Disclosures
June 6, 2016

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

Dr. Dan Arber has disclosed that he sits on the Advisory Boards of Agios and Dava Oncology and that he consults for Celgene. The planners have determined that this financial relationship is not relevant to the case being presented and does not present a conflict of interest.

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

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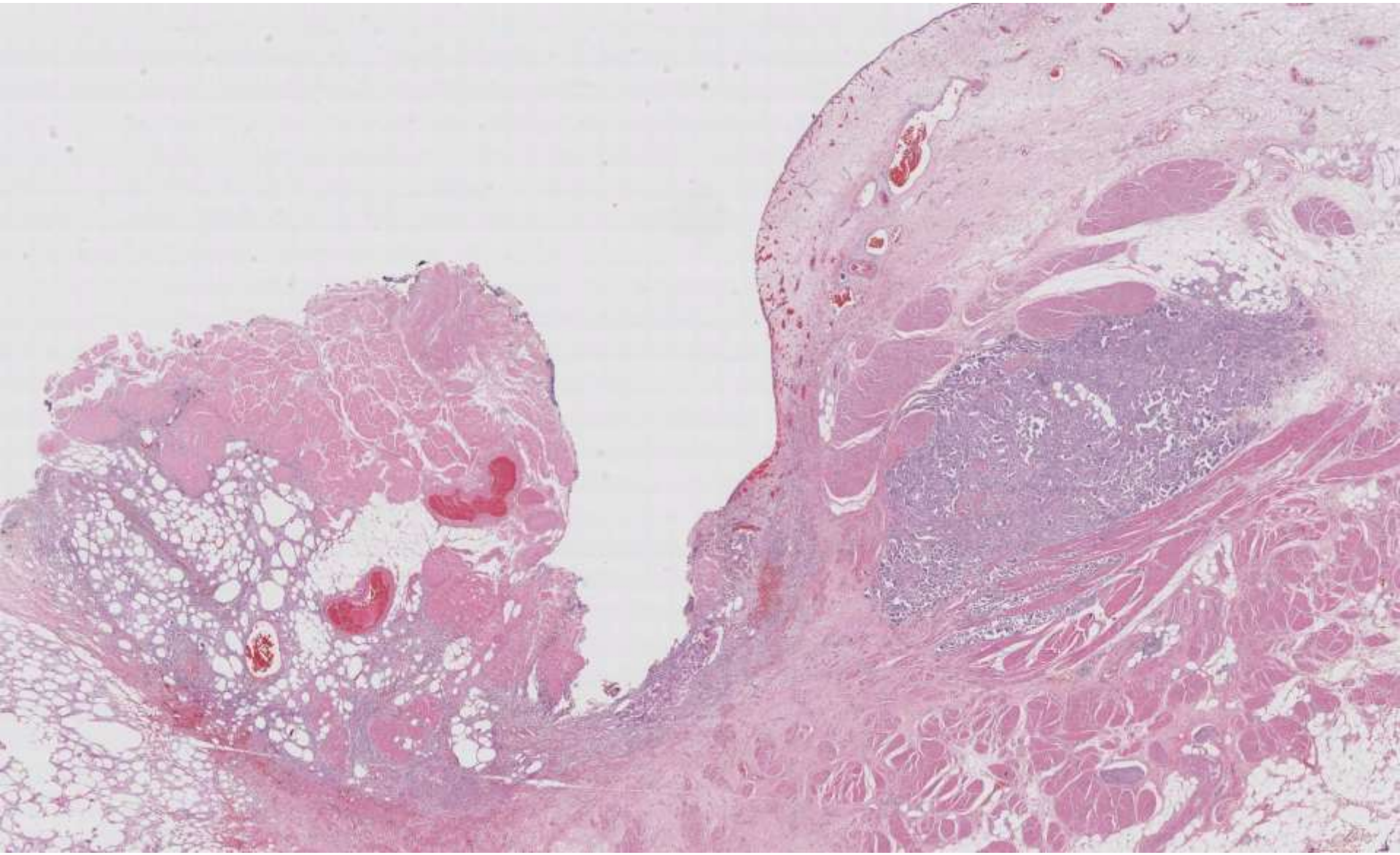
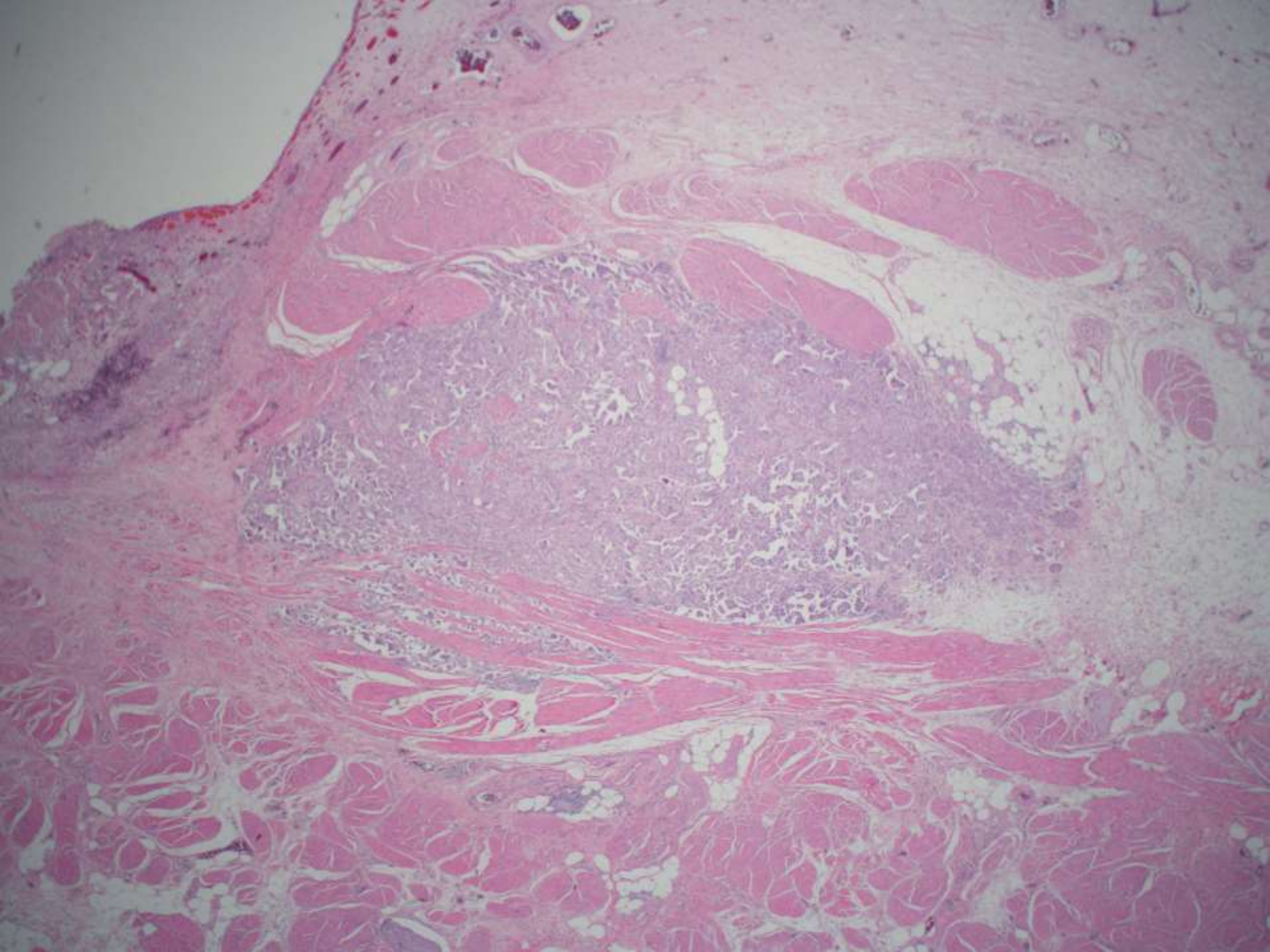
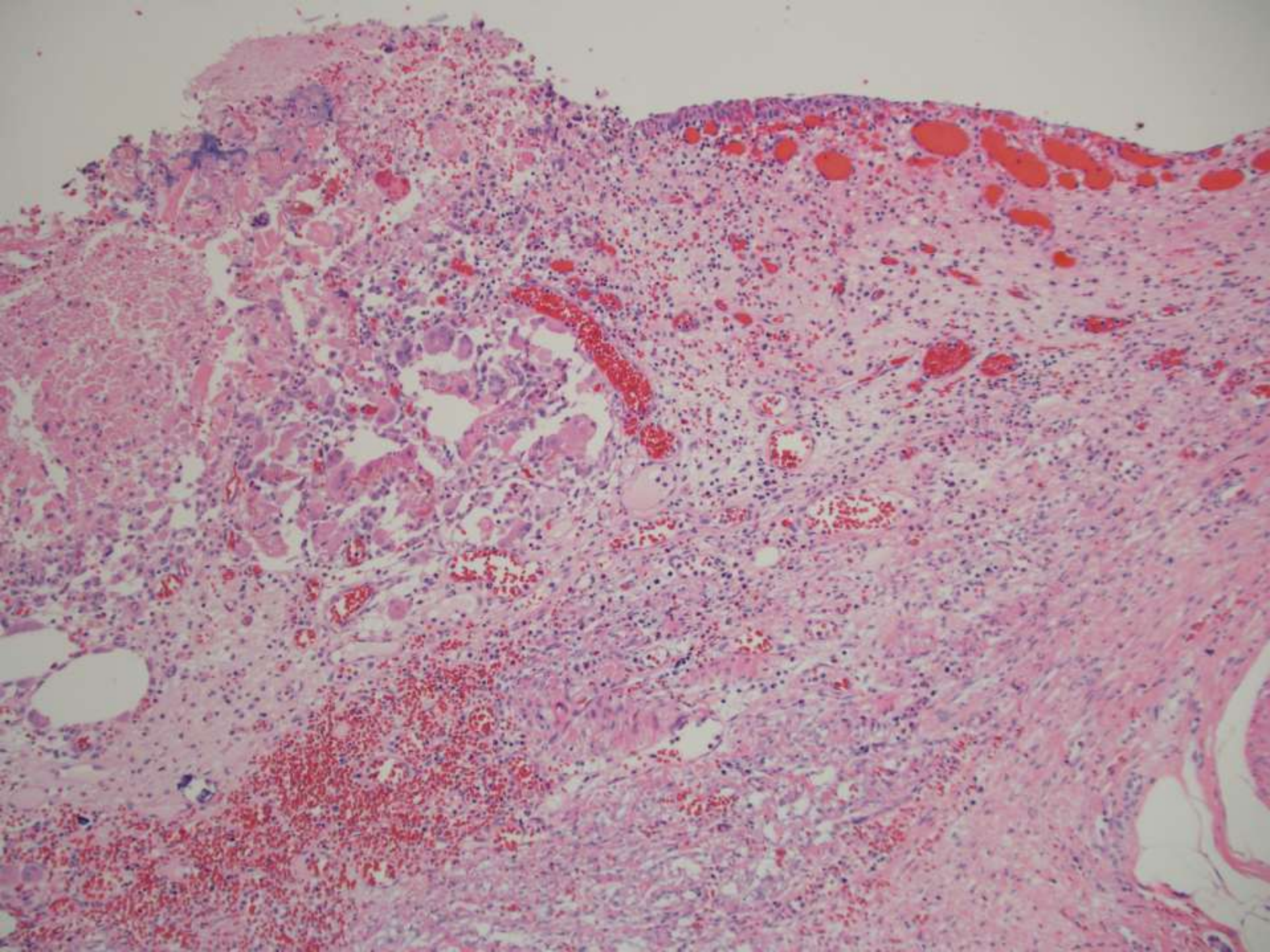
SB 6051

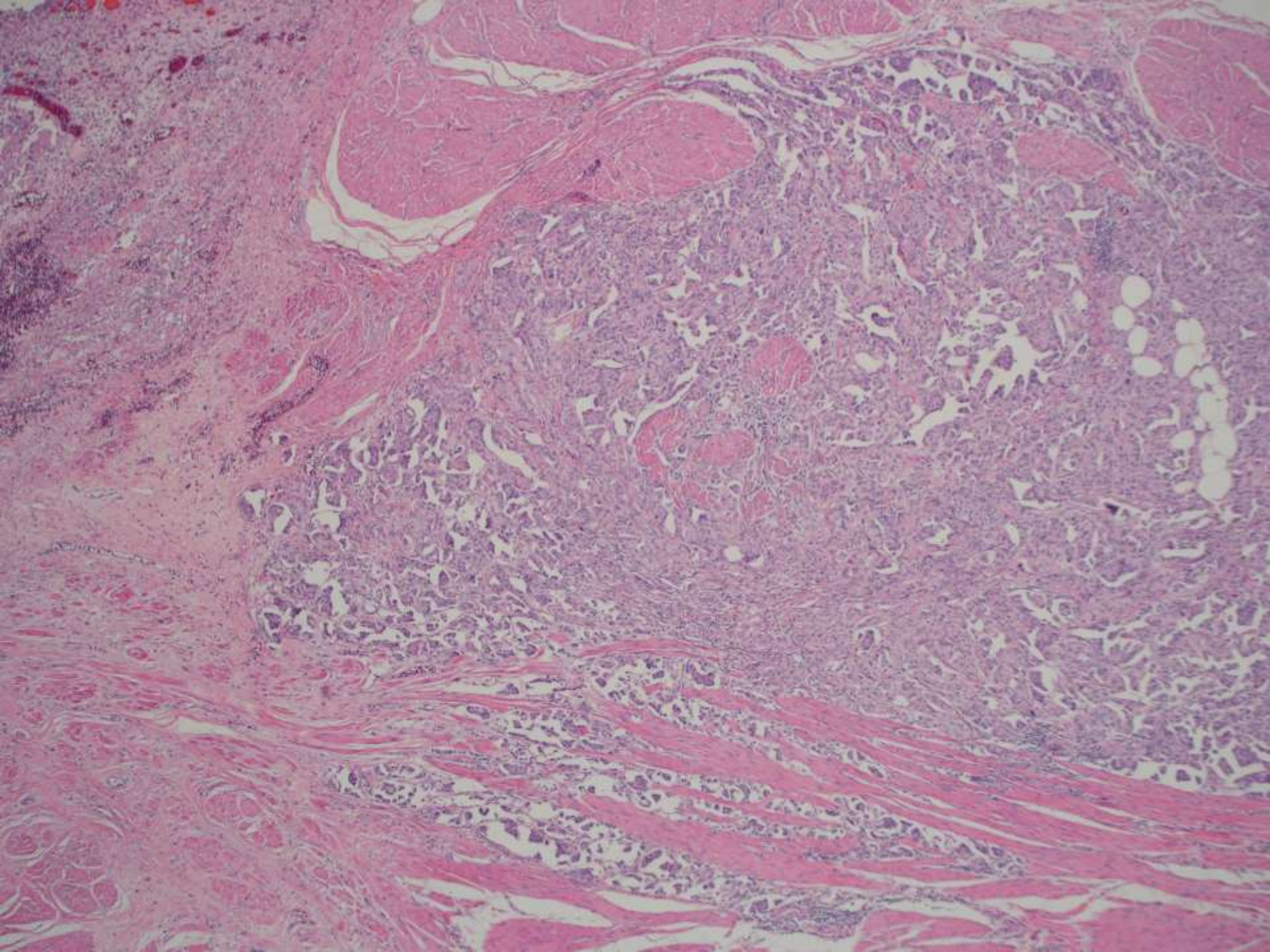
David Levy/Megan Troxell; Stanford

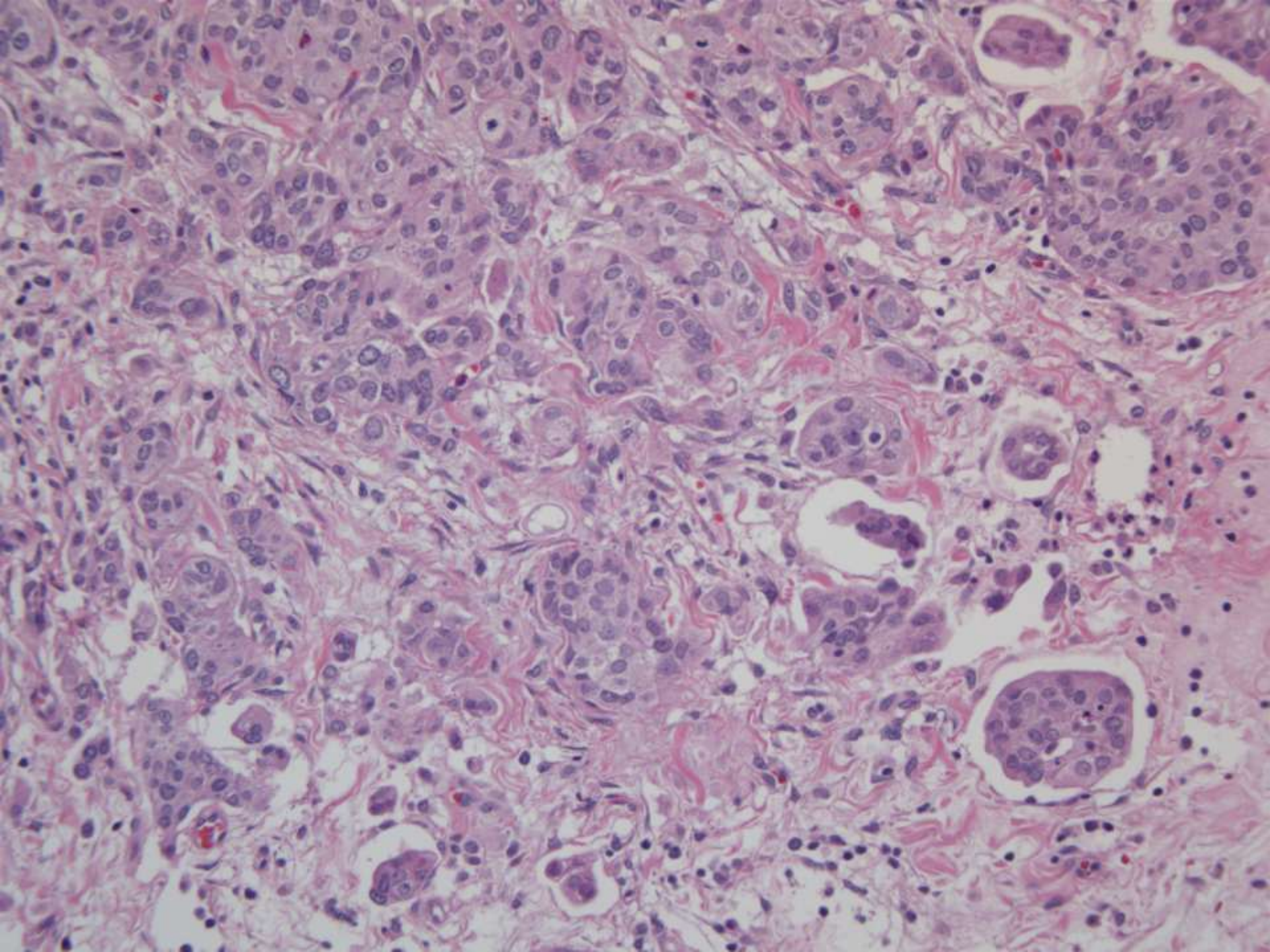
33-year-old kidney transplant recipient. TURBT then cystectomy.

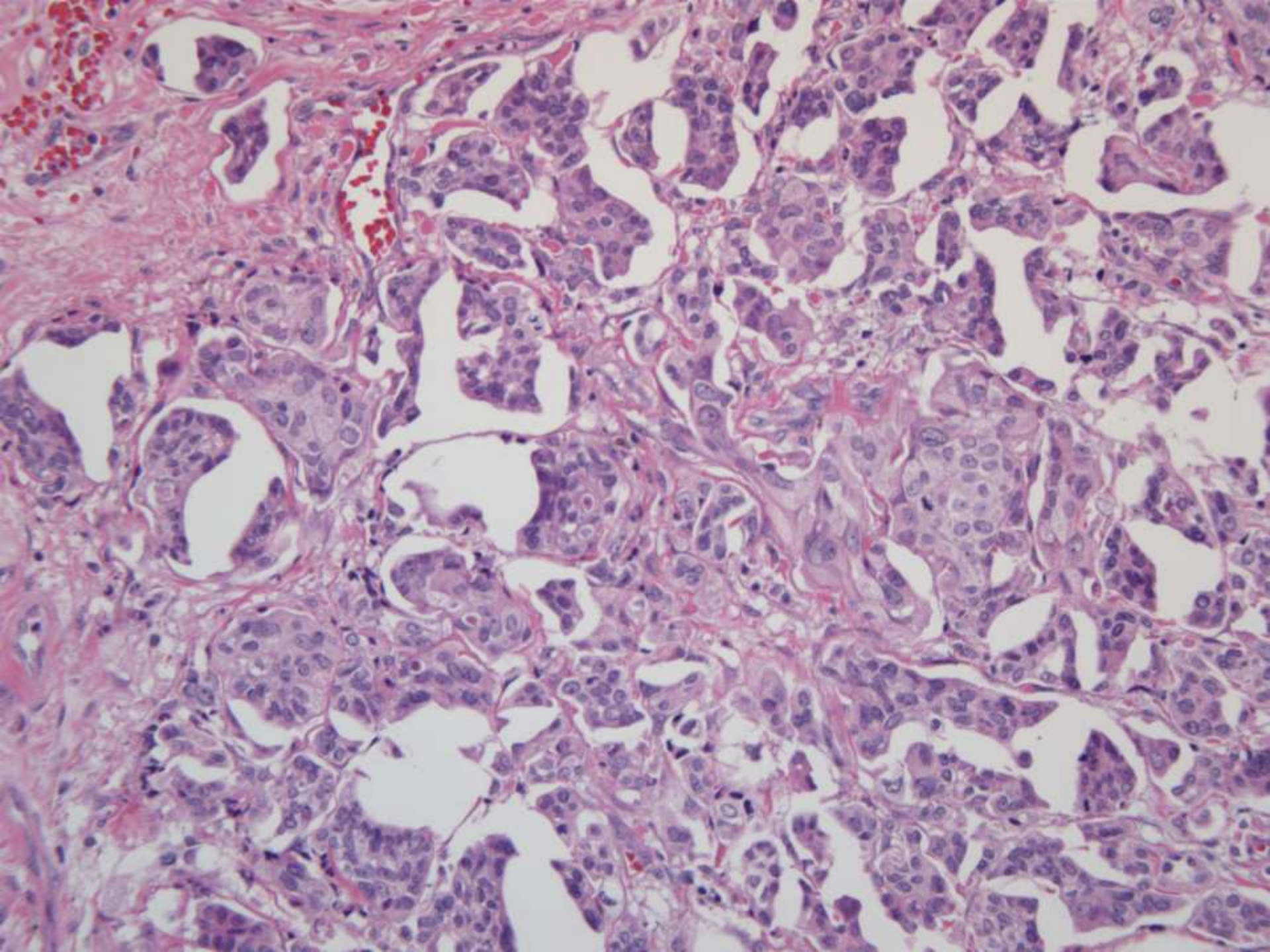


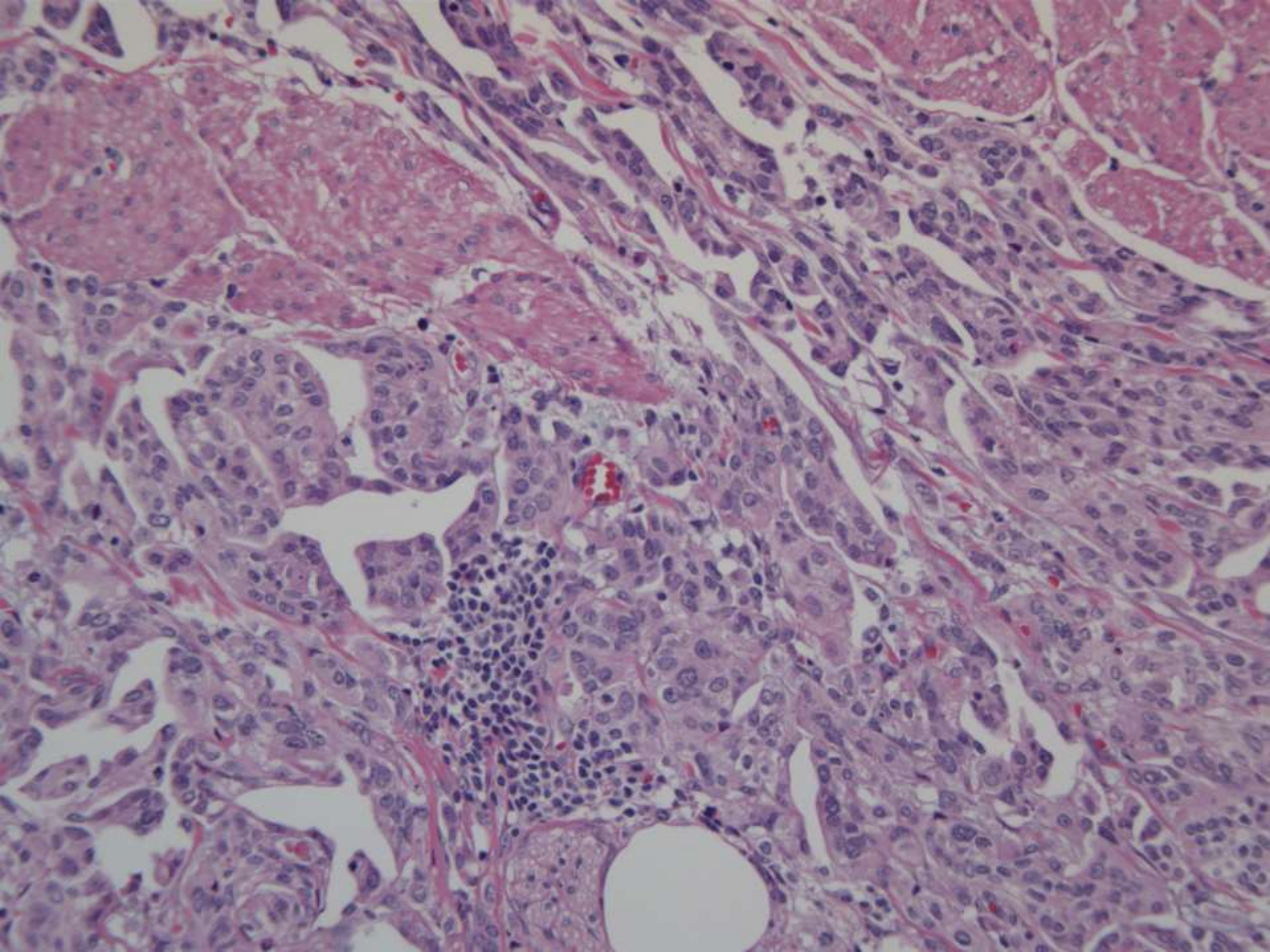


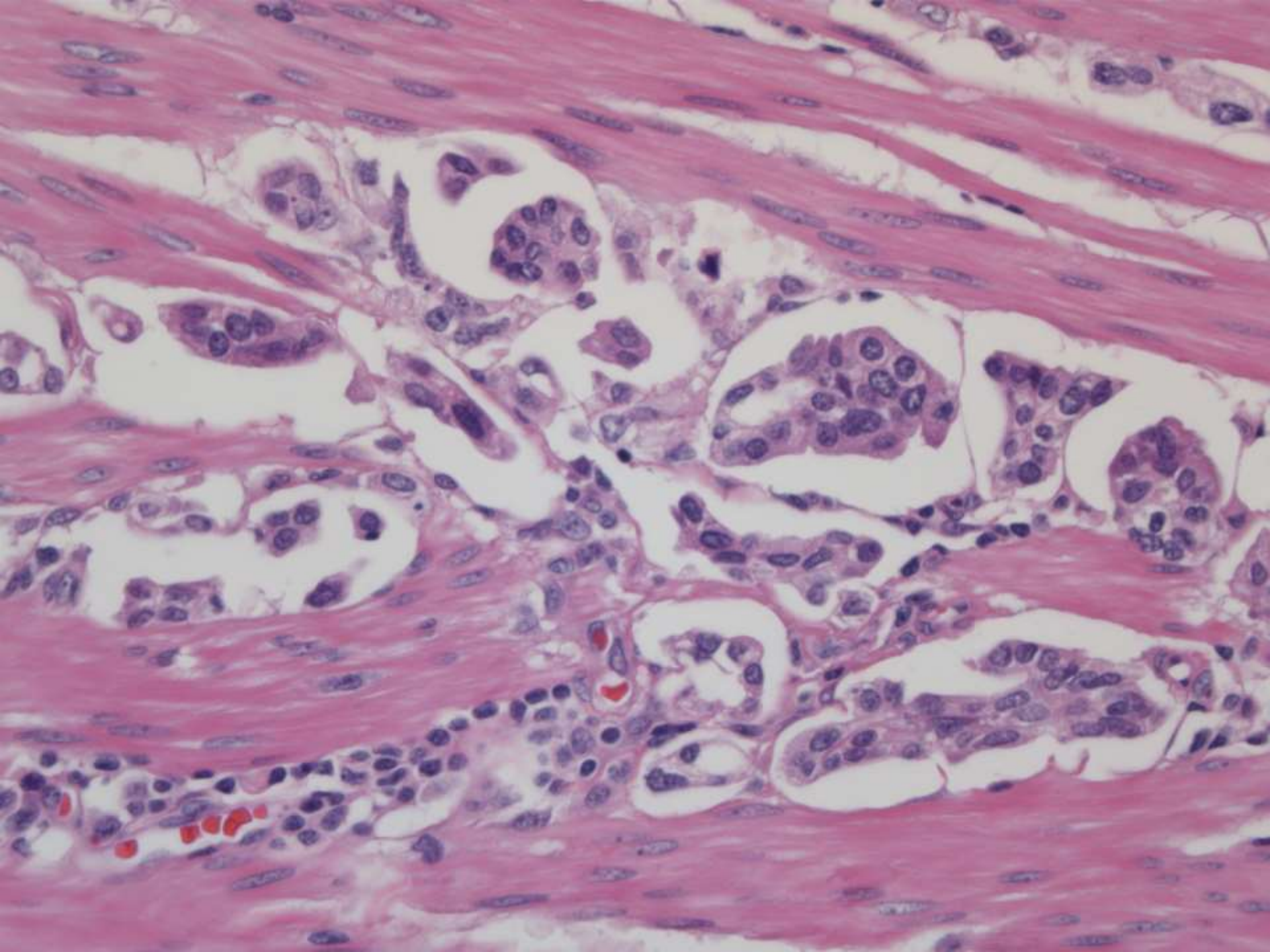












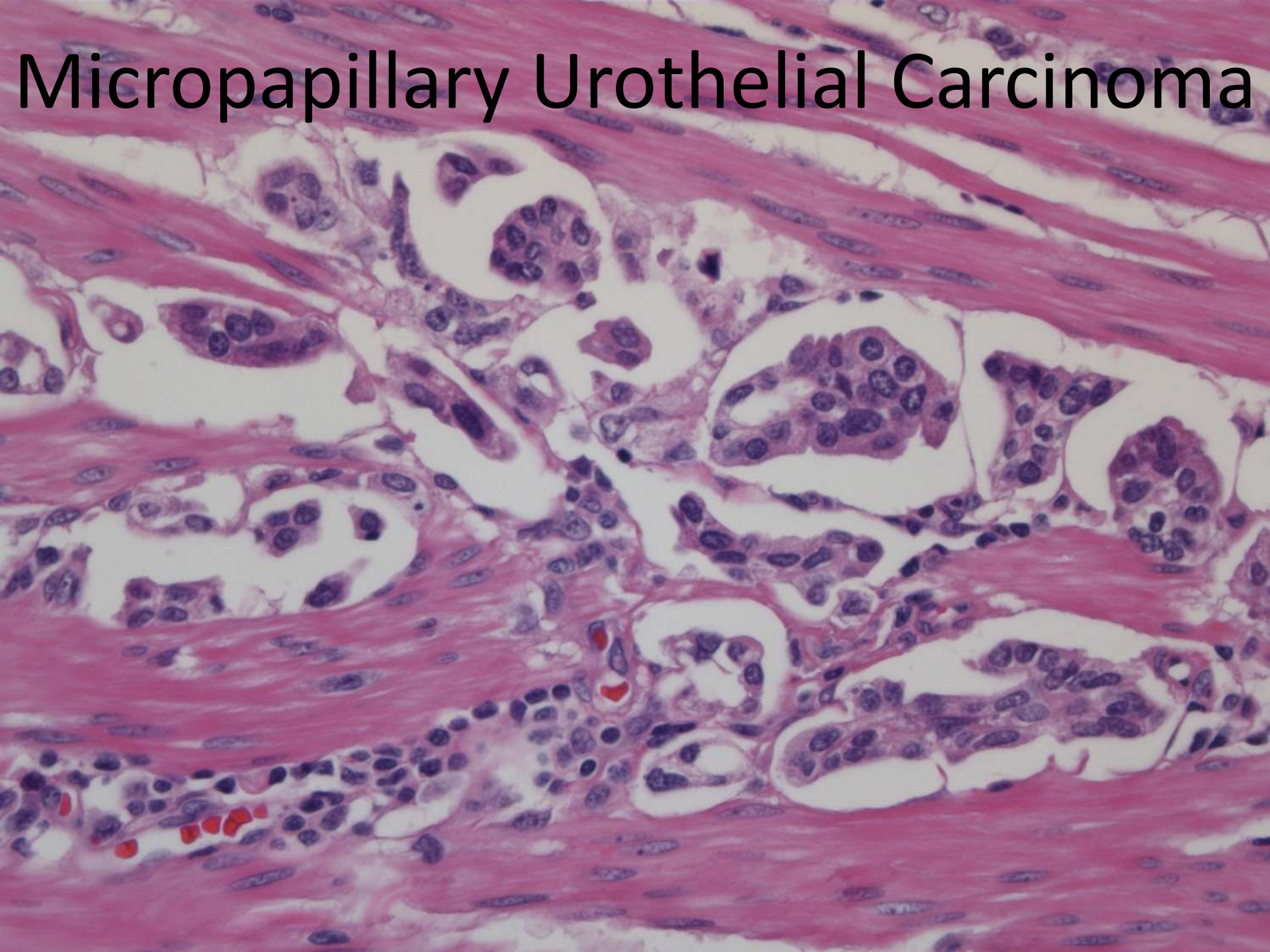
DIAGNOSIS?

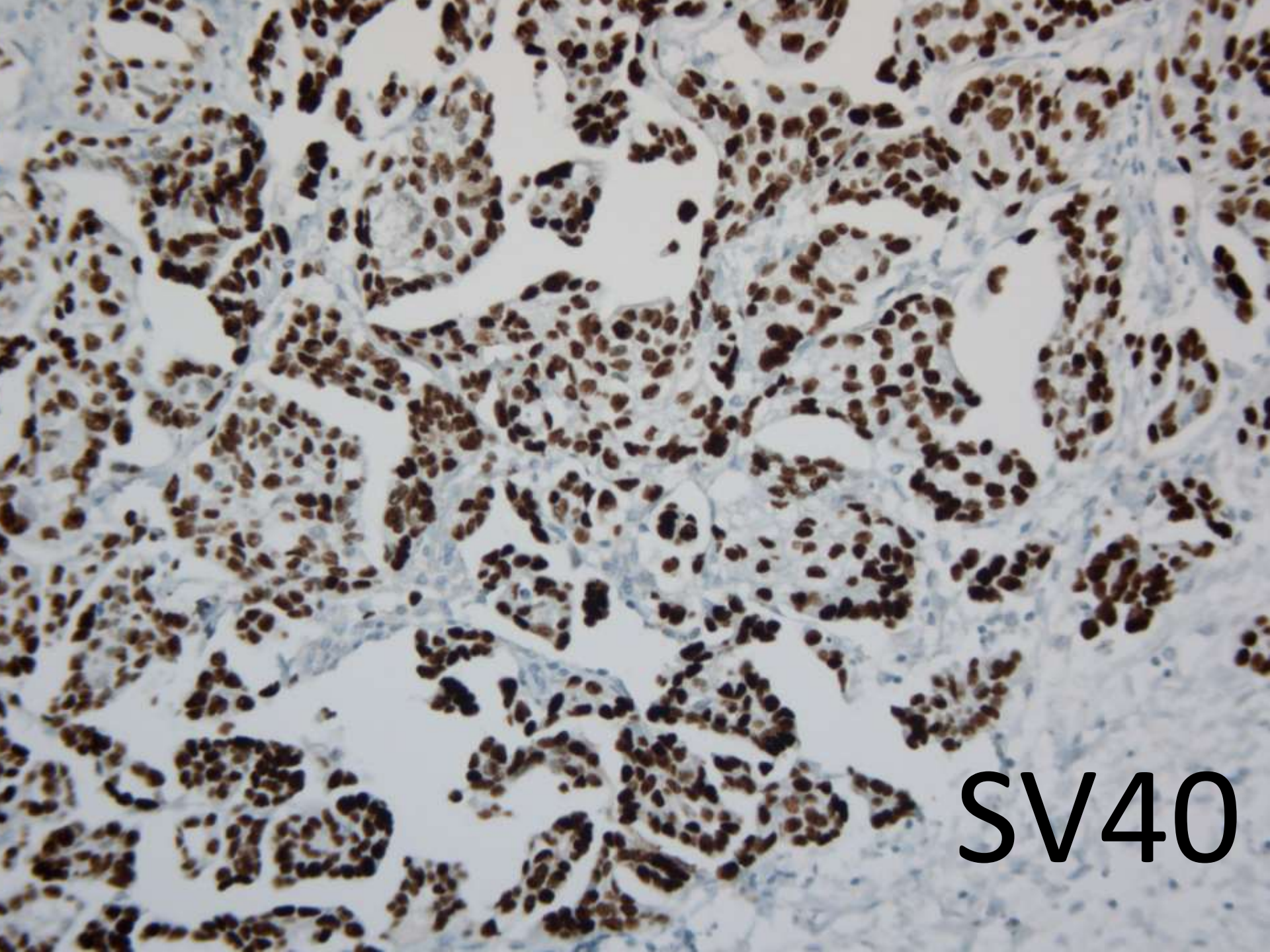
33 year old kidney transplant recipient with hematuria; TURBT then cystectomy

David Levy, Megan Troxell

Stanford

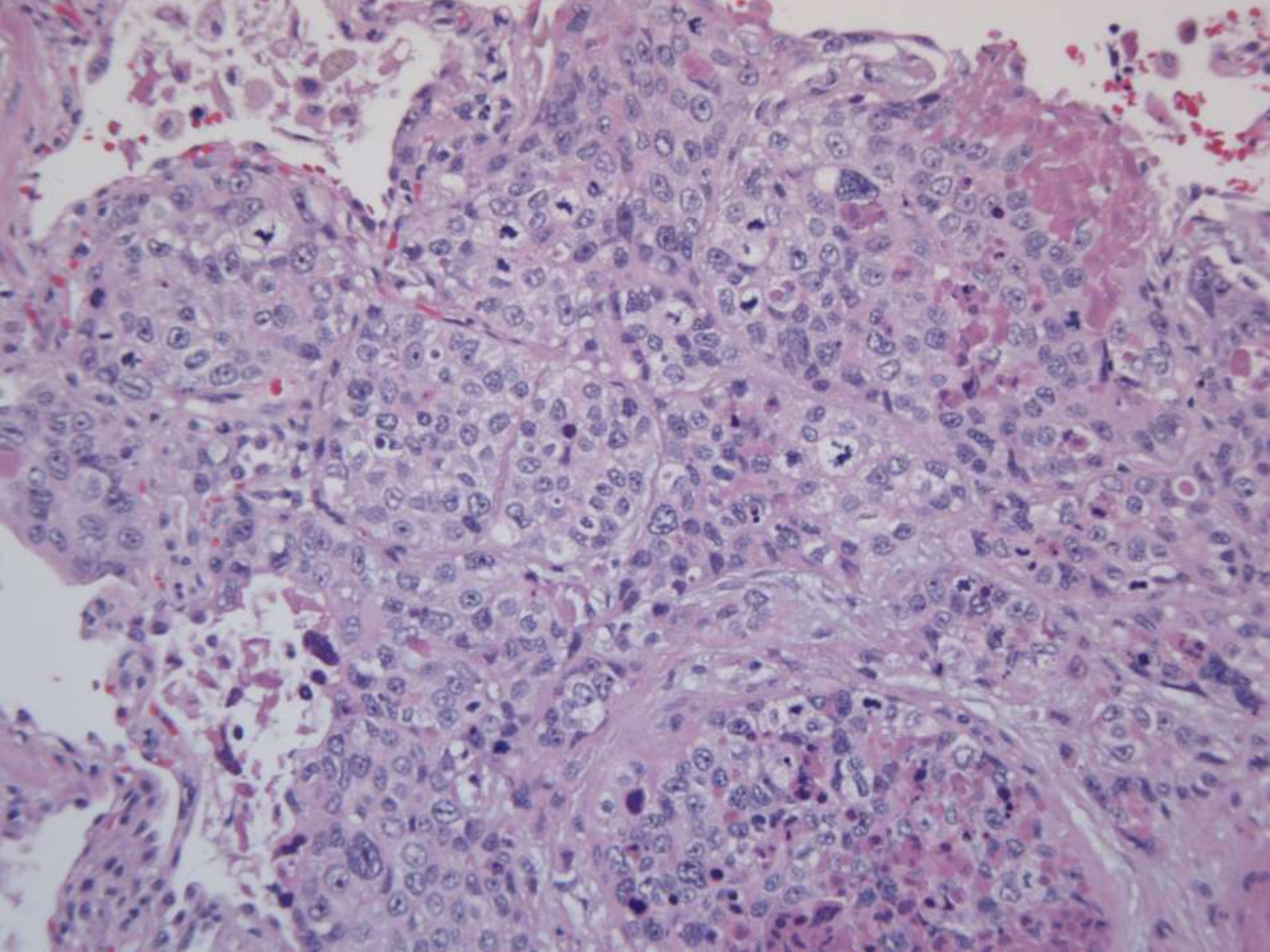
Micropapillary Urothelial Carcinoma

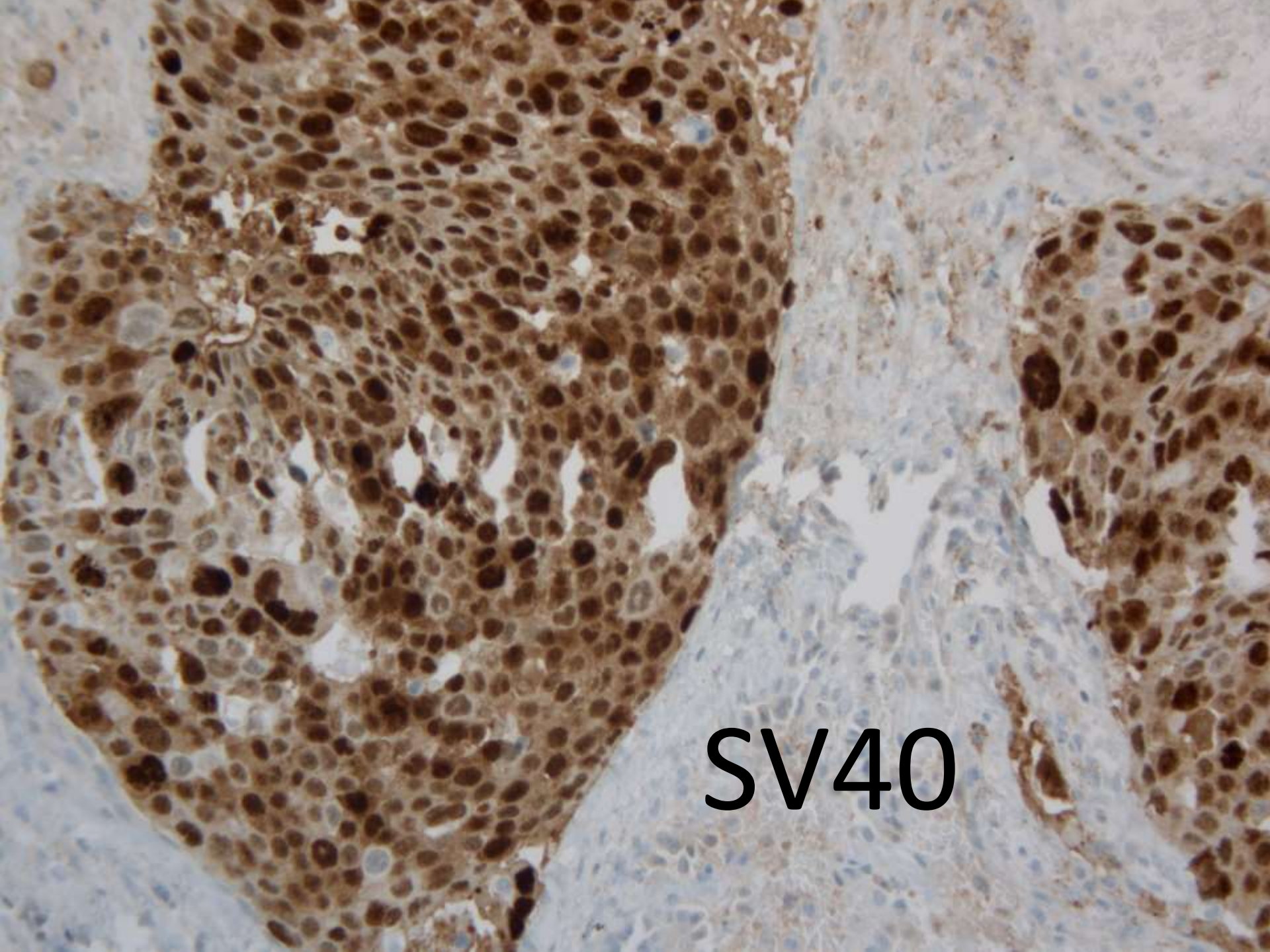



SV40

Clinical Course and Outcome

- 33 year old kidney transplant recipient
  - Kidney transplant at age 23
  - Post transplant biopsies negative for viral nephropathy
  - 10 years post transplant, developed UC
  - Cystoprostatectomy
    - BK polyoma viremia (uptrending)
    - Lung and brain metastasis




SV40

Post Transplant Viral Induced Oncogenesis

- Anogenital carcinomas (HPV)
- PTLD (EBV)
- Kaposi sarcoma (HHV8)
- Urothelial carcinoma:
  - Immunosuppressed renal transplant patients are 3-4x more likely to develop urothelial carcinoma
    - BK virus?

Polyomavirus large T antigen is prevalent in urothelial carcinoma post–kidney transplant

Table 2 Clinical parameters and outcome of UC cases in post–kidney transplant patients

Patient no.	Age (y)/sex at cancer diagnosis	Large T IHC	Polyoma viremia	Cr level at cancer diagnosis (mg/dL)	Clinical outcome
1	33, Male	+	Yes	1.6	Died of bladder cancer
2	50, Male	+	Yes	1.6	Persistent high creatinine
3	31, Male	+	Yes	1.85	Elevated creatinine
4	71, Male	+	Neg	1.4	Persistent high creatinine
5	58, Female	−	Neg	1.1	Died of bladder cancer
6	35, Female	−	ND	1.3	Died of cancer, sepsis
7	76, Male	−	Neg	1.4	Lost to follow-up
8	86, Male	−	ND	<1	Normal creatinine
9	80, Male	−	Yes	1.1	Normal creatinine
10	66, Female	−	ND	0.9	Normal creatinine
11	49, Female	−	ND	3.7	First allograft failed; normal creatinine with subsequent 2nd transplant

Abbreviations: UC, urothelial carcinoma; IHC, immunohistochemistry; Cr, serum creatinine; FSGS, focal segmental glome
urine BK studies tested during transplant course, and negative; ND, not done; GN, glomerulonephritis.

- **POST-TRANSPLANT UROTHELIAL CARCINOMA**
- Common features:
  - Younger patients, ~10.5 years post transplant
  - High grade and muscle invasive
  - May be associated with polyoma virus (SV40+)

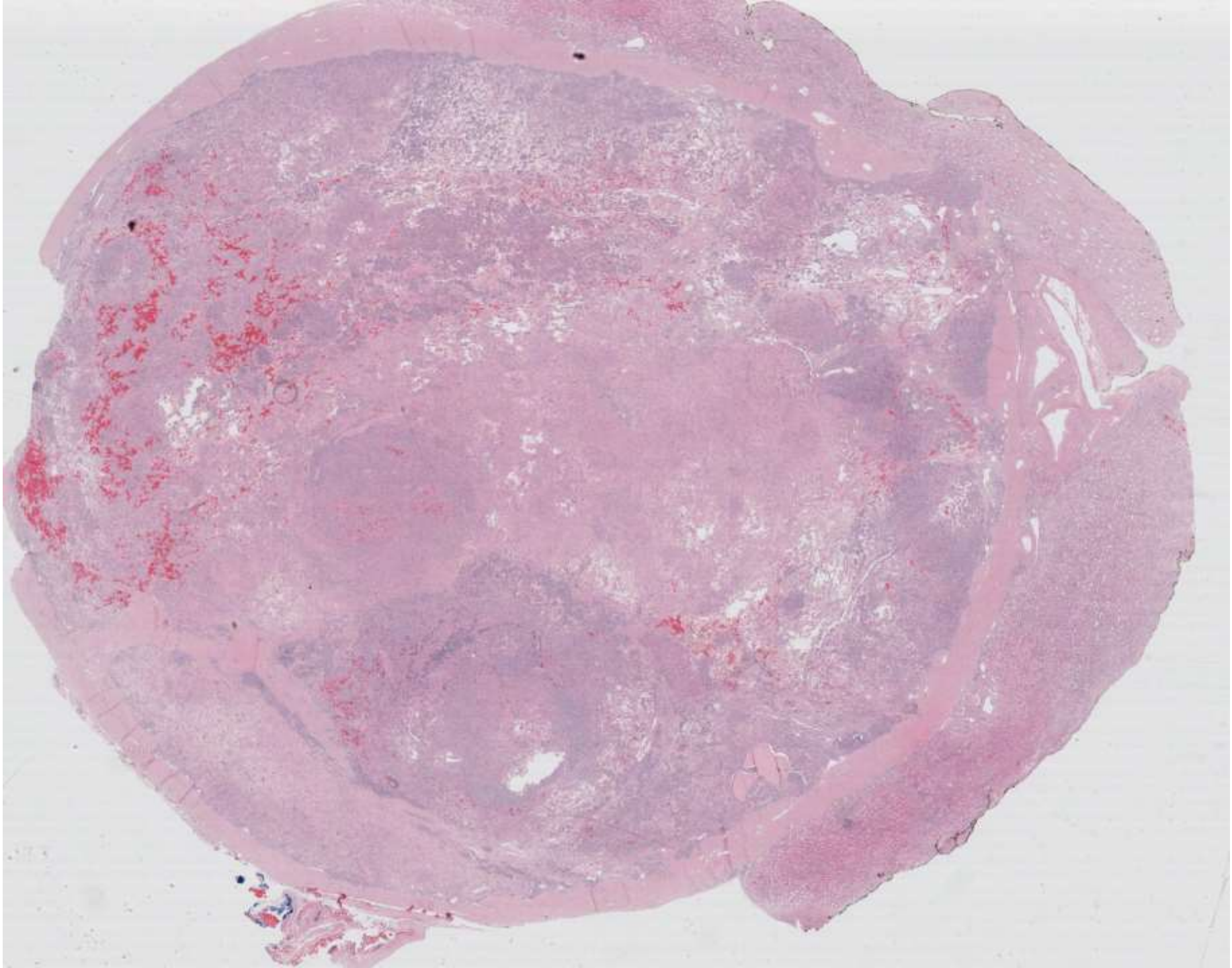
Questions?

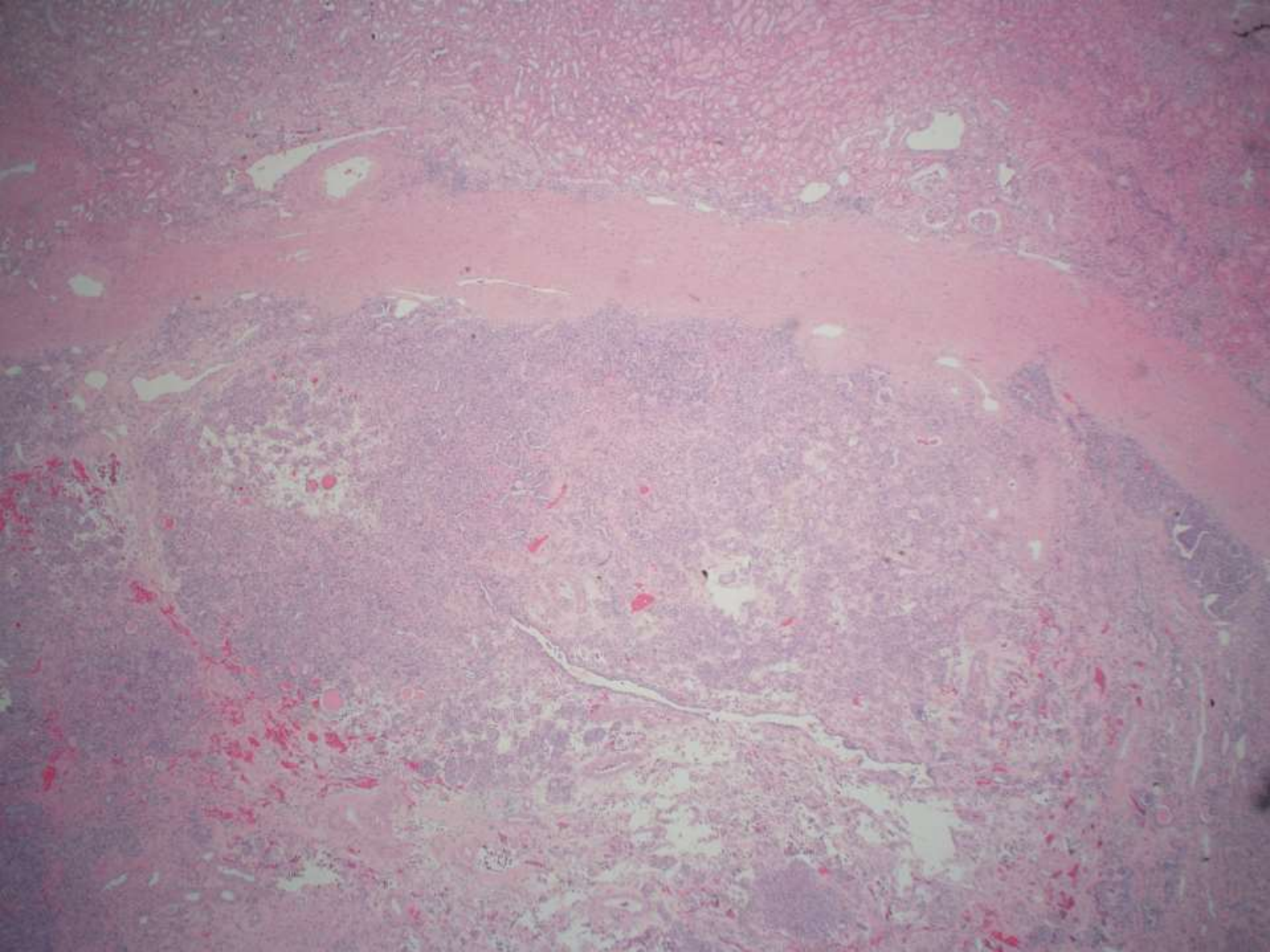
- Yan et al. Polyoma virus large T antigen is prevalent in urothelial carcinoma post-kidney transplant. Human Pathology (2015), Volume 48, 122-131.
- Kenan et al. The oncogenic potential of BK-polyomavirus is linked to viral integration into the human genome. The Journal of Pathology (2015); 237:379-89

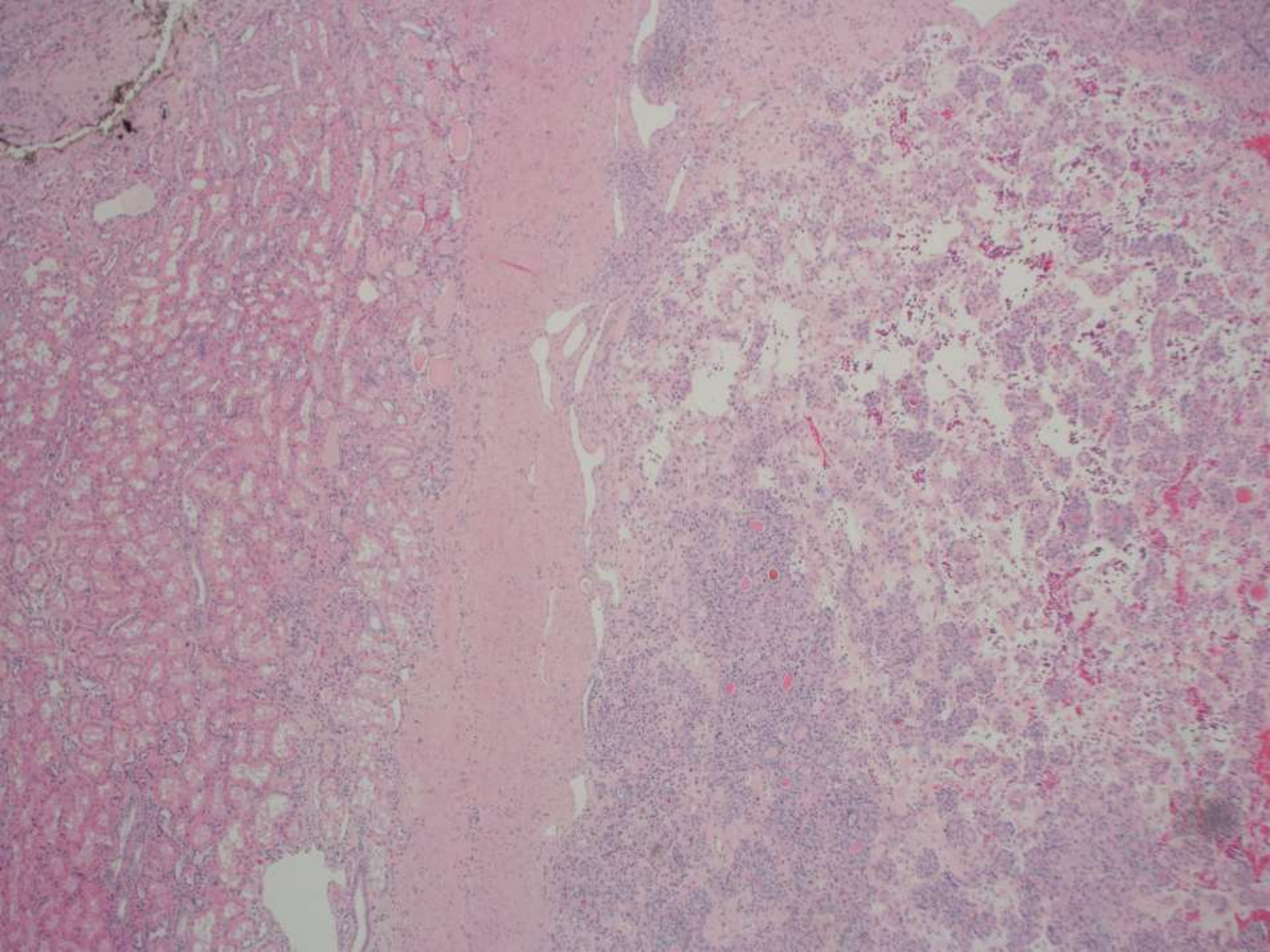
SB 6052

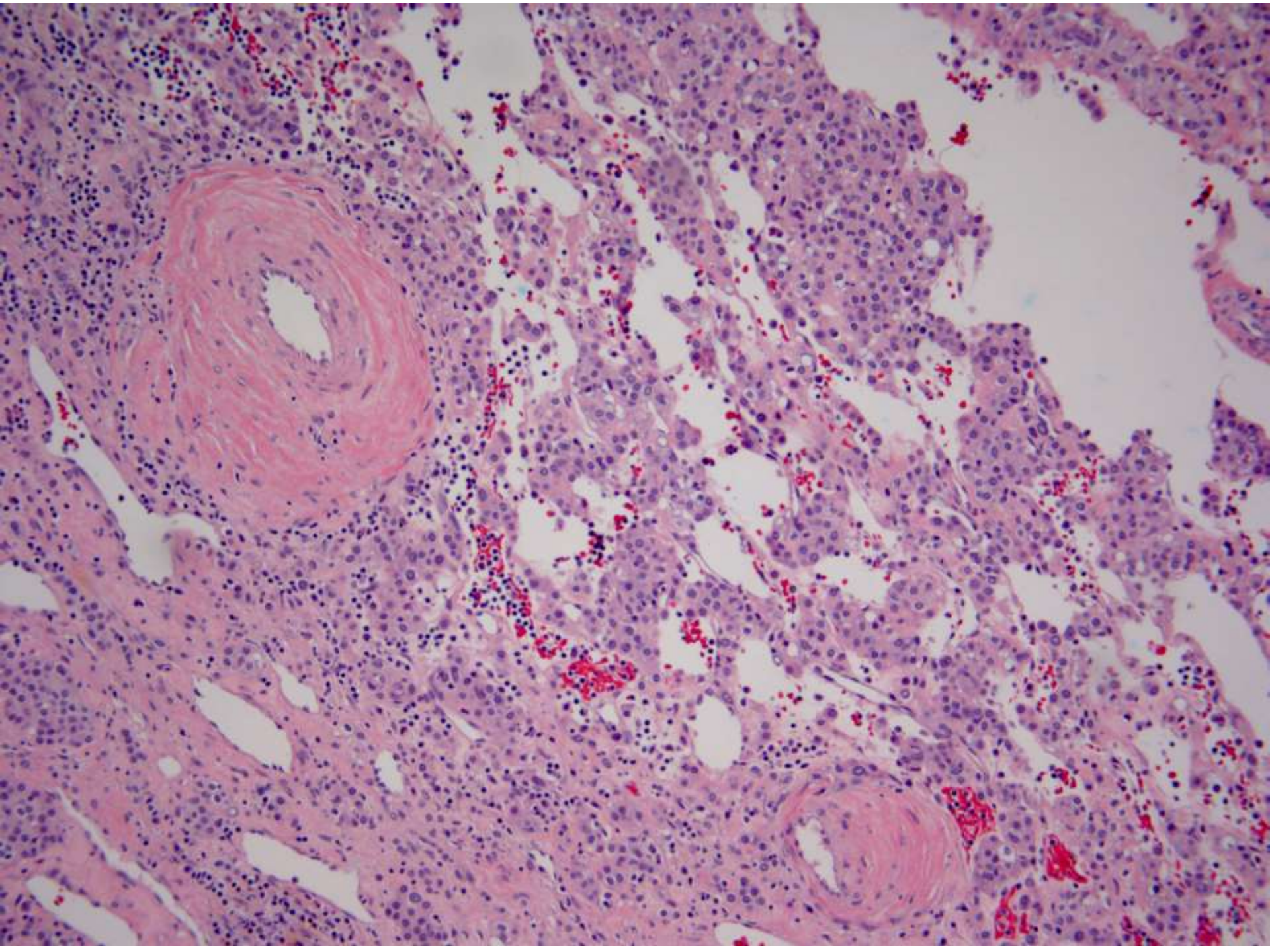
David Levy/Megan Troxell; Stanford

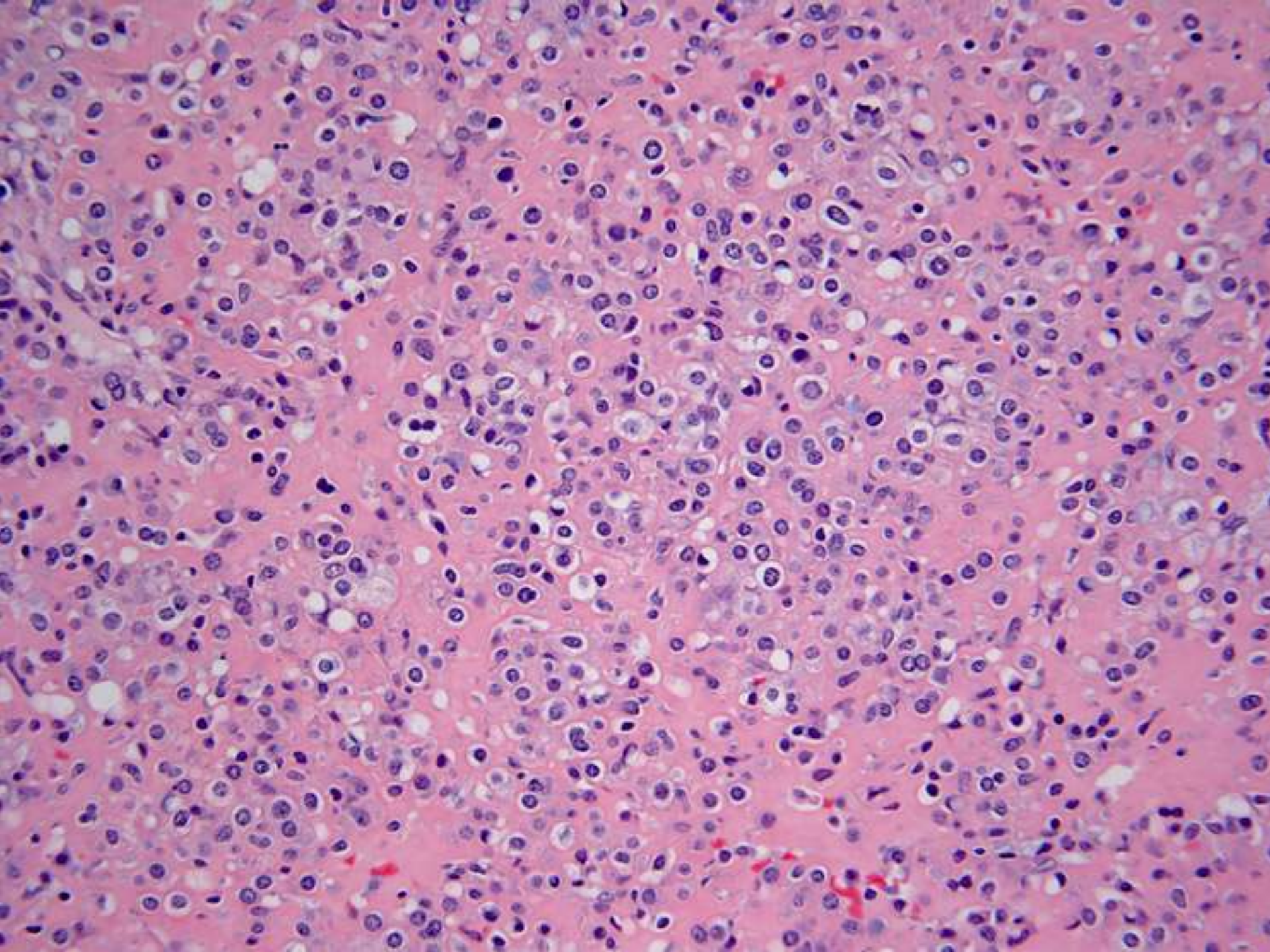
37-year-old woman with incidentally-discovered kidney tumor.

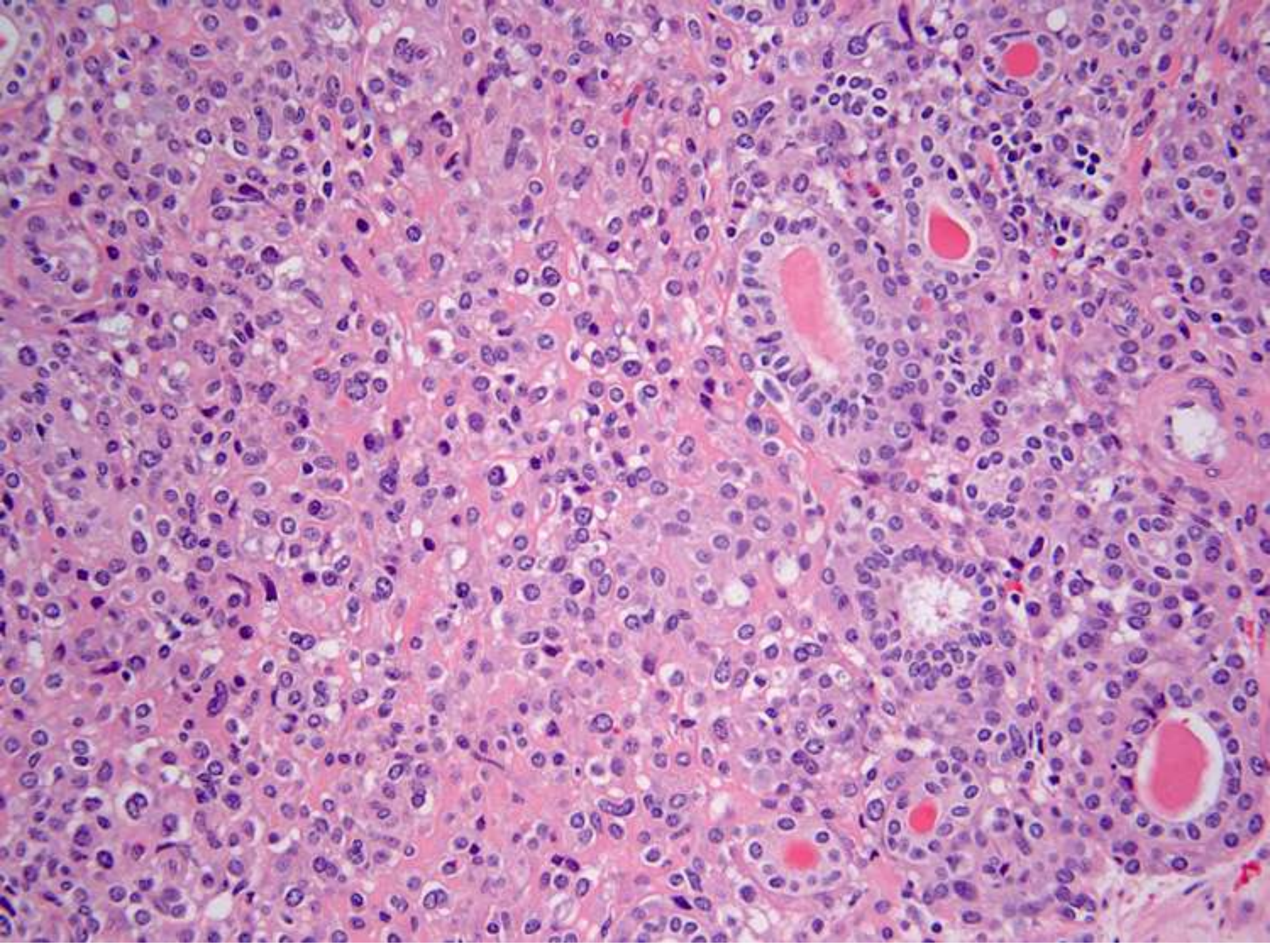


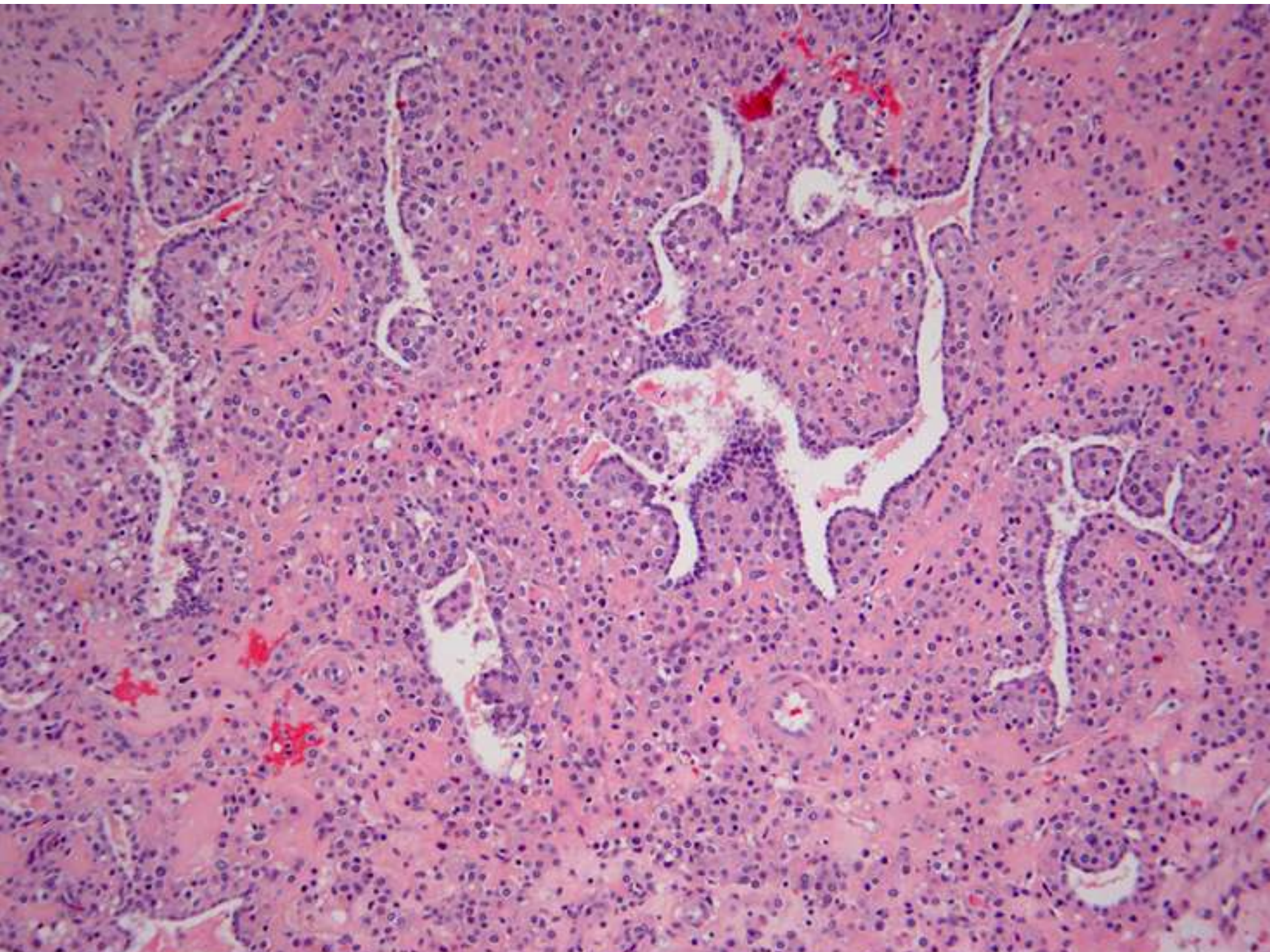












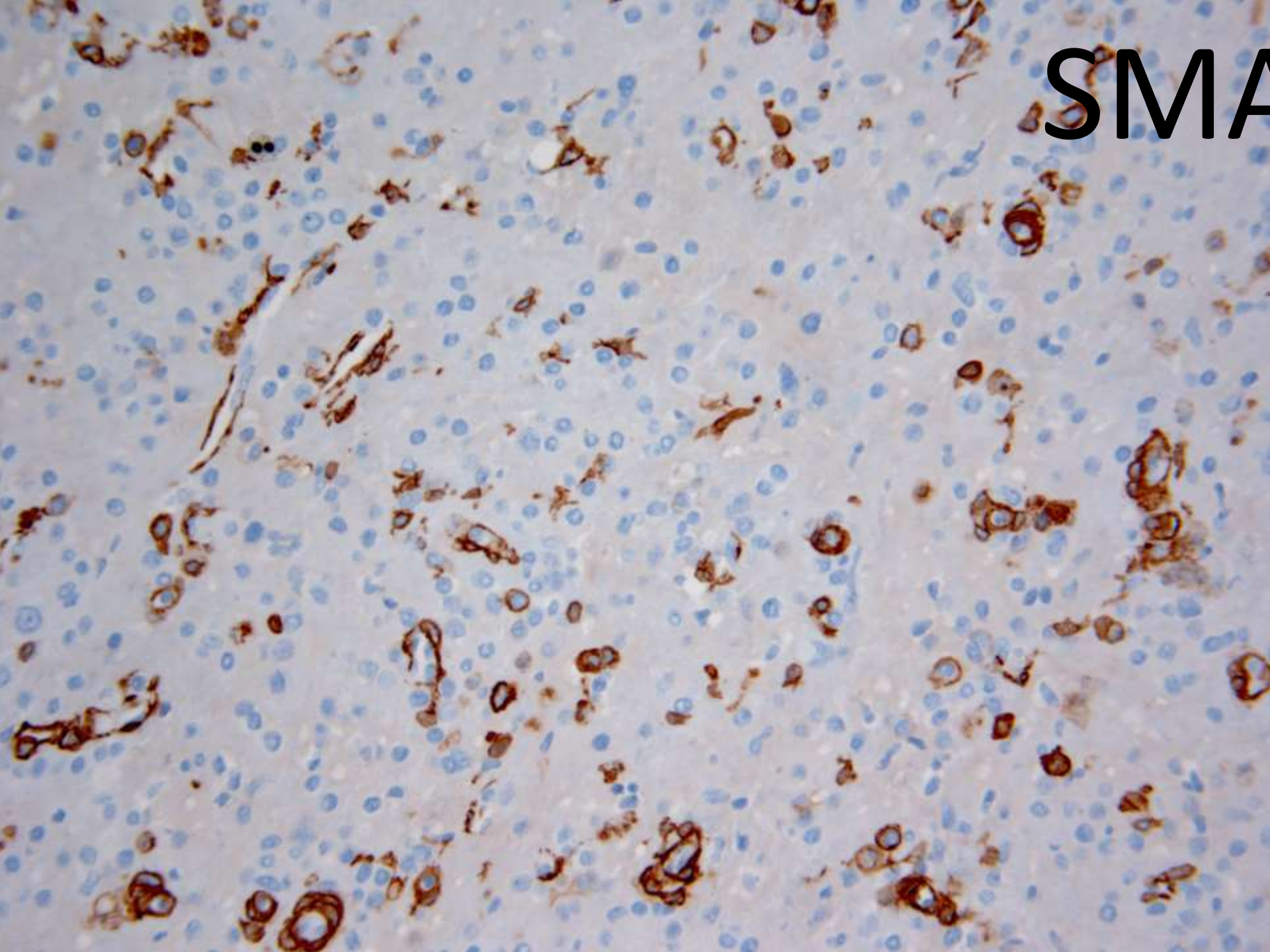
DIAGNOSIS?

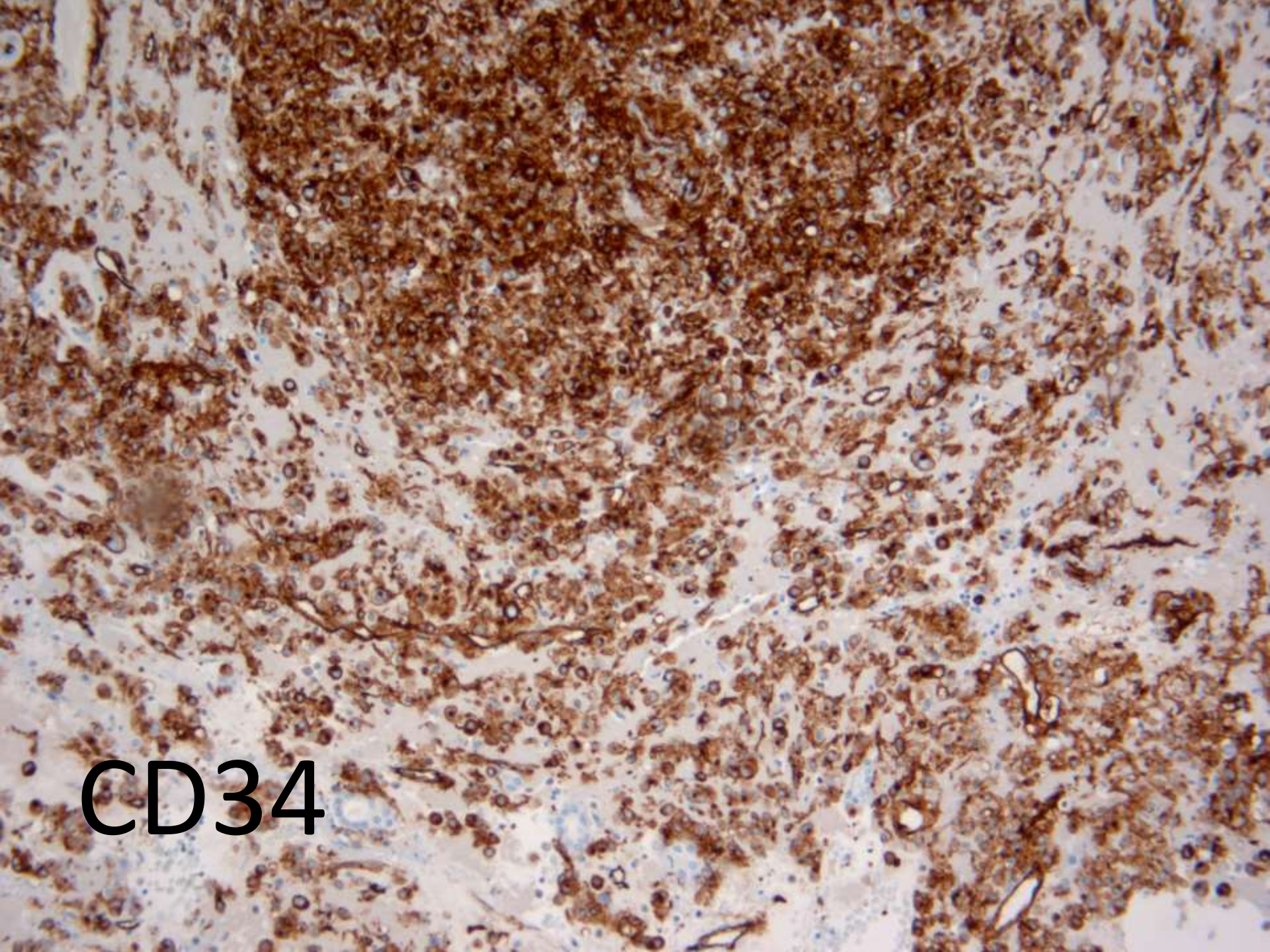
37-year-old woman with incidentally discovered kidney tumor.

David Levy and Megan Troxell
(Stanford)

Differential Diagnosis

- Chromophobe RCC
- Papillary RCC
- JG cell tumor
- Glomus tumor
- Solitary Fibrous Tumor/Hemangiopericytoma


SMA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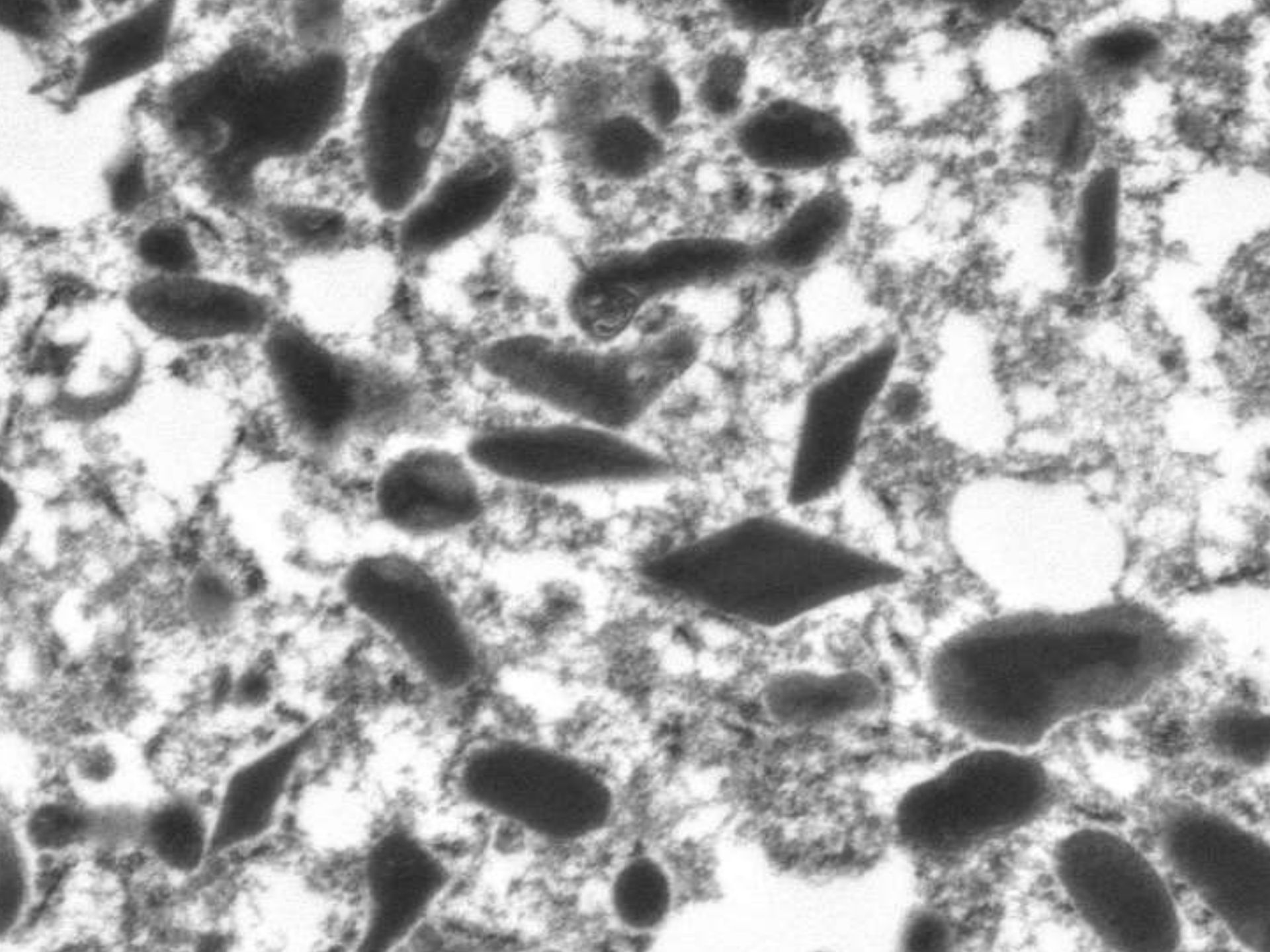


JG cell tumor

Background

- Renin producing tumor derived from smooth muscle cells of the JG apparatus
- Classic presentation:
  - Young adult with severe hypertension variably responsive to medical therapies.
- Rare: less than 100 cases reported
- Prognosis:
  - Predominantly benign outcome
  - 1 case of 52 y/o with lung metastasis

JG cell tumor

- Microscopic features:
  - **Typical**: "Glomus tumor-like" architecture
    - Sheets of uniform polygonal cells with clear to eosinophilic cytoplasm and distinct cell borders.
    - Numerous capillaries and branching vessels.
    - Entrapped tubules along the periphery
    - Mitotic activity and necrosis are uncommon
    - EM: Sharply angulated rhomboid protorenin crystals
    - IHC: Renin

Clinical Course and Follow-up

- 37 year old female with incidentally discovered kidney tumor
- Medically managed HTN and hypokalemia in 1994 (age 21)
  - HTN recognized in association with pregnancy
  - 1994 IVP and renal ultrasound: no renal mass identified
  - 1997: Serum aldosterone reported as normal
  - 2010: Resection

- **JUXTAGLOMERULAR CELL TUMOR**
  - Well circumscribed, small (2-3 cm) tumor
  - Young, hypertensive, hypokalemia
  - Variable architecture/"Glomus-like features"

- Benign clinical course
  - 1 documented case of metastasis

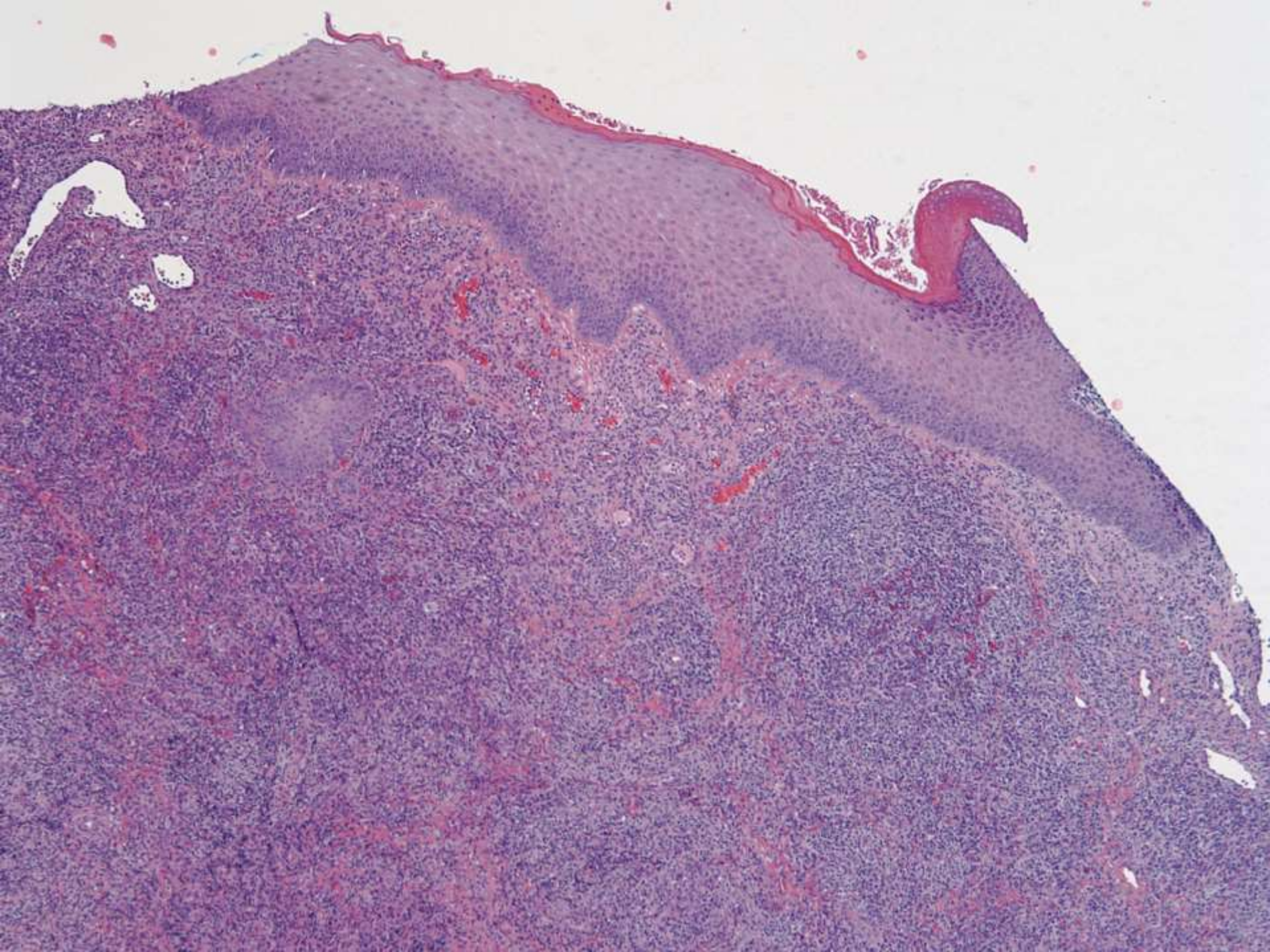
Questions?

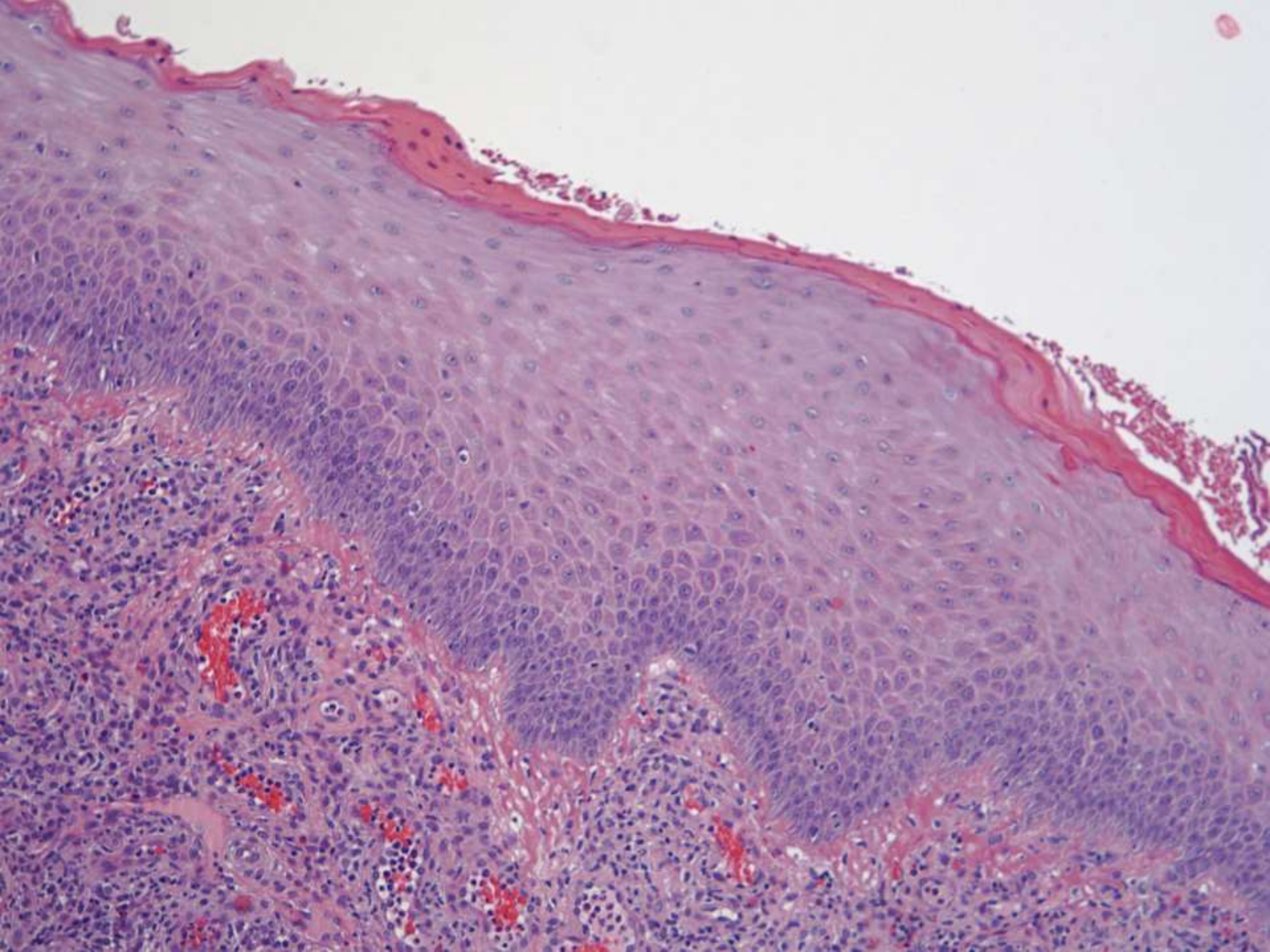
- Amin M. & Tickoo S. *Diagnostic Pathology: Genitourinary* 2nd ed. Salt Lake City, UT, Elsevier Inc. 2016.
- Moch. H, Humphrey P, Ulbright T, et al, editors. WHO classification of tumours of the urinary system and male genital organs. Lyon: IARC Press, 2016.

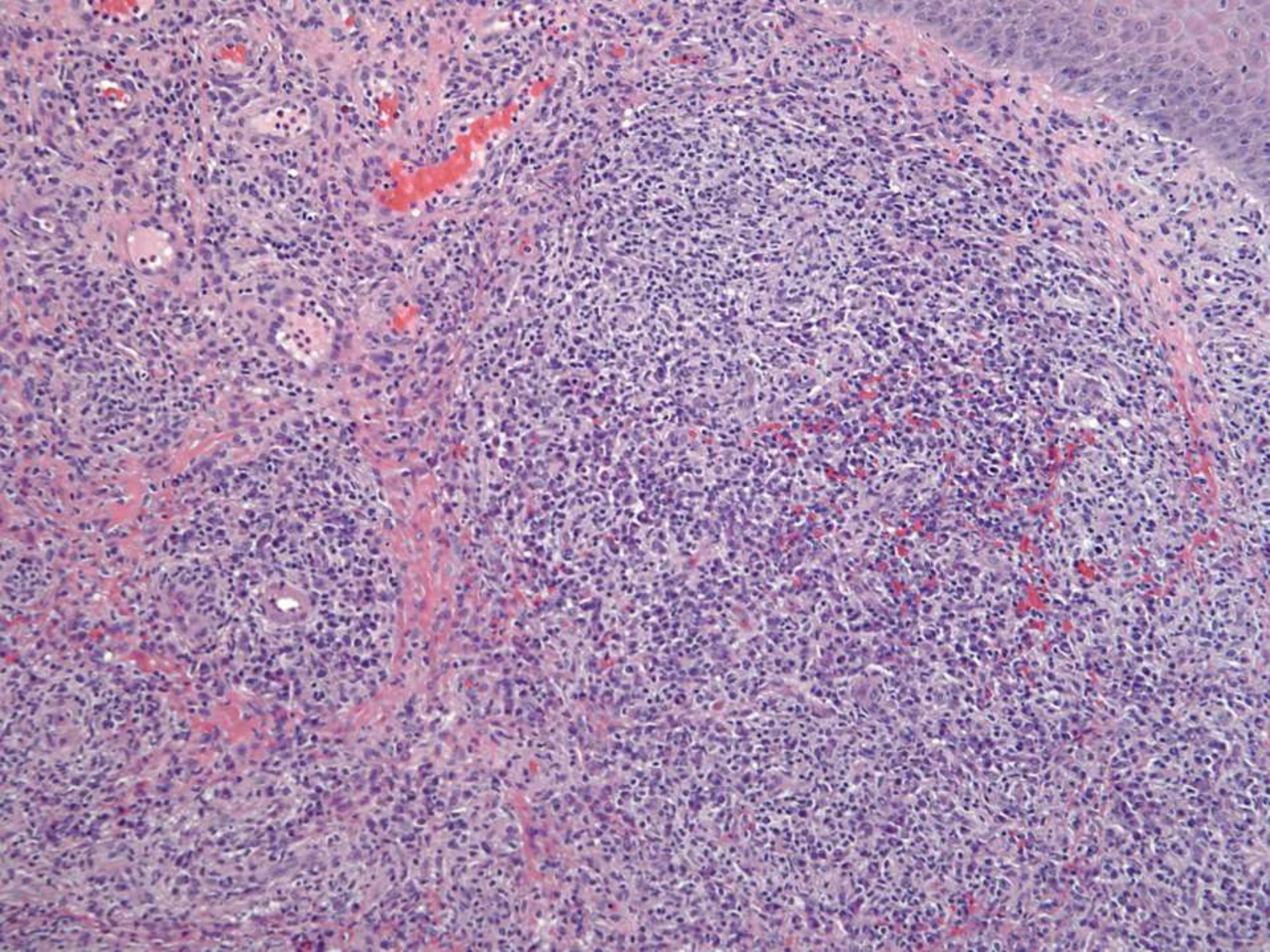
SB 6053

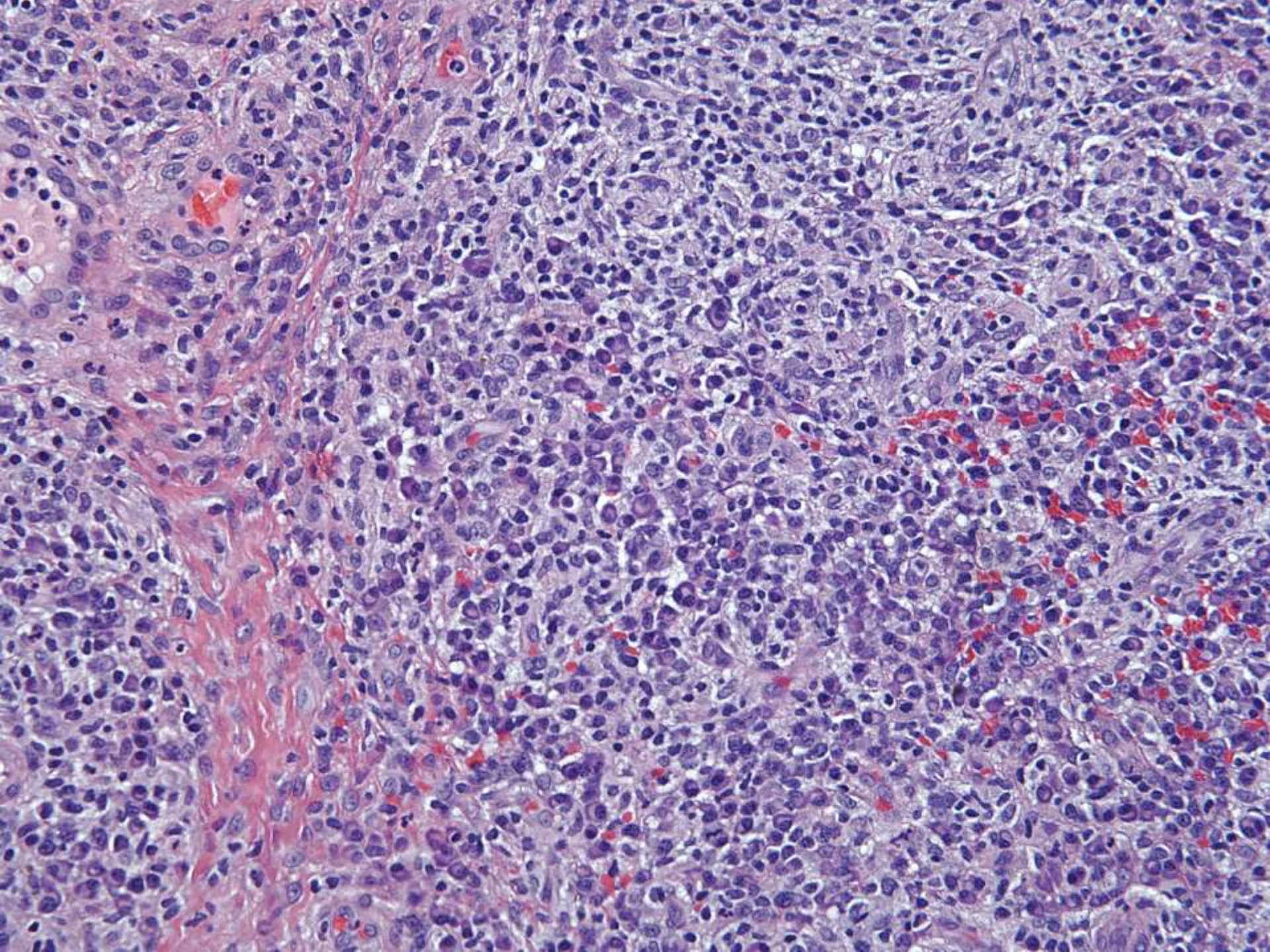
Christine Louie/Teri Longacre; Stanford

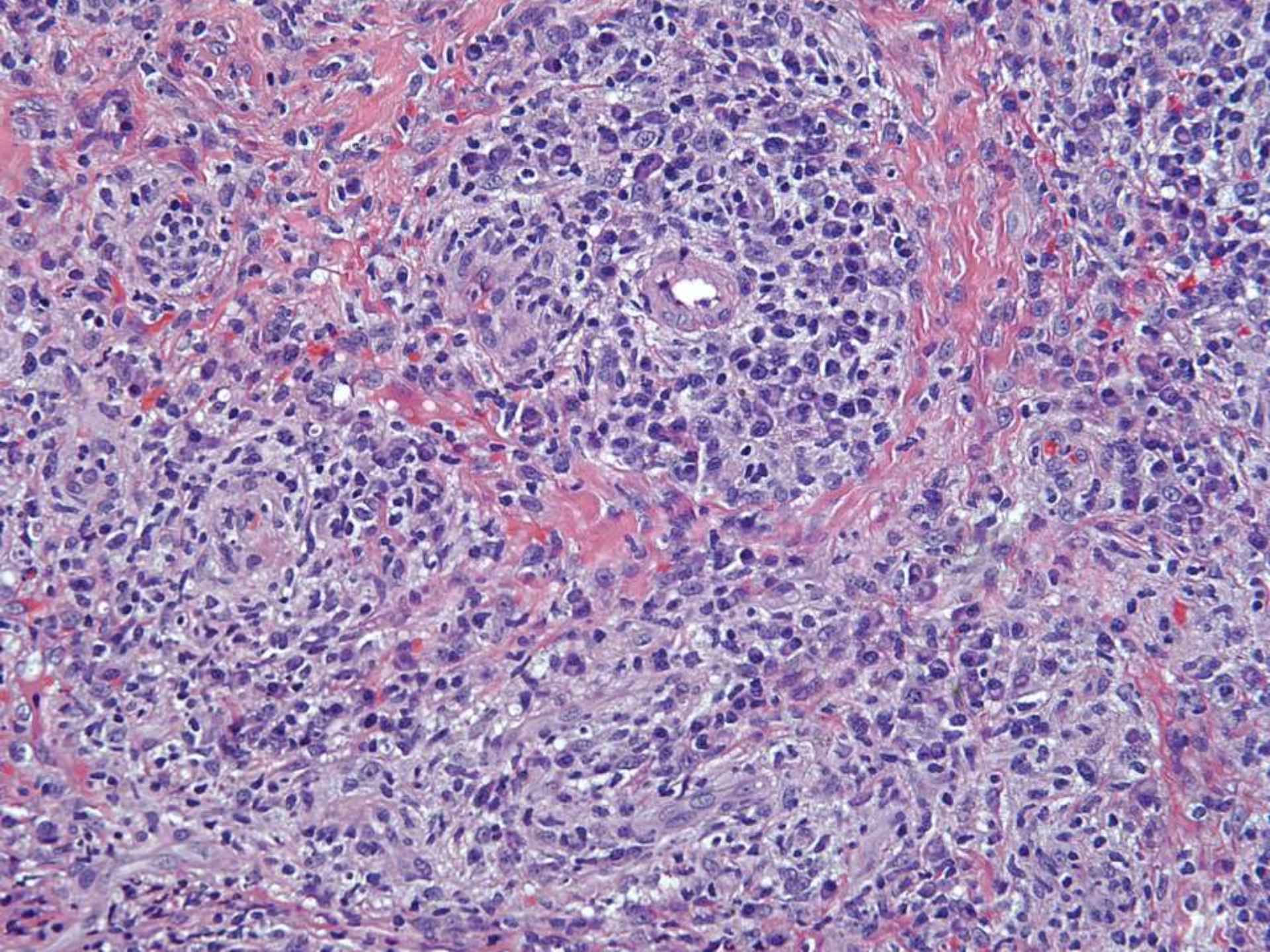
25-year-old man with indurated perianal lesion.



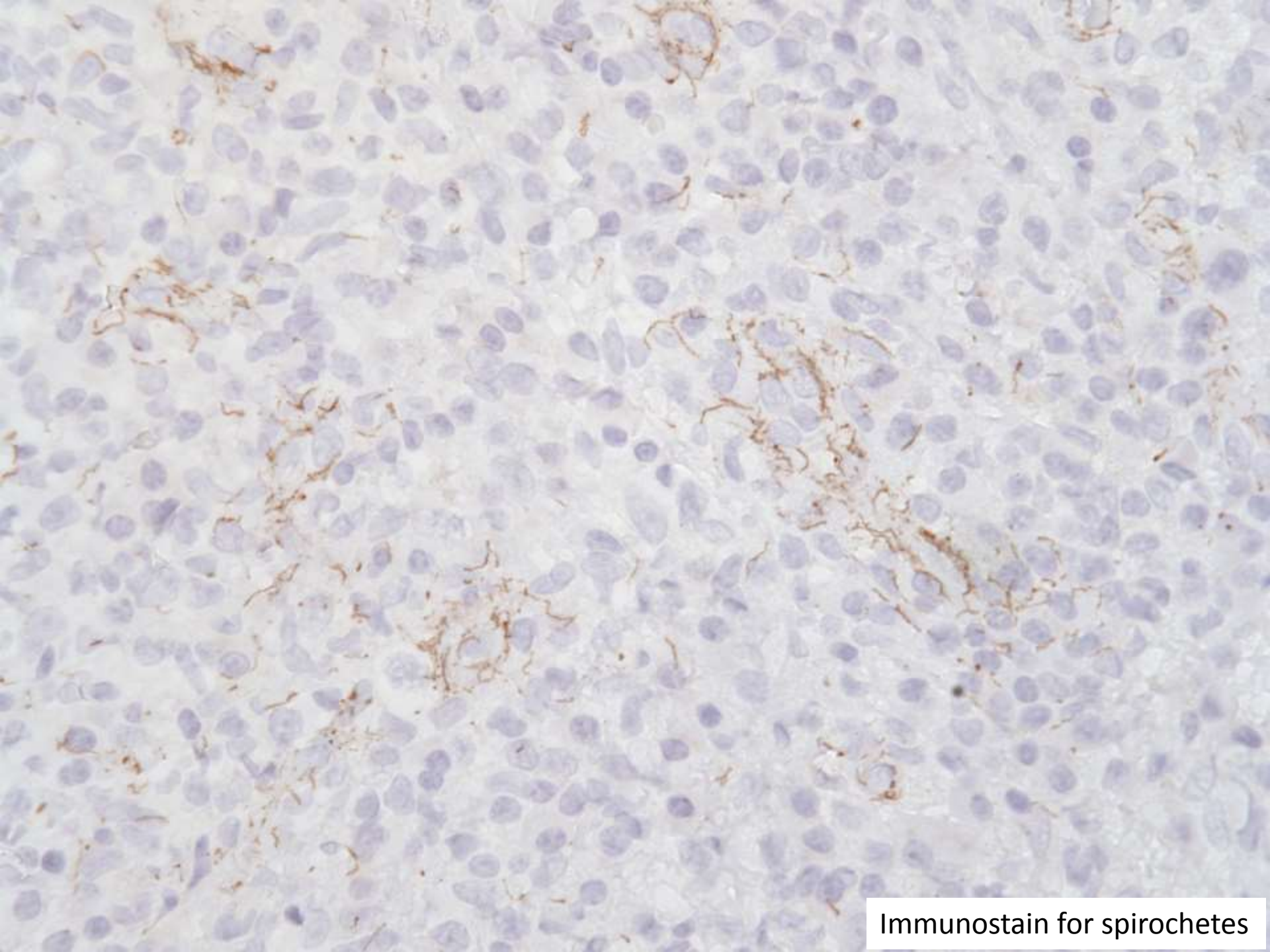


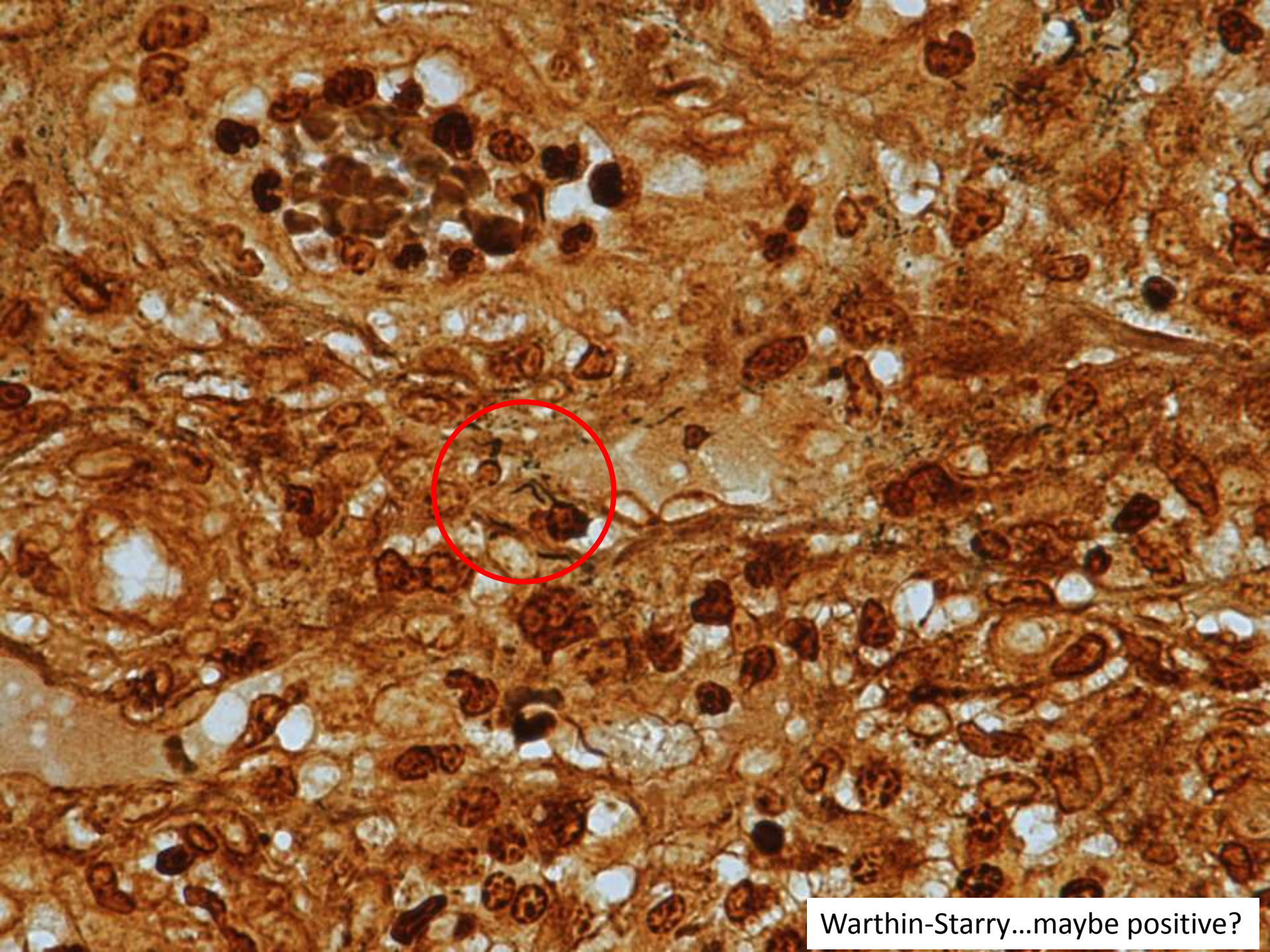


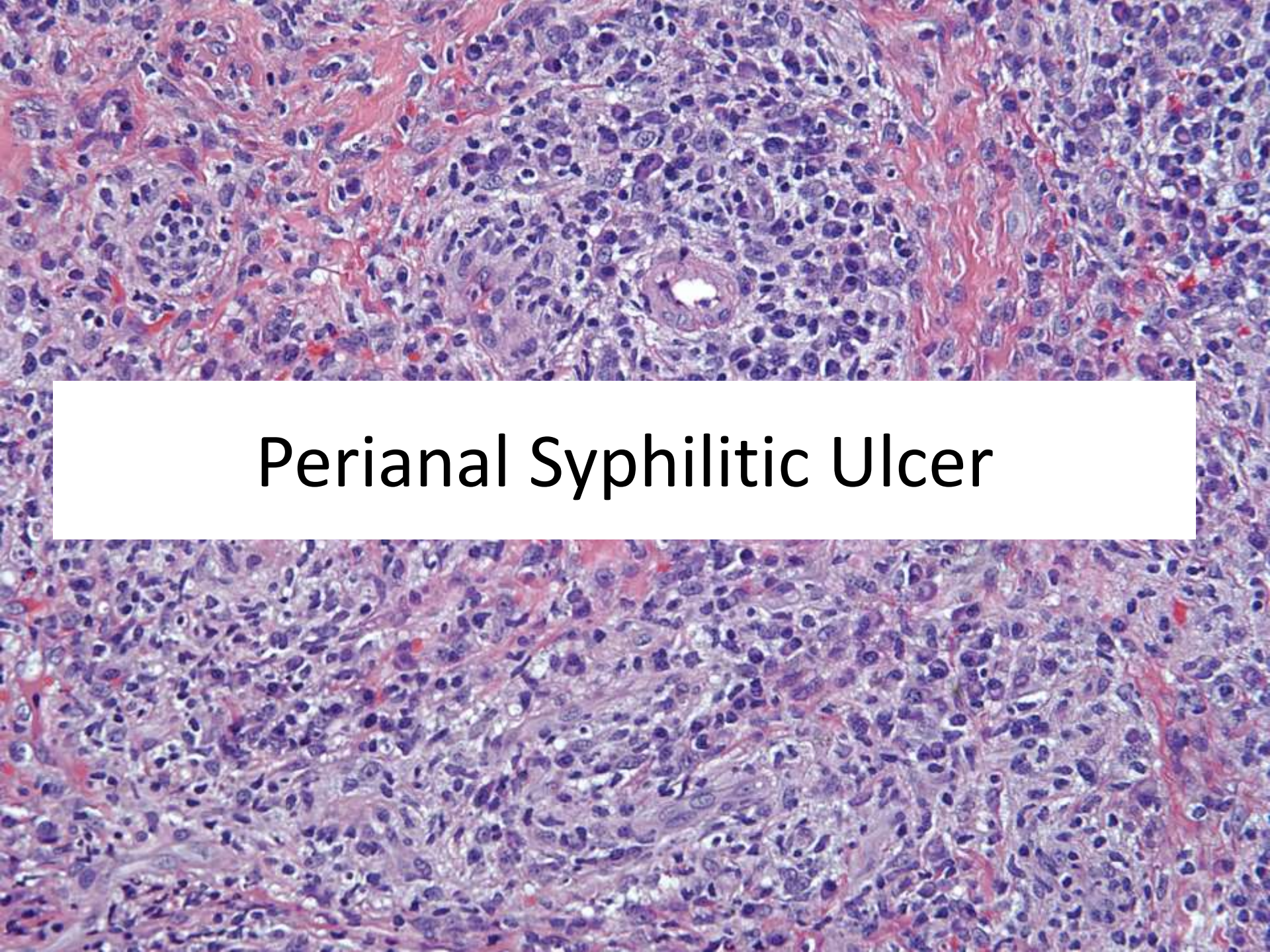




DIAGNOSIS?


Immunostain for spirochetes


Warthin-Starry…maybe positive?


Perianal Syphilitic Ulcer

Primary syphilis - features

- Sharply punched out painless ulcer “chancre”
- Marked acanthosis at periphery of lesion
- Dermal infiltrate of lymphocytes and plasma cells
- Perivascular inflammatory infiltrate rich in plasma cells with endothelial cell swelling

Secondary syphilis

- Maculopapular lesions
- Band-like infiltrate in upper dermis
- Much more superficial infiltrate of lymphocytes, histiocytes, plasma cells
- Parakeratosis, necrotic keratinocytes
- Poorly formed granulomas may be present

Human Pathology (2009) 40, 624–630

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Original contribution

Treponema pallidum distribution patterns in mucocutaneous lesions of primary and secondary syphilis: an immunohistochemical and ultrastructural study

Gemma Martín-Ezquerra MD[a,*], Alex Fernandez-Casado MD[a], Dídac Barco MD[b], Anna Jucglà MD[c], Núria Juanpere-Rodero MD[h], Josep Maria Manresa PhD[j], Luis Miguel Soares de Almeida MD[d], Jose Luis Rodríguez-Peralto MD[e], Heinz Kutzner MD[f], Lorenzo Cerroni MD[g], Carles Barranco MD[h], Josep Lloreta MD[h], Luis Requena MD[i], Ramon M. Pujol MD[a]

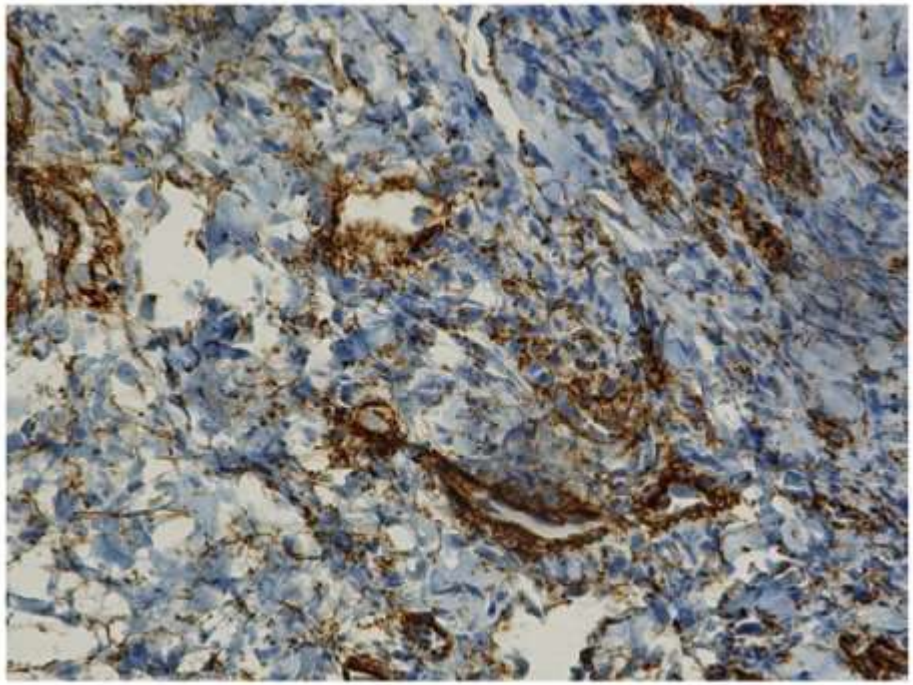
Primary vs. Secondary

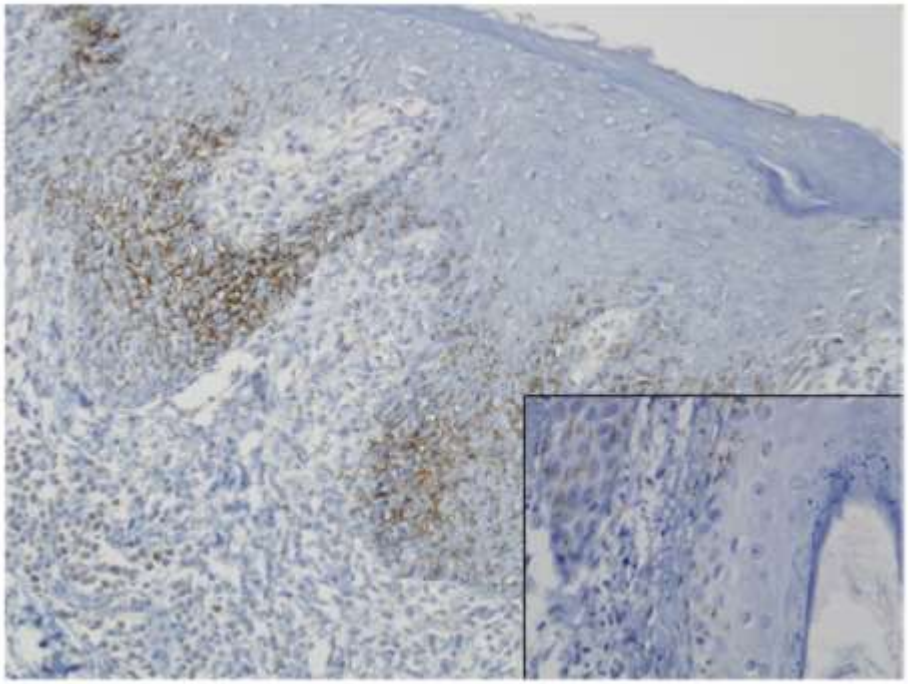
- 8 cases of primary syphilis: All cases were ulcers
- 26 cases of secondary syphilis: Most cases were maculopapular lesions with 4 cases of erosions

Stain detection rates

- Warthin Starry: 4/8 cases of primary syphilis, 13/26 cases of secondary syphilis
- IHC for spirochetes: 8/8 cases of primary syphilis, 21/26 cases of secondary syphilis

IHC patterns: 1º vs 2º





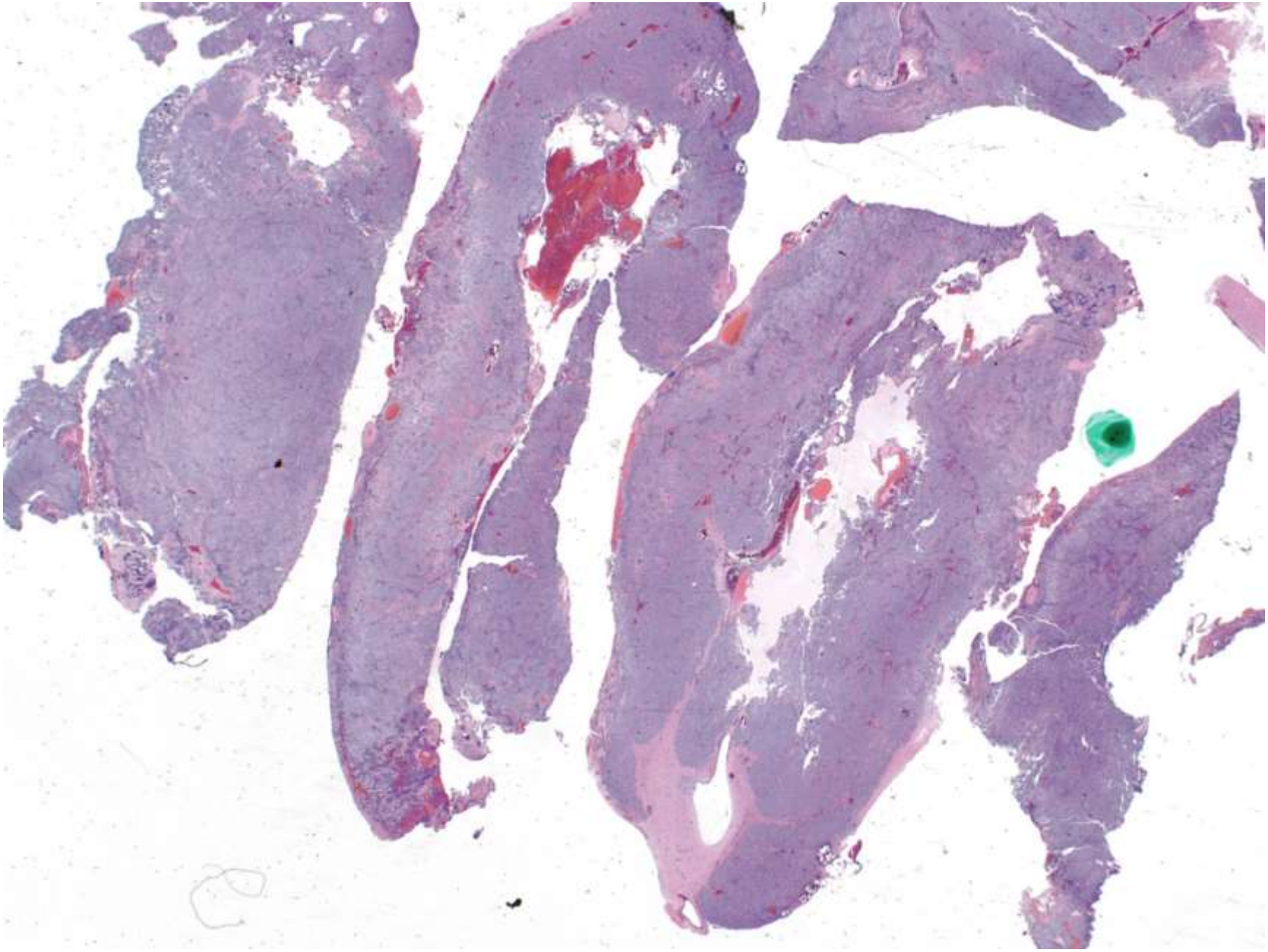
Take home points

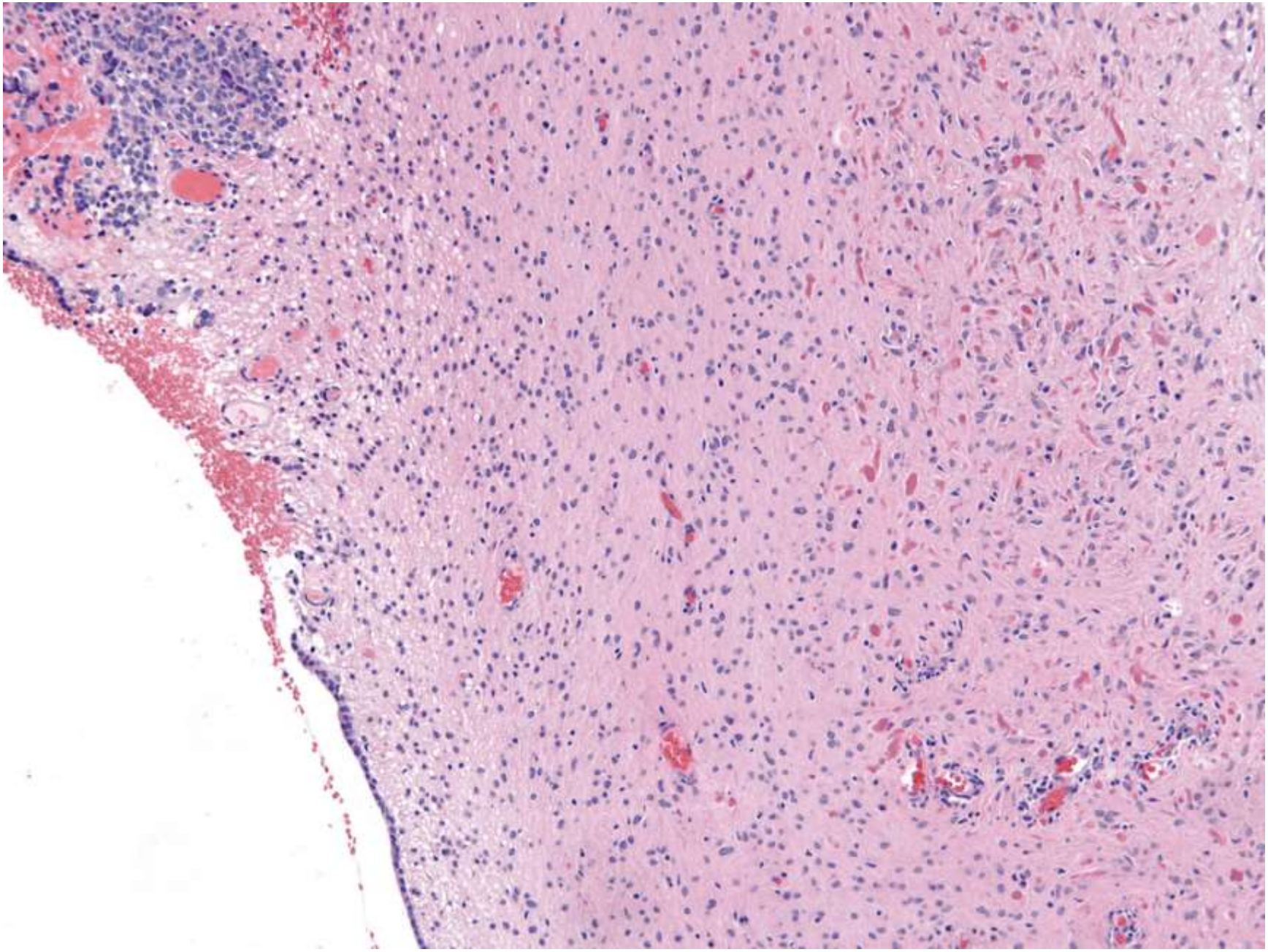
- Consider primary syphilis in an ulcer with perivascular plasma cells
- Secondary syphilis if maculopapular lesions with lichenoid infiltrate
- IHC should be done in all cases of suspected syphilis but sensitivity is not 100%

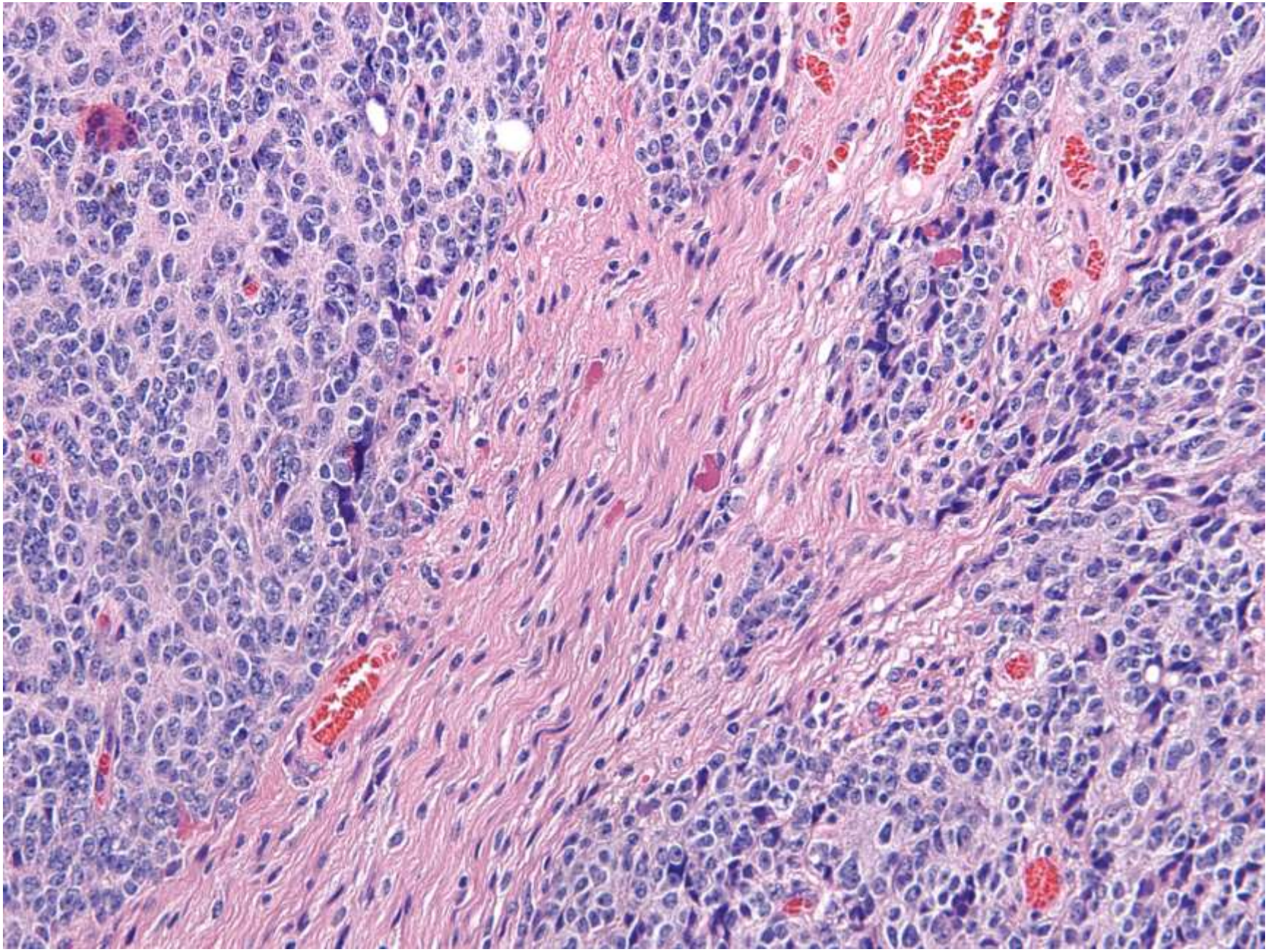
SB 6054

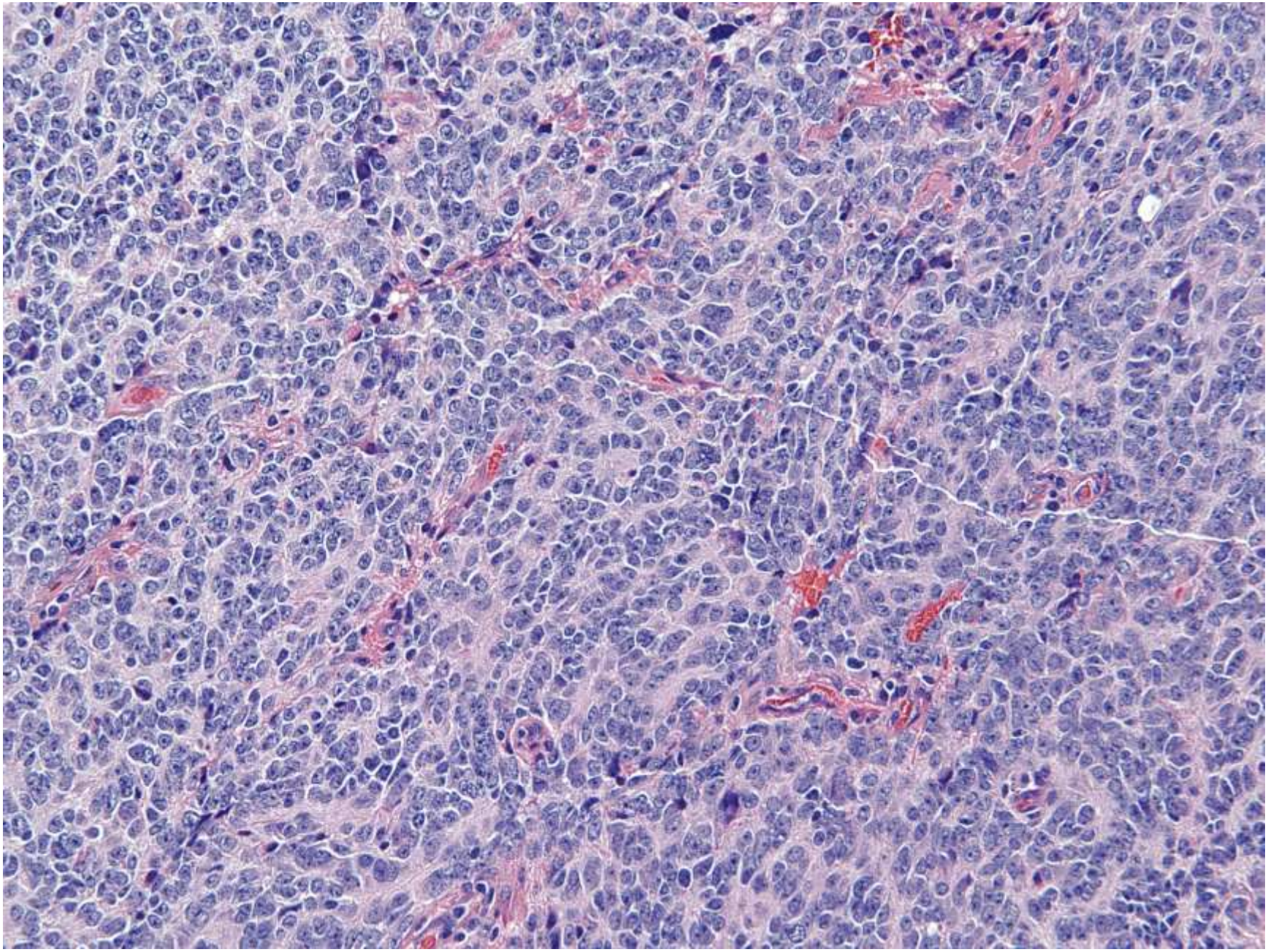
Peyman Samghabdi/Hannes Vogel; Stanford

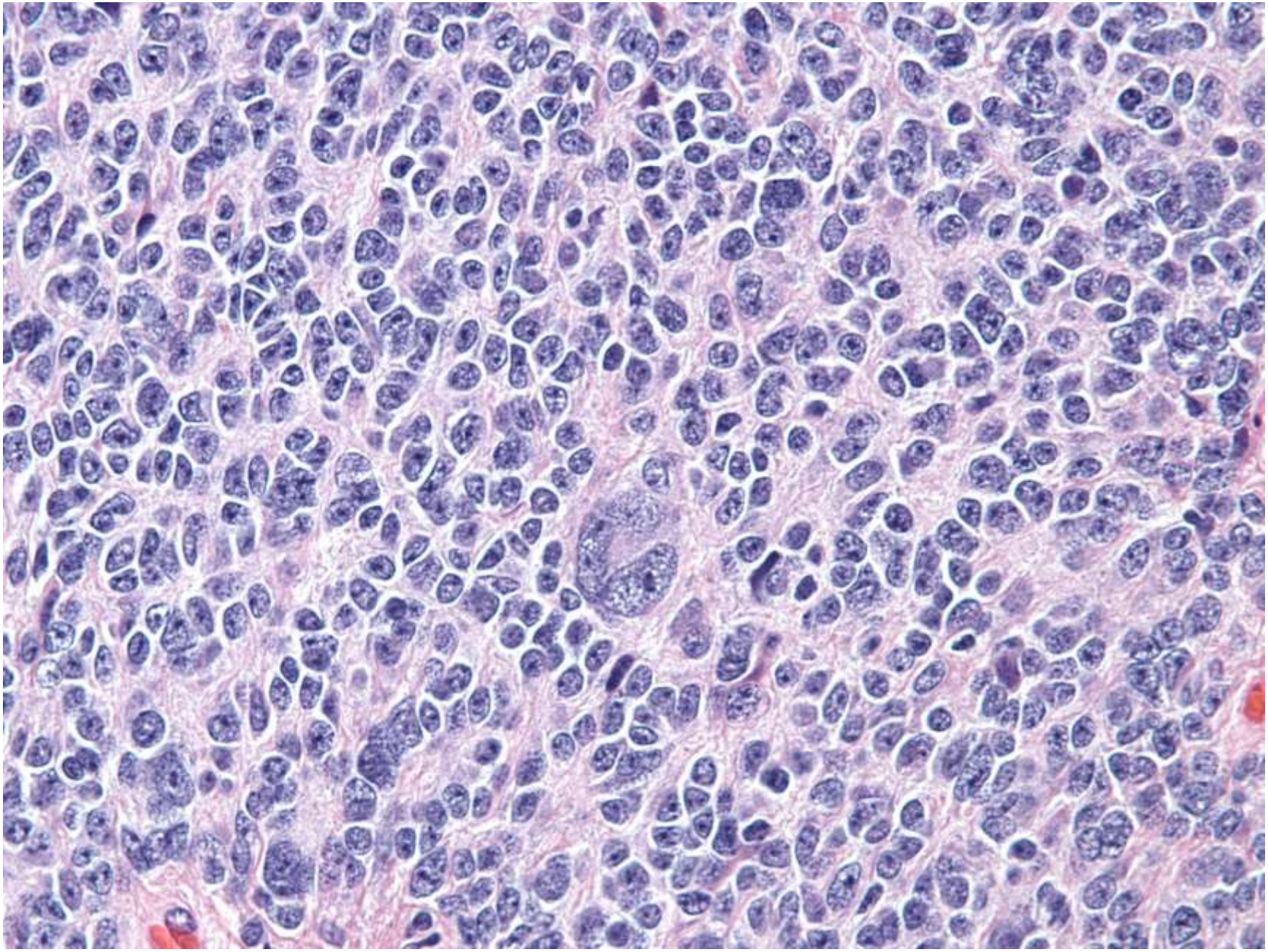
34-year-old man with heterogenous pineal mass measuring 2cm.

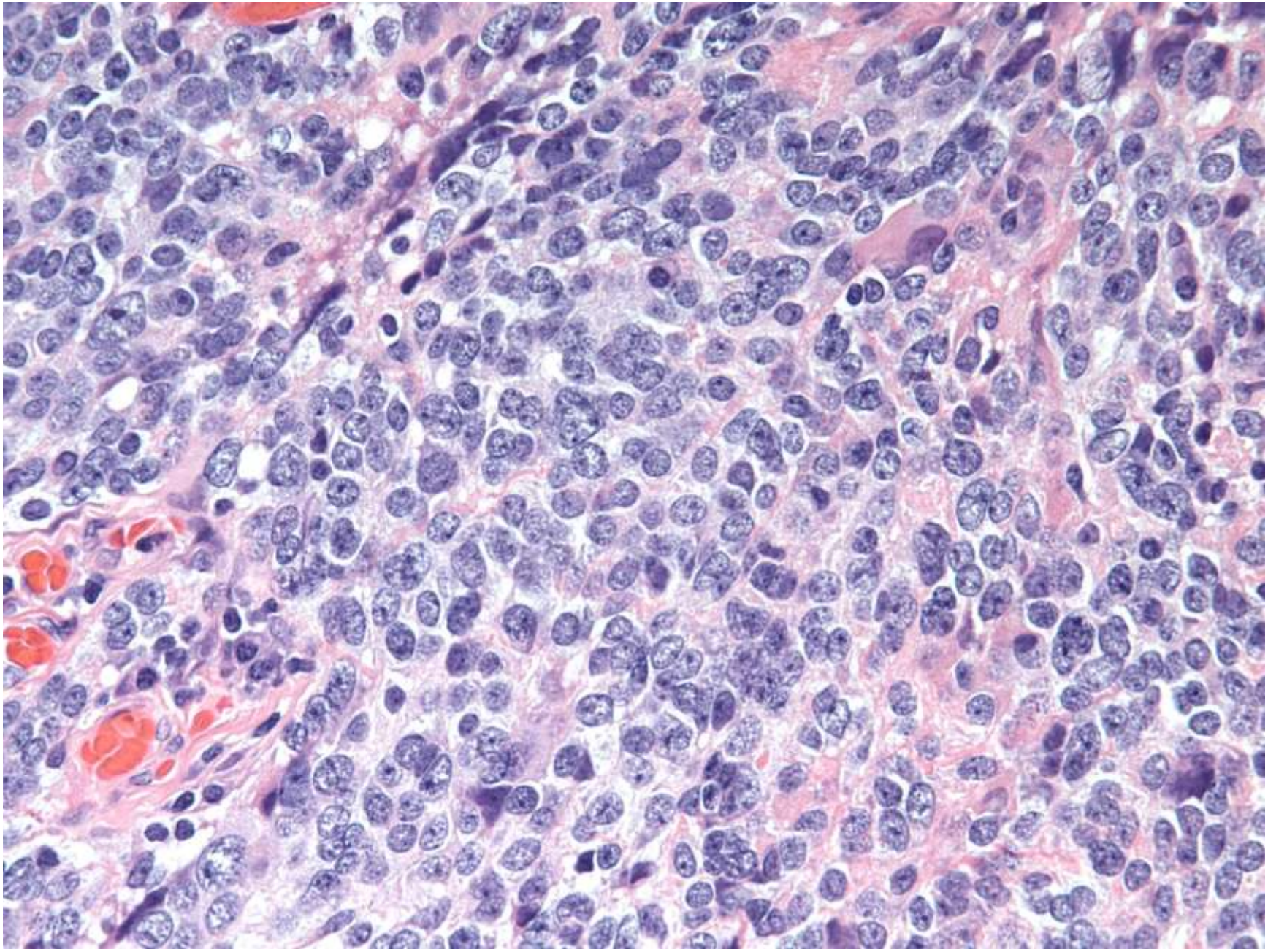










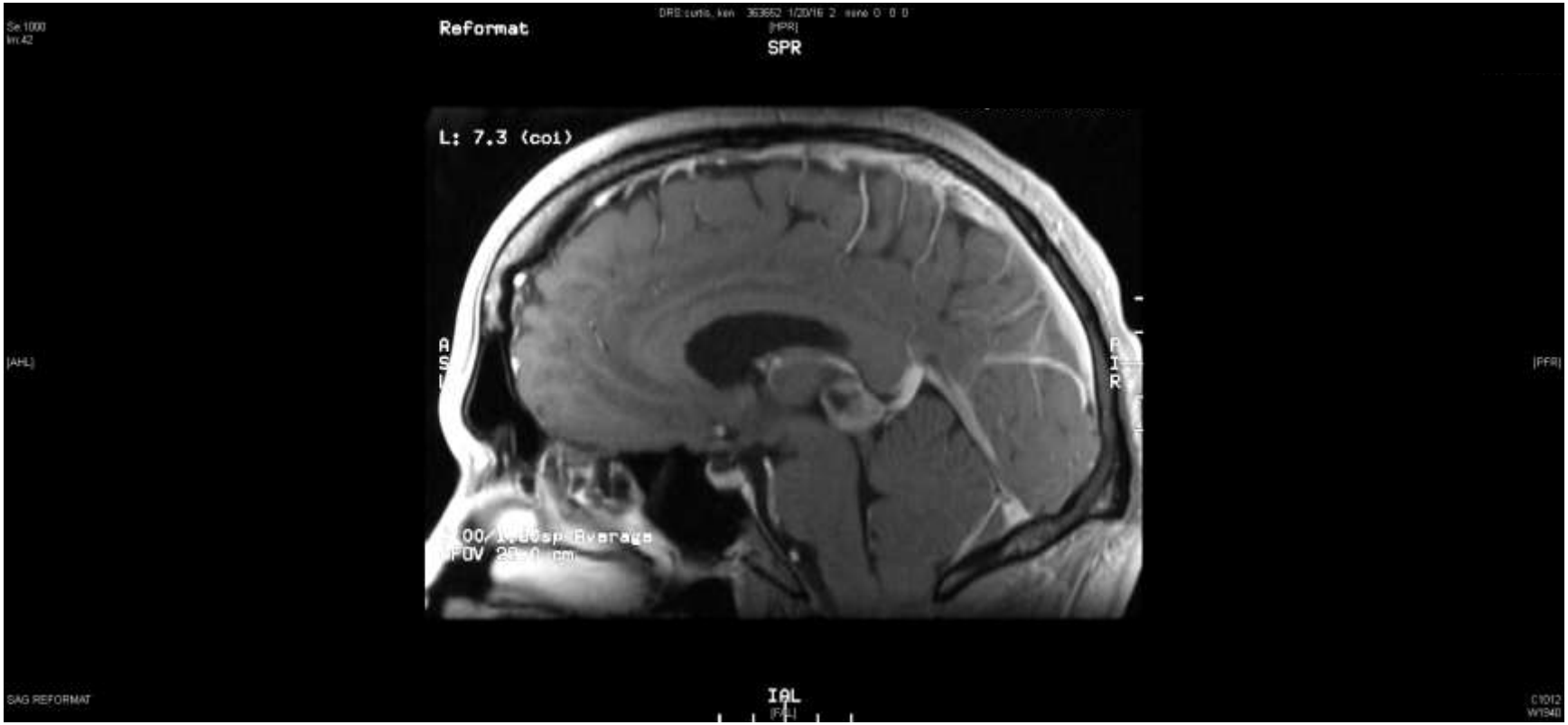


DIAGNOSIS?

Stanford Neuropathology Case Presentation June 2016

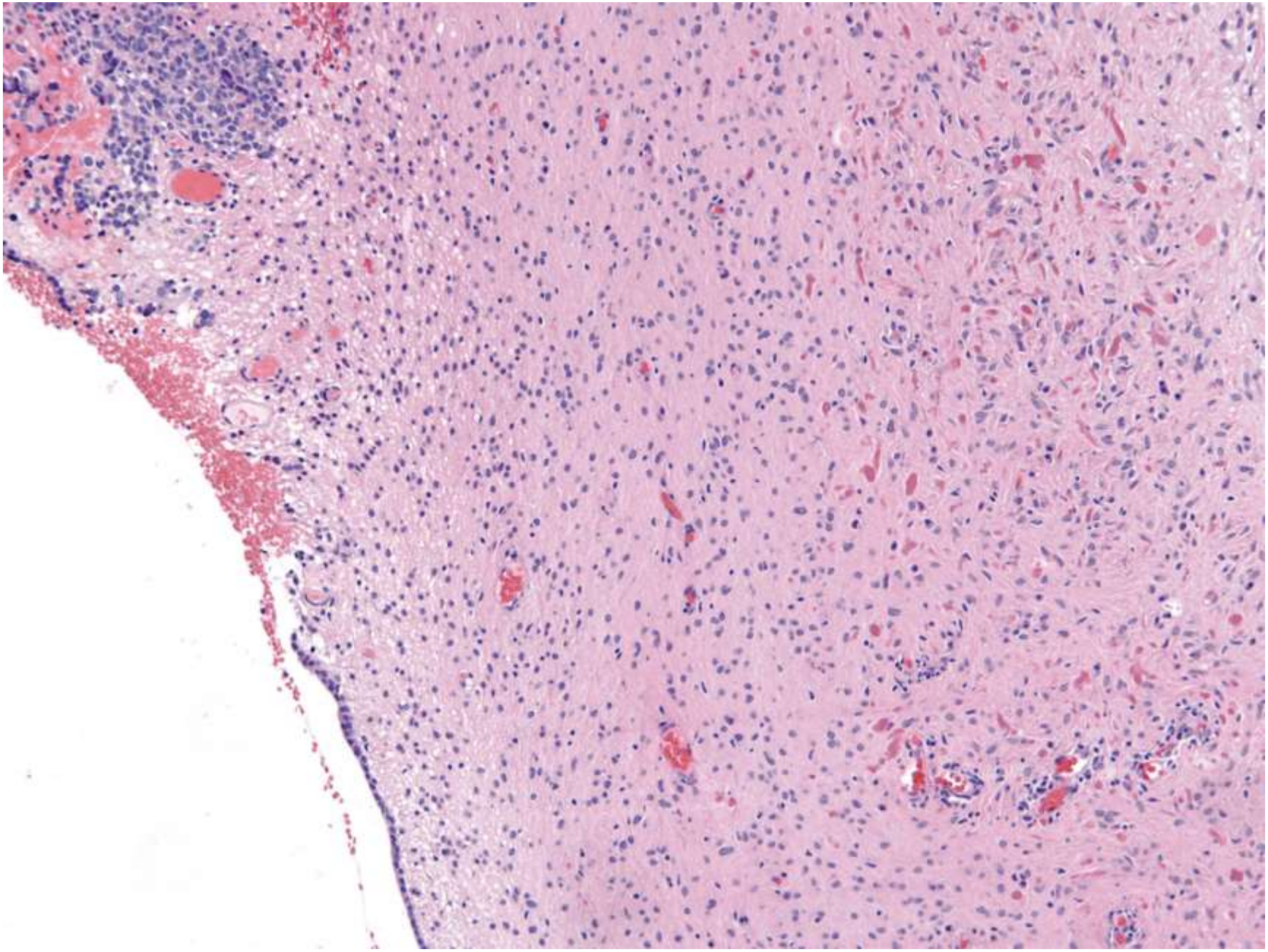
Peyman Samghabadi M.D.
Edward Plowey M.D., Ph.D.
Hannes Vogel M.D.

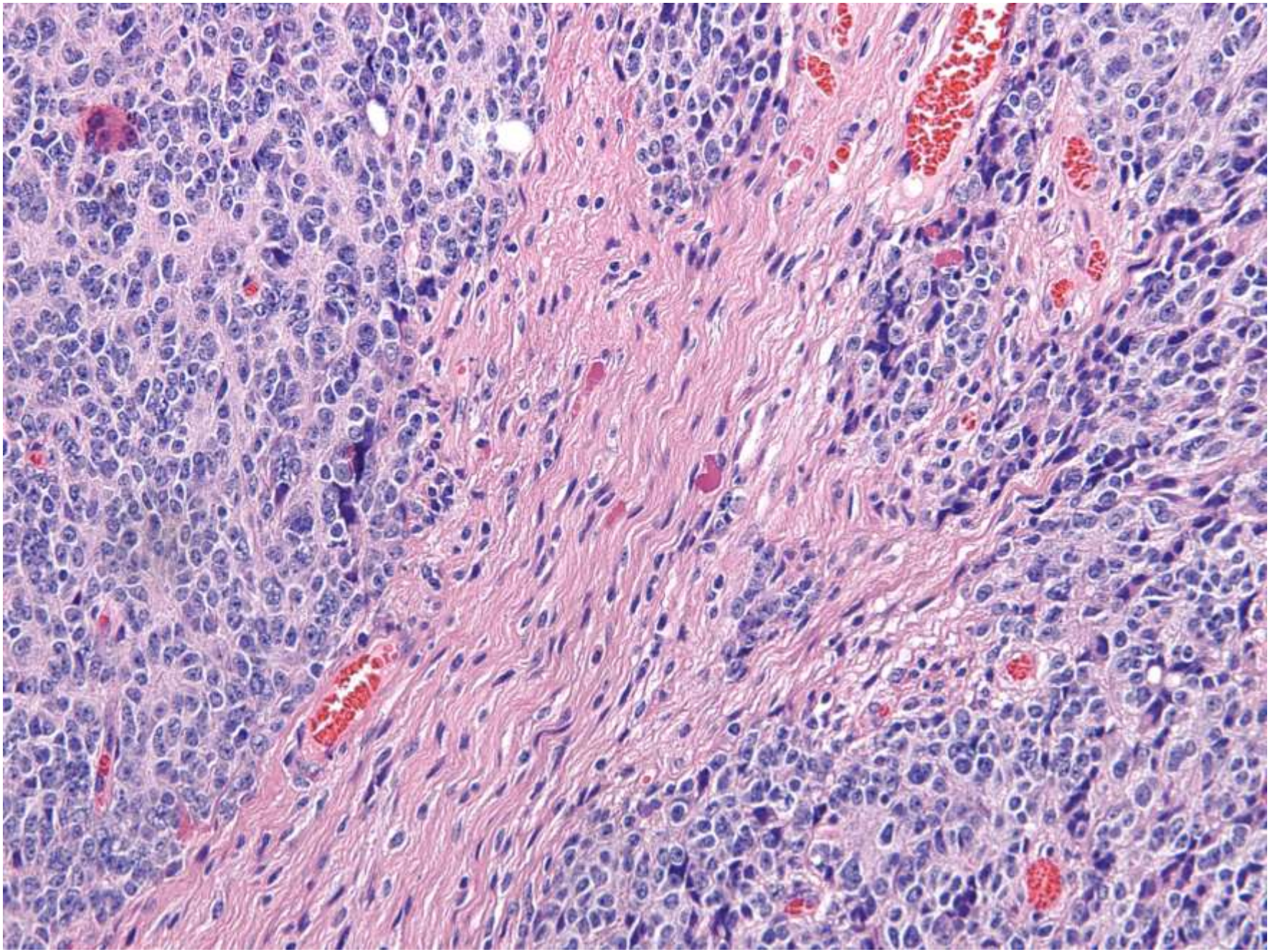
MRI, T1

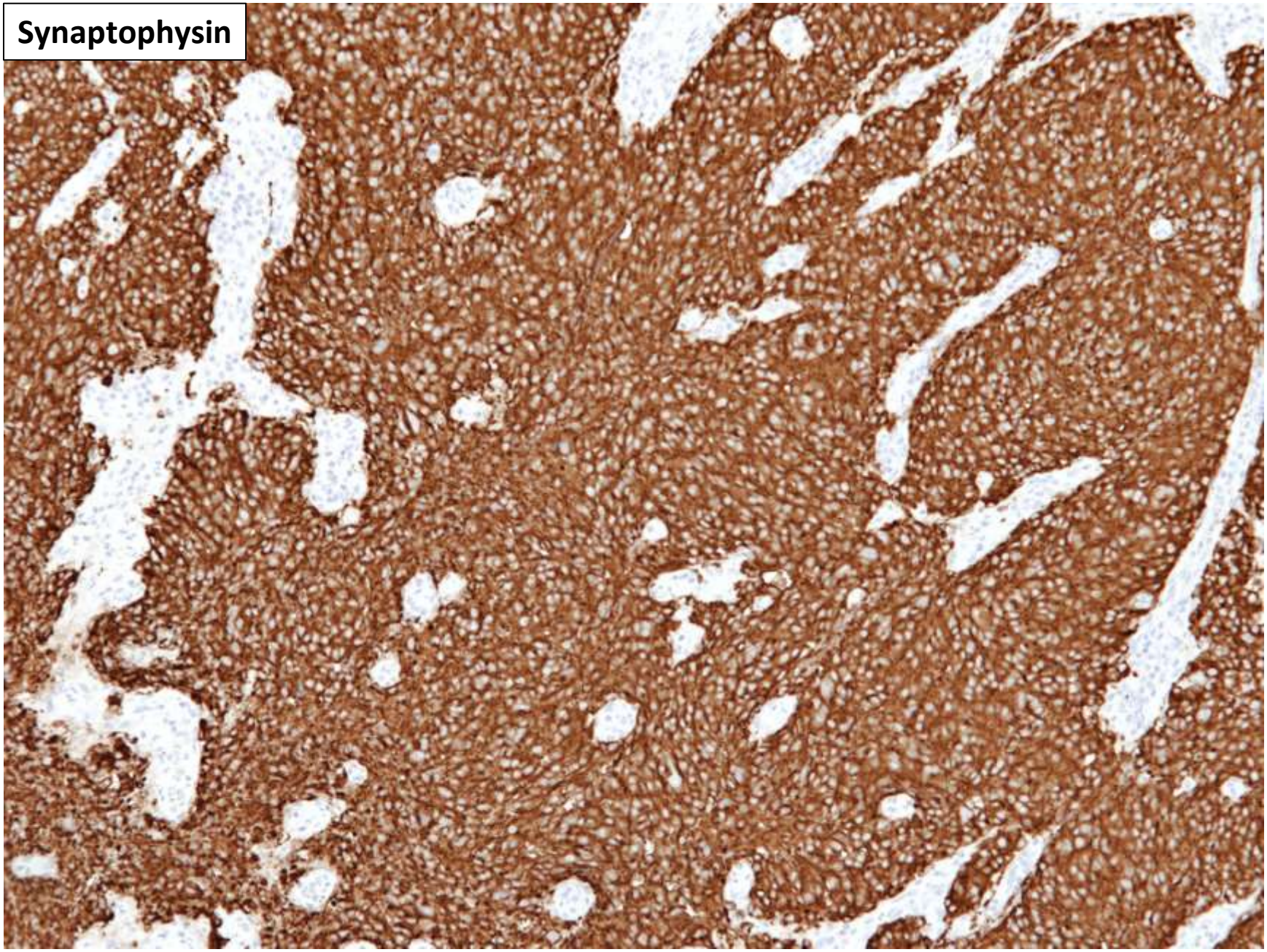


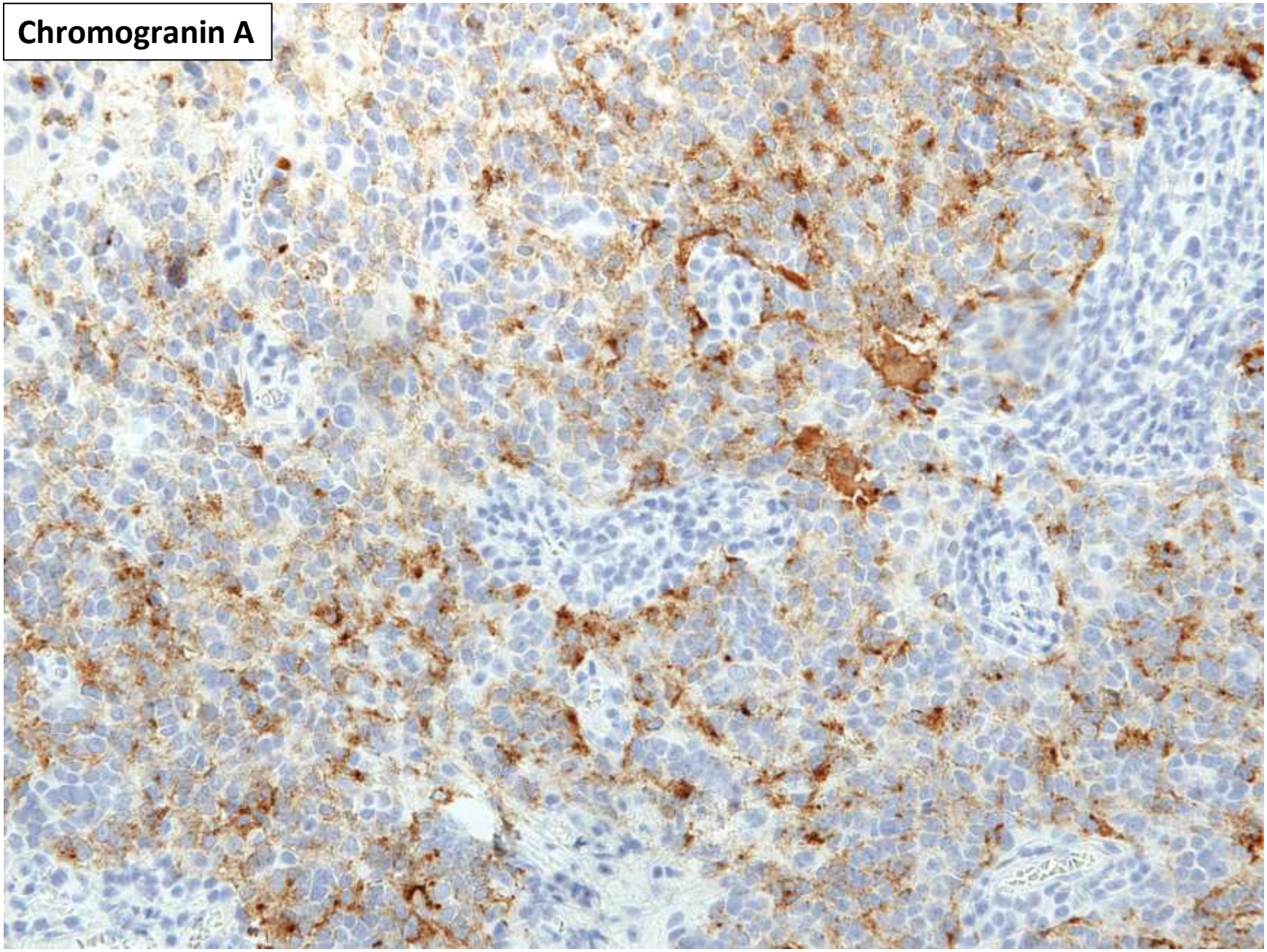
Differential Diagnosis of Pineal Region Tumors

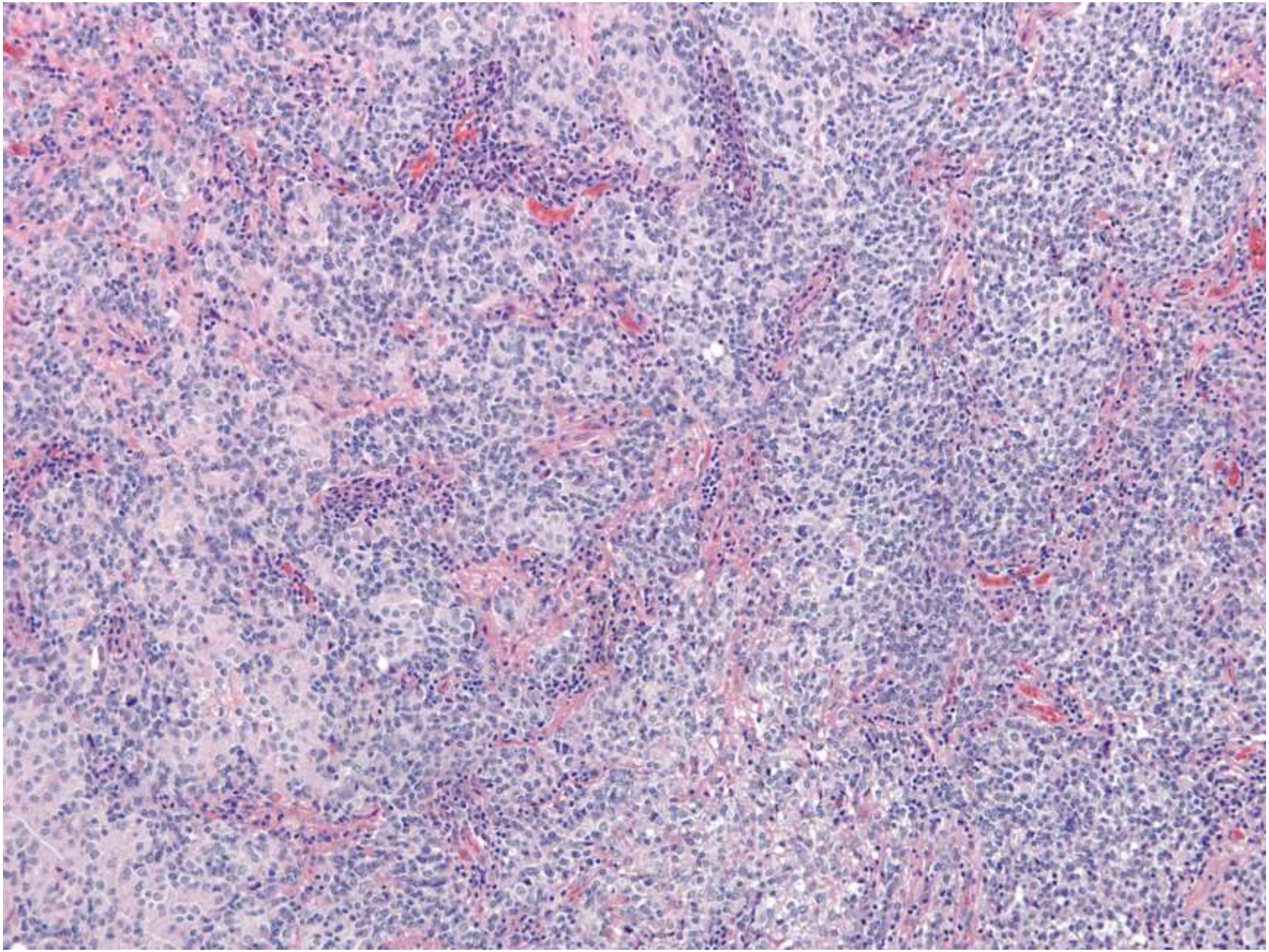
- Germ cell tumors
- Pineal Parenchymal Tumor (Pineocytoma, PPTID, Pineoblastoma)
- Gliomas
- Other Neoplastic (AT/RT, Papillary Tumor of the Pineal Region, Meningioma, Metastasis)
- Non-neoplastic (pineal cyst, vascular malformation, arachnoid cyst)

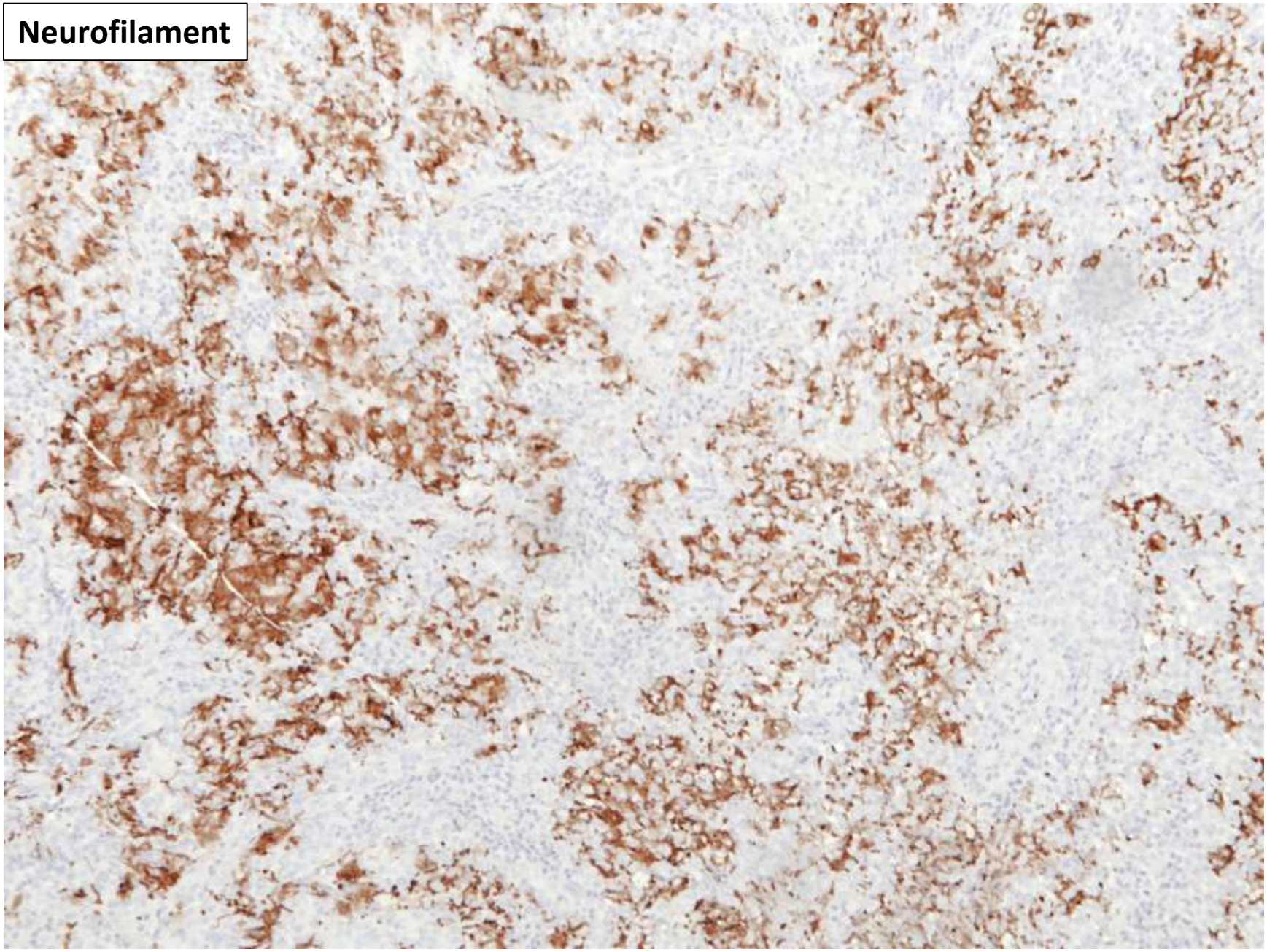


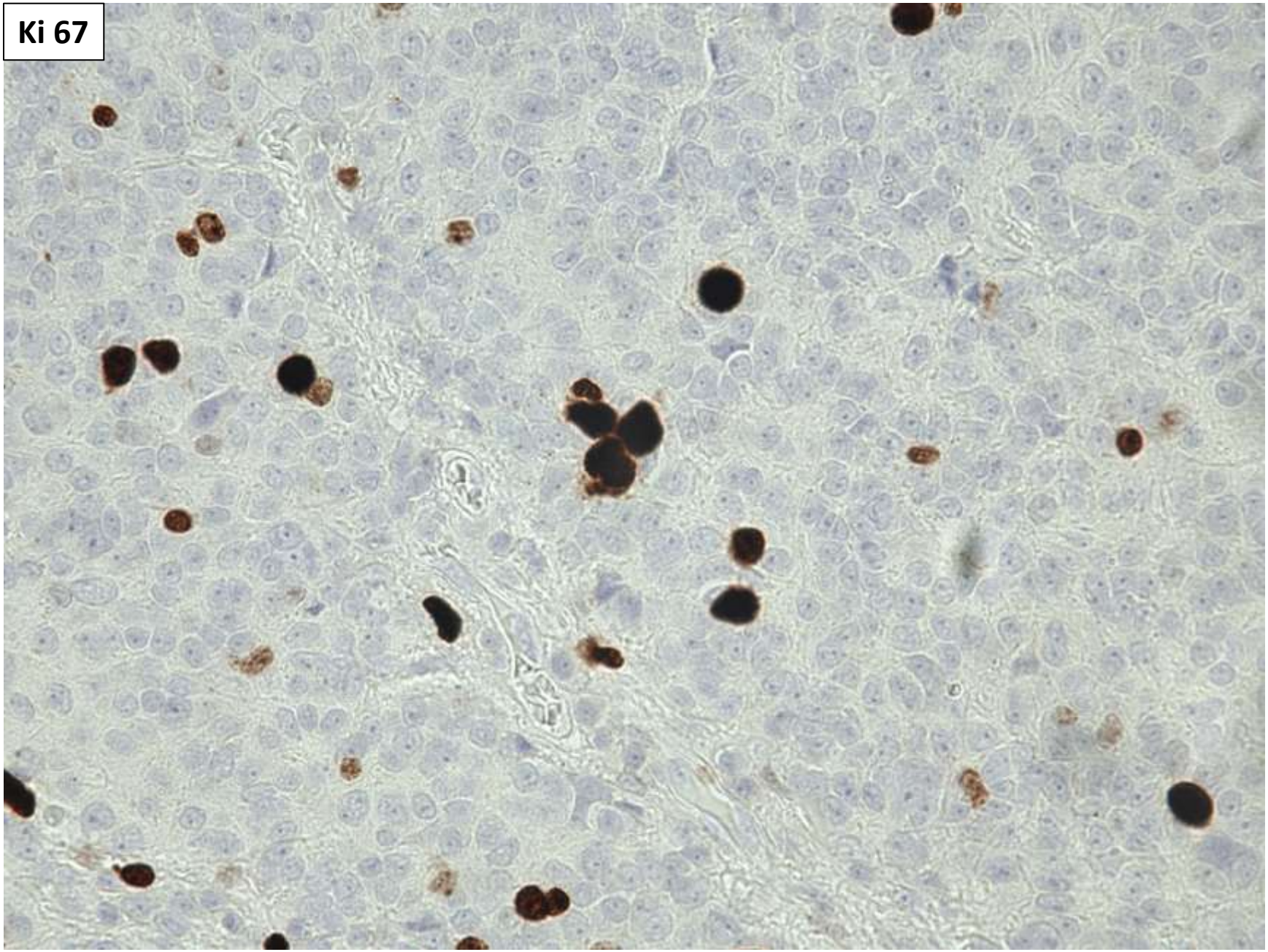



Synaptophysin


Chromogranin A




Neurofilament


Ki 67

DIAGNOSIS?

DIAGNOSIS

PINEAL PARENCHYMAL TUMOR OF INTERMEDIATE DIFFERENTIATION, WHO GRADE II

Demographics

- Pineal Region Tumors
  - Less than 1% of CNS neoplasms
  - 25% accounted for by Pineal Parenchymal Tumors*
    - Pineocytomas: 36-47 years (I)
    - PPTID: 27.4 (III) to 40.3 years (II)
    - Pineoblastoma: 12-18 years (IV)

Clinical Manifestations

- Obstruction of cerebral aqueduct → hydrocephalus:
  - Headache, nausea, vomiting, AMS
- Compressive effects:
  - Superior Colliculi: upward gaze palsy
  - Hypothalamic region: DI, Hypogonadism, Precocious Puberty
  - Cerebellum: Ataxia

Histopathology

- PC (I): Well differentiated, diffuse or lobular, pineocytomatous rosettes, delicate vessels, non-mitotic
- PB (IV): Small round blue cell tumor: Homer Wright rosettes, necrosis, vascular proliferation, infiltration, Photoreceptor-type differentiation (Flexner-Wintersteiner rosettes or fleurettes), mitotic

Histopathology

- PPTID (II-III): Increased N:C ratios (visible cytoplasm), stippled chromatin, variable atypia, diffuse vs. lobulated pattern, variable rosettes, variably mitotic

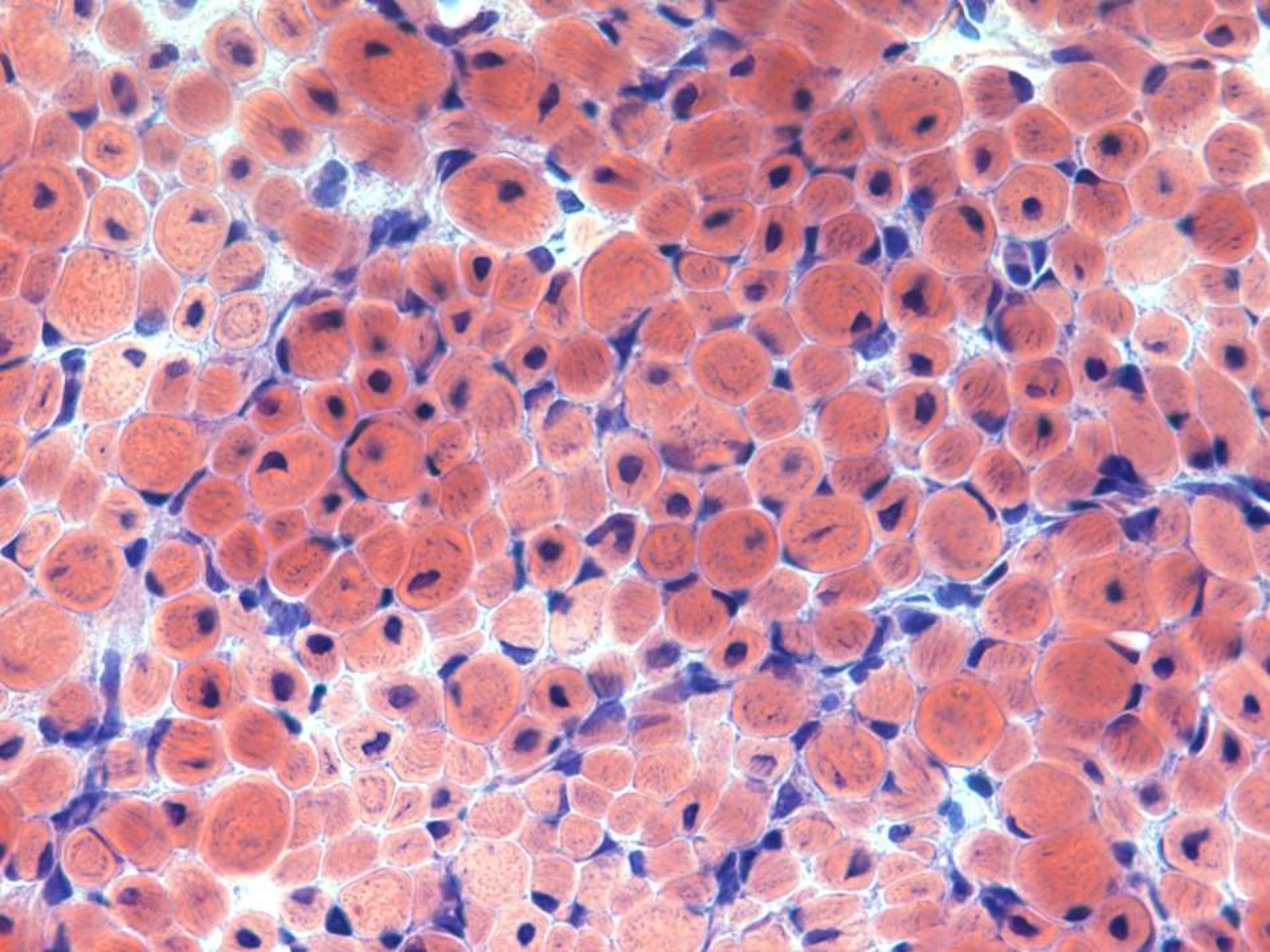
Grading

Histologic Type	PC	PPTID (Low Grade)	PPTID (High Grade)	PB
Synaptophysin	Strong	Weak to Moderate	Weak to Moderate	Weak
Mitoses	0	<6	<6, ≥ 6	Variable
Neurofilament	+++	++	+/-, ++	+/-
Treatment	Surgery	Surgery, Adjuvant	Surgery, Adjuvant	Surgery, Radiation, Chemotherapy
Prognosis	91% at 5 years	74% at 5 years (local recurrence)	39% at 5 years (metastatic)	10% at 5 years

SB 6055

Kelli Devereaux/Hannes Vogel; Stanford

3-month-old male with hypotonia, facial weakness, ventilator dependent. Ex-32 week premature. MRI showed small subdurals, likely birth related. Normal CK. Testing negative for myotonic dystrophy. Submitted image. Right soleus muscle, H&E cryosection.

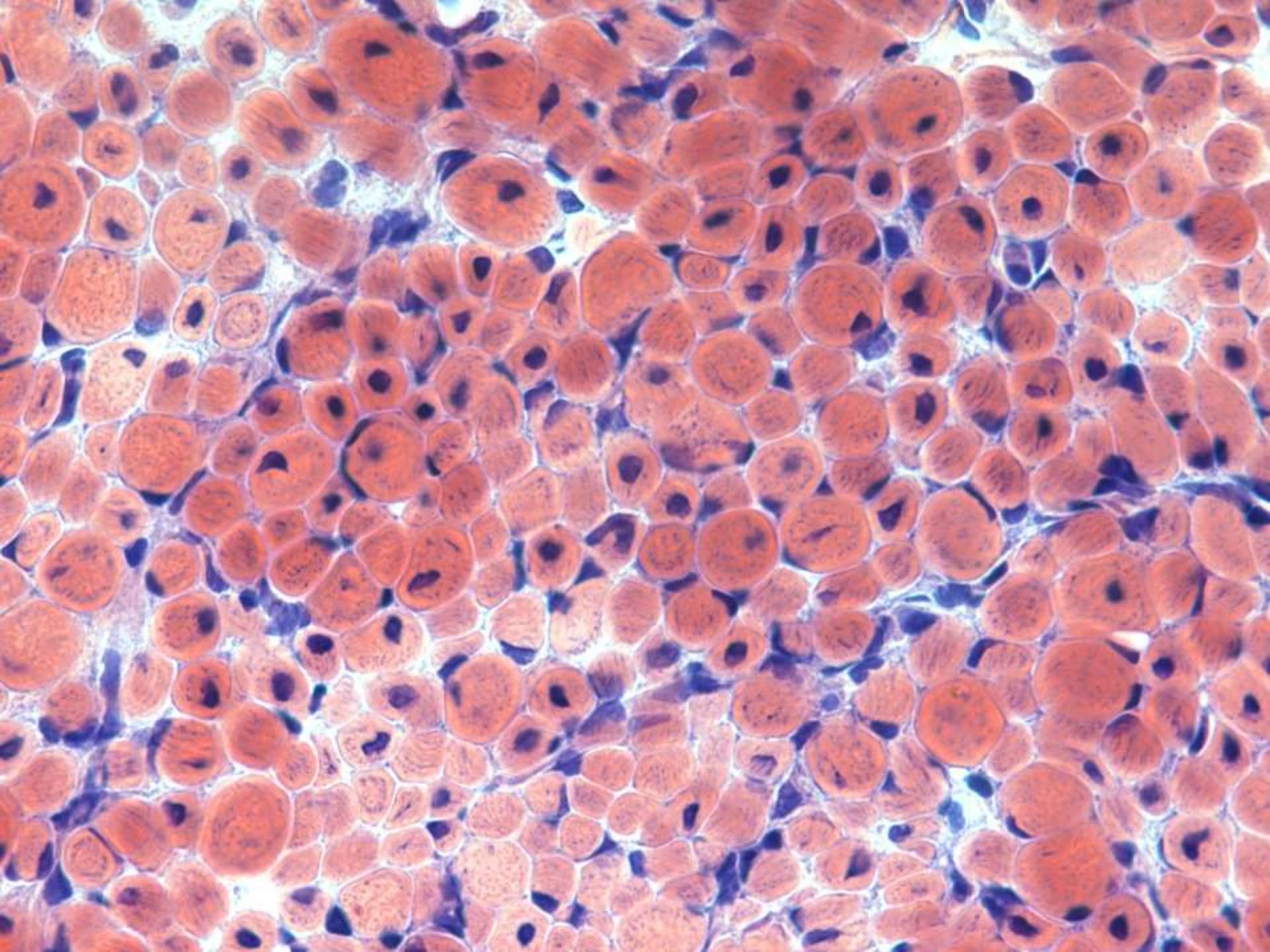


DIAGNOSIS?

June South Bay Pathology Society June 2016
Kelli Devereaux MD and Hannes Vogel MD

3 month old male with hypotonia, facial weakness, ventilator dependent. Ex-32 week premature. MRI showed small subdurals, likely birth related. Normal CK. Testing negative for myotonic dystrophy.

Submitted image. Right soleus muscle, H&E cryosection



Differential diagnosis

1. **Infantile myotonic dystrophy**
2. **Centronuclear myopathy: X-linked “Myotubular myopathy”**
3. **Centronuclear myopathy: autosomal**

Myotubularin (MTM1); Chromosome Xq28; Recessive

- Epidemiology: 1 male in 50,000
- Gene mutations: Spread unevenly across whole gene
- Clinical features
  - Onset: Infancy
  - Polyhydramnios: 50%
  - Severe hypotonia, proximal & distal weakness; symmetric
  - Respiratory insufficiency
  - Ophthalmoplegia & ptosis at birth (60%), or with disease progression

Myotubularin (MTM1); Chromosome Xq28; Recessive

- Prognosis
  Early death: Mean = 5 months
  Weakness non-progressive
  Survivors often
    Respirator dependent (80%)
    Feeding tube dependent

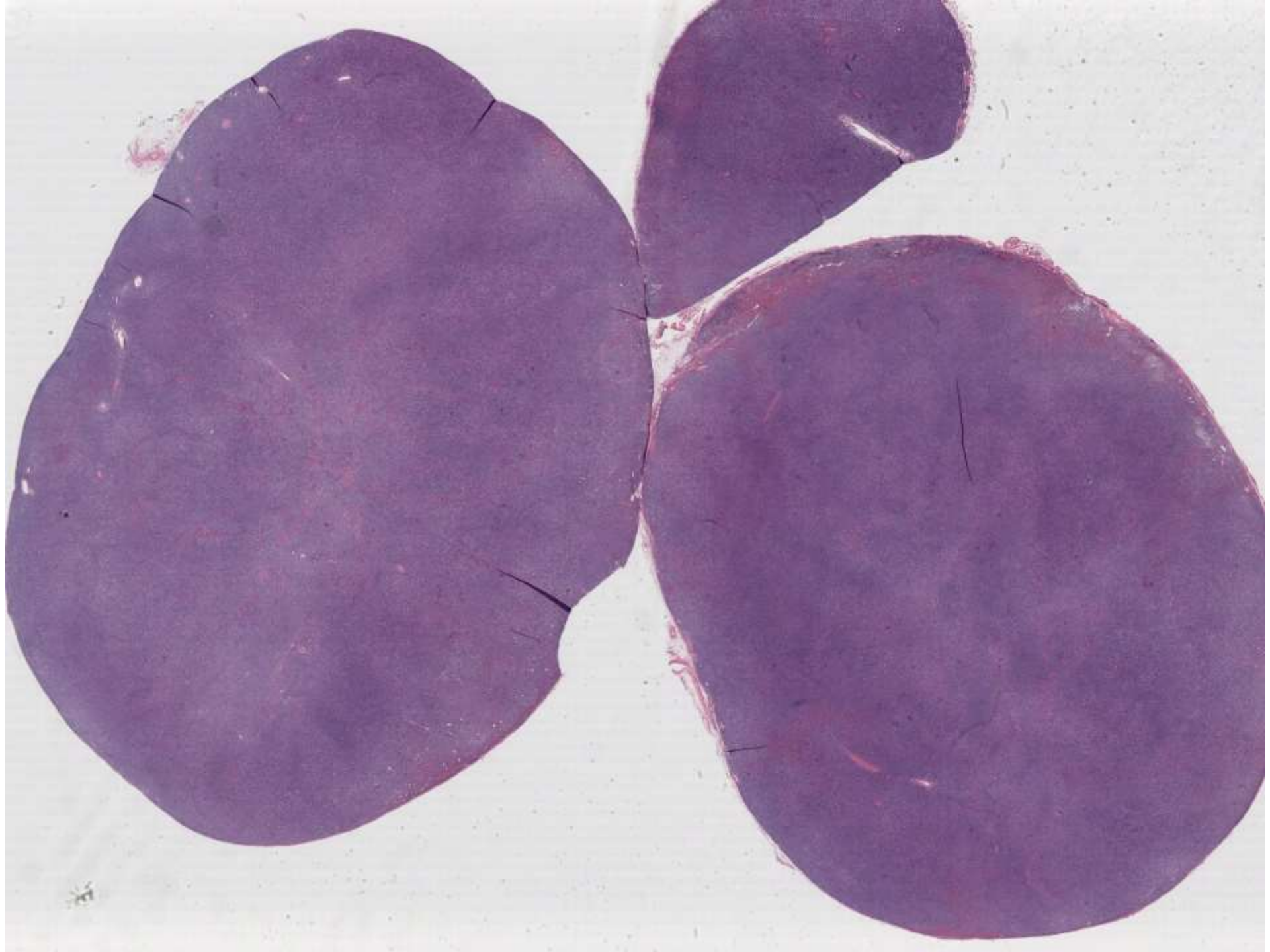
- Female carriers may be symptomatic: mild weakness or history of easy fatigability

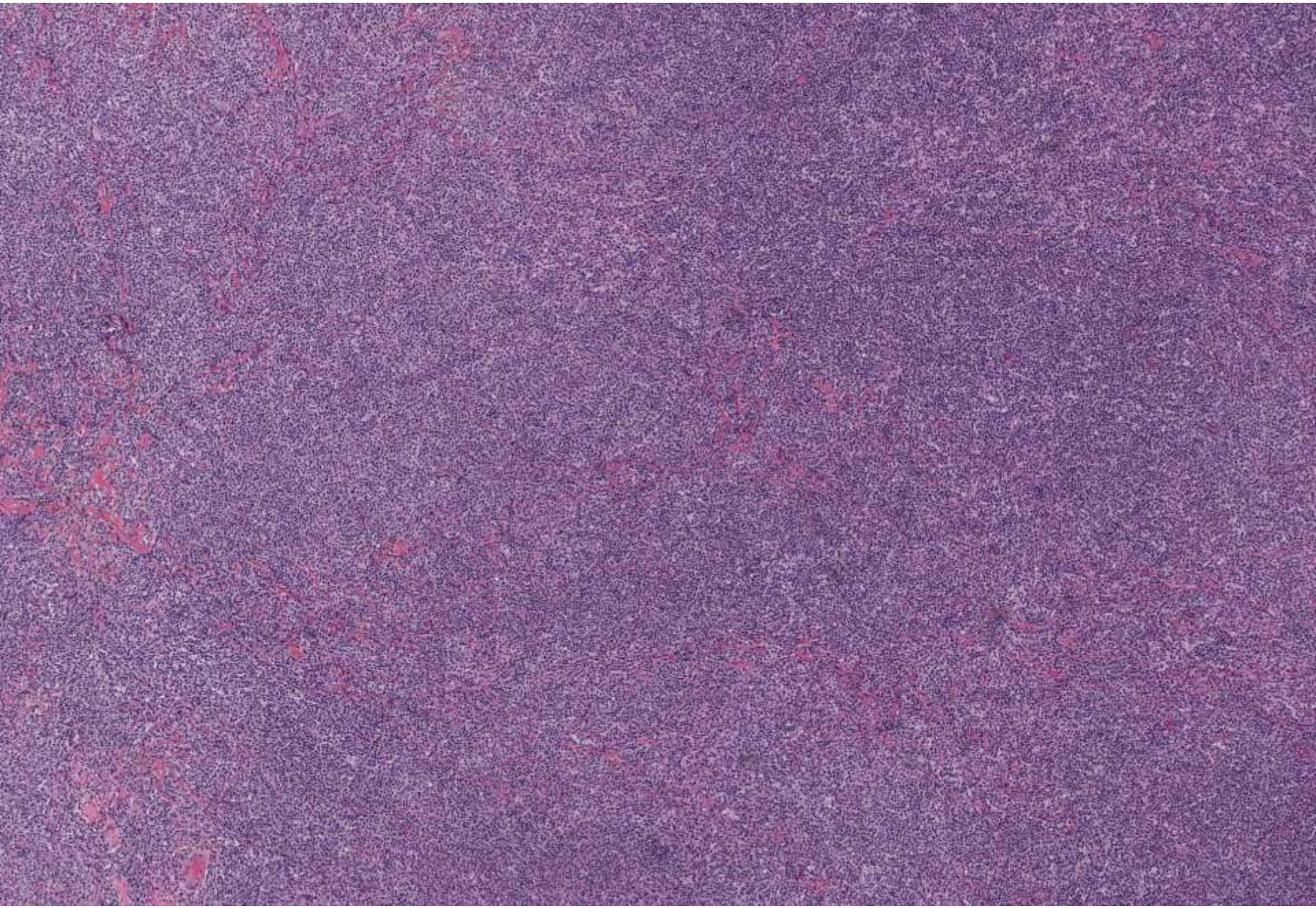
- Gene therapy trials in progress

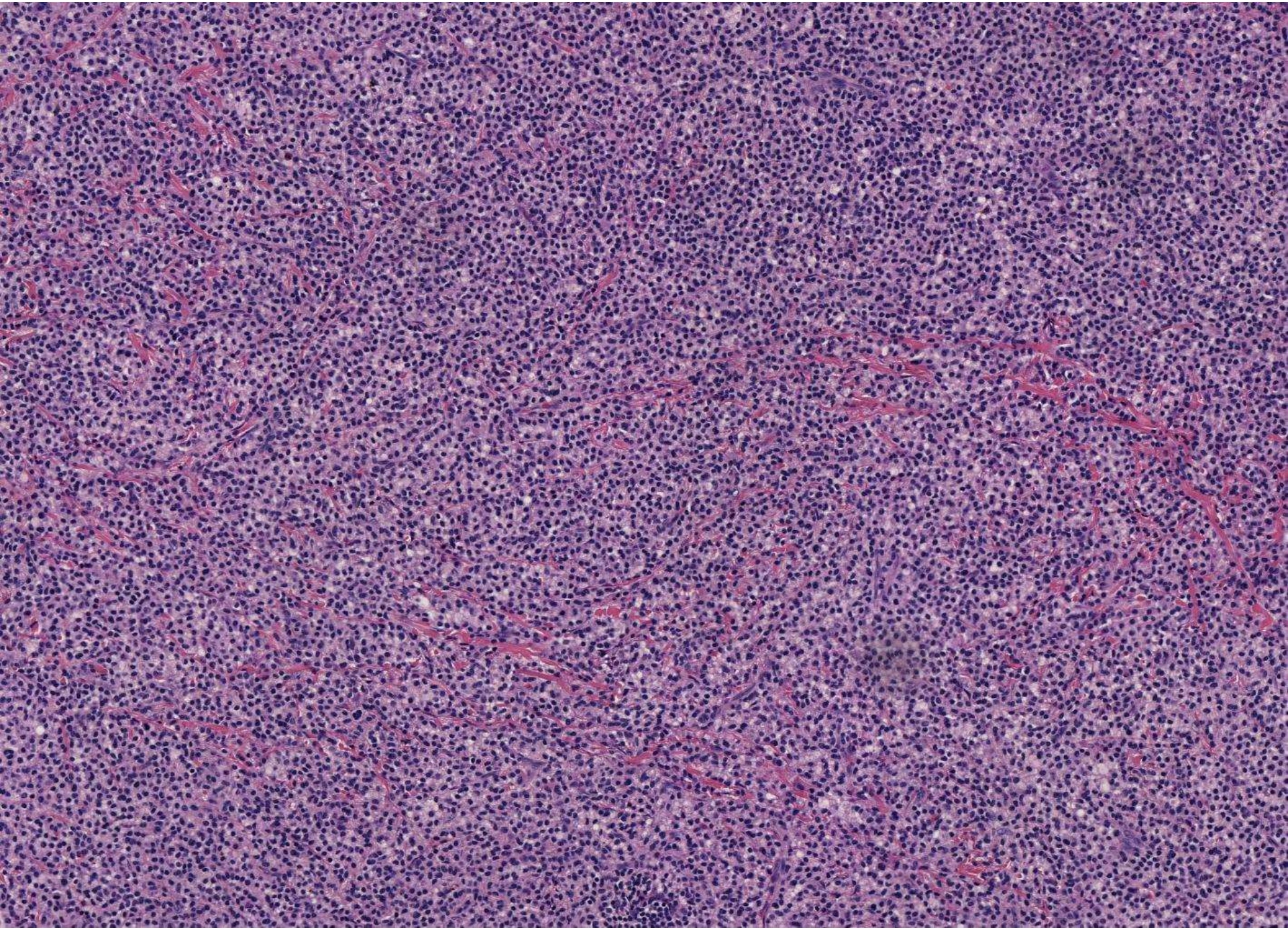
SB 6056

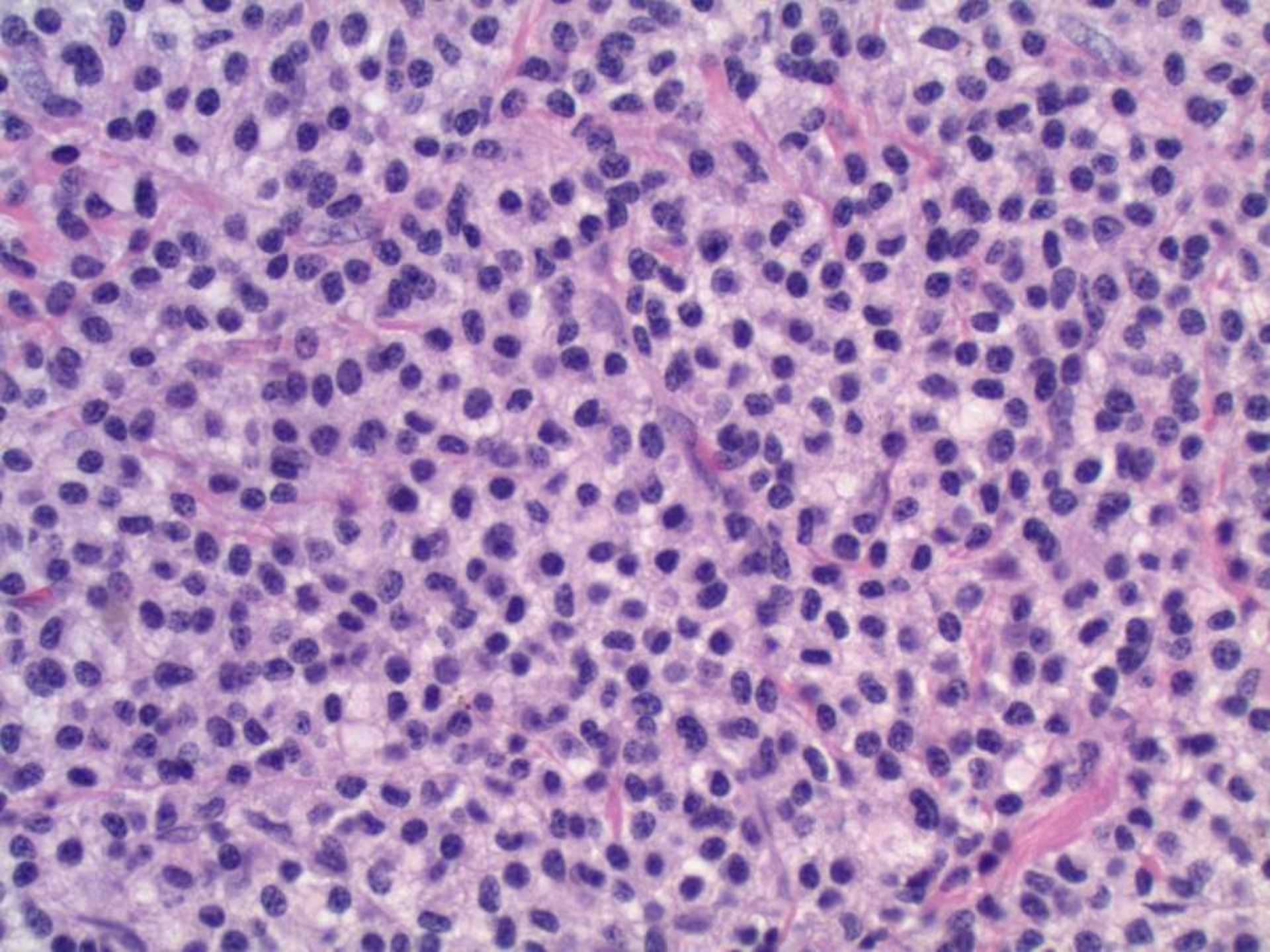
Keith Duncan; Mills-Peninsula

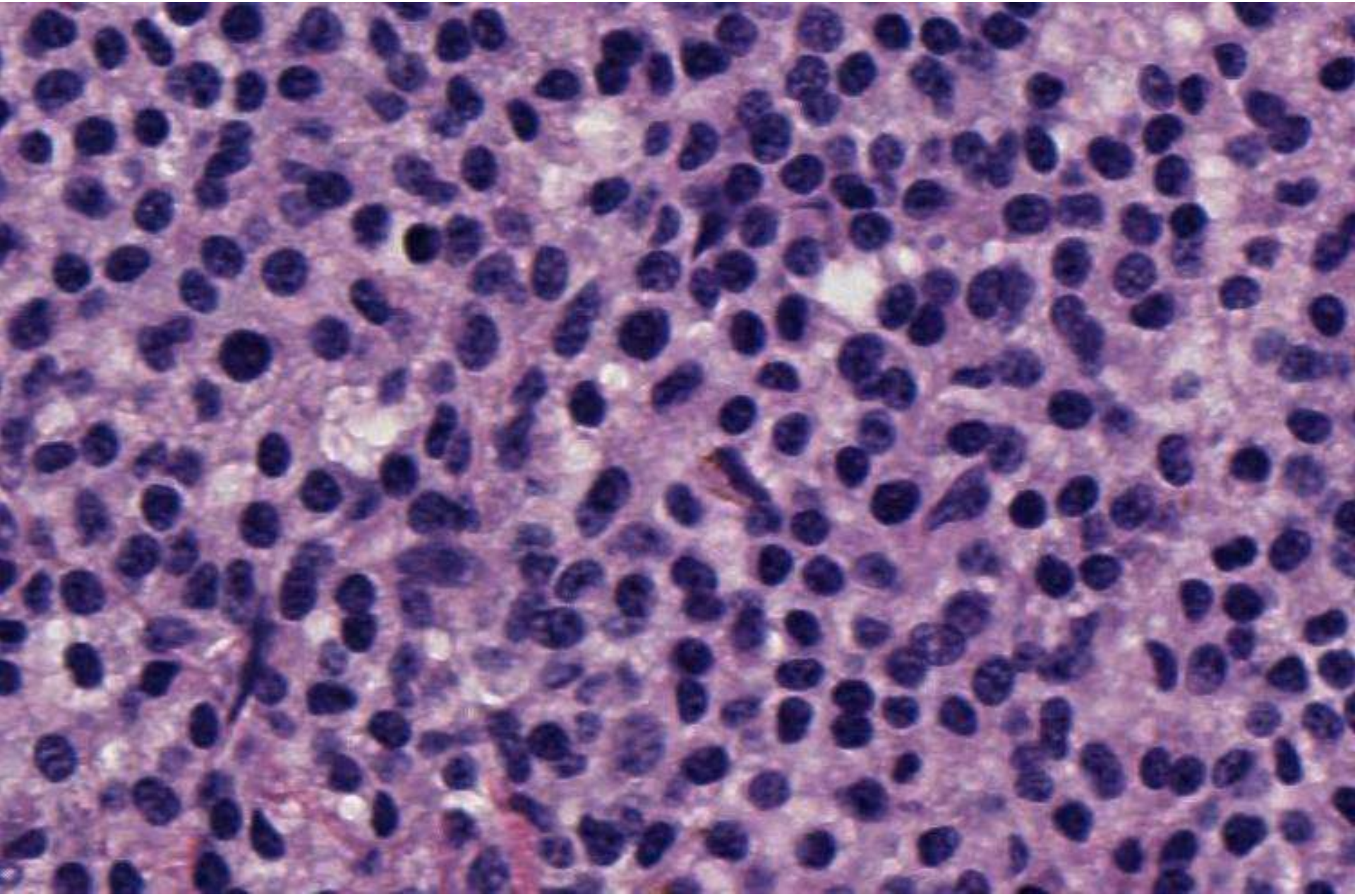
47-year-old woman with left neck mass x3 months.











DIAGNOSIS?

PLASMACYTOMA

- 3–5% of plasma cell neoplasms
- Isolated plasma cell neoplasm, usually of bone or soft tissue (oropharynx)

- **Solitary plasmacytoma of bone**, extramedullary plasmacytoma or primary lymph node plasmacytoma

- LN rare, must exclude metastatic multiple myeloma (40% of high stage myelomas metastasize to lymph nodes), metastatic upper respiratory tract plasmacytomas (15% metastasize cervical LN)

- Often involves cervical nodes, mean 5 cm, 40% had serum monoclonal proteins, most patients had localized disease and were cured after local excision or radiation, similar to other extramedullary plasmacytomas

Plasma cell neoplasm

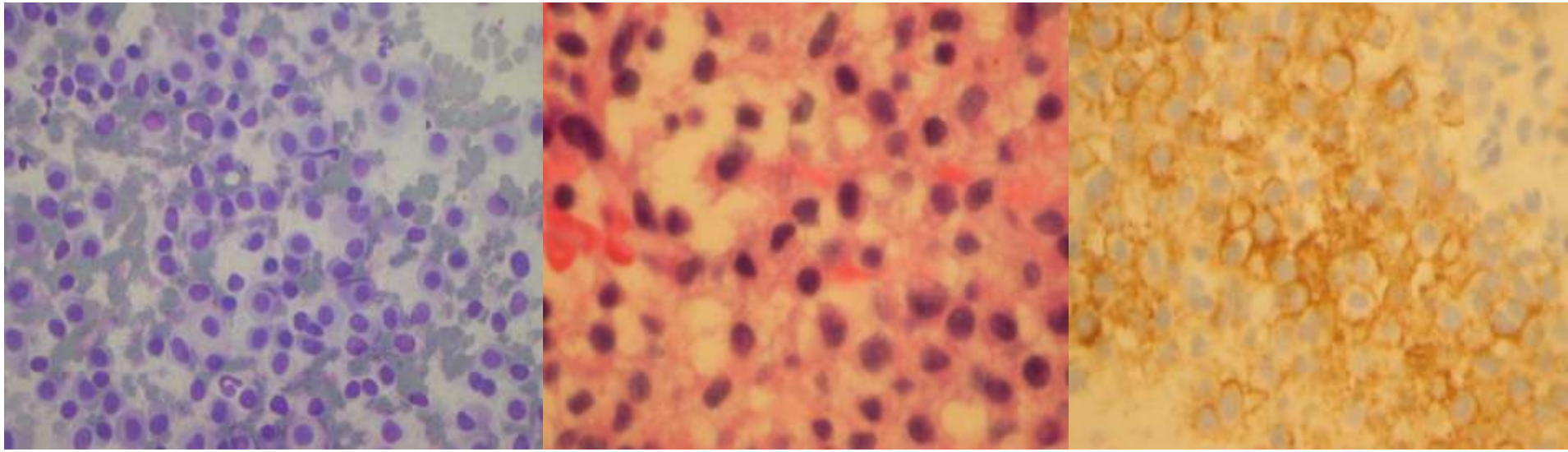
FISH POSITIVE FOR CCND1 GENE REARRANGEMENT
T(11:14) TRANSLOCATION
NO LIGHT CHAIN EXPRESSED

CD138 & CD43 POSITIVE, CD20 VARIABLE, CYCLIN D1 POSITIVE
KI-67 10%

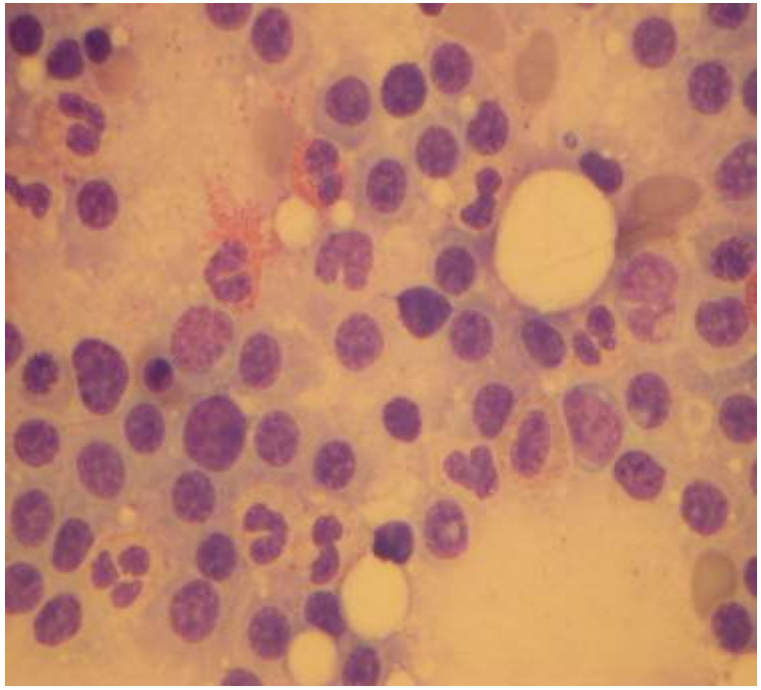
NEG: ALL CYTOKERATINS, PAX5, CD3, CD45, CD34, CD68

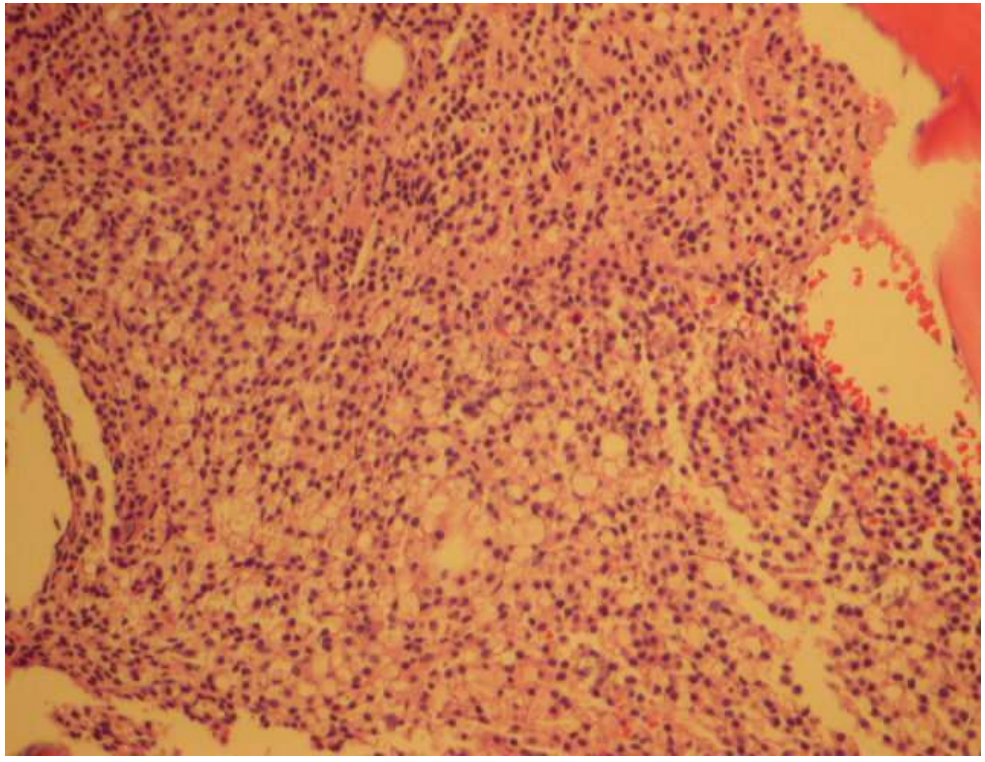
EBV, HHV8 NEG (EXCLUDING PLASMABLASTIC LYMPHOMA)
BRAF V6003 & CD25 NEG- NOT HAIRY CELL LEUKEMIA
SOX11 NEG- NOT MANTLE CELL LYMPHOMA

ORIGINAL FNA
smears, cell button, CD138



BONE MARROW:
Aspirate smears & Bx





FOLLOW UP

PET in 2015 was negative except for a sellar mass which is most likely pituitary adenoma.
Workup: hypogammaglobulinemia & elevated beta-2 microglobulin

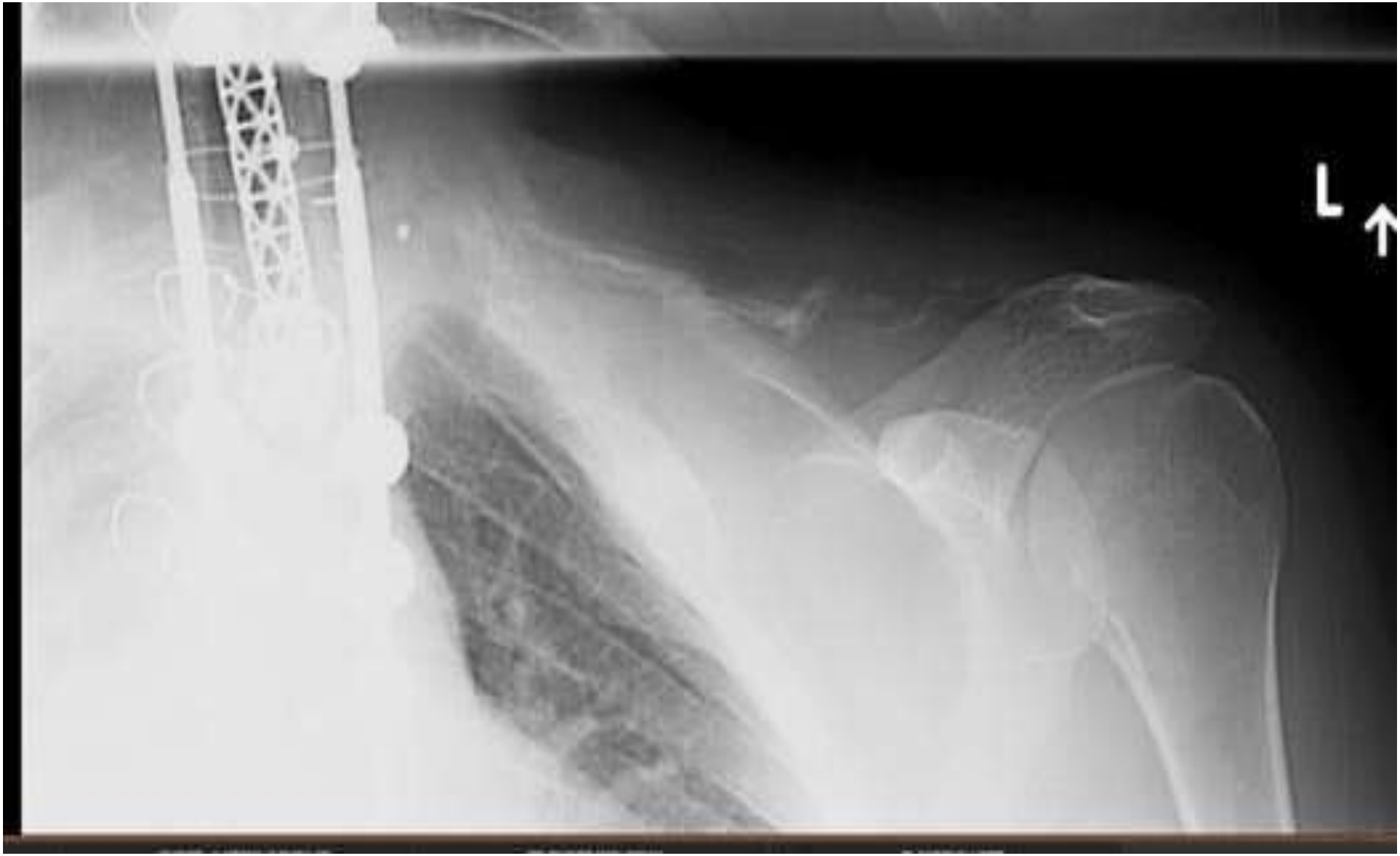
Recent MRI:
1. Heterogeneous enhancing calvarium compatible with known multiple myeloma.
2. 1.7 cm expansile pituitary intrasellar mass with moderate mass effect on the optic chiasm c/w pituitary macroadenoma.

SB 6057
(2 slides)

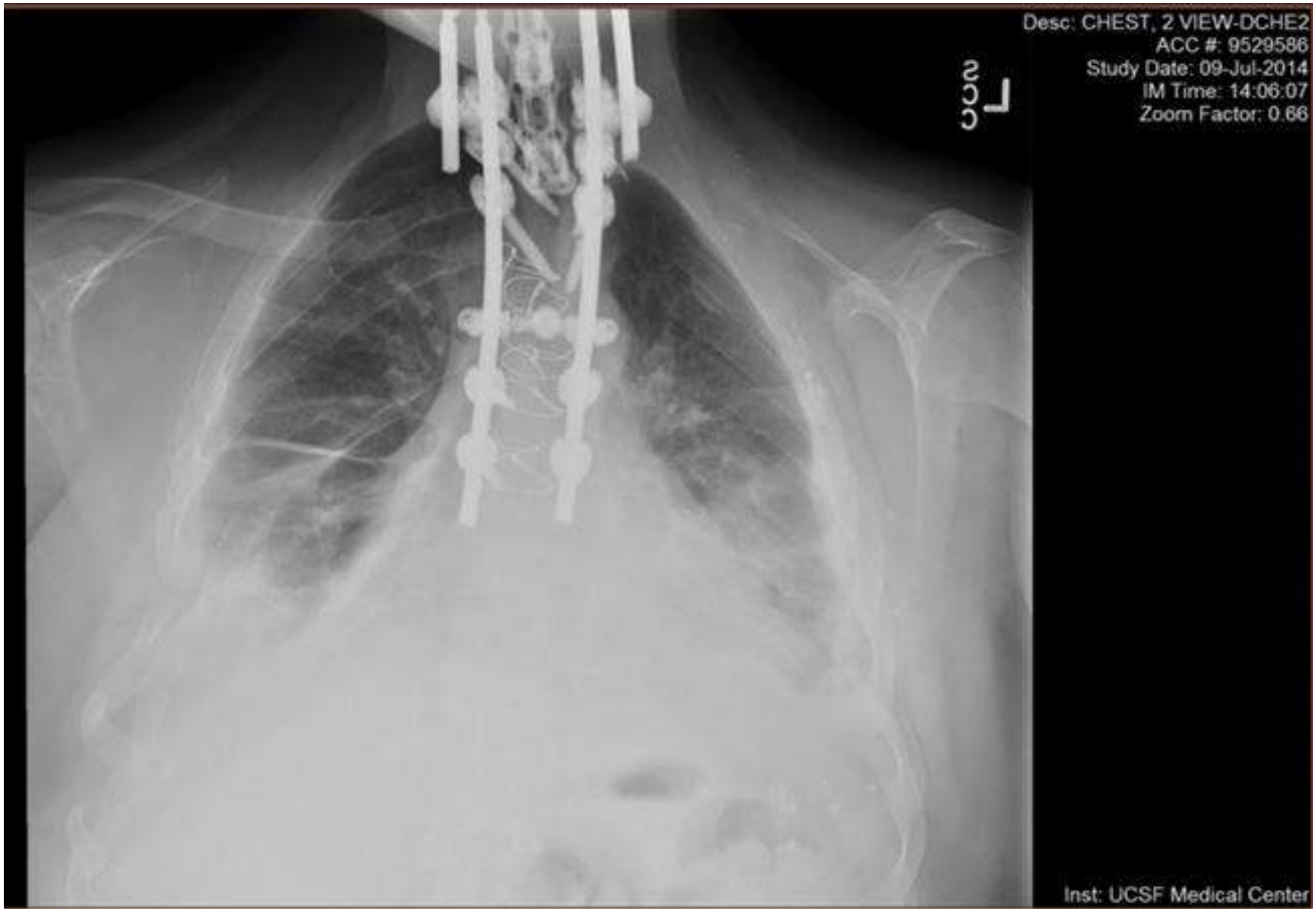
Emily Chan/Andrew Horvai; UCSF

25-year-old man with multiple lymphangiomas who died from complications of aspiration pneumonia in the setting of small thorax due to chronic compression fractures.

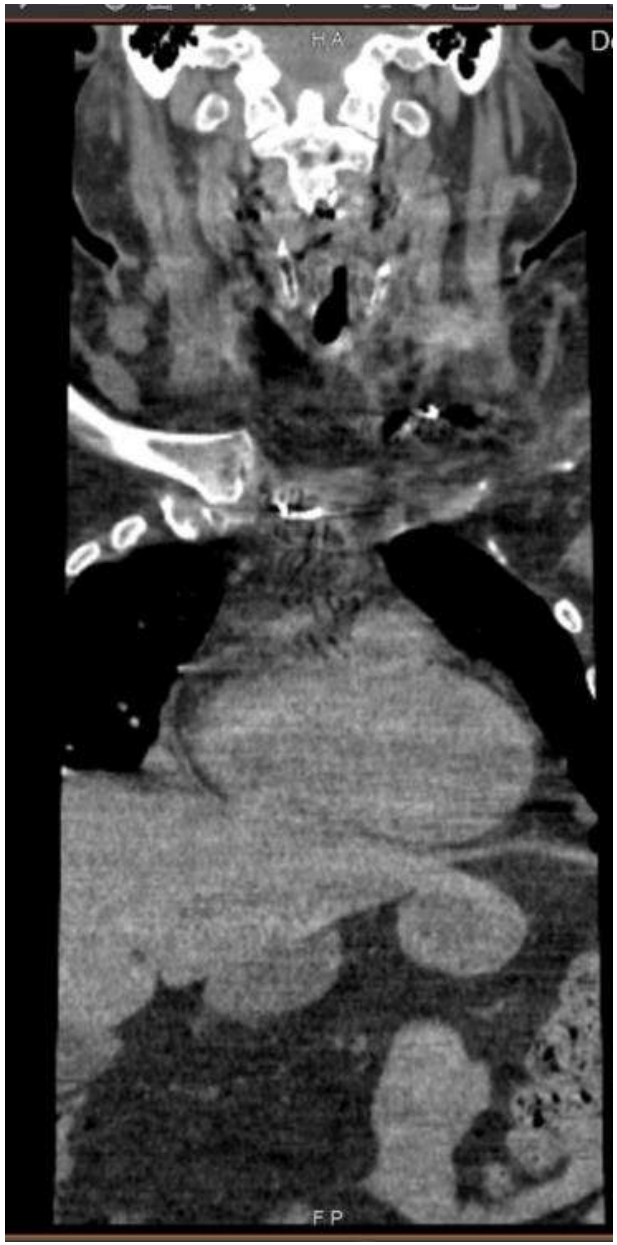
AP Shoulder 6/2010

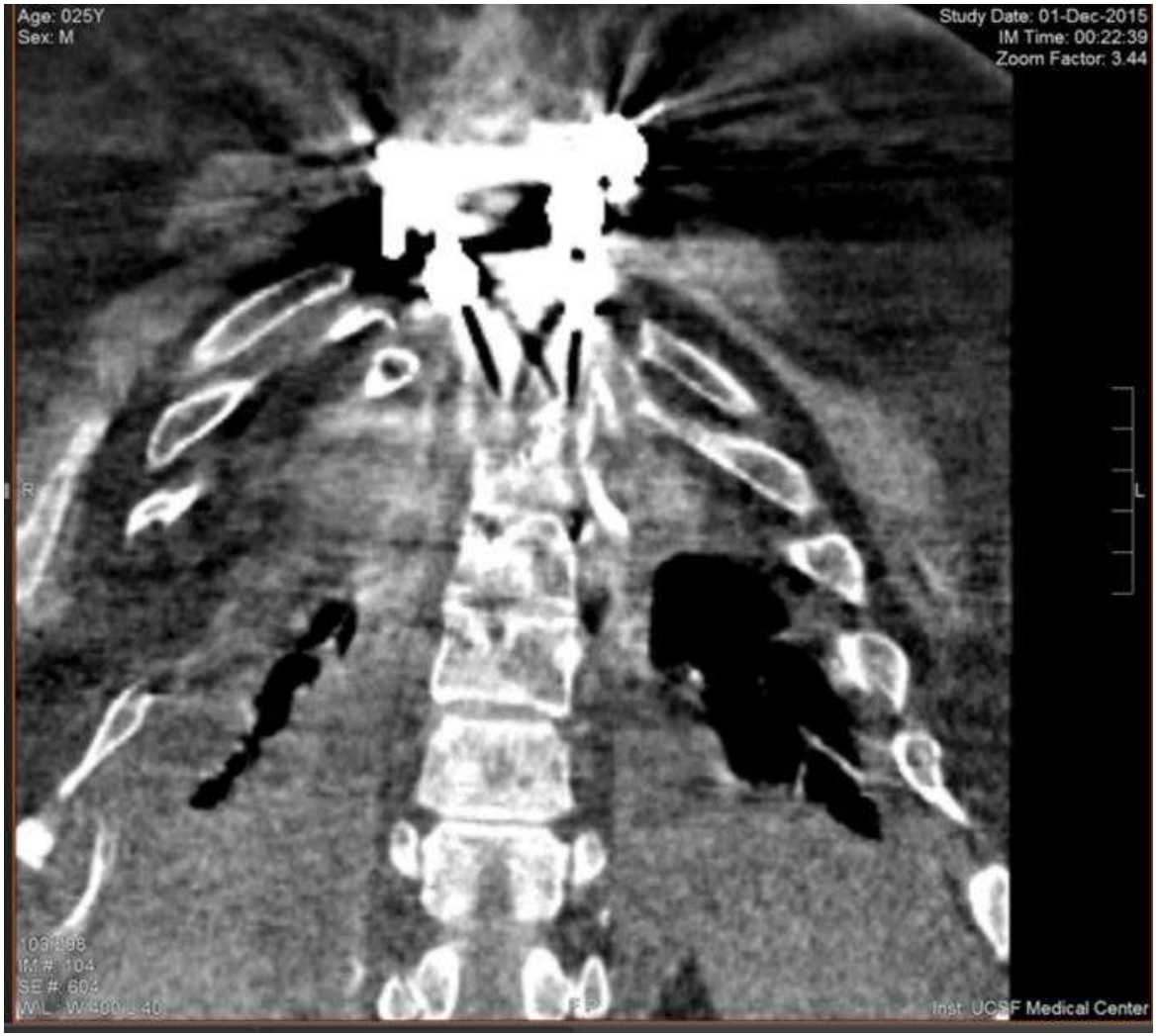


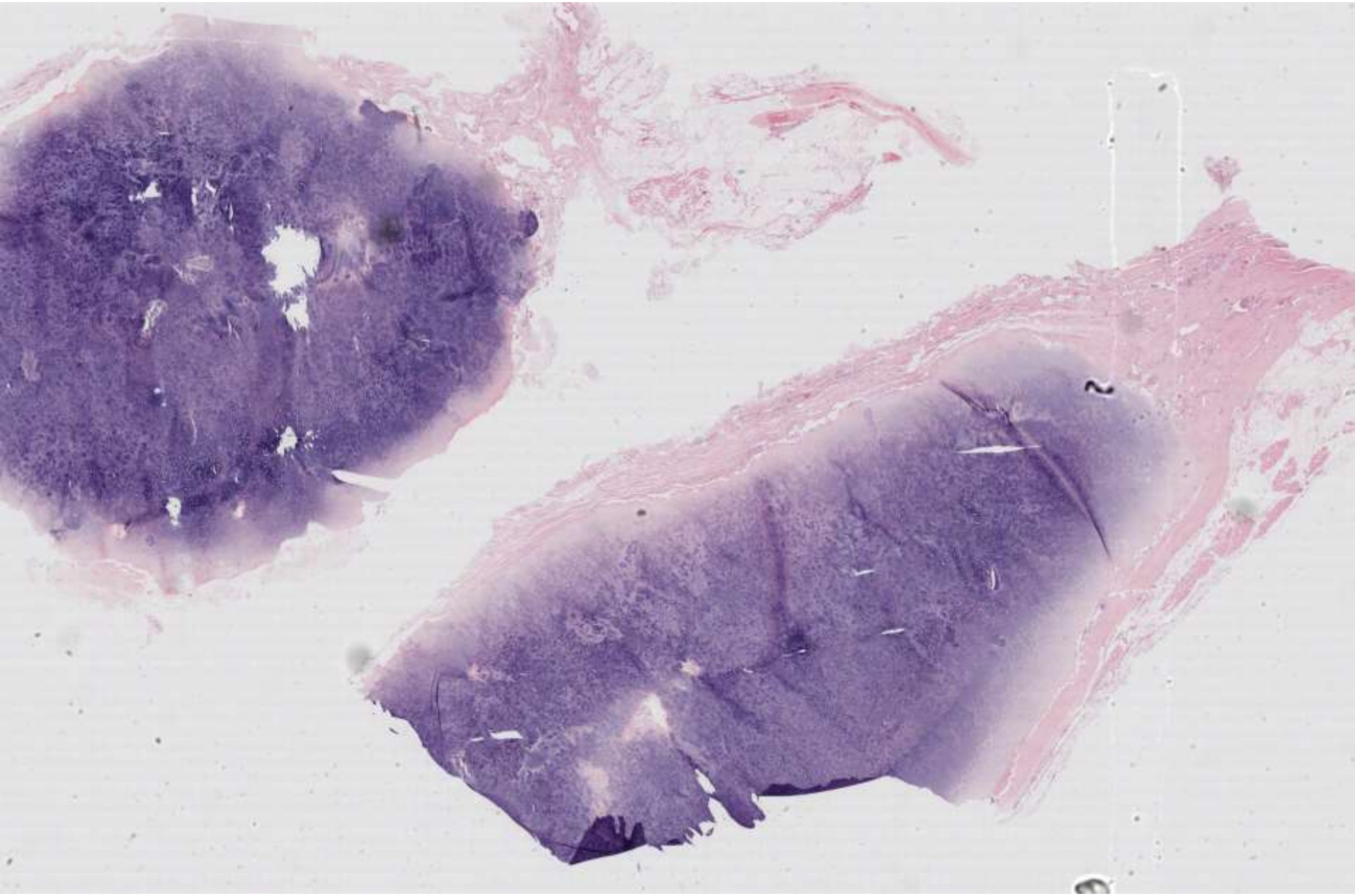
AP Chest Film 6/2014

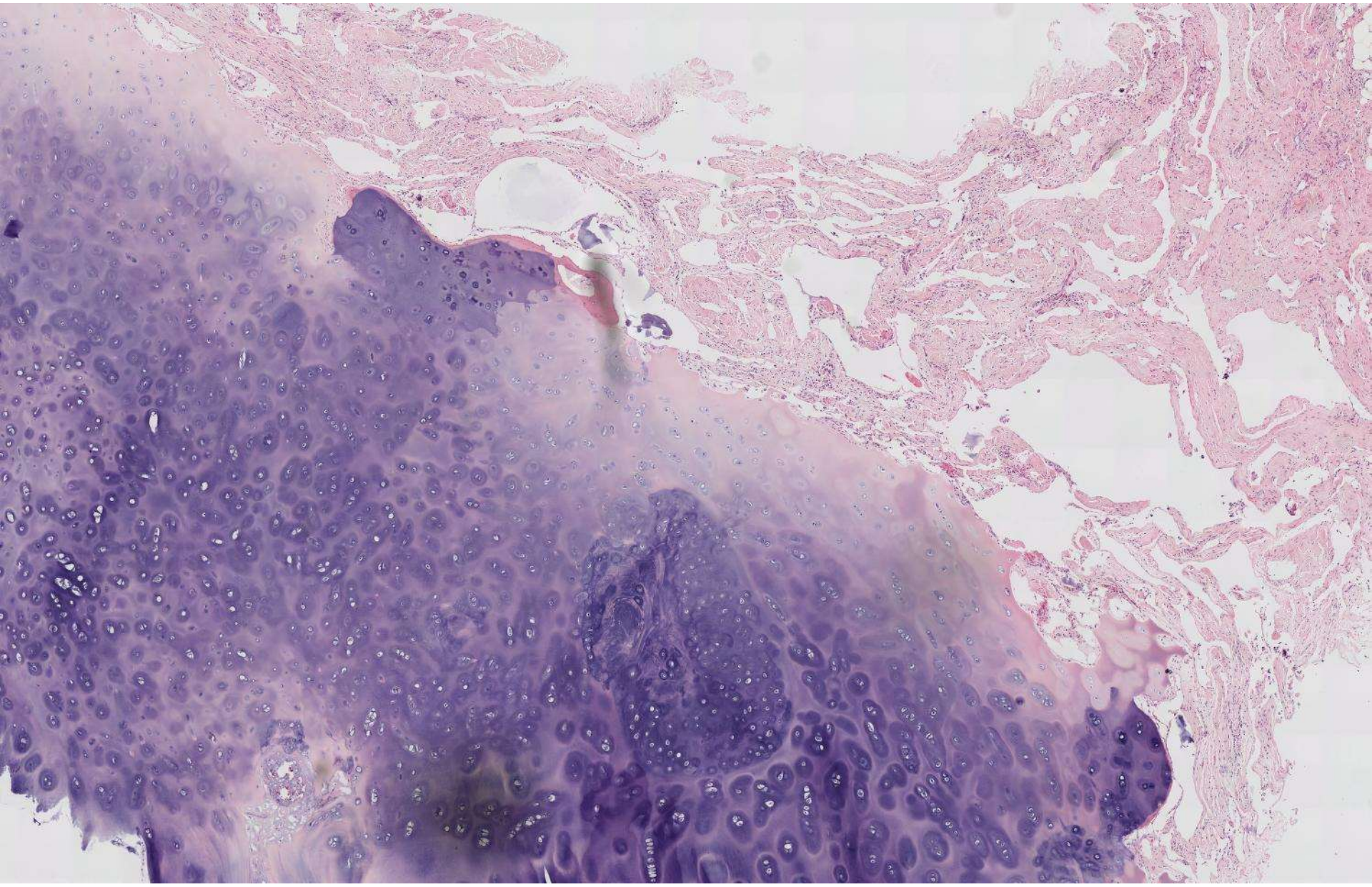


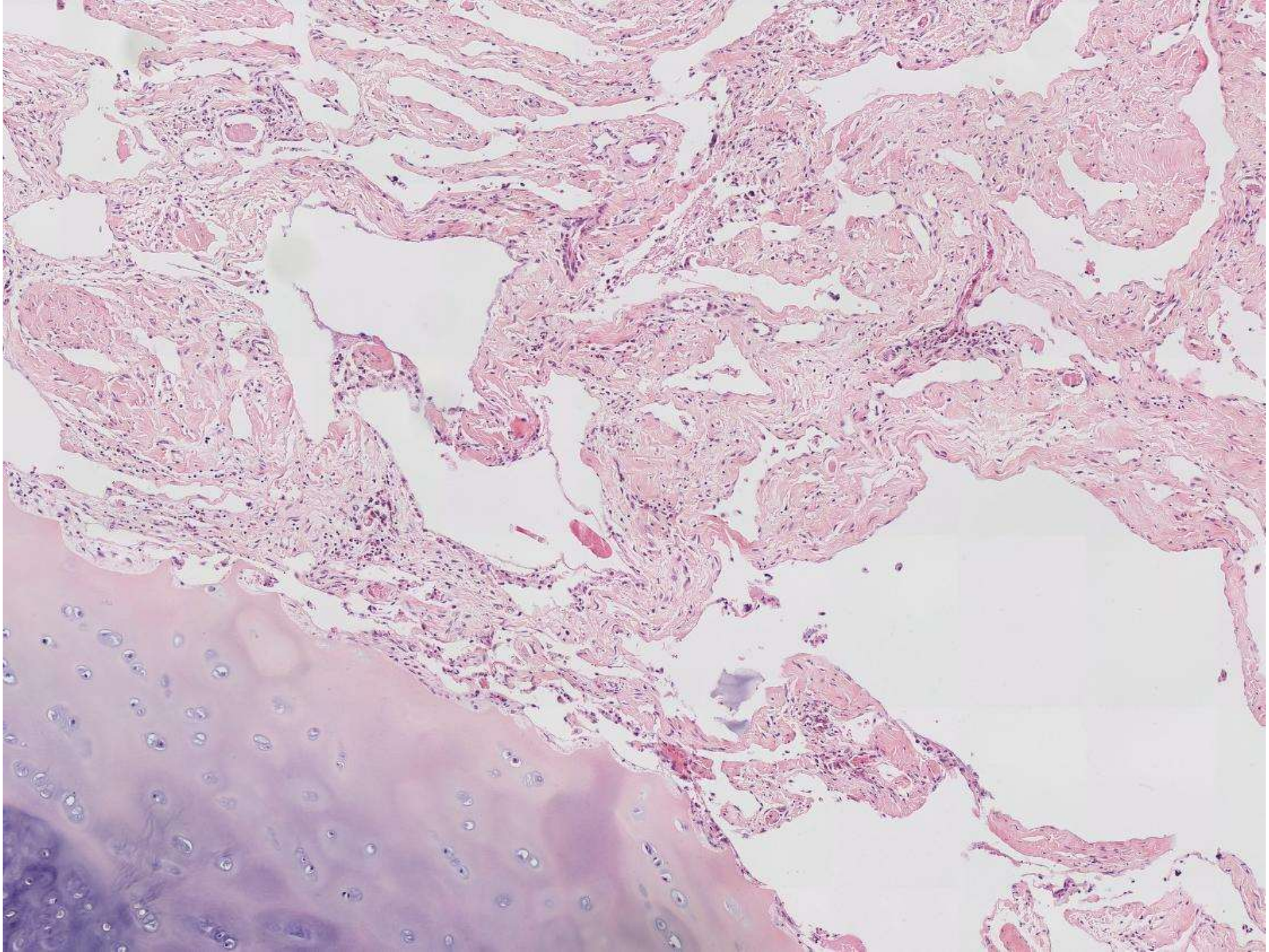
Coronal CT 12/1/15

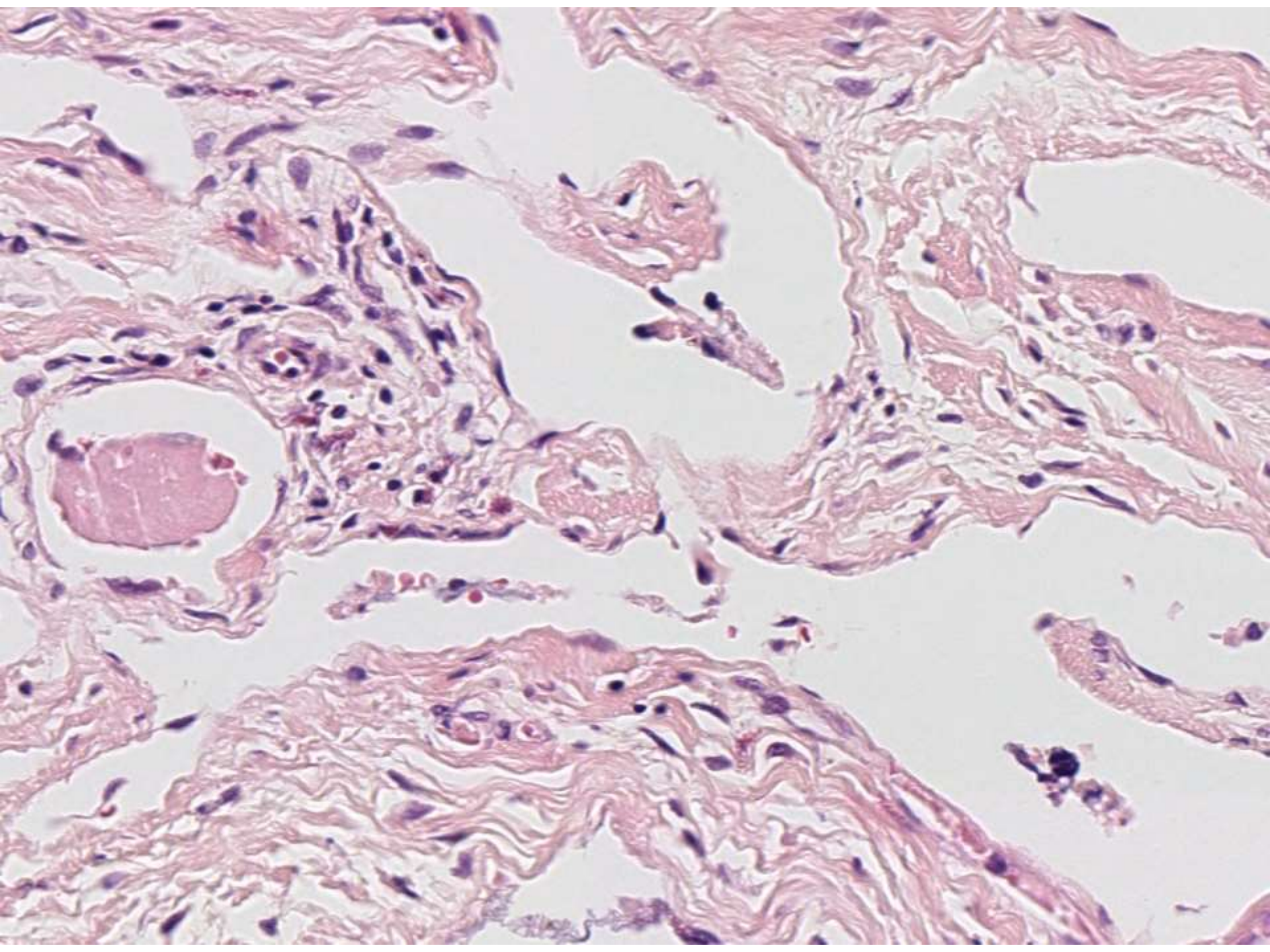


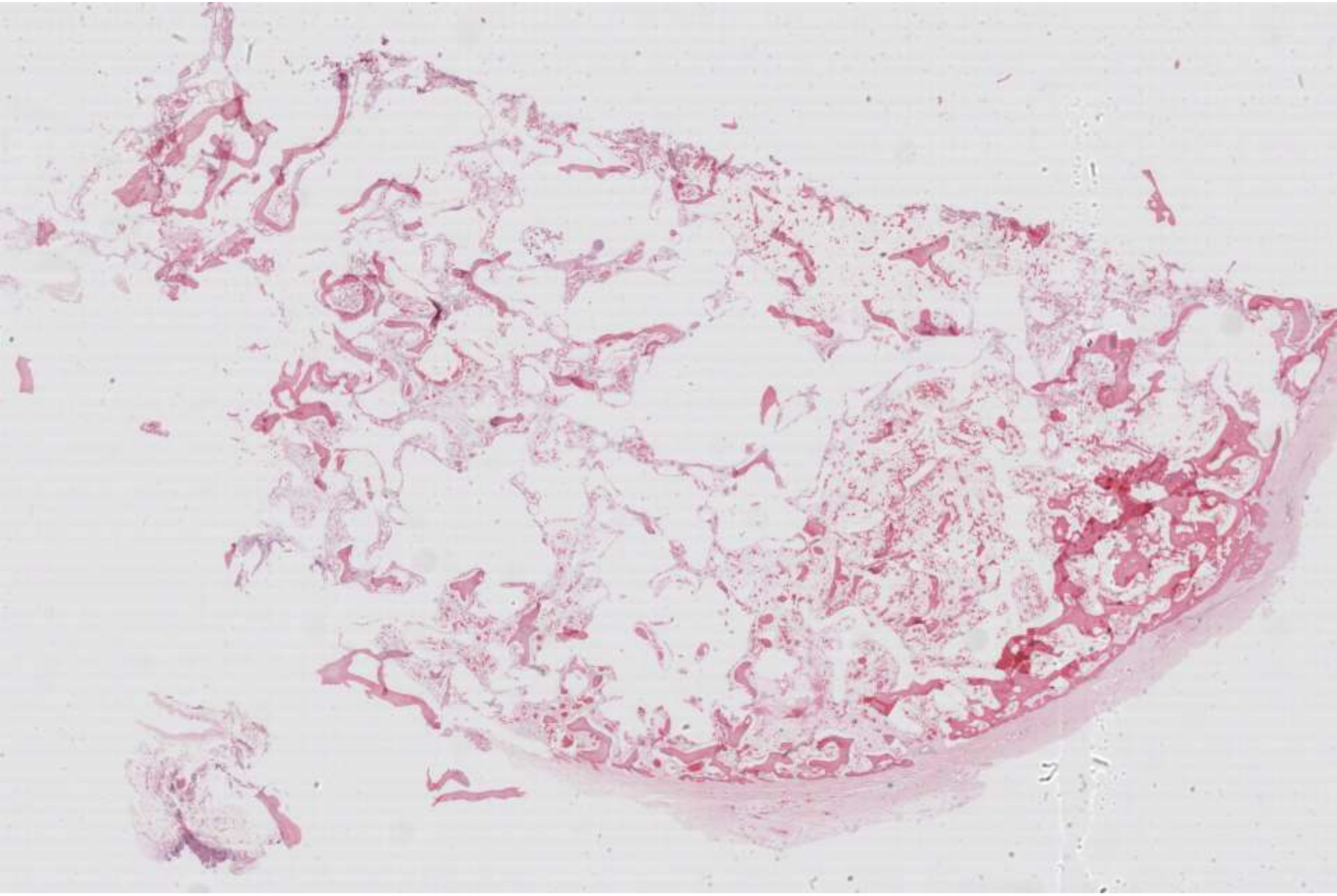


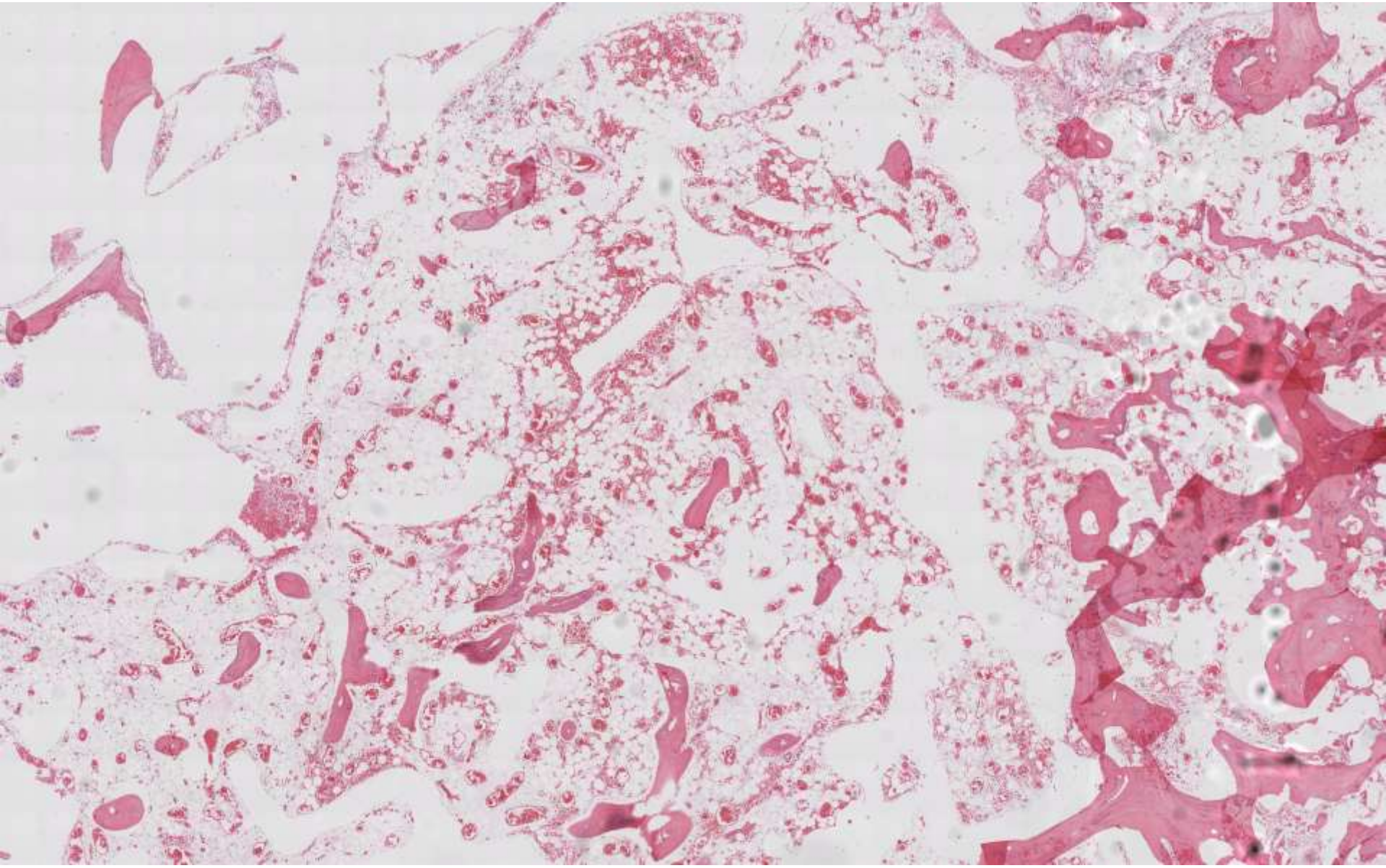


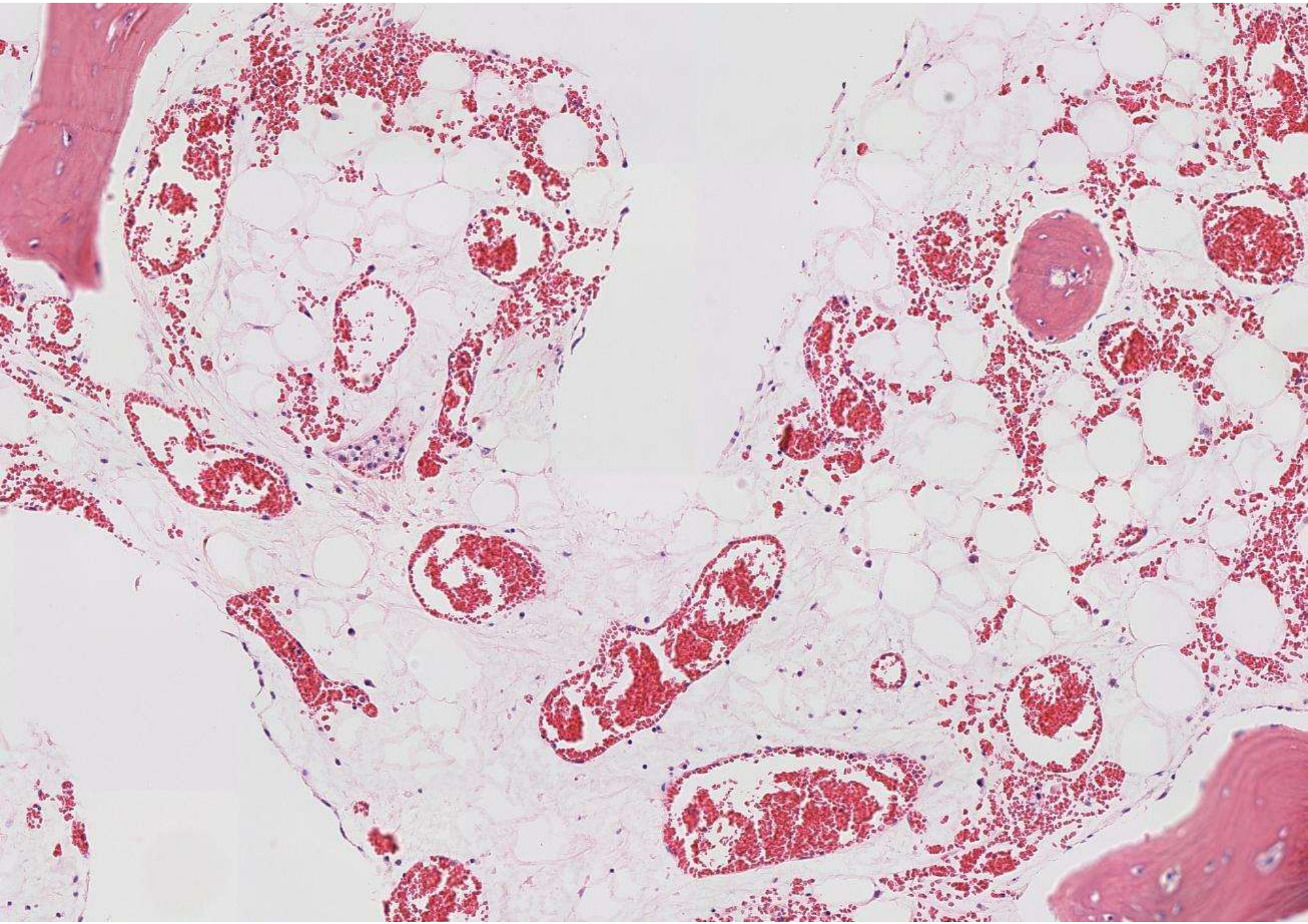


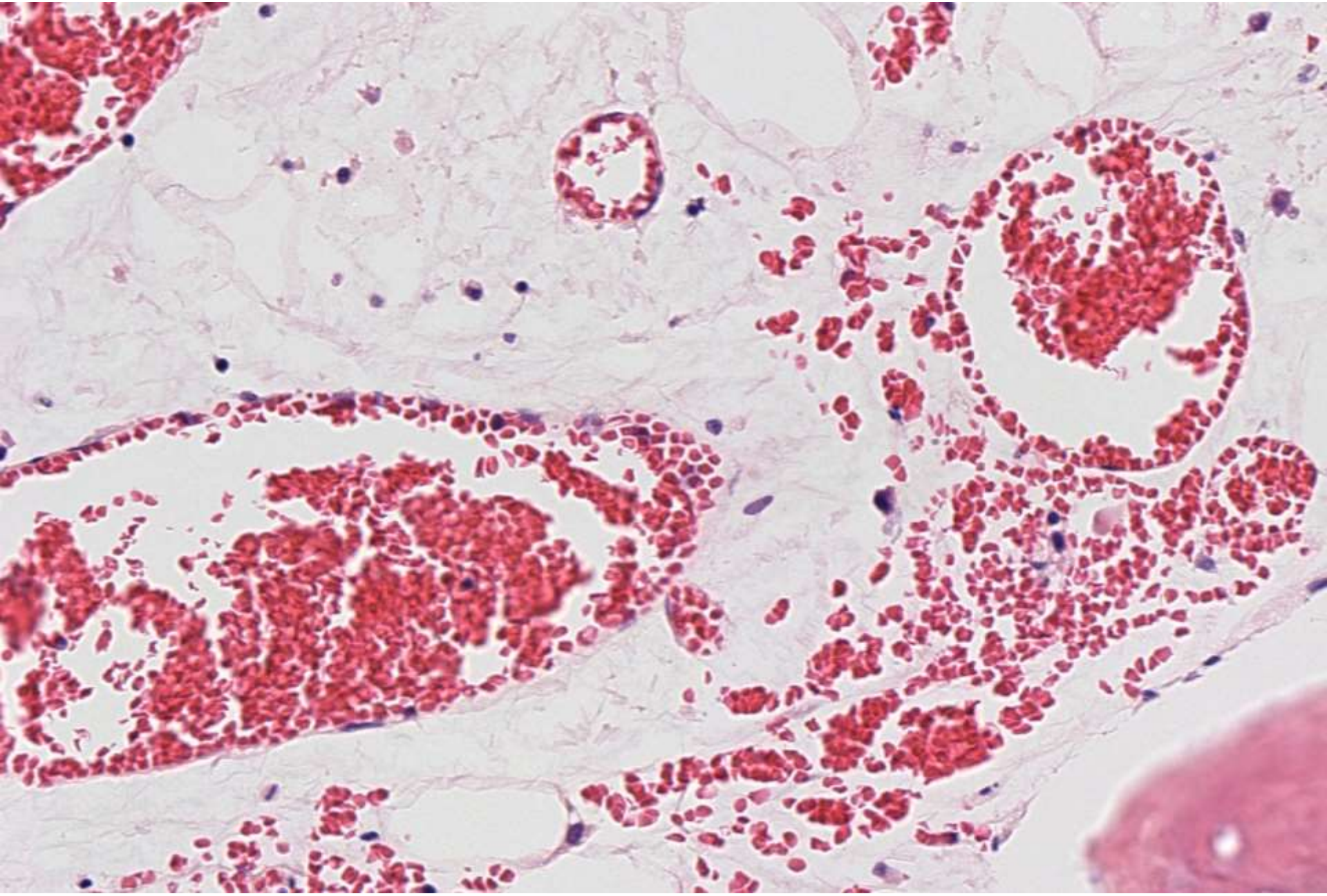


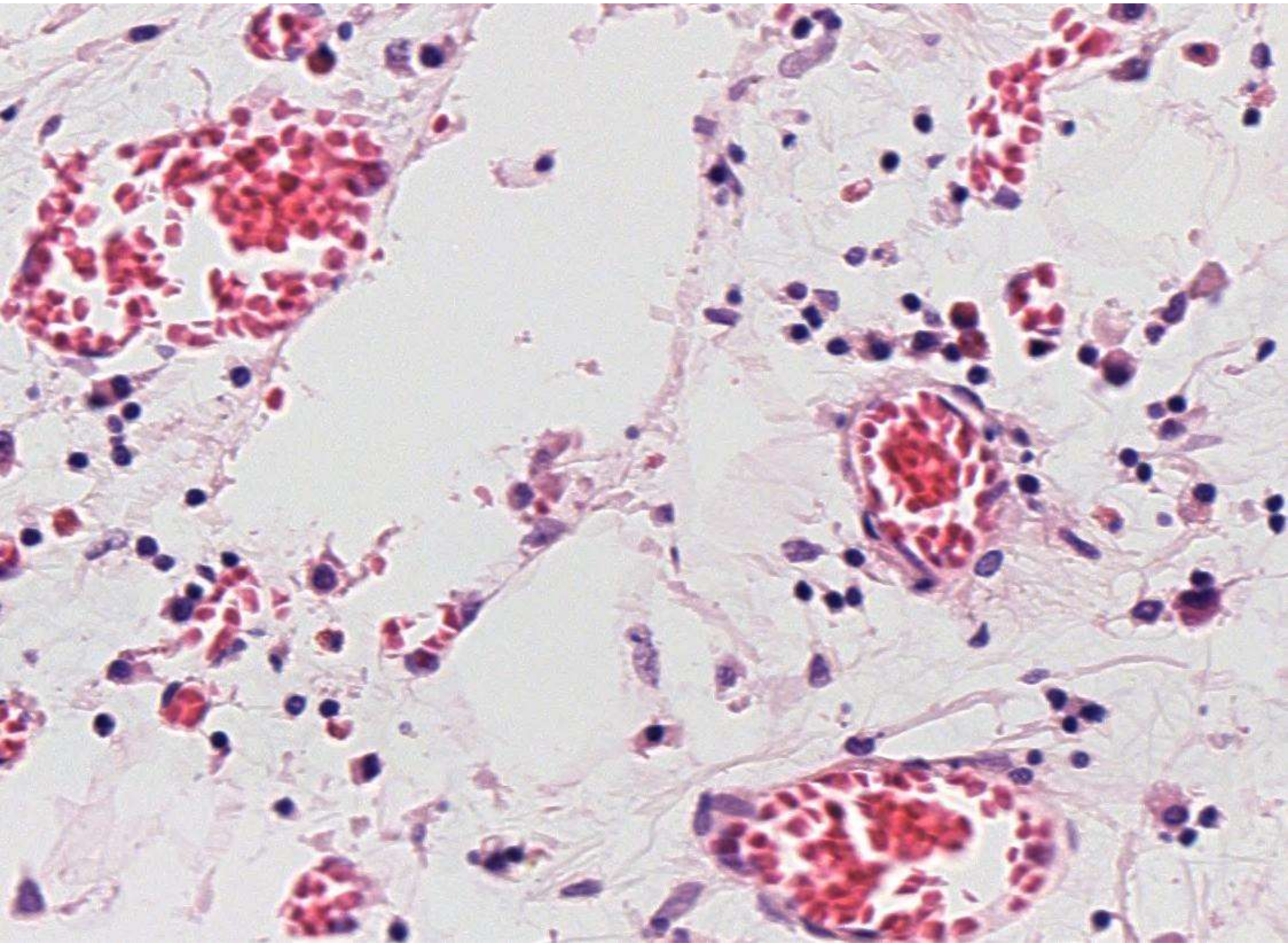












DIAGNOSIS?

South Bay Presentation

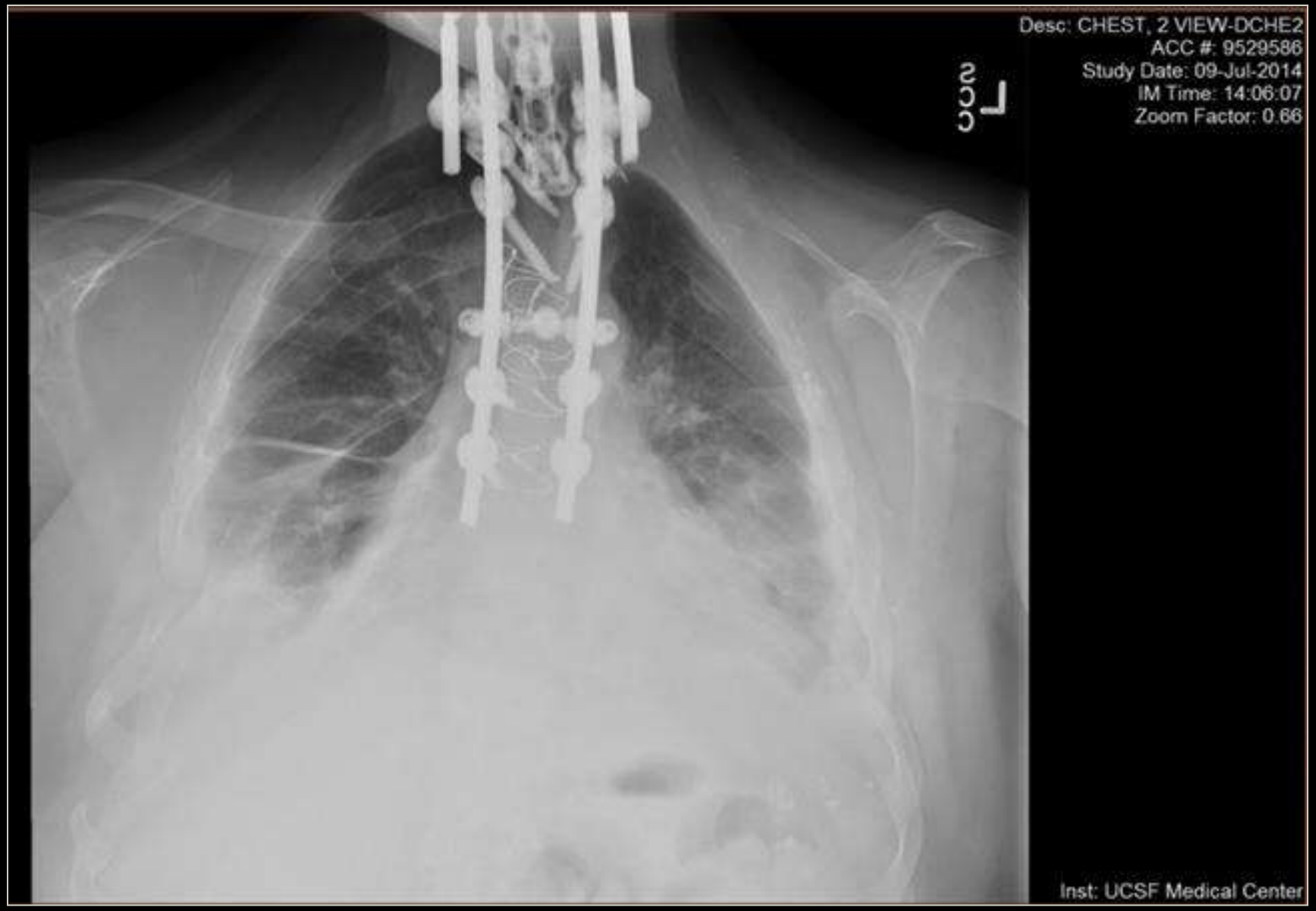
June 6, 2016

Emily Chan, PGY1
Dr. Andrew Horvai (Faculty Sponsor)
UCSF

Patient history

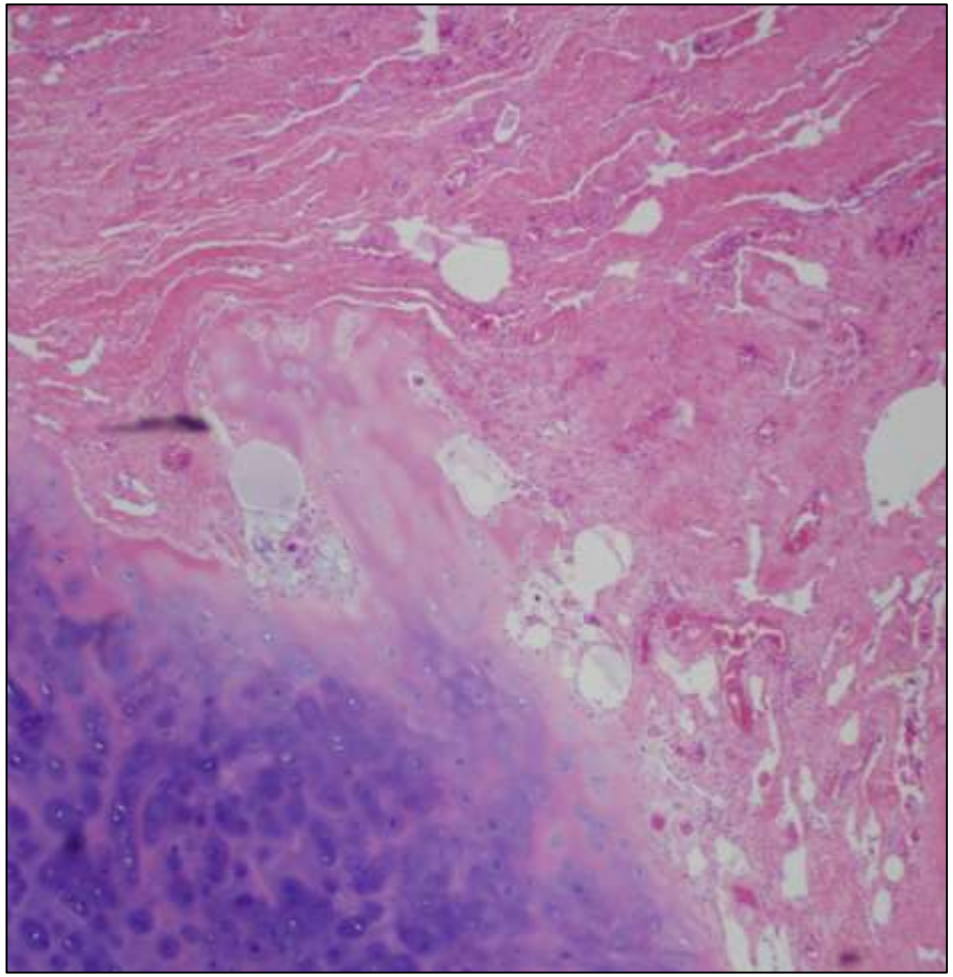
- 25 year old man
- Removal of multiple “hemangiomas” from spine in Mexico at age 13
- Reconstructions and complex spinal surgeries involving C3-T9 from ages 13-23
- Chronic pleural effusions and chylothorax
- Aspiration pneumonia, deceased

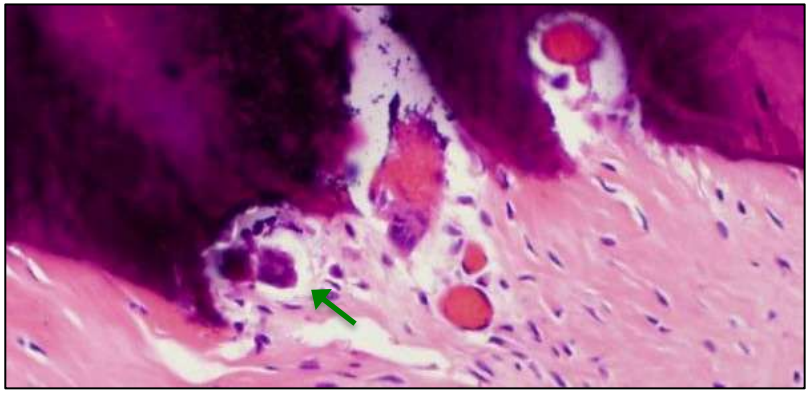
AP Chest Film 6/2014

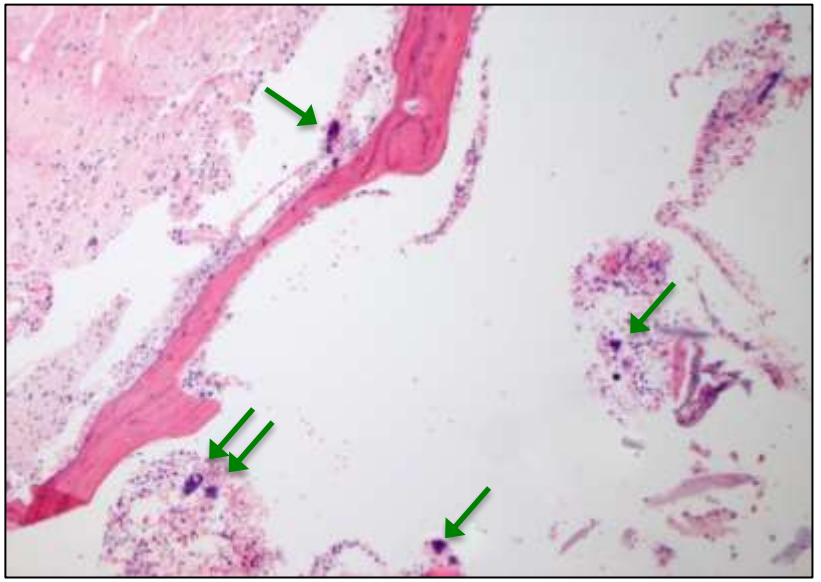


Histology

- Vascular malformation involving bone and cartilage, with bone showing resorption

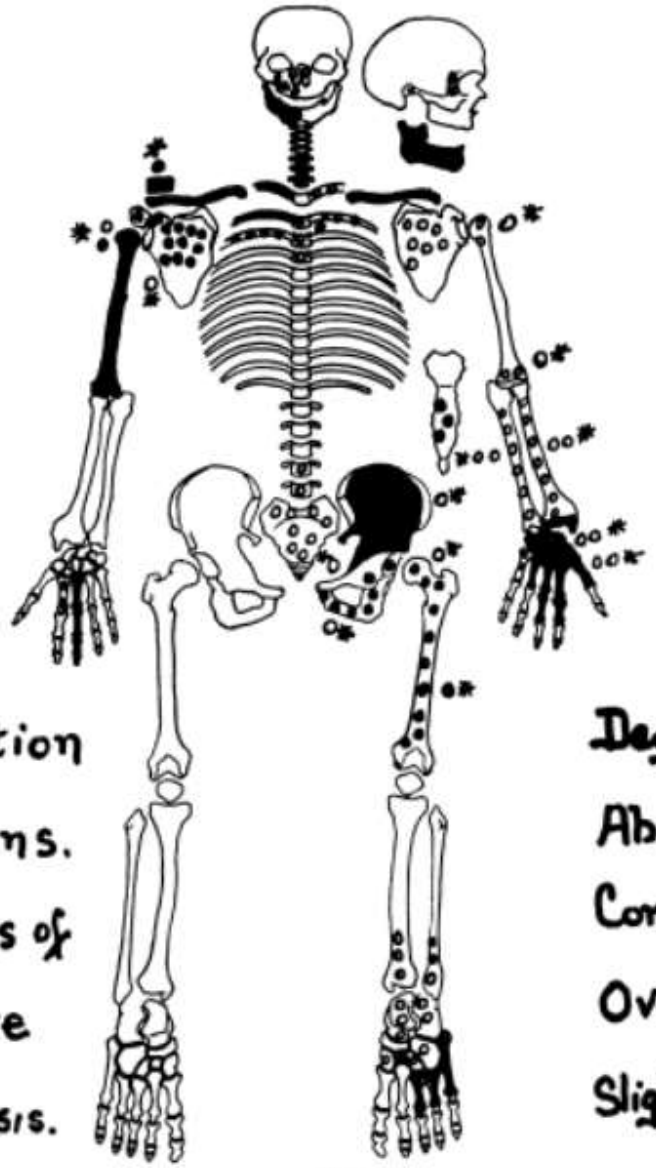






Diagnosis: Gorham Stout Disease

- **Synonym**: Massive osteolysis
- **Clinical**
  - ~200 cases reported worldwide
  - Children and young adults <40 years
  - Pain/swelling/path Fx over affected bones
  - Loose teeth, meningitis
  - Chylothorax, respiratory compromise
- **Pathology**:
  - Multiple bones with lymphatic malformations
  - Increased resorption of medulla and cortex
- **Pathogenesis**:
  - Unknown
  - Local ischemia from compression by lymphatics/slow blood flow promotes resorption?



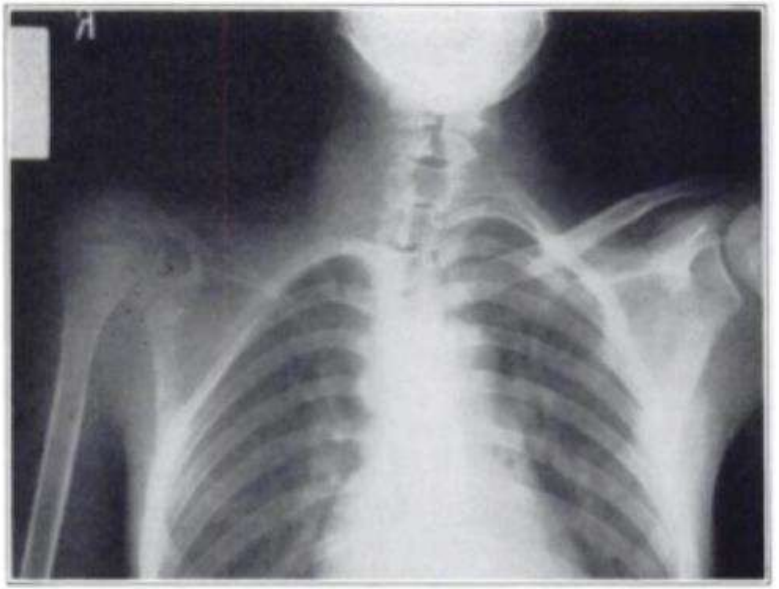
Distribution of lesions. 18 Cases of Massive Ostedysis.

Degree of Absorption

Complete 3+

Over 50% 2+

Slight-moderate 1+



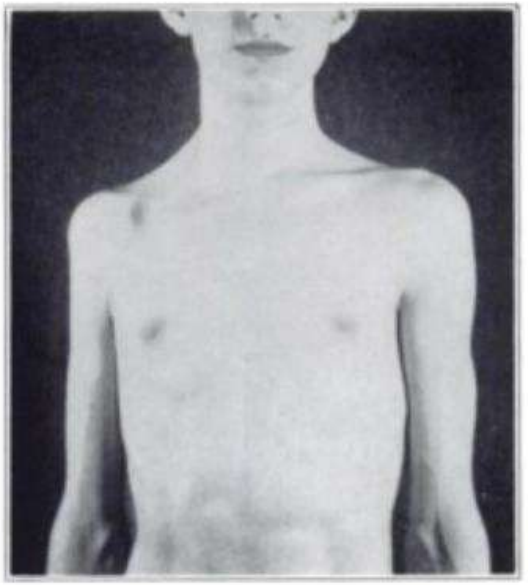
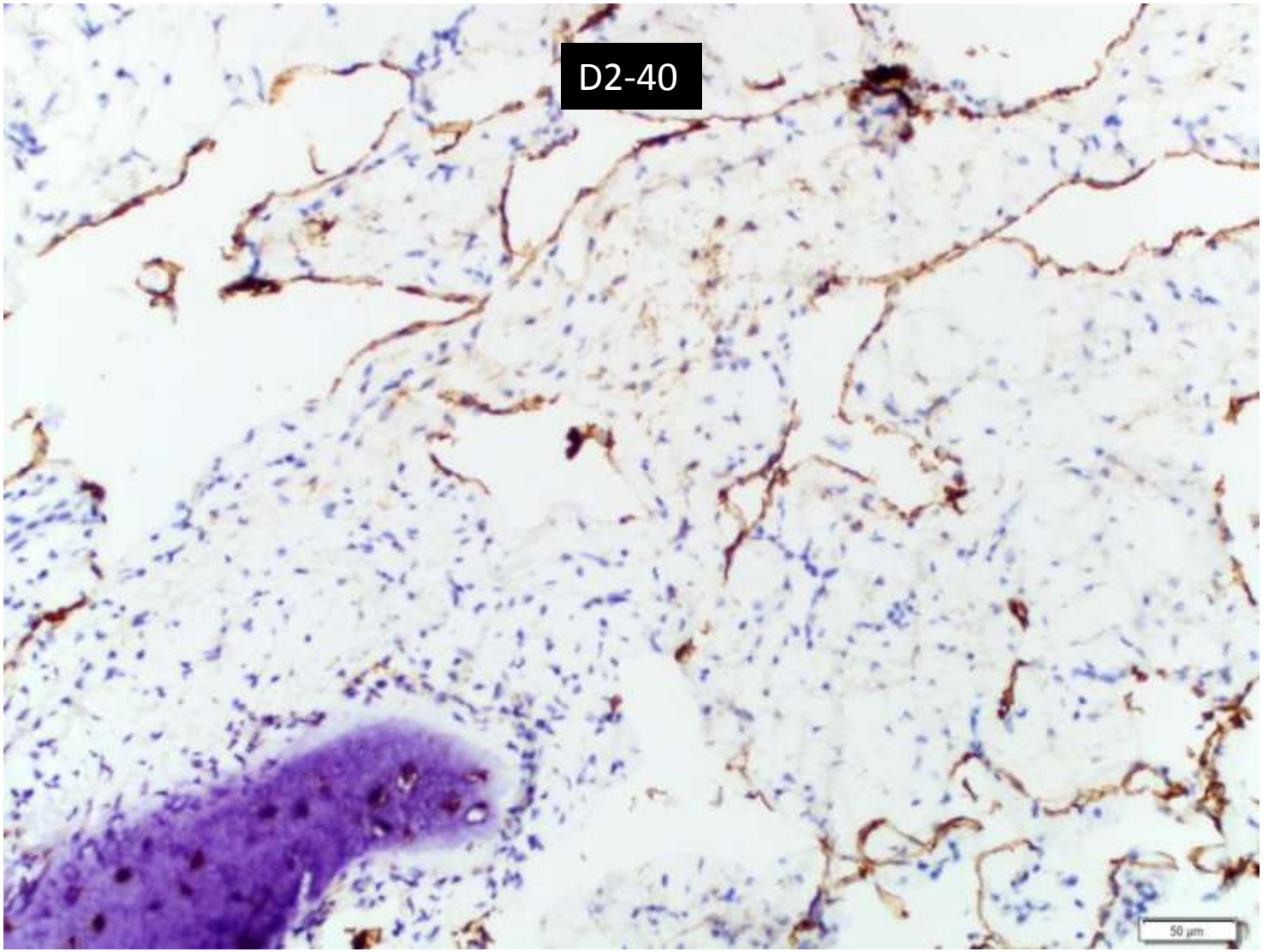


Fig. 1

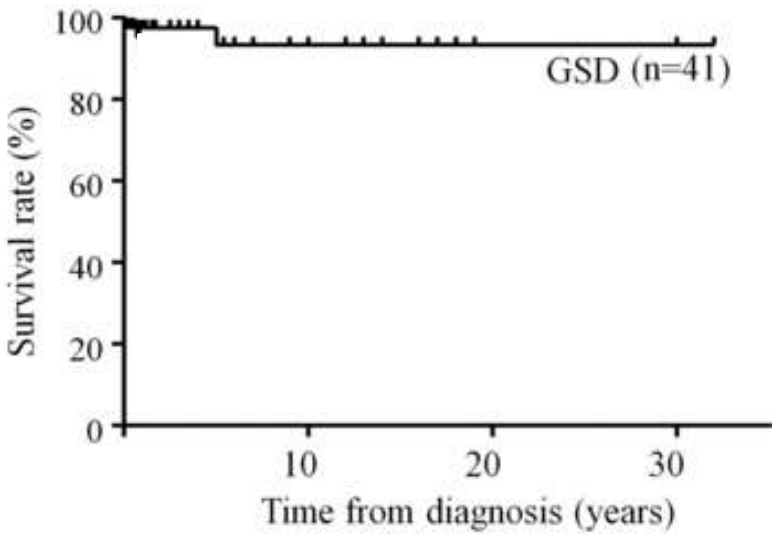
Gorham et al Am J Med, 1954

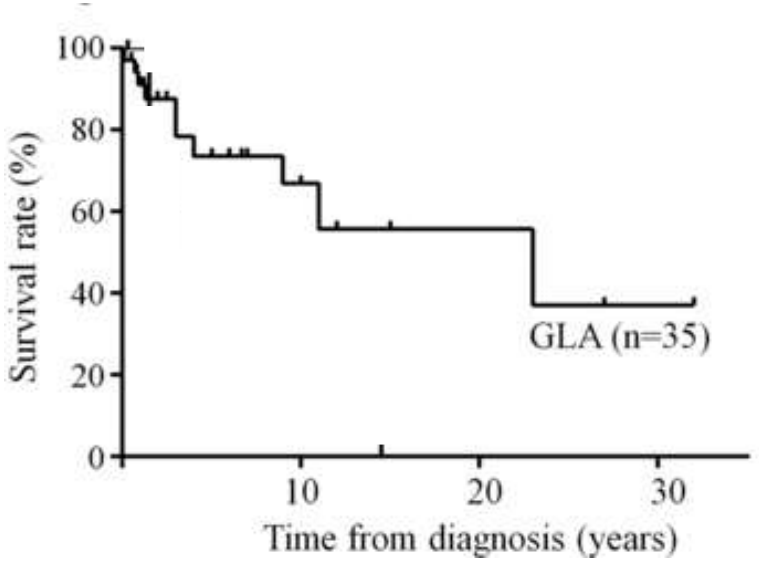
Lymphatic-type endothelium



Gorham Stout Disease vs Lymphangiomatosis

	Gorham Stout Disease	Lymphangiomatosis
Histopathology	Proliferation of thin-walled anastomosing lymphatic vessels	
Predominant radiographic findings	Lytic lesions and resorption of cortical bone	Diffuse involvement of soft tissue, viscera, or bone. Lytic areas confined to medullary bone





Modified from Ozeki et al Pediatr Blood Cancer 2016

Treatment and Prognosis

- No standard therapy
  - Radiation and surgery
  - Bisphosphonates
  - Alpha-2b interferon
  - Thoracic duct ligation for chylothorax
- Prognosis unpredictable
- Early recognition and treatment key!

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- Patel DV, Gorham's disease or massive osteolysis. Clin Med Res. 2005 May;3(2):65-74
- Tie et al, Chylothorax in Gorhams syndrome. A common complication of a rare disease. Chest. 1994 105(1):208-13.
- Hirayama, et al, Cellular and humoral mechanisms of osteoclast formation and bone resorption in Gorham-Stout disease. J Pathol 2001; 195: 624-530.
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- Saify and Gosavi, Gorham's disease: A diagnostic challenge. J Oral Maxillofac Pathol. 2014 18(3):411-4.
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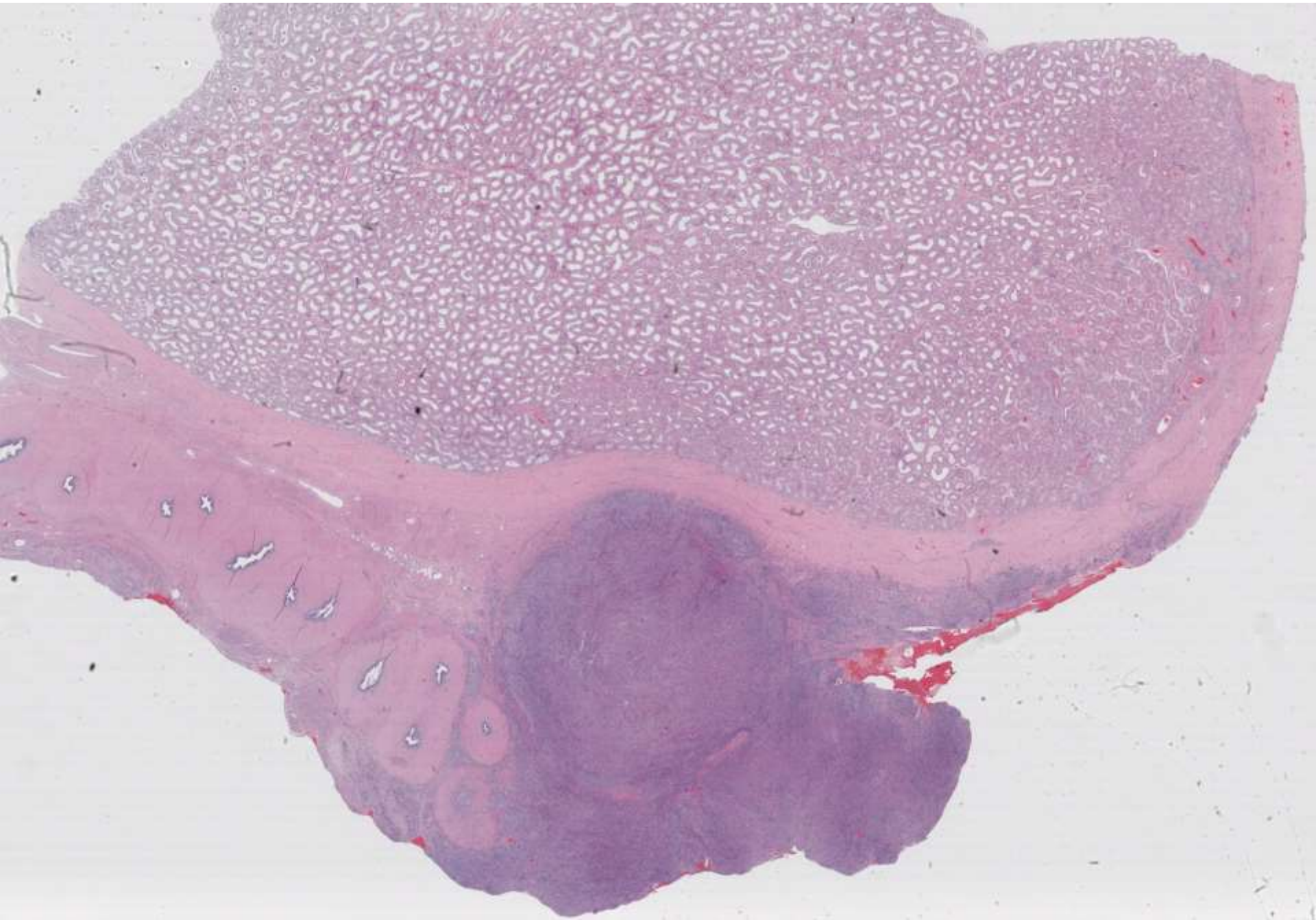
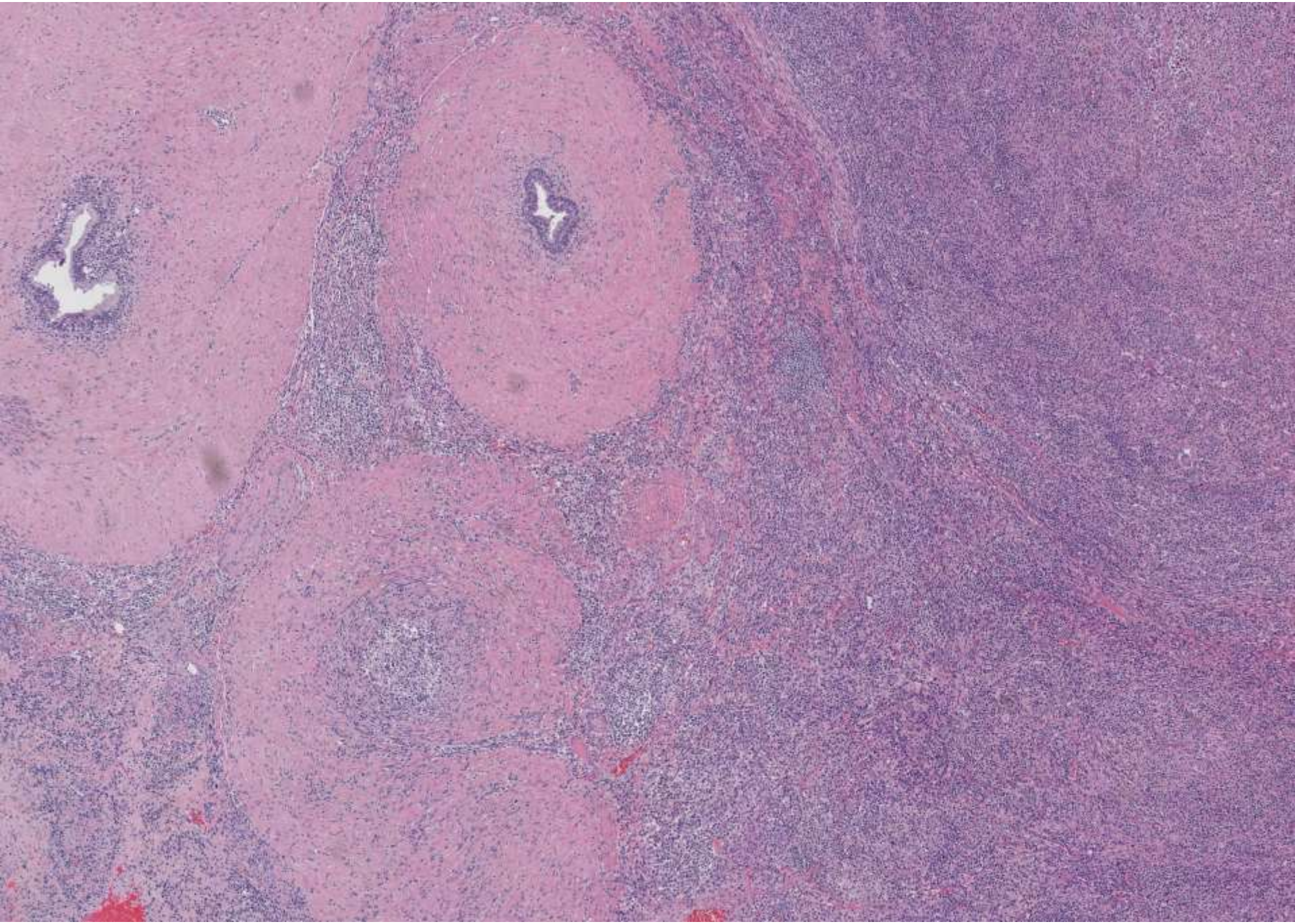
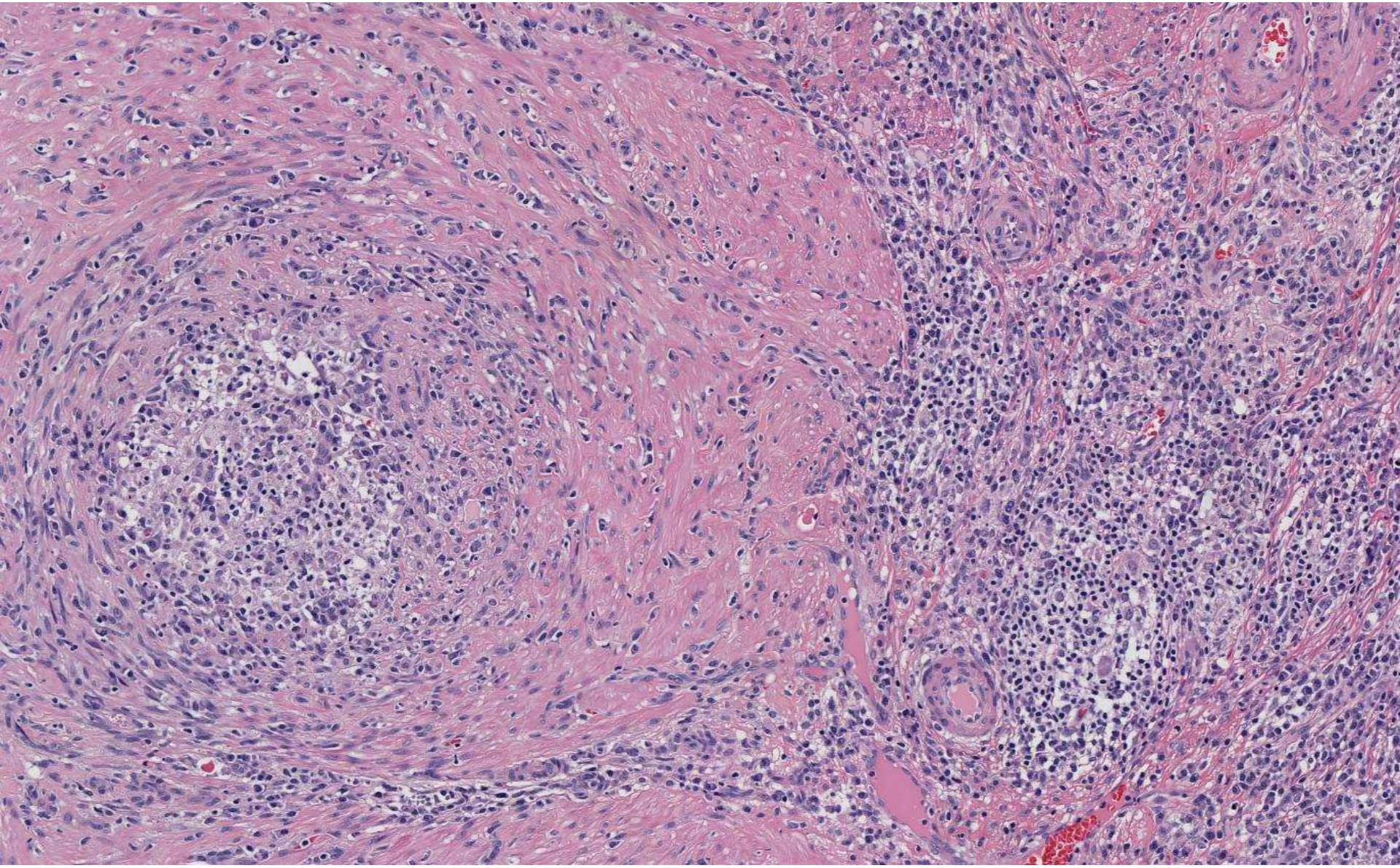
SB 6058

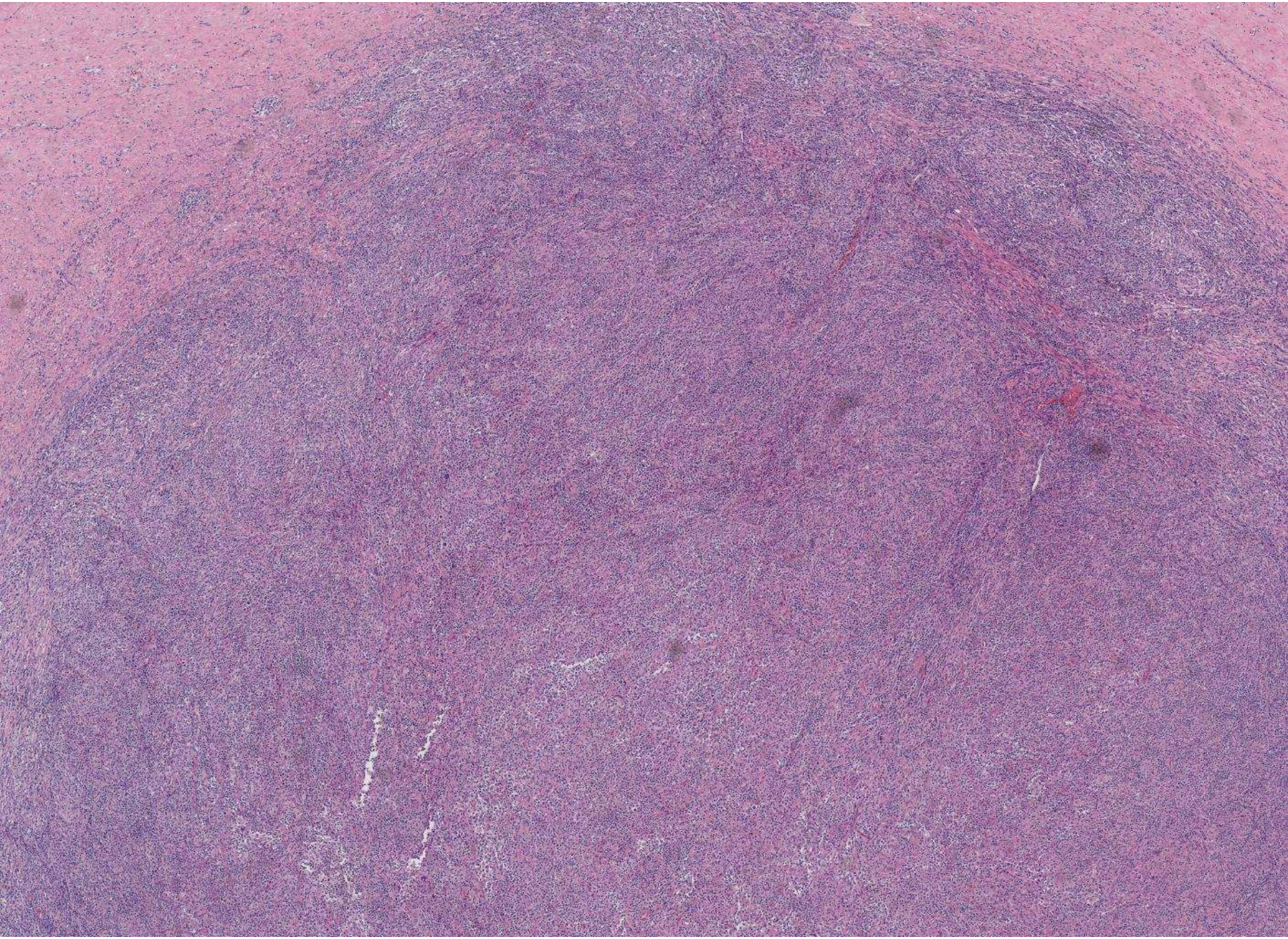
Sunny Kao; Stanford

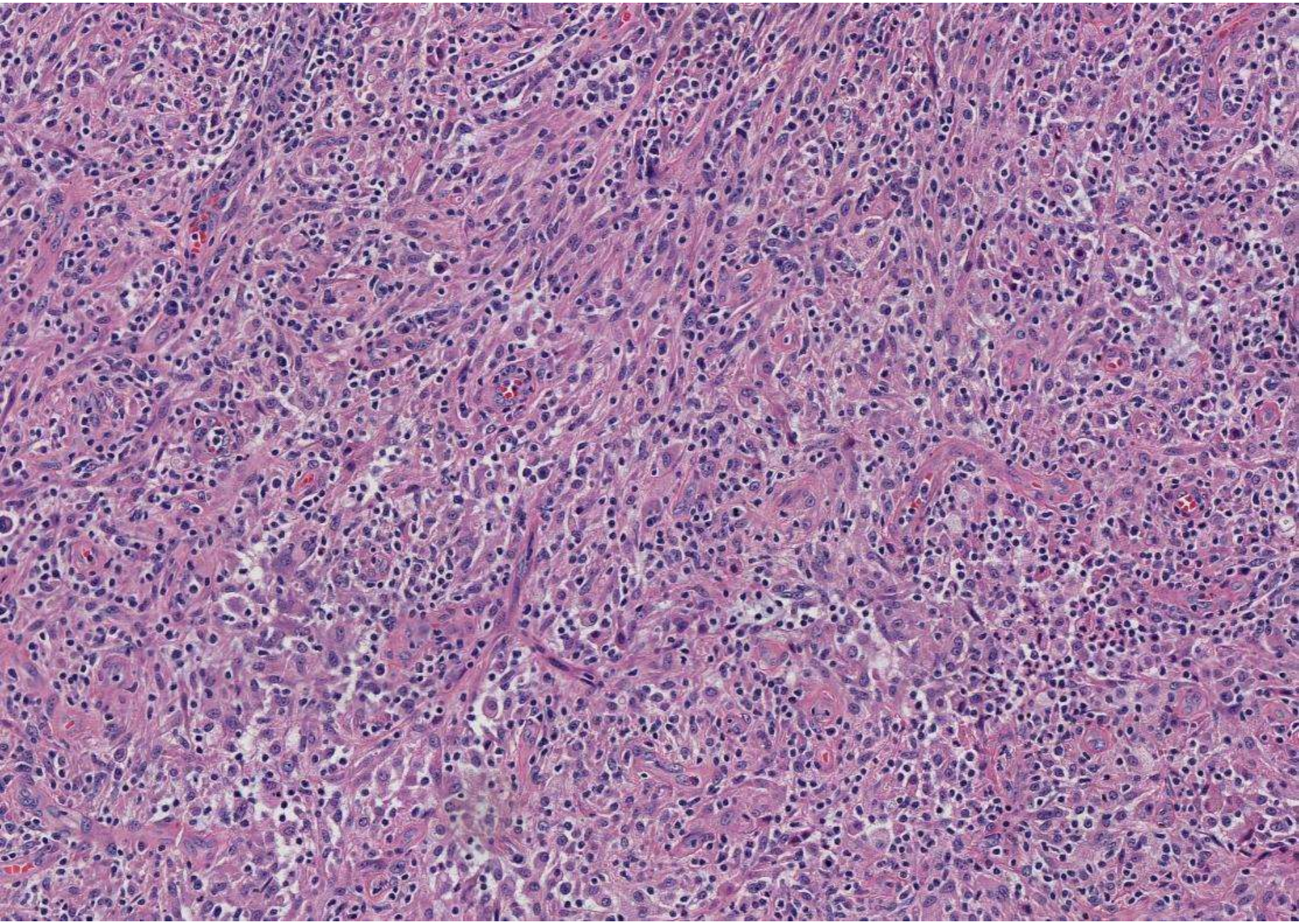
80-year-old man with right testicular tumor.

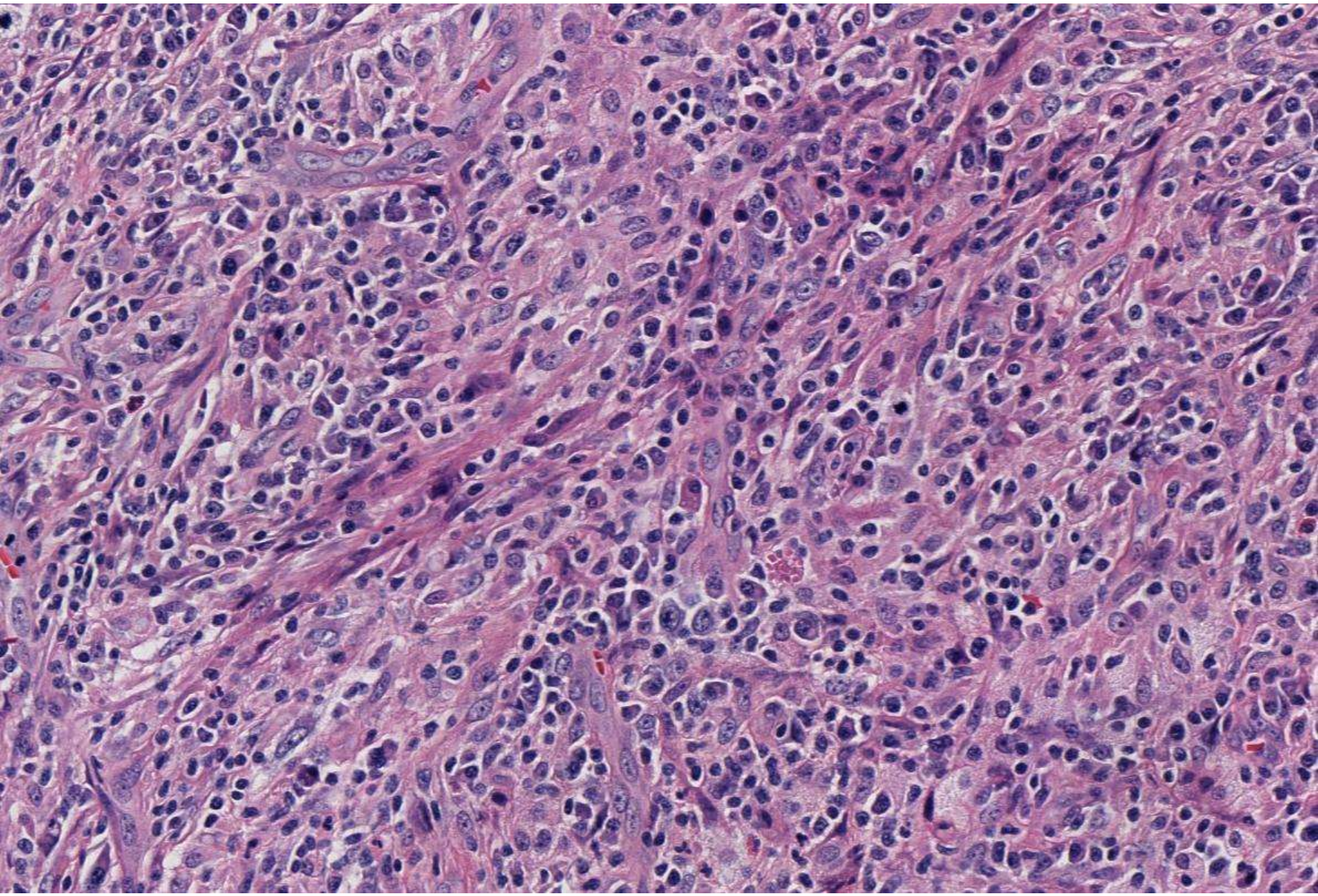


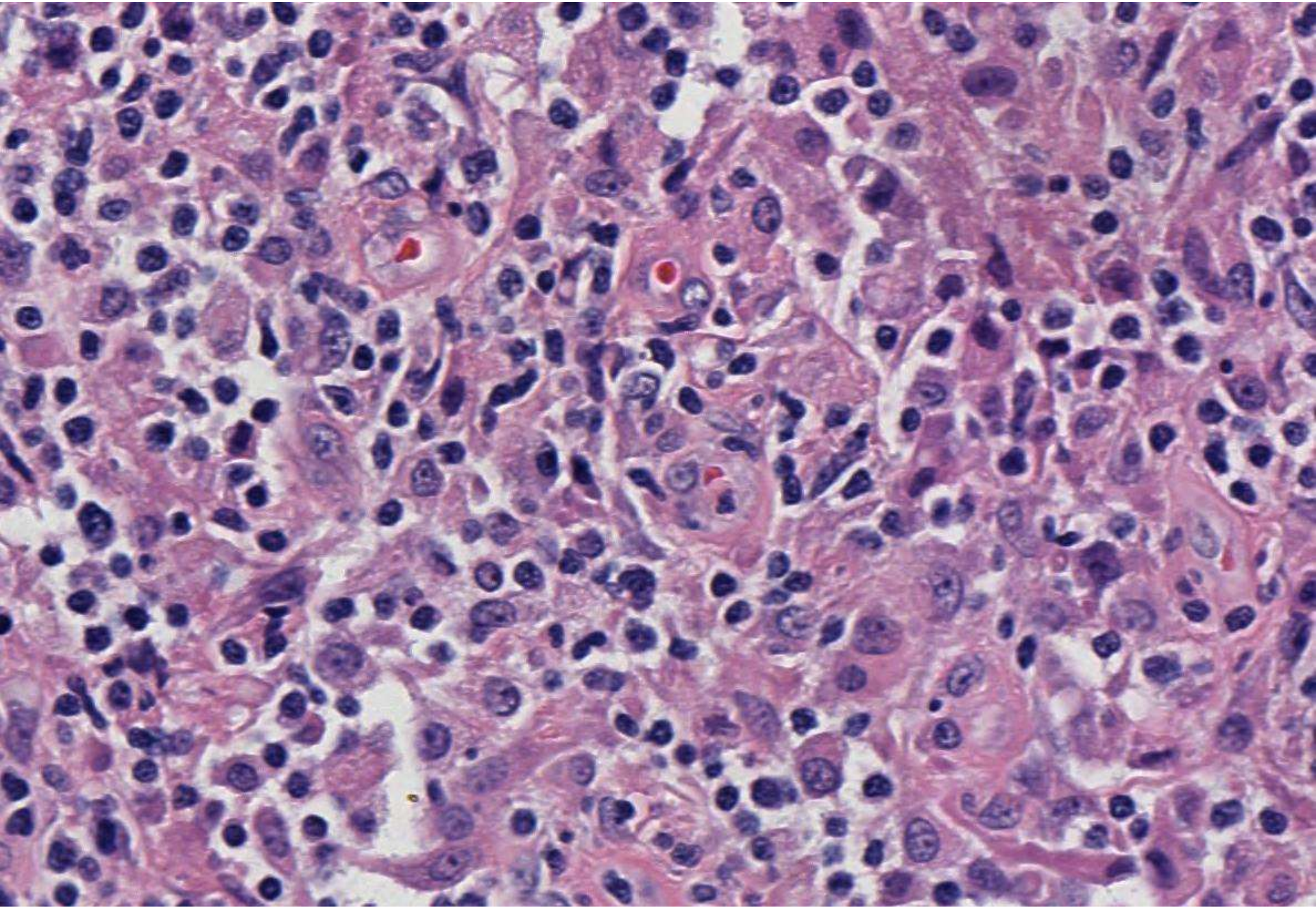


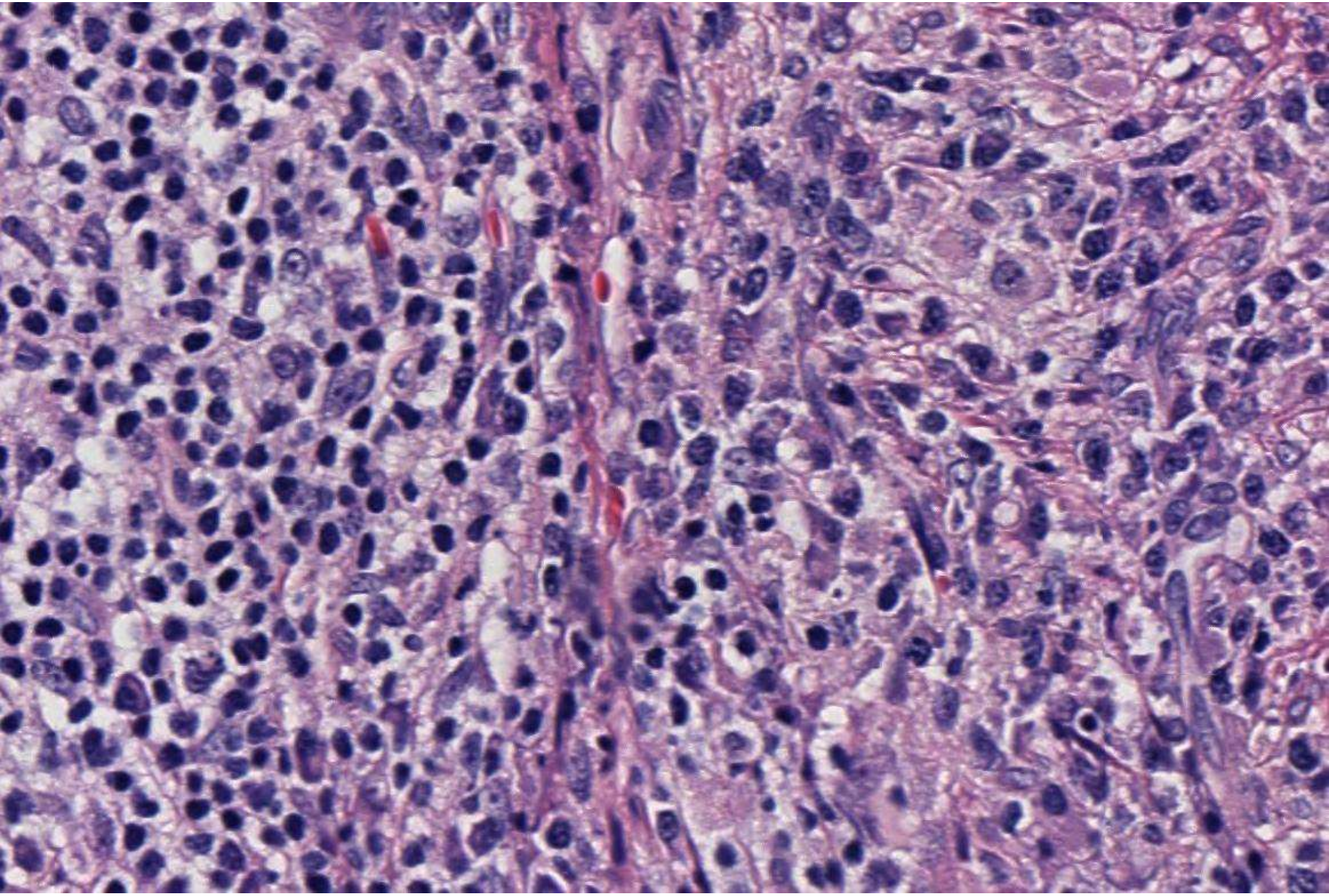












DIAGNOSIS?

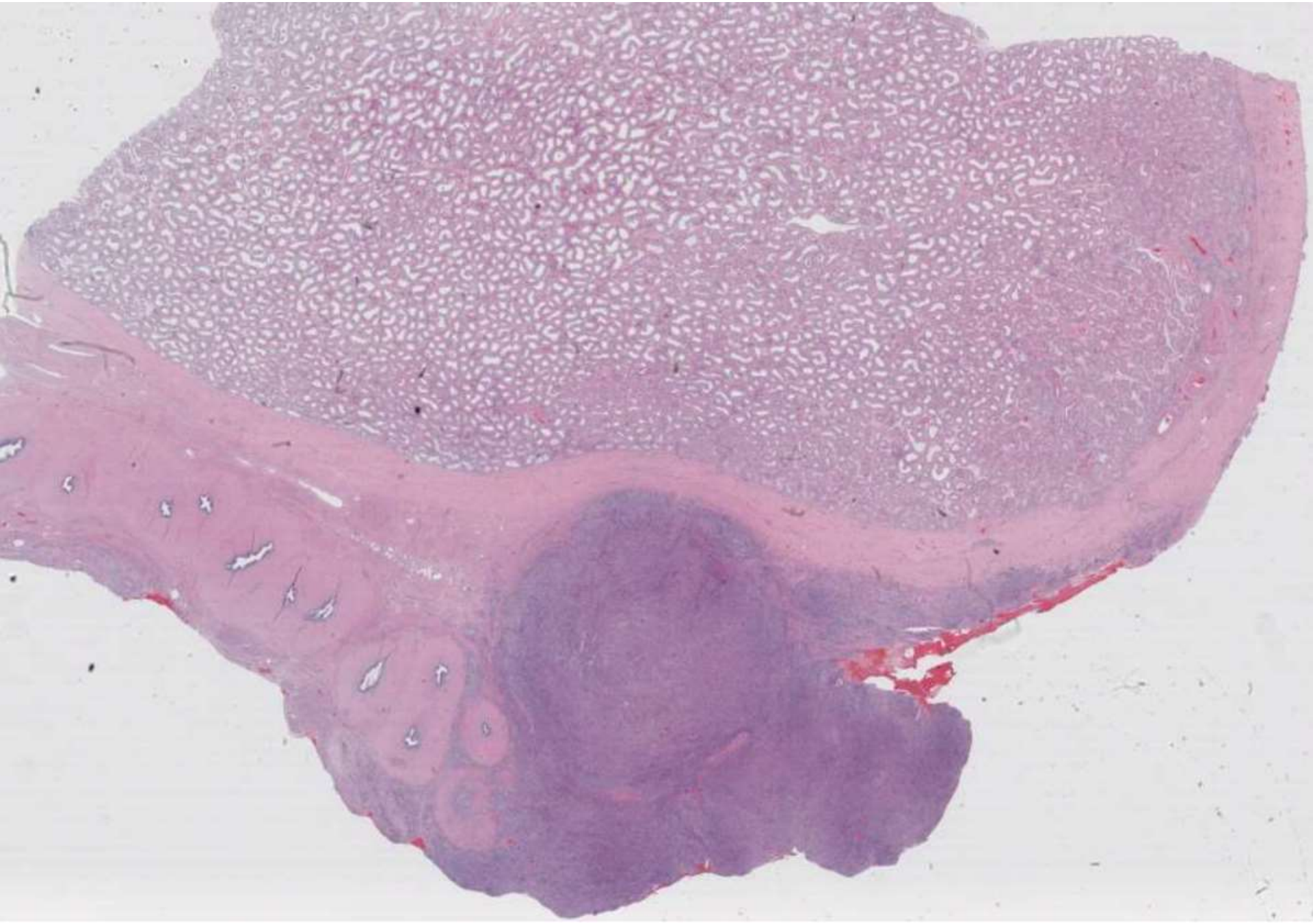
SB 6058

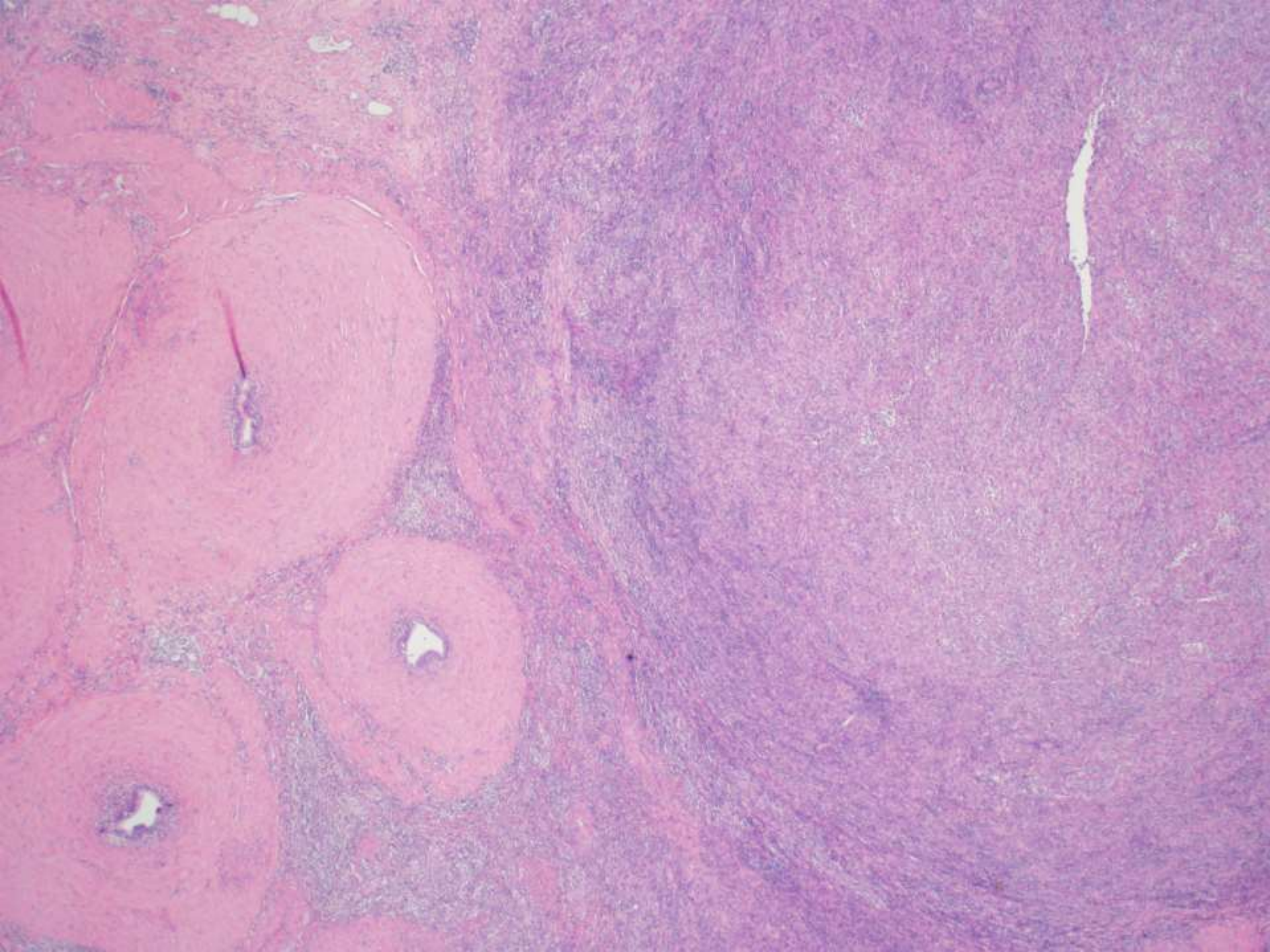
Sunny Kao; Stanford

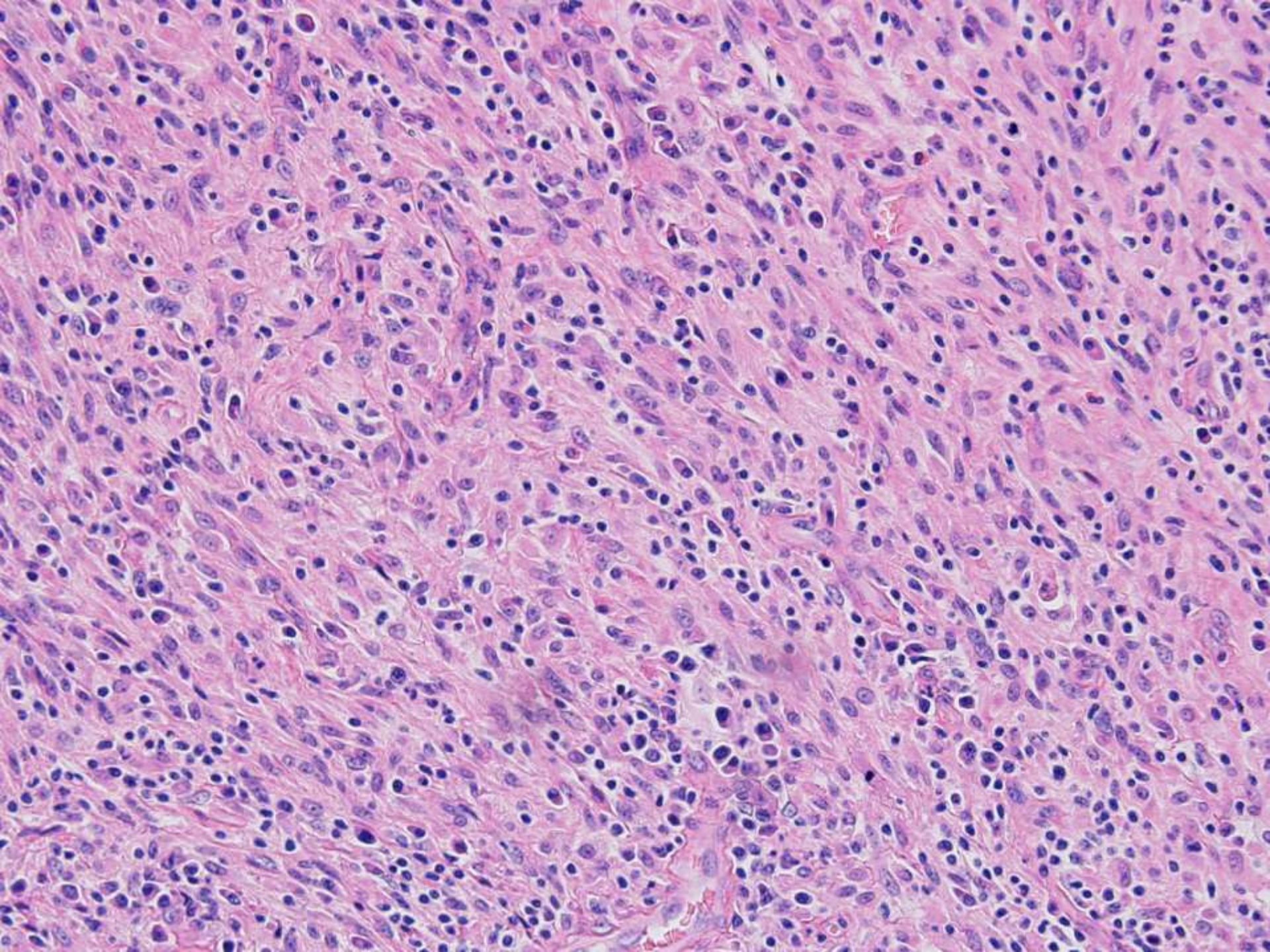
80 year-old male with right “testicular” mass

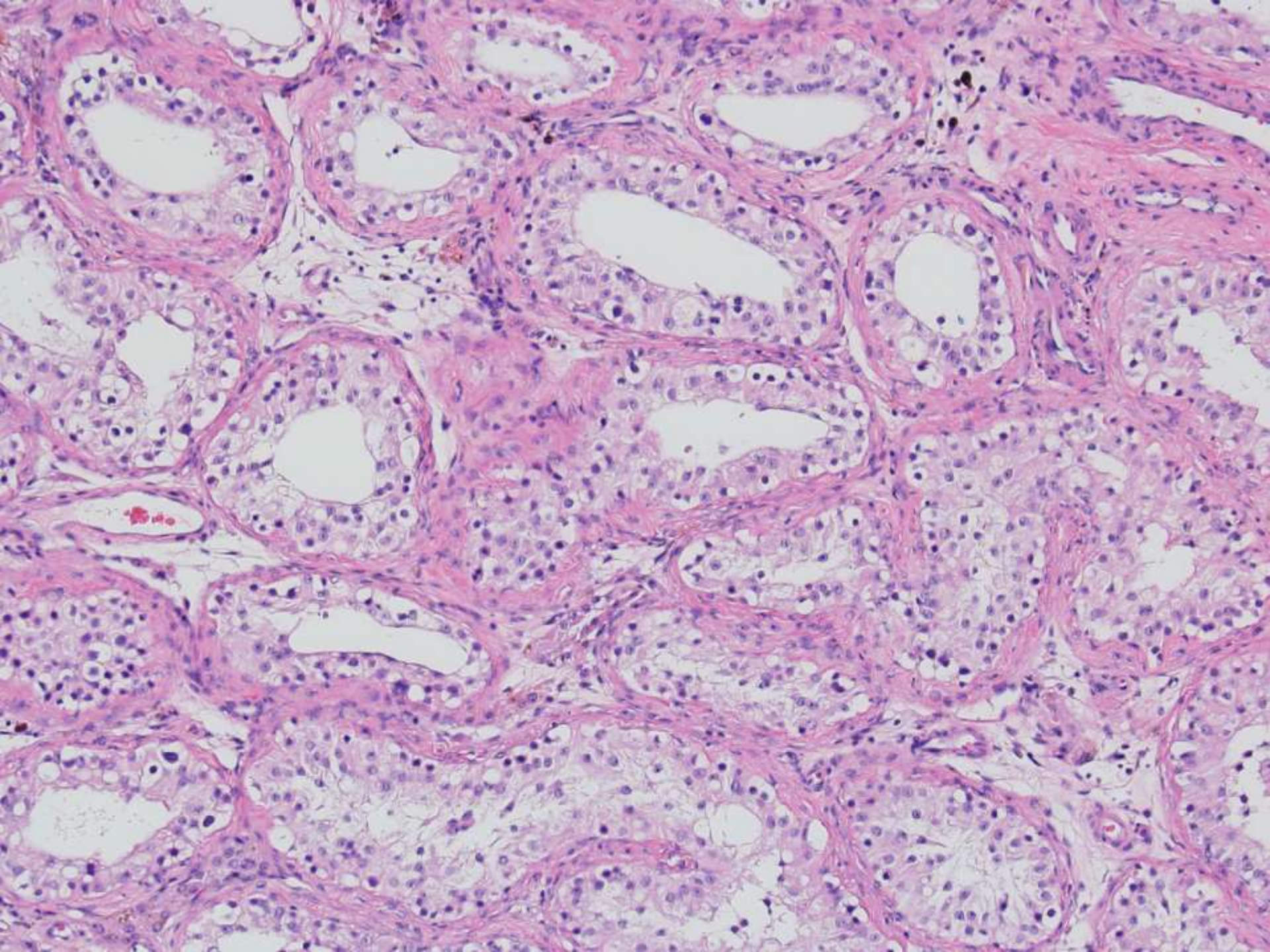
Gross Description

The specimen is received in formalin labeled with the patient's name, demographics and identified as "right testis". It consists of a 42 g testis with attached spermatic cord and overlying epididymis. The testis measures 6 x 3.6 x 2.9 cm and is somewhat distorted and focally firm. The attached spermatic cord measures 2.6 cm in length x 0.3 cm in diameter. The tunica vaginalis is tightly adherent to the testis and is retracted at the distal region. The tunica albuginea is raised and roughened at the distal region. The testis is inked blue and it is sectioned to reveal a bilocular cystic space in the proximal region, between the tunica vaginalis and tunica albuginea. The cystic space contains a small amount of thin clear fluid. The testis parenchyma is yellow orange and spongy. The seminiferous tubules strip with ease and no lesions are identified.









Differential Diagnosis

- Lymphoma
- Sarcoma
- Infarcted adenomatoid tumor
- Rosai-Dorfman disease
- Malakoplakia/Infectious
- Inflammatory pseudotumor/pseudosarcomatous myofibroblastic proliferation (“proliferative funiculitis”)

Staining results

- CD3, CD20 show mixture of B- and T-cells
- Kappa/Lambda-ISH show no light chain restriction
- No increase in IgG4 plasma cells
- S100 and CD21 both negative
- GMS/PAS/von Kossa all negative
- FISH for MDM2 negative
- SMA is positive in spindle cells
- ALK-1 is negative

“Proliferative Funiculitis”

- Spermatic cord is the most common location; rarely epididymis
- Potential to recur if not completely excised; by definition, NON-METASTASIZING
- Heterogeneous appearance with variable cellularity and intensity of inflammatory infiltrates; can resemble nodular fasciitis
- Mits: <1/10 HFPs; NO atypical mitosis
- Vascular; granulation tissue-like
- IHC supports myofibroblastic lineage

Major pitfall

- **Not considering lymphoma or sarcoma (<u>inflammatory liposarcoma!!!</u>)**
- **Reactive/variable appearance is helpful in confirming non-neoplastic nature**
- **Make sure there is NO cytologic atypia (hyperchromatic nuclei), admixed atypical adipocytes, or atypical mitosis**

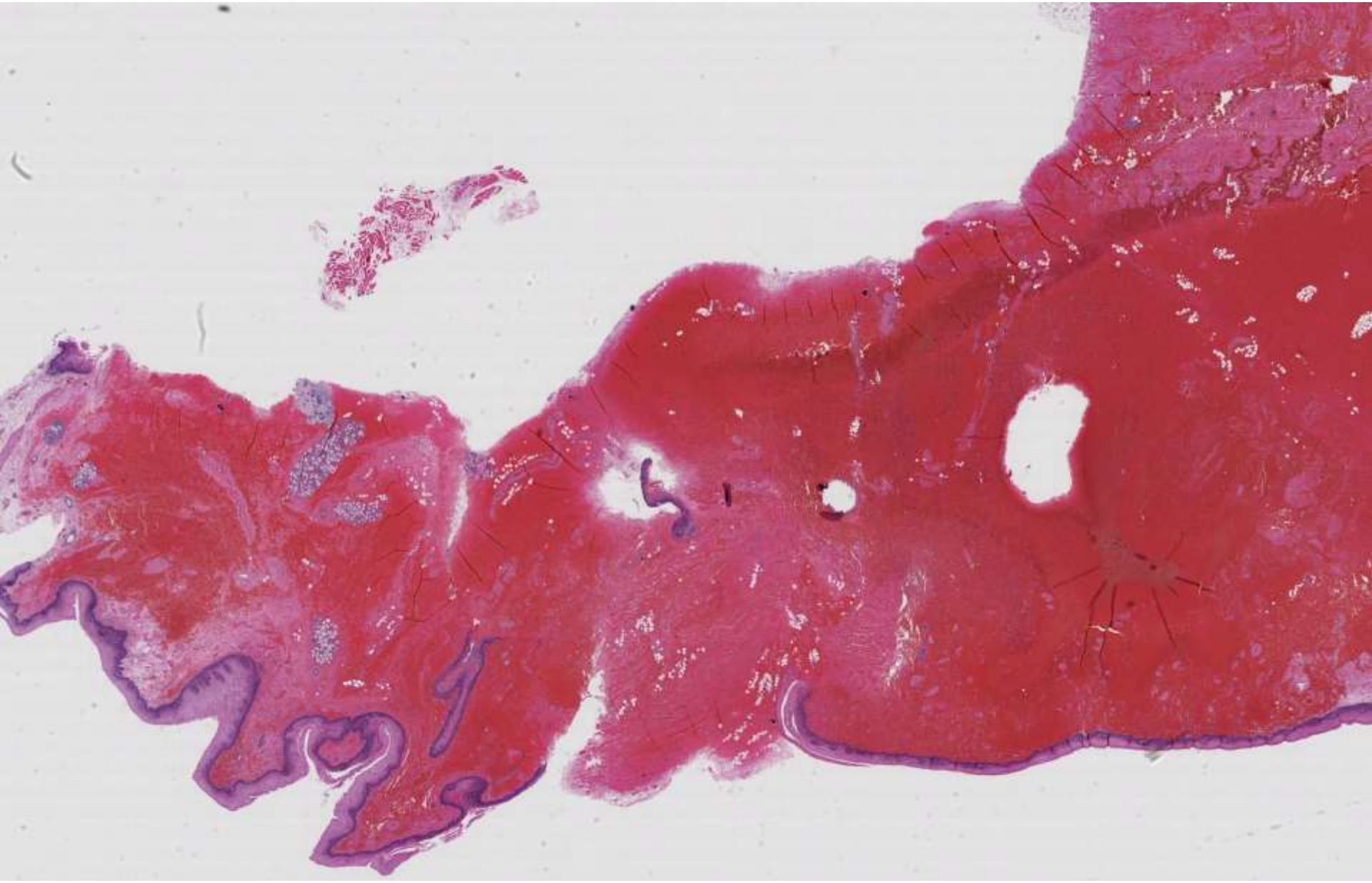
References

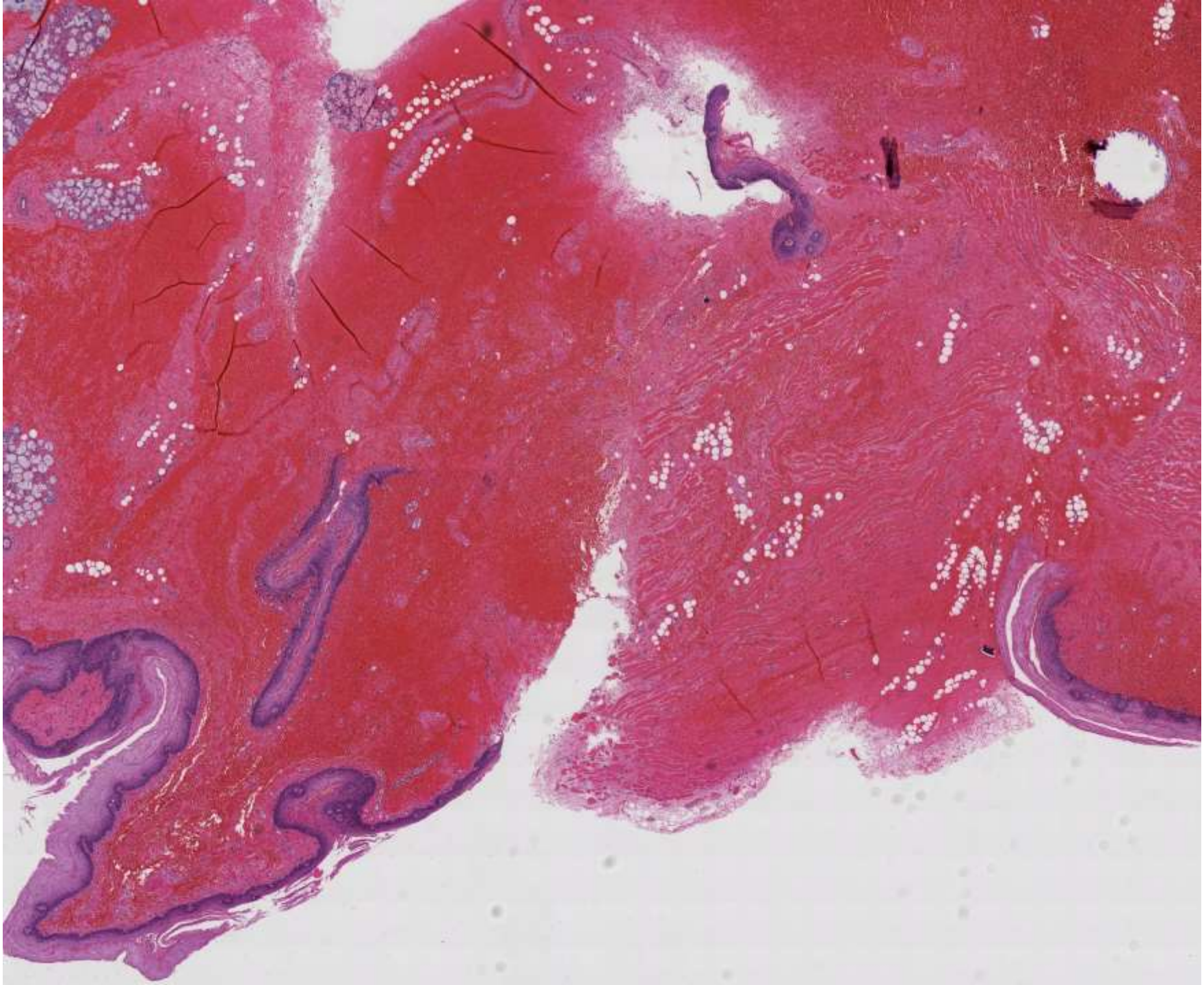
- Hollowood K, Fletcher CD. Pseudosarcomatous myofibroblastic proliferations of the spermatic cord ("proliferative funiculitis"). Histologic and immunohistochemical analysis of a distinctive entity. Am J Surg Pathol. 1992 May;16(5):448-54.
- Milanezi MF, Schmitt F. Pseudosarcomatous myofibroblastic proliferation of the spermatic cord (proliferative funiculitis). Histopathology. 1997 Oct;31(4):387-8.

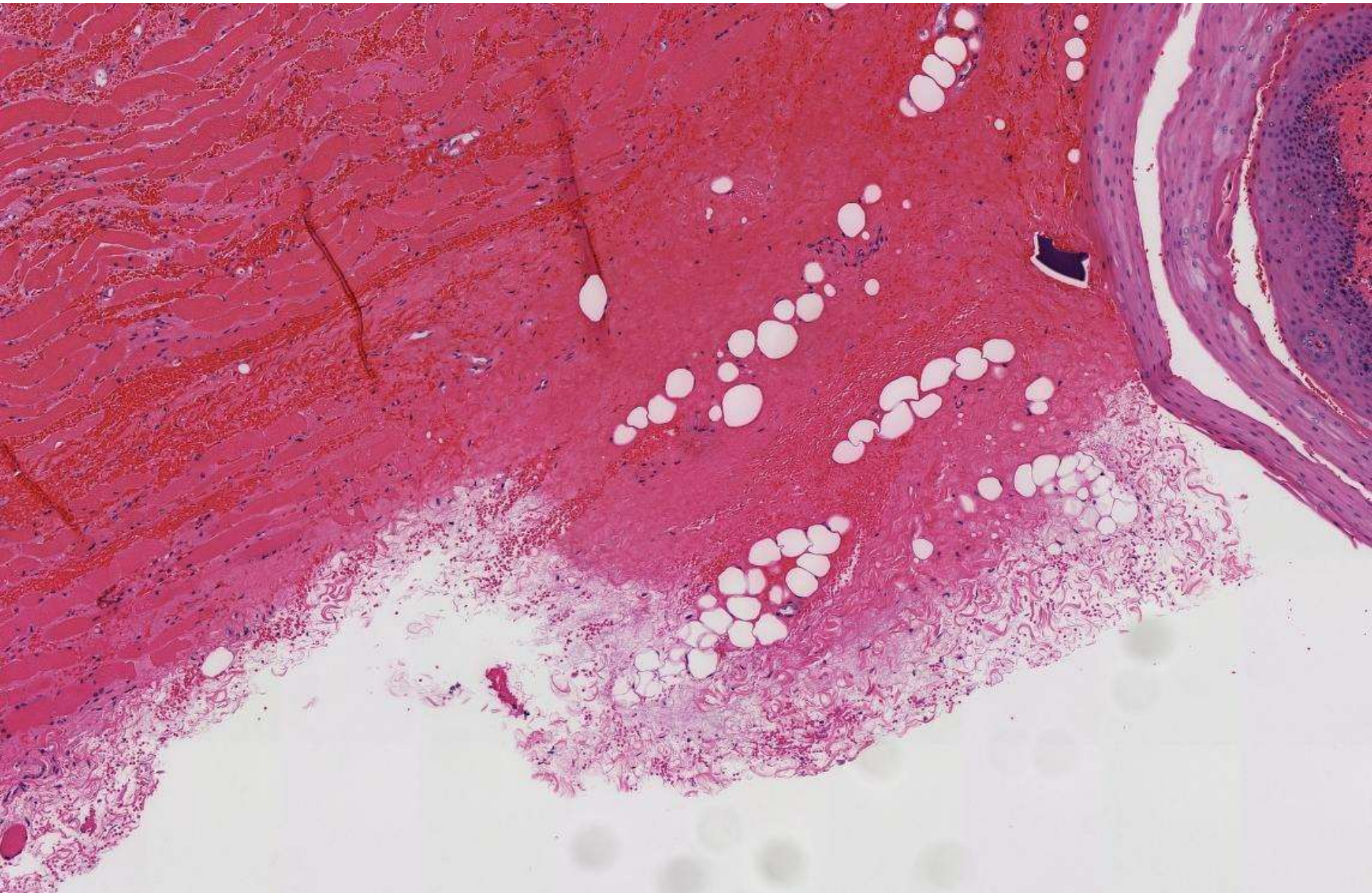
SB 6059

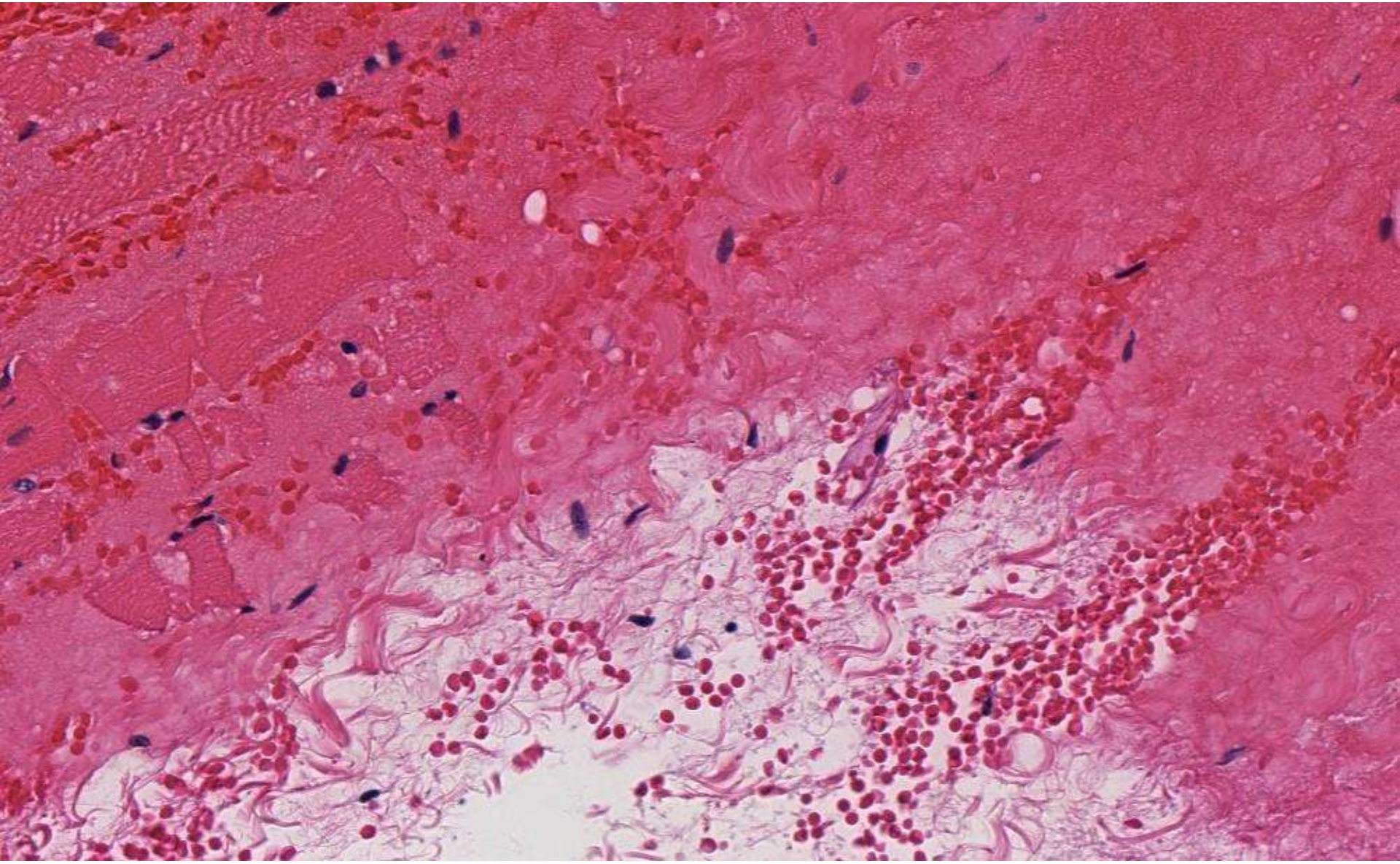
Ankur Sangoi; El Camino Hospital

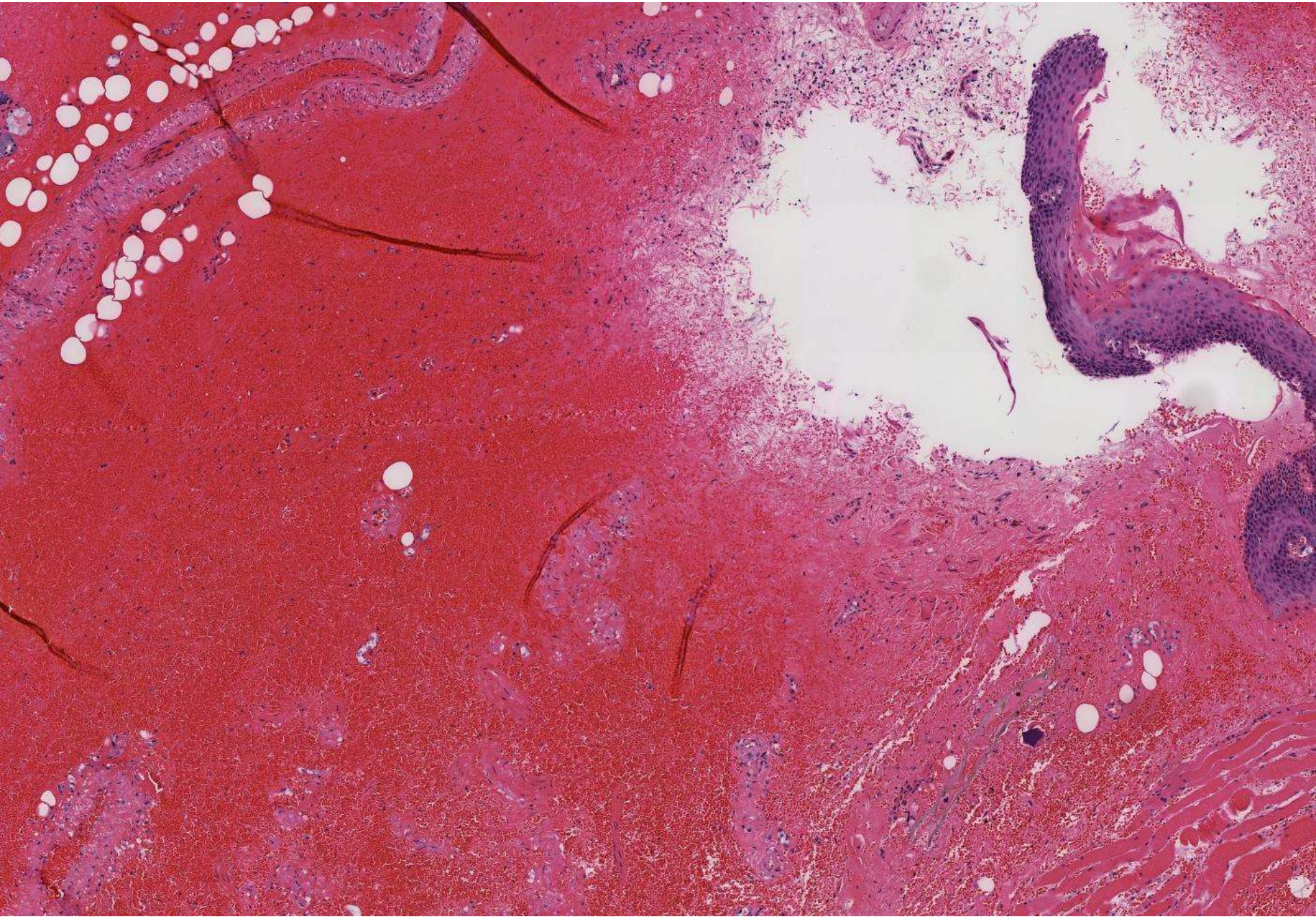
79-year-old man with a remote history of esophageal cancer status post resection, end-stage renal disease (etiology unknown), and hypertension presented to the ER with fatigue. He was found to be hypotensive and anemic with elevated postassium and mild acidosis. Stools were guaic positive with a negative CT abdomen/pelvis. During attempted jugular vein catheter placement, he became further hypotensive and unresponsive. The patient died despite persistent transfusion and coding. Autopsy requested given clinical concern for iatrogenic artertial disruption during catheter placement. Section of esophagus submitted.

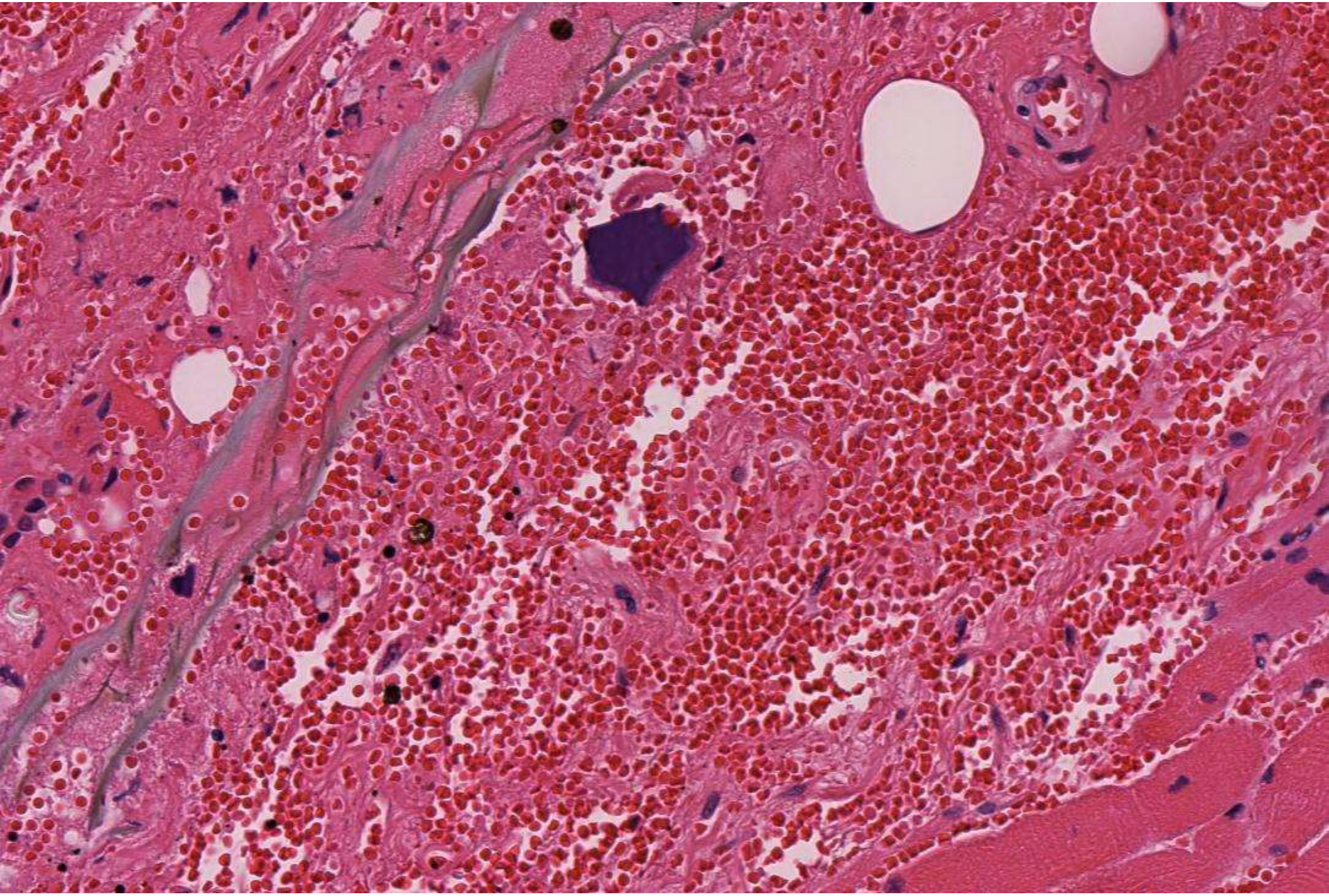


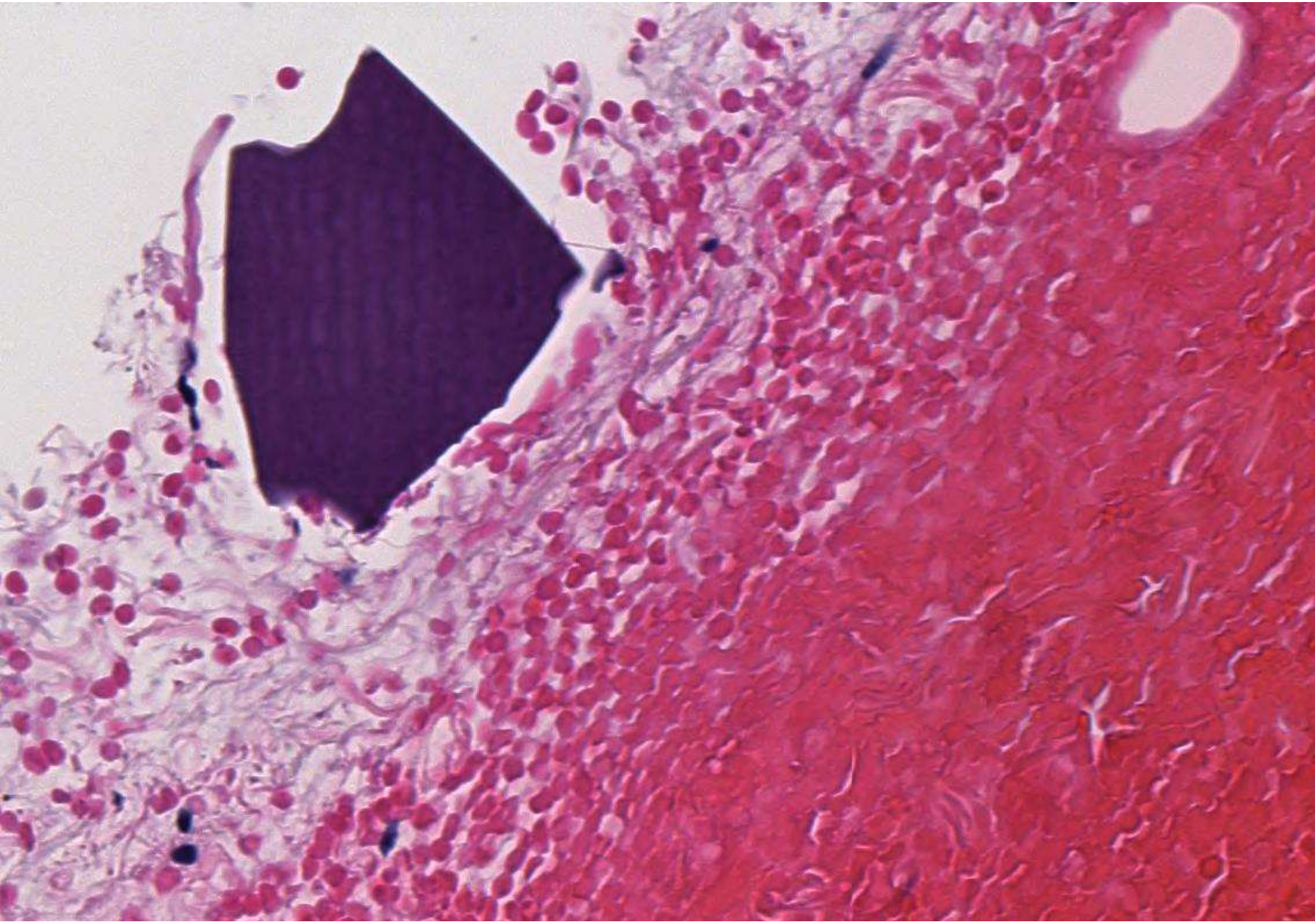


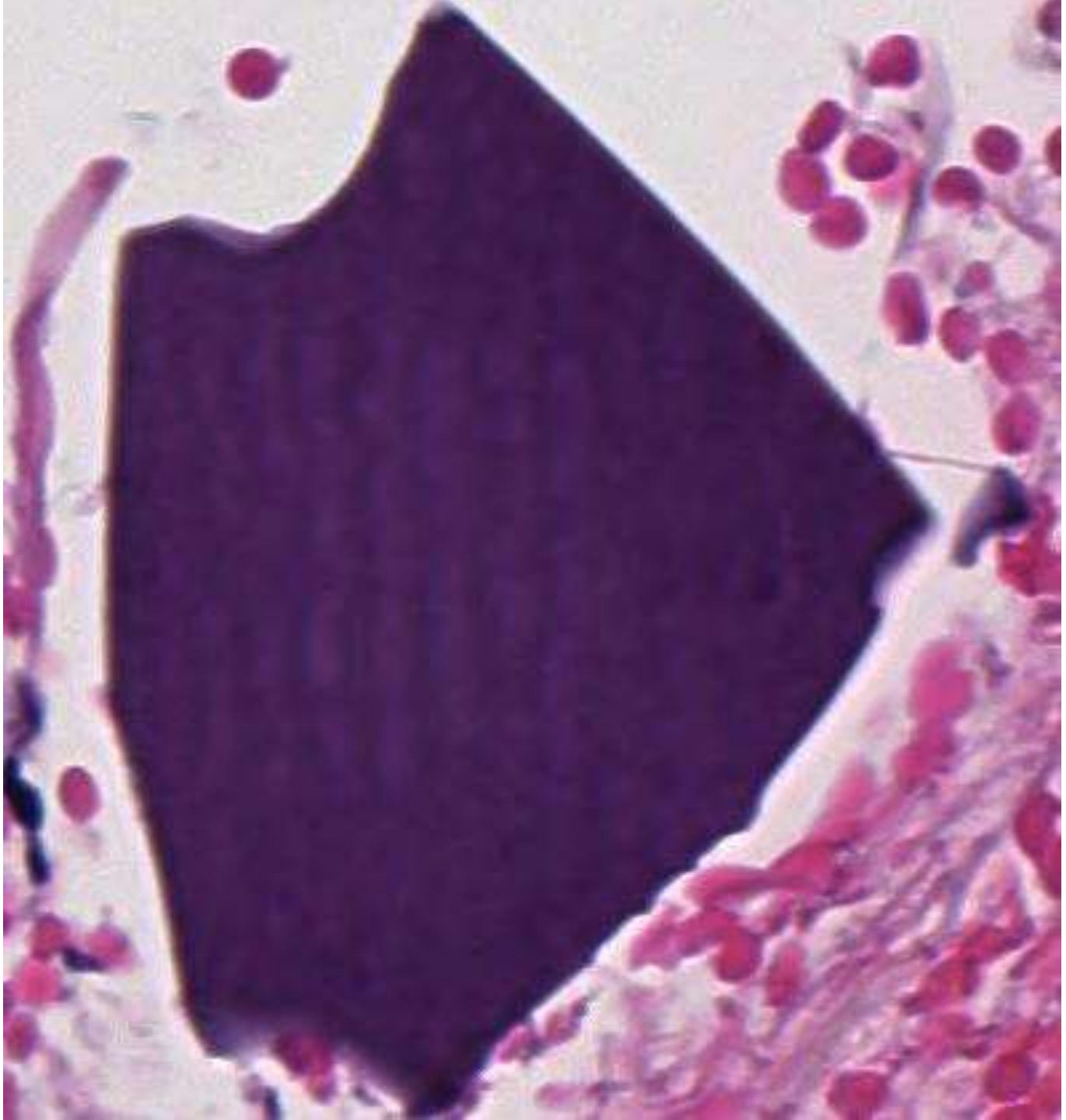




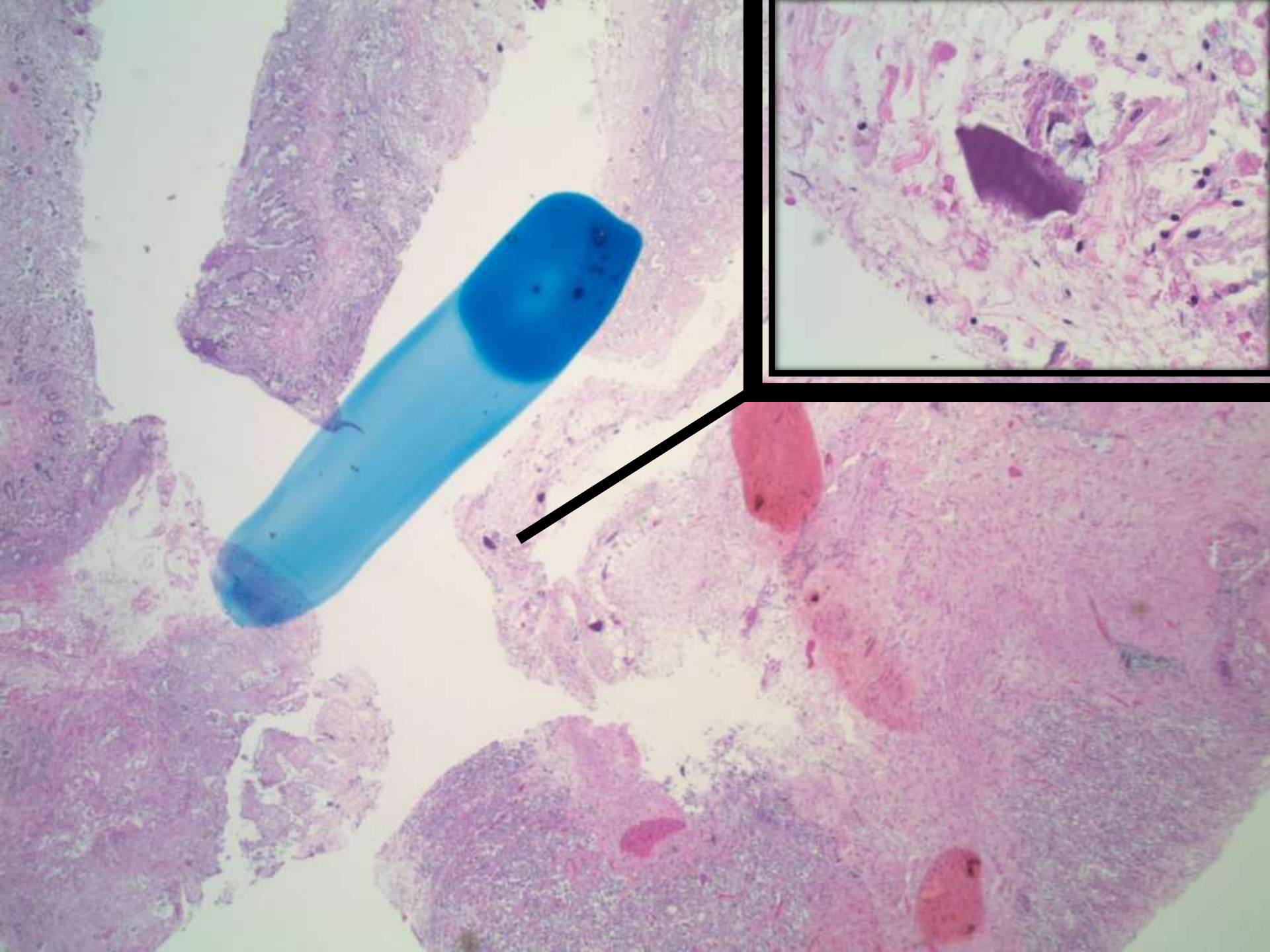


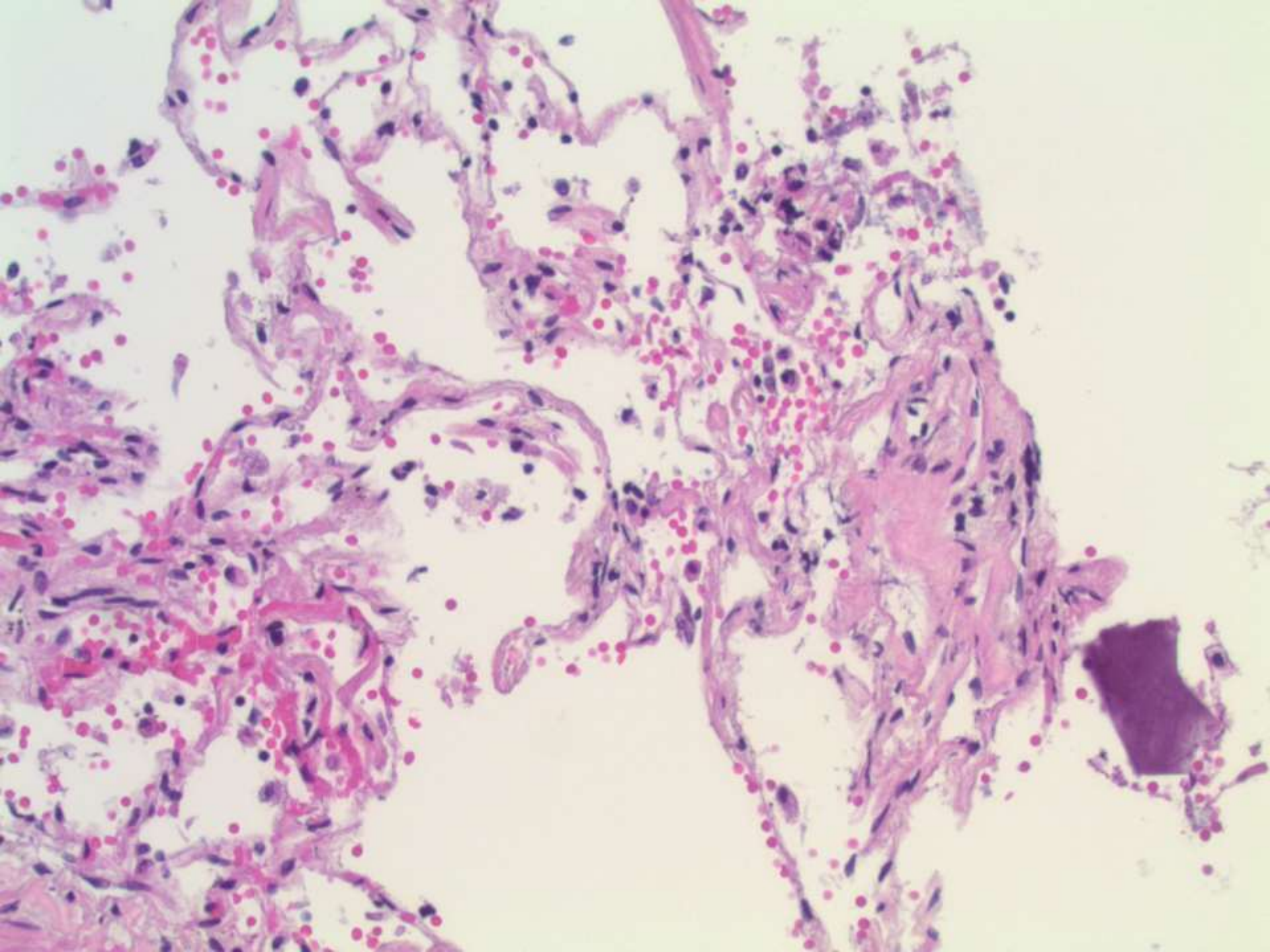


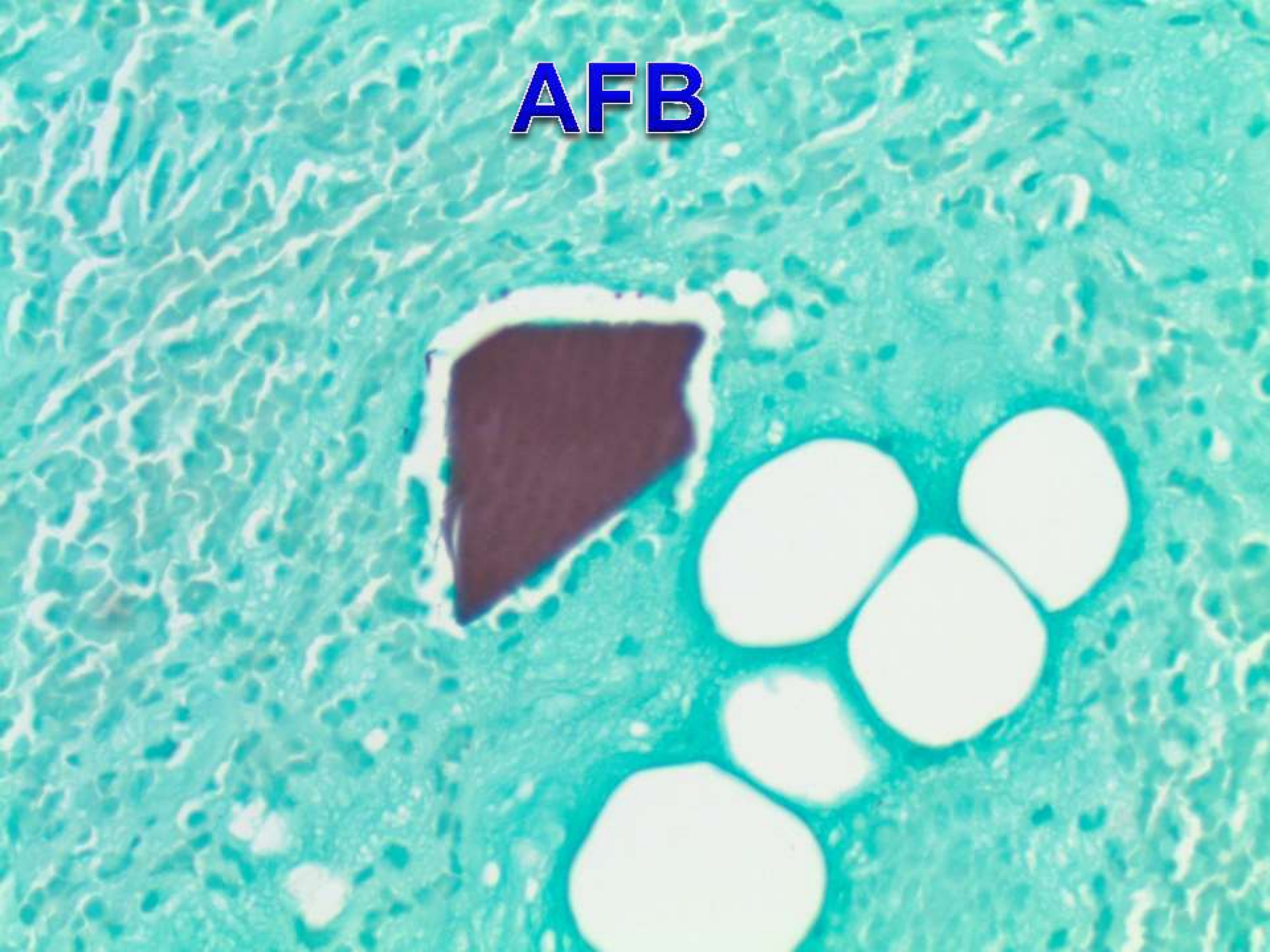




DIAGNOSIS?






AFB

DIAGNOSIS

- **Kayexalate-associated upper GI tract mucosal necrosis**

DIAGNOSIS

- **Kayexalate-associated upper GI tract mucosal necrosis**

FINAL PATHOLOGIC DIAGNOSIS:

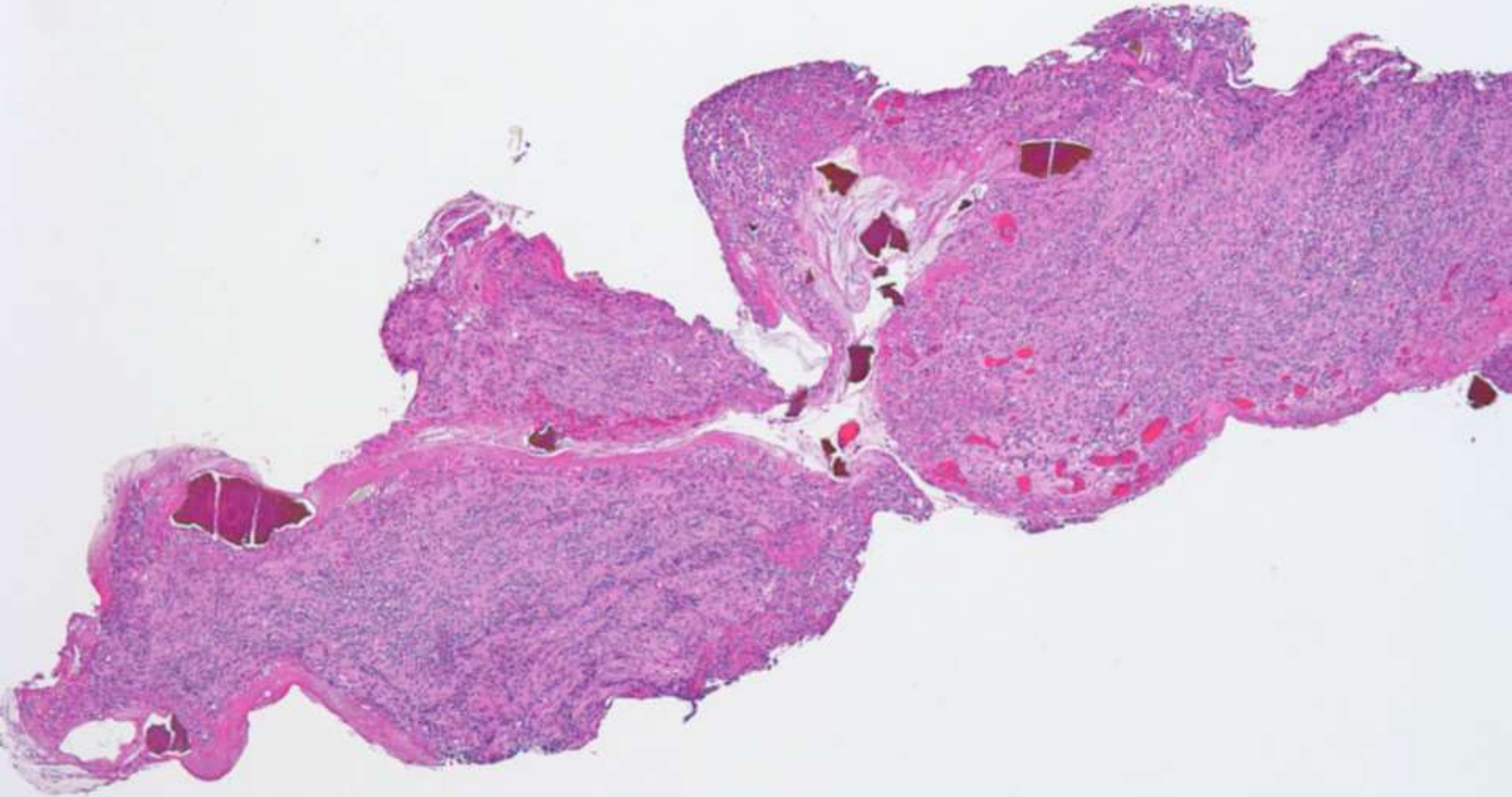
I. Intact bilateral jugular veins without associated arterial disruption (status post attempted right and successful left dialysis catheter placement)
II. Upper gastrointestinal tract mucosal necrosis
    A. Upper and lower esophagus, with paraesophageal hemorrhage
    B. Duodenum
    C. Right hemothorax (2L)
III. Bilateral atrophic kidneys (history of end-stage renal disease)
IV. Atherosclerotic cardiovascular disease and hypertension
    A. Moderate to severe coronary artery narrowing
    B. Mild arthrosclerosis of aorta
    C. Mild left ventricular hypertrophy
V. Stomach with gastrointestinal tract stromal tumor (3.6cm)
VI. Bilateral lung nodules with changes consistent with chronic aspiration
VII. Prostatic glandular and stromal hyperplasia

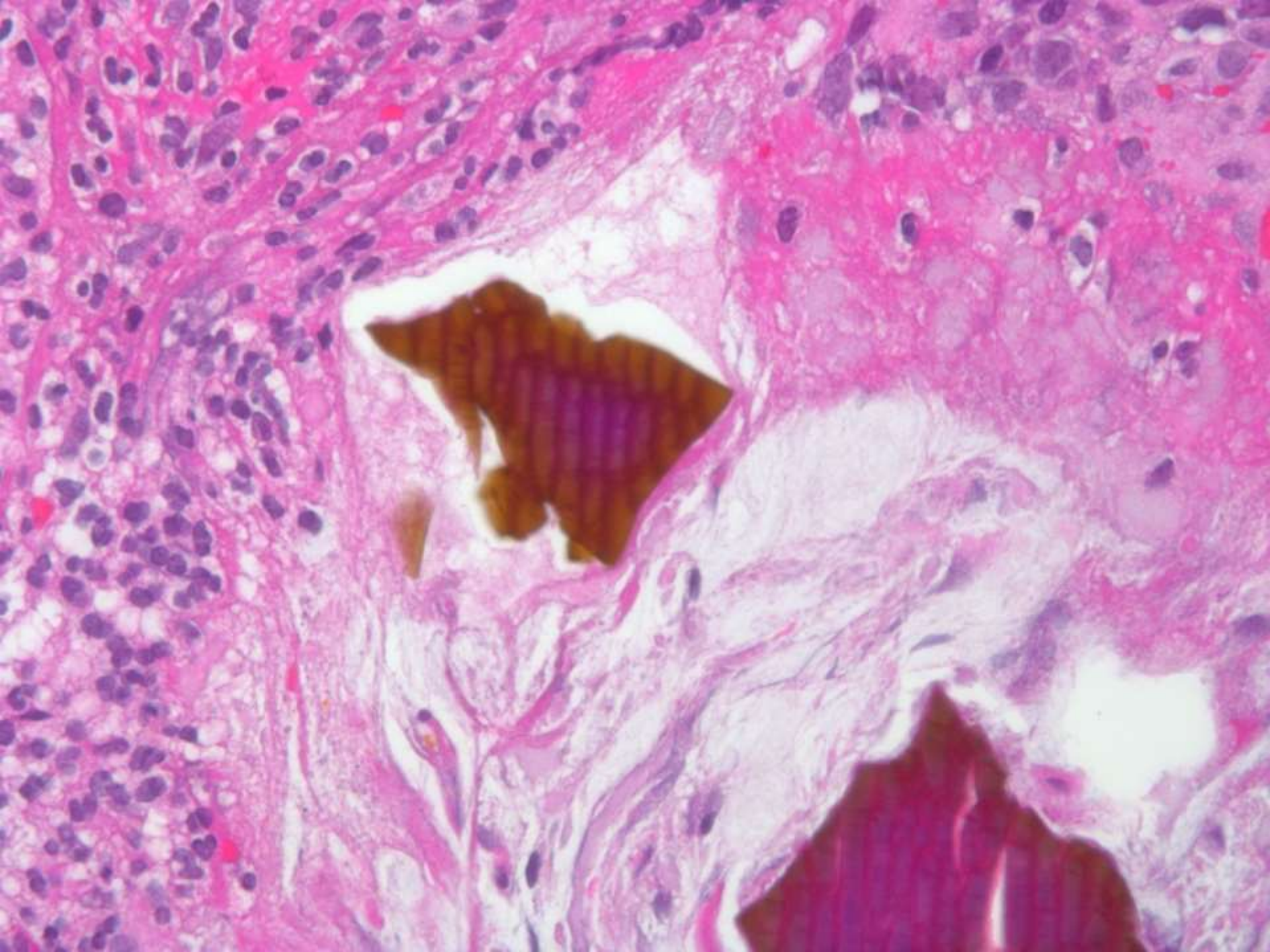
Differential diagnosis of GI tract resins

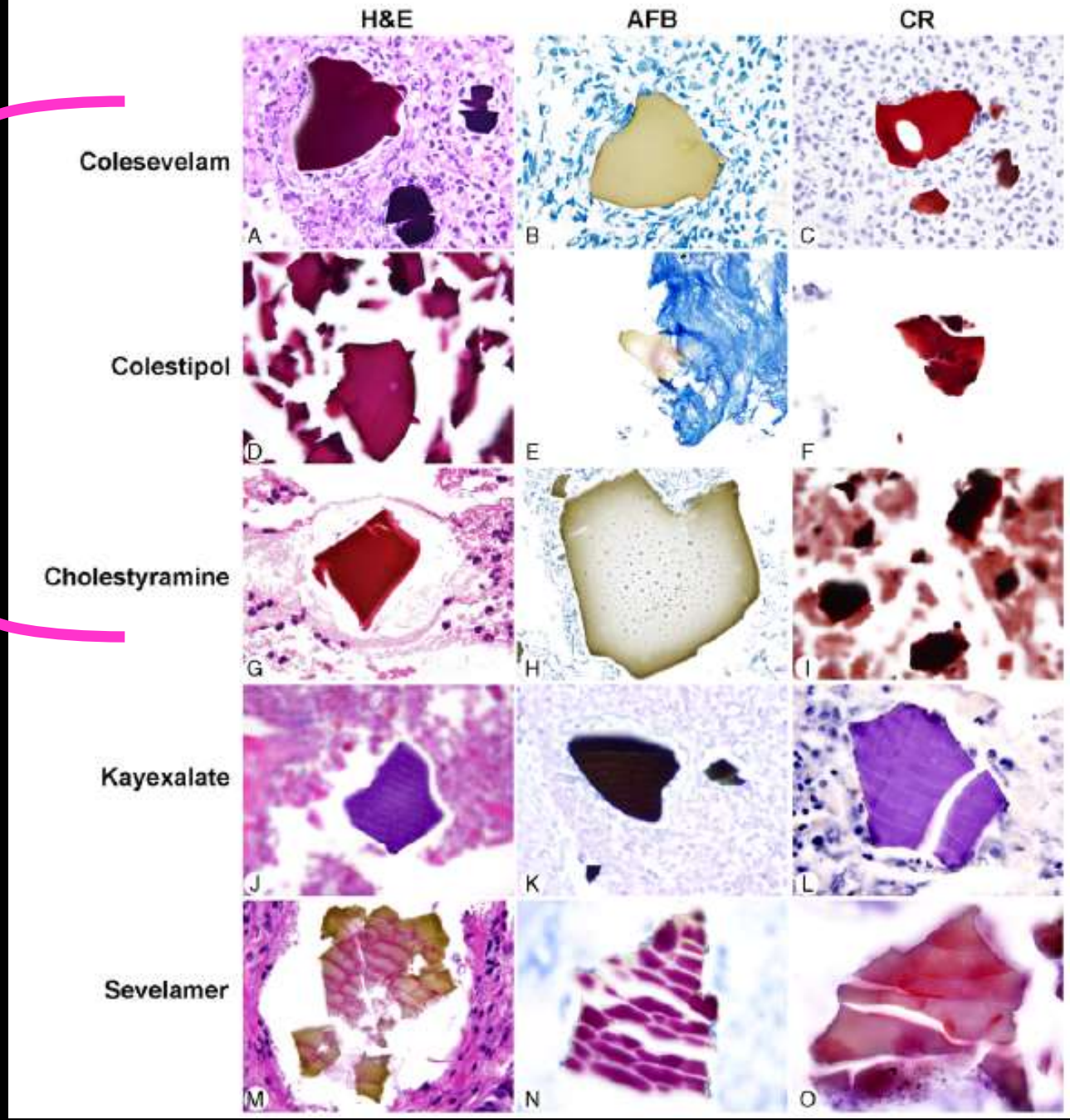
Resin = non-absorbable drugs that serve as platforms for ion exchange

- **Kayexalate crystals**
  - treat hyperkalemia usually administered with osmotic laxative sorbitol
- **Sevelamer crystals**
  - used in chronic renal disease to lower phosphate
- **Bile acid sequestrant crystals**
  - Cholestyramine, colesevelam, colestipol used to treat hypercholesterolemia/dyslipidemia

SB 5820 (March 2014)






H&E
AFB
CR
Colesevelam
Colestipol
Cholestyramine
Kayexalate
Sevelamer
A
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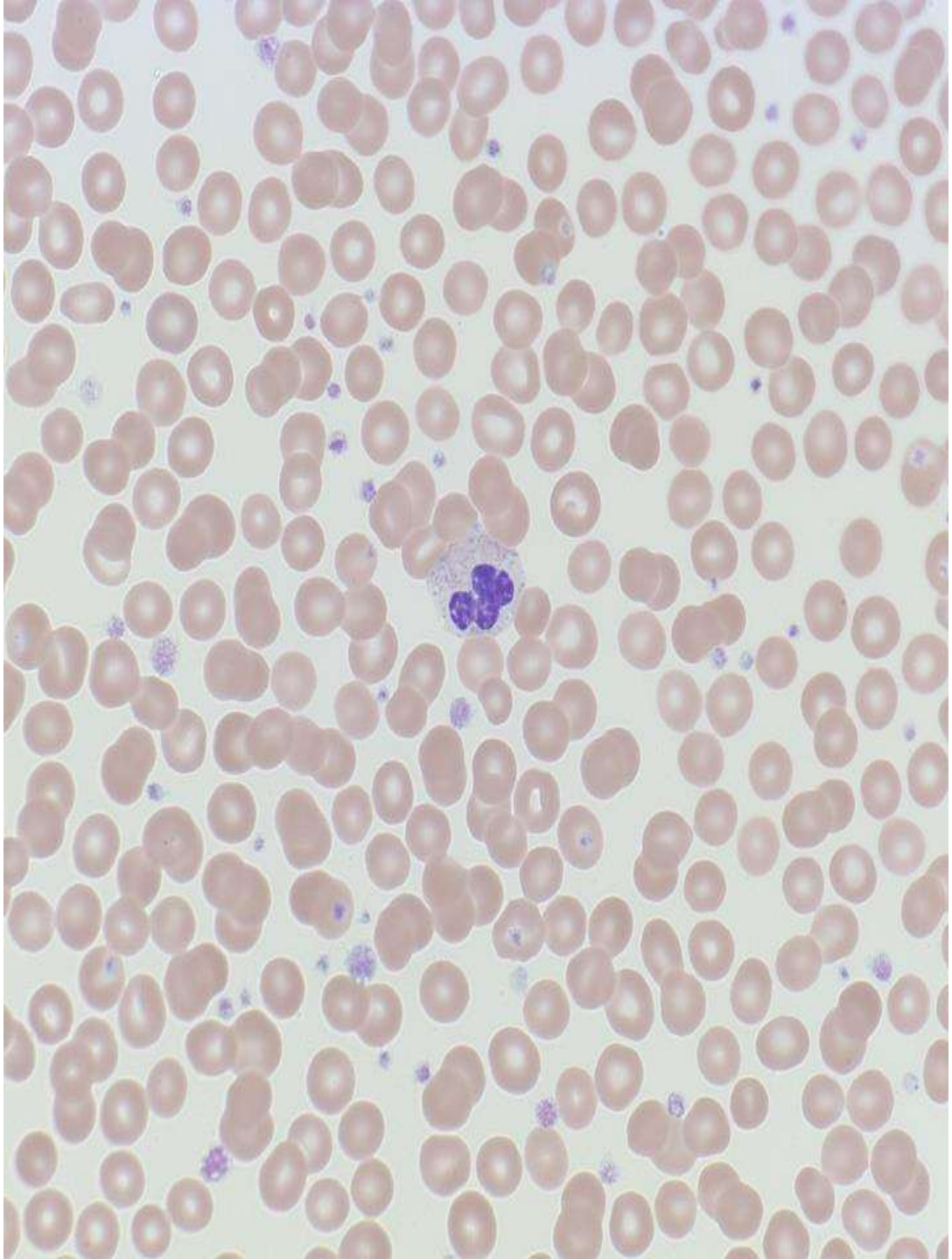
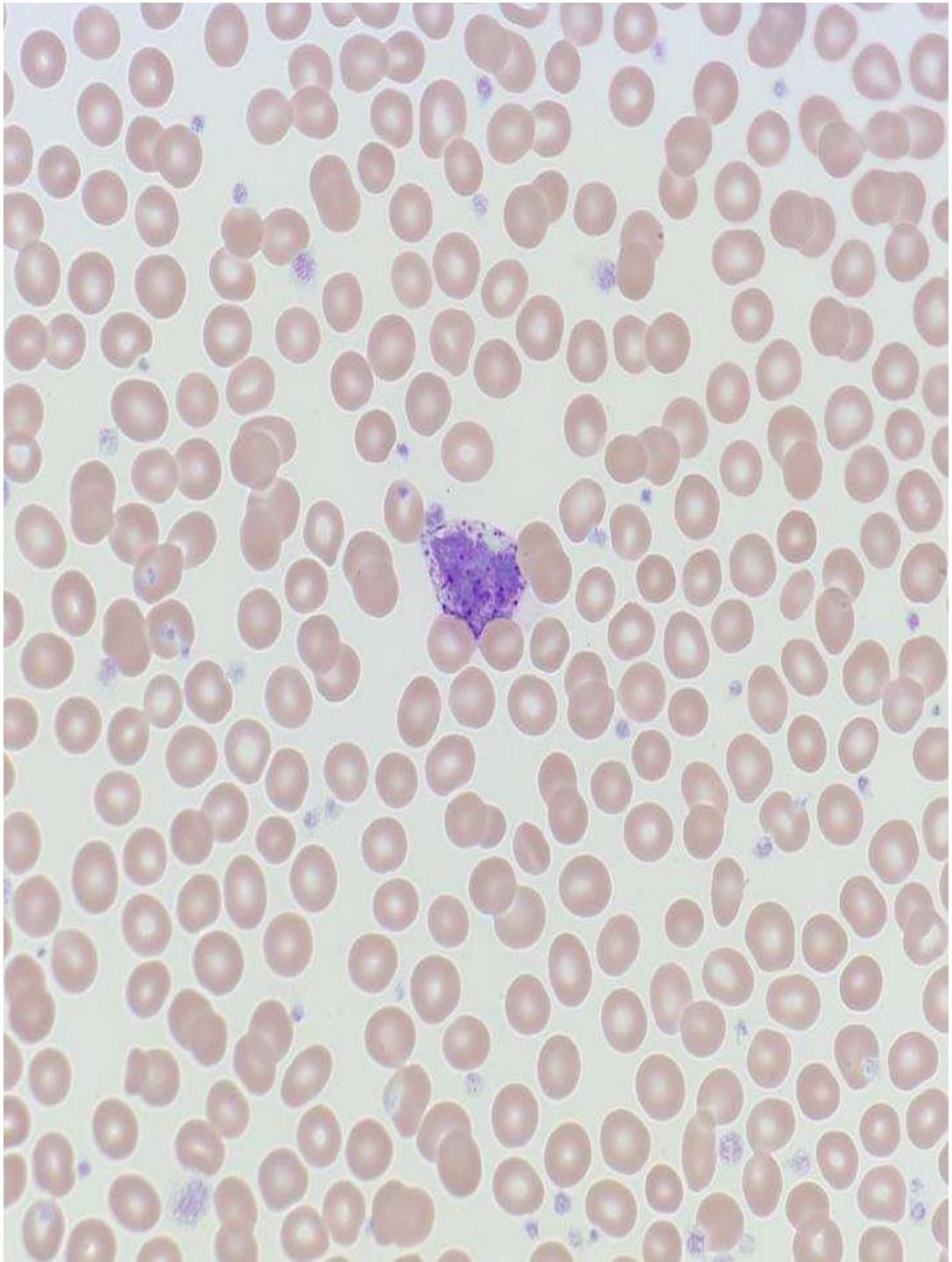
SB 6060

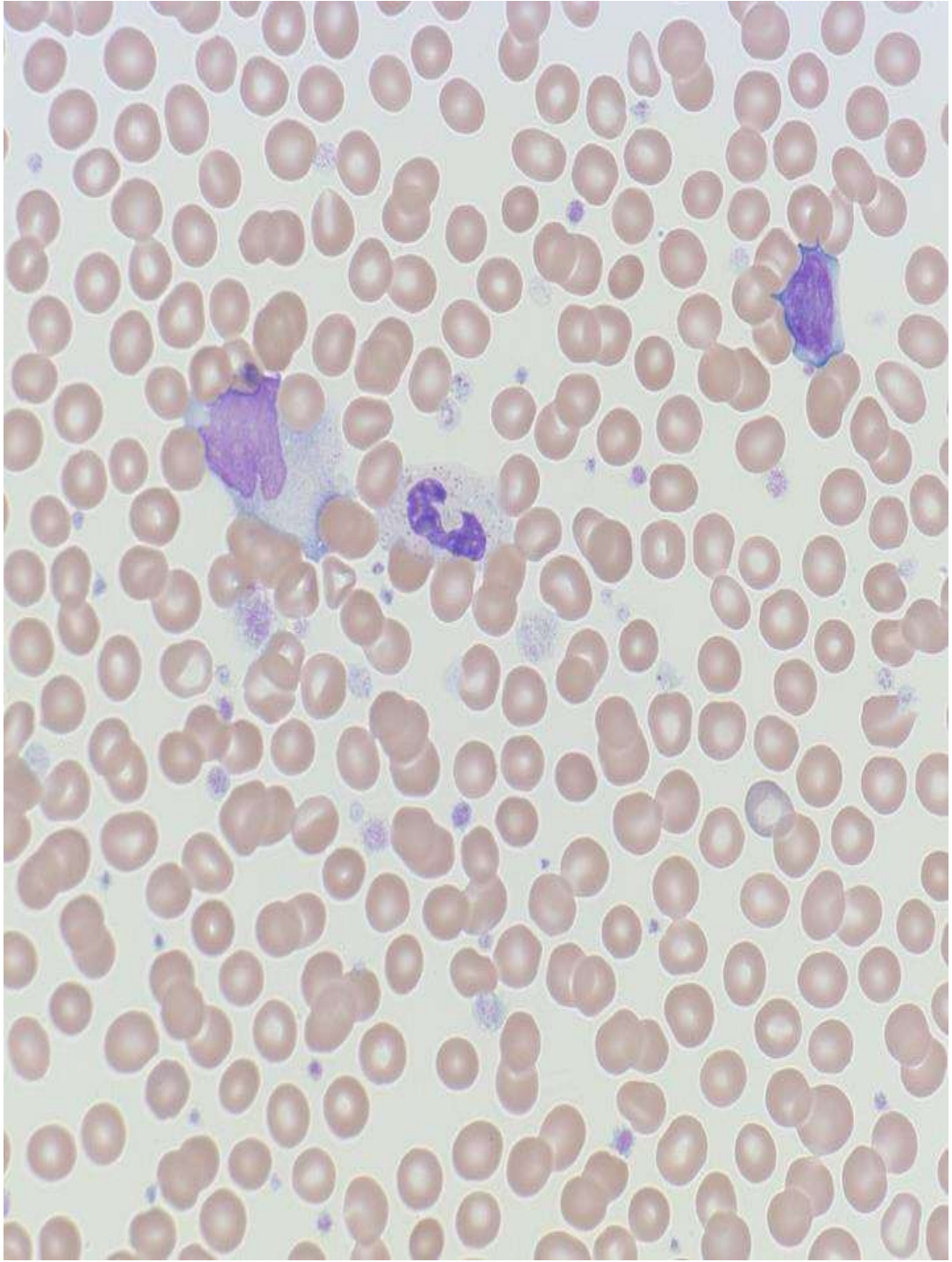
Peng Li/Daniel Arber/Robert Ohgami; Stanford

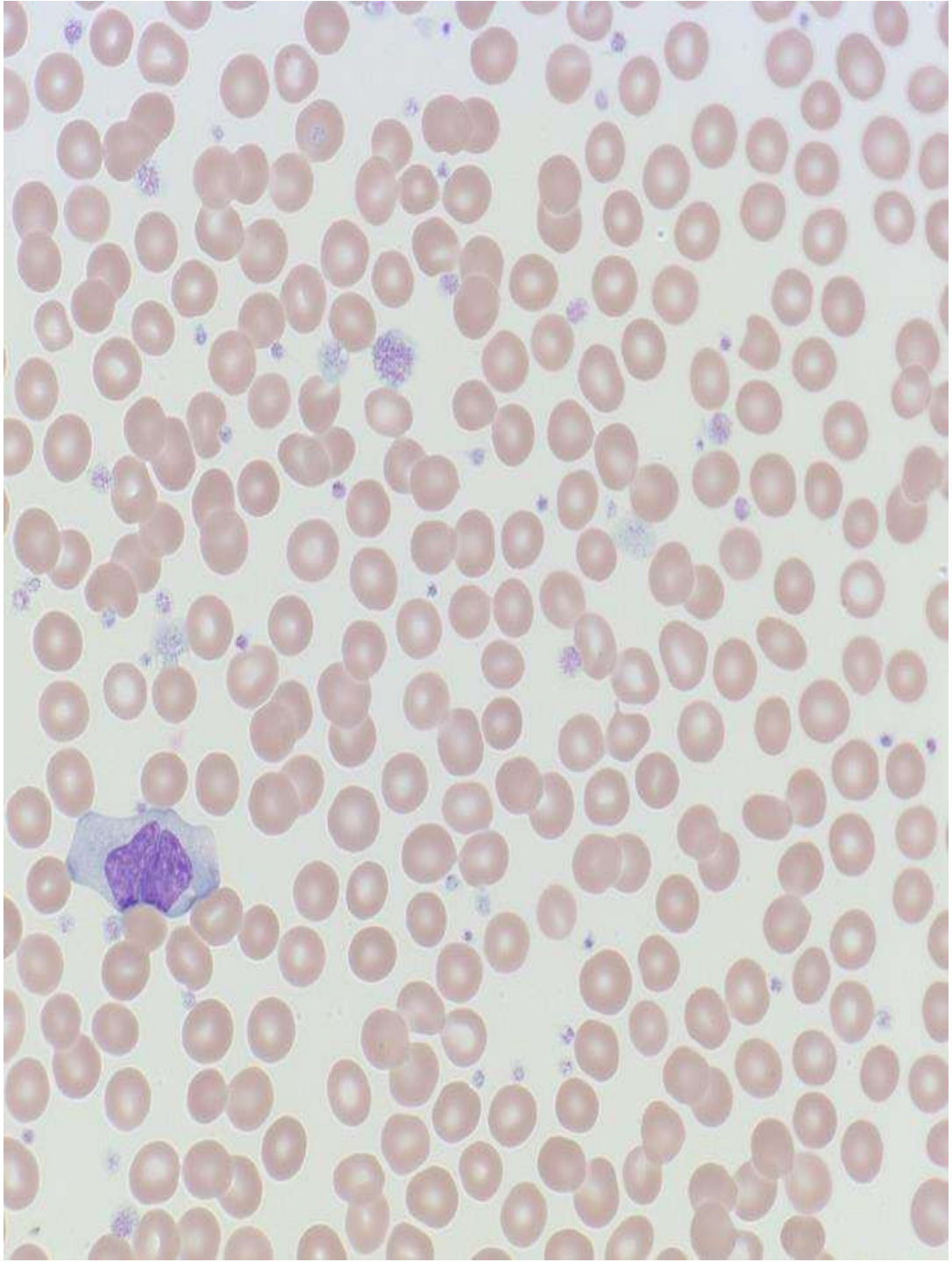
57-year-old woman with a history of thrombocytosis. A concurrent cytogenetics study shows normal female karyotype, and positive for RNA splicing factor 3B, subunit 1 (*SF3B1*) mutation and negative for JAK2 mutation and BCR-ABL in a peripheral blood specimen.

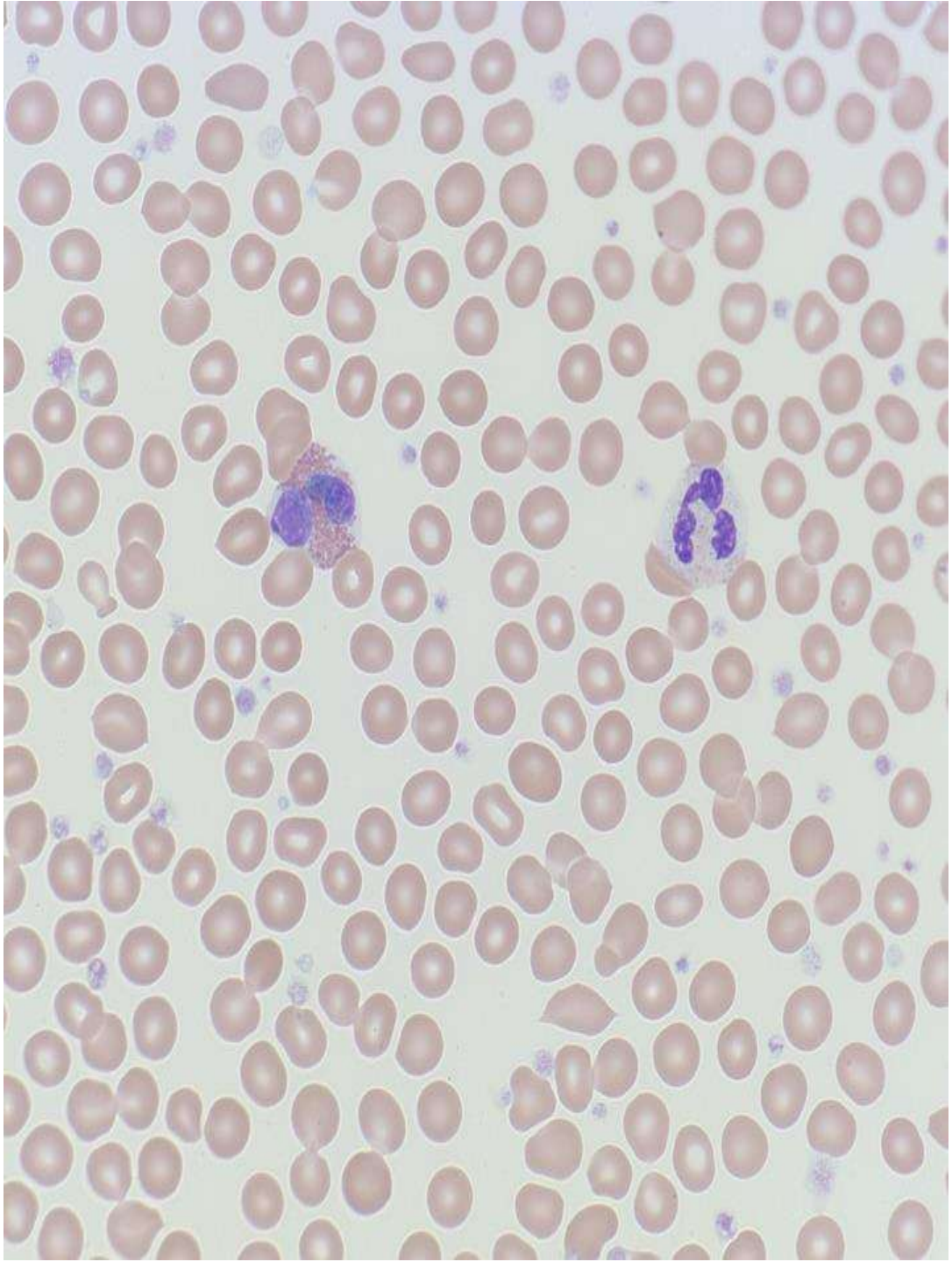
Peripheral blood



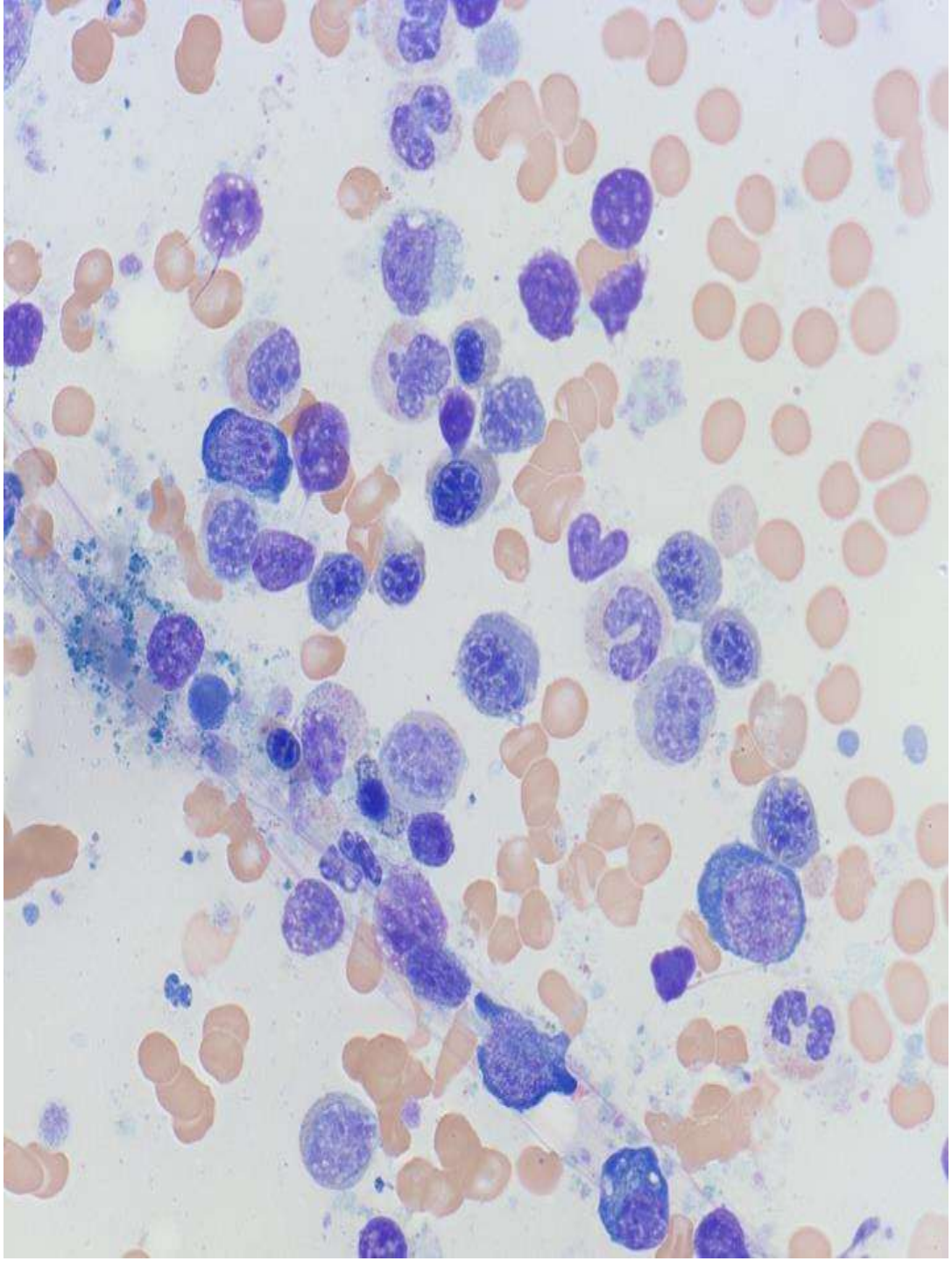


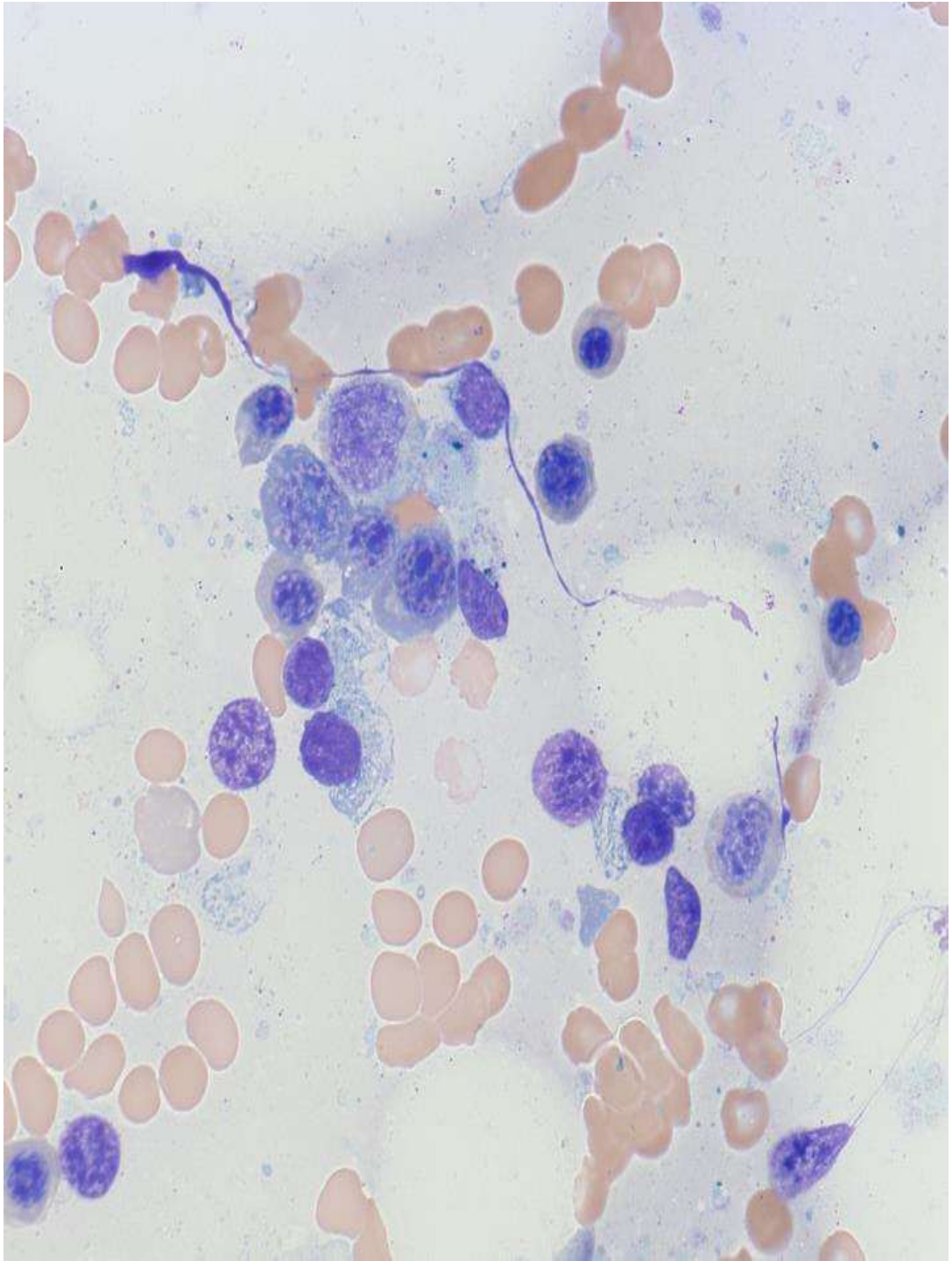


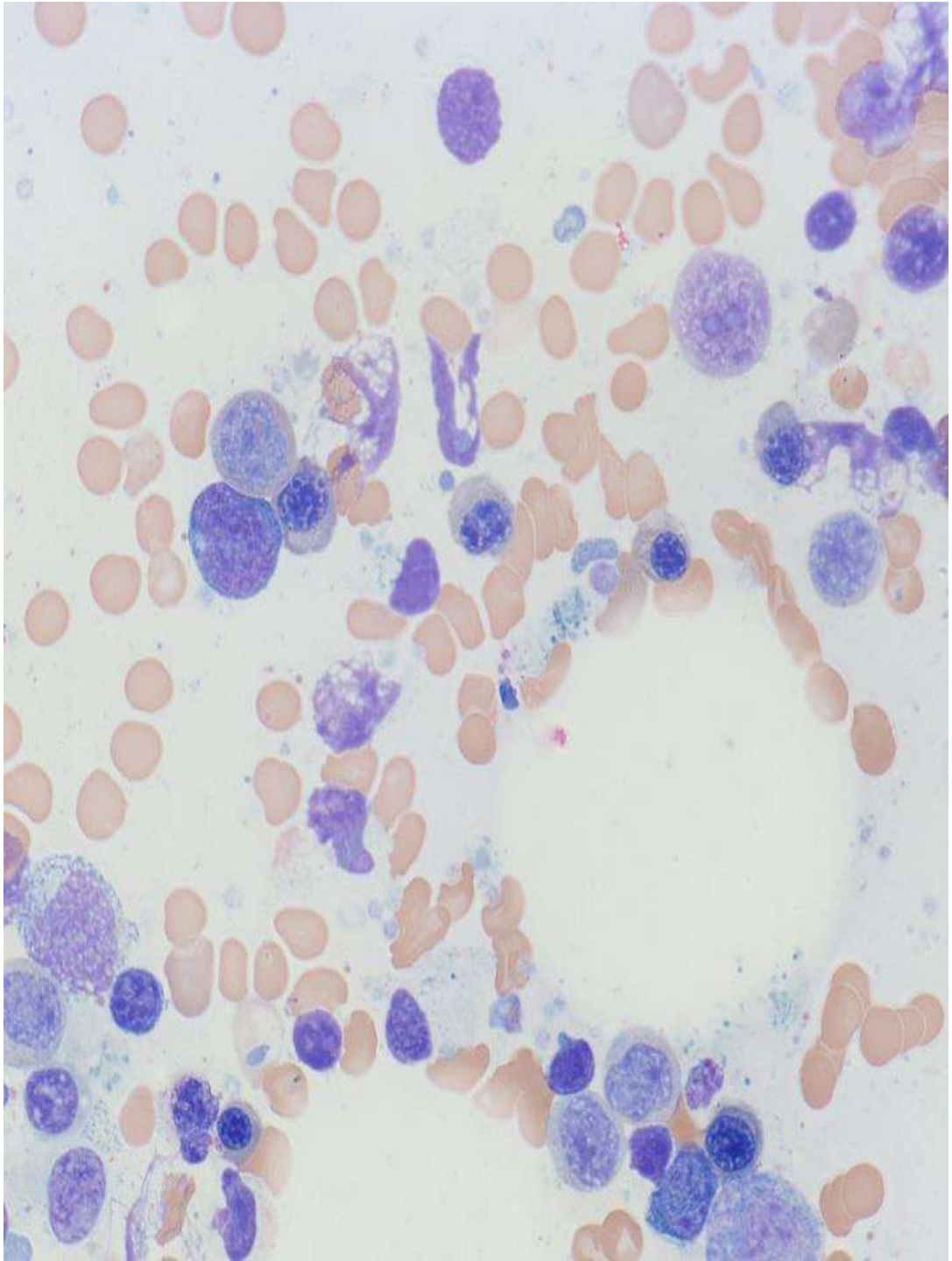


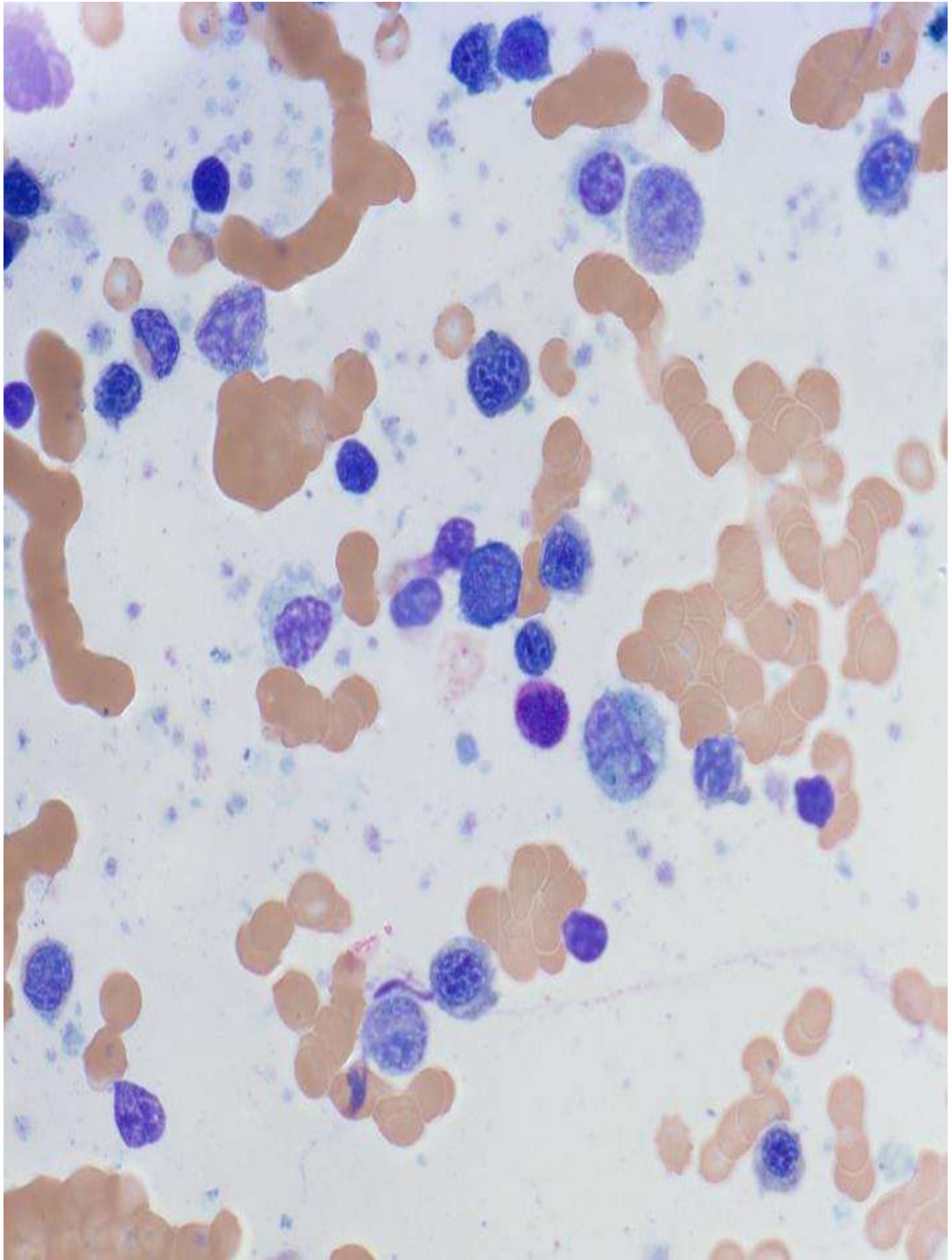


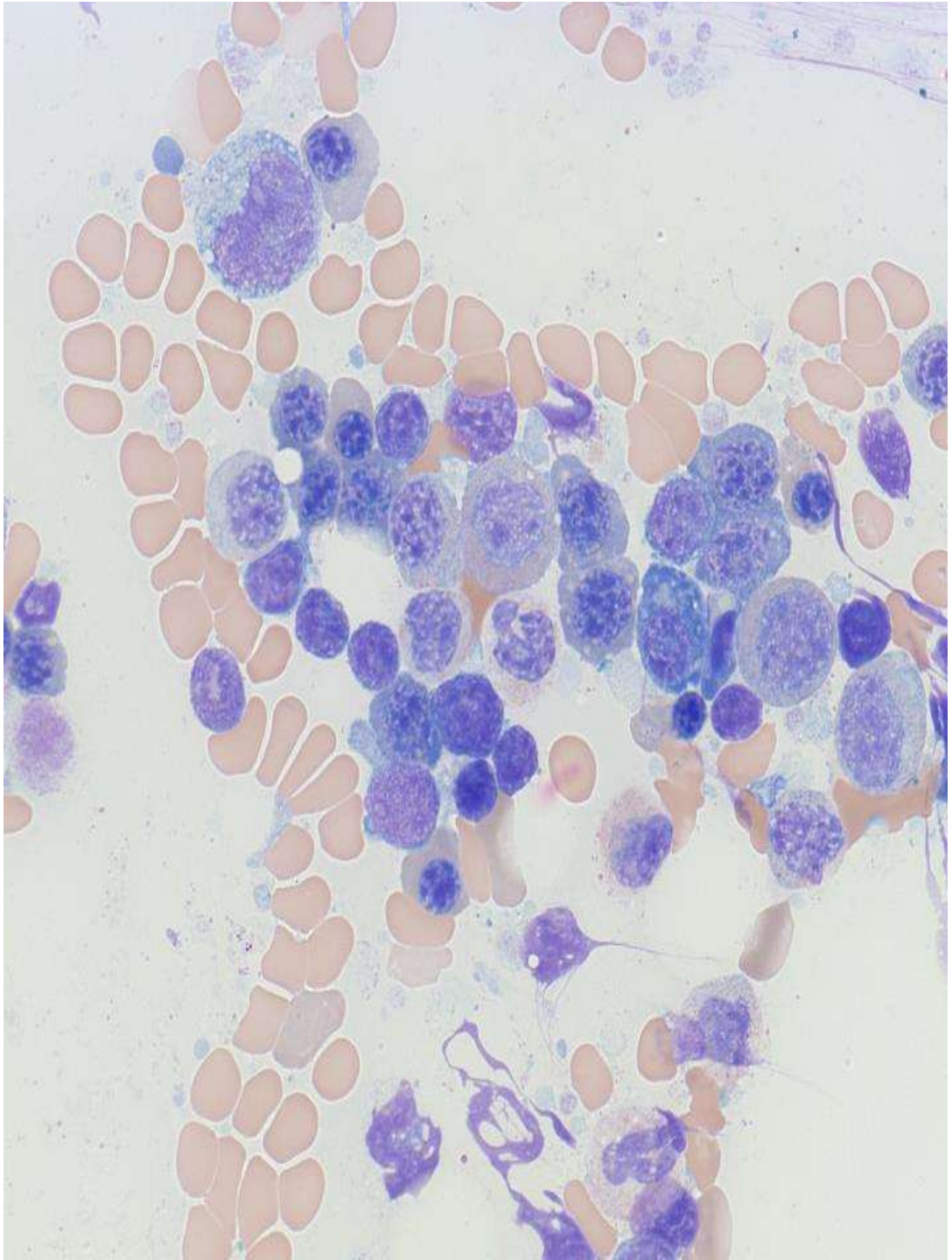
Bone marrow aspirate

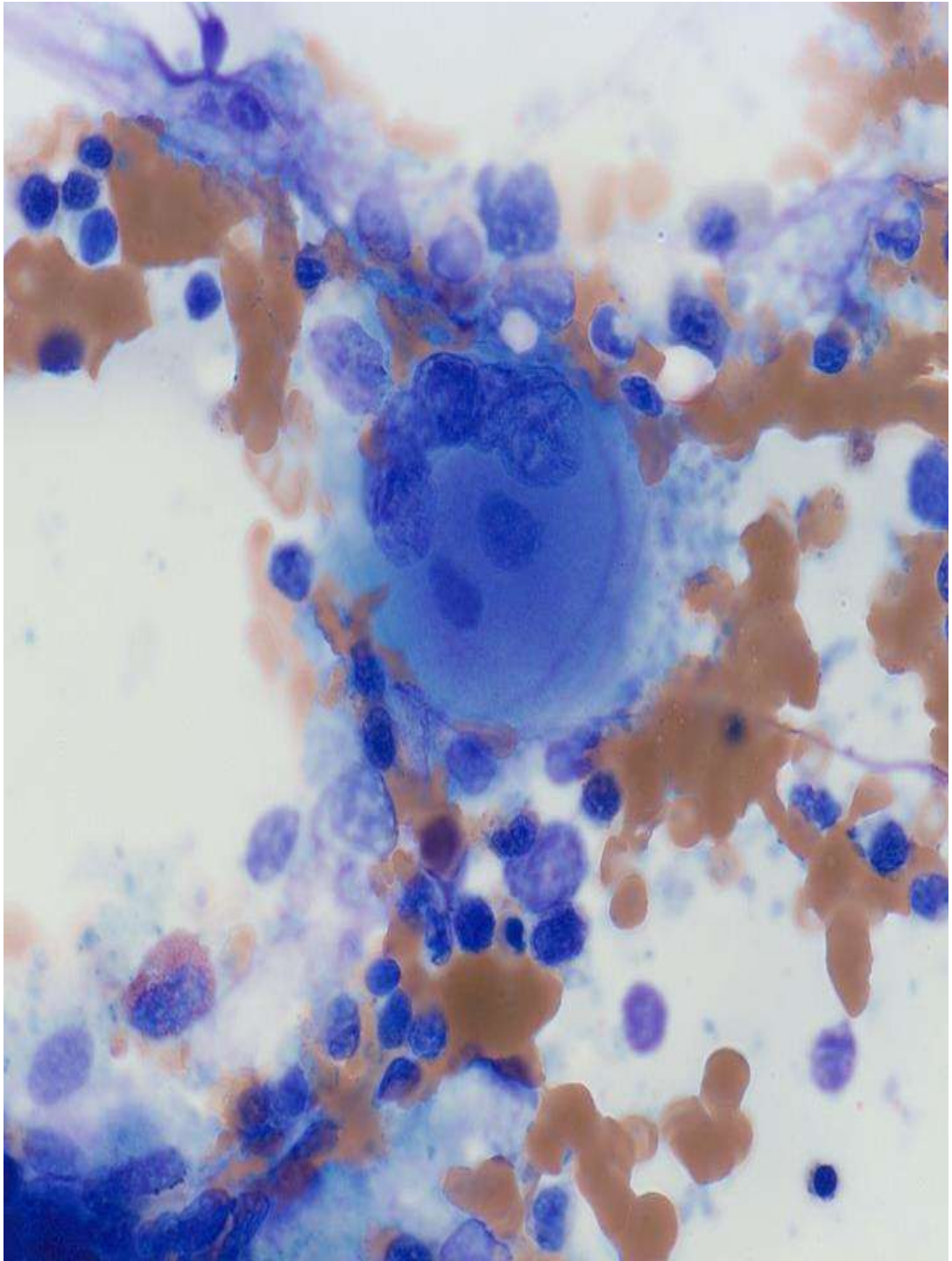


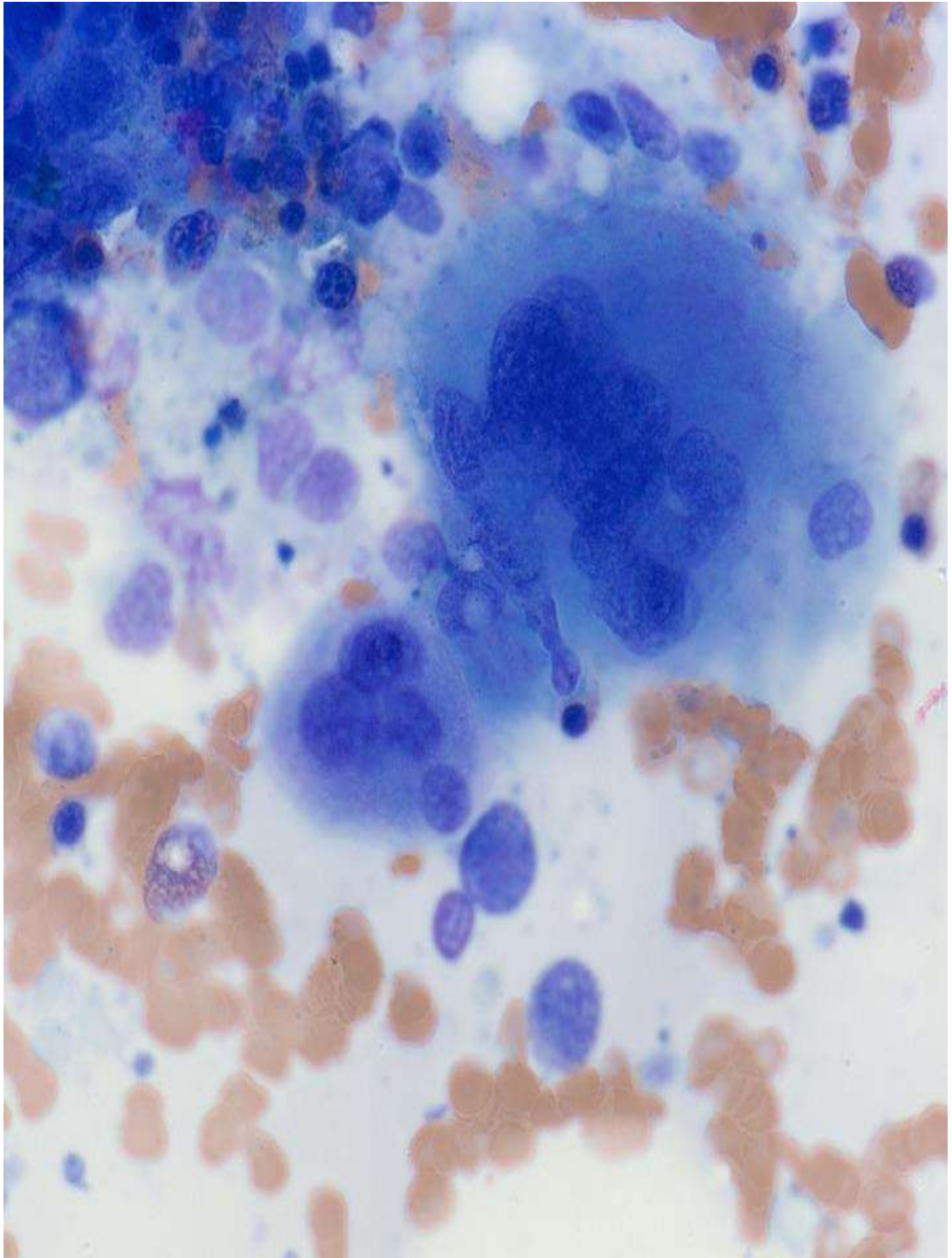


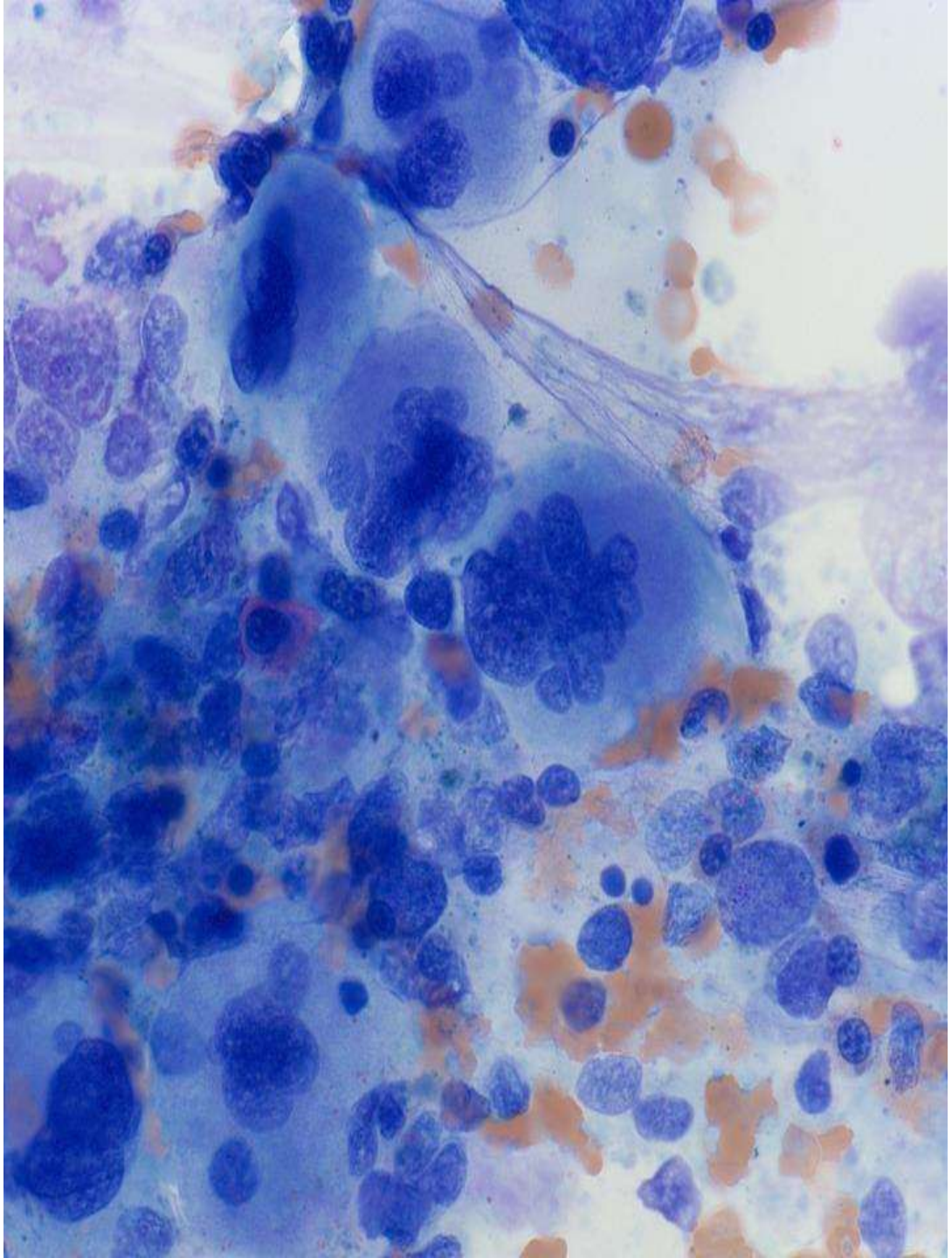


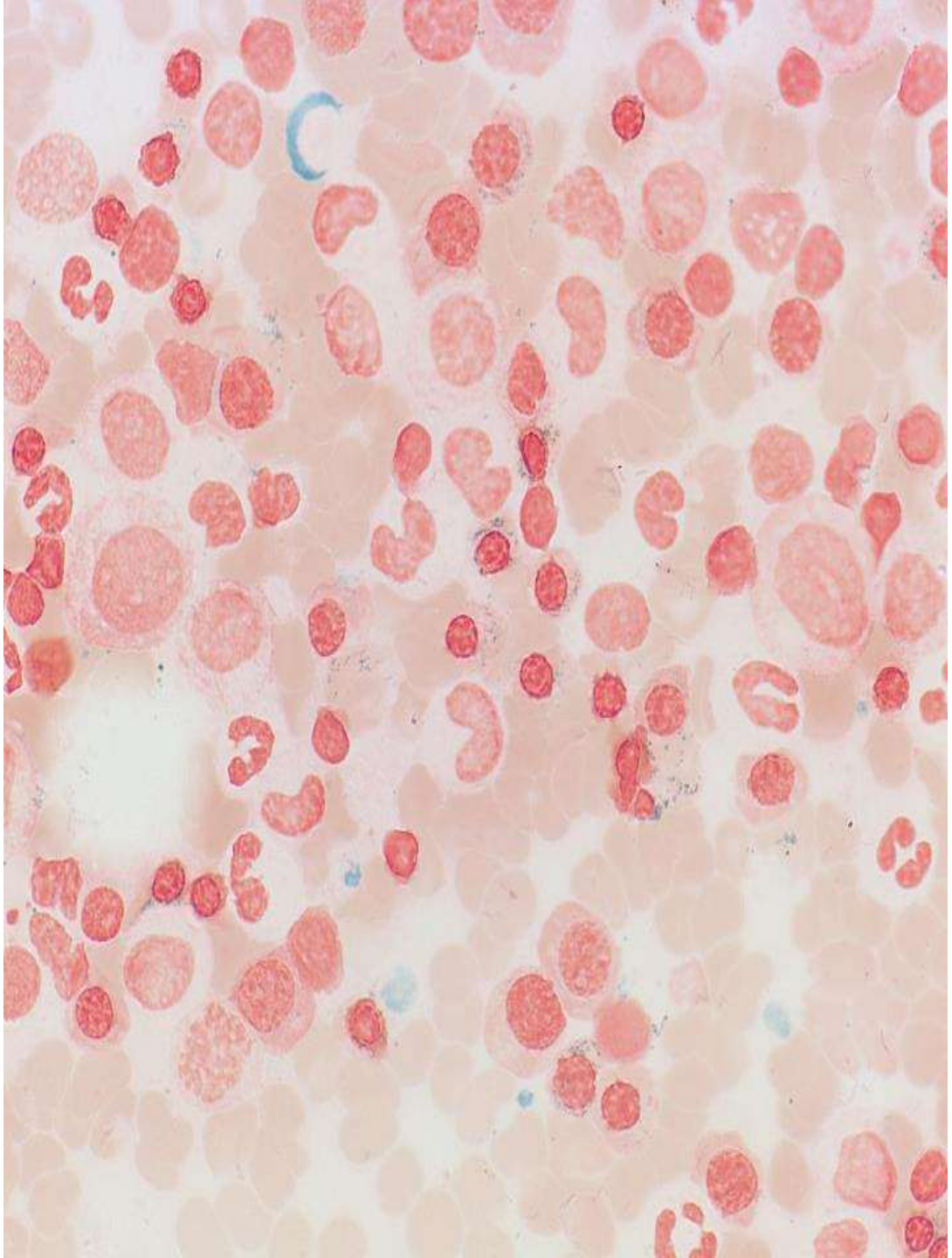


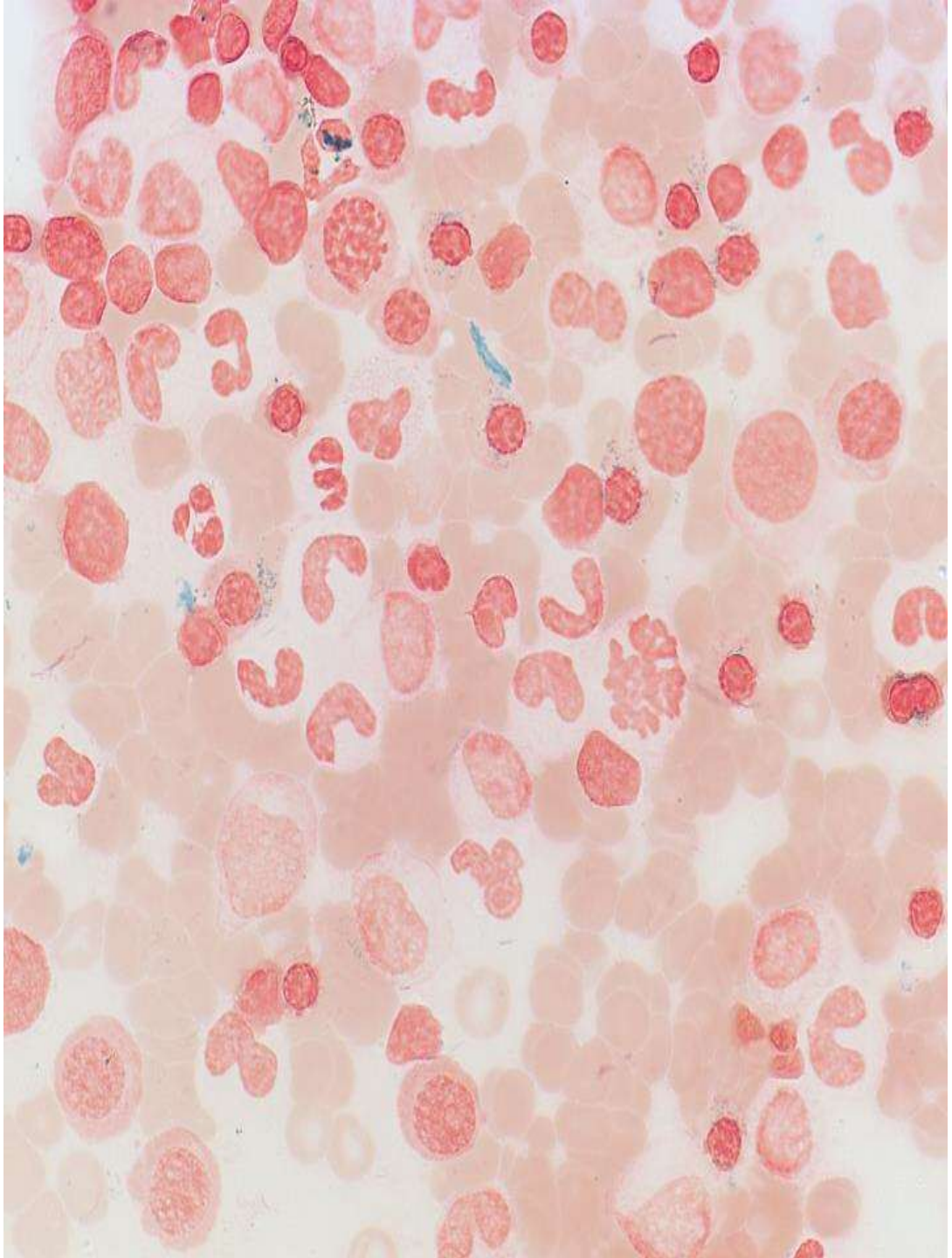


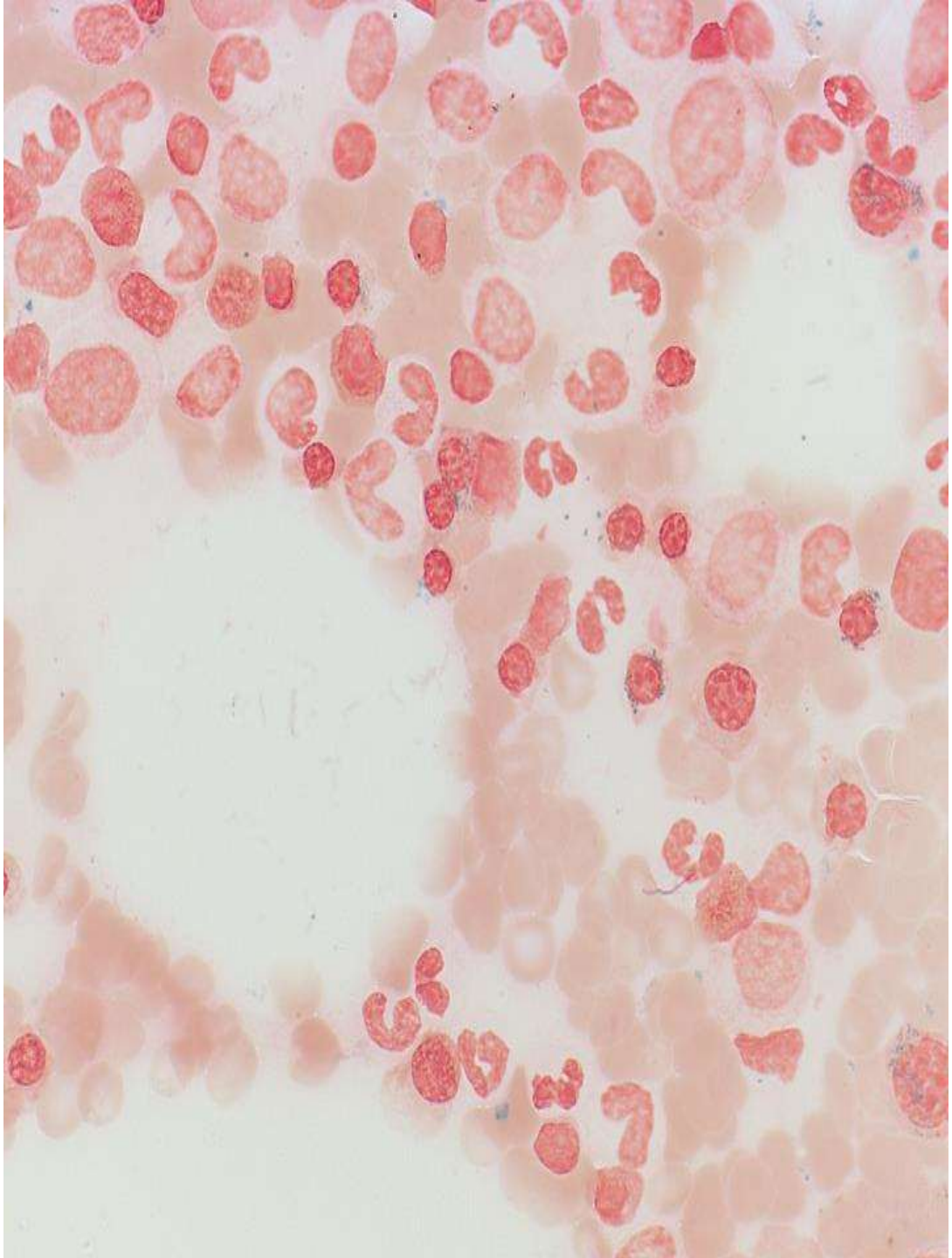




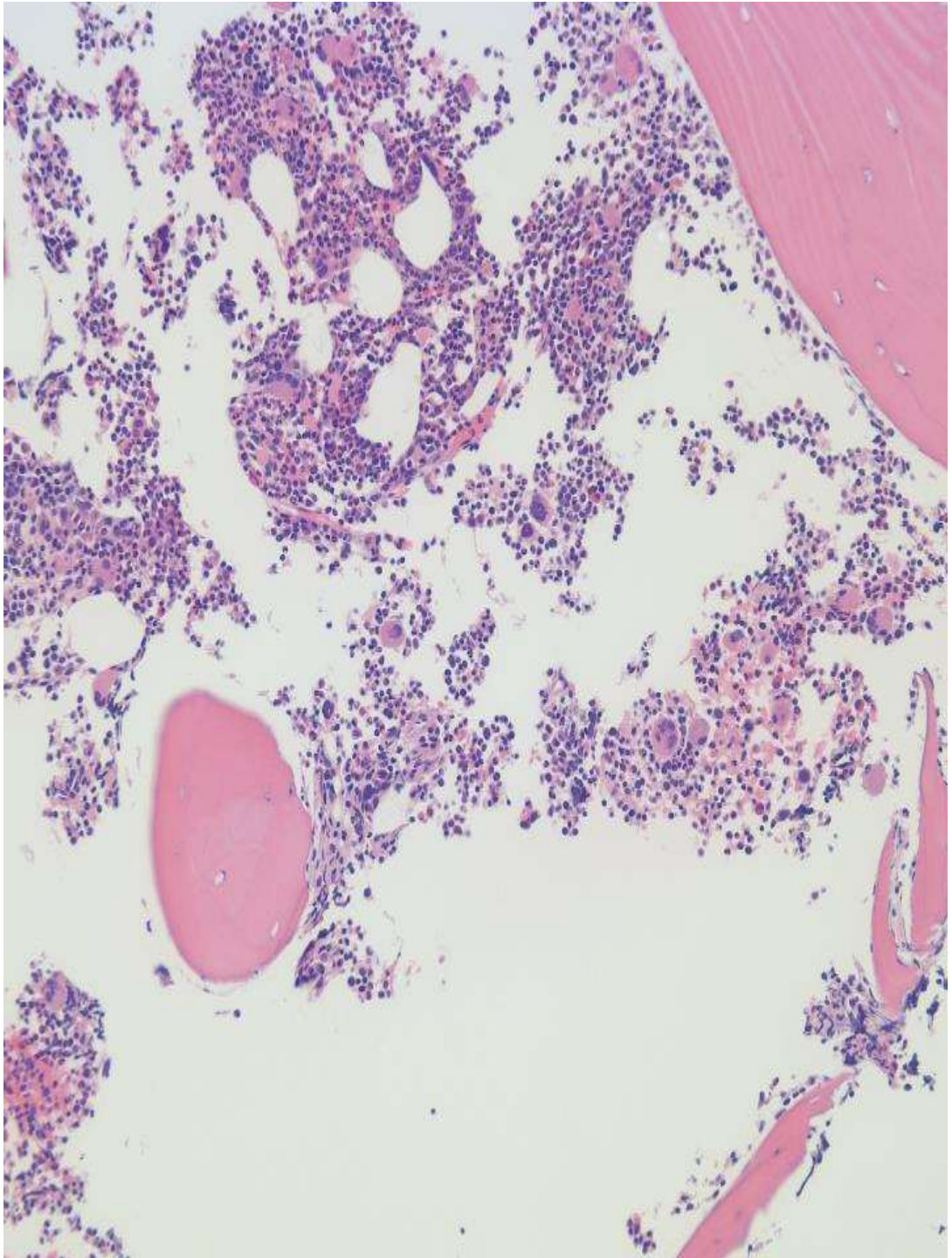


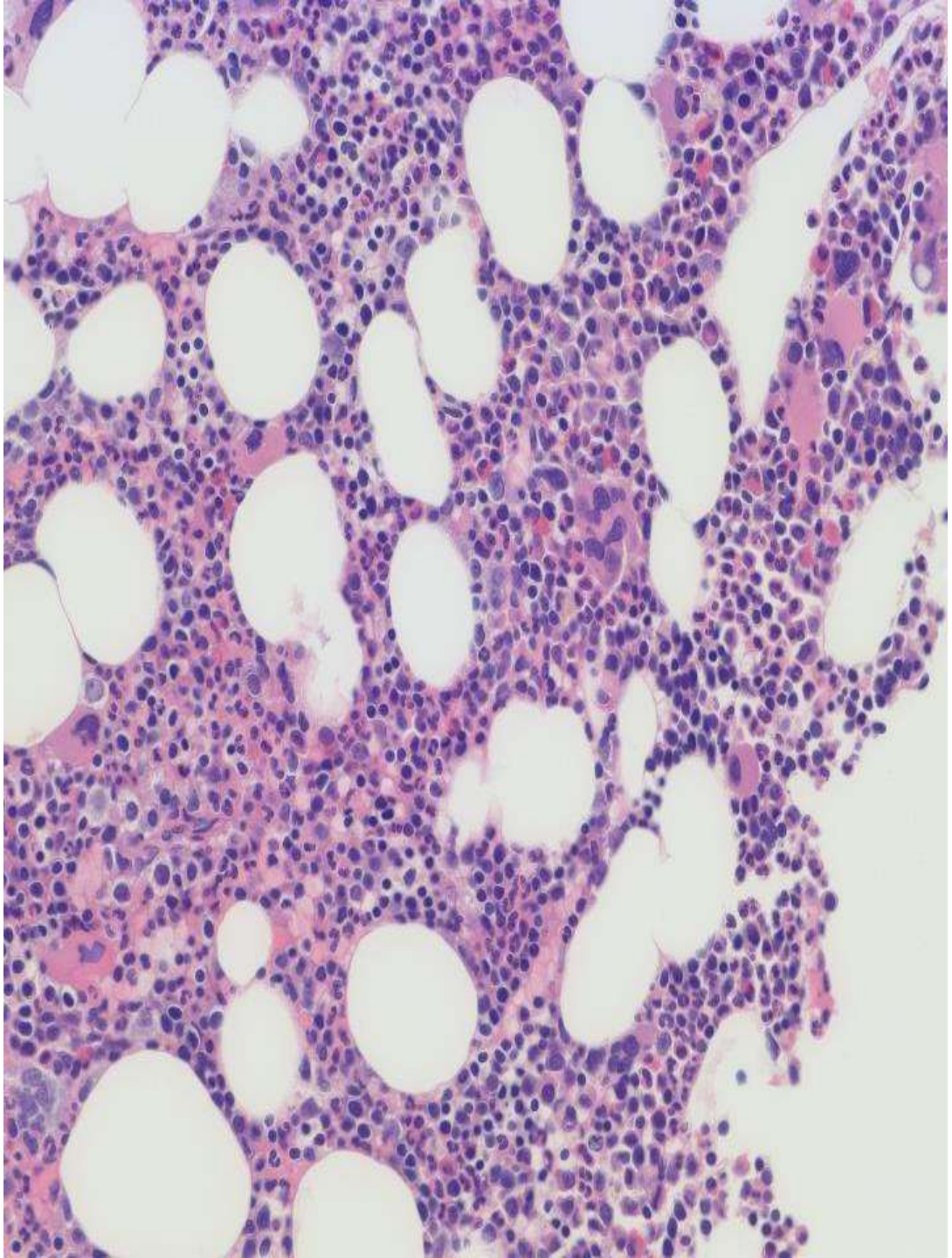


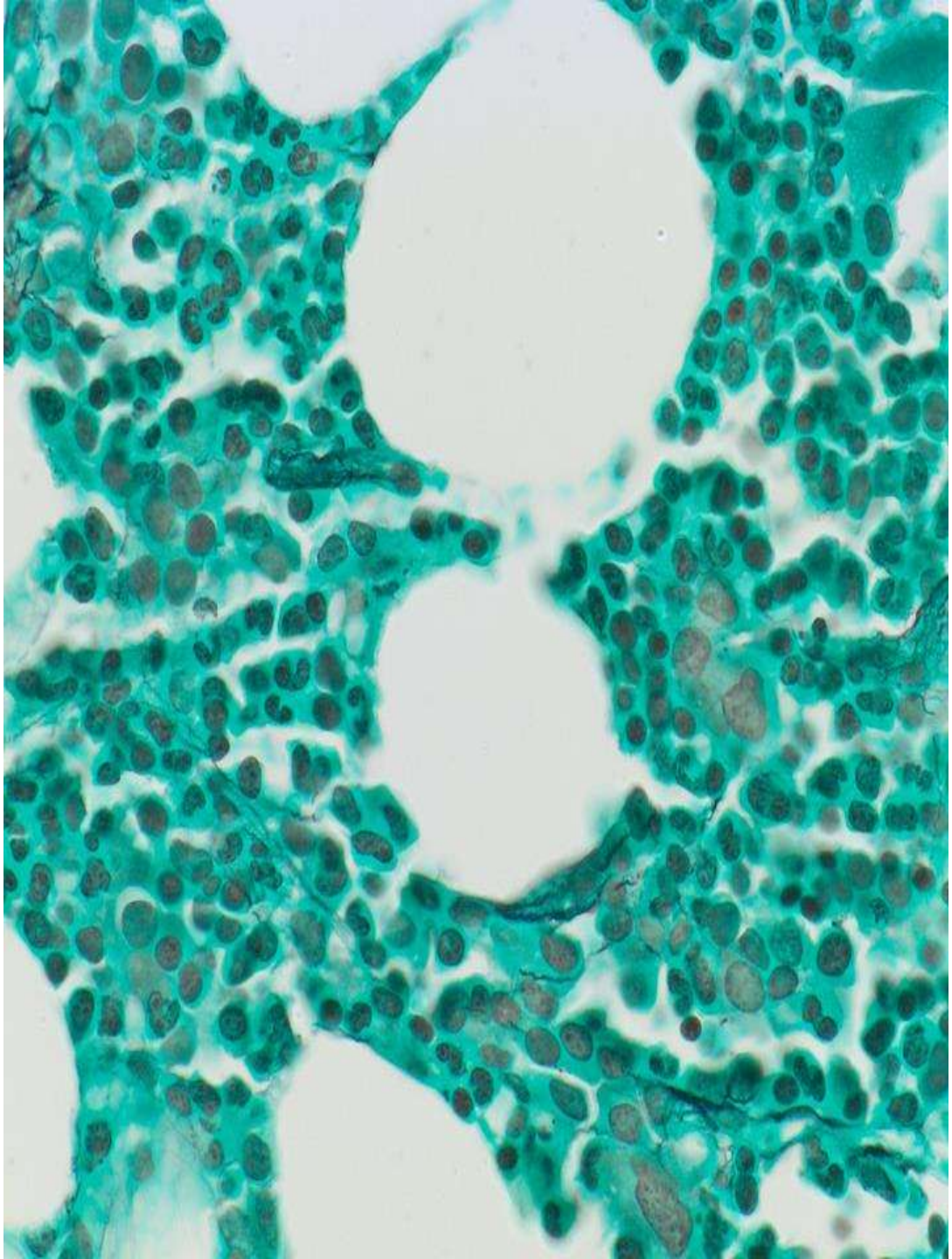


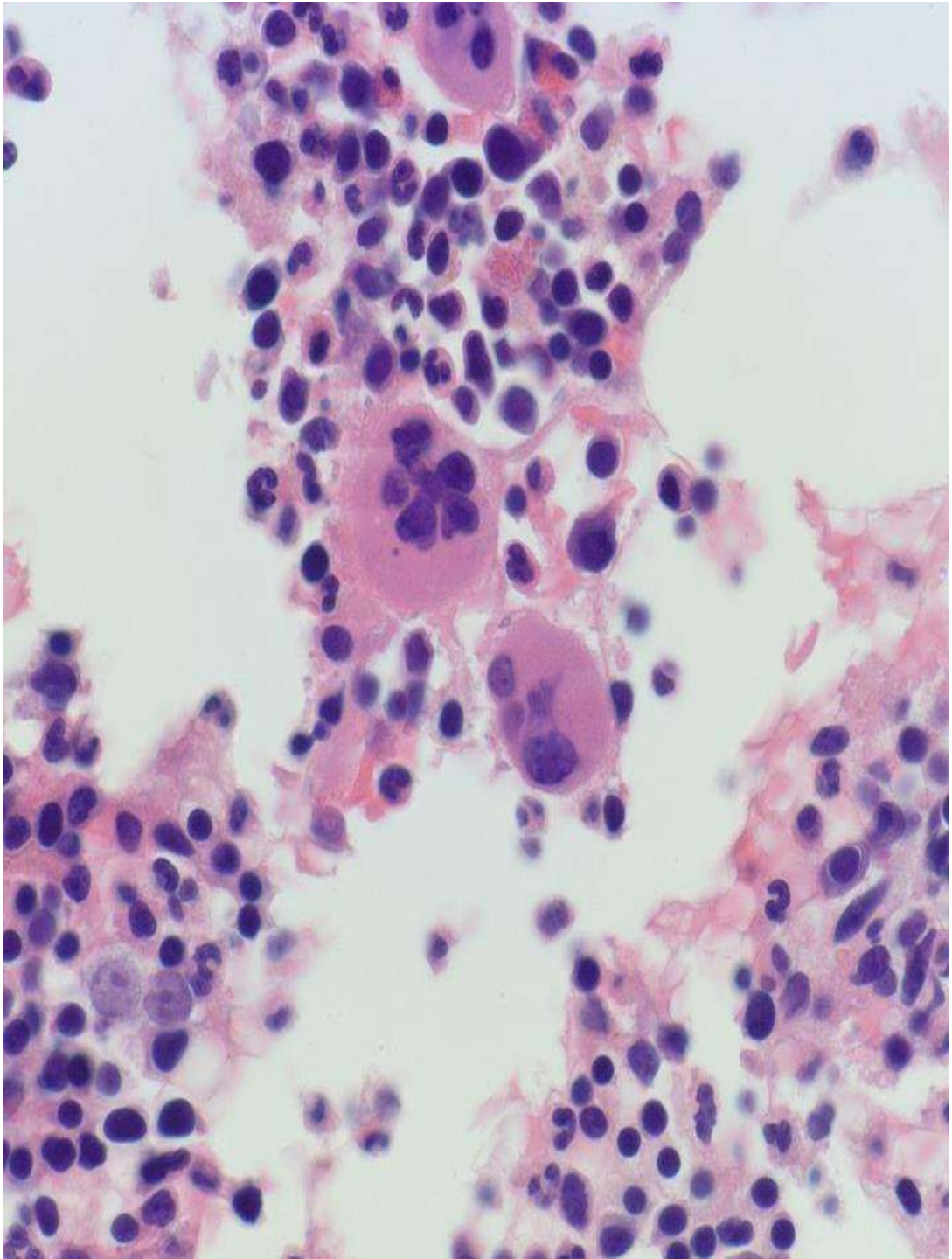


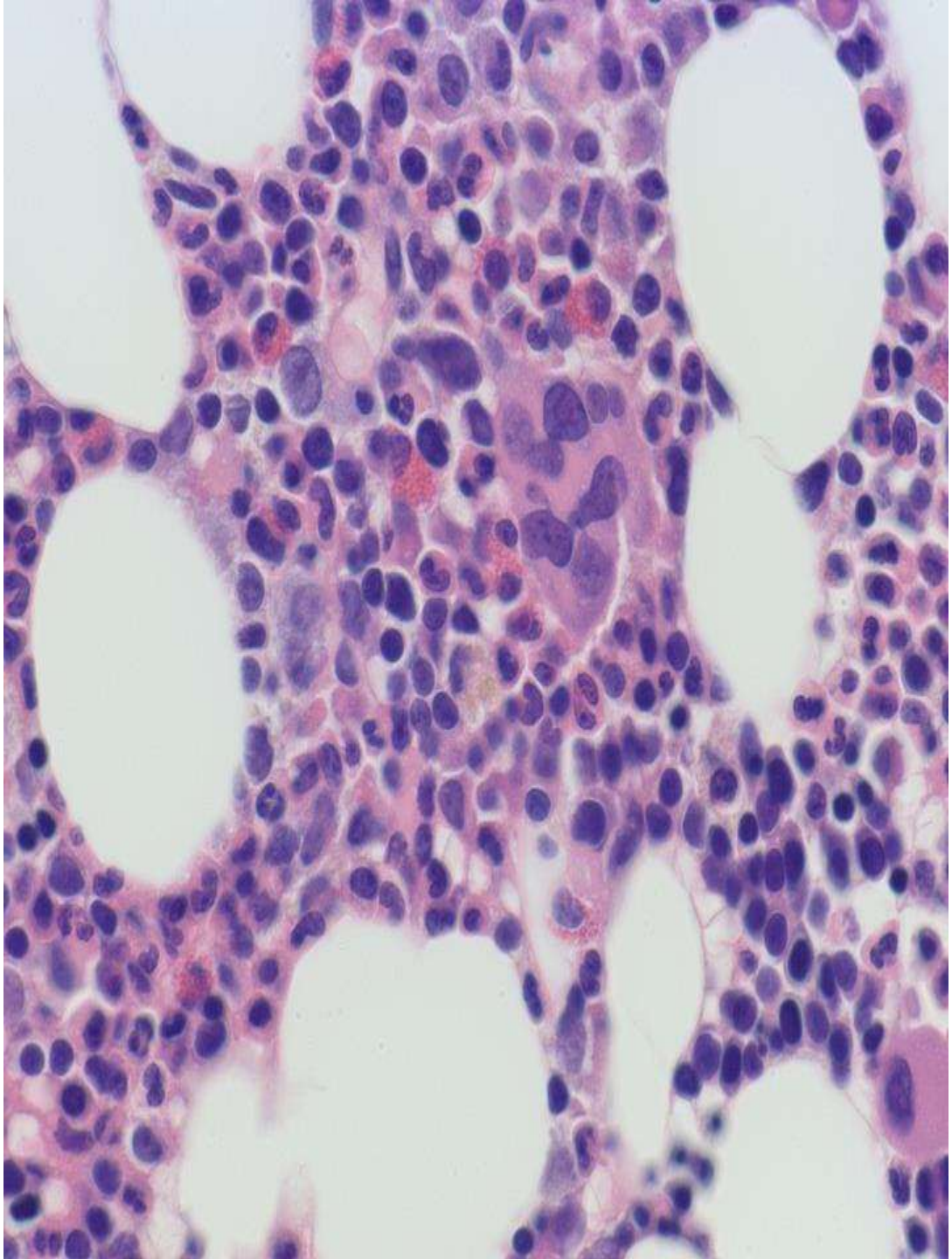
Bone marrow biopsy

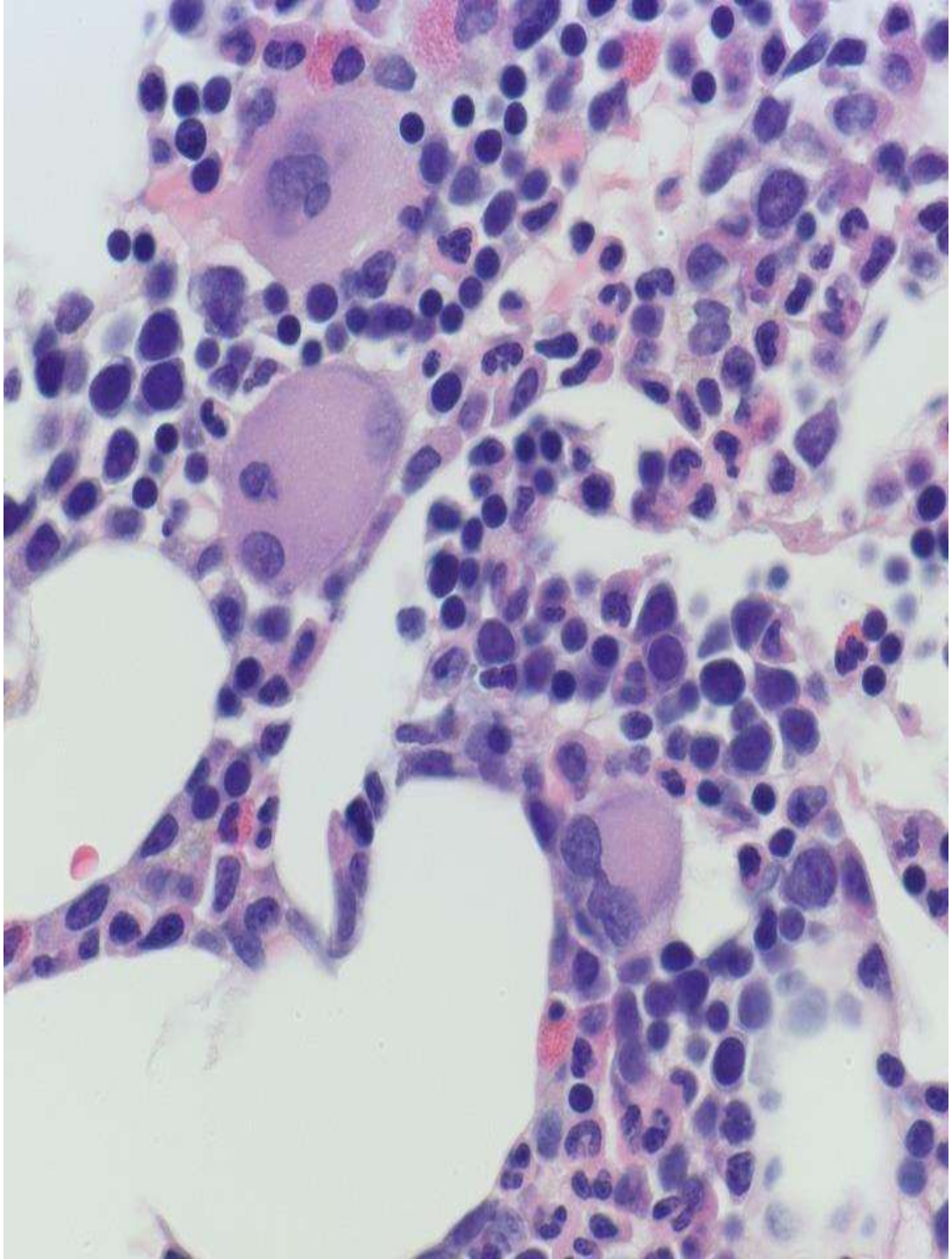












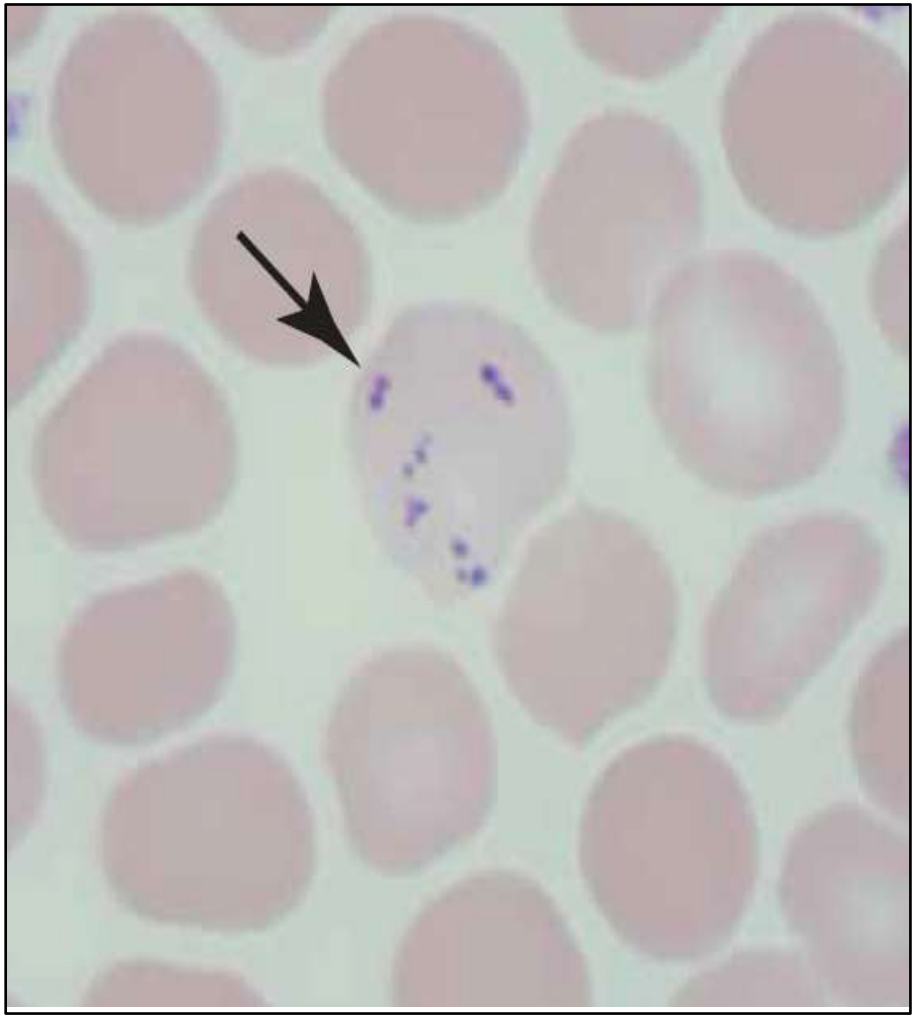
DIAGNOSIS?

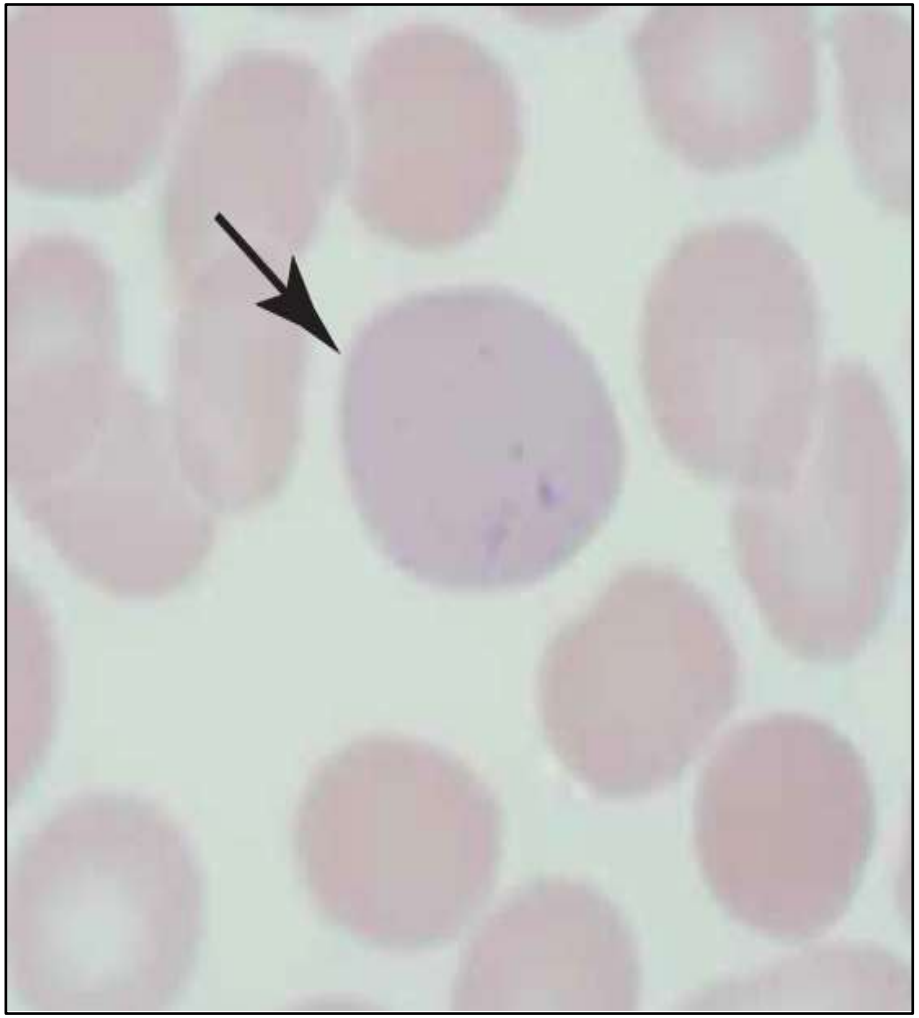
South Bay Pathology Society Unknown Case

Peng Li MD, PhD, Daniel A. Arber MD and Robert Ohgami MD, PhD

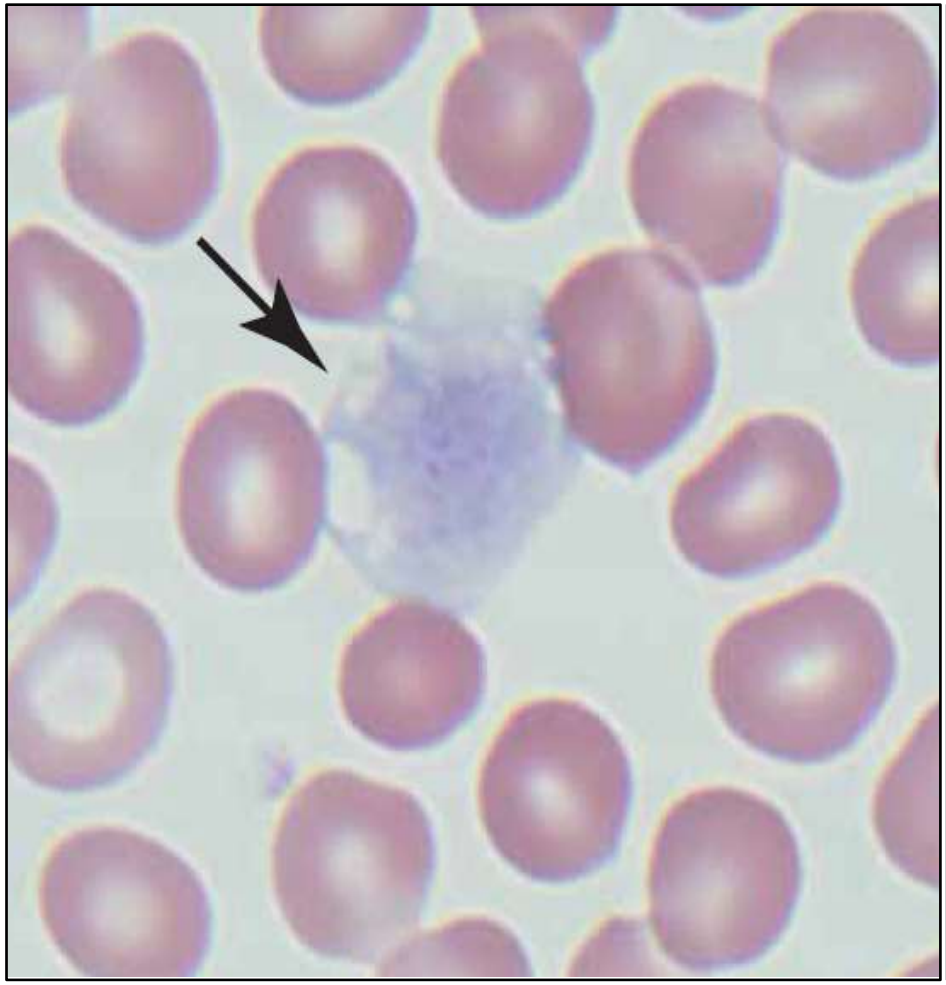
Department of Pathology, Stanford University School of Medicine

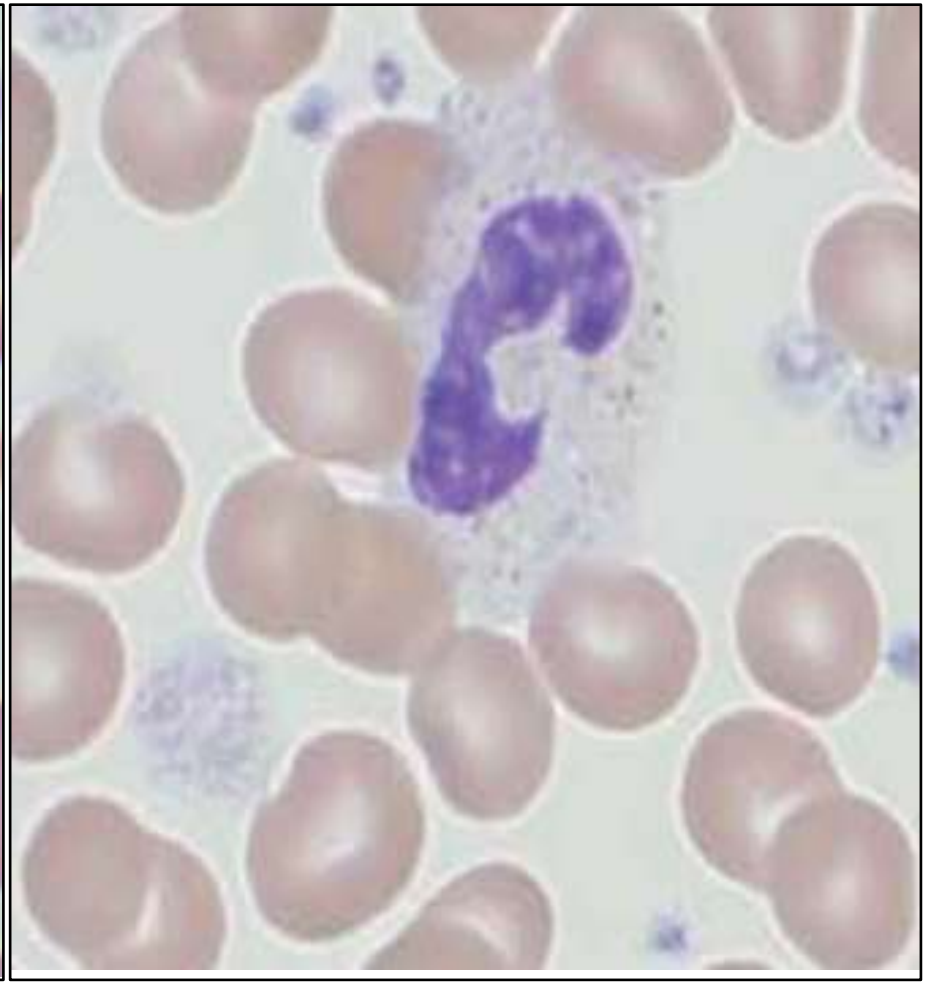
Summary of Peripheral Blood Findings



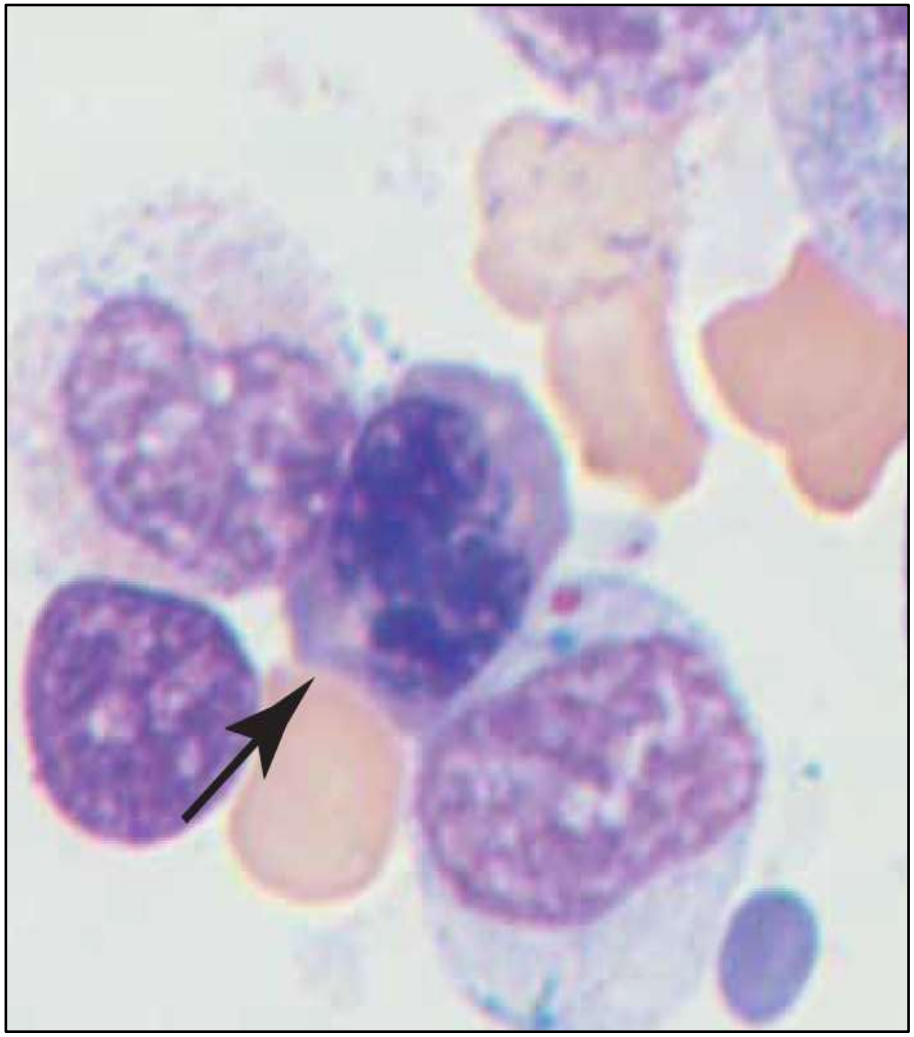


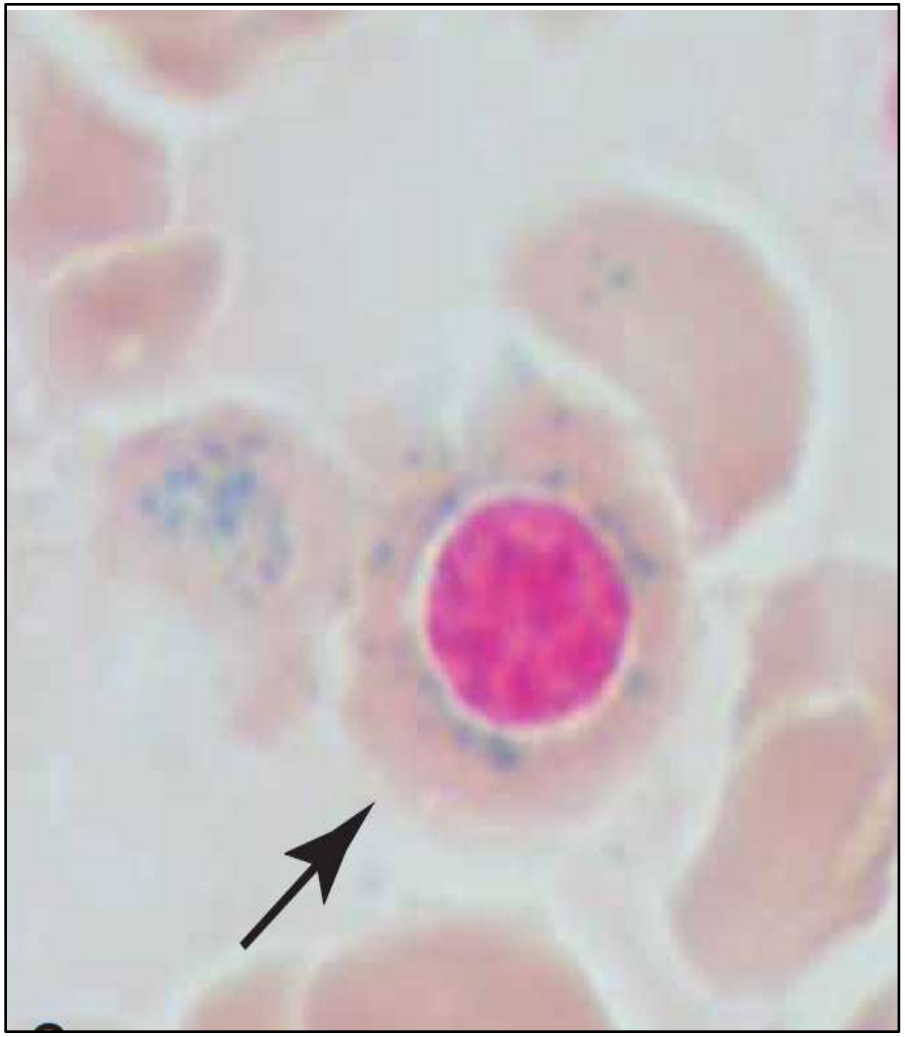
Summary of Peripheral Blood Findings



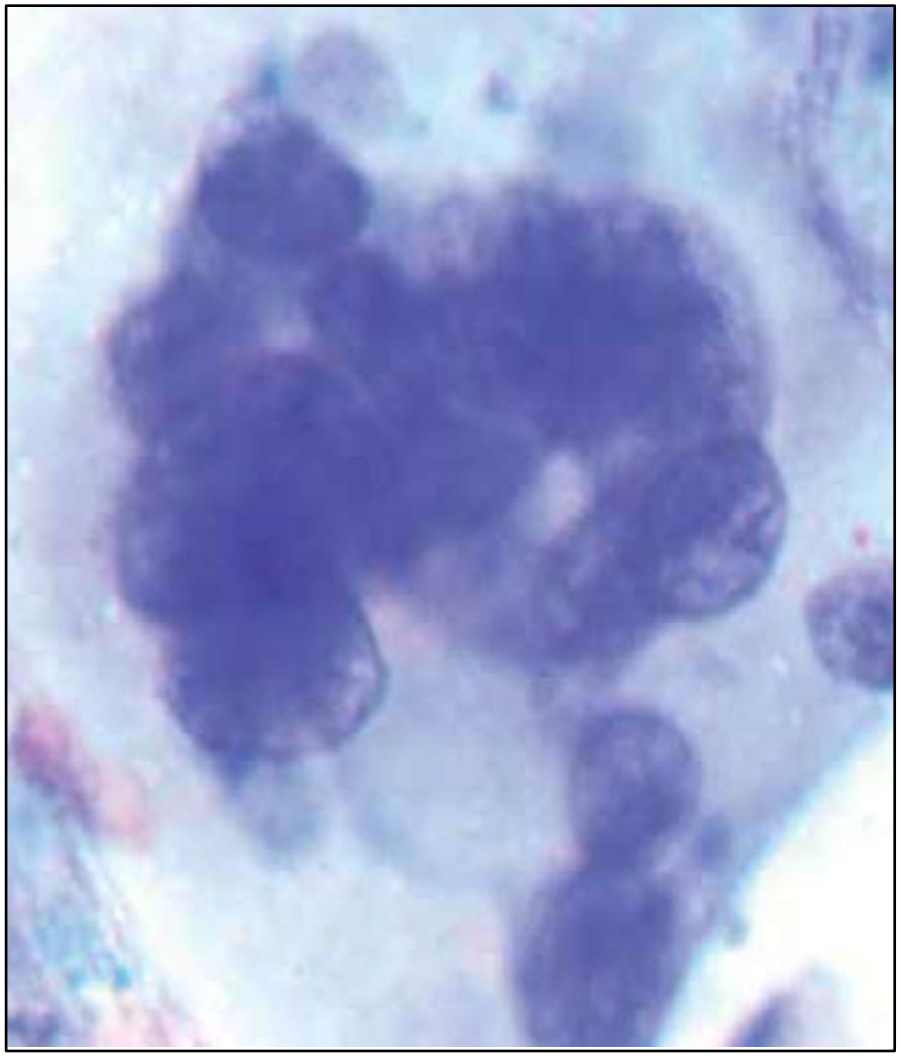


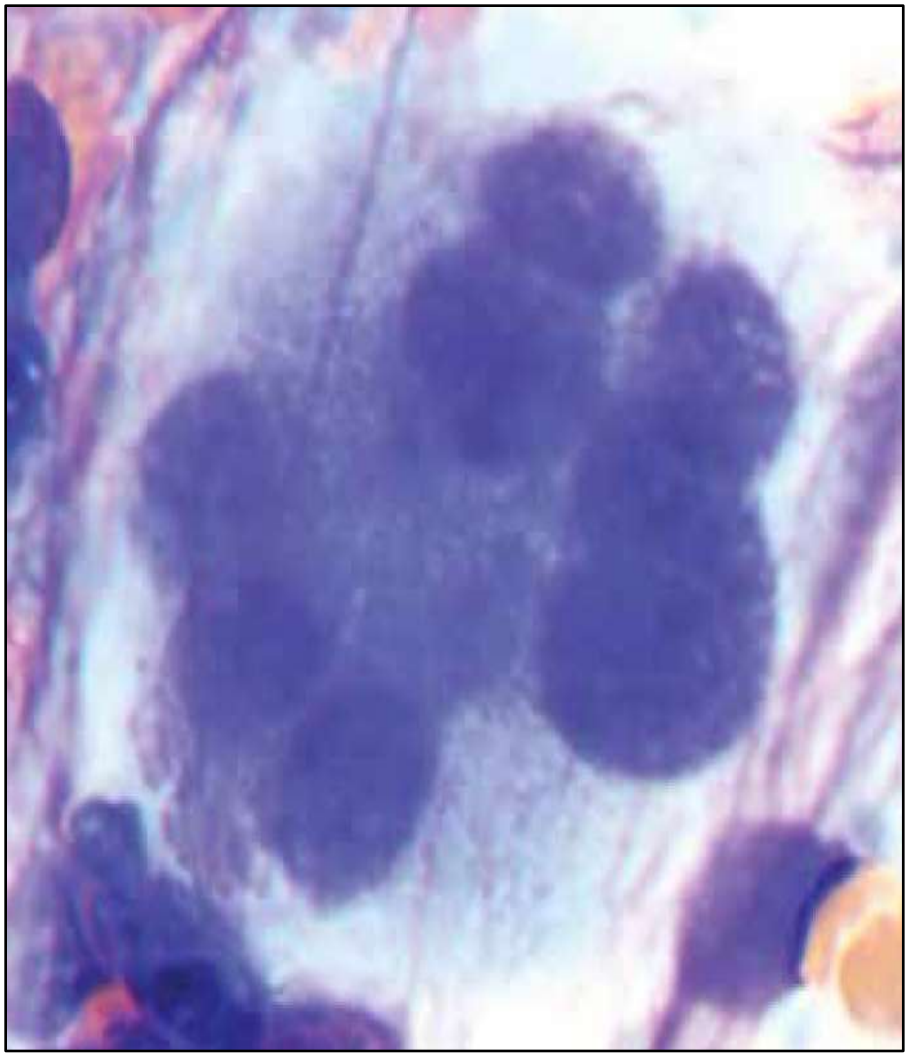
Summary of Bone Marrow Findings





Summary of Bone Marrow Findings





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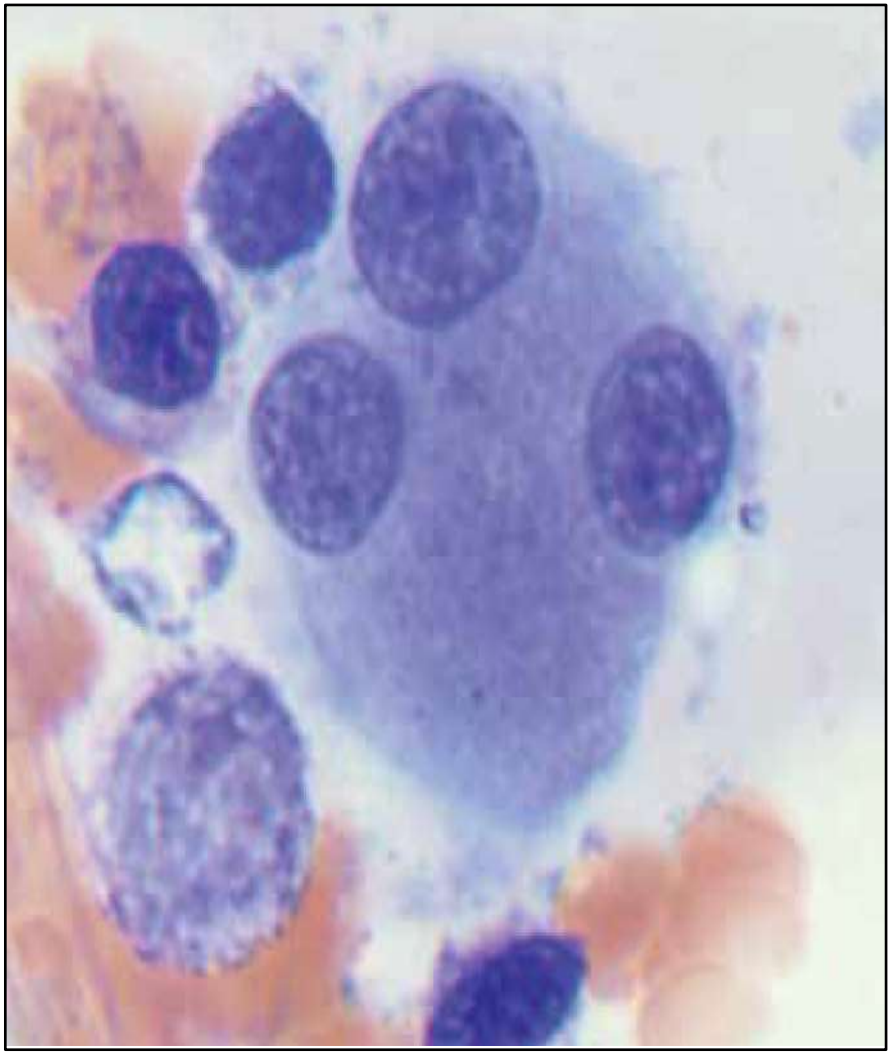

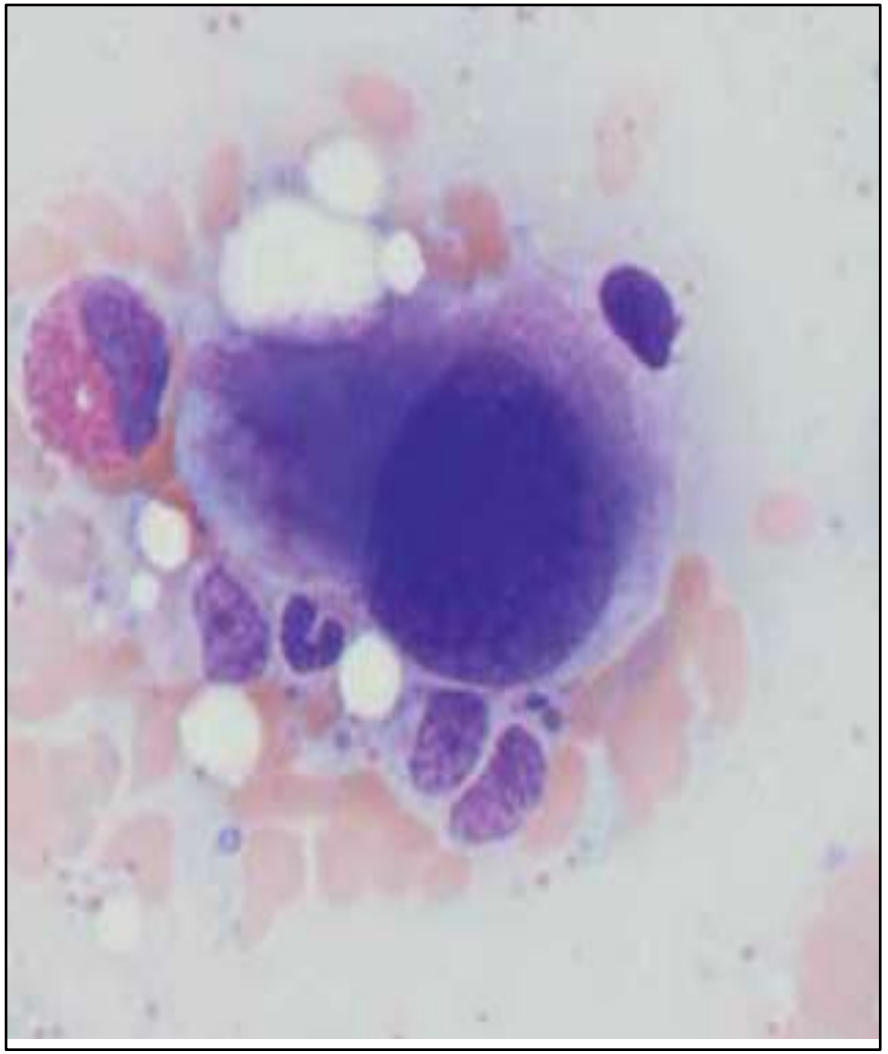

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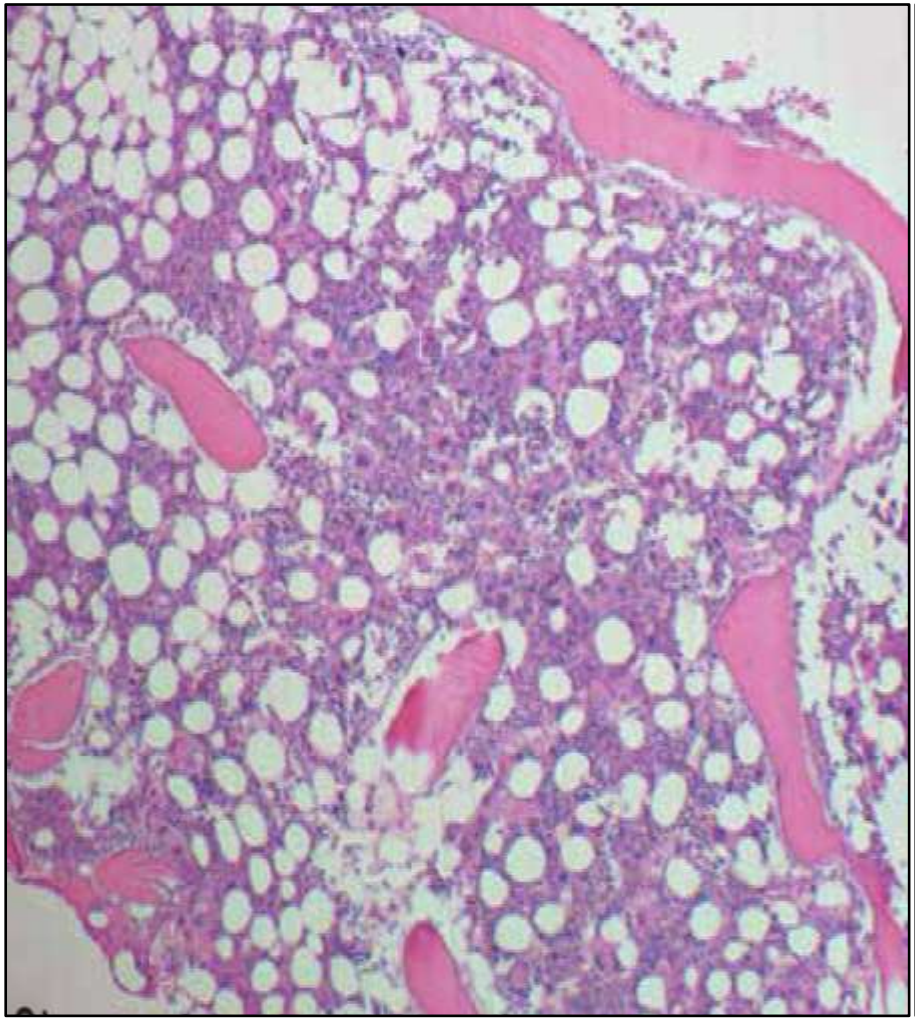

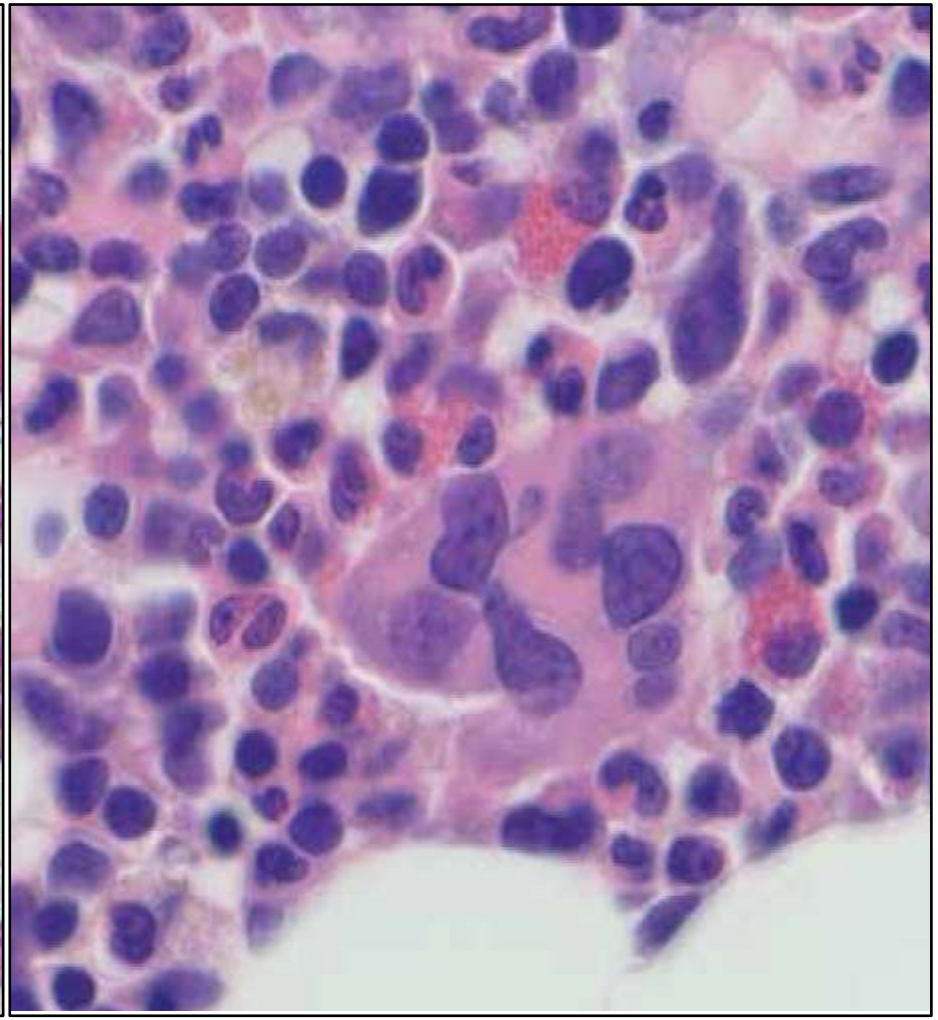

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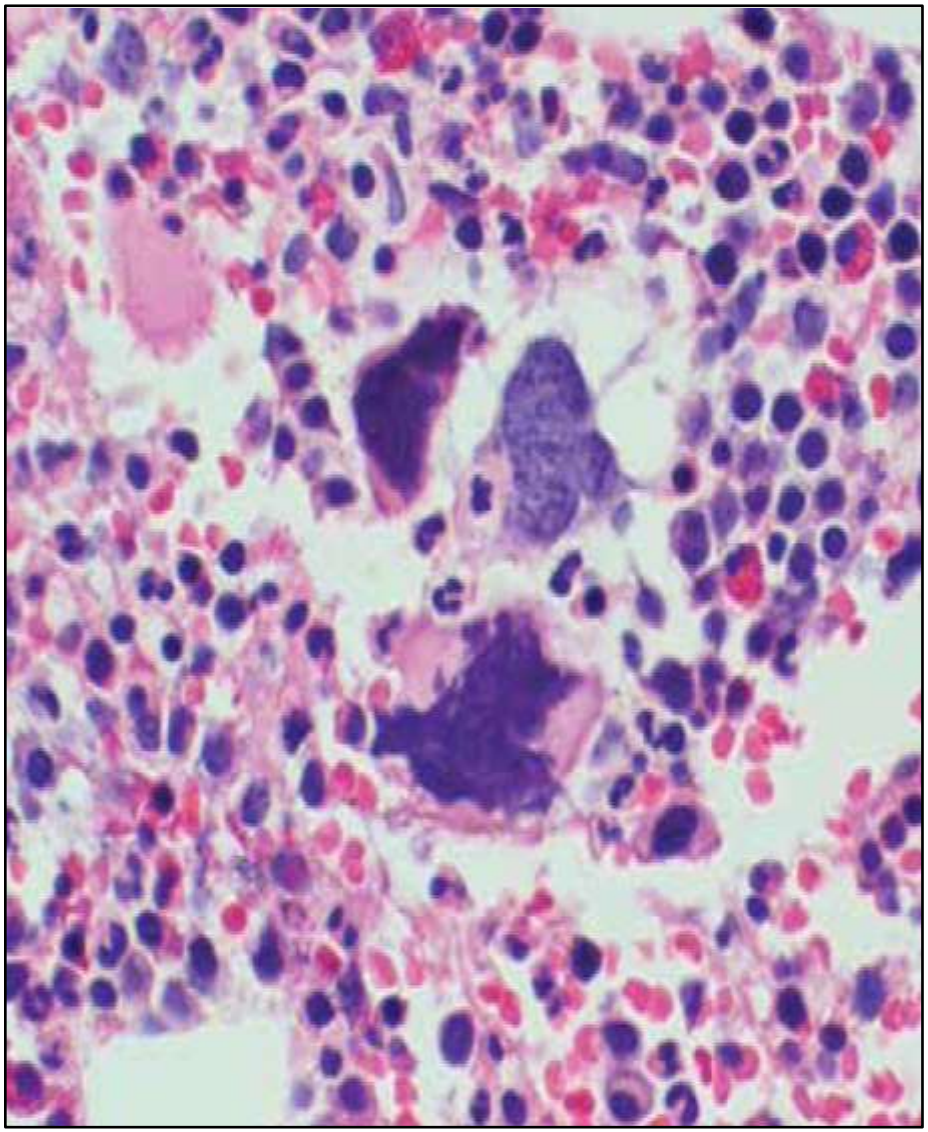

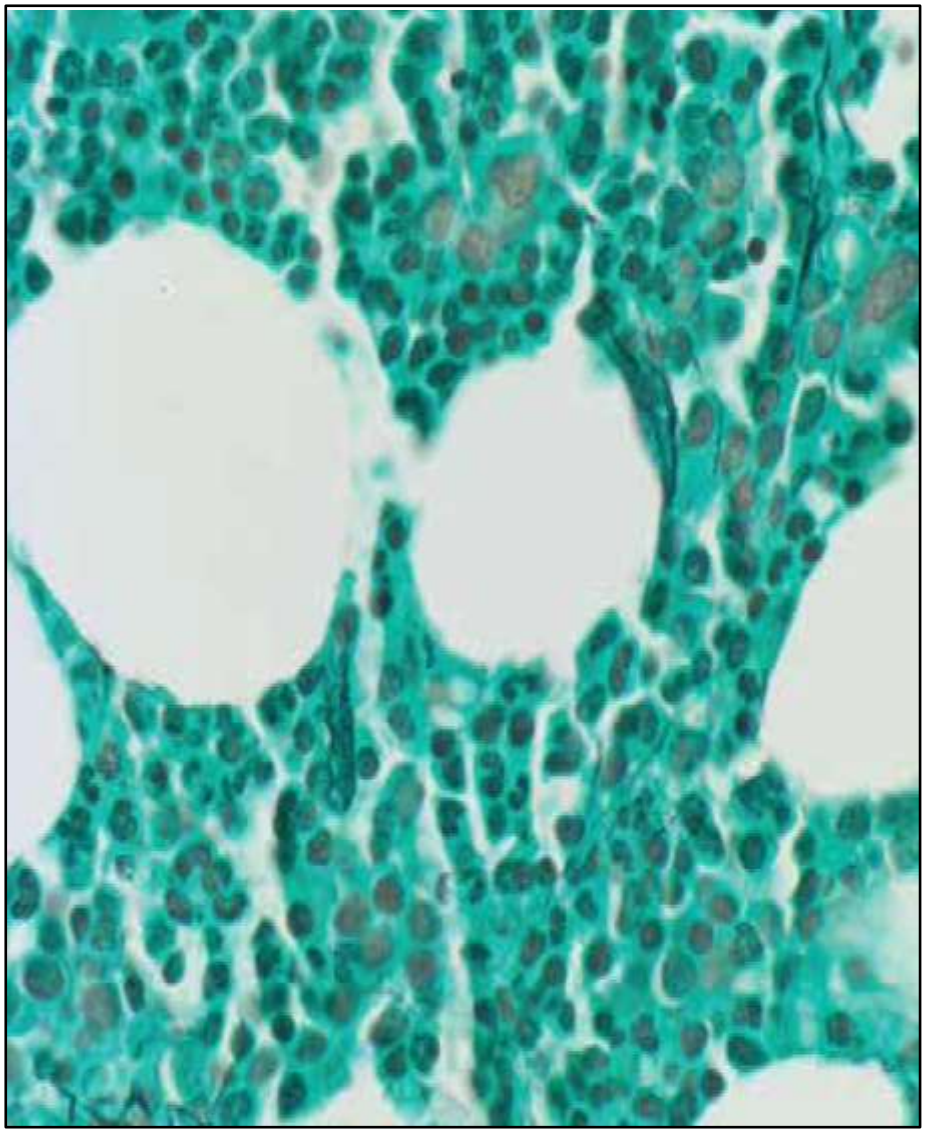

Summary of Morphologic Findings

- Myeloproliferative features
  - Persistent thrombocytosis without anemia
  - Hyperlobated megakaryocytes
- Dysplastic features
  - Erythrocytes: peripheral blood findings, ring sideroblasts and nuclear irregularity
  - Megakaryocytes: hypogranular giant platelets
  - Myeloid cells: hypogranulation
- Bone marrow cellularity: Normal
- Myelofibrosis: No

Summary of Cytogenetic and Molecular Findings

- Karyotype: Normal
- Molecular findings
  - JAK2: negative
  - BCL-ABL: negative
  - MPL: negative
  - SF3B1: Positive

Differential Diagnoses

- ❑ MDS/MPN with ring sideroblasts and thrombocytosis (RARS-T)
- ❑ ET with acquired ring sideroblasts
- ❑ MDS/MPN NOS
- ❑ RARS

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MDS/MPN with Ring Sideroblasts and Thrombocytosis

- A new full entity in the 2016 revision
- Previously a provisional entity: RARS-T

Diagnostic criteria in Updated WHO

- Anemia associated with erythroid lineage dysplasia
- ≥15% ring sideroblasts* even if *SF3B1* mutation is detected
- No increase in blasts (<1% in PB, <5% in BM)
- Persistent thrombocytosis ≥450 x 10^9/L
- SF3B1 mutation
- No history of recent cytotoxic or growth factor therapy, no history of MPN, MDS (except MDS-RS), or other type of MDS/MPN
- No *BCR-ABL1* fusion gene, no rearrangement of *PDGFRA*, *PDGFRB* or *FGFR1*; or *PCM1-JAK2*; no t(3;3)(q21;q26), inv(3)(q21q26) or del(5q)

Arber, Blood, 2016

MDS/MPN with Ring Sideroblasts and Thrombocytosis

A mixed group exhibiting a spectrum of morphologic and molecular findings

- All patients had thrombocytosis and anemia
- Leukocytosis: +/-
- Ring sideroblasts: 8% to 75%
- SF3B1 mutation: >80%, strongly correlates with RS
  - JAK2(V617F): ~60%
  - MPL(W515L): <5%
  - CALR: <5%
- Cytogenetics: normal

Gurevich et al, Am J Clin Pathol, 2011
Patnaik et al, Am J Hematol, 2015

Unique Findings in the Current Case

- ?Anemia

A Case Series of MDS/MPN-RS-T without Anemia

	Case 1	Case 2	Case 3	Case 4
Age at original presentation	52	54	57	82
Gender	M	M	F	F
Hgb (g/dL)	16.8	14.8	14.3	12.5
MCV (fL)	78.1	95.0	91.2	90
Plt (K/uL)	690	652	626	>450
Cellularity	Normocellular	Normocellular	Normocellular	hypercellular
Increase of blast	No	No	No	No
Dyspoiesis	Dysmegakaryopoiesis	Dysmegakaryopoiesis	Dyserythropoiesis and dysmegakaryopoiesis	Dysmegakaryopoiesis
Ring	+ (17%)	+ (1%)	+ (15%)	+ (>15%)
Myelofibrosis	MF0	MF0-1	MF0	n/a
Karyotype	5q-	Normal	Normal	n/a
JAK2	+	+	-	+
MPL and CalR	n/a	n/a	-	n/a
SF3B1	?	?	+	?
Follow up	16 years	19 years	1 year	n/a

MDS/MPN-RS-T with and without Anemia

- Clinical manifestations
- Morphologic features
- Cytogenetic findings
- Molecular findings
- Prognosis

Are similar in cases WITH and WITHOUT anemia

Take Home Points

- A new full WHO entity: MDS/MPN with ring sideroblasts and thrombocytosis
- Both MPN and MDS morphologic features
- Presence of a SF3B1 mutation
- ANEMIA MAY BE ABSENT