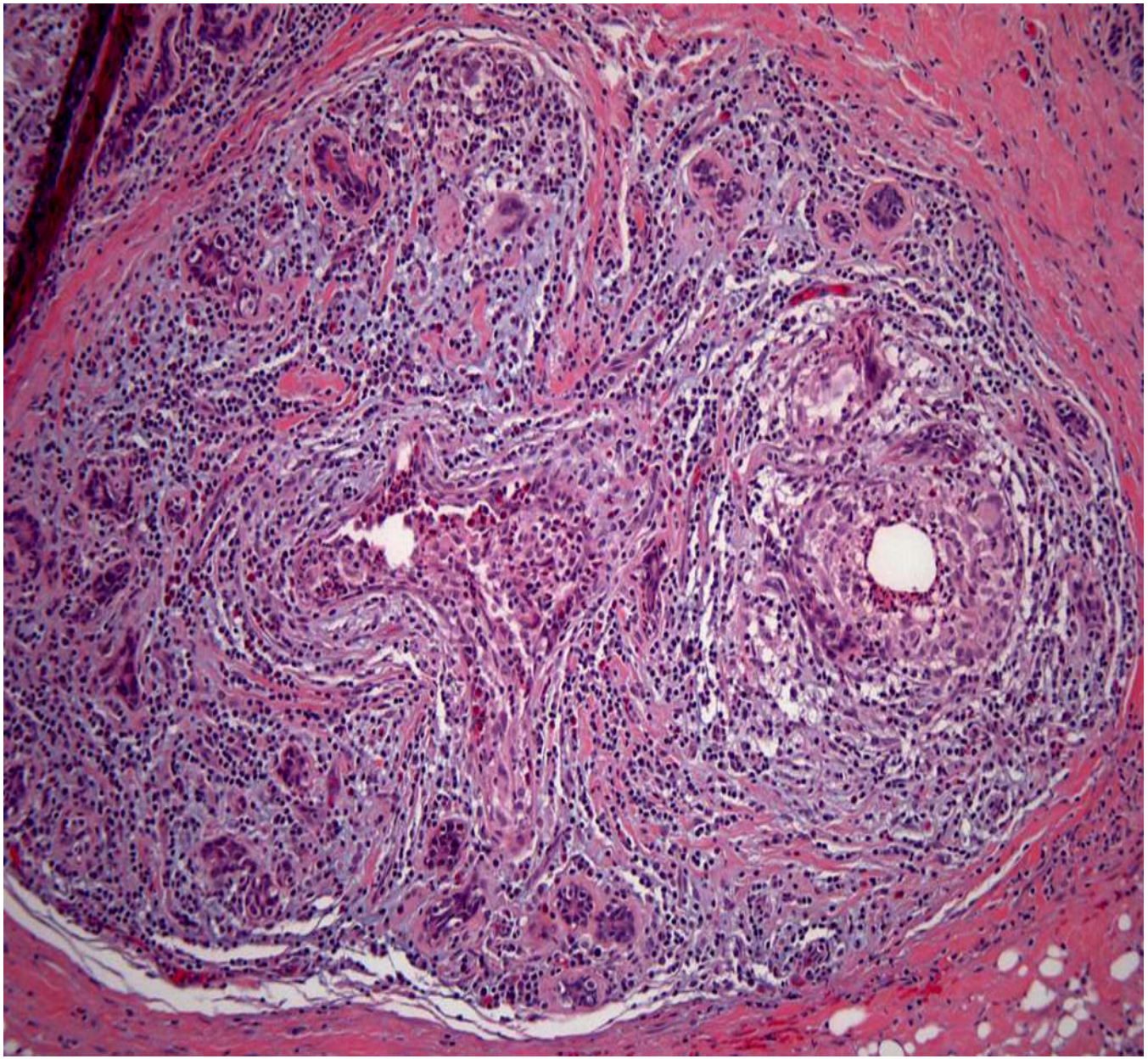
Thanks to Megan Troxell for extra images!

CNGM has a specific histologic pattern

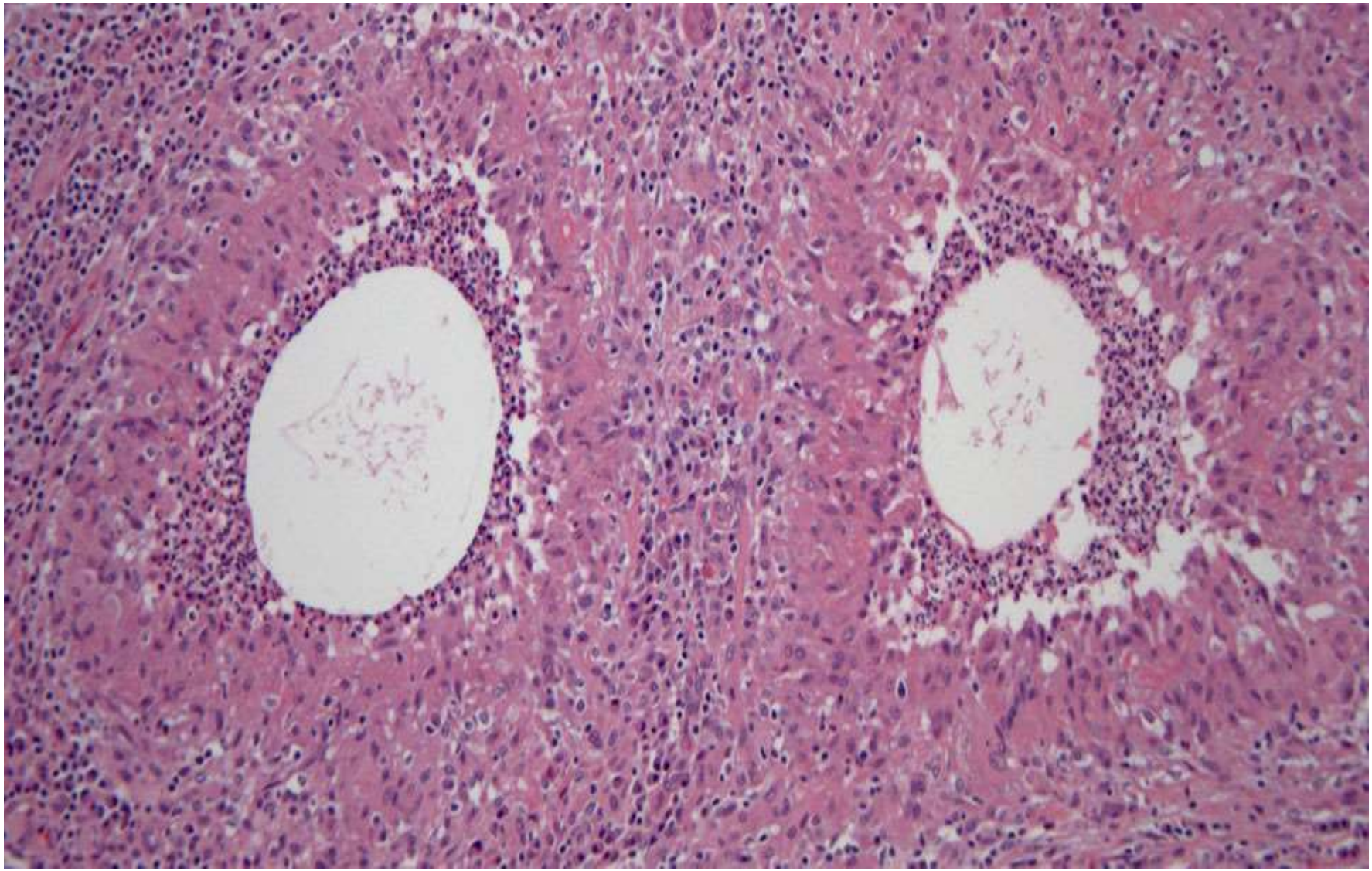
- First described in 2002 (Taylor et al, New Zealand)
- Lobulocentric location
- Granulomatous and neutrophilic inflammation
- Discrete cystic spaces surrounded by neutrophils surrounded by histiocytes
  - Cystic spaces are variably sized but larger than surrounding adipocytes

- CNGM *may* represent a subset of cases previously diagnosed as:
  - granulomatous lobular mastitis
  - idiopathic granulomatous mastitis

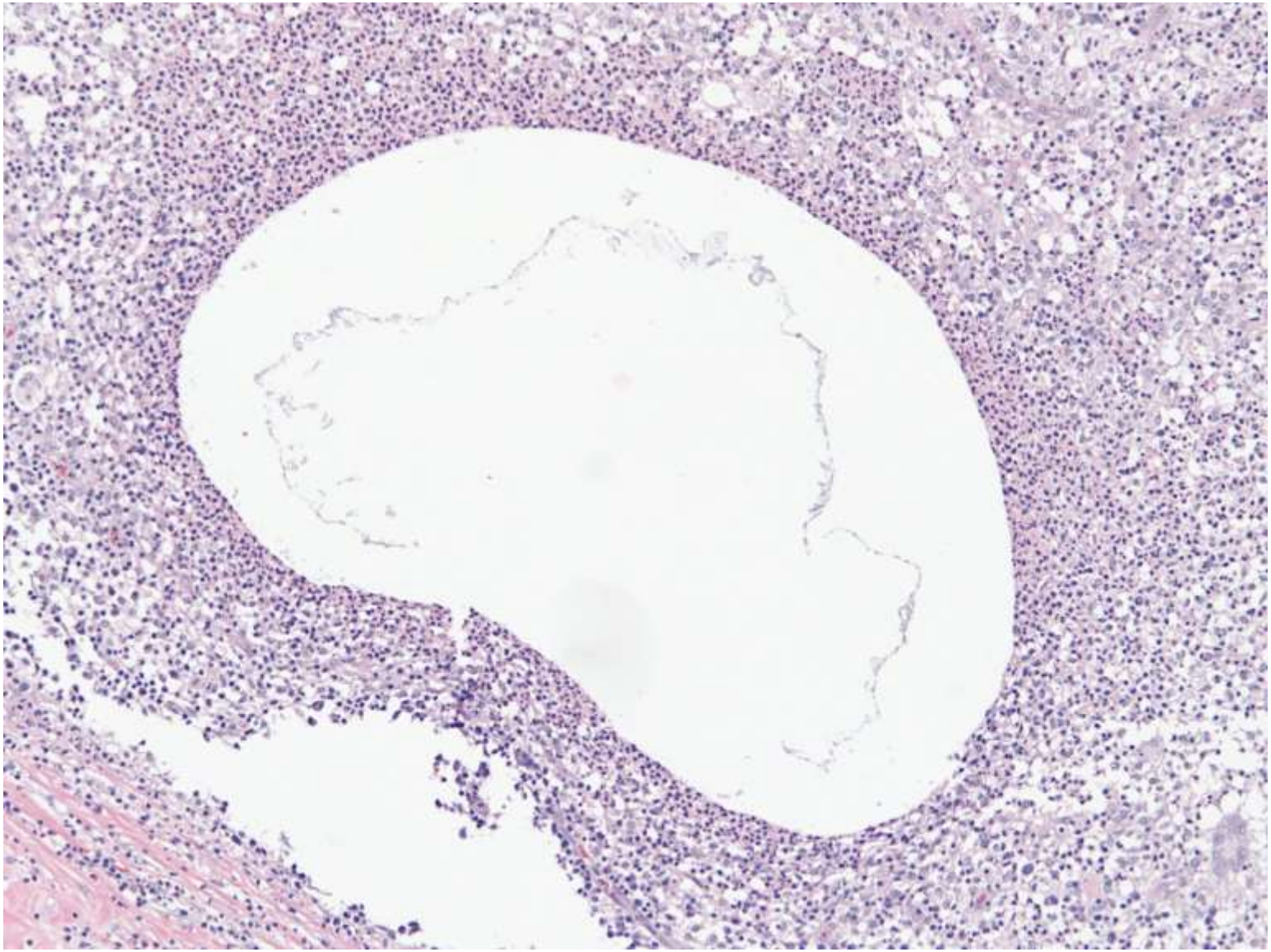
Taylor et al. Pathology, 2003. PMID: 12745457
Troxell et al. AJCP, 2016. PMID: 27247368
Renshaw et al. AJCP, 2011. PMID: 21846918



Lobulocentric
(separate case)



Cystic spaces, surrounded by neutrophils, surrounded by histiocytes
(separate case)

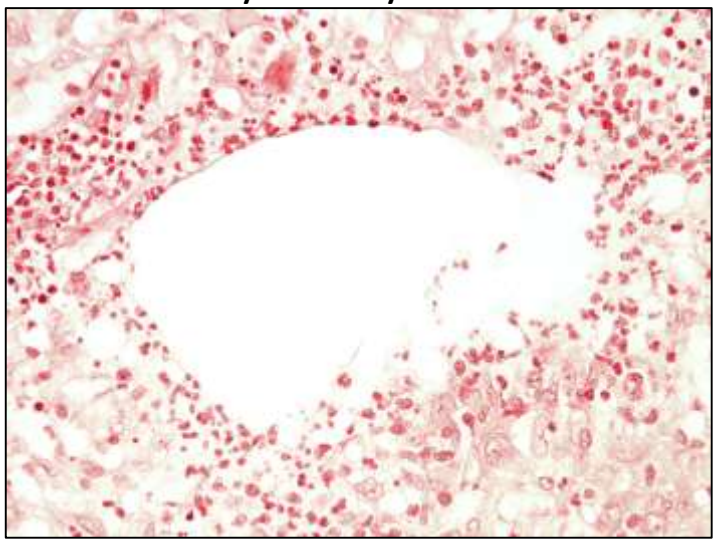


Cystic spaces, surrounded by neutrophils, surrounded by histiocytes

CNGM is associated with *Corynebacterium*

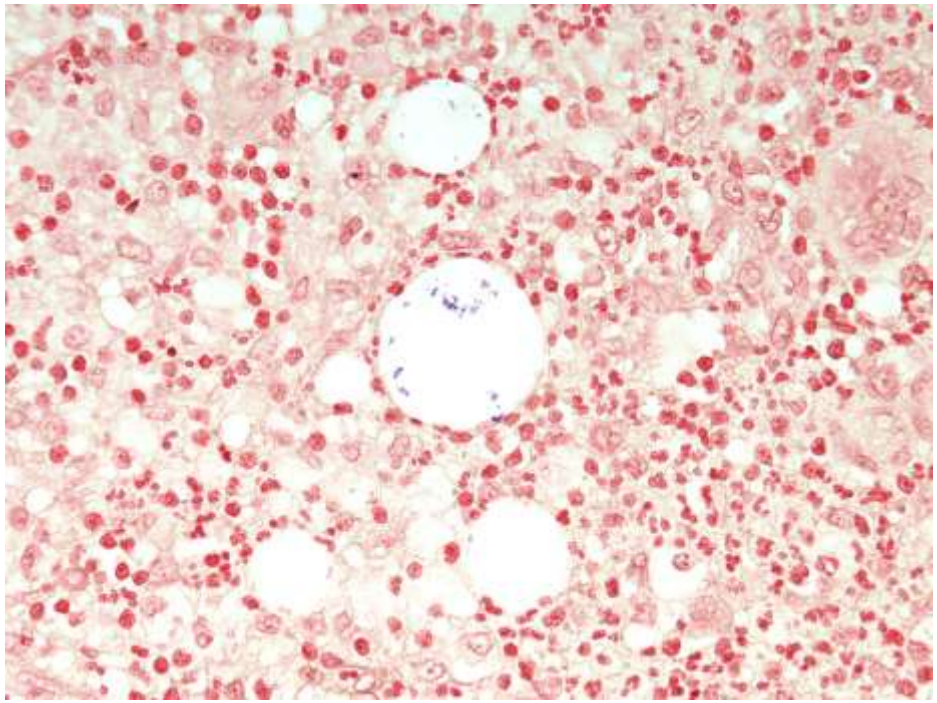
- **Rare** Gram-positive bacilli
- Look for them in the cystic spaces
- Frequently only seen within one of the spaces

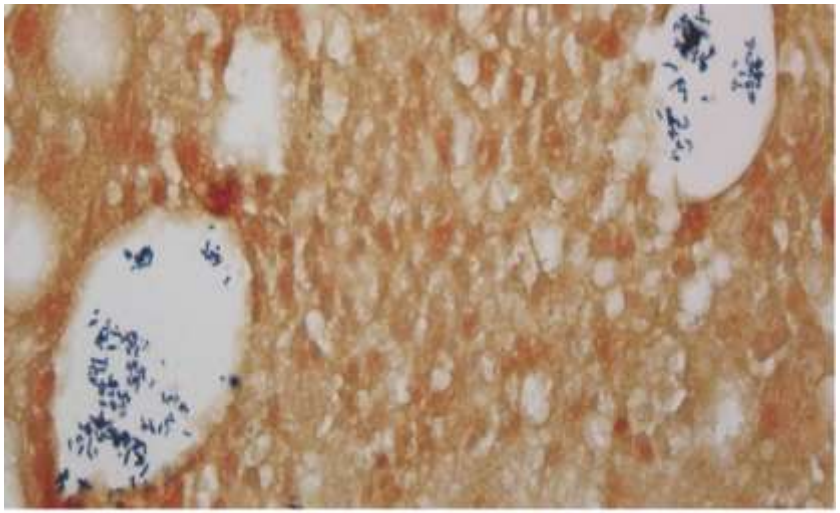
If at first you only see this:

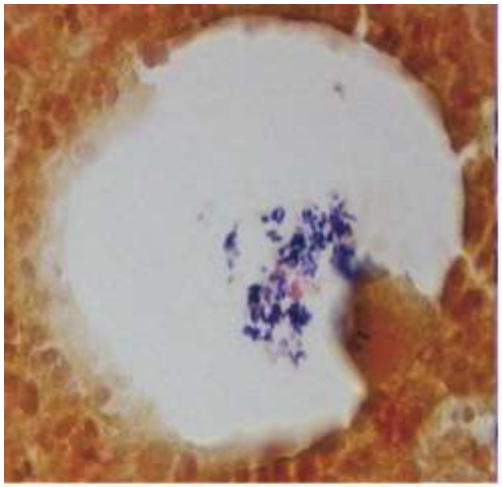


keep looking….

Troxell et al. AJCP, 2016. PMID: 27247368
Renshaw et al. AJCP, 2011. PMID: 21846918







Corynebacterium

- Fastidious organisms – hard to grow / need specialized growth media
- Many labs will dismiss as skin flora, "diphtheroids", or commensal / contaminant
  - Recent study by Leal et al (UNC) showed 11/11 isolates of *C. kroppenstedtii* from breast tissue cultures were clinically significant
- In addition to gram stain, AFB / Fite (and GMS) is recommended
  - Some mycobacteria are variably gram positive

Leal et al. JCM, 2016. PMID: 27629905
Troxell et al. AJCP, 2016. PMID: 27247368
Renshaw et al. AJCP, 2011. PMID: 21846918

CNGM – Unique Demographics

- Compared to other forms of mastitis, CNGM is more frequently seen in women who are:
  - Hispanic
  - Pacific island origin
  - Younger
  - Several years post-partum
  - Born outside the U.S.

Taylor et al. Pathology, 2003. PMID: 12745457
Troxell et al. AJCP, 2016. PMID: 27247368

CNGM Treatment – Highly Variable

Typically chronic / recurring disease course:

- Multiple rounds of surgery / debridement
- Prolonged courses of antibiotics
- Immunomodulatory therapy (steroids, methotrexate)

Will *Corynebacterium* association inform treatment options in the future?

Studies / data are currently lacking

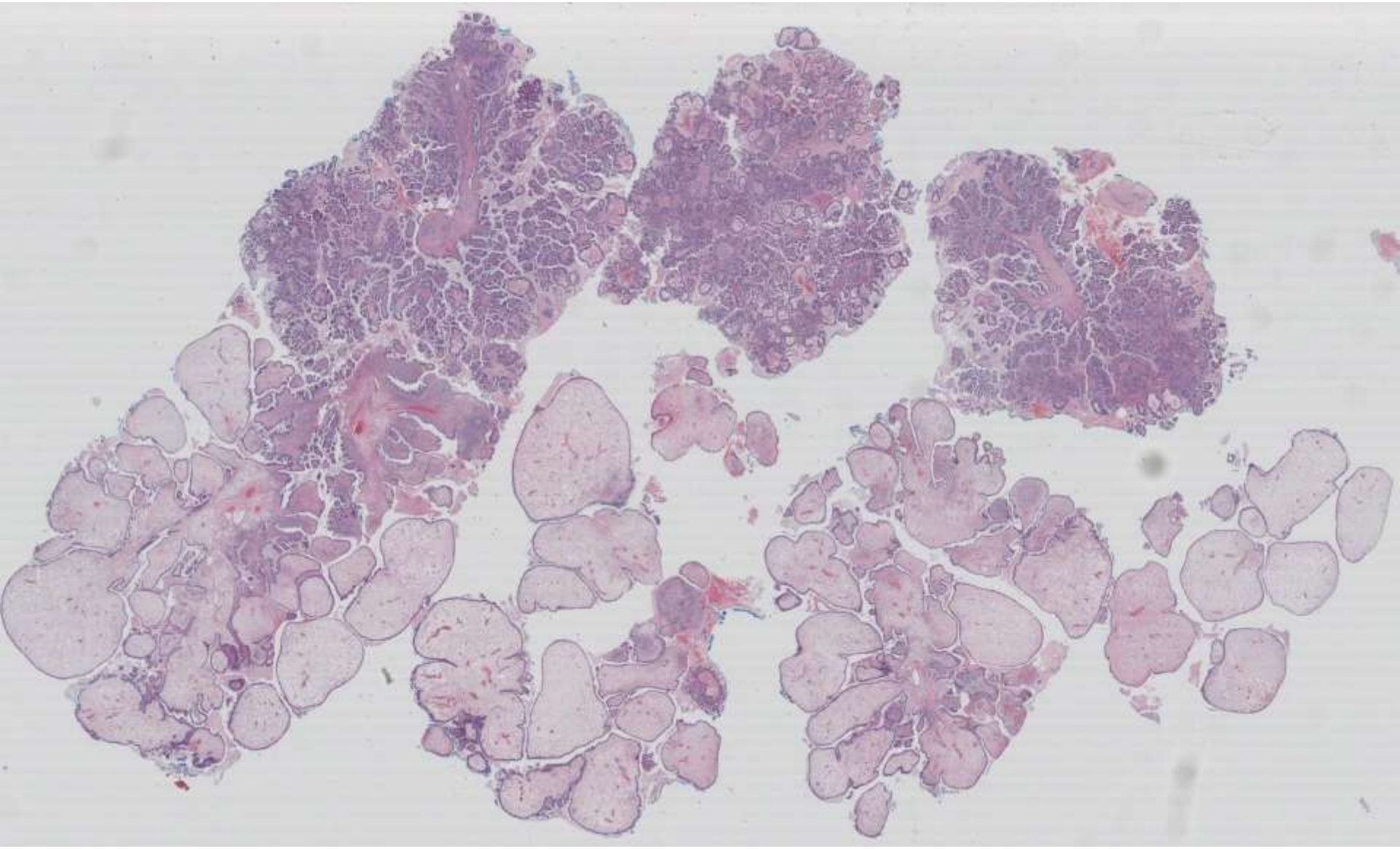
References

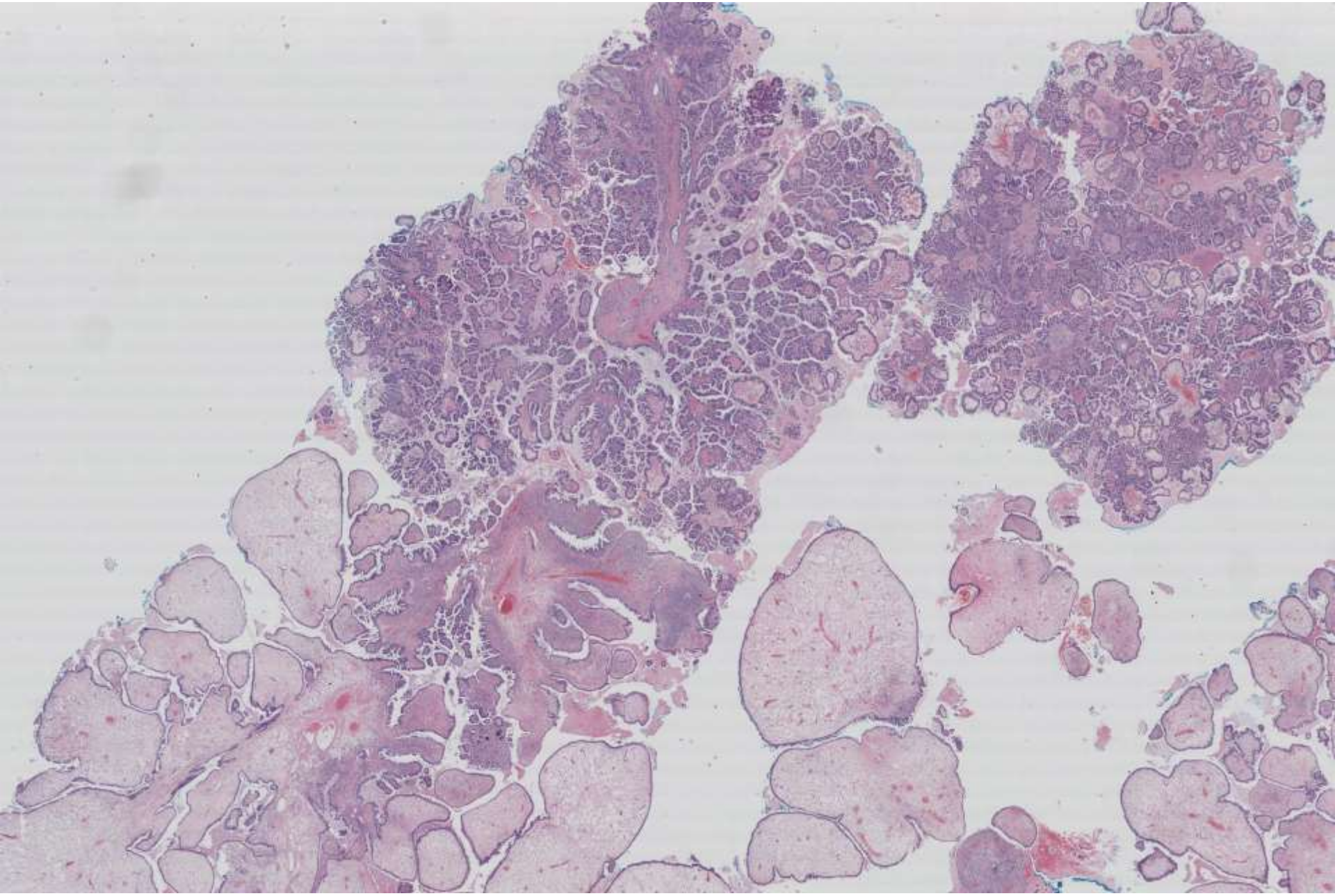
1. Taylor, G. B., Paviour, S. D., Musaad, S., Jones, W. O. & Holland, D. J. A clinicopathological review of 34 cases of inflammatory breast disease showing an association between corynebacteria infection and granulomatous mastitis. *Pathology* **35,** 109–119 (2003).
2. Renshaw, A. A., Derhagopian, R. P. & Gould, E. W. Cystic neutrophilic granulomatous mastitis: An underappreciated pattern strongly associated with gram-positive bacilli. *Am. J. Clin. Pathol.* **136,** 424–427 (2011).
3. D'Alfonso, T. M. *et al.* Cystic Neutrophilic Granulomatous Mastitis: Further Characterization of a Distinctive Histopathologic Entity Not Always Demonstrably Attributable to Corynebacterium Infection. *Am. J. Surg. Pathol.* **39,** 1440–7 (2015).
4. Troxell, M. L. *et al.* Cystic Neutrophilic Granulomatous Mastitis. *Am. J. Clin. Pathol.***145,** 635–645 (2016).
5. Leal SM, Jones M, Gilligan PH. Clinical significance of commensal gram-positive rods routinely isolated from patient samples. J Clin Microbiol. 2016;54(12):2928–36.
6. Johnson MG, Leal SM, Plongla R, Leone PA, Gilligan PH. The Brief Case - Recurrent Granulomatous Mastitis Due to Corynebacterium kroppenstedtii. J Clin Microbiol. 2016;54(8):1938–41.

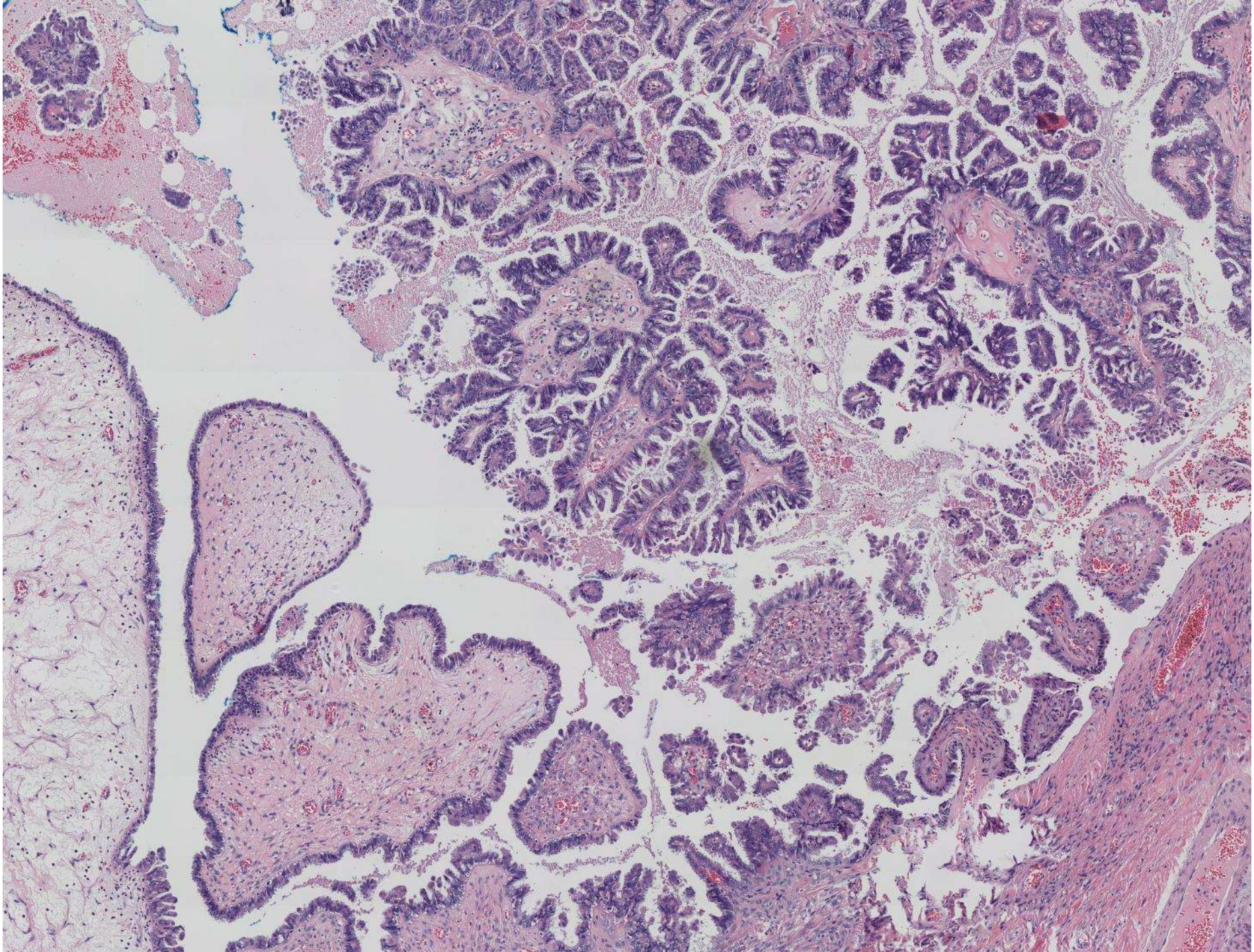
SB 6149
[scanned slide available]

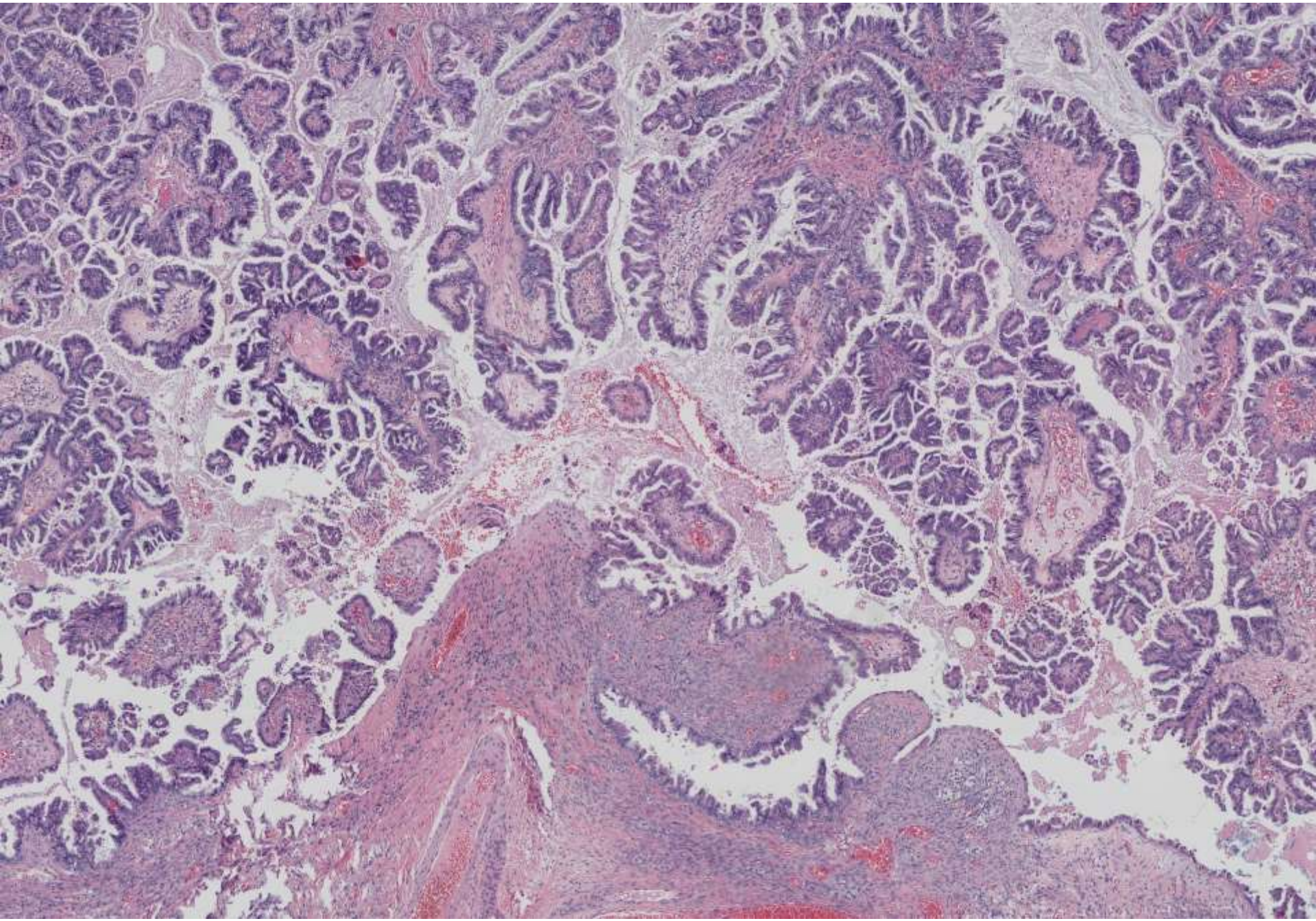
Sunny Kao; Stanford

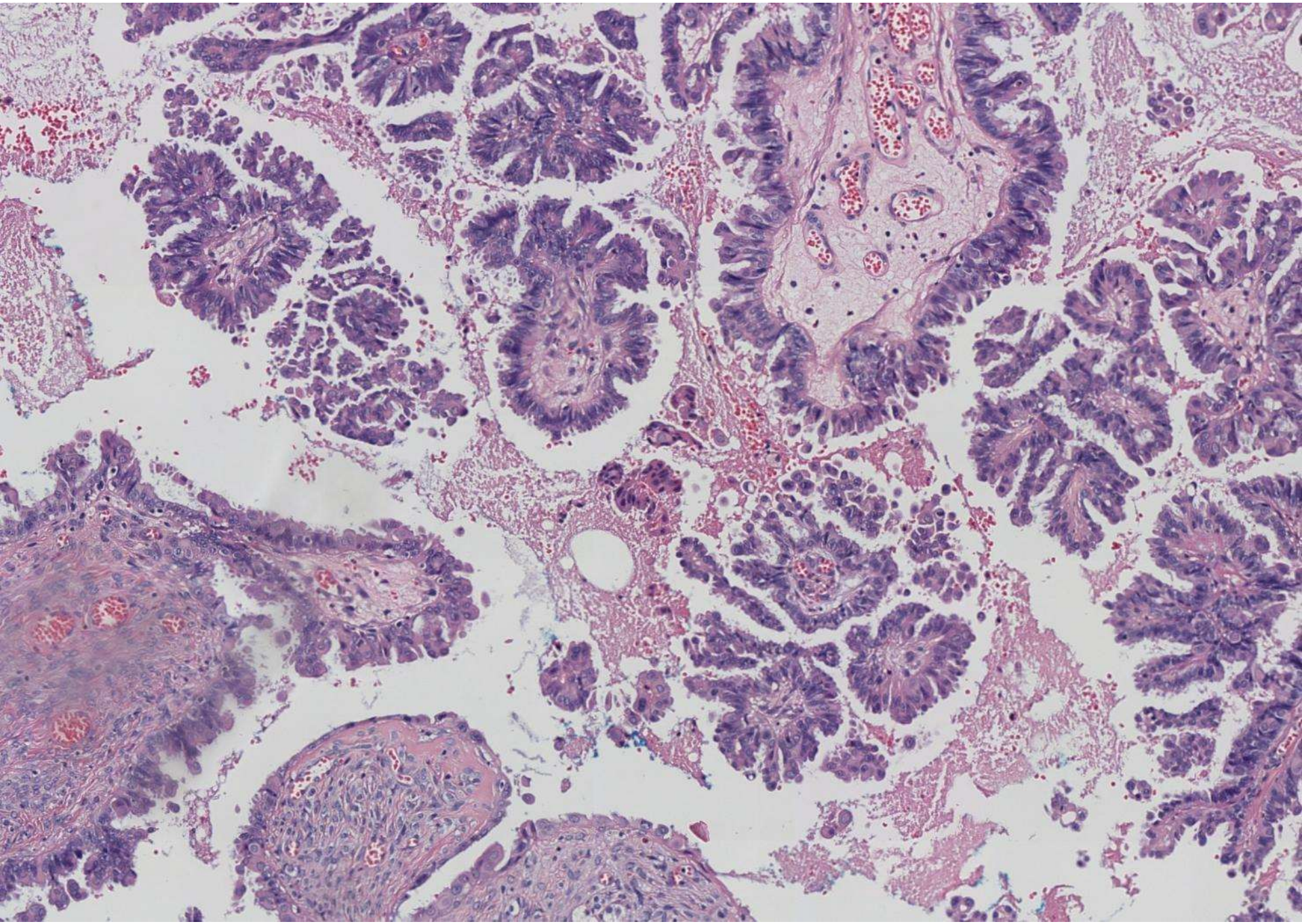
16-year-old M with left hydrocele/testicular tumor.

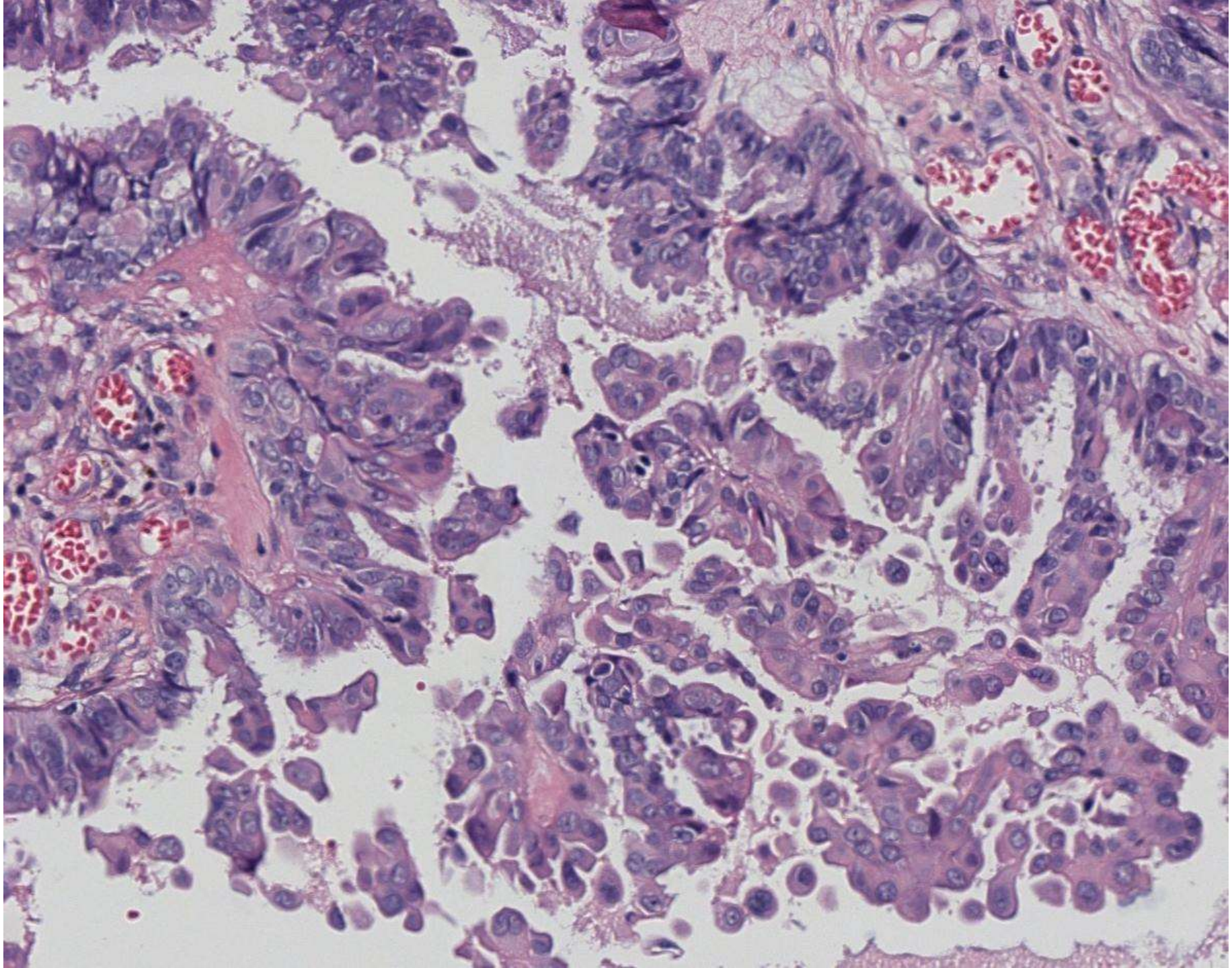




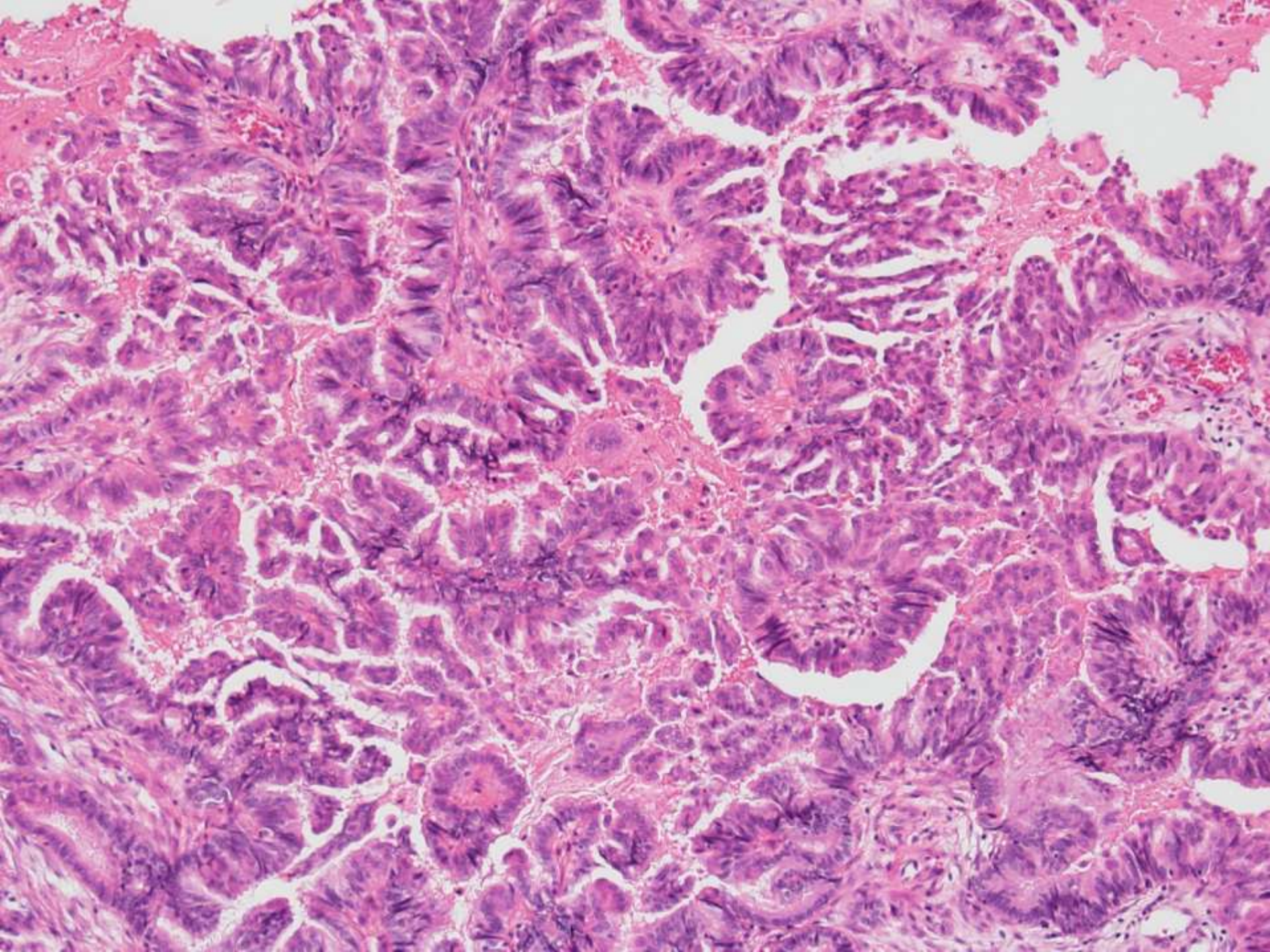


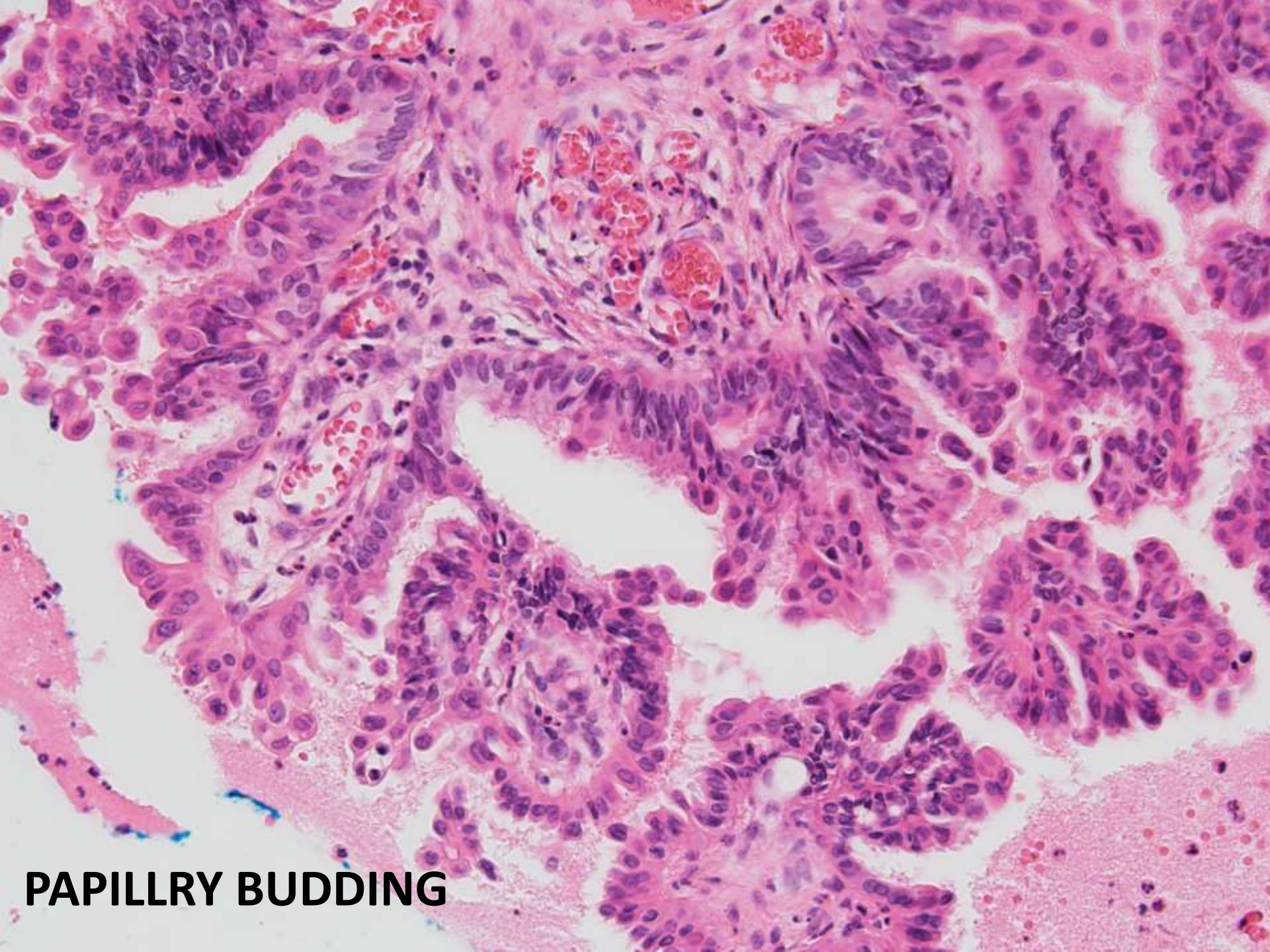




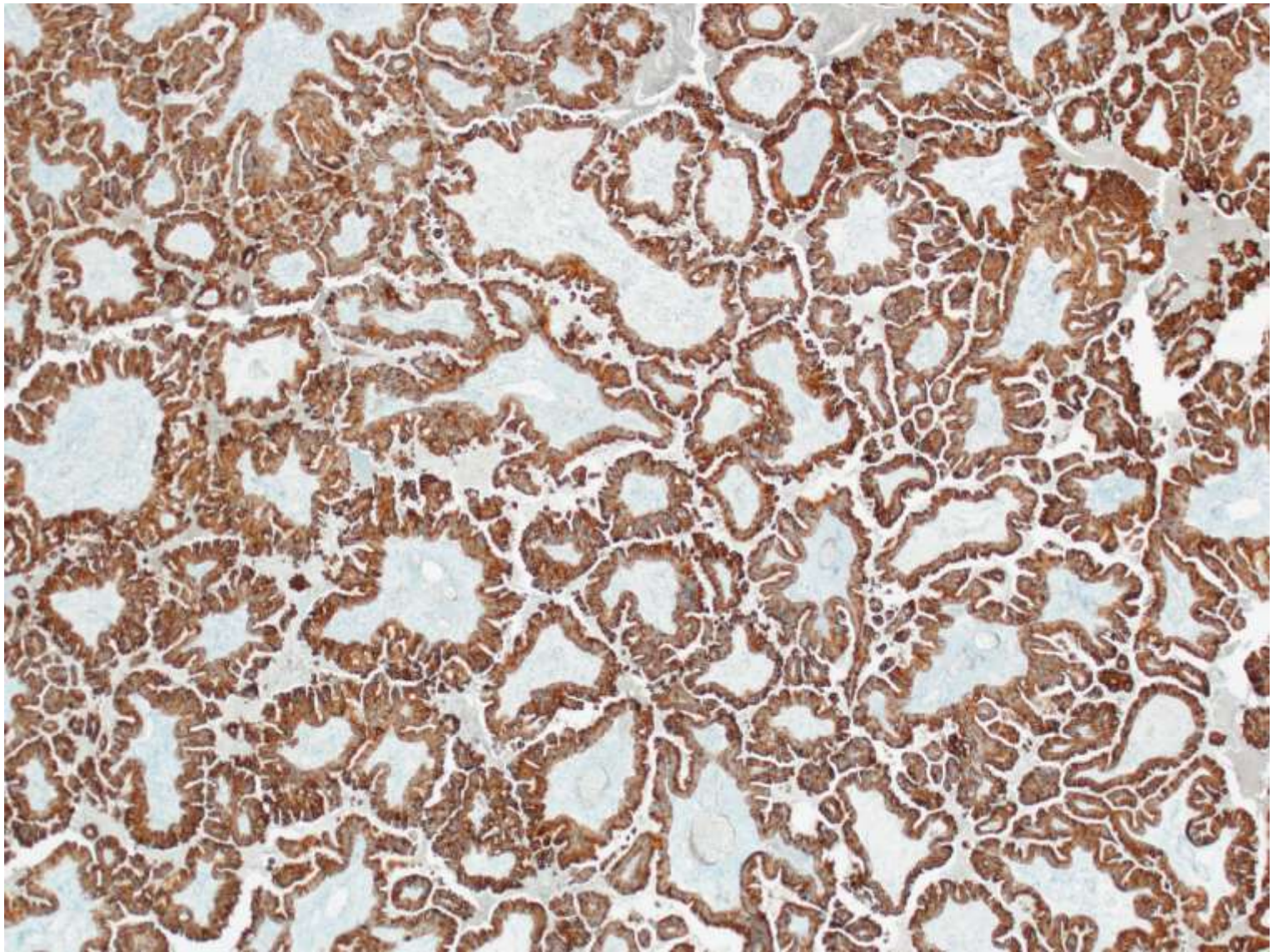


DIAGNOSIS?

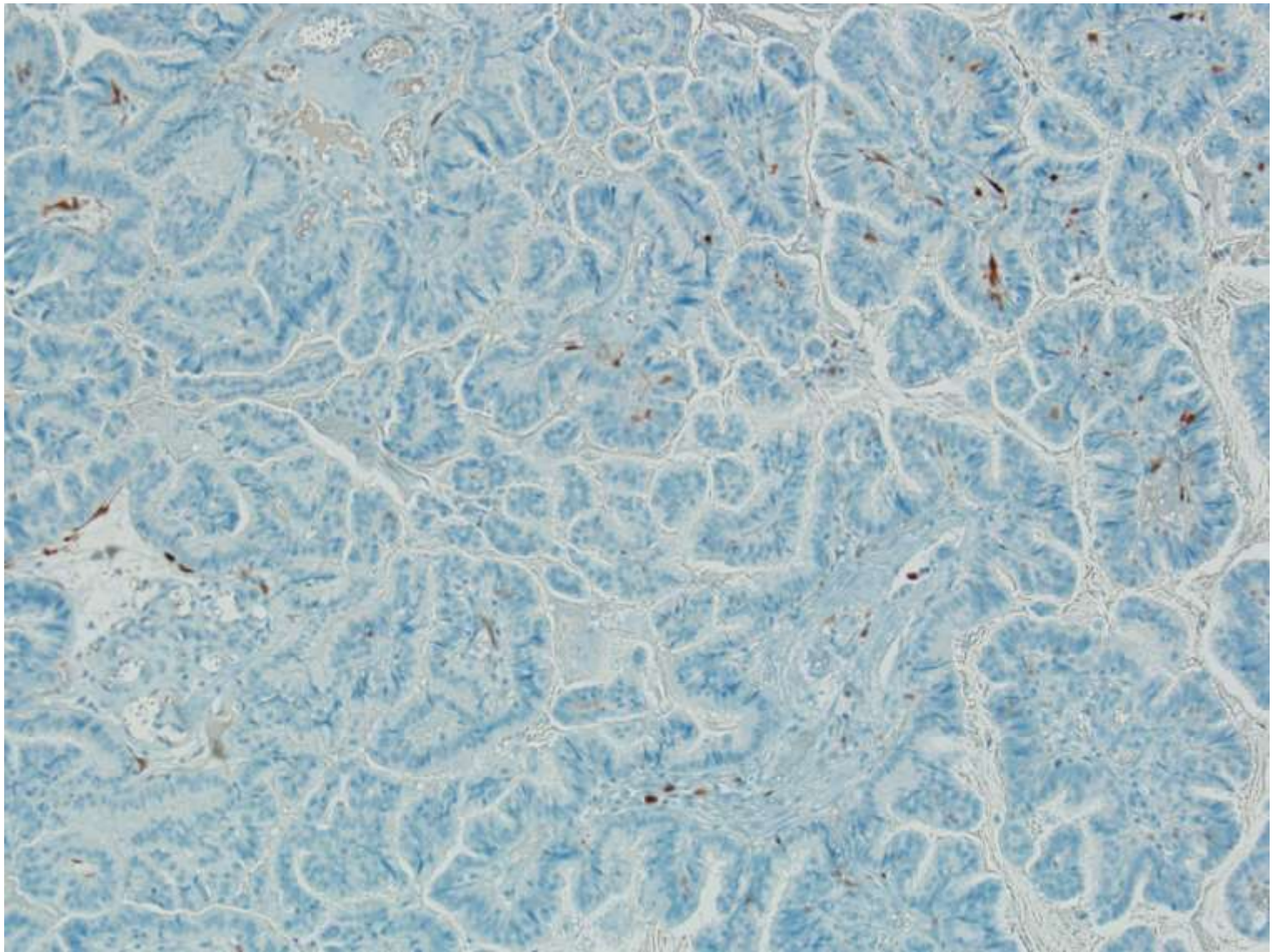



PAPILLRY BUDDING

EMA



Calretinin



Serous borderline tumor

- Slightly more serous than mucinous tumors in the paratestis
- Varying age
- Usually presents as mass +/- hydrocele
- Origin: appendix testis and/or Mullerian metaplasia of the peritoneal lining
- Favorable outcome

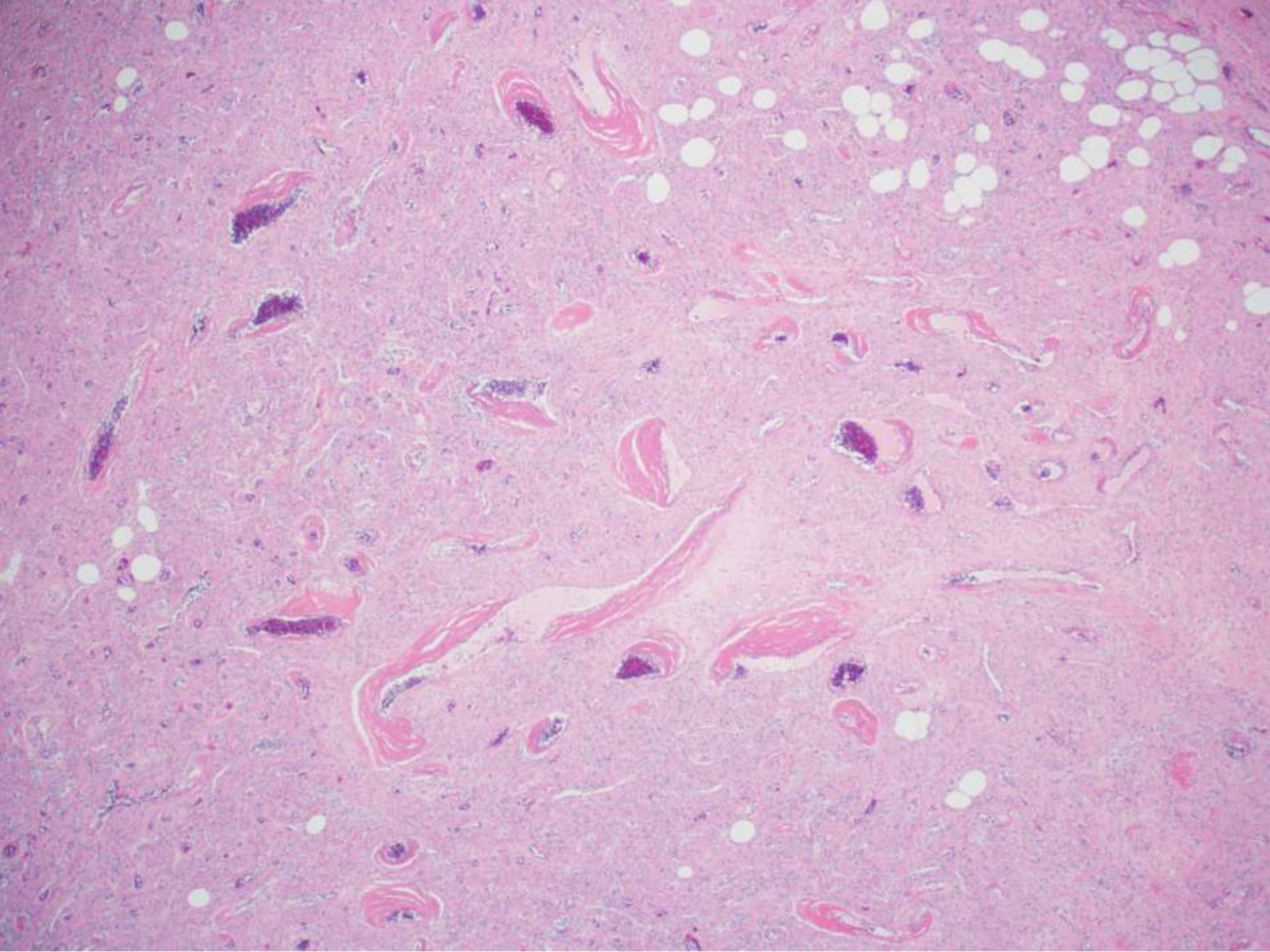
Differential Diagnosis

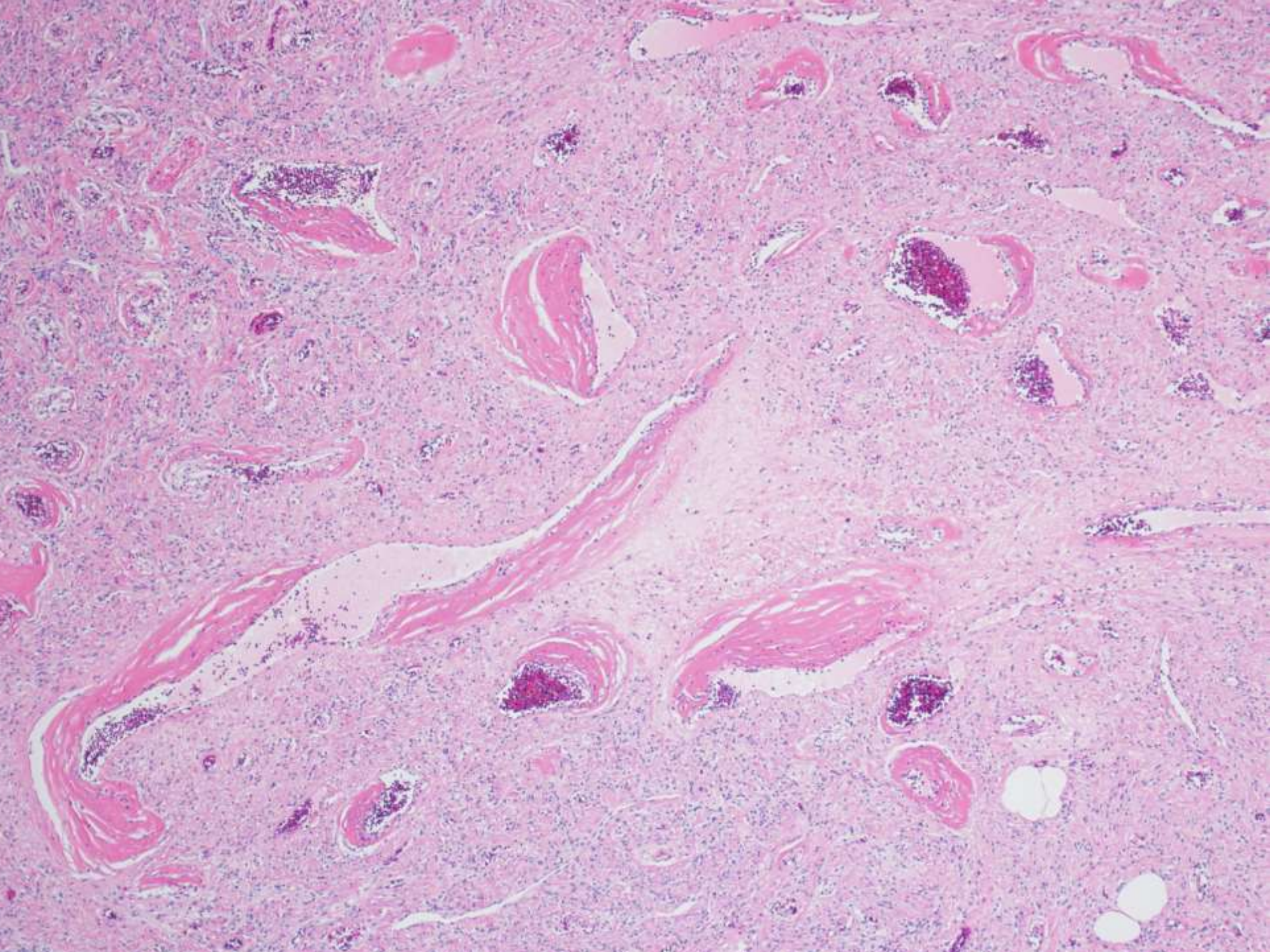
- Rete testis carcinoma
  - Hilum; associated with dilated rete channels
  - Highly atypical cells
- Well-differentiated mesothelioma
  - Cuboidal cells
  - Less cellular stratification
  - Cilia absent
  - Calretinin+, CEA-, CD15-

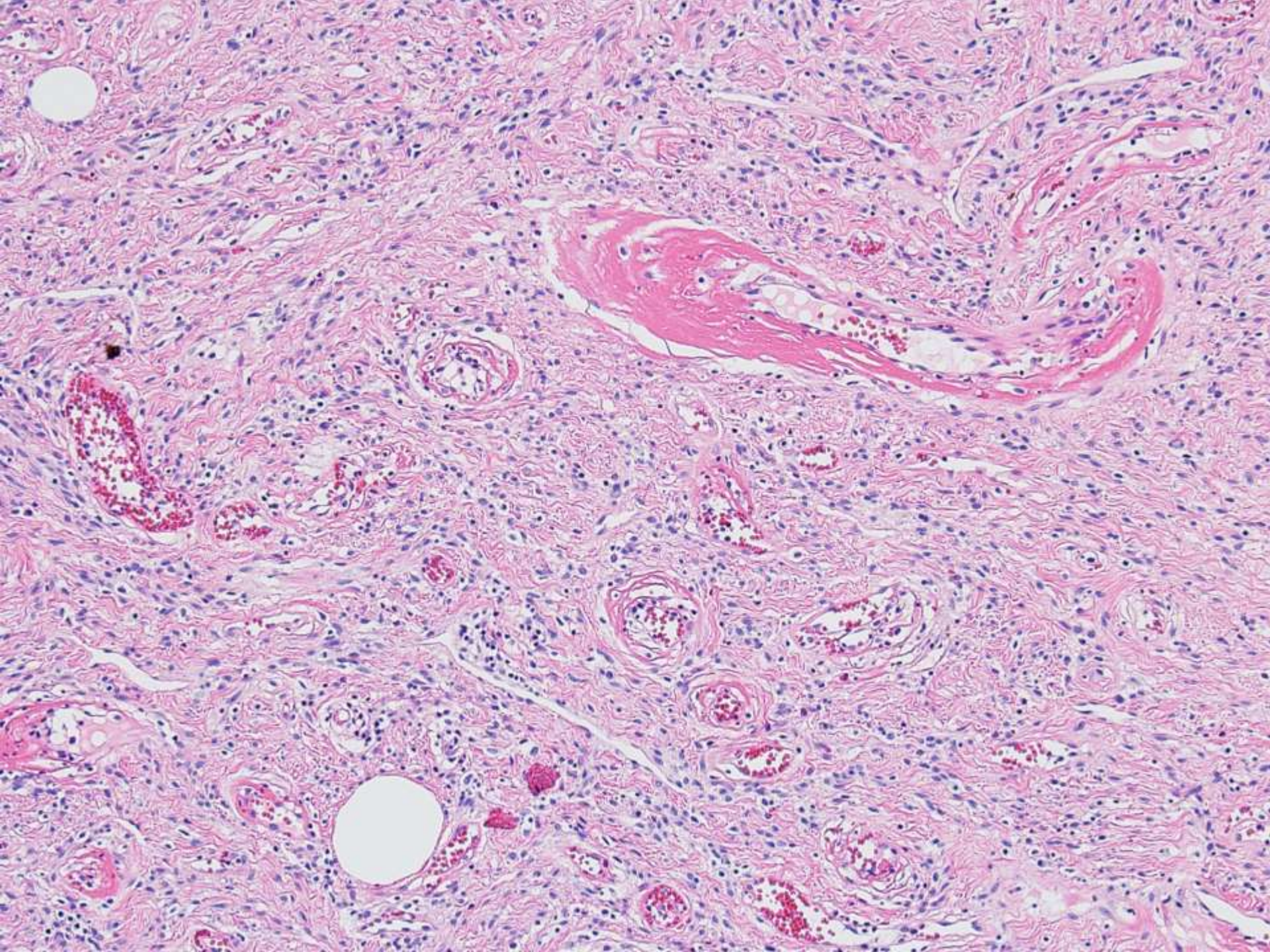
SB 6150

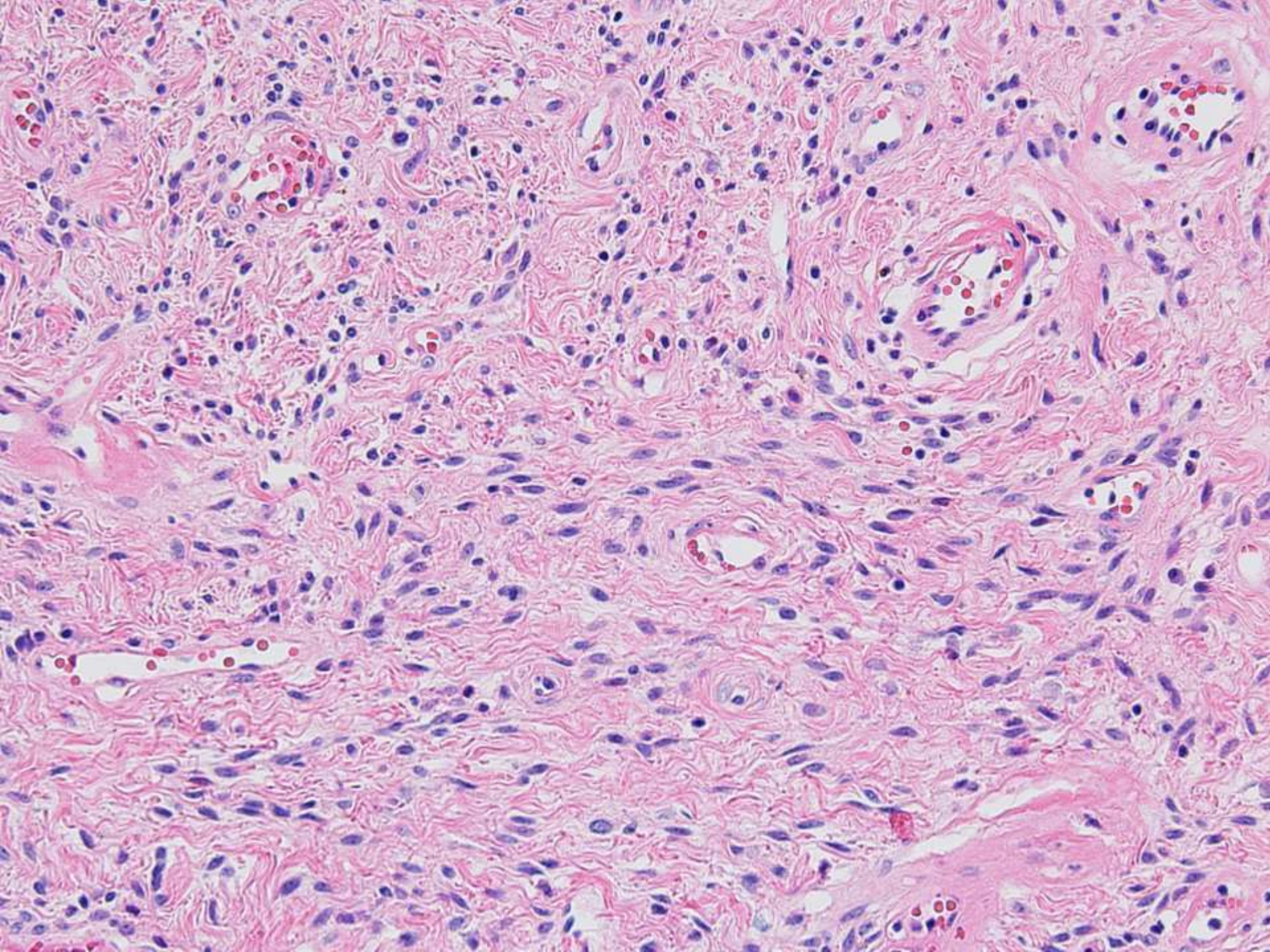
Sunny Kao; Stanford

58-year-old M with right groin mass.

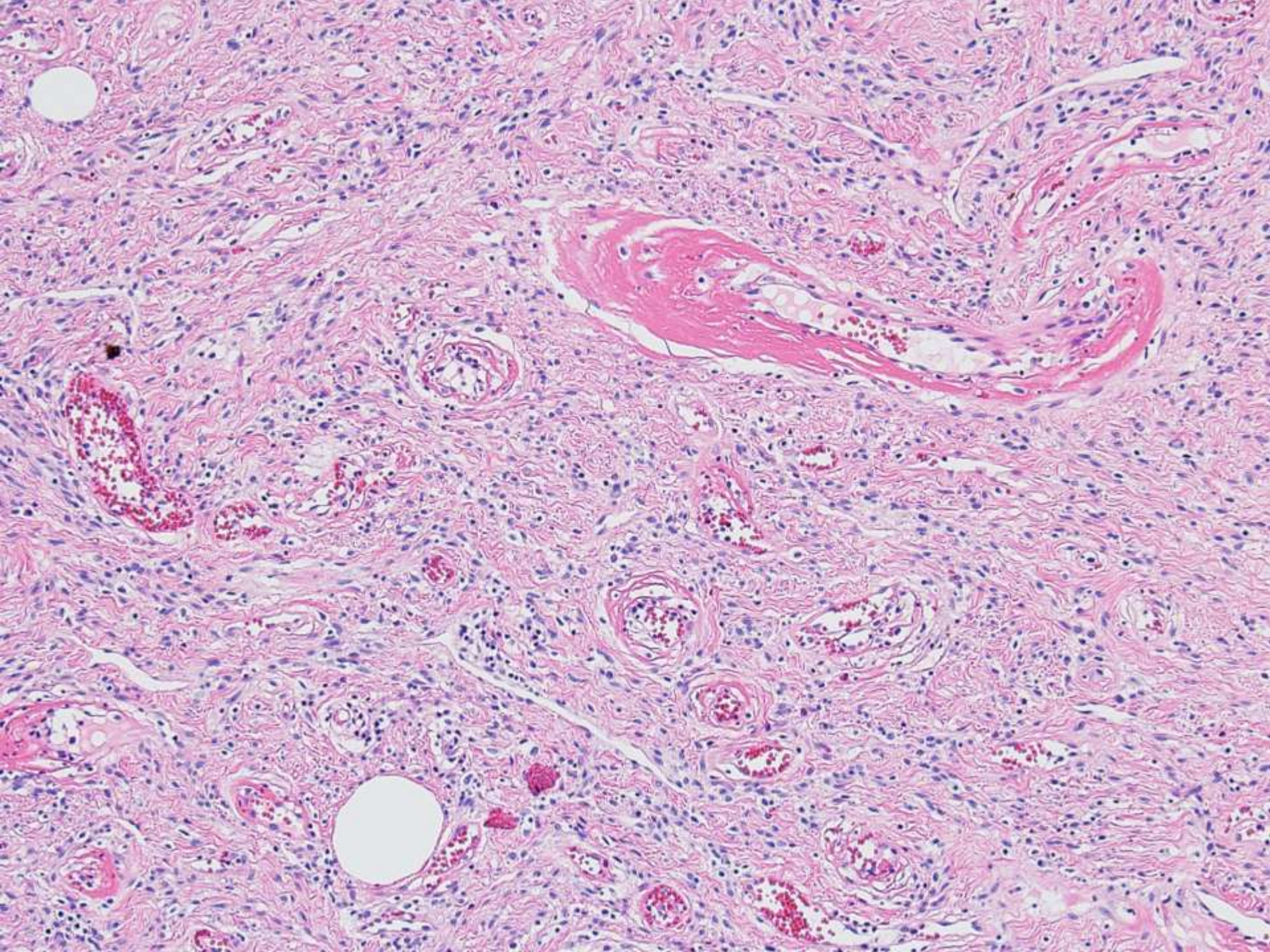


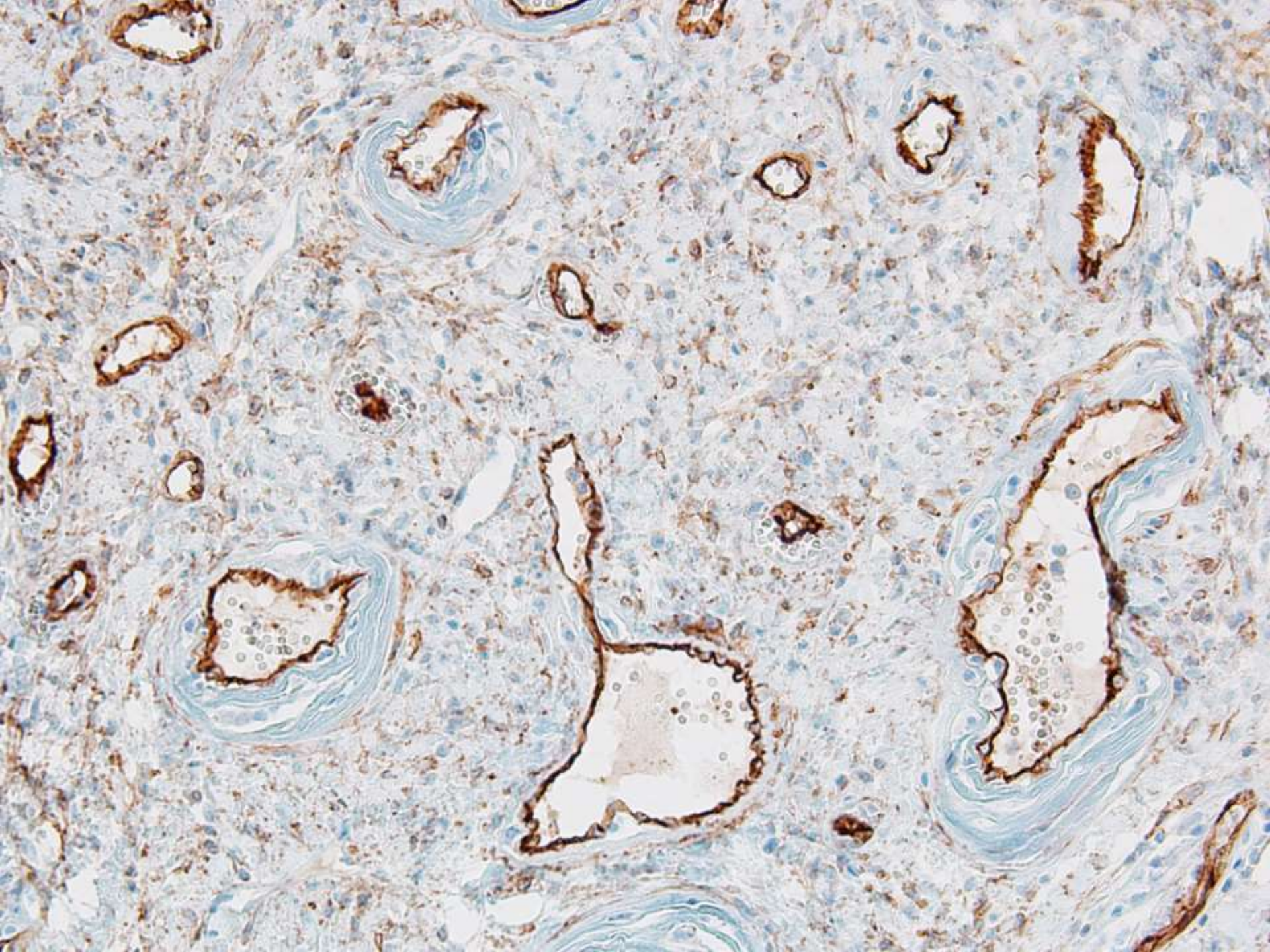




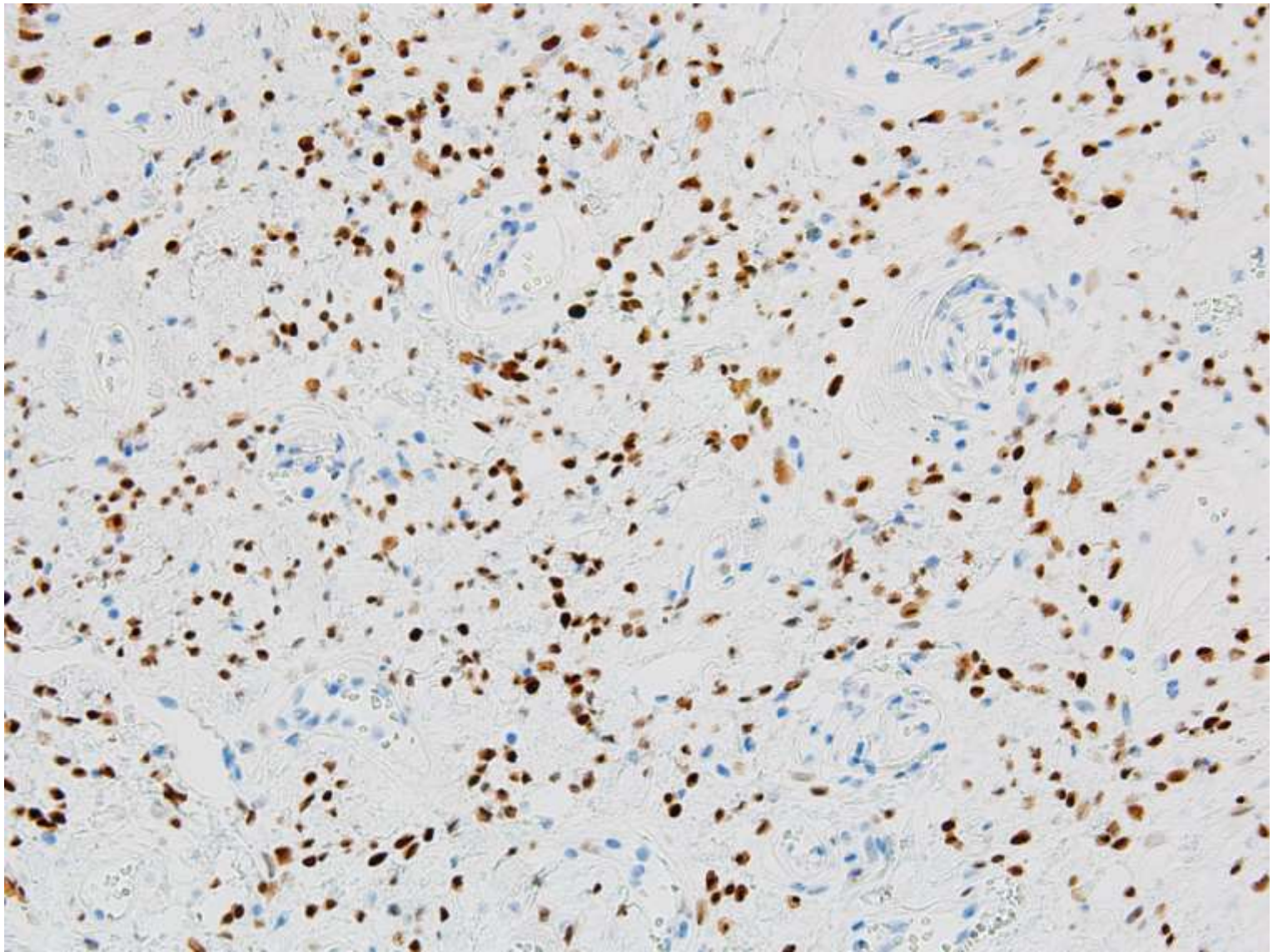


DIAGNOSIS?

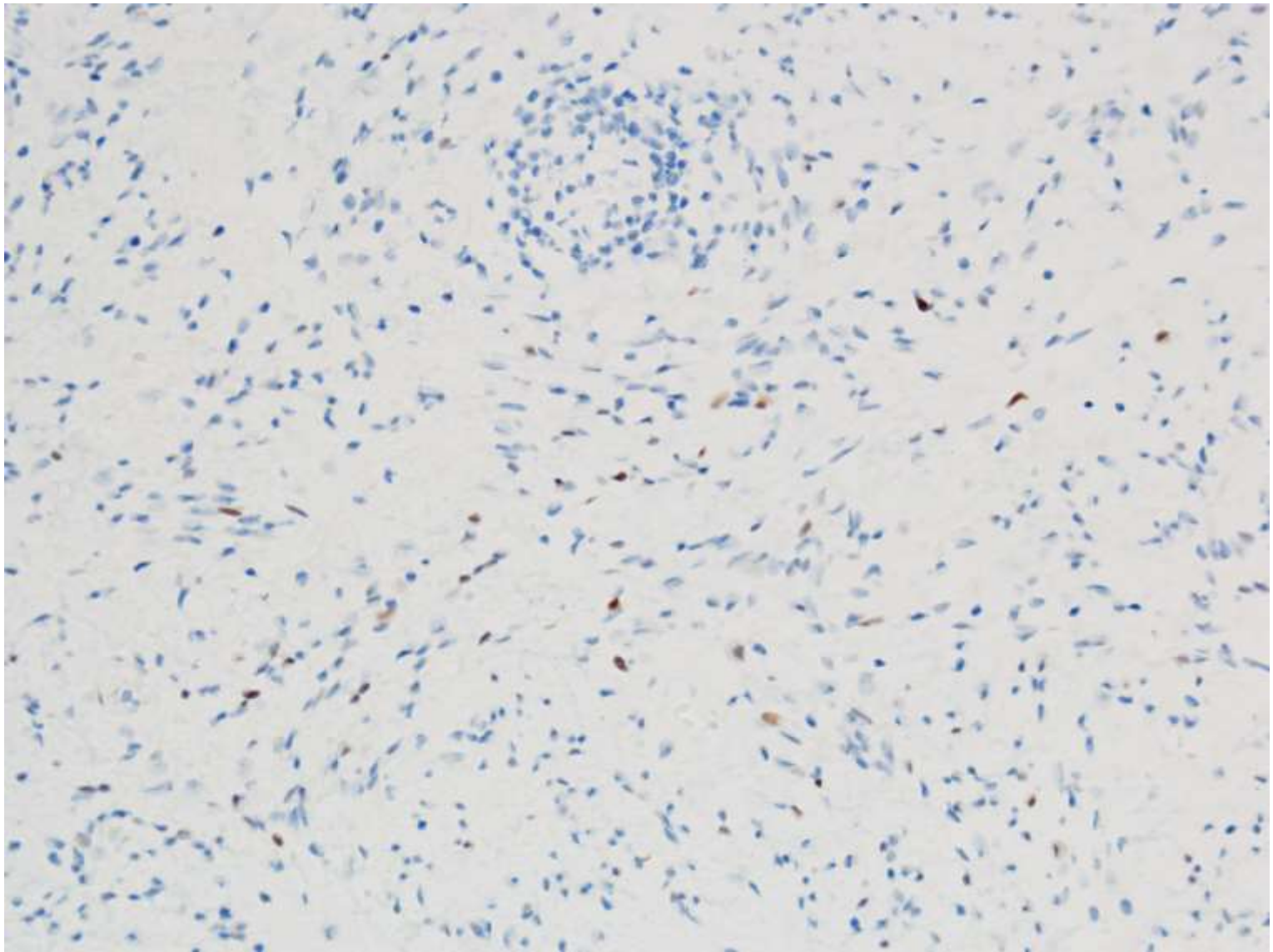




ER



PR



Cellular angiofibroma

- Aka “angiomyofibroblastoma-like tumor”
- Middle aged to elderly men (median 60 Y)
- Usually presents as painless scrotal/inguinal mass thought to represent hernia
- CD34+ (75%), ER (20%), PR (20%), S100-
- Benign→ local excision

Differential Diagnosis

- Aggressive angiomyxoma!!
  - Variable age 1-82 (mean 46)
  - Infiltrative nature
  - Lesser cellularity
  - Attenuated cells
  - More commonly desmin+