Disclosures
February 2, 2015

Dr. Sonam Prakash has disclosed that she received monetary benefits from Incyte Corporation in her role as advisor for the Hematopathology Publications Steering Committee. The activity planners have determined that this financial relationship is not relevant to the case being presented.

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

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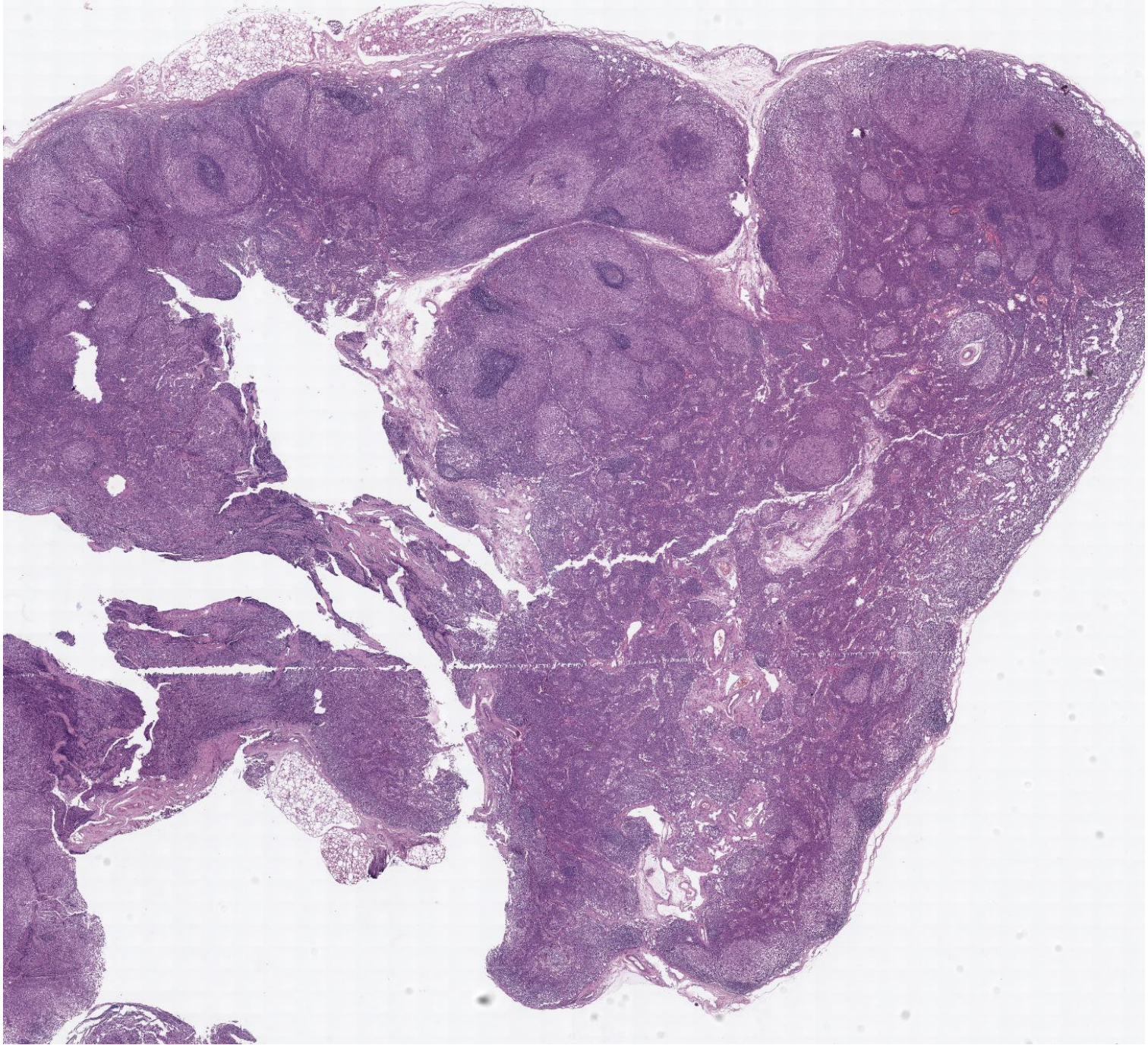
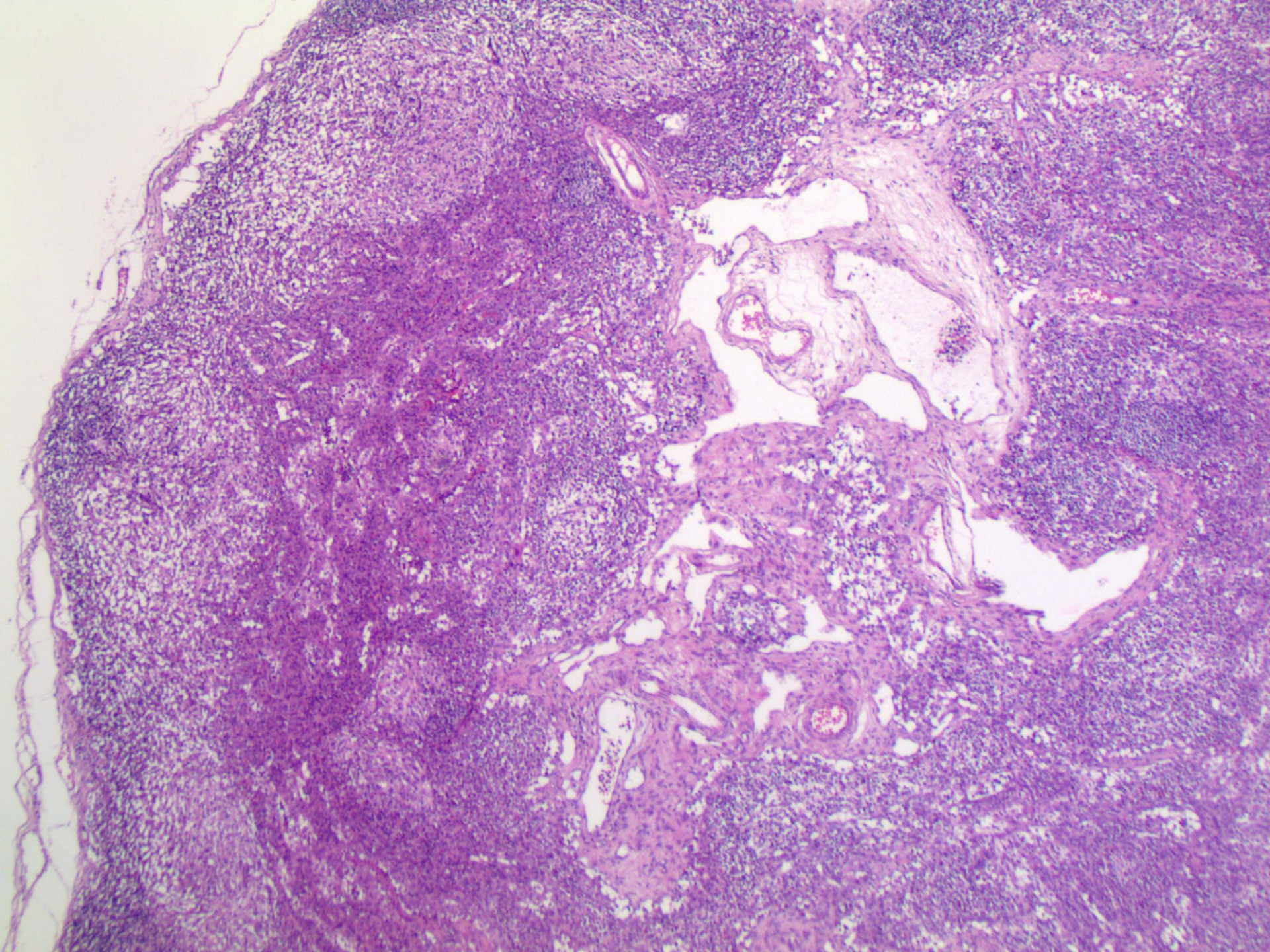
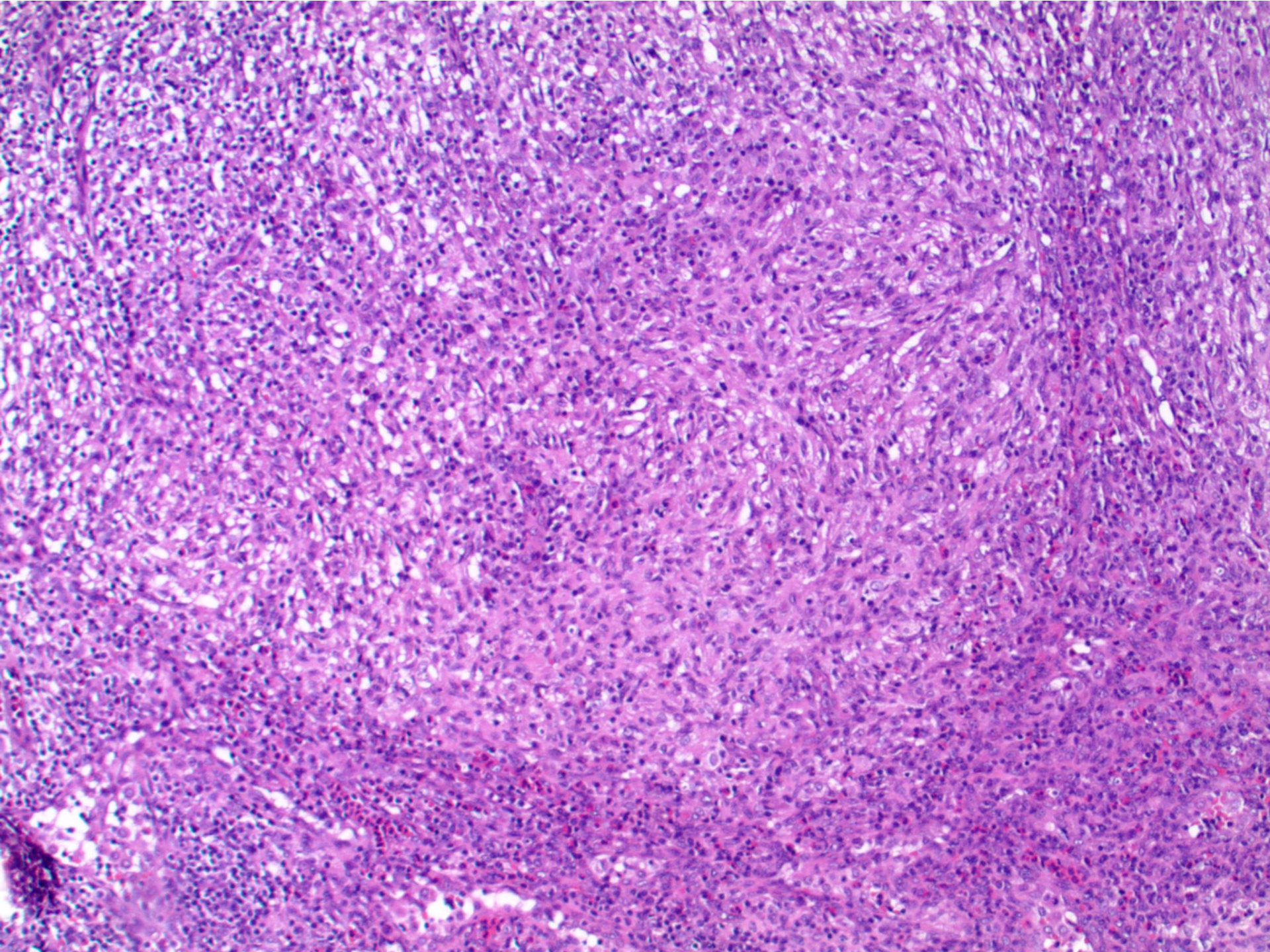
SB 5911

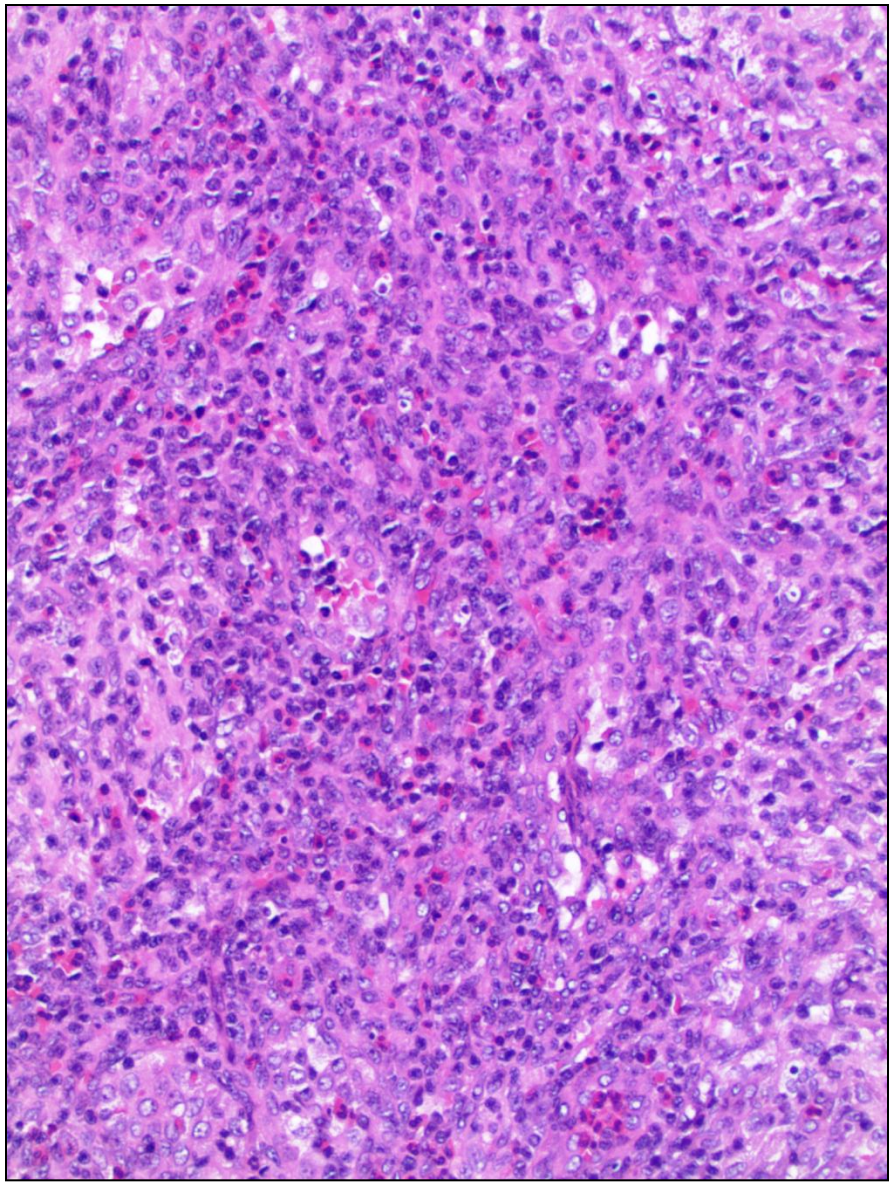
Nabeen Nayak; Sir Ganga Ram Hospital (New Delhi)

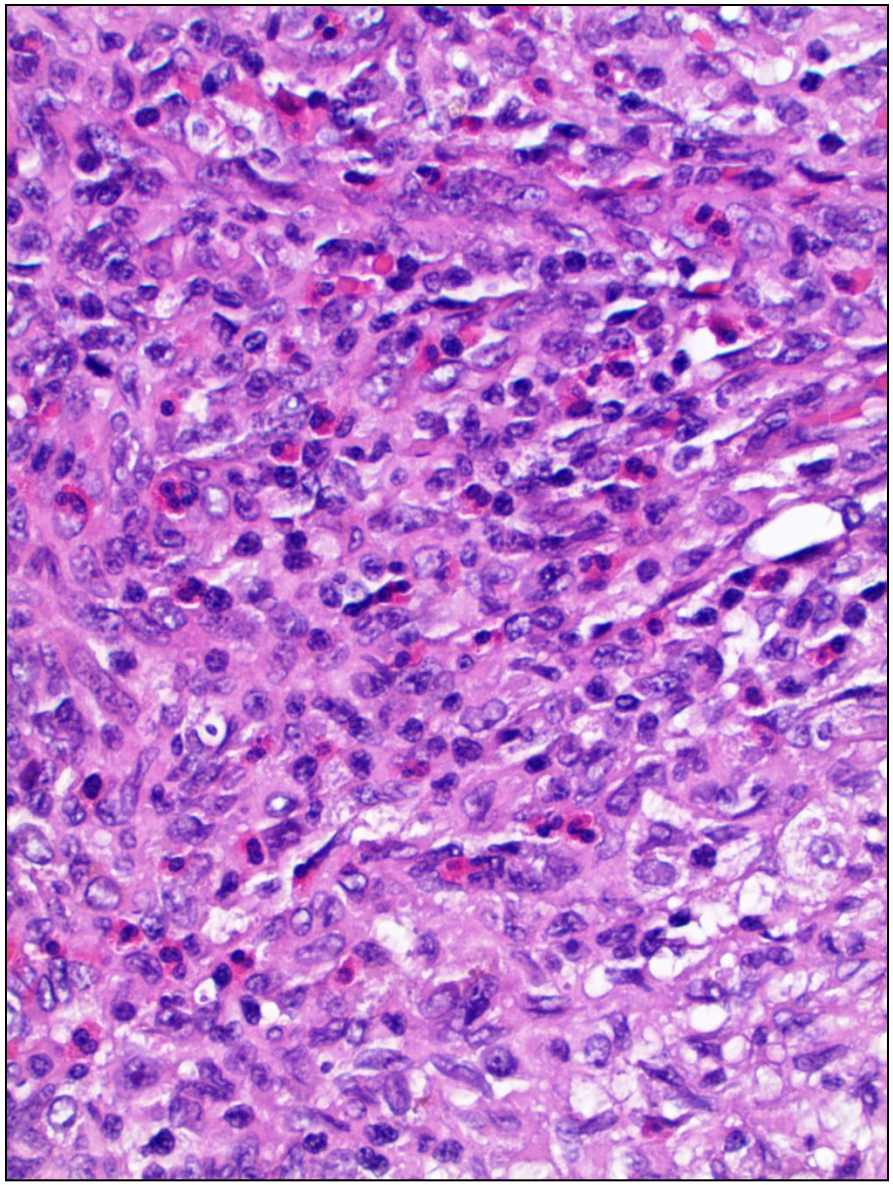
8-week-male infant (firstborn after 3 first trimester abortions) was brought in for evaluation of multiple swellings in axilla and groin first noticed at 6 week age. He had diffuse maculopapular rash on the face and trunk at birth resembling atopic rash which persisted together with seborrheic dermatitis in the scalp. The child however had no diarrhea and was active and thriving well. The swellings (considered to be lymph nodes) were excised.

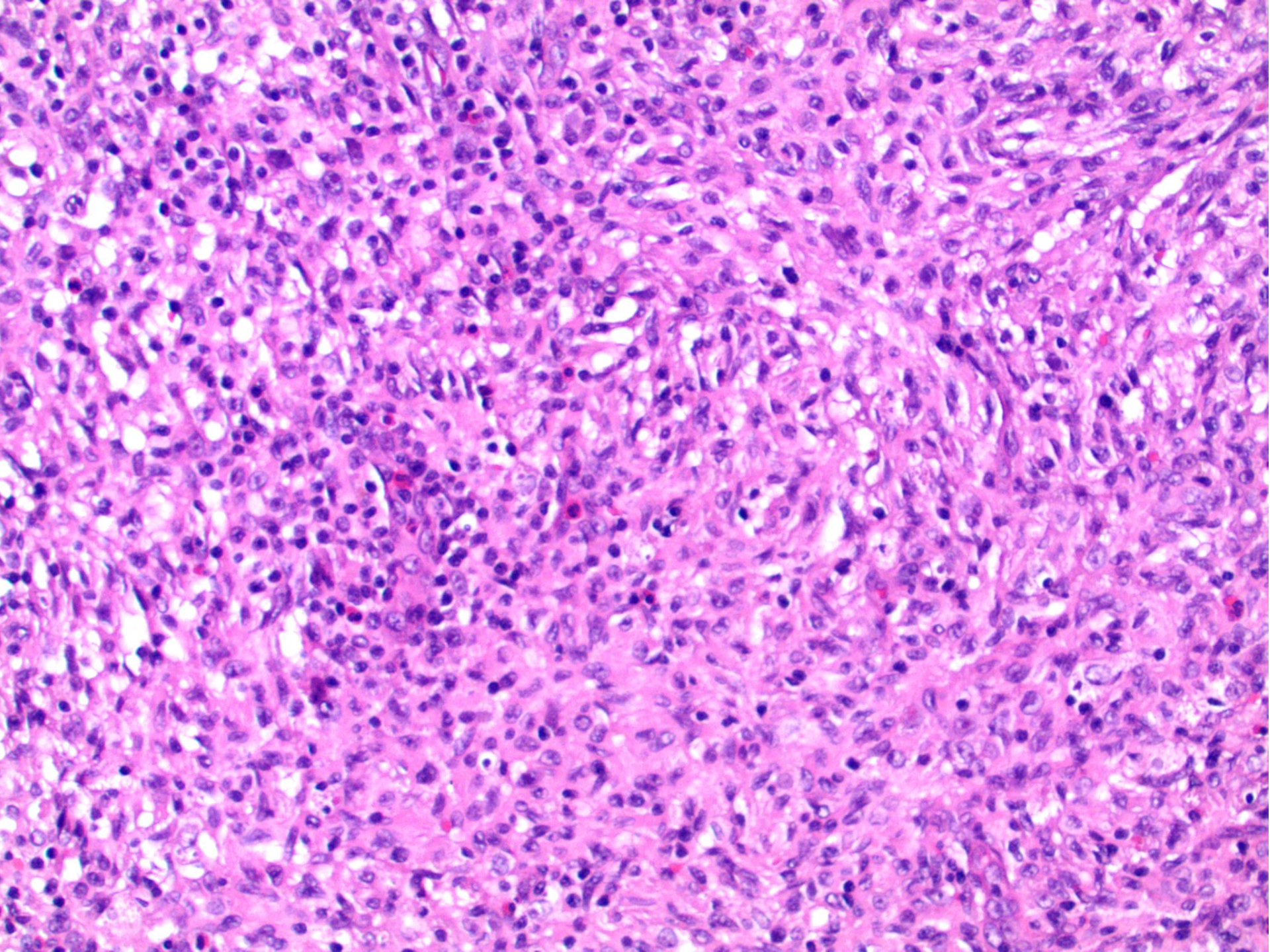


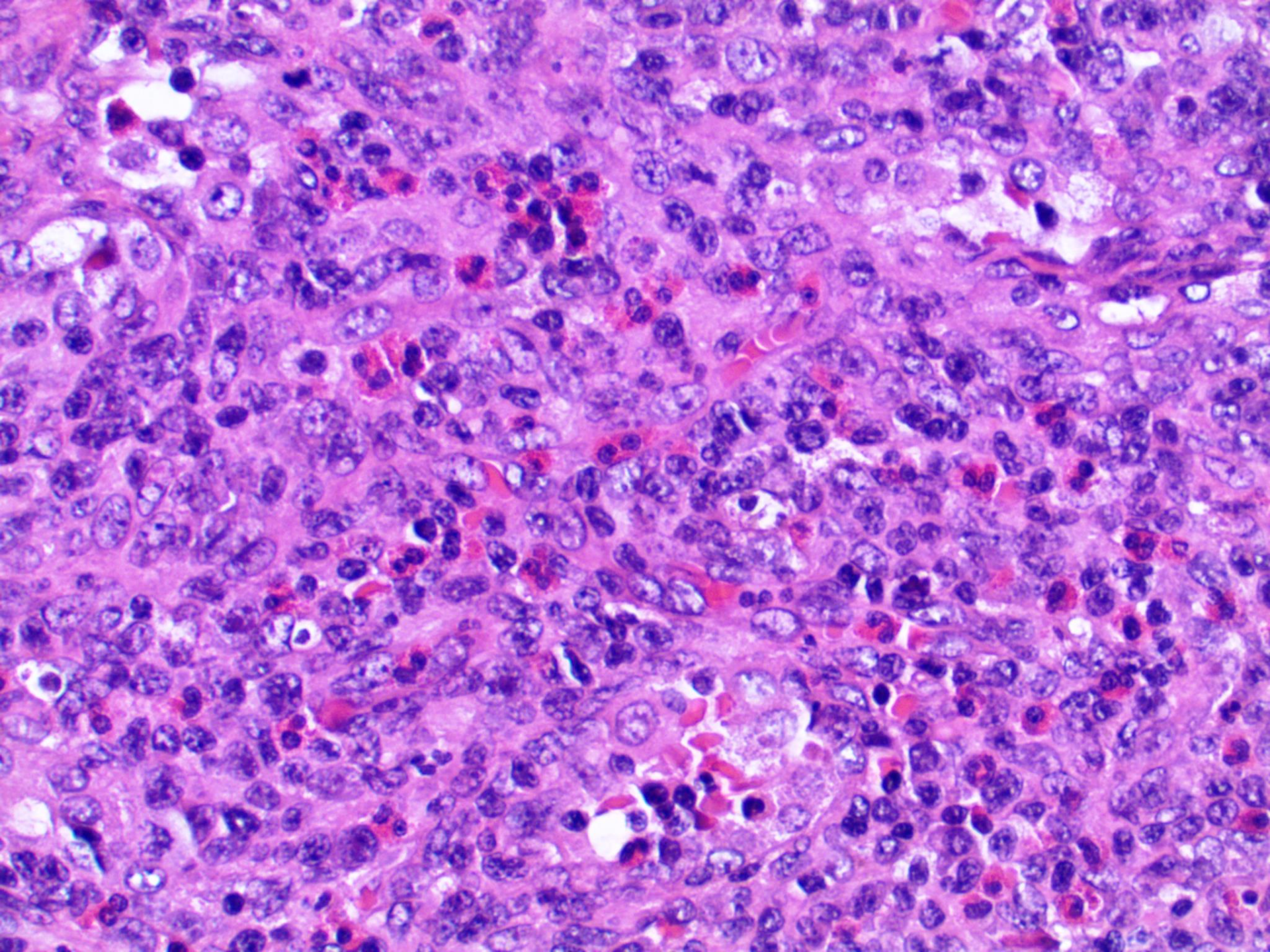












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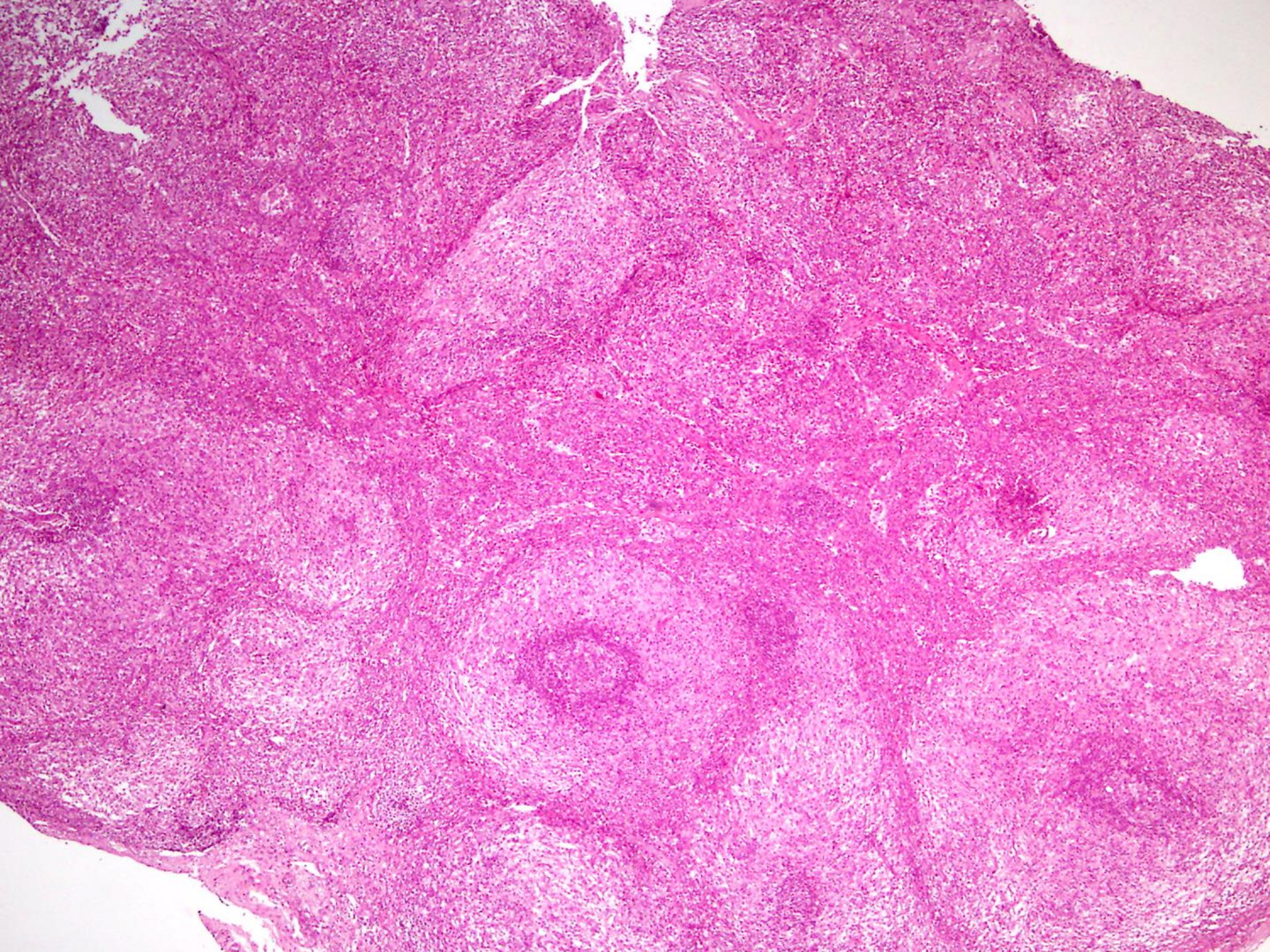

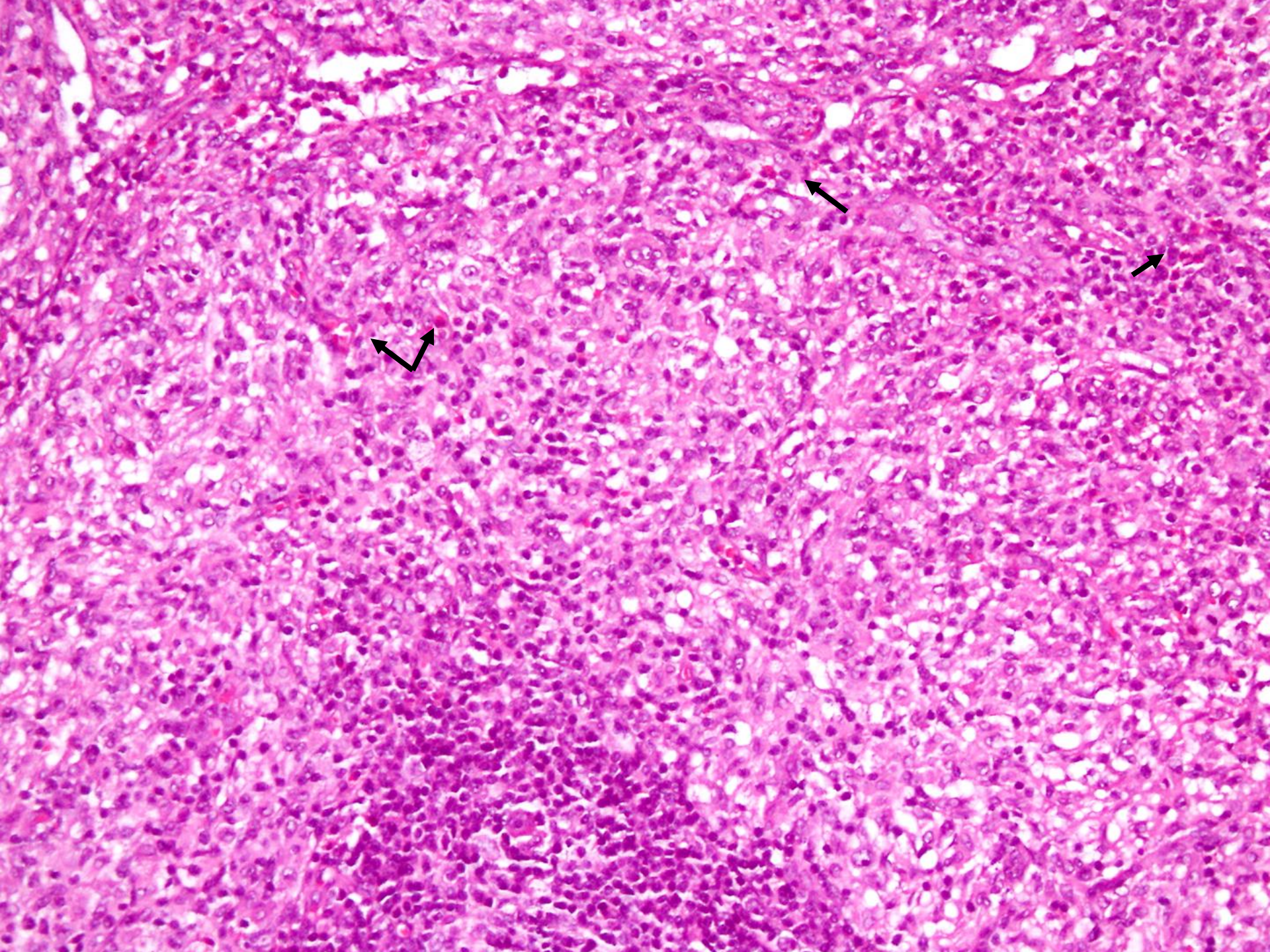

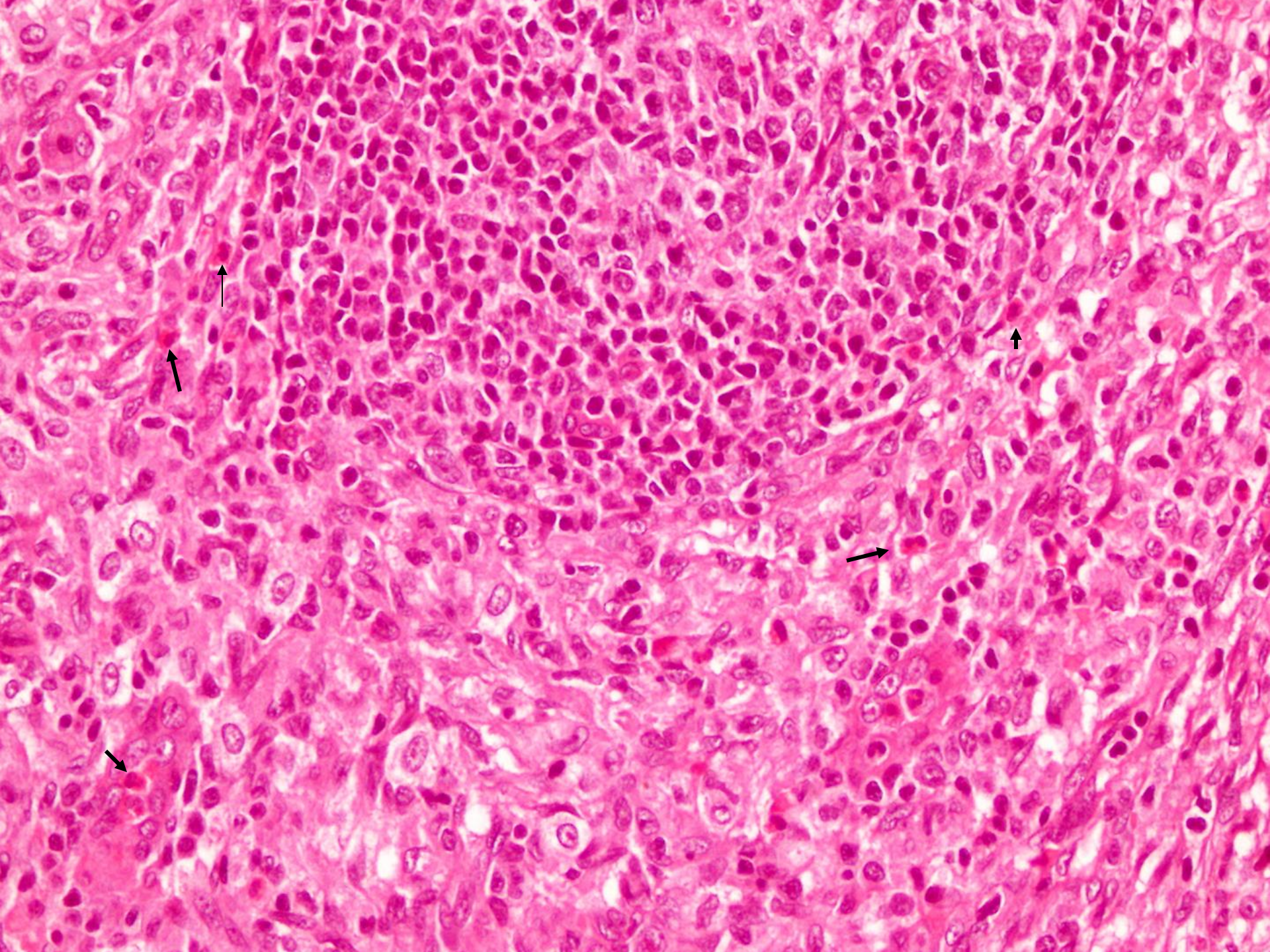

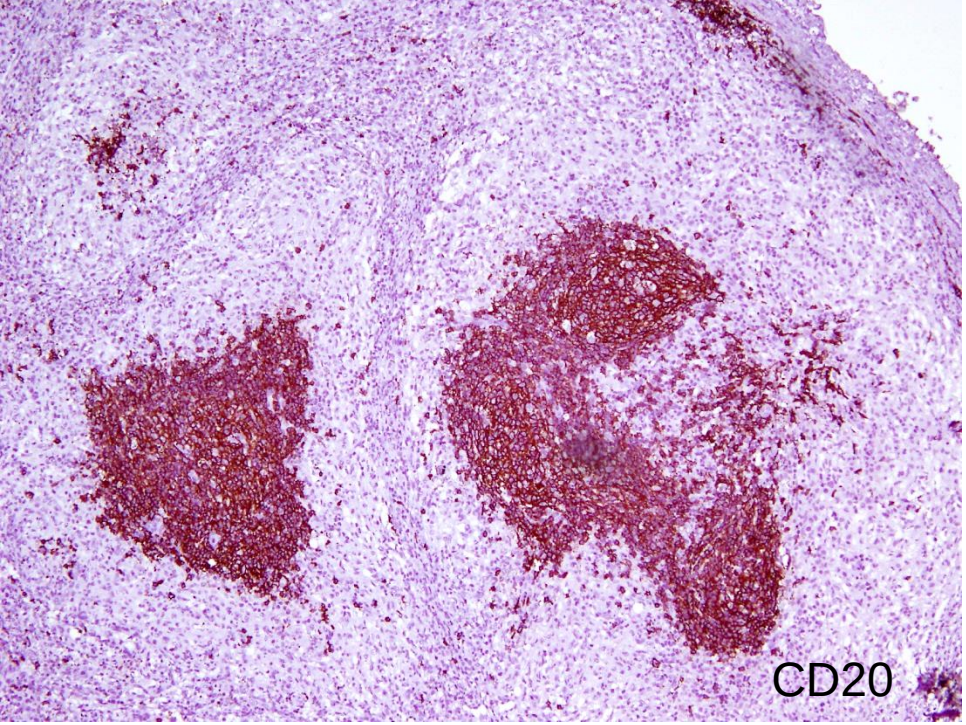
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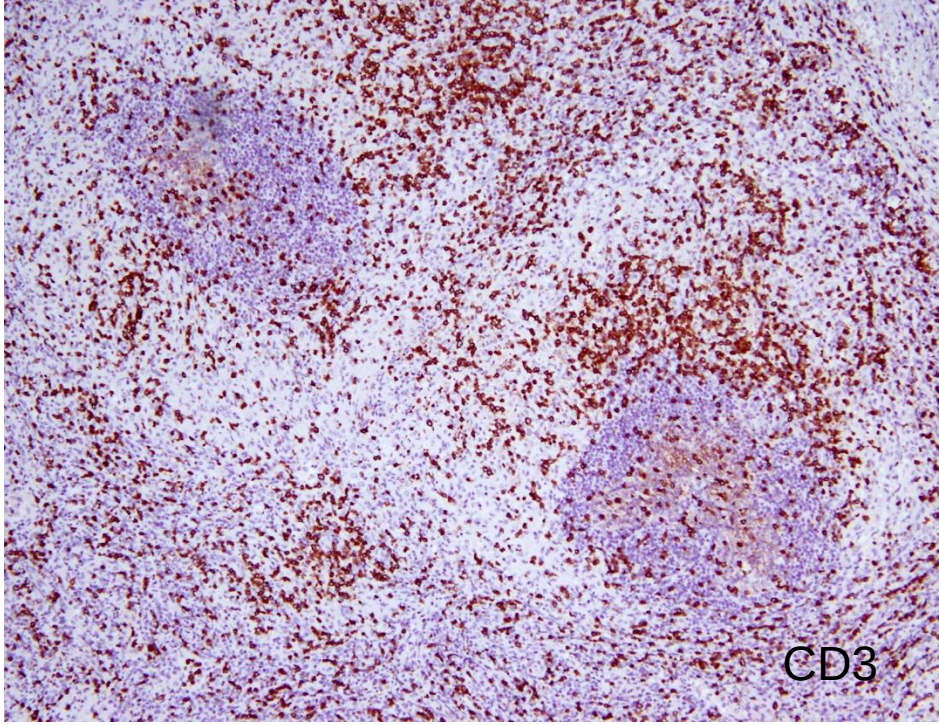
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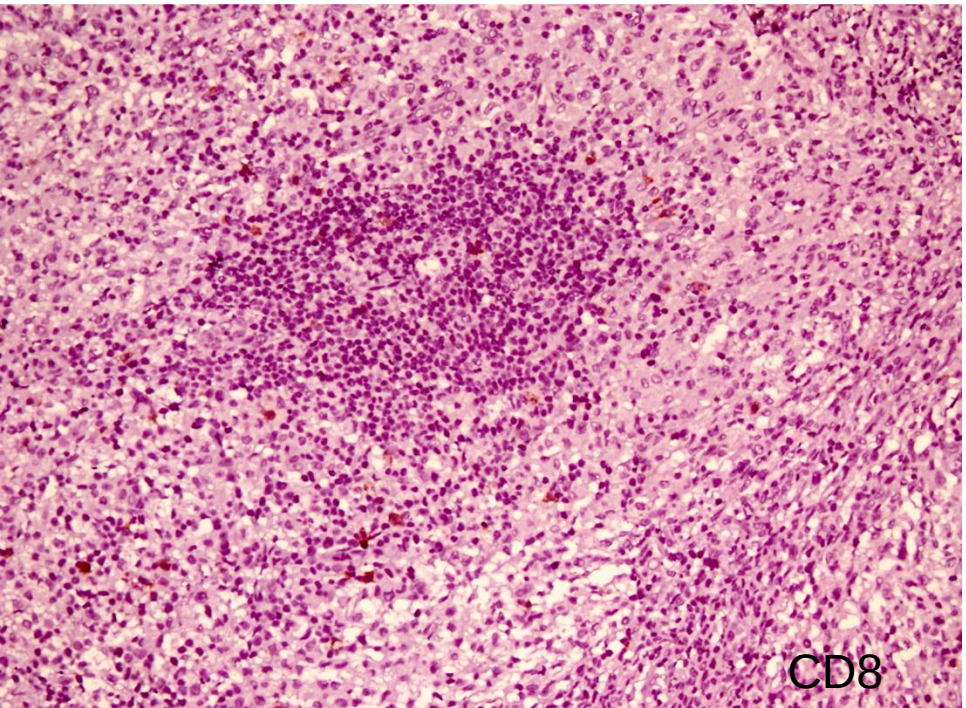
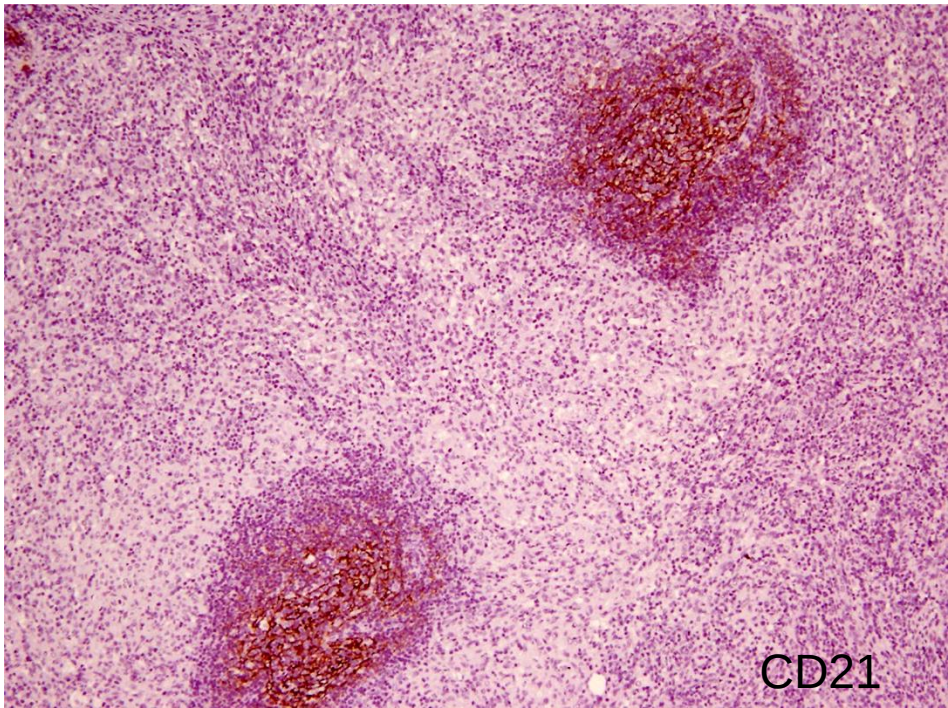

CD8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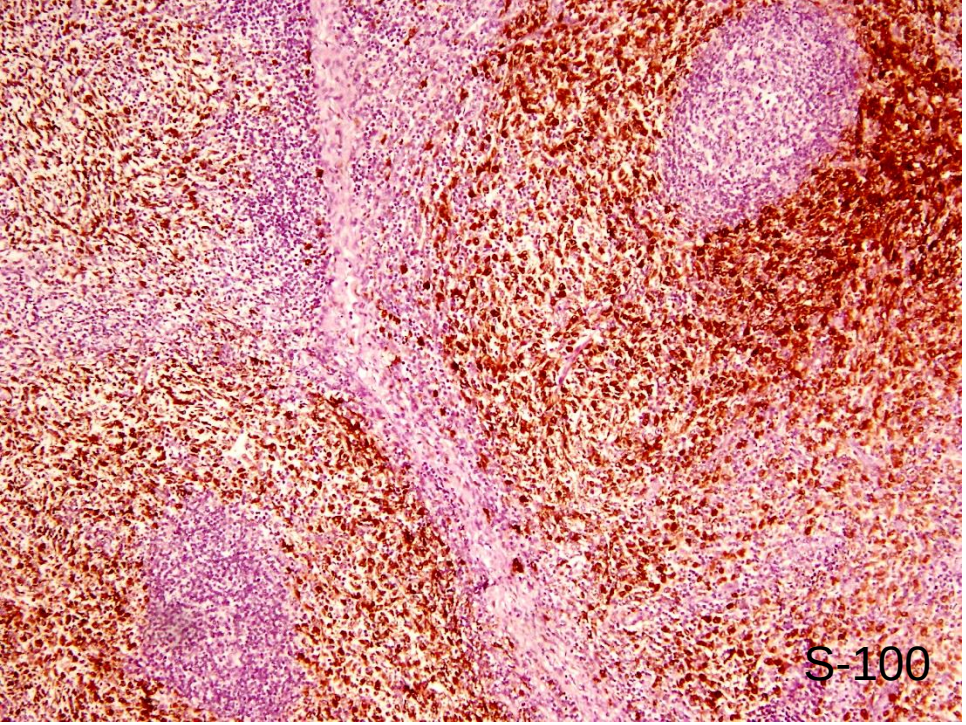
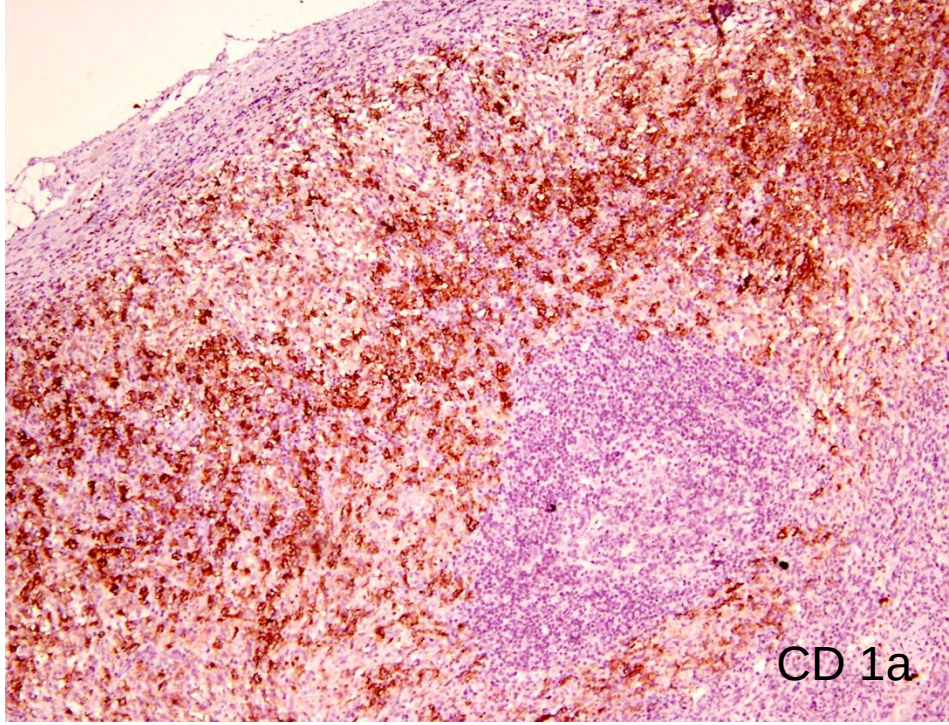
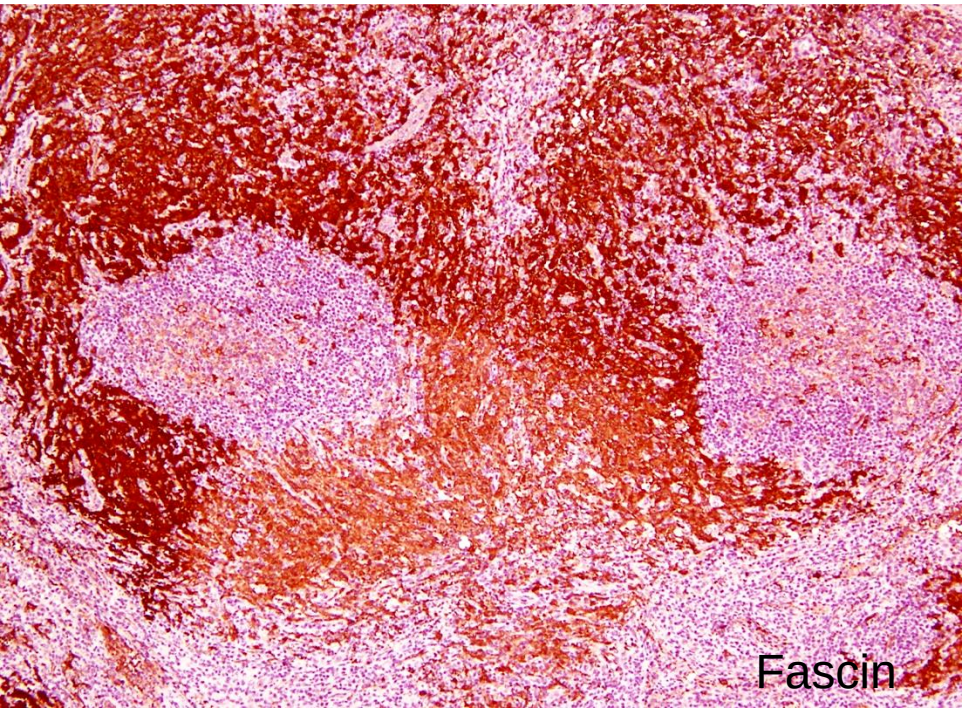
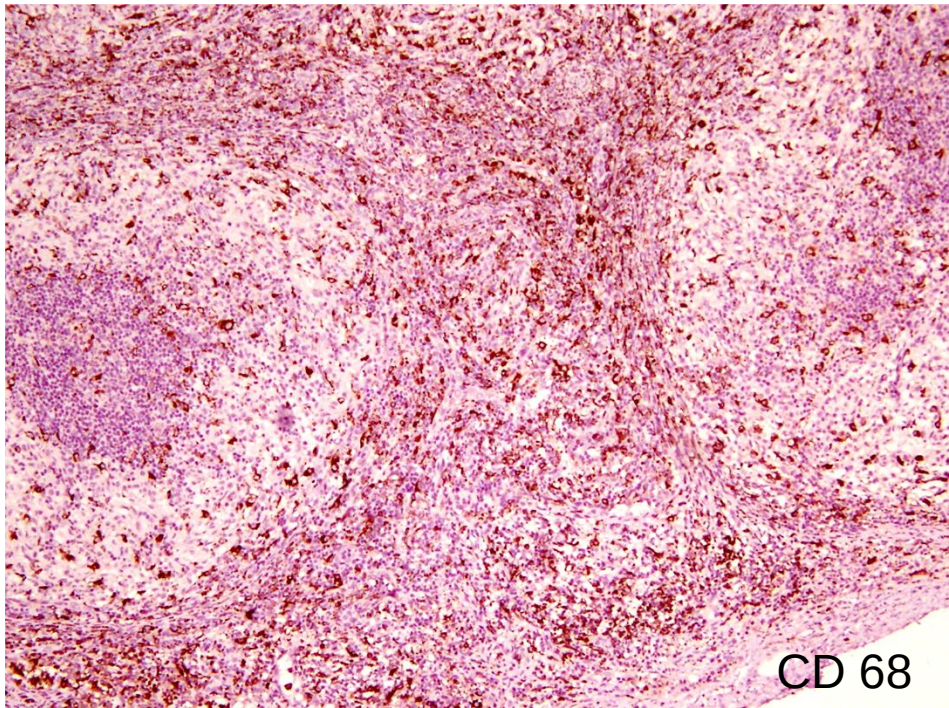

S-100


CD 1a


Fascin


CD 68

IHC profile of proliferated large cells in our case *

POSITIVE	NEGATIVE
S-100	CD 20
CD 1a (80% cells)	CD 3
FASCIN	CD 8
CD 68 (50% cells)	CD 21

Immunophenotypic Characterization of Dendritic cell subsets & Histiocytes (Intl. Lymphoma Study Group: Histopathology 2002;41:1-29)

Cell Type	CD68	Lysozyme	CD1a	S-100	CD21	Fascin
Langerhans cell H	+	Variable	+	+	-	+
Interdigitating D cell	Variable	Variable	-	+	-	+
Follicular D cell	Variable	-	-	-	+	Variable
Histiocyte	+	+	-	Variable	-	-

*

*In view of this the large cell population in our case is likely to be a mixture of Langerhans cells and Interdigitating dendritic cells (Birbeck granules status not evaluated)

Skin Biopsy - Chronic non-specific eczematoid dermatitis without any significant proliferation of Dendritic cells

DIAGNOSIS : **Omenn syndrome**

Pathologic changes in lymphnode and skin and the clinical features in this young child are characteristic of this disease. His peripheral blood had lymphopenia (low CD-3 cells, low CD-19 cells, normal NK cells) Eosinophilia (absolute Eosinophil count -19000 / microL) and low Immunoglobulins except for IgE which was significantly raised (135 IU / ml).

One among about a dozen *Severe Combined Immunodeficiency Diseases (SCID)* which have an autosomal recessive inheritance pattern (all except one), **Omenn syndrome (GS Omenn, 1965)** is caused by mutations in the RAG1/RAG2 genes. These result in immaturity of T cells that are oligoclonal and autoreactive, and in virtual absence of B lymphocytes. Death Is due to fatal infections. Only curative Rx is compatible Bone Marrow or Cord Blood Stem cell transplantation.

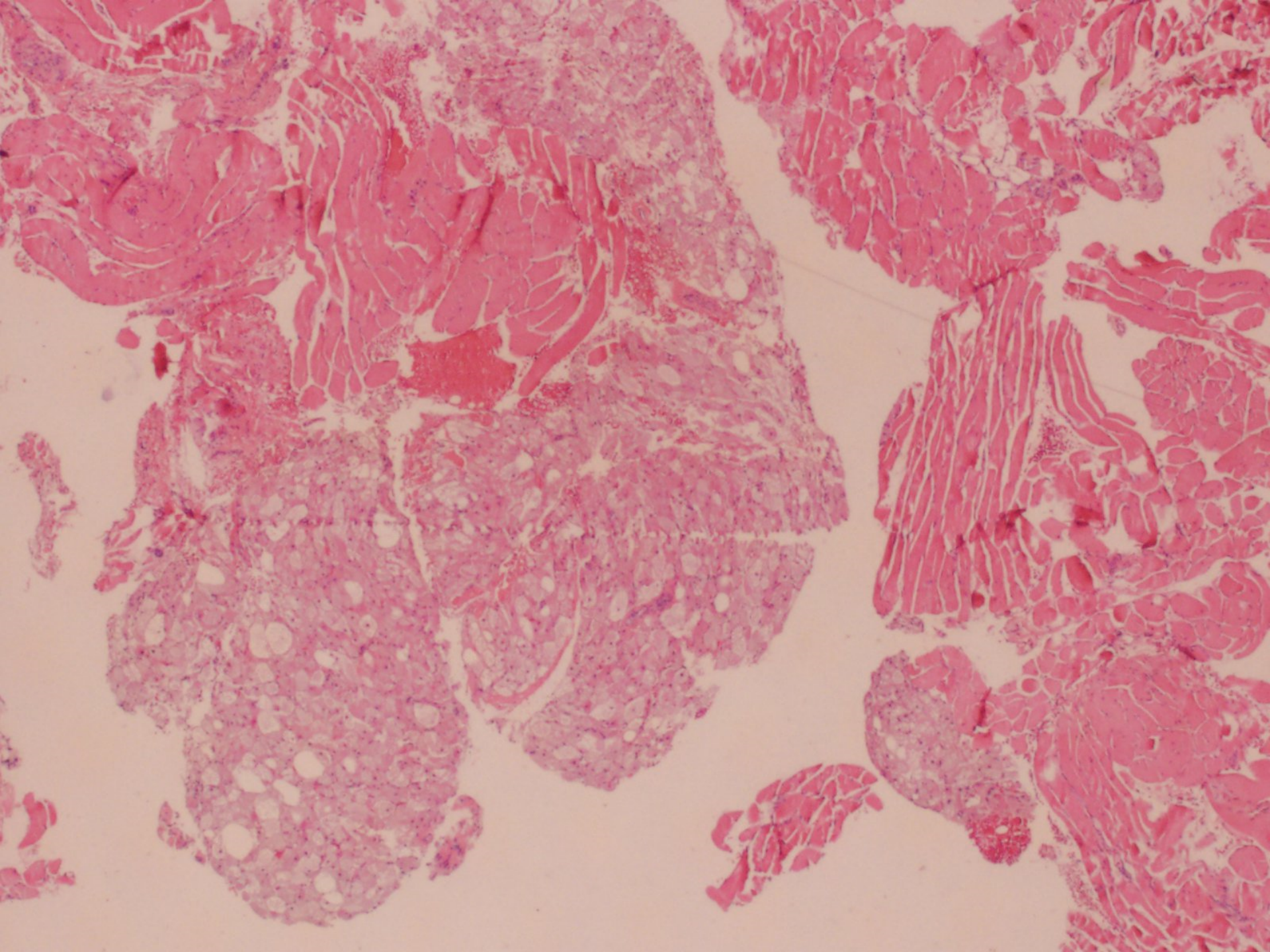
Bone marrow transplantation could not be done in our patient as no HLA-matched related donor could be found, cord blood banking had not been done and the family could not afford an unrelated donor transplantation.

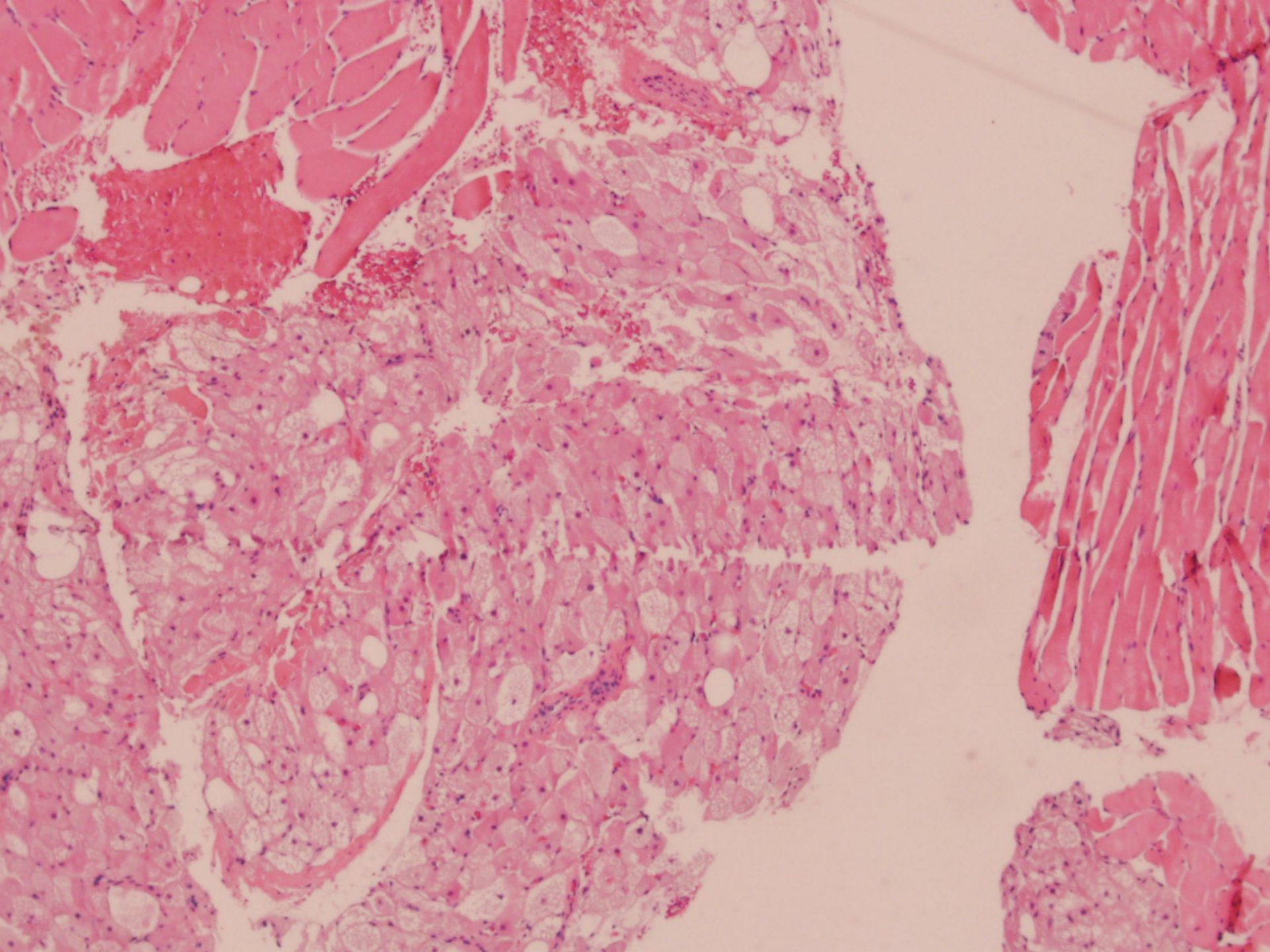
The child subsequently developed sepsis and succumbed to multi-organ Failure at the age of 14 weeks. Genetic studies have not been carried out.

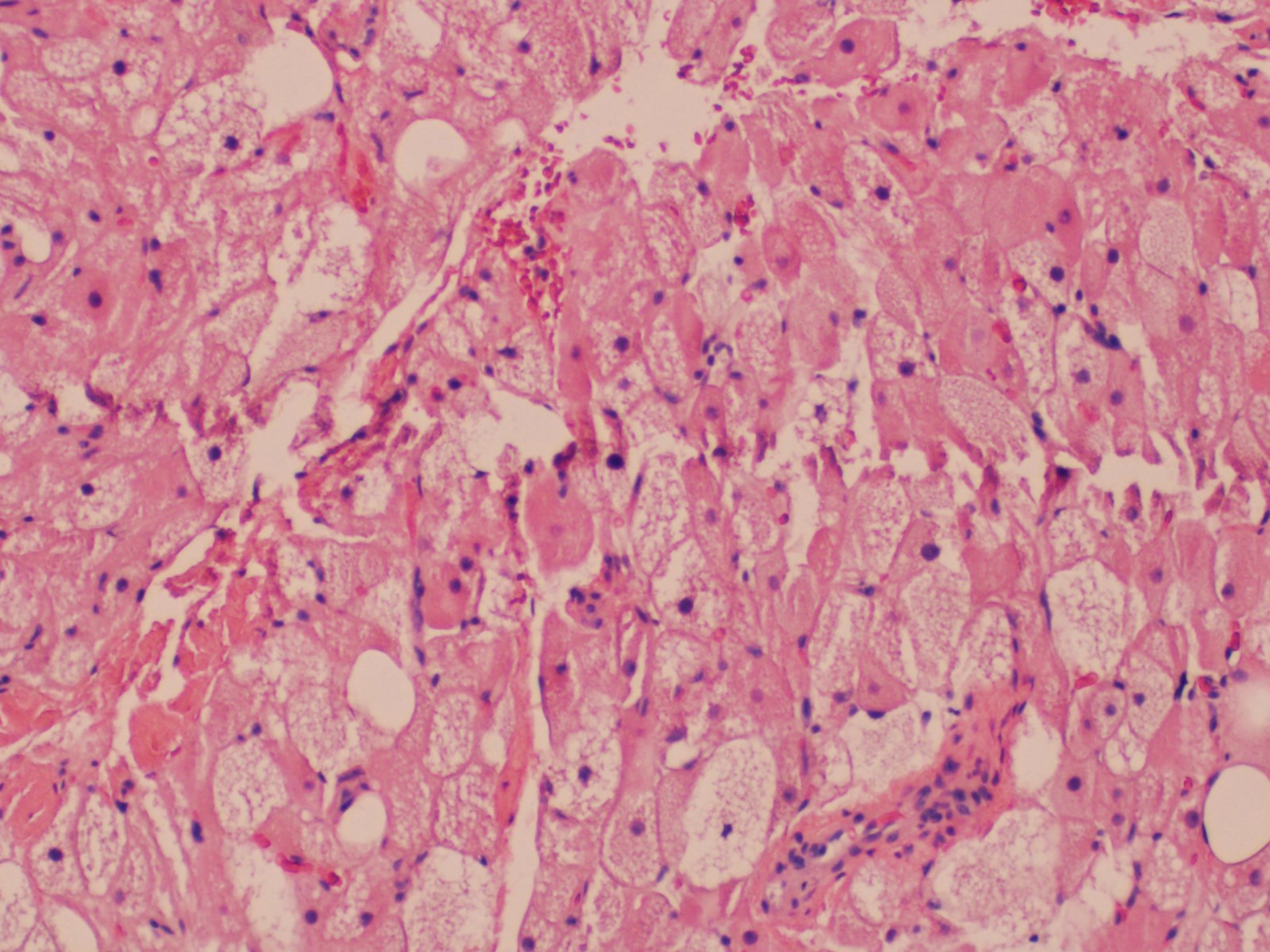
SB 5912

Sarah Cherny; Kaiser South San Francisco

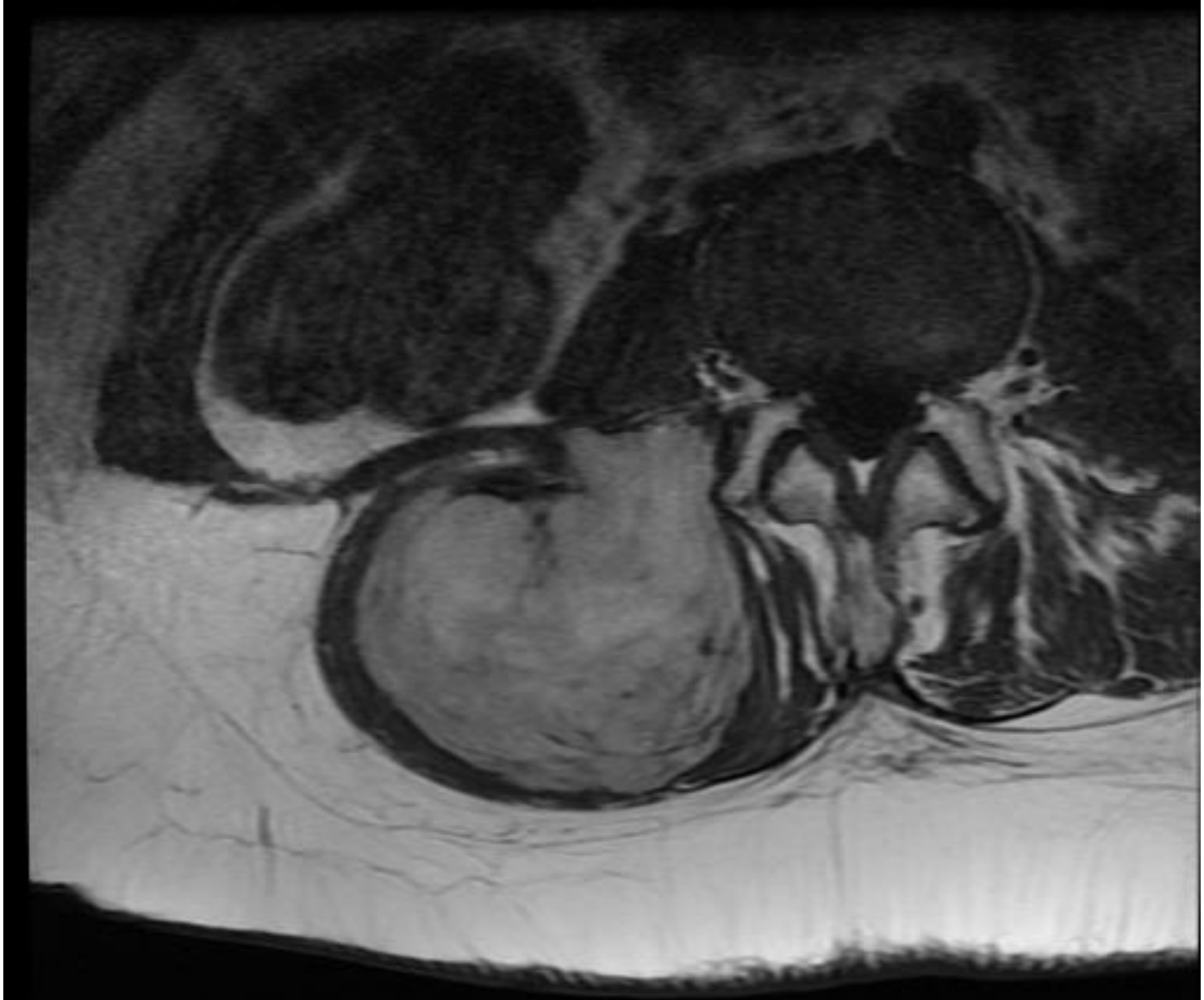
62-year-old woman with right lower back pain. MRI shows 11.8x7.1x5.8cm mass centered within right posterior paraspinous muscles which courses close to the right L3-4 neuroforamen.





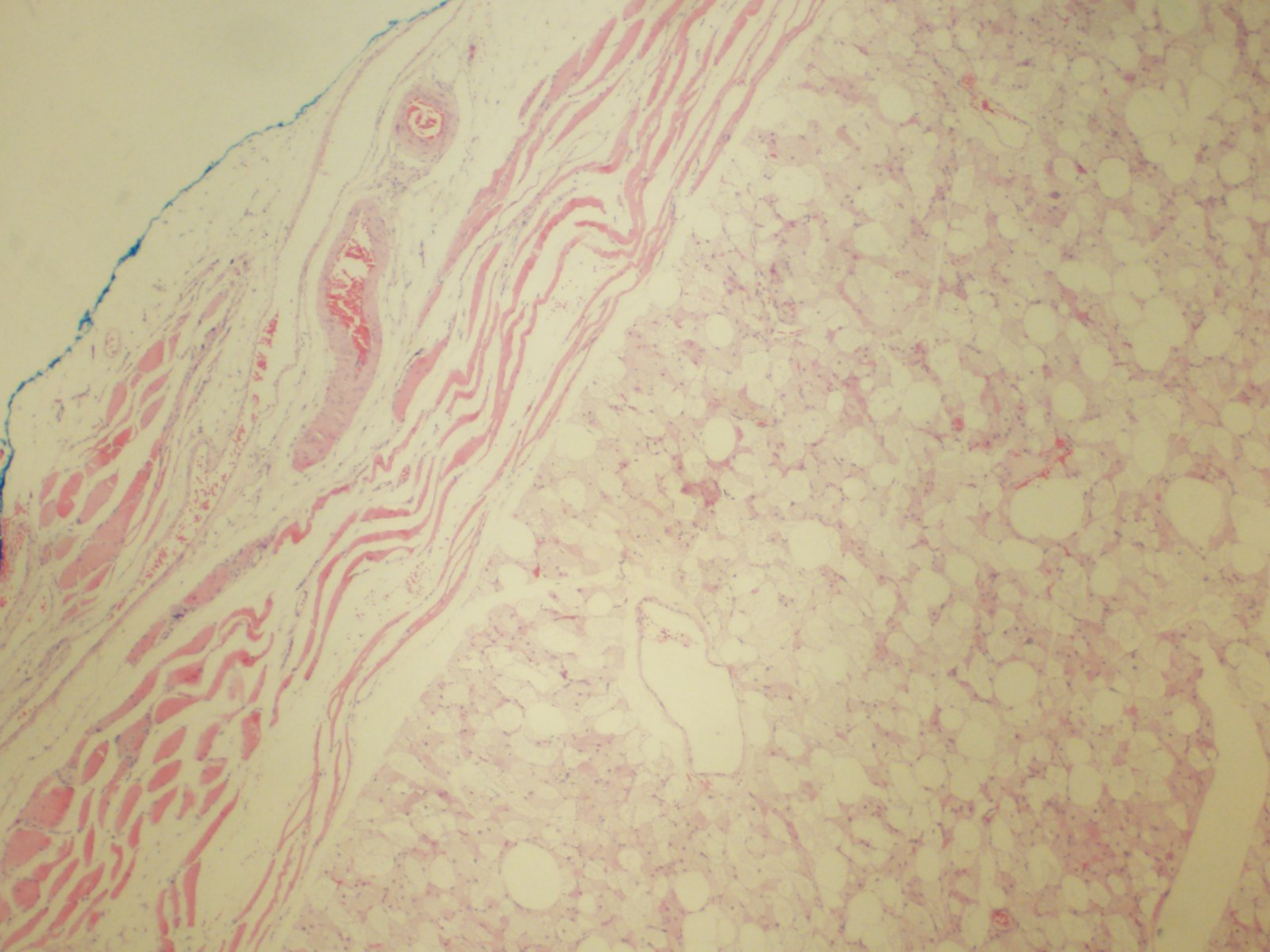


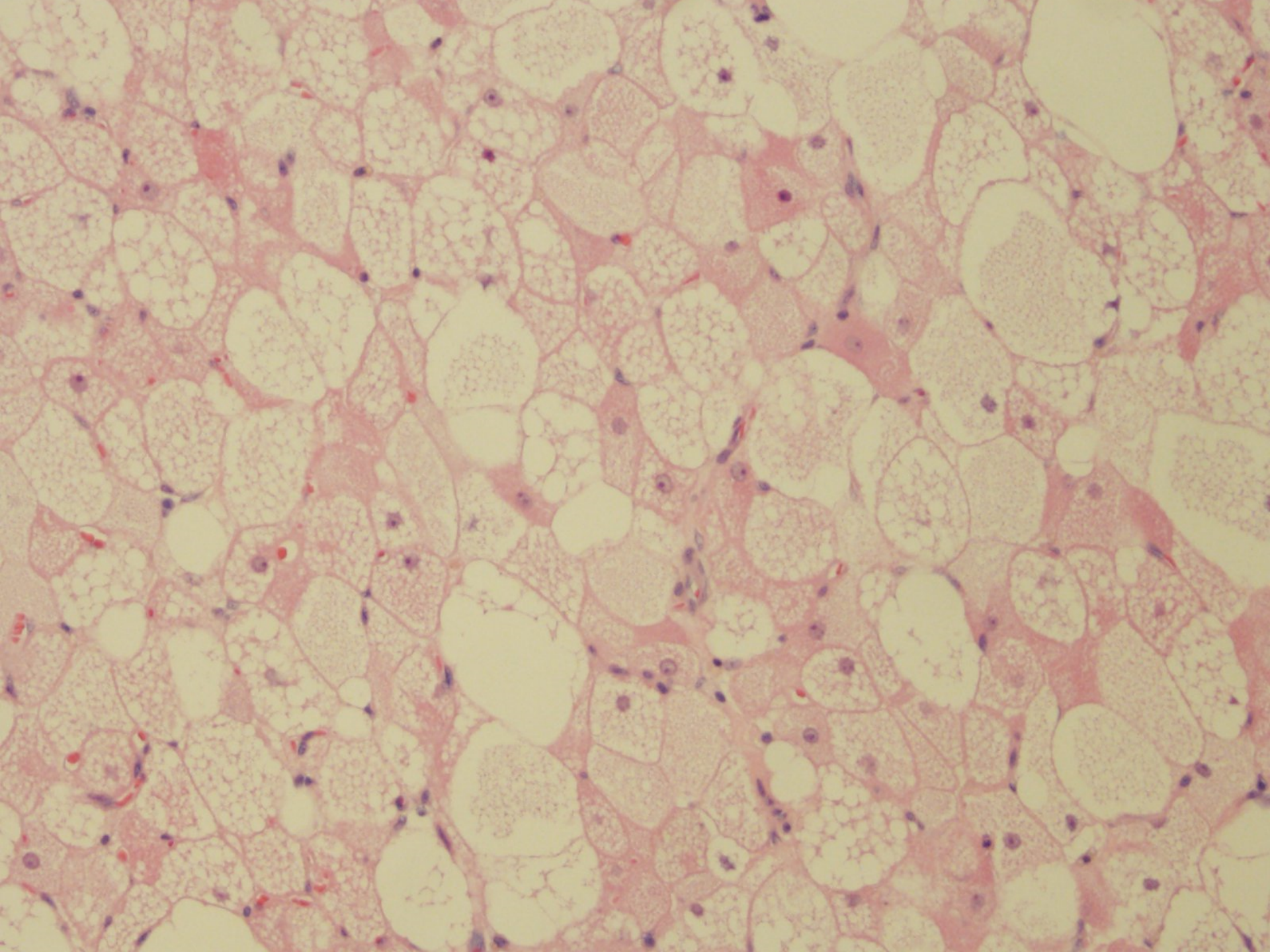
DIAGNOSIS?



-Heterogeneous 11.8 x 7.1 x 5.8 cm mass centered within right posterior paraspinous muscles with associated enhancement, coursing close to right L3-4 foramina

-Ddx includes nerve sheath tumor versus liposarcoma





Hibernoma

- Rare, benign fatty tumor composed, at least in part, of brown fat cells with granular, multivacuolated cytoplasm

- 1.1% of all adipocytic tumors
  - 1.6% of all benign adipocytic tumors

- 6 morphologic variants
  - Granular (or eosinophilic) – most common
  - Mixed
  - Pale
  - Lipoma-like
  - Myxoid - rare
  - Spindle cell - rare

Hibernoma

- Young adults, mean age of 38 years
  - ~5% in children
  - ~5% in adults over 60 years
- Slight male predominance

Hibernoma

- Wide variety of locations: thigh > trunk > upper extremity > head & neck
  - <10% occur in the intra-abdominal and thoracic cavities
- Large majority (90%) present as slow-growing tumors in the subcutis
  - 10% are intramuscular
- Median size = 9.3 cm (range = 1-24 cm)

Hibernoma

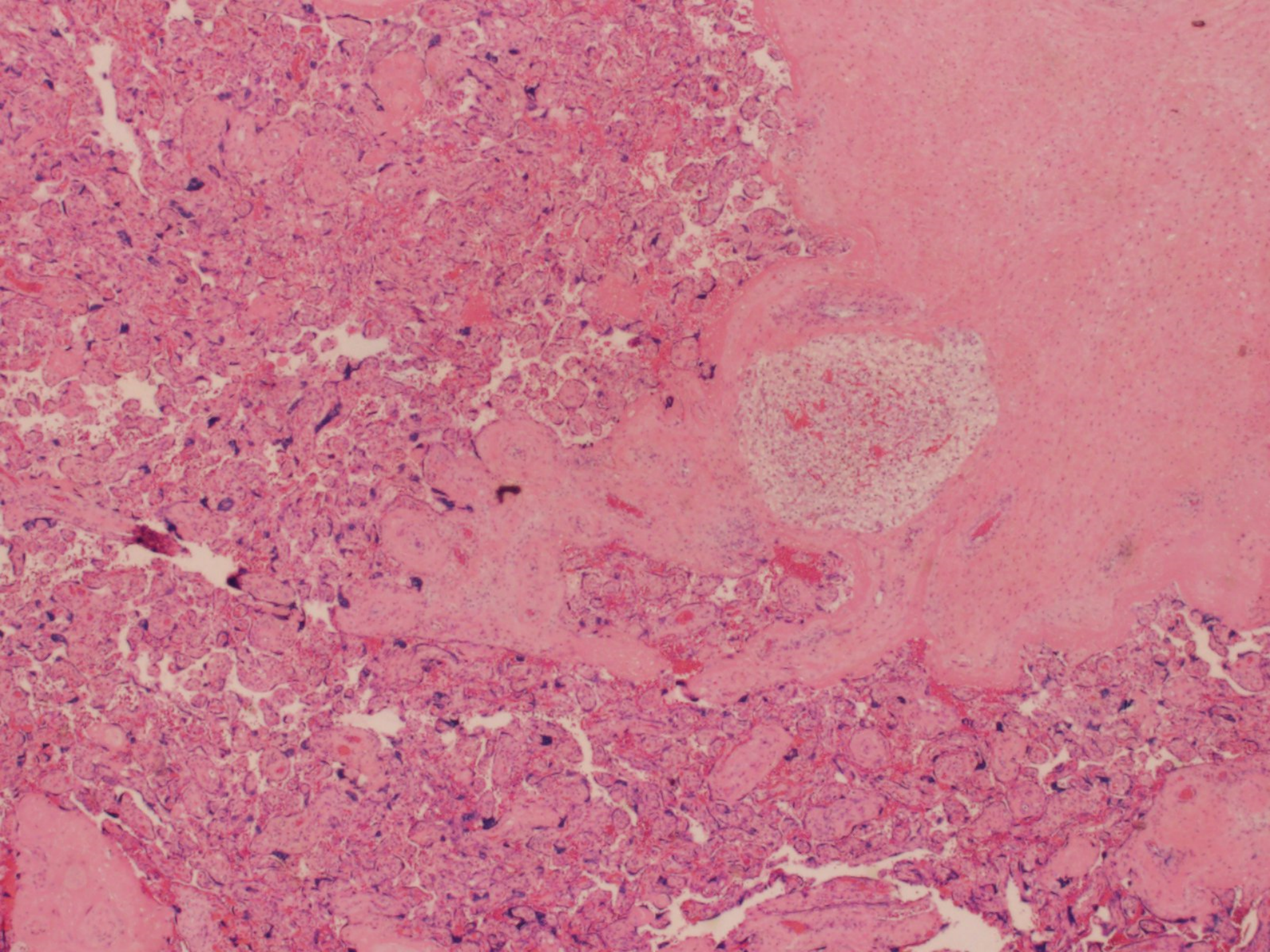
- Benign – no recurrence with complete local excision

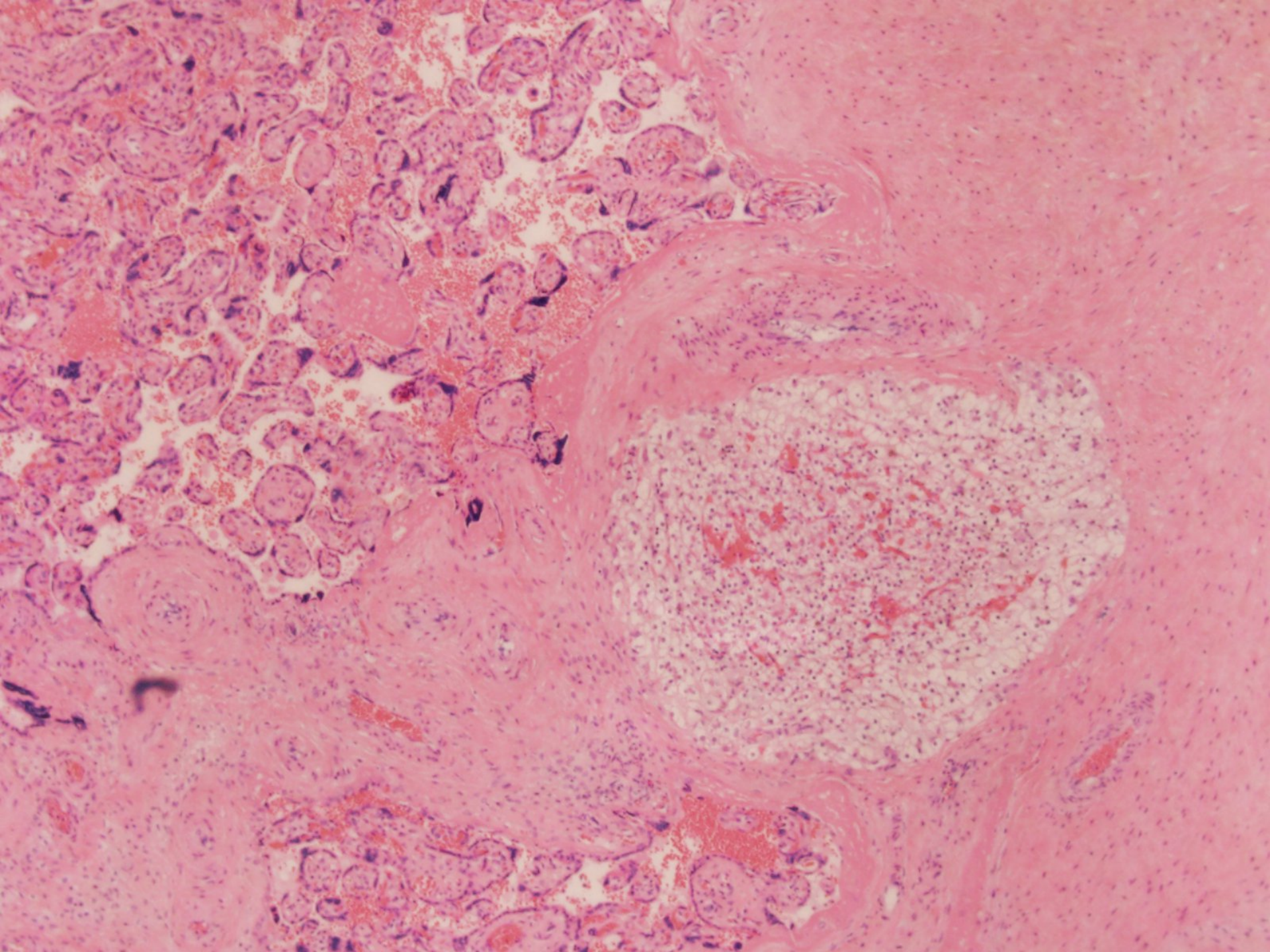
- Follow up: Patient recovered from her excision, doing well

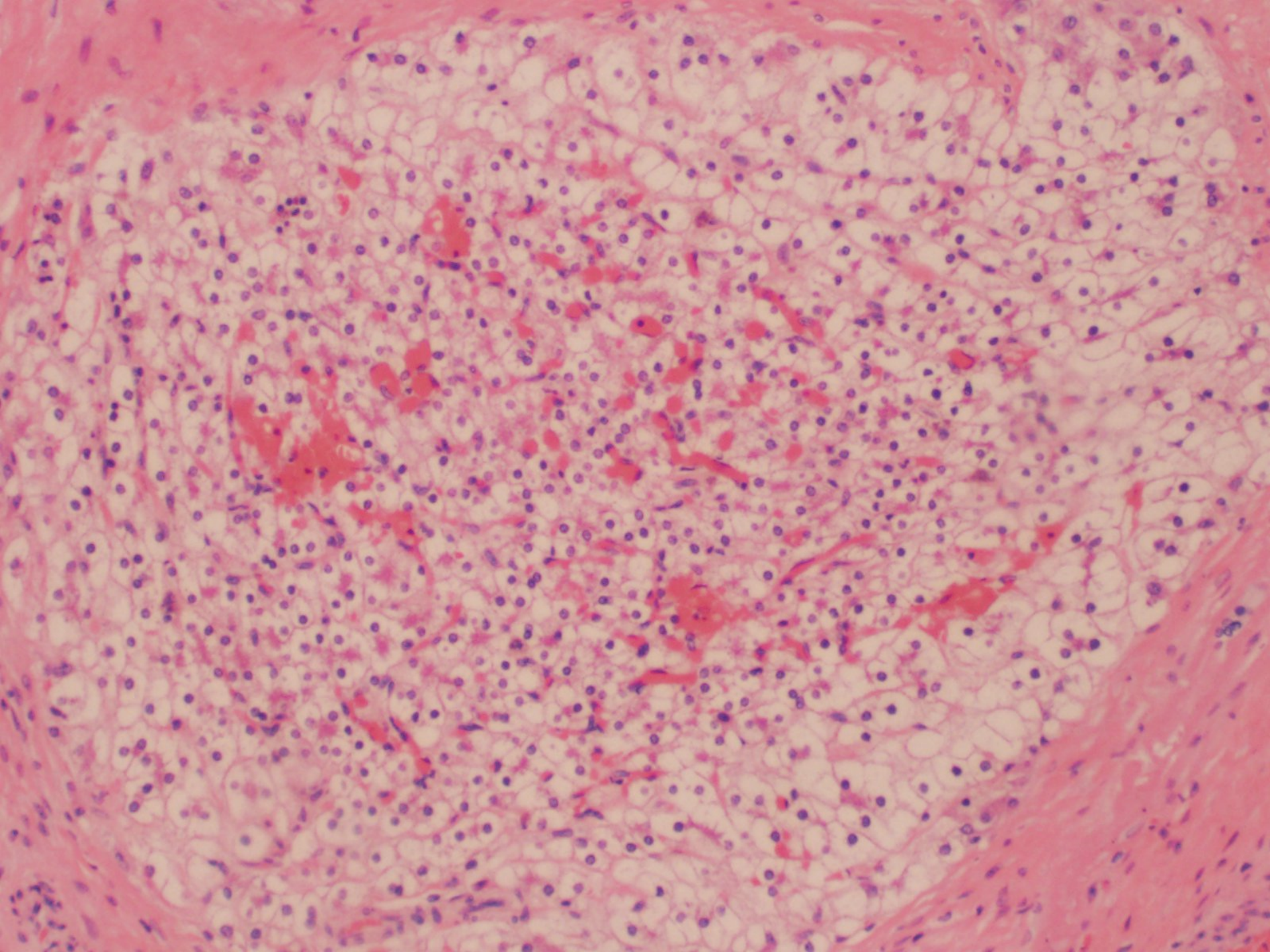
SB 5913

Sarah Cherny; Kaiser South San Francisco

39-year-old with di-di twin placenta.







DIAGNOSIS?

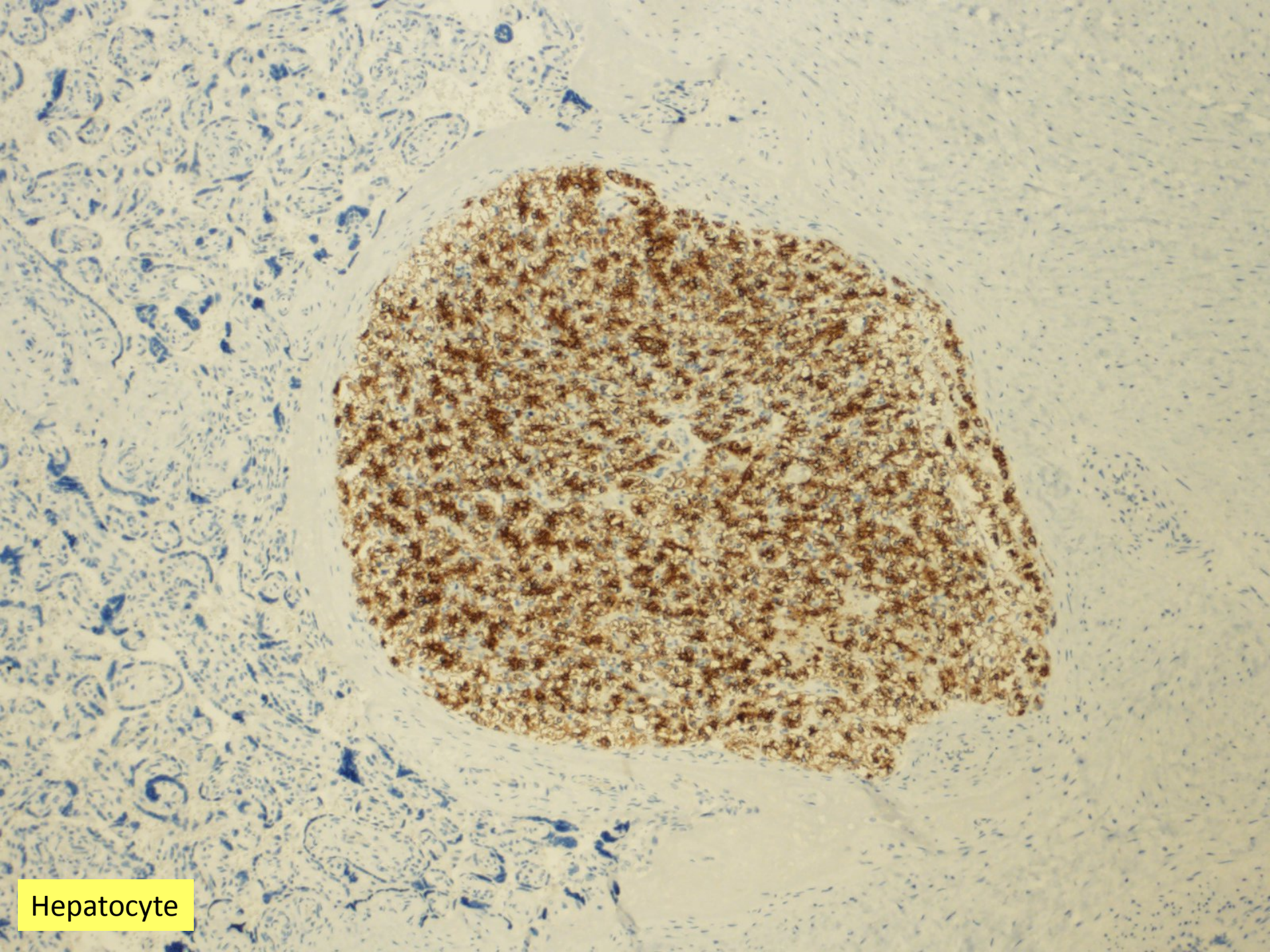
3

ATLAS OF NONTUMOR PATHOLOGY

Placental Pathology

Frederick T. Kraus, MD
Raymond W. Redline, MD
Deborah J. Gersell, MD
D. Michael Nelson, MD, PhD
Jeffrey M. Dicke, MD

AFIP
AHP

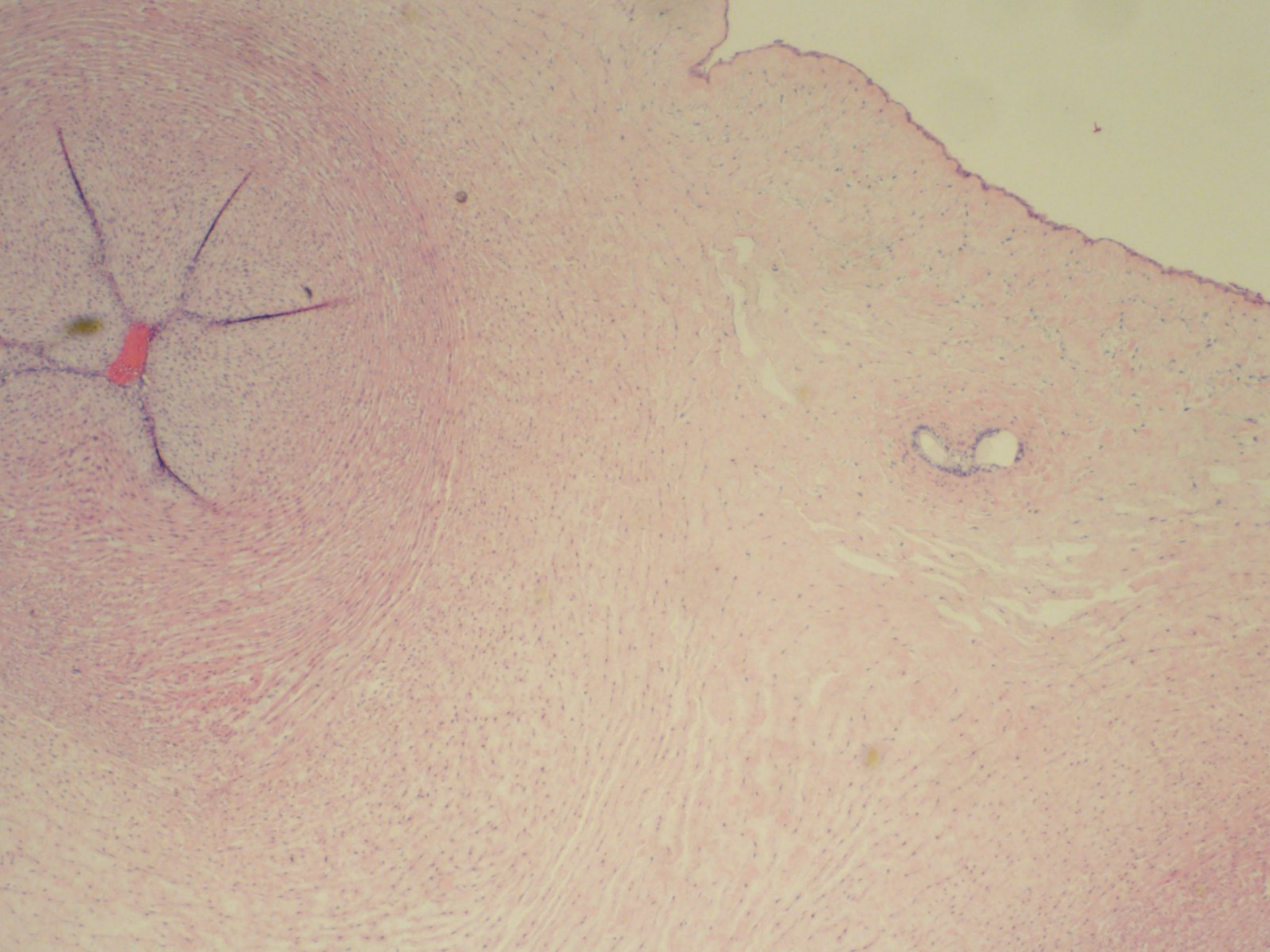

Hepatocyte

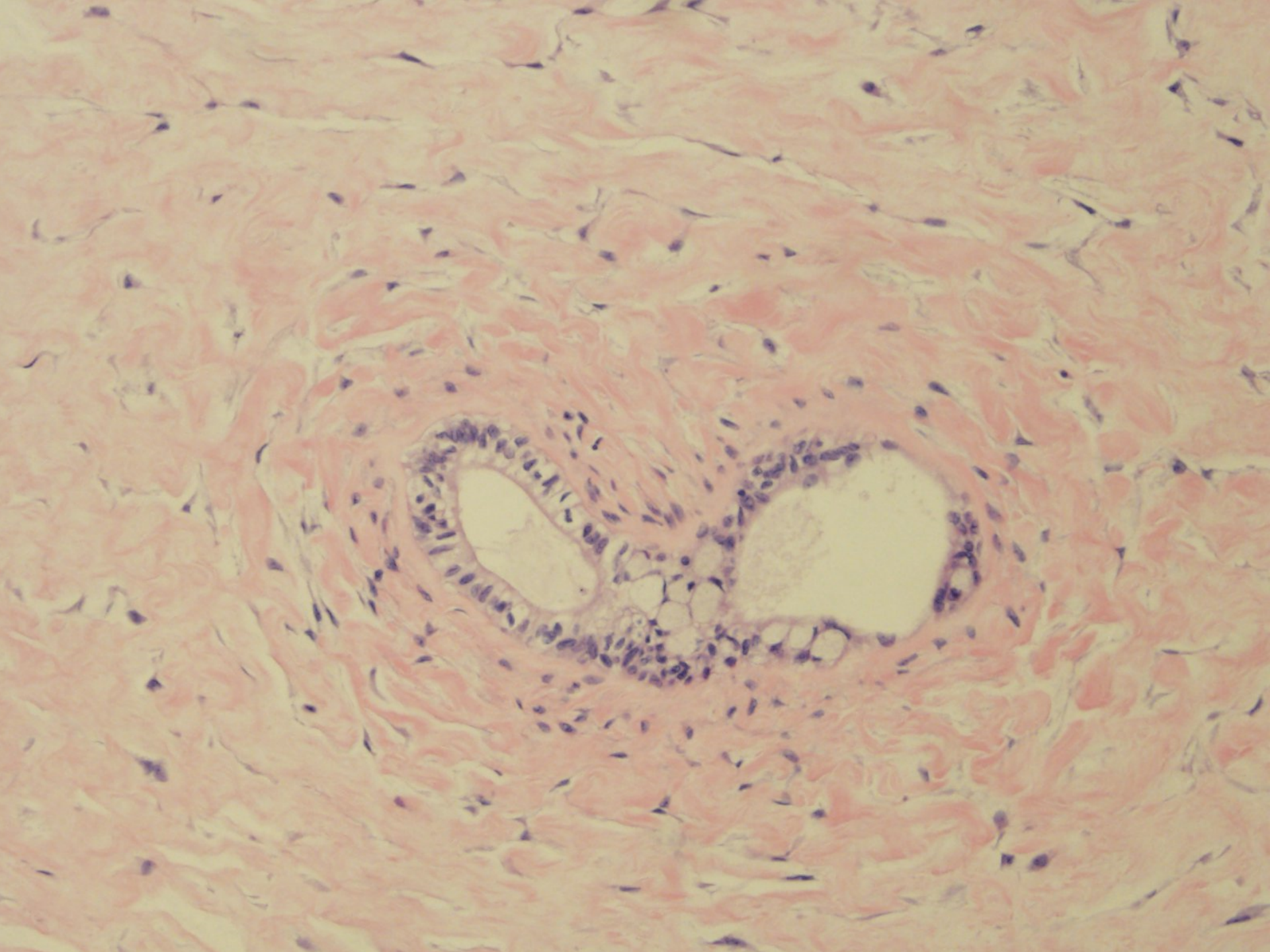
- Variably reported as
  - Hepatic heterotopia or ectopia
  - Hepatic adenomas
  - Monodermal teratoma

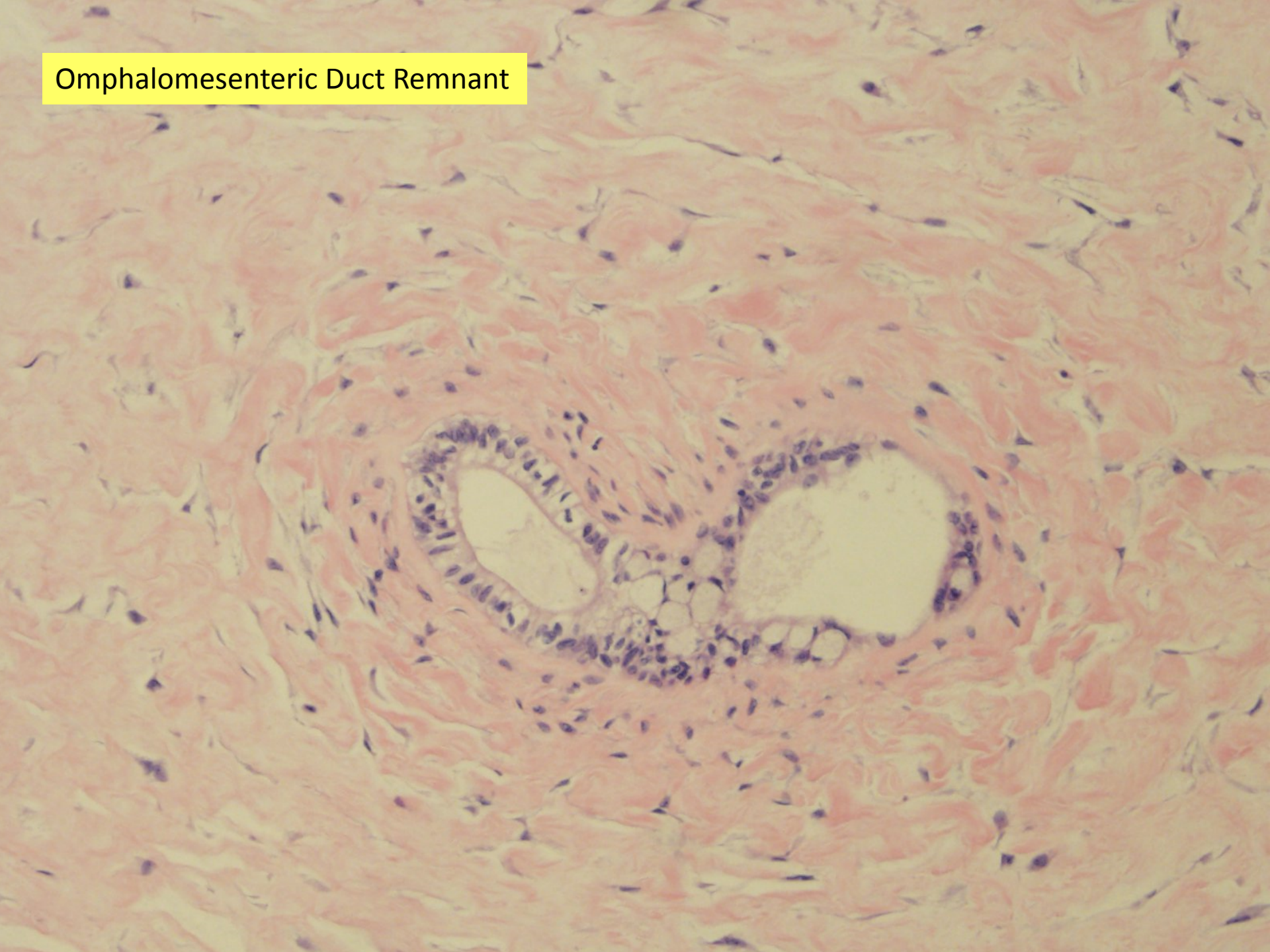
- Histogenesis uncertain, but displaced embryonic yolk sac elements with hepatic differentiation is favored

- Exceedingly rare
- Benign, with no known implications for pregnancy or fetus
- Small (usually <1 cm) well-circumscribed nodules of hepatocytes
  - Up to 7 cm
- May contain hematopoiesis
- IHC: AFP, α1AT, CEA, Hepatocyte, HepPar1
- Has also been reported in the umbilical cord

- CLC…
  - Only found in (placentas of) reproductive age females.






Omphalomesenteric Duct Remnant

Utility of High-Throughput Sequencing: Improving Diagnosis, Staging, and Clinical Management of CTCL Patients

Jinah Kim, MD PhD
Departments of Pathology and Dermatology

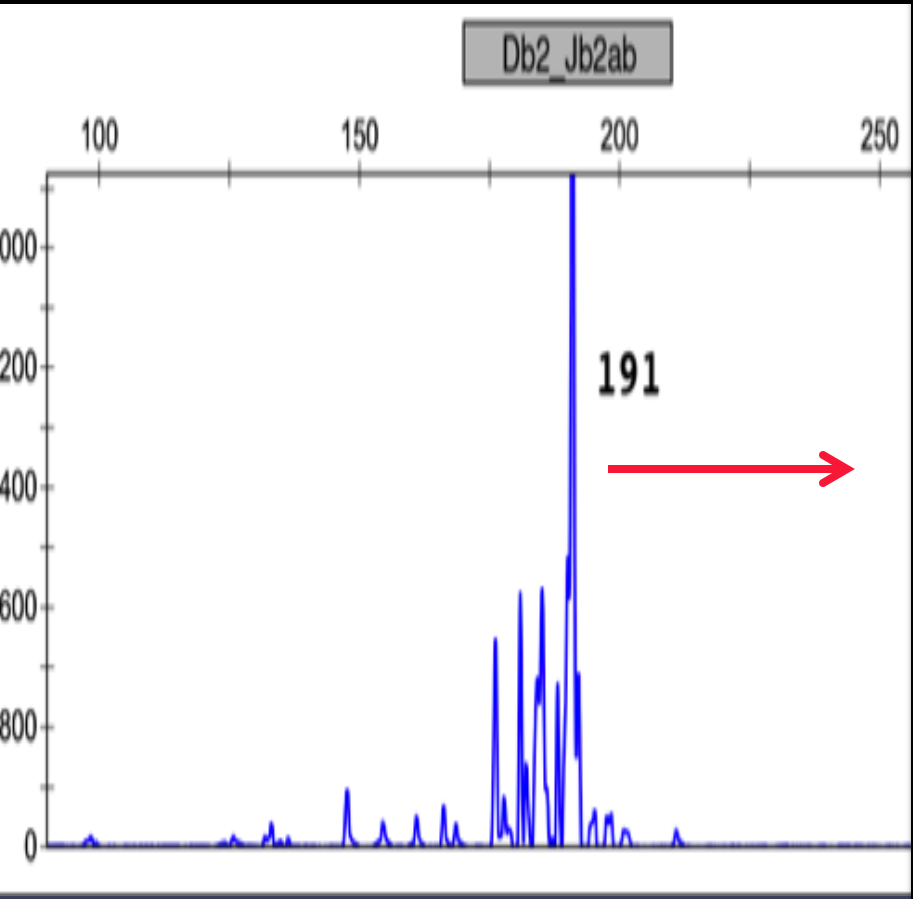
Diagnosis of CTCL

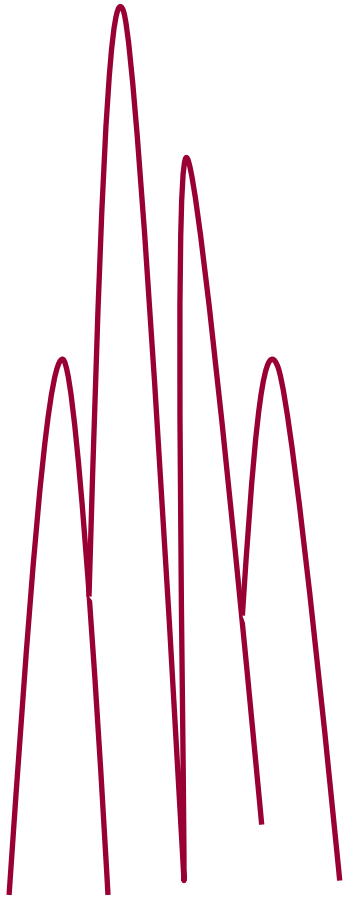
- Clinical findings
- Histopathology
- Immunohistochemical stains
- Flow cytometry
- Molecular Clonality

Limitations of standard TCR-PCR

- Identification of clonal TCR rearrangements found in chronic benign inflammatory disorders (false positive)
- Fails to identify true clonal TCR gene rearrangements in disease (false negative)
- Challenges in accurate assessment of minimal disease burden under therapy and the distinction from reactive conditions

Standard TCR-PCR Lacks Specificity

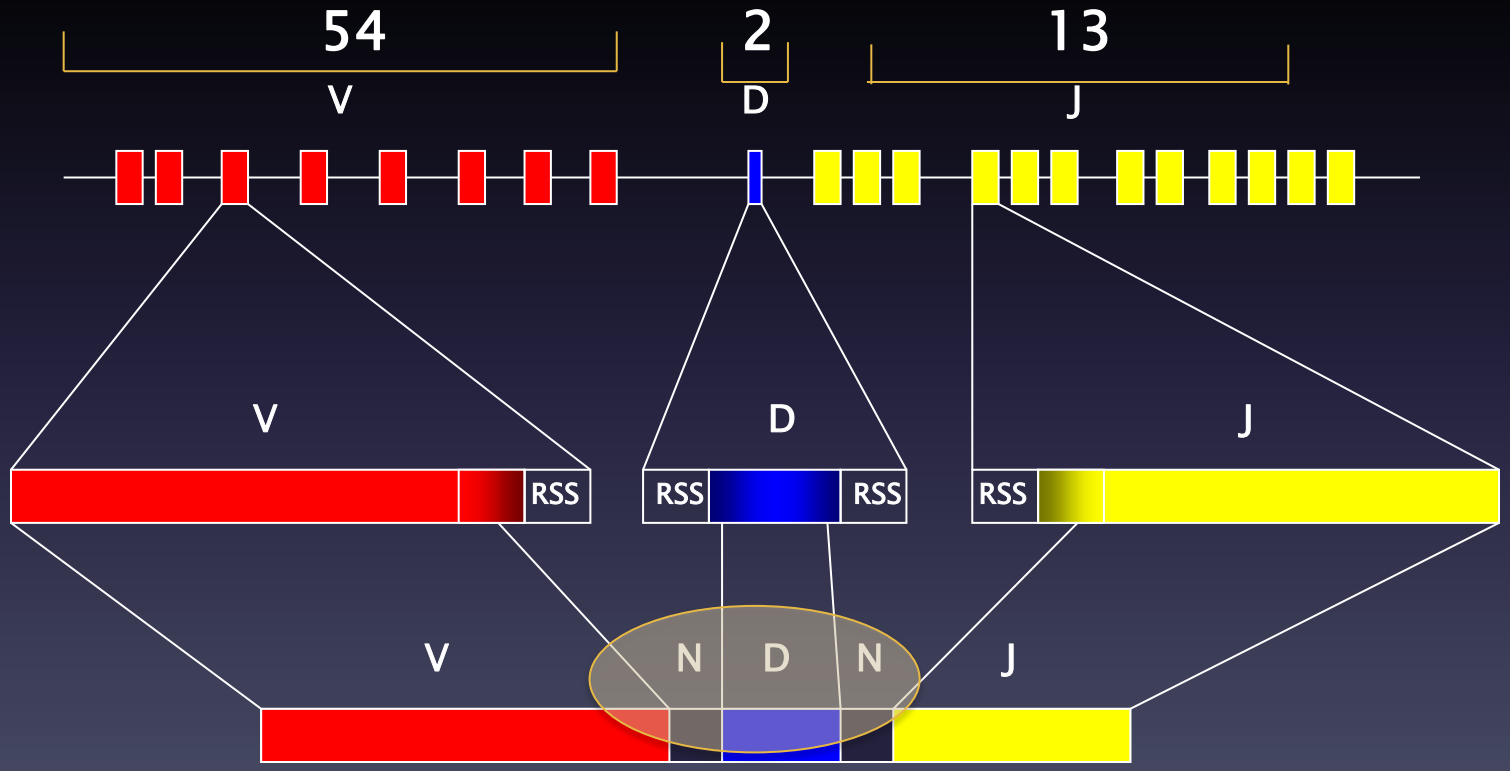




- Multiple small peaks may appear as one peak
- Data acquired is independent of specific sequence

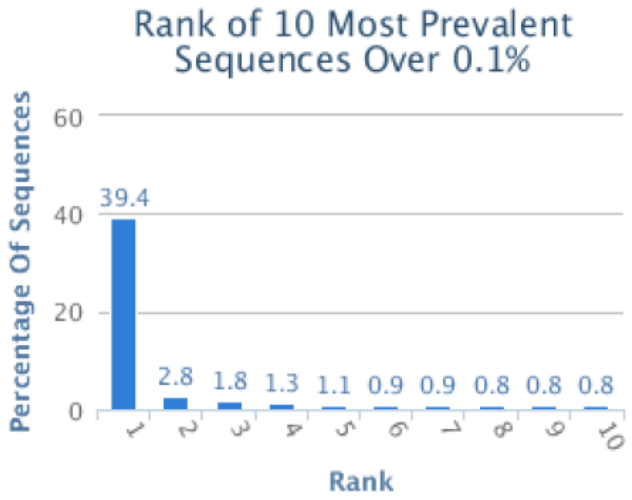
High Throughput Sequencing: Immune Profiling of T cell Receptor Repertoire

- Multiplex PCR that determines DNA sequences of rearranged T cell receptors
- Simultaneous amplification of all V(D)J rearrangements in one reaction



In collaboration with Adaptive Biosystems, Seattle WA

HTS-TCR



Summary Results:

Dominant clone identified

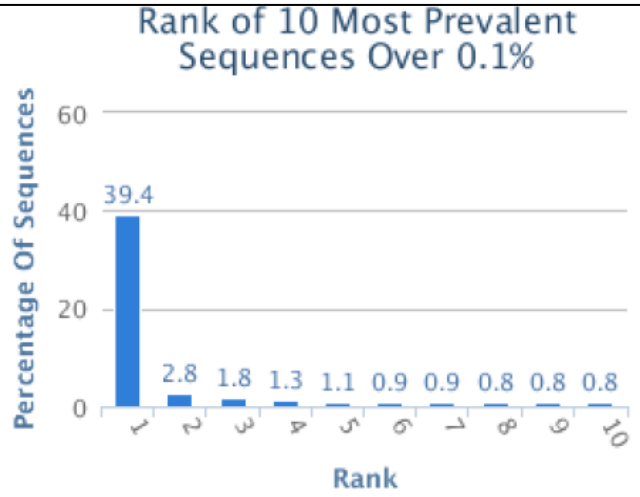
TCRB CDR3 gene fragments were amplified using multiplex PCR amplification. Gene sequences were analyzed and cataloged, and the highest frequency clone(s) observed is reported.

Rank	Sequence	Frequency
1	ACATCGGCCCAAAAGAACCCGACAGCTTTCTATCTCTGTGCCAGTAGTATCGGGACAGGGGACTTTTACGAGCAGTACTTCGGGCCG	39.4

- Specific dominant clones identified
- Frequency of clone measured
- Sequences tracked and compared

In collaboration with Adaptive Biosystems, Seattle WA

Tumor-specific TCR Sequences are tracked



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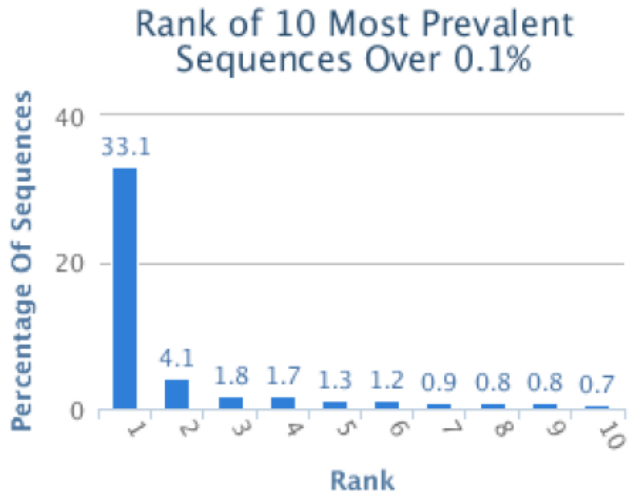

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1	ACATCGGCCCAAAAGAACCCGACAGCTTTCTATCTCTGTGCCAGTAGTATCGGGACAGGGGACTTTTACGAGCAGTACTTCGGGCCG	33.1

High Throughput Sequencing in TCL

- Dominant clones identified
- Identify and quantitatively track TCR rearrangement sequences from a complex background of cells

High Throughput Sequencing of T cell Repertoire

- Identification of a tumor-specific dominant rearrangement sequence
- Improves accuracy of diagnosis
- Improved utility in diagnosis and management of CTCL, especially with minimal disease

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RESEARCH ARTICLE

CANCER

Minimal Residual Disease Monitoring with High-Throughput Sequencing of T Cell Receptors in Cutaneous T Cell Lymphoma

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Examine the role of HTS-TCR in CTCL

Diagnosis and Staging of CTCL

- Reduced False positive of inflammatory disorders
- Reduced False negative in mild disease

Clinical management of CTCL patients

- Monitoring treatment efficacy/ identification of minimal disease
- Differentiating from lymphomatoid drug reaction

Comparison of HTS-TCR and TCR-PCR

- 75 cases of inflammatory disorders of patients followed at Stanford Dermatology Clinics:
  - Lichenoid dermatitis
  - Spongiotic dermatitis
  - Psoriasis
- HTS-TCR and TCR-PCR performed on all cases

Higher Frequency of Clonality in Standard TCR-PCR over HTS-TCR

Clinical Diagnosis	PCR-TCRβ	PCR-TCRγ	HTS-TCRβ	total cases
Lichenoid dermatitis	8 (30.8%)	10 (38.5%)	2 (7.7%)	26
Spongiotic dermatitis	1 (6.3%)	3 (18.8%)	0 (0%)	16
Psoriasis	10 (30.3%)	8 (24.2%)	0 (0%)	33

Examine the role of HTS-TCR in CTCL

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- Reduced False positive of inflammatory disorders
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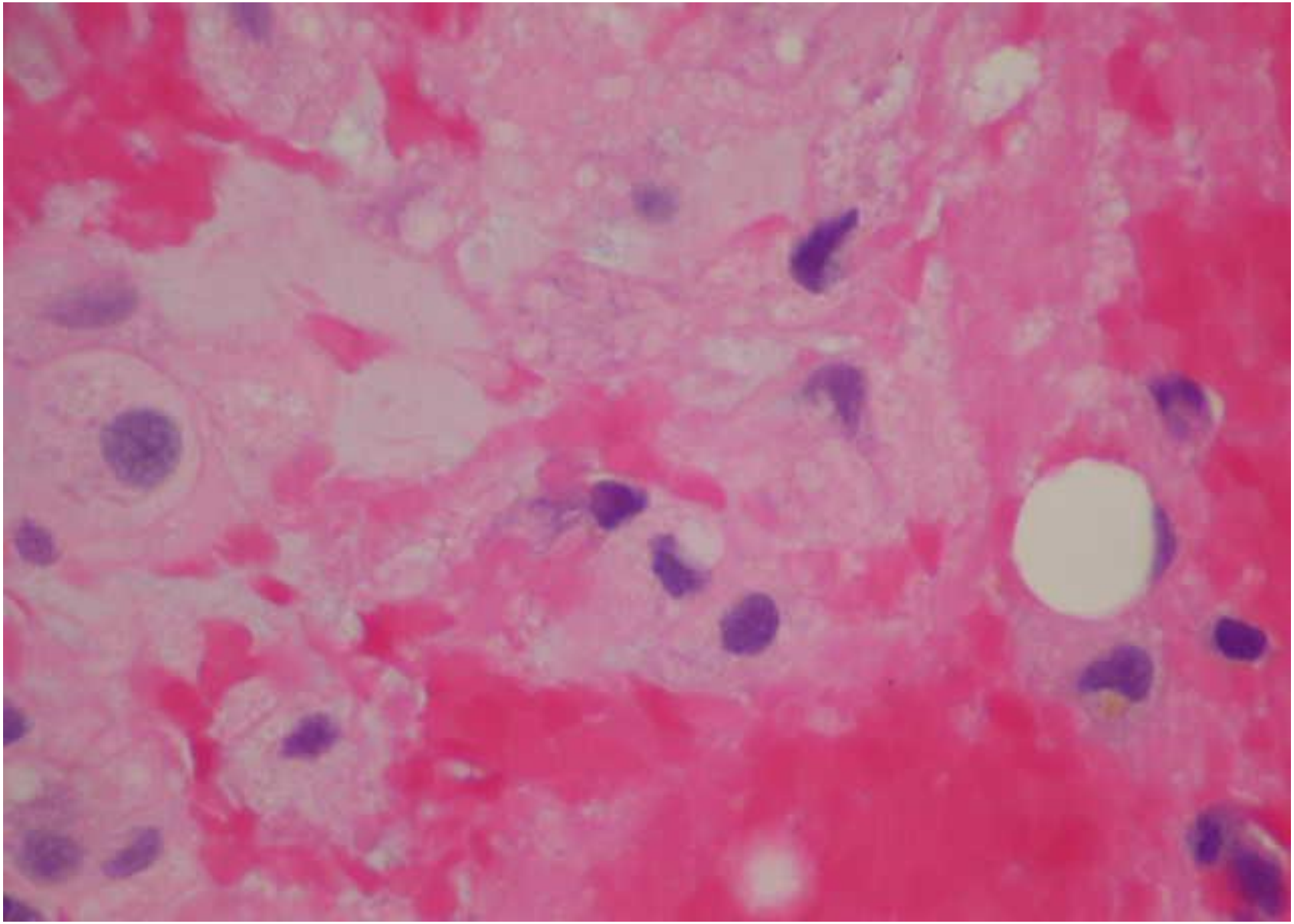
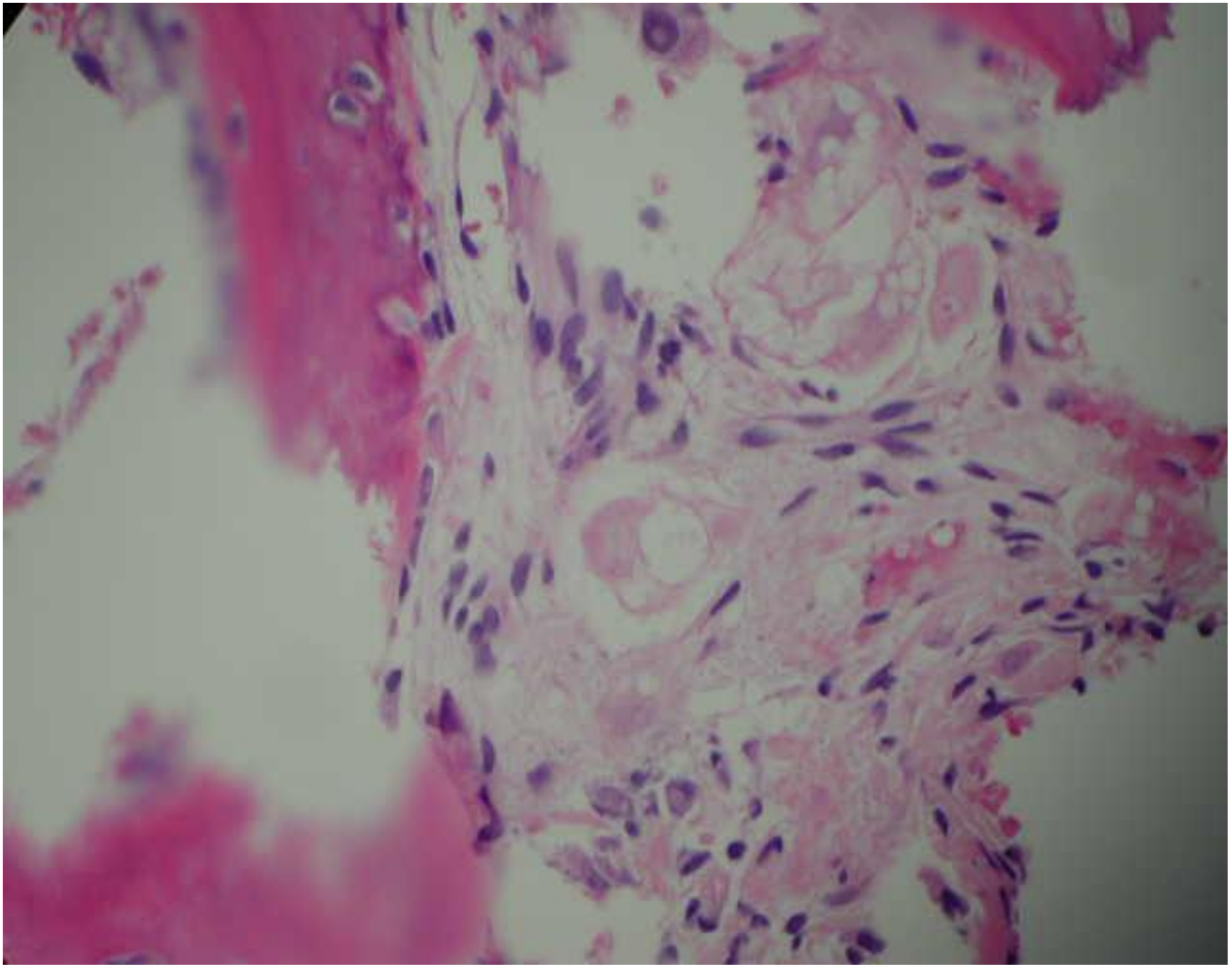
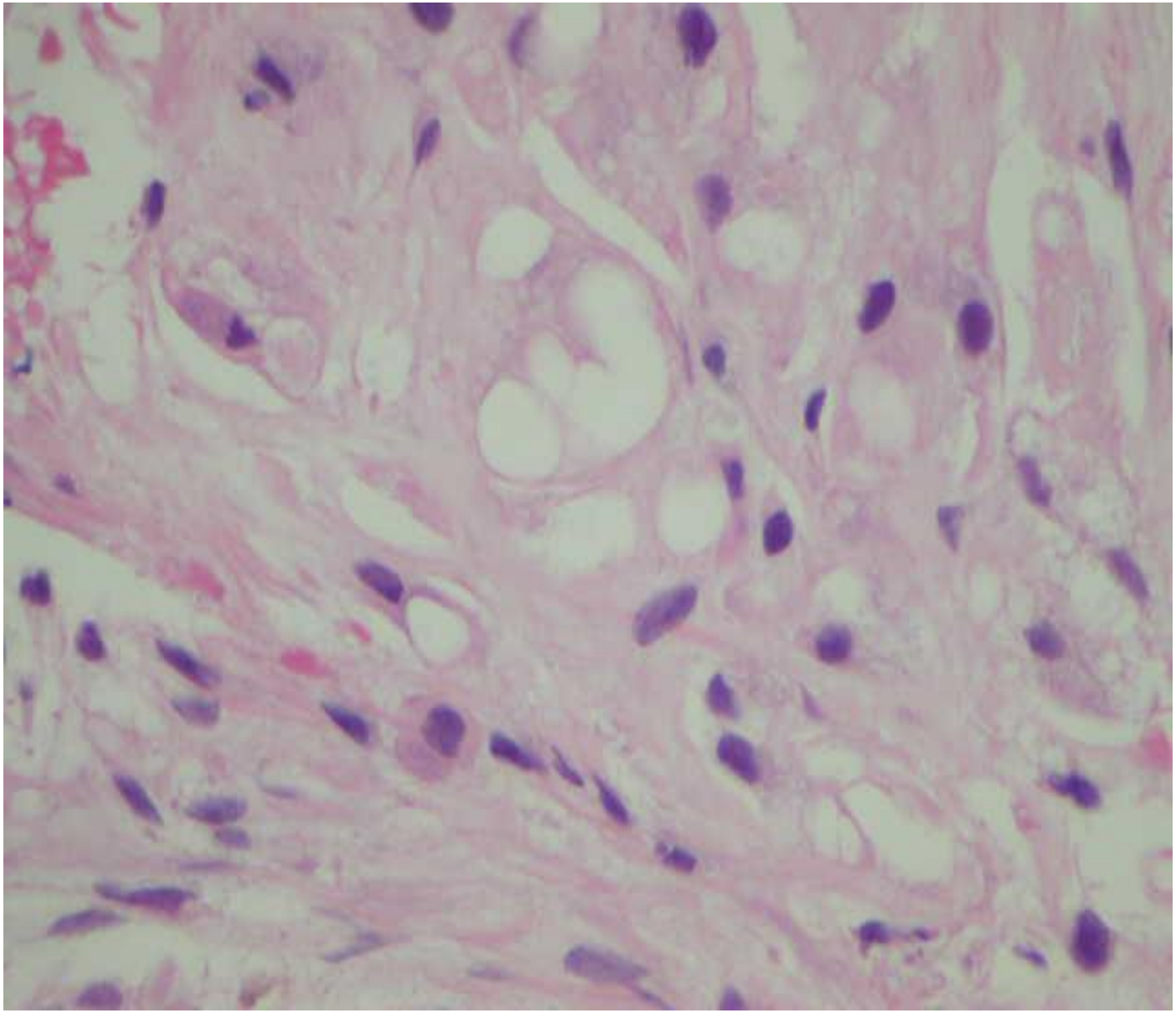
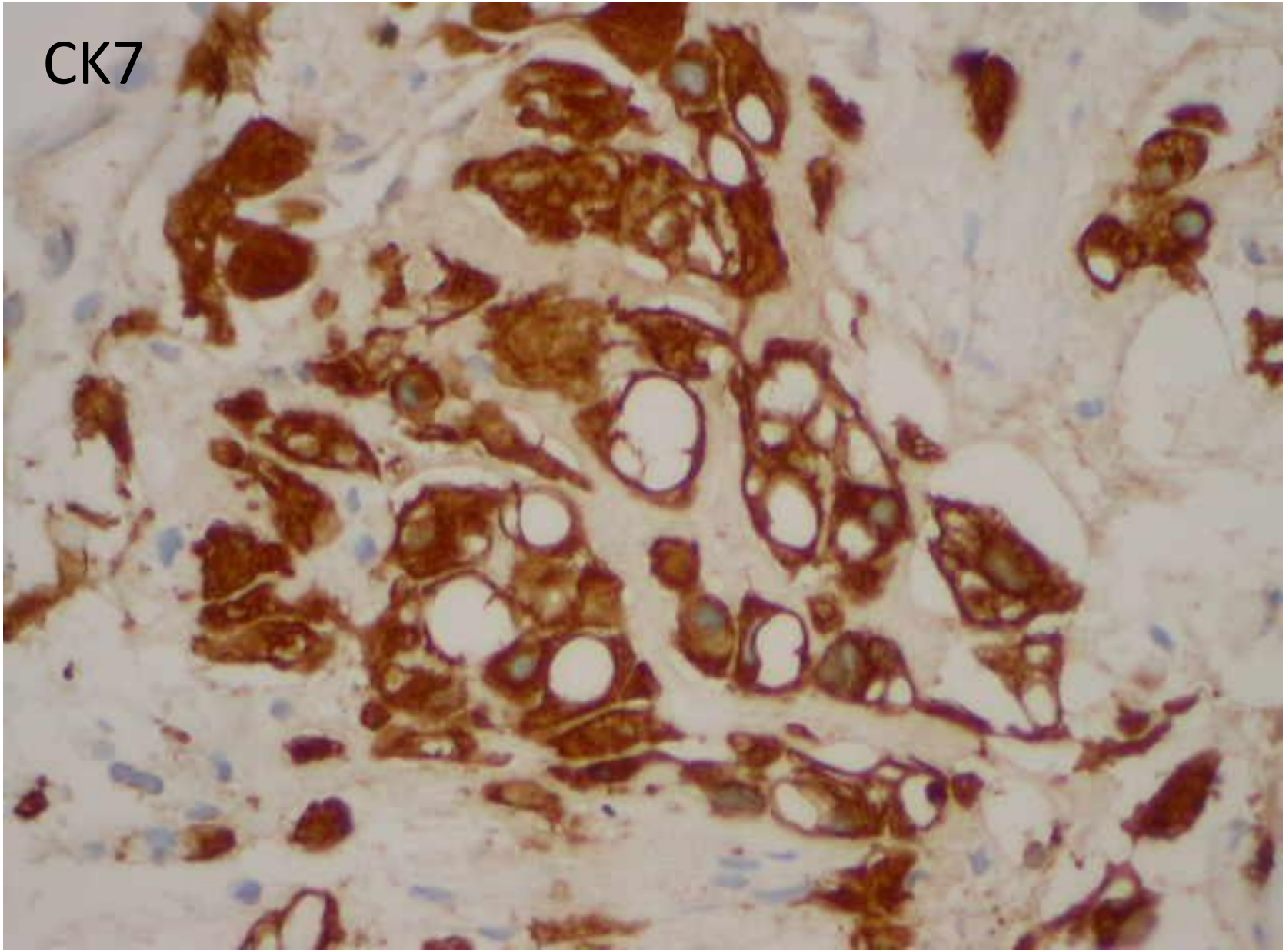




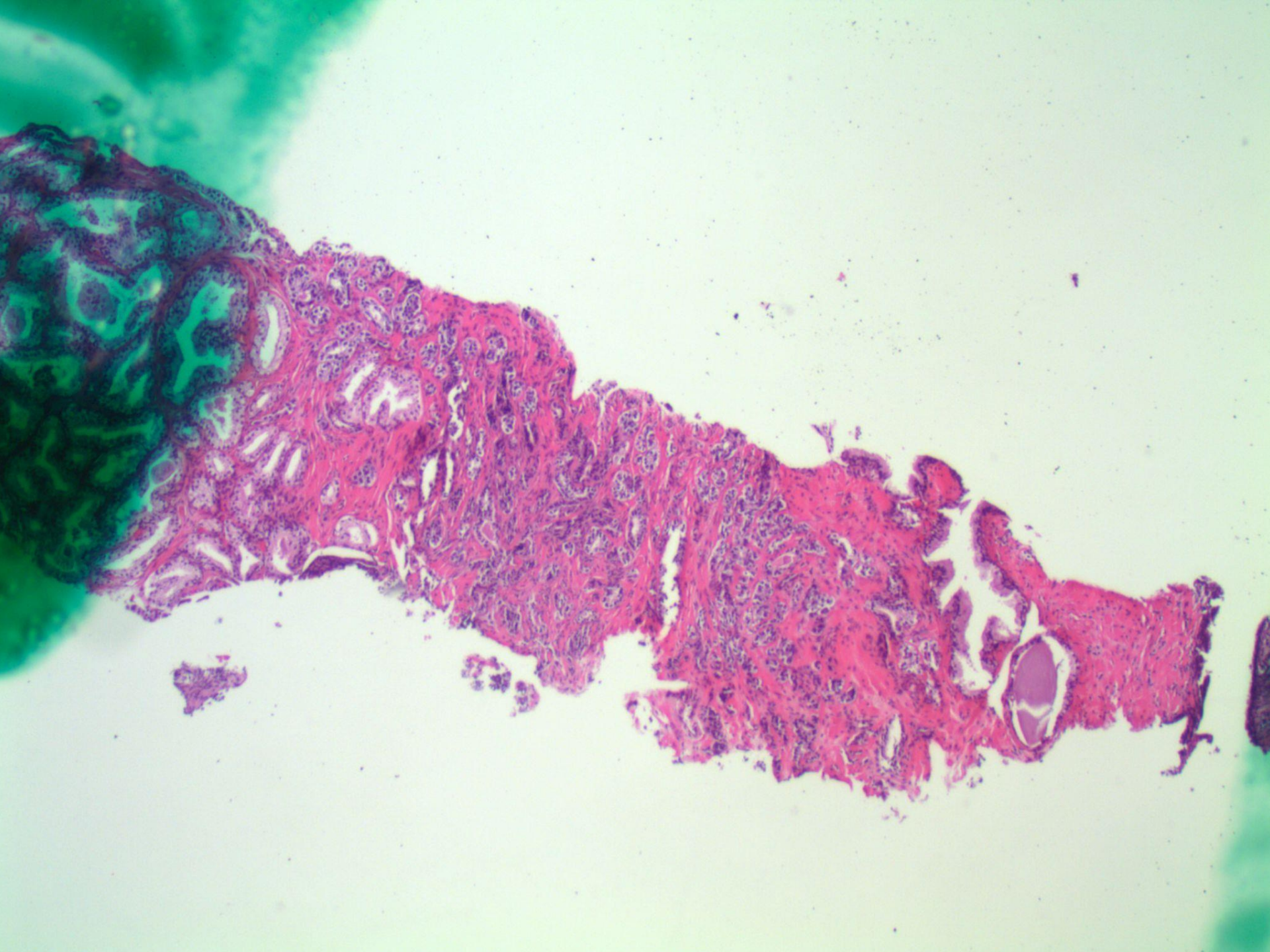


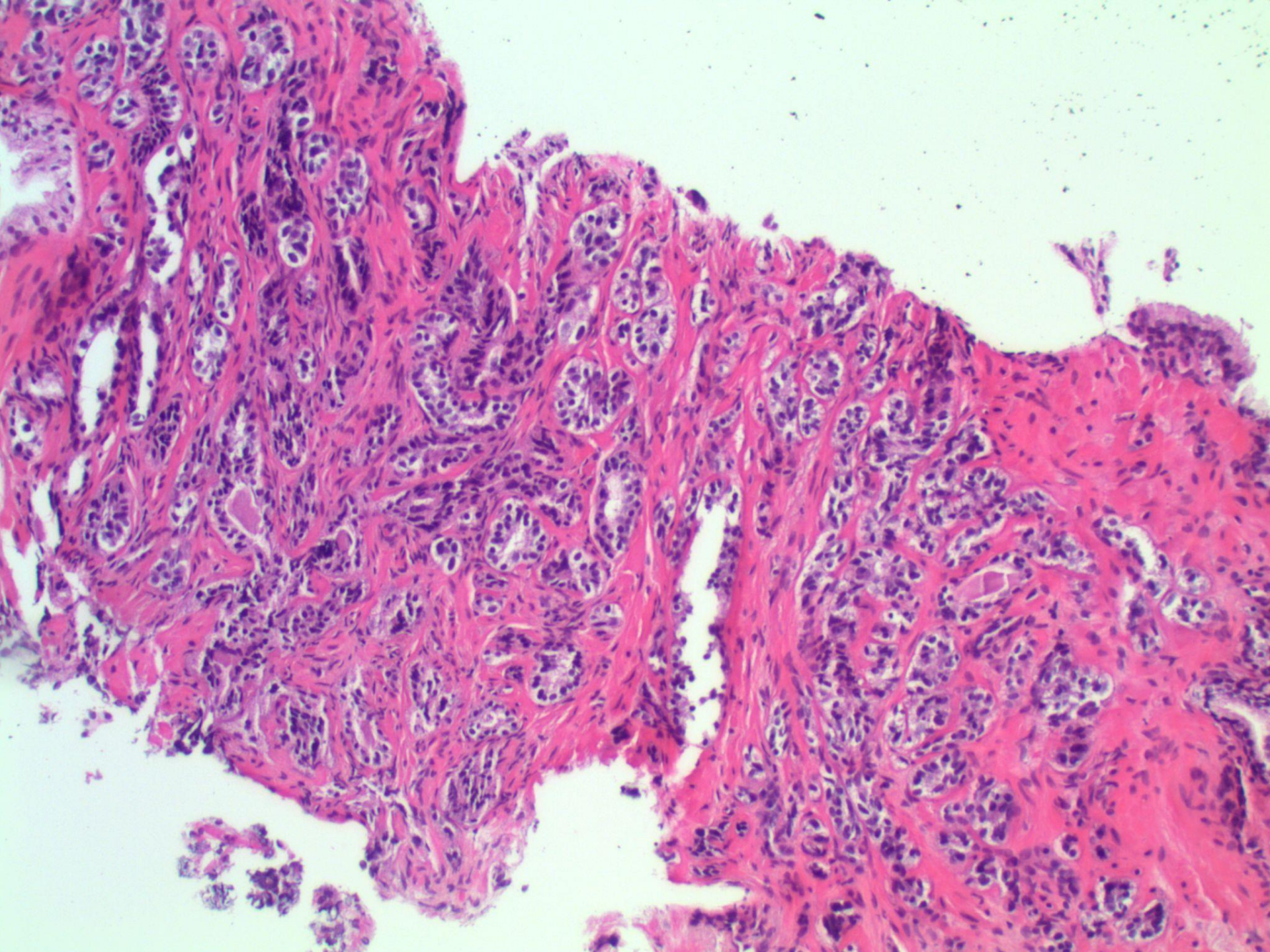

CK7

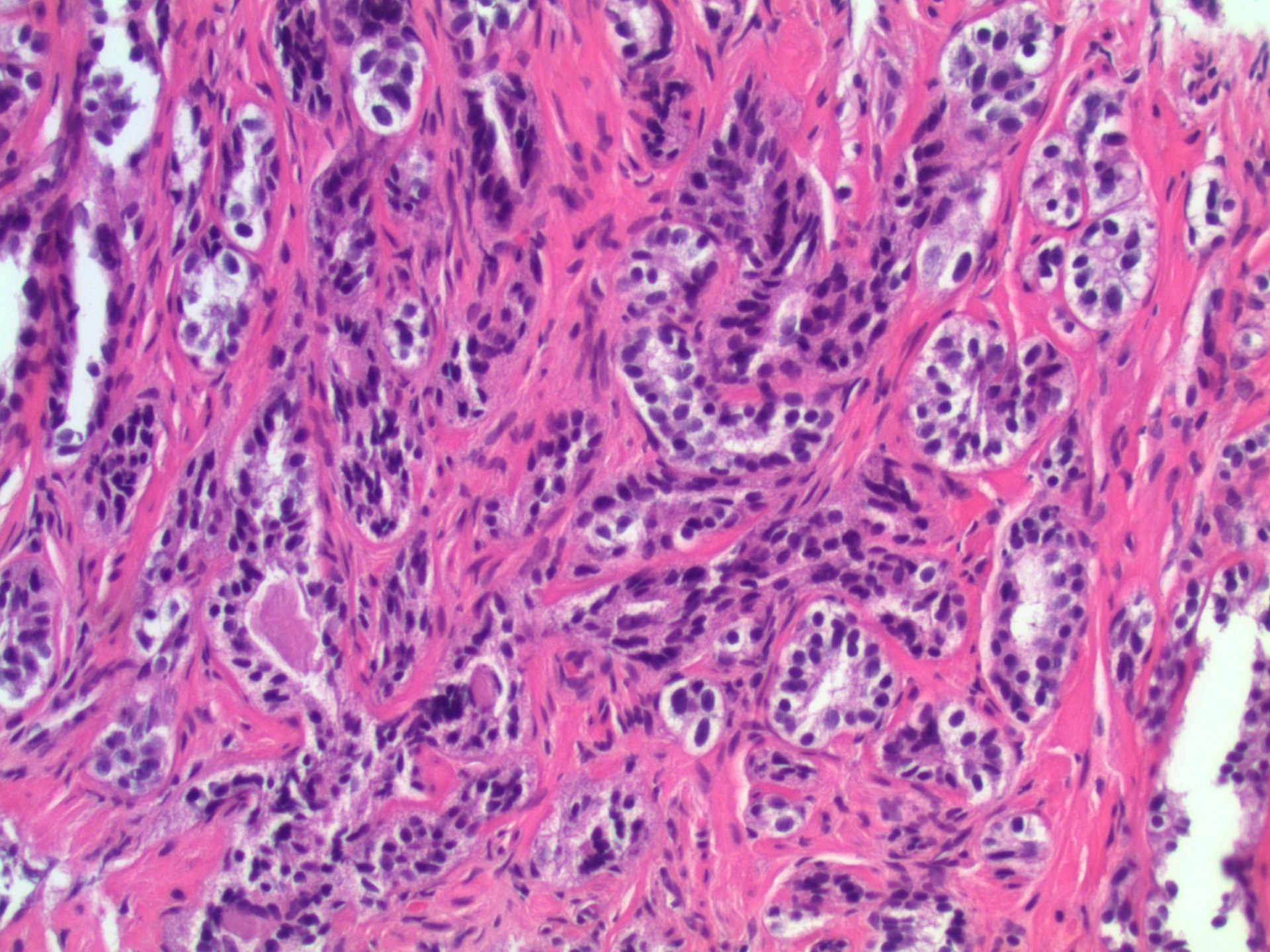
SB 5914

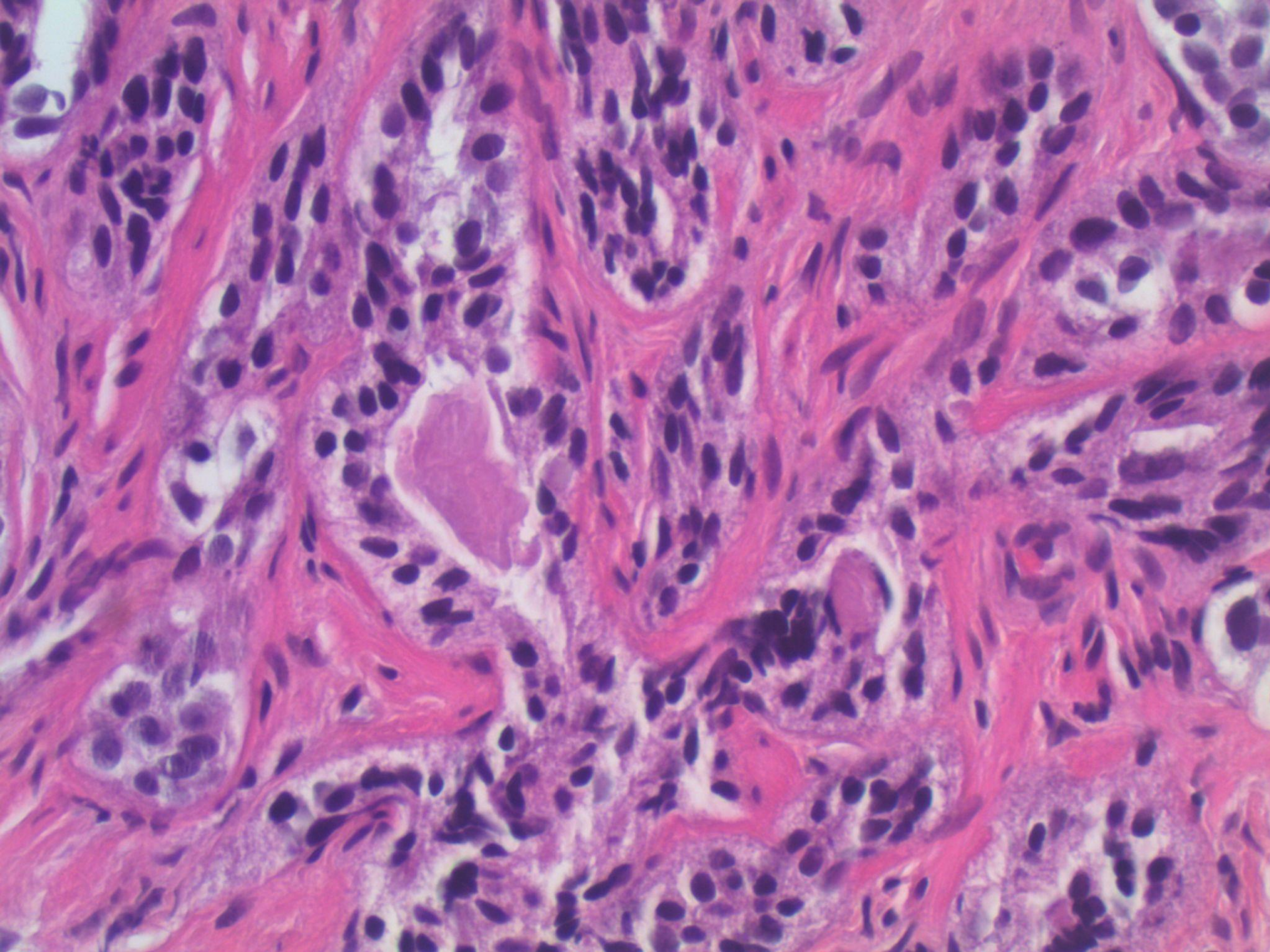
Ankur Sangoi; El Camino Hospital

65-year-old male with PSA of 3.84. Prostate biopsies submitted.







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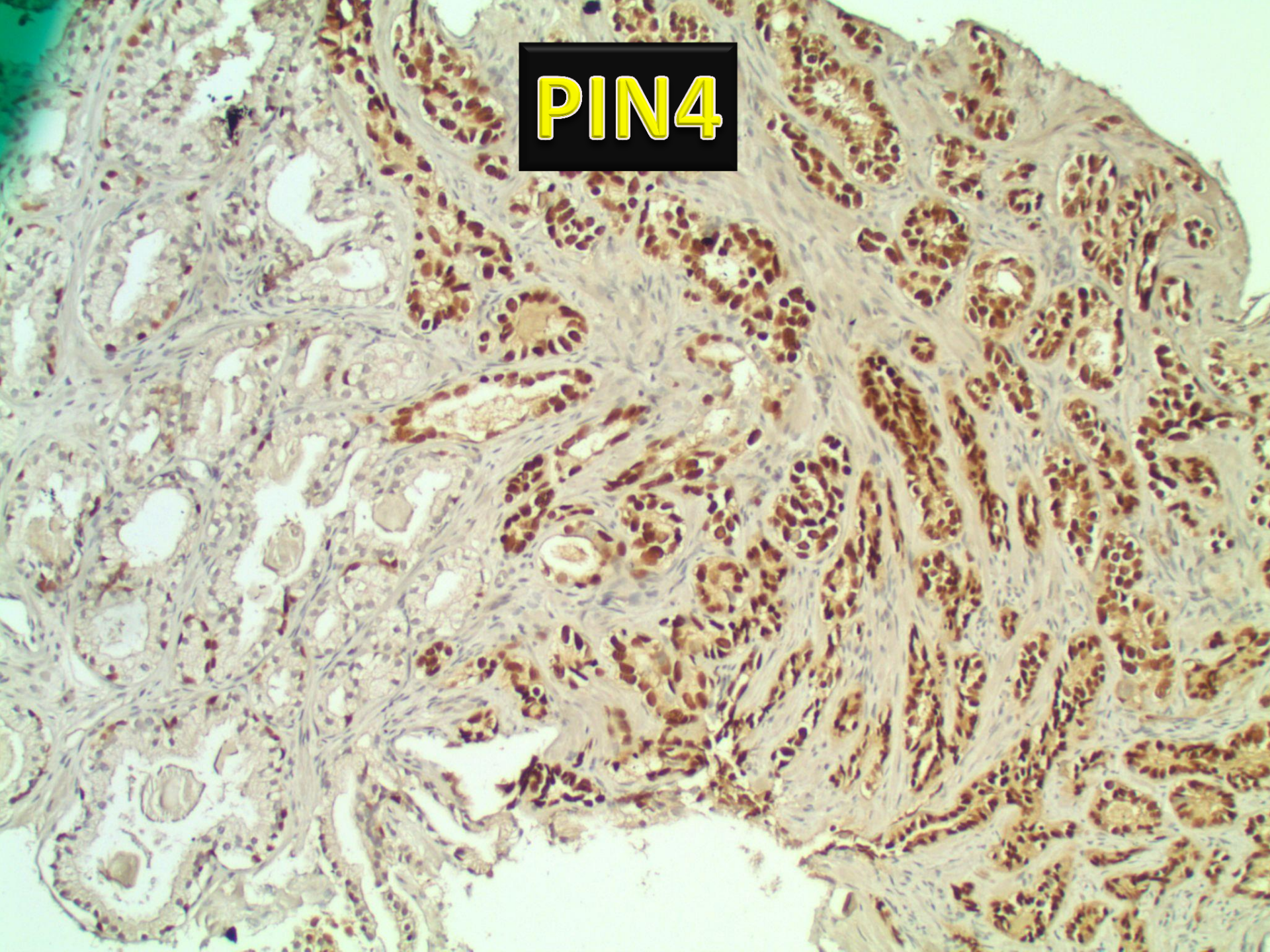
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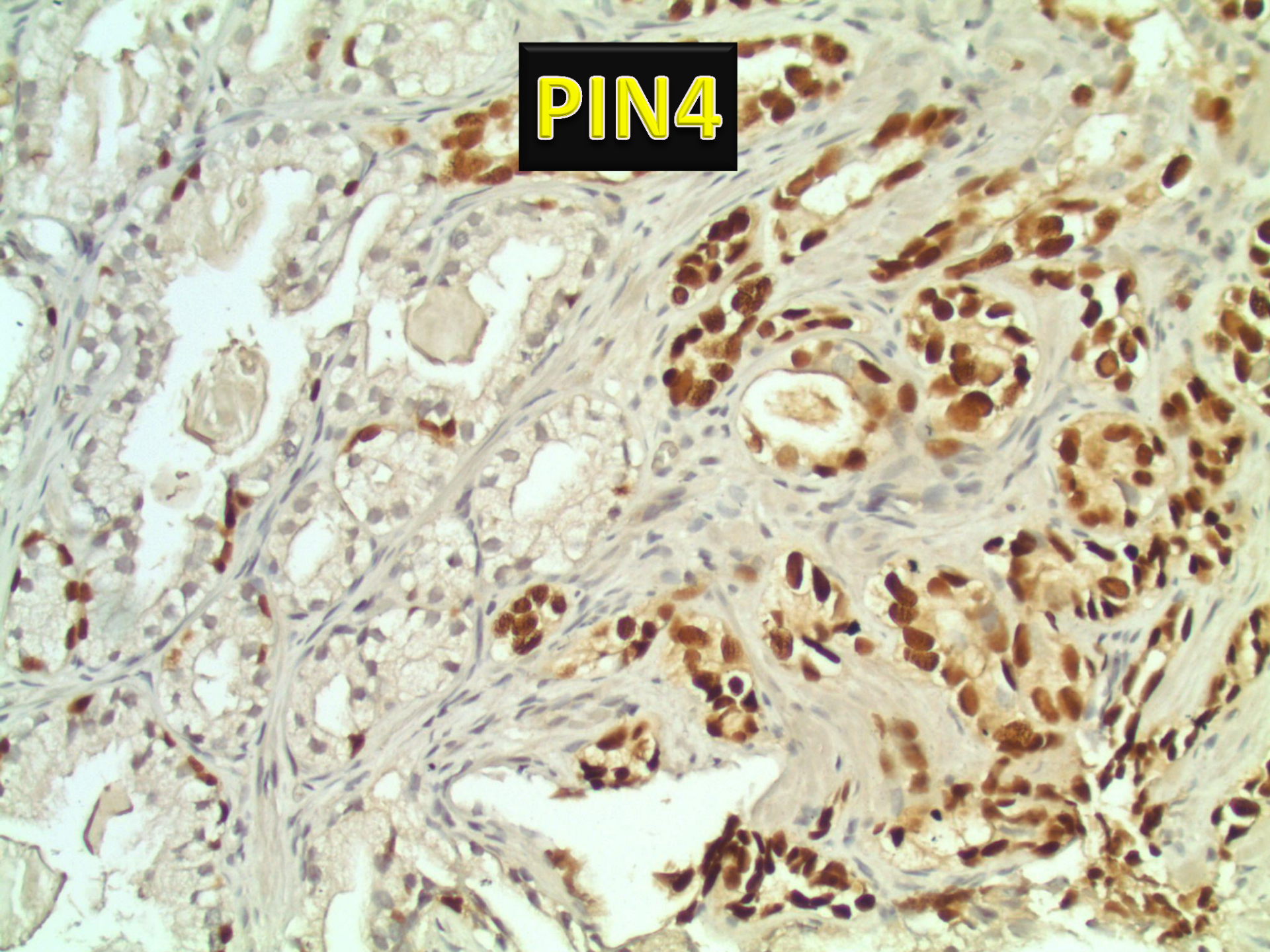
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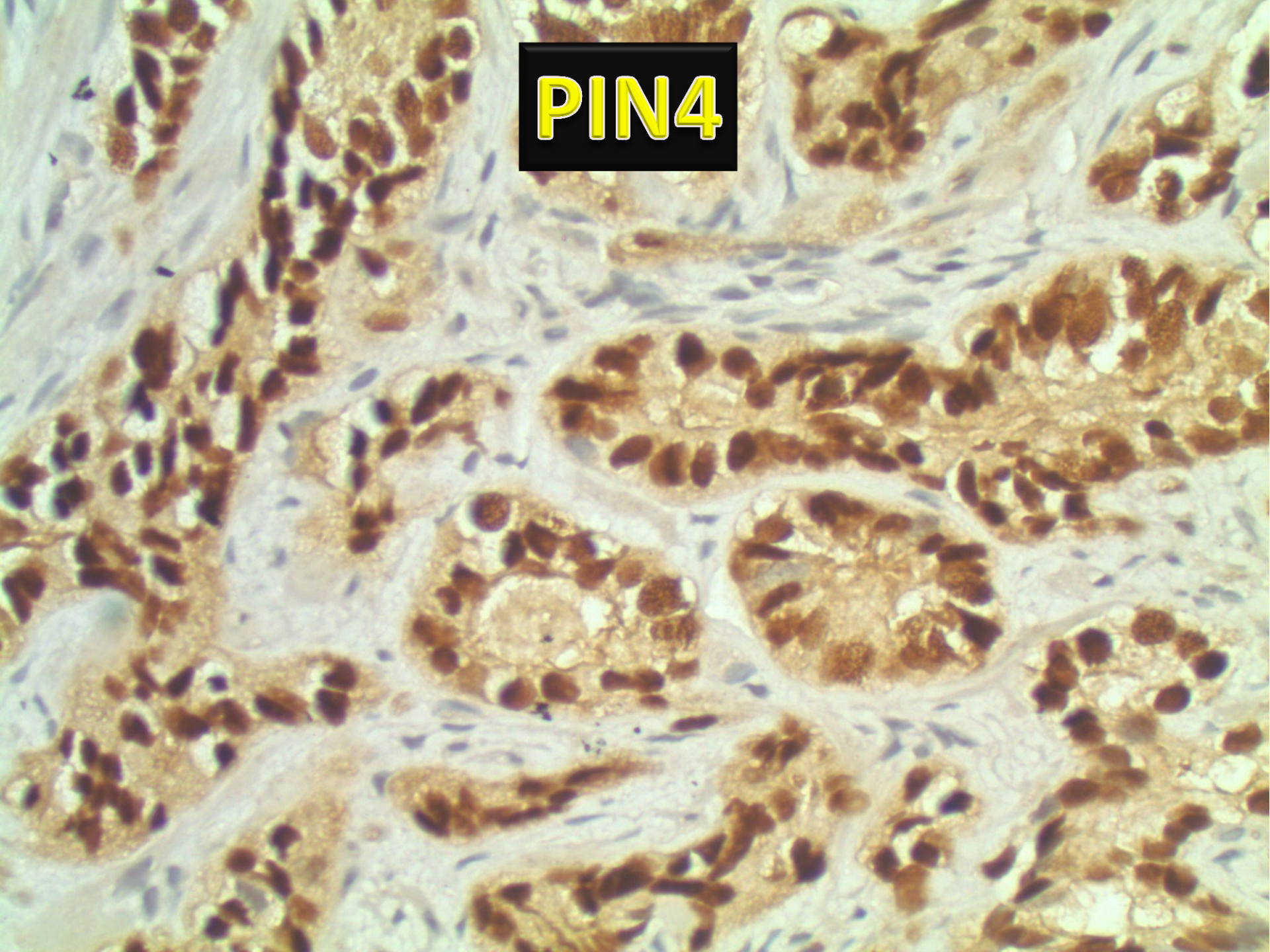
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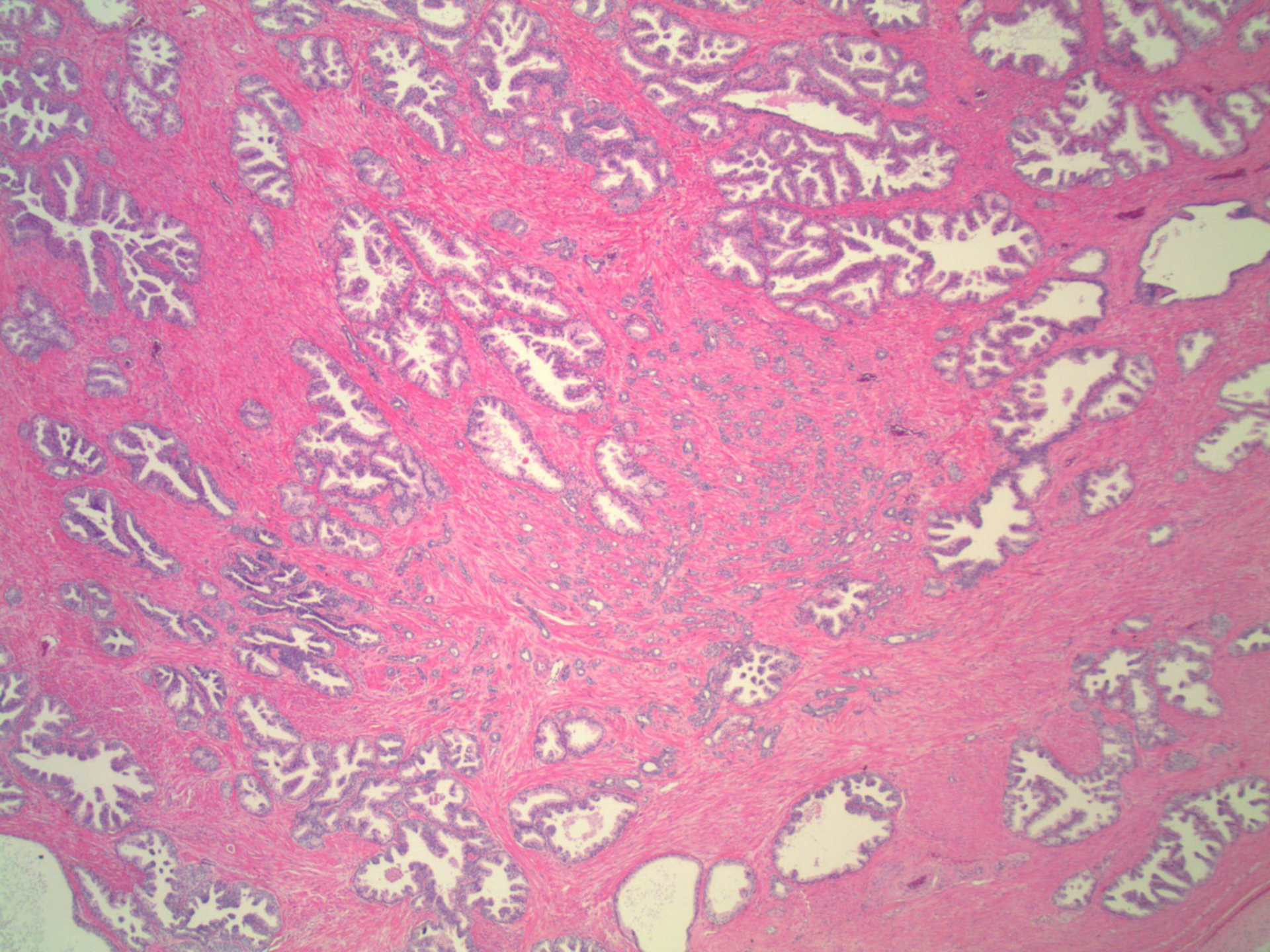
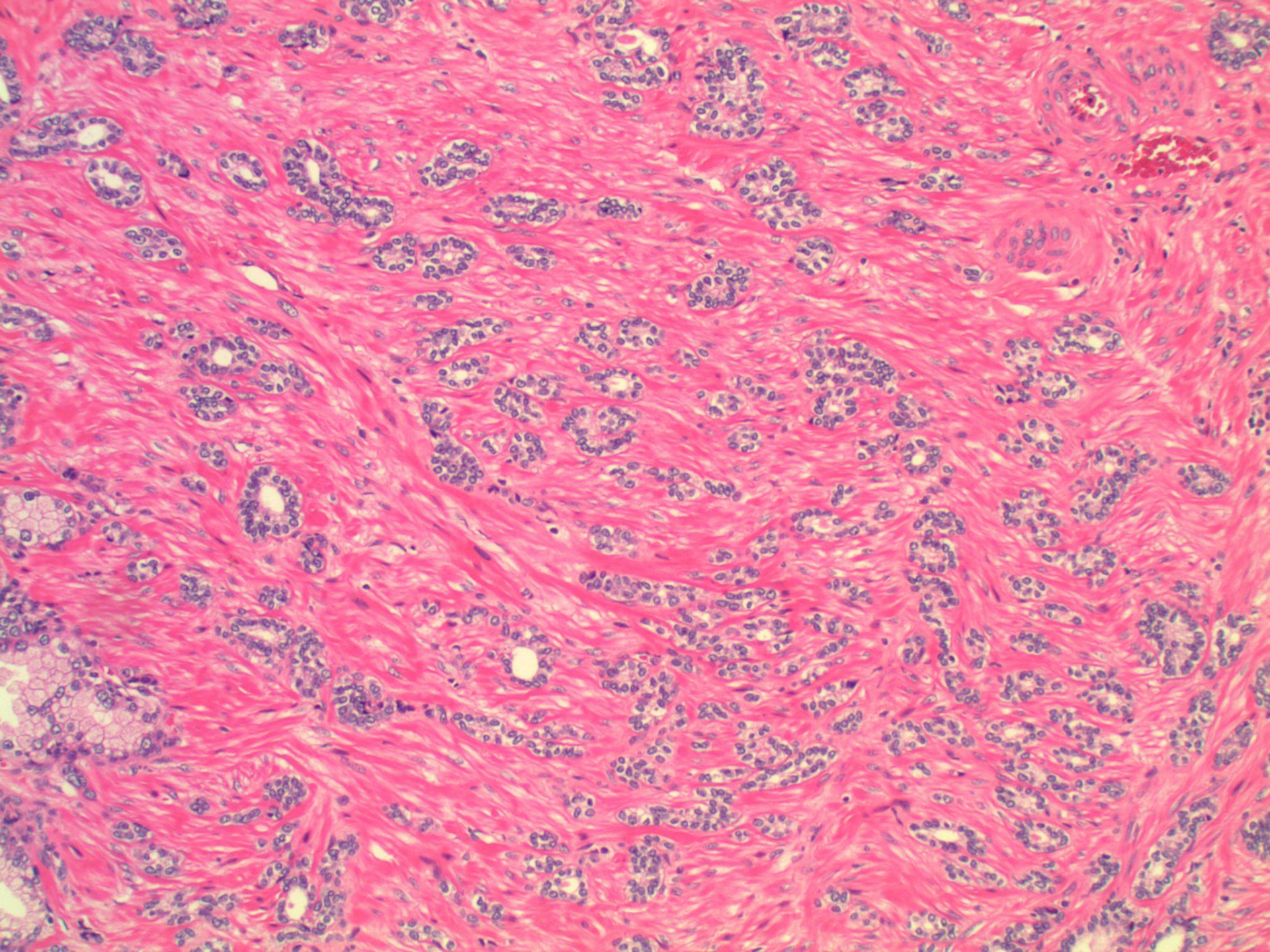
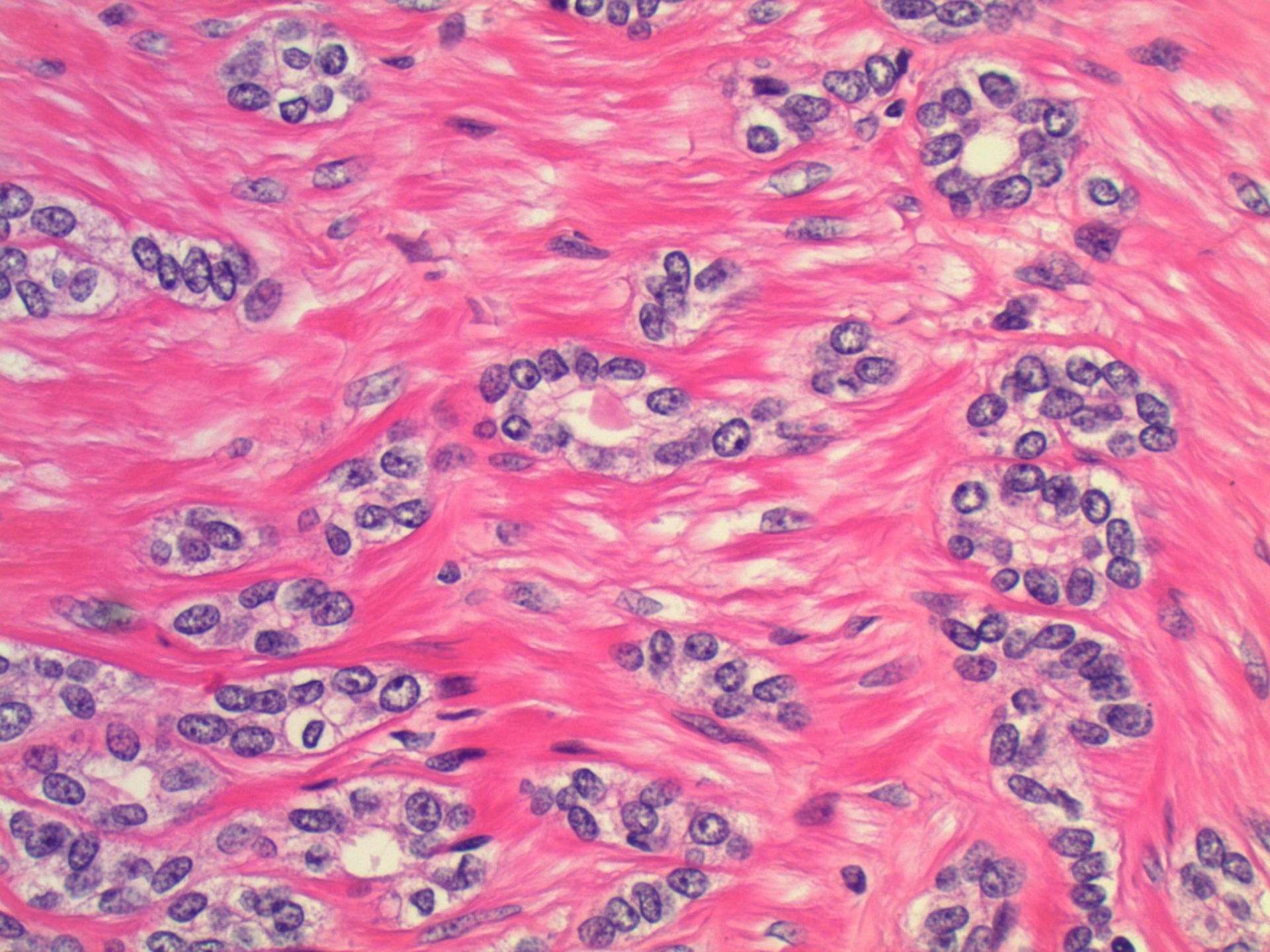
DIAGNOSIS?

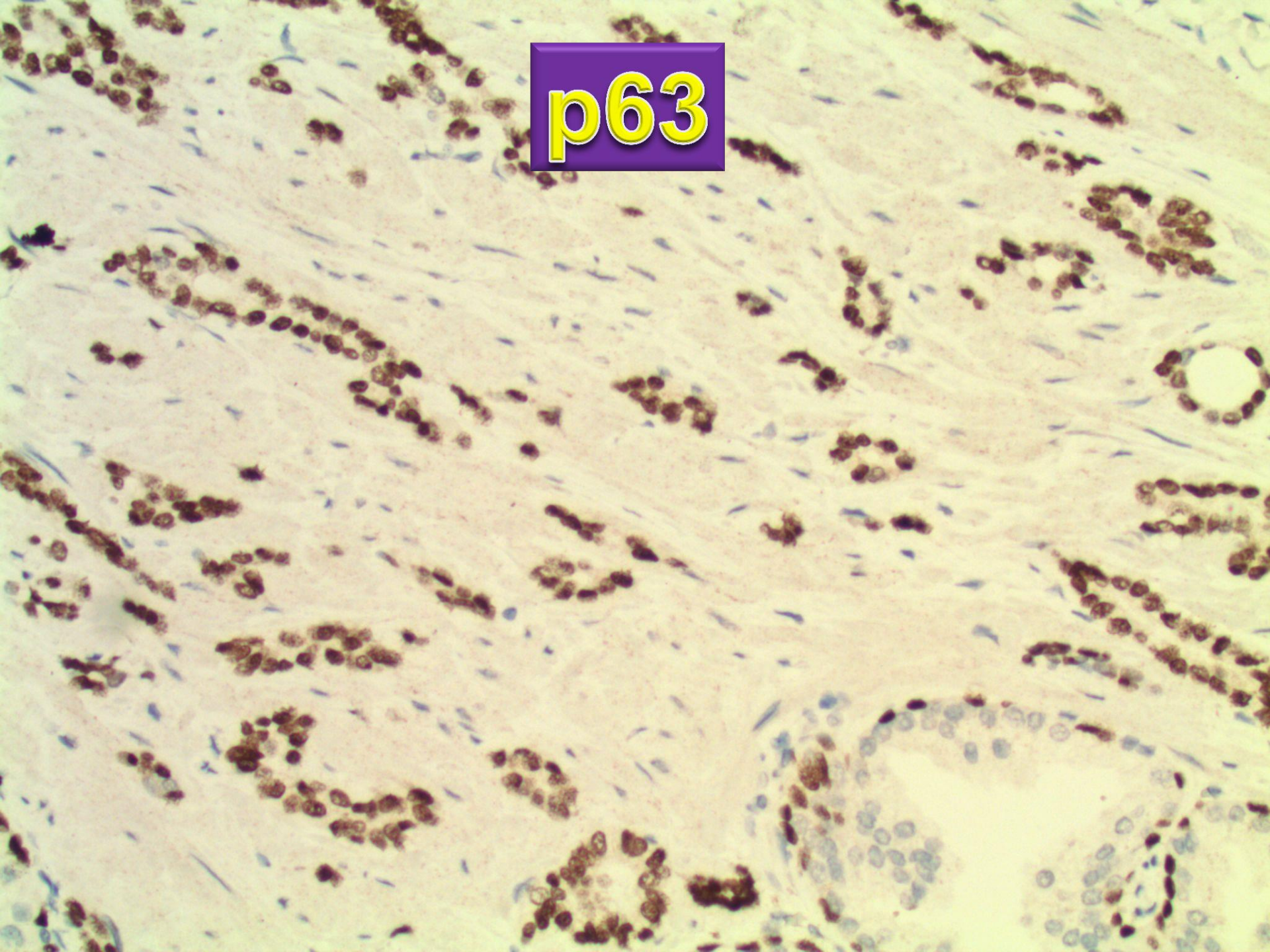
DIAGNOSIS

p63-positive prostatic carcinoma








p63

Aberrant Diffuse Expression of p63 in Adenocarcinoma of the Prostate on Needle Biopsy and Radical Prostatectomy: Report of 21 Cases

Adeboye O. Osunkoya, MD, Donna E. Hansel, MD, PhD,† Xinlai Sun, MD,‡ George J. Netto, MD,* and Jonathan I. Epstein, MD*§‖*

Am J Surg Pathol • Volume 32, Number 3, March 2008

Aberrant Expression of p63 in Adenocarcinoma of the Prostate

A Radical Prostatectomy Study

Giovanna A. Giannico, MD, Hillary M. Ross, MD,† Tamara Lotan, MD,† and Jonathan I. Epstein, MD†‡§*

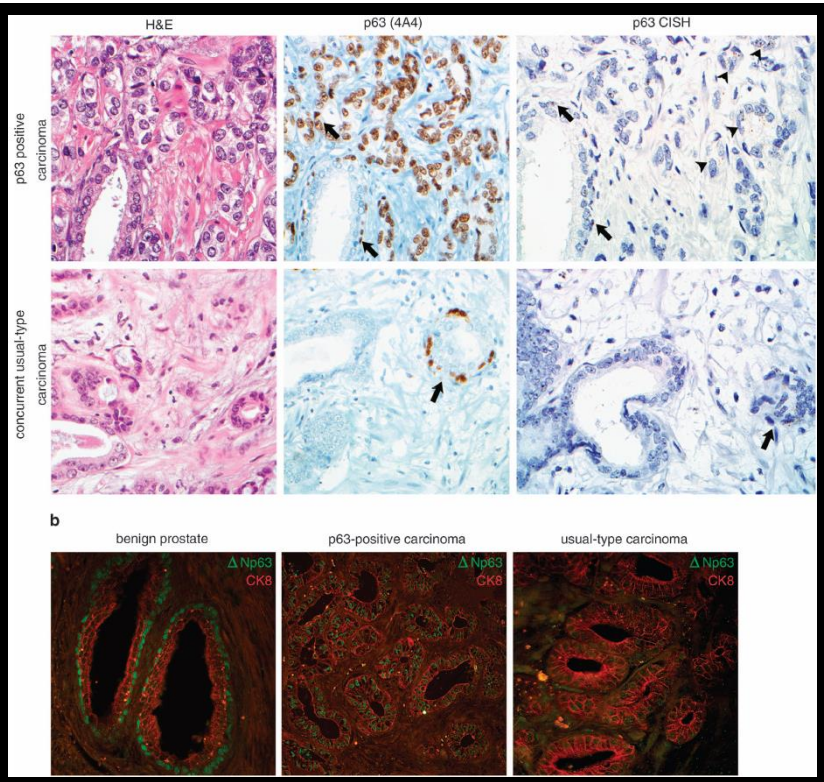
Am J Surg Pathol • Volume 37, Number 9, September 2013

p63-positive prostate ca

- **Uncommon**
- **Often co-exist with usual-type prostatic adenocarcinoma**
- **Usually distinct atrophic, basaloid morphology**
- **Do not Gleason grade**
  - Discuss relative good prognosis at RP

Prostate adenocarcinomas aberrantly expressing p63 are molecularly distinct from usual-type prostatic adenocarcinomas

Hsueh-Li Tan[1], Michael C Haffner[2], David M Esopi[2], Ajay M Vaghasia[2], Giovanna A Giannico[3], Hillary M Ross[1], Susmita Ghosh[1], Jessica L Hicks[1], Qizhi Zheng[1], Ankur R Sangoi[4], Srinivasan Yegnasubramanian[2], Adeboye O Osunkoya[5], Angelo M De Marzo[1,2,6], Jonathan I Epstein[1,2,6] and Tamara L Lotan[1,2]



2015 [epub ahead of print]

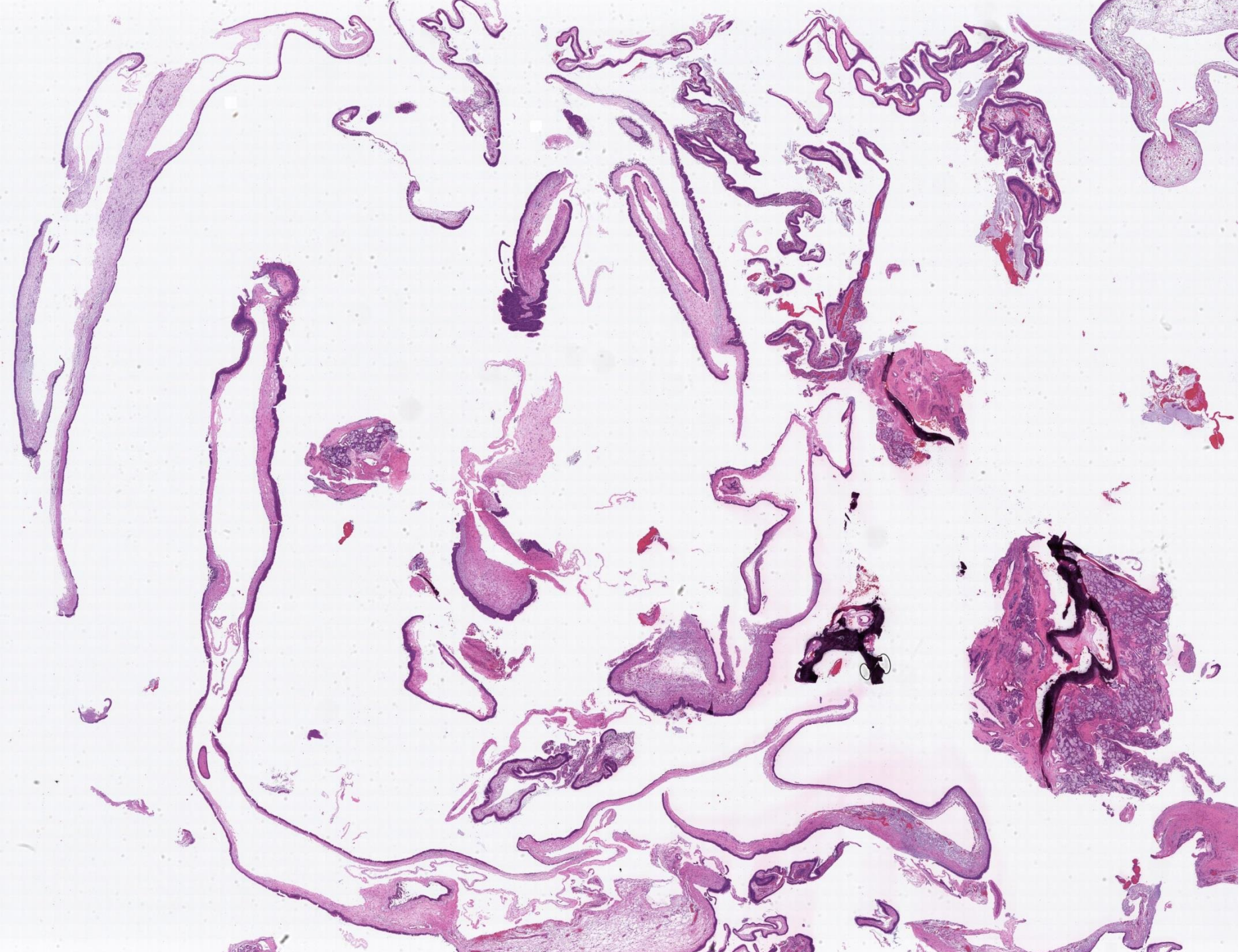
p63-positive prostate ca

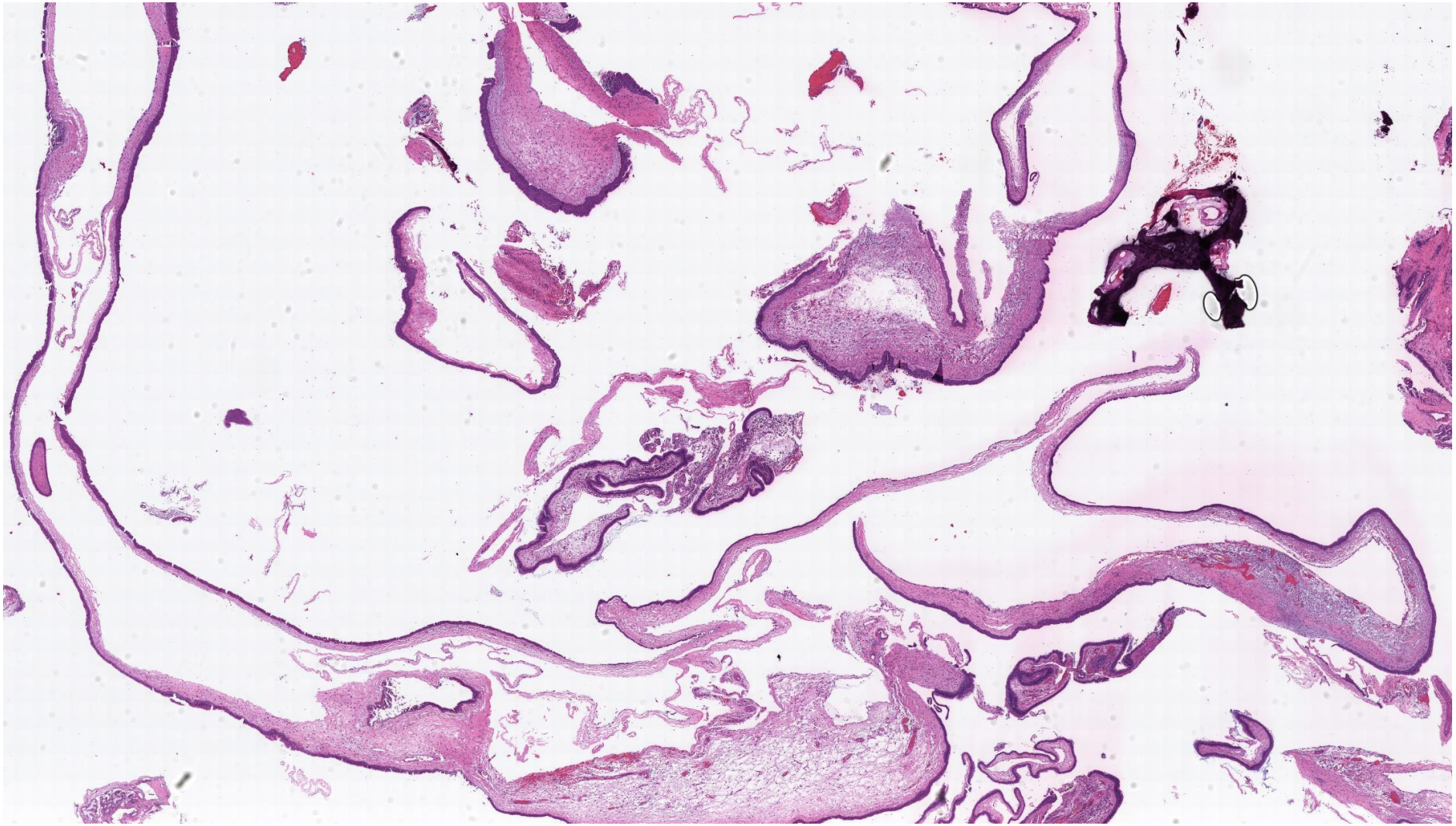
- Positive IHC: p63, CK8/18, AR, NKX3.1
- Negative IHC: HMWCK (CK5/6 weakly+)
- Lack ERG rearrangement
- No SPINK1 expression
- No PTEN loss
- Mixed luminal/basal phenotype
- Distinct molecular variant

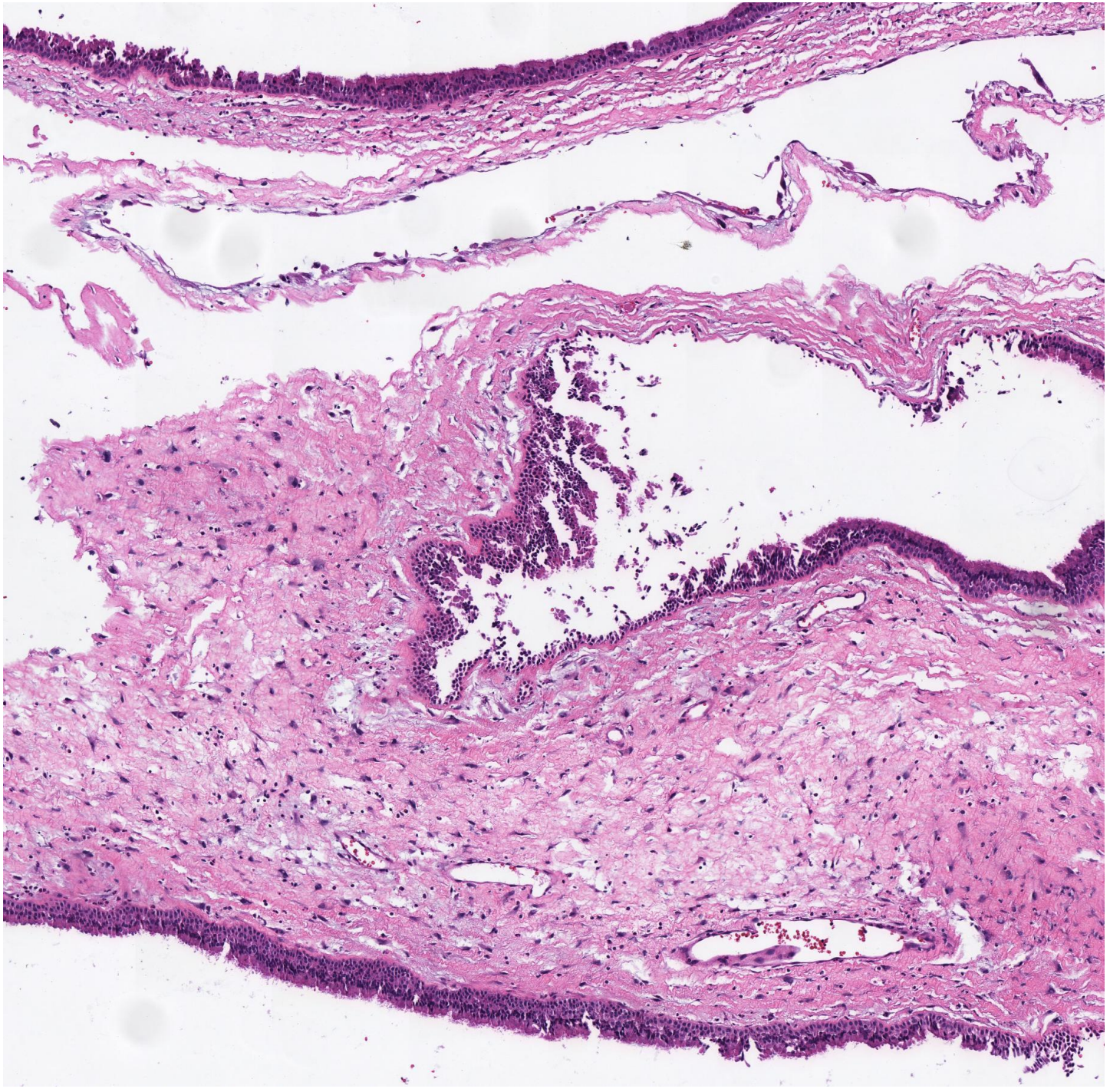
SB 5915

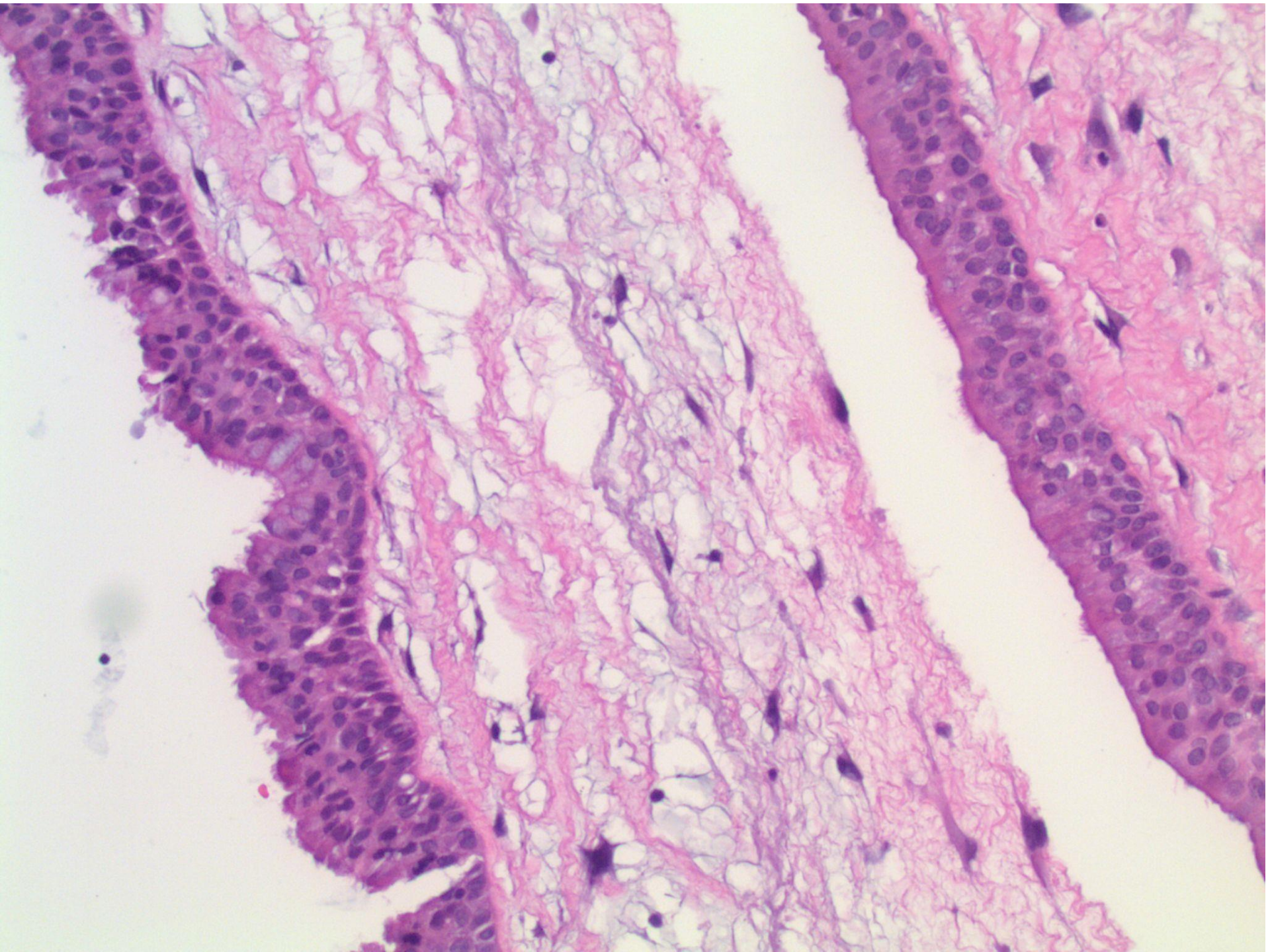
Ankur Sangoi; El Camino Hospital

27-year-old female with right nasal polyp. Polypectomy submitted.







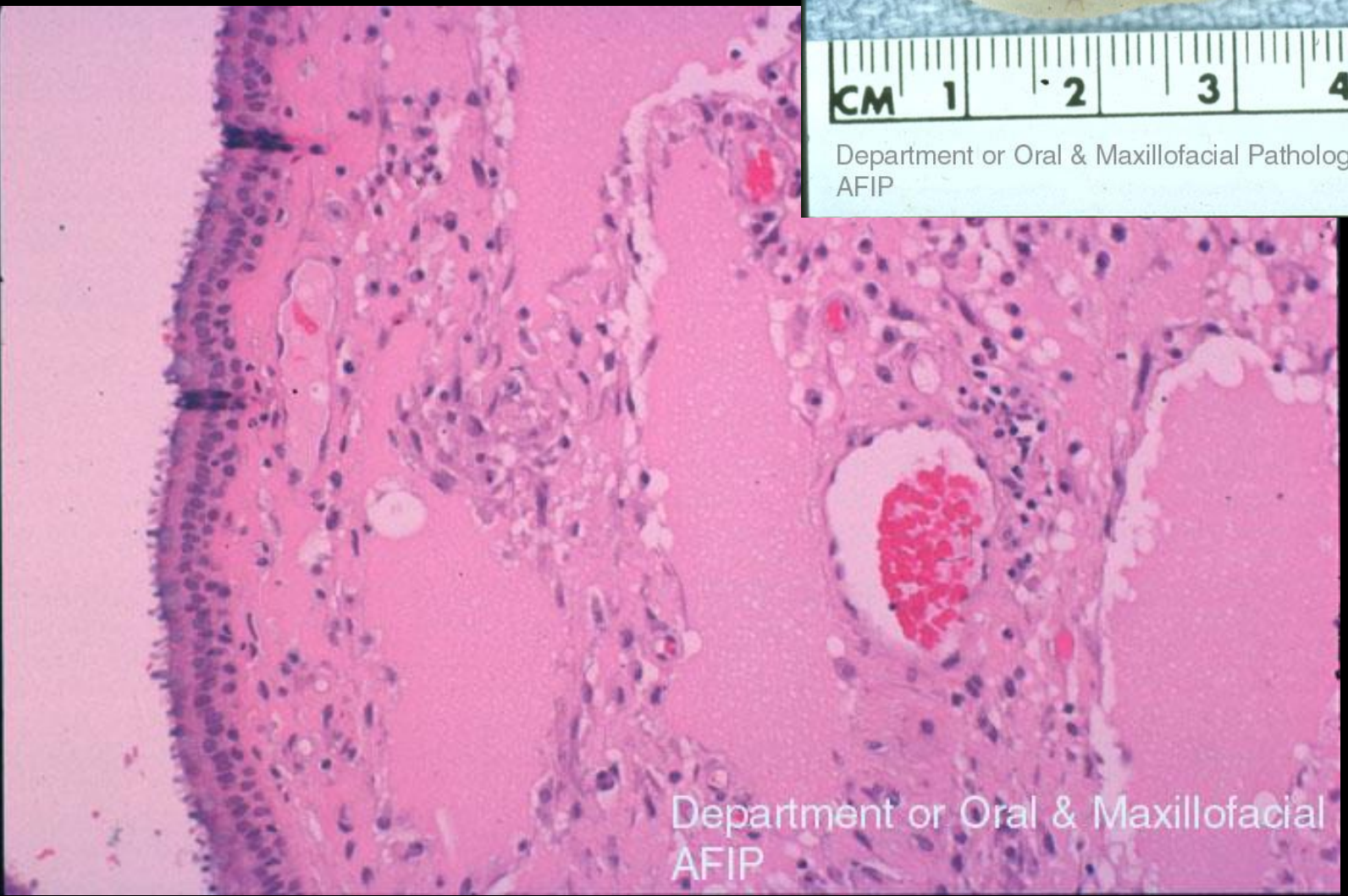


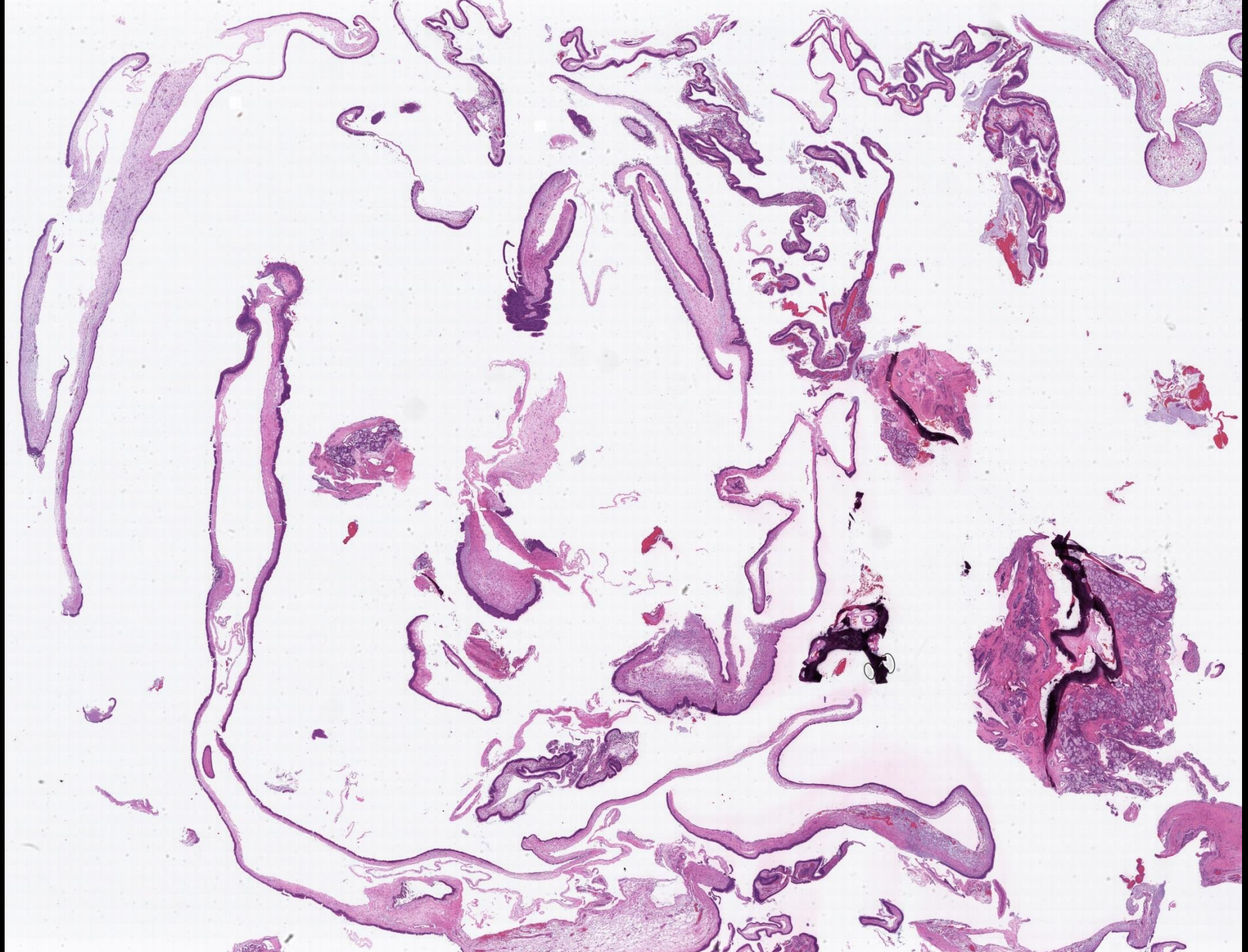
DIAGNOSIS?

DIAGNOSIS

Antrochoanal polyp

Antrochoanal Polyp





Antrochoanal Polyp

- 4-6% of nasal polyps
- Frequently occur in childhood
- 90% solitary
- Arise from wall of maxillary antrum, extending through large primary or secondary maxillary ostium into nasal cavity
- May pass into choanae or nasopharynx
- Usually not associated with allergic sinusitis

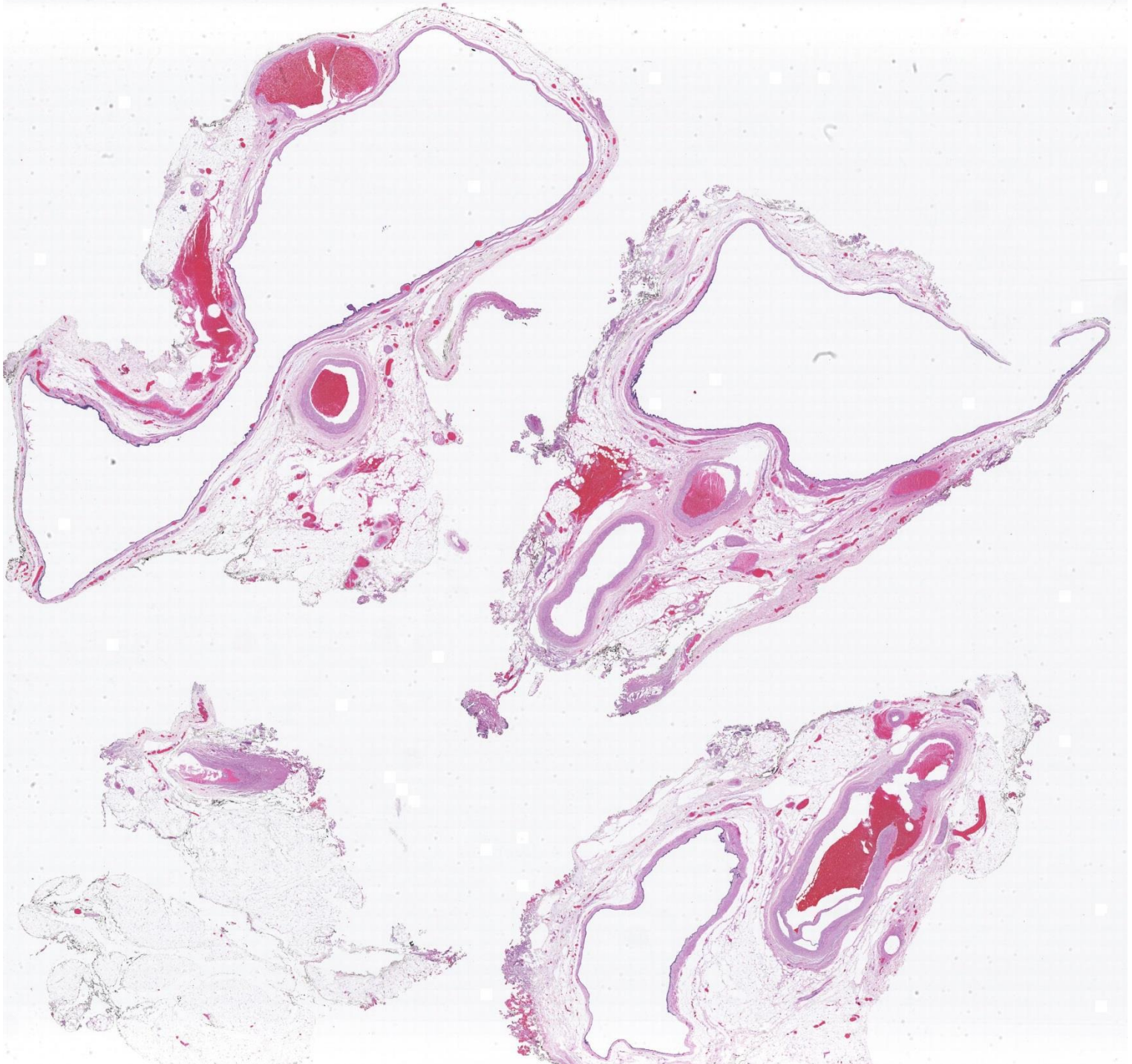
Antrochoanal Polyp

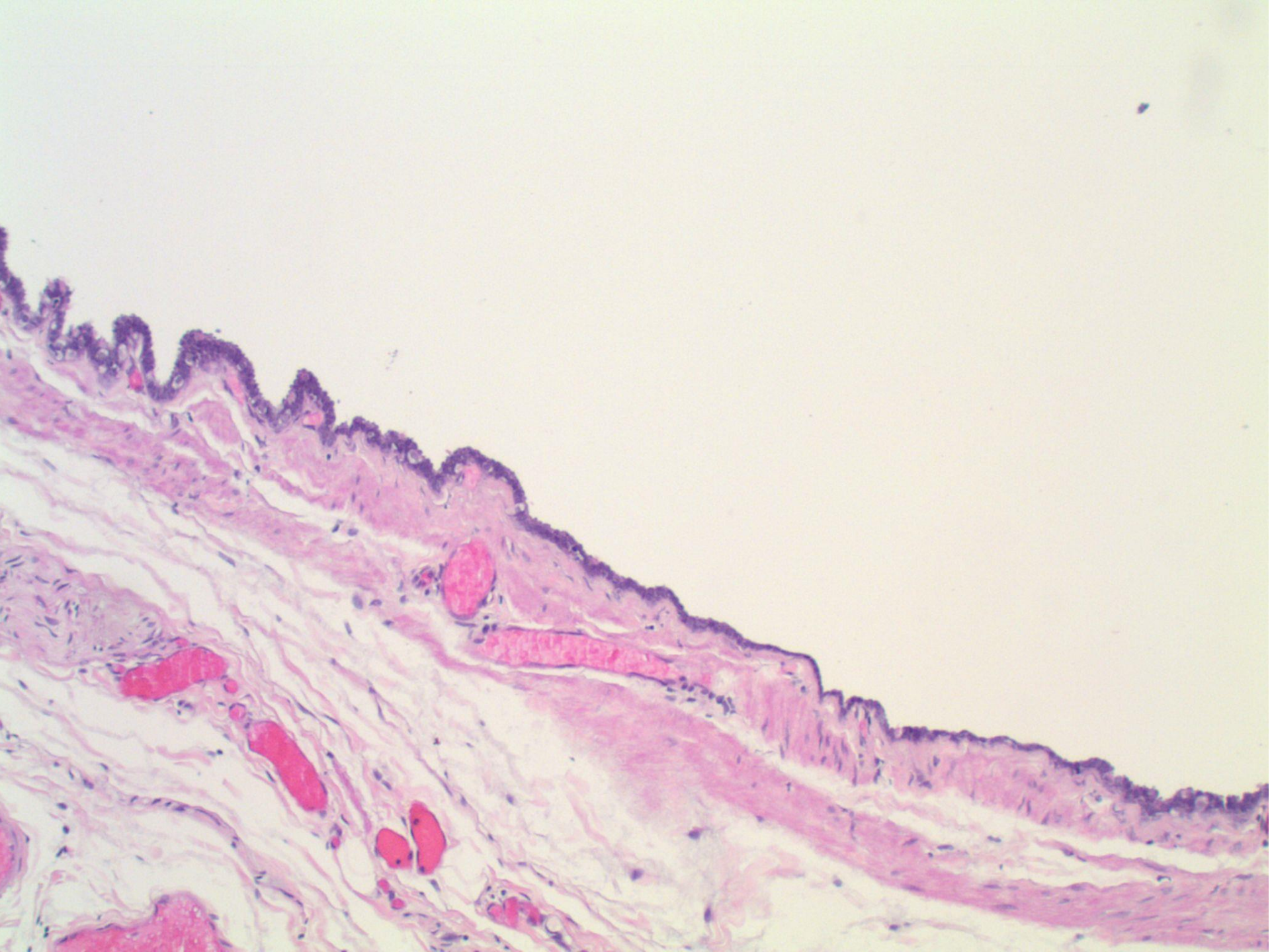
- **<u>Gross:</u> long narrow stalk with firm, fibrous body**
- **<u>Micro:</u> (vs. inflammatory polyp)**
  - thin surface mucosa with no thickened basement membrane
  - less edema and fewer glands than inflammatory polyp
  - may have prominent dilated vessels with thrombosis or infarct
  - prominent eosinophils in only 20%

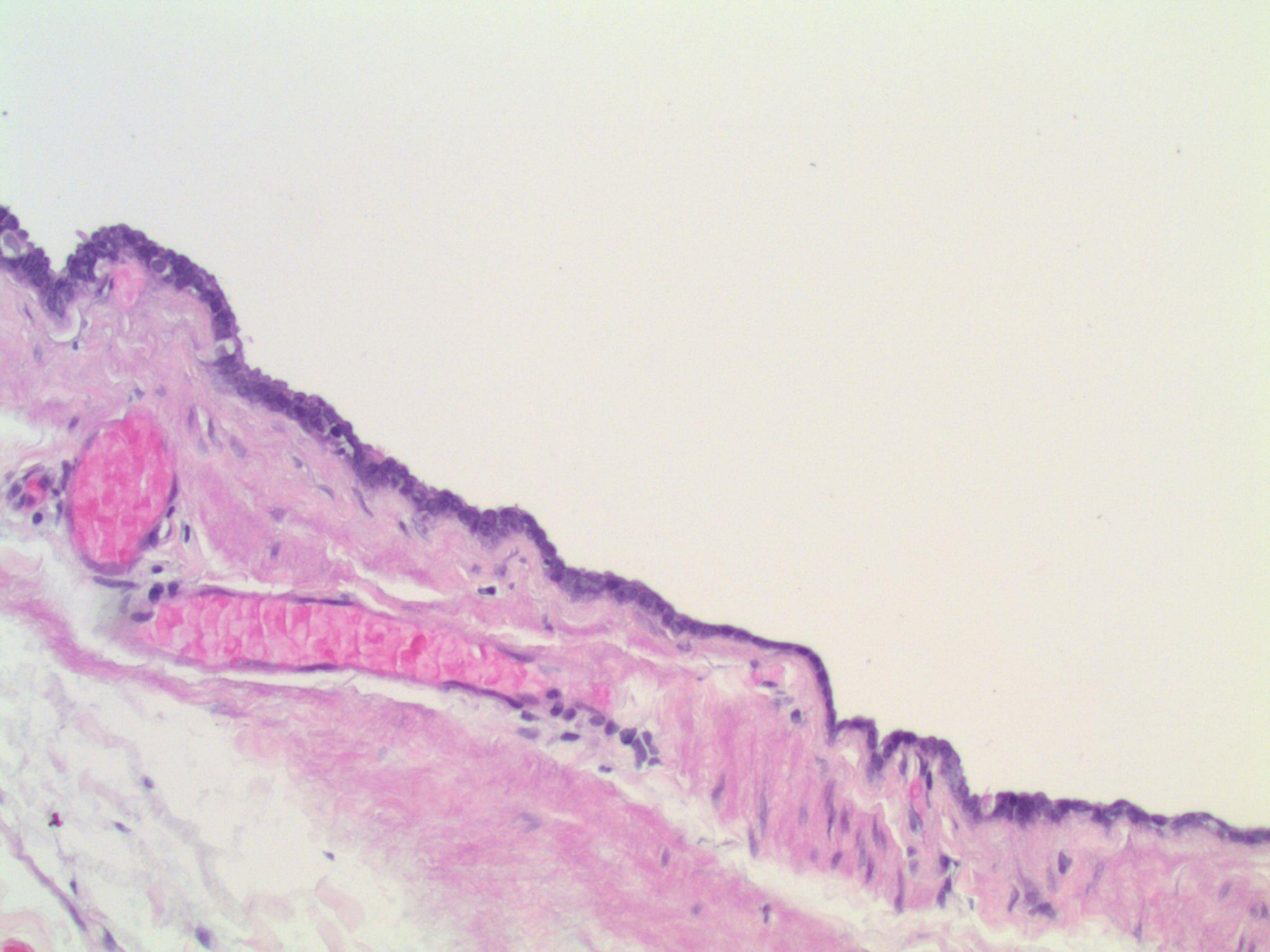
SB 5916

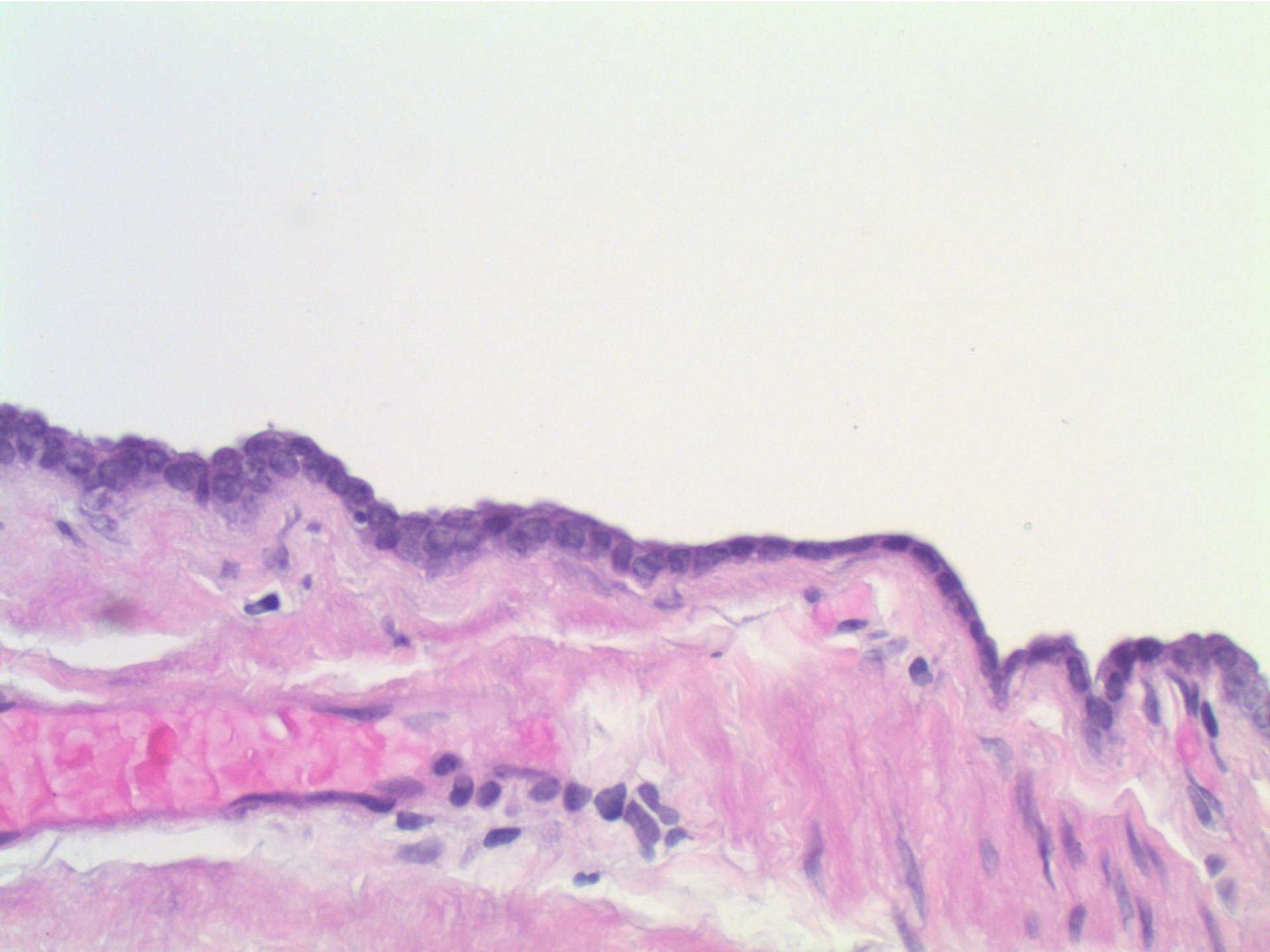
Ankur Sangoi; El Camino Hospital

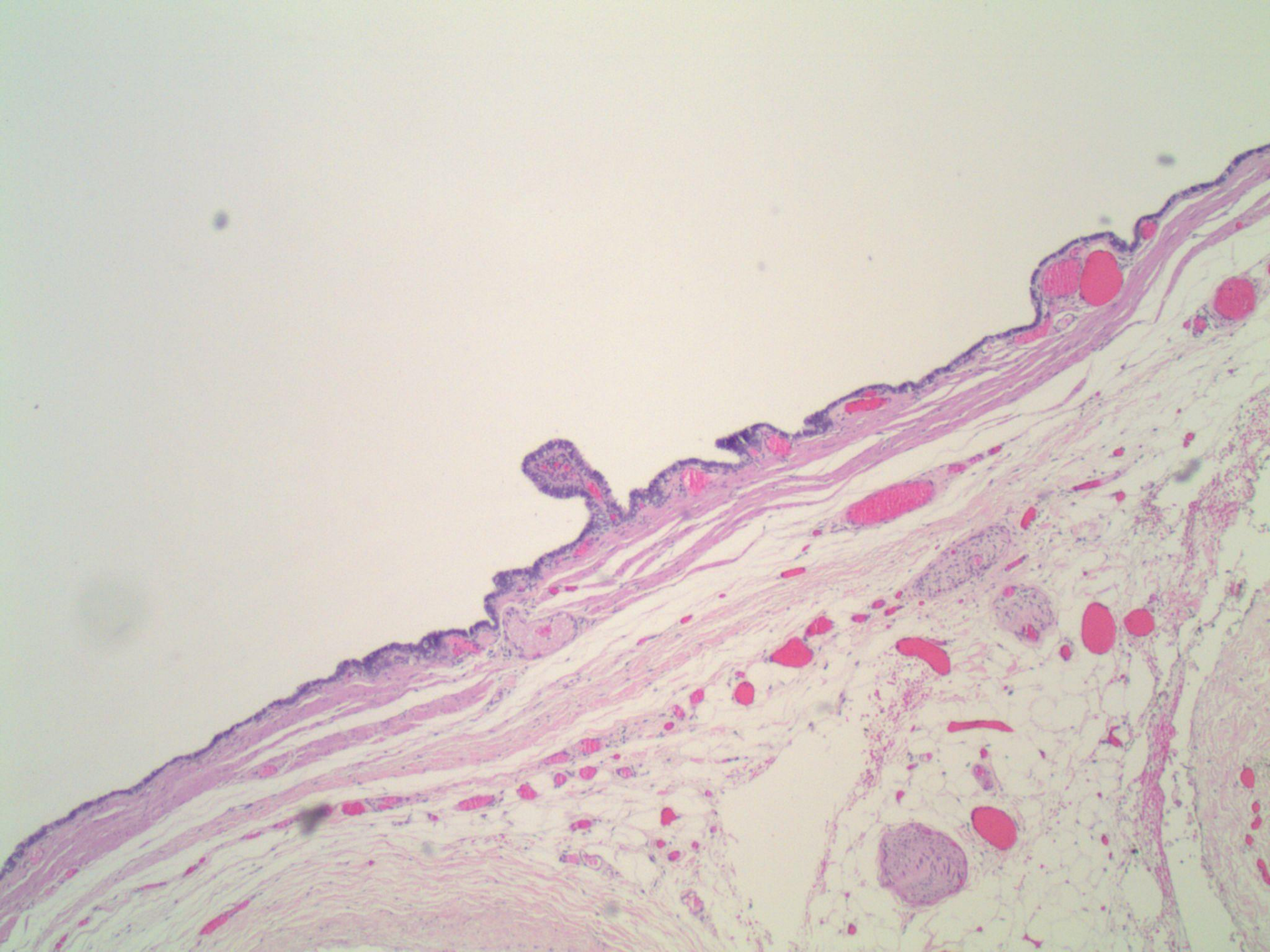
45-year-old female with 5.3cm mediastinal cyst which was excised.

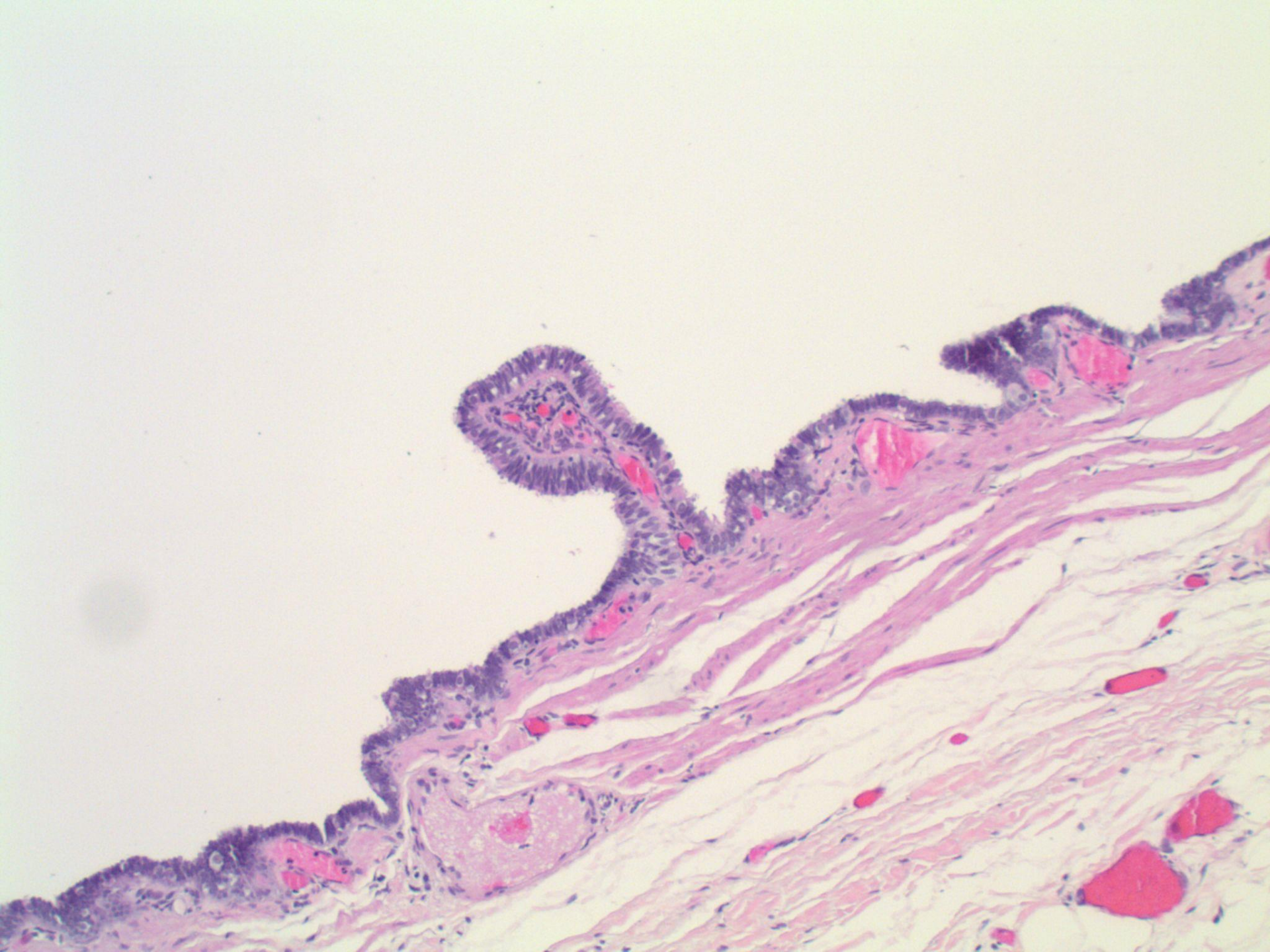


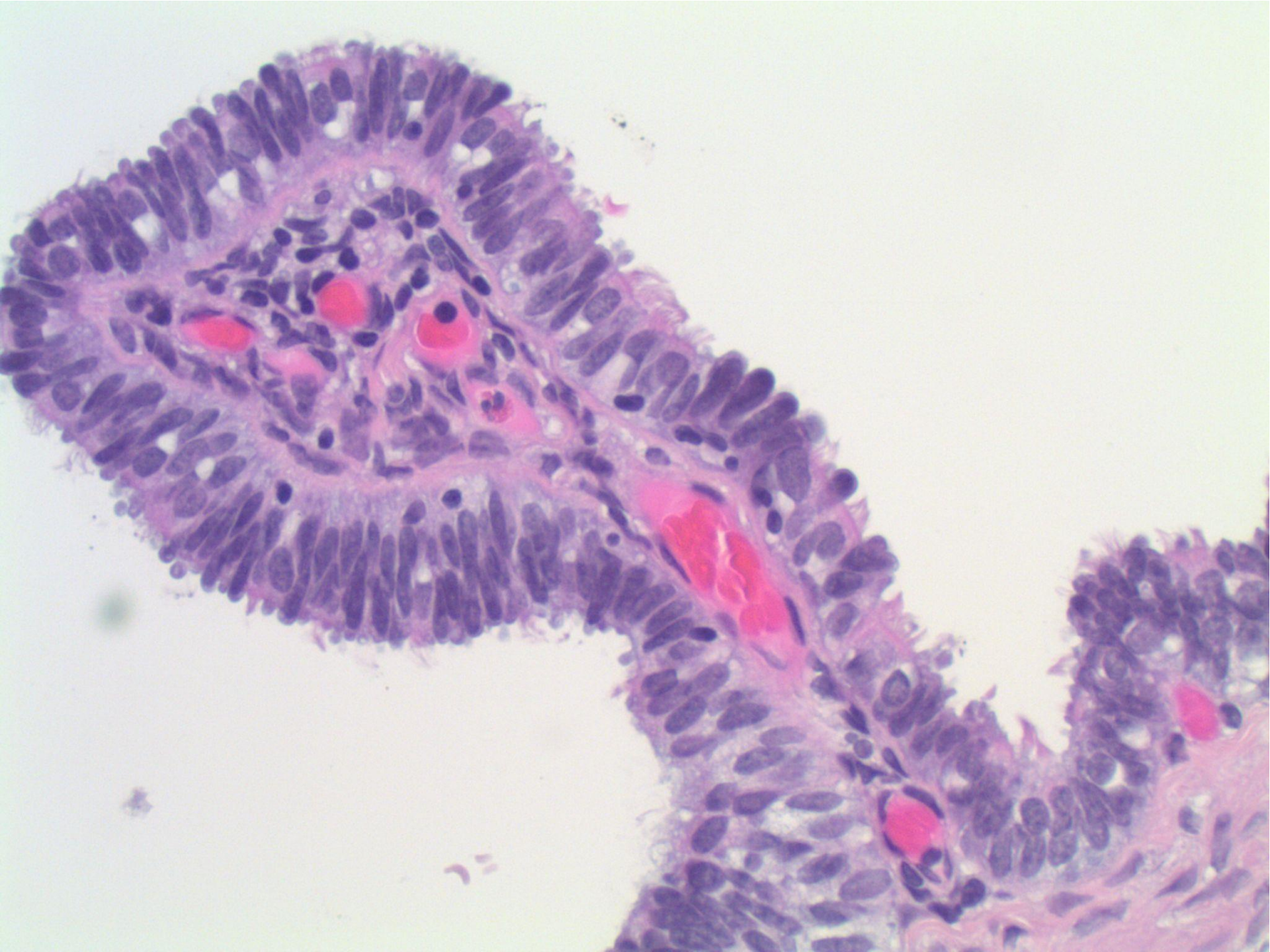




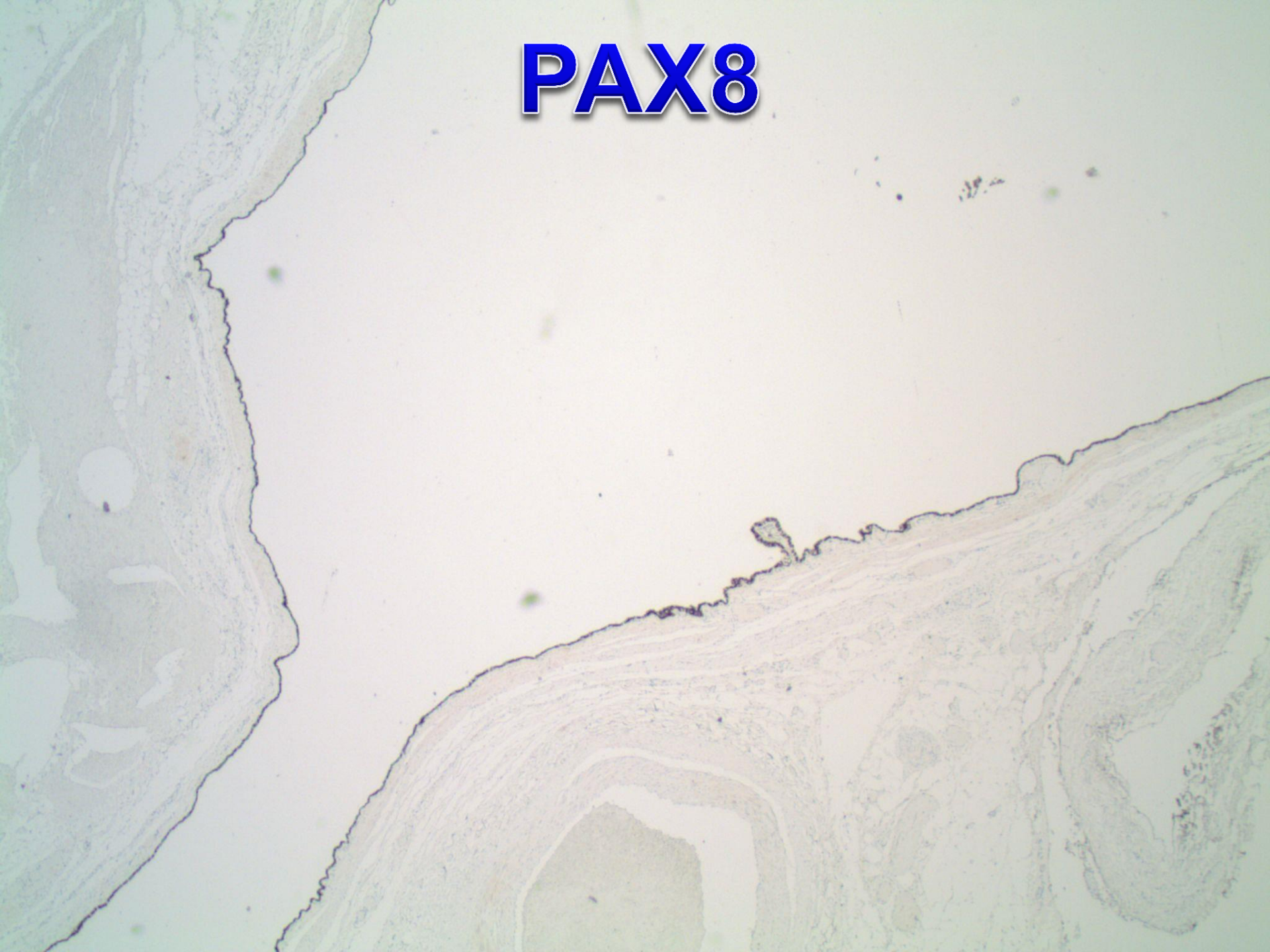




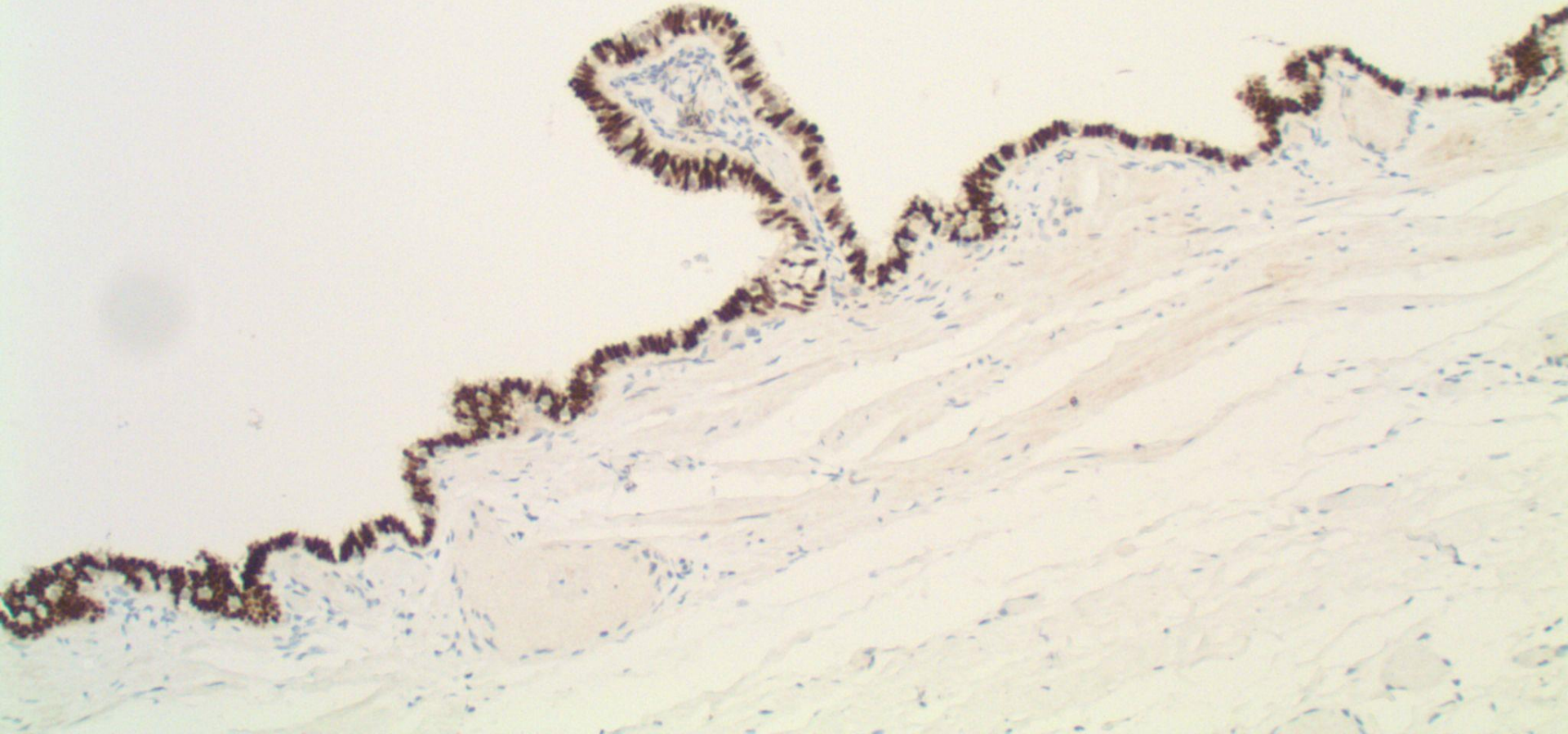




DIAGNOSIS?


PAX8

PAX8



"More and more patients are going to the Internet for medical advice. To keep my practice going, I changed my name to Dr. Google."


Dr. Google™
Google Search
I'm Feeling Lucky


Dr. Google™
mediastinal mullerian cyst
Google Search
I'm Feeling Lucky

About 32,300 results (0.26 seconds)

Mullerian cysts of the posterior mediastinum: report of two ...

www.ncbi.nlm.nih.gov/... ▾ National Center for Biotechnology Information ▾

by M Simmons - 2013 - Cited by 2 - Related articles

Cystic lesions can be occasionally be found in the **mediastinum**, and typically include bronchogenic **cysts**, esophageal duplication **cysts**, and neuroenteric **cysts**.

A case of Mullerian cyst arising in posterior mediastinum.

www.ncbi.nlm.nih.gov/... ▾ National Center for Biotechnology Information ▾

by S Kobayashi - 2012 - Cited by 3 - Related articles

Ann Thorac Cardiovasc Surg. 2012;18(1):39-41. Epub 2011 Aug 26. A case of **Mullerian cyst** arising in posterior **mediastinum**. Kobayashi S(1), Inoue T, Karube ...

Pathogenesis of mediastinal paravertebral müllerian cysts of ...

www.ncbi.nlm.nih.gov/... ▾ National Center for Biotechnology Information ▾

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Int J Gynecol Pathol. 2010 Nov;29(6):546-51. doi: 10.1097/PGP.0b[illegible]13e3181[illegible]

Pathogenesis of **mediastinal** paravertebral **müllerian cysts** of H[illegible]

Mediastinum - Mullerian cyst (Hattori's Cyst)

www.pathologyoutlines.com/topic/**mediastinummulleriancyst**.hu[illegible] ▾

Mediastinum. **Cystic** lesions. **Mullerian cyst** (Hattori's **Cyst**). Reviewer: Hanni Gulwani, M.D. (see Reviewers page) Revised: 16 March 2013, last major update ...

Pathogenesis of Mediastinal Paravertebral Müllerian Cysts ...

journals.lww.com/.../Pathogenesis_of_**Media**... Lippincott Williams & Wilkins ▾

by RE Batt - 2010 - Cited by 5 - Related articles

Hattori reported isolated posterior **mediastinal** paravertebral **müllerian cysts** of undetermined pathog.

[PDF] Paravertebral mediastinal Mullerian cyst resected by vide...

www.jthoracdis.com/article/viewFile/3730/4159 ▾

J Thorac Dis 2015 www.jthoracdis.com. Introduction. The **Mullerian cyst** was first

CLC

Cysts of the posterior mediastinum showing müllerian differentiation (Hattori's cysts)

Vincent Thomas-de-Montpréville, MD*, Elisabeth Dulmet, MD

Department of Pathology, Marie Lannelongue Surgical Center, 92350 Le Plessis Robinson, France

Annals of Diagnostic Pathology 11 (2007) 417–420

Table 1
Main clinicopathologic data of the 9 mediastinal cysts with müllerian differentiation

Age (y)	Symptoms	Paravertebral location	Size (cm)	Preoperative diagnosis	Histologic initial typing
40	Chest pain, dysphagia	Left T4	1.5	Neurinoma	Benign serous cyst
46	Cough	Left T4	3.3	Neurinoma	Bronchogenic cyst
47	Cough	Right T4/T5	5	Neurinoma	Bronchogenic cyst
48	Asymptomatic, known for 7 y	Left T5	3	Bronchogenic cyst	Benign serous cyst
50	Ancient asthma, chest pain	Right T3/T4	3.2	Neurinoma or cyst	Bronchogenic cyst
51	Asymptomatic	Left T3/T4	3	Cyst	Bronchogenic cyst
56	Asymptomatic	Left T8	1.3	Neurinoma	Bronchogenic cyst
58	Cough	Prevertebral T5	4.5	Bronchogenic cyst	Benign serous cyst
59	Chest pain	Right T2 through T4	2.5	Neurinoma	Bronchogenic cyst

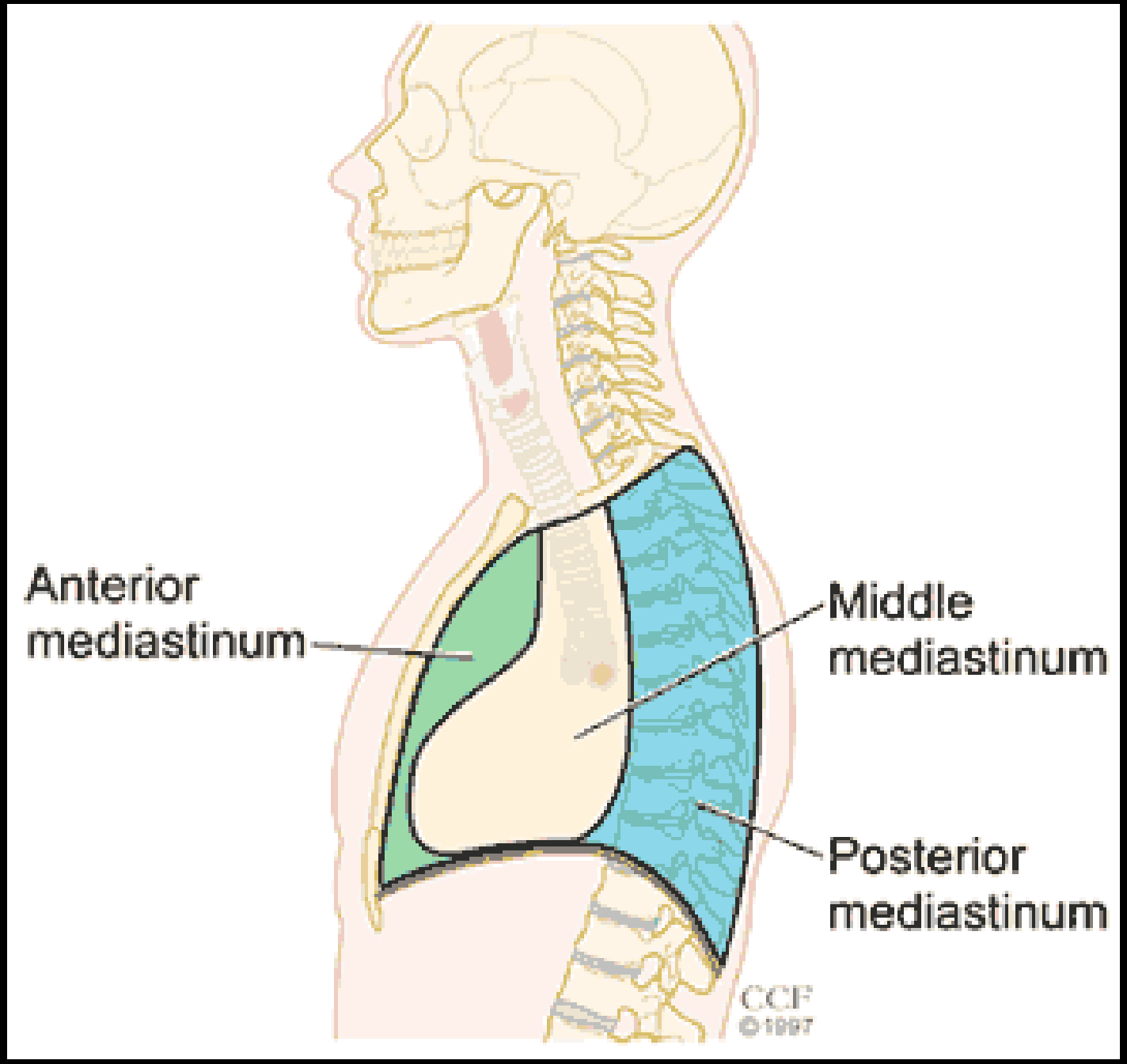
T3, T4, T5, and T8 indicate third, fourth, fifth, and eighth thoracic vertebrae.

DIAGNOSIS

Hattori's cyst
(posterior mediastinal Muellerian cyst)

Hattori's cyst (posterior mediastinal Muellerian cyst)

- First described in 2005
- Typically women, in posterior mediastinum, showing müllerian differentiation
- Initially classified as bronchogenic or unspecified benign serous cysts


Anterior
mediastinum
Middle
mediastinum
Posterior
mediastinum
CCF
©1997

Mediastinal cysts

- **ANTERIOR**
  - germ cell, lymphoma, thymoma/thymic, thyroid
- **MIDDLE**
  - bronchogenic, LAD, pericardial, thyroid, trachea
- **POSTERIOR**
  - EMH, LAD, neuroenteric, neurogenic

Examine the role of HTS-TCR in diagnosis of CTCL

Diagnosis and Staging of CTCL

- Reduced False positive of inflammatory disorders
- Reduced False negative in mild disease

Clinical management of CTCL patients

- Monitoring treatment efficacy/ identification of minimal disease
- Differentiating from lymphomatoid drug reaction

Case 1

- 88 year-old woman with pruritus, erythema and scaling for approximately 6 months. The eruption was initially present on her legs and then became generalized

CASE 1

- Sezary panel negative
- Skin and Blood TCR-PCR clonality tests performed

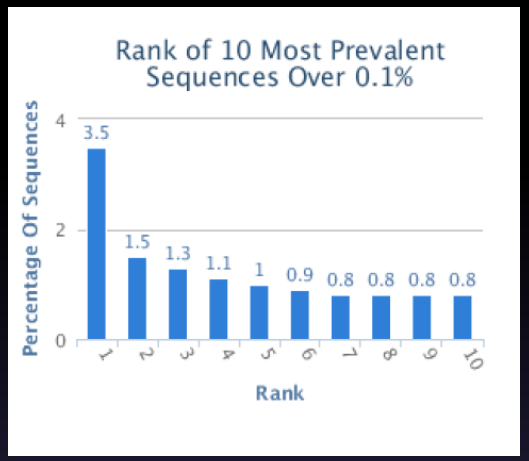
Patient 1:
Standard TCR-PCR performed on skin and blood samples

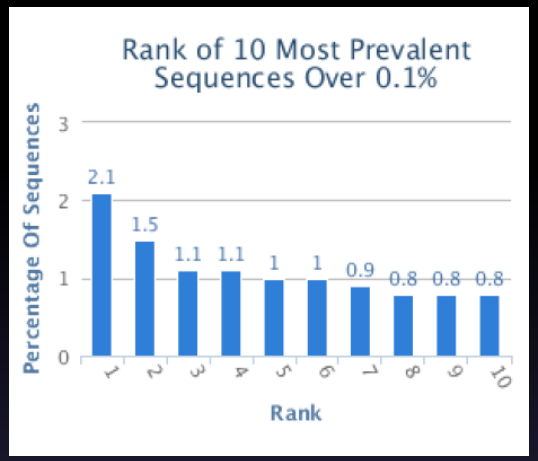
	PCR-TCRB	PCR-TCRG
BLOOD	OLIGO	POS*
BLOOD	OLIGO	POS*
TISSUE	NEG	POS*
TISSUE	NEG	POS*
TISSUE	WEAK**	NEG
TISSUE	WEAK**	NEG

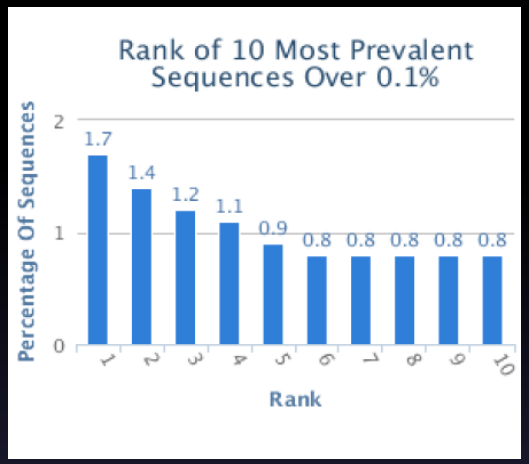
**, ** denotes shared clonality*

Patient 1: HTS tests fail to identify tumor-specific sequence

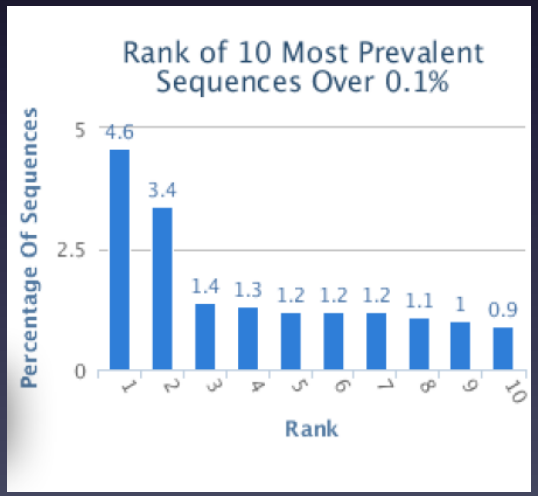
TCR-B

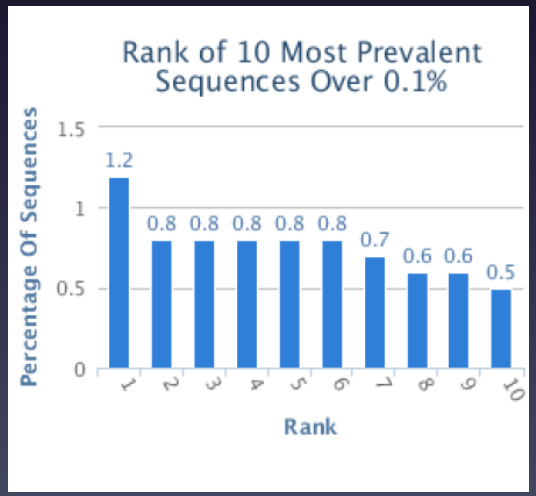


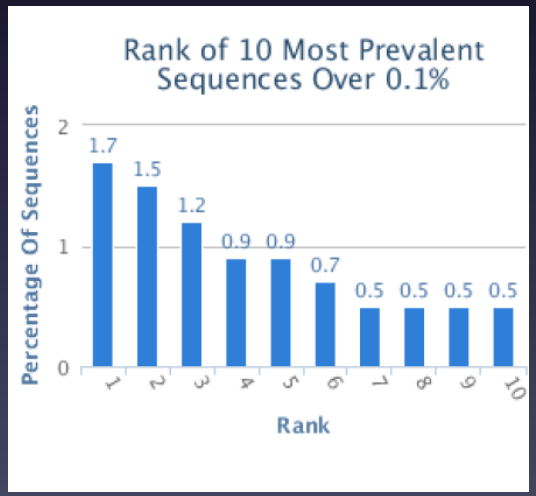




TCR-G





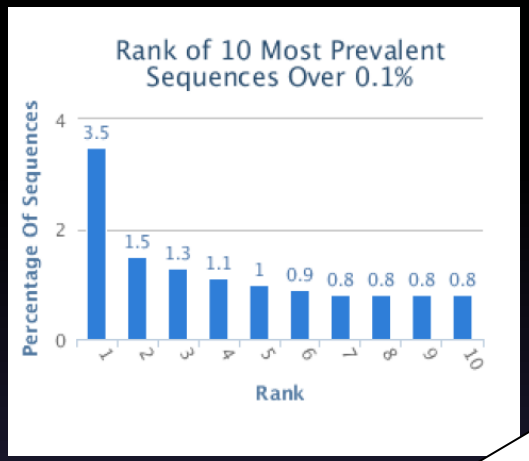


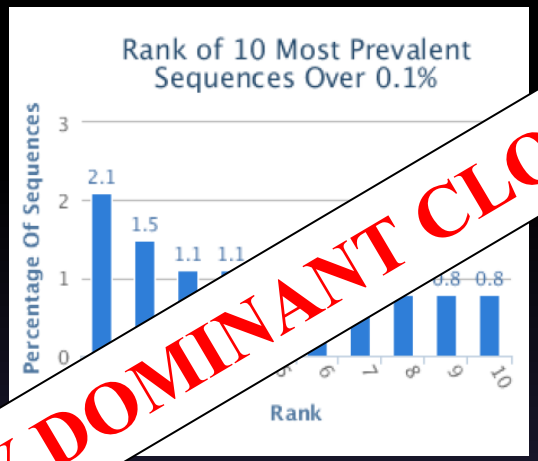
Skin Biopsy: 1 2 3

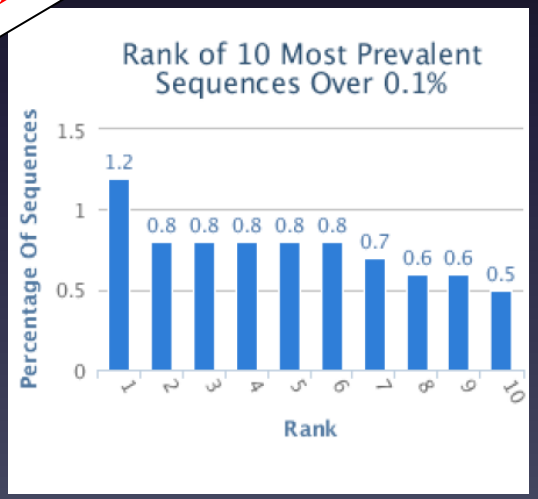
Patient 1: HTS tests fail to identify tumor-specific sequence

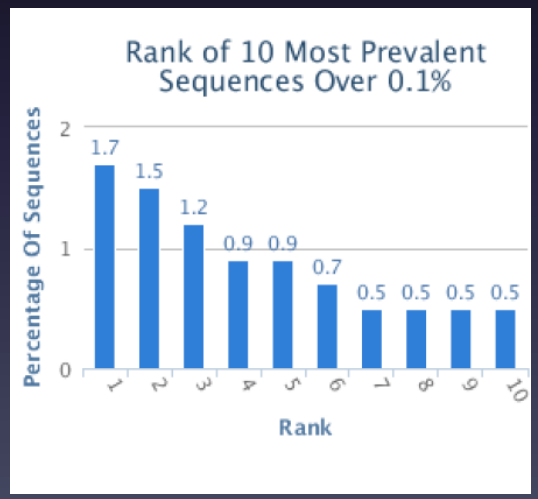
TCR-B

TCR-G









FAIL TO IDENTIFY DOMINANT CLONE BY HTS

Skin Biopsy: 1 2 3

Examine the role of HTS-TCR in CTCL

Diagnosis and Staging of CTCL

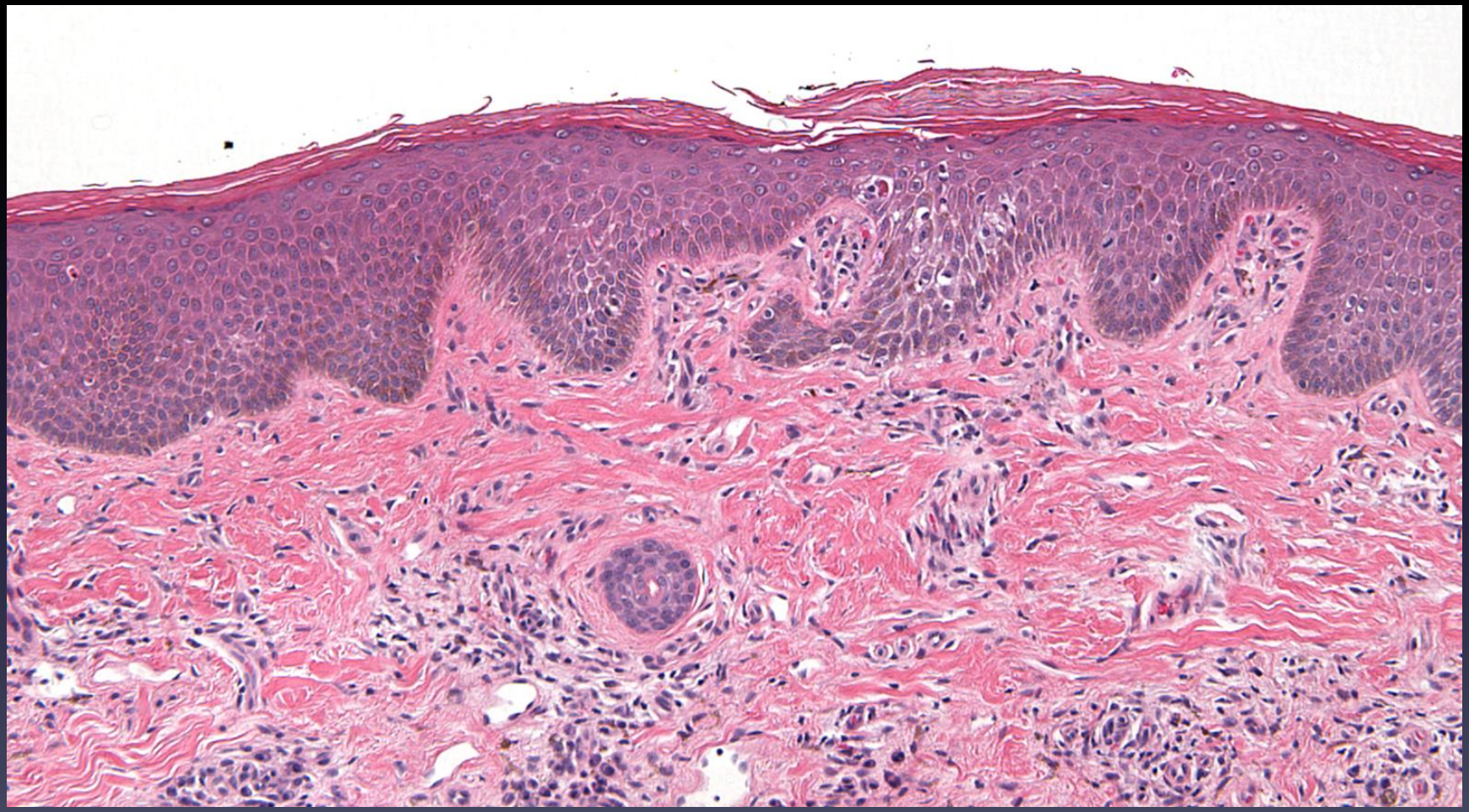
- Reduced False positive of inflammatory disorders
- Reduced False negative in mild disease

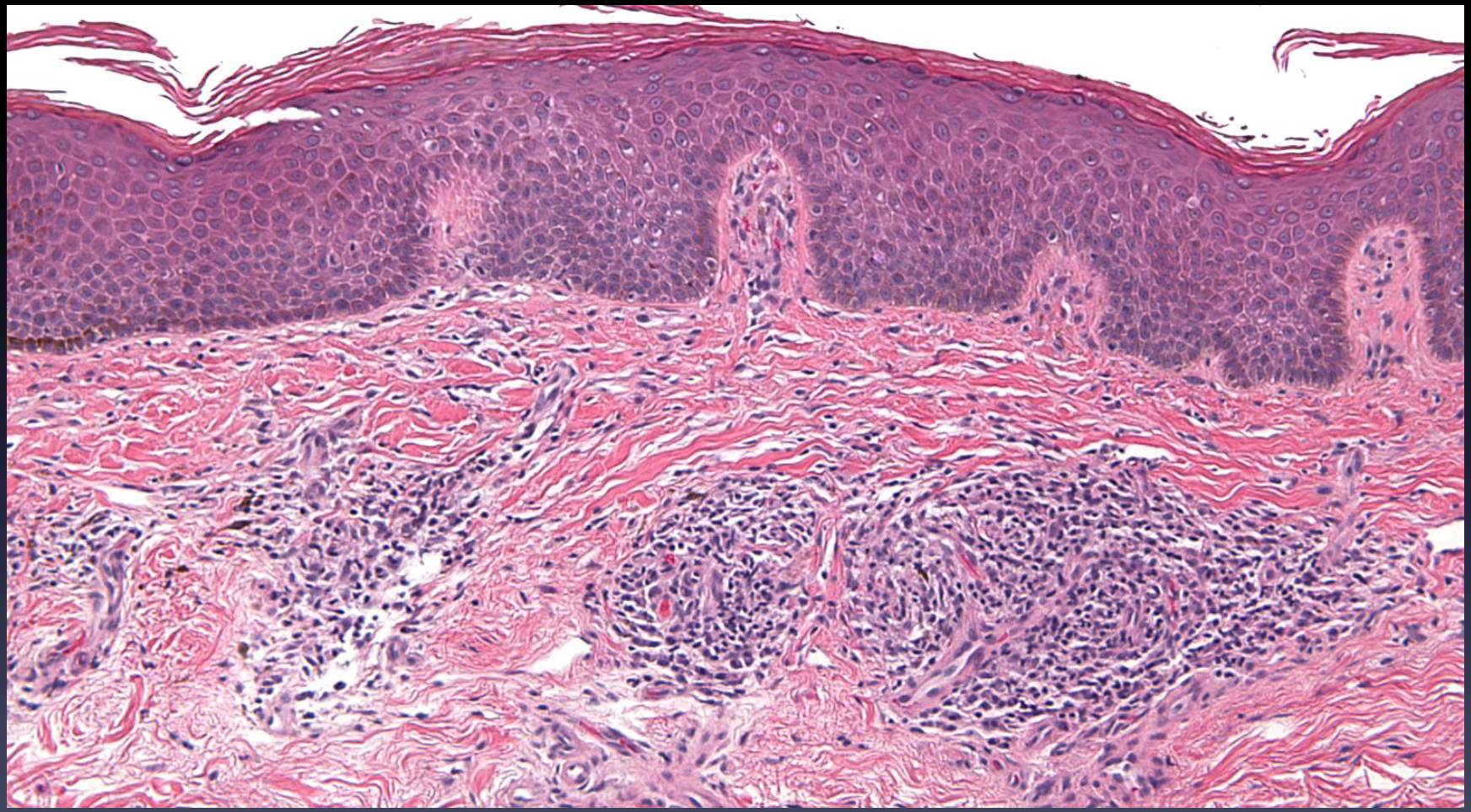
CASE 2

- 71 y/o male with 10 h/o generalized pruritus and scaling received therapy for eczema and psoriasis
- Previously treated with prednisone, adalimumab, and cyclosporine without significant improvement

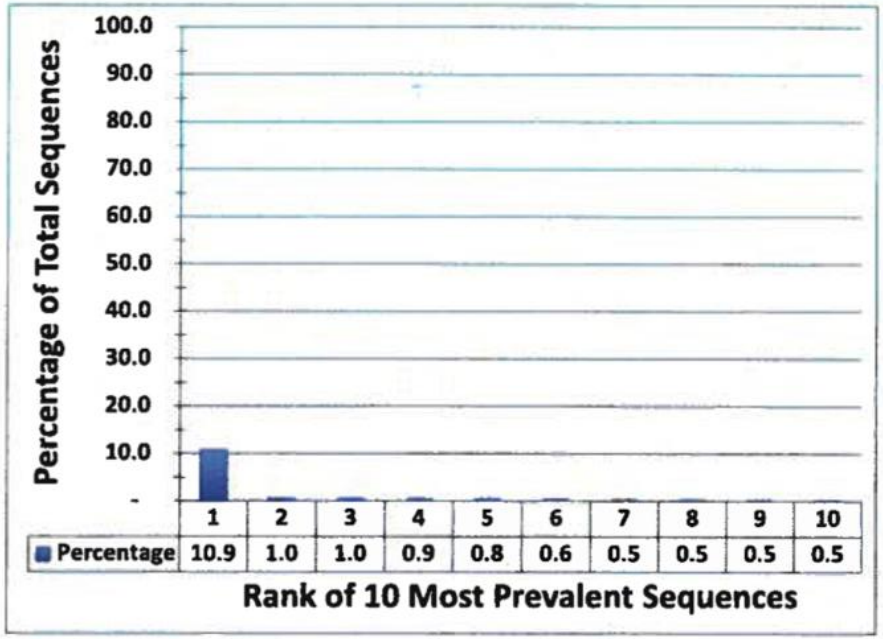
CASE 2

- Skin biopsy: ALI
- TCR-PCR: negative
- Sézary flow: small abnormal population
- TCR-PCR in PB: negative





RESULTS



Summary Results:

Dominant clone detected

TCRB CDR3 gene fragments were amplified using multiplex PCR amplification. Gene sequences were analyzed and cataloged, and the highest frequency clone(s) observed is reported.

Rank	Sequence	Frequency
1	ACTGTGACATCGGCCCAAAAGAACCCGACAGCTTTCTATCTCTGTGCCAGTAGTATGTCAGGAGGTCAGCCCCAGCATTTTGGTGAT	10.9

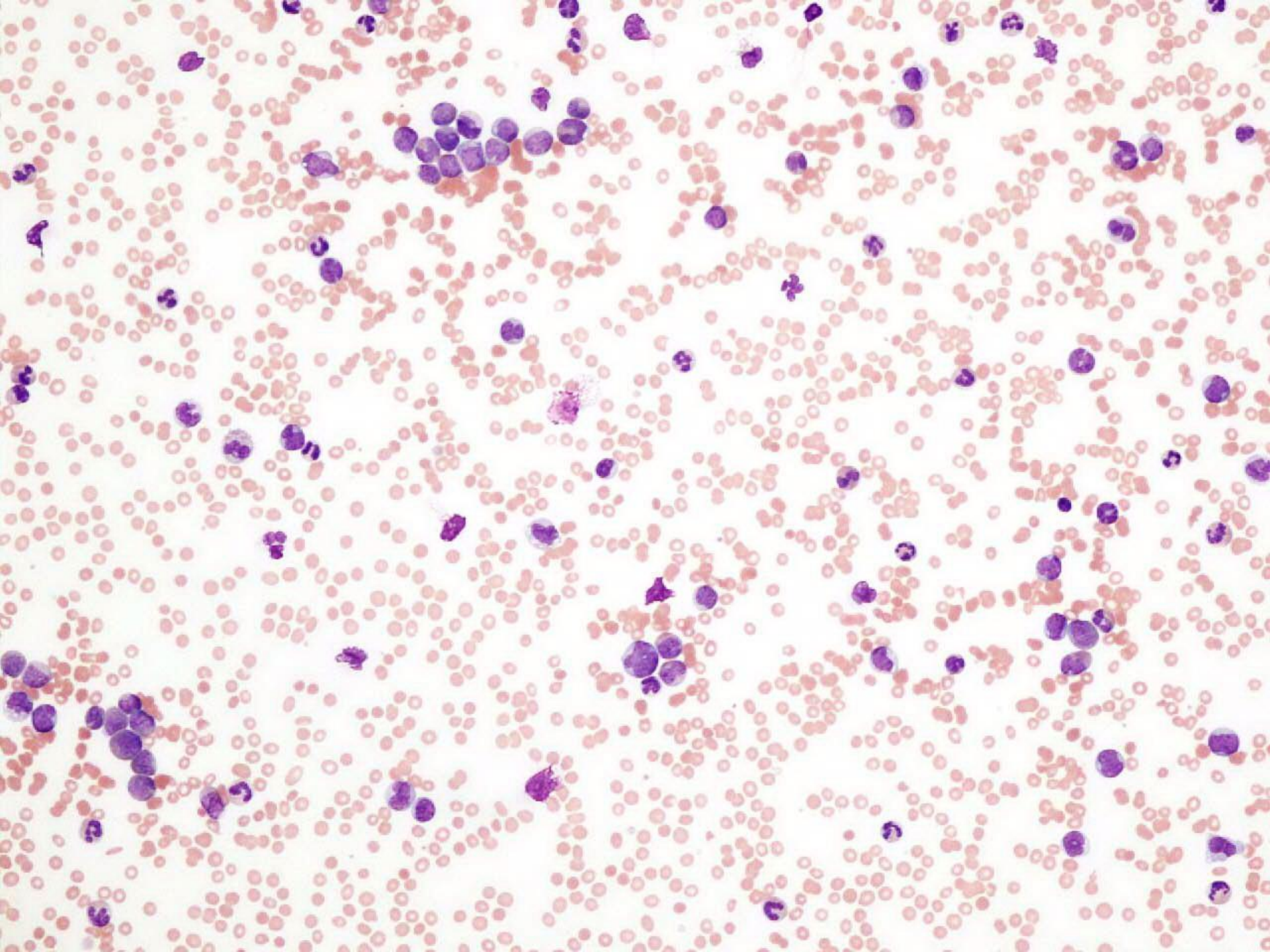
Clinical Course

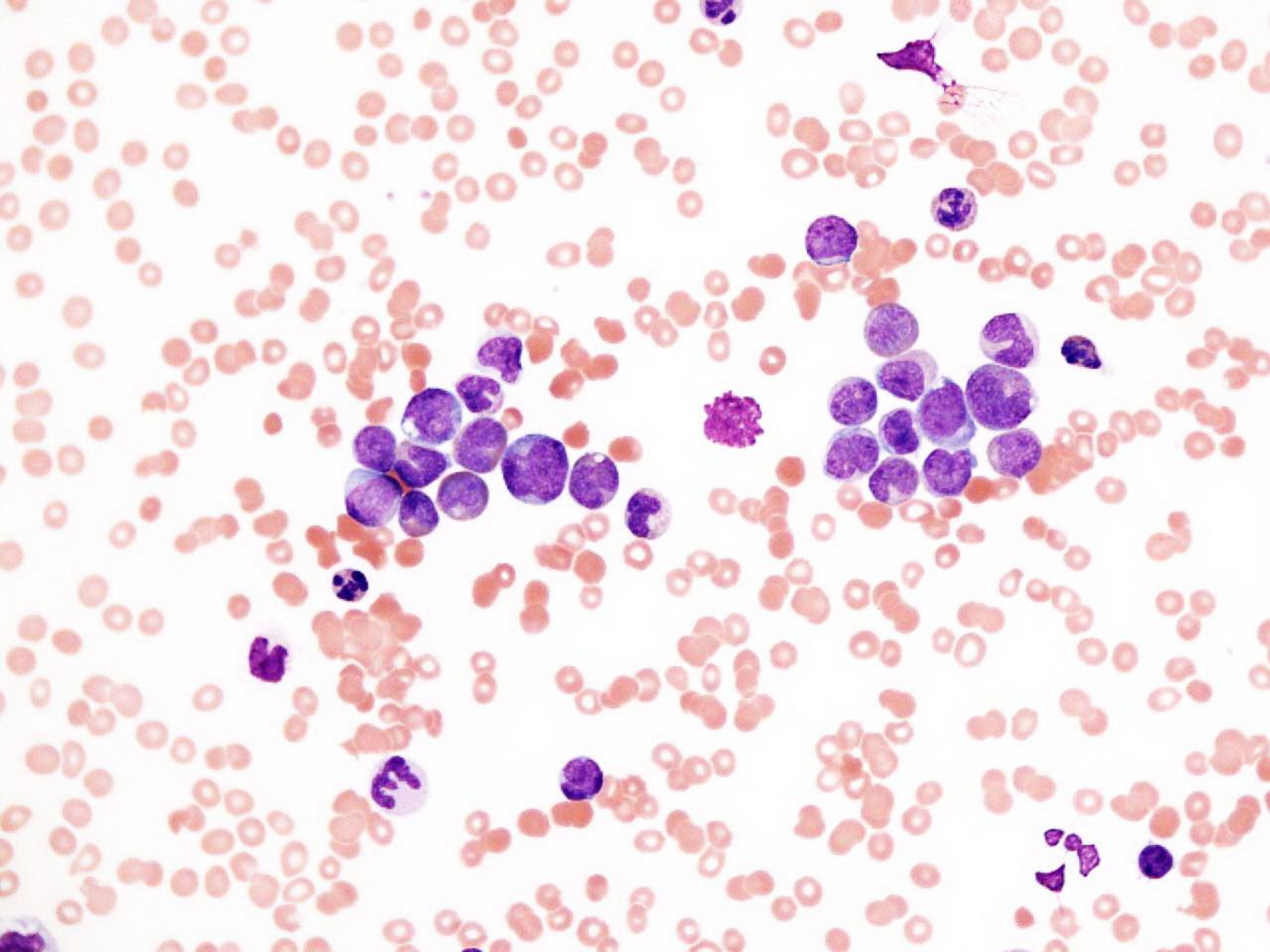
- Bexarotene 300 mg BID
- Triamcinolone 0.1 % ointment
- Near complete remission sustained for almost a year

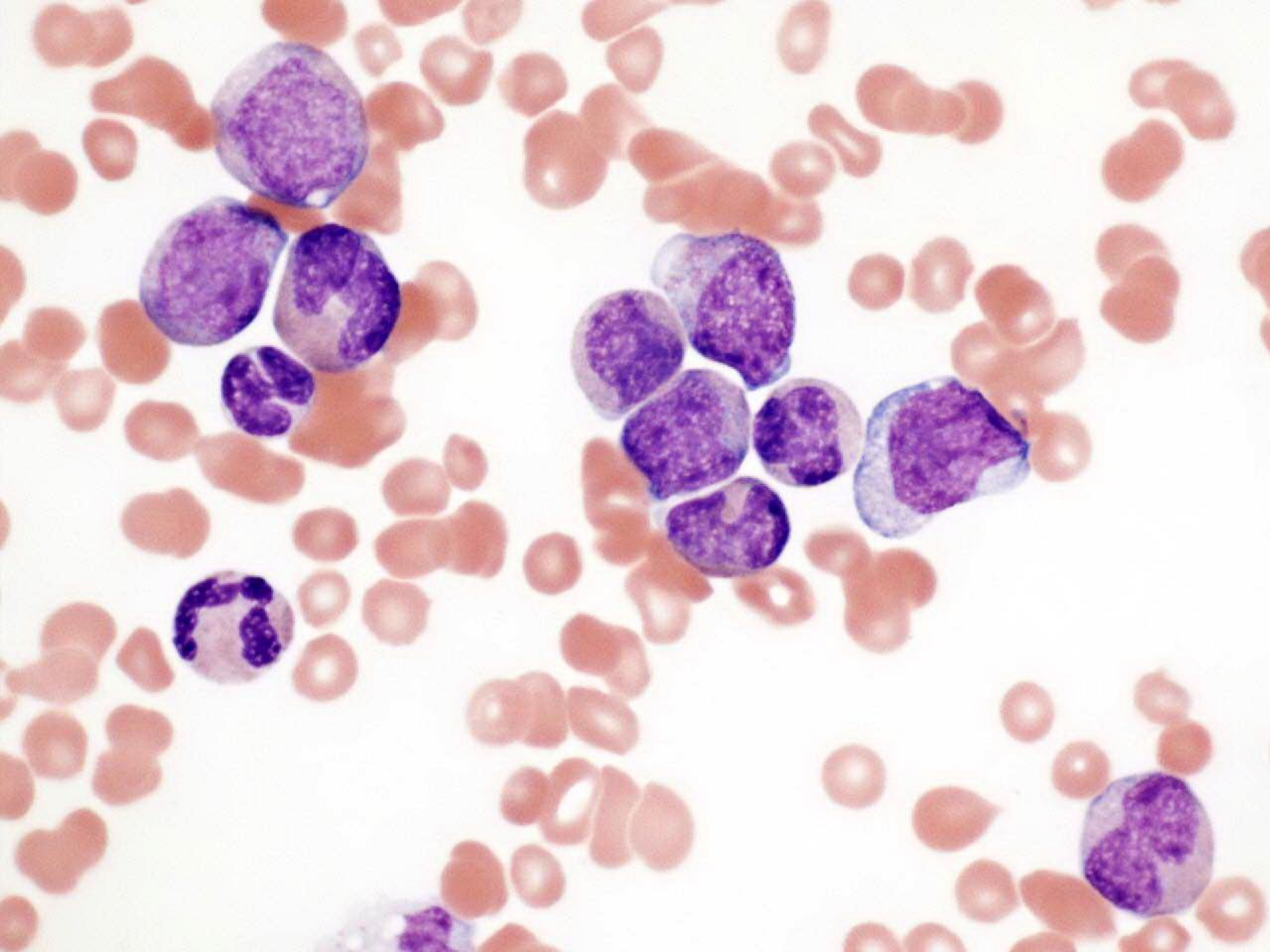
SB 5917

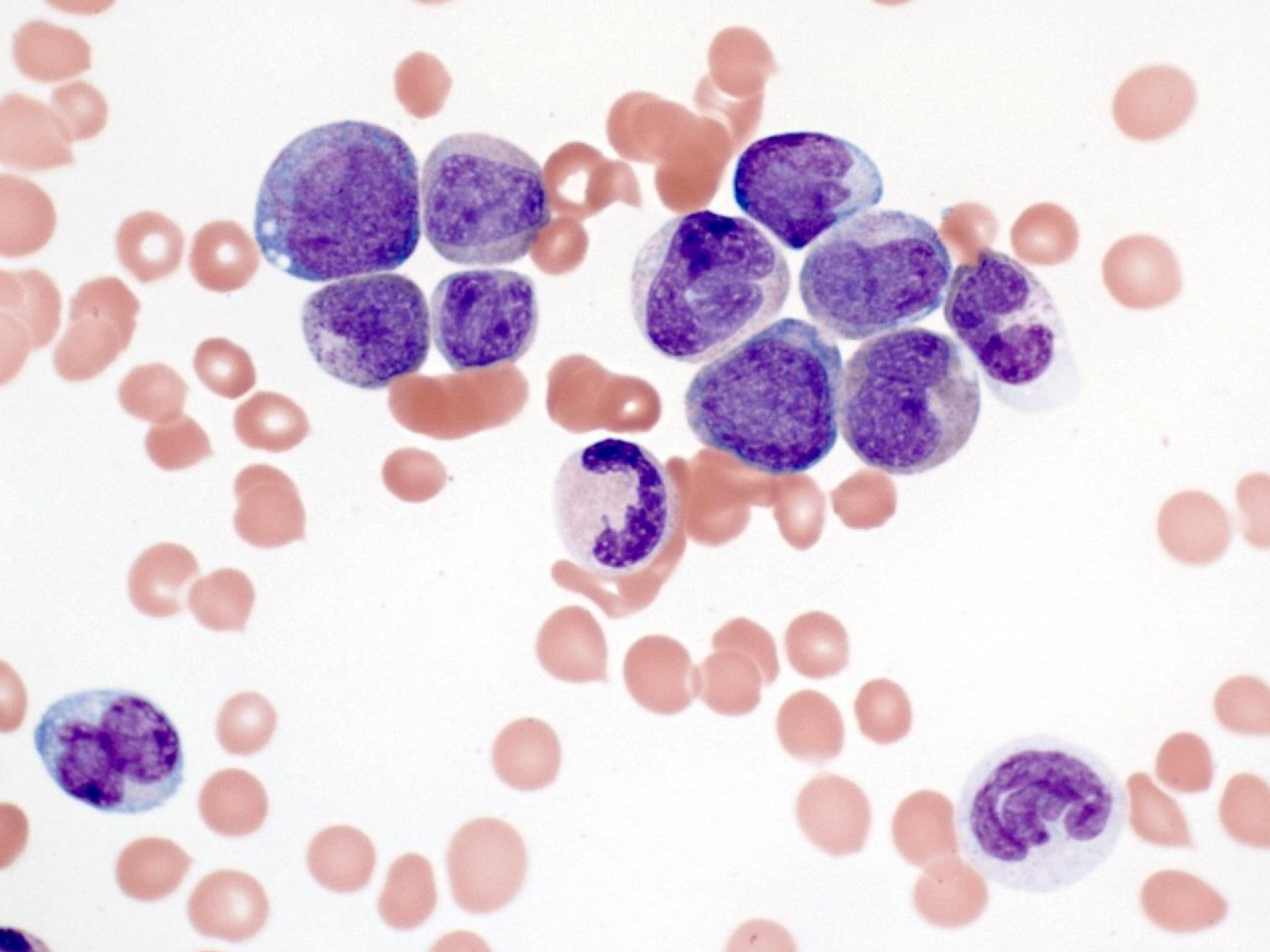
Linlin Wang/Sonam Prakash; UCSF

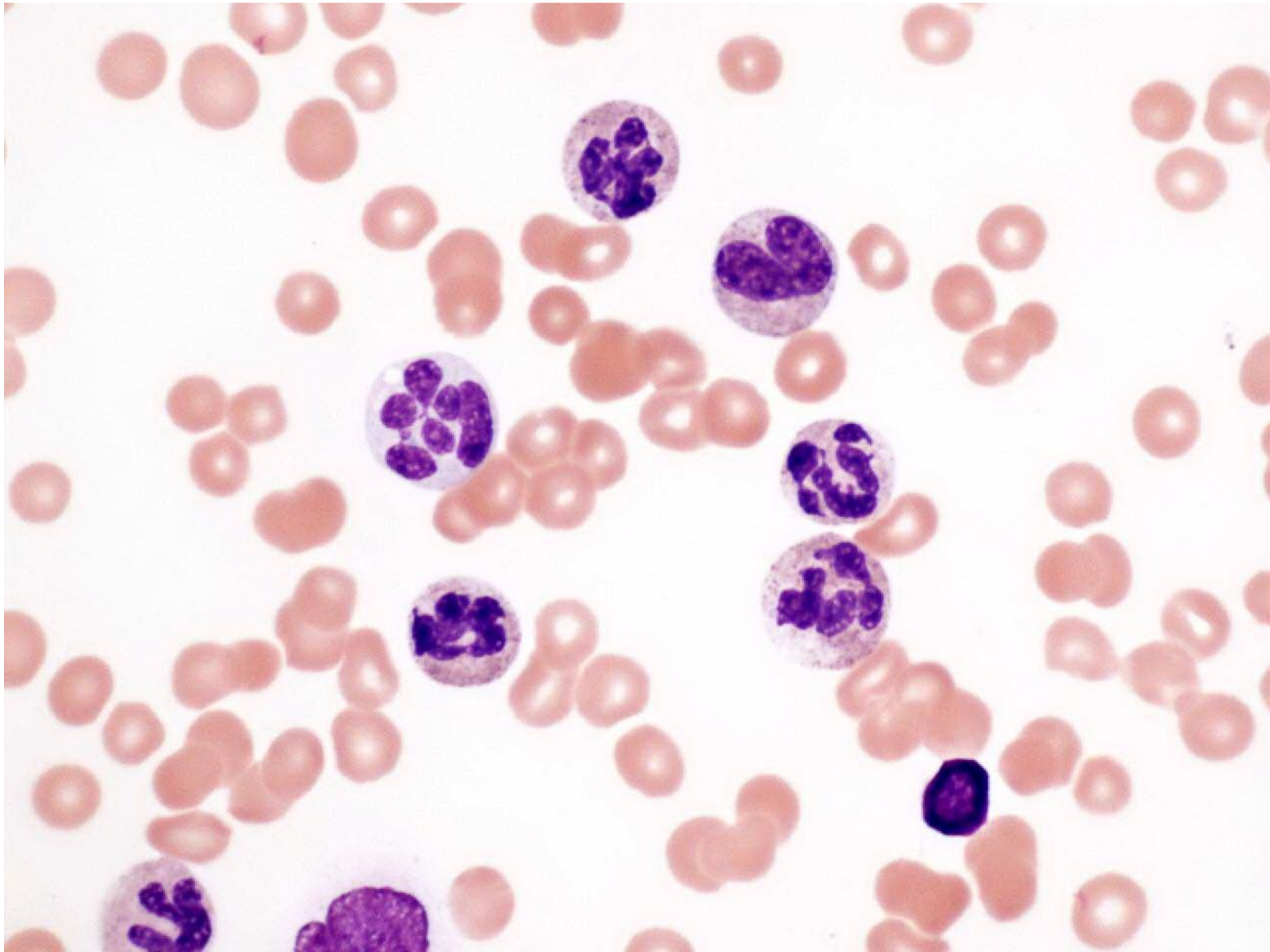
60-year-old man with initially presented with anemia and thrombocytopenia now has increasing number of circulating blasts. The imaging shows extensive lymphadenopathy, sclerotic/lytic bone lesion, and splenomegaly. WBC 79.5, HgB 8.3, MCV 89, Plt 30. Peripheral blood smear submitted.





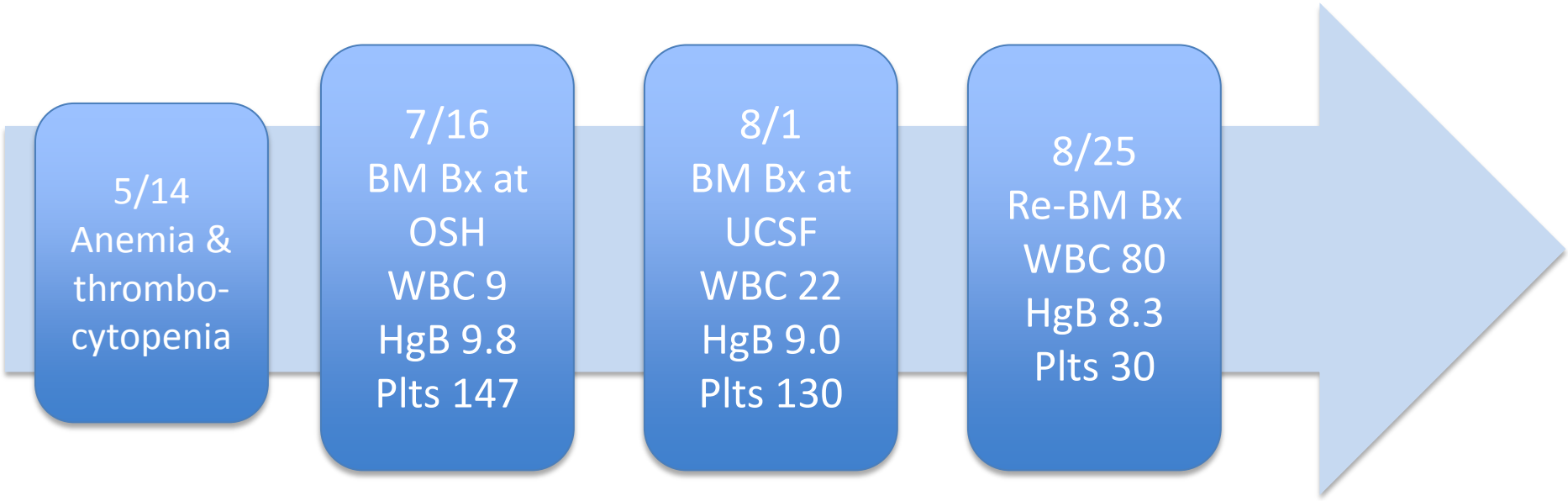






DIAGNOSIS?

Patient: A 60-year-old Man



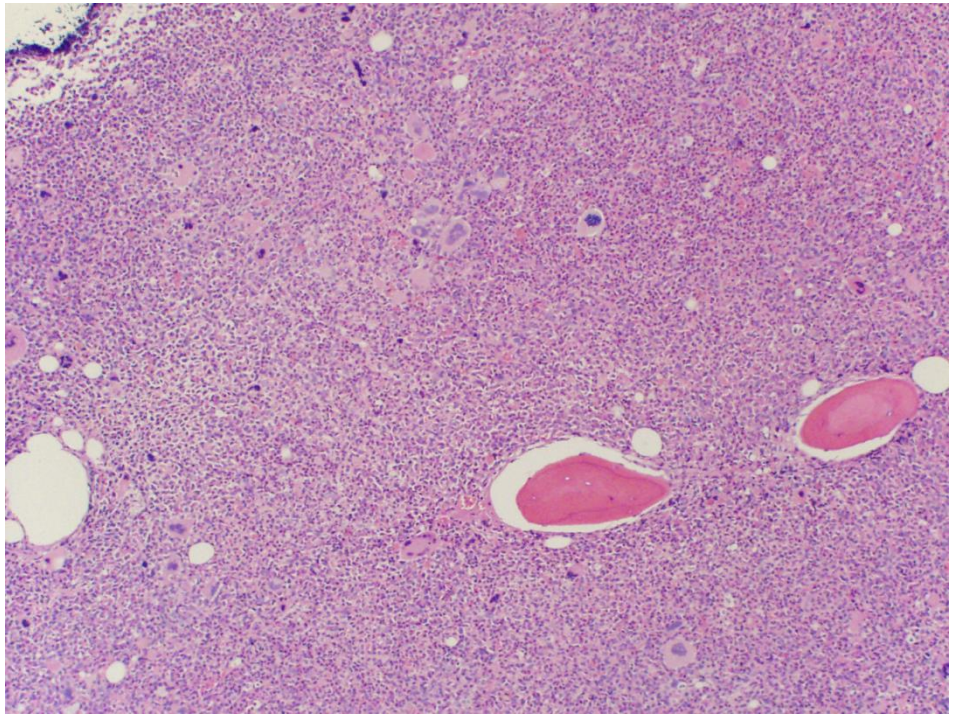
PB and BM 8/1

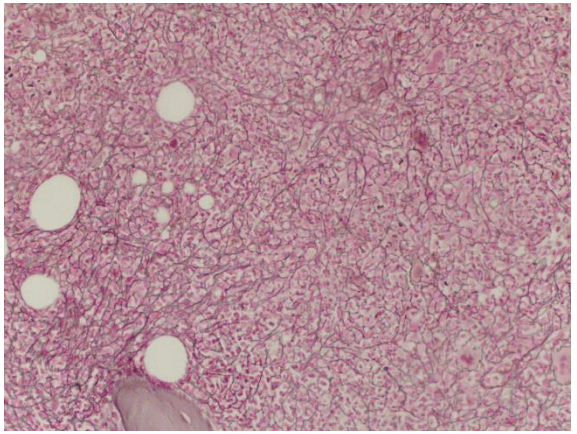
- Leukocytosis (WBC 22.5 x 10E9/L)

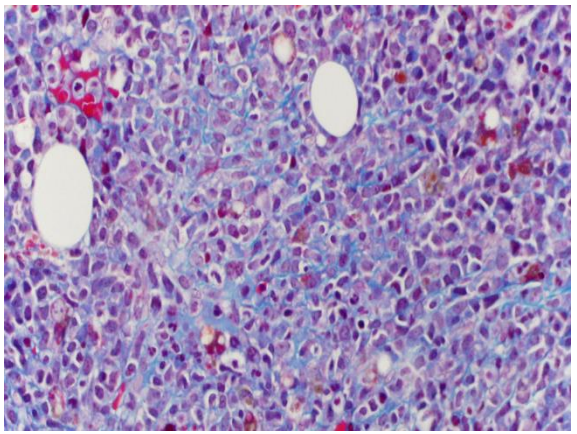
  Mostly neutrophils with immature granulocytes (8%)

  A few circulating blasts (3%)

  Few hypersegmented neutrophils

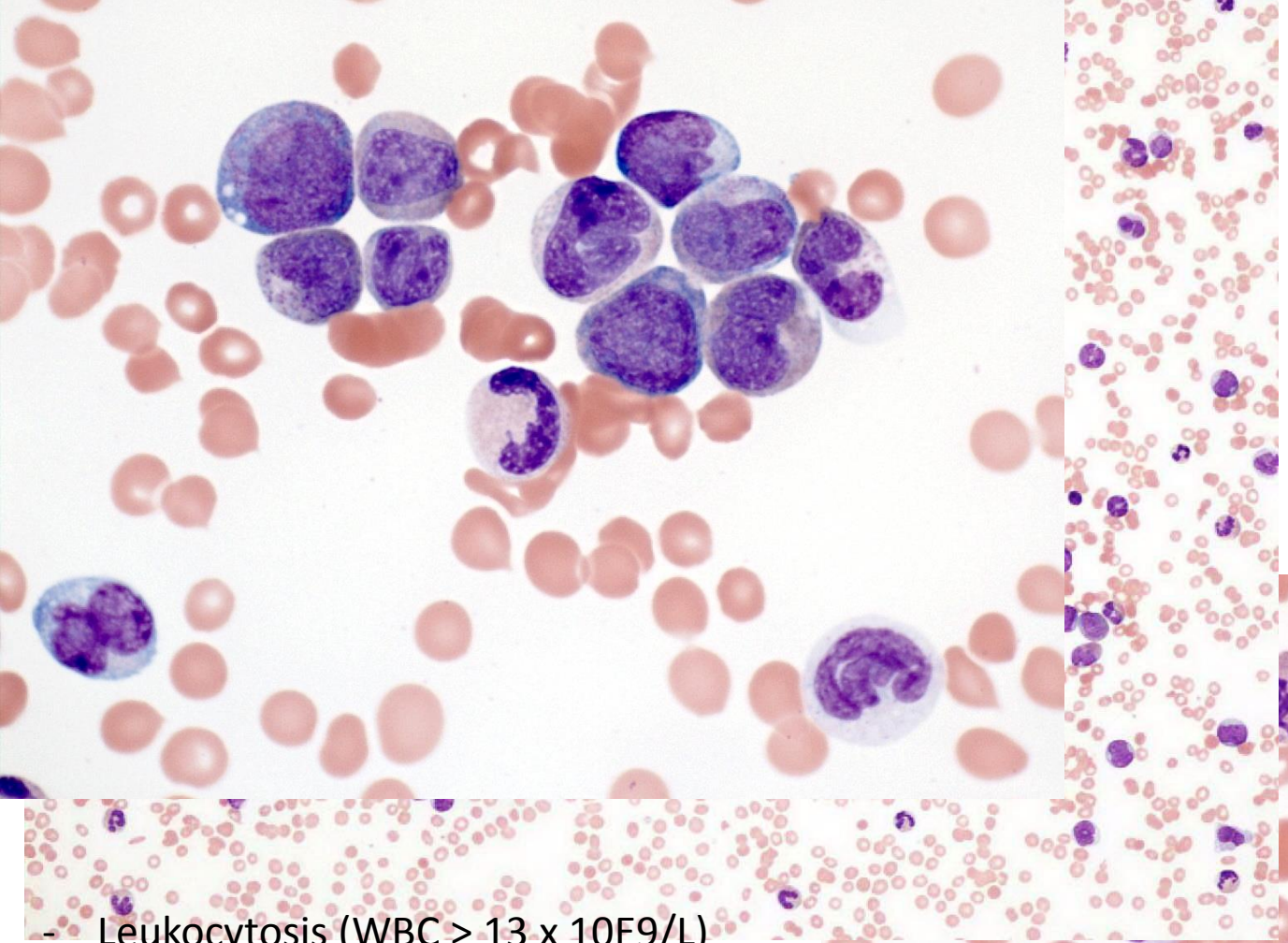






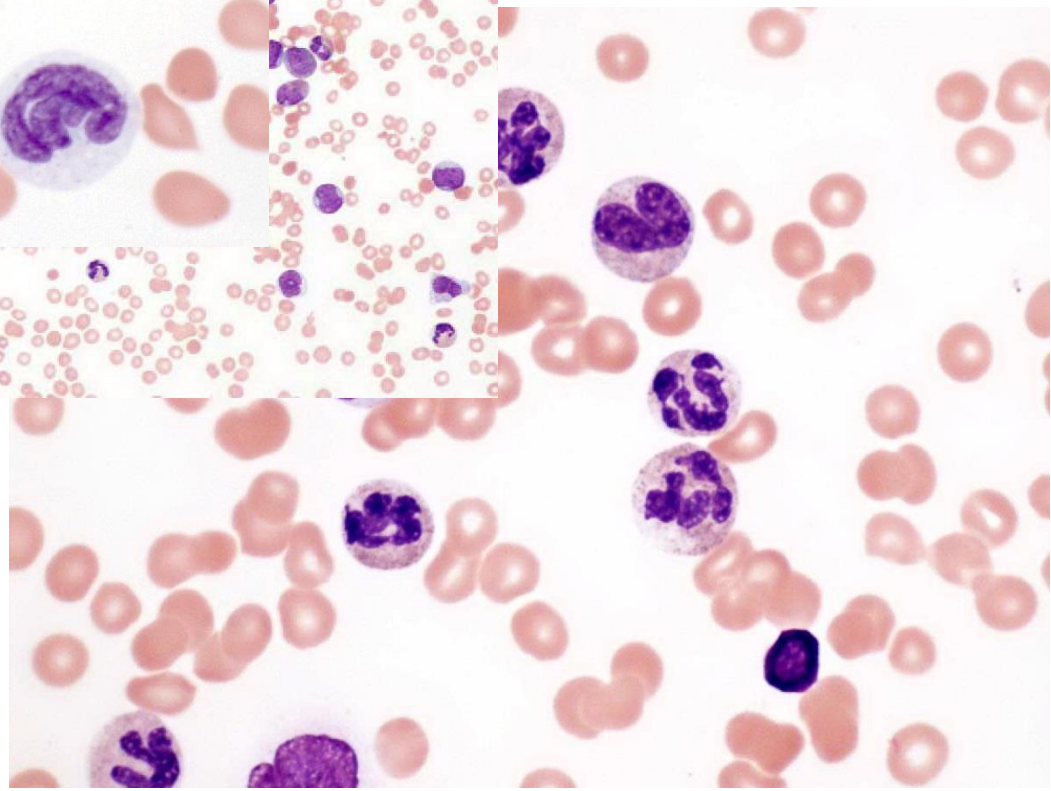
Ancillary Studies

- Flow: 2.7% atypical myeloid population (myeloid blasts with CD7)
- Cytogenetics: normal
- MDS FISH: normal
- Negative: JAK2, Calreticulin, MPL, BCR/ABL, MPN panel (ASXL1, EZH2, IDH1, IDH2, KRAS, NRAS and TET2)
- Negative: PDGFRA, PDFGRB, FGFR1



8/25

WBC 79.5 x10E9
HGB 8.3g/dl
MCV 89fl
Plt 30x10E9/L

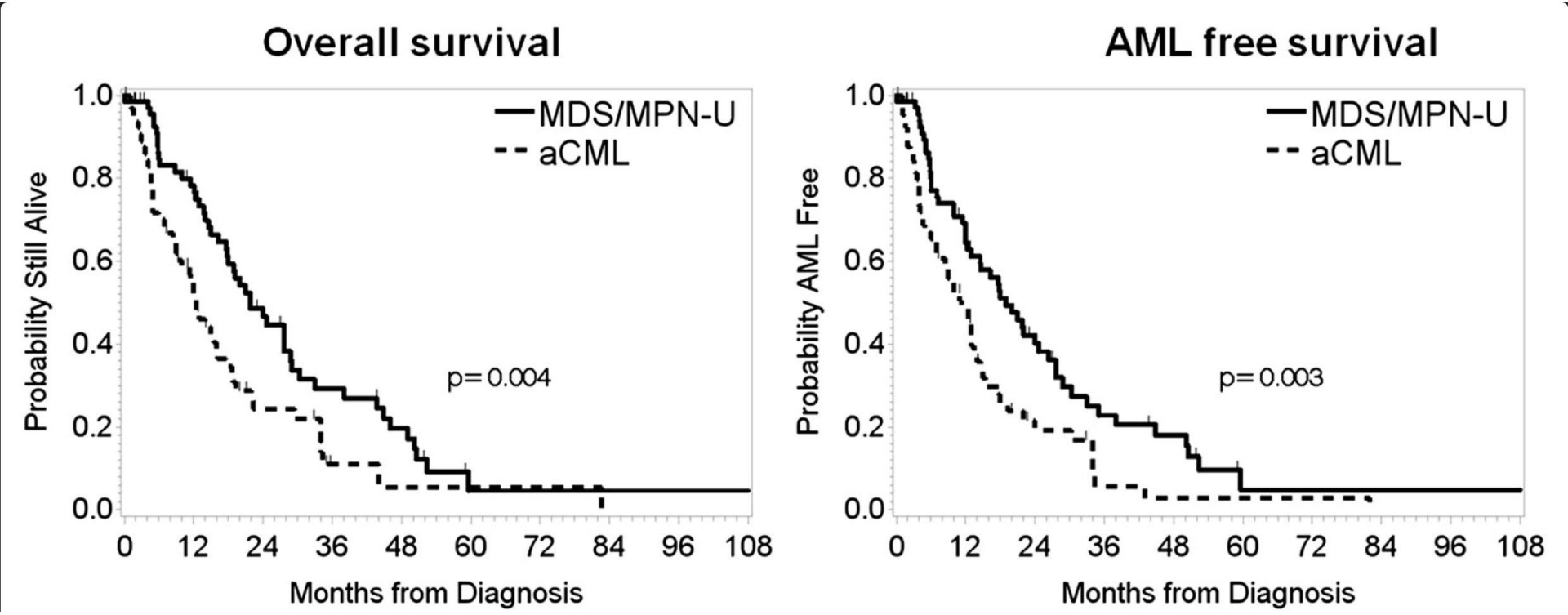


- Leukocytosis (WBC > 13 x 10E9/L)
- Circulating myeloid precursors > 10% of WBC
- Marked dysgranulopoiesis
- No monocytosis

Atypical Chronic Myeloid Leukemia, BCR-ABL negative

- MDS/MPN neoplasm
- Diagnosis criteria:
  - Leukocytosis (WBC > 13 x 10E9/L)
  - Circulating myeloid precursors > 10% of WBC
  - Marked dysgranulopoiesis
  - Absence of monocytosis/basophilia
  - No BCR-ABL, PDGFRA, PDGFRB, FGFR1 rearrangement
- Prognosis: poor

Compared with MDS/MPN-U, Patients with aCML Showed a Significant Inferior OS



OS: (**12.4 months**, 95% CI [9.0-16.1] vs **21.8 months**, 95% CI[17.6-28.8])

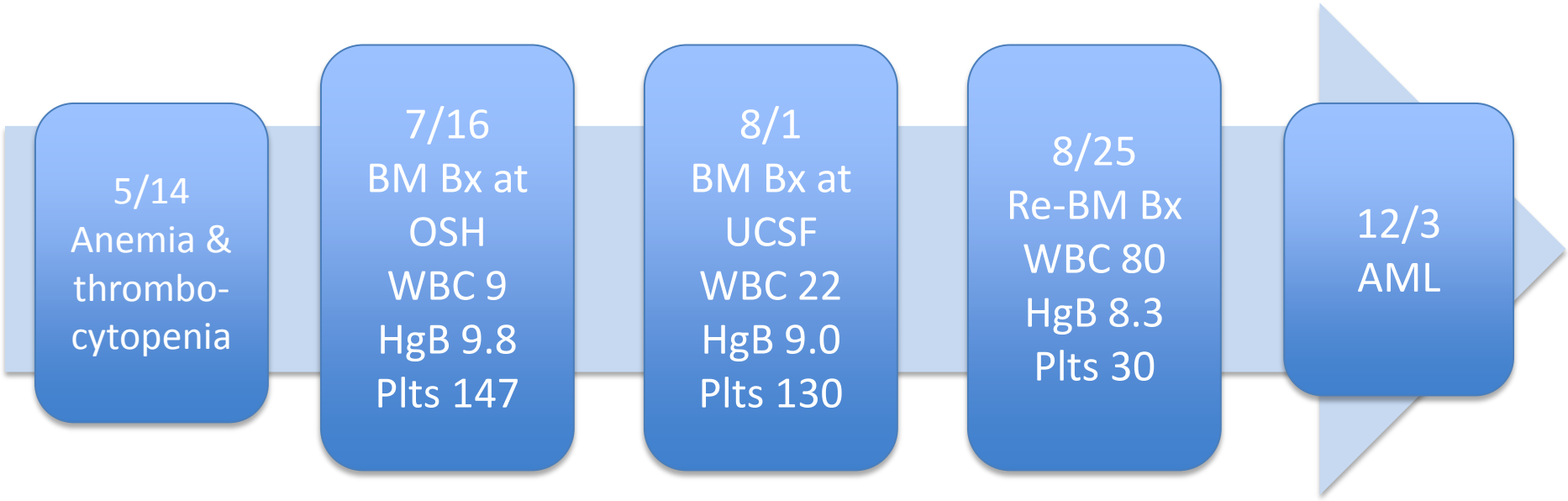
AML-free survival (**11.2 months**, 95% CI [7.0-13.5] vs **18.9 months**, 95% CI [12.3-26.3]).

Wang, SA, et al. Blood 2014

Clonal Marker?

- CSF3R T6181 mutation: controversy
- SETBP1: 30% +
- RAS(KRAS/NRAS): 30% +
- Calreticulin: negative
- JAK2 V617F: 7% +

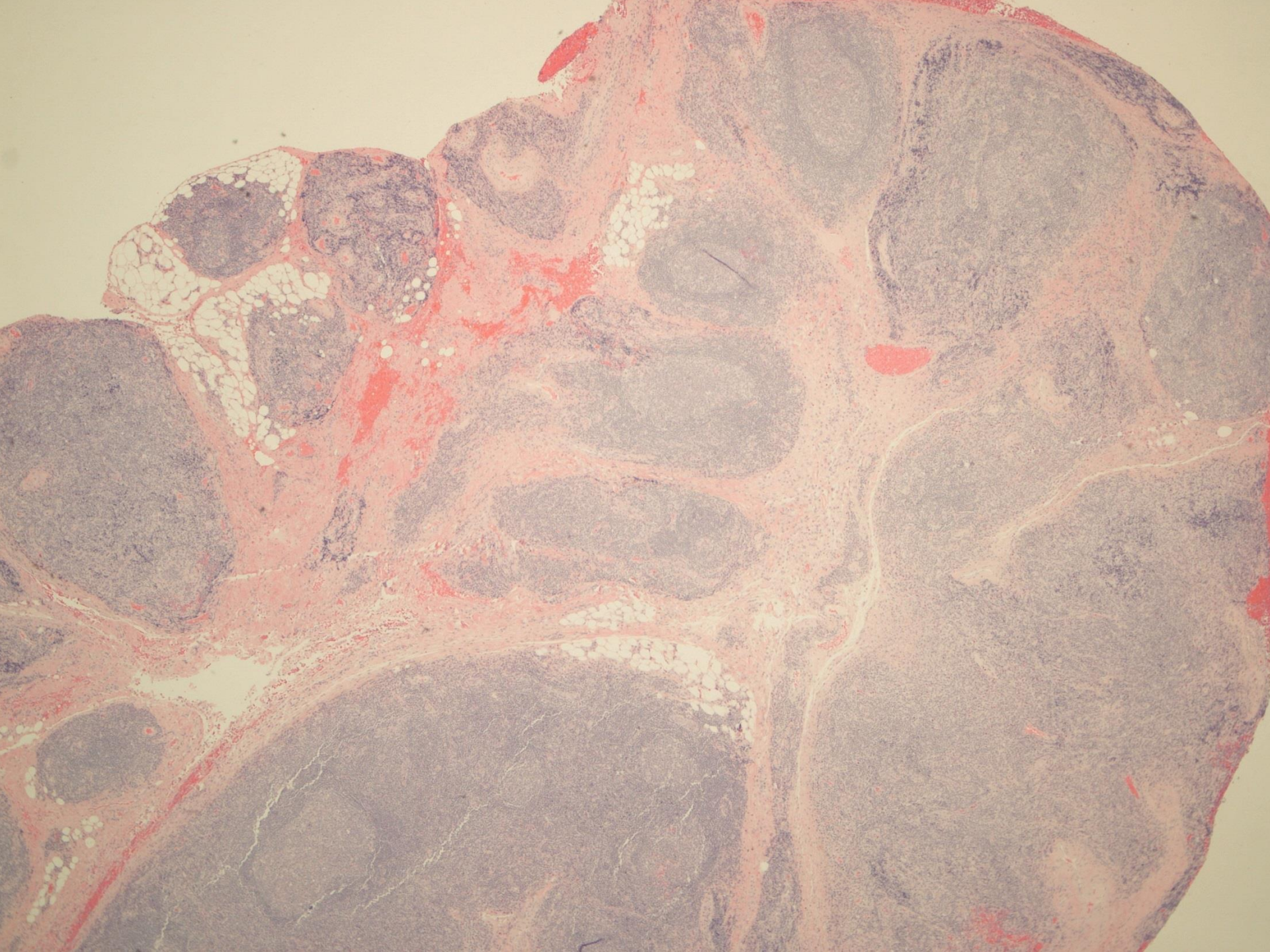
Atypical CML Progression

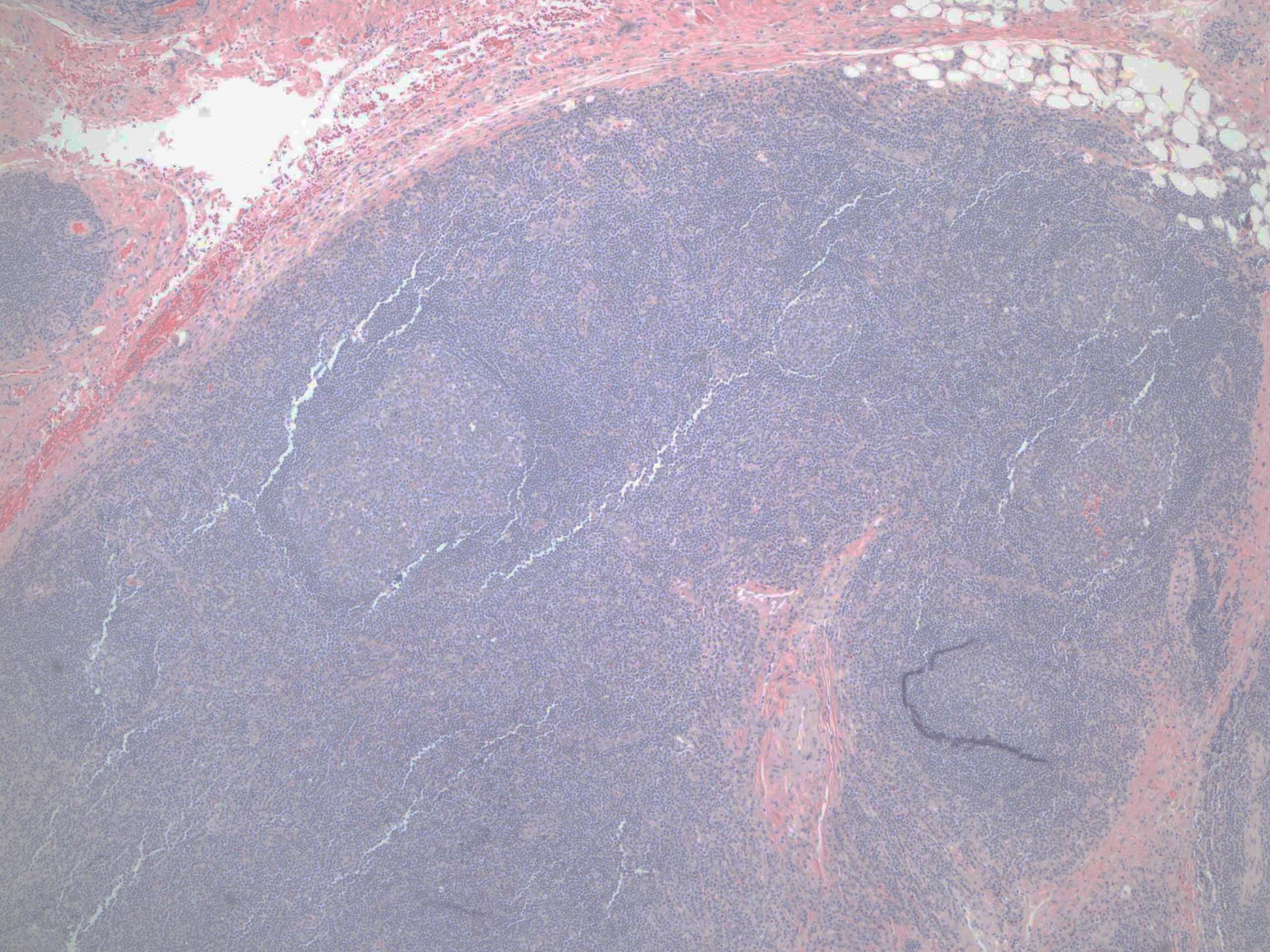


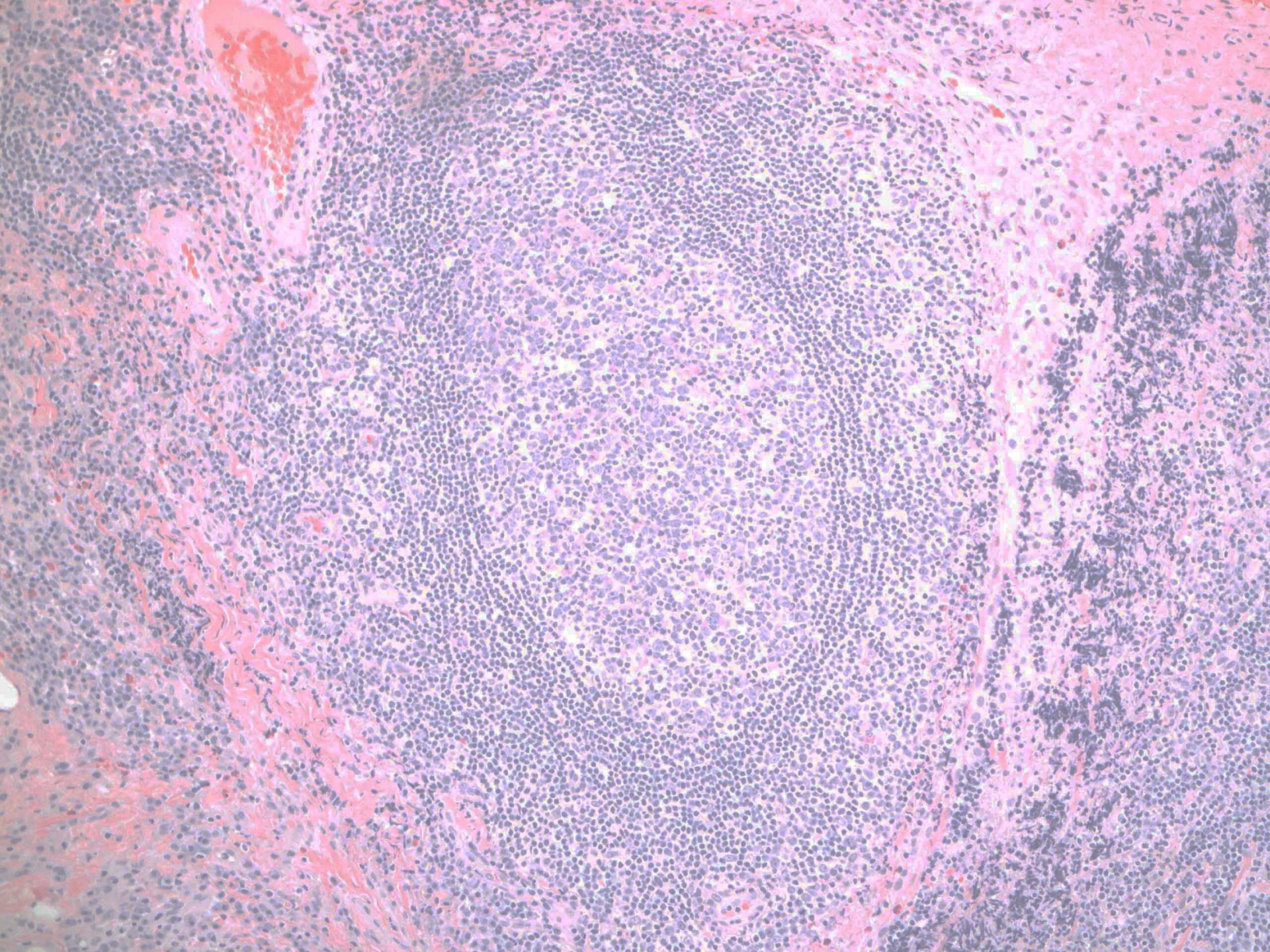
SB 5918

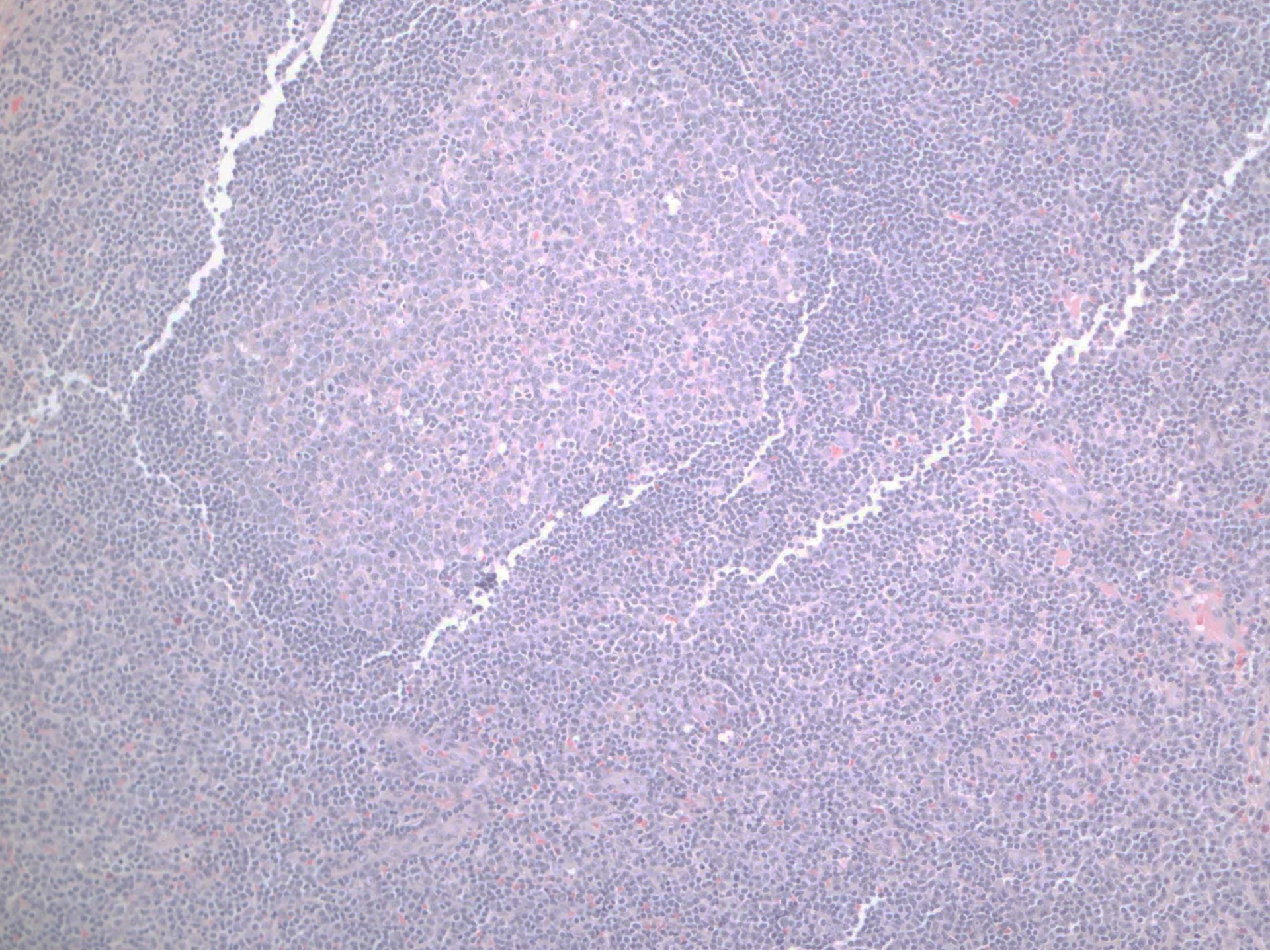
Linlin Wang/Patrick Treseler; UCSF

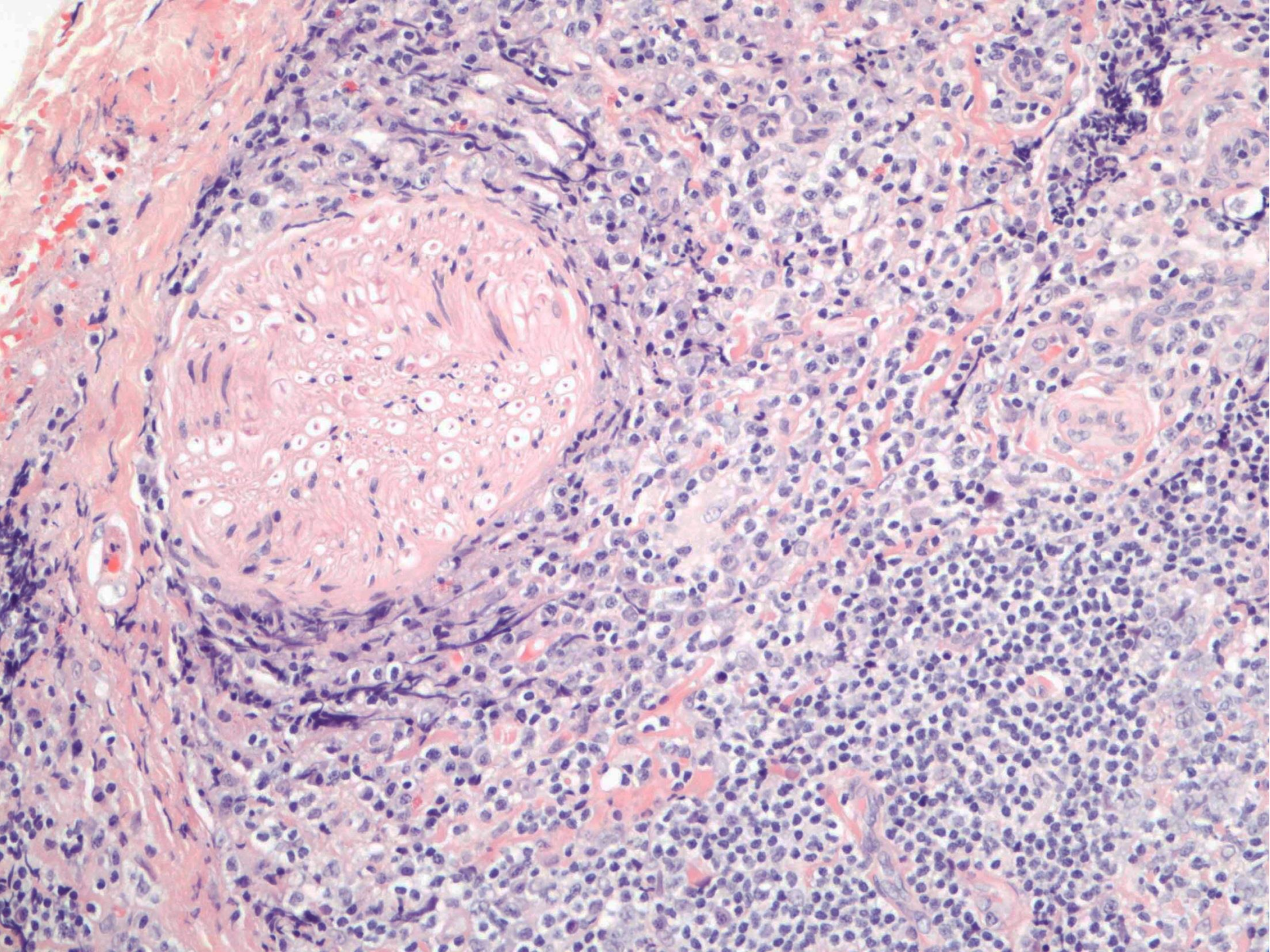
72-year-old man with long-standing history of recurrent reactive peri-orbital lymphoid hyperplasia who presented with progression of disease. Imaging studies show peri-orbital, peri-optic nerve, submandibular gland and mediastinal lymphoid hyperplasia. Lacrimal gland submitted.

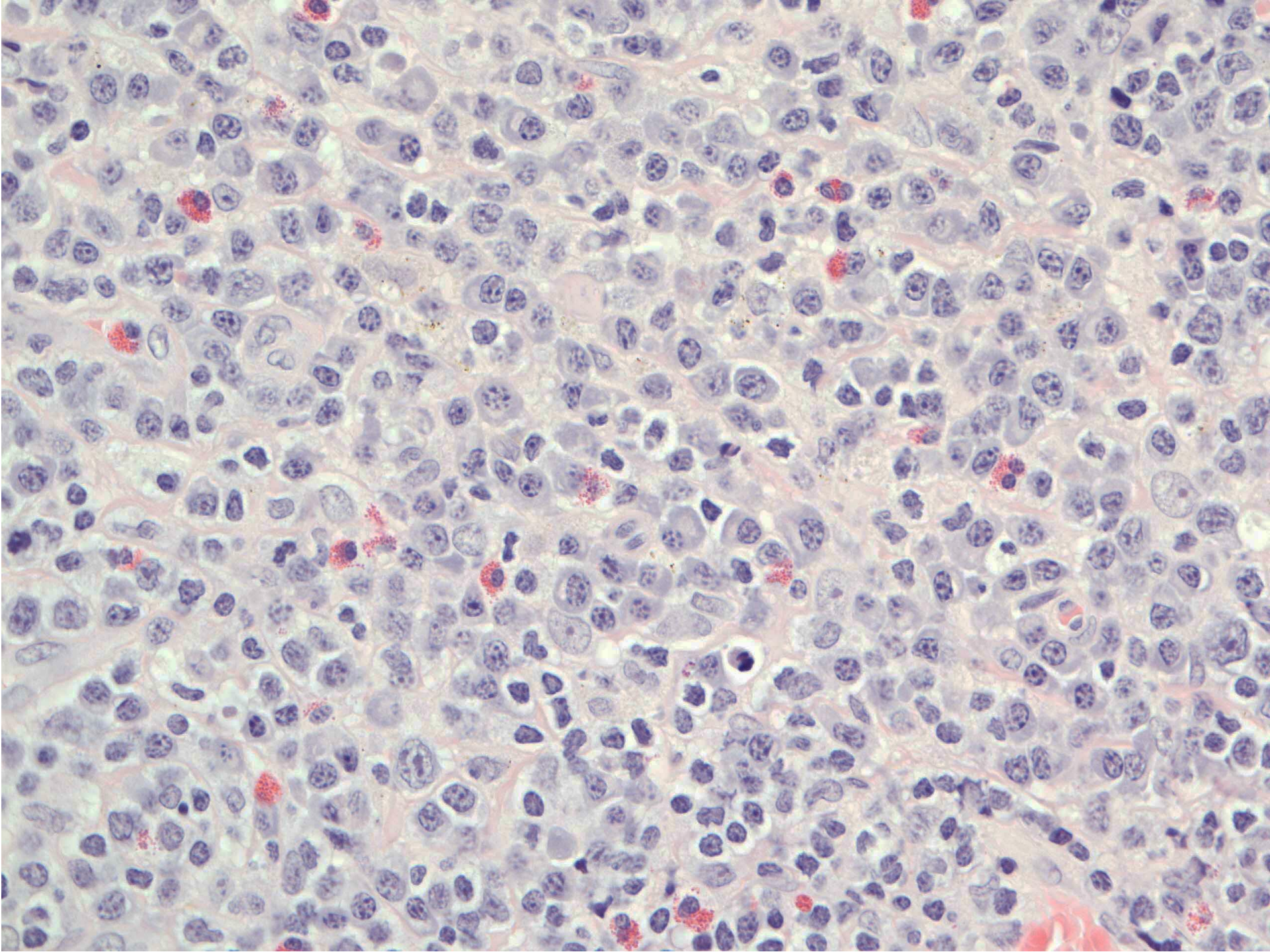


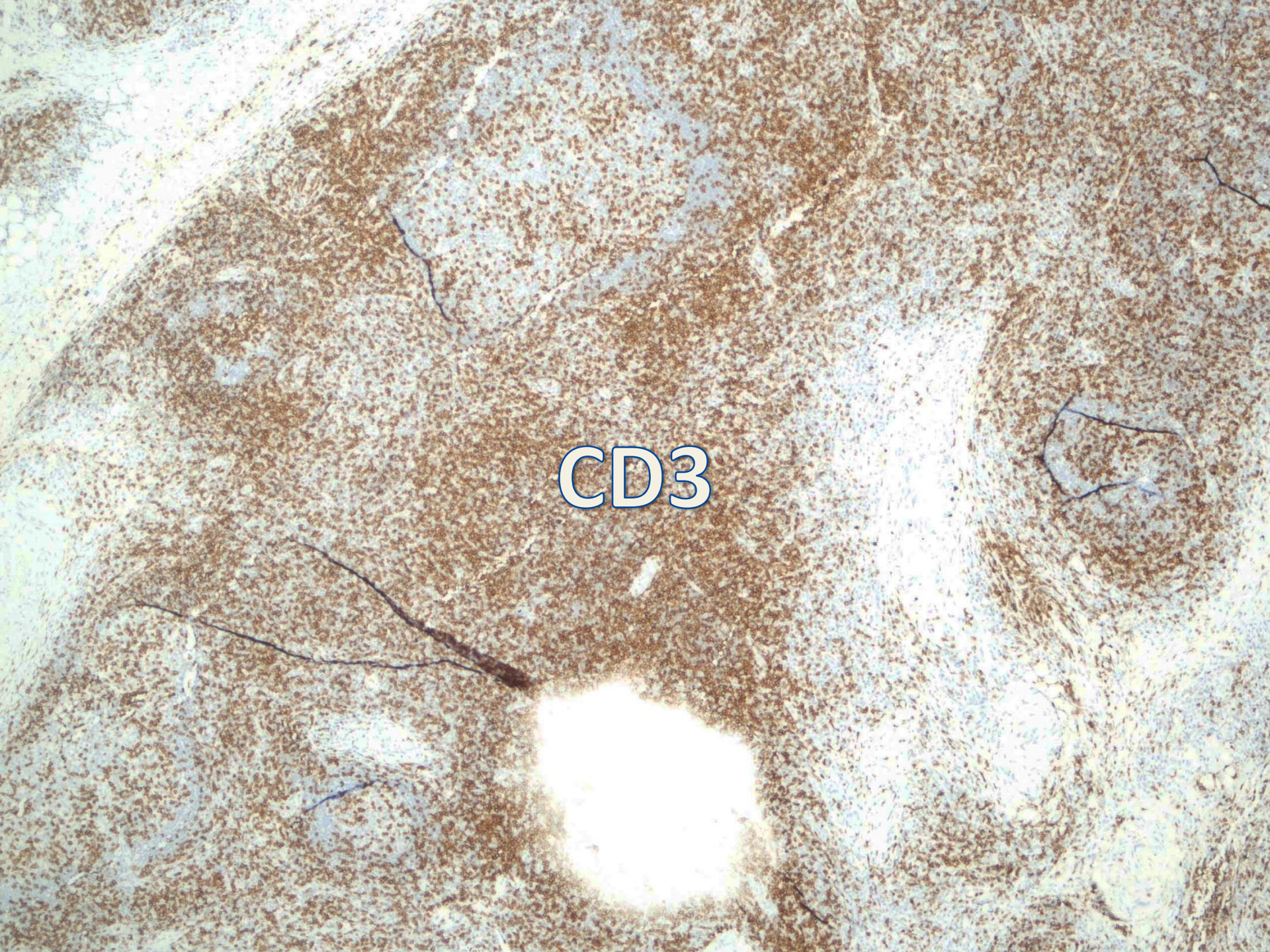


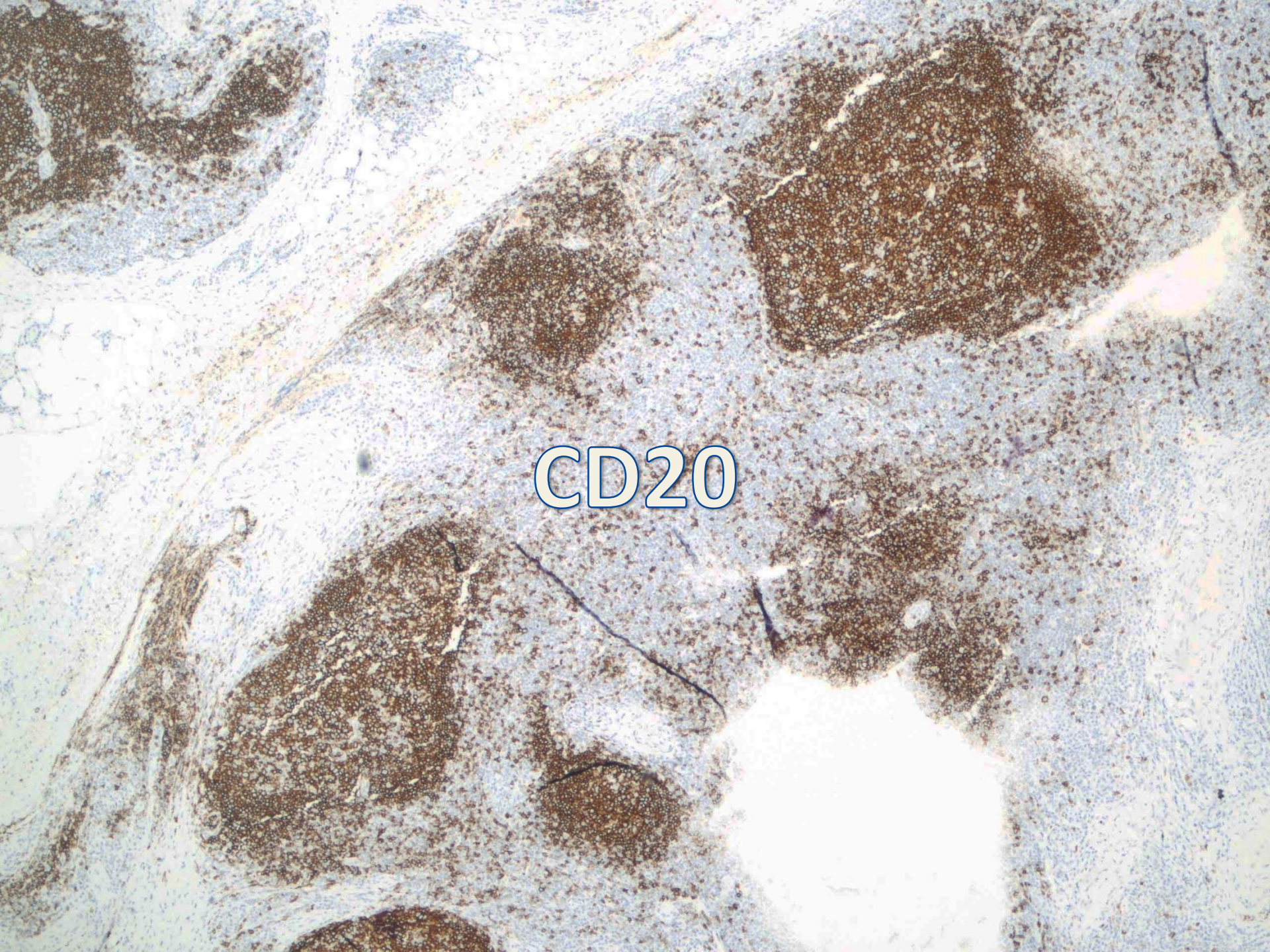




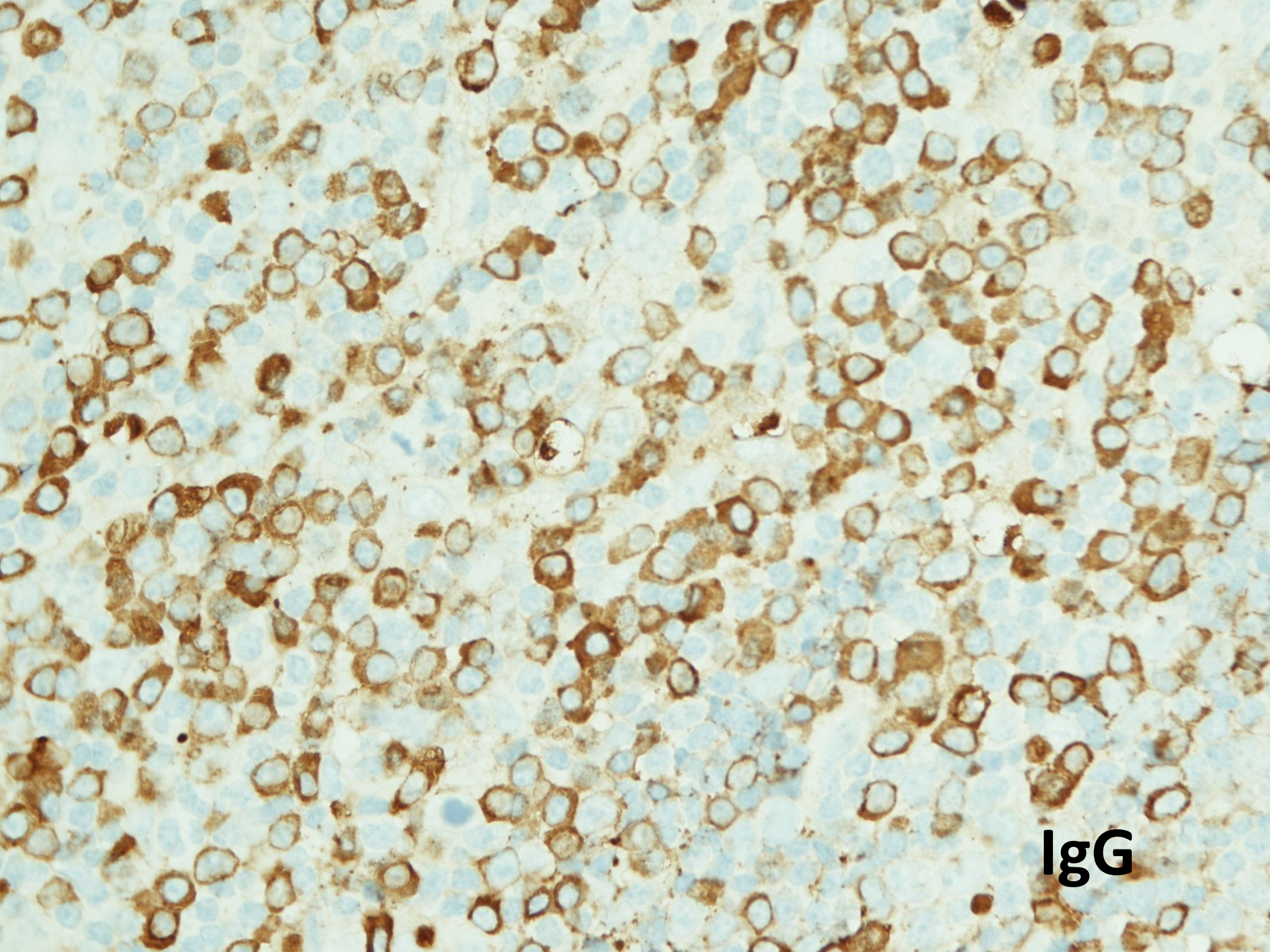


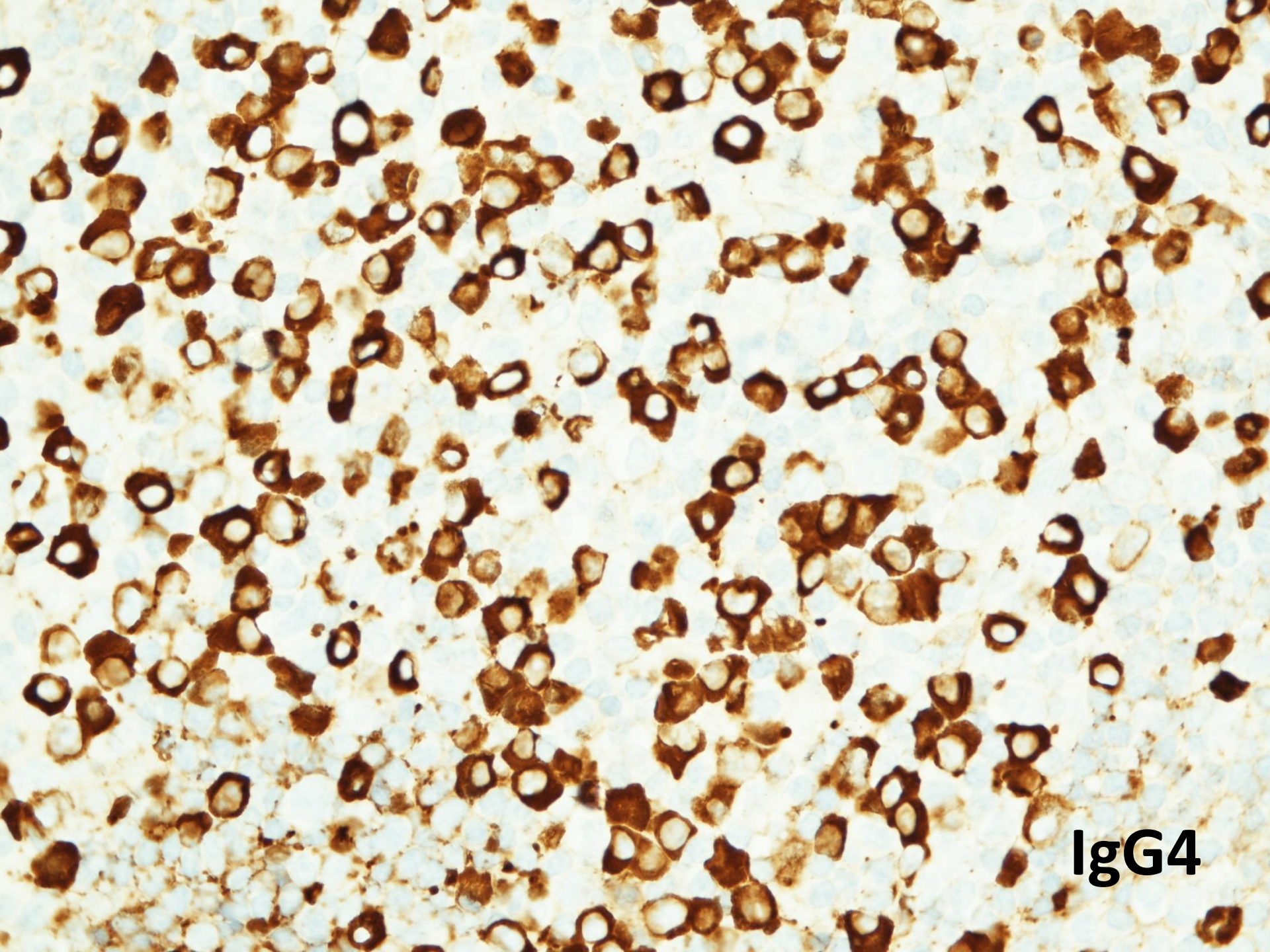



CD3


CD20

DIAGNOSIS?


IgG


IgG4

Diagnosis

IgG4-related disease

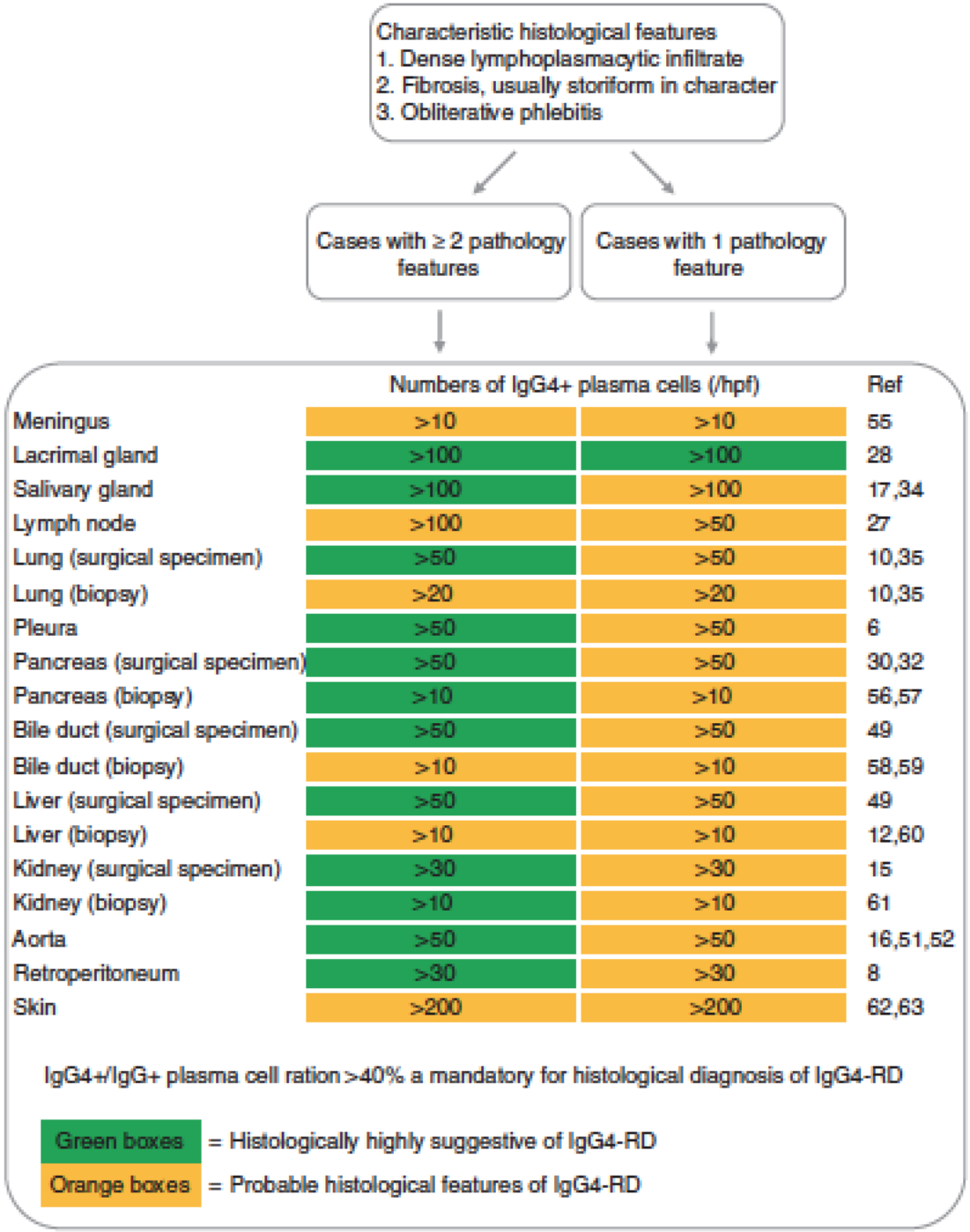
- Morphological features
    1. Dense lymphoplasmacytic infiltrate
    2. Fibrosis, arranged at least focally in a storiform pattern
    3. Obliterative phlebitis
- Increased numbers of IgG4+ plasma cells (IgG4+/IgG+ ratio > 40%)

Mod Pathol. 2012 Sep

Diagnosis Criteria

- Generally, want to see two of the three histological features for biopsy to be highly suggestive of IgG4-RD.
- *Exceptions!:* In lacrimal glands, lymph nodes, lung, and minor salivary glands storiform-type fibrosis and obliterative phlebitis may be absent in true IgG4-RD.

Mod Pathol. 2012 Sep

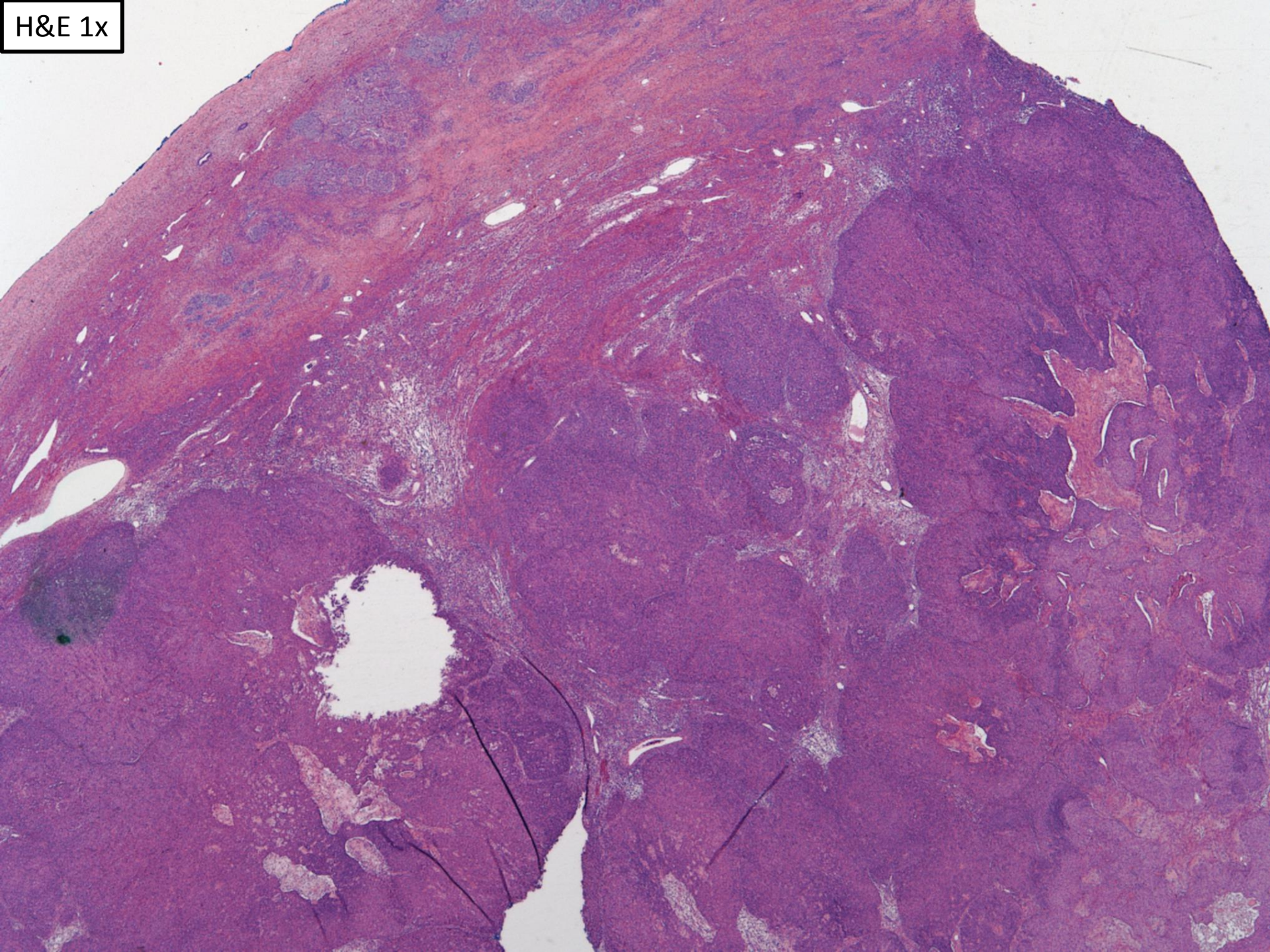


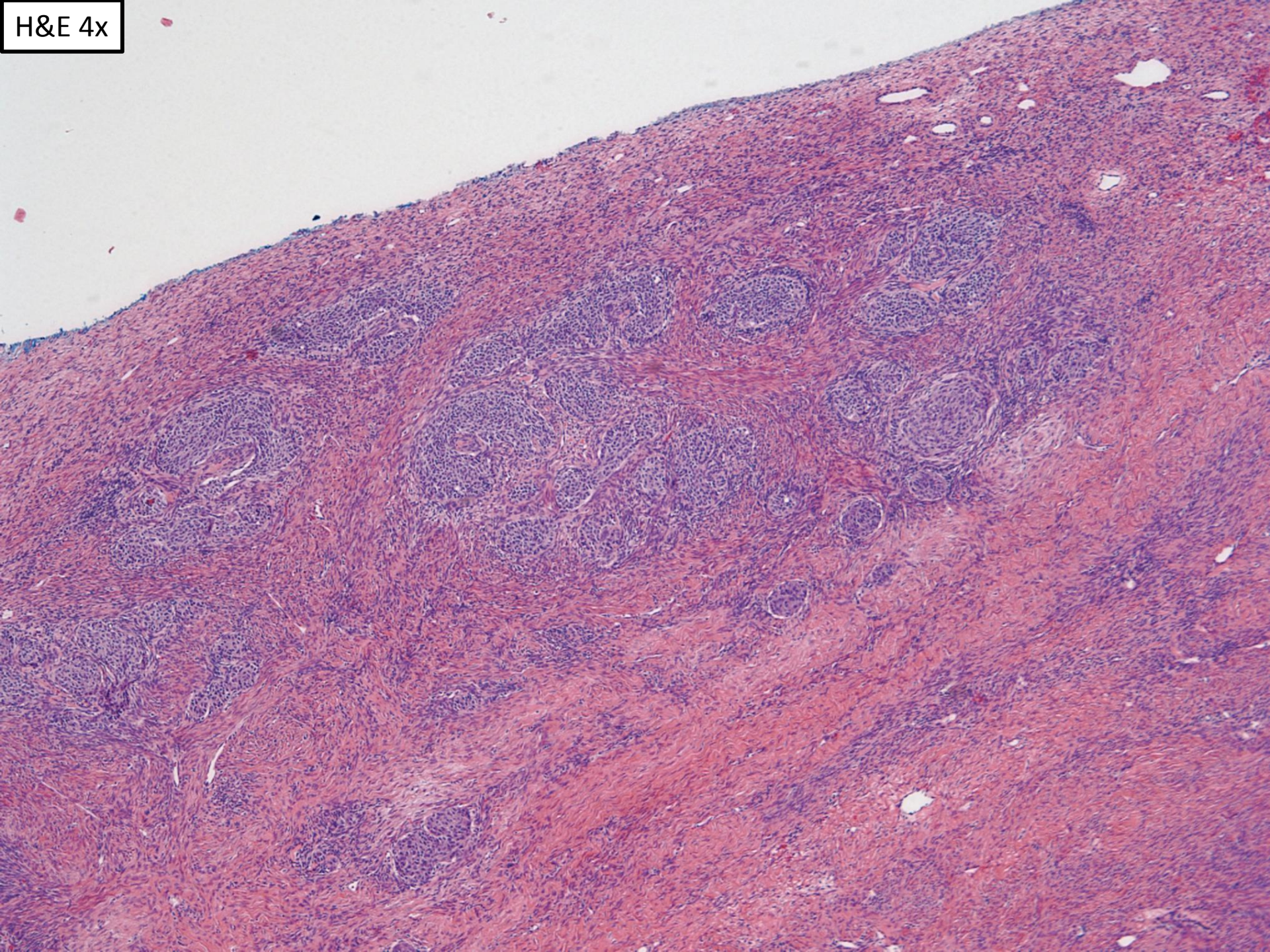
Mod Pathol. 25: 1150; 2012.

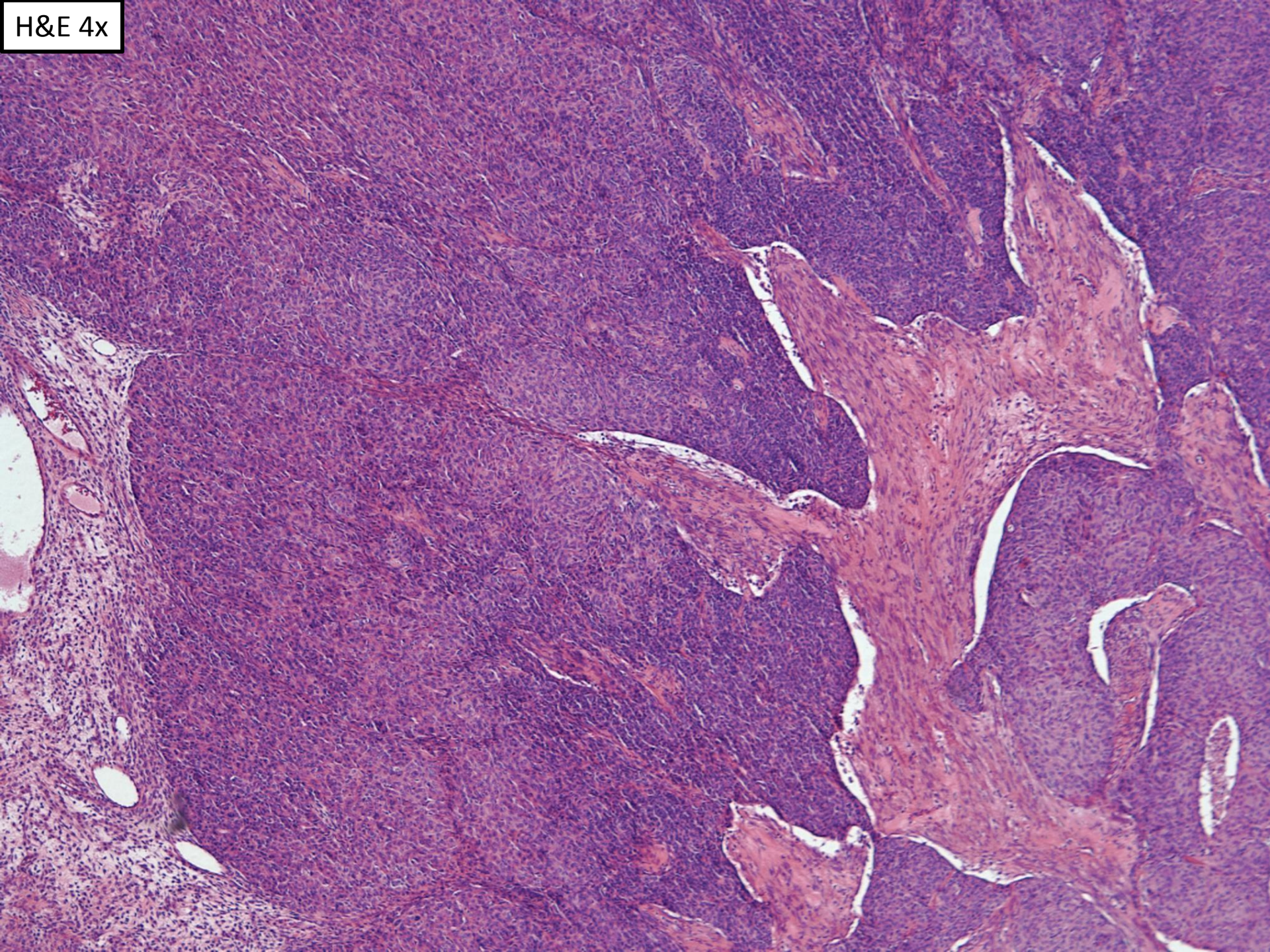
SB 5919

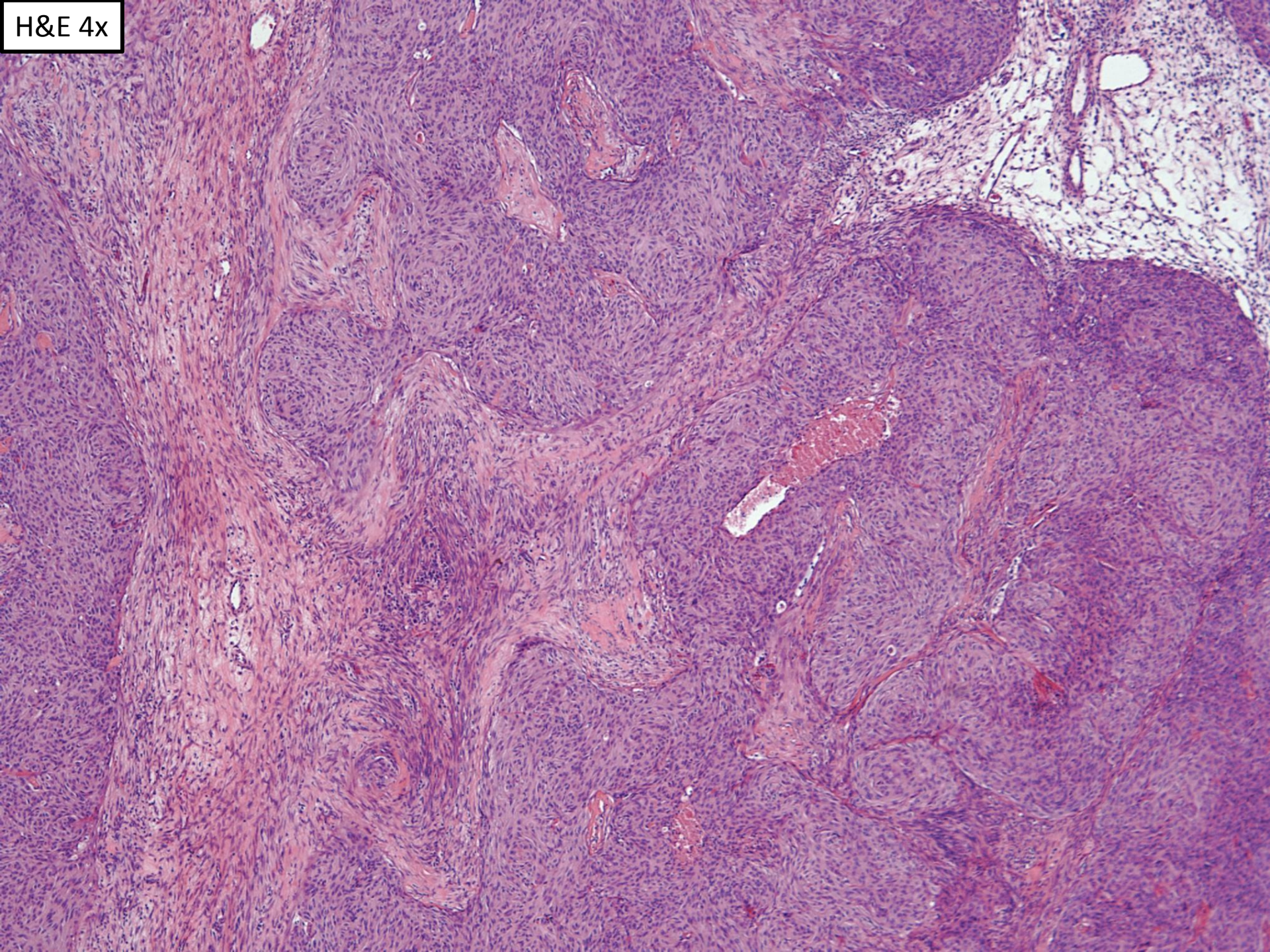
Natalia Isaza/Richard Kempson; Stanford

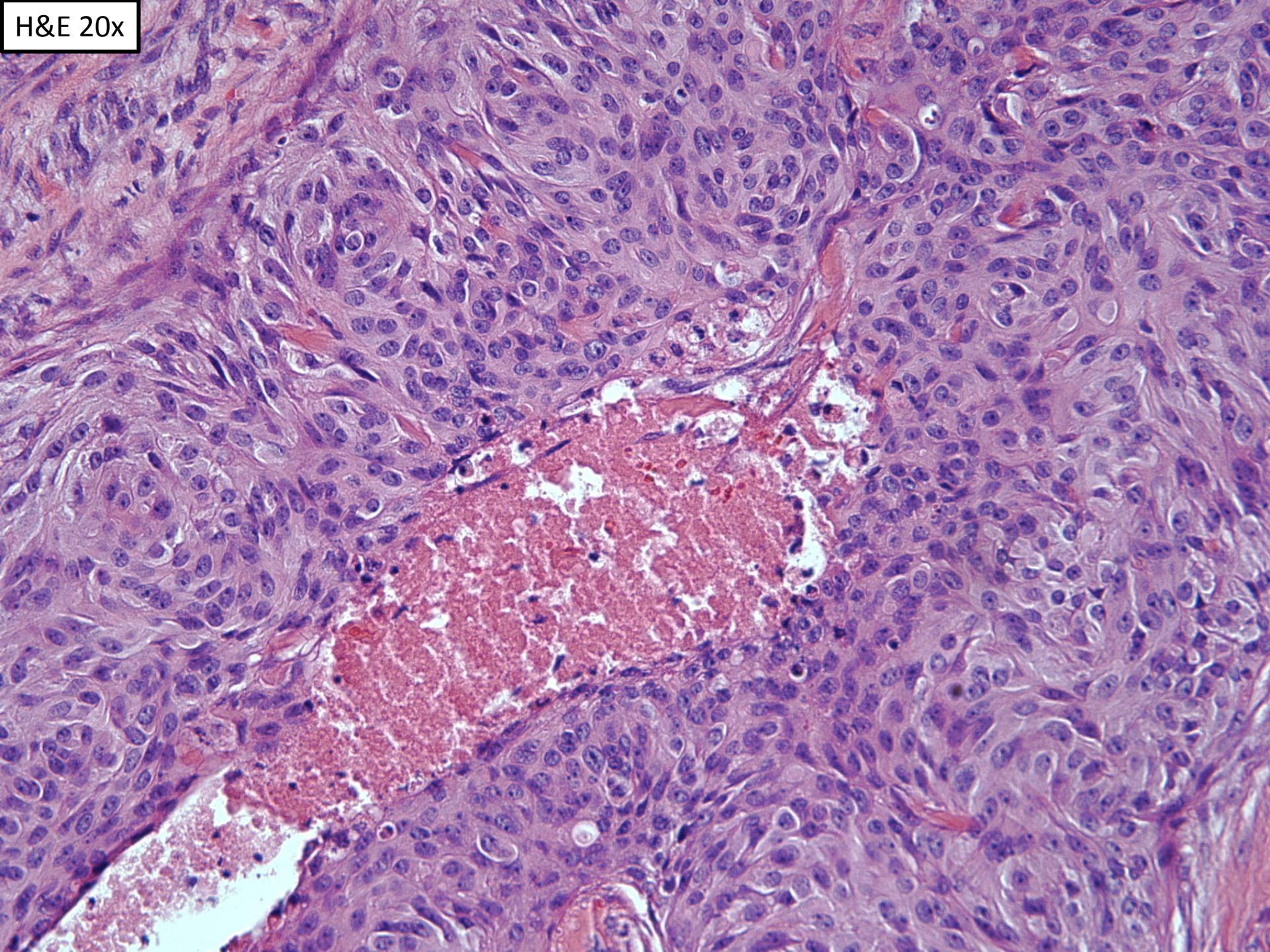
66-year-old woman presents with 10.2cm solid unilateral left ovarian mass and history of myeloproliferative disorder. There was no evidence of spread beyond the ovary at the time of surgery.

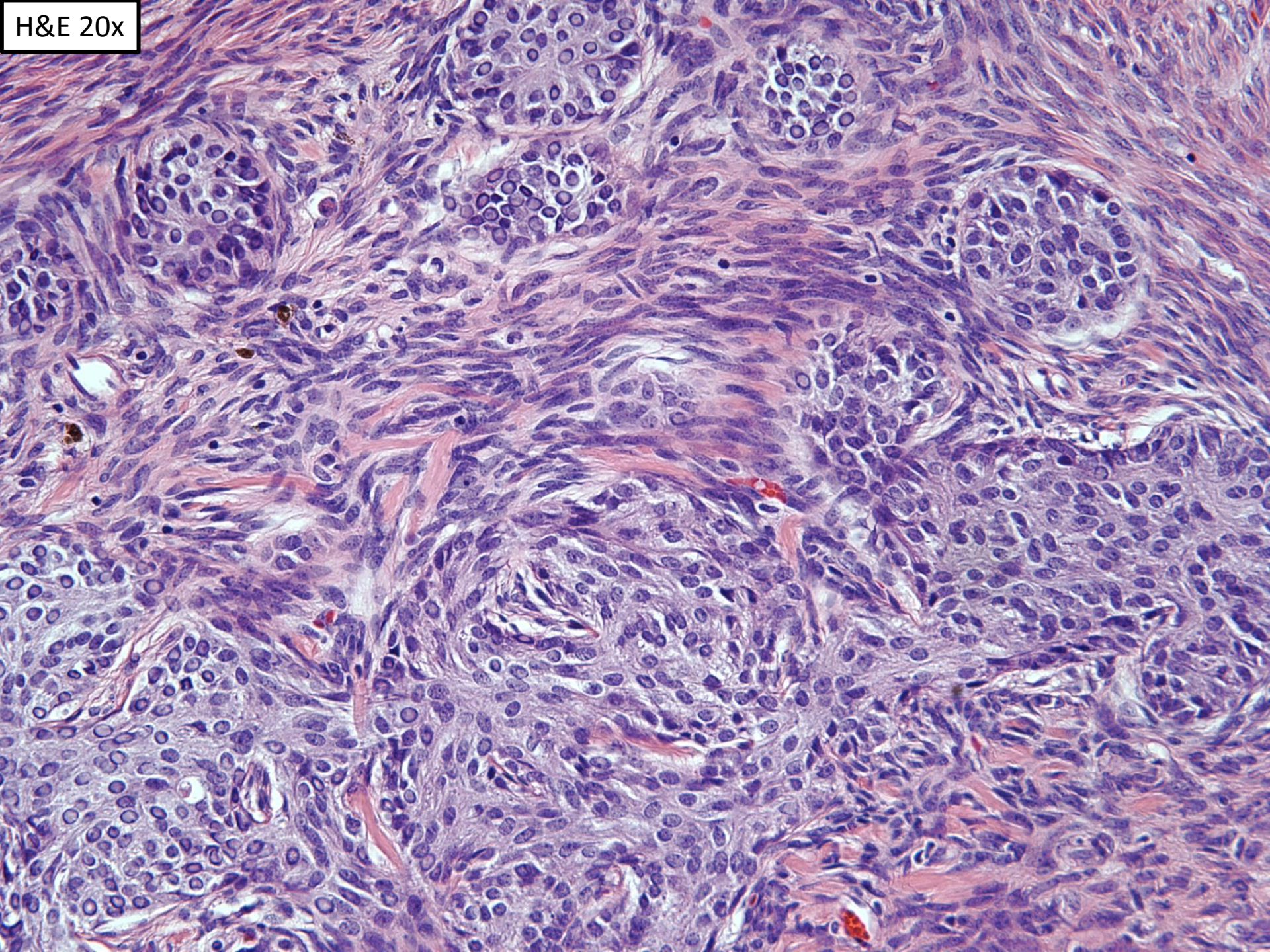

H&E 1x

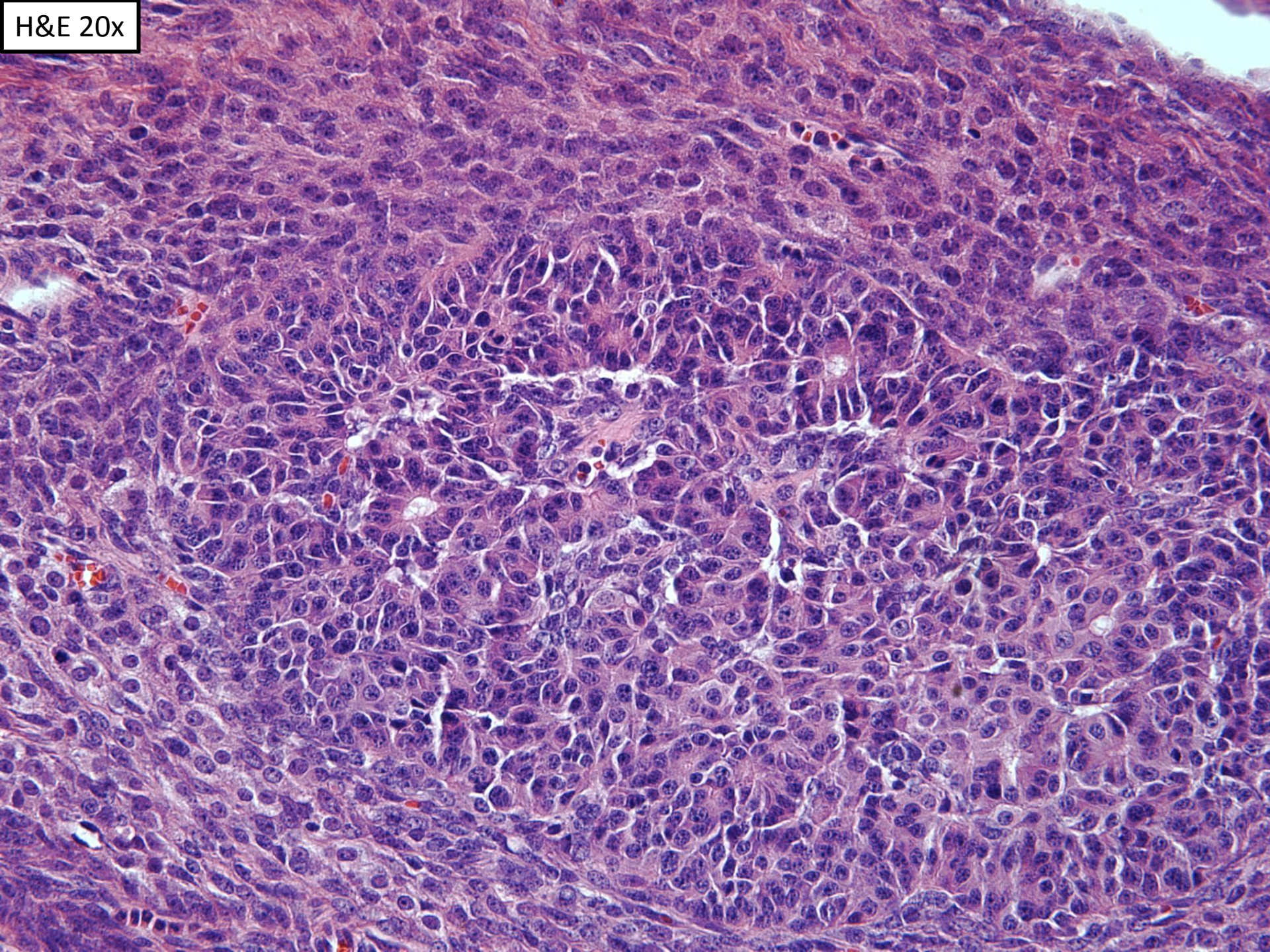

H&E 4x


H&E 4x

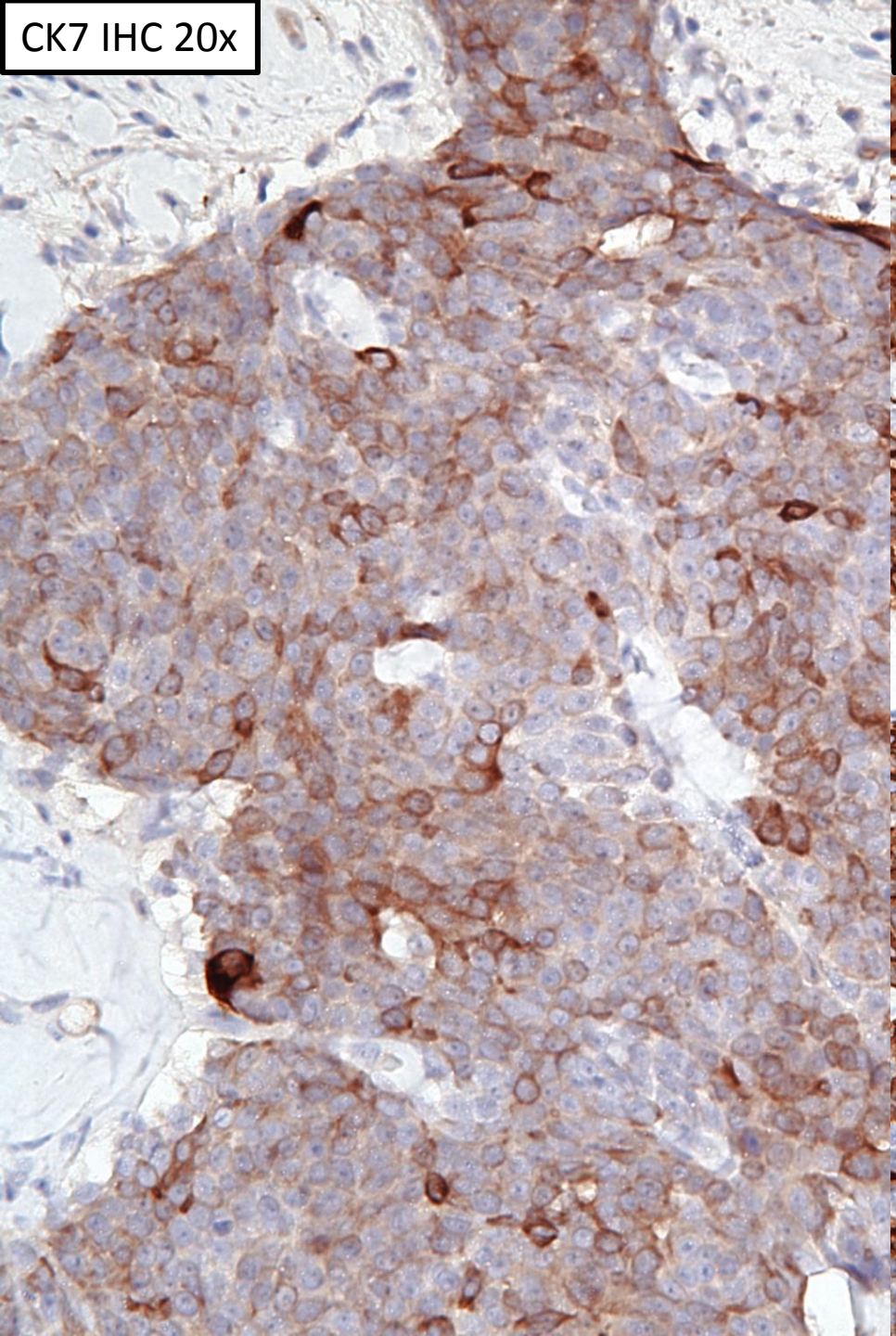

H&E 4x

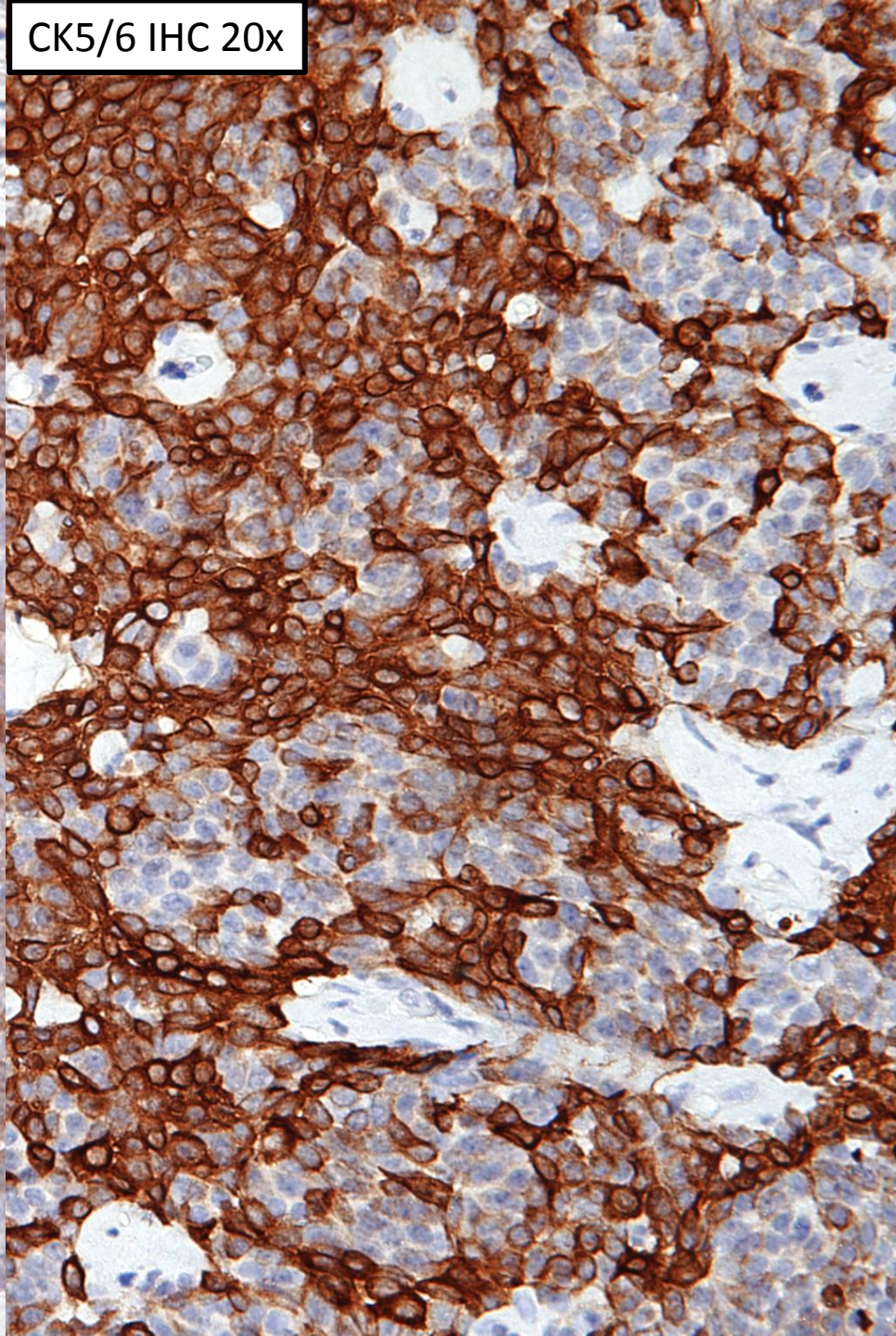

H&E 20x

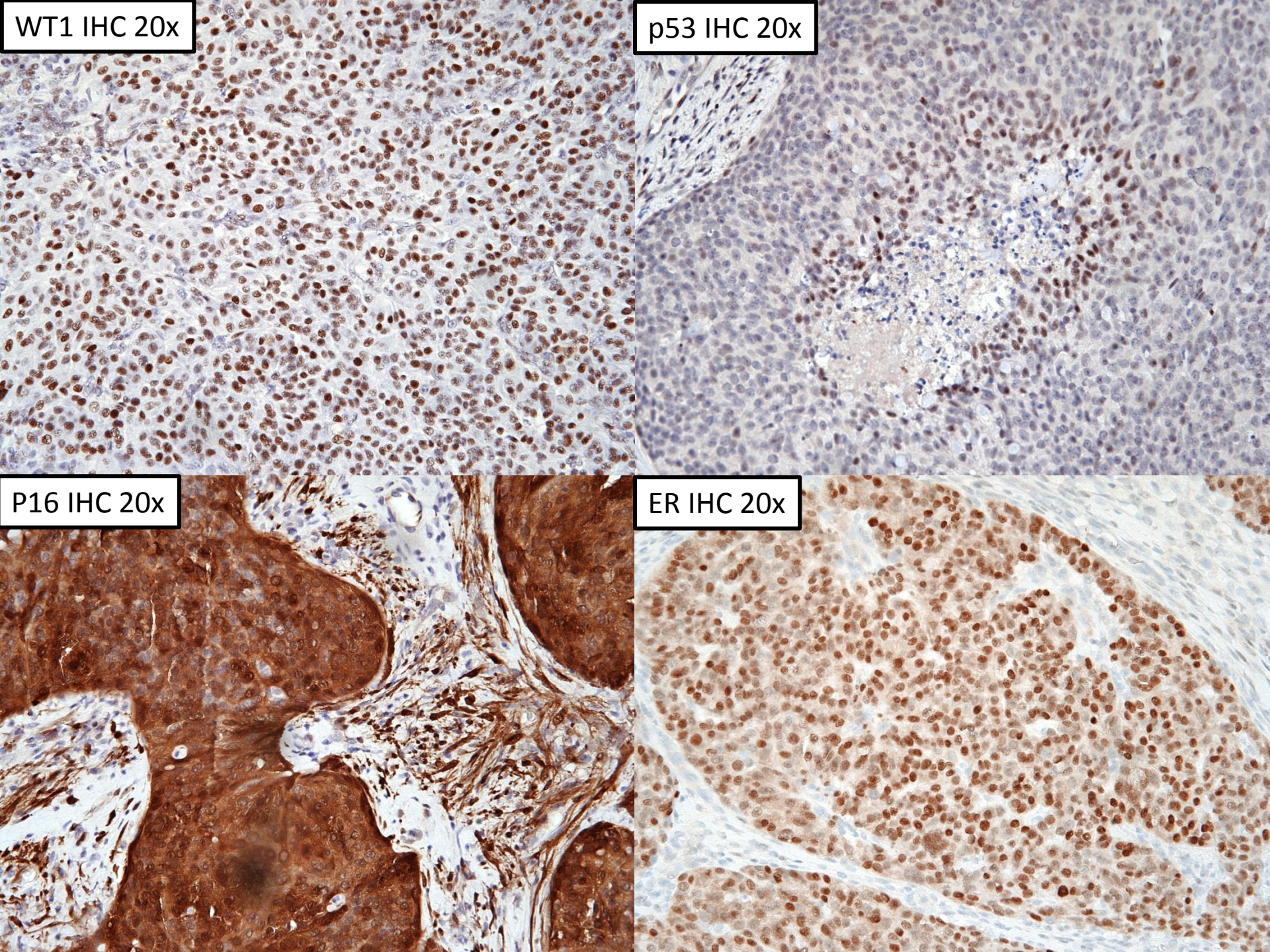

H&E 20x


H&E 20x

DIAGNOSIS?


CK7 IHC 20x


CK5/6 IHC 20x


WT1 IHC 20x
p53 IHC 20x
P16 IHC 20x
ER IHC 20x

Diagnosis

- **OVARY, LEFT, OOPHORECTOMY**
  - **ENDOMETRIOID CARCINOMA WITH PROMINENT SPINDLE CELL COMPONENT, FIGO GRADE 1 (SEE COMMENT)**

Tornos C, Silva EG, Ordonez NG, Gershenson DM, Young RH, Scully RE. *Endometrioid carcinoma of the ovary with a prominent spindle-cell component, a source of diagnostic confusion. A report of 14 cases.* Am J Surg Pathol. 1995 Dec;19(12):1343-53.

Take Home Points

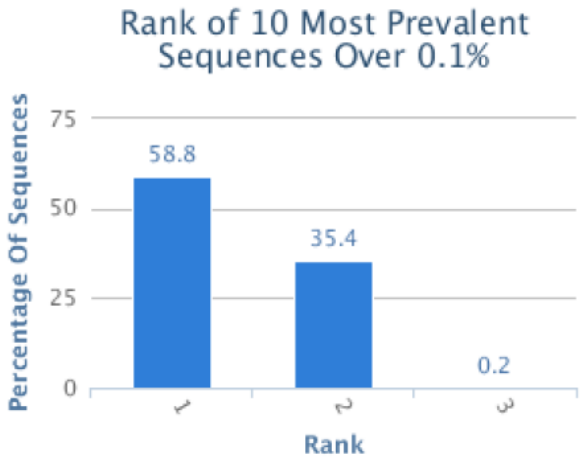
- Should be graded based on the glandular component using FIGO grading
- The most helpful features to identify these are:
  - Areas of typical endometrioid adenocarcinoma
  - Squamous differentiation
  - Adenofibromatous component
  - Intraluminal mucin
  - Keratin and EMA positivity

Case 3

68 yo man with Sezary syndrome (IVA)

PCR positive in skin biopsy

RESULTS



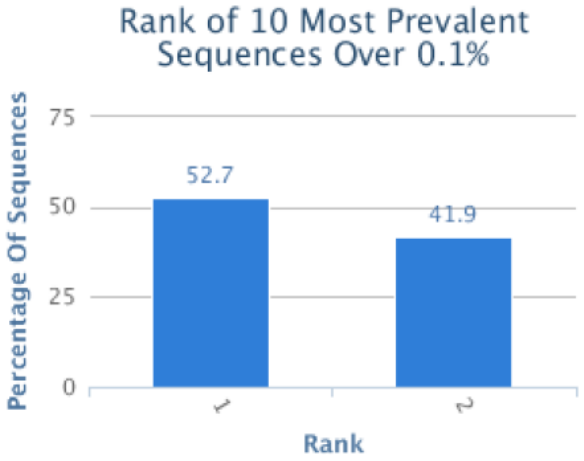
Summary Results:

Dominant clone identified

TCRB CDR3 gene fragments were amplified using multiplex PCR amplification. Gene sequences were analyzed and cataloged, and the highest frequency clone(s) observed is reported.

Rank	Sequence	Frequency
1	GCCCAAAAGAACCCGACAGCTTTCTATCTCTGTGCCAGTAGCCCAGGTCGGGGGACAGGGGGCAATCAGCCCCAGCATTTTGGTGAT	58.8
2	GCGCACAGAGCAGGGGGACTCGGCCATGTATCTCTGTGCCAGCAGCTTCGGACTAGCGGGAGTACAGATACGCAGTATTTTGGCCCA	35.4

RESULTS



Summary Results:

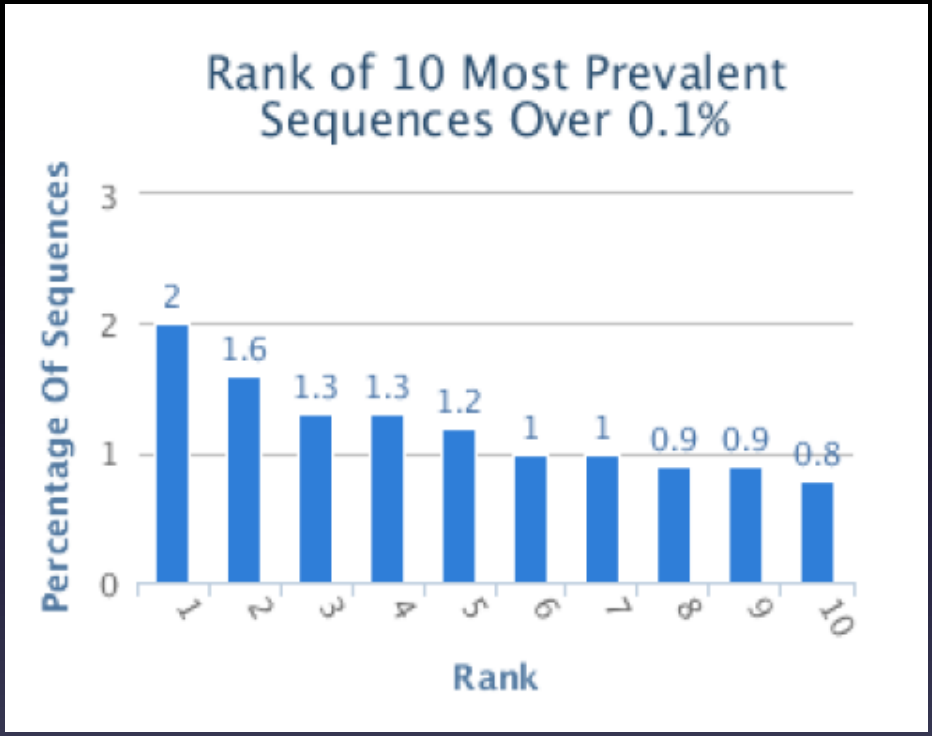
Dominant clone identified

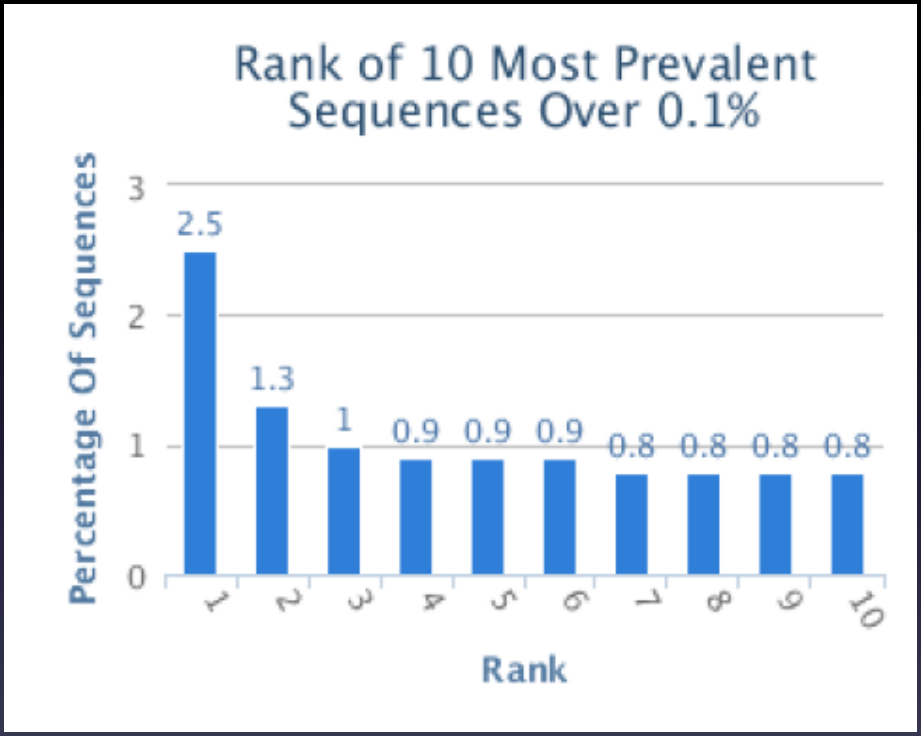
TCRB CDR3 gene fragments were amplified using multiplex PCR amplification. Gene sequences were analyzed and cataloged, and the highest frequency clone(s) observed is reported.

Rank	Sequence	Frequency
1	GCCCAAAAGAACCCGACAGCTTTCTATCTCTGTGCCAGTAGCCCAGGTCGGGGGACAGGGGGCAATCAGCCCCAGCATTTTGGTGAT	52.7
2	GCGCACAGAGCAGGGGGACTCGGCCATGTATCTCTGTGCCAGCAGCTTCGGACTAGCGGGAGTACAGATACGCAGTATTTTGGCCCA	41.9

- Developed generalized rash after 2months on anti-CCR4 therapy
- Positive TCR-PCR on skin

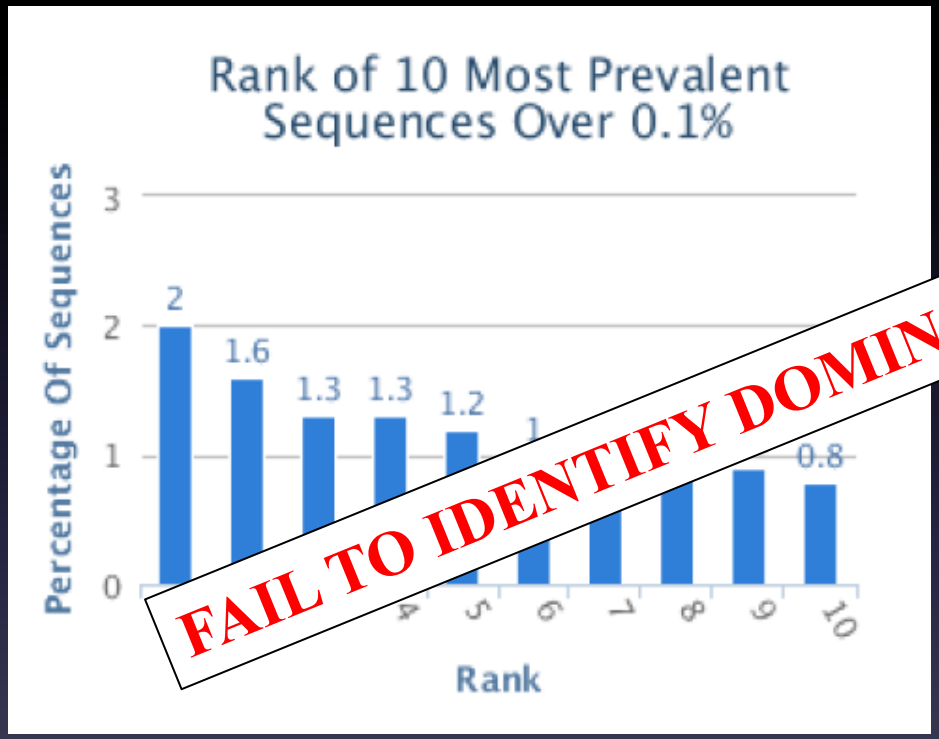
HTS-TCR negative





Negative for dominant clones

HTS-TCR negative



FAIL TO IDENTIFY DOMINANT CLONE BY HTS

Negative for dominant clones

Clinical utility of TCR HTS in CTCL

1. Quantitative utility in following minimal residual disease
2. Clonal evolution under targeted therapy
3. In diagnostic evaluation or re-staging
4. Real-time use in clinics

Summary

- HTS is a useful ancillary test for the diagnosis of CTCL
- Identification of dominant clones may reduce the false positive rate in inflammatory disorders
- Identification of dominant clone permits diagnosis of minimal disease and post-treatment

Summary

- Tracking dominant clones may be useful in establishing tumor burden in treatment
- Differentiating from lymphomatoid drug reactions

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Robert LeBlanc
Laurel Stevens

Adaptive Biosystems:

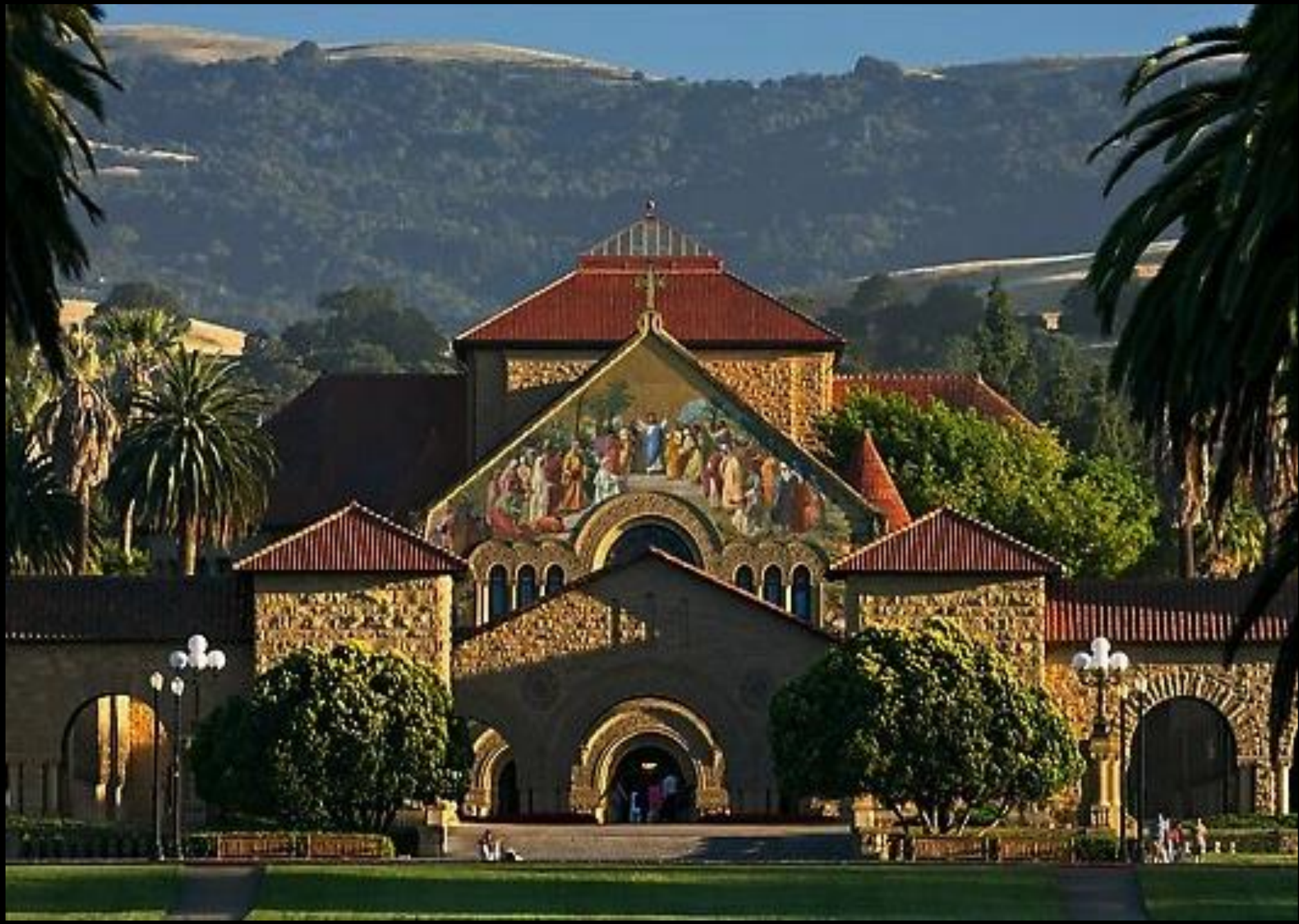
Ilan Kirsch

BMT:

Wen-Kai Weng

Molecular Pathology:

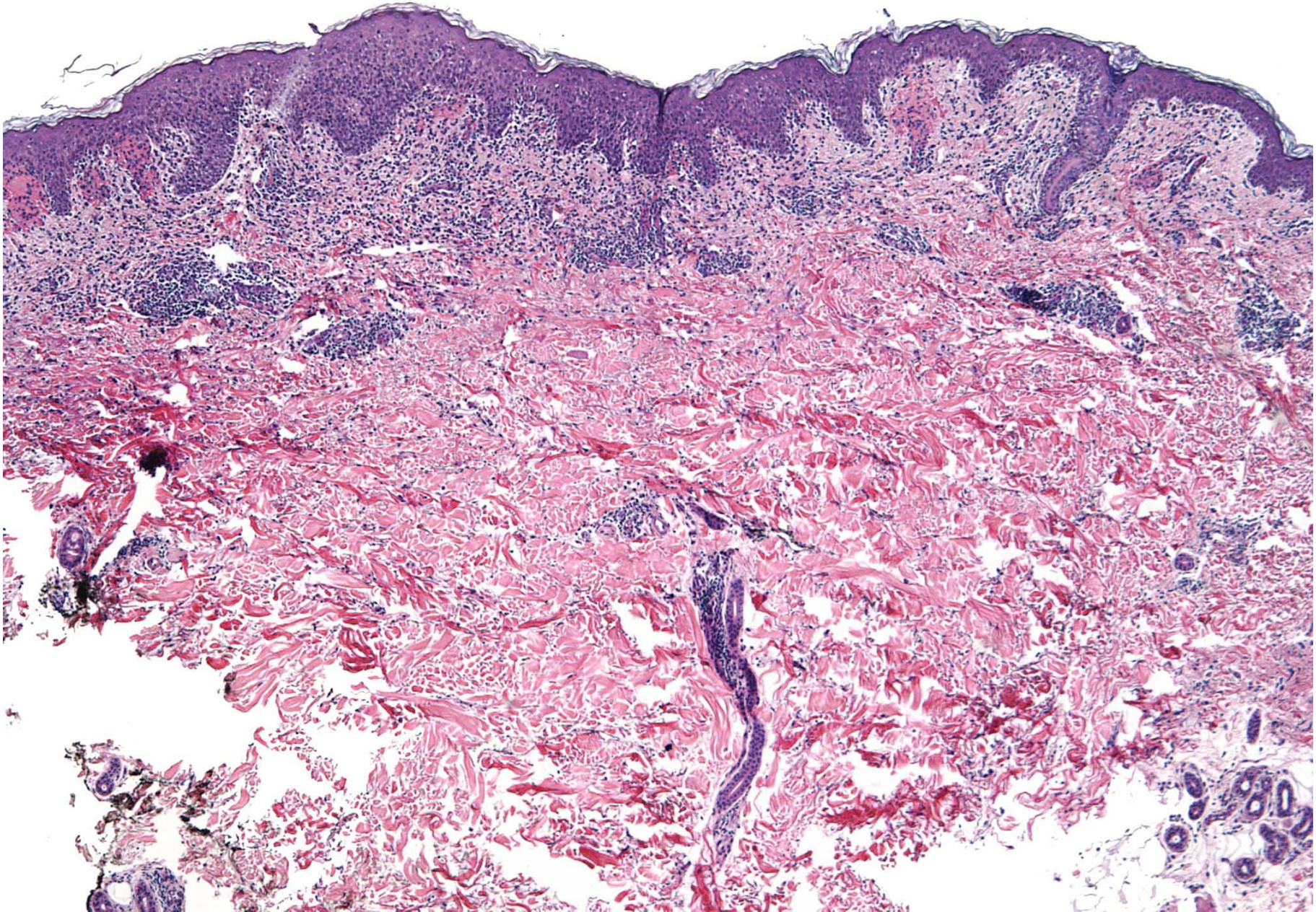
Dan Arber
James Zehnder

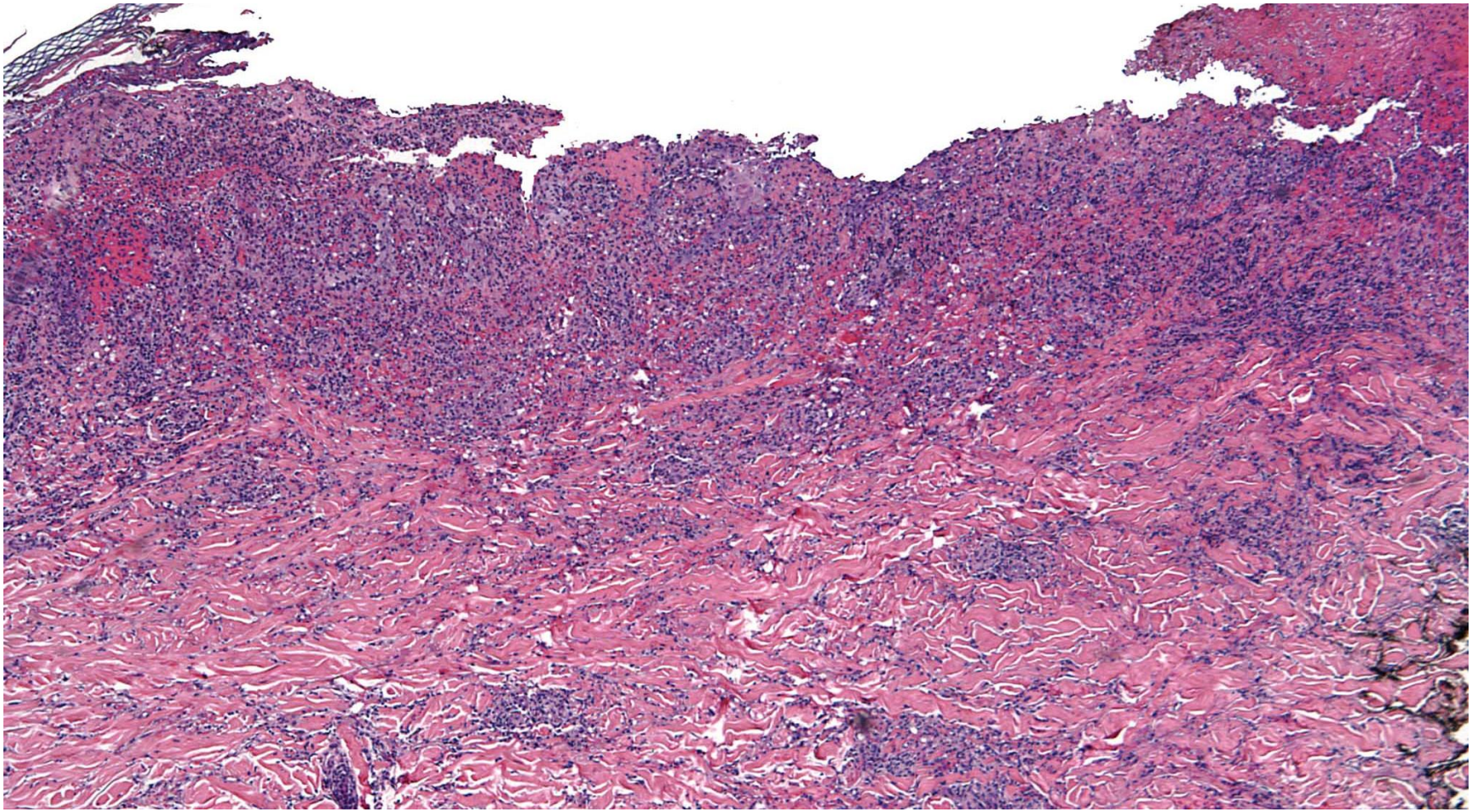


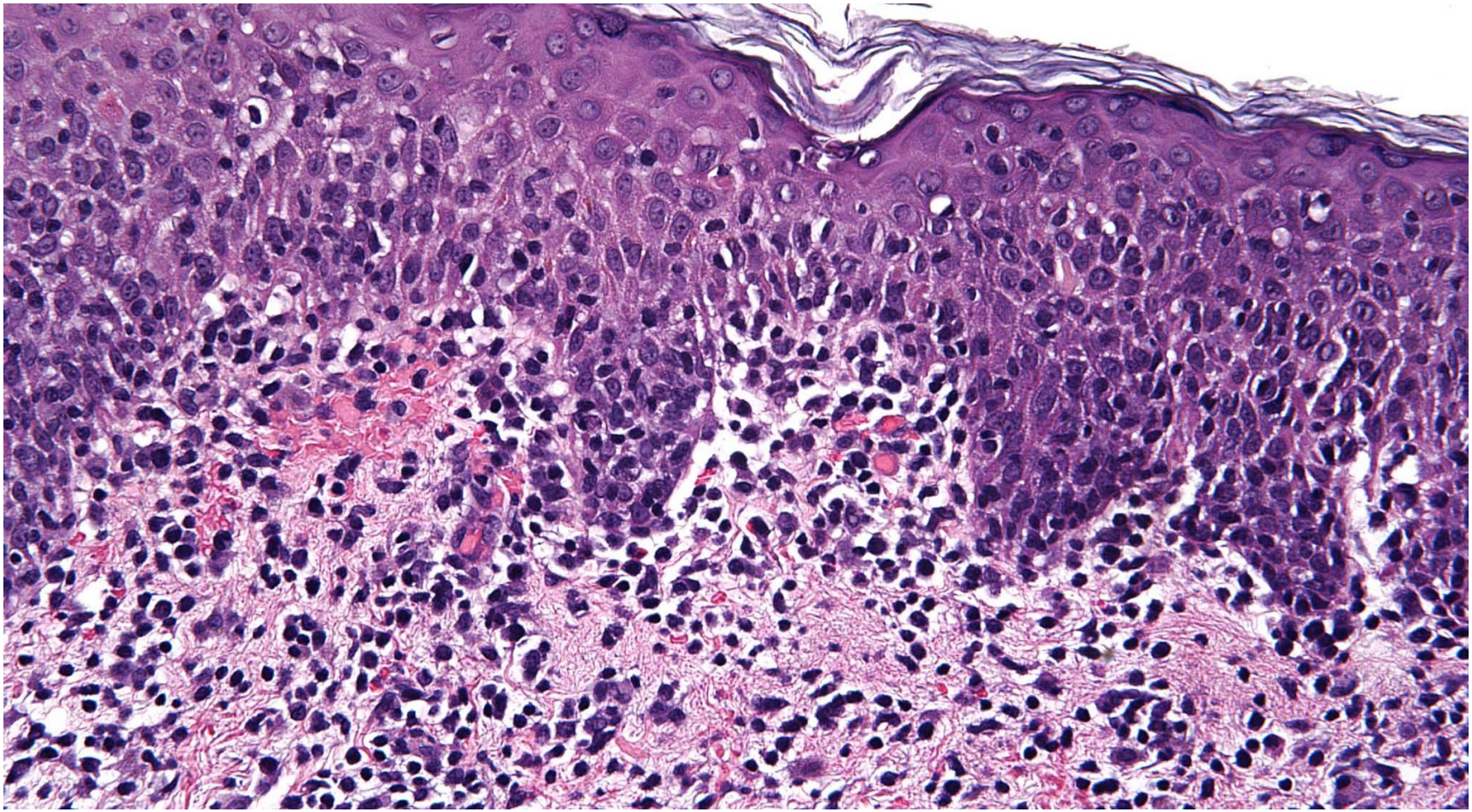
SB 5920

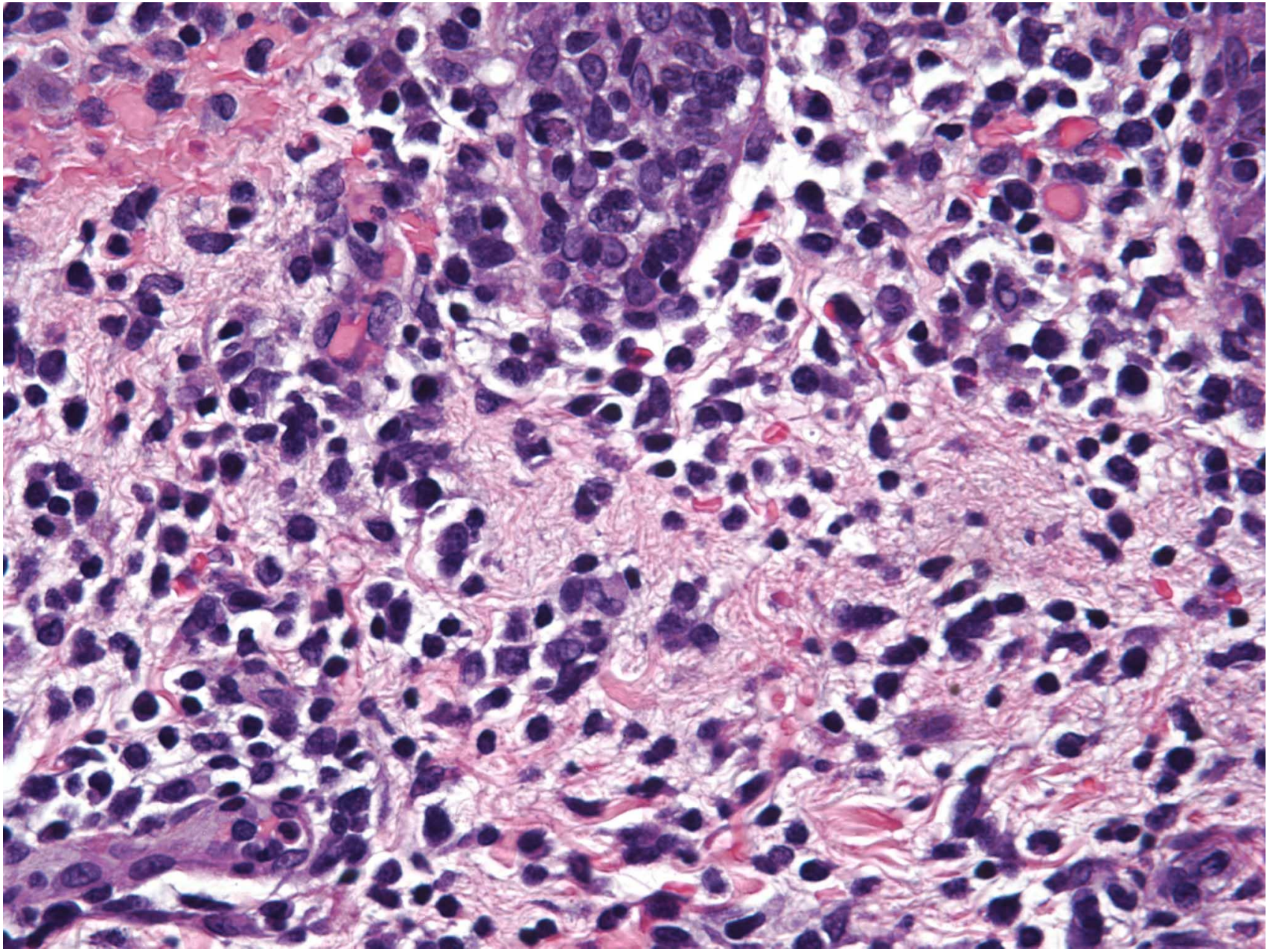
Jinah Kim; Stanford

76-year-old man with a 2-month history of erythematous to violaceous papules present on his extremities, trunk, and back.

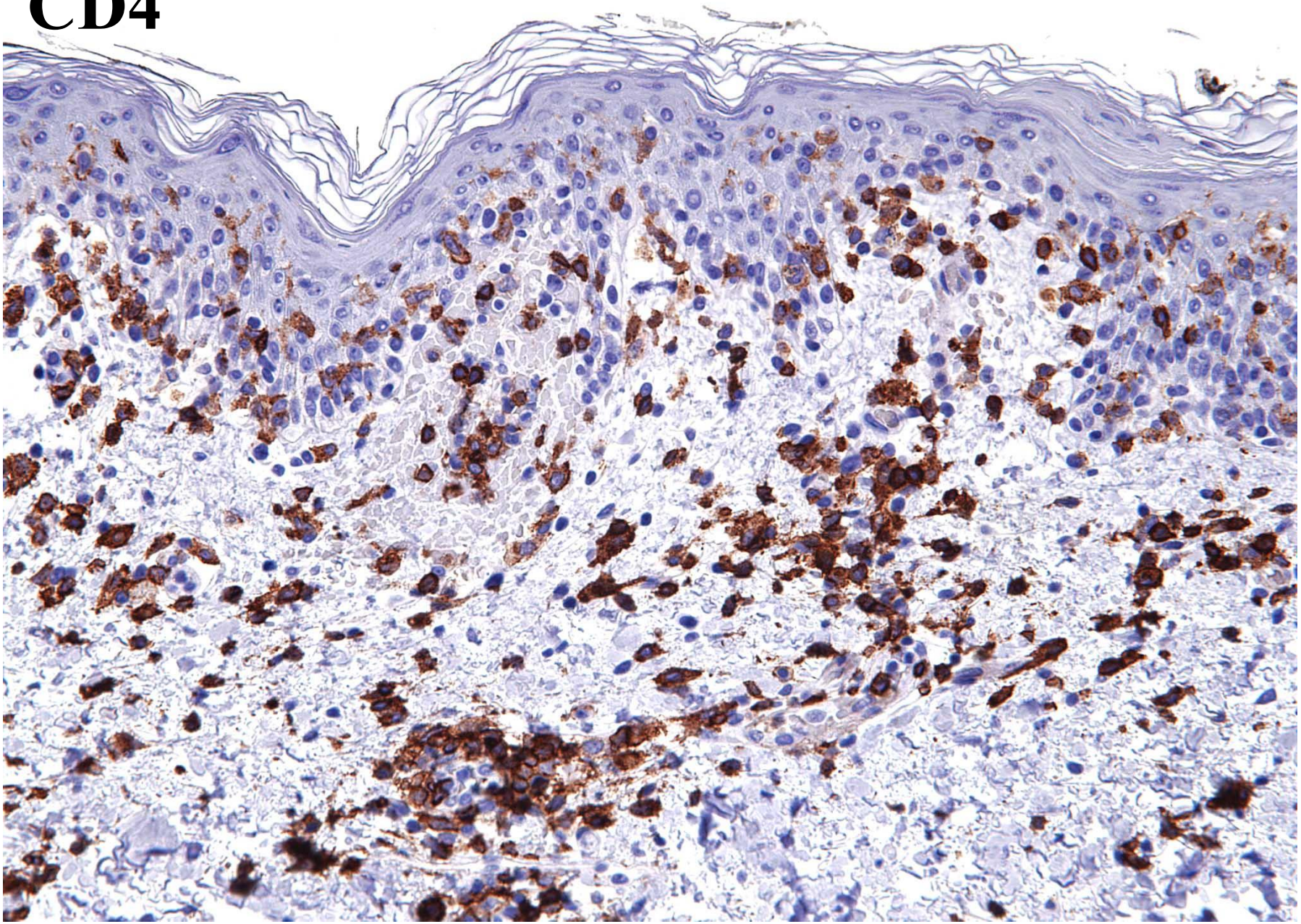


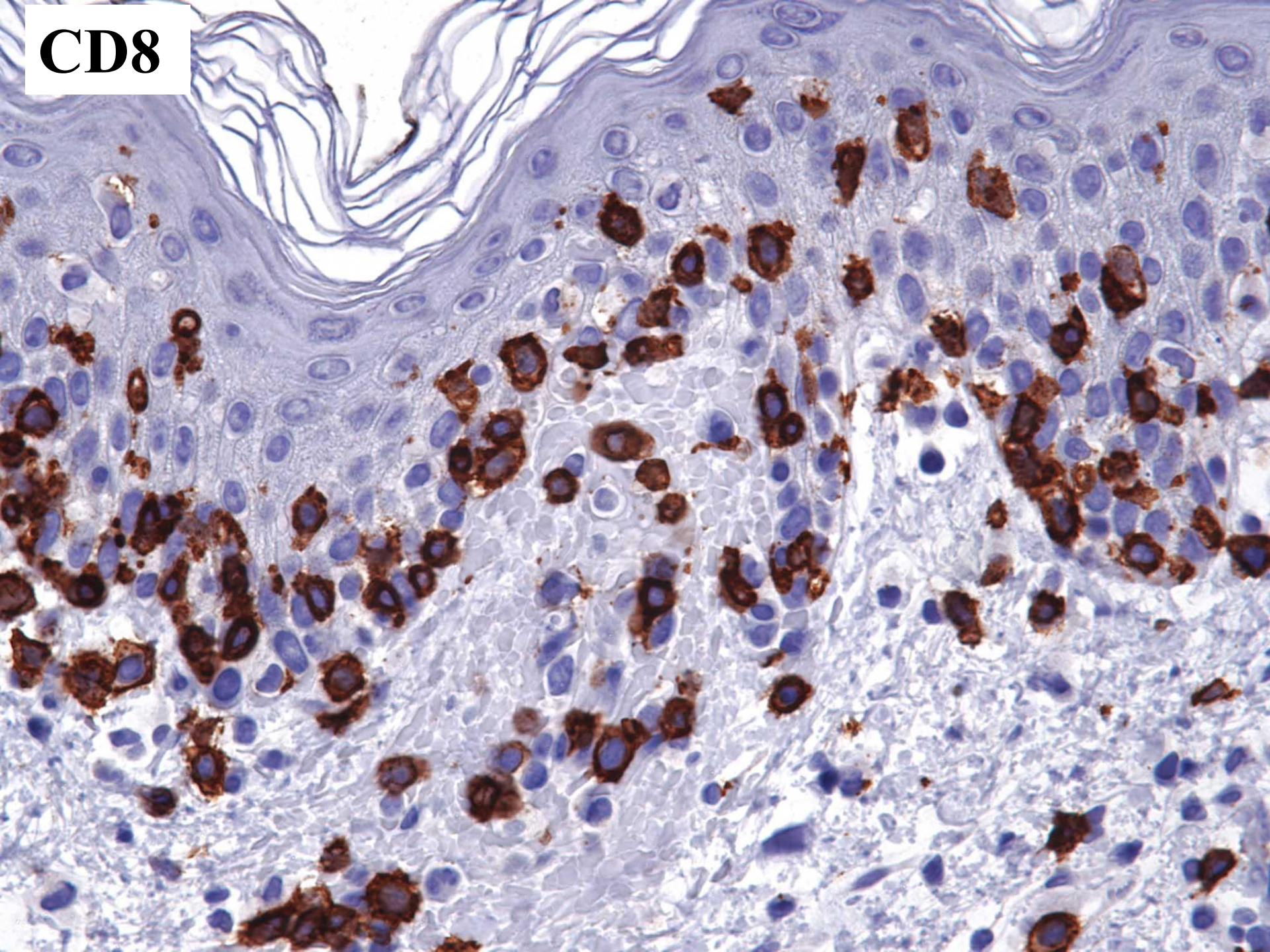


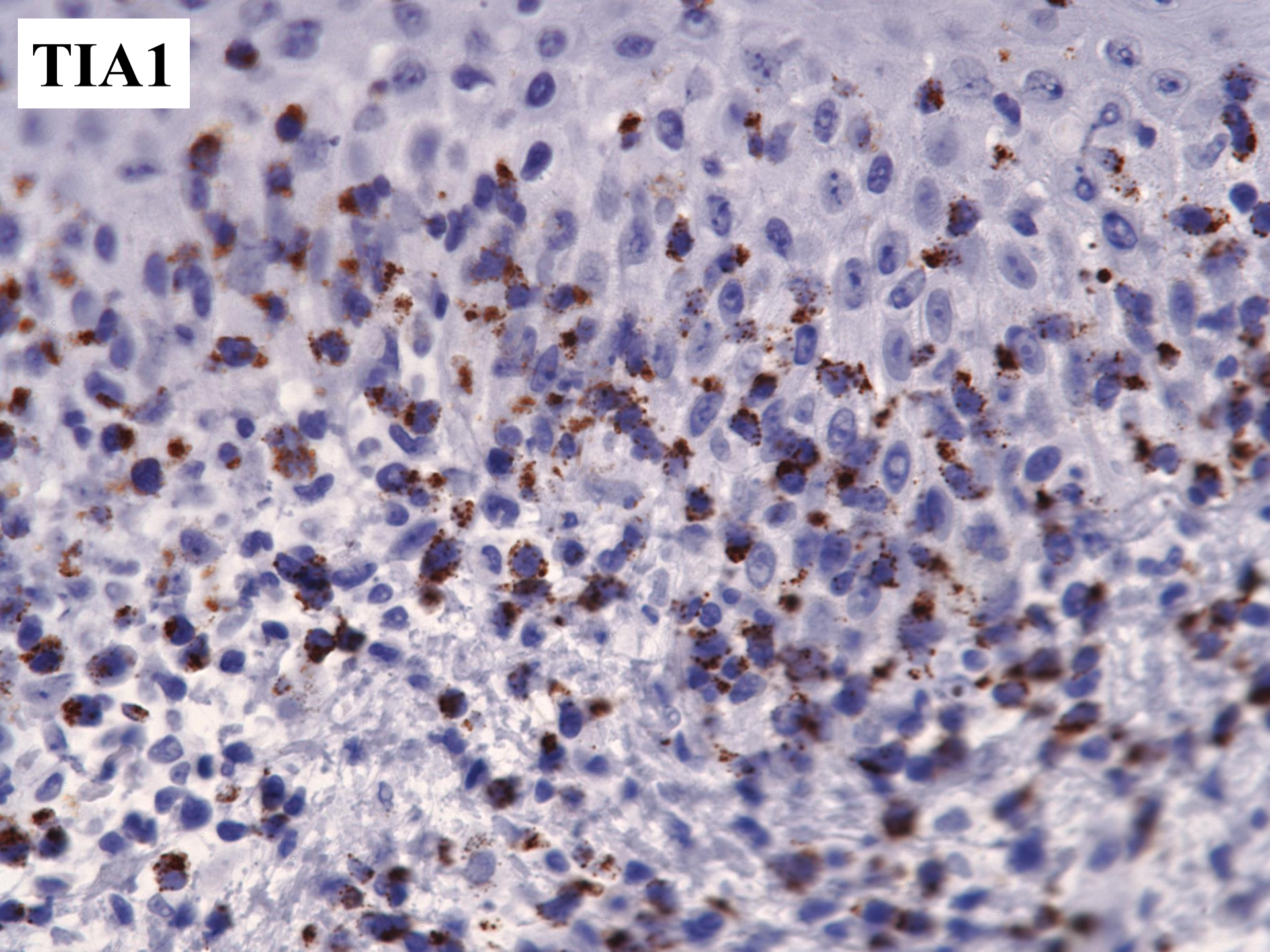




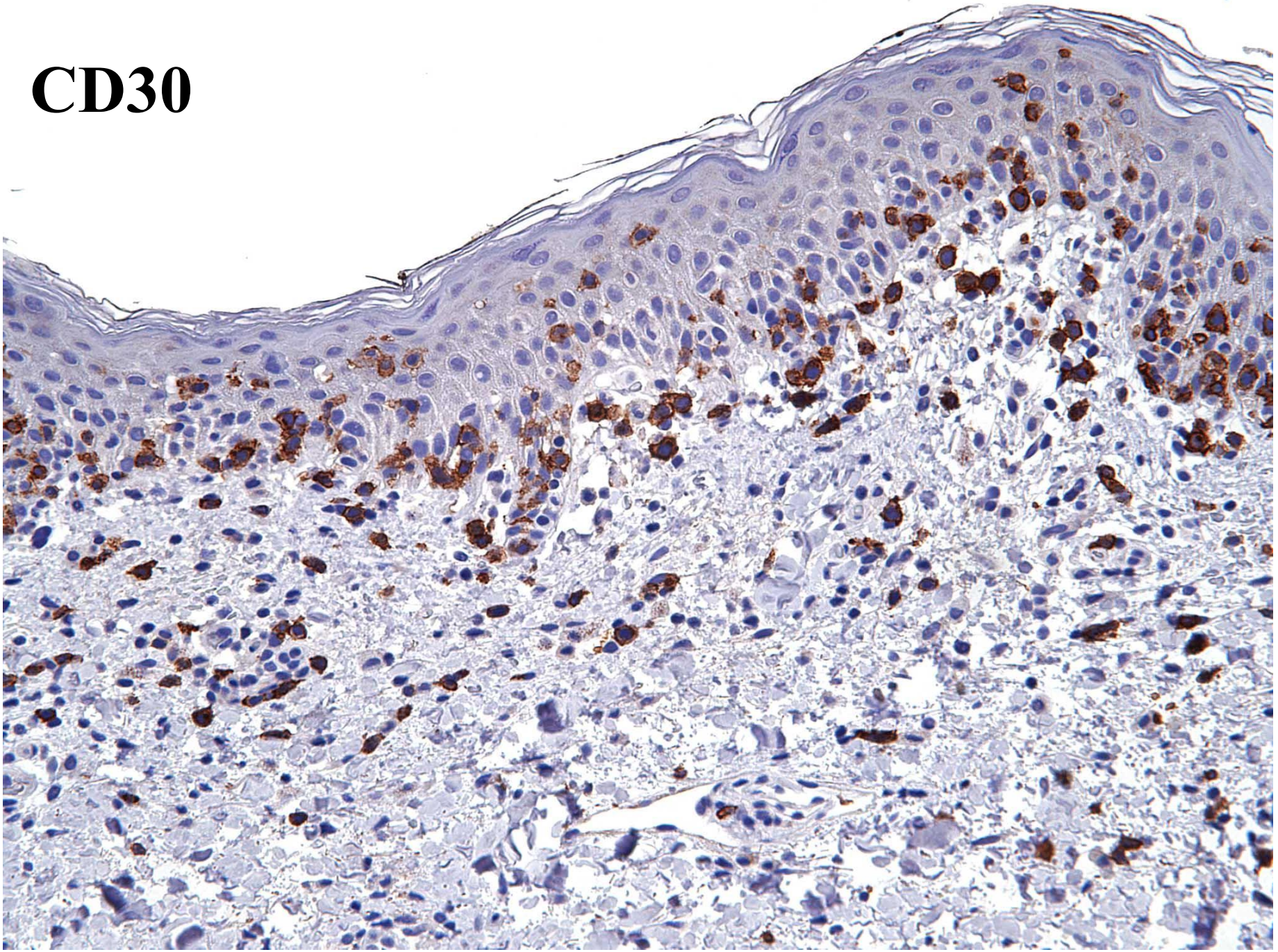
CD4




CD8

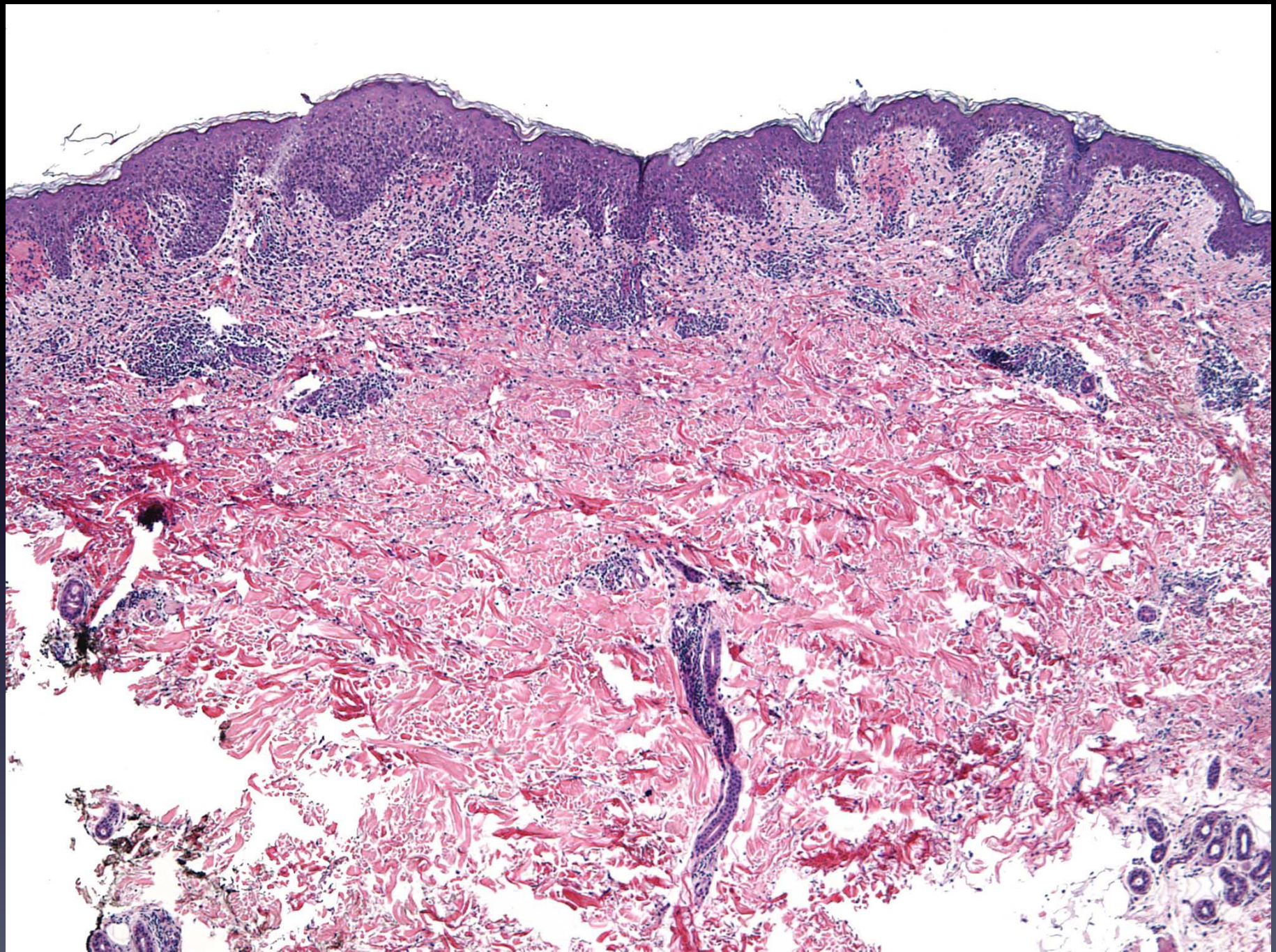

TIA1

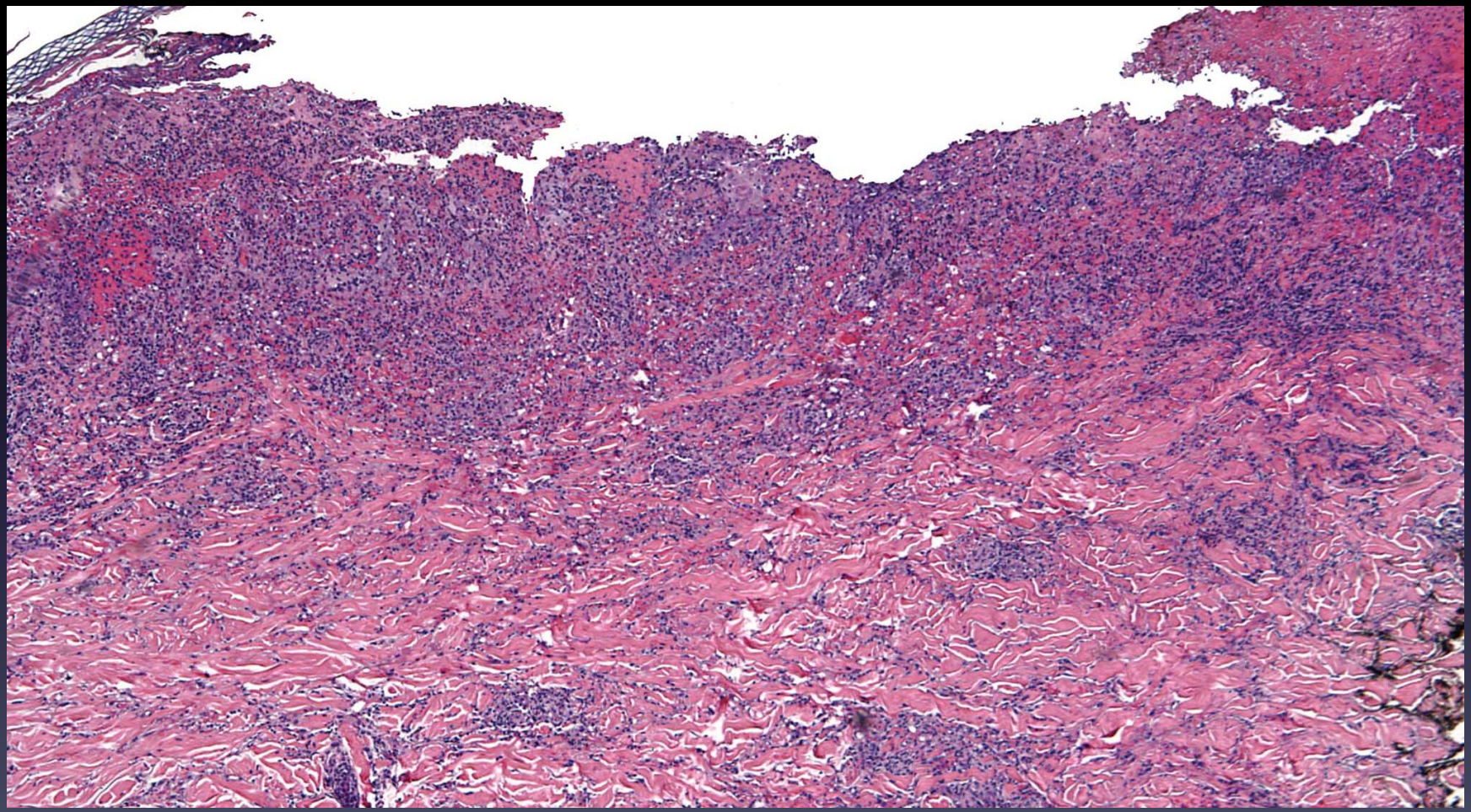
CD30

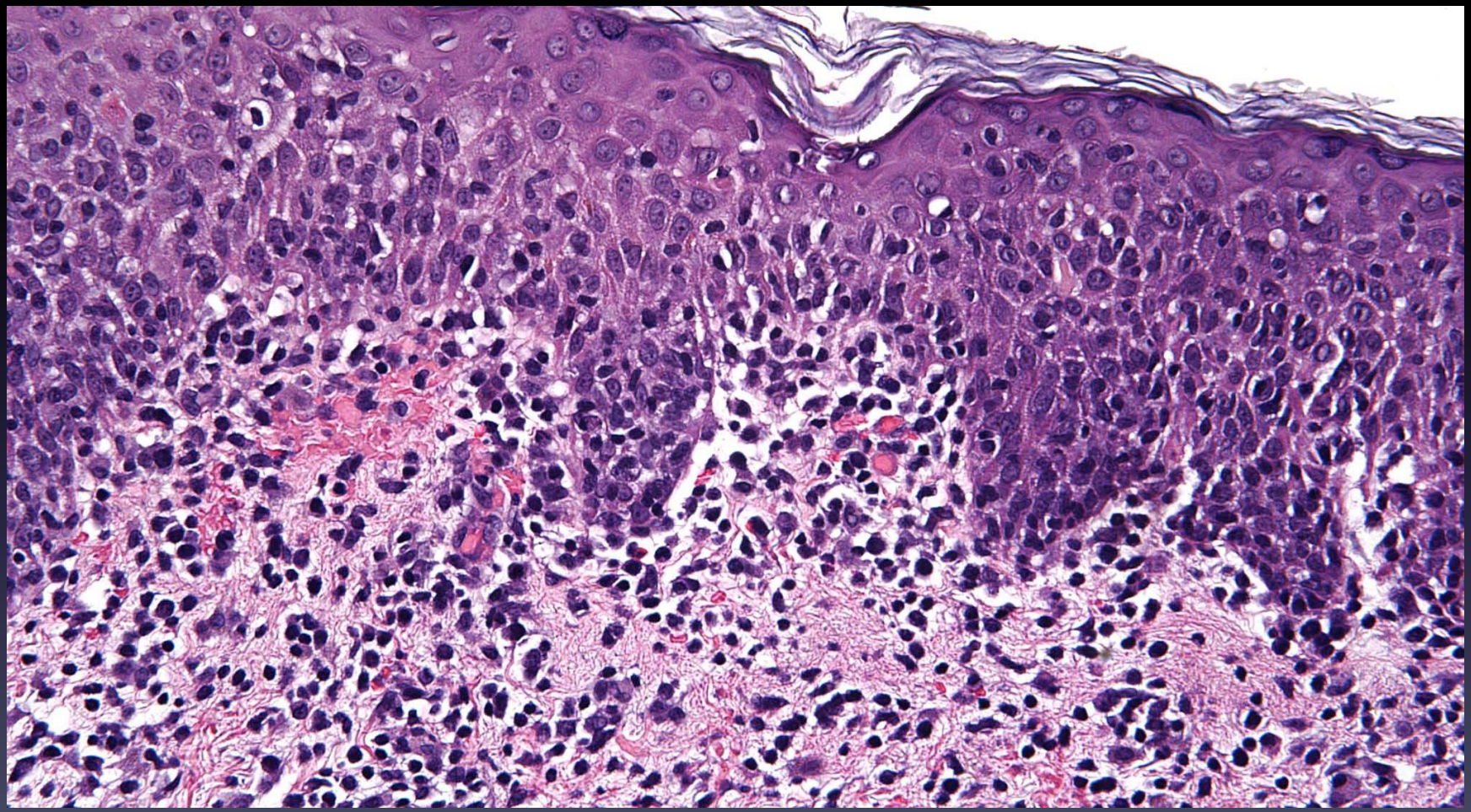


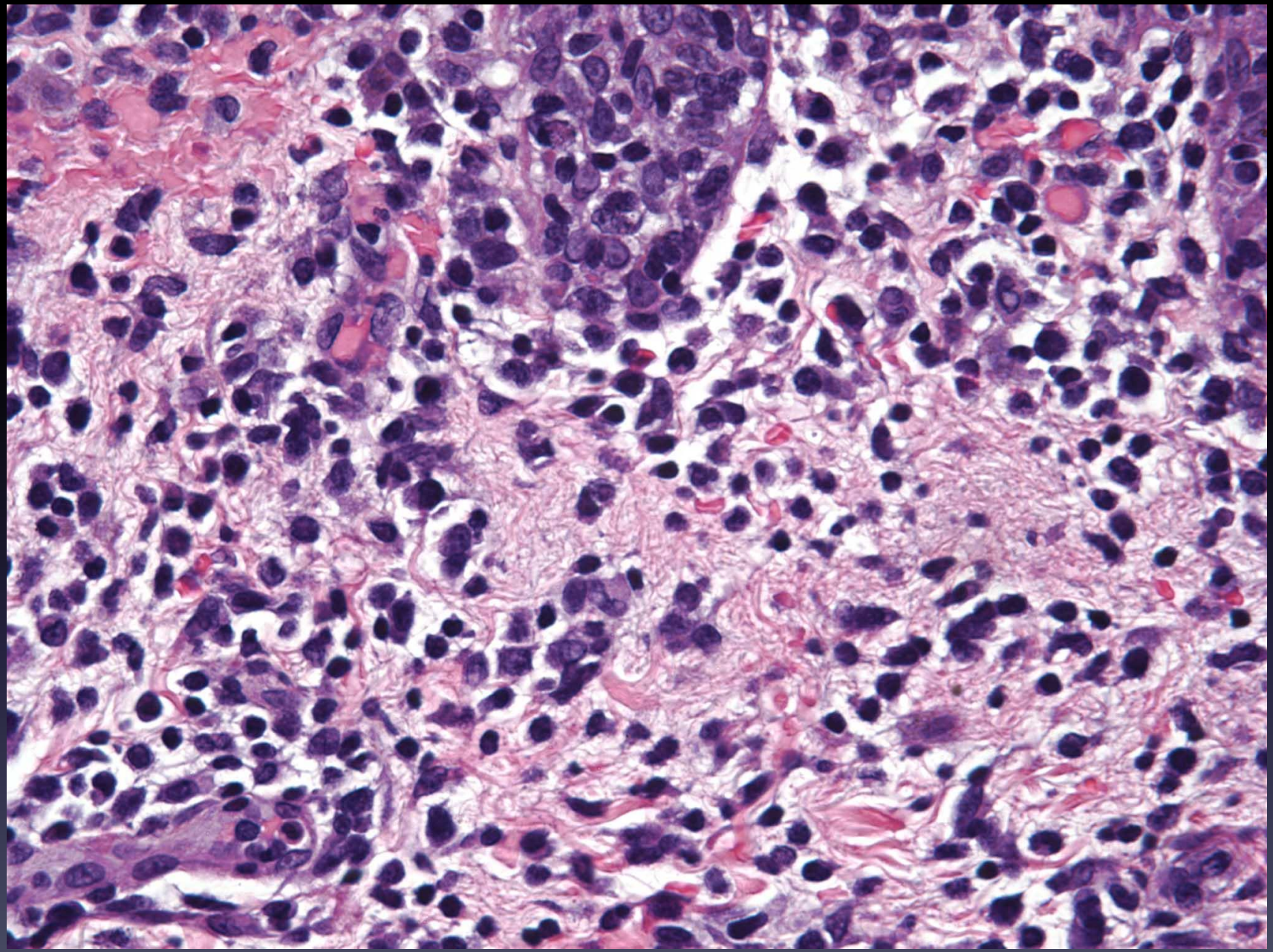
DIAGNOSIS?

- 76 year-old man with a 2-month history of erythematous to violaceous papules present on his extremities, trunk and back

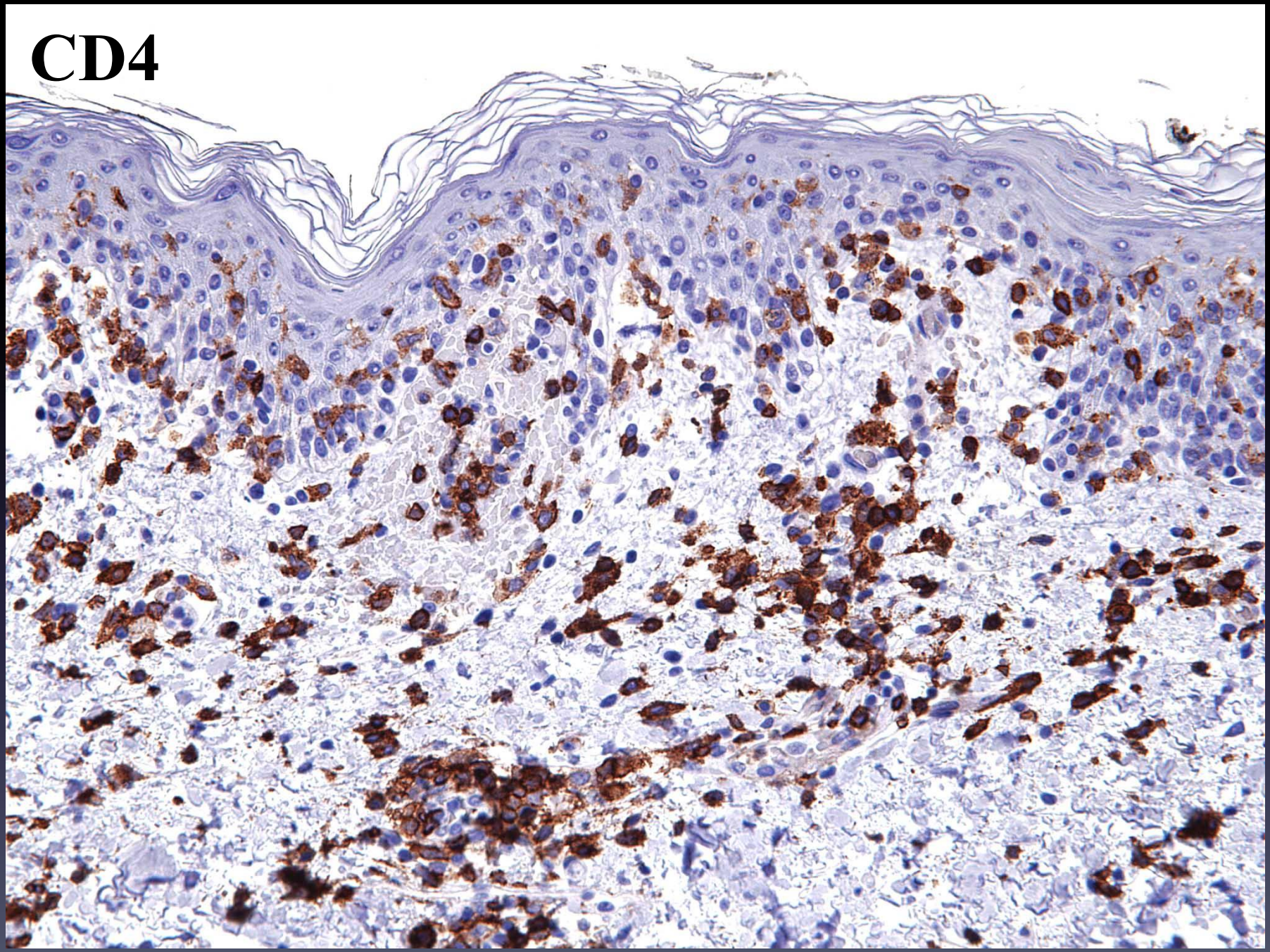


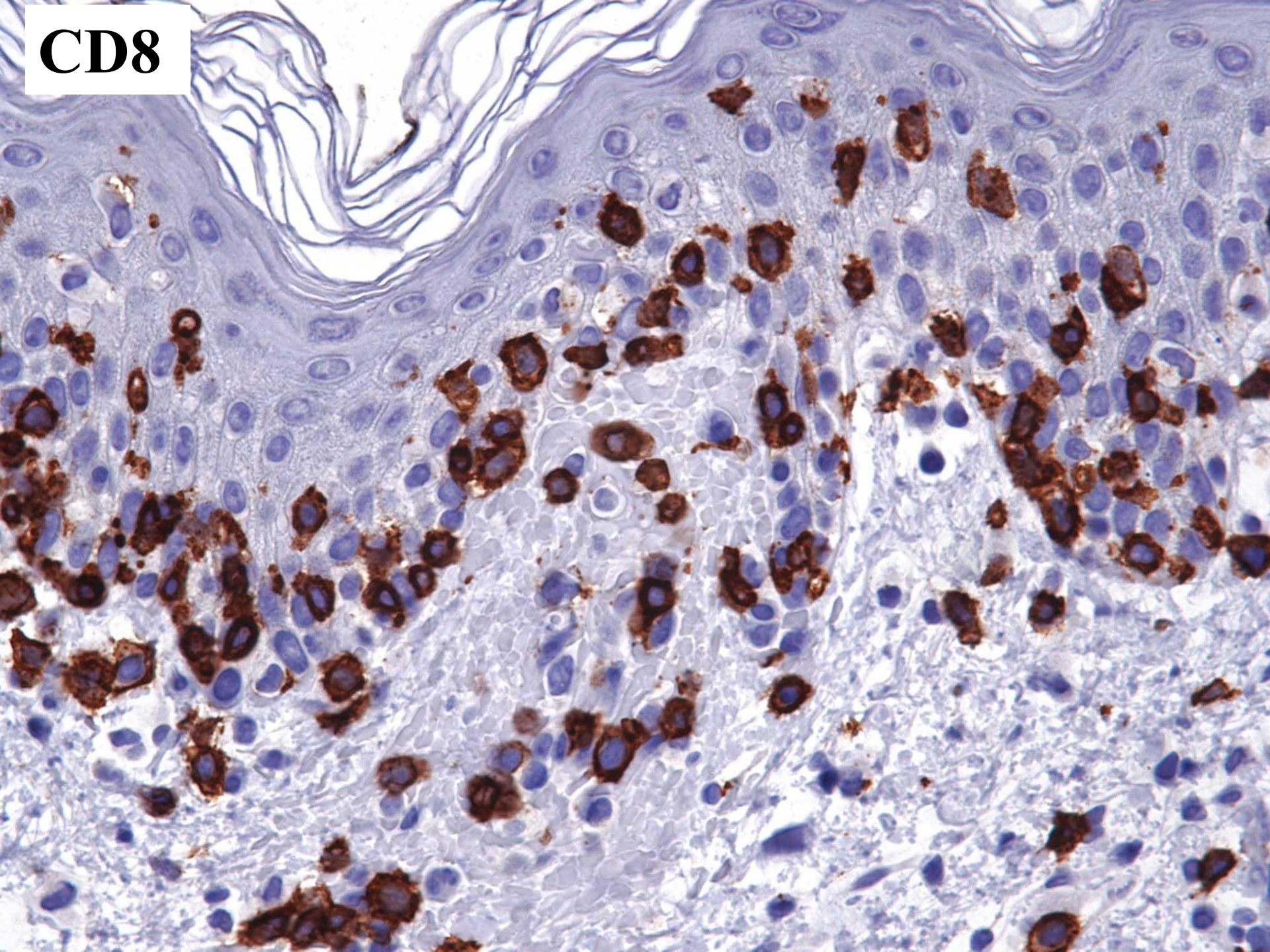


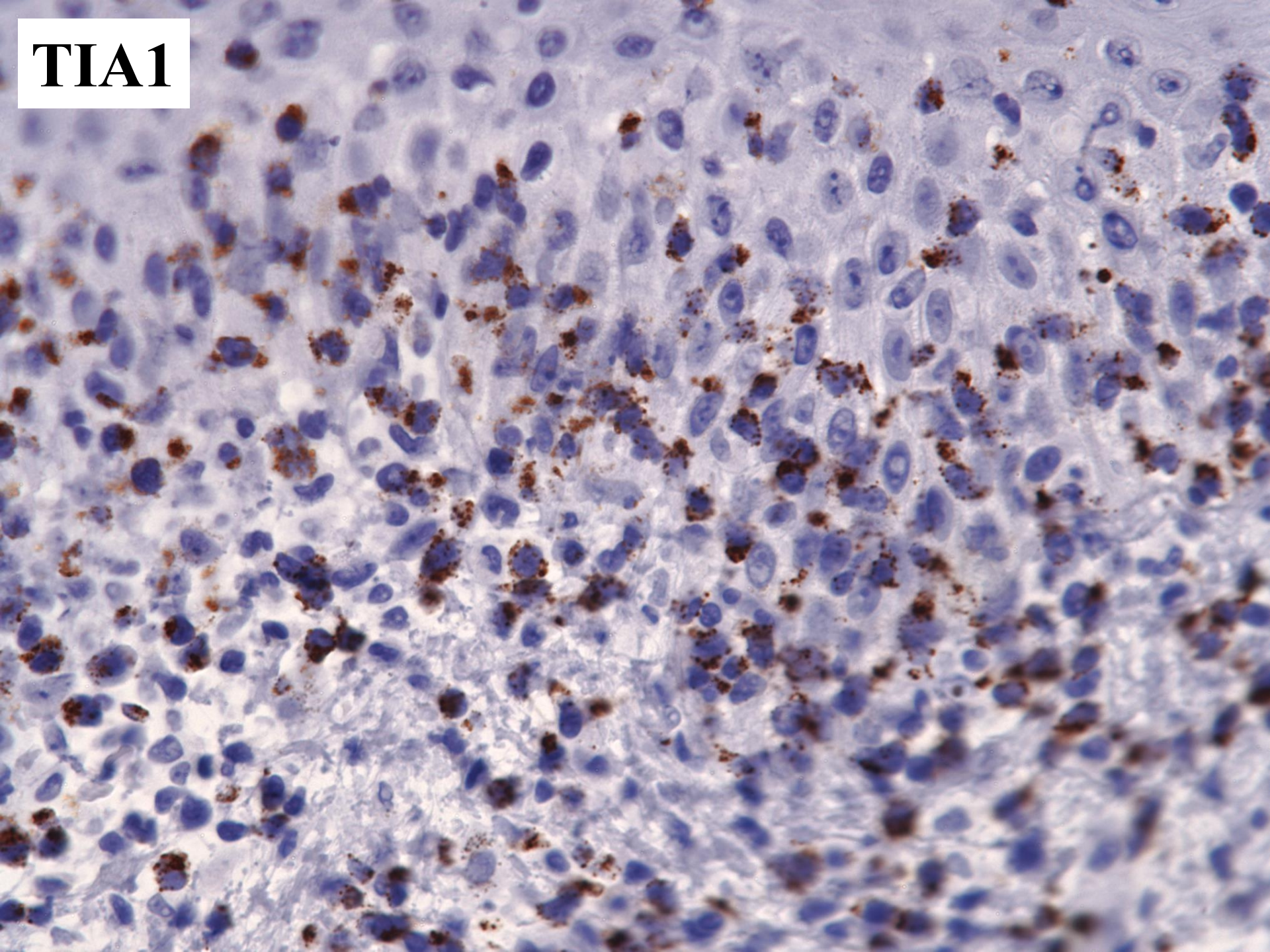




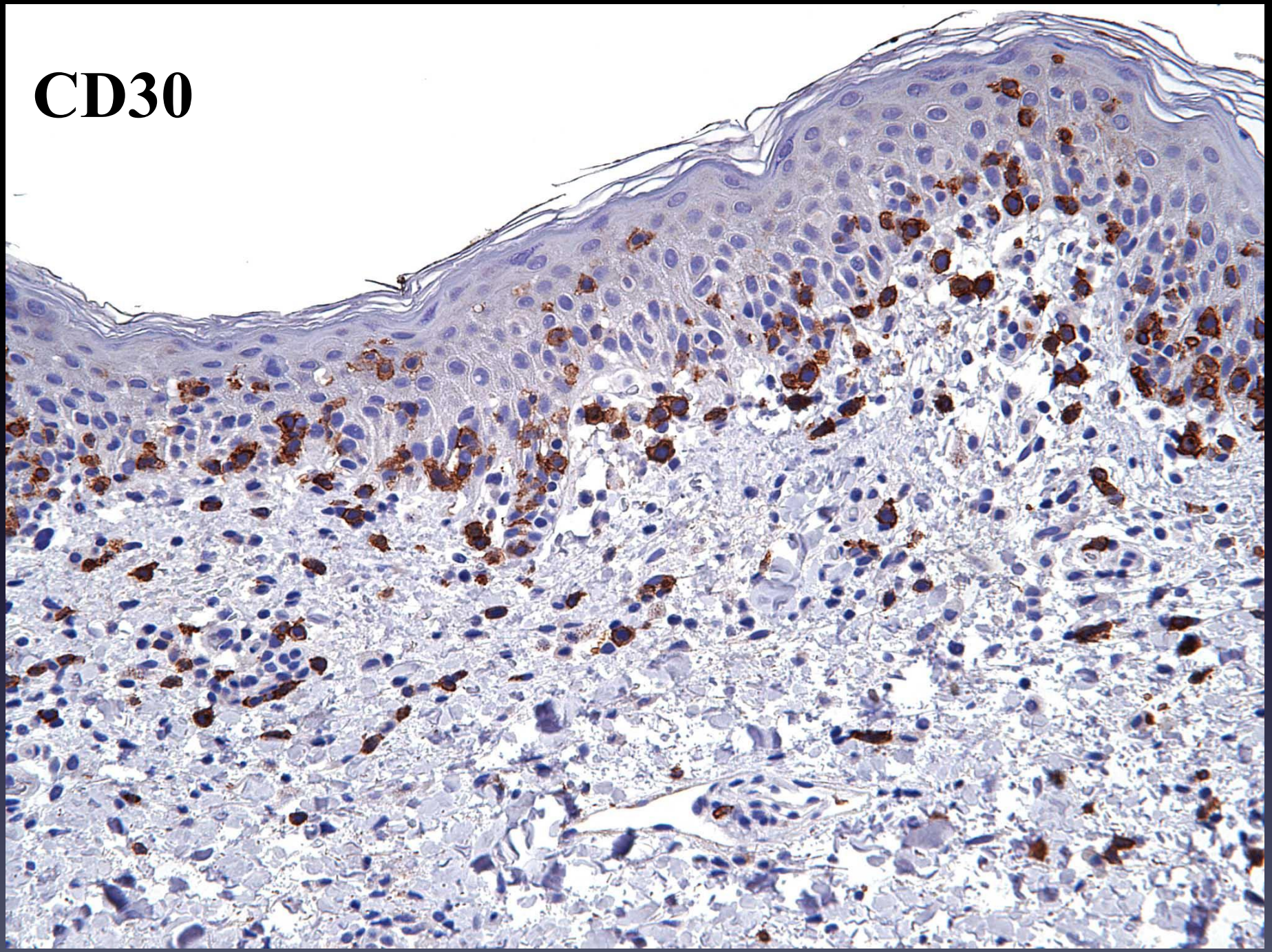
CD4




CD8


TIA1

CD30



Diagnosis?

Differential diagnosis:

- Aggressive epidermotropic CD8+ T cell lymphoma
- CD8+ MF
- LyP, type D

CD8+ cytotoxic T-cell lymphoma

- Rapid onset of patches, plaques, nodules and tumors
- Ulcerations and necrosis
- Aggressive course with a median survival of 32 months

LyP, Type D

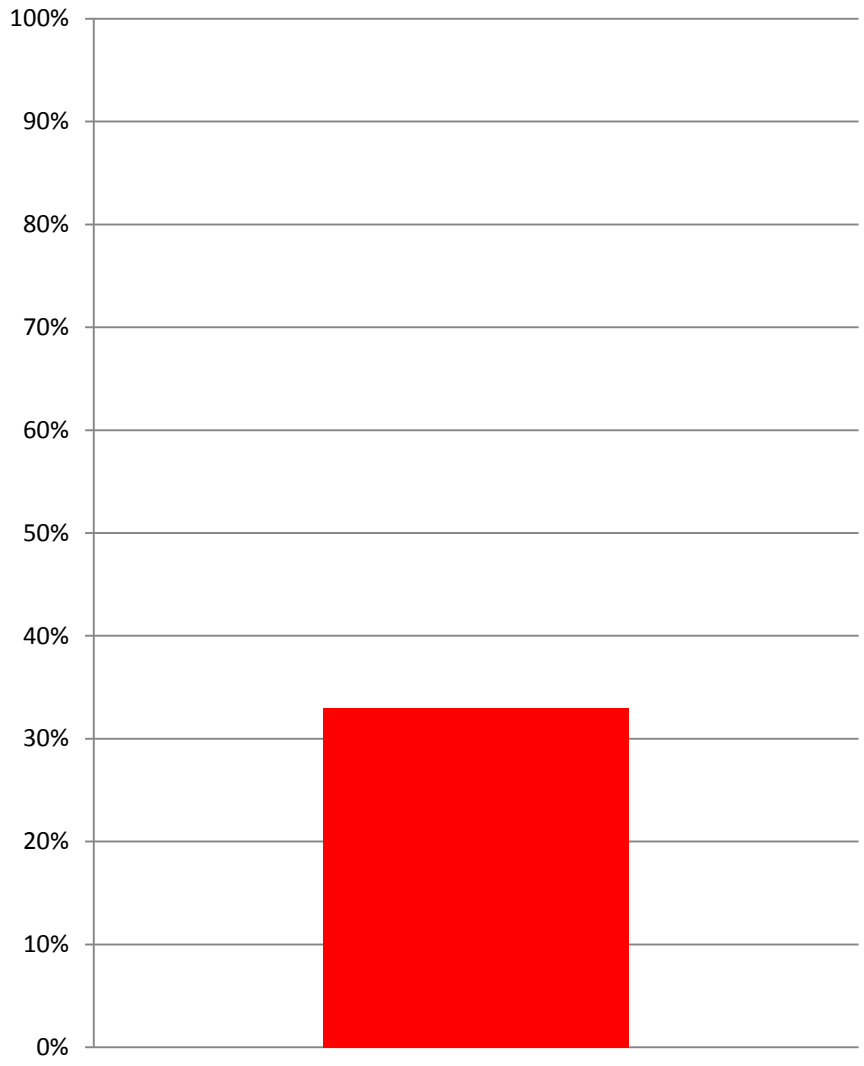
- Indolent waxing, waning clinical course
- Crops of papules, nodules
- May ulcerate
- Important to avoid overtreatment

Membership Dues

- 2014:
  - 107 memberships
- 2015:
  - YTD: 35 memberships
  - 4 new members!!!

PLEASE GET YOUR DUES PAID BY MARCH 31.

  - $50 late fee after March 31



South Bay Pathology Society

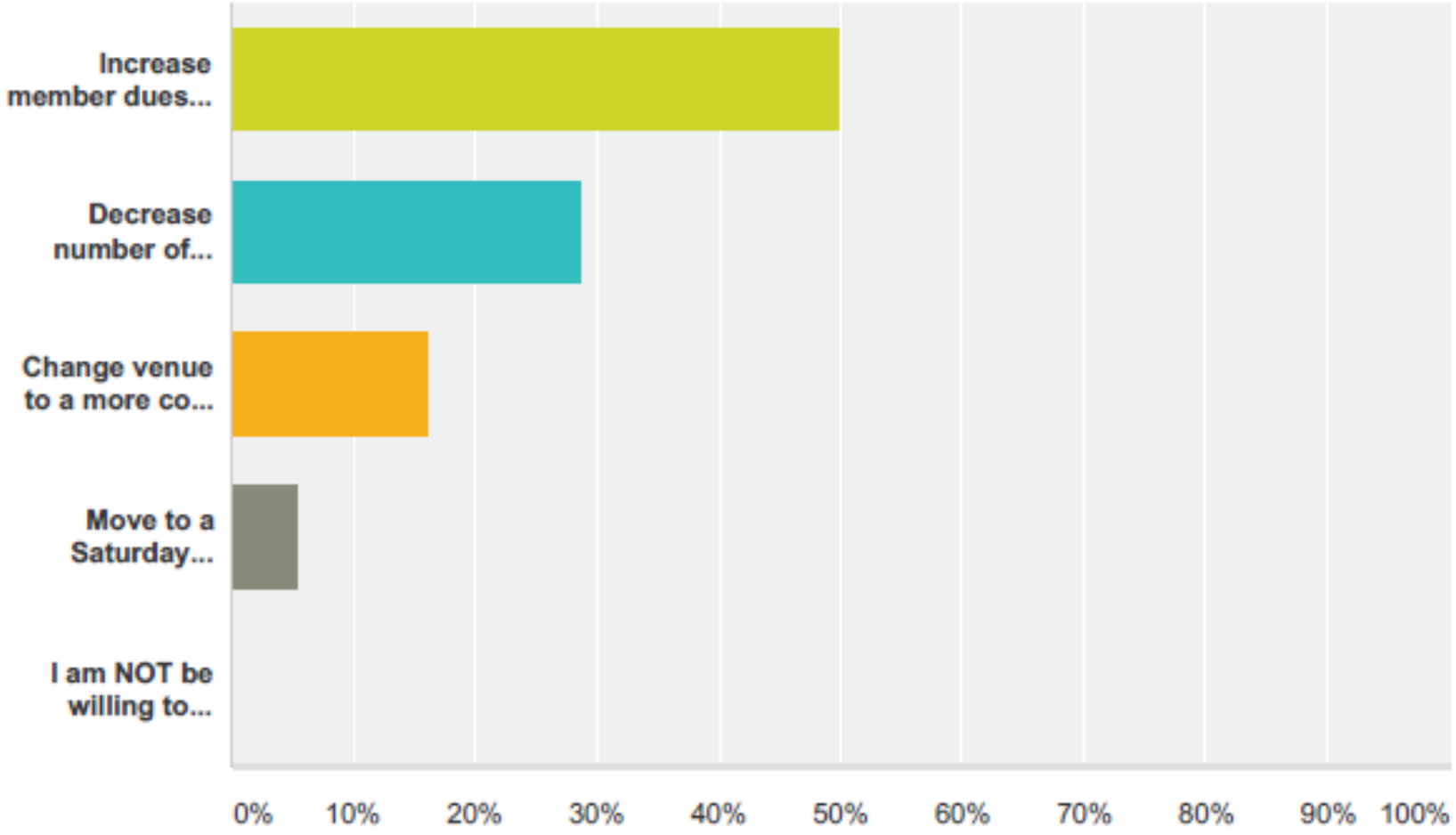
2014 Member Survey

2014 Member Survey

- Sent somewhat urgently with question about raising annual dues because of financial situation and need to contract with Garden Court Hotel for 2015
- Sent to current membership roster
- Completed by 56 individuals

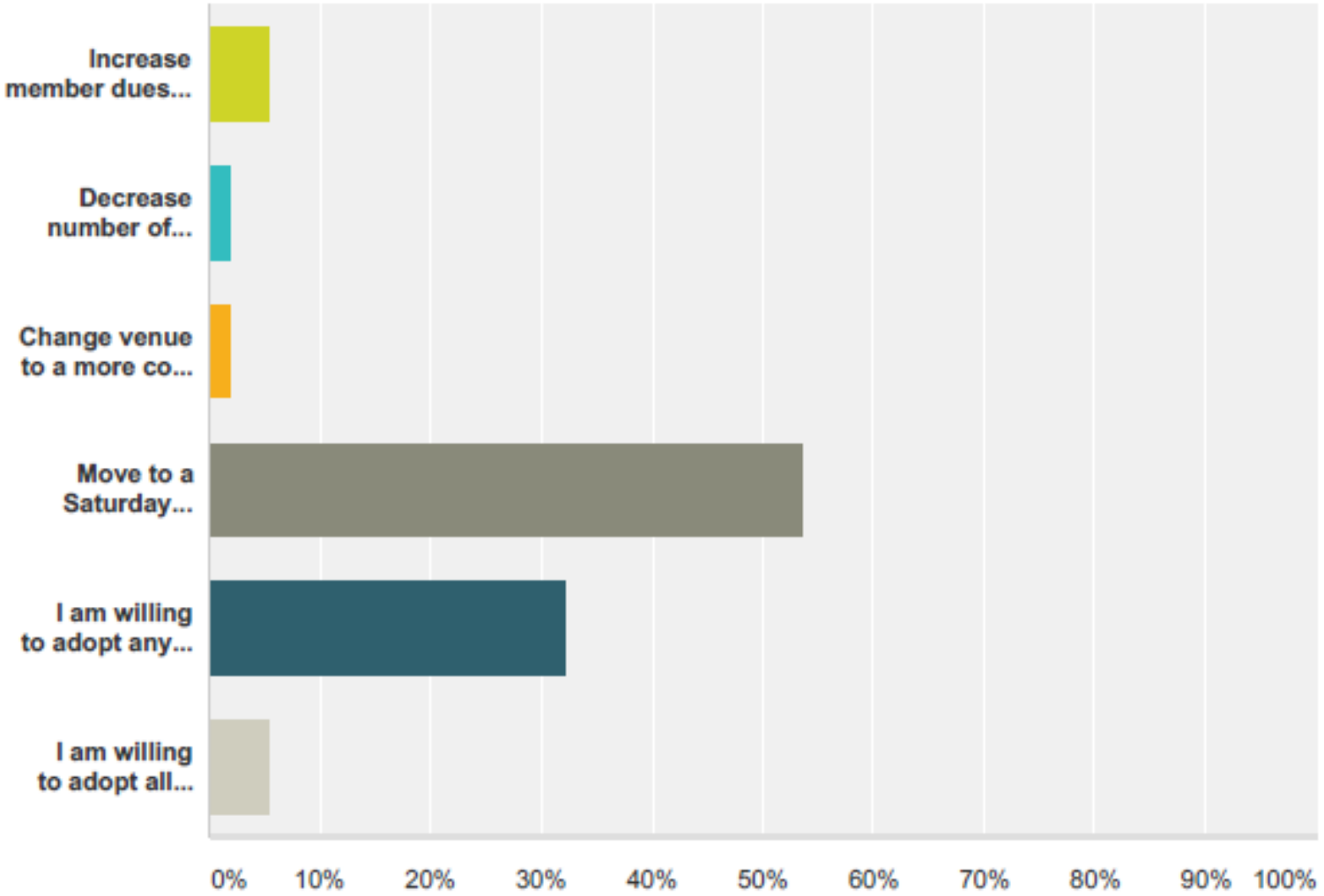
Q1 Which ONE of the following options would you be willing to adopt to maintain the Society's financial viability?

Answered: 56 Skipped: 0



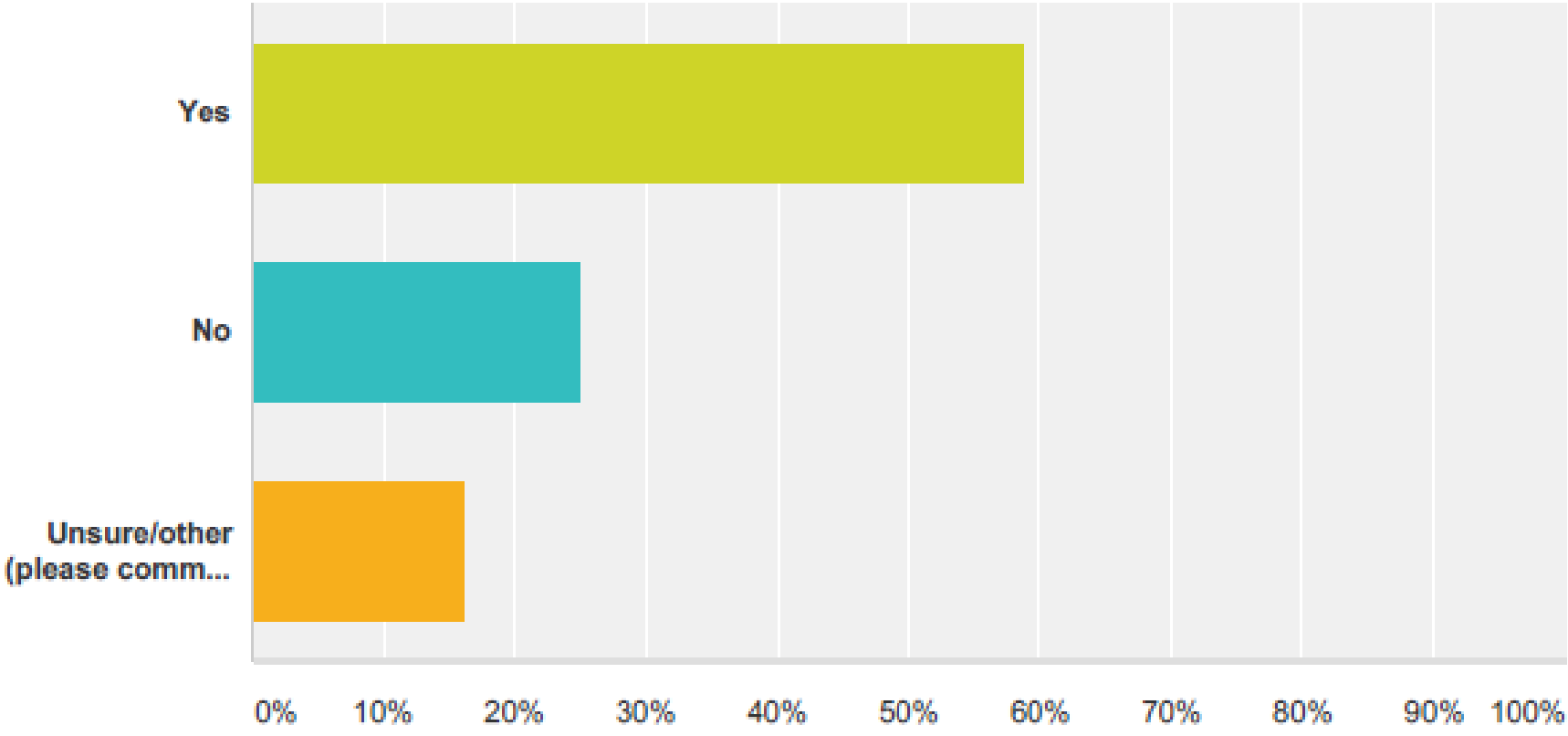
Q2 Which ONE of the following options would you absolutely refuse to adopt in order to maintain the Society's financial viability?

Answered: 56 Skipped: 0



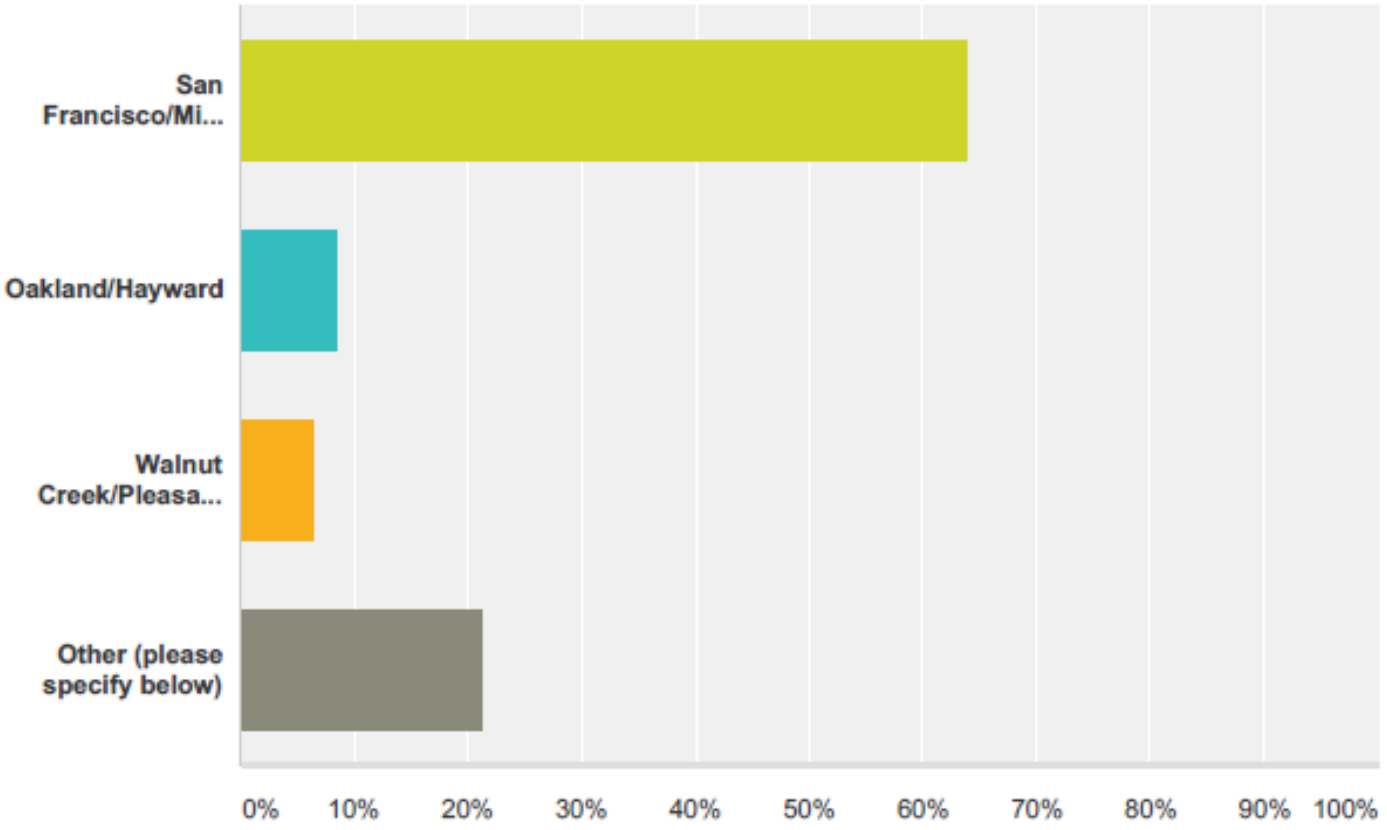
Q3 If the only way for the Society to remain financially viable is to move some meetings outside of Palo Alto, would you vote in favor of changing the by-laws?

Answered: 56 Skipped: 0



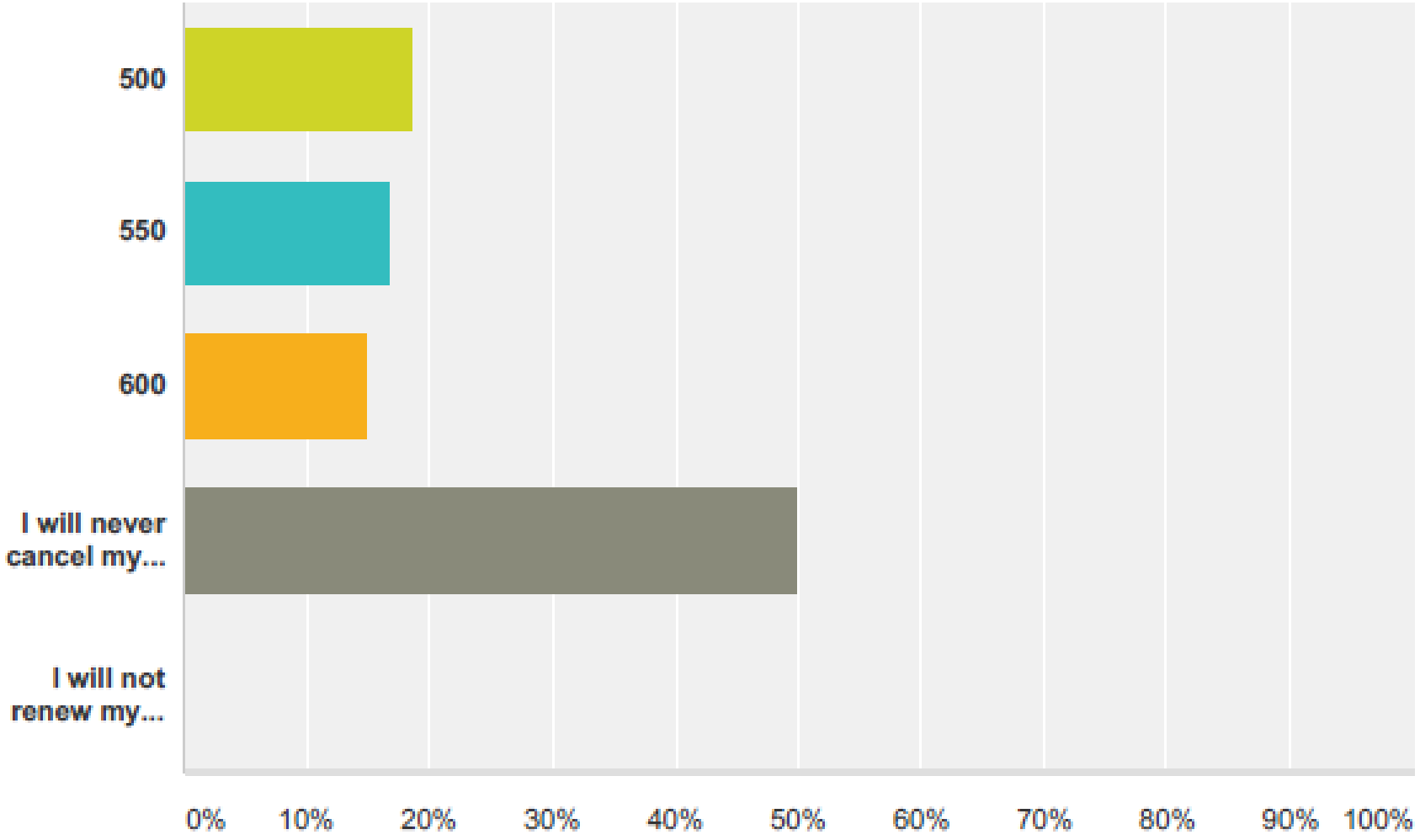
Q4 Currently, the by-laws do NOT allow the meeting to be held outside of the South Bay and Mid Peninsula. Assuming the Society changes the by-laws and the majority of the membership approves the ability to host the meeting in an alternate venue ... what region should the alternate venue be?

Answered: 47 Skipped: 9



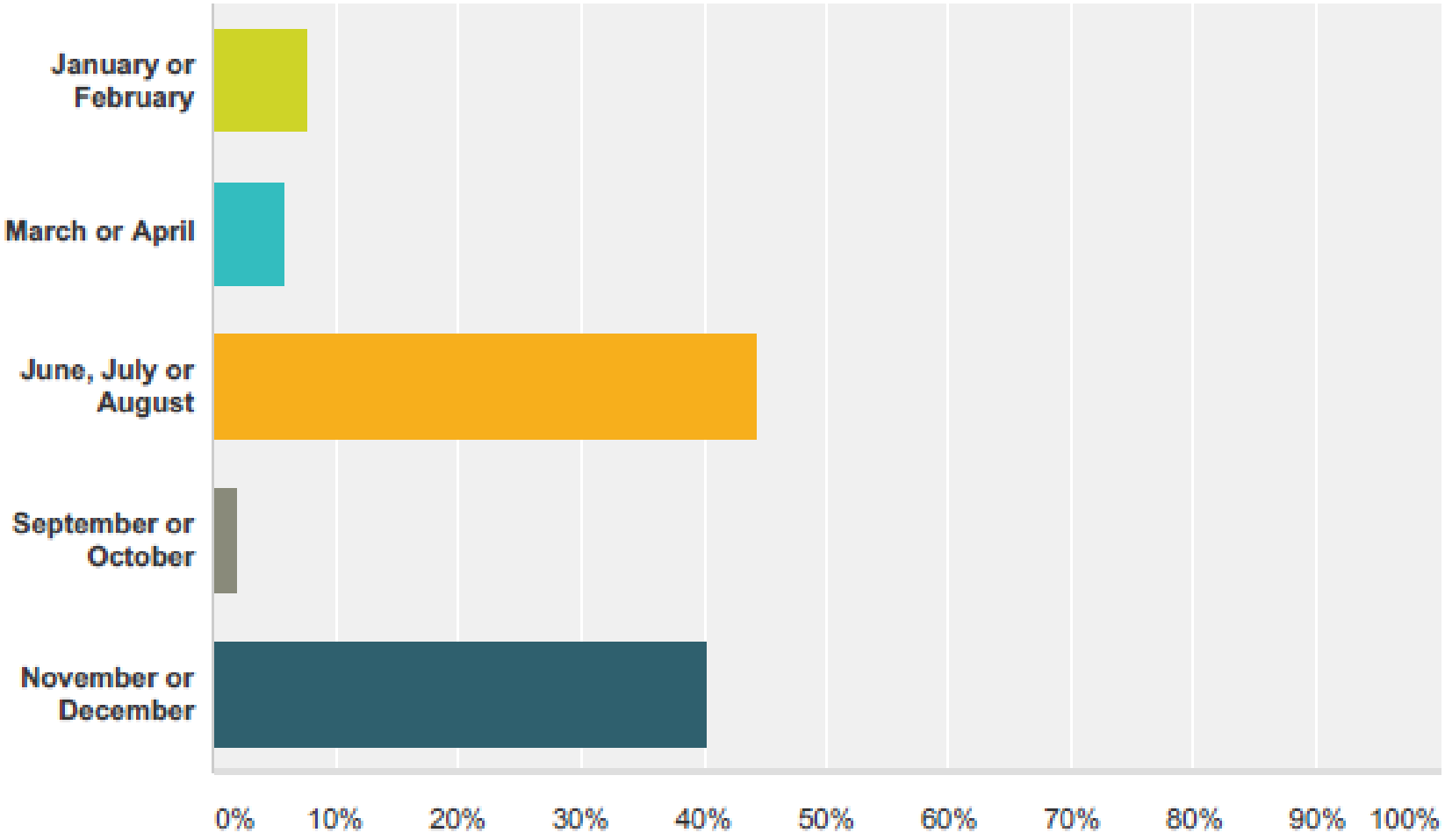
Q6 Currently, the membership dues are $450. At what point would you NOT renew your membership?

Answered: 54 Skipped: 2



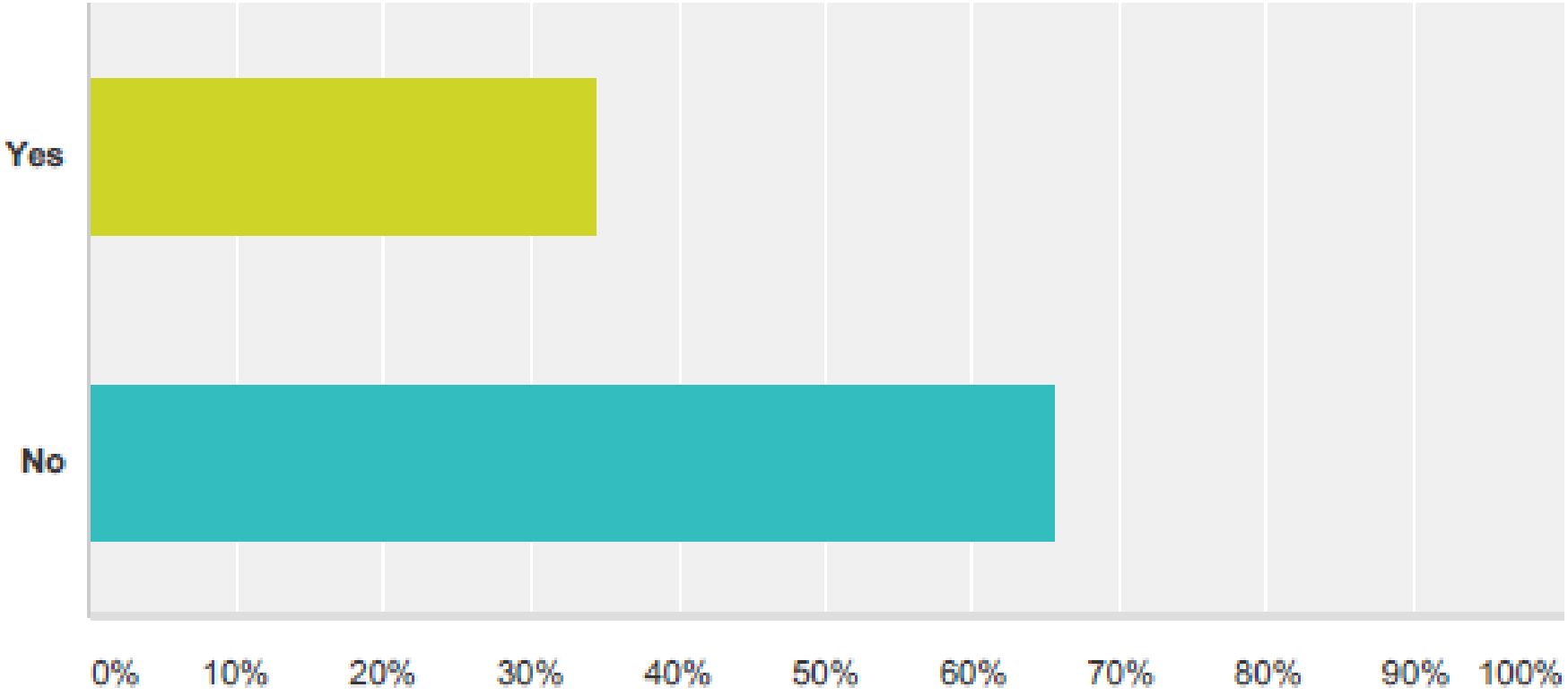
Q7 If the Society had to reduce the number of meetings from 11 to 10, when should we skip a meeting?

Answered: 52 Skipped: 4



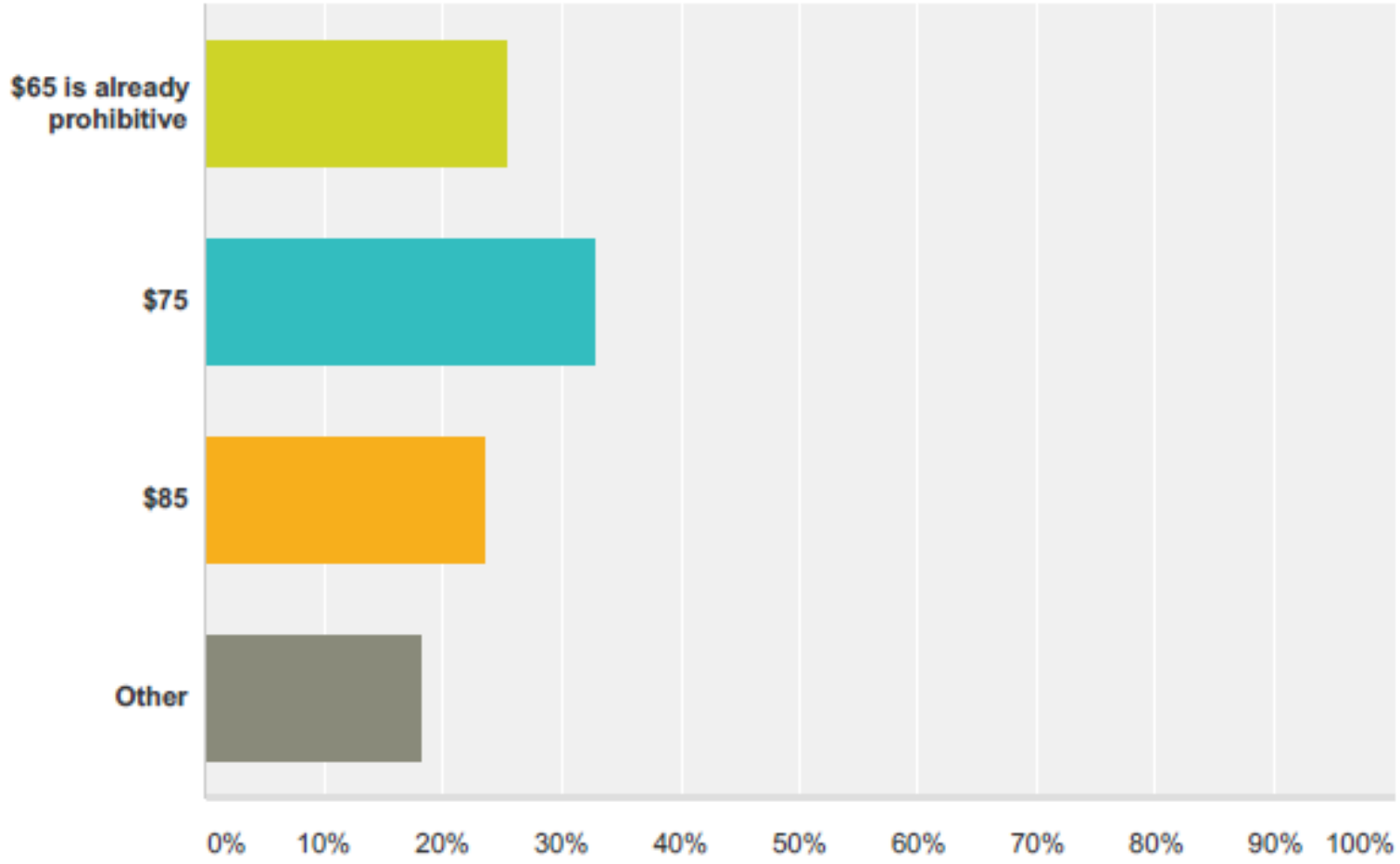
Q8 If the general membership voted in favor of moving one or some meetings to Saturday, would you attend?

Answered: 55 Skipped: 1



Q13 The current guest fee is $65 per meeting, which covers the cost of the meal and wine. At what point would you consider the guest fee prohibitive?

Answered: 55 Skipped: 1



Q14 If the Society determines that a decreased membership for first year members (many of whom may be fresh out of residency or fellowship) in order to attract more members, what discounted rate would you consider appropriate?

Answered: 55 Skipped: 1