Disclosures
April 6, 2015

Dr. Keith Duncan has disclosed that he/his group received a consultation fee from Abbvie (Redwood City) and Oxford Biotherapeutics (San Jose) for review of immunohistochemical stains. Dr. Sonam Prakash has disclosed that she receives monetary benefits from Incyte Corporation as an advisor for the Hematopathology Publications Steering Committee. The activity planners have determined that these financial relationships are not relevant to the cases being presented.

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

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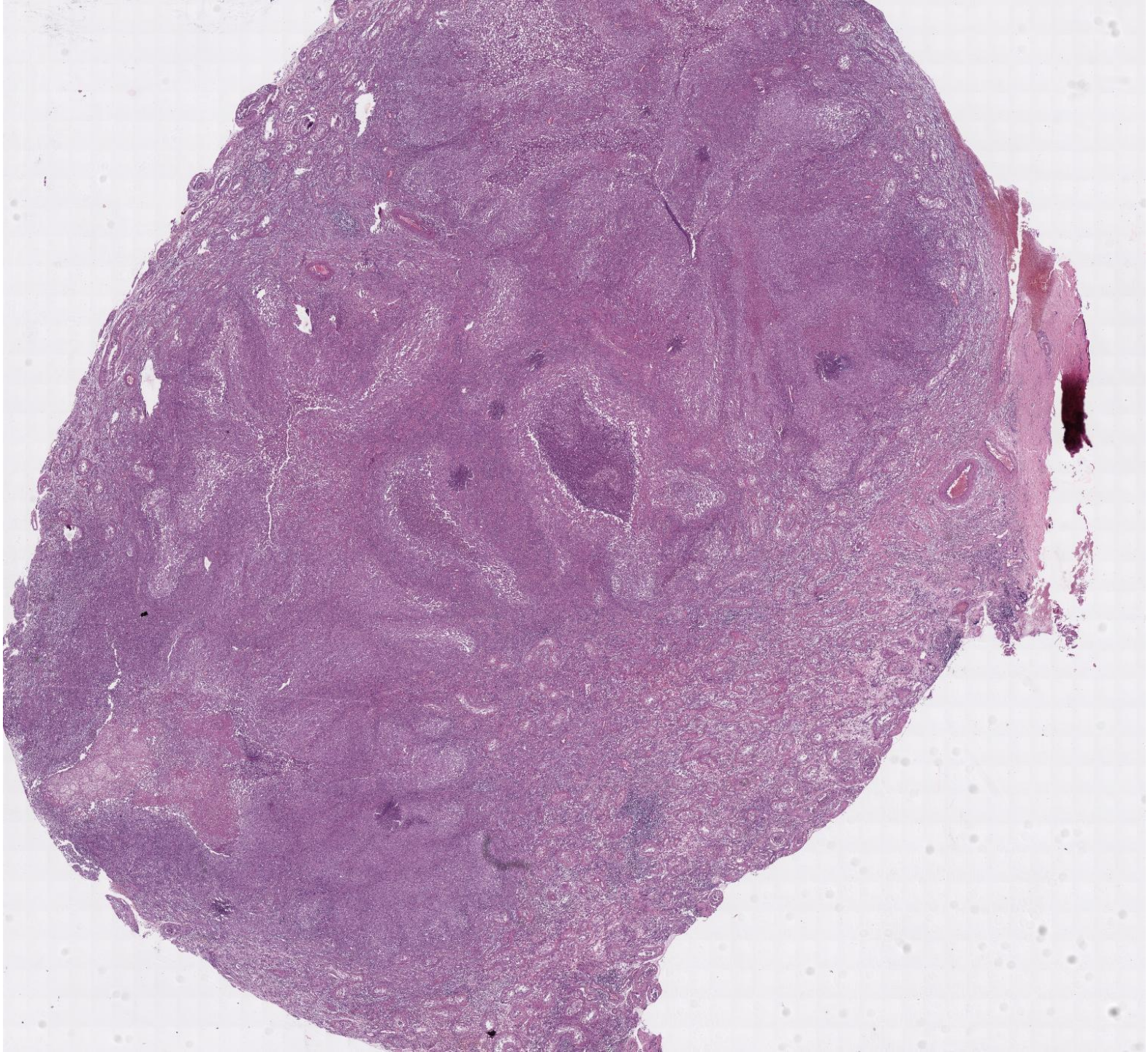
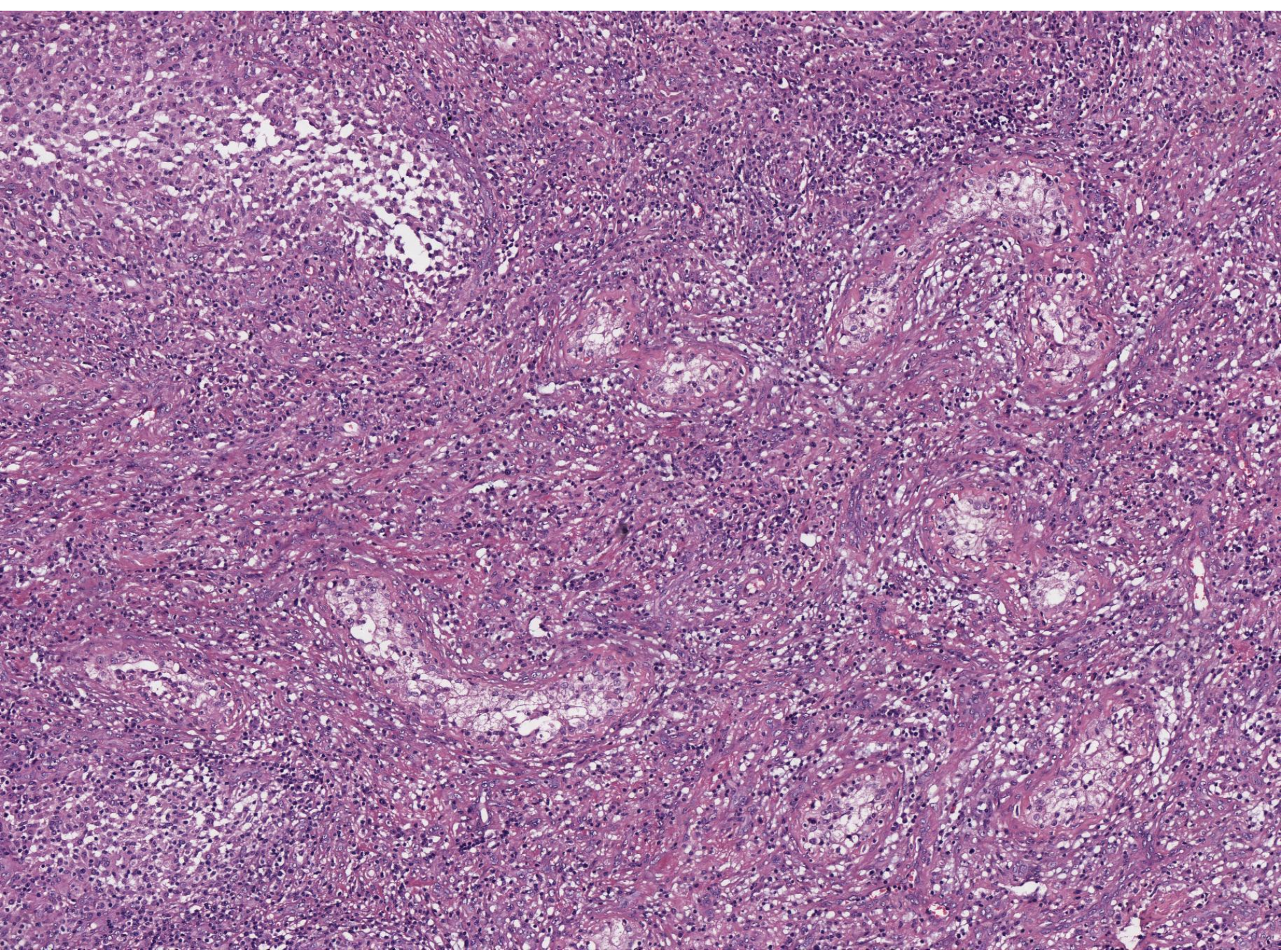
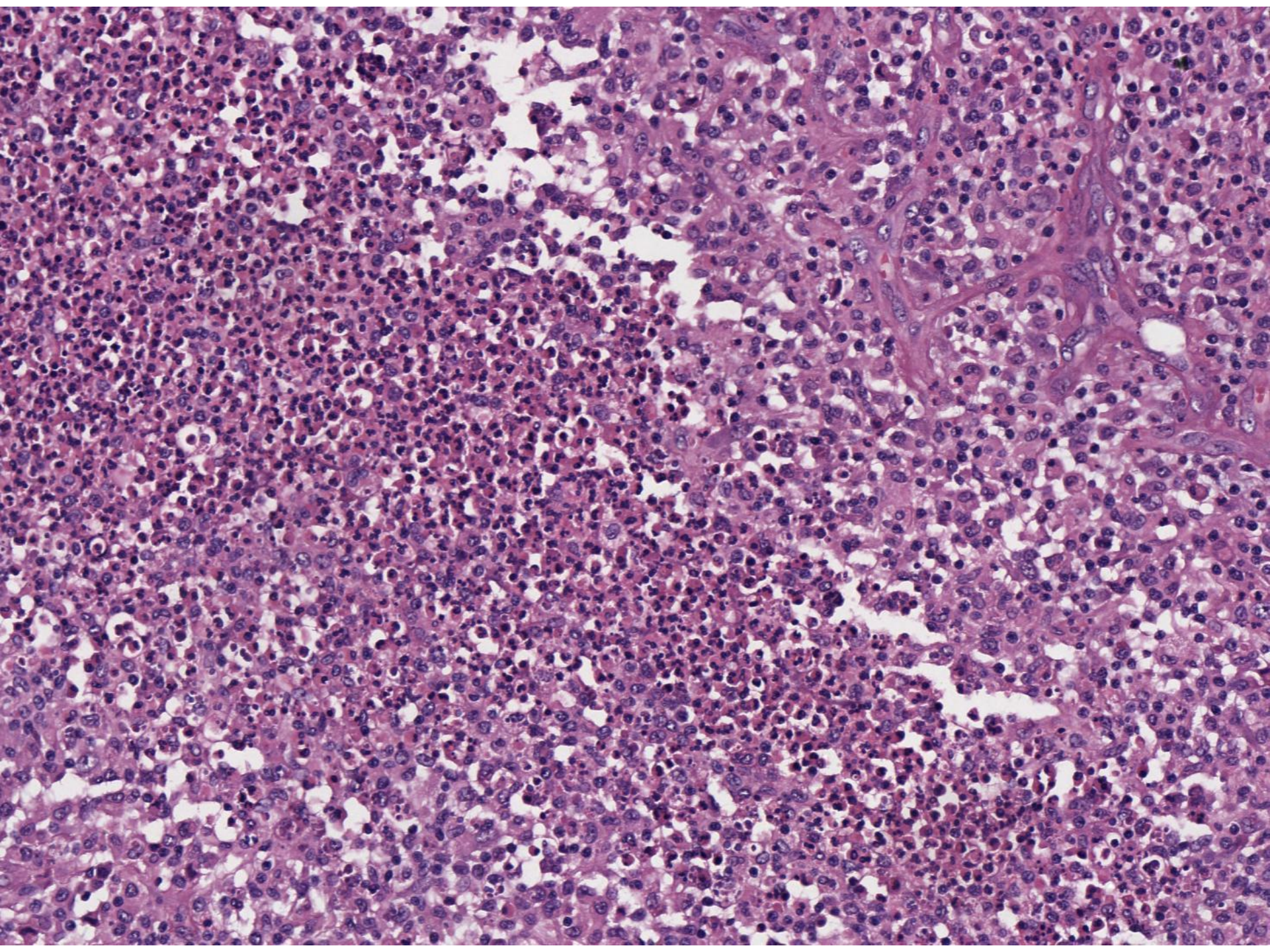
SB 5931

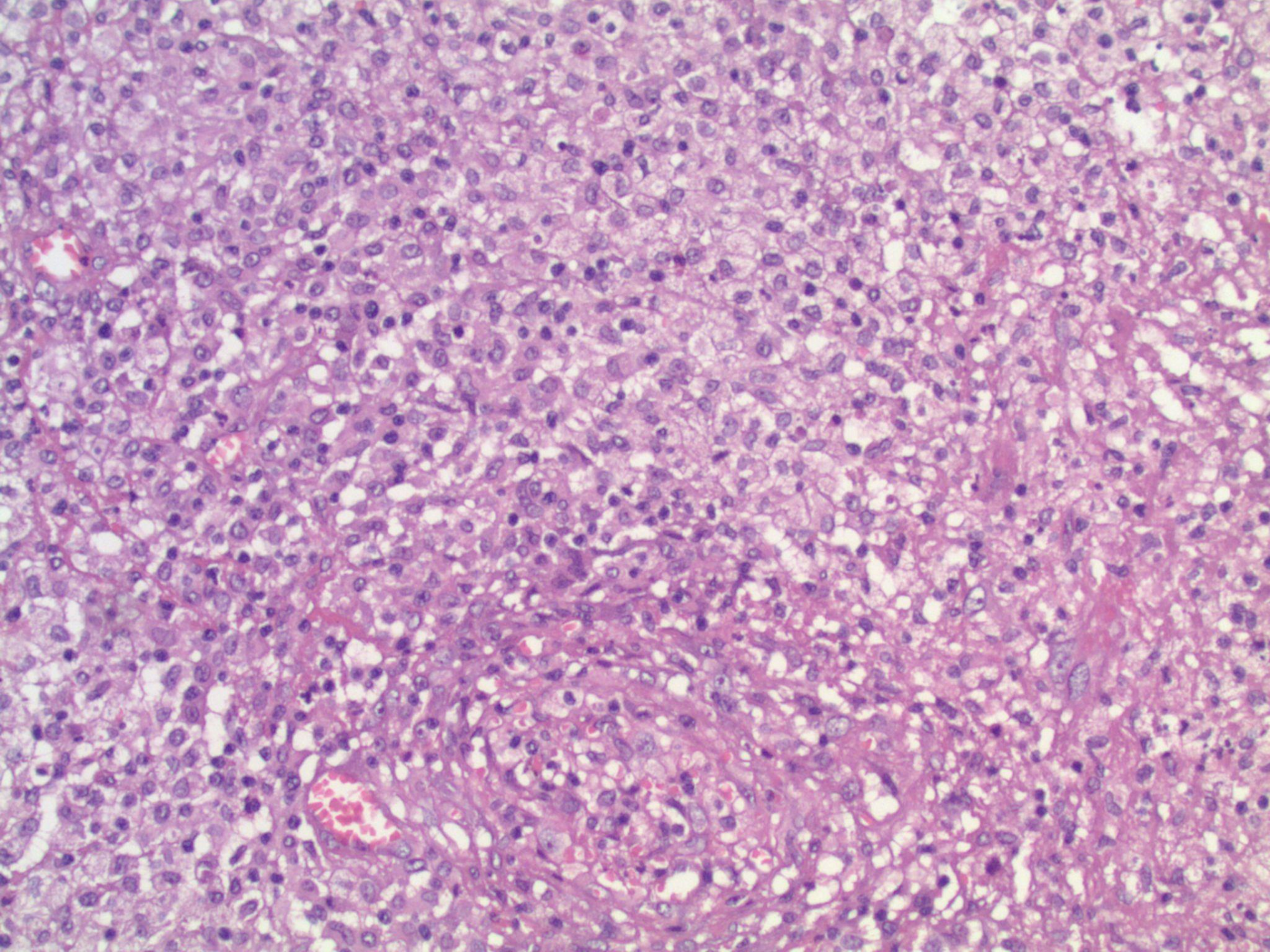
Nabeen Nayak; Sir Ganga Ram Hospital (New Delhi)

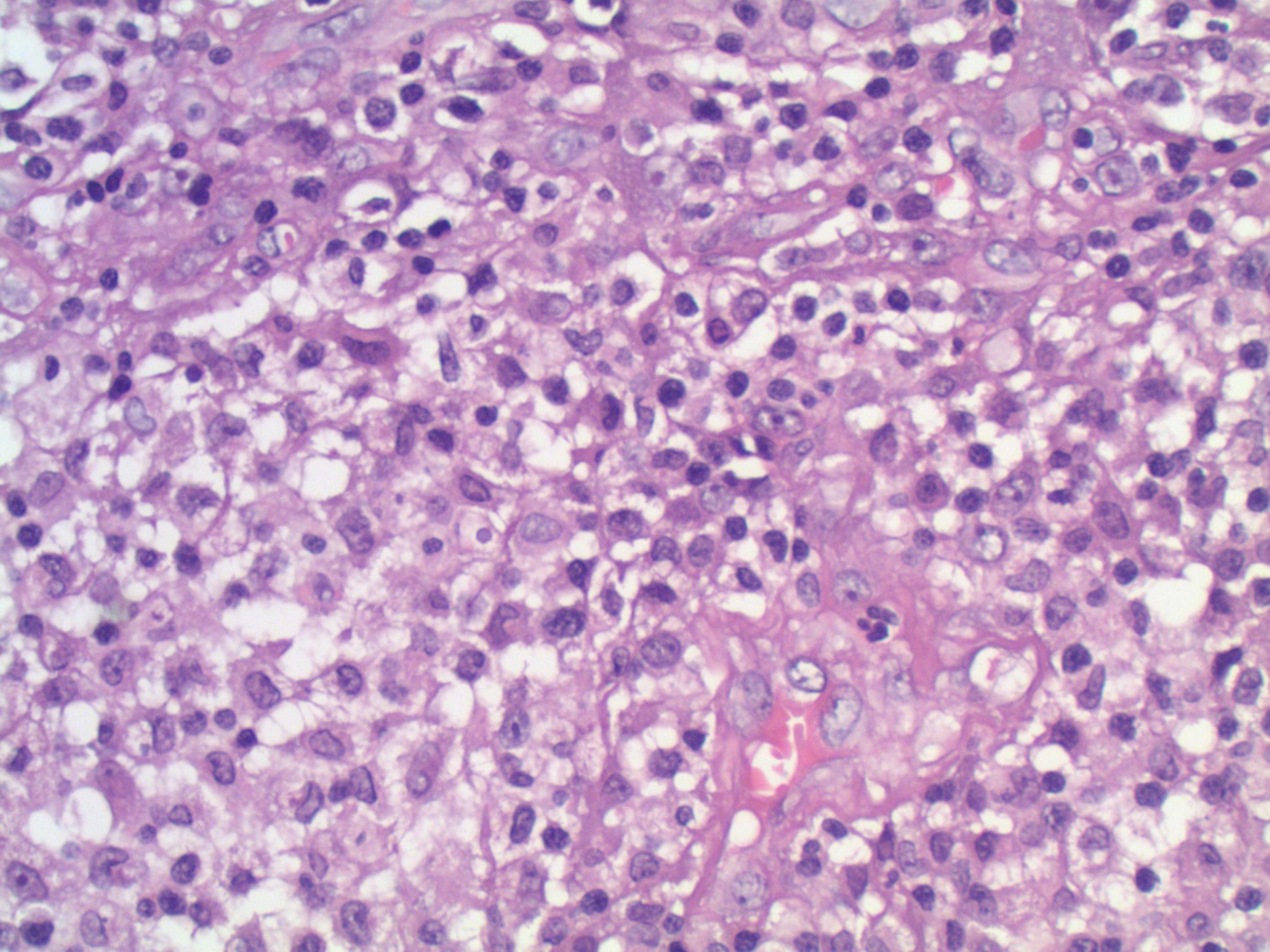
32-year-old male presented with swelling and pain in his right testis. Had similar swelling in his left testis 10 years earlier for which an orchiectomy was done. MRI and US of the present testicular mass were suggestive of malignant neoplasm. Right orchiectomy performed.



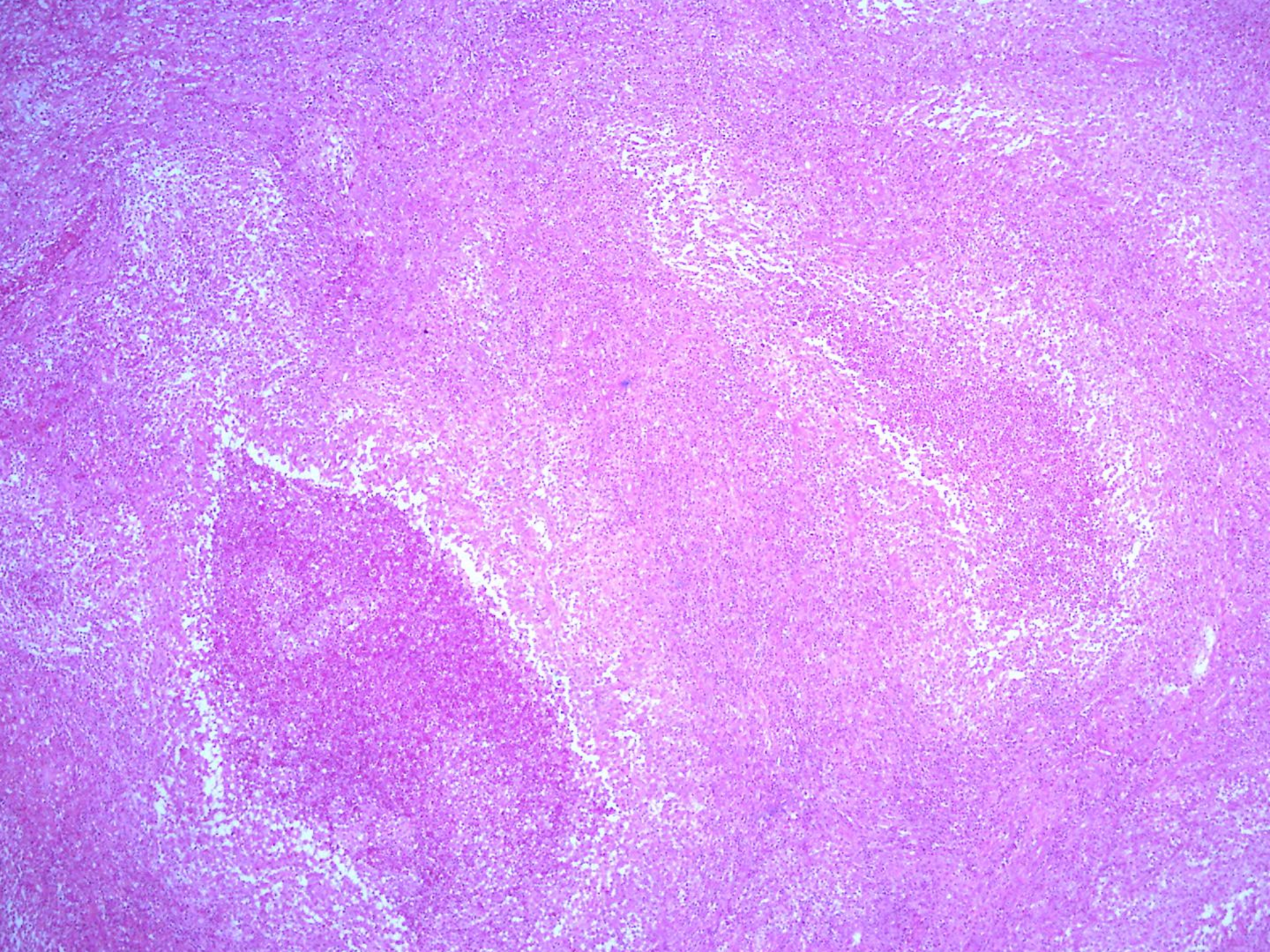


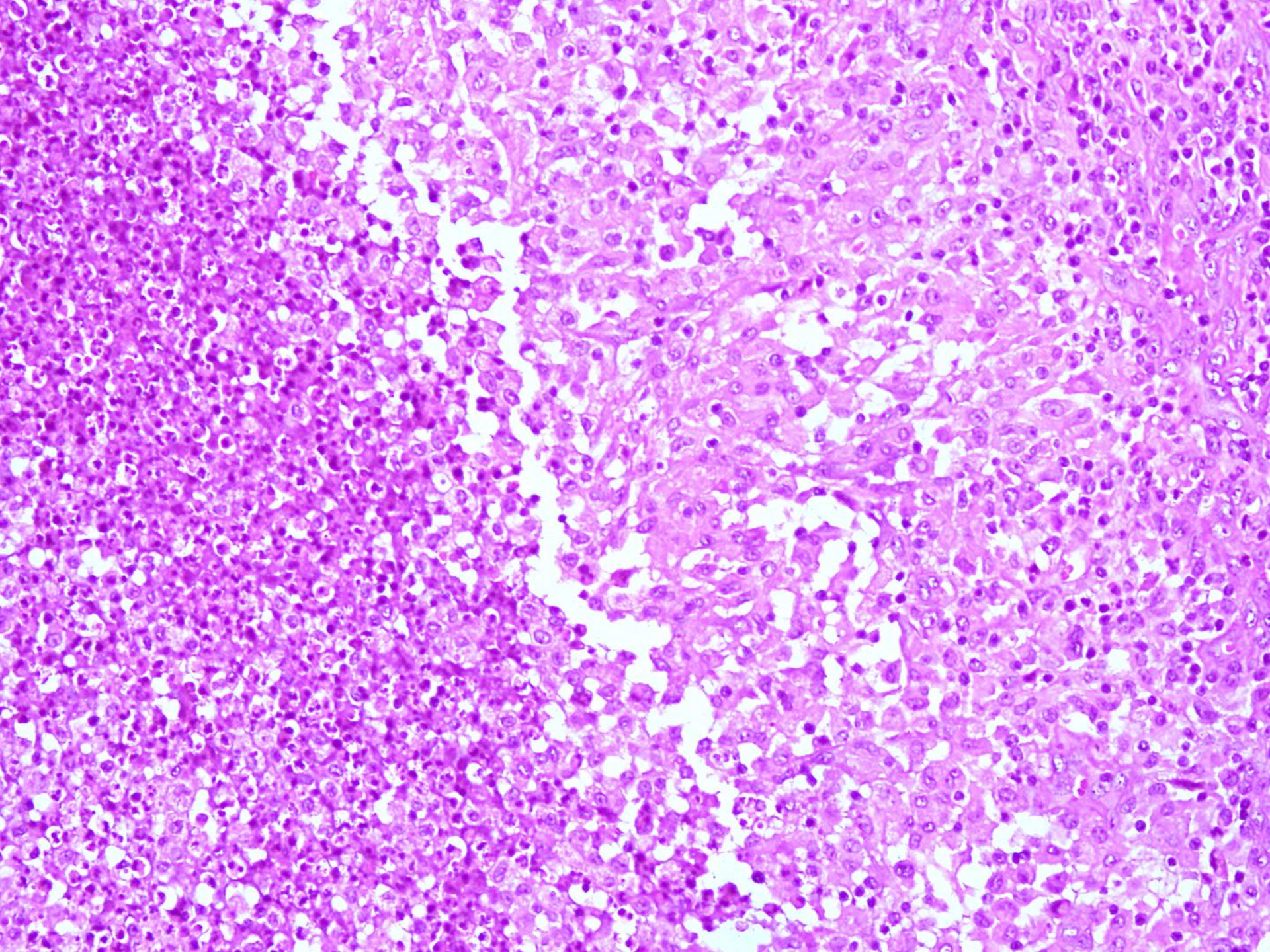


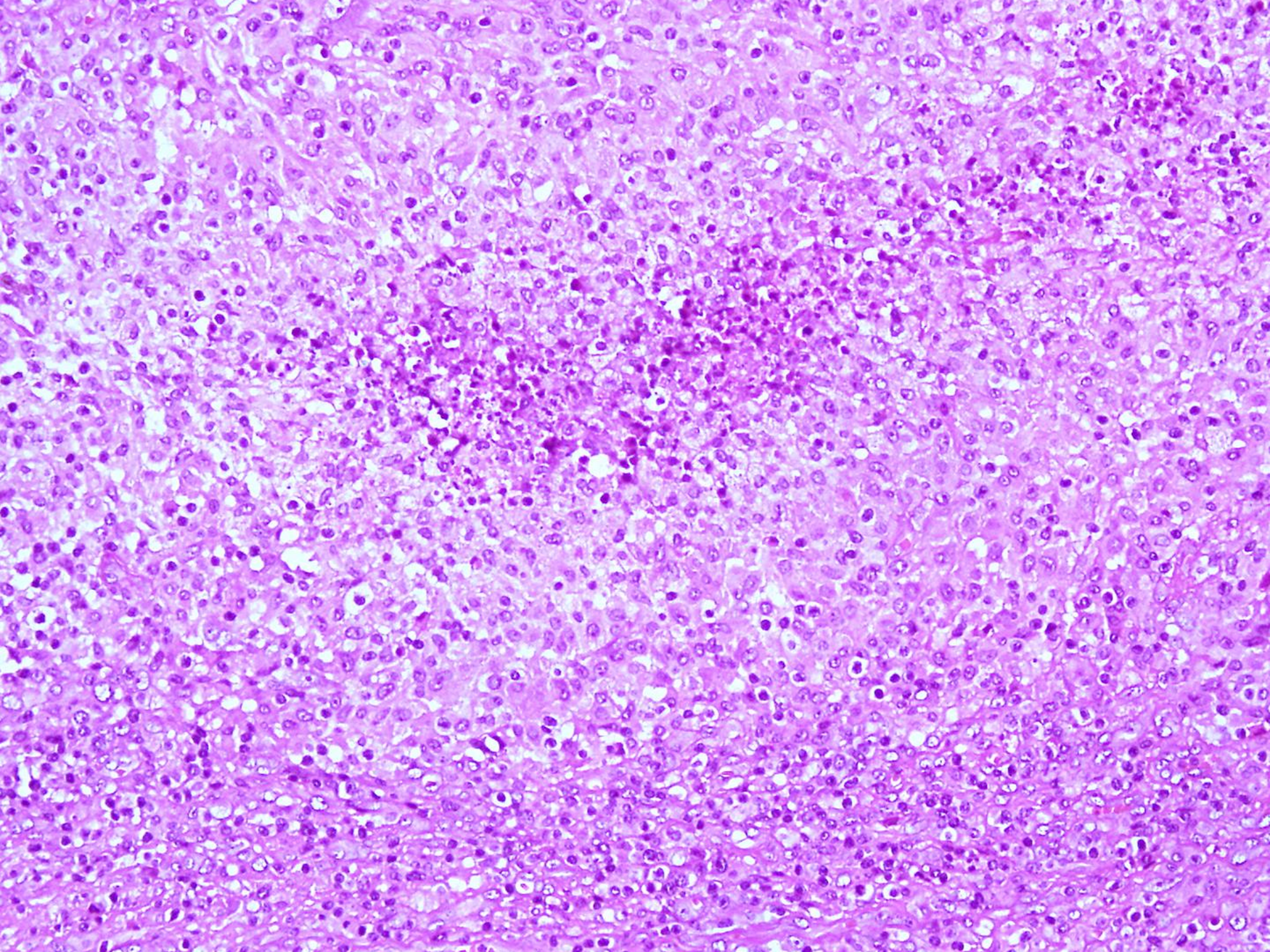


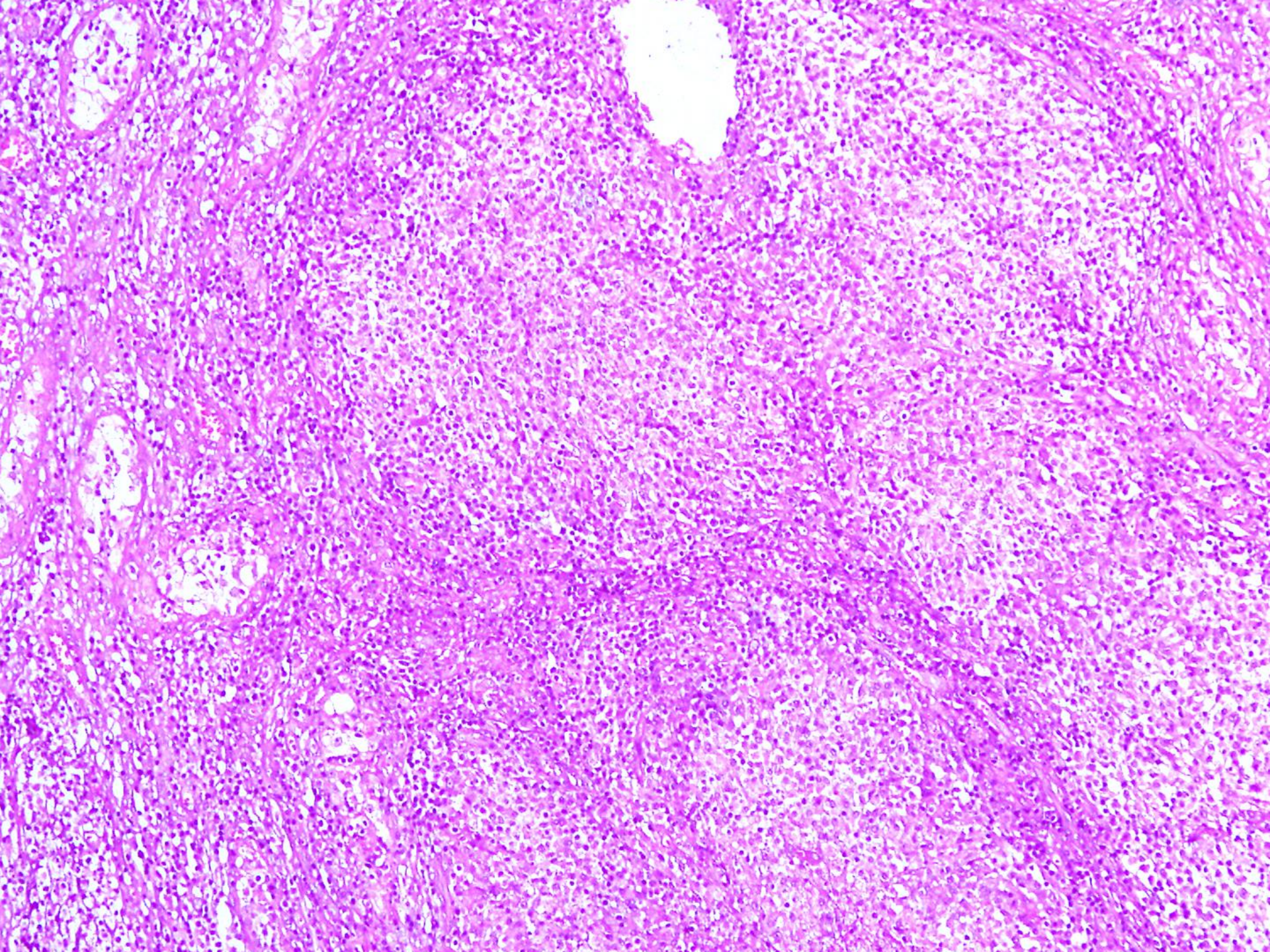


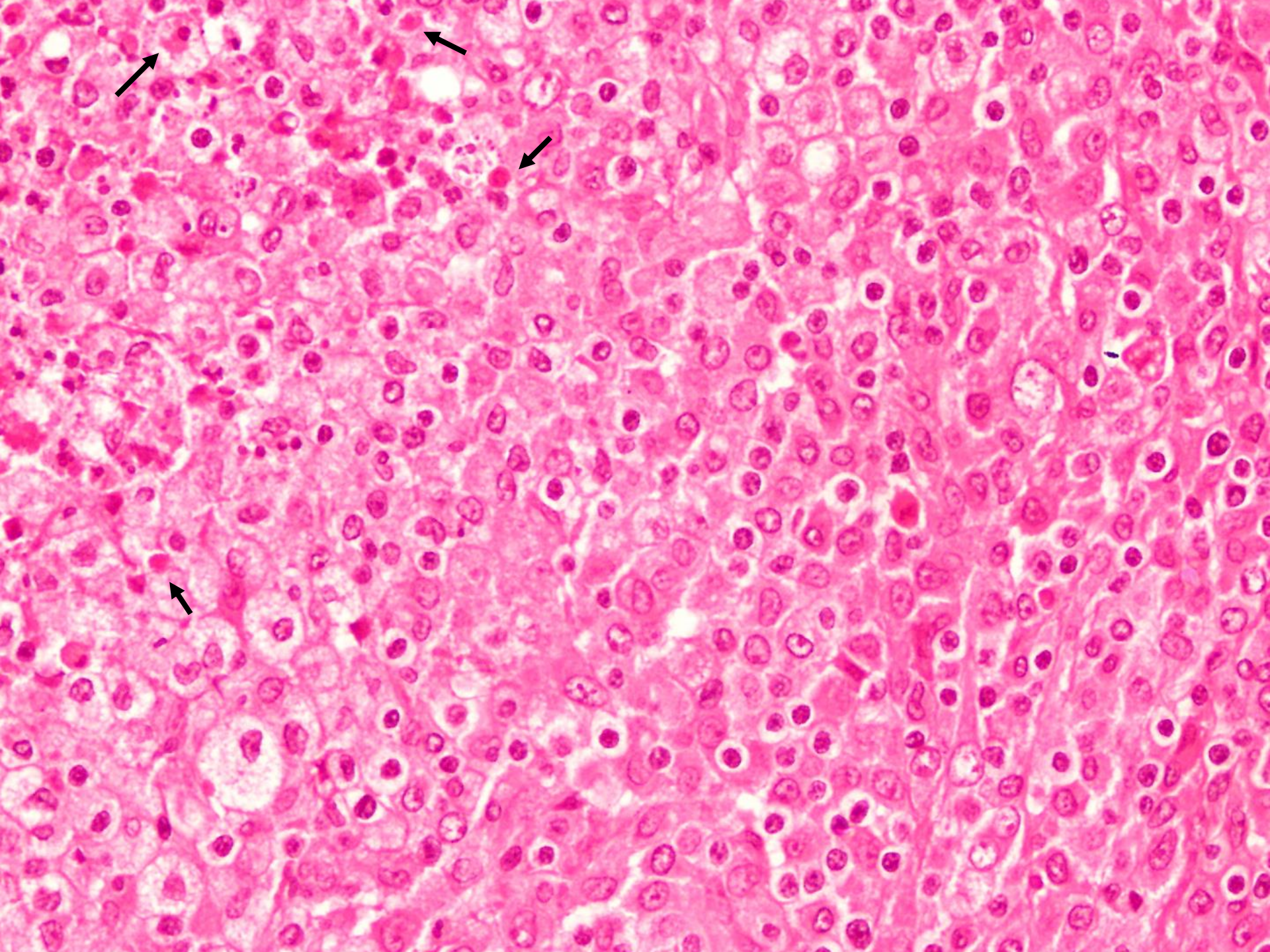
DIAGNOSIS?

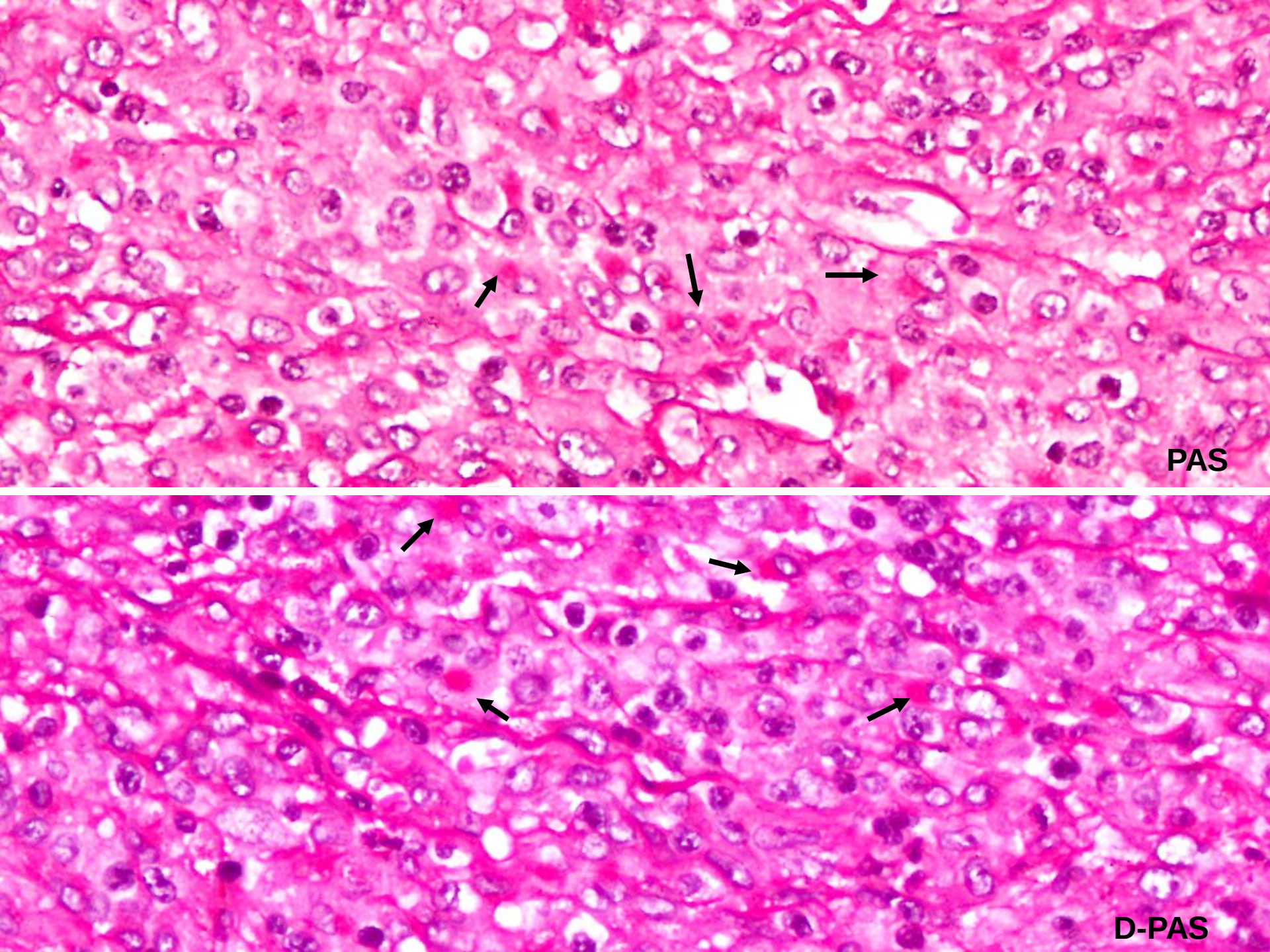


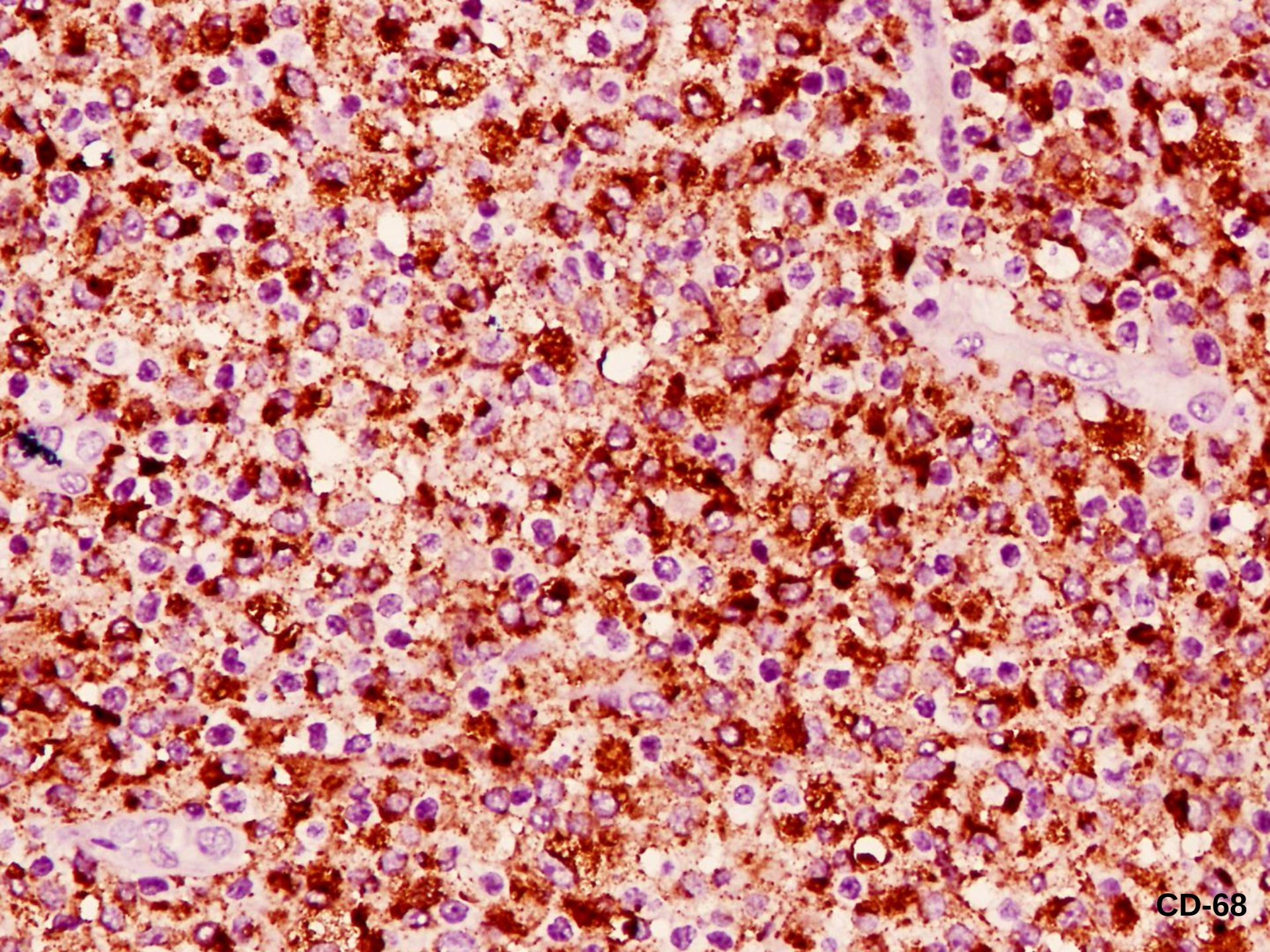









PAS
D-PAS


CD-68

SPECIAL STAINS:

Positive	Negative
-PAS, D-PAS for cytoplasmic globules	- Z-N stain for Acid fast bacilli
-CD-68 IPOX	- GMS stain for fungi
	- Warthin Starry & Gram's for bacteria
	- PLAP IPOX
	- Iron & Calcium stain for Michaelis Gutmann bodies

INFECTIONS:

-Per-operative tissue and urine cultures negative for bacteria and fungi

-Tuberculin skin test negative

-Serologic test for anti-B.henselae IgM & IgG negative

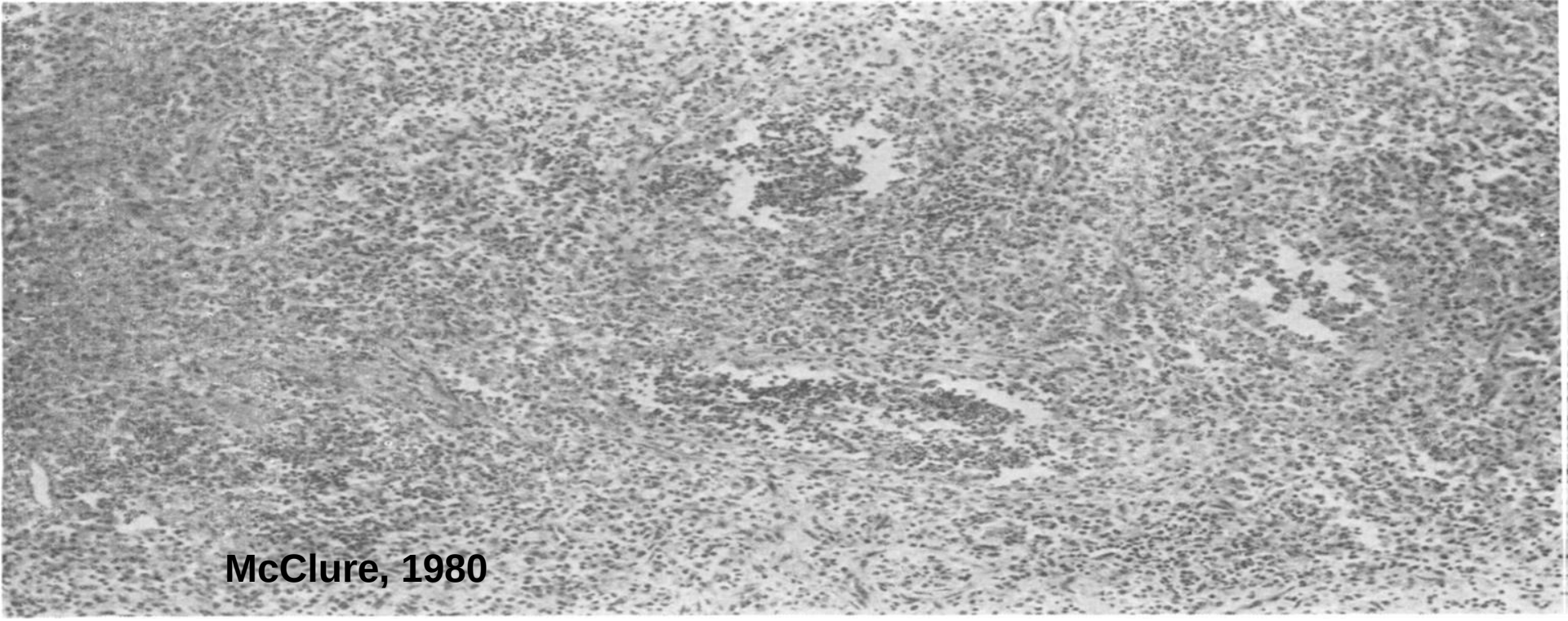
CONTRALATERAL ORCHIDECTOMY: (10 years earlier)

-Reported in another hospital as Tuberculous orchitis

DIAGNOSIS: **MALAKOPLAKIA, TESTIS**

- Ultrastructural studies not done; MG bodies not identified.
- Presence of MG bodies not mandatory for diagnosis.

  These are later developments in the D-PAS positive phagolysosomes within the histiocytes (von Hansemann cells) when the latter become larger and subsequently get encrusted with iron and calcium.
- Most of the ‘ granulomatous orchitis’ of unidentified etiology in fact belong to the category of Malakoplakia. In some of these CSD-like granulomas have been described (Mikuz, G. Virchows Arch. 1973; McClure J. J Clin Pathol. 1980)

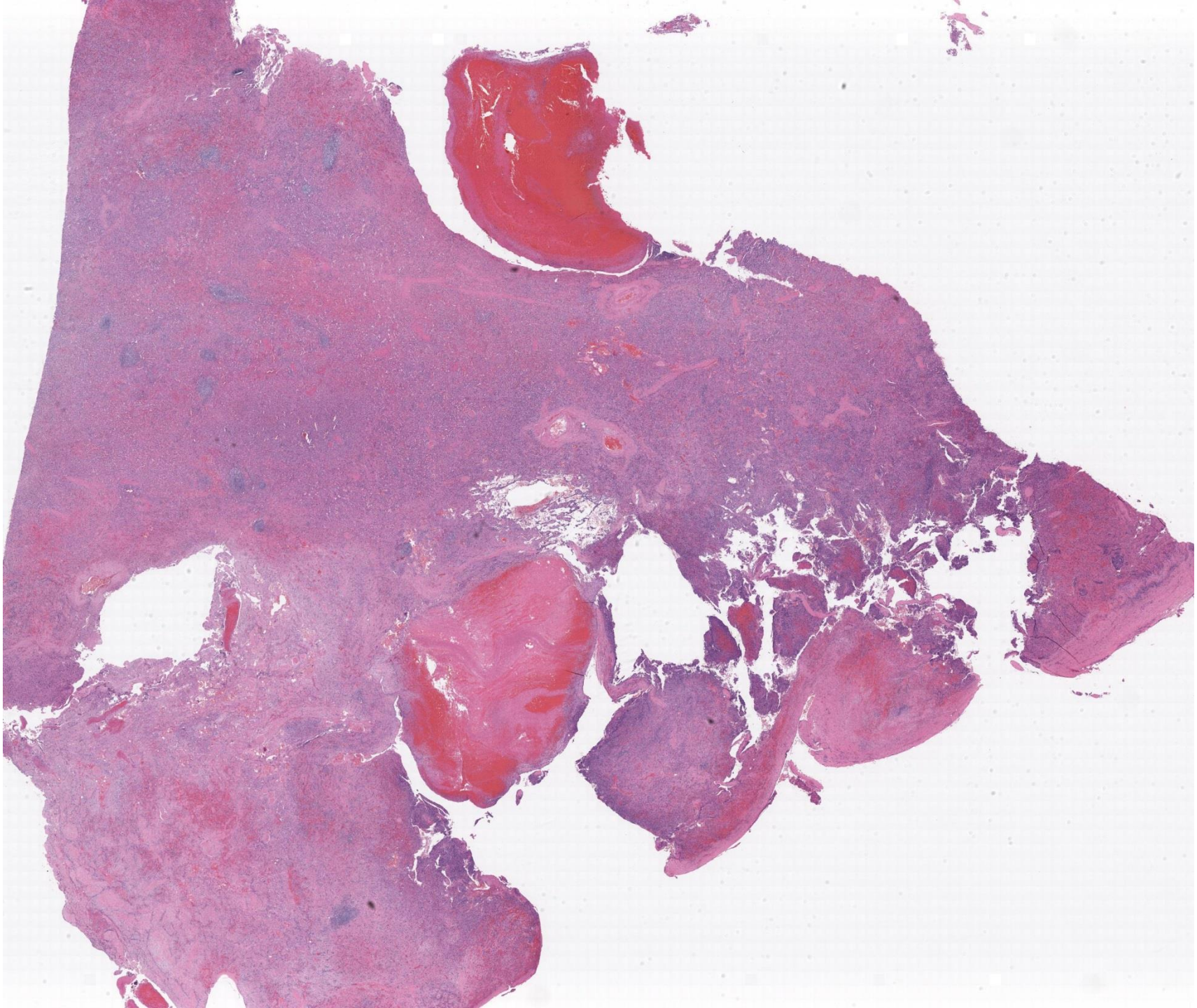

McClure, 1980

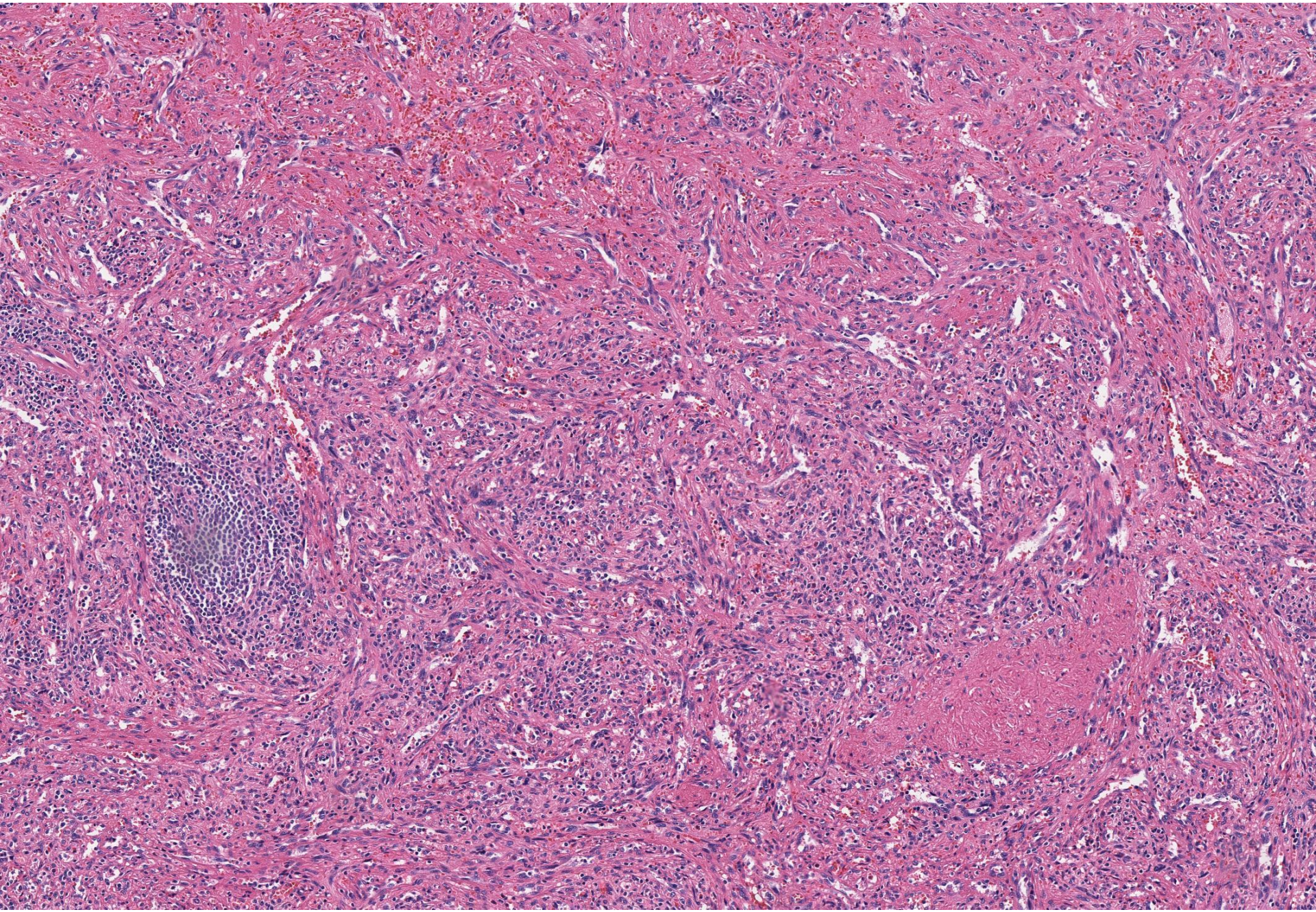
"We'll widen the clogged artery by inserting a balloon."

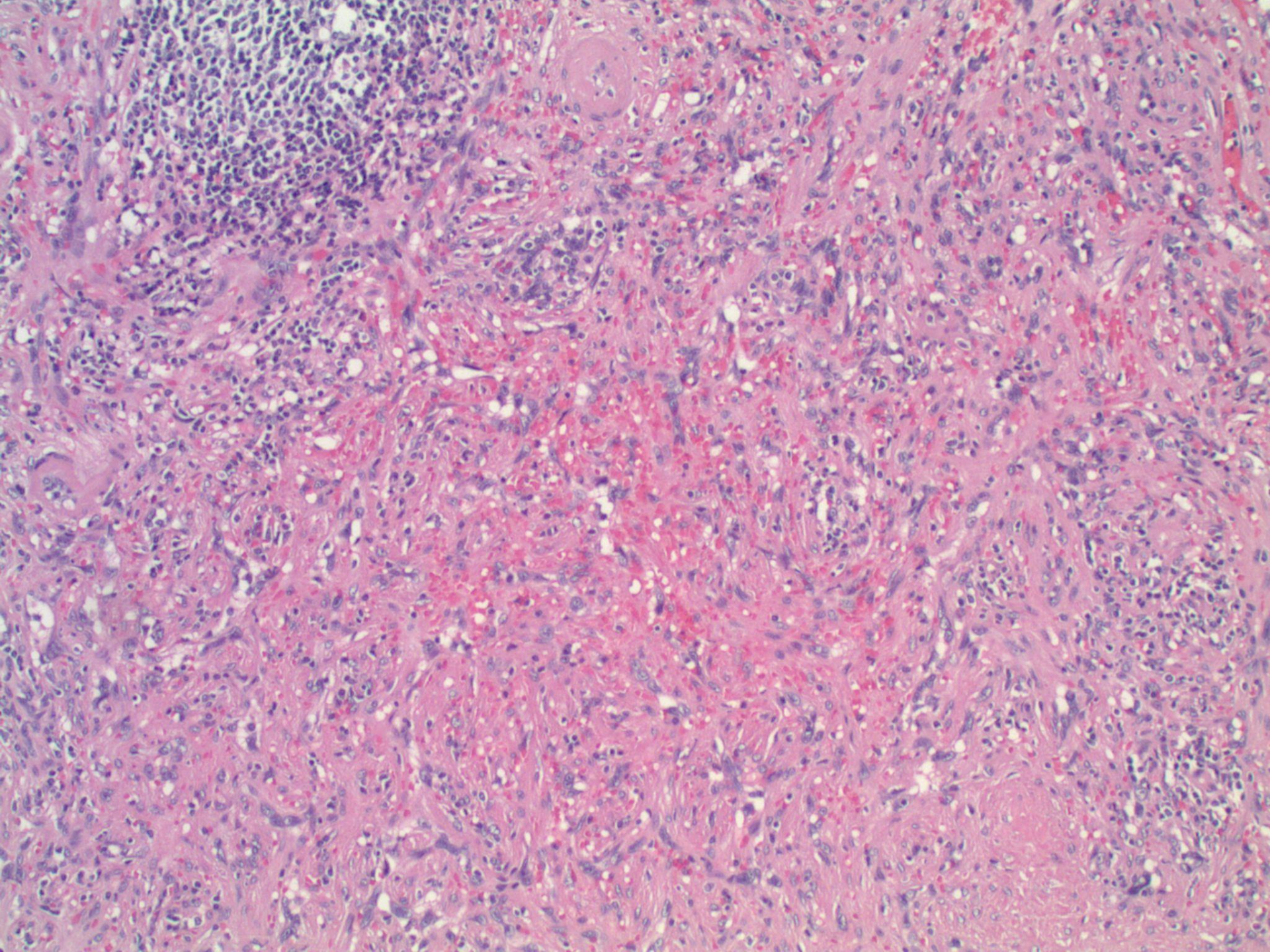
SB 5932

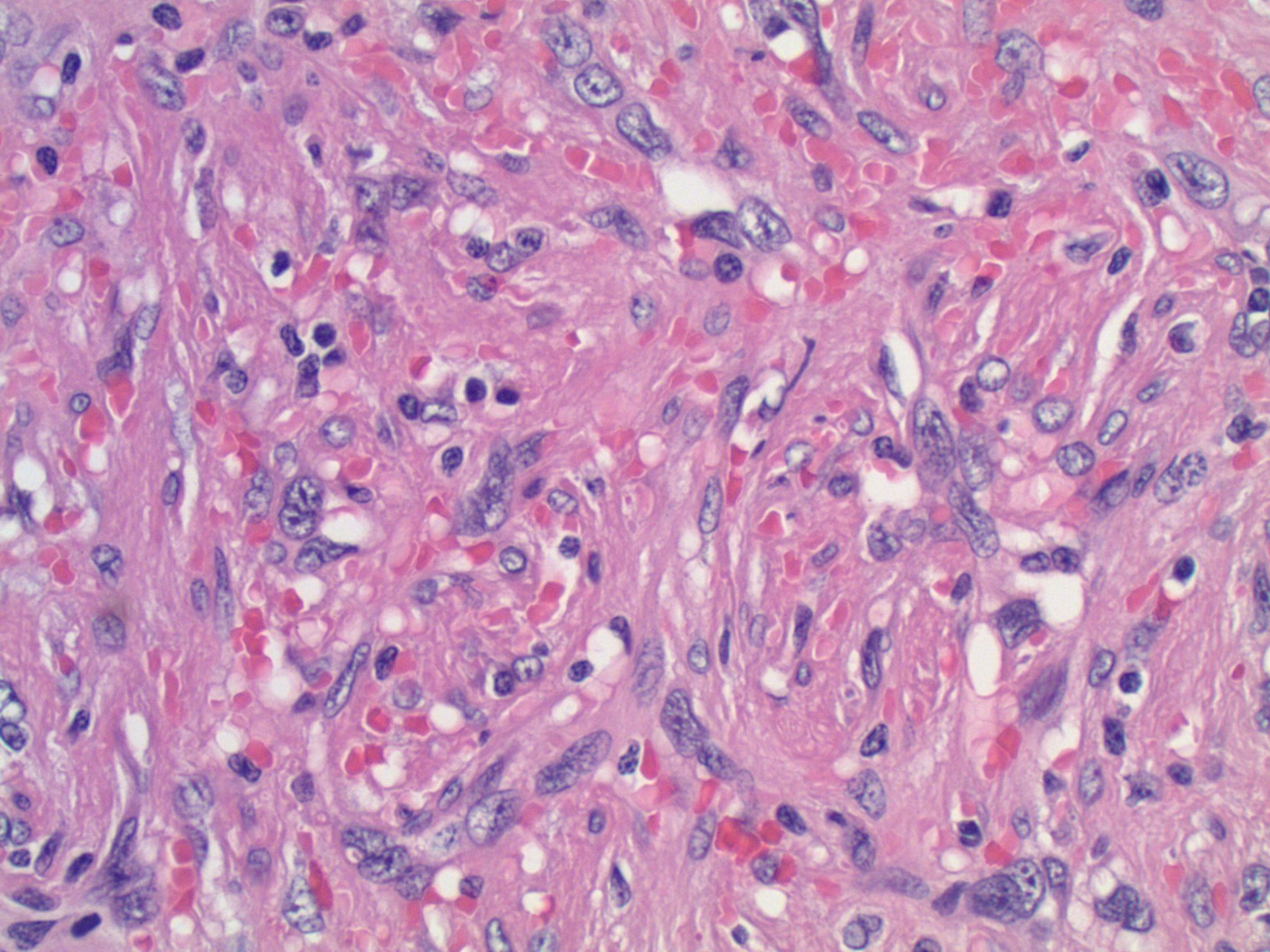
Keith Duncan; Mills-Península

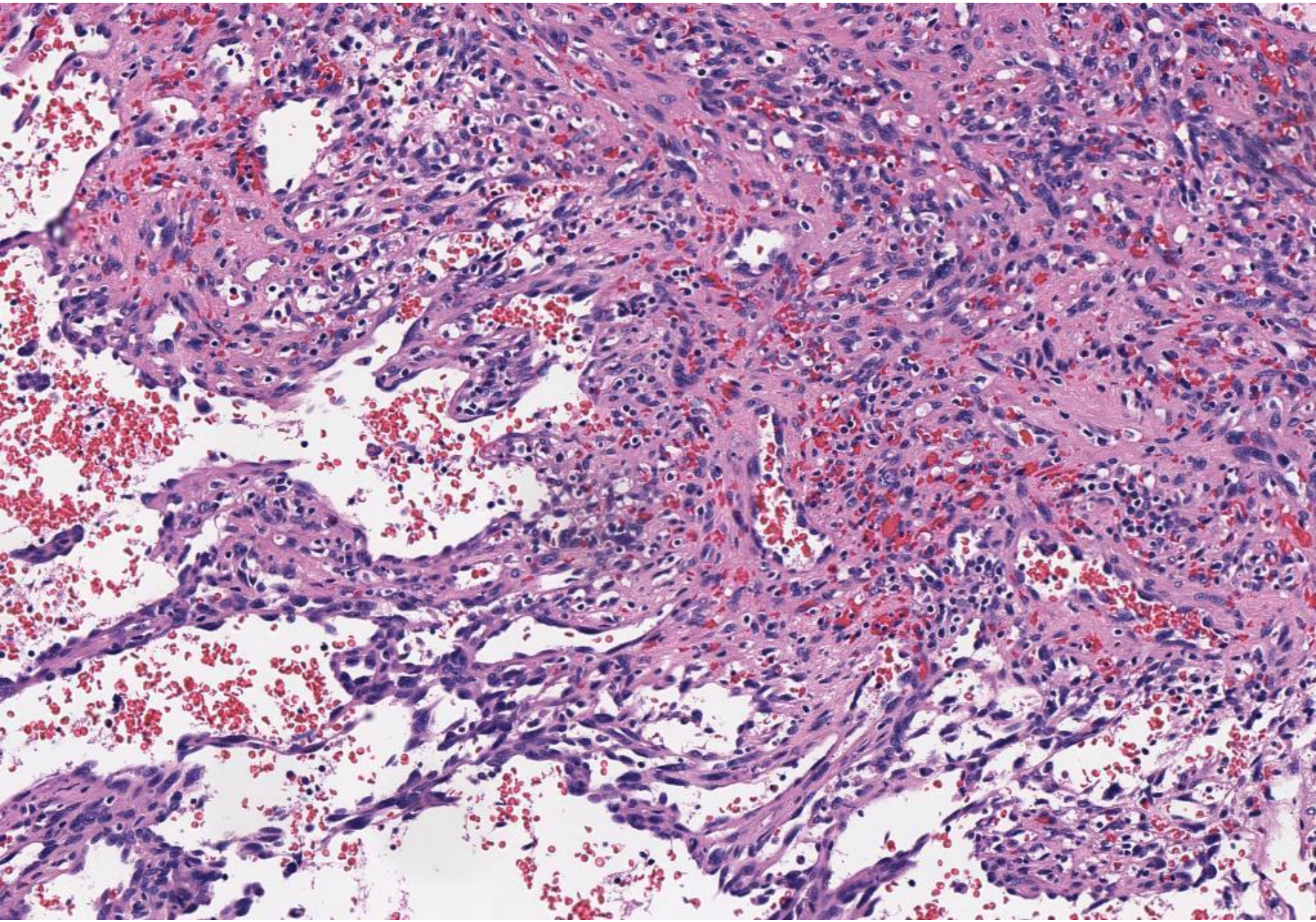
55-year-old male with “bleeding spleen.” Splenectomy performed.

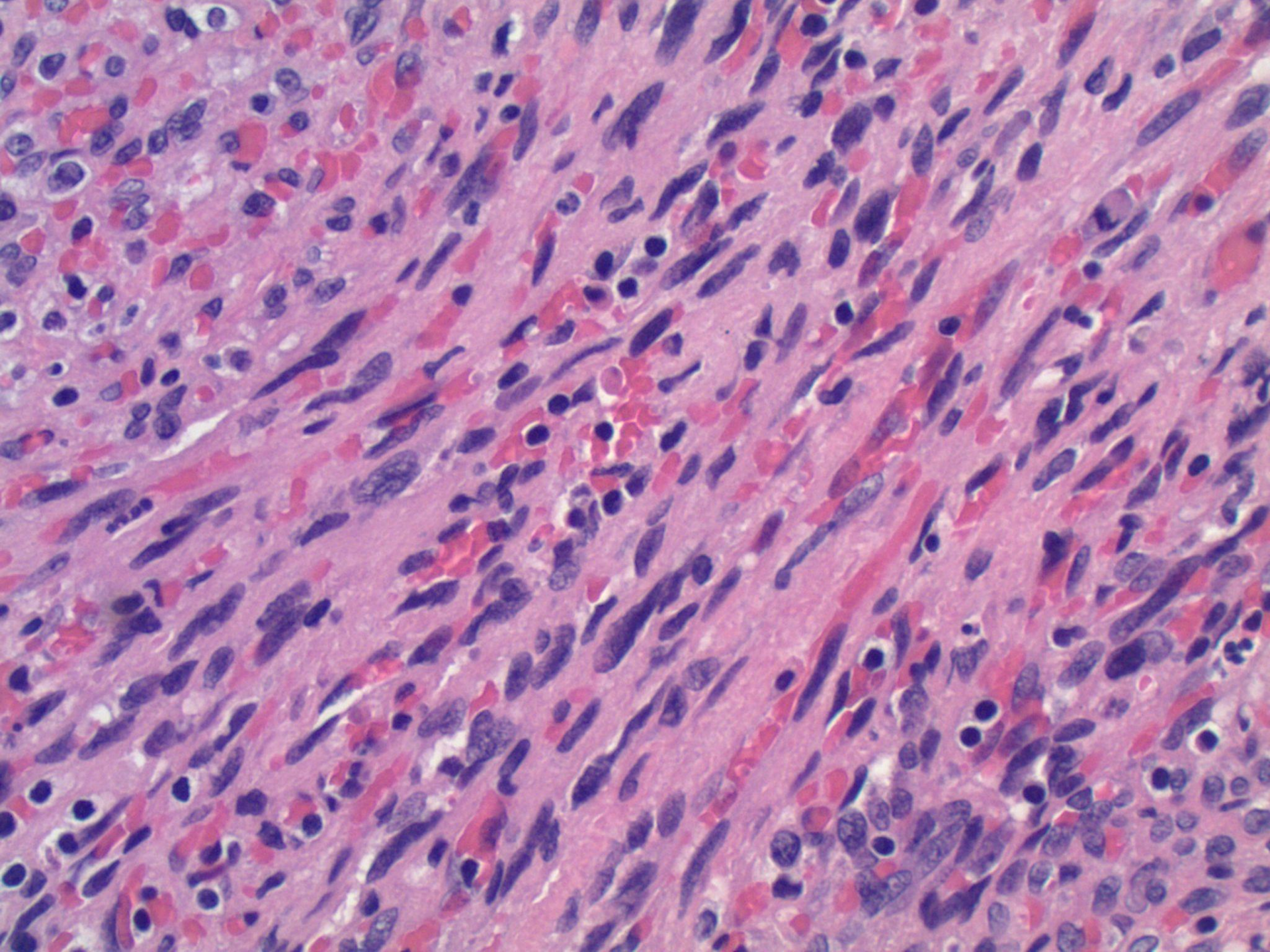












DIAGNOSIS?

Angiosarcoma of the Spleen

- Rare, but most common malignant nonlymphoid tumor of spleen
- Mean age 60 years, range 29-85 years, slight male preponderance
- Associated with microangiopathic anemia, thrombocytopenia, consumptive coagulopathy

Angiosarcoma of the Spleen

- **Pathophysiology**
- Uncertain, can develop from preexisting hemangioma or hemangioendothelioma
- Hx of Therapeutic irradiation, thorium dioxide & polyvinyl chloride exposure
-

Clinical features

- Nonspecific symptoms/findings: upper abdominal pain/fullness, weight loss, splenomegaly and anemia
- Leukopenia, elevated LDH levels and thrombocytopenia may be the first manifestation
- Up to 30% present with splenic rupture
- Aggressive (median survival 6 months), almost uniformly fatal with widespread metastases to liver, bone or bone marrow

Microscopic features of angiosarcoma

- Solid, papillary or freely anastomosing vascular channels (variable), lined by atypical, hyperchromatic cells with intracytoplasmic hyaline globules (may be epitheloid)
- Hemorrhage, necrosis, hemosiderin, extramedullary hematopoiesis
- Kaposi sarcoma-like pattern

IHC FINDINGS

- Endothelial markers (CD31, CD34, factor VIII- use of panel is recommended) & histiocytic markers (CD68) positive
- Variable S100
- Keratin (may be focally positive)

Angiosarcoma of the spleen

- Mod Pathol 2000;13(9):978–987
- **Splenic Angiosarcoma: A Clinicopathologic and Immunophenotypic Study of 28 Cases**
- Thomas S Neuhauser et al
- AFIP: approx. ¼ cases in their splenectomy archives were angiosarcomas;
- Am J Surg Path: July 1997 - Vol 21 - Iss 7 - pp 827-835
- Splenic Vascular Tumors: A Histologic, Immunophenotypic, and Virologic Study
- Arber, Daniel A. M.D et al. 4 cases of angiosarc of 22 vascular lesions

Differential diagnosis

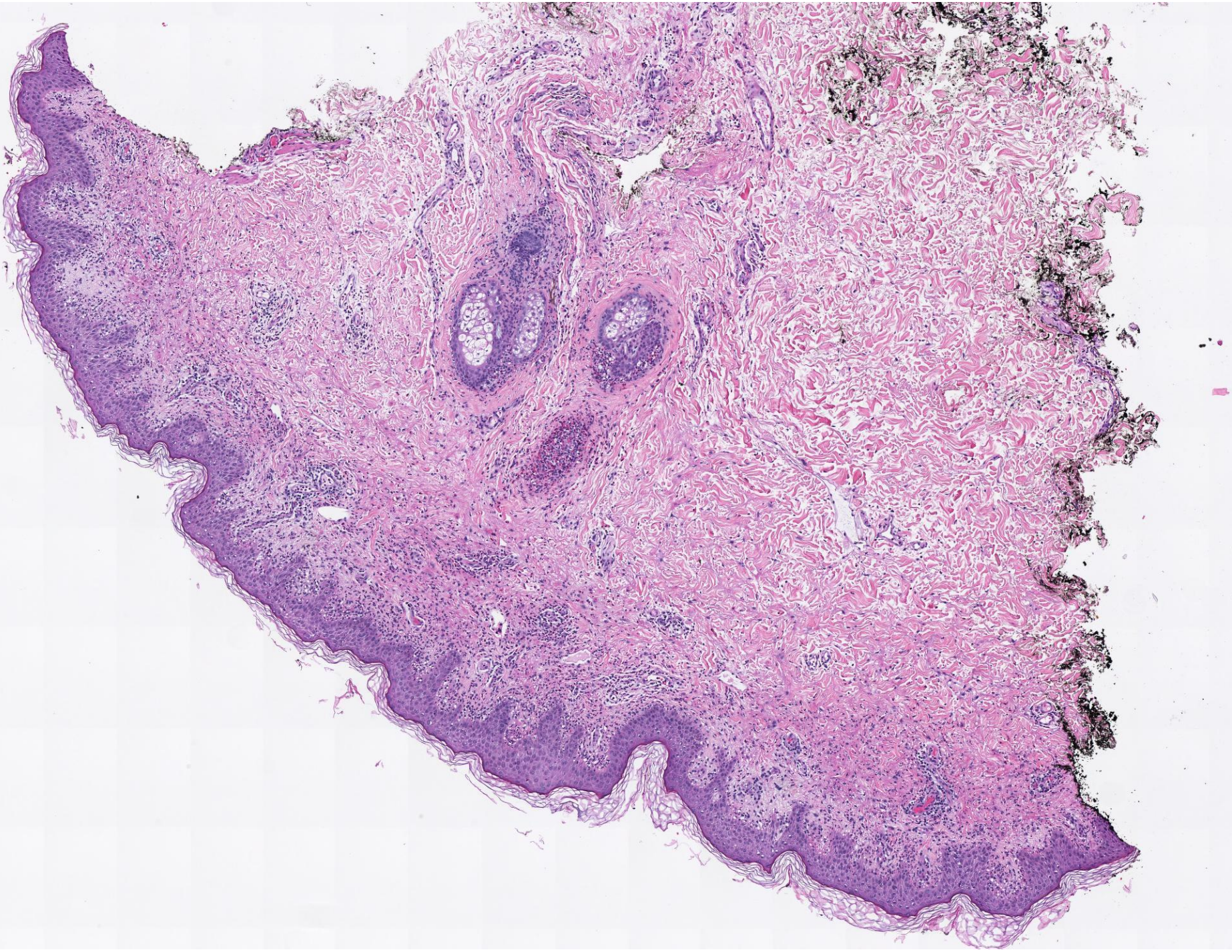
- Hematoma
- Hemangioma
- Metastatic lesions

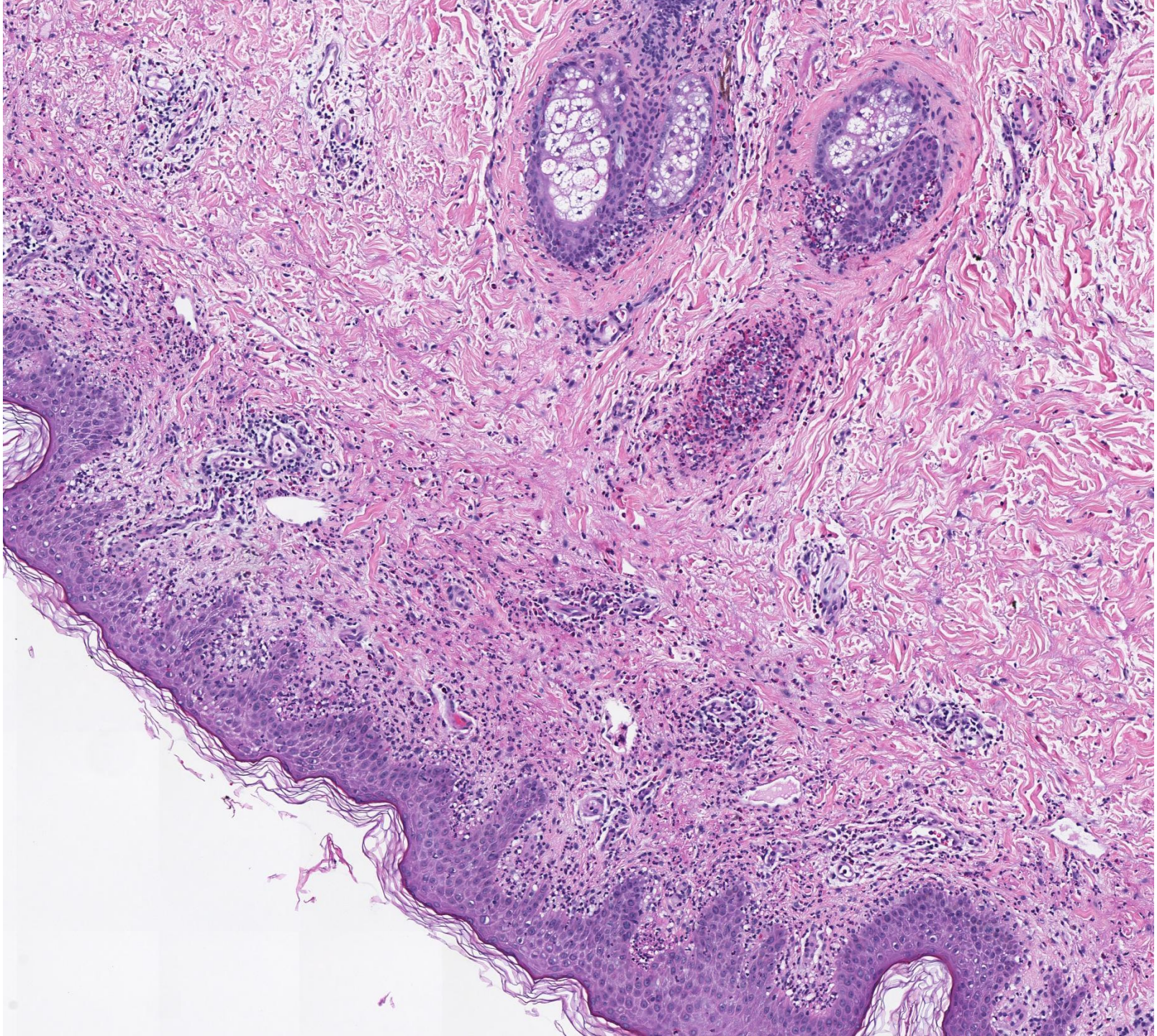
"Well, Bob, it looks like a paper cut, but just to be sure let's do lots of tests."

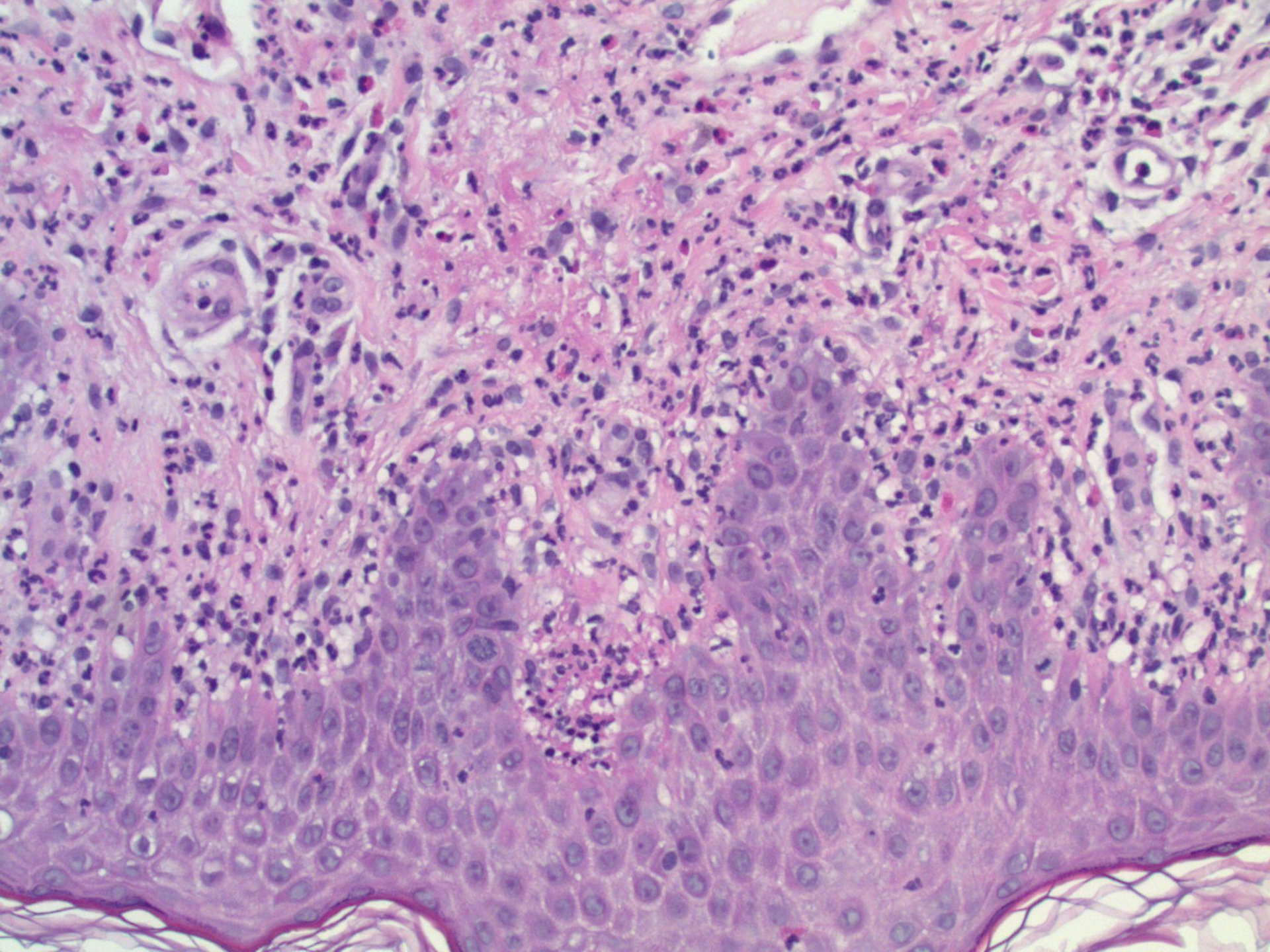
SB 5933

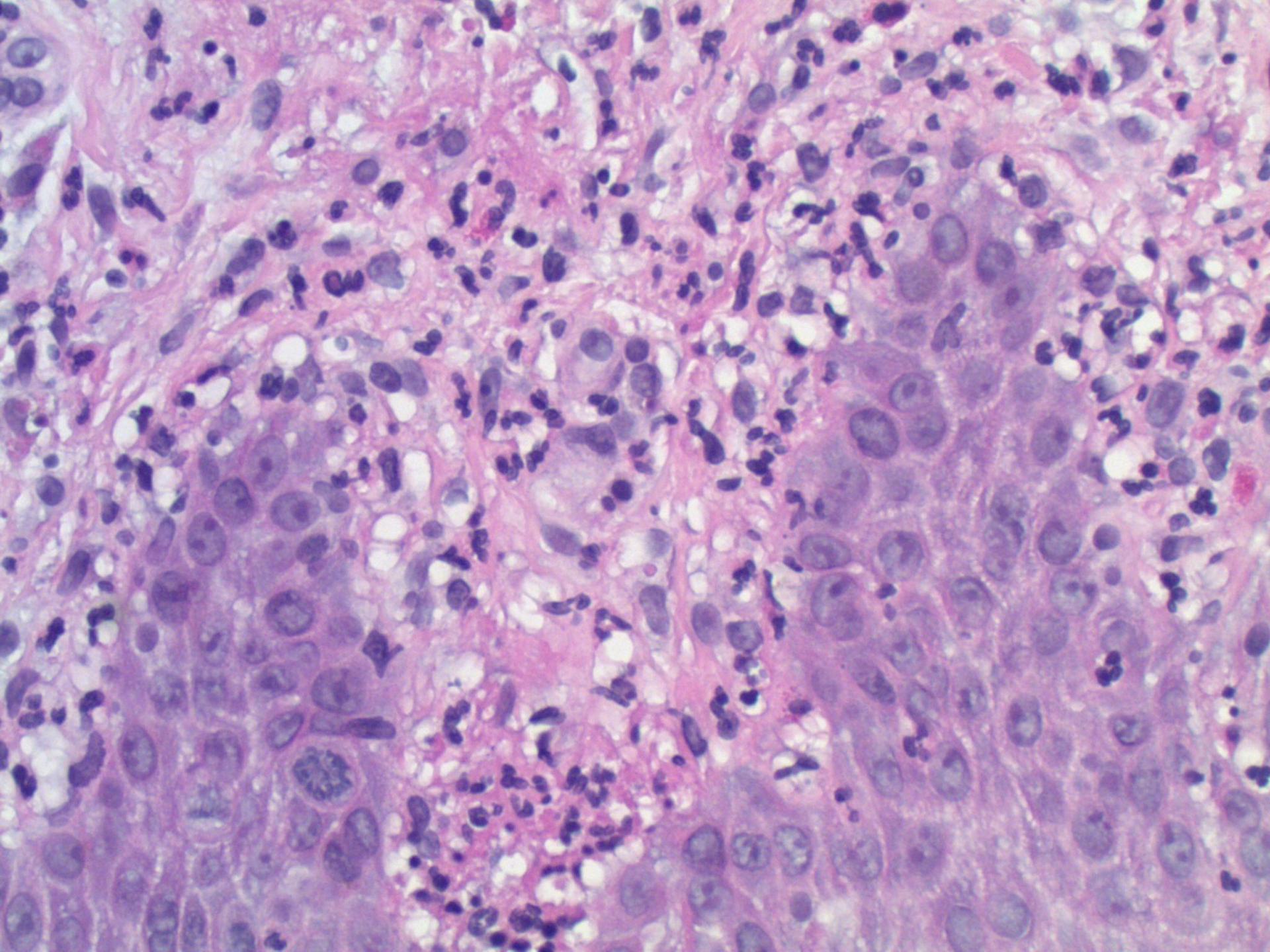
John Collin; El Camino Hospital

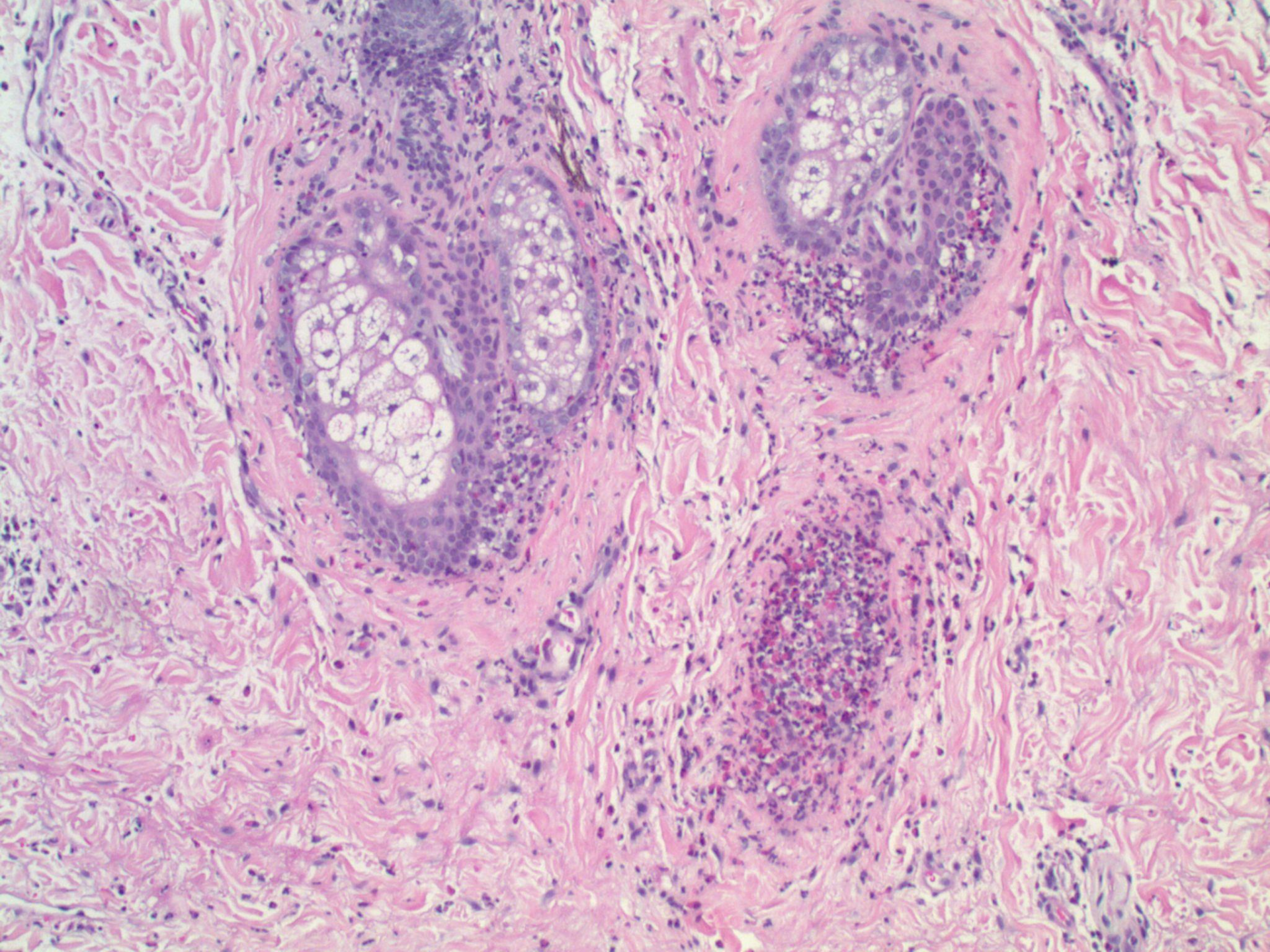
68-year-old male with history of endocarditis on multiple antibiotics. New rash x 3 days, vesicles and small bullae on the extensors, axilla, inguinal region.





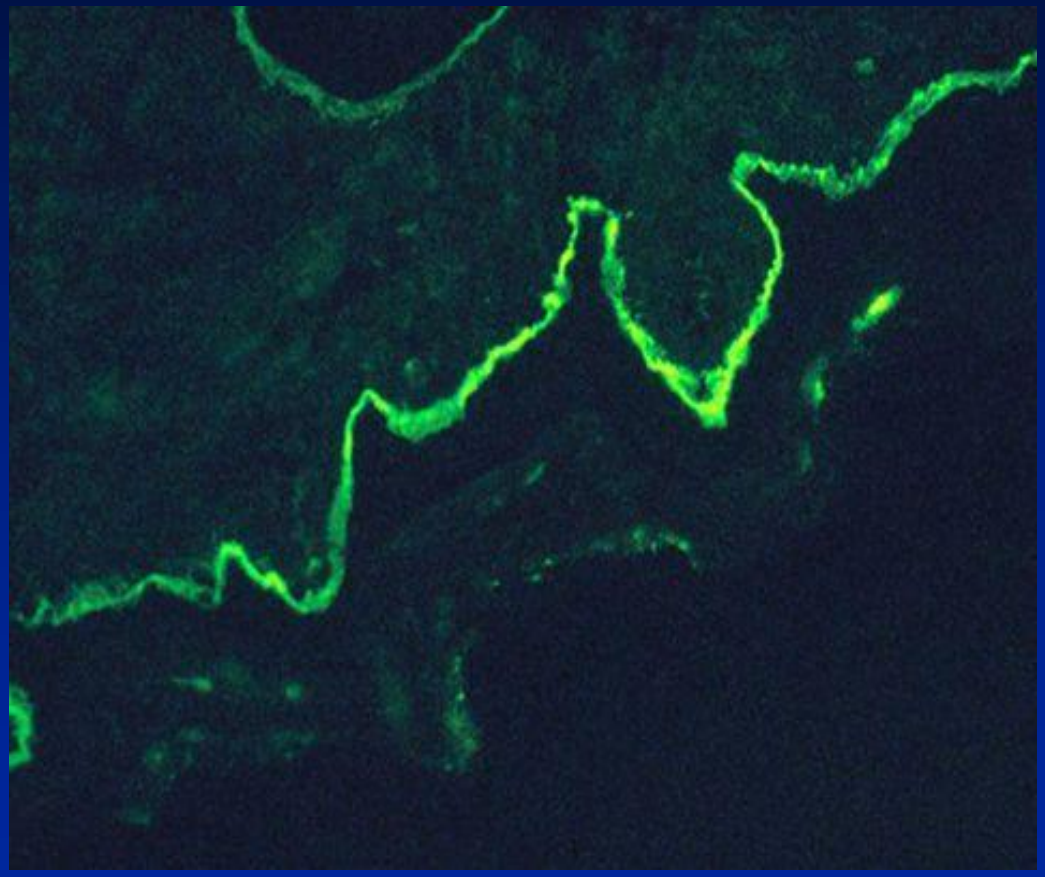






DIAGNOSIS?

Linear IgA disease



Linear IgA disease

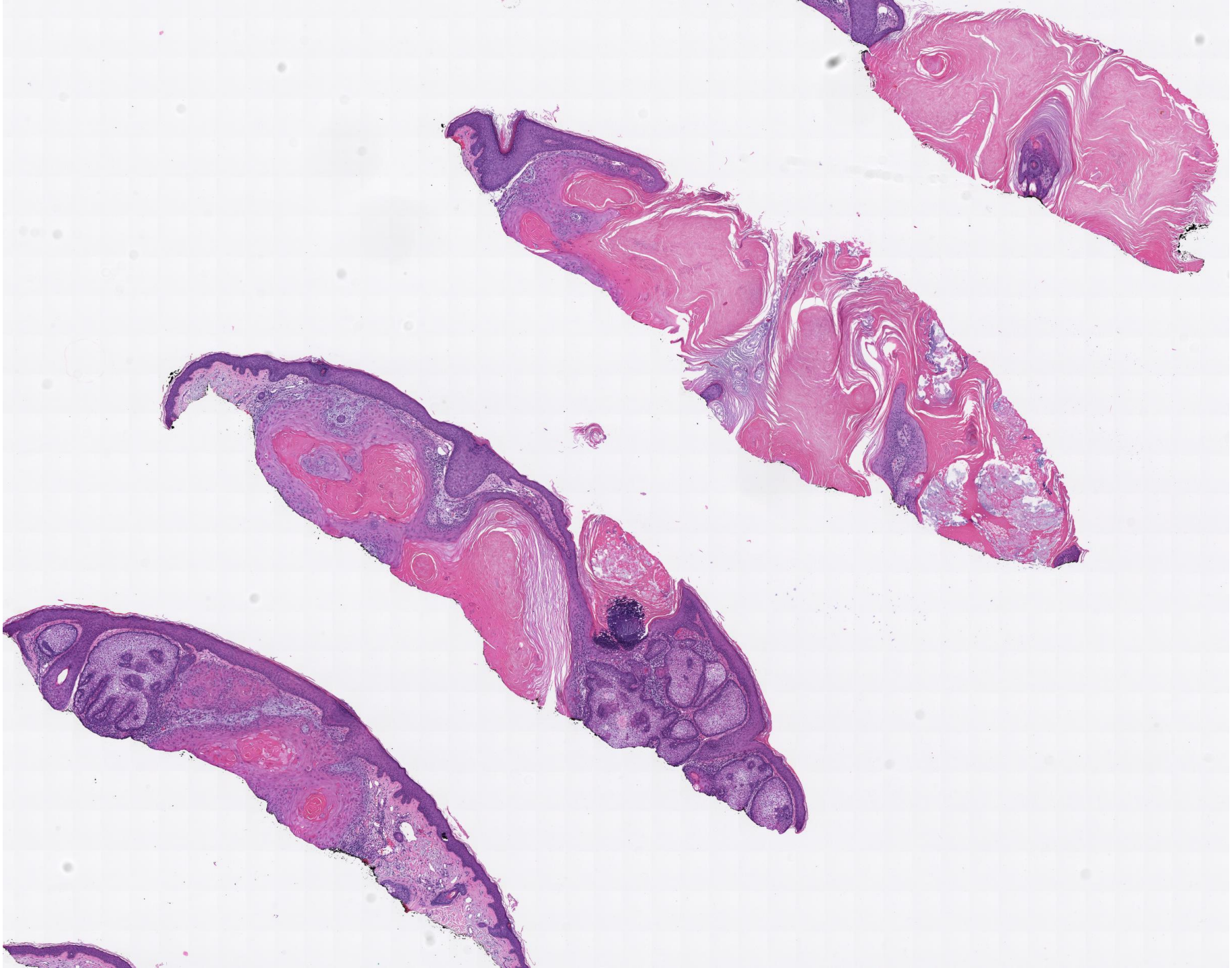
- Autoimmune disorder characterized by linear deposition of IgA along the basement membrane.
- Bimodal age distribution
  - 4.5 years and 52 years
- Drug related vs non-drug related
- Non drug related: cause mostly unknown, some after variety of infections, typhoid, brucella, tuberculosis, varicella, herpes zoster
- Drug related: Vancomycin main one
- Clinical: Pruritic, red, urticarial, targetoid and bullous lesions on trunk, extremities, palms and soles.

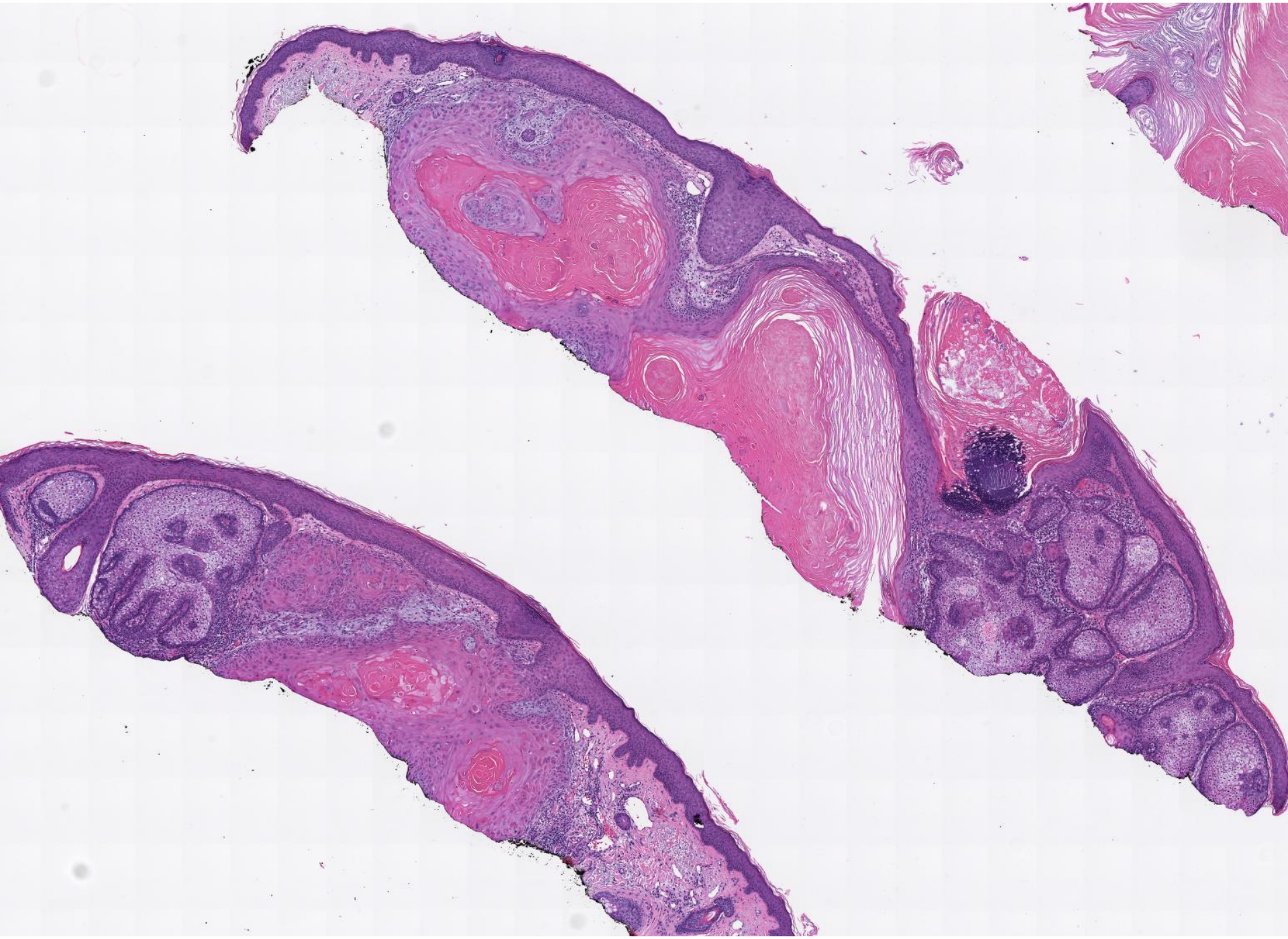
"I don't think it's anything serious, but, just to be sure, I'm going to bill you as if it is."

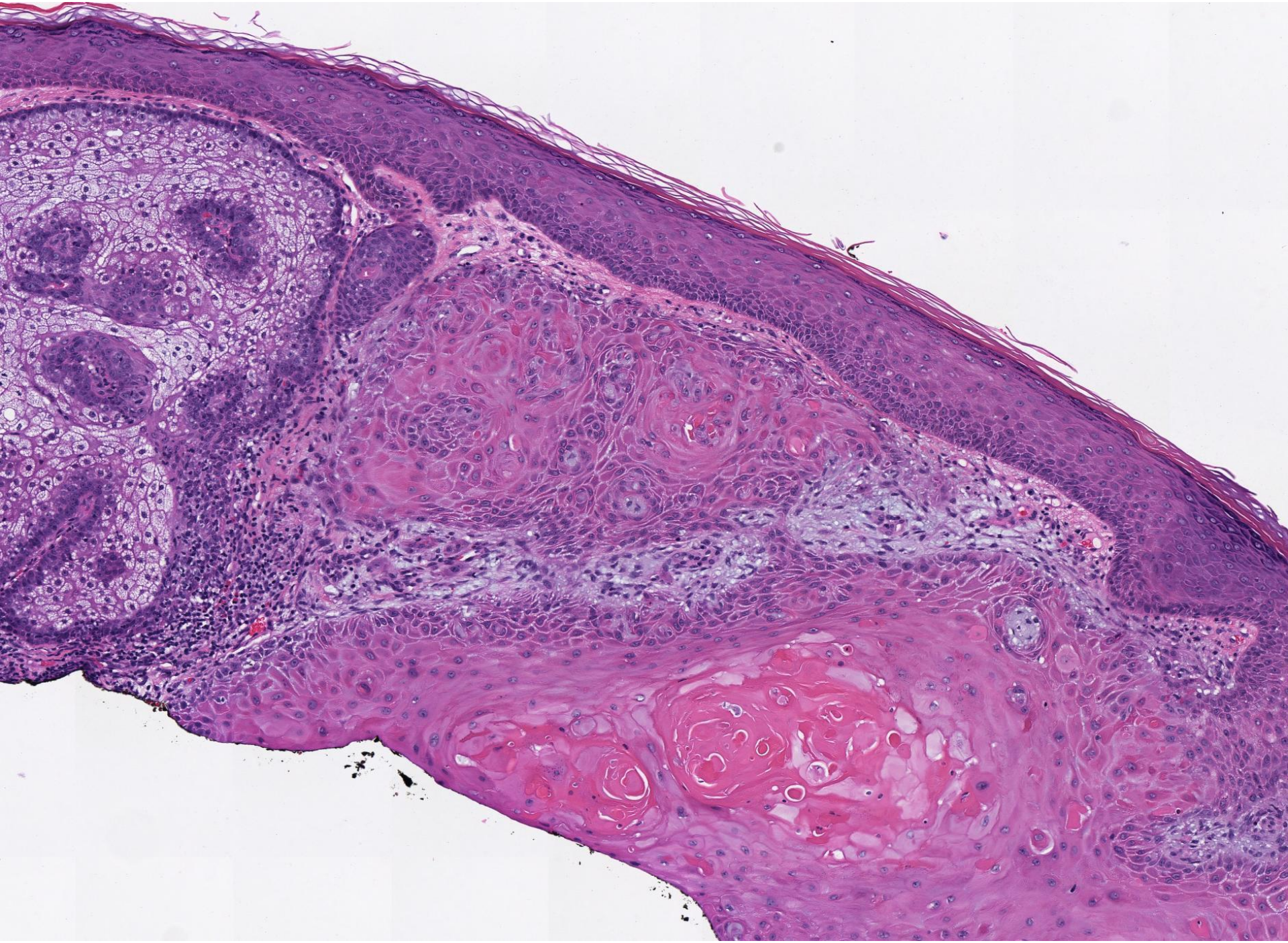
SB 5934

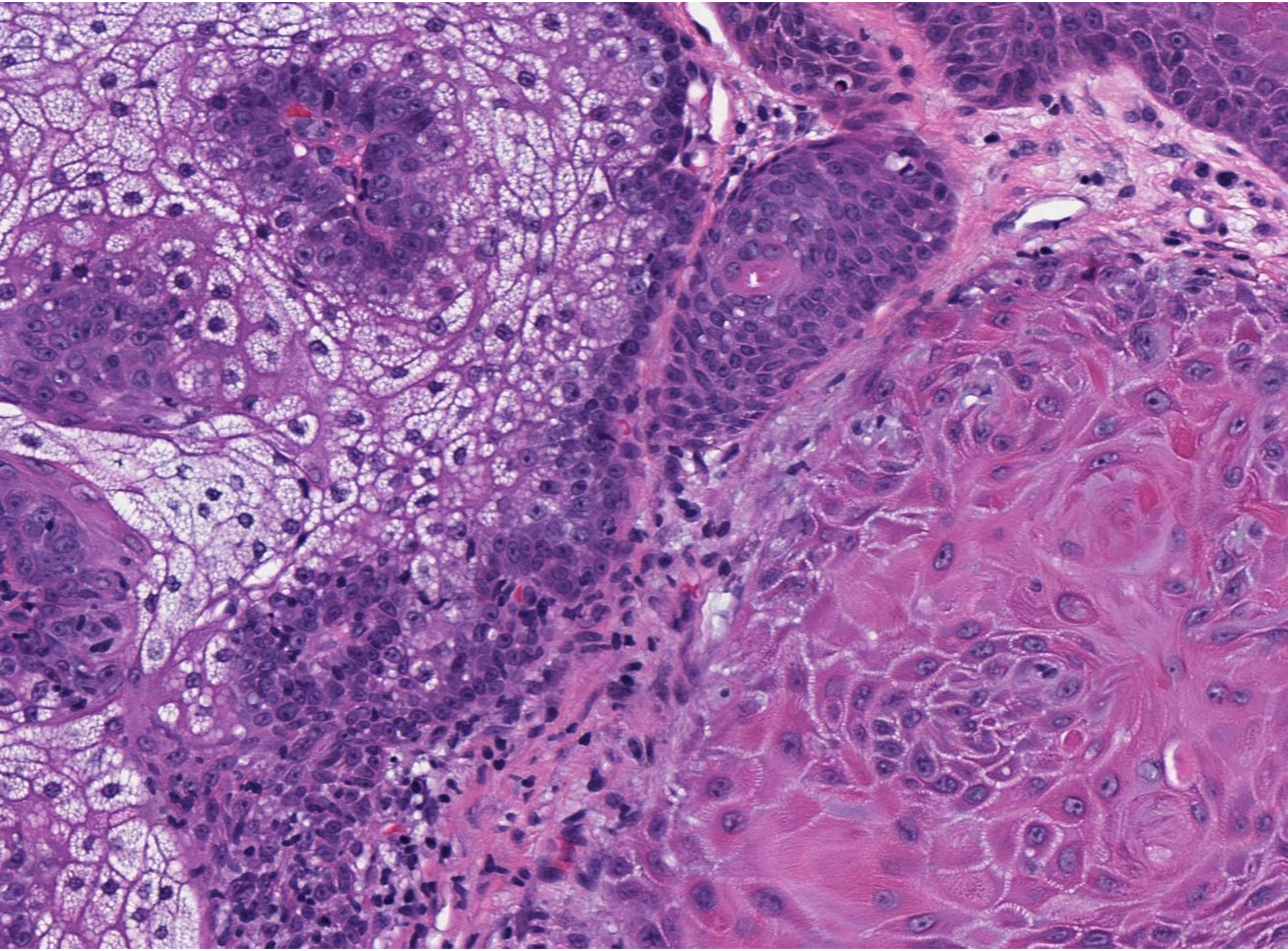
Charles Lombard; El Camino Hospital

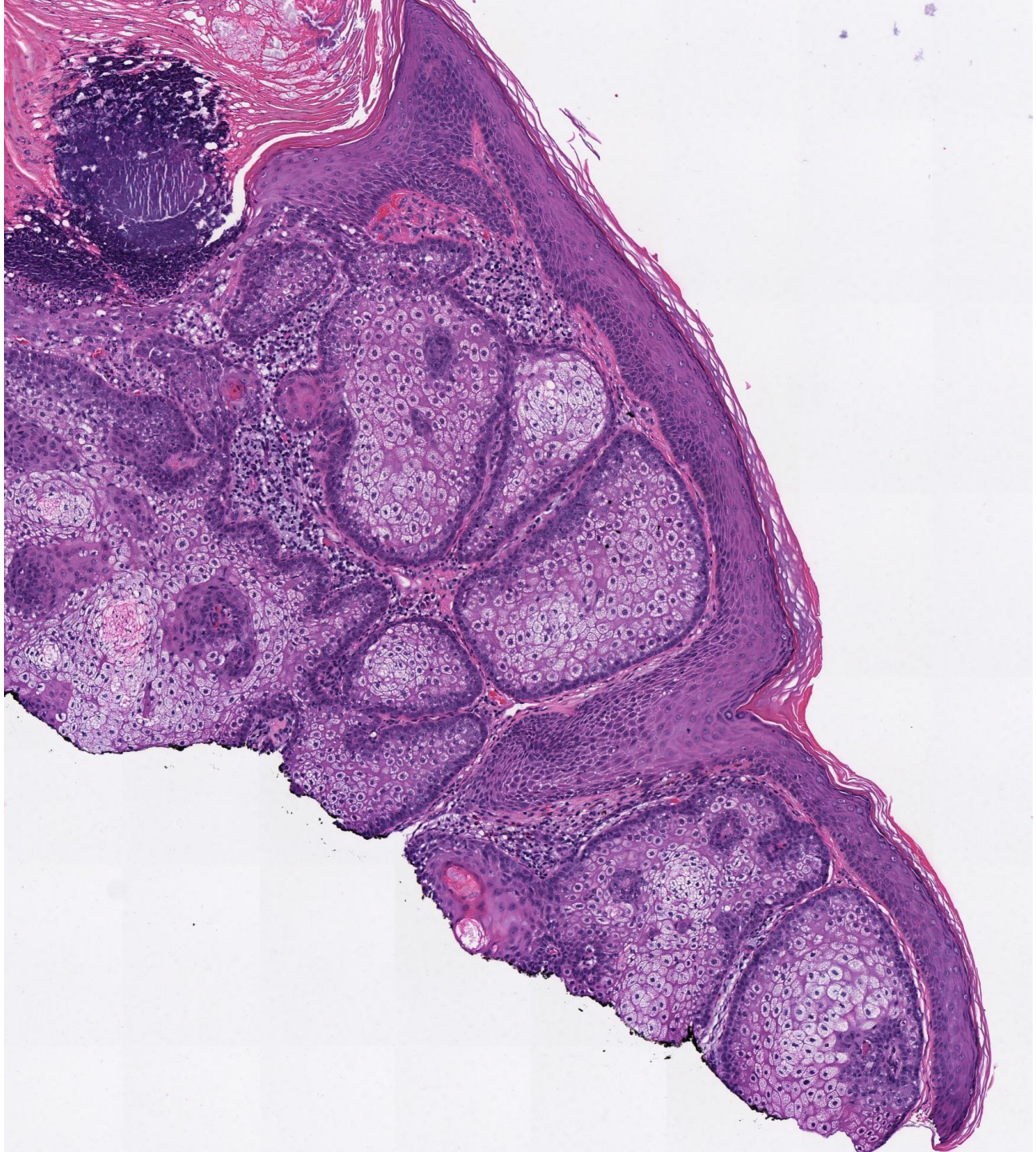
71-year-old male with scalp lesion.

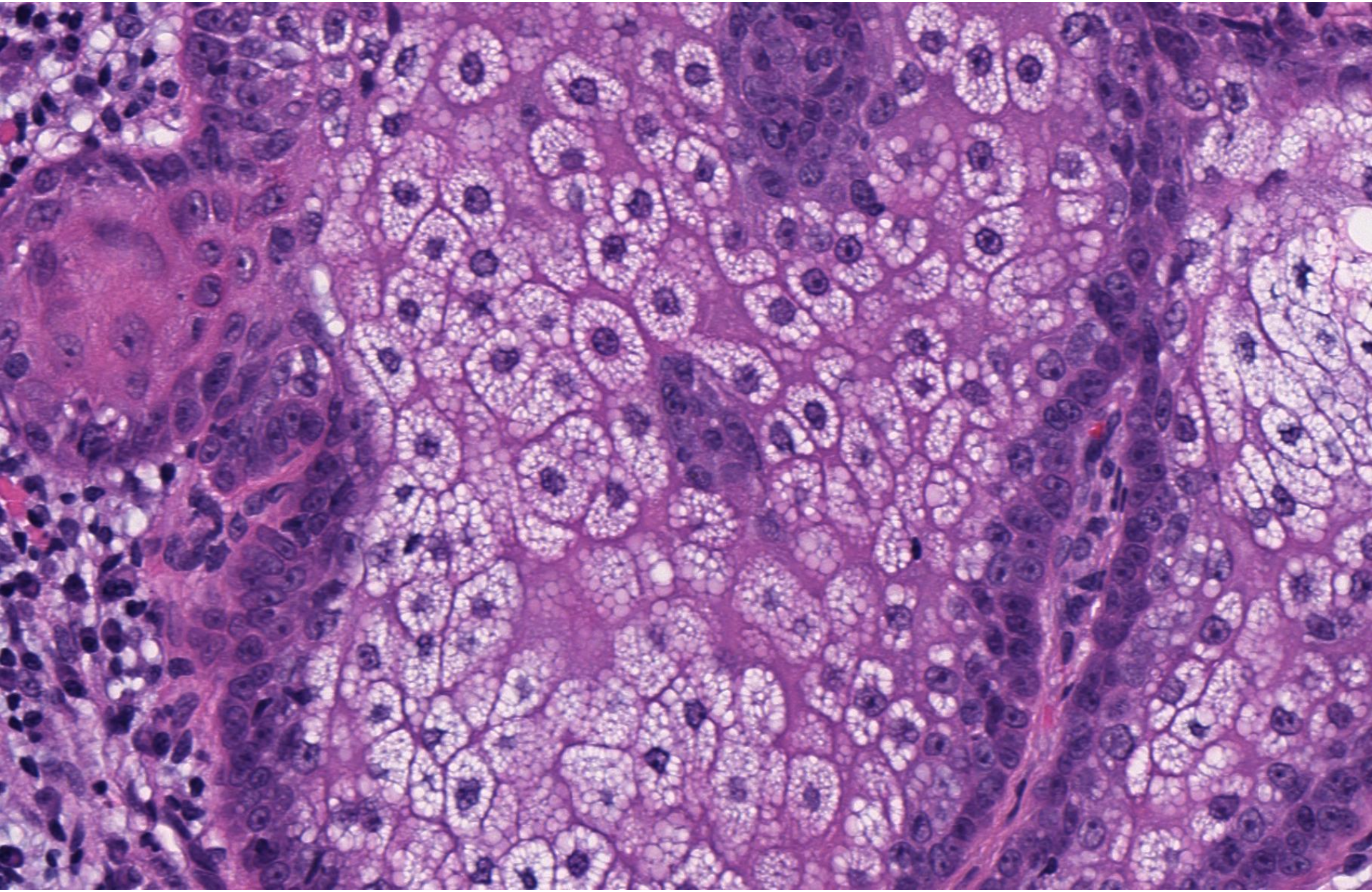












DIAGNOSIS?

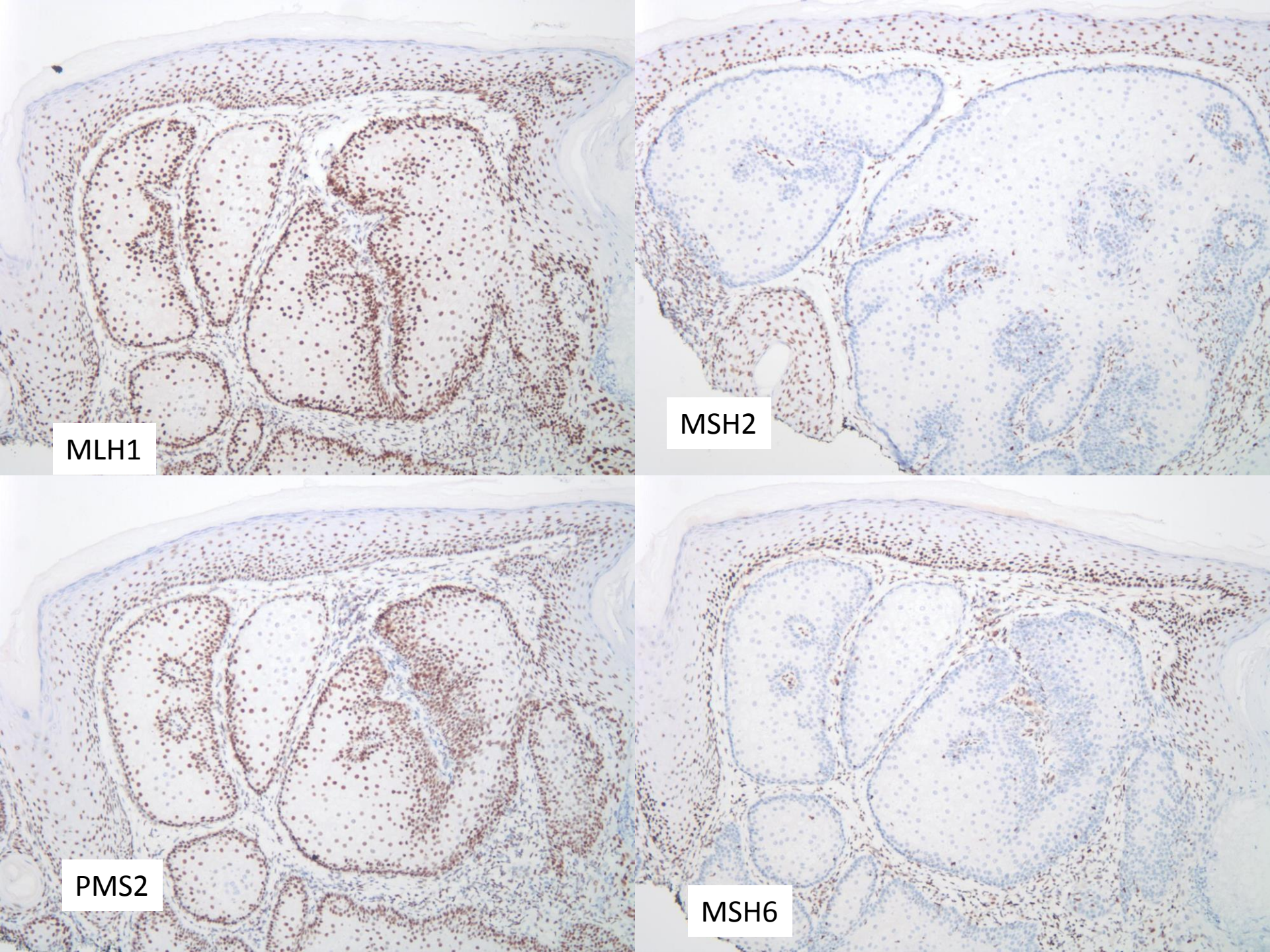
Sebaceous neoplasm (see comment)

What’s next???

Mismatch repair protein deficiency is common in Sebaceous Neoplasms and suggests the importance of screening for Lynch Syndrome.

Plocharczyk et al.

Am J Dermatopathol 2013;35:191-195


MLH1
MSH2
PMS2
MSH6

MSI testing of sebaceous lesions

- 43 cases (Seb ca, adenoma, hyperplasia, sebaceoma, sebaceous NOS)
  - 33% with abnormal MMRP by IHC
    - No case of sebaceous hyperplasia
    - Corrected % is 40%
  - In this series 63% of patients with abnormal MMRP were confirmed to have Lynch Syndrome

Routine testing of all sebaceous neoplasms for MMRP abnormalities

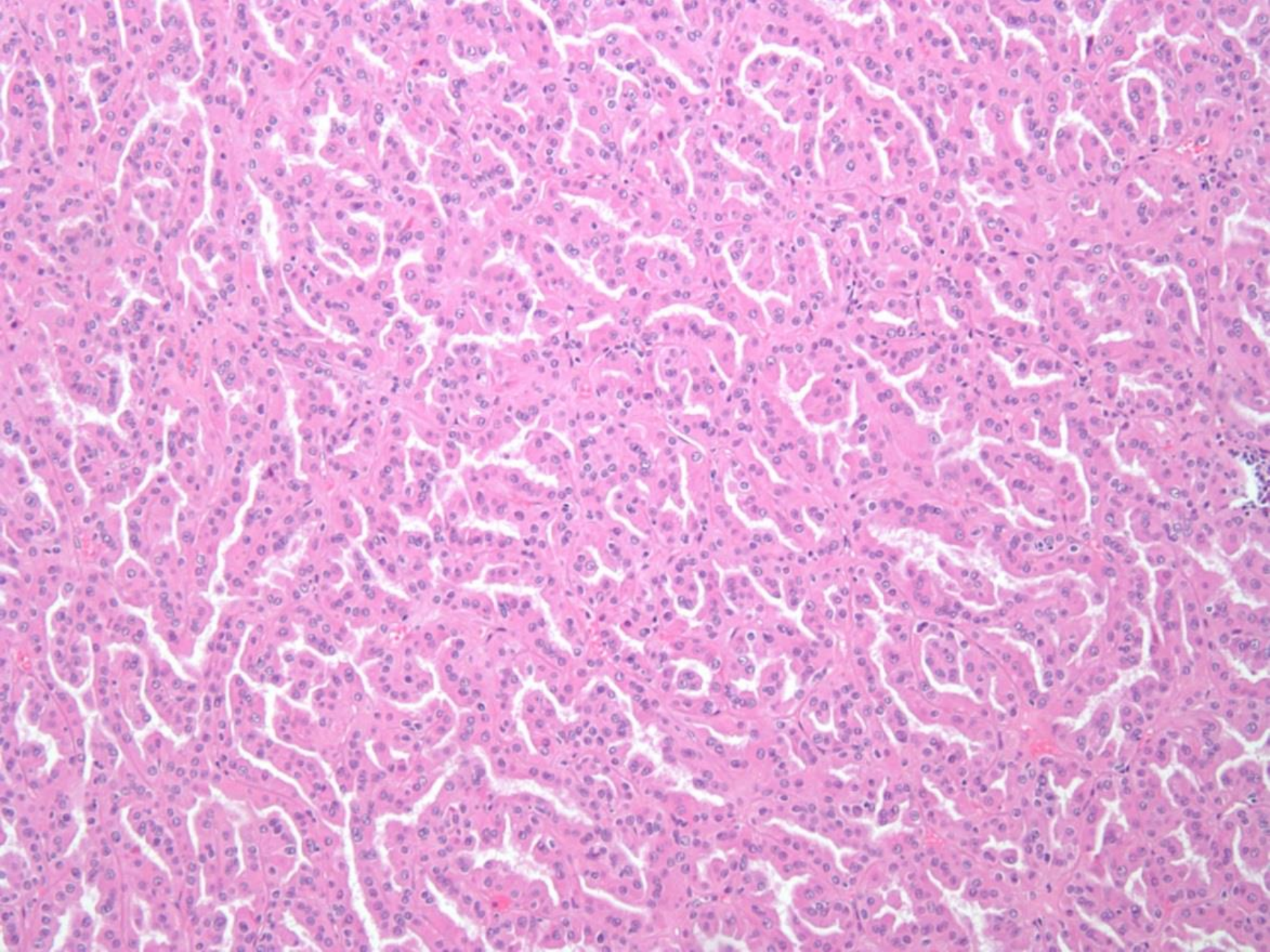
- Incidence of sebaceous neoplasms (excluding sebceous hyperplasia) is low 0.36% of all skin biopsies in one series
- Yield for MMRP abnormality is high (40%)
- When MMRP abnormality is present incidence of Lynch syndrome is high (50-60%)
- Sebaceous tumors often present before the onset of visceral malignancy providing opportunity for enhanced surveillance/screening

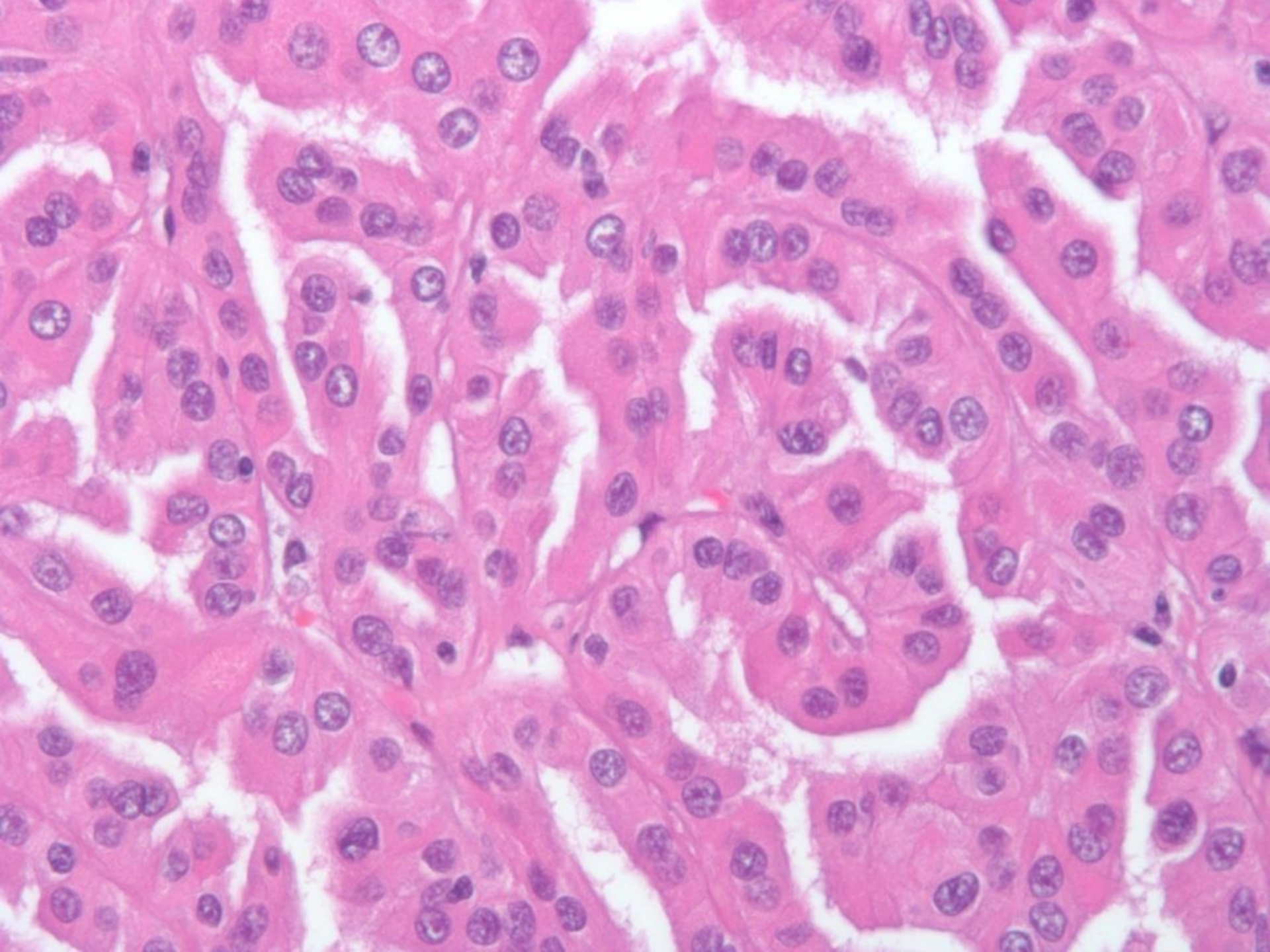
"The gentleman at the other register would like to cover your co-pay."

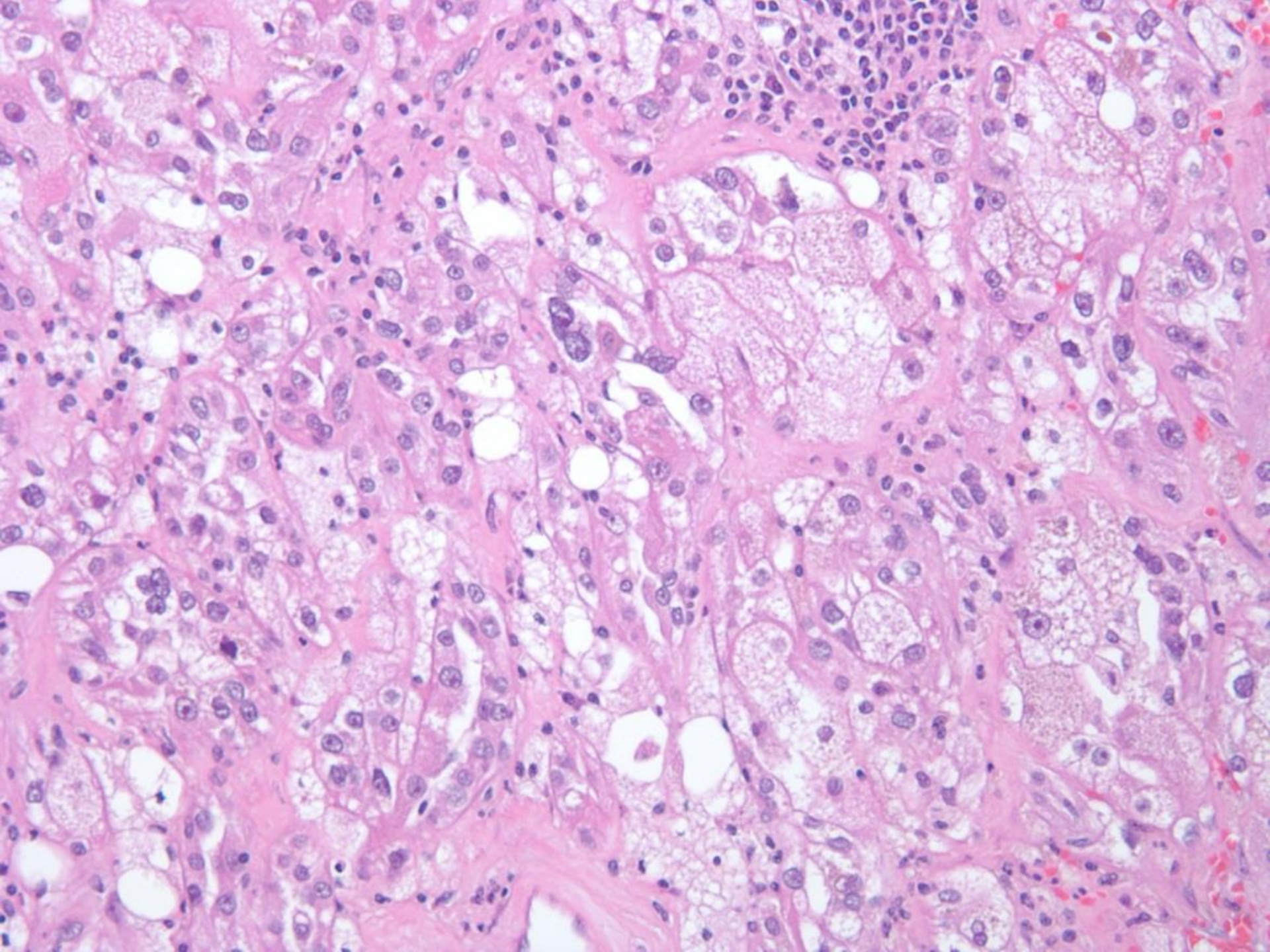
SB 5935

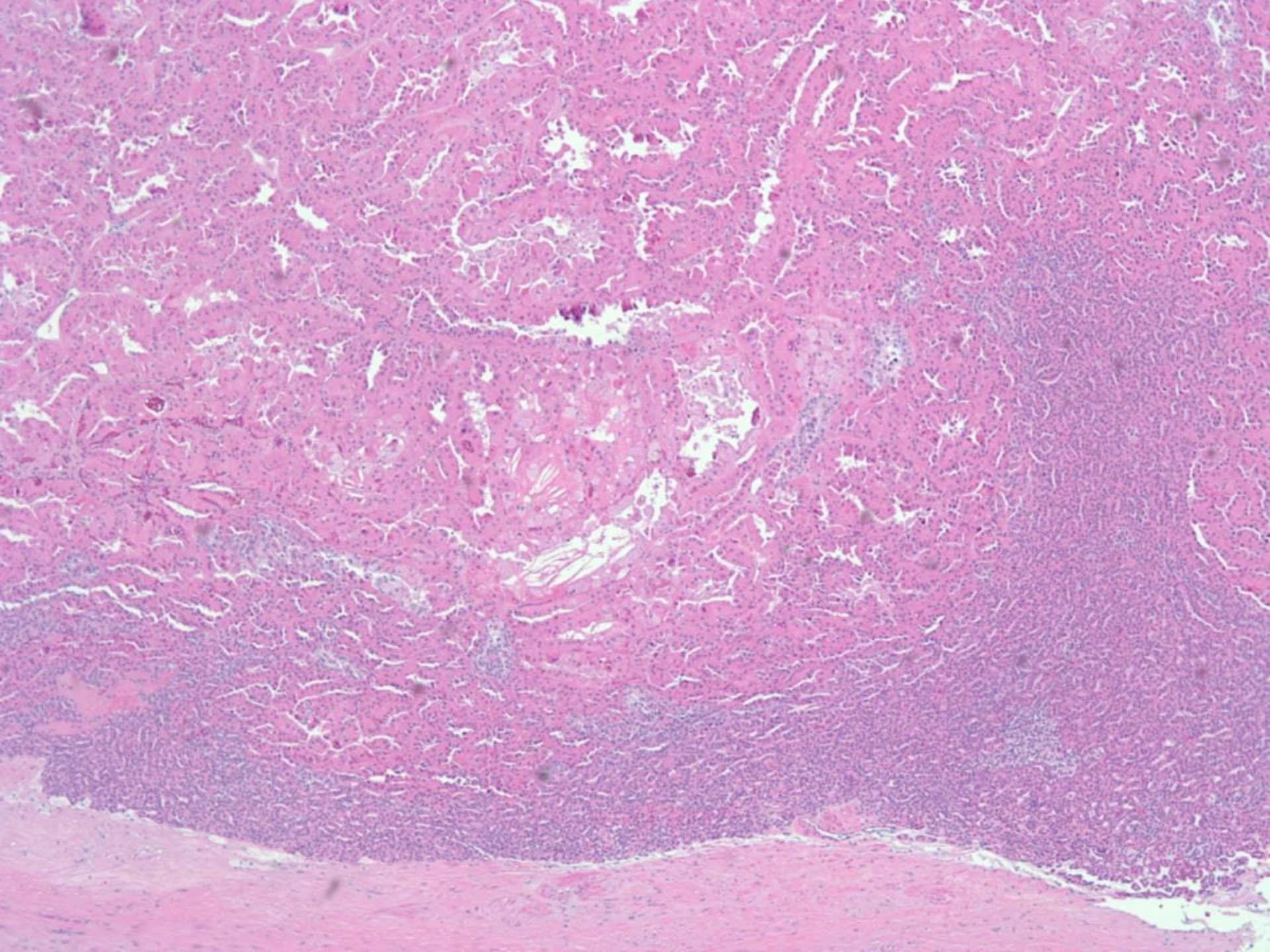
Charles Lombard; El Camino Hospital

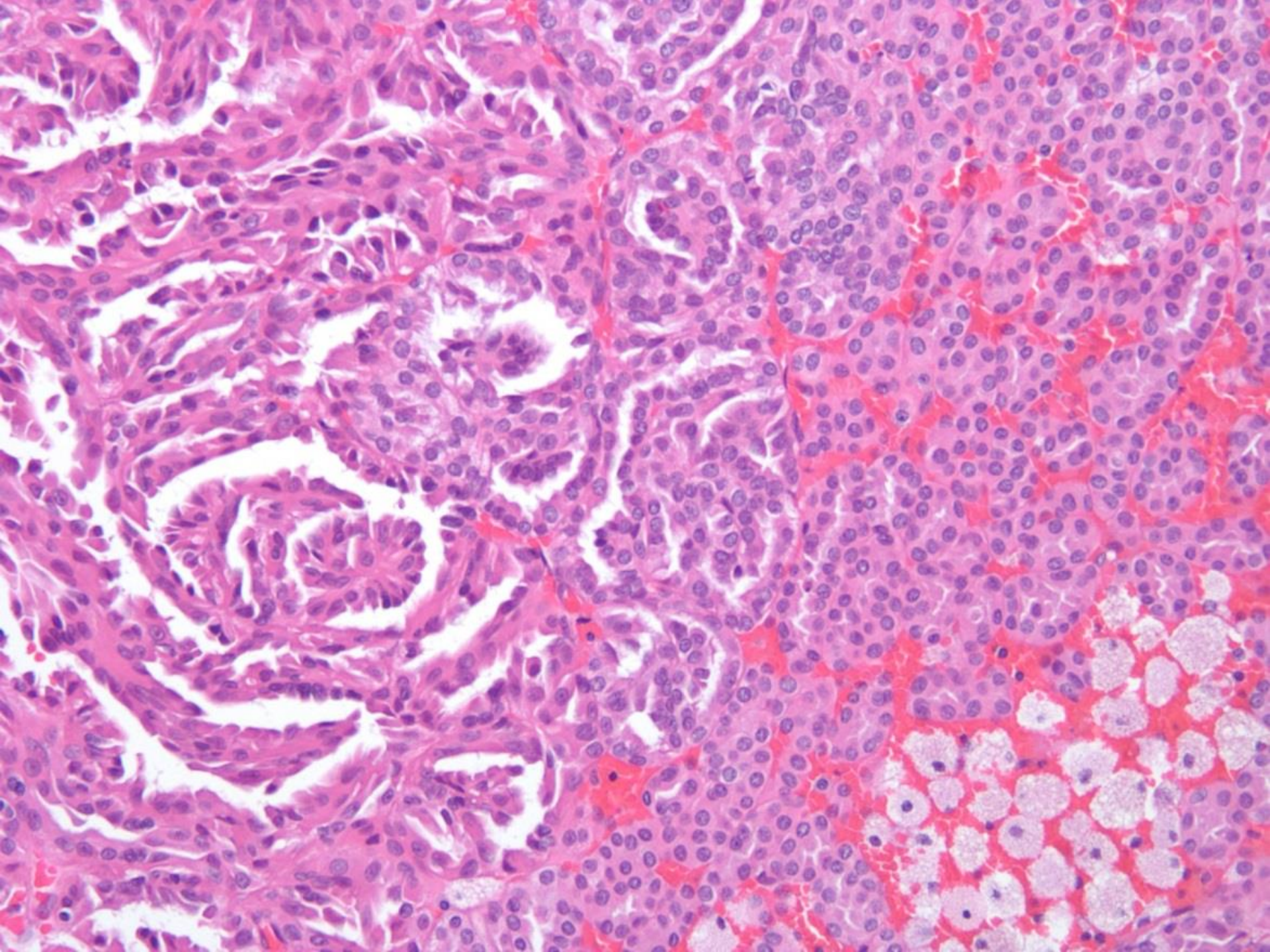
81-year-old female with 2.8cm left renal mass. Partial nephrectomy performed.











DIAGNOSIS?

Papillary renal cell carcinoma, Type 2

With Mixed component of Papillary renal cell carcinoma, Type 1

Papillary renal cell carcinoma

- Common to have “overlapping patterns”
  - 47 % of cases in 1 series had “overlapping” features
    - Predominantly type 1 tumors with focal areas of type 2-like is most common pattern
- Unusual pattern “true mixed” with predominantly type 2 tumor and focal type 1 areas
  - 2 series report incidence of 2% in papillary RCC

“The morphologic and ipox spectrum of papillary RCC”. AJSP 2014;38:887-894.

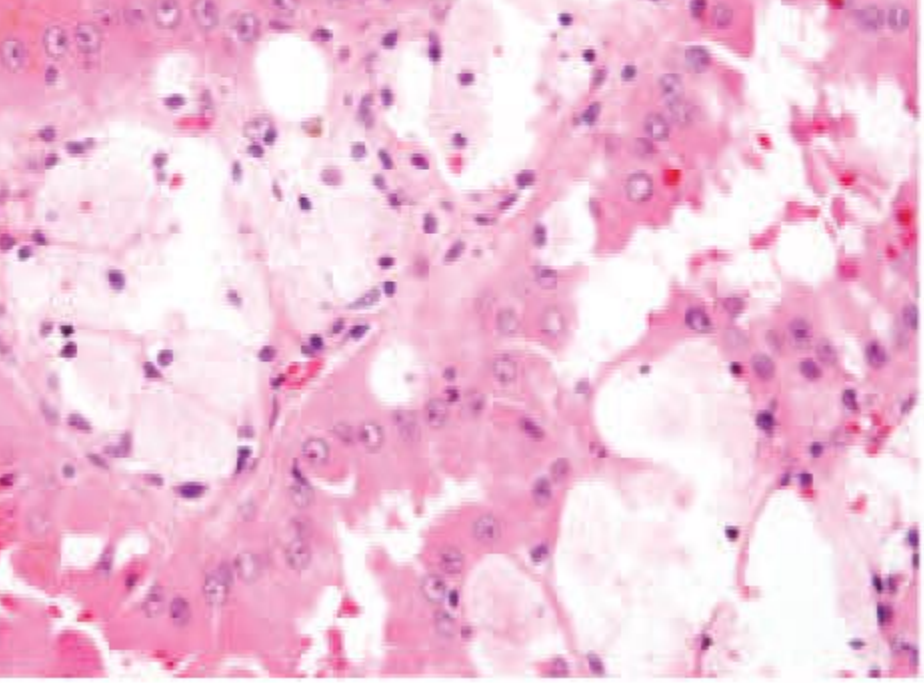
DDX: oncocytic renal cell neoplasms

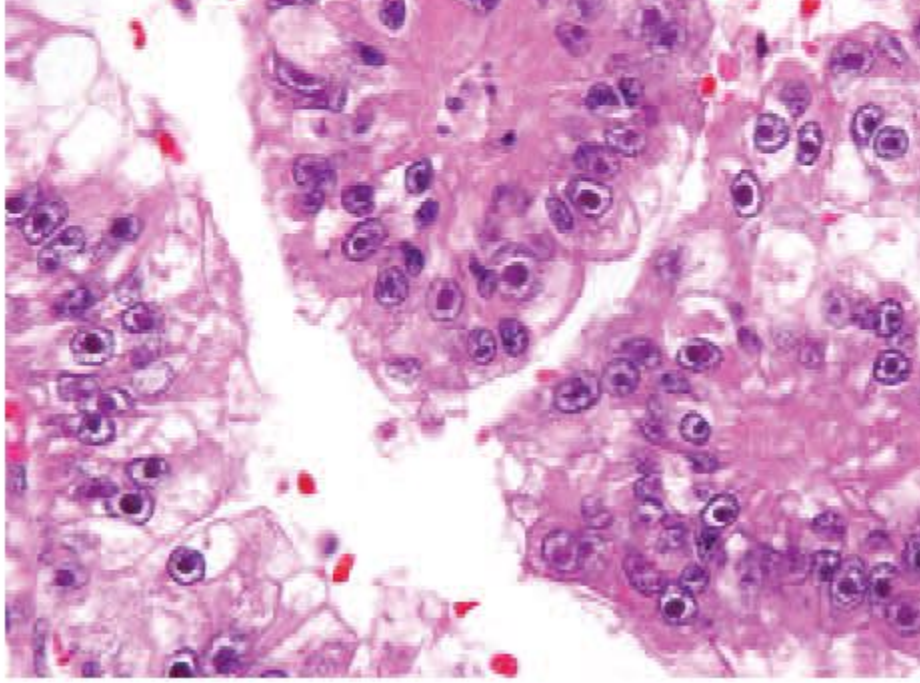
- Oncocytoma
- Chromophobe RCC
- Hybrid tumor
- Tubulocystic carcinoma
- Papillary RCC
- Clear cell (conventional) RCC
- Follicular thyroid-like carcinoma
- Hereditary leiomyomatosis–associated RCC
- Acquired cystic kidney disease–associated RCC
- Rhabdoid RCC
- MiTF translocation carcinomas
- Epithelioid angiomyolipoma
- Unclassified RCC

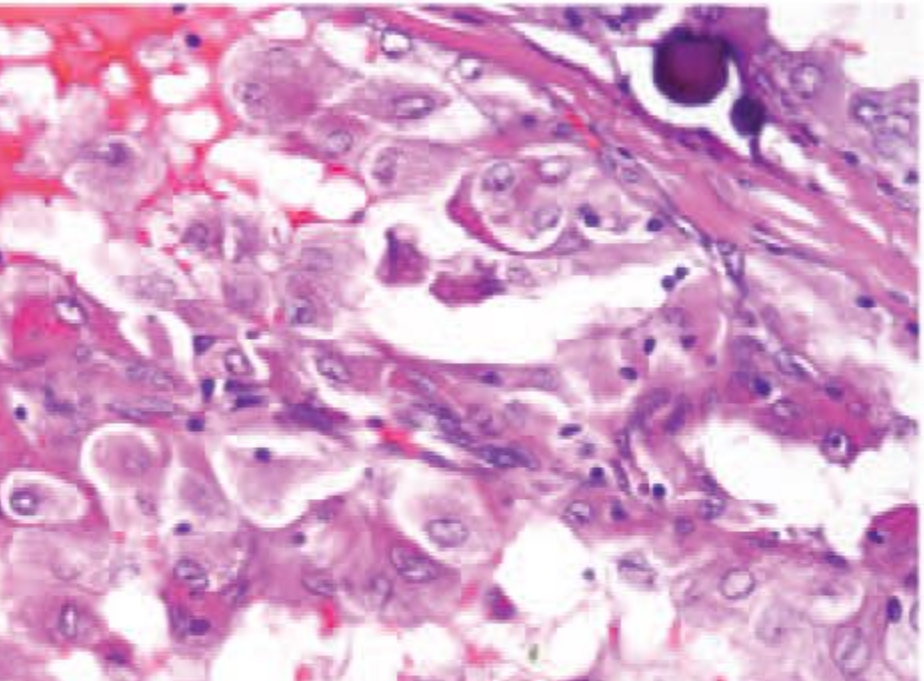
From Epstein: Diagnostic approach to Eosinophilic Renal Neoplasms. APLM 2014;138:1531-41.

DDX: Renal papillary oncocytic neoplasms

- Papillary renal cell carcinoma, type 2
  - "oncocytic papillary renal cell carcinoma
- Hereditary leiomyomatosis-associated RCC
- Translocation RCC
  - Xp11.2 (TFE3)
  - T 6;11 (TFEB)







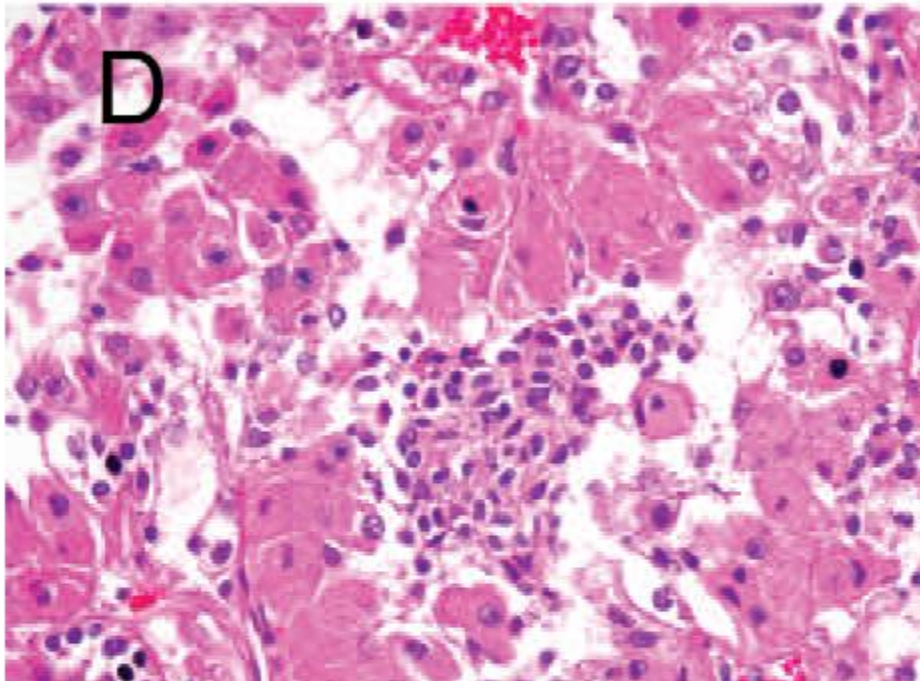

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Table 4. Useful Immunomarkers in the Diagnosis of Renal Epithelial Neoplasms[a]

Antibodies	CRCC	PRCC	ChRCC	CPRCC	Onco	CDC	MTSCC	UUC
EMA	+	+	+	+	+	+	+	+
CK7	−	+	+	+	−	+	+	+
CK20	−	−	−	−	−	−	−	+/−
CK903	−	−	−	+/−	−	+	−	+
p63	−	−	−	−	−	−	−	+
CD10	+	+	−/+	+/−	−/+	−	−	−
CAIX	+	+/−, focal	−	+	−	−/+	ND	+
P504S	−/+	+	−	−	−	−/+	+/−	−/+
KIM-1	+	+	−	ND	−	−	ND	−
PAX2/PAX8	+	+	+/−	+	+	+	−	−
RCCma	+	+	−/+	+/−	−	−	−	−
CD117	−	−	+	−	+	+	−	−
S100A1	+	+/−	−	ND	+	−	−	−
S100P	−	−	−	−	−	−	−	+
GATA3	−	−	−	−	−	−	−	+
CD15	−	−	−	−	+/−	−	−	+/−
Vim	+	+/−	−	+/−	−	+	−	−
ksp-cad	−/+	−	+	ND	+	−	−	−

Abbreviations: CDC, collecting duct carcinoma; ChRCC, chromophobe renal cell carcinoma; CPRCC, clear cell papillary renal cell carcinoma; CRCC, clear cell renal cell carcinoma; MTSCC, mucinous tubular and spindle cell carcinoma; Onco, oncocytoma; PRCC, papillary renal cell carcinoma (type I); UUC, upper urinary tract urothelial carcinoma.

[a] Please refer to Tables 1 and 2 for definitions of symbols and antibody abbreviations.

Wilkerson et al: “Application of IHC in urololgic surgical pathology”. APLM 2014;138:1643-65

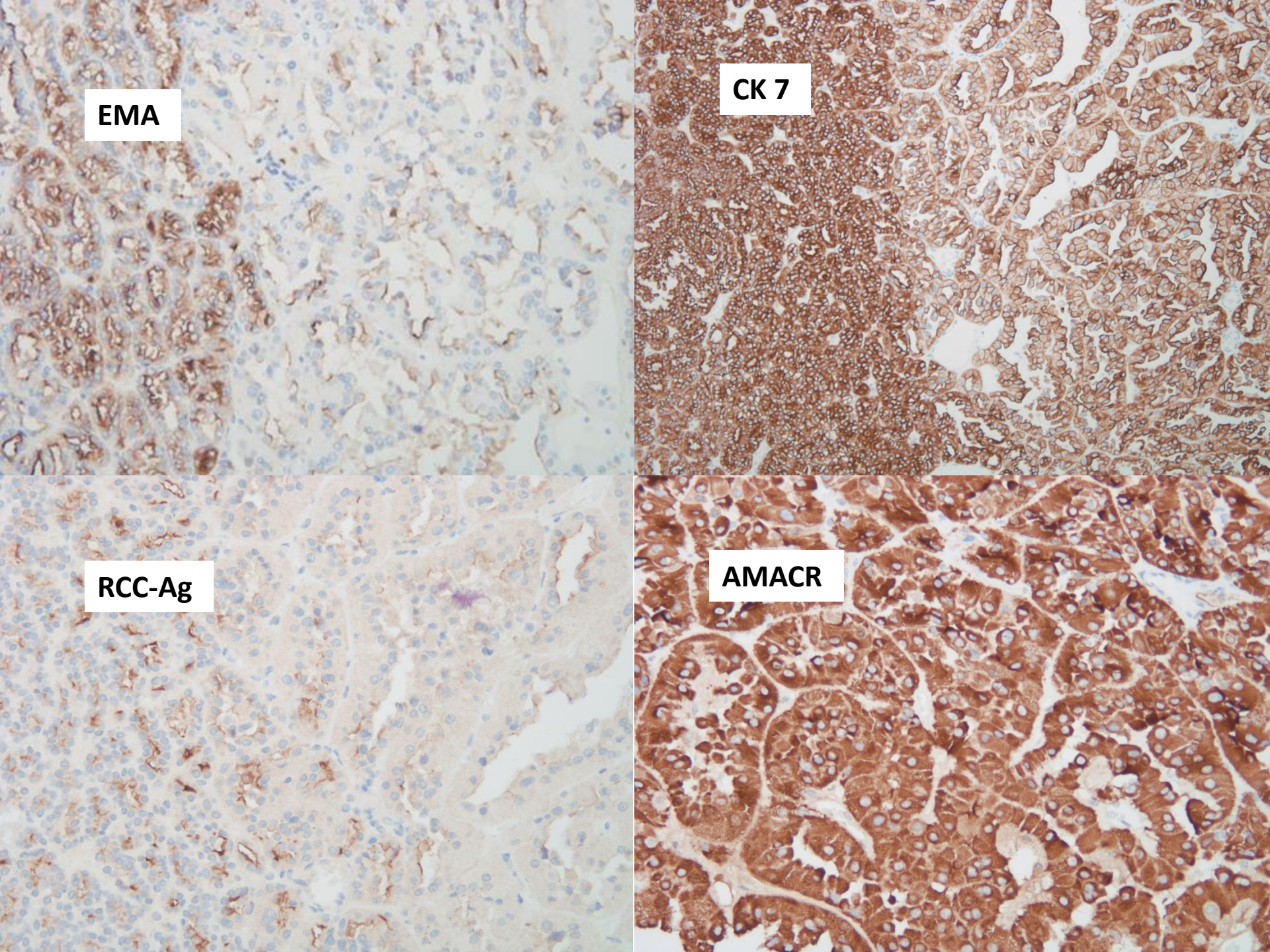
IHC: Papillary RCC

- CK 7, EMA positive (type 1 usually stronger and more uniform than type 2)
- AMACR: Positive

Table 6. Differential Diagnosis of Renal Cell Tumors With Both Clear Cell and Papillary Features[a]

Marker	CPRCC	CRCC	PRCC	TRCC
CK7	+	−	+	−/focally +
CAIX	+	+	Focally +	Focally +
P504S	−	−/+	+	+
CD10	−/focal +	+	+/−	+
34BE12	+/−	−	−	−
Paraf	N+	−	−/+	ND
RCCma	−	+	+	+
TFE3	−	−	−	+
GLUT1	+	+	−	ND

Wilkerson et al: “Application of IHC in urololgic surgical pathology”. APLM 2014;138:1643-65.


EMA
CK 7
RCC-Ag
AMACR

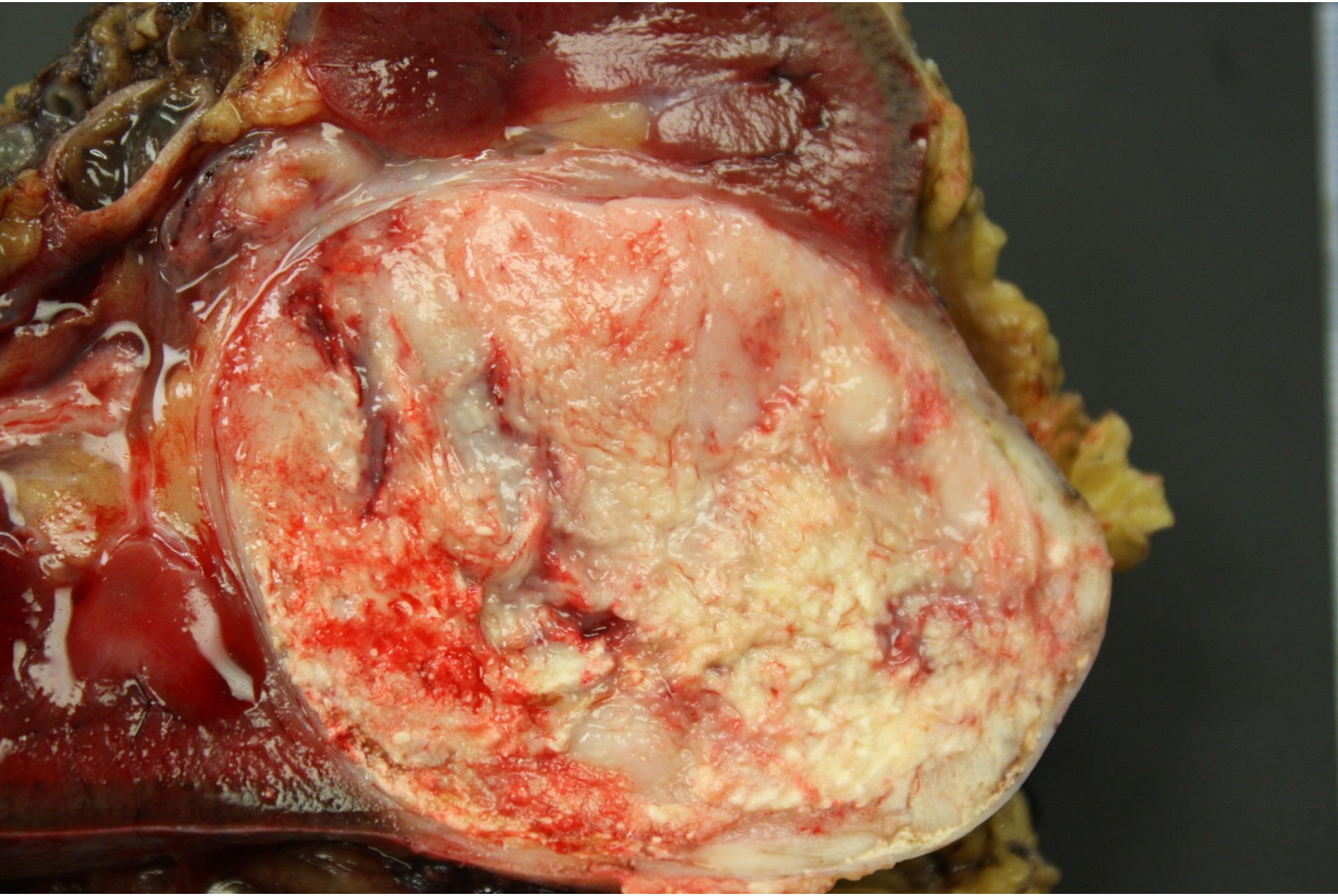
"If it's any consolation, toward the end he was high as a kite."

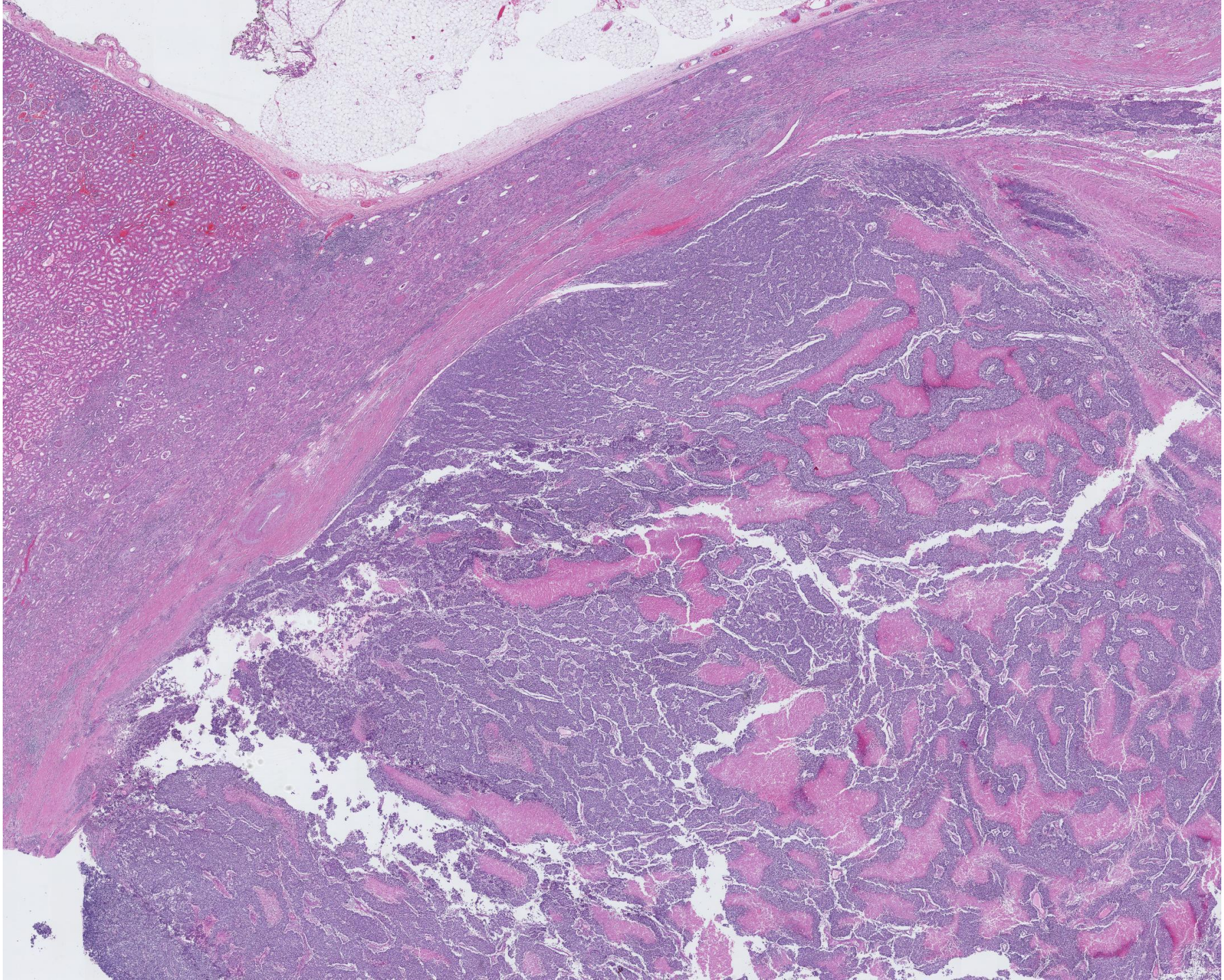
SB 5836

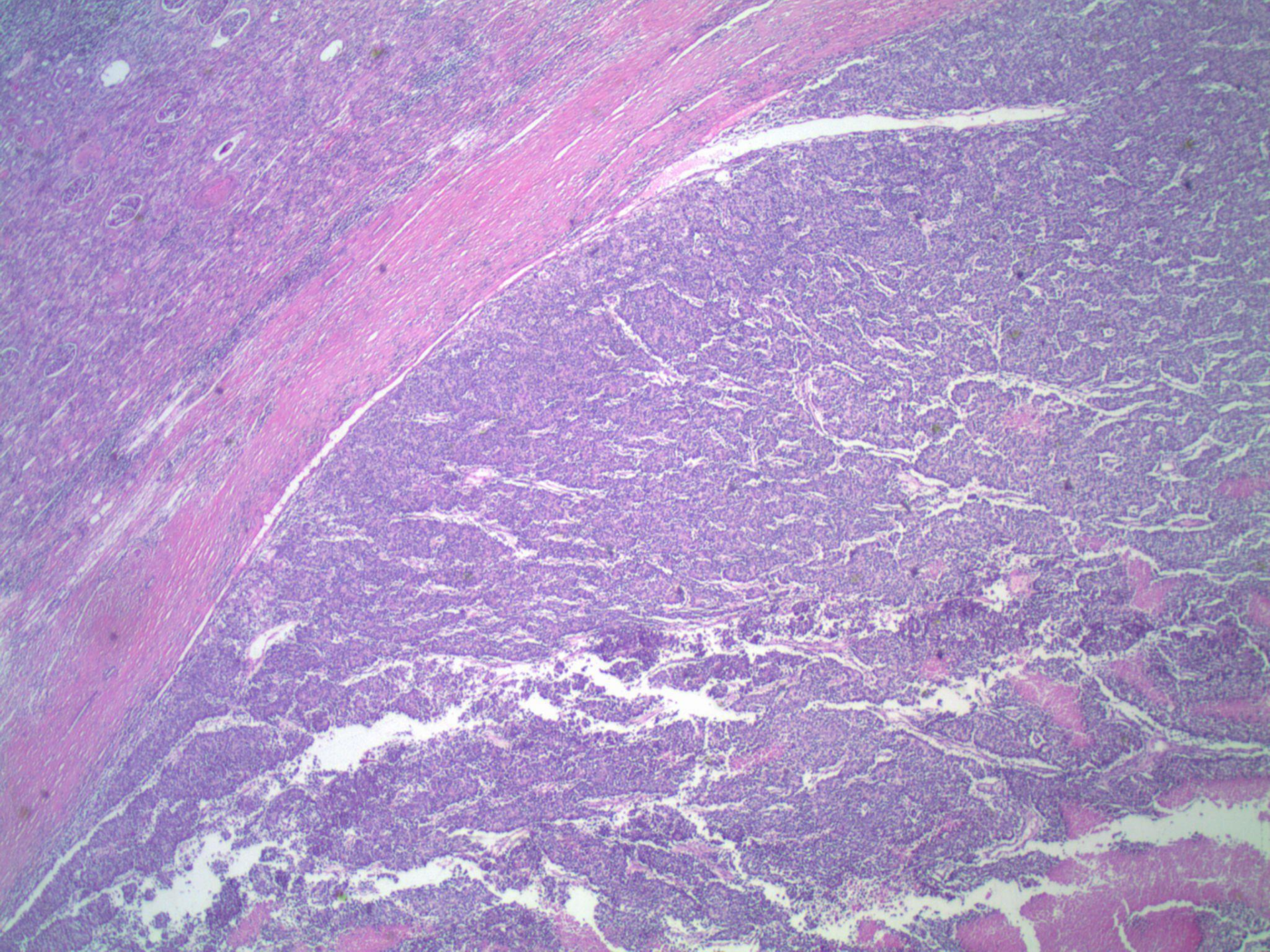
Ankur Sangoi; El Camino Hospital

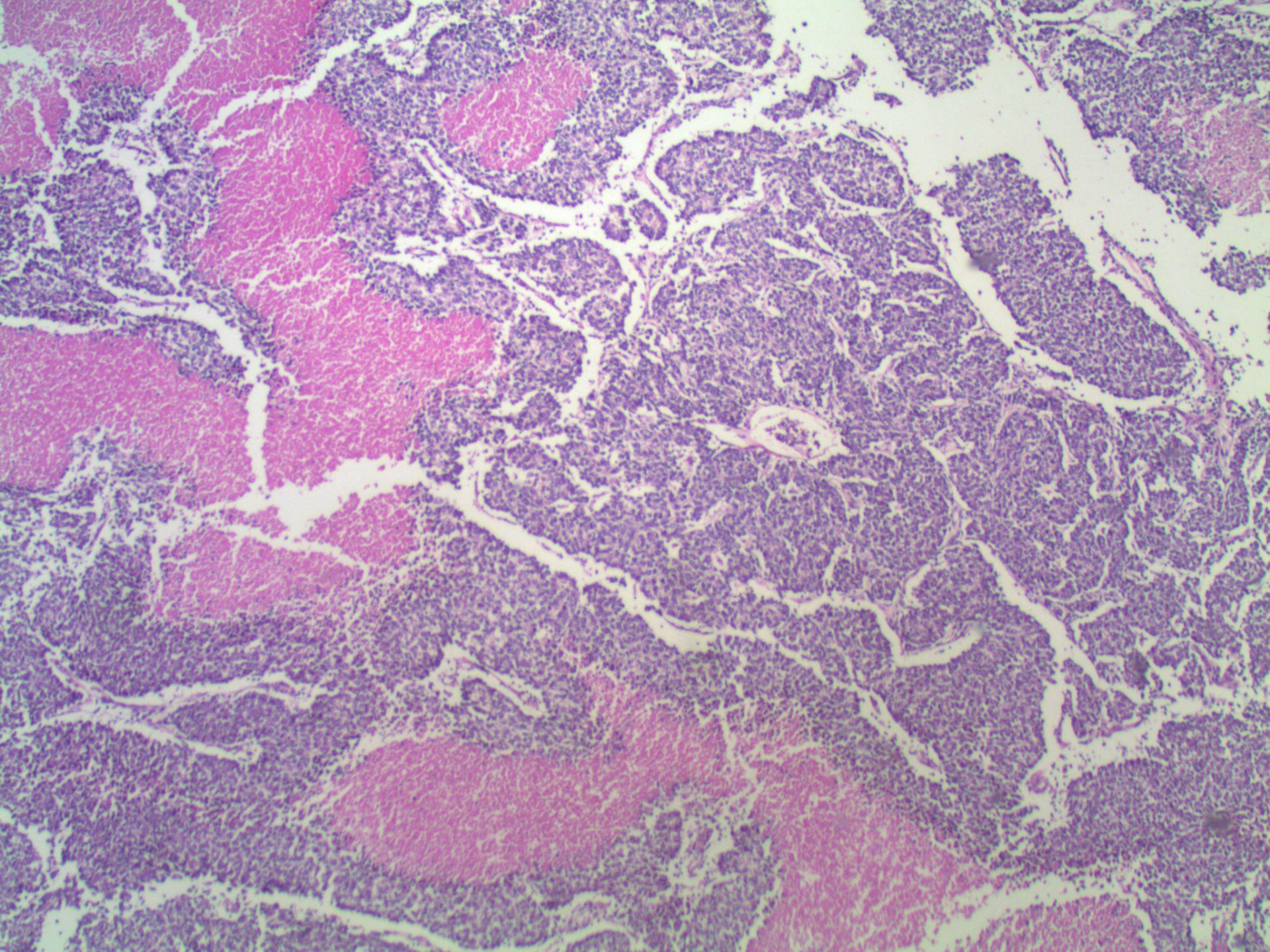
32-year-old female with left lower pole renal mass suspicious for renal cell carcinoma. Radical nephrectomy performed.

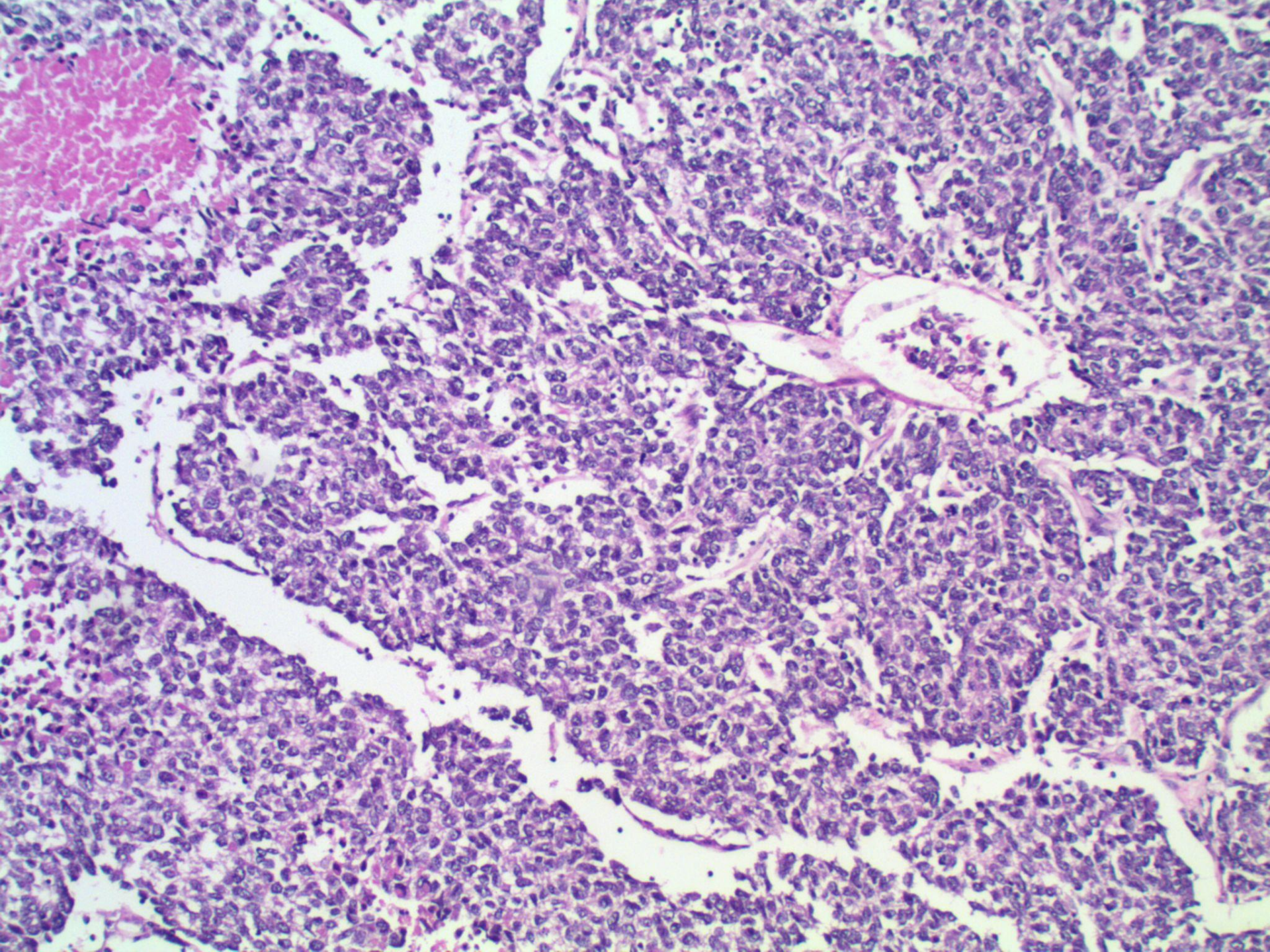

CENTIMETERS
INCHES
Cat. No. 09-016
Fisher Scientific

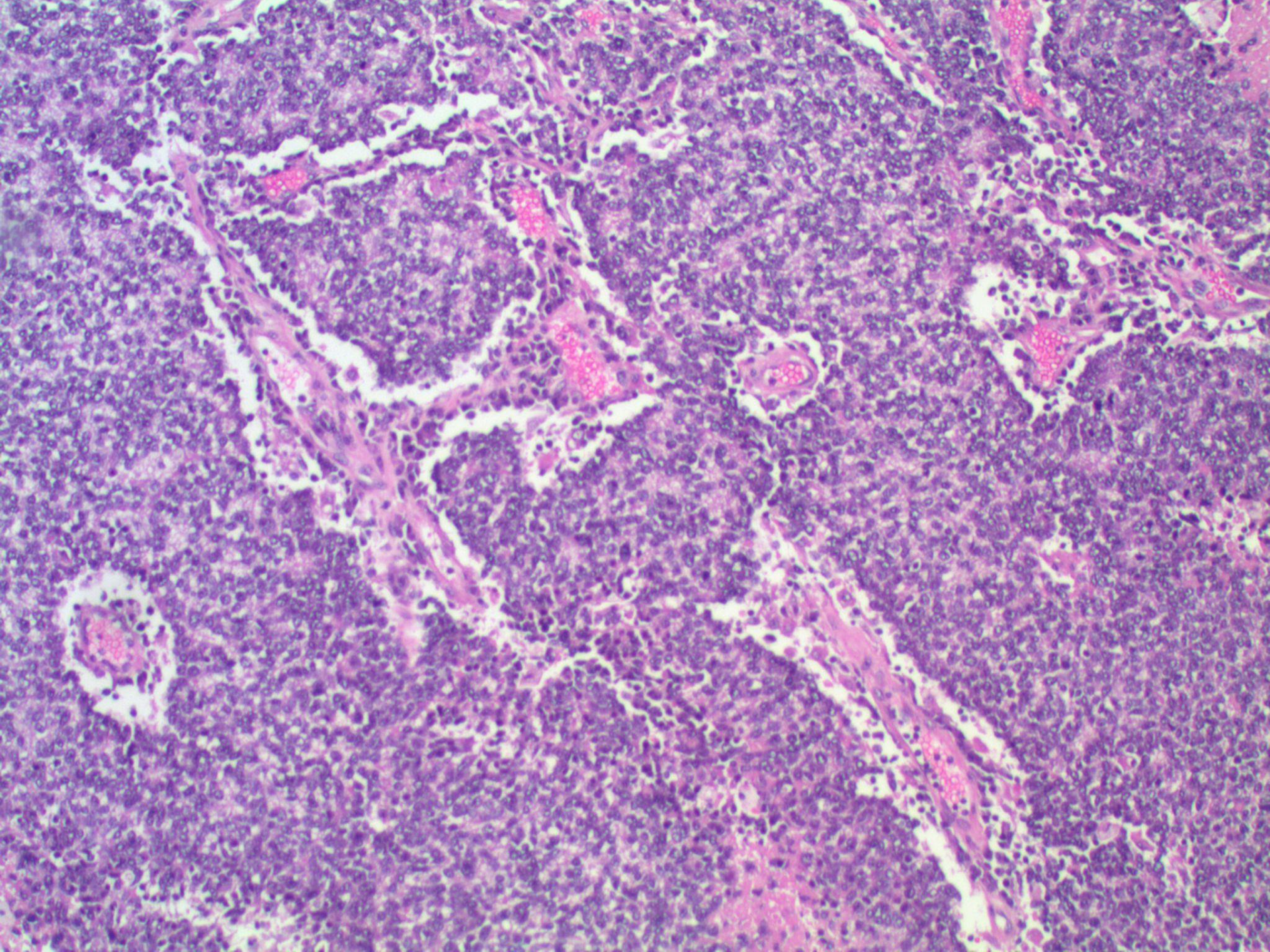


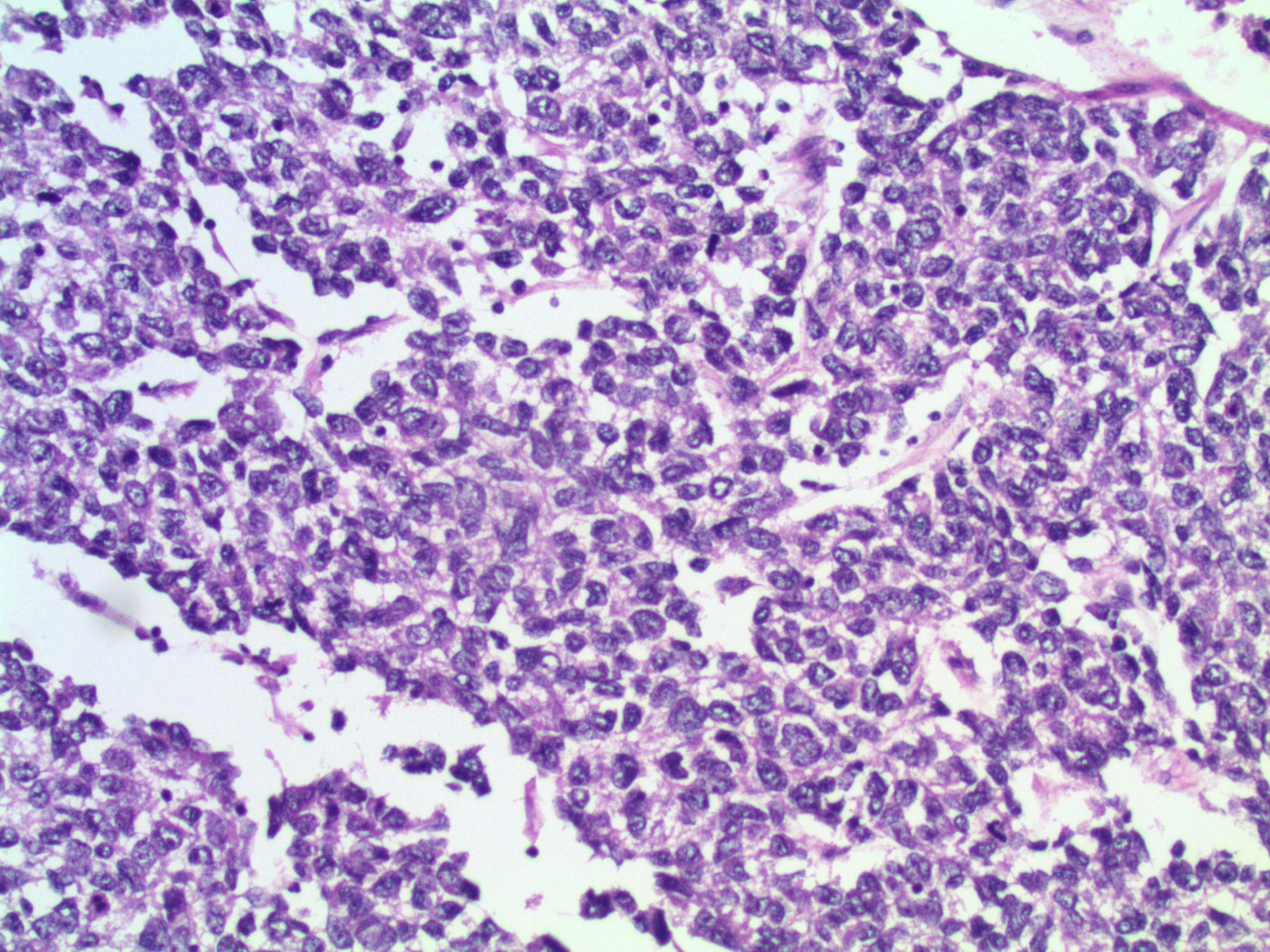


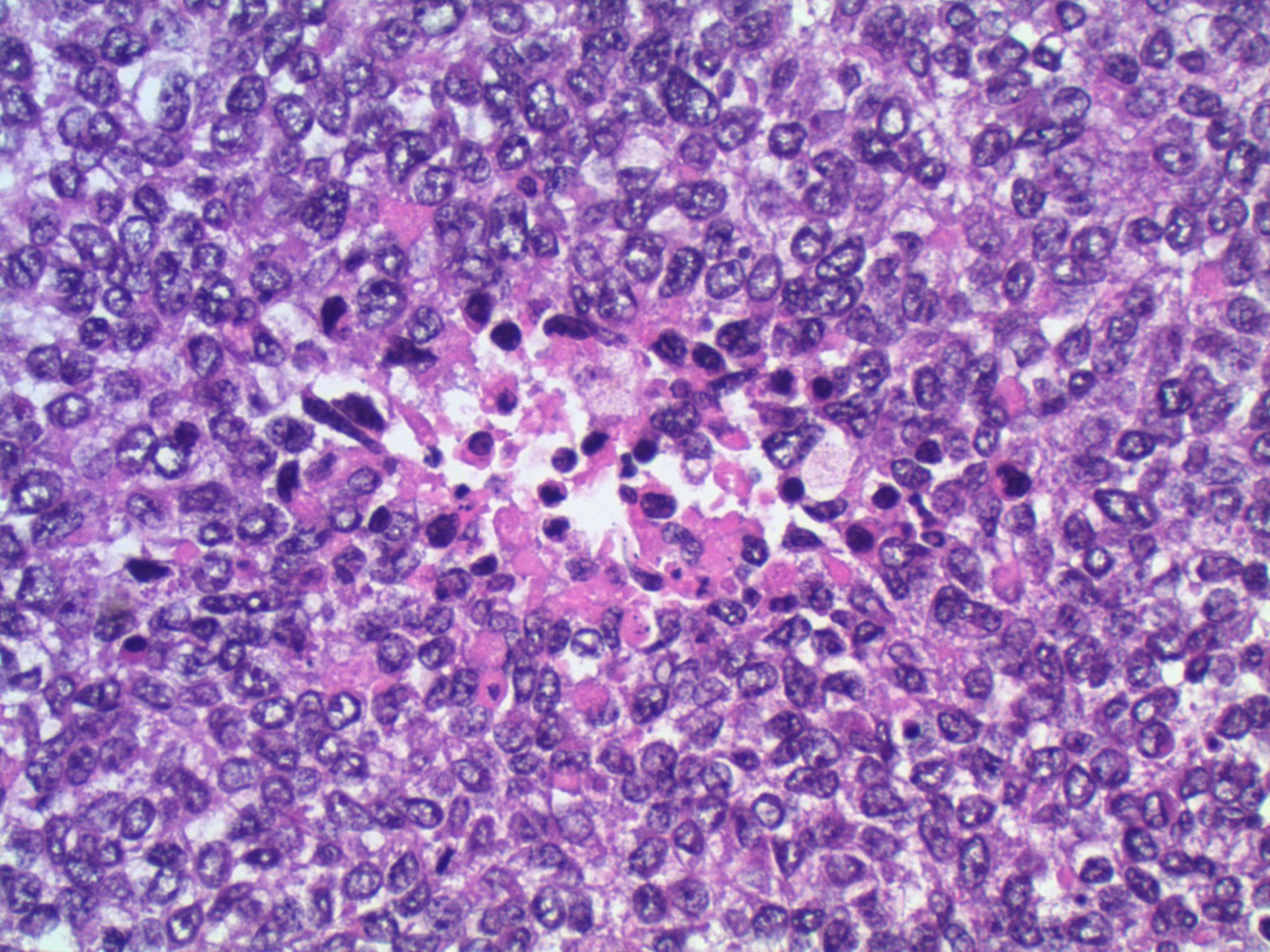








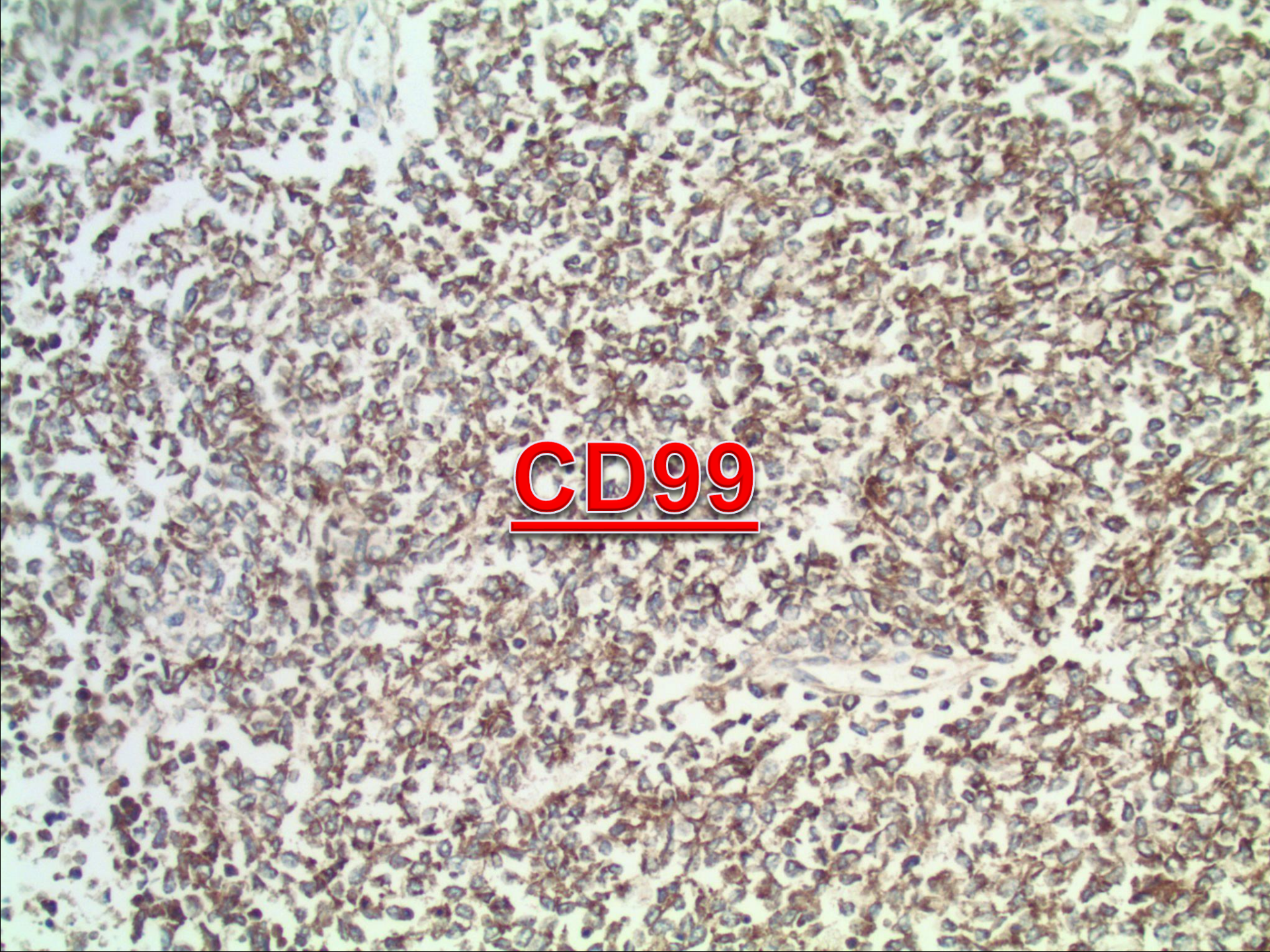




DIAGNOSIS?

IMMUNOHISTOCHEMISTRY

- AE1/AE3
- BCL2
- CD43
- CD99
- CHROMOGRANIN
- DESMIN
- EMA
- ERG
- GATA3
- OSCAR
- PAX8
- P63
- S100
- SYNAPTOPHYSIN
- VIMENTIN
- WT1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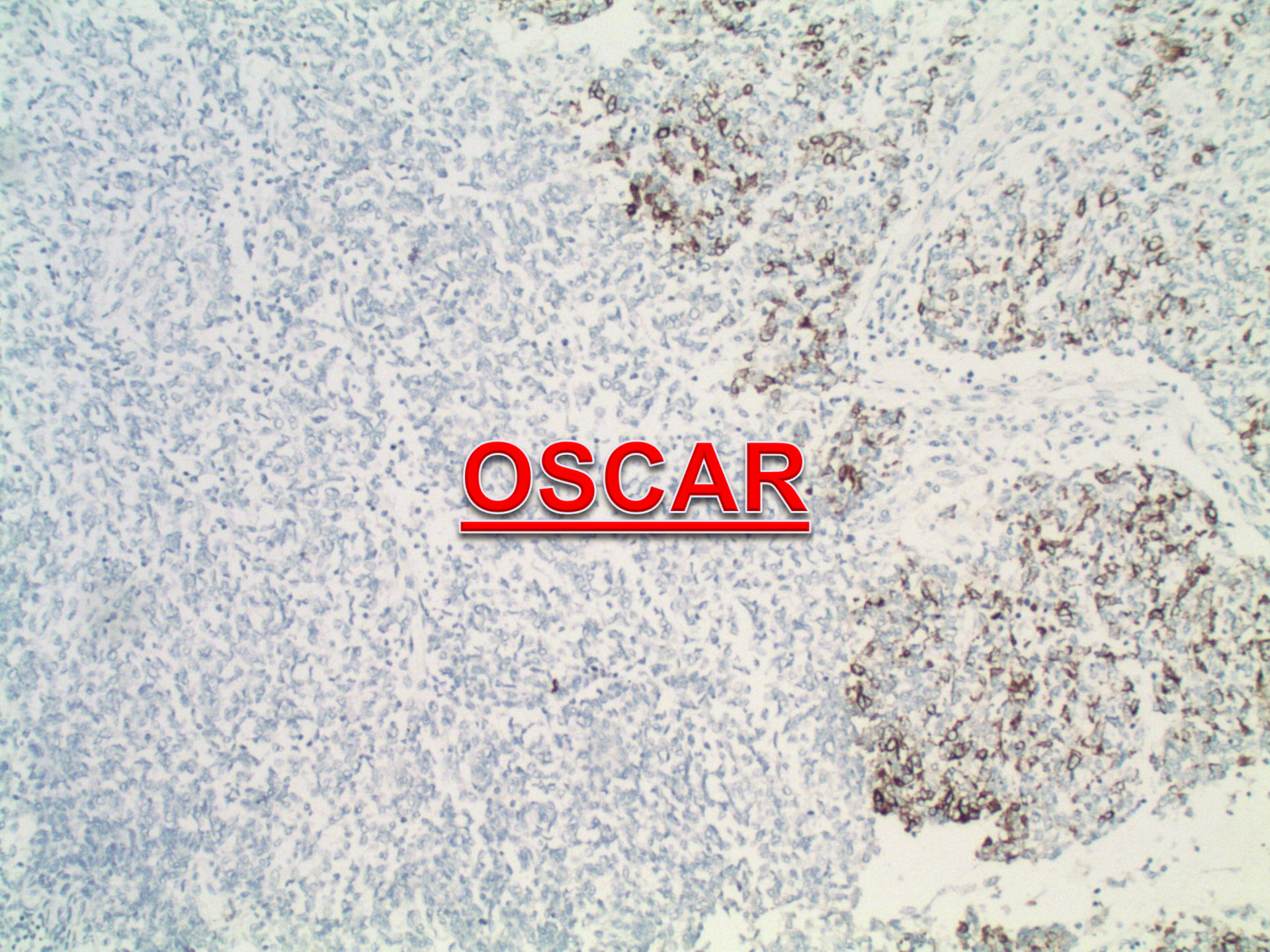
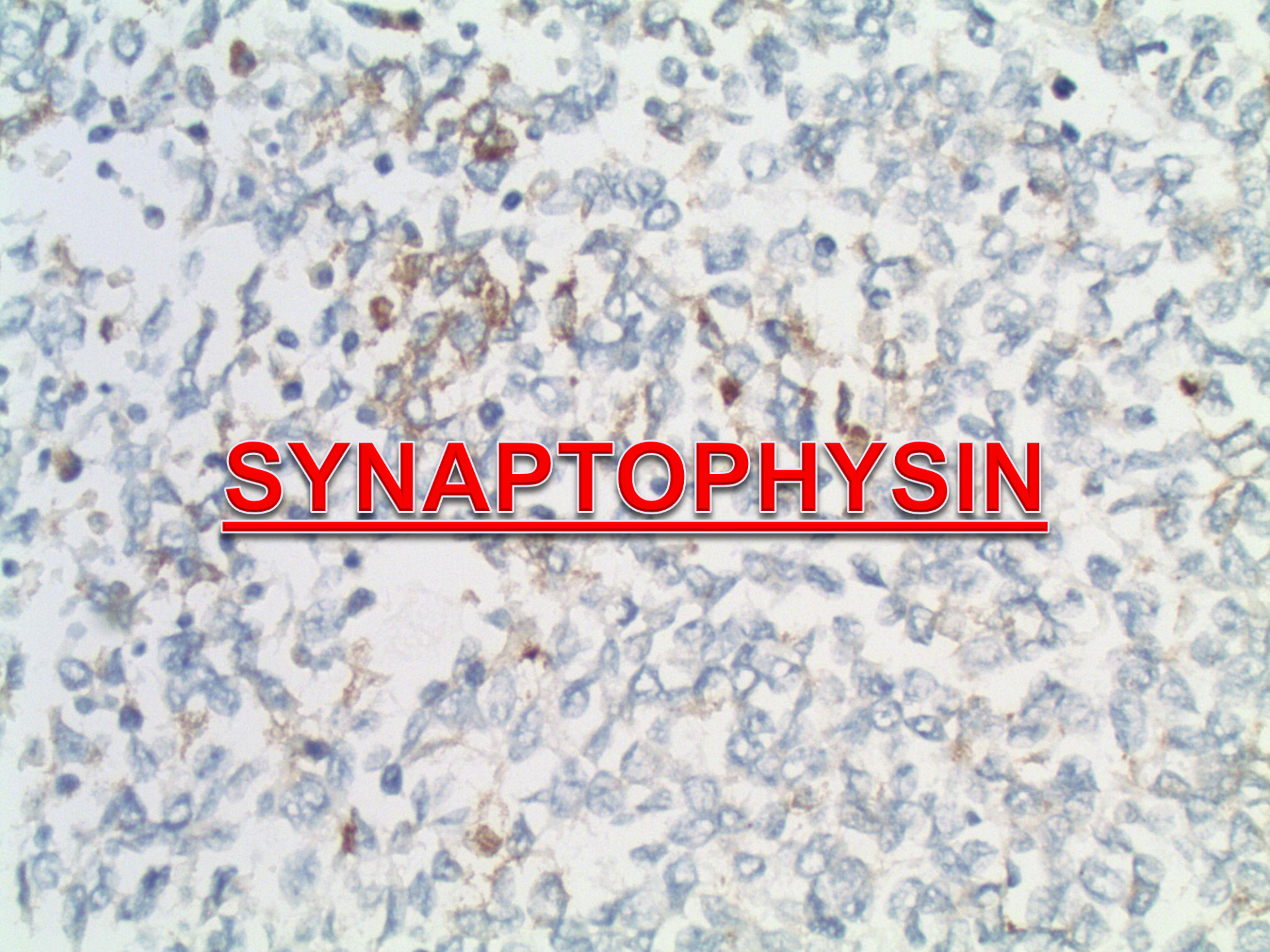
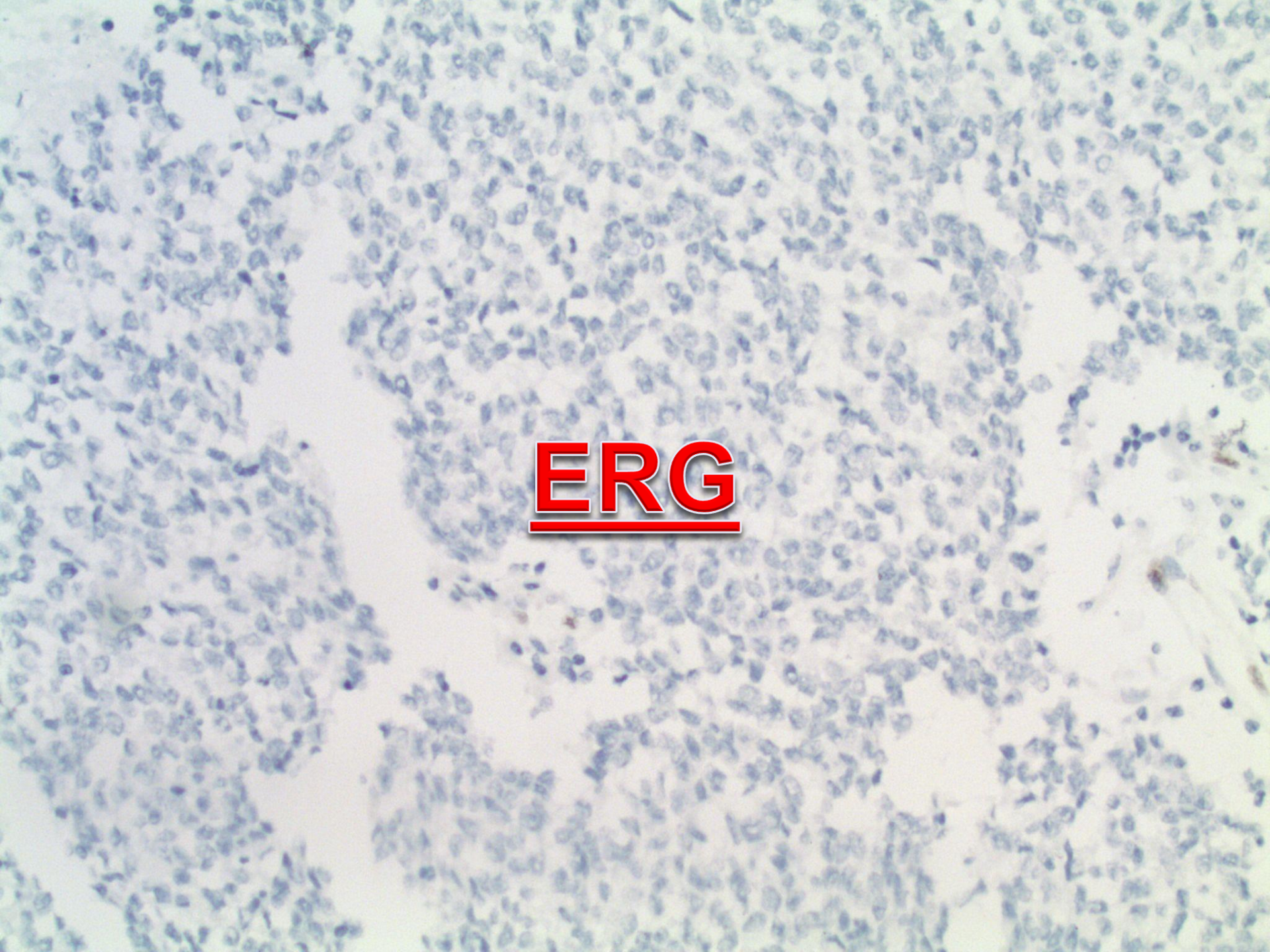

OSCAR


SYNAPTOPHYSIN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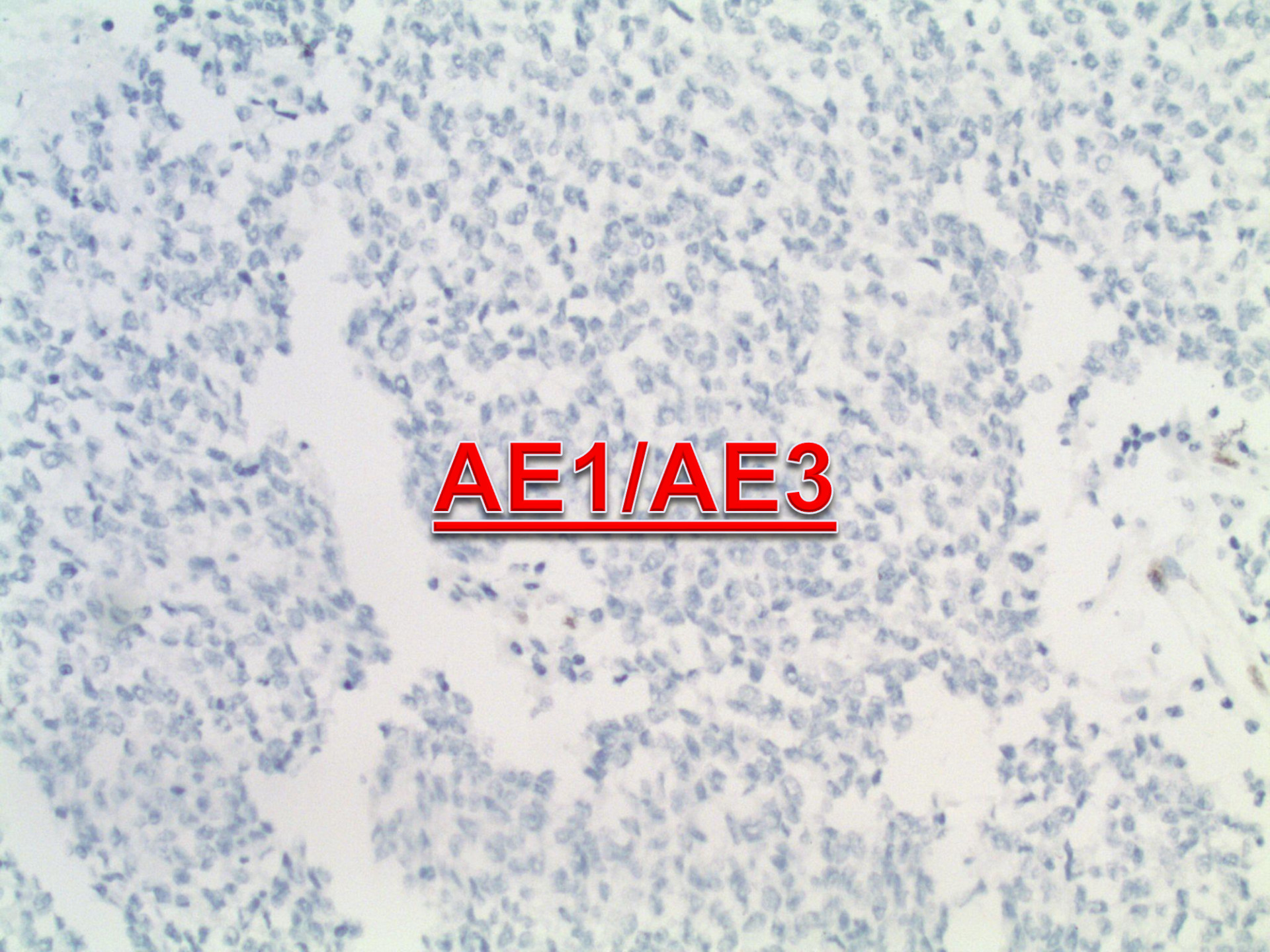
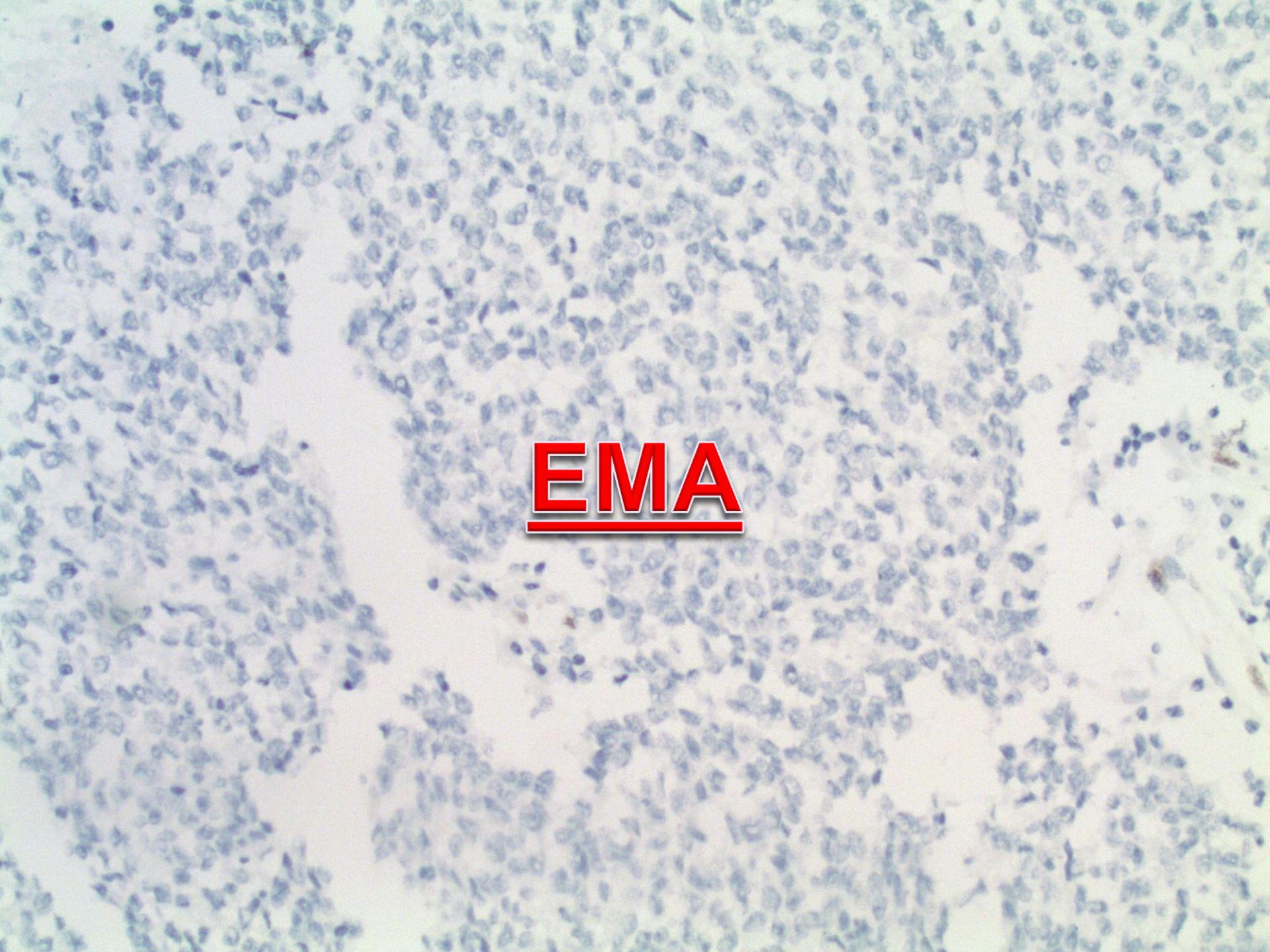
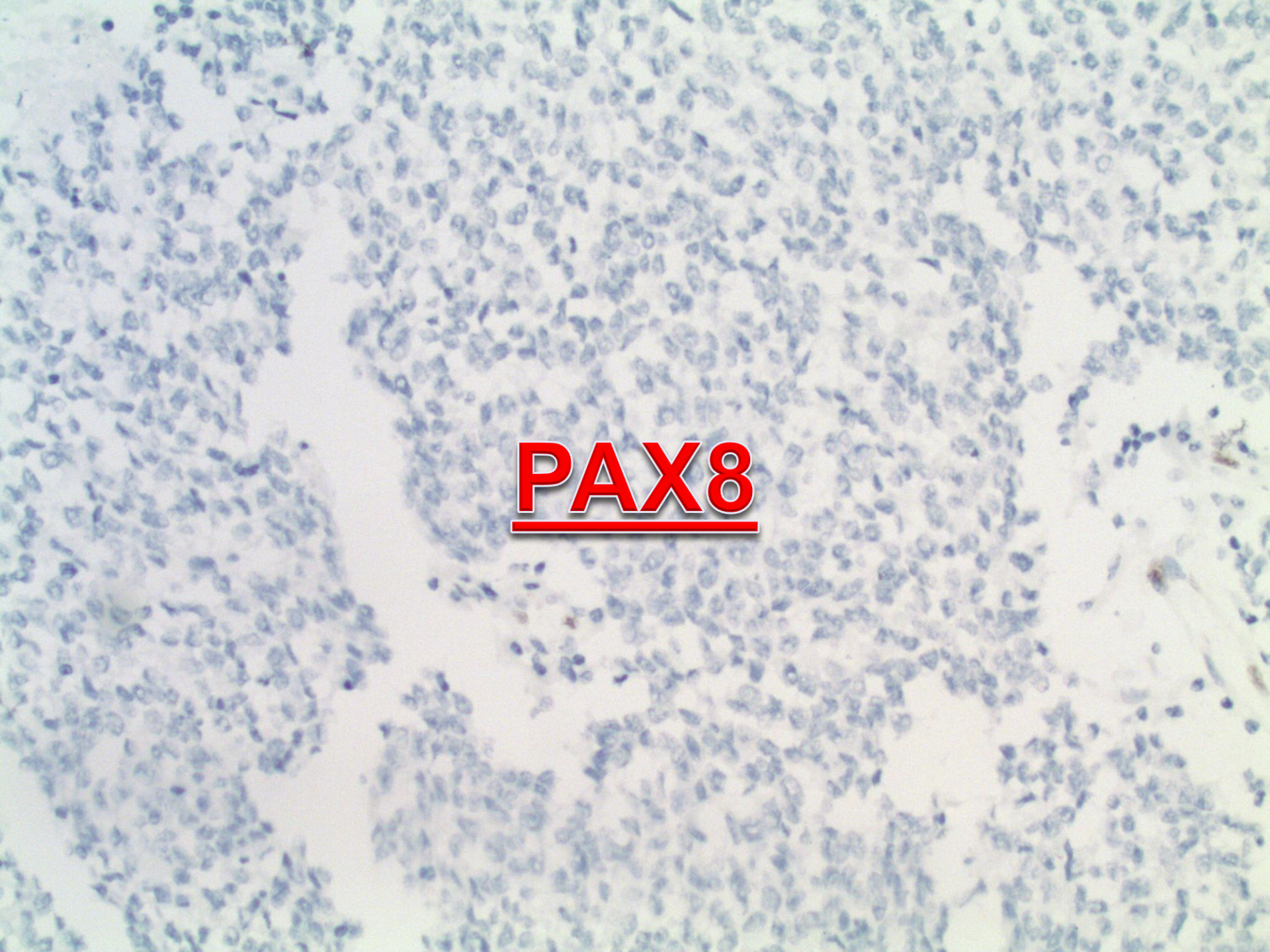
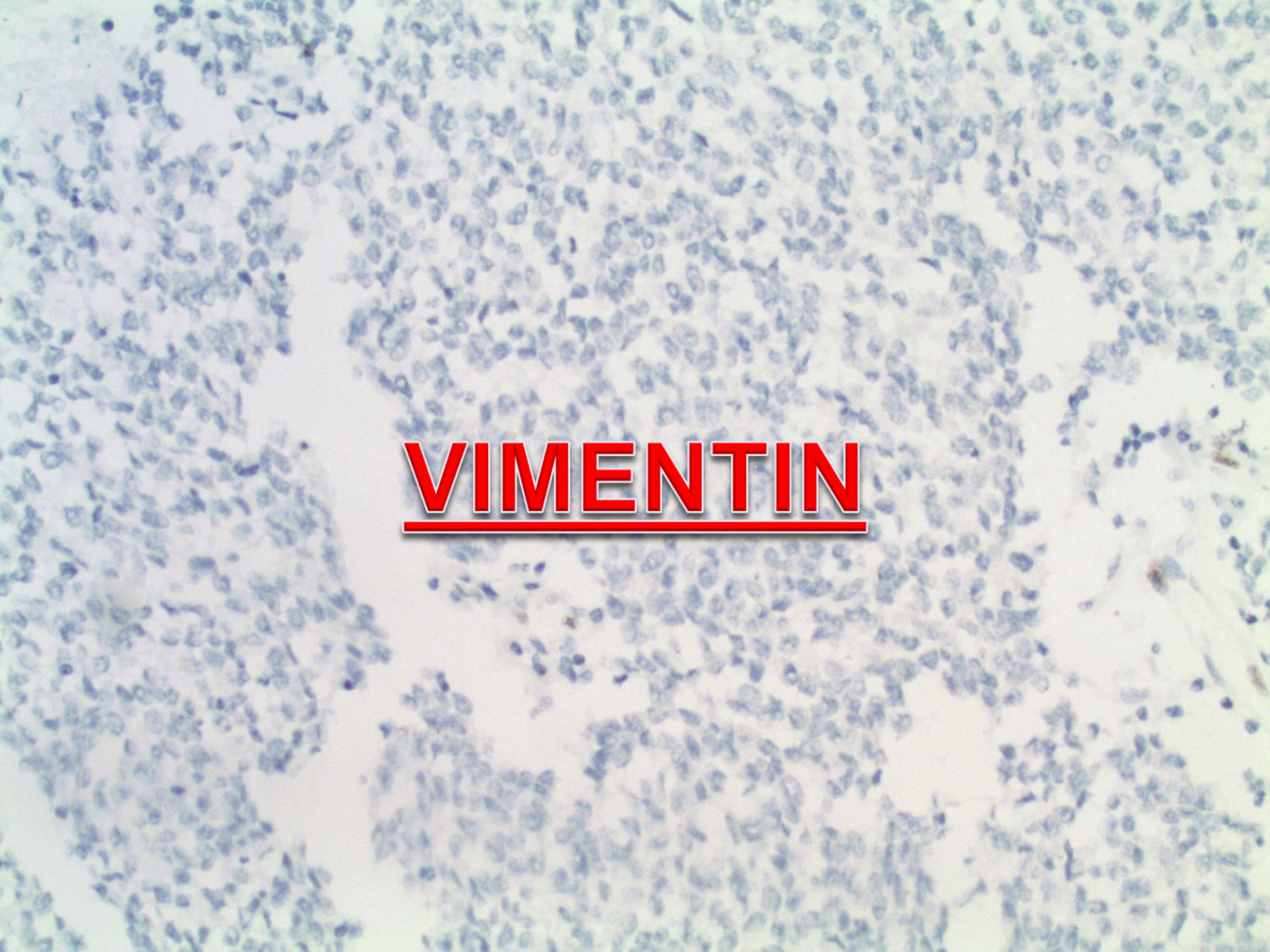
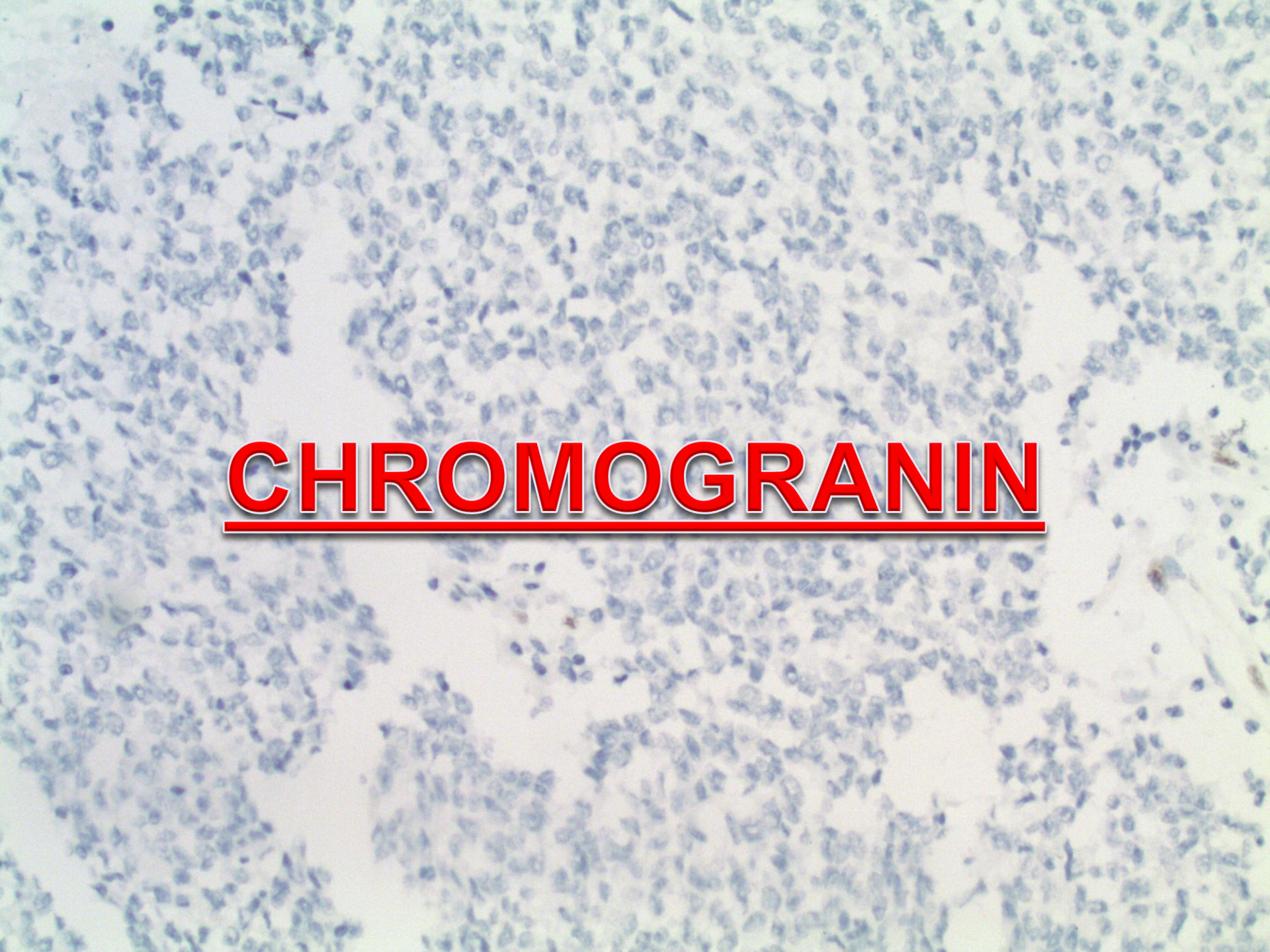
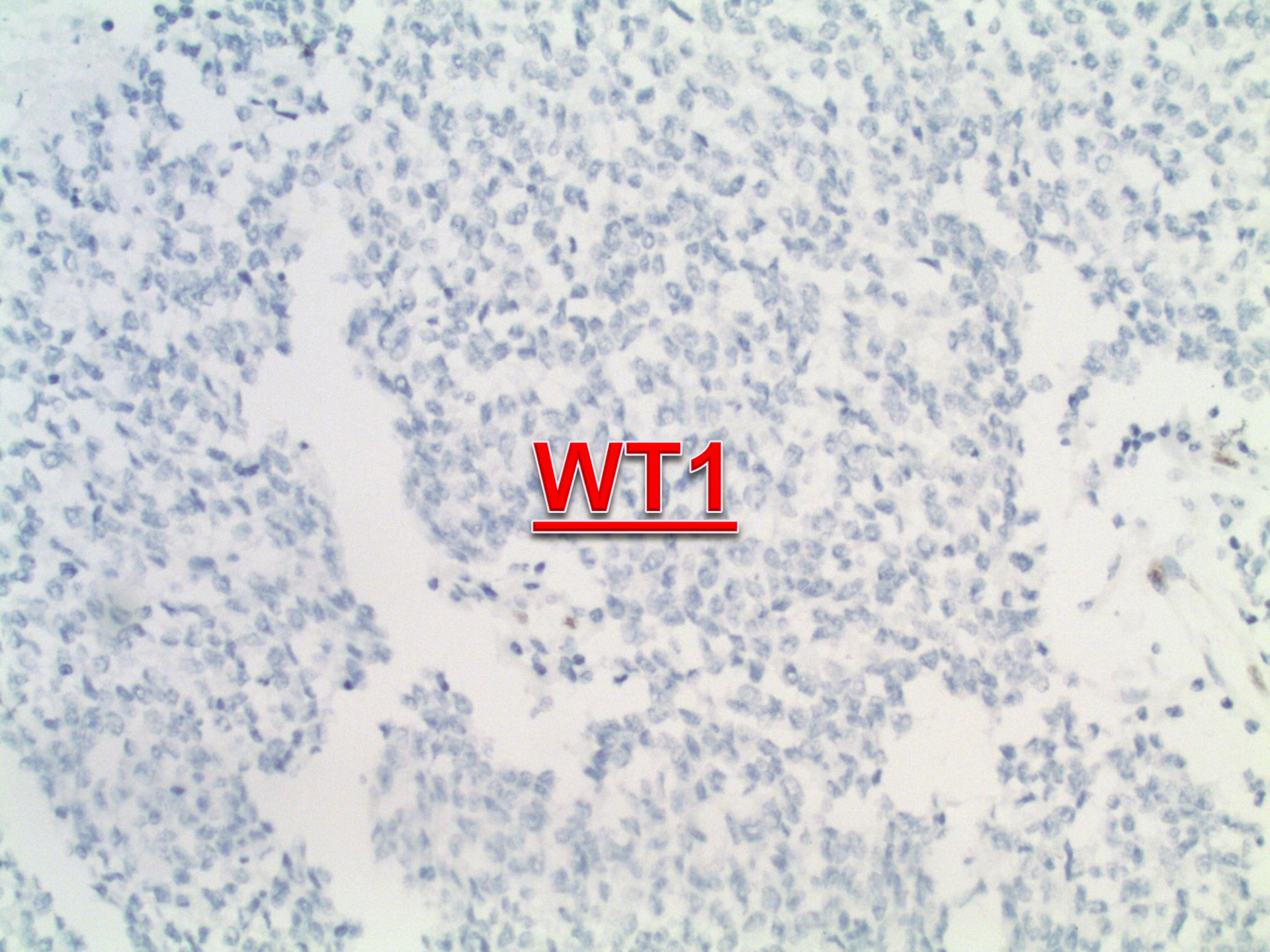

AE1/AE3


EMA


PAX8


VIMENTIN


CHROMOGRANIN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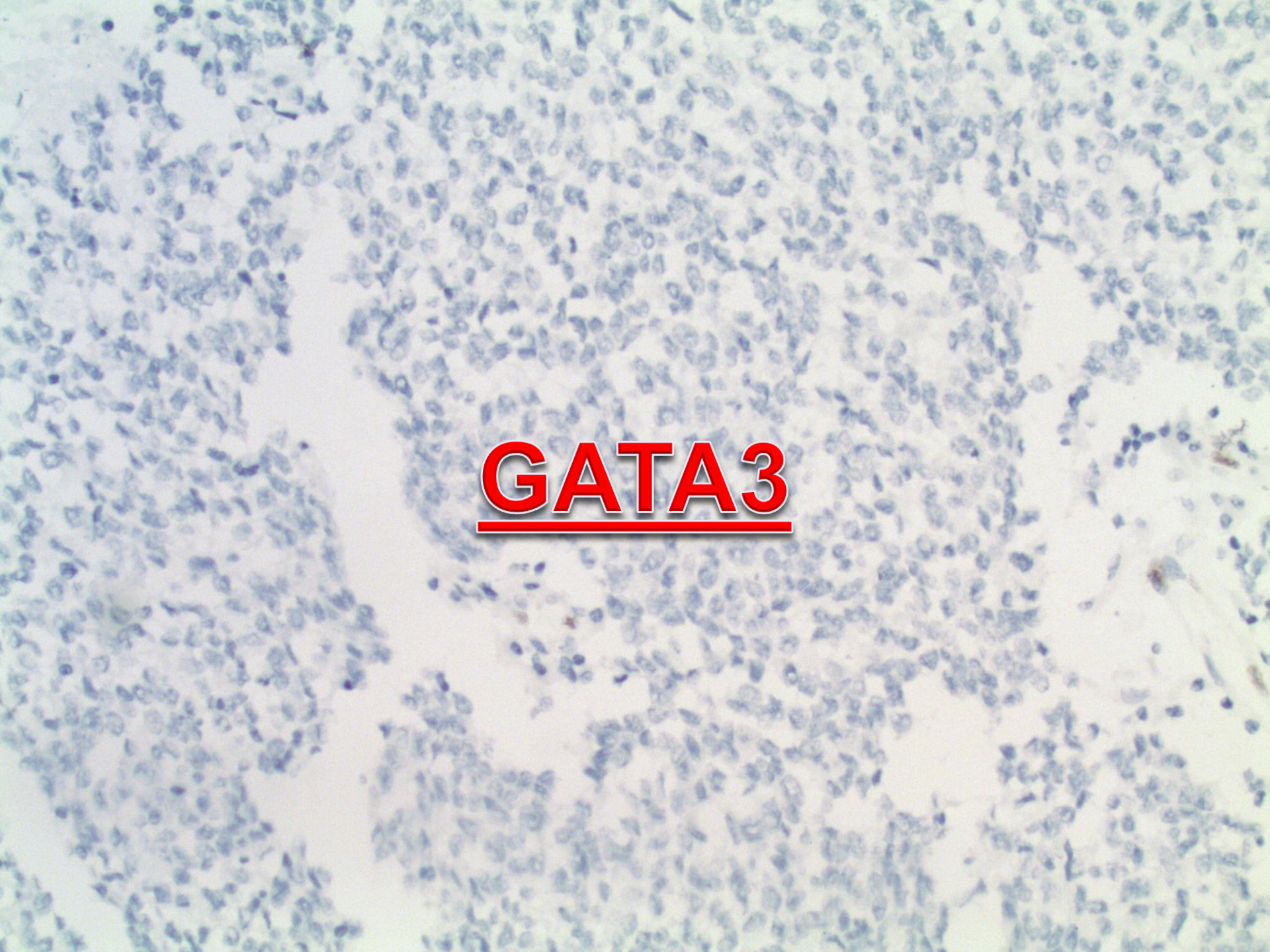
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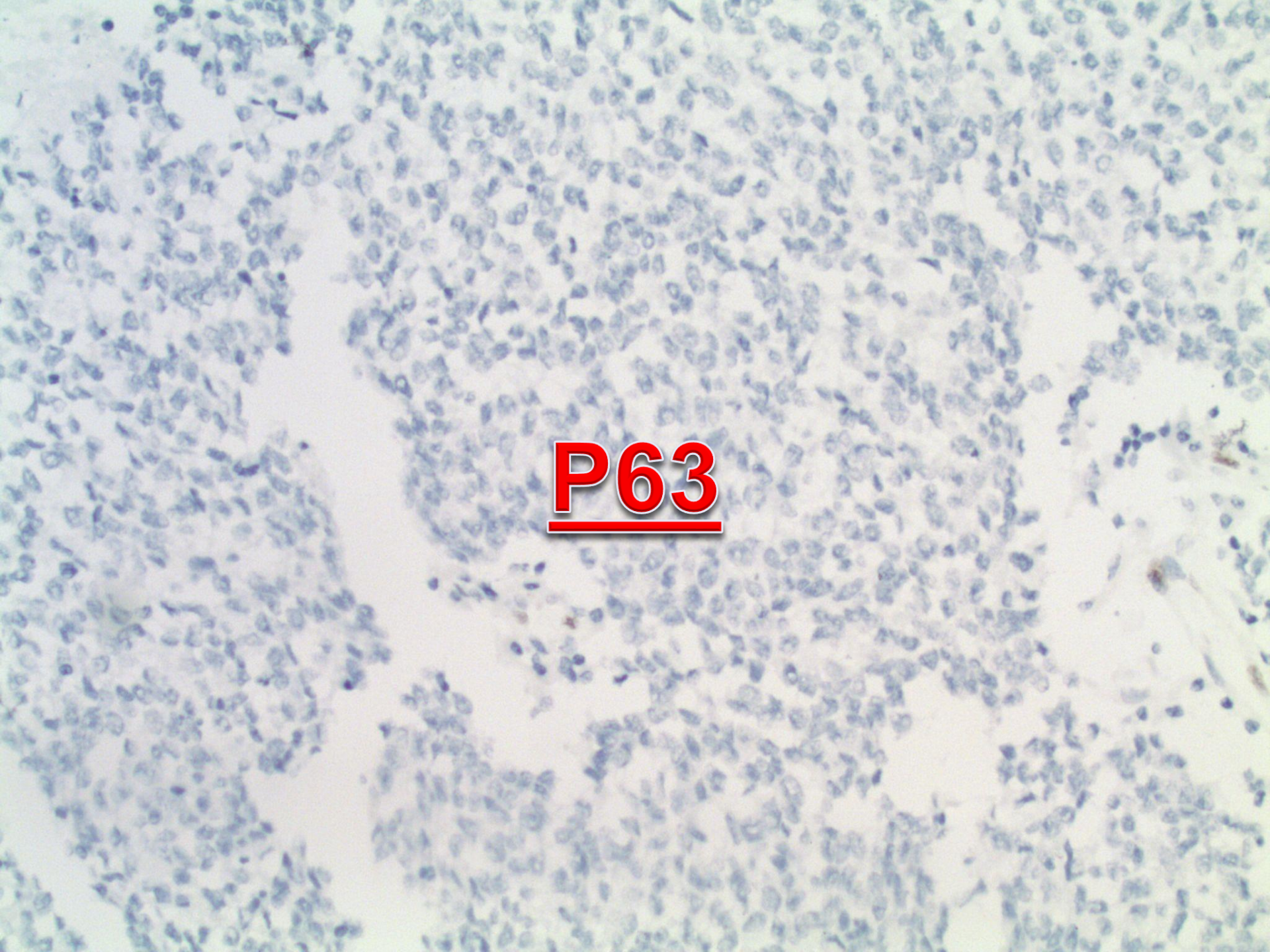
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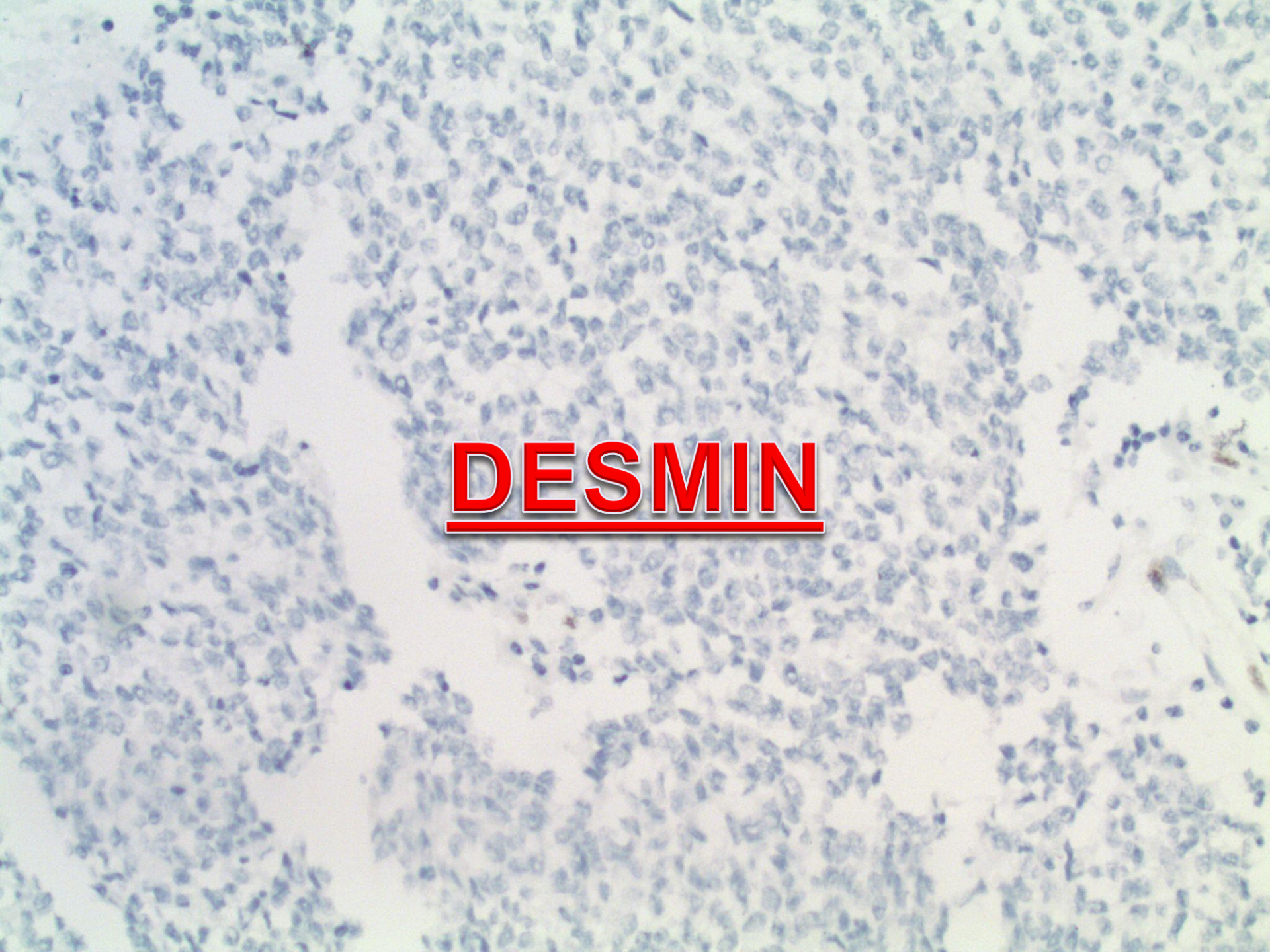
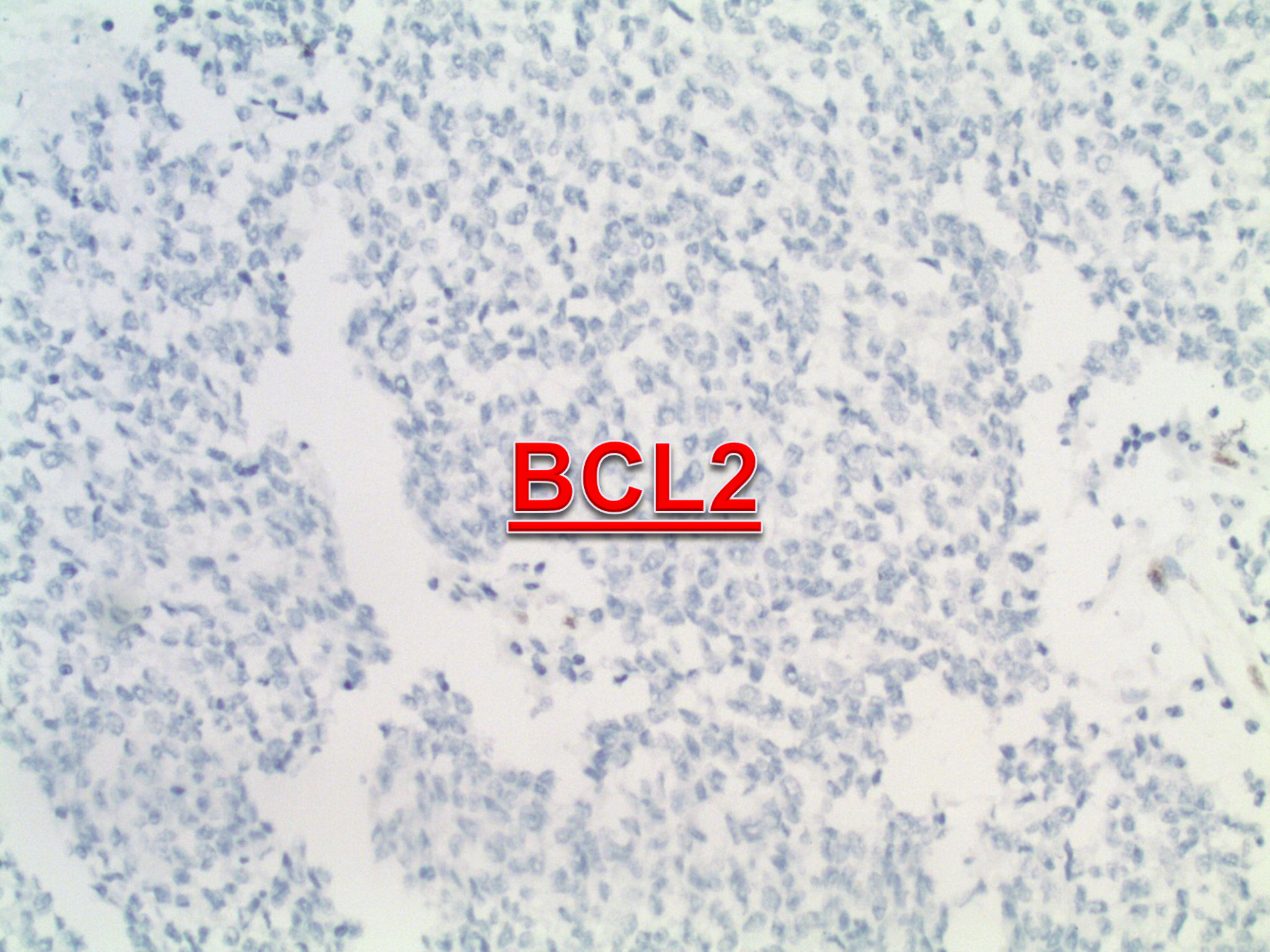
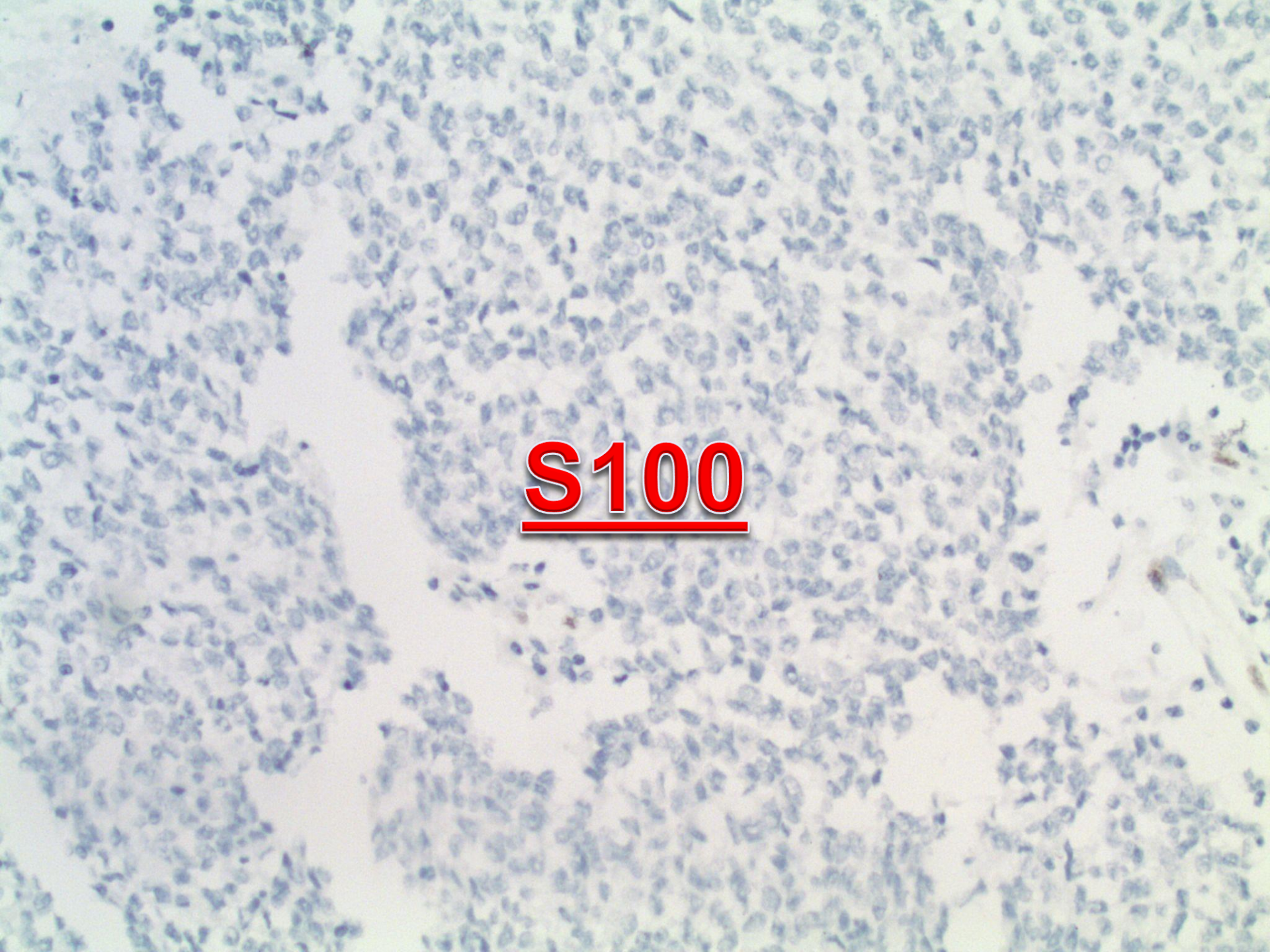
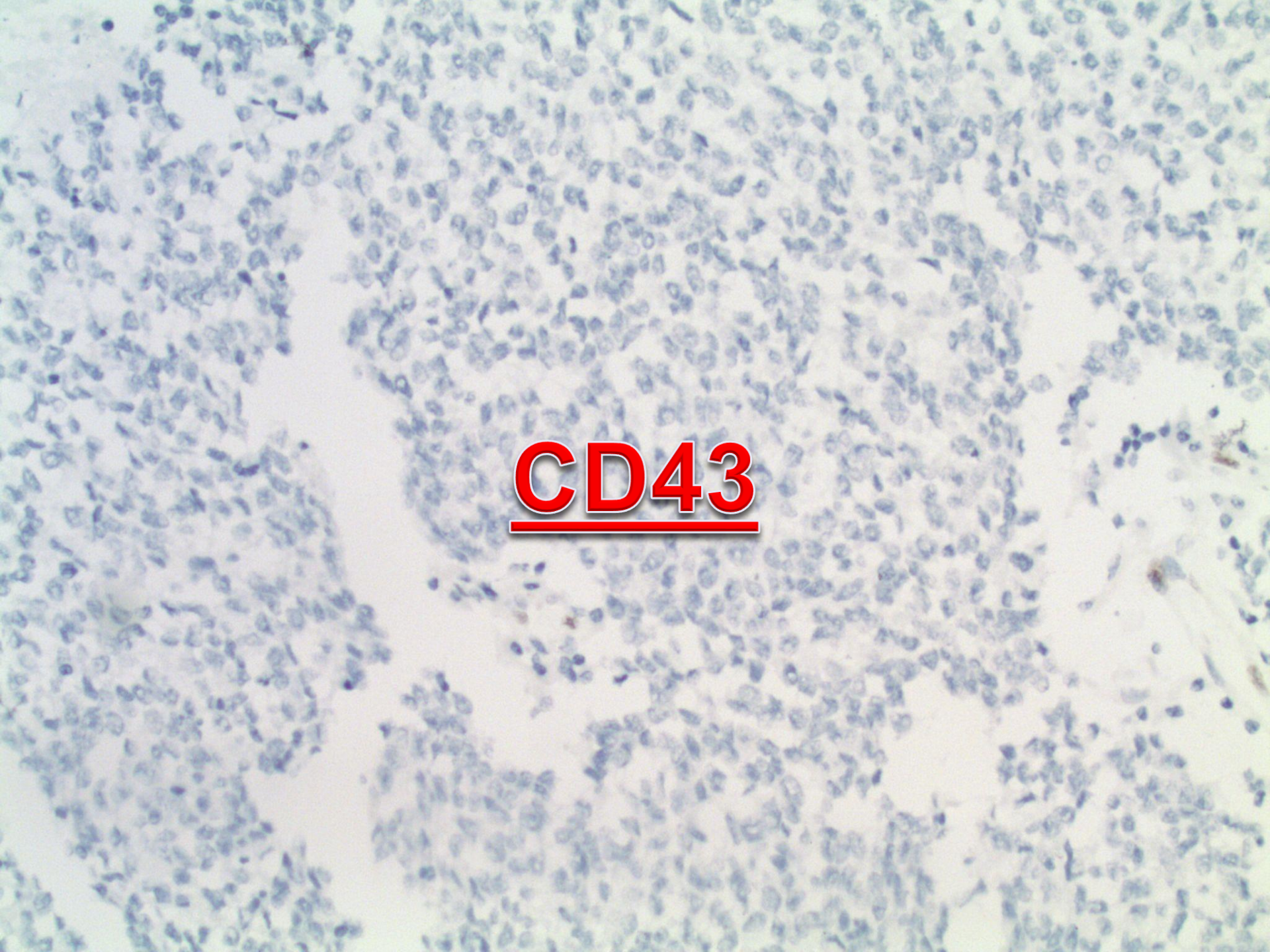

DESMIN


BCL2


S100


CD43

Additional molecular testing

FISH FOR *EWSR1*:

Procedure Results and Interpretation
FISH for *EWSR1* (22q12) Translocations

RESULT: Positive for *EWSR1*(22q12) translocation

DIAGNOSIS

Ewing sarcoma/PNET
(primary renal)

DDx

- **Ewing sarcoma/PNET**
  - NEKT
- **Adult-type Wilm's tumor**

Primary Malignant Neuroepithelial Tumors of the Kidney

A Clinicopathologic Analysis of 146 Adult and Pediatric Cases from the National Wilms' Tumor Study Group Pathology Center

David M. Parham, M.D., Gary J. Roloson, M.D., Michael Feely, B.S., Daniel M. Green, M.D., Julia A. Bridge, M.D., and J. Bruce Beckwith, M.D.

Am J Surg Pathol, Vol. 25, No. 2, 2001

Primary Ewing's Sarcoma/Primitive Neuroectodermal Tumor of the Kidney

A Clinicopathologic and Immunohistochemical Analysis of 11 Cases

Rafael E. Jimenez, M.D., Andrew L. Folpe, M.D.,
Rosanna L. Lapham, M.D., Jae Y. Ro, M.D., Patricia A. O'Shea, M.D.,
Sharon W. Weiss, M.D., and Mahul B. Amin, M.D.

Am J Surg Pathol 26(3): 320–327, 2002

TABLE 2. *Immunohistochemical results*

Antibody to	Renal Ewing's sarcoma/ primitive neuroectodermal tumor (%)	Wilms' tumors (%)
CD99	11/11 (100)	1/5 (20)
Fli-1	5/8 (63)	0/10 (0)
WT-1	0/10 (0)	7/9 (78)
Pan-cytokeratin	2/8 (25)*	Not performed

* Cytokeratin expression was focal (<10%) in both positive cases.

Am J Surg Pathol 26(3): 320–327, 2002

Clinical and Pathological Features of Primary Neuroectodermal Tumor/Ewing Sarcoma of the Kidney

Emanuela Risi, Roberto Iacovelli, Amelia Altavilla, Daniele Alesini, Antonella Palazzo, Claudia Mosillo, Patrizia Trenta, and Enrico Cortesi

UROLOGY 82 (2), 2013

Pubmed search 195-2012 → 116 cases
55% men
Median age 28 years; 22% of patients ≤15 years
All had clinical symptoms as 1st presentation
(usually pain 54%, hematuria 29%, mass 28%)
One third metastatic at diagnosis
40% non-metastatic developed mets after surgery

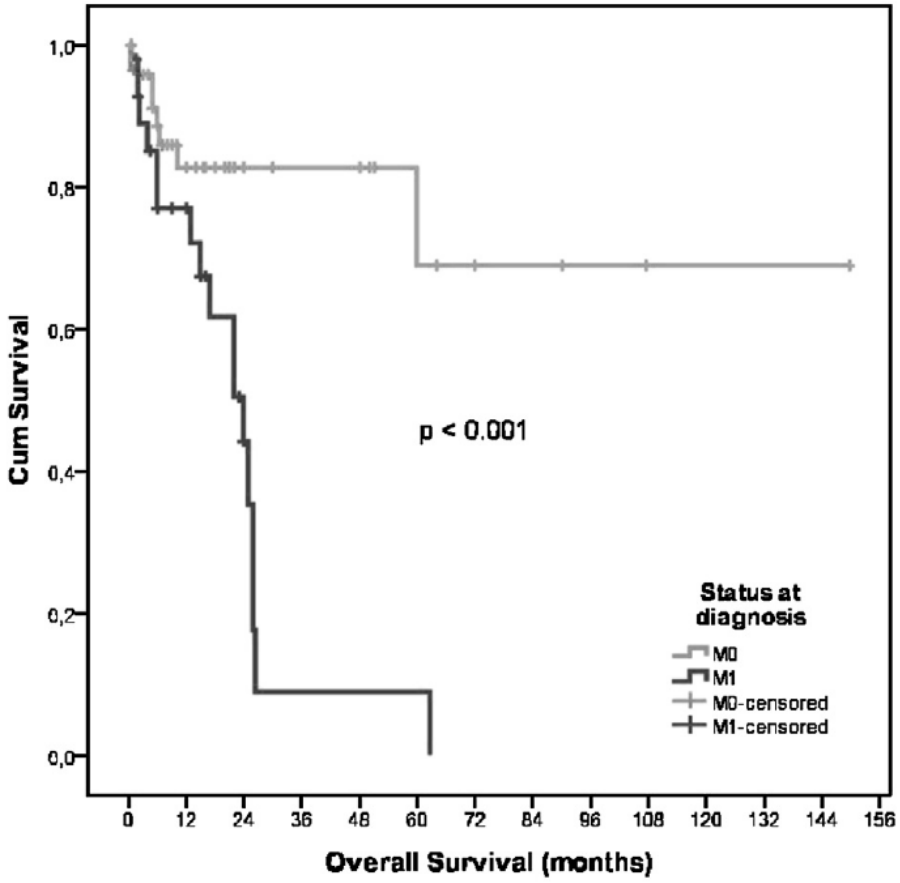
Clinical and Pathological Features of Primary Neuroectodermal Tumor/Ewing Sarcoma of the Kidney

Emanuela Risi, Roberto Iacovelli, Amelia Altavilla, Daniele Alesini, Antonella Palazzo, Claudia Mosillo, Patrizia Trenta, and Enrico Cortesi

UROLOGY 82 (2), 2013

Table 2. Immunohistochemical expression of tumor markers in primary renal PNET/EWS

HIC test	No. of Cases	Expression (%)
VIM	33	81.8
NSE	34	88.2
CD99	96	99
FLI-1	33	60.6
CKs	65	7.7
CD117	6	33.3
CHR	34	5.9
SYN	28	32.1
CD45	25	0
TdT	7	0
WT-1	39	23.1
CD56	10	30
CD57	1	100
S100	26	38.5
EMA	13	15.4
NF	7	0
DES	22	4.5
MYOG	7	0
SMA	5	0
PGP9.5	1	100
GFAP	2	100

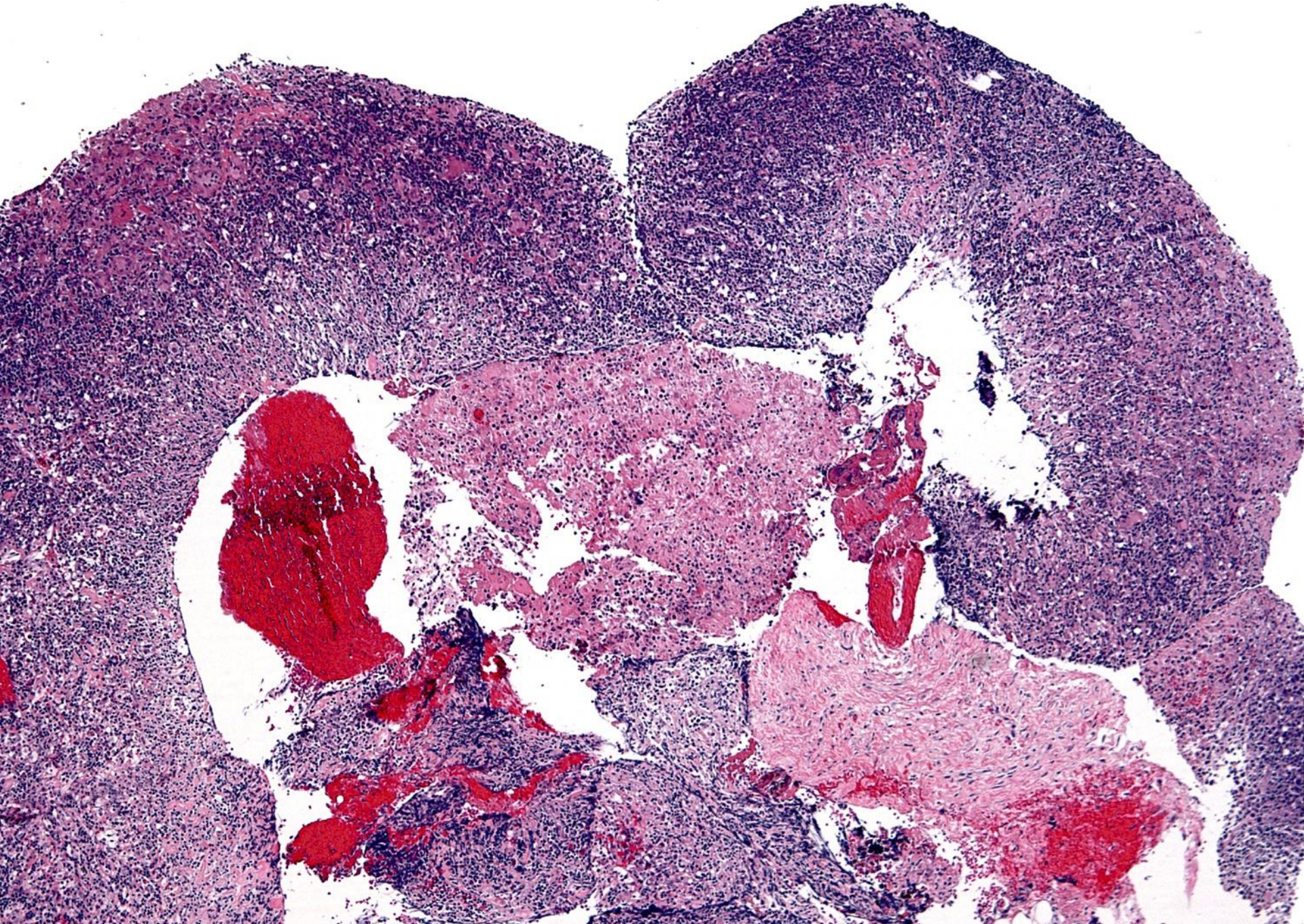


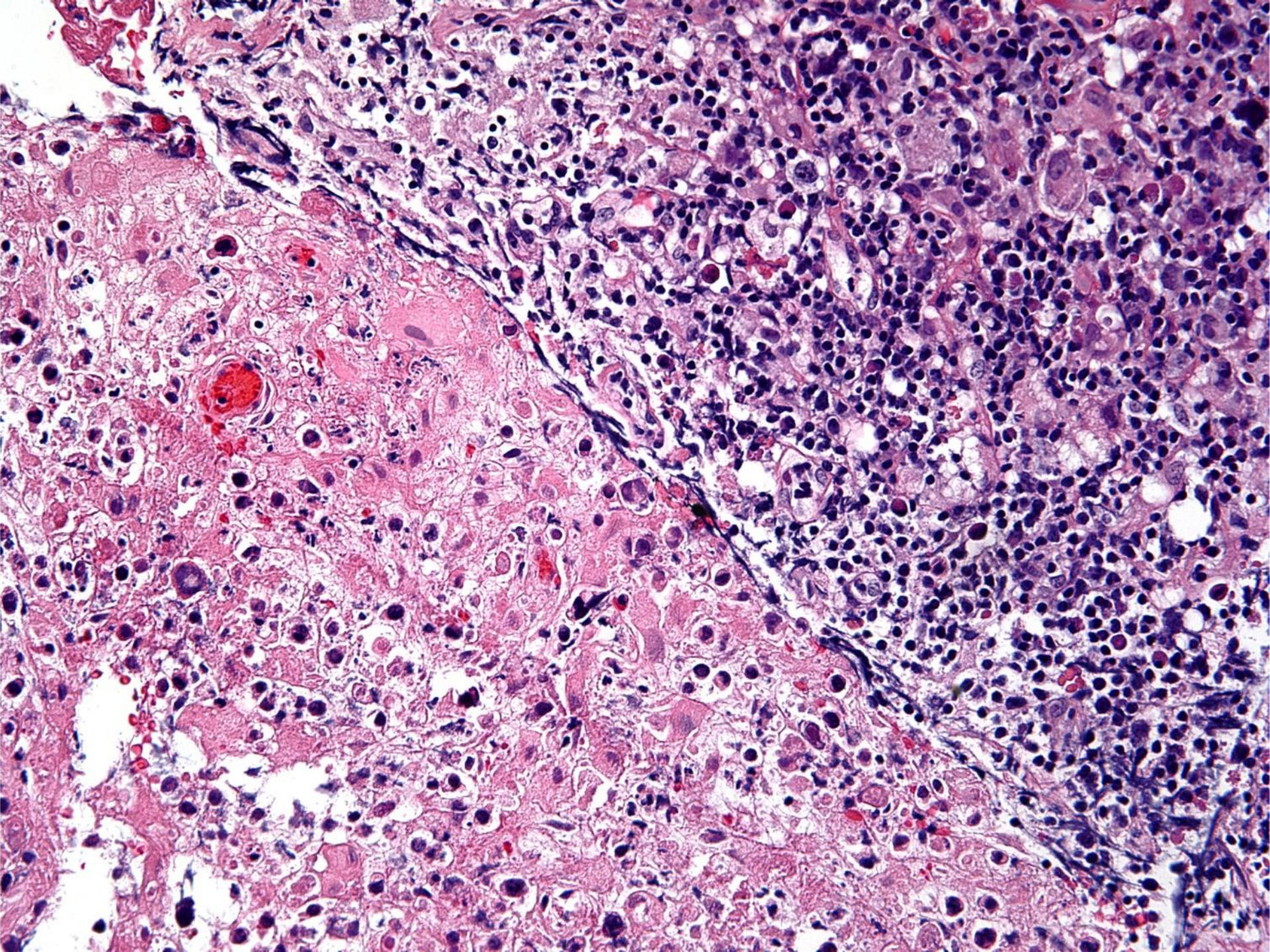
"If there's anything more we can do for you, don't hesitate to fill out the proper forms."

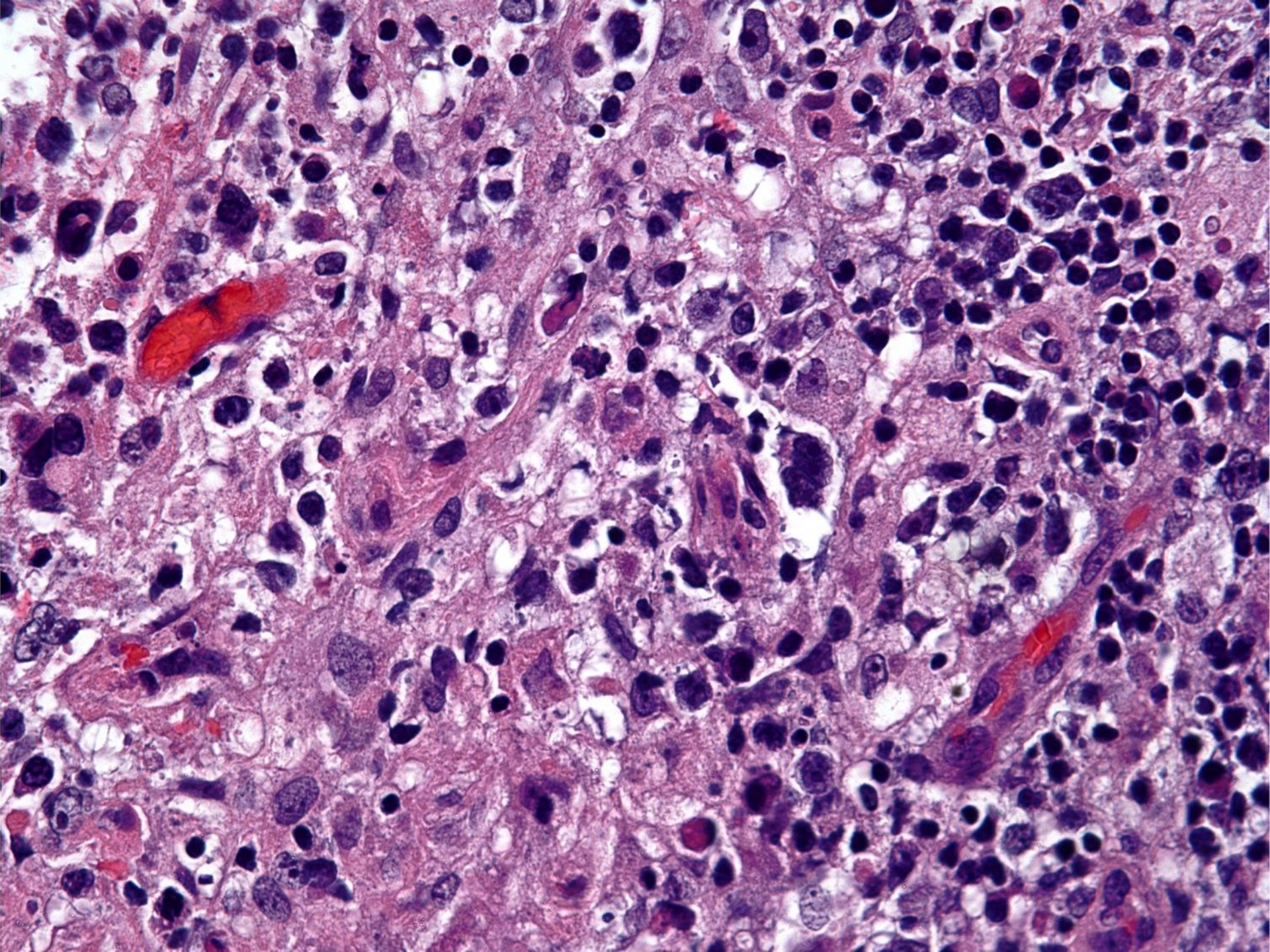
SB 5837

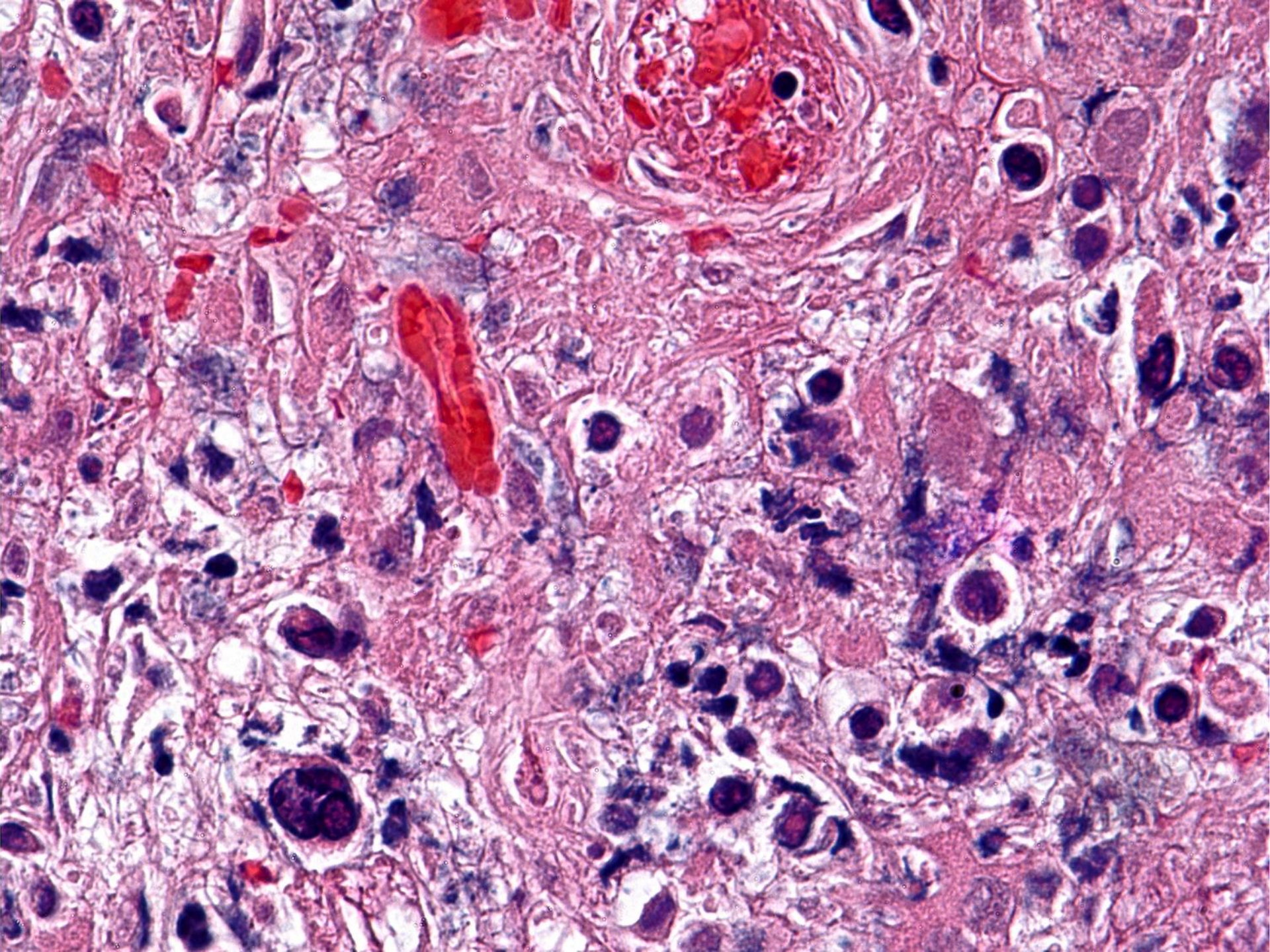
Jenny Hoffmann/Dita Gratzinger; Stanford

70-year-old man with history of CLL presents with recurrent fevers and worsening lymphadenopathy. A core biopsy of an axillary lymph node is performed.

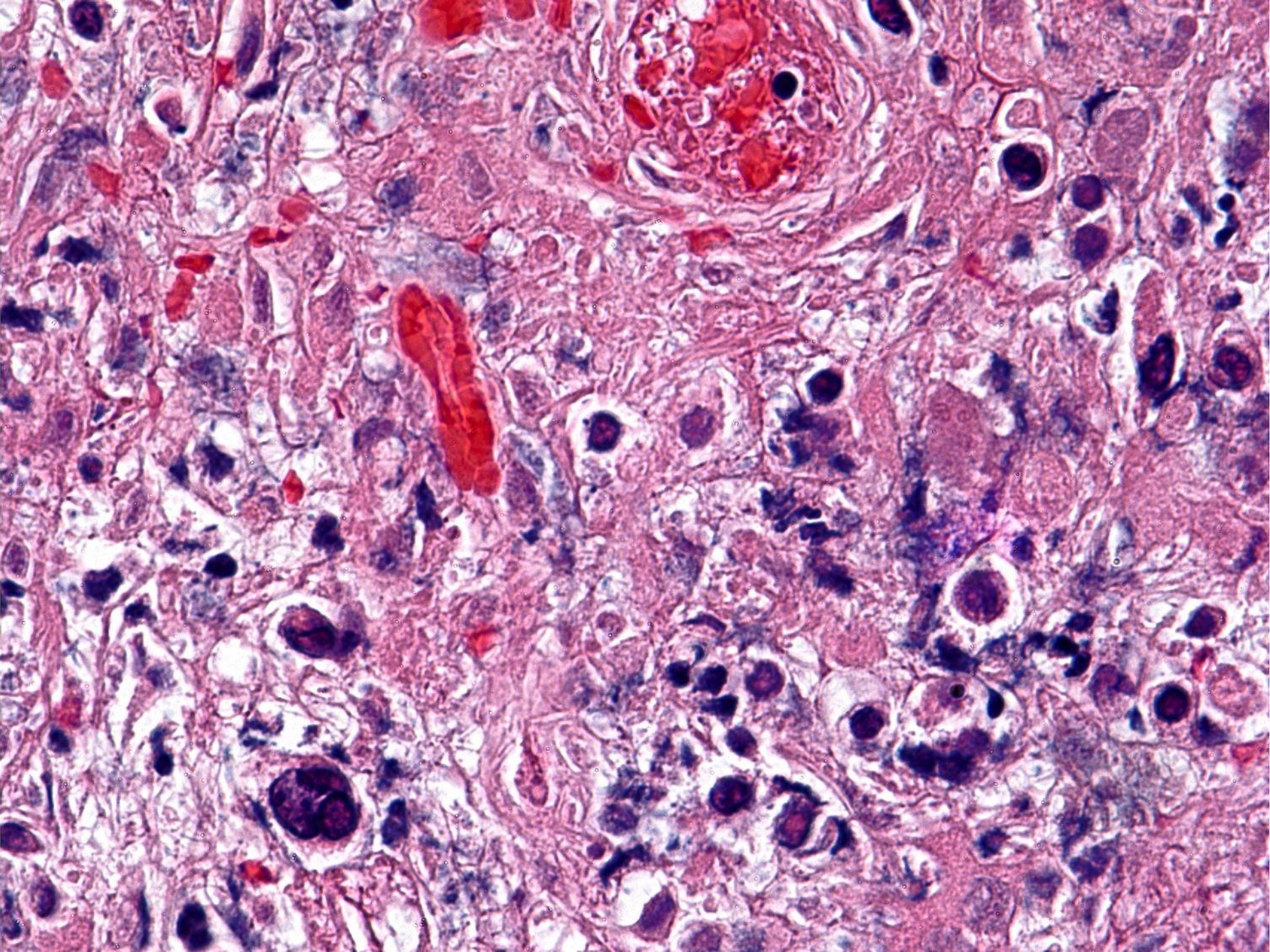


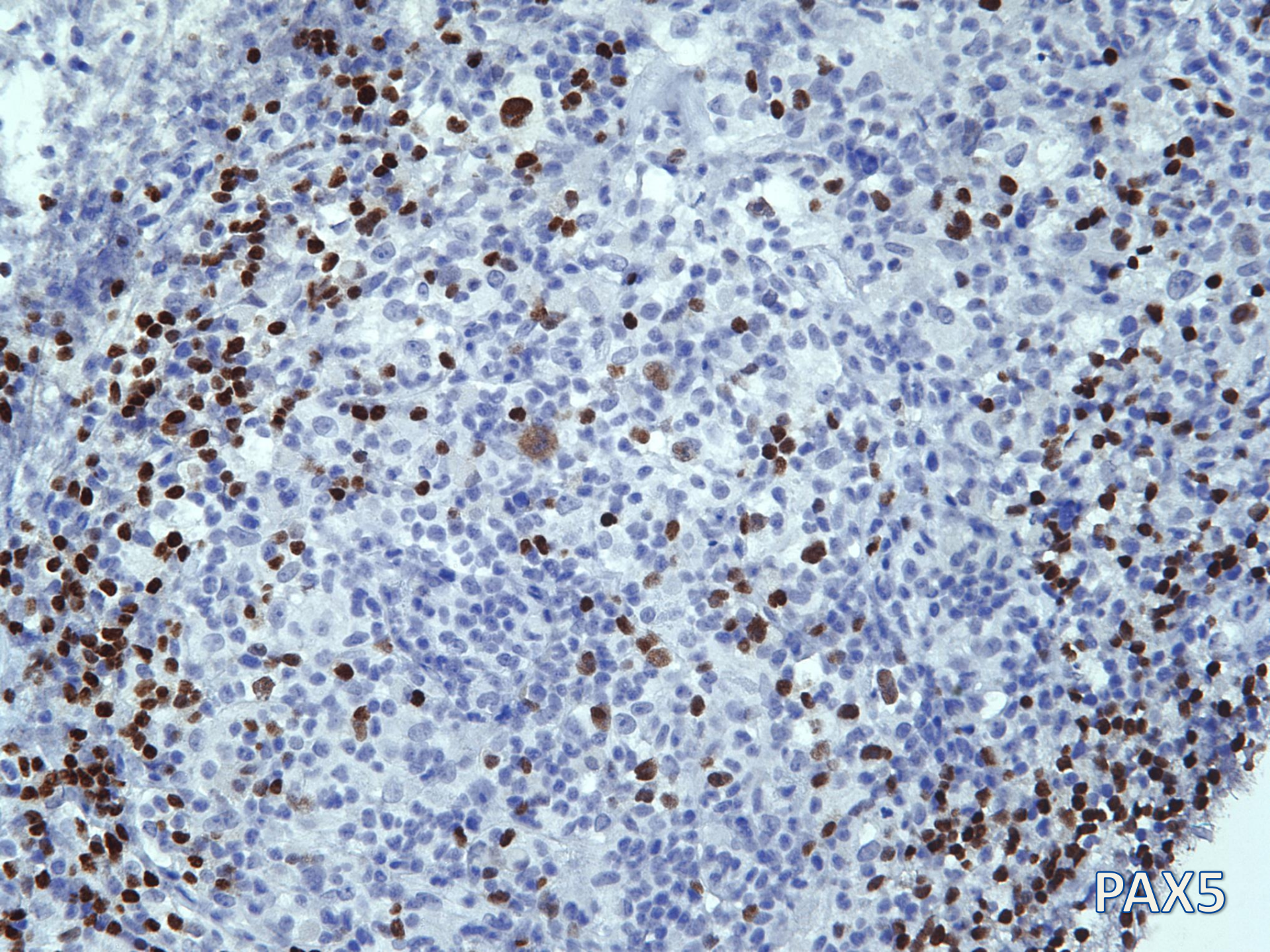


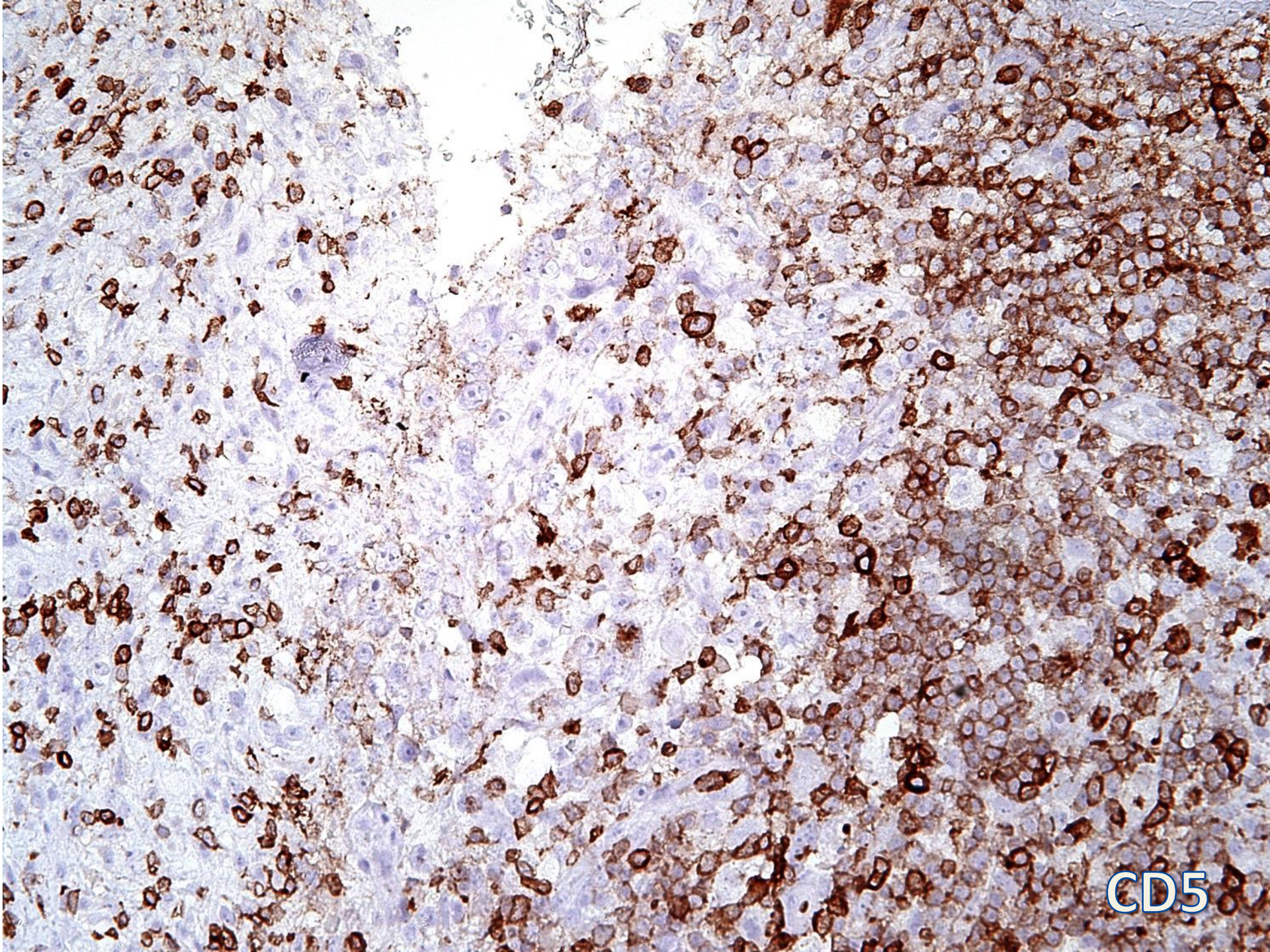


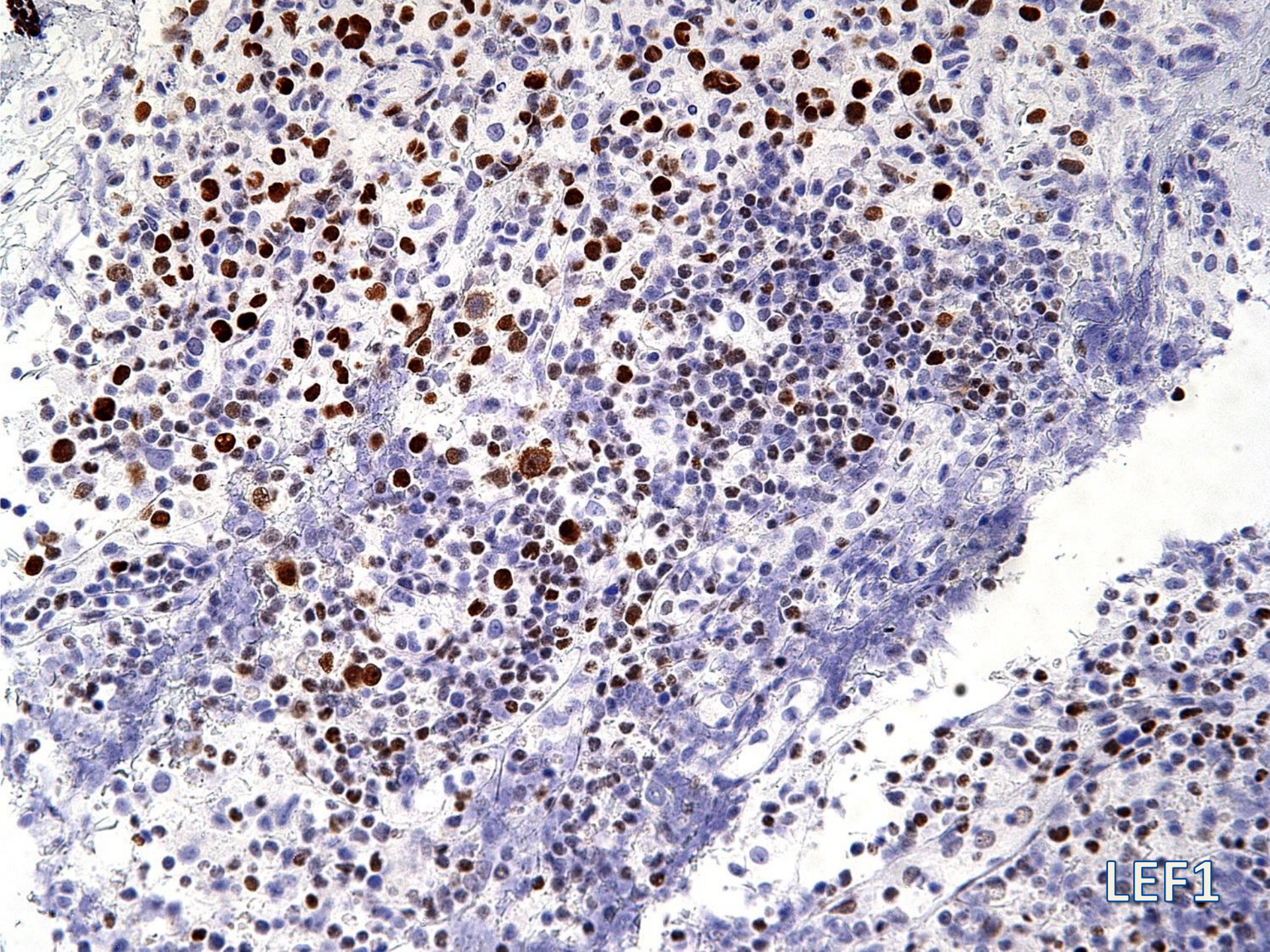


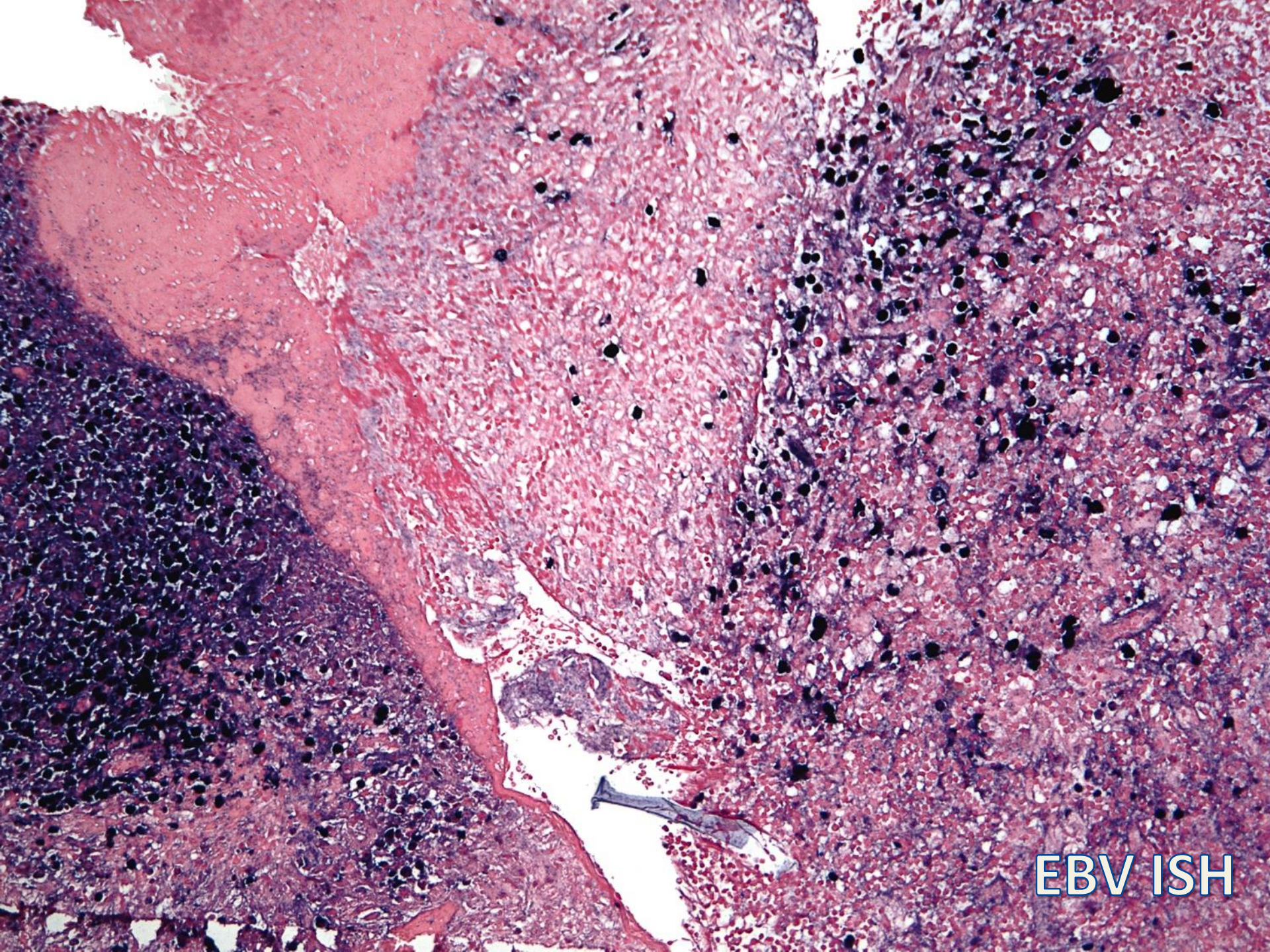
DIAGNOSIS?

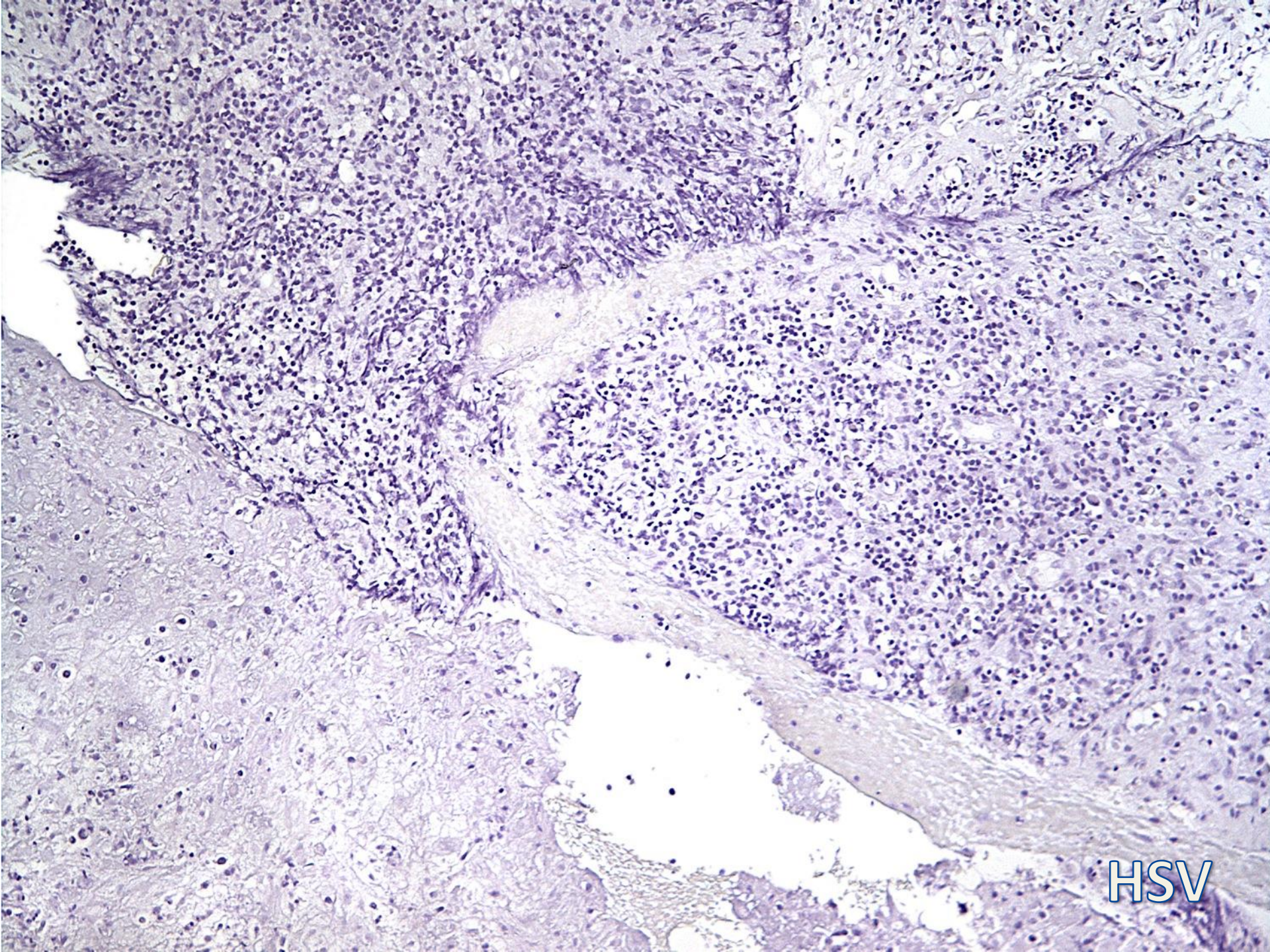



PAX5


CD5


LEF1


EBV ISH


HSV

Differential Diagnosis

- Herpes lymphadenitis in association with chronic lymphocytic lymphoma
- Hodgkin transformation
- Large cell transformation (NHL)
- (Polymorphous PTLD-like picture/Immunodeficiency-associated lymphoproliferative disorders)

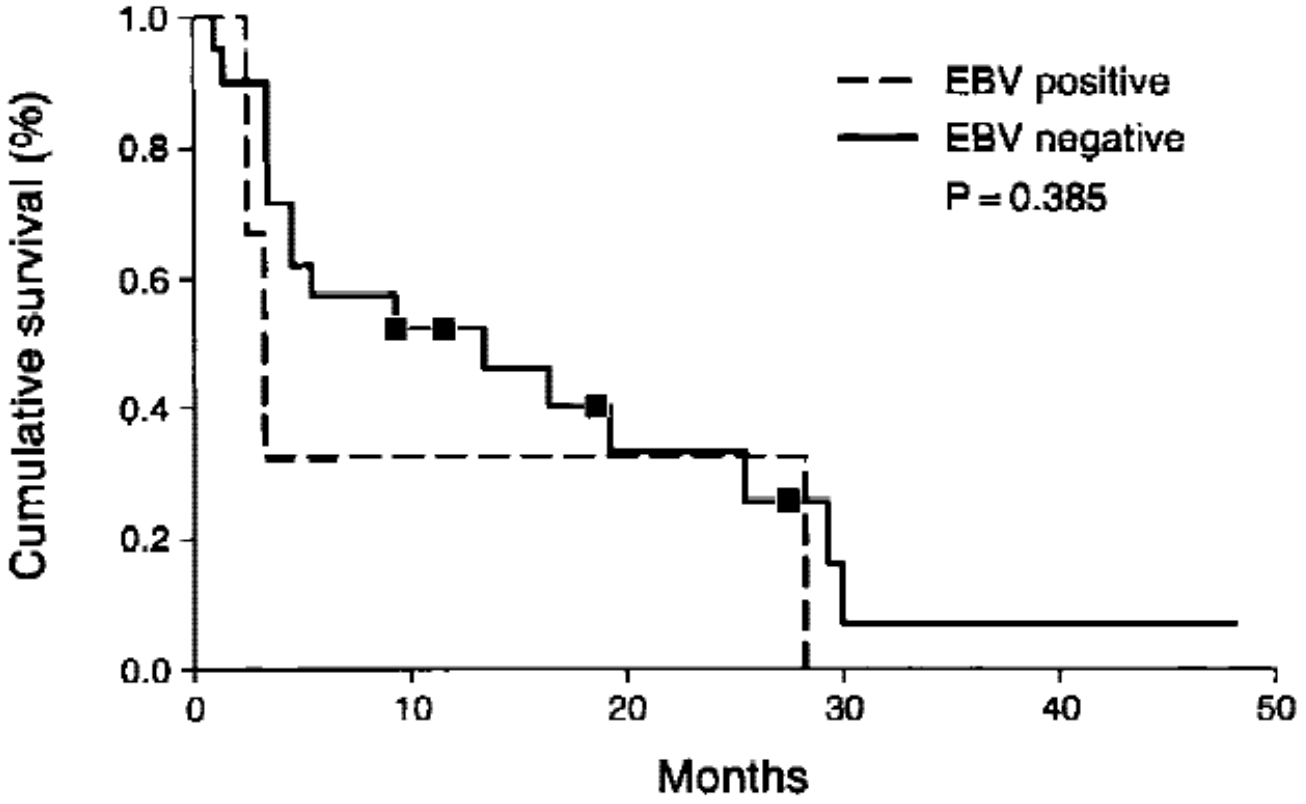
DIAGNOSIS

-- **EBV POSITIVE LARGE CELL TRANSFORMATION OF CLL/SLL**

LEF1 Expression identifies CLL/SLL in Small B-cell Lymphomas

B-cell lymphoma[a]	*Nuclear overexpression of LEF1 (positive cases/total cases)*
Chronic lymphocytic leukemia/small lymphocytic lymphoma (n=92)	92/92 (100%), positive in ~100% cells
Without Richter's transformation	84/84 (100%; CD5+: 80; CD5−: 2)
With Richter's transformation	8/8 (100%; all CD5+)
Mantle cell lymphoma (n=53)	0/53
Classical type	0/47
Small cell variant	0/2
Pleomorphic/blastoid variant	0/4
Marginal zone lymphoma (n=31)	0/31
Nodal	0/15 (CD5−: 13; CD5+: 2)
Splenic	0/3 (CD5−: 2; CD5+: 1)
Mucosa-associated lymphoid tissue	0/13 (all CD5−)
Follicular lymphoma (n=43)	
Grade 1–2	0/31
Grade 3	6/12 (50%), positive in 5–15% cells
Diffuse large B-cell lymphoma (n=71)	27/71 (38%), significant staining variability
De novo	23/51 (45%)
Diffuse large B-cell lymphoma, NOS	22/48
Primary mediastinal large B-cell lymphoma	1/3
Transformed from follicular lymphoma	4/17 (24%)
Transformed from marginal zone lymphoma	0/2
Post-transplant lymphoproliferative disorder	0/1

EBV Infection in Richter's Transformation



References

1. Ansell SM, Li CY, Lloyd RV, Phyliky RL. Epstein-Barr virus infection in Richter's transformation. Am J Hematol. 1999 Feb;60(2):99-104.
2. Tandon B, Peterson L. Gao J, Nelson B, Ma S, Rosen S, Chen YH. Nuclear overexpression of lymphoid-enhancer-binding factor 1 identifies chronic lymphocytic leukemia/small lymphocytic lymphoma in small B-cell lymphomas. Mod Pathol. 2011 Nov;24(11):1433-43.

"You should relax less."

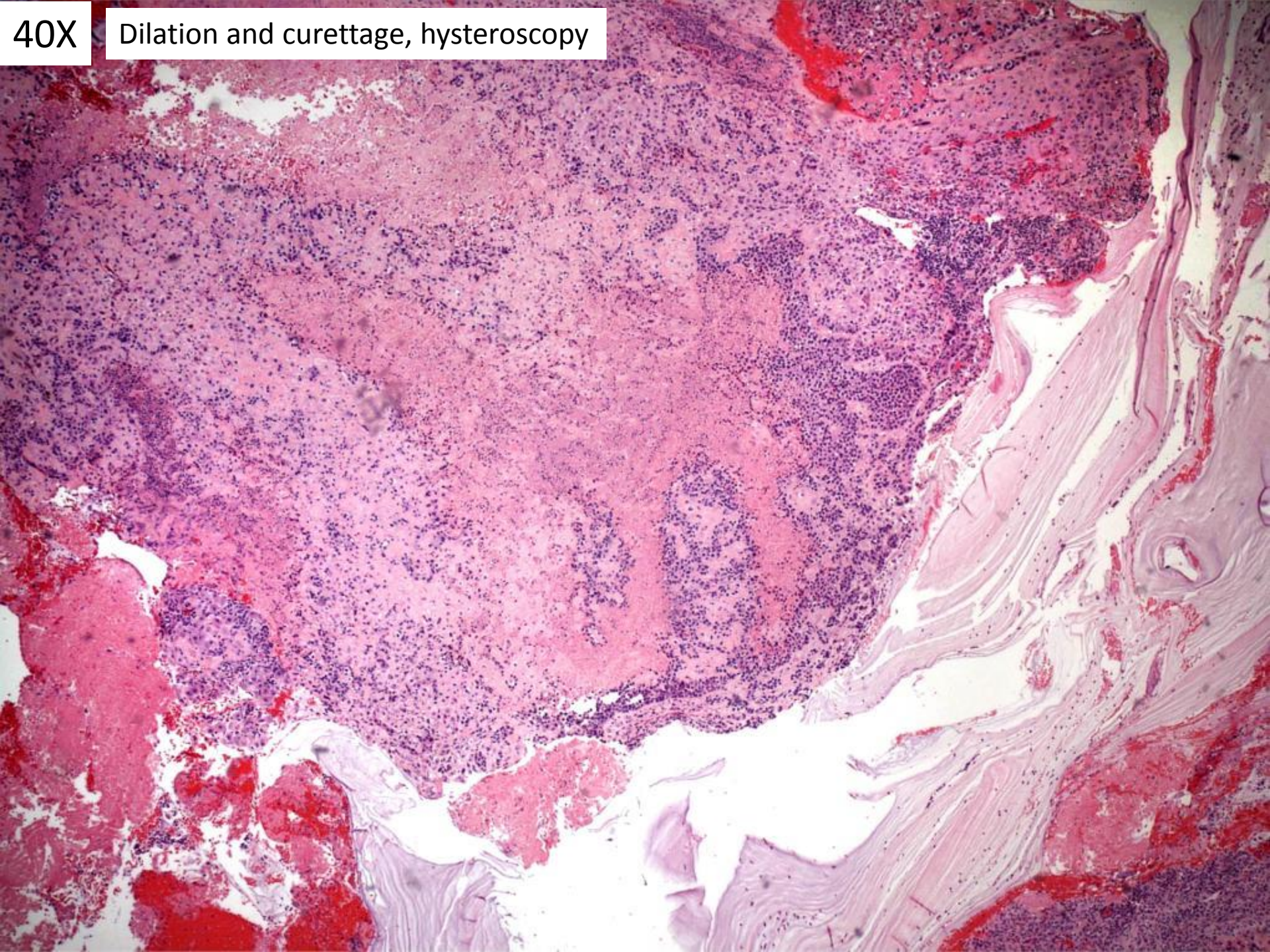
SB 5838

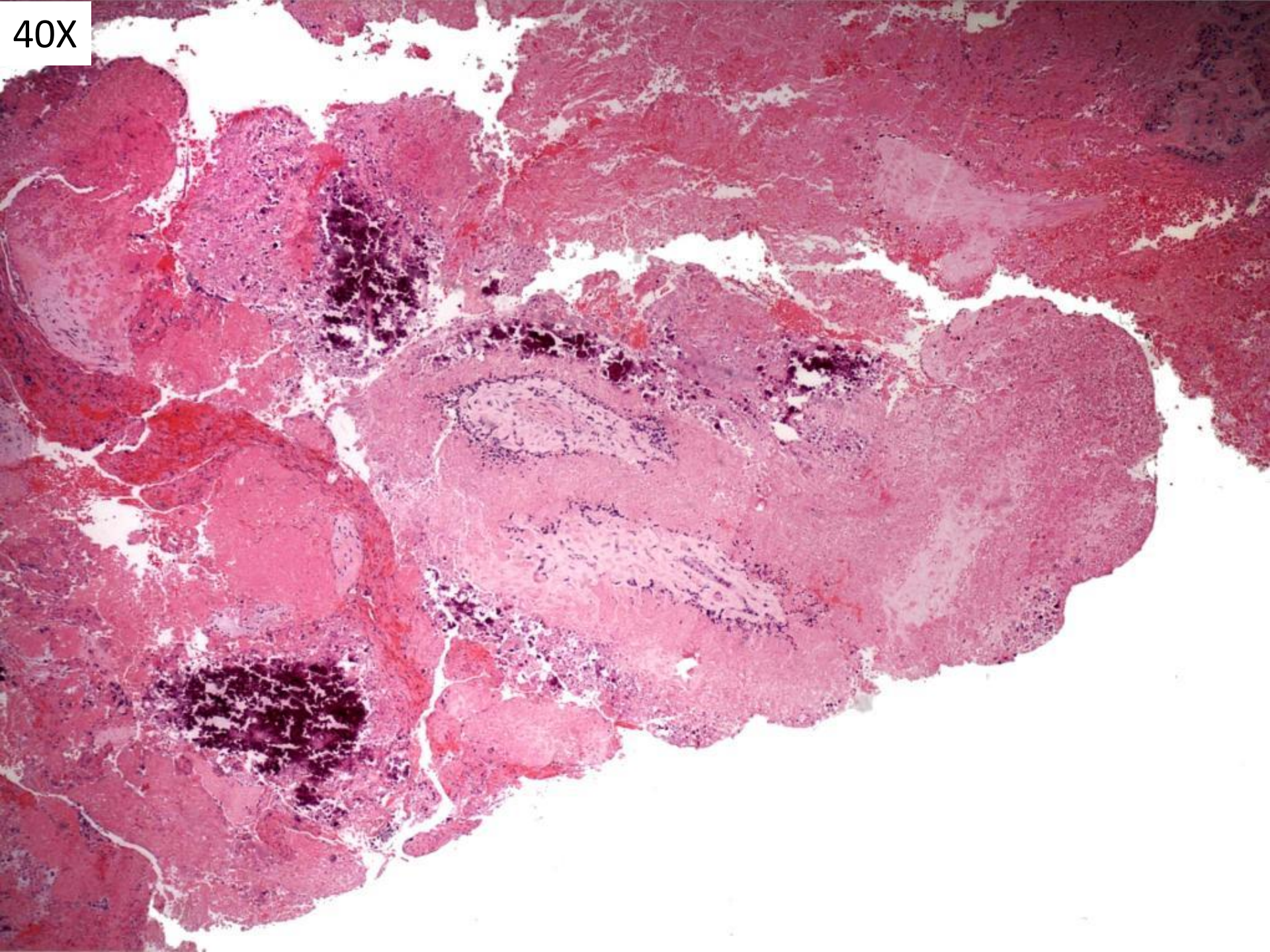
Sebastian Fernandez-Pol/Ann Folkins/Christina Kong; Stanford

37-year-old female with endometrial curettage. Rule out trophoblastic disease

40X

Dilation and curettage, hysteroscopy

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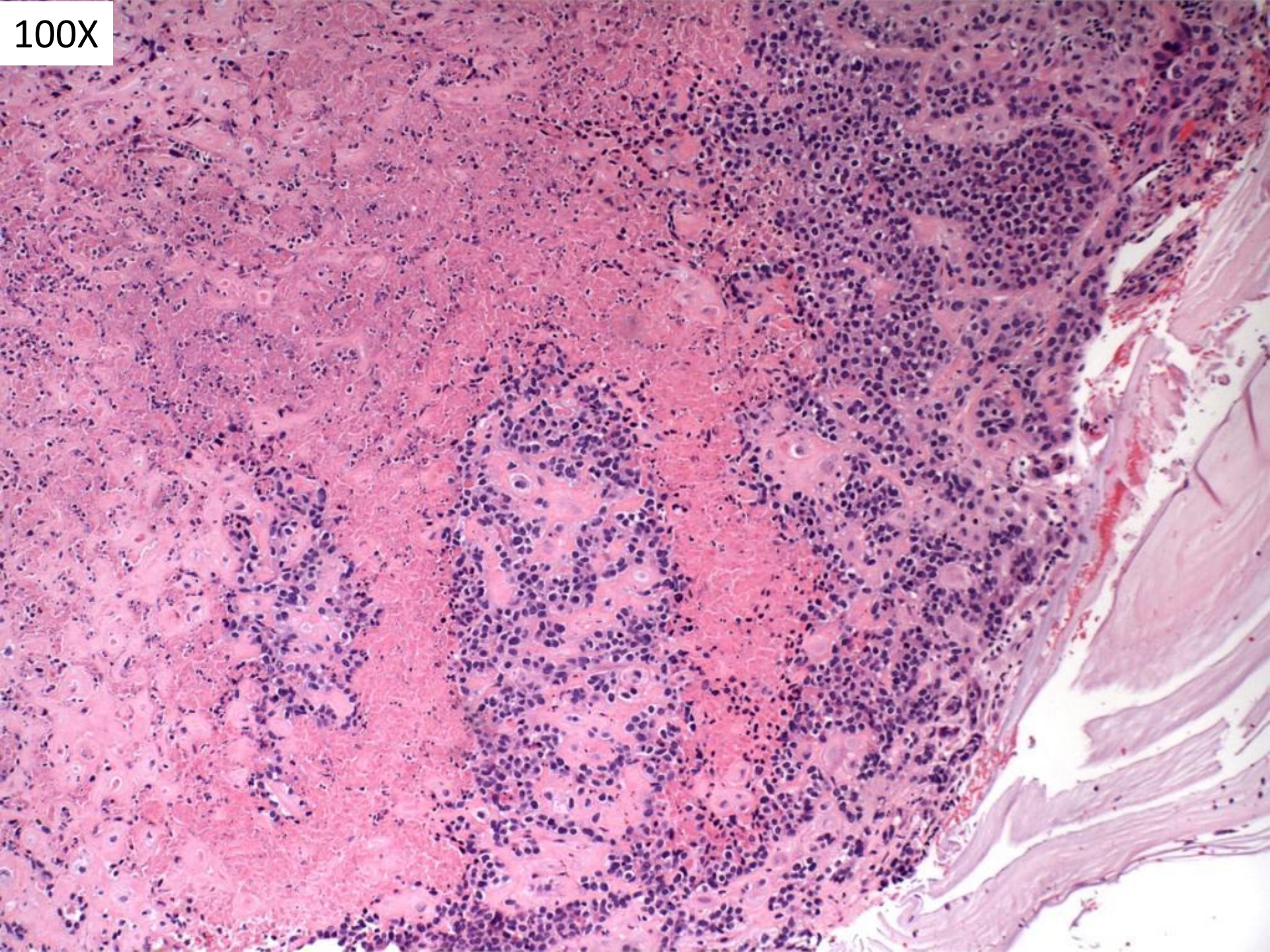
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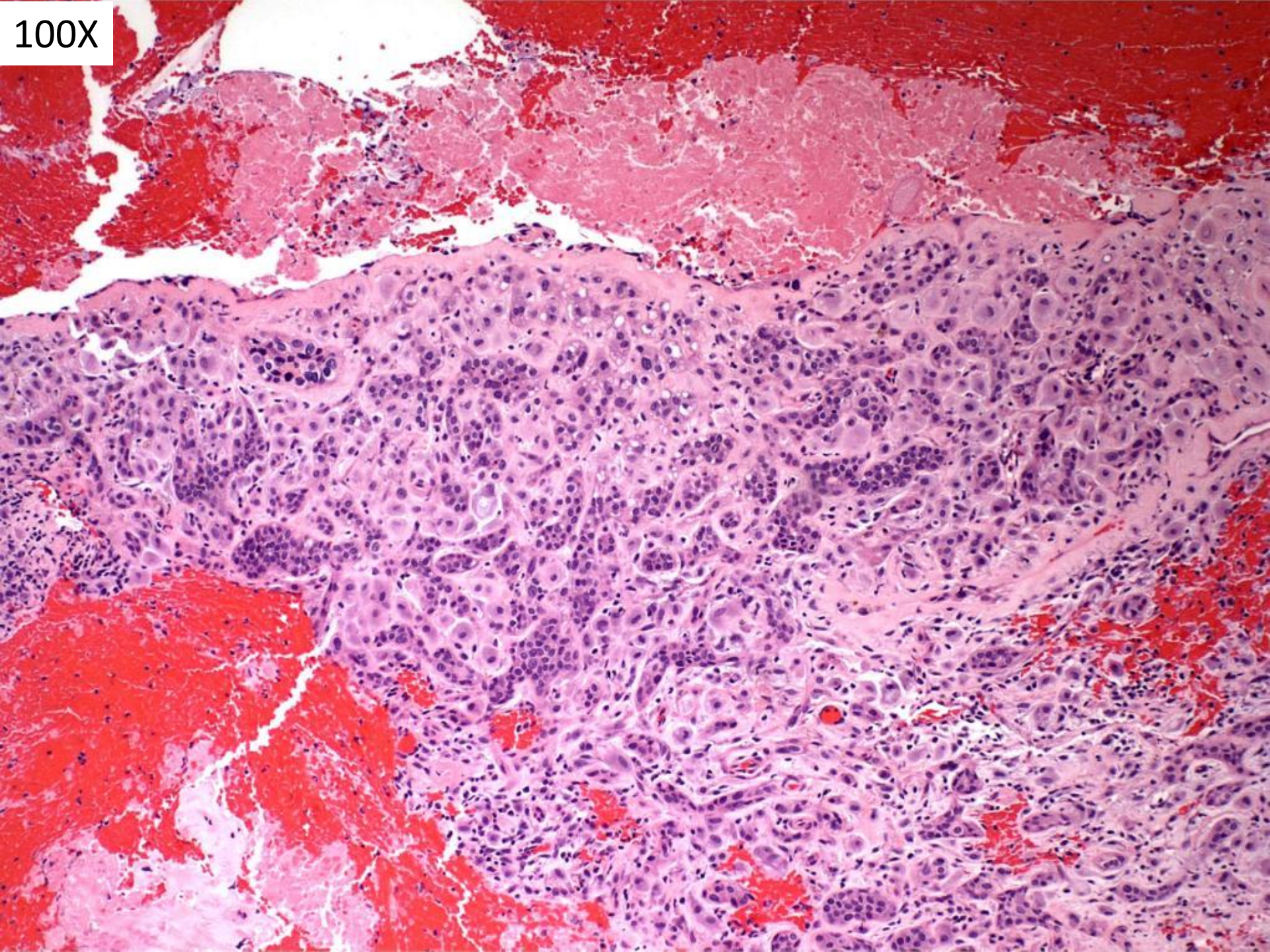
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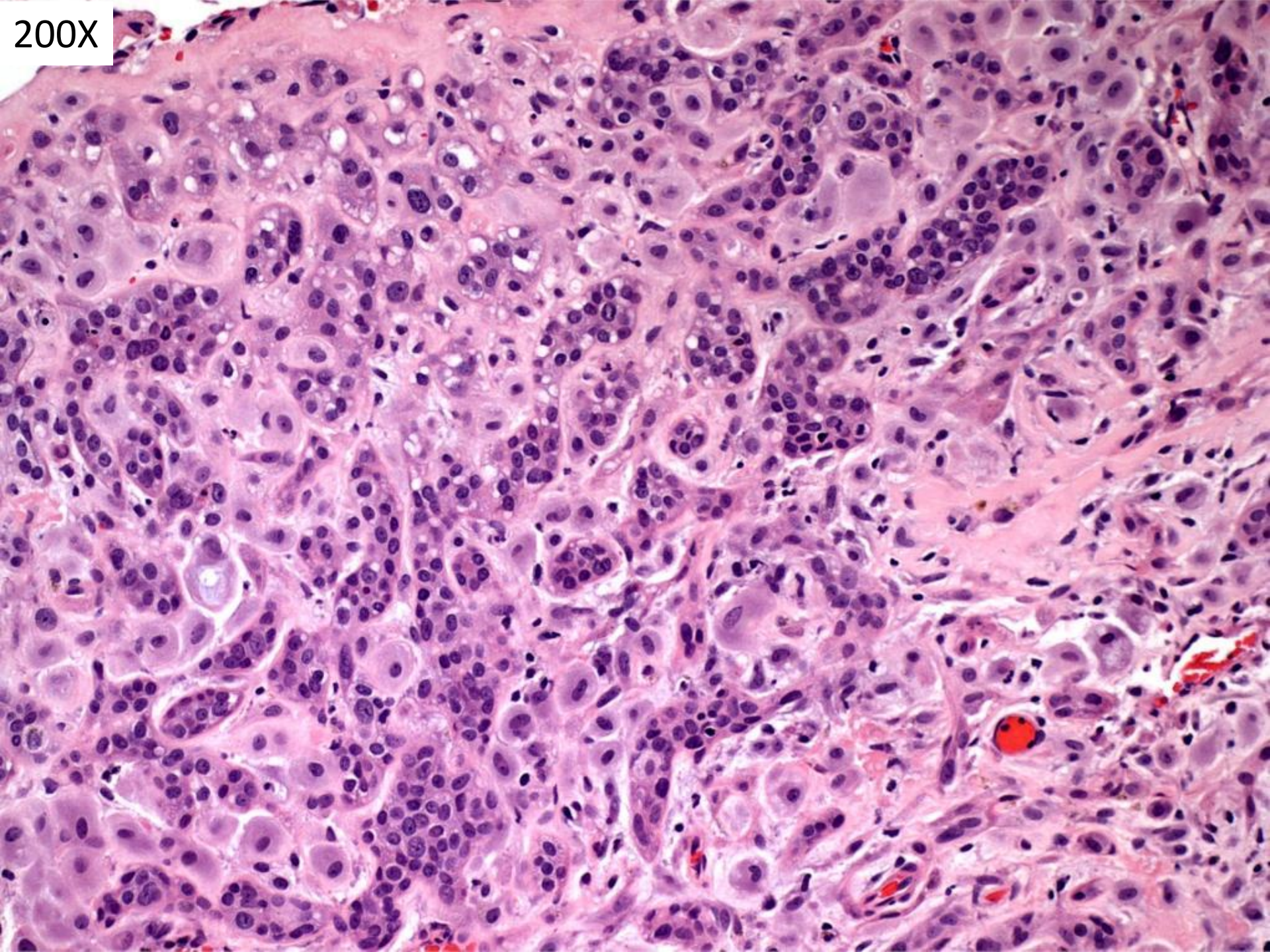
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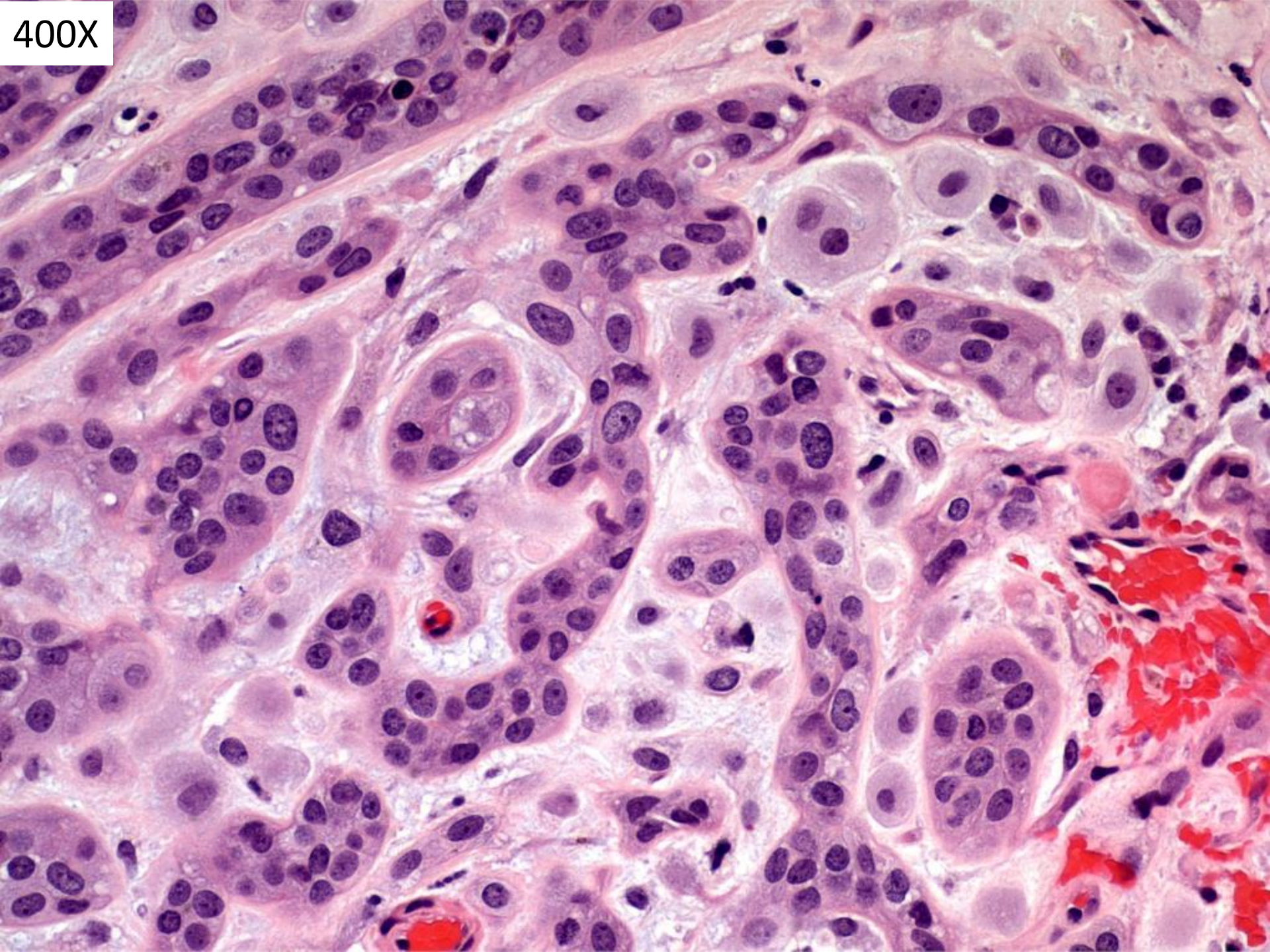
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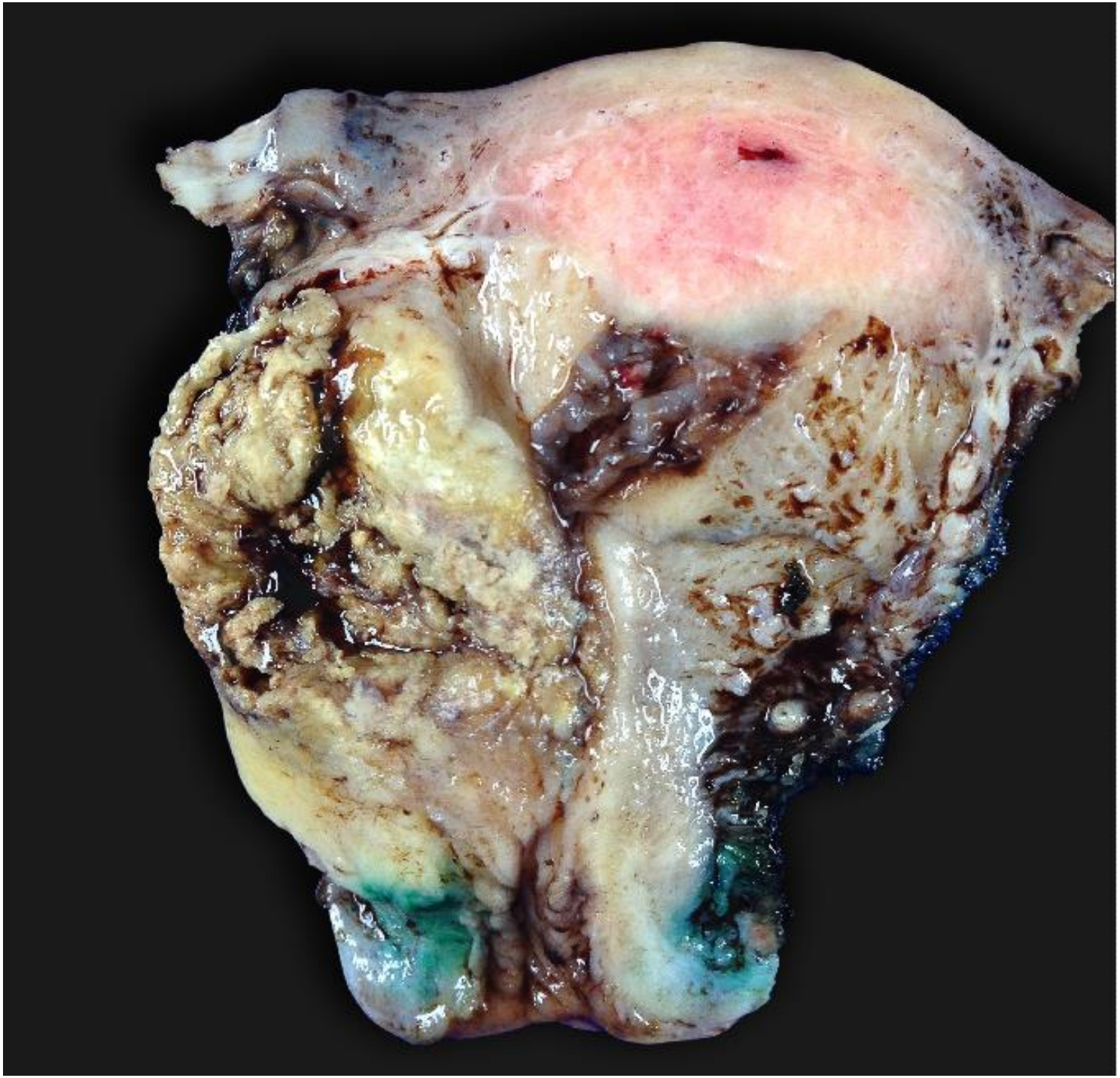
DIAGNOSIS?



Differential diagnosis

Benign

- Exaggerated placental site
- Placental site nodule

Malignant

- Placental site trophoblastic tumor
- Epithelioid trophoblastic tumor
- Choriocarcinoma
- Epithelioid smooth muscle tumor
- Keratinizing squamous cell carcinoma of the cervix

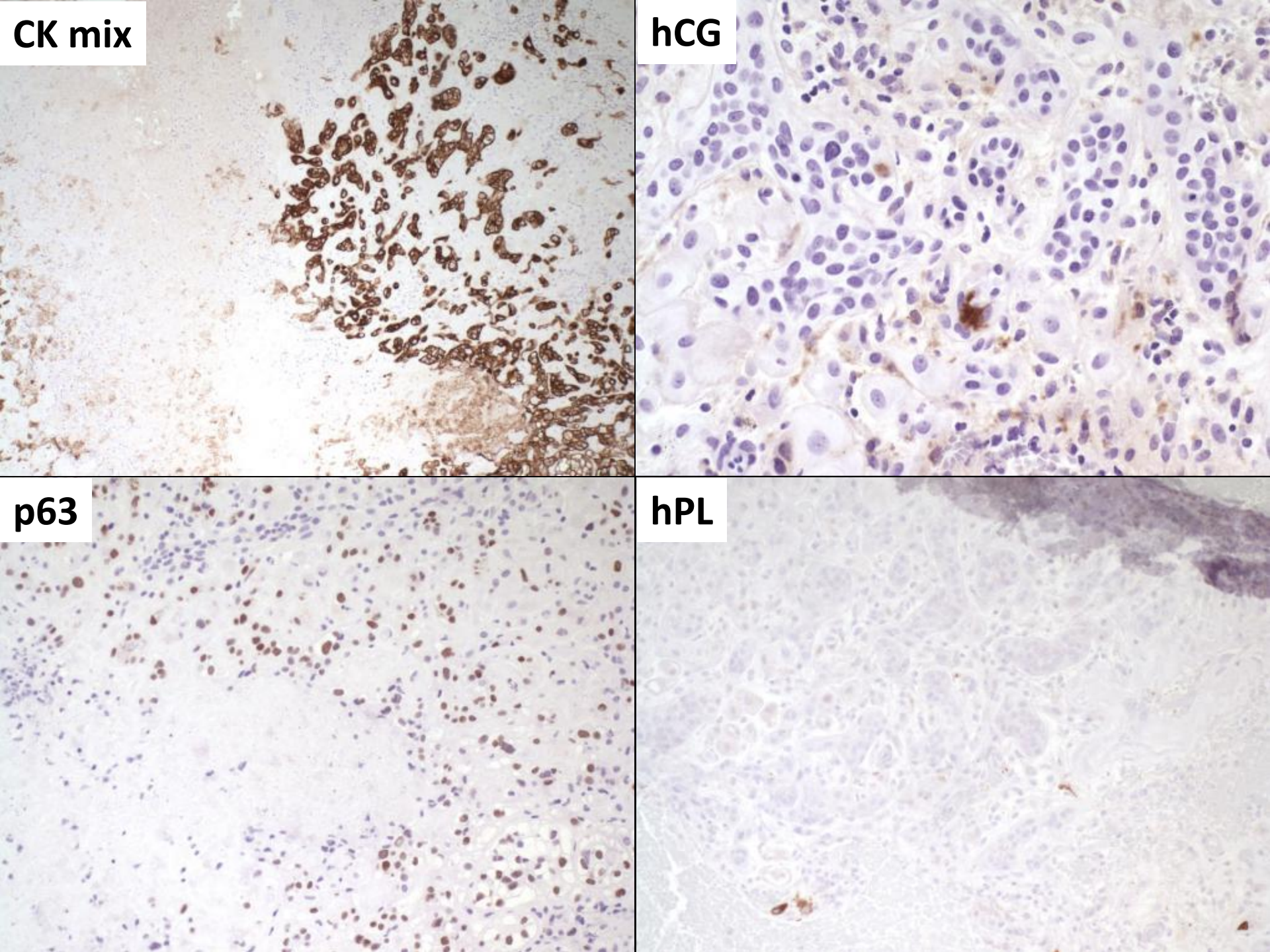
Differential diagnosis

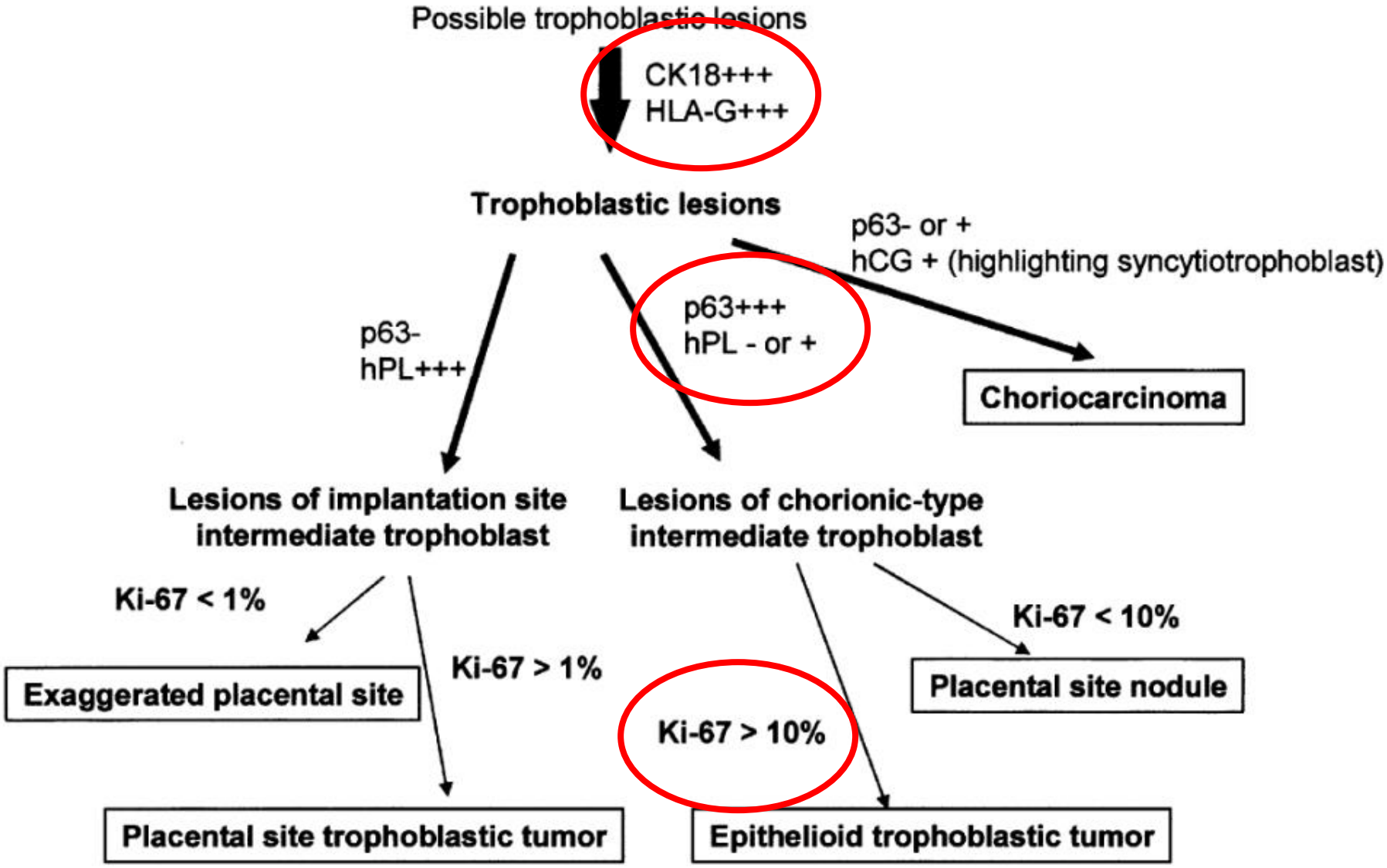
Benign

- Exaggerated placental site
- Placental site nodule

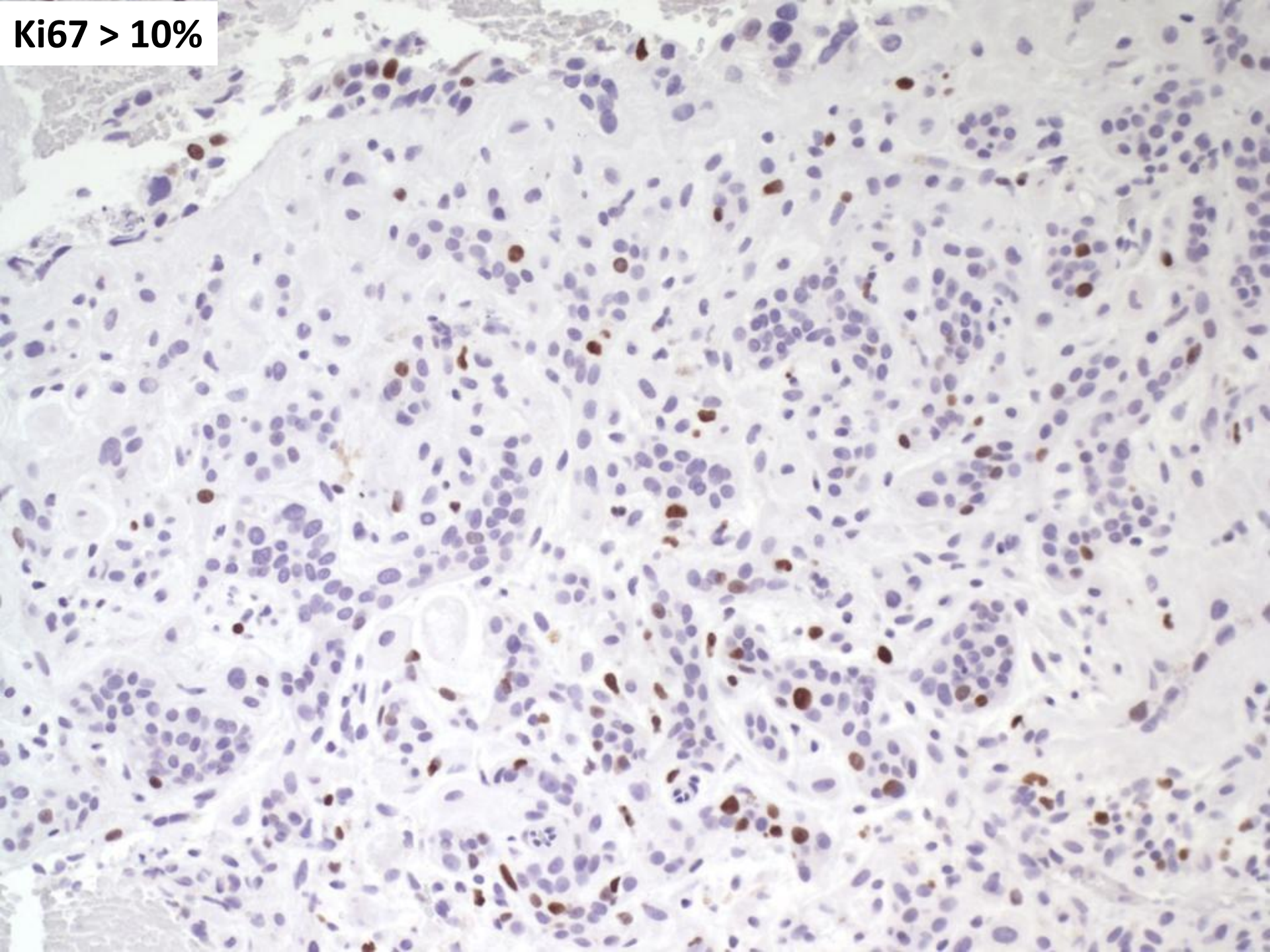
Malignant

- Placental site trophoblastic tumor
- **Epithelioid trophoblastic tumor**
- Choriocarcinoma
- Epithelioid smooth muscle tumor
- Keratinizing squamous cell carcinoma of the cervix


CK mix
hCG
p63
hPL

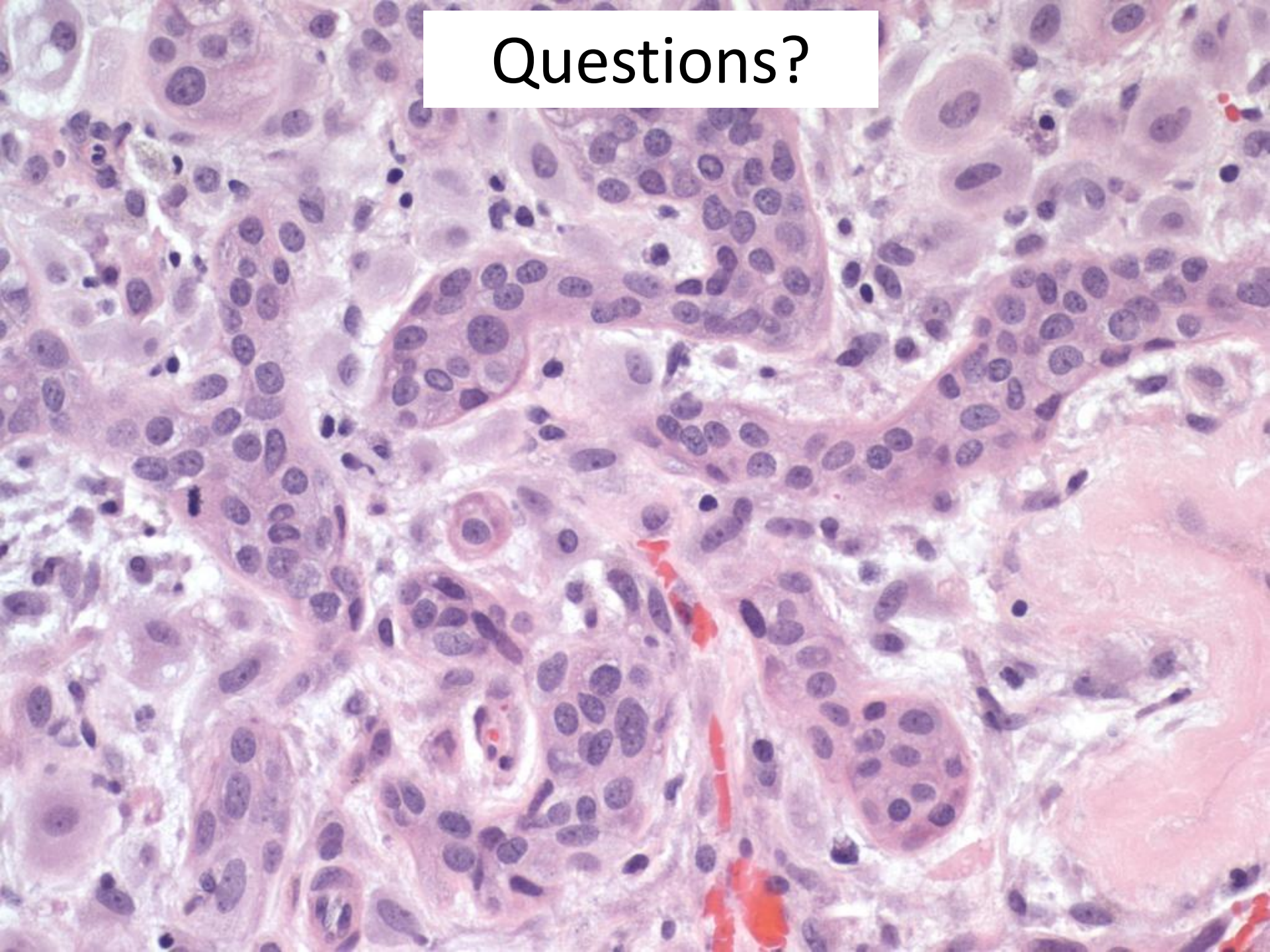


Shih IM, Kurman RJ. p63 expression is useful in the distinction of epithelioid trophoblastic and placental site trophoblastic tumors by profiling trophoblastic subpopulations. Am J Surg Pathol. 2004; 28:1177–1183.


Ki67 > 10%

Epithelioid trophoblastic tumor (ETT)	Placental Site Nodule (PSN)
0.5 to 4.0 cm	Microscopic (<0.4 cm)
Calcifications usually present	No calcifications (or not prominent)
Necrosis (palisading)	No necrosis
	Extensive eosinophilic extracellular matrix
	Circumscribed

Blaustein's Pathology of the Female Genital Tract, 6th Edition
Sternberg 2014

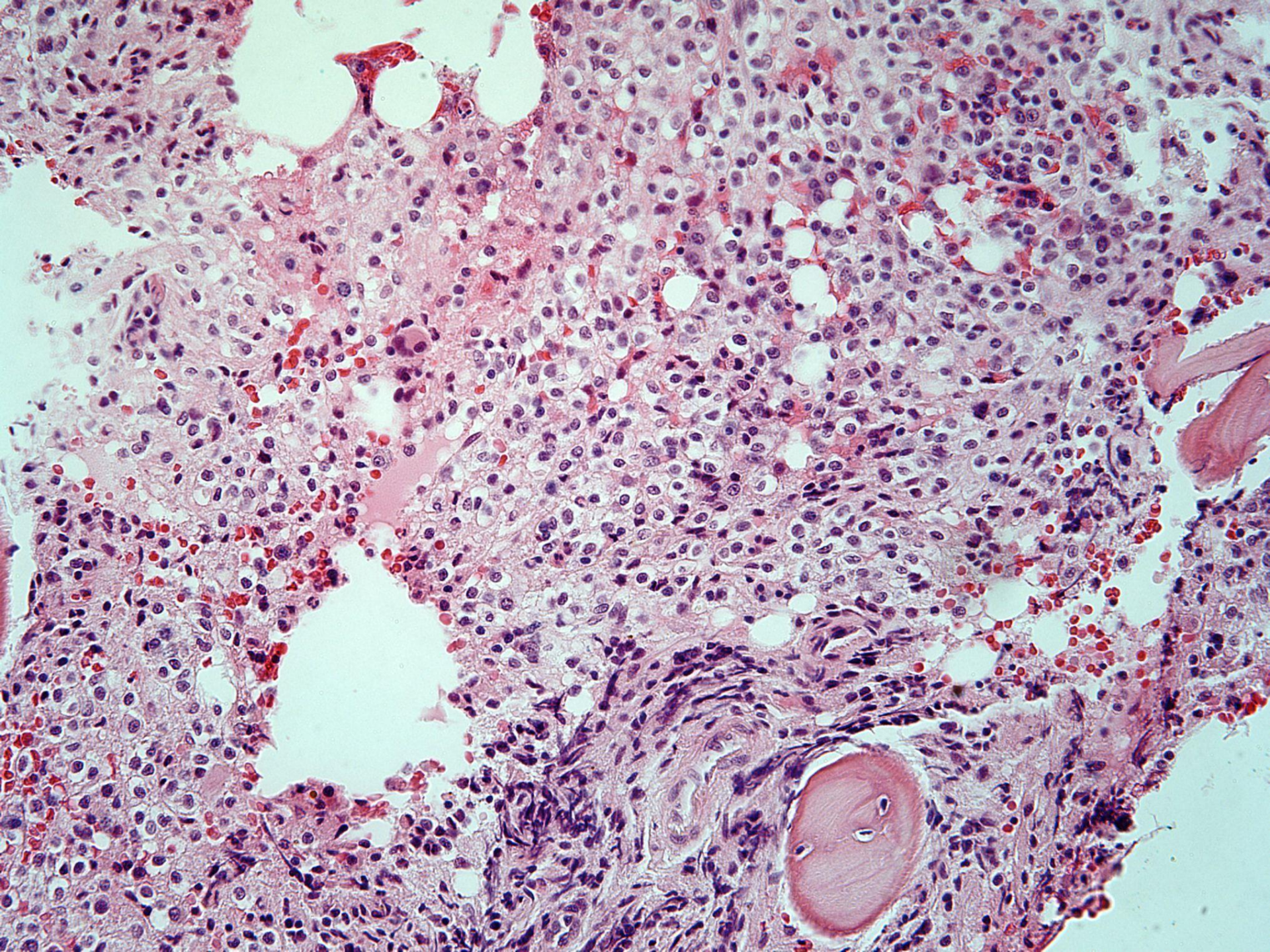

Questions?

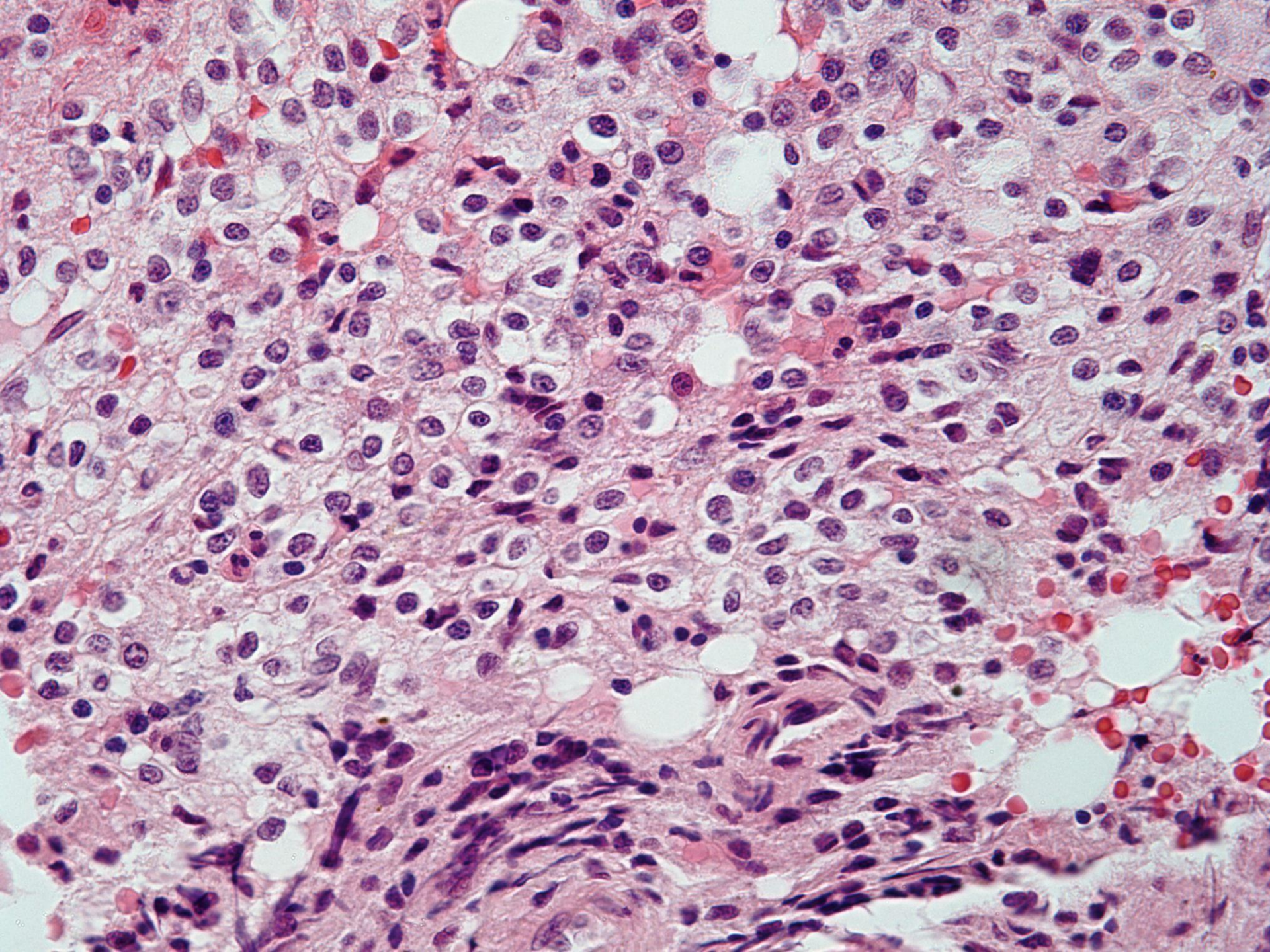
"Prozac? Alright! Kickin' it old school."

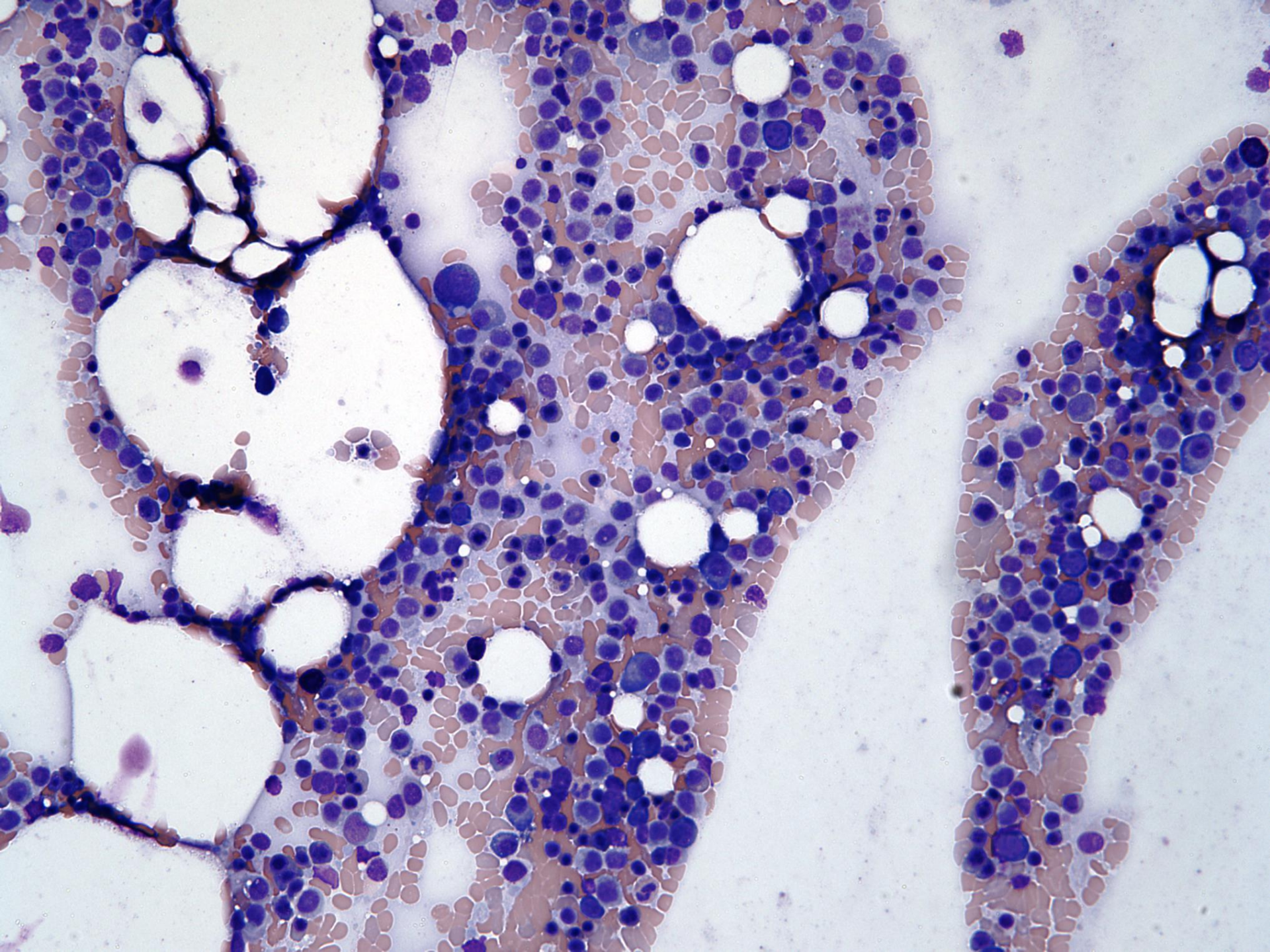
SB 5939

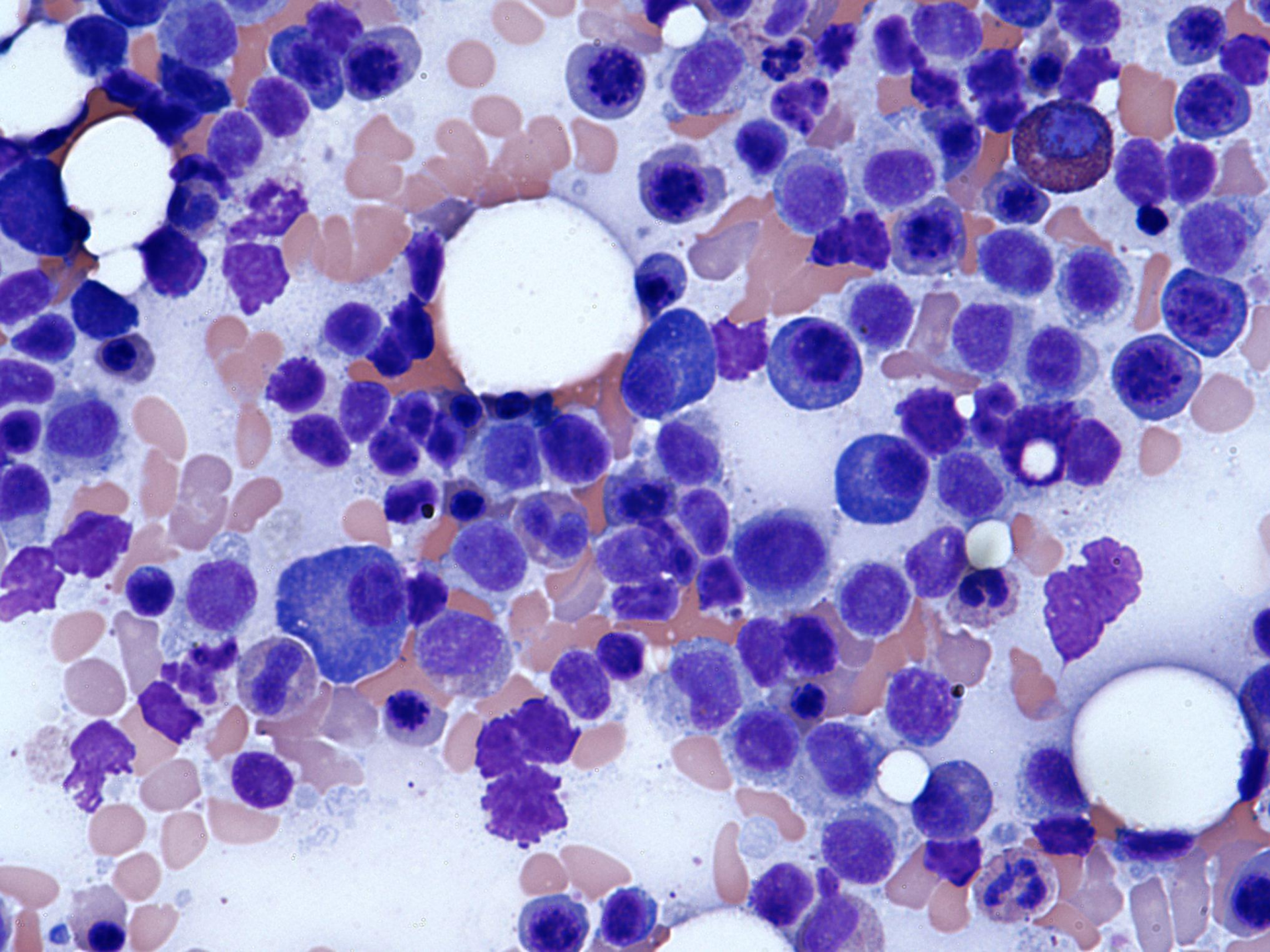
Alana Shain/Dean Fong; Stanford

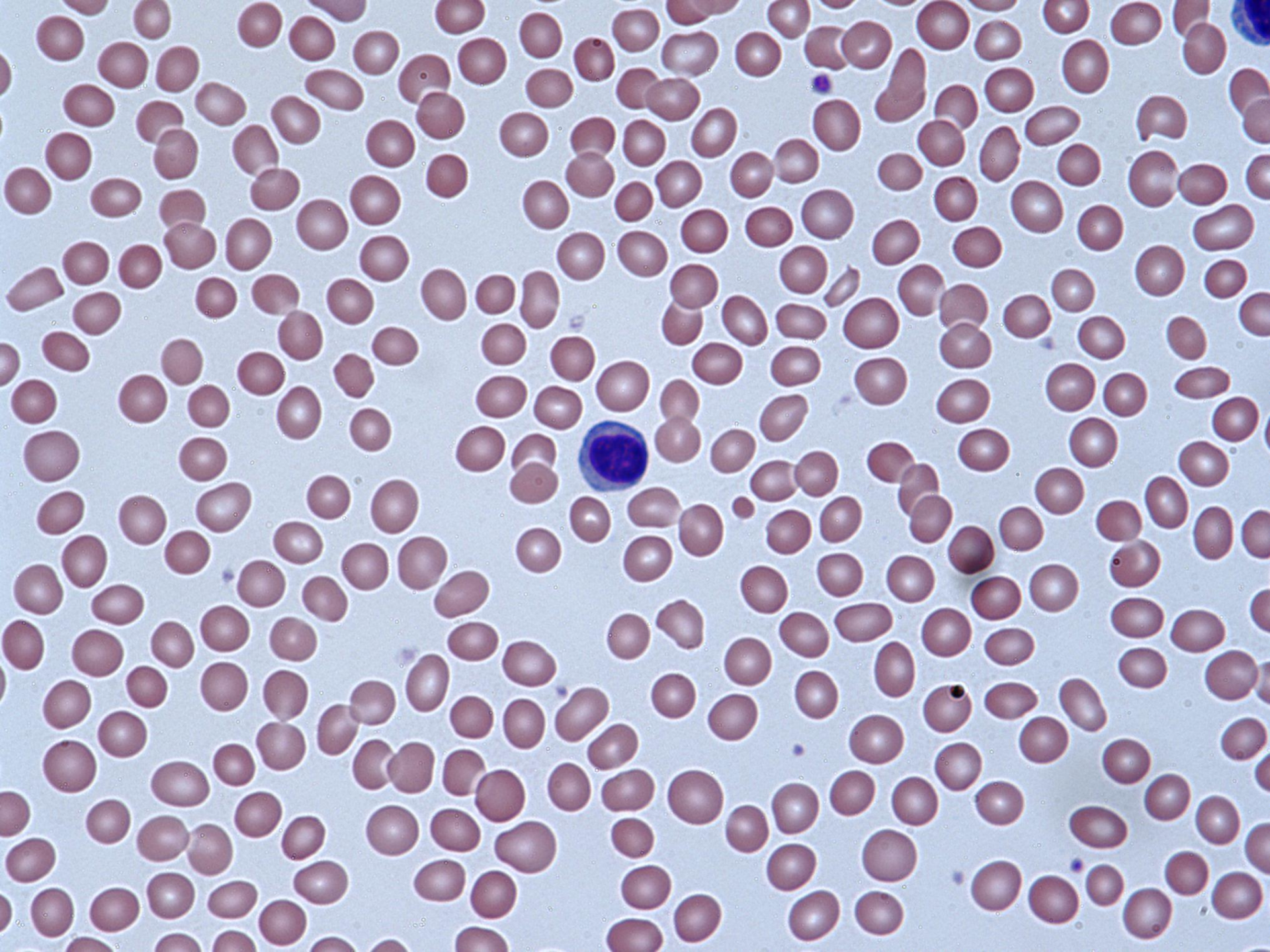
75-year-old male with IgG kappa monoclonal gammopathy of undetermined significance, now with progressive leukopenia and neutropenia.



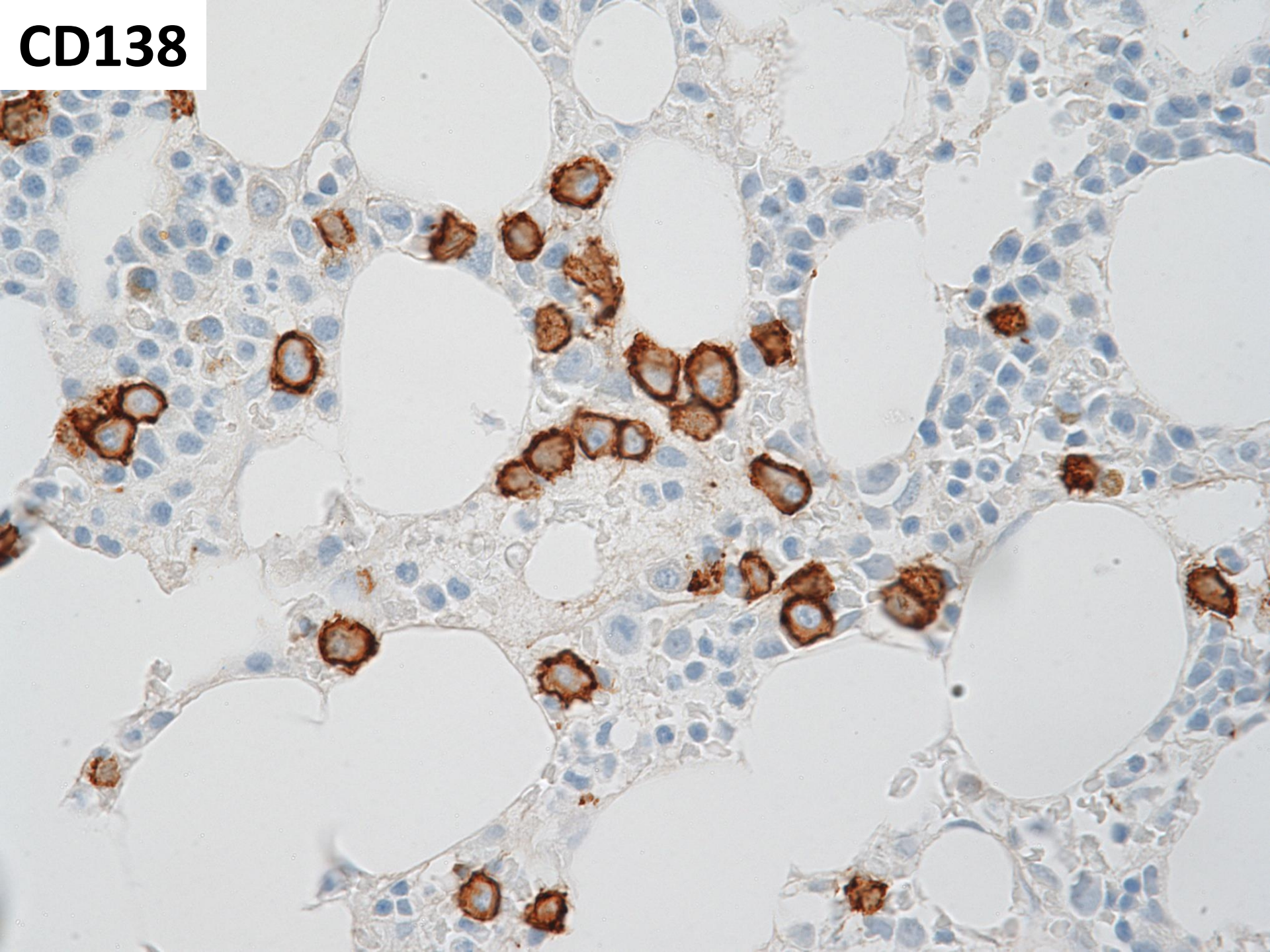


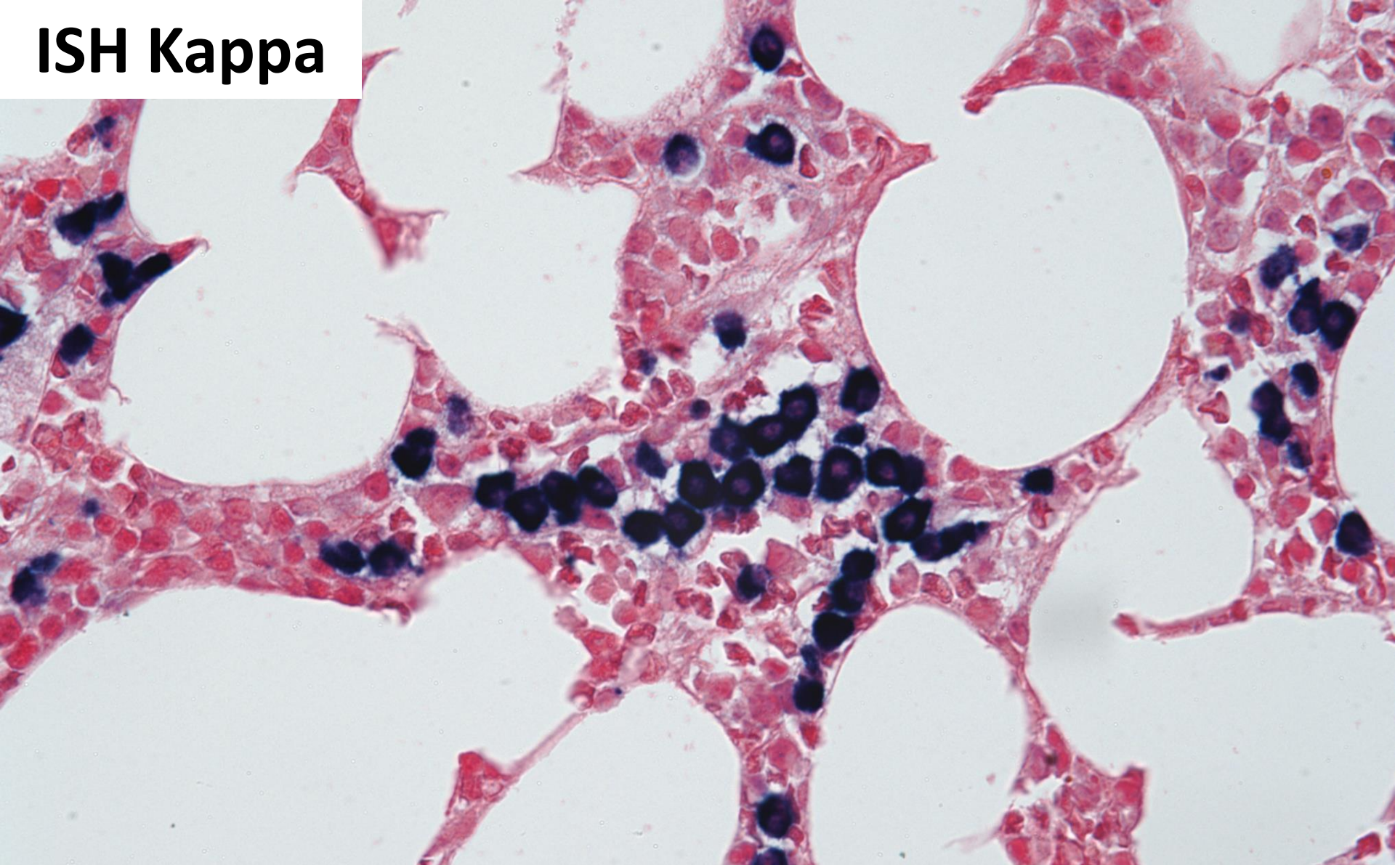




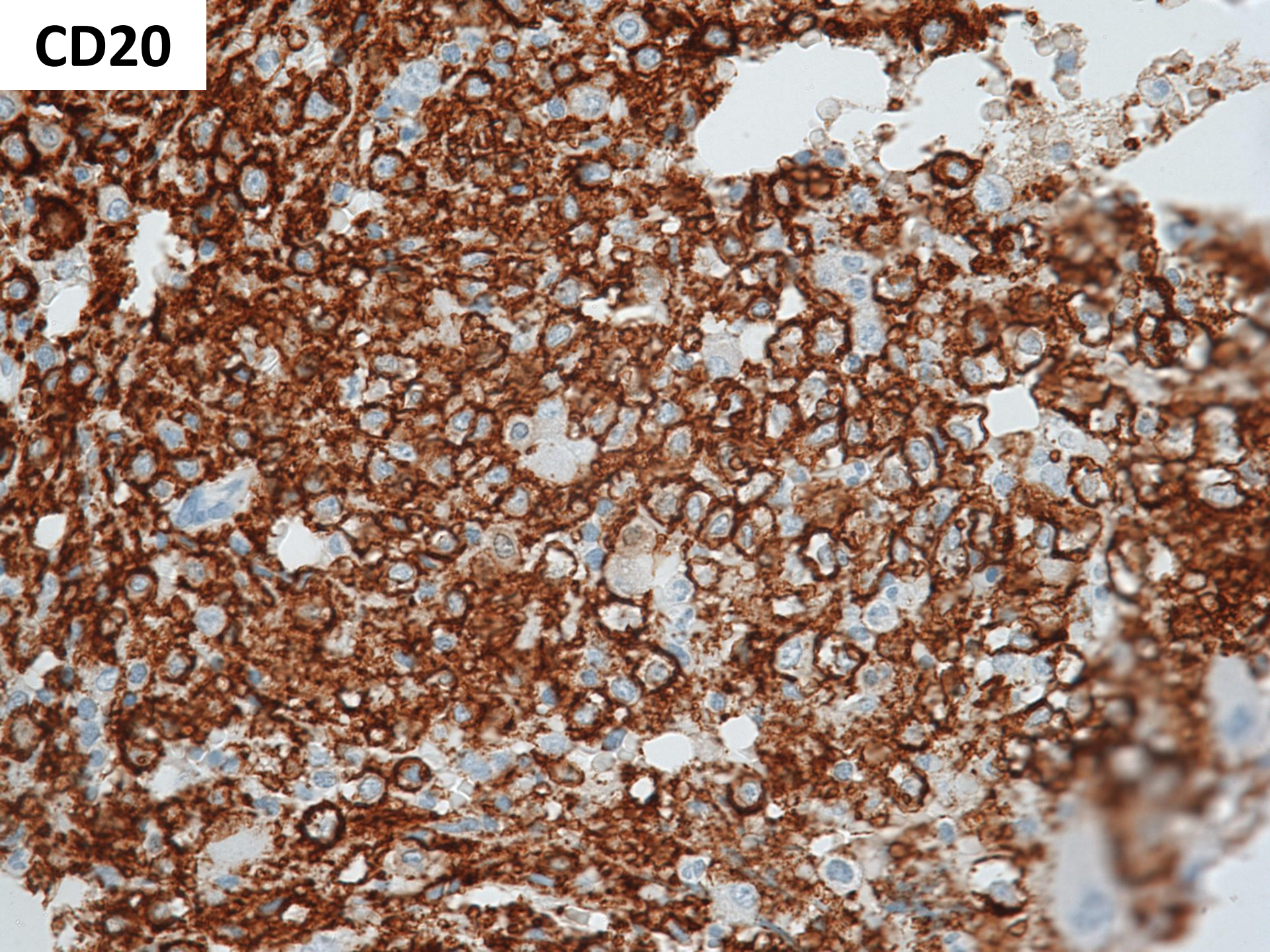


DIAGNOSIS?


CD138



Diagnosis 1:
Kappa monotypic plasma cell dyscrasia


CD20

Flow Cytometry

Clonal plasma cell population

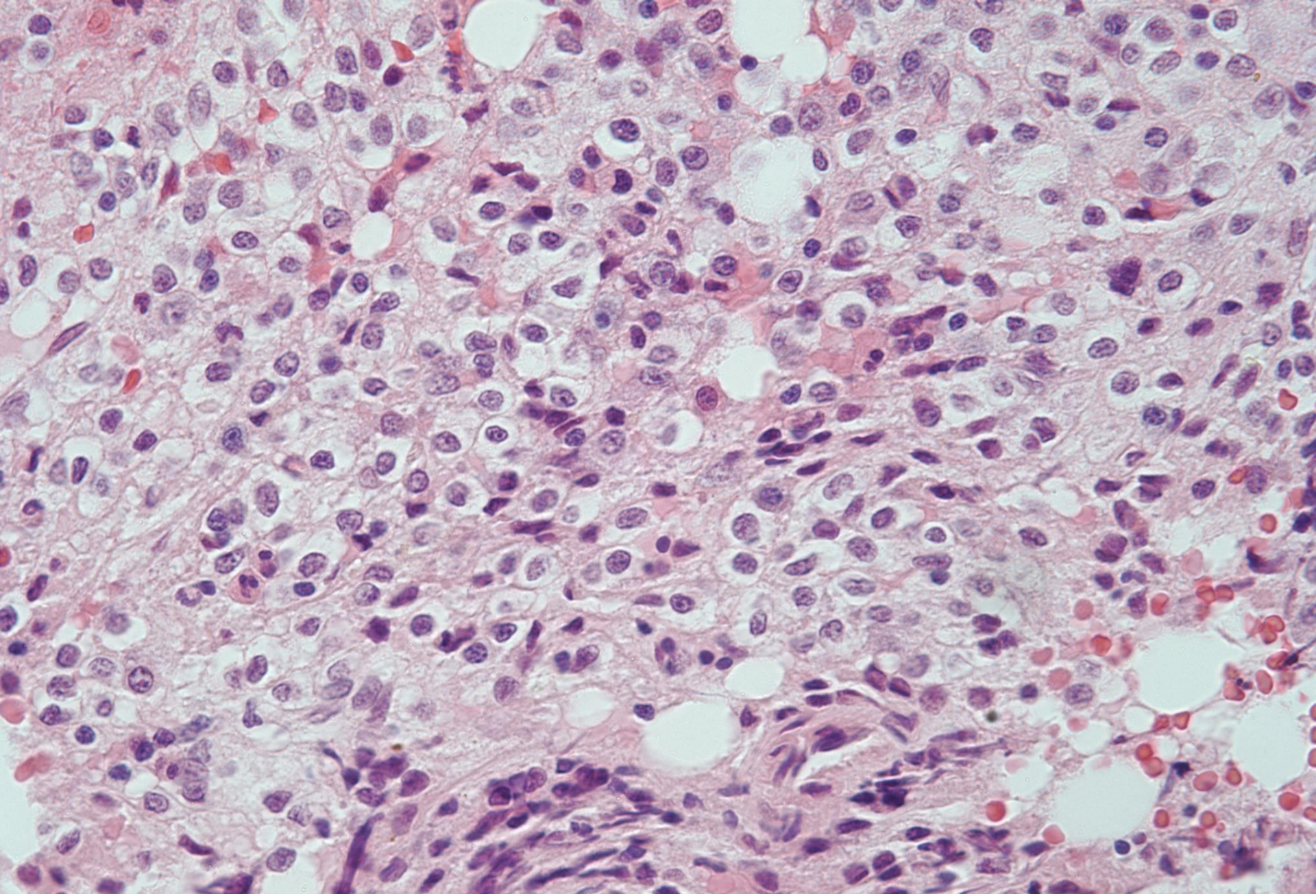
+: CD38, CD138, CD56, kappa

-: CD19

Abnormal B lymphocyte population

+: CD19, CD20, CD11c, CD25, CD103, lambda

-: CD5, CD23



Diagnosis 2: Hairy Cell Leukemia

Hairy Cell Leukemia

Presentation

- Cytopenias (**monocytopenia = sensitive marker of disease**)
- Splenomegaly

Differential Diagnosis:

- Splenic marginal zone lymphoma: Short polar villi. Nodular BM pattern. Annexin negative.
- HCL-variant: Annexin negative. CD25 negative.
- Plasma cell leukemia (Tanioka et al. Jpn J Clin Oncol 2003)

Stains: Annexin, DBA.44, TRAP

* Annexin can stain granulocytes *

* Bcl1 (Cyclin D1) can be positive in both HCL and myeloma *

Flow: CD19, CD20, **CD11c, CD25, CD103**

* CD103 also seen in splenic MZL (15%), HCL-v, T-cell lymphomas *

Second Malignancies

Hairy cell leukemia (Hisada et al., 2007)

- Increased relative risk Hodgkin lymphoma, non-Hodgkin lymphoma, thyroid cancer based on SEER data
- Absolute risk of second cancers small (34 second primaries per year in 10,000 hairy cell leukemia patients)

Myeloma (Engelhardt et al., 2014)

- Estimated incidence 1-10%
- Solid tumor (78%) > hematologic malignancies (22%) (Hasskarl et al., 2011)
- Rare to have mature B-cell neoplasm as secondary malignancy
- VA: 33/197 (16.8%) had other cancers (prostate), most diagnosed before or concomitantly (Munker et al., 2014)

References

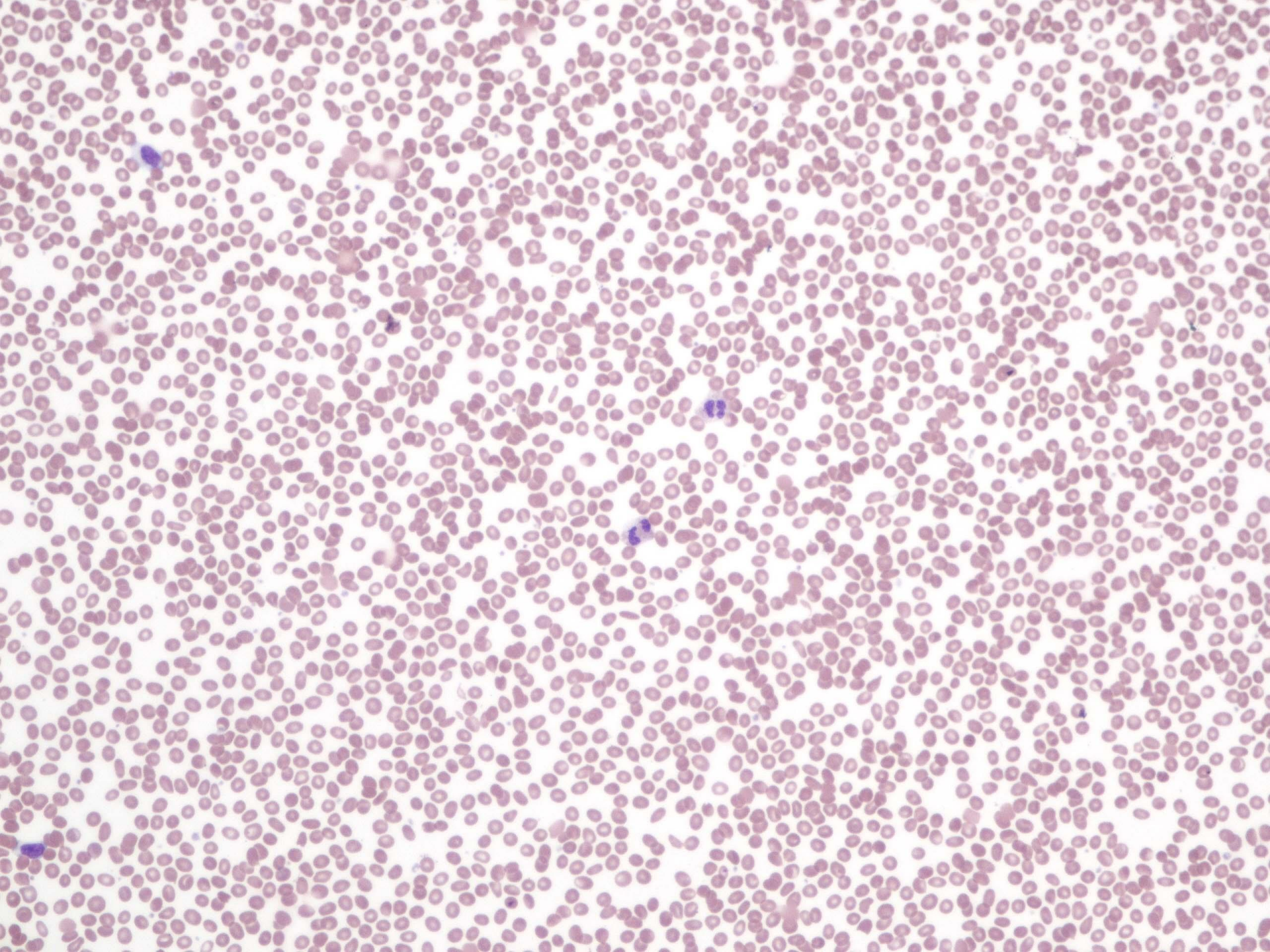
- Engelhardt et al. “Multiple Myeloma and Second Malignancies.” Clinical Lymphoma, Myeloma & Leukemia 2014, Vol. 14, No. 2, 98-101.
- Hasskarl J et al. “Association of multiple myeloma with different neoplasms: systematic analysis in consecutive patients with myeloma. Leuk Lymphoma 2011; 52:247-59.
- Hisada et al. “Second Cancer Incidence and Cause-Specific Mortality Among 3104 Patients With Hairy Cell Leukemia: A Population-Based Study.” J Natl Cancer Inst 2007;99: 215 – 22.
- Munker R et al. “Multiple myeloma and other malignancies: a pilot study from the Houston VA.” Clinical Lymphoma, Myeloma & Leukemia 2014, Vol. 14, No. 2, 102-6.
- Tanioka et al. “A Case of Primary Plasma Cell Leukemia with Hairy-cell Morphology and Lambda-type Bence–Jones Protein. Immunohistochemical and Molecular Analysis.” Jpn J Clin Oncol 2003;33(5)232–237.

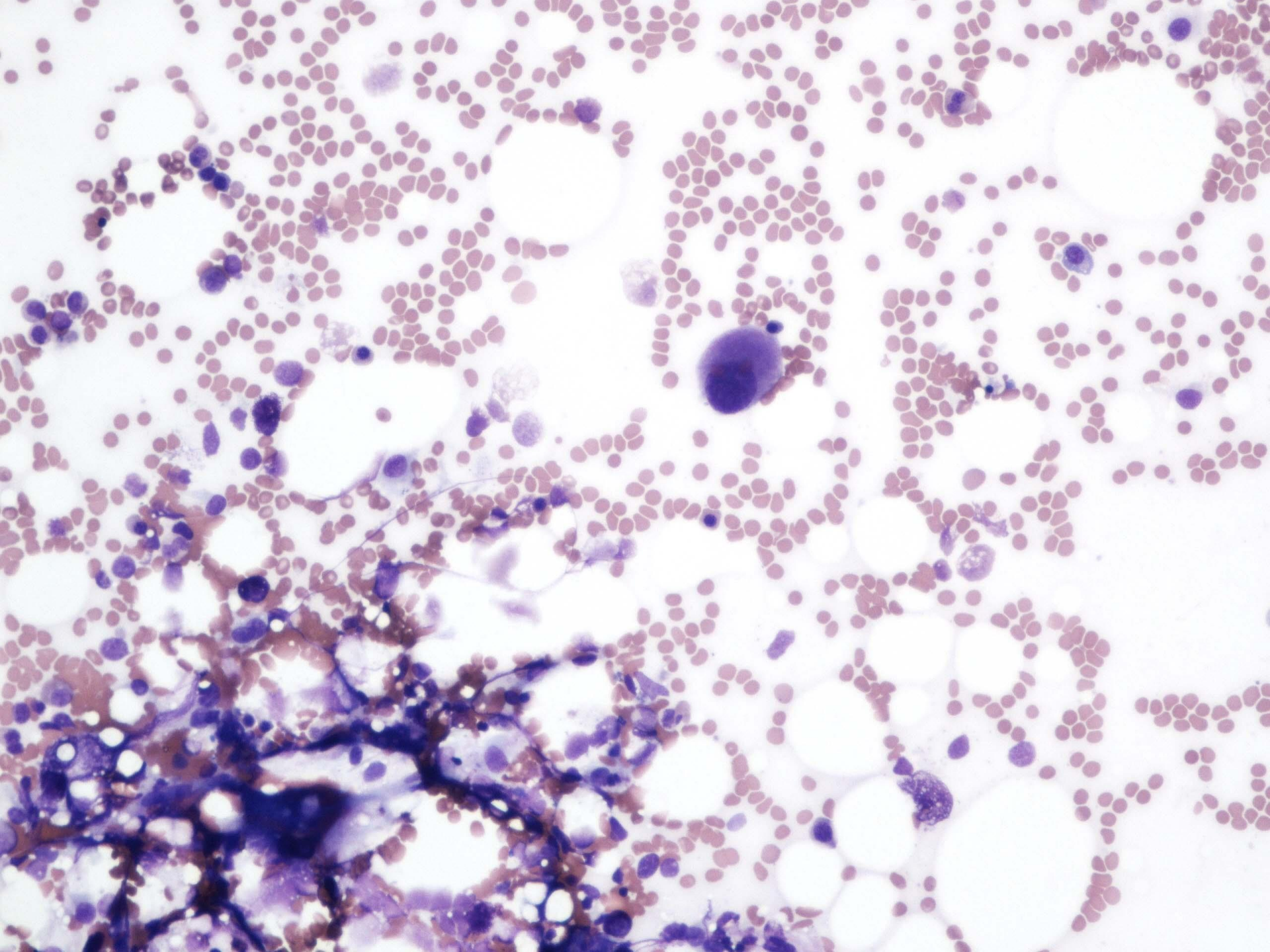

SO, COULD WE HAVE ALL YOUR STUFF AFTER YOU DIE?
DOCTORS WITHOUT BOUNDARIES
CN COLLECTION

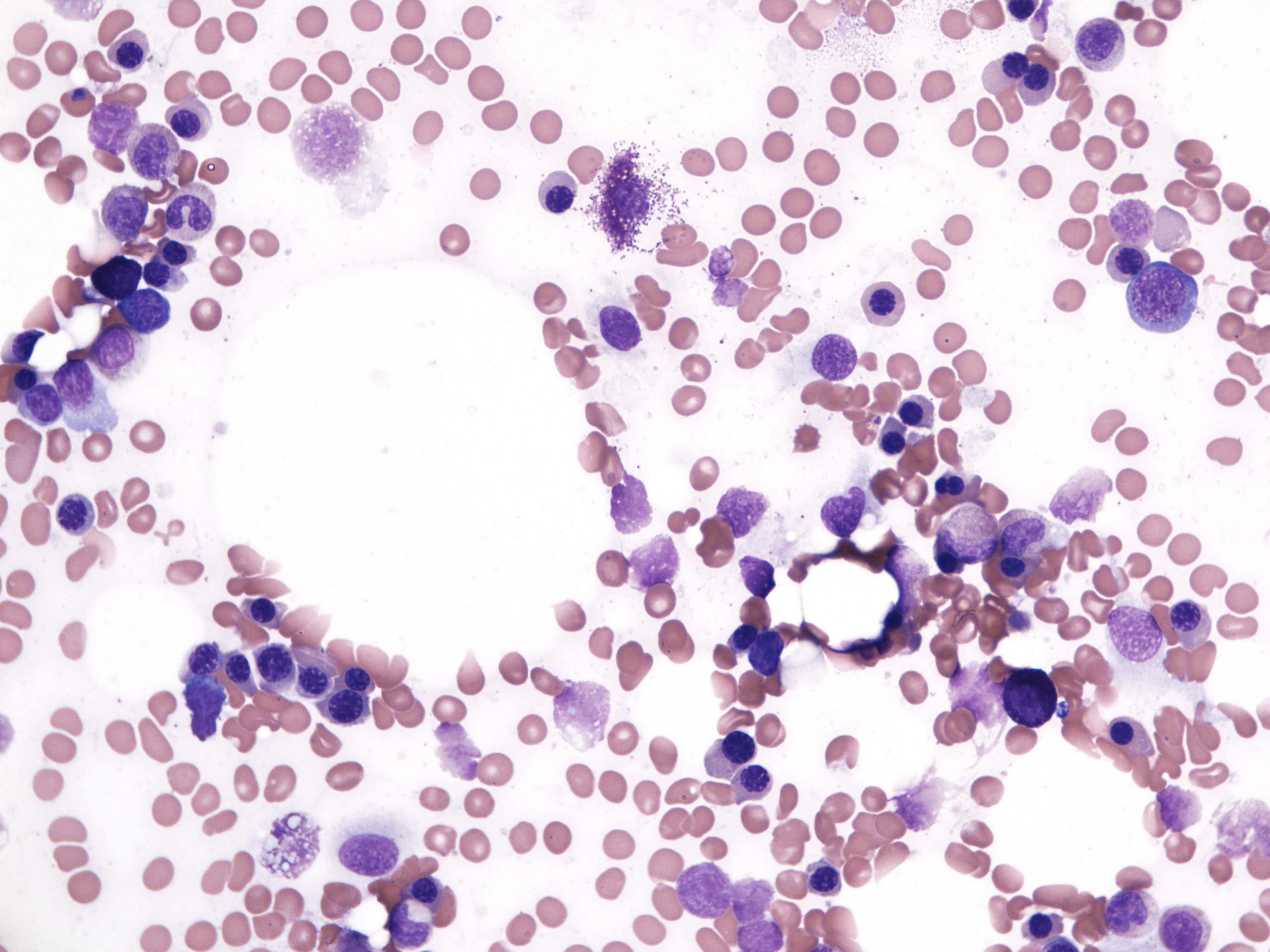
SB 5940

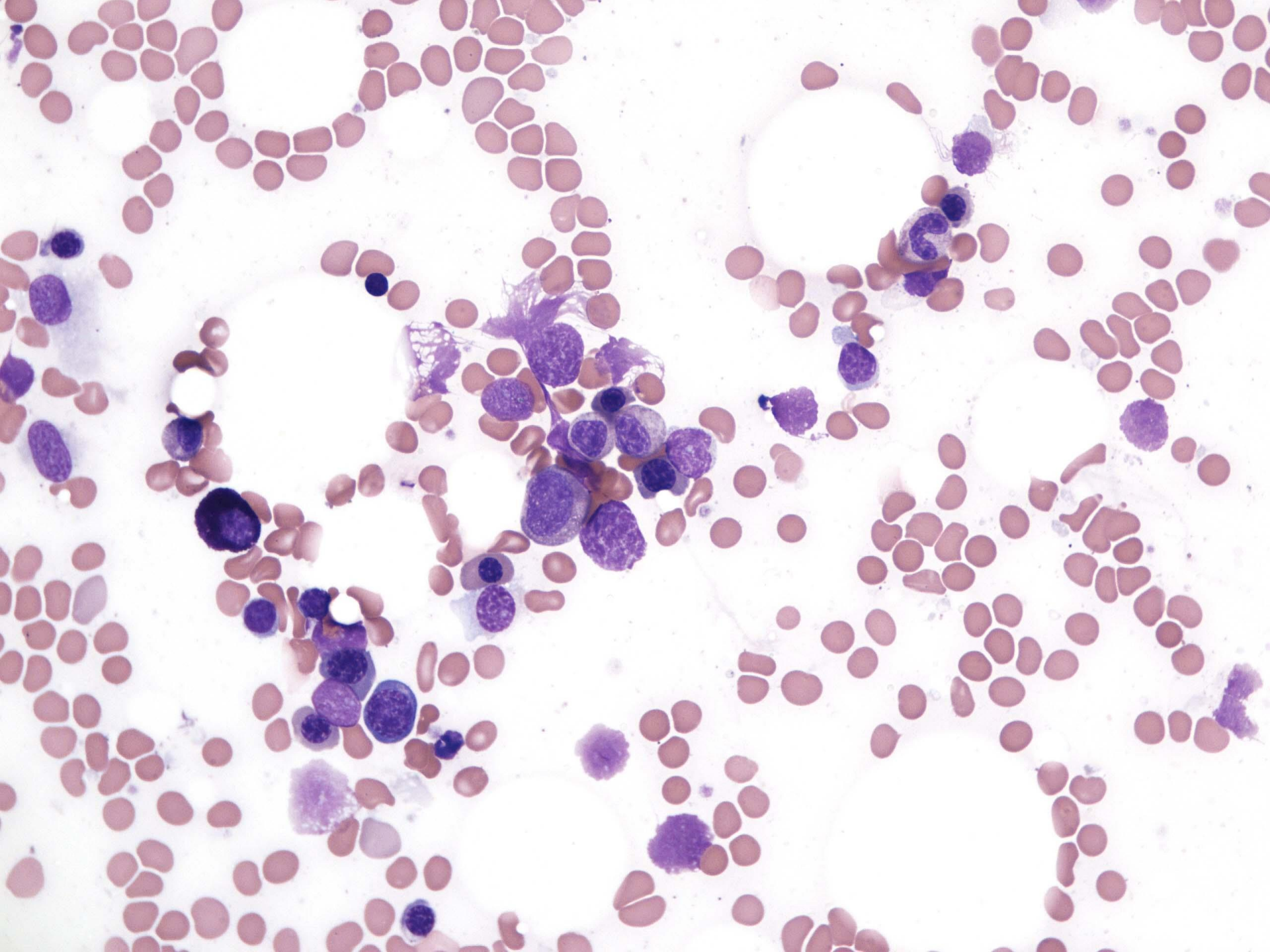
Linlin Wang/Sonam Prakash; UCSF

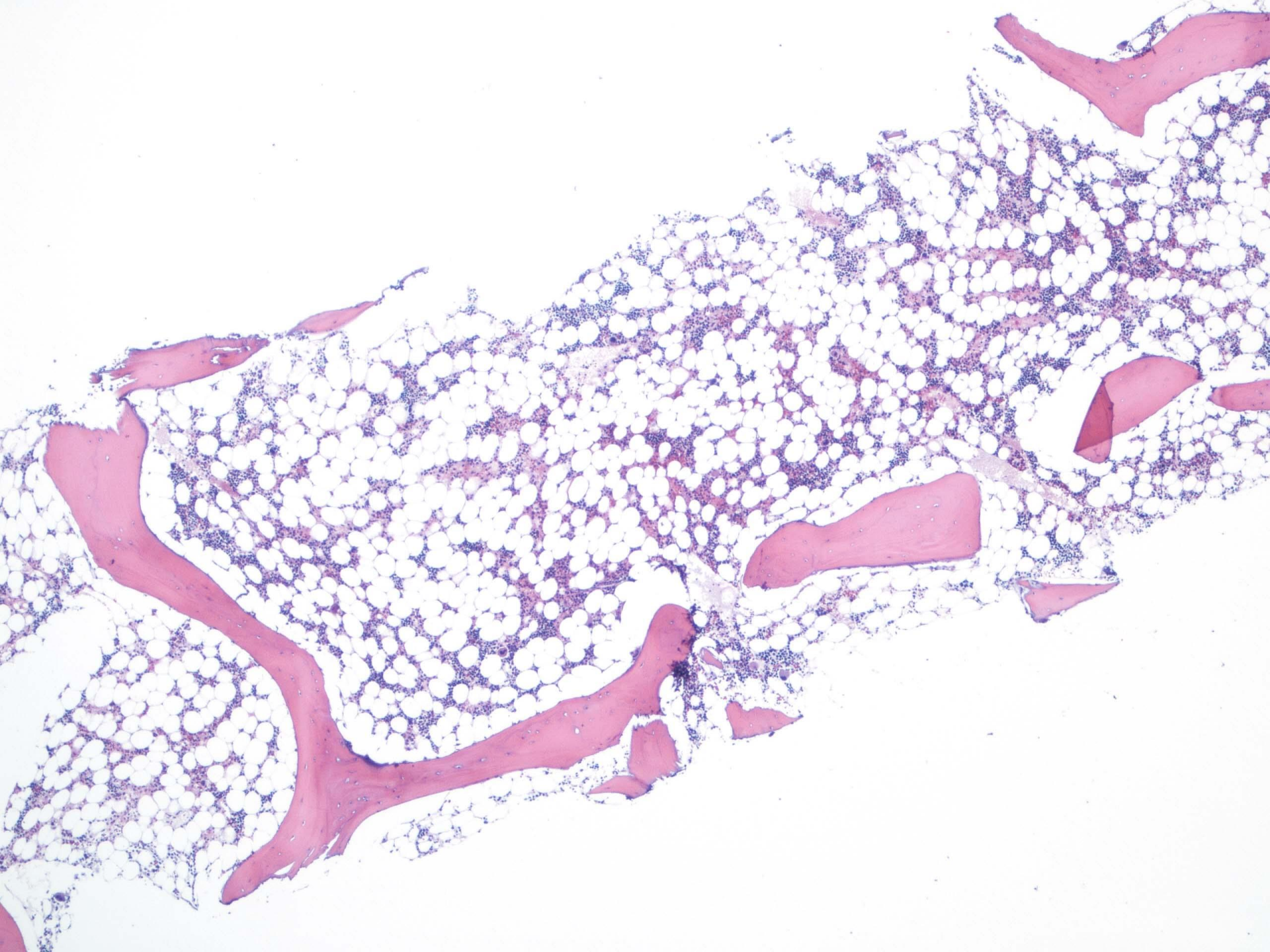
21-year-old man with scabies, mycobacterium infection and a reported history of ITP, now with pancytopenia. His aunt had AML at age 34, and his brother had MDS at age 17. CBC: WBC 2.6 x10E9/L (Neut 66%, Lymph 34%), HGB 9g/dl, MCV 88fl, Plt 79x10E9

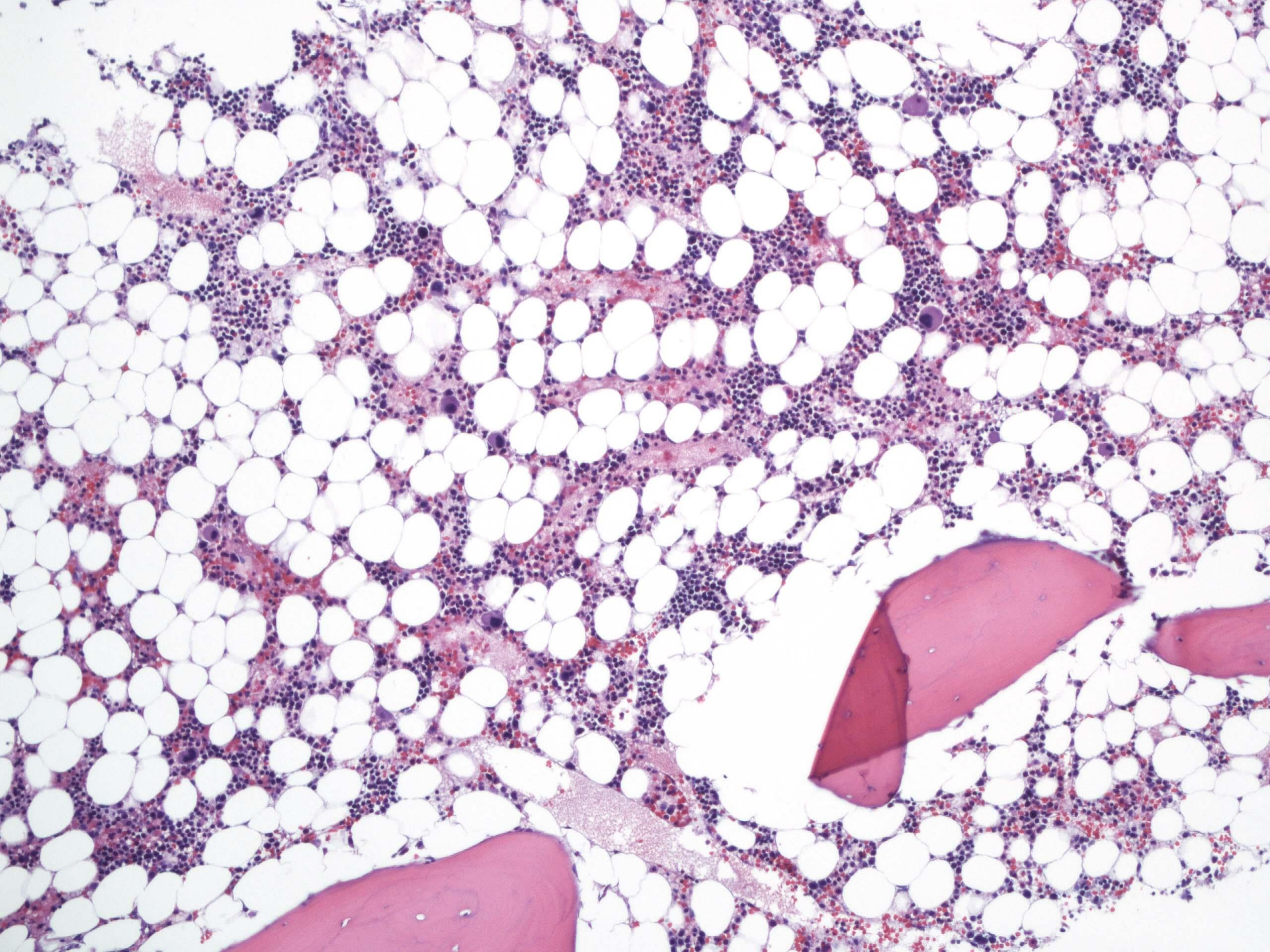


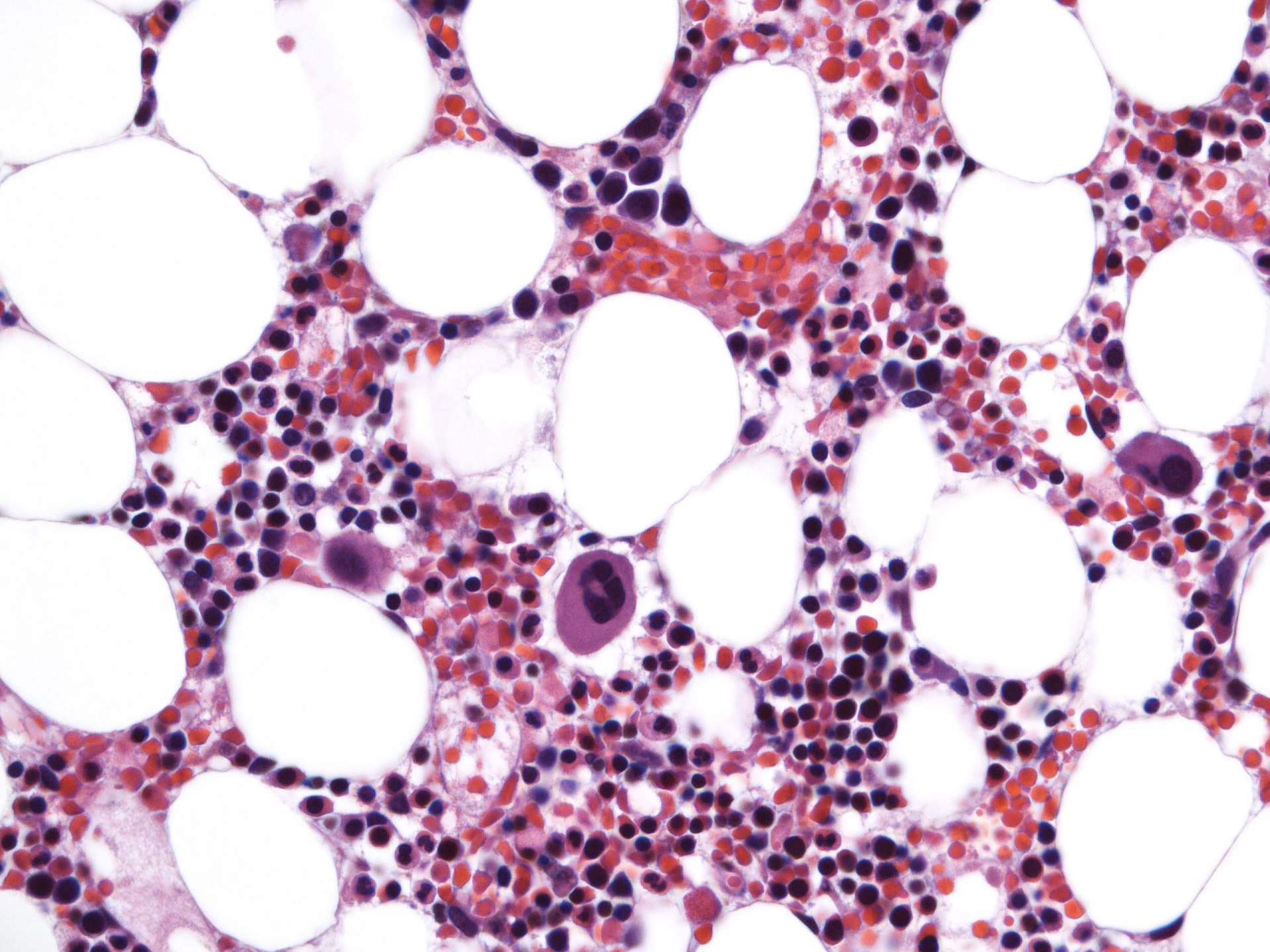


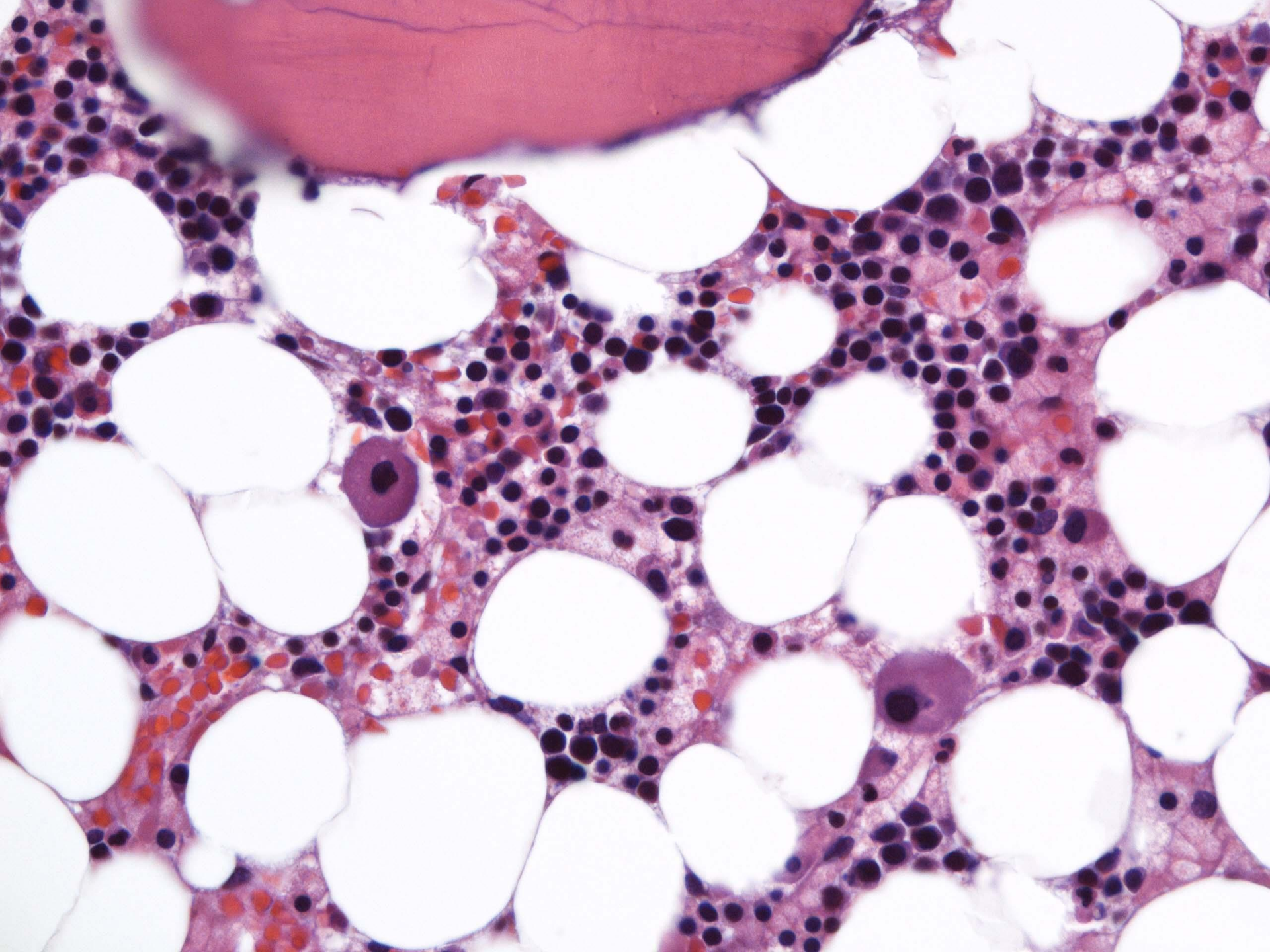












DIAGNOSIS?

Summary

- PB:
  - Pancytopenia
  - A subset of neutrophils with hypolobation
  - Monocytopenia
- BM:
  - Hypocellular marrow with erythroid predominant trilineage hematopoiesis
  - A subset of hypolobated megakaryocytes
- Flow cytometry:
  - No immunophenotypically abnormal cell population
  - Inverted CD4: CD8 ratio
  - Decreased B-cells (1%)
- Cytogenetics:
  - Normal karyotype

Differential Diagnosis

- Hypocellular MDS versus aplastic anemia?
  - Morphologic dysplasia and cytopenias
  - No increase in blasts
  - Normal cytogenetics
  - Does not meet the criteria for aplastic anemia

	AA	Patient
HGB (g/dL)	<10	9
ANC (x10E9)	<1.5	1.7
PLT (x10E9)	<50	79

- Monocytopenia?
- Specific infections

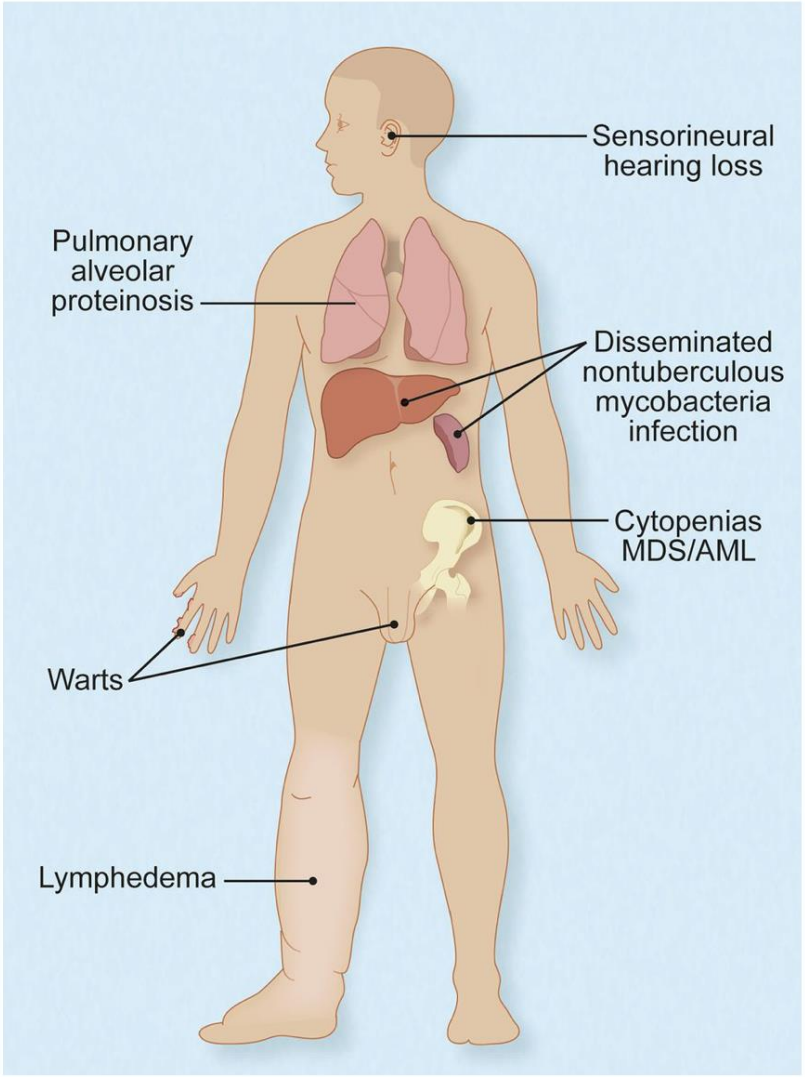
MonoMac syndrome

An immunodeficiency syndrome with

- Infection with disseminated nontuberculous mycobacteria, HPV and/ or fungi.
- PB with absence of monocytes, NK cells and B-cells.
- Propensity to develop MDS/AML in half of the patients.
- Occasional pedigrees with two or more affected generations.

GATA2 Deficiency

- MonoMac
- Familial MDS/AML
- Emberger syndrome (primary lymphedema with MDS)
- Dendritic cells, monocyte, B and NK-cell deficiency



blood

Home / September 8, 2011; Blood: 118 (10)

Mutations in *GATA2* are associated with the autosomal dominant and sporadic monocytopenia and mycobacterial infection (MonoMAC) syndrome

Amy P. Hsu[1], Elizabeth P. Sampaio[1], Javed Khan[2], Katherine R. Calvo[3], Jacob E. Lemieux[4], Smita Y. Patel[5], David M. Frucht[6], Donald C. Vinh[1], Roger D. Auth[6], Alexandra F. Freeman[1], Kenneth N. Olivier[1], Gulbu Uzel[1], Christa S. Zerbe[1], Christine Spalding[1], Stefania Pittaluga[7], Mark Raffeld[7], Douglas B. Kuhns[8], Li Ding[1], Michelle L. Paulson[1,8], Beatriz E. Marciano[1], Juan C. Gea-Banacloche[9], Jordan S. Orange[10], Jennifer Cuellar-Rodriguez[1], Dennis D. Hickstein[9], and Steven M. Holland[1]

GATA2 Deficiency Marrow

- Hypocellular marrow
- Severely reduced monocytes, B-cells and NK-cells
- Atypical megakaryocytes
- Flow cytometry:
  - Absent hematogones
  - Inverted CD4: CD8 ratios
- Abnormal cytogenetics

blood Prepublished online October 30, 2014; doi:10.1182/blood-2014-06-580340

GATA2 deficiency-associated bone marrow disorder differs from idiopathic aplastic anemia

Karthik A. Ganapathi, Danielle M. Townsley, Amy P. Hsu, Diane C. Arthur, Christa S. Zerbe, Jennifer Cuellar-Rodriguez, Dennis D. Hickstein, Sergio D. Rosenzweig, Raul C. Braylan, Neal S. Young, Steven M. Holland and Katherine R. Calvo

Summary of Findings

- Nontuberculous mycobacterial infection
- Monocytopenia
- Atypical megakaryocytes
- Family history of AML/MDS
- Additional Studies:
  - Lymphocyte subset study in PB: decreased B-cell and NK-cells.
  - Confirmed GATA2 mutation
    - cDNA 1082G>A causing the substitution of histidine for arginine at amino acid 361 (R361H)