SEPT 2018 DIAGNOSIS LIST

6301: PEComa (ovary; GYN pathology)
6302: Ganglioneuroma with prominent adipocytic component (pleural/soft tissue pathology)
6303: Follicular T-cell lymphoma (lymph node; hematopathology)
6304: Blastic plasmacytoid dendritic cell neoplasm (soft tissue/hematopathology)
6305: Myeloid neoplasm with atypical plasmacytoid dendritic cell proliferation (bone marrow/hematopathology)
6306: Blastoid variant of mantle cell lymphoma (lymph node; hematopathology)
6307: metastatic prostatic adenocarcinoma (mediastinum; GU pathology)
6308: mesenchymal chondrosarcoma (brain; soft tissue pathology)
6309: adult T-cell leukemia/lymphoma (bone marrow; hematopathology)
6310: metastatic low grade fibromyxoid sarcoma (pancreas; soft tissue pathology)

Disclosures
Sept 10, 2018

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

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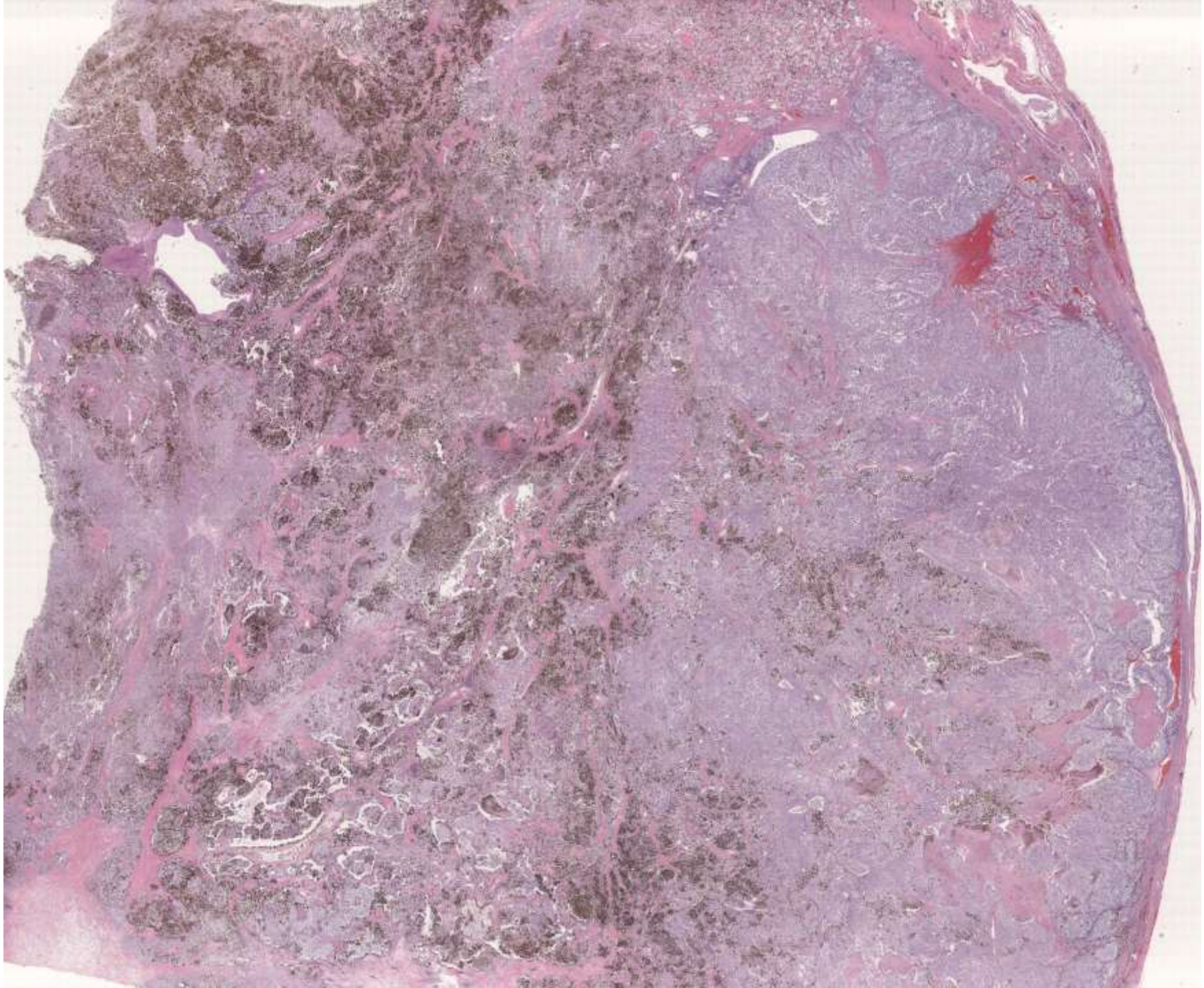
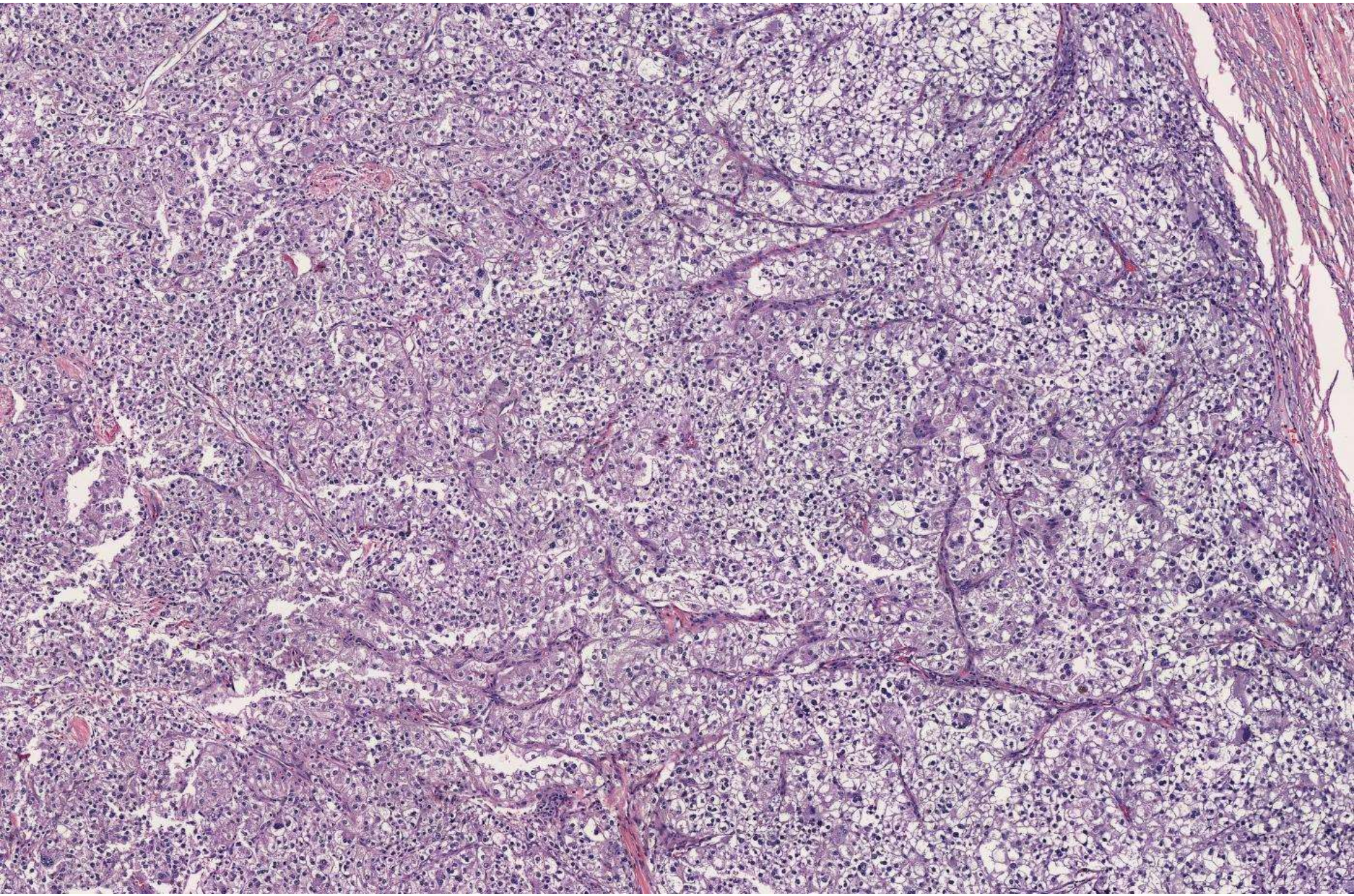
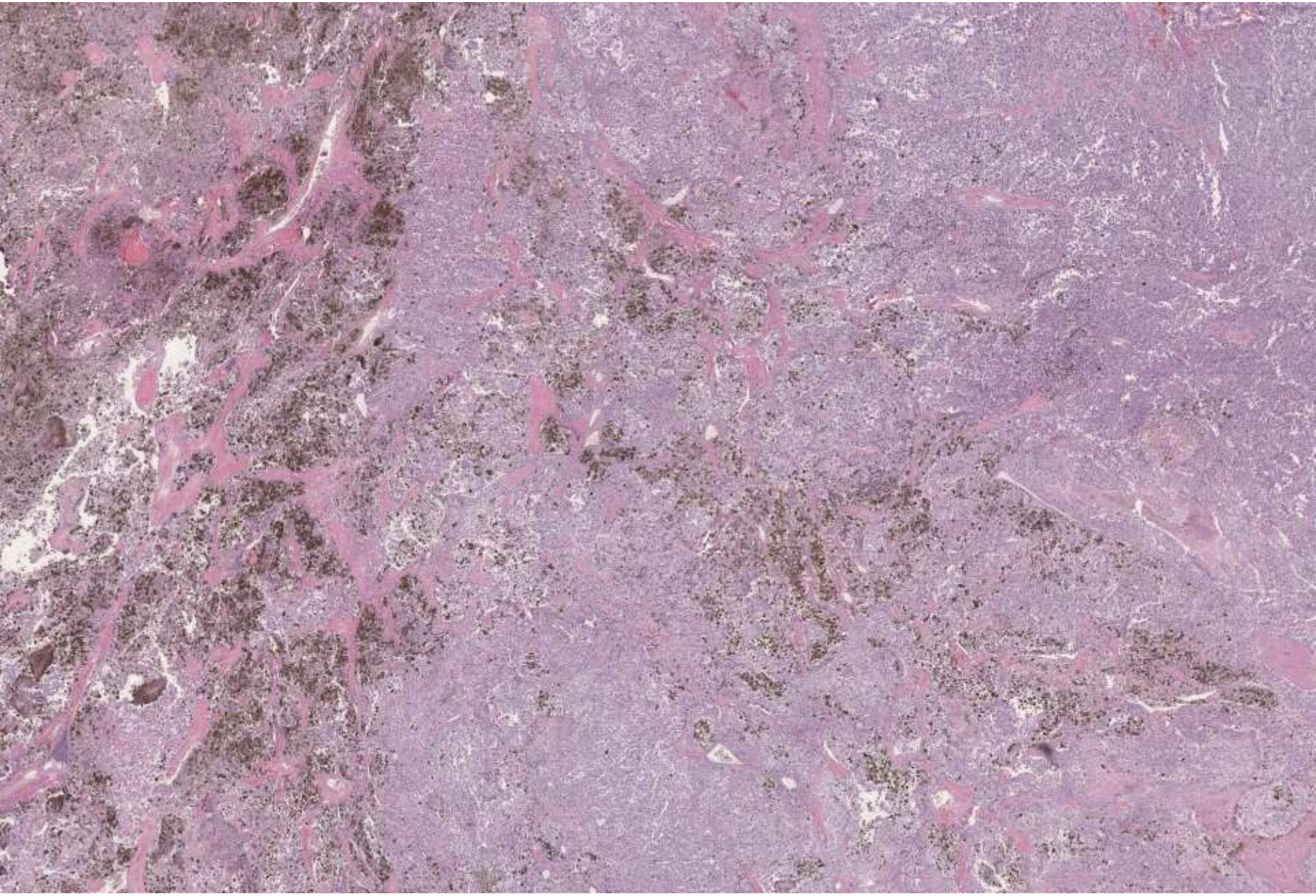
SB 6301
(scanned slide available)

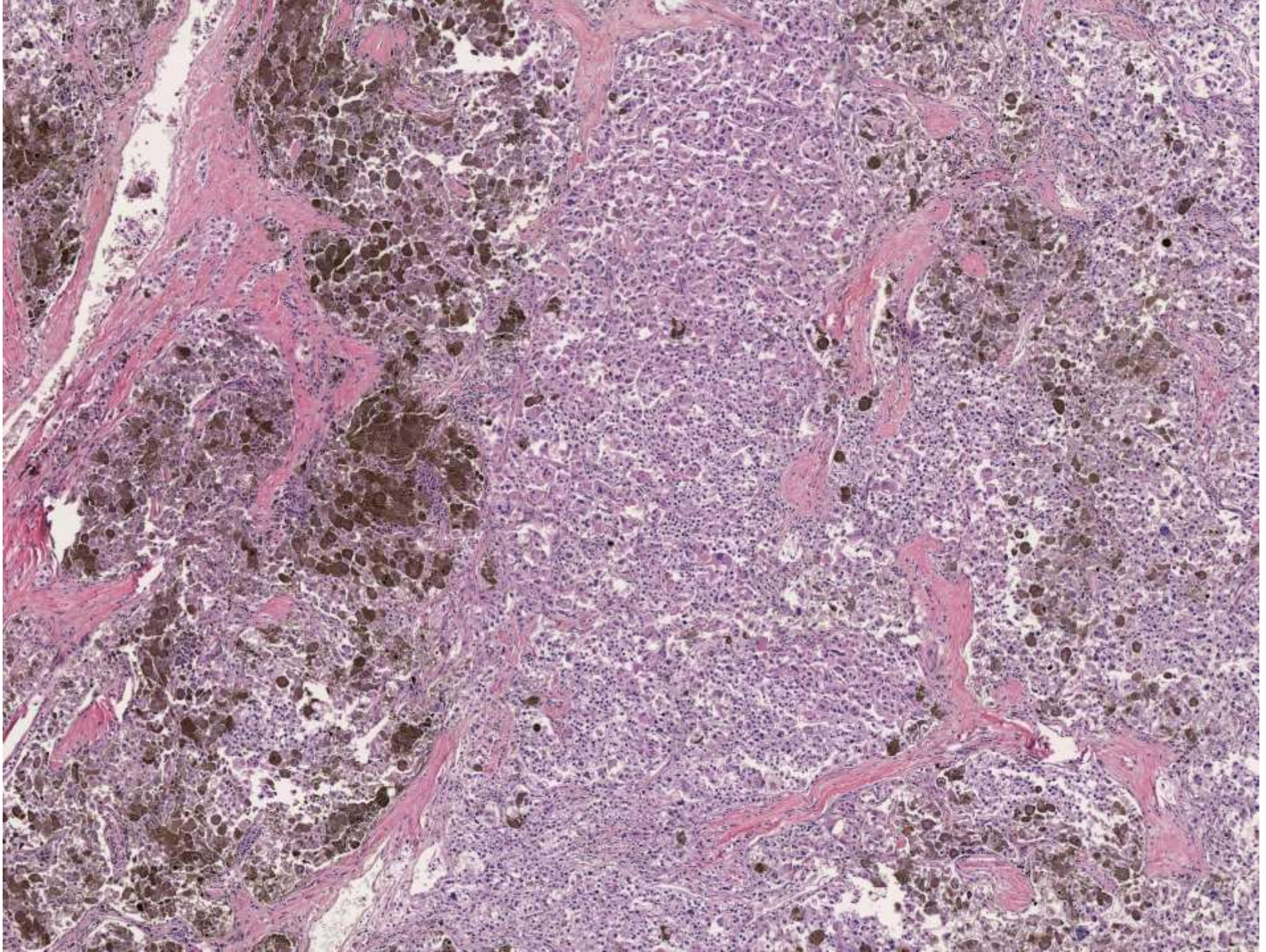
Mahendra Ranchod; Good Samaritan Hospital

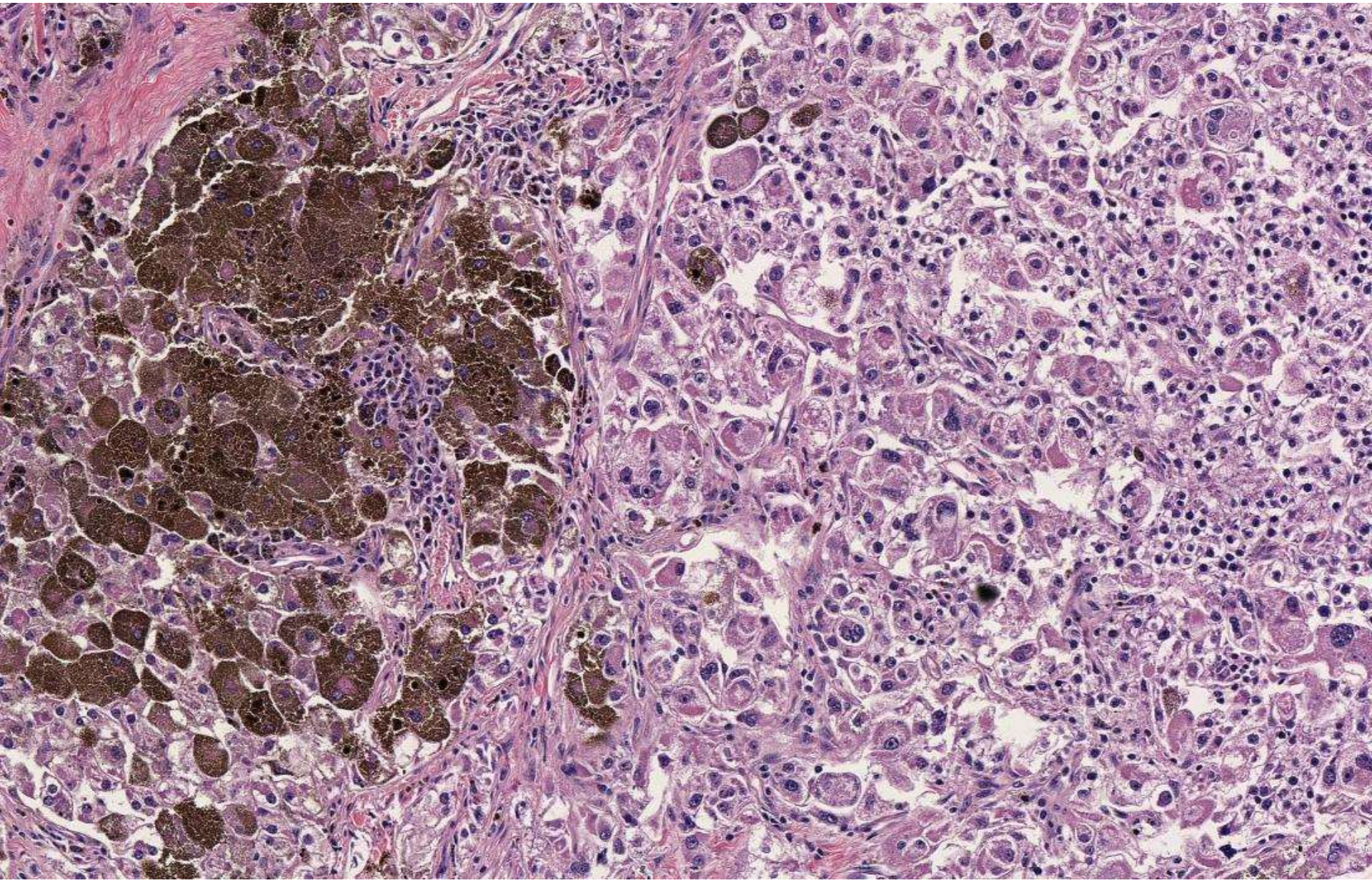
48-year-old female underwent TAH/BSO for 9cm ovarian mass.

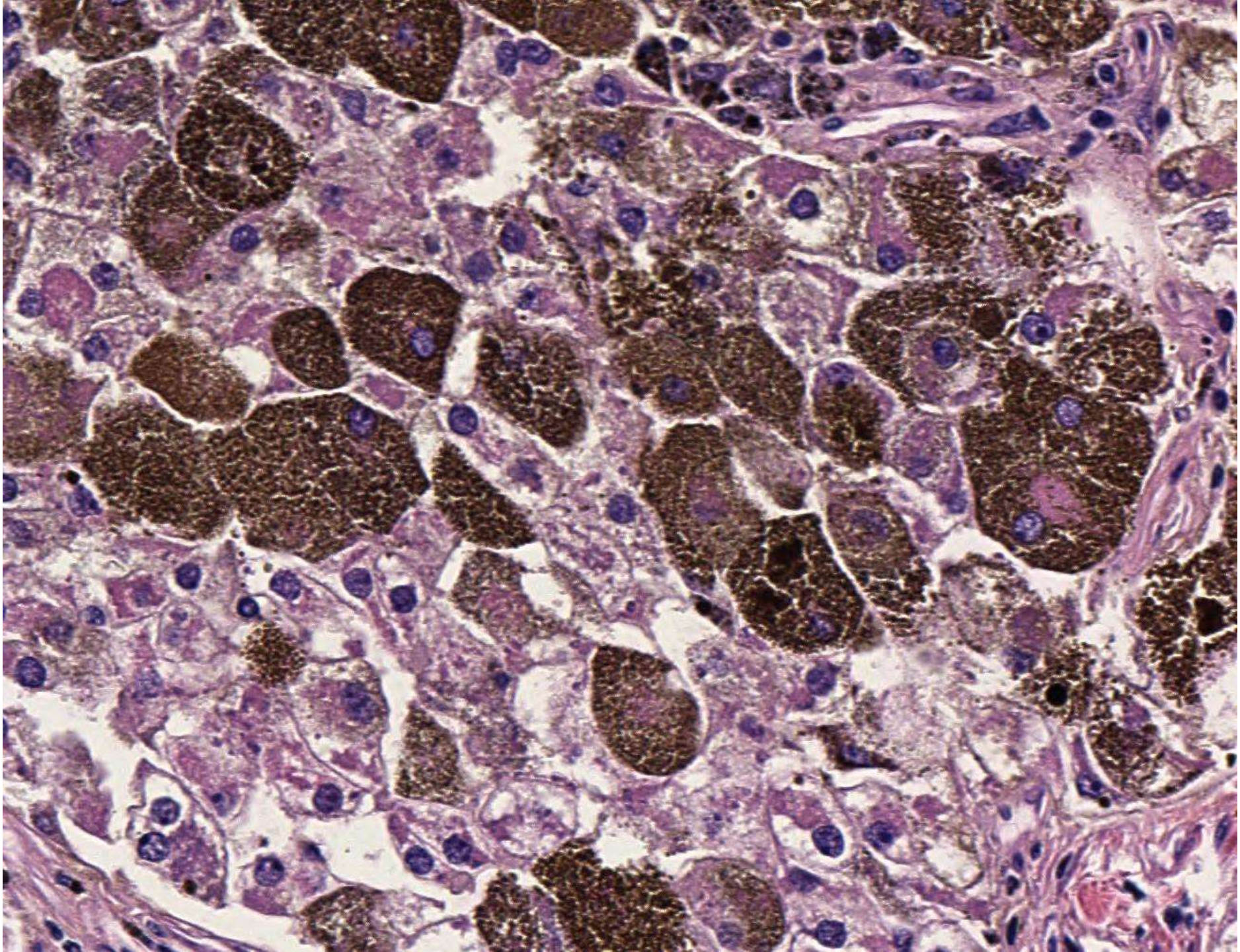


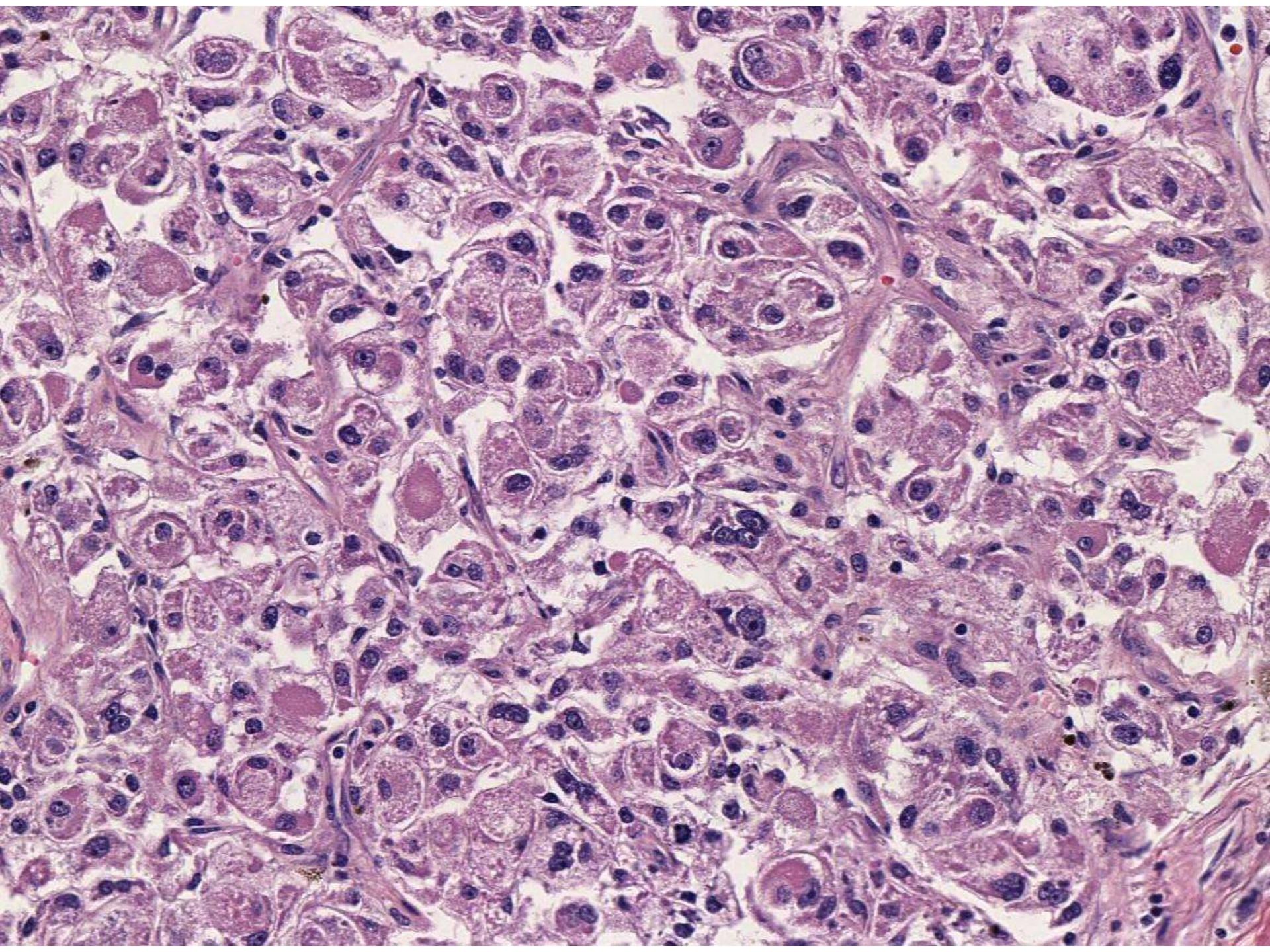


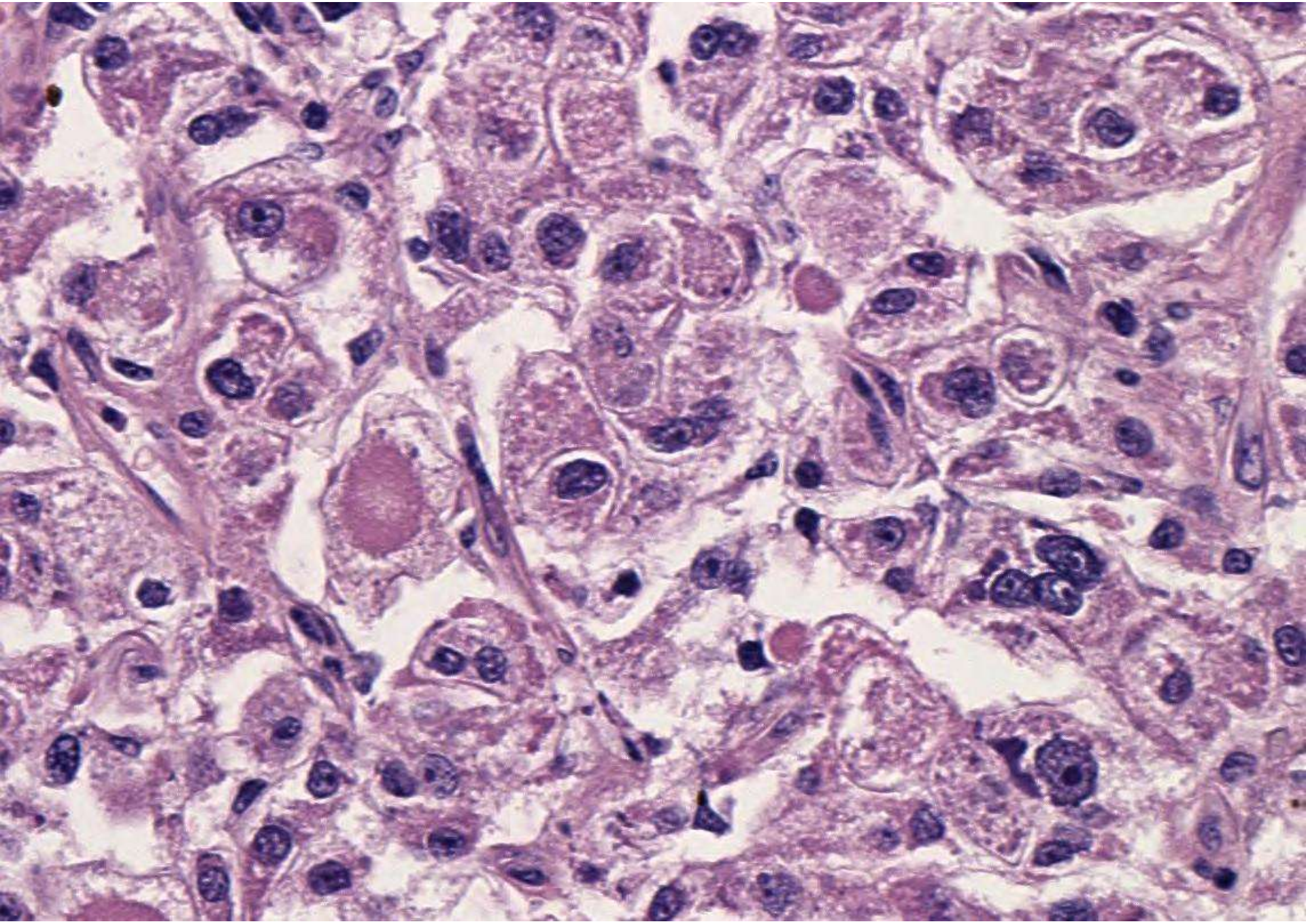




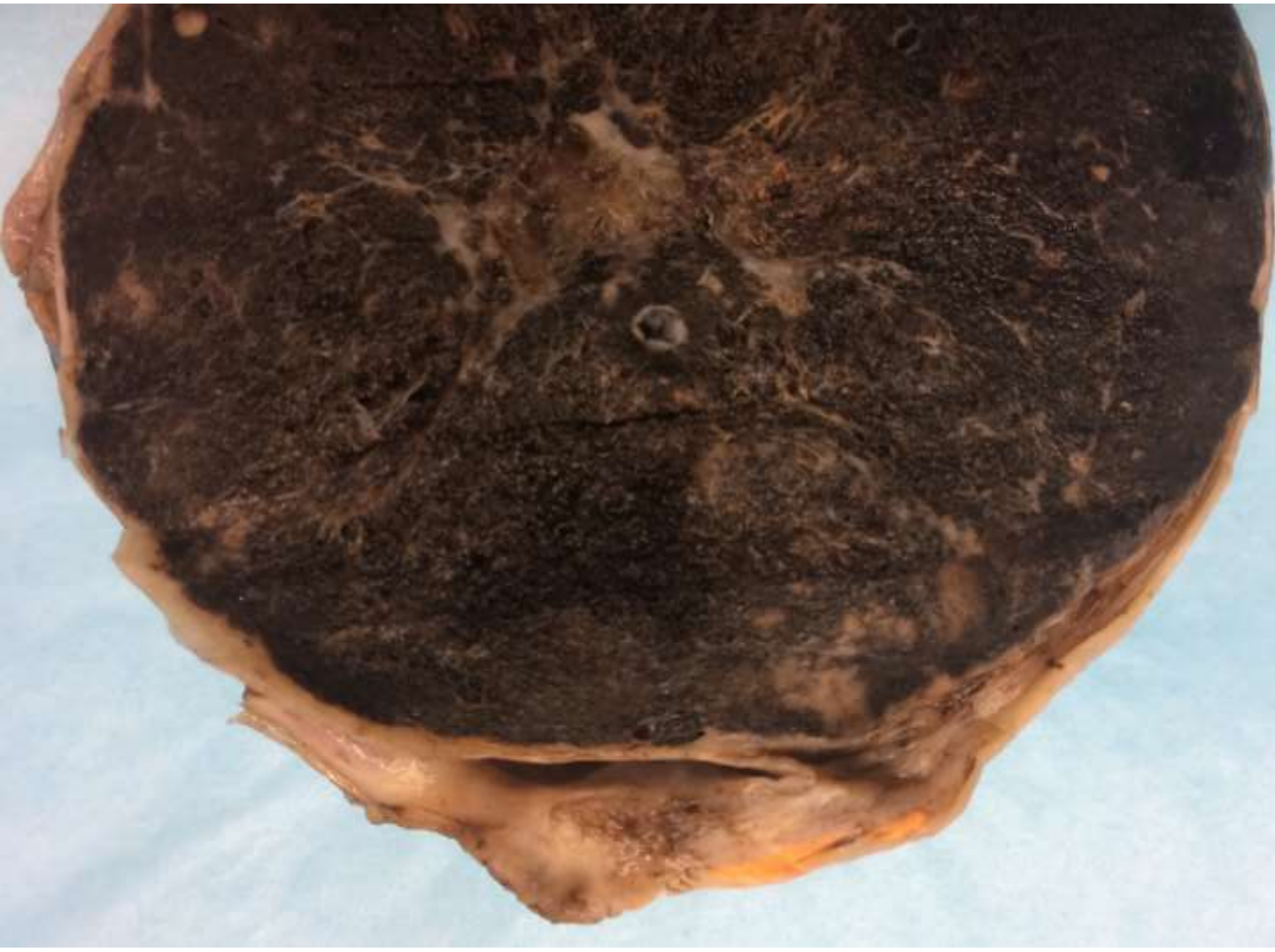








DIAGNOSIS?



SB 6301 ?Diagnosis

Metastatic Melanoma

- **No clinical support**
- **IHC**
  - **S100 - Negative**
  - **SOX 10 - Negative**
  - **Melan A - Patchy positive**

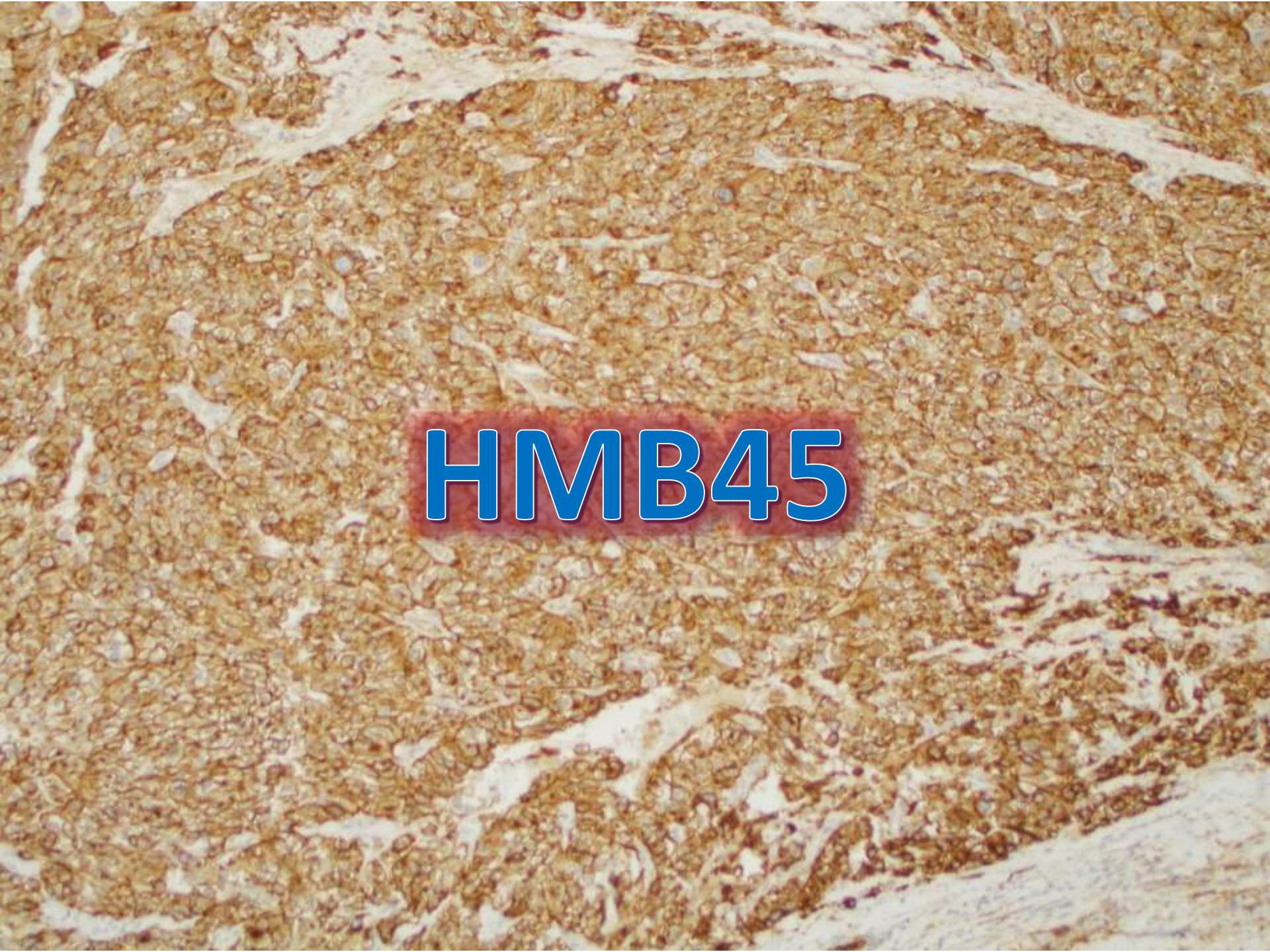
SB 6301

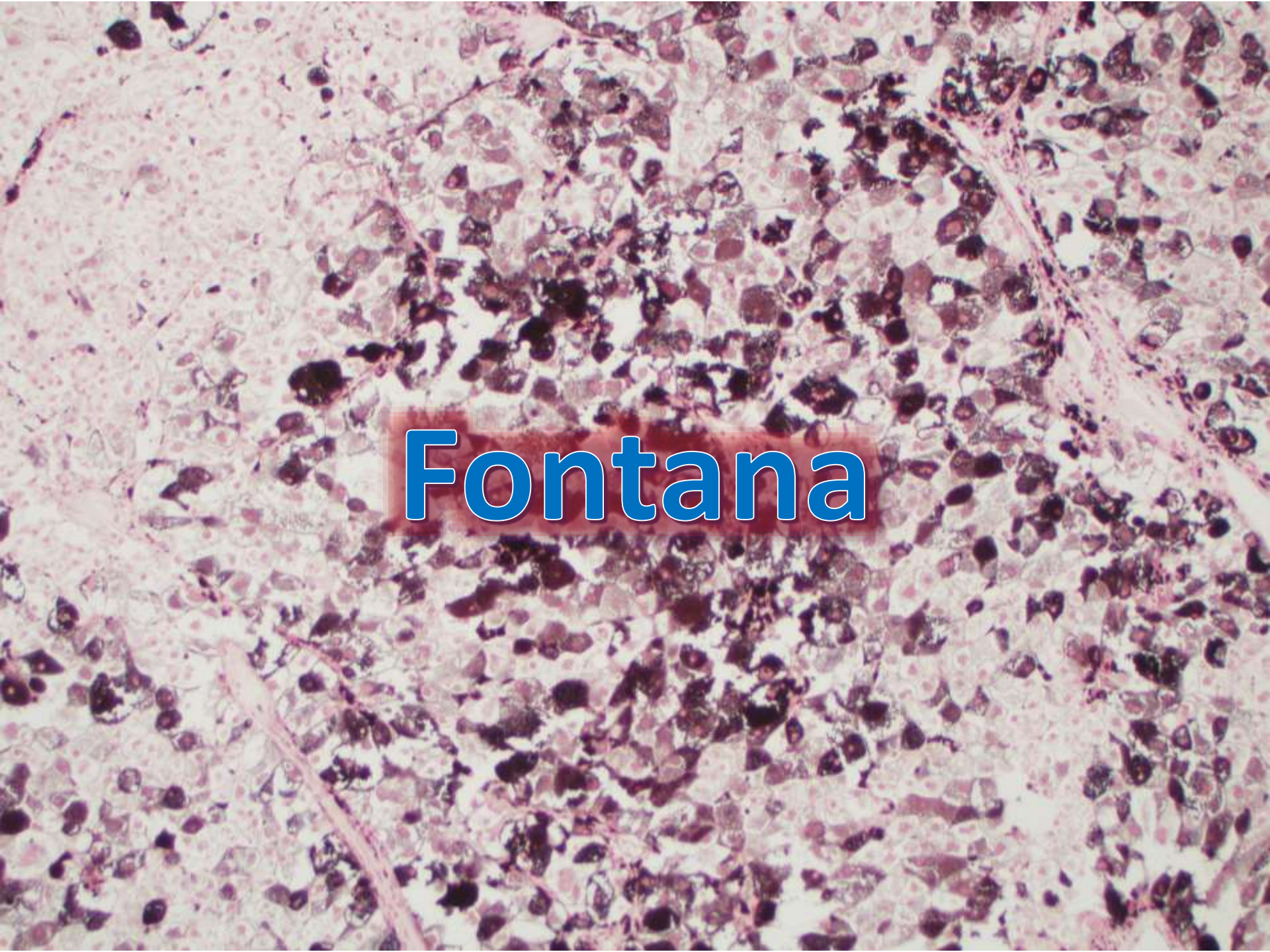
Additional IHC

HMB 45 - Positive
SMA - Negative
Desmin - Negative

PAX8 - Negative
Inhibin - Negative

What is this??


HMB45


Fontana

TFE3 Translocation-associated PEComa

- Schoolmeester et. al Am J Surg Pathol 2015
- 6 cases (Mayo & S-K)
  - TFE3 translocation 6/6
  - HMB 45 6/6
  - Melan A 3/6
  - SOX10 0
  - S100 not done
  - SMA 1/6
  - Desmin 1/6
  - Caldesmon 1/6
  - Cathepsin 6/6

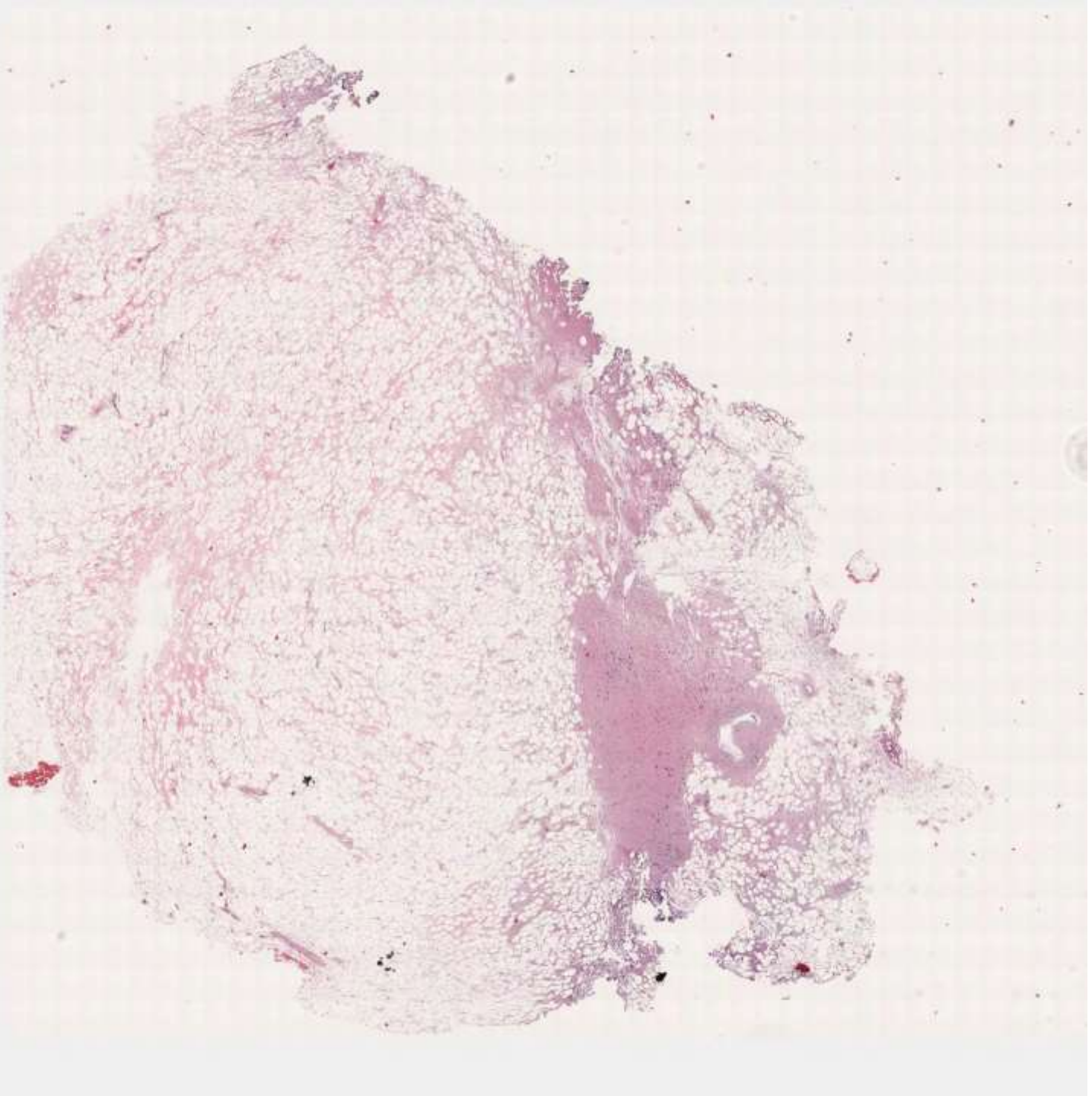
Criteria for Malignancy

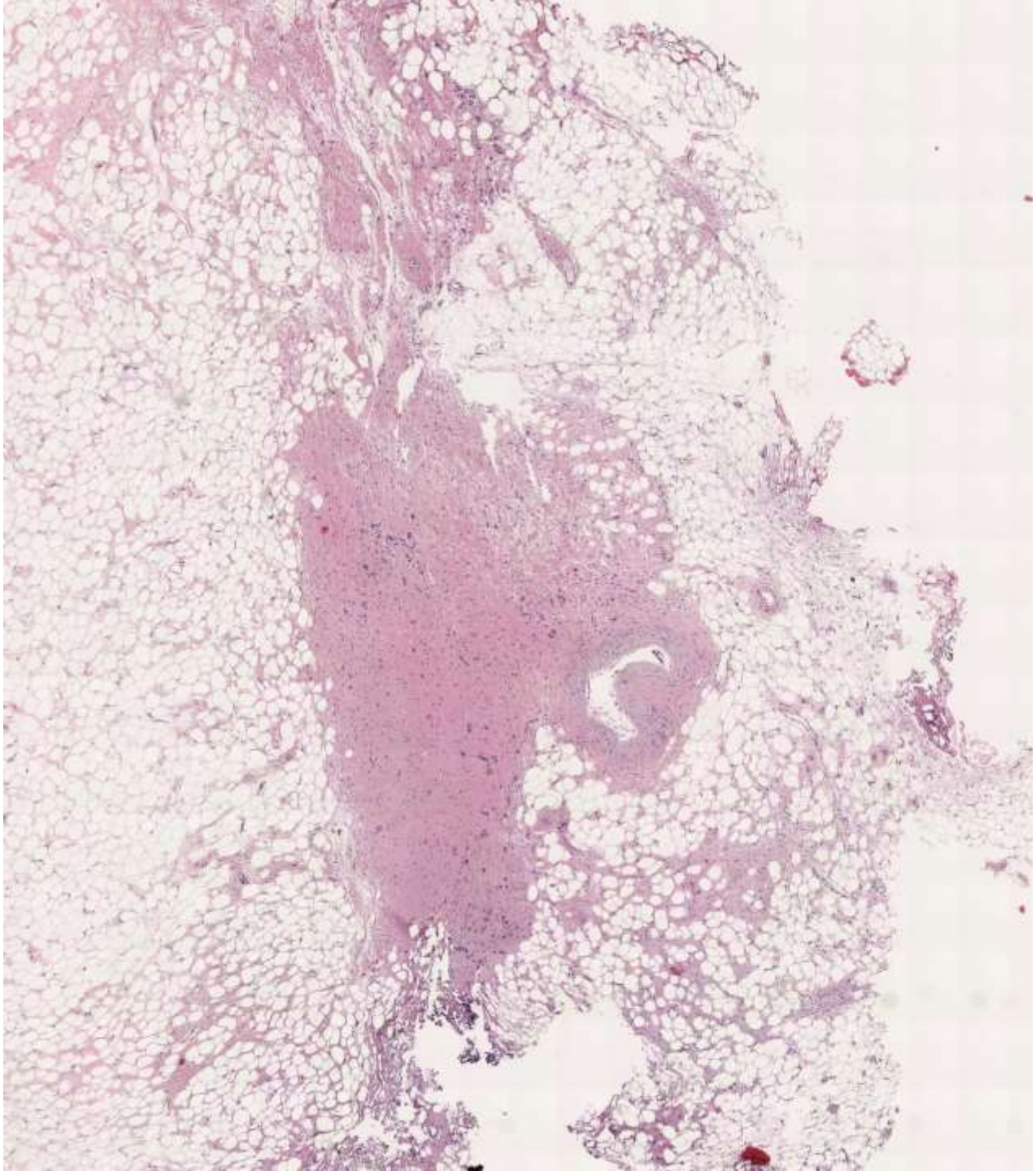
- **Size: >5cm**
- **Infiltrative growth**
- **High grade nuclear features**
- **Necrosis**
- **Vascular invasion**
- **Mitoses >1/50HPF**

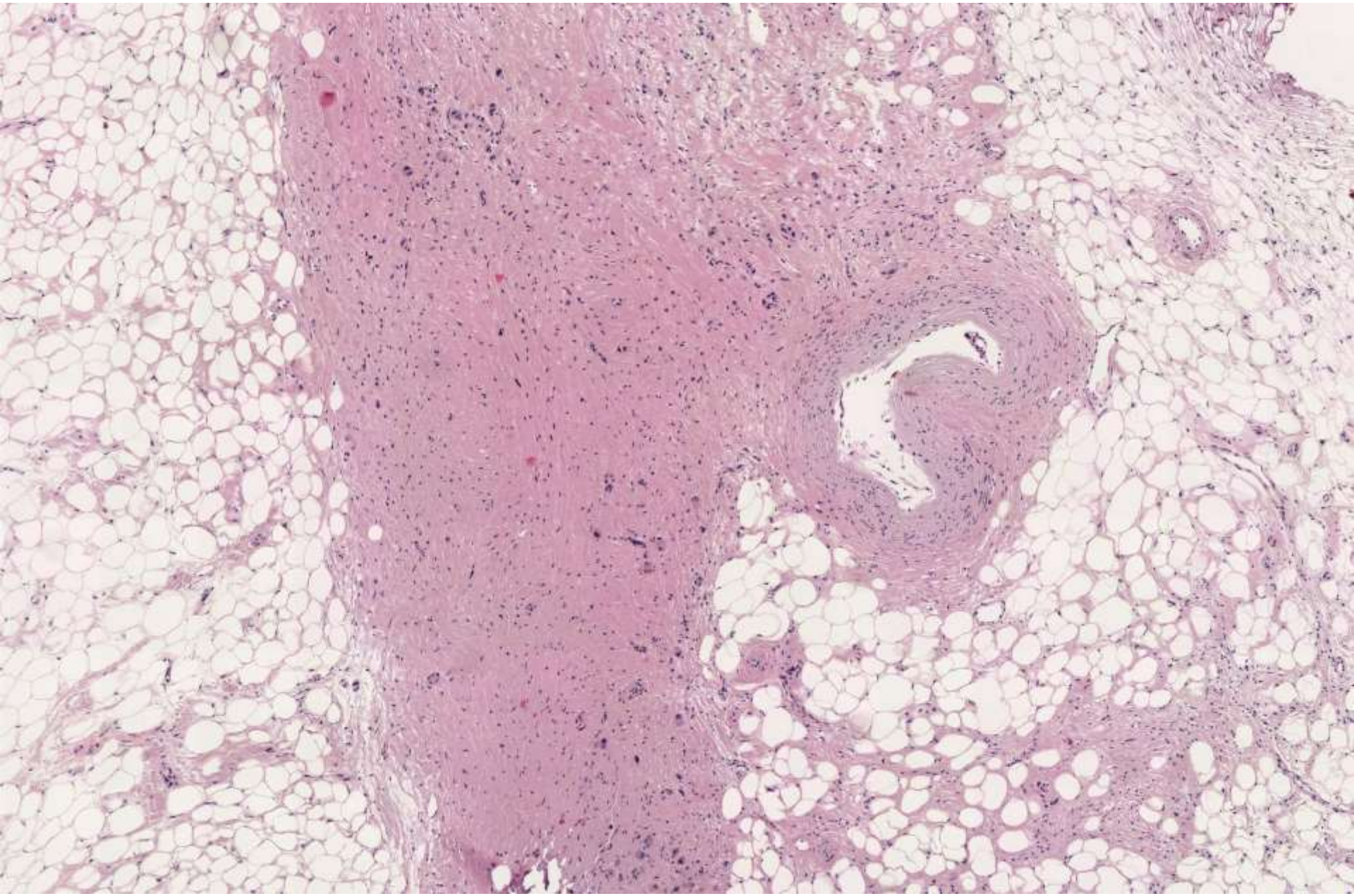
SB 6302
(scanned slide available)

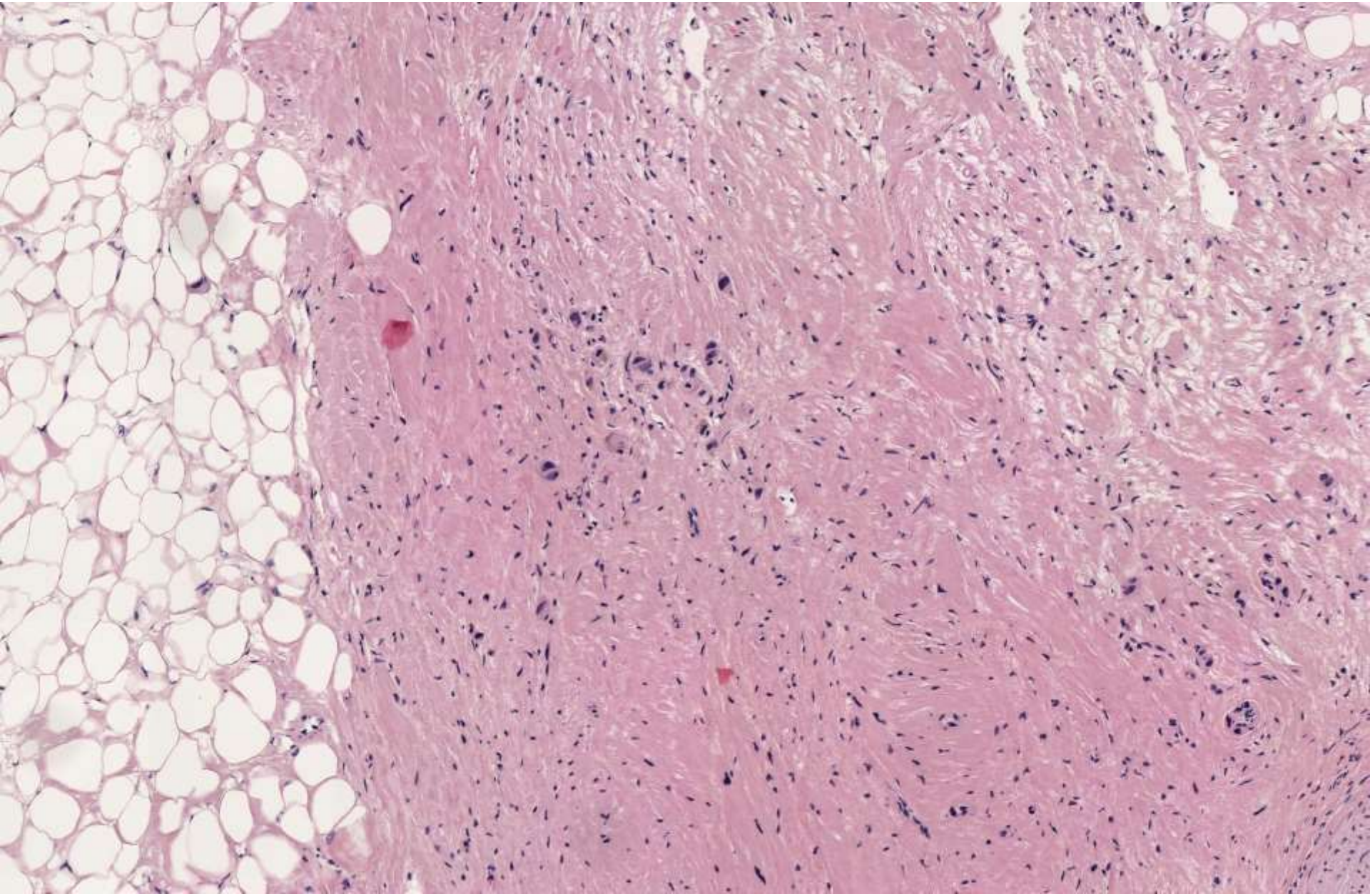
Justin Cuff; Mills-Peninsula

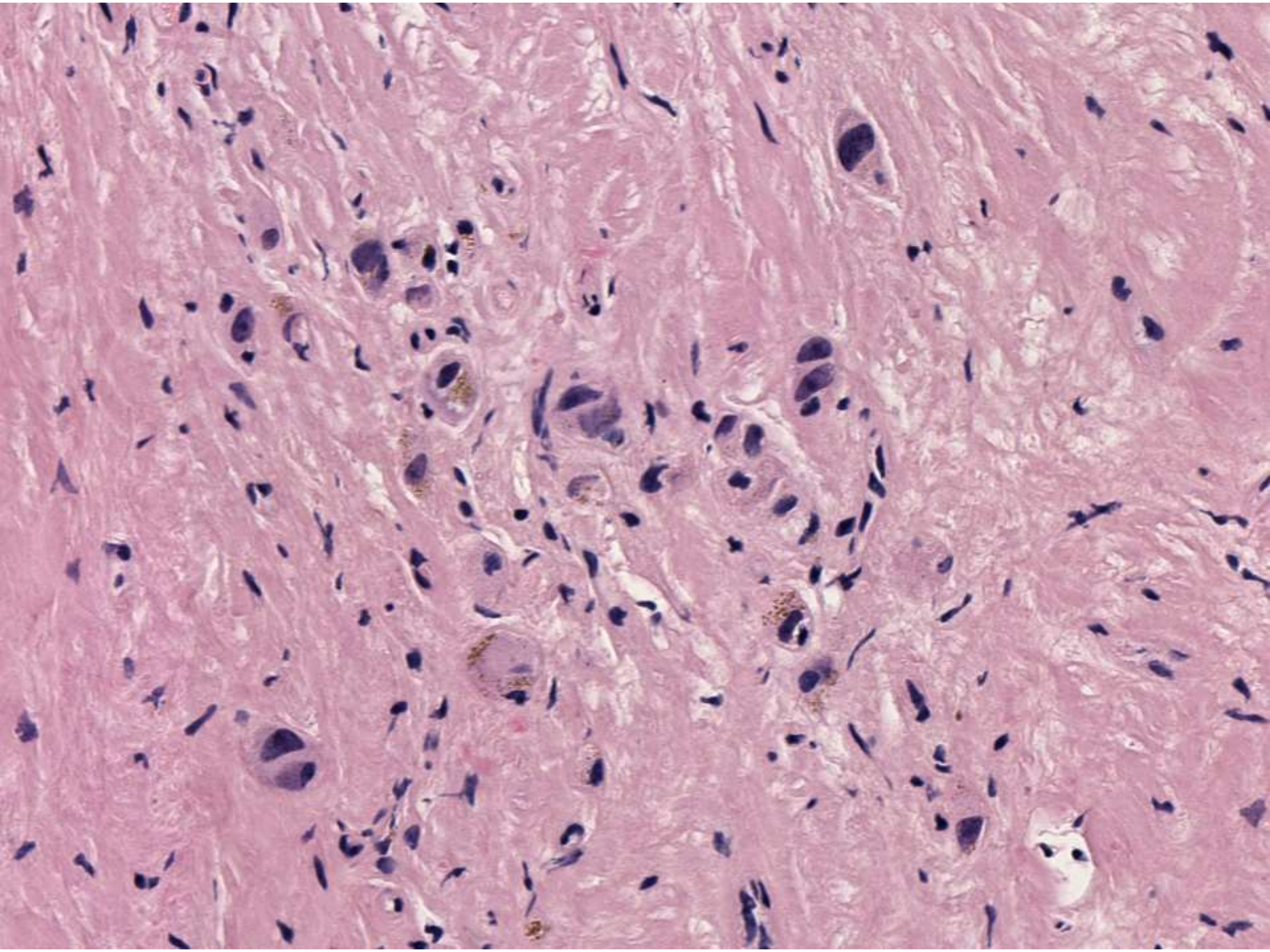
63-year-old female with left pleural mass.

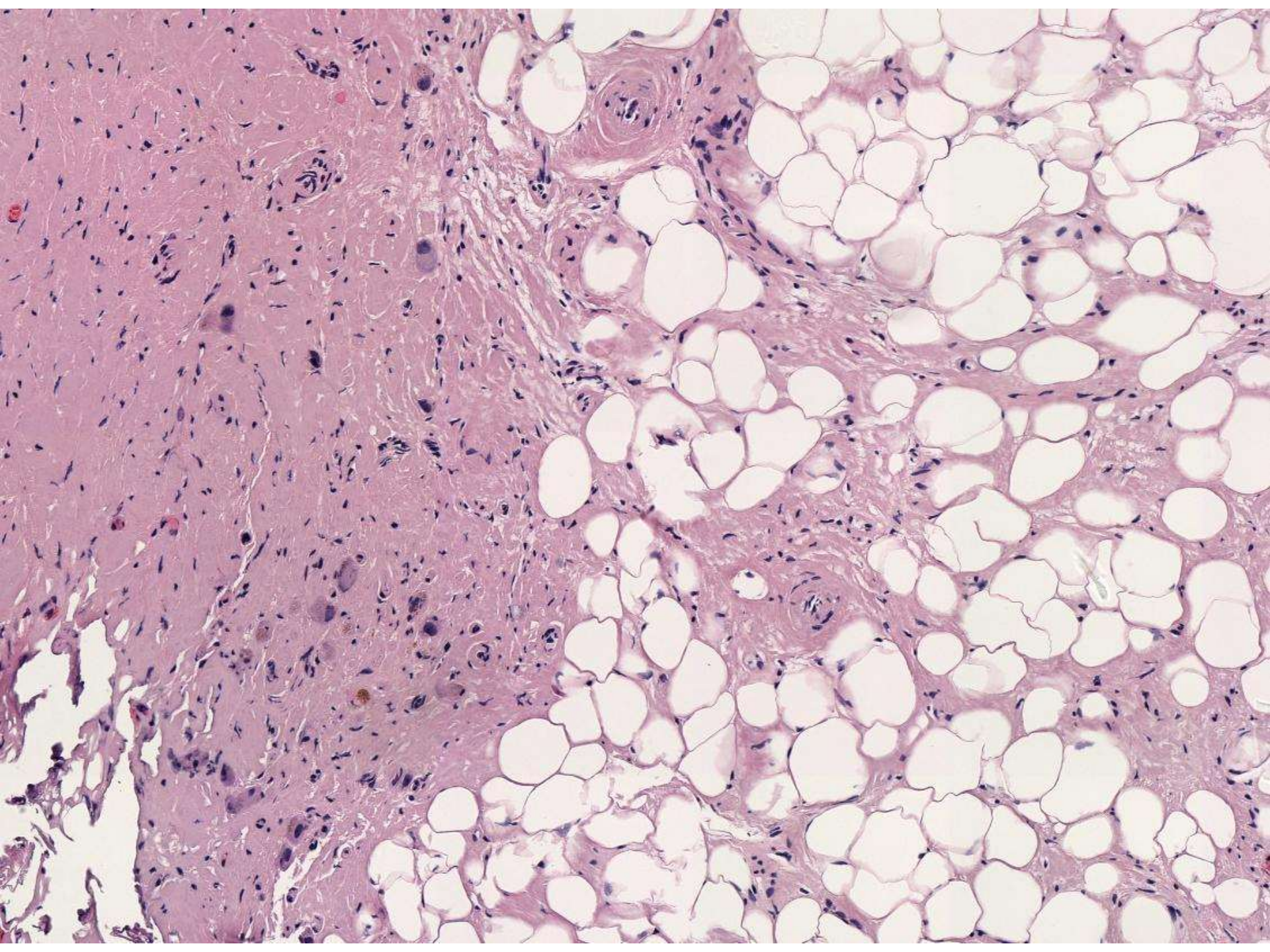


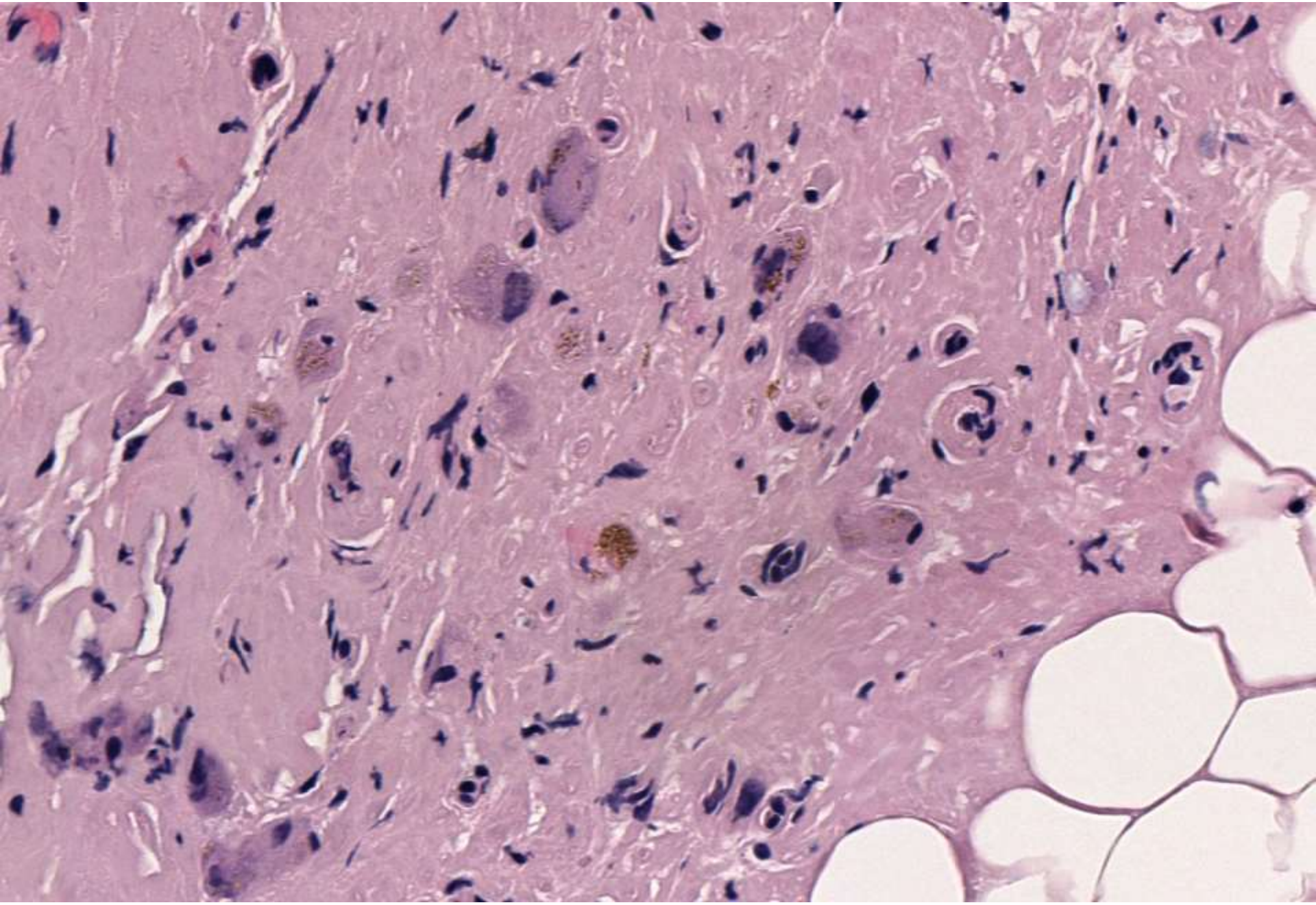


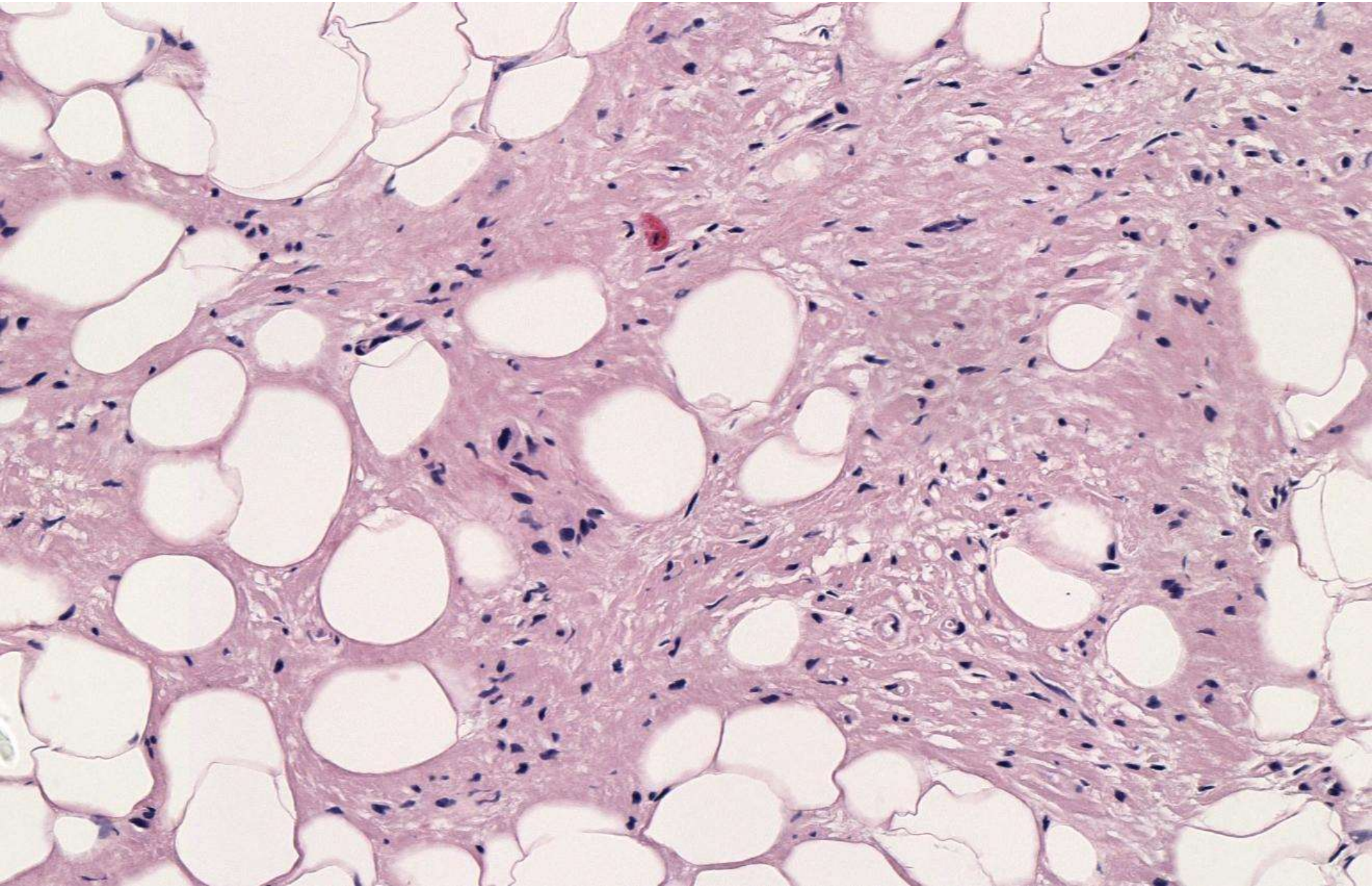










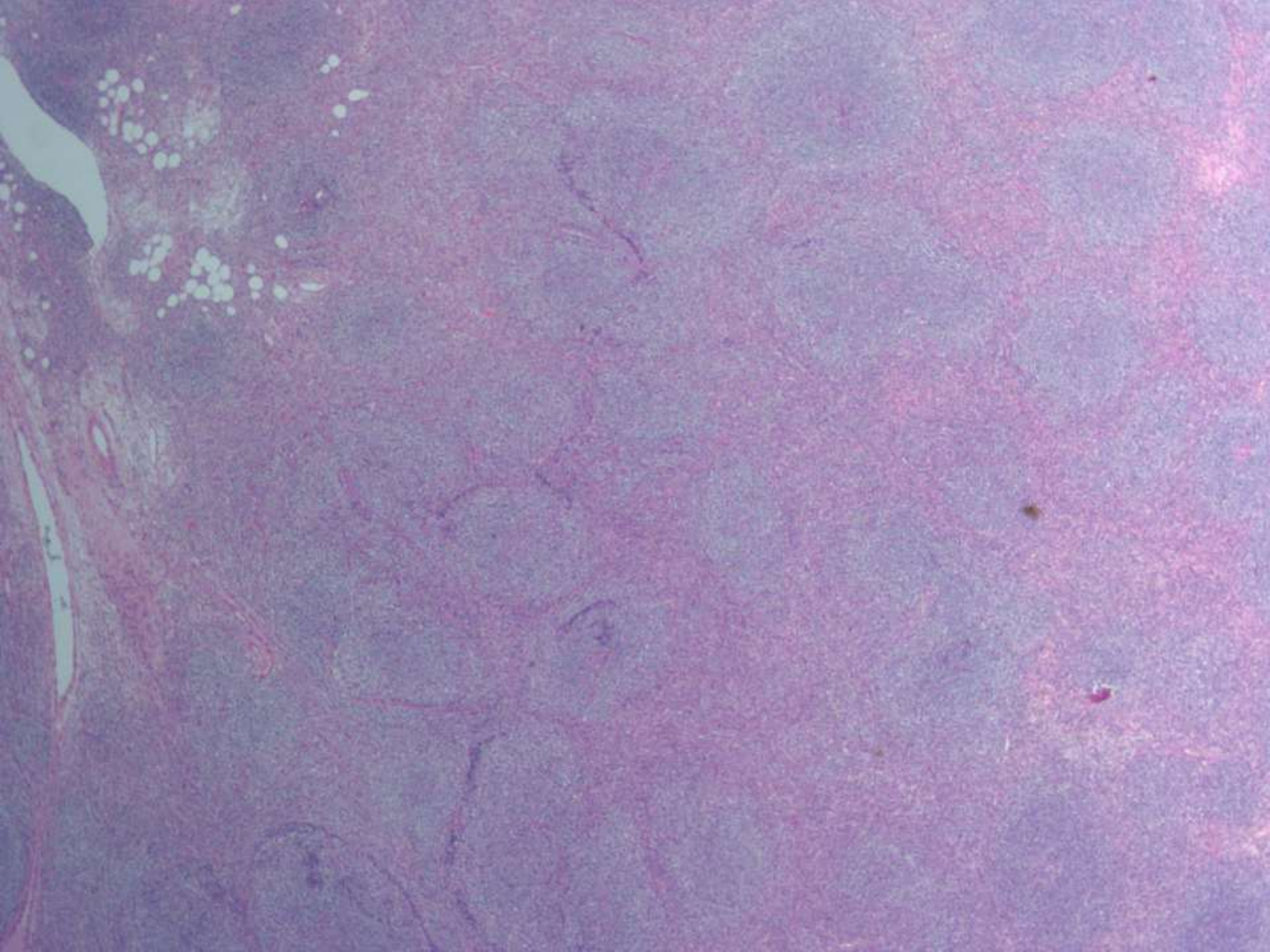


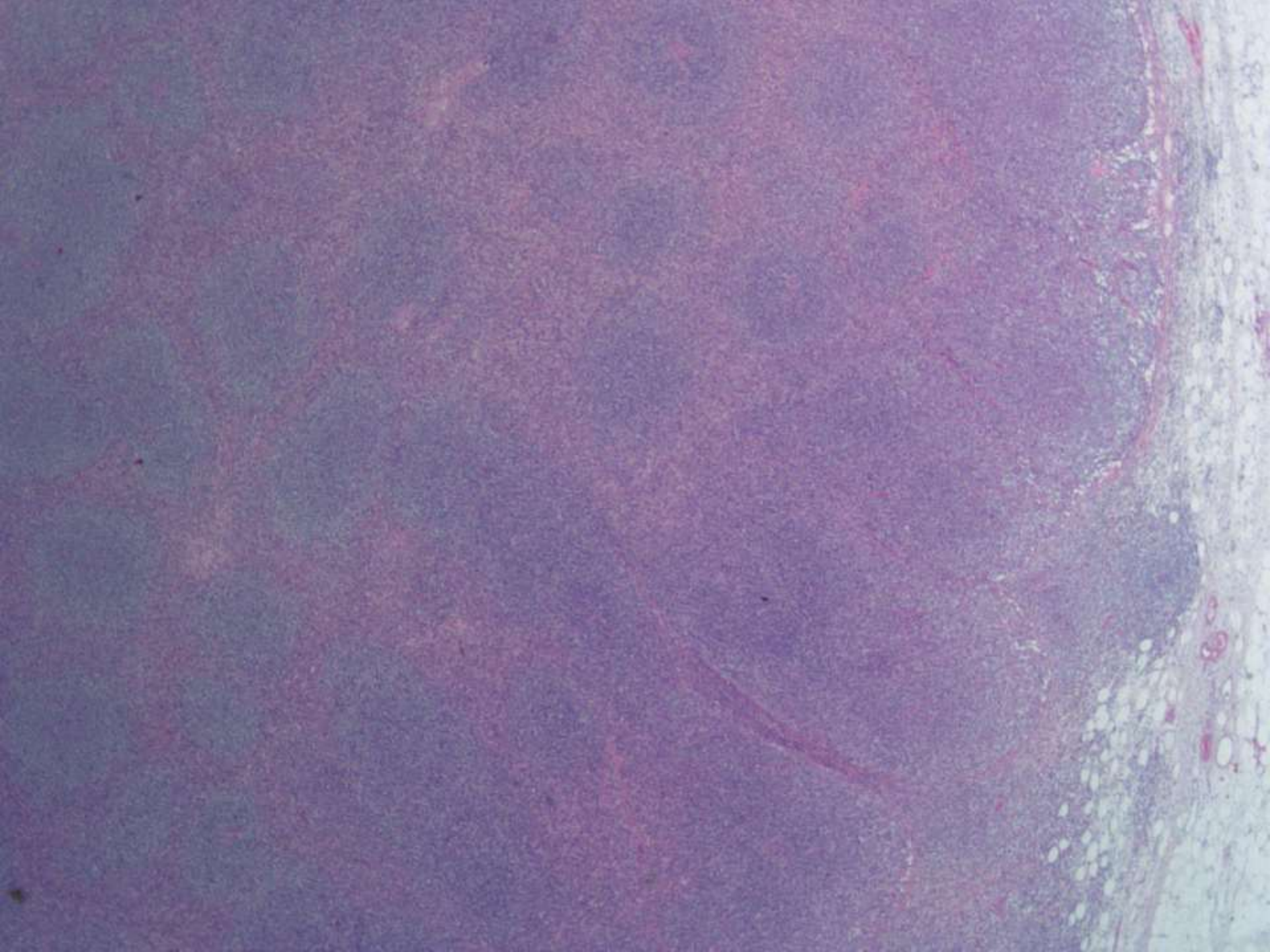
DIAGNOSIS?

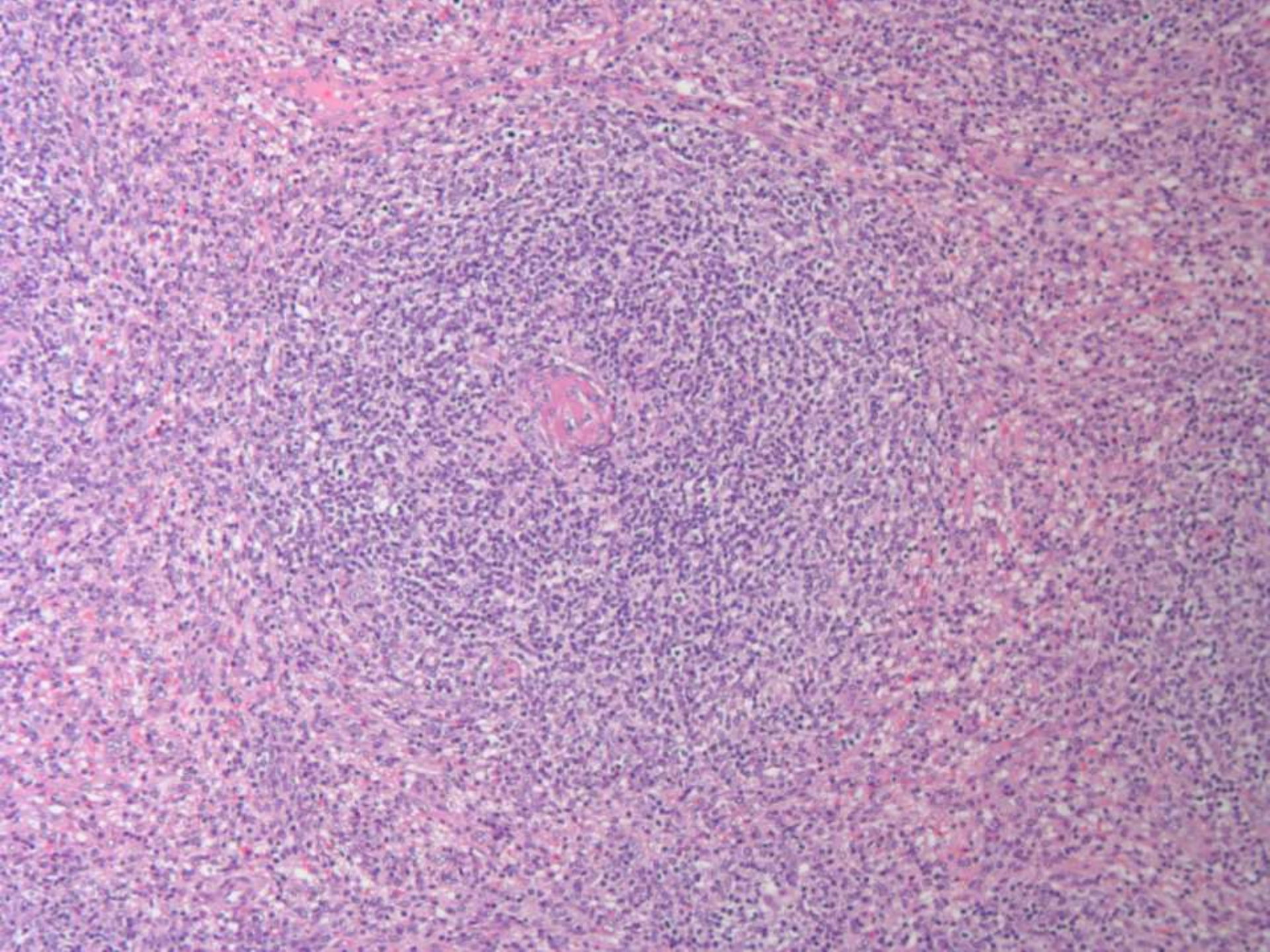
SB 6303

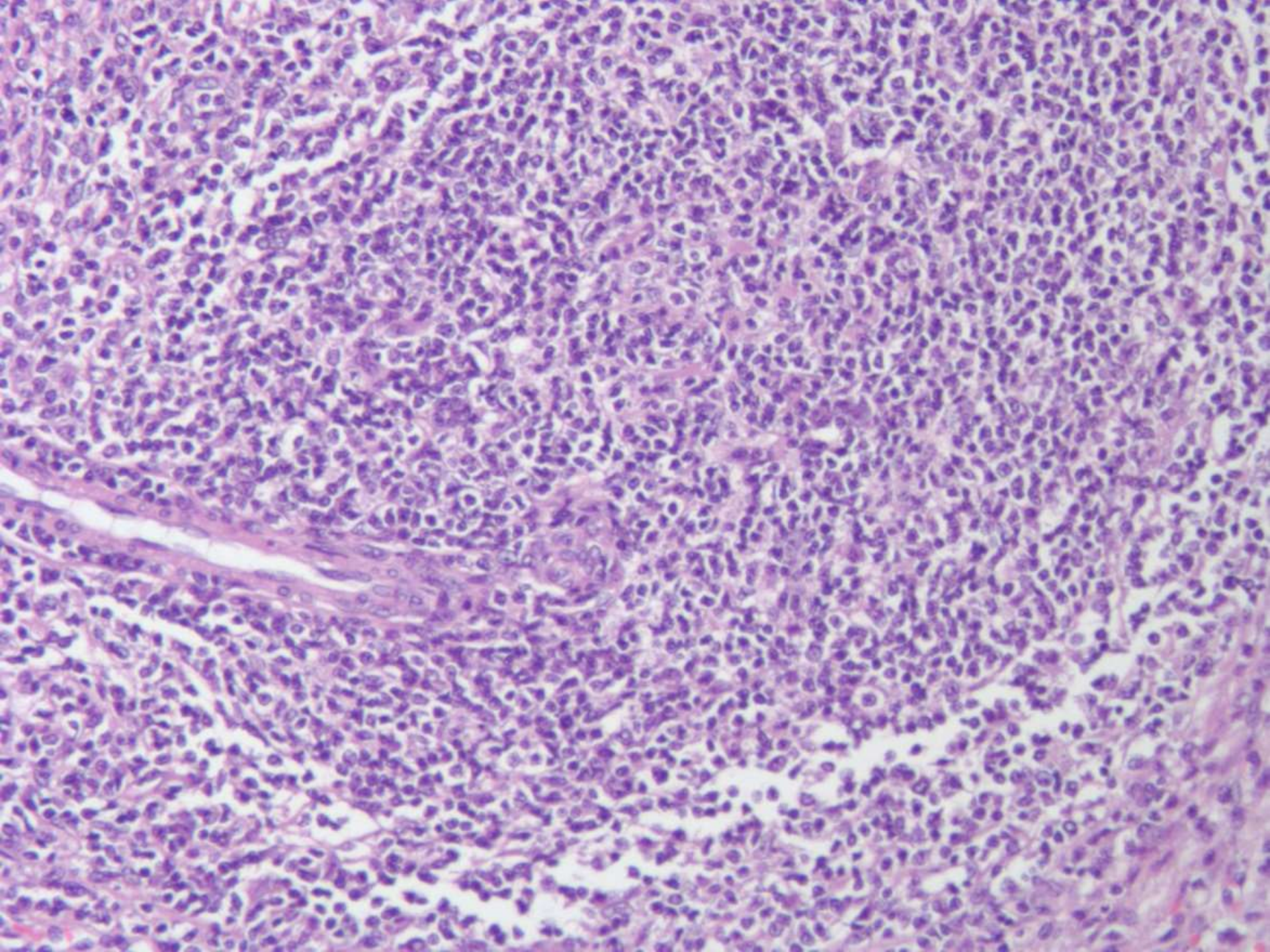
Charles Lombard; El Camino Hospital

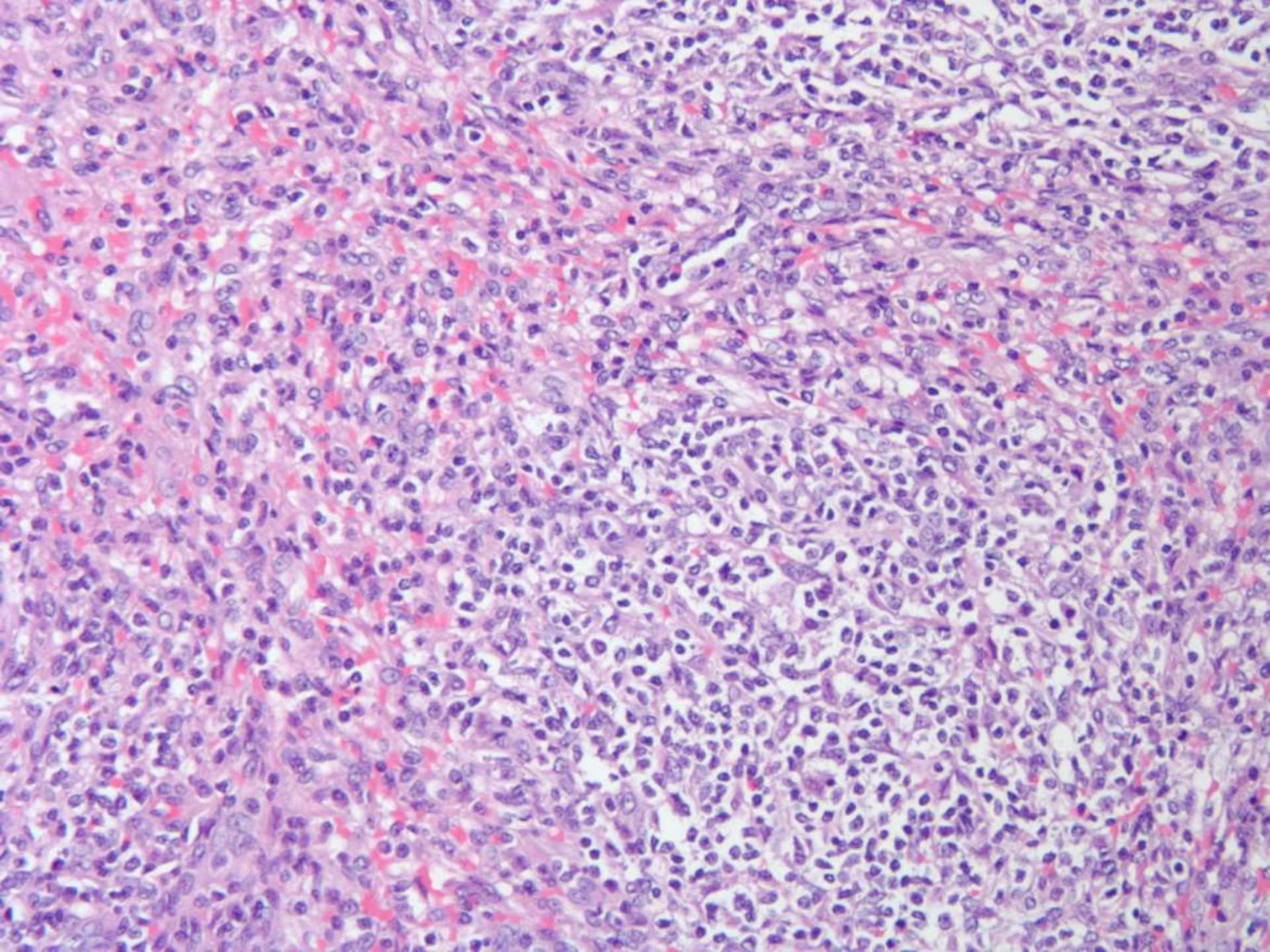
64-year-old female with diffuse lymphadenopathy without hepatosplenomegaly. Prior needle biopsy negative for T-cell receptors, beta/gamma rearrangements negative, B-cells gene rearrangement study negative.

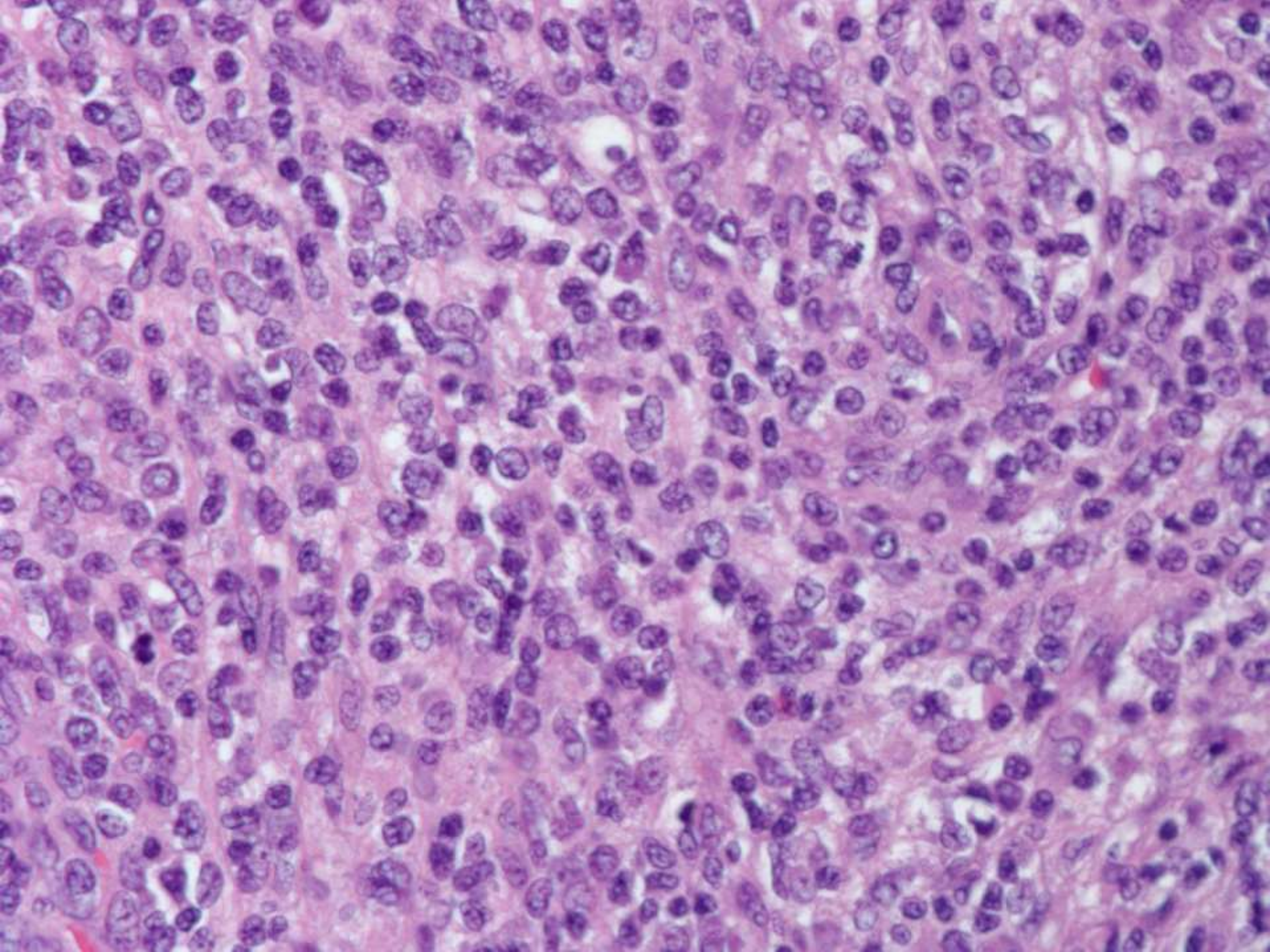


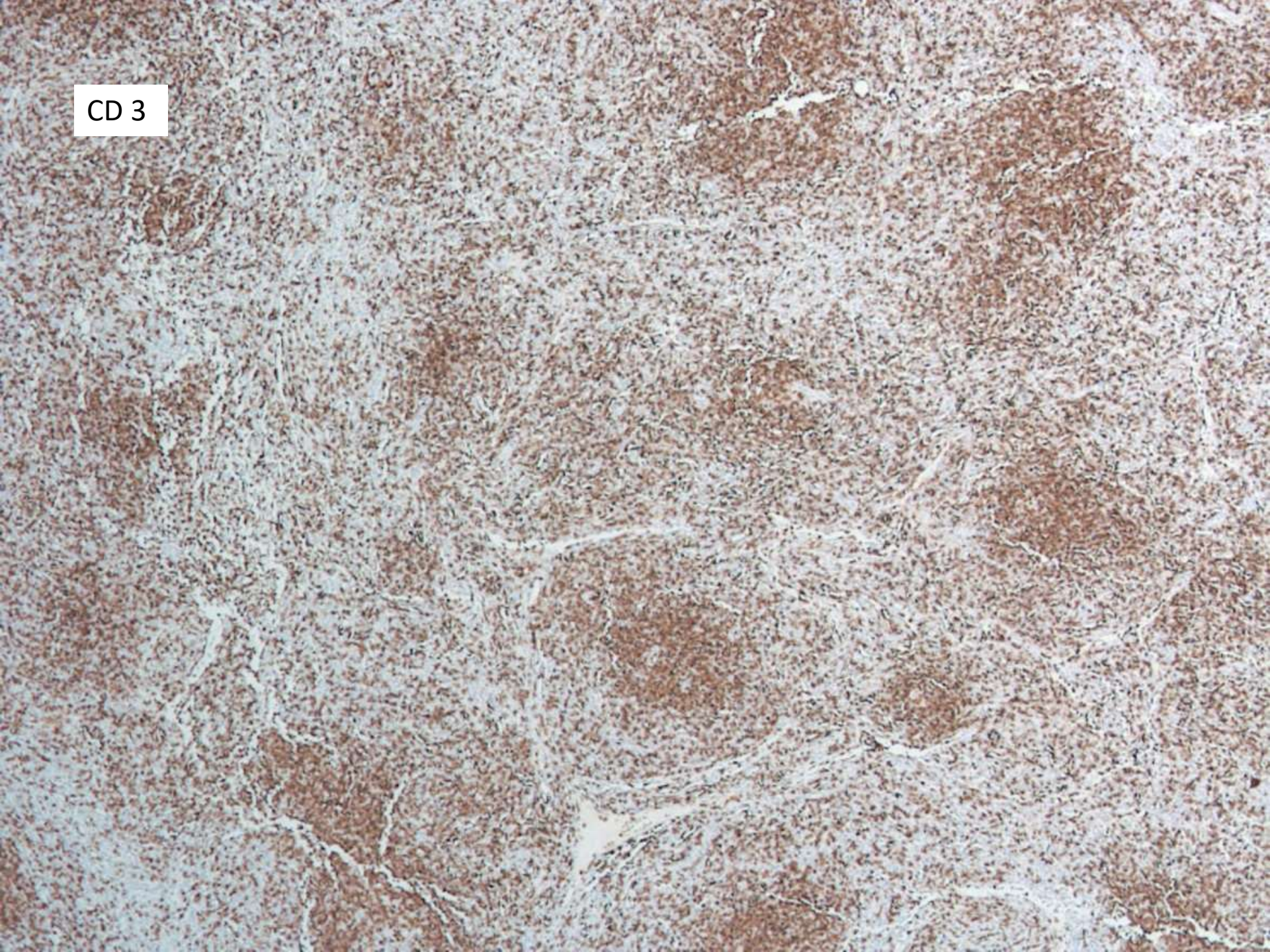








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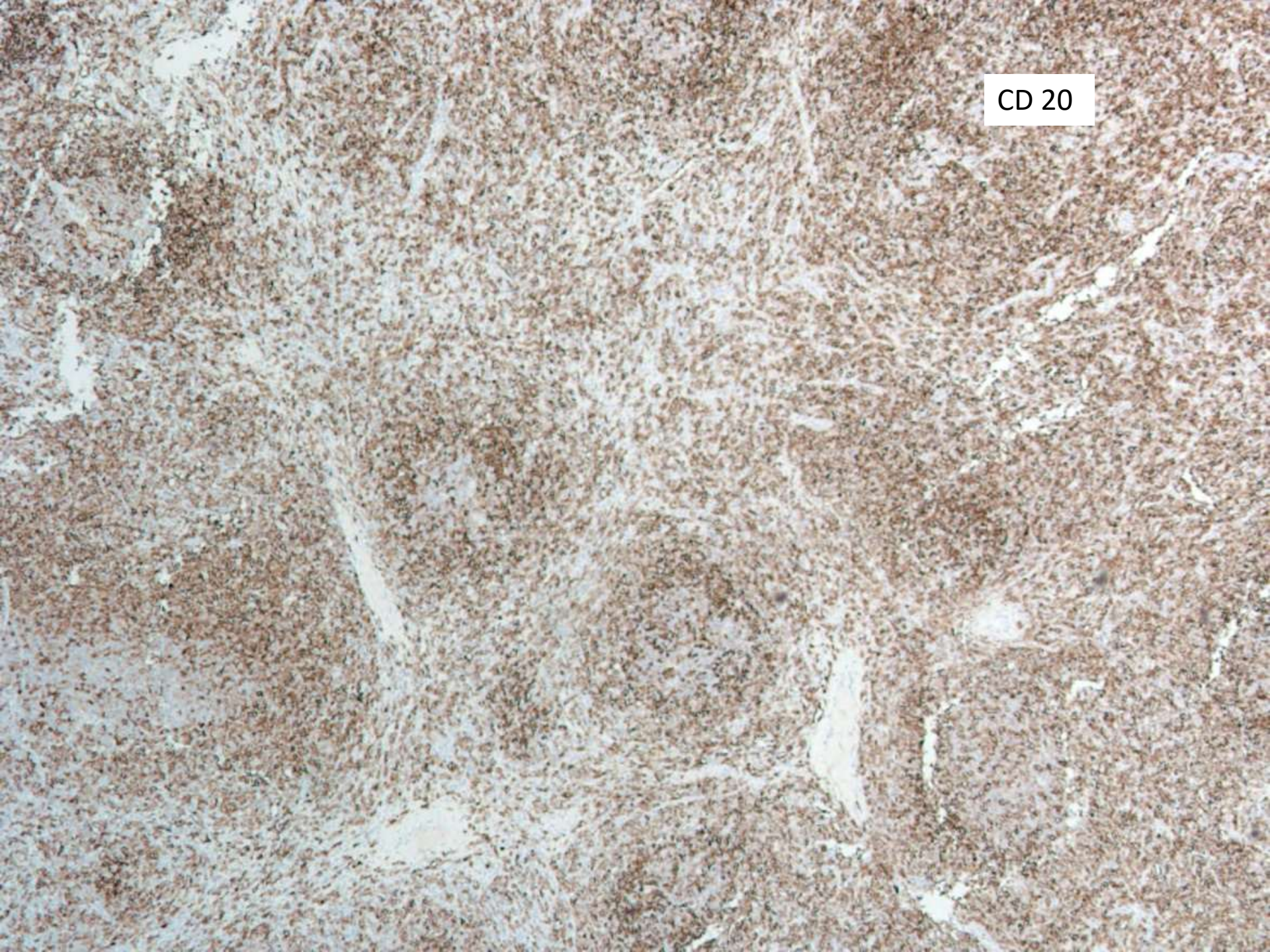
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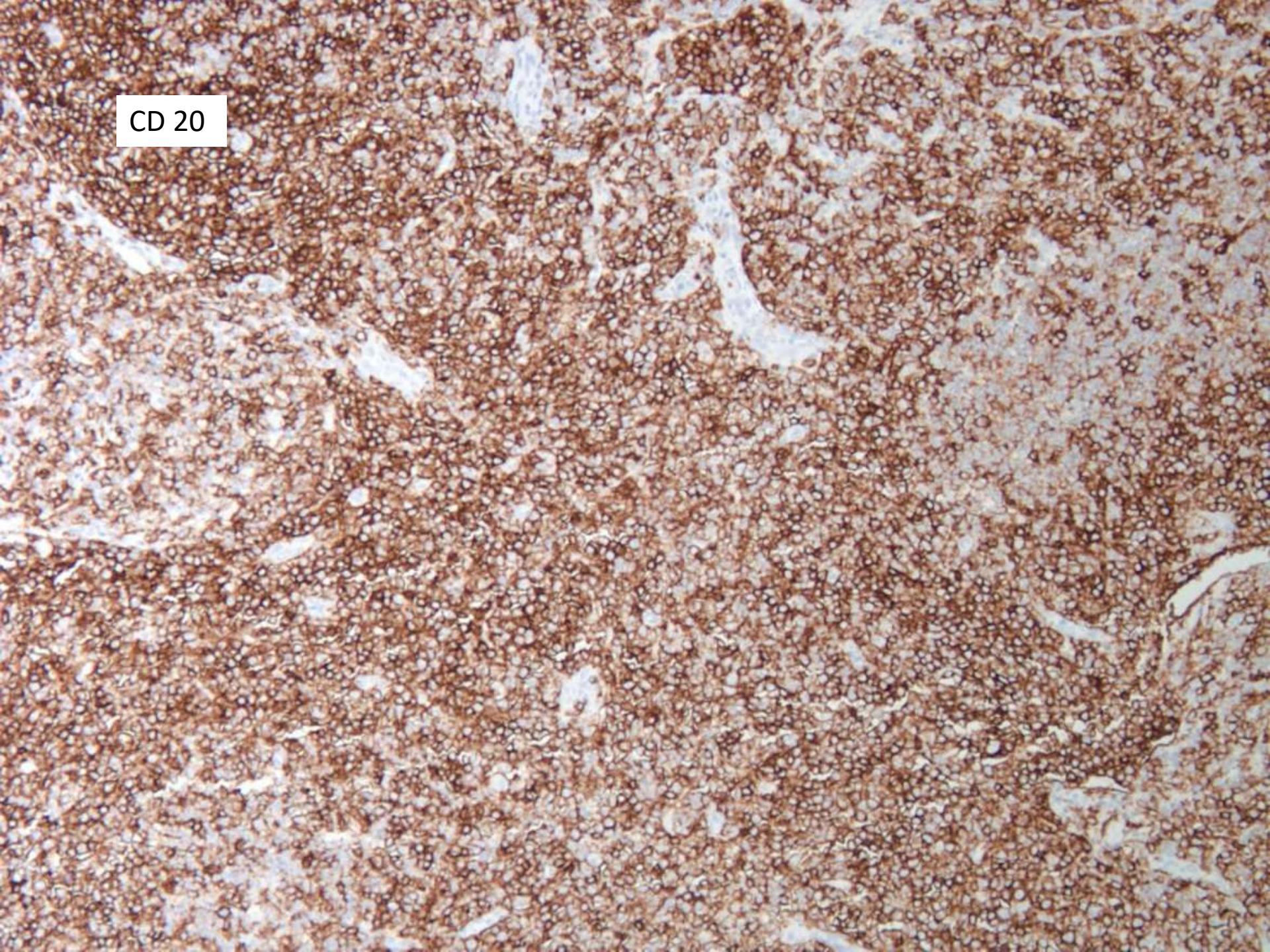
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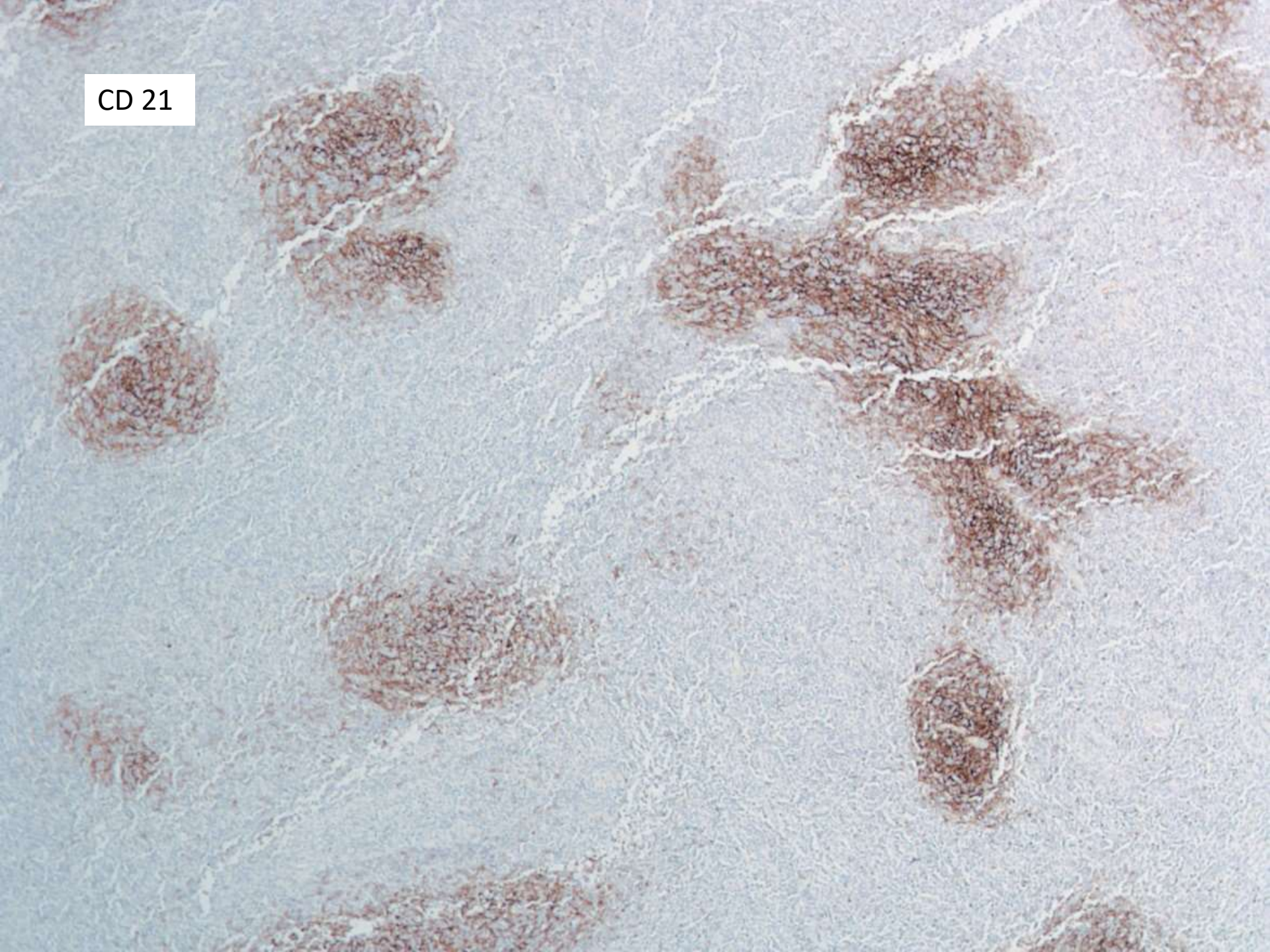
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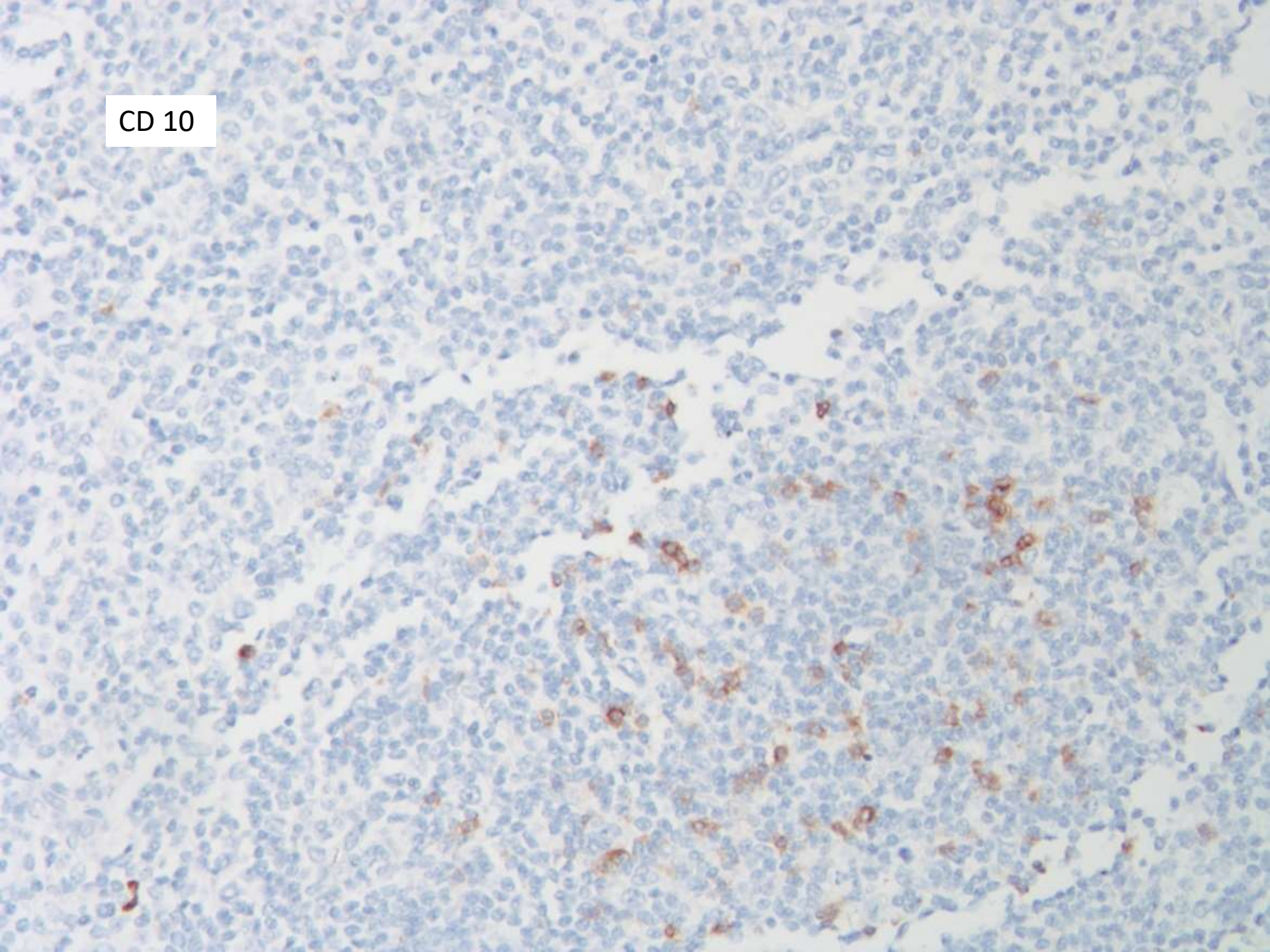
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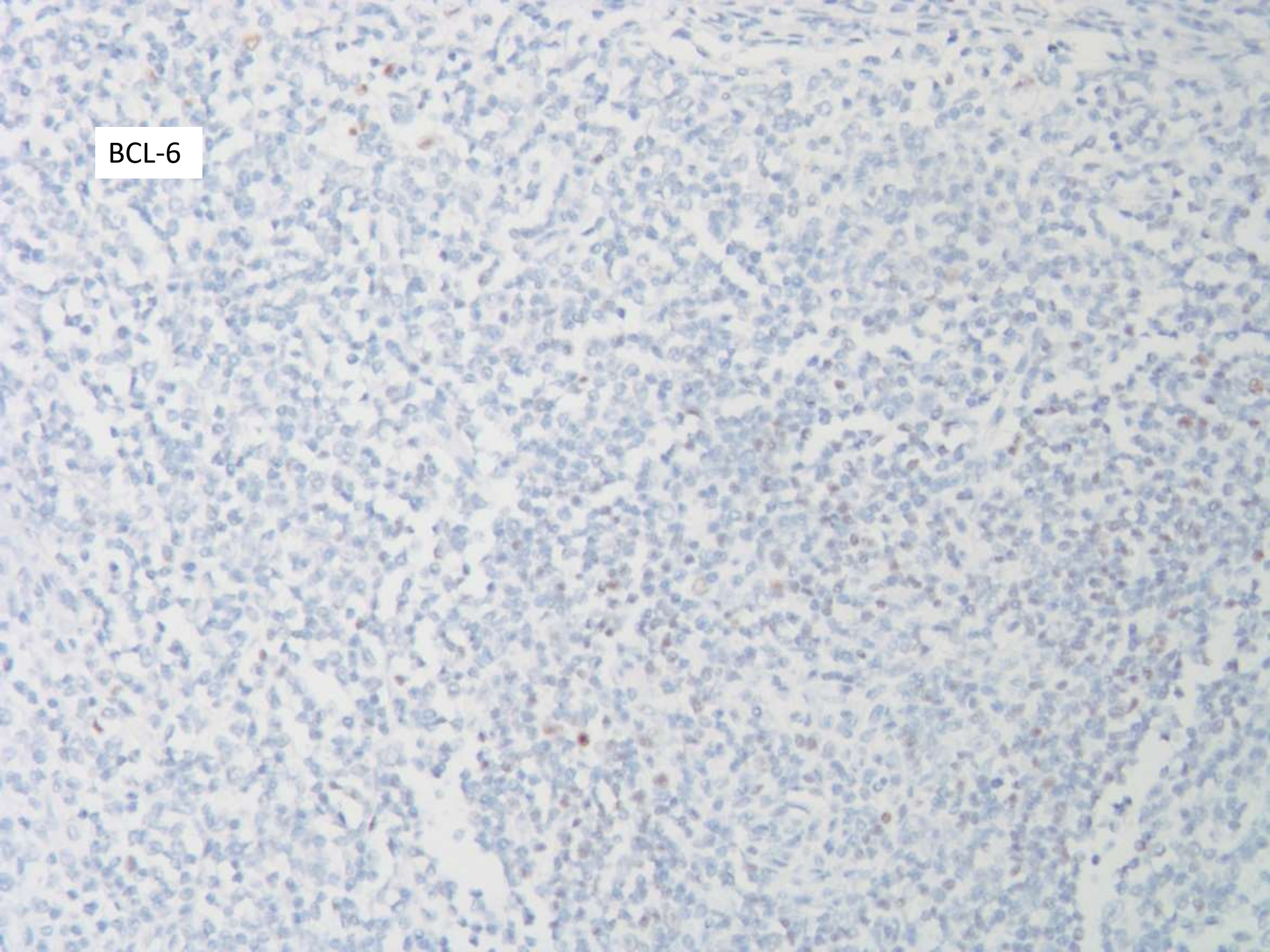
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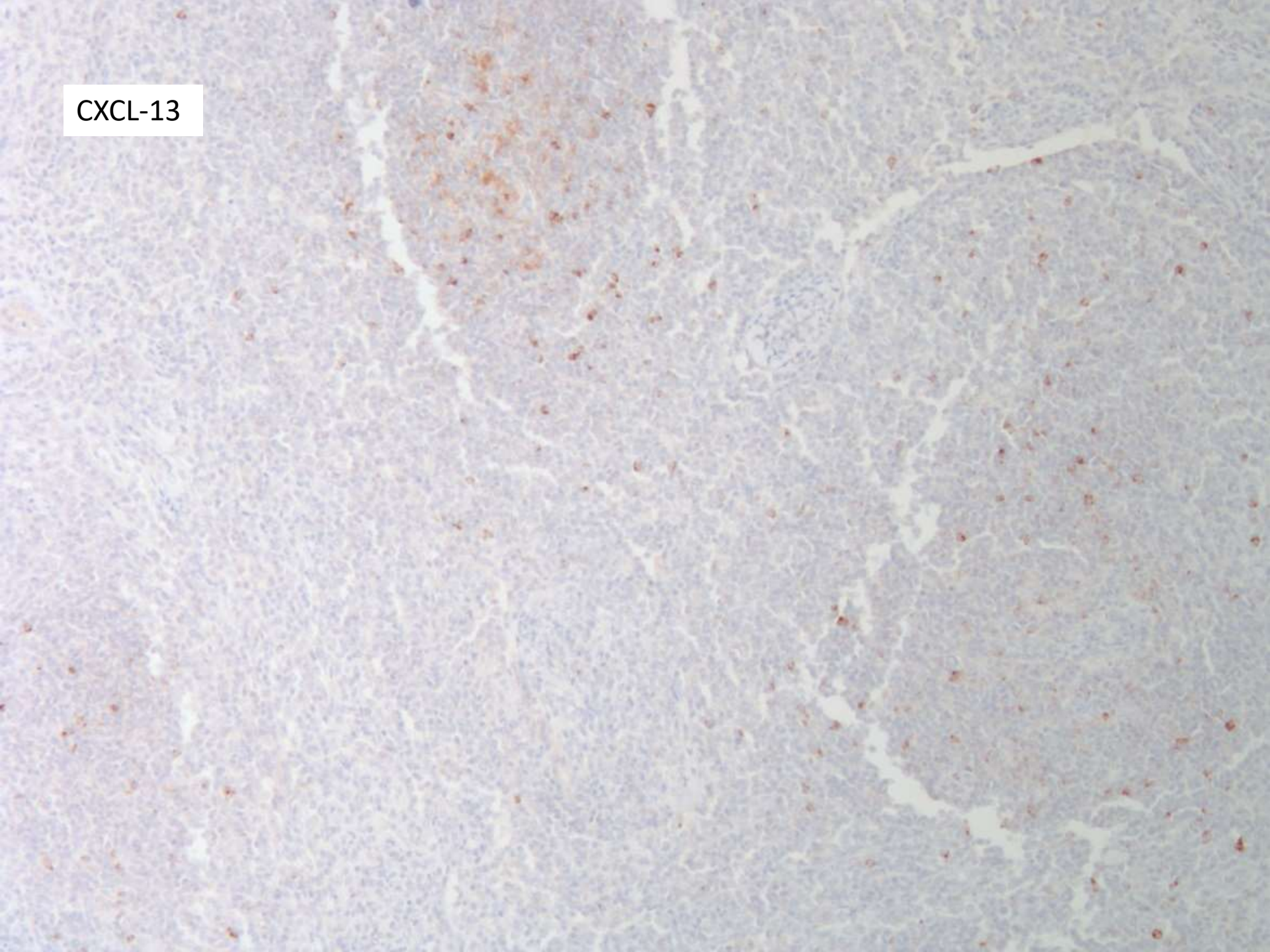
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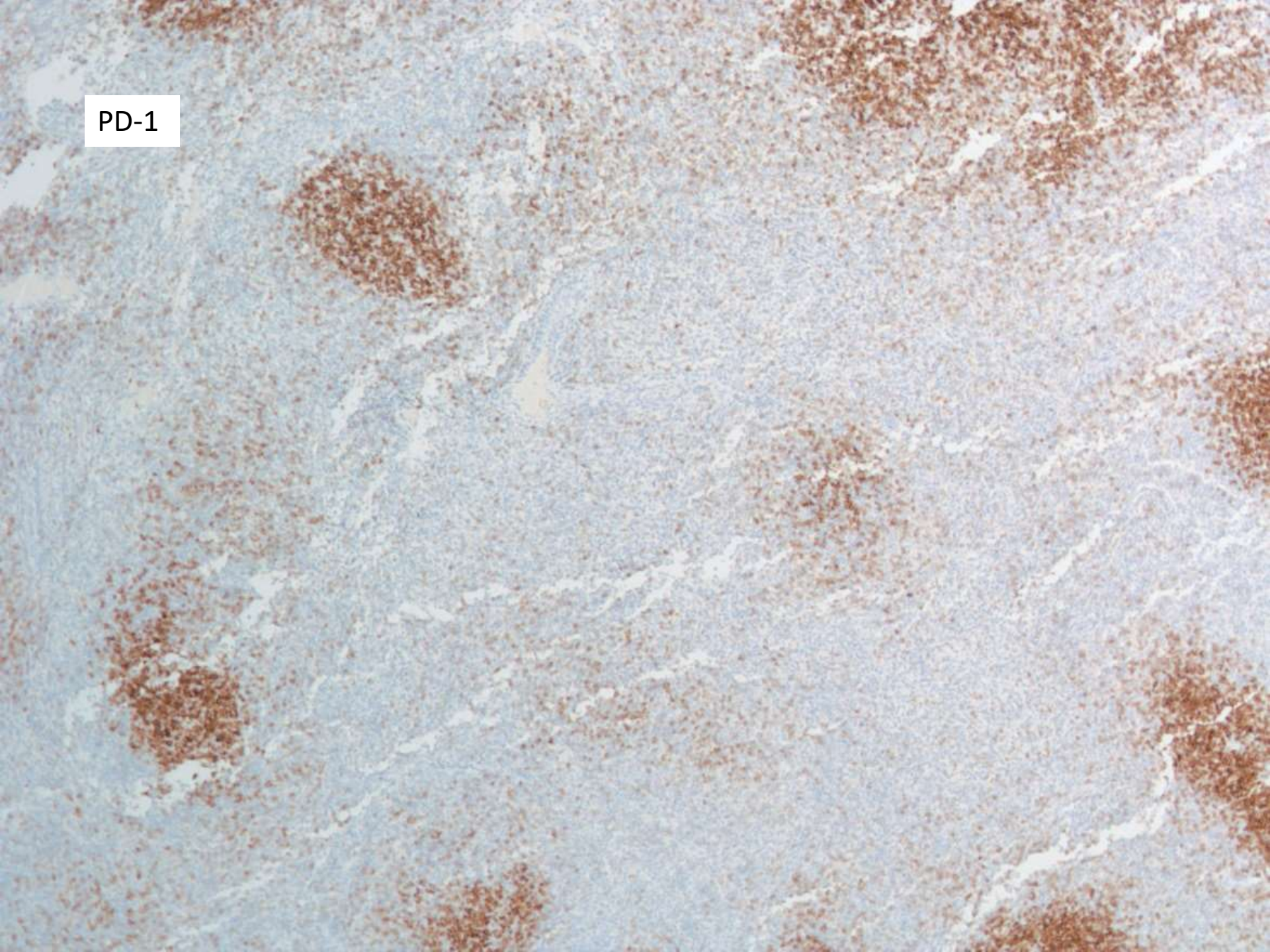
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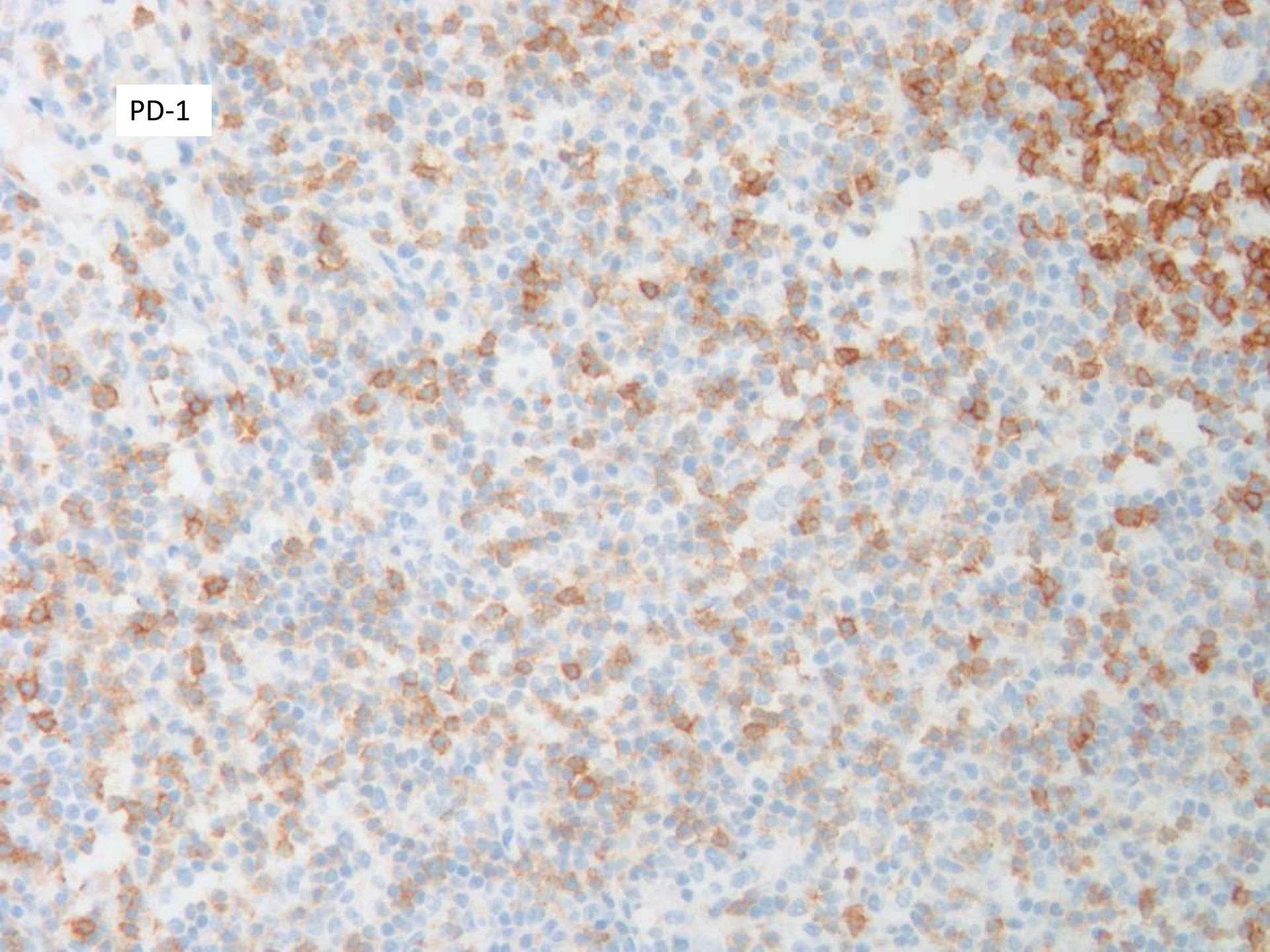
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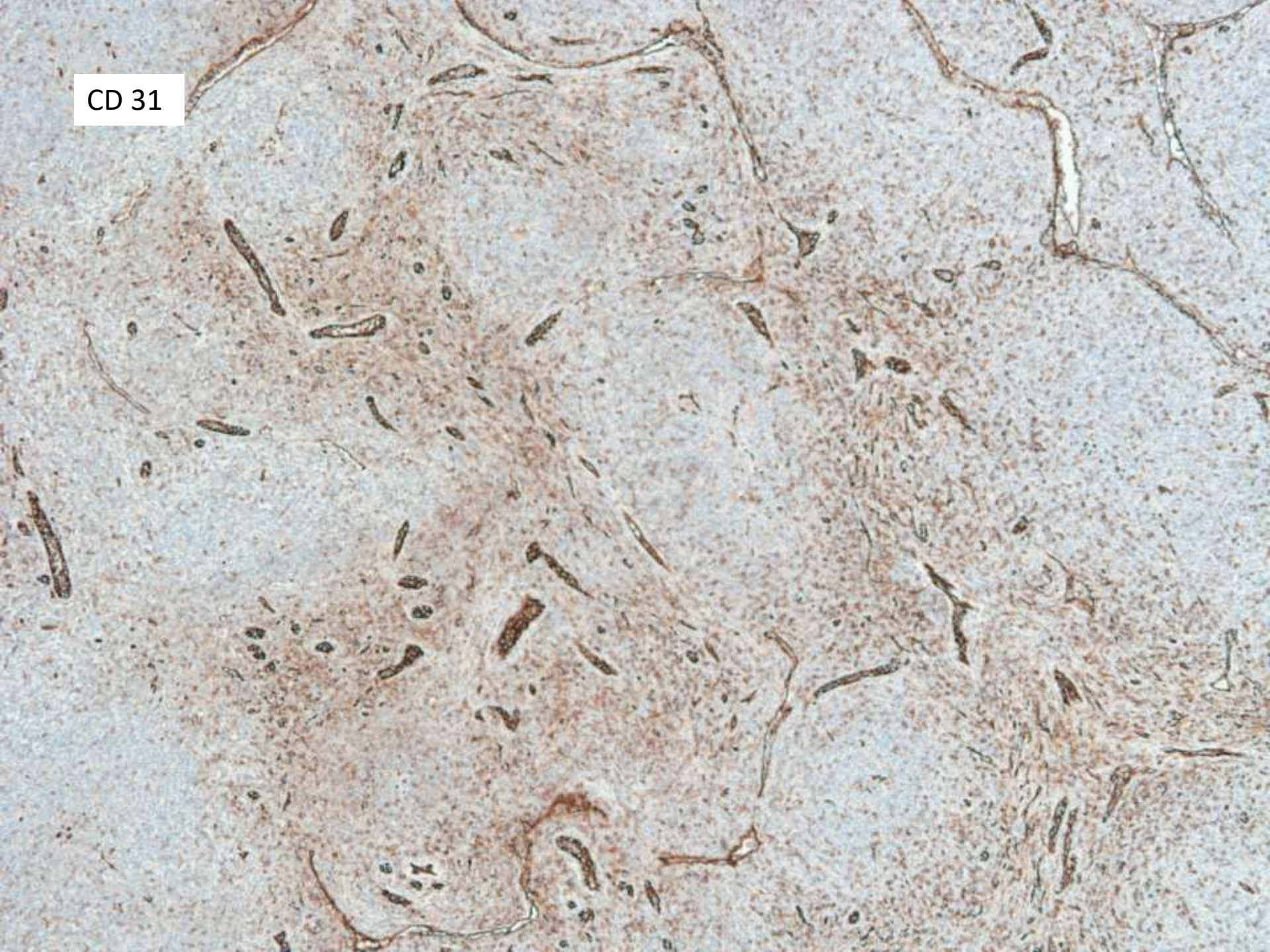
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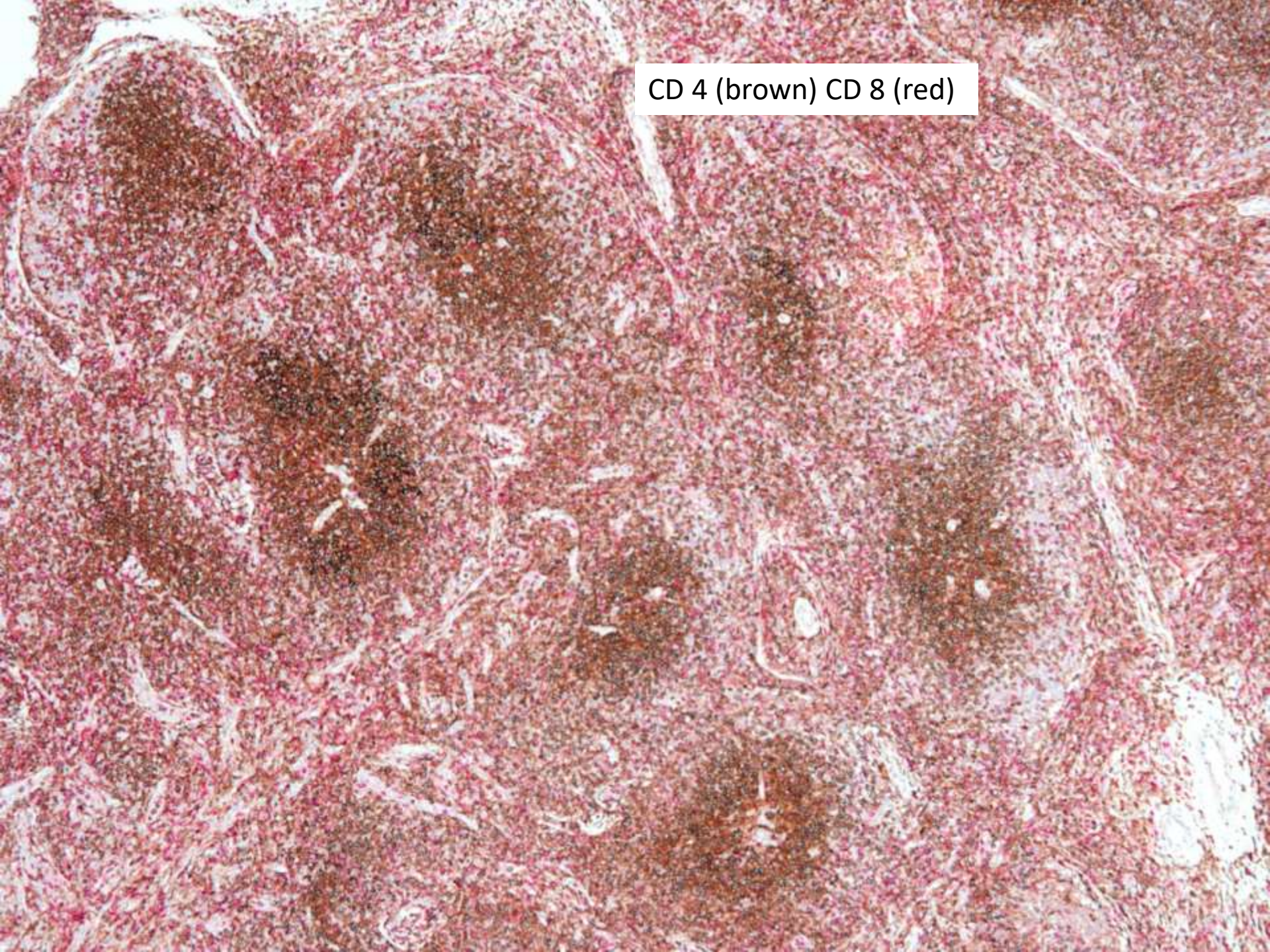
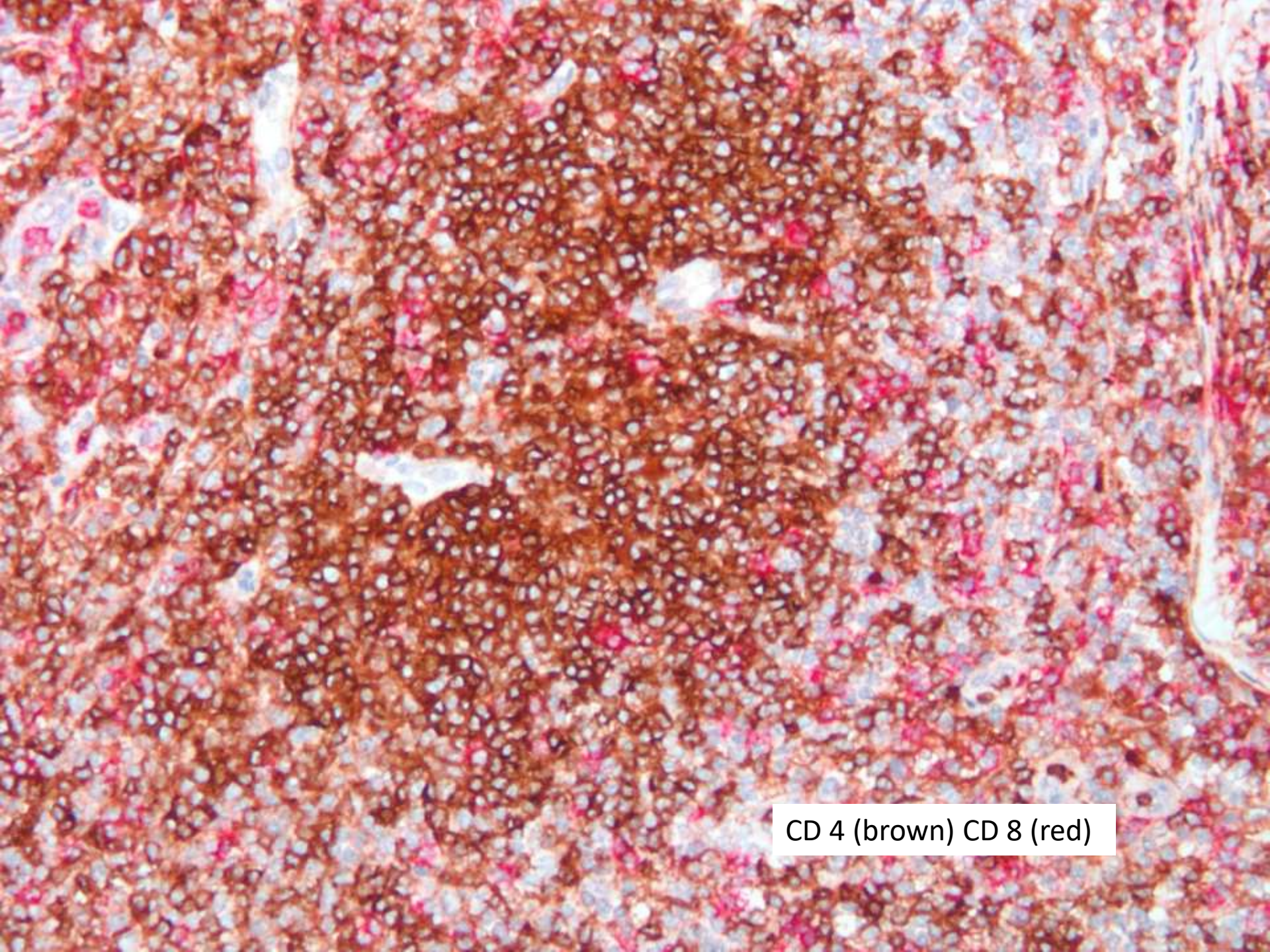

CD 4 (brown) CD 8 (red)


CD 4 (brown) CD 8 (red)

DIAGNOSIS?

Follicular T-cell lymphoma Histology

- Follicular growth pattern
  - PTGC-like
  - Follicular lymphoma-like
- Intermediate sized monotonous lymphoid cells
- Interfollicular areas typically lack polymorphous infiltrate and vascular proliferation characteristic of AITL
- Immunoblasts and RS-like cells may be present

Follicular T cell lymphoma
IHC

- CD3/CD4: stains majority of cells in follicles
- CD8: few cells in follicles; CD 4:8 ratio 1:1 in interfollicular areas
- CD20: prominent numbers of B cells in the interfollicular areas
- CD10/BCL6: few cells in follicles; no T cell coexpression
- PAX5/CD30: No Hodgkin-like staining
- PD-1: positive staining of follicles and interfollicular cells
- CD 21: retained follicular meshwork in follicles
- HHV8, EBV, CMV: negative

Follicular T cell lymphoma

Interpretation
Molecular Genetics
T-Cell Receptor Beta Gene Rearrangement:

RESULTS:

TEST:	RESULT:
T-CELL RECEPTOR BETA GENE REARRANGEMENT	NEGATIVE

Interpretation
Molecular Genetics
T-Cell Receptor Gamma Gene Rearrangement:

RESULTS:

TEST:	RESULT:
T-CELL RECEPTOR GAMMA GENE REARRANGEMENT	NEGATIVE

Follicular T cell lymphoma

Interpretation
Molecular Genetics
B-Cell Gene Rearrangement:

RESULTS:

TEST:	RESULT:
B CELL GENE REARRANGEMENT	NEGATIVE

Follicular T cell lymphoma

- In study by Medeiros et al
  - 85% had monoclonal TCR gene rearrangement
  - 5 % had oligoclonal TCR patterns
  - 10 % had a polyclonal pattern

  - Reference:
  - Hu et al: “Follicular T cell lymphoma: A number of an emerging family of follicular helper T-cell derived T-cell lymphomas.”Human Pathology 2012;43:1789-1798.

Follicular T cell lymphoma

- Most peripheral T-cell lymphomas are B cell poor
- Follicular T cell lymphoma is frequently a B-cell rich variant of T-cell lymphoma
- This pattern of lymphoma may be confused with reactive processes including
  - Reactive follicular hyperplasia
  - Progressive transformation of germinal centers

- Molecular: ITK-SYK Fusion (?specific for FTCL); seen in 20%

- Reference:
- Ruiz and Cotta: “Follicular helper T-cell lymphoma: A B-cell rich variant of T-cell lymphoma”. Annals of diagnostic pathology 2015; 19: 187-192.

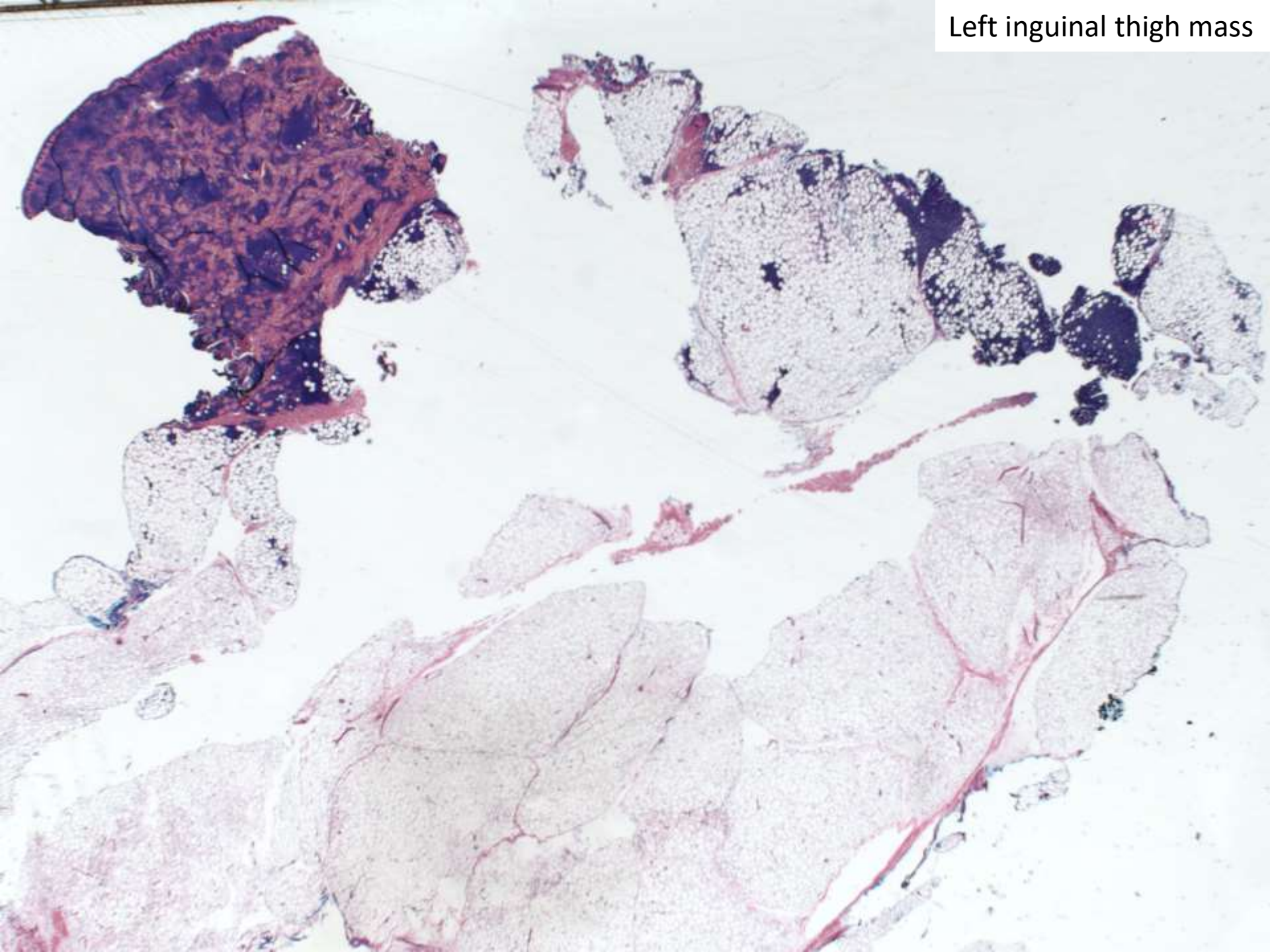
Follicular T-cell lymphoma

- Middle-aged and elderly
- Rare;< 1% of T-cell neoplasms
- Lymph nodes, sometimes involving BM
- Present with advanced stage/B symptoms
- Clinically aggressive (although not well characterized) 50% dead within 24 months of diagnosis

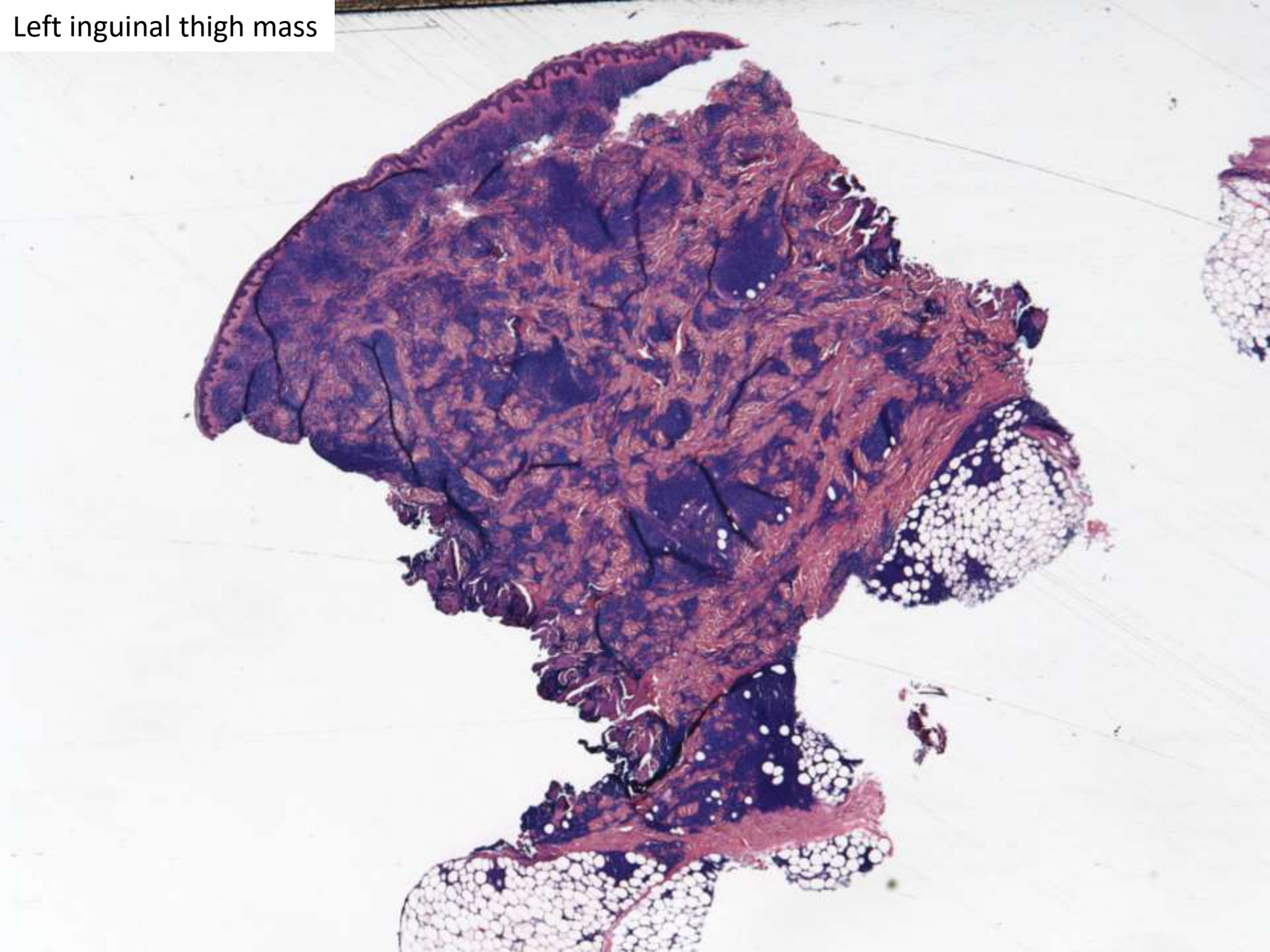
SB 6304

Sebastian Fernandez-Pol/Roger Warnke; Stanford

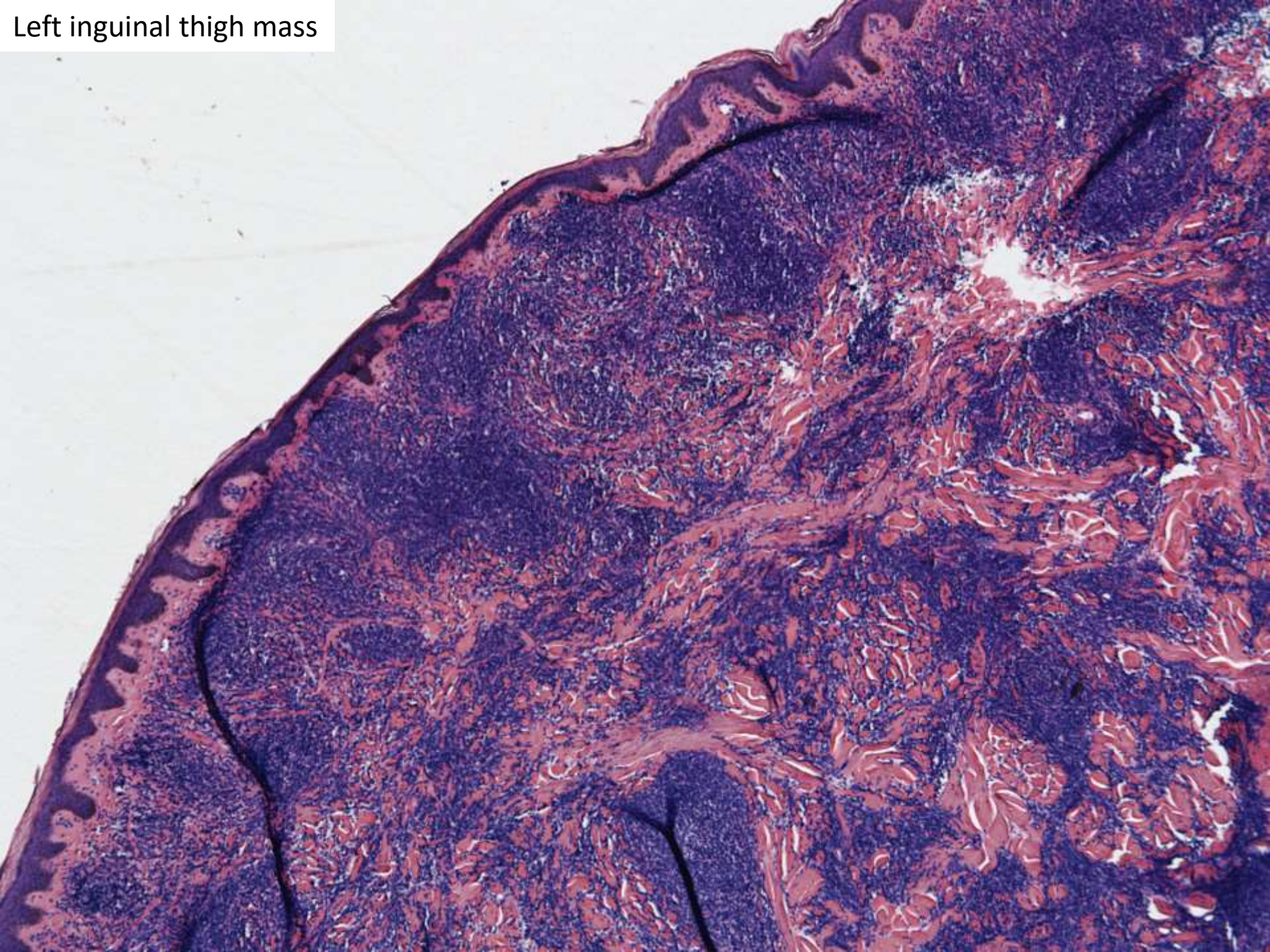
19-year-old male with history of lump in proximal left thigh and tenderness in left inguinal region. The mass is located on the left leg, anterior aspect of the thigh and has been present for 2 years. Sections of the thigh mass and lymph node submitted.

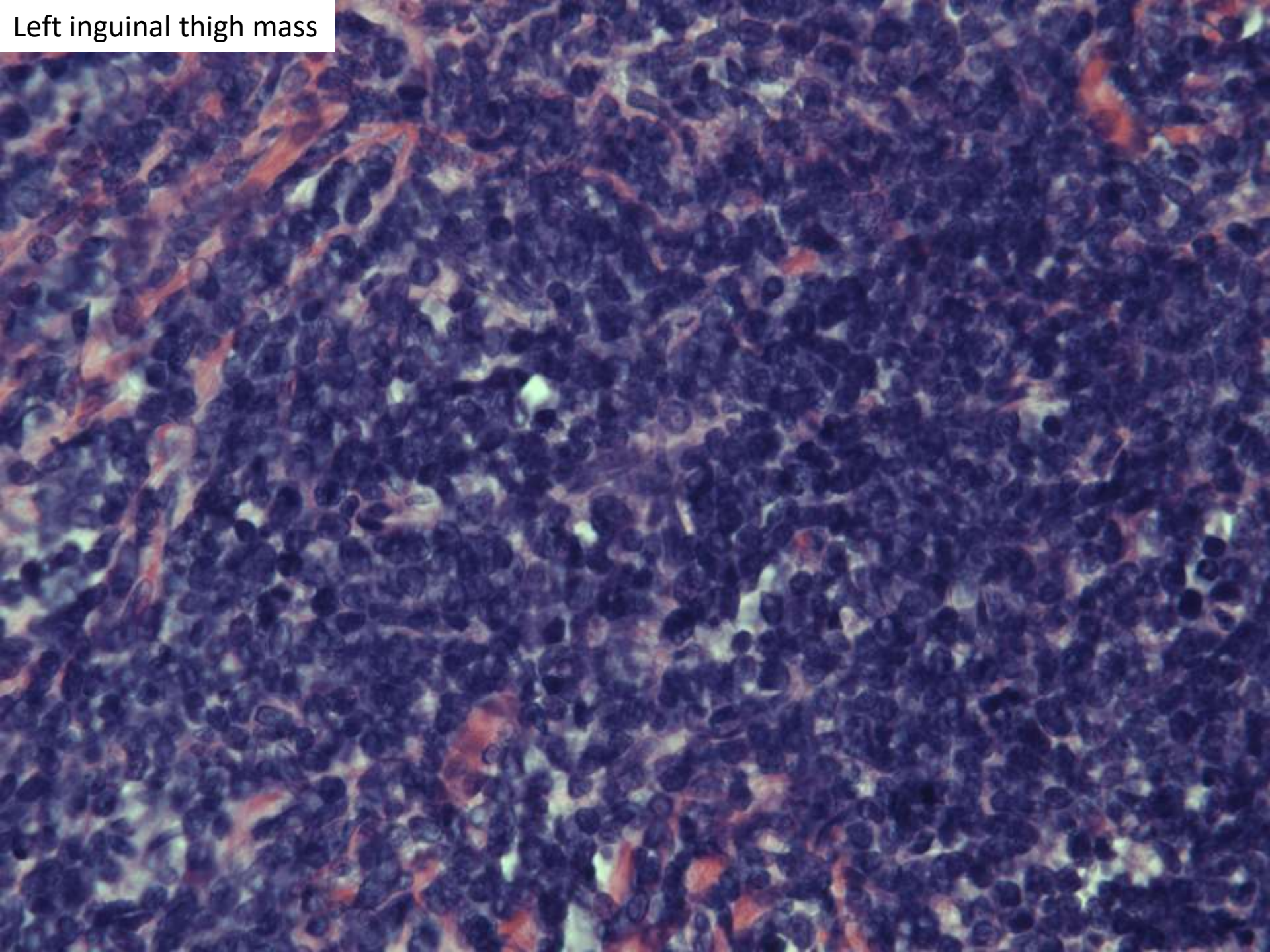

Left inguinal thigh mass

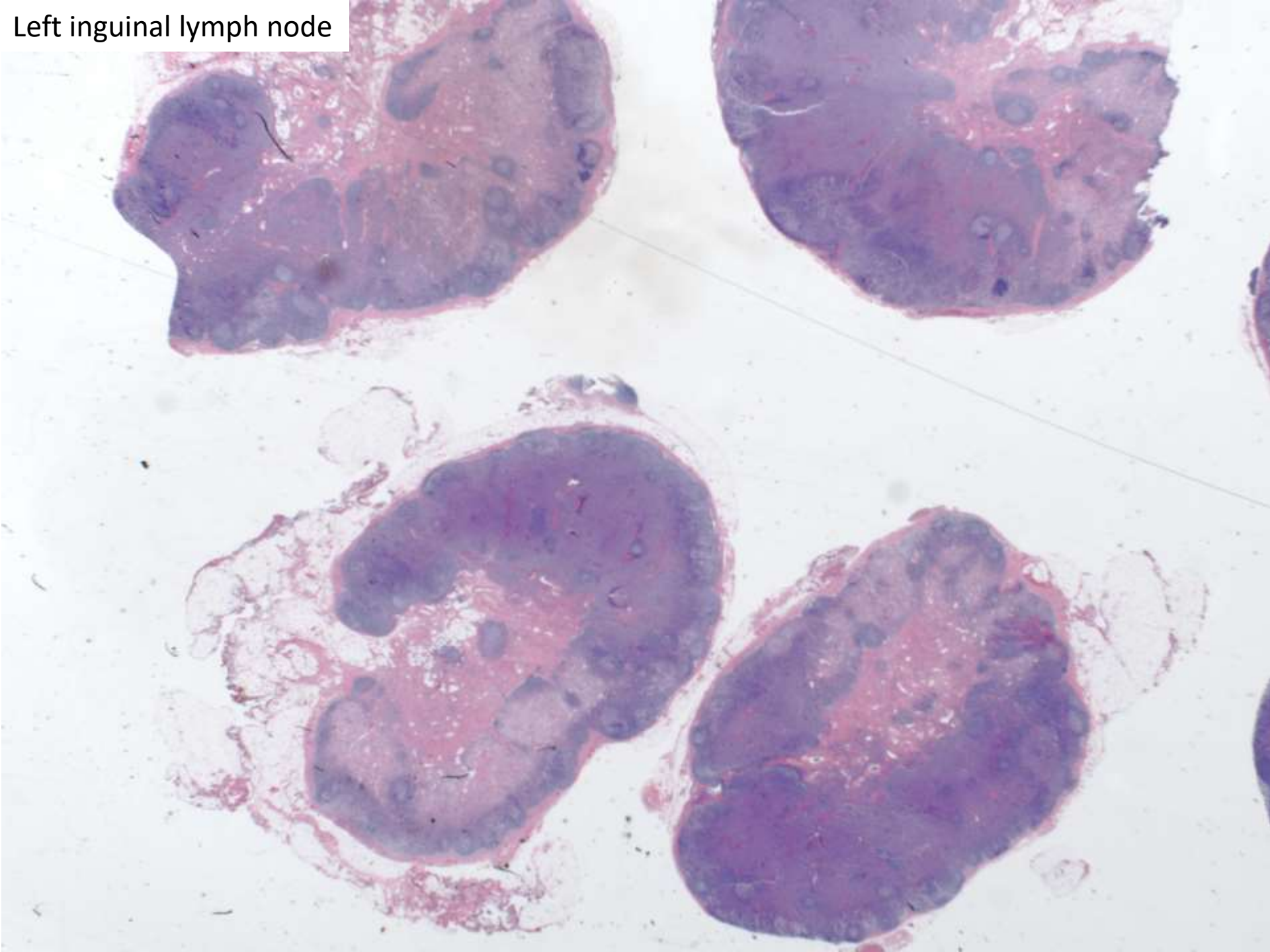
Left inguinal thigh mass



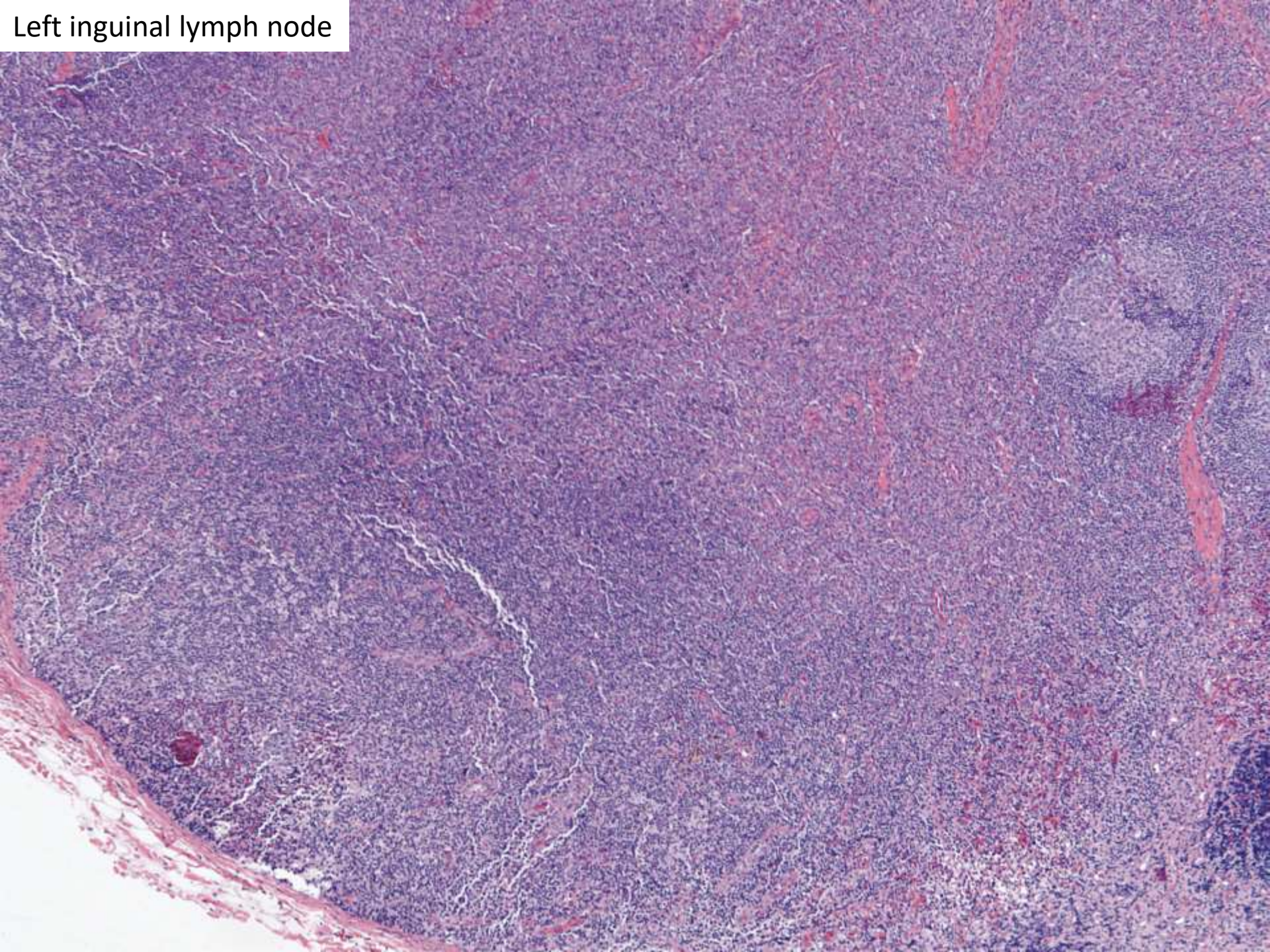
Left inguinal thigh mass

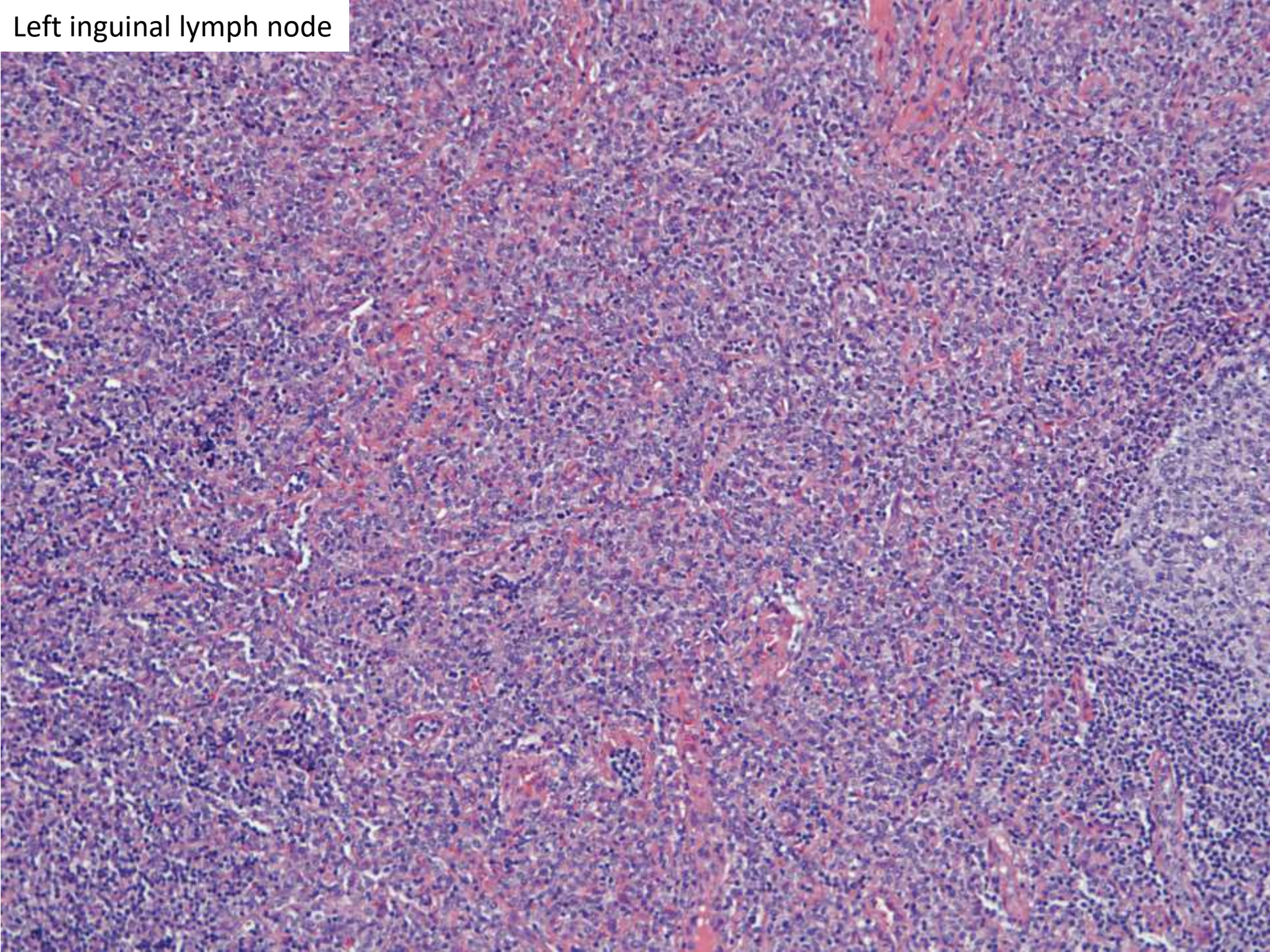


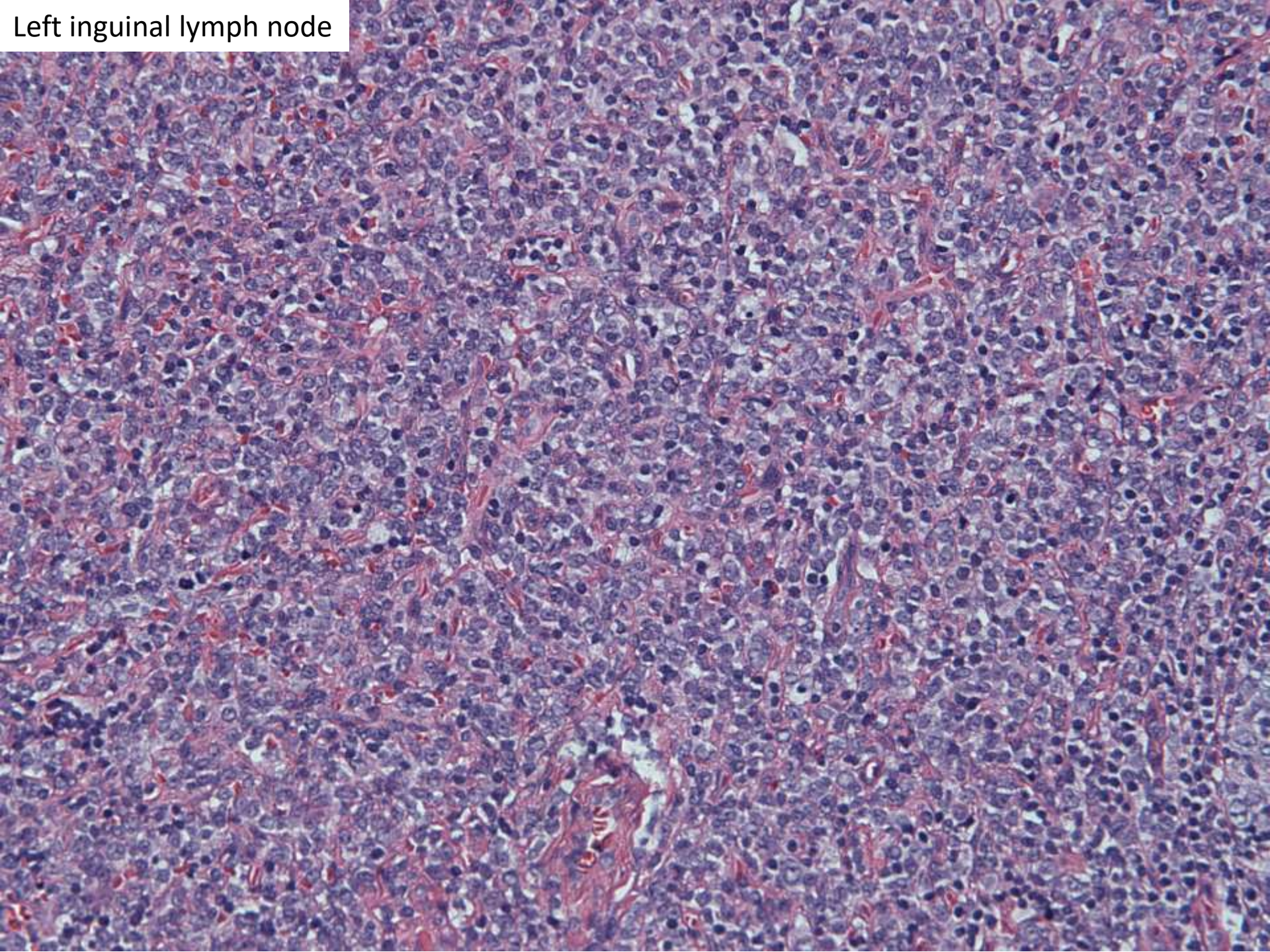

Left inguinal thigh mass

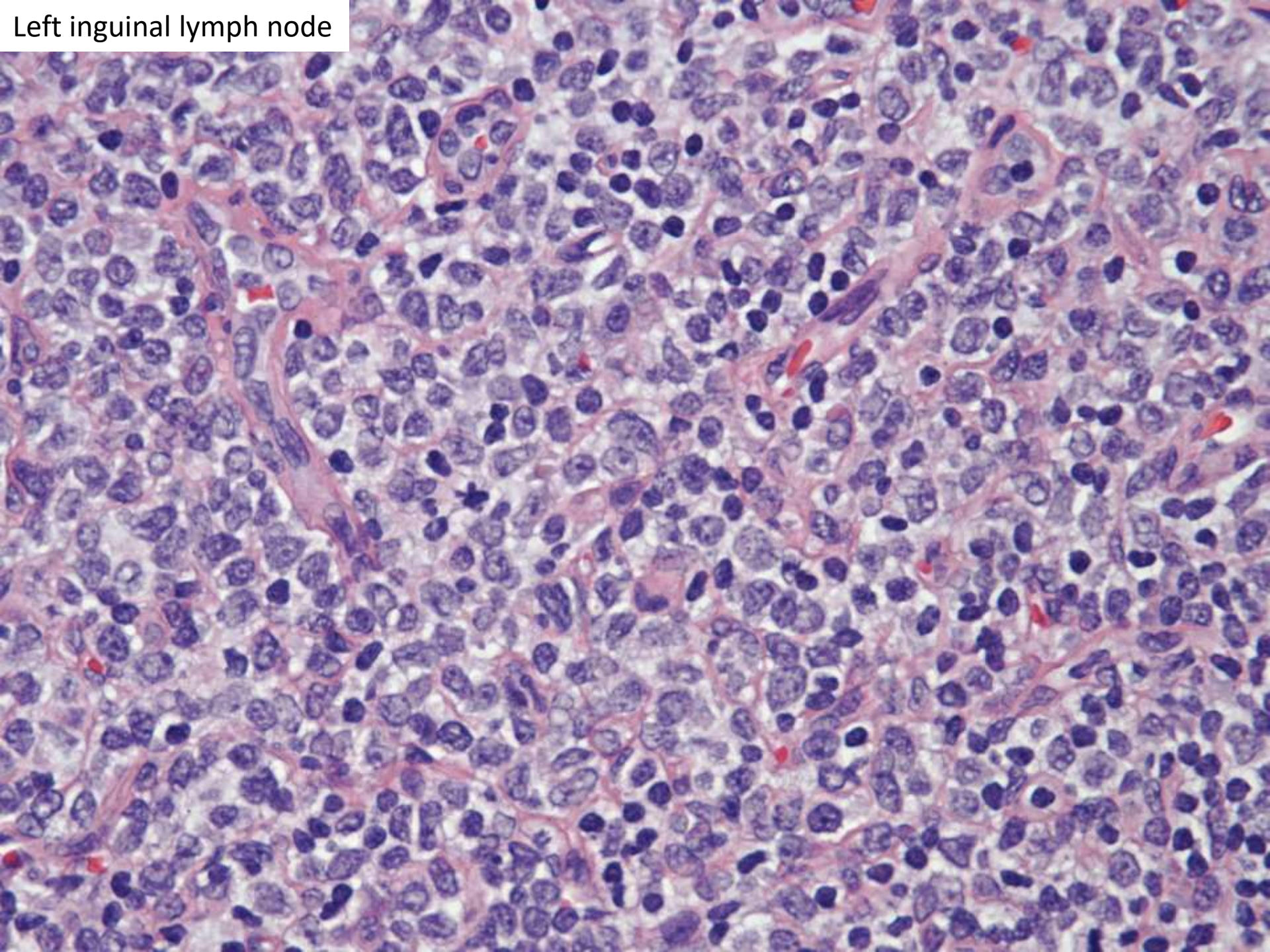

Left inguinal lymph node

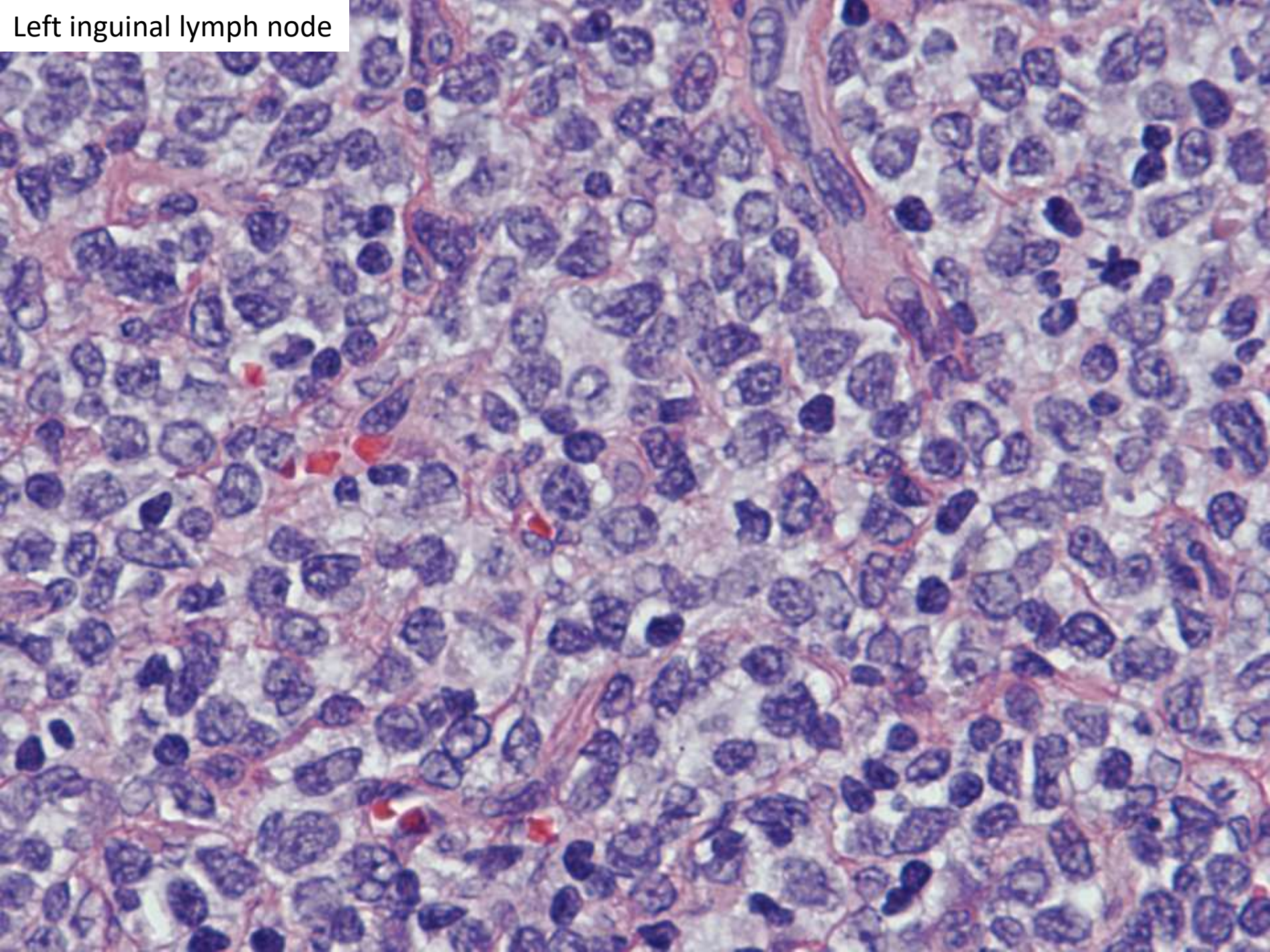

Left inguinal lymph node


Left inguinal lymph node

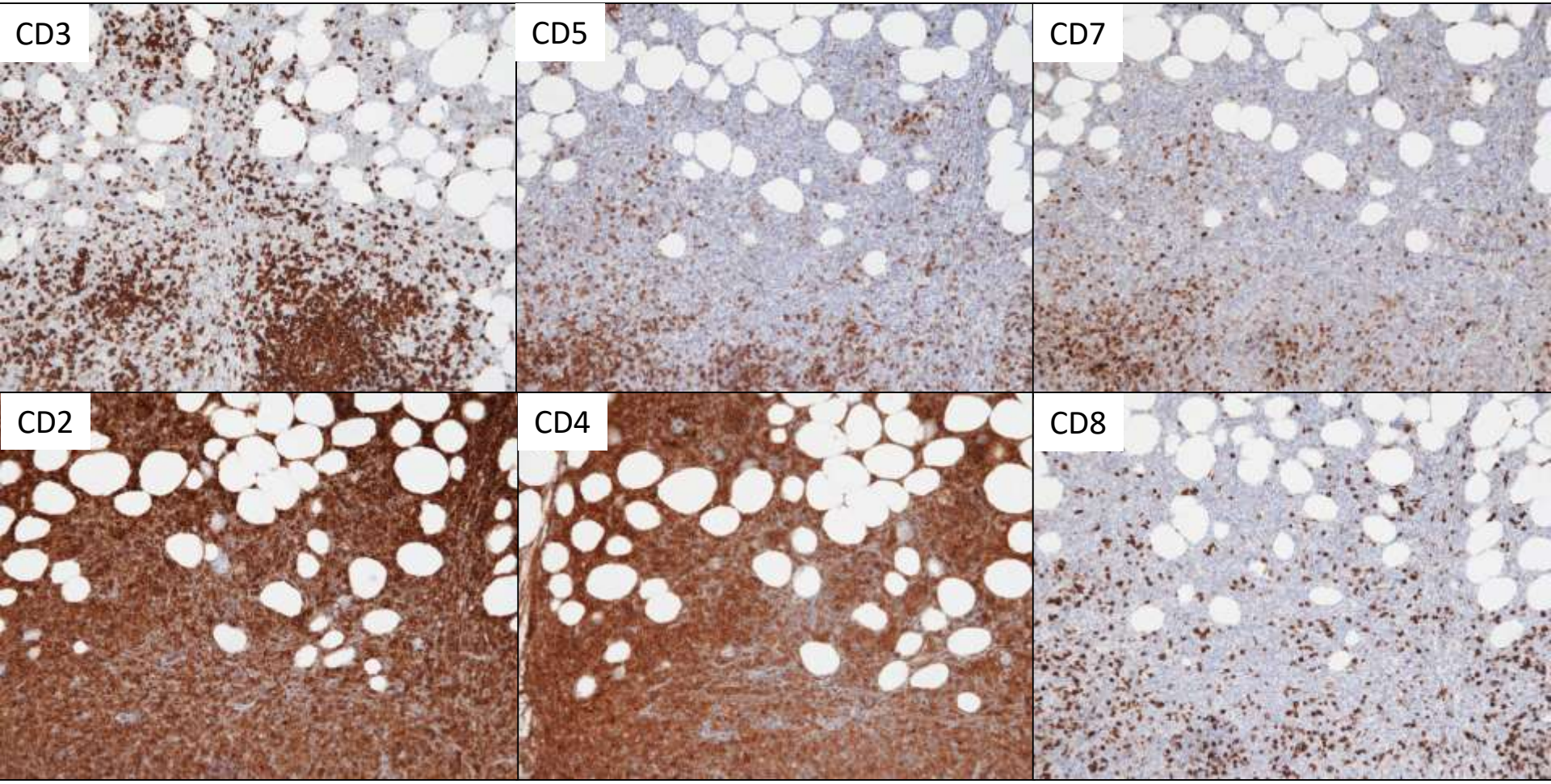

Left inguinal lymph node


Left inguinal lymph node

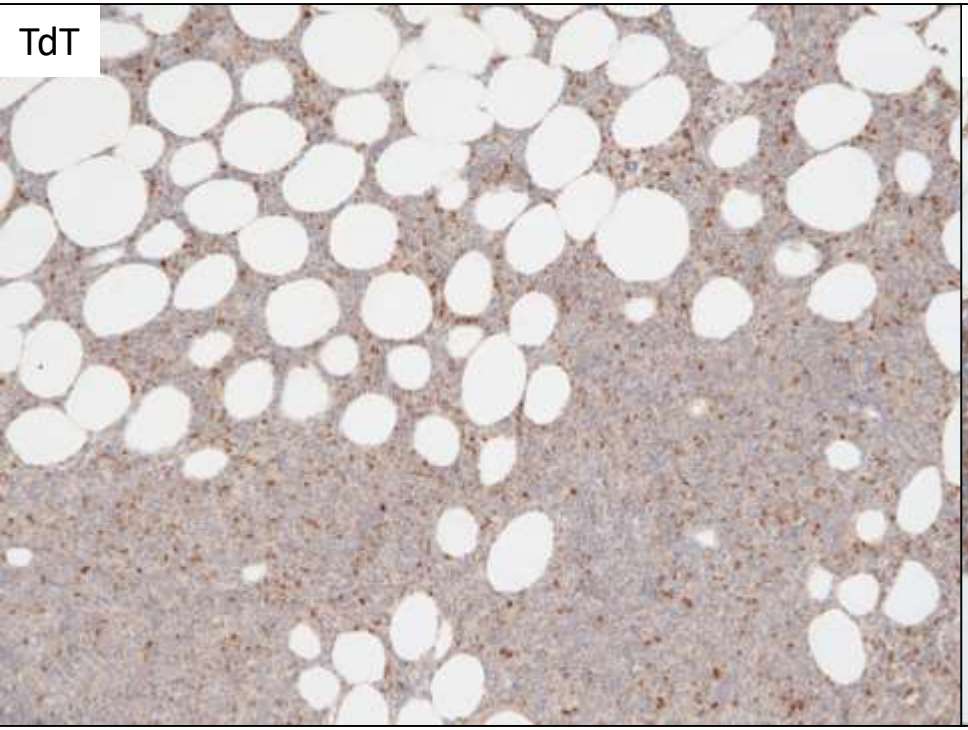

Left inguinal lymph node

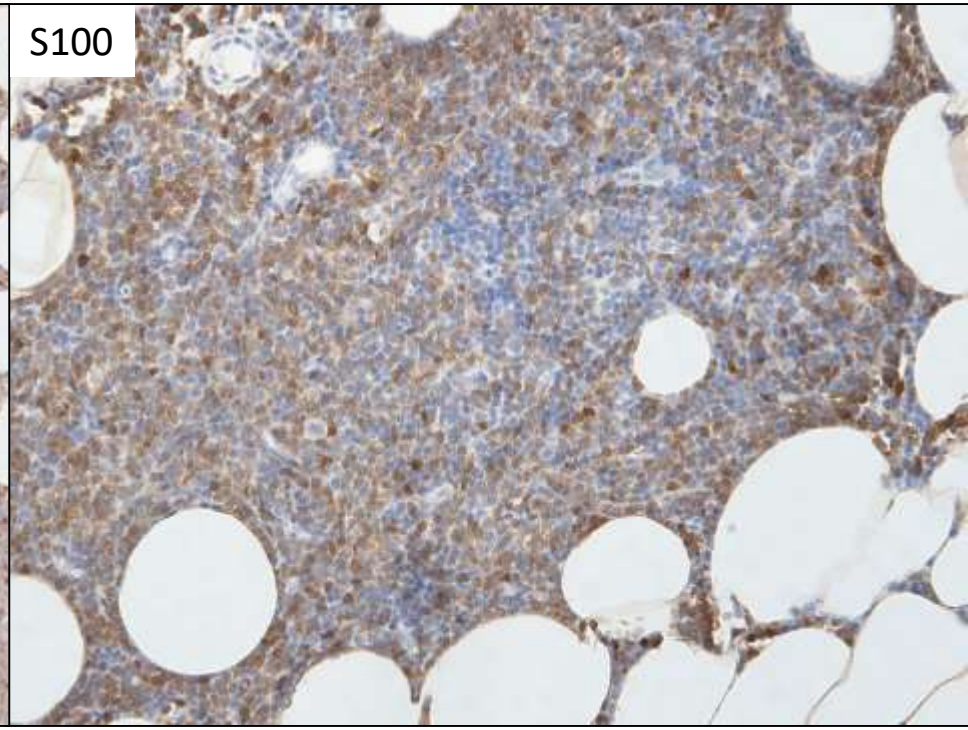

Left inguinal lymph node

Left inguinal thigh mass



Left inguinal thigh mass



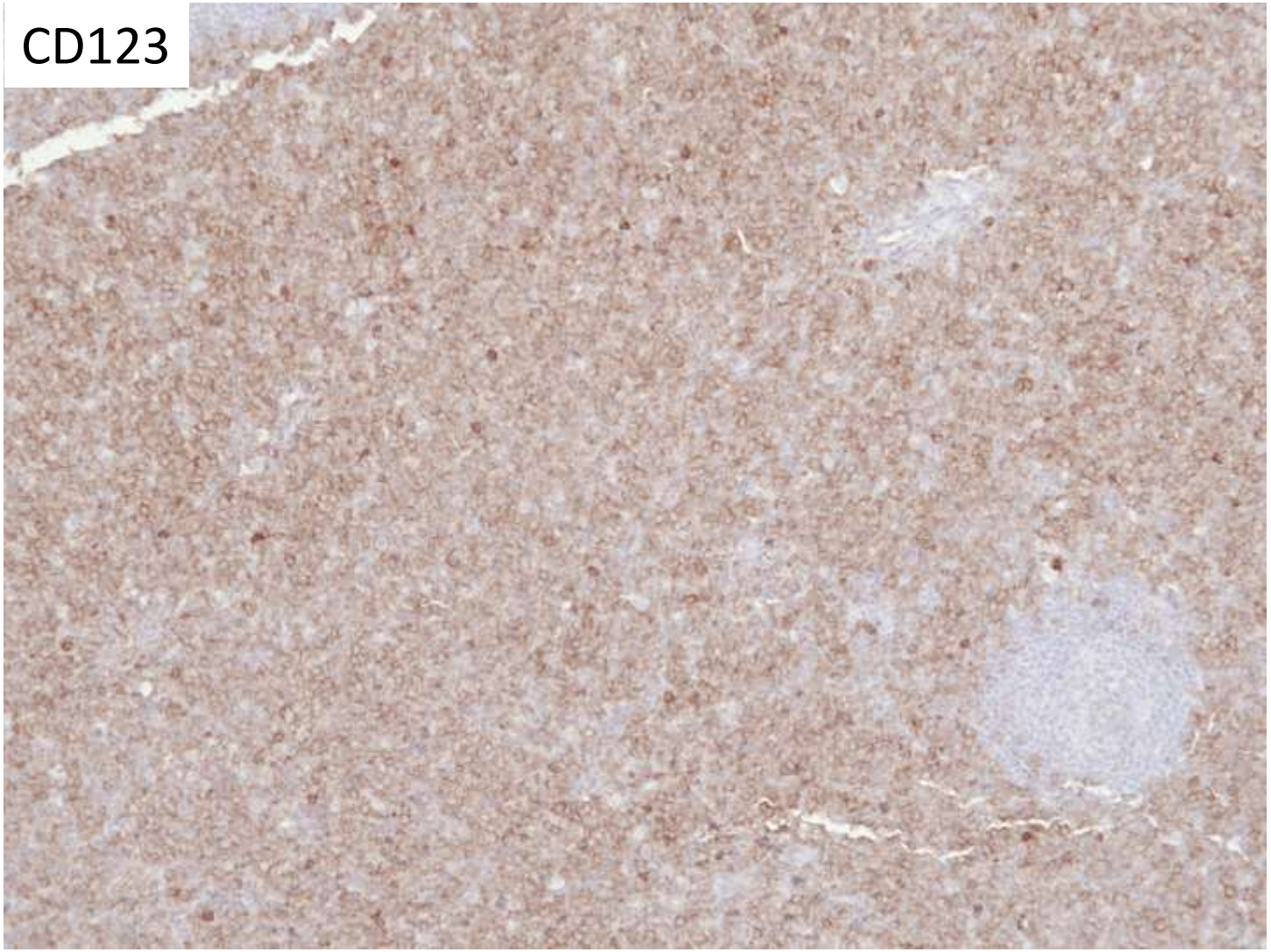


DIAGNOSIS?

Differential diagnosis

- Acute leukemia – leukemia cutis, myeloid or ambiguous lineage
- T-cell lymphoma with antigen loss
- Blastic plasmacytoid dendritic cell neoplasm

TCL1


CD123

Immunophenotype of our case

Positive	Negative
CD4	MPO
CD56	CD34
CD123	CD117
TCL1	CD20
CD2	CD3
S100 (subset dim)	CD7
TdT (subset dim)	CD5
	CD8
	Lysozyme

Blastic plasmacytoid dendritic cell neoplasm

- Frequently presents in the skin
- Leukemic phase, either present at initial diagnosis (approximately 50% of cases) or in the subsequent course of the disease
- Diagnosis rests on immunophenotype:
  - CD4 and CD56 coexpression
  - Expression of plasmacytoid dendritic cell markers (CD123, CD303, TCL1)
  - Absence of any specific myeloid, T-lymphoid, B-lymphoid, or NK-lymphoid lineage markers

Blastic Plasmacytoid Dendritic Cell Neoplasms

Clinico-immunohistochemical Correlations in a Series of 91 Patients

Fanny Julia, MD, Stephane Dalle, MD, PhD,* Gerard Duru, PhD,† Brigitte Balme, MD,‡ Béatrice Vergier, MD, PhD,§ Nicolas Ortonne, MD, PhD,‖ Marie D. Vignon-Pennamen, MD,¶ Valérie Costes-Martineau, MD, PhD,# Laurence Lamant, MD, PhD,** Sophie Dalac, MD,†† Claire Delattre, MD,‡‡ Pierre Déchelotte, MD, PhD,§§ Philippe Courville, MD,‖‖ Agnès Carlotti, MD,¶¶ Anne De Muret, MD,## Sylvie Fraitag, MD,*** Annie Levy, MD,††† Andrew Mitchell, MD,‡‡‡ and Tony Petrella, MD§§§‖‖‖*

Antibody	% of Positivity
CD4	98
CD56	93
CD123	97
CD303	63
TCL1	99
MX-1	65
CD68	84
CD2	37
CD7	11
TdT	19
S100	32

4 of the 5 markers

BPDCN	Acute leukemia
CD4	CD4
CD56	CD56
CD123	CD123
TCL1	TCL1 (rare)
CD303 (only specific marker)	MPO
	MNDA
	CD13
	CD11c
	CD14
	Lysozyme
	CD3
	CD79a
	CD19
	PAX5
	LAT

Clinical behavior

- Median overall survival ranging from 9 to 20 months
- Follow up for this case unavailable

BPDCN summary

- Consider BPDCN in a skin proliferation that looks like blasts
- BPDCN can express a wide variety of markers that may lead to confusion (e.g. S100, TdT)
- Need an extensive immunohistochemistry panel:
  - CD4, CD56, CD123, TCL1, CD303 (at least 4 of the 5)
  - Exclude acute myeloid leukemia, B-lymphoblastic leukemia, T-lymphoblastic leukemia

References

- Julia F, Dalle S, Duru G, et al. Blastic plasmacytoid dendritic cell neoplasms: clinico-immunohistochemical correlations in a series of 91 patients. Am J Surg Pathol. 2014;38(5):673–680.
- Johnson RC, Kim J, Natkunam Y, et al. Myeloid Cell Nuclear Differentiation Antigen (MNDA) Expression Distinguishes Extramedullary Presentations of Myeloid Leukemia From Blastic Plasmacytoid Dendritic Cell Neoplasm. Am J Surg Pathol. 2016 Apr;40(4):502-9.
- Facchetti F., Cigognetti M., Fisogni S., Rossi G., Lonardi S., Vermi W. Neoplasms derived from plasmacytoid dendritic cells. *Modern Pathology*. 2016;29(2):98–111.

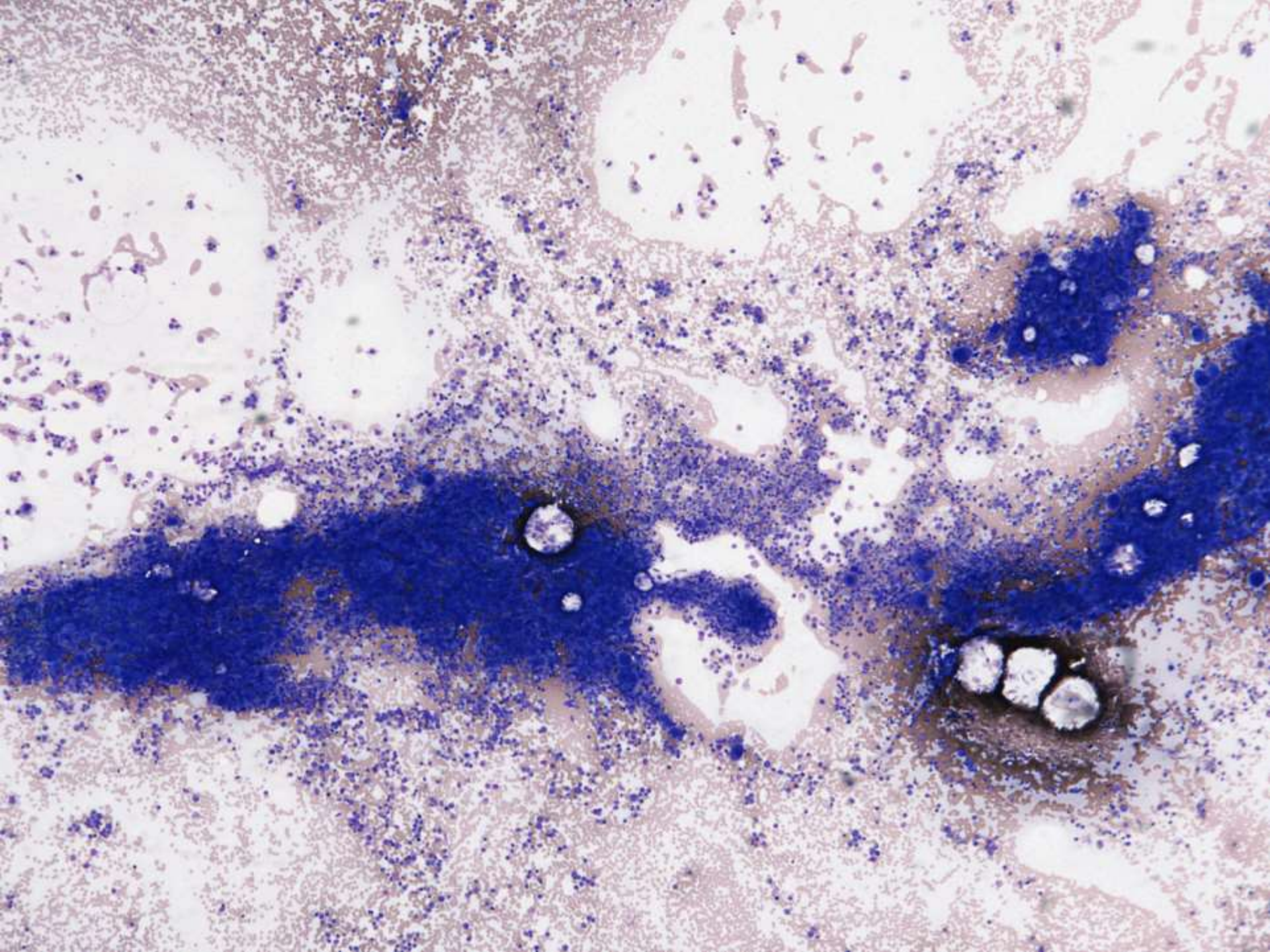
SB 6305

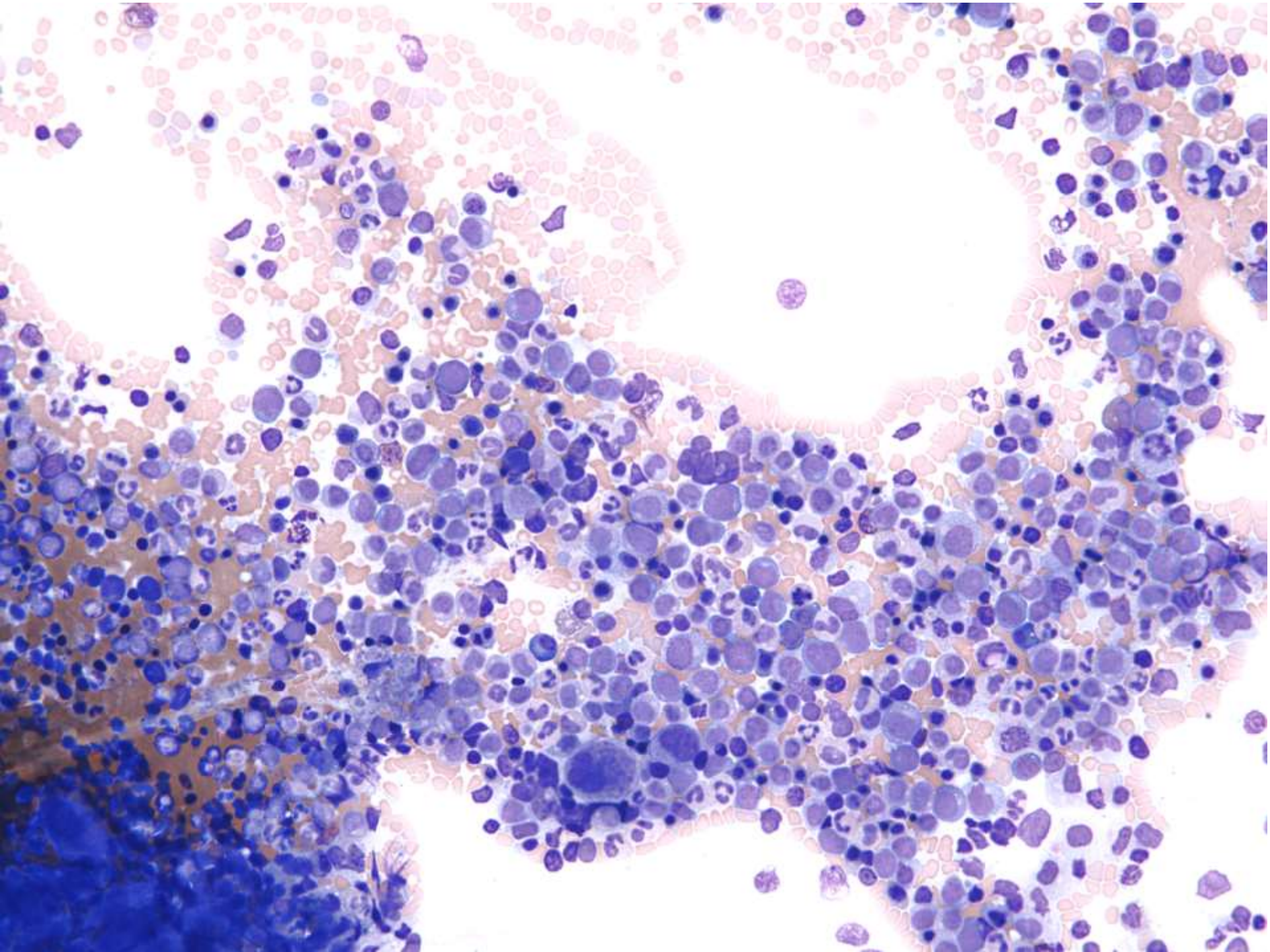
Joshua Menke/Brent Tan; Stanford

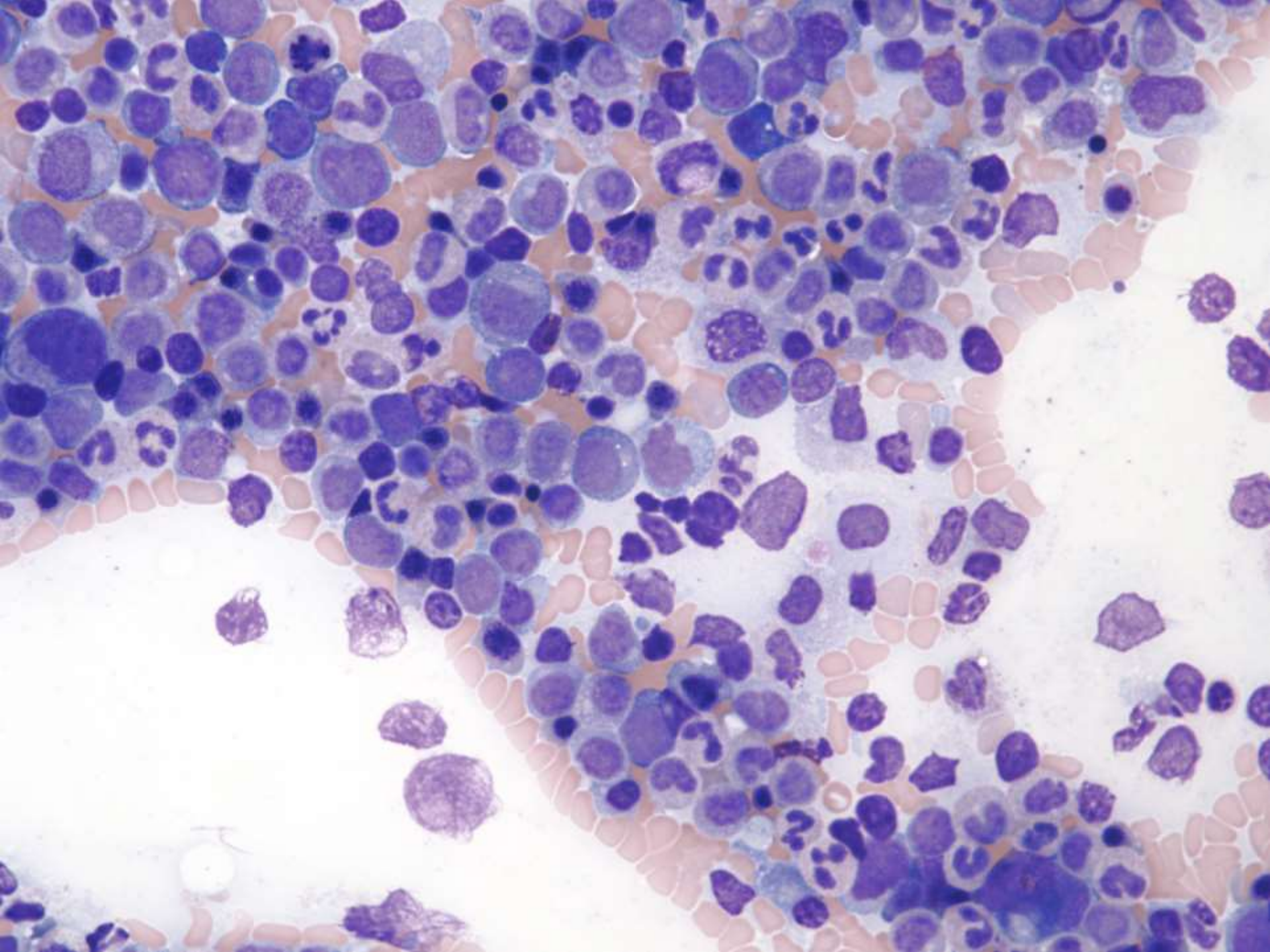
54-year-old male with anemia, splenomegaly, peripheral monocytosis. Bone marrow submitted.

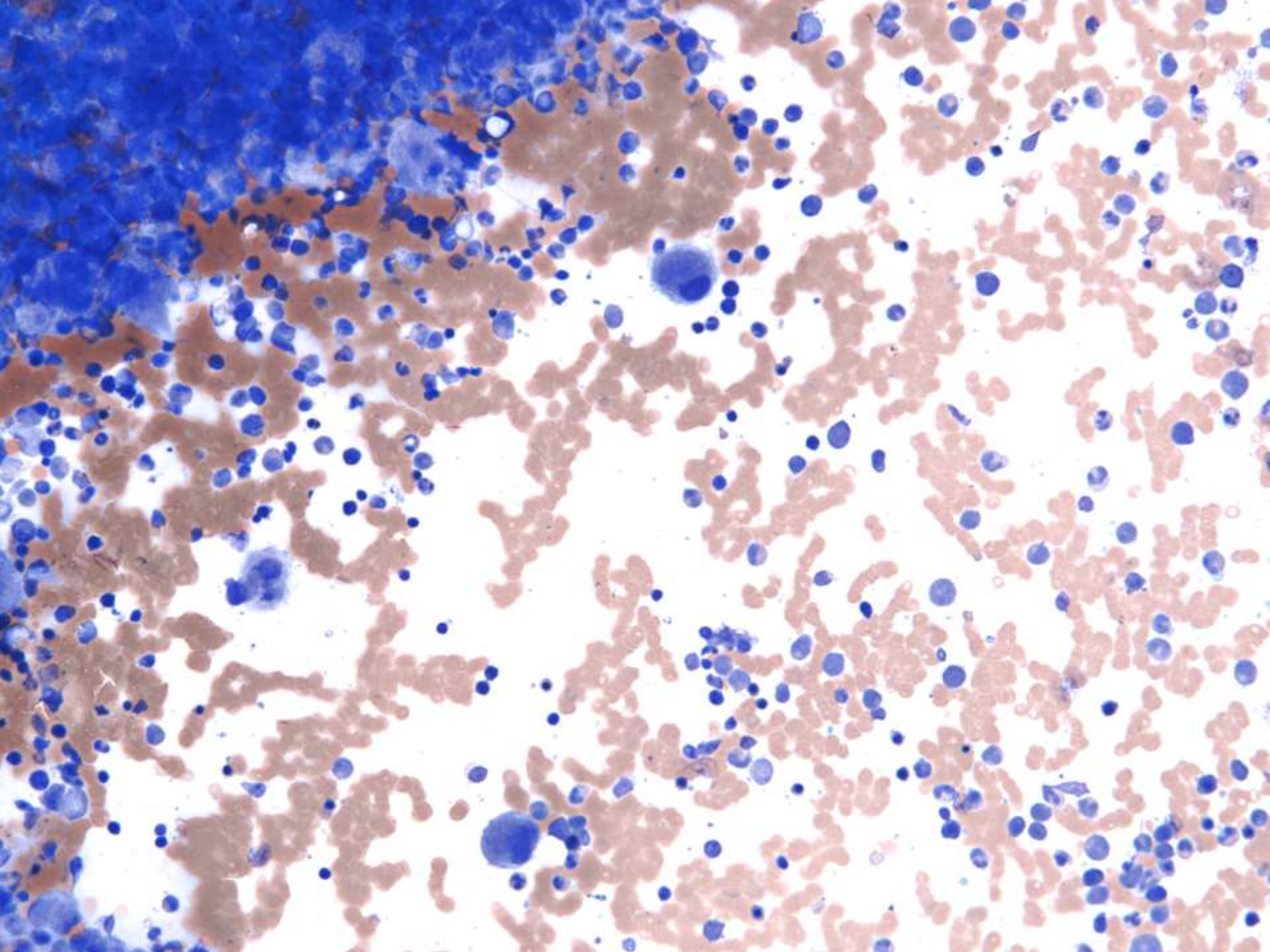
Clinical history

- 54 year old man with anemia, splenomegaly
- CBC: WBC: 5.8 K/uL HGB: 10.7 g/dL MCV: 74 fL RDW: 18% PLT: 345 K/uL
- Diff: NEUTS 43% LYMPHS 20% MONOS 32%
- ABS NEU: 2.49 K/uL **ABS MONO 1.86 K/uL**



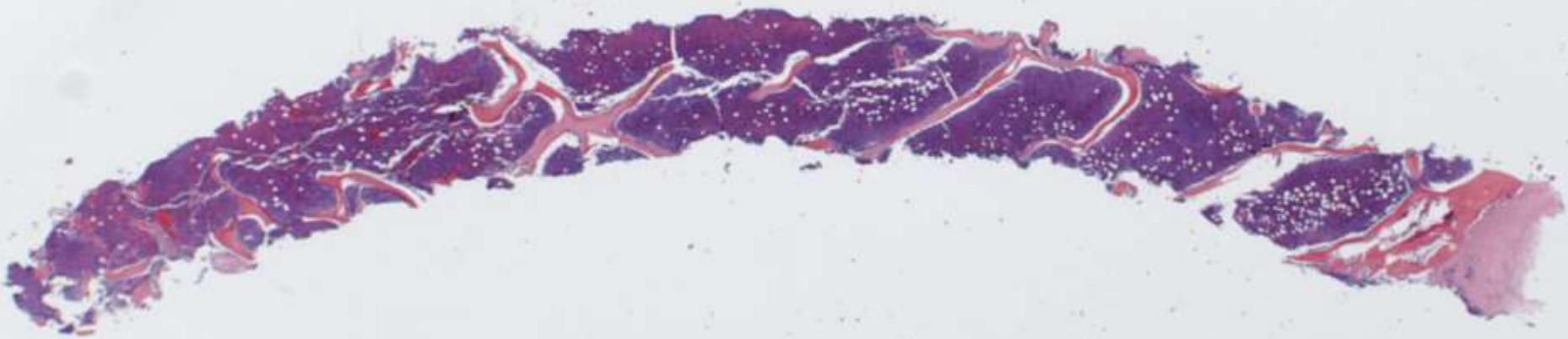


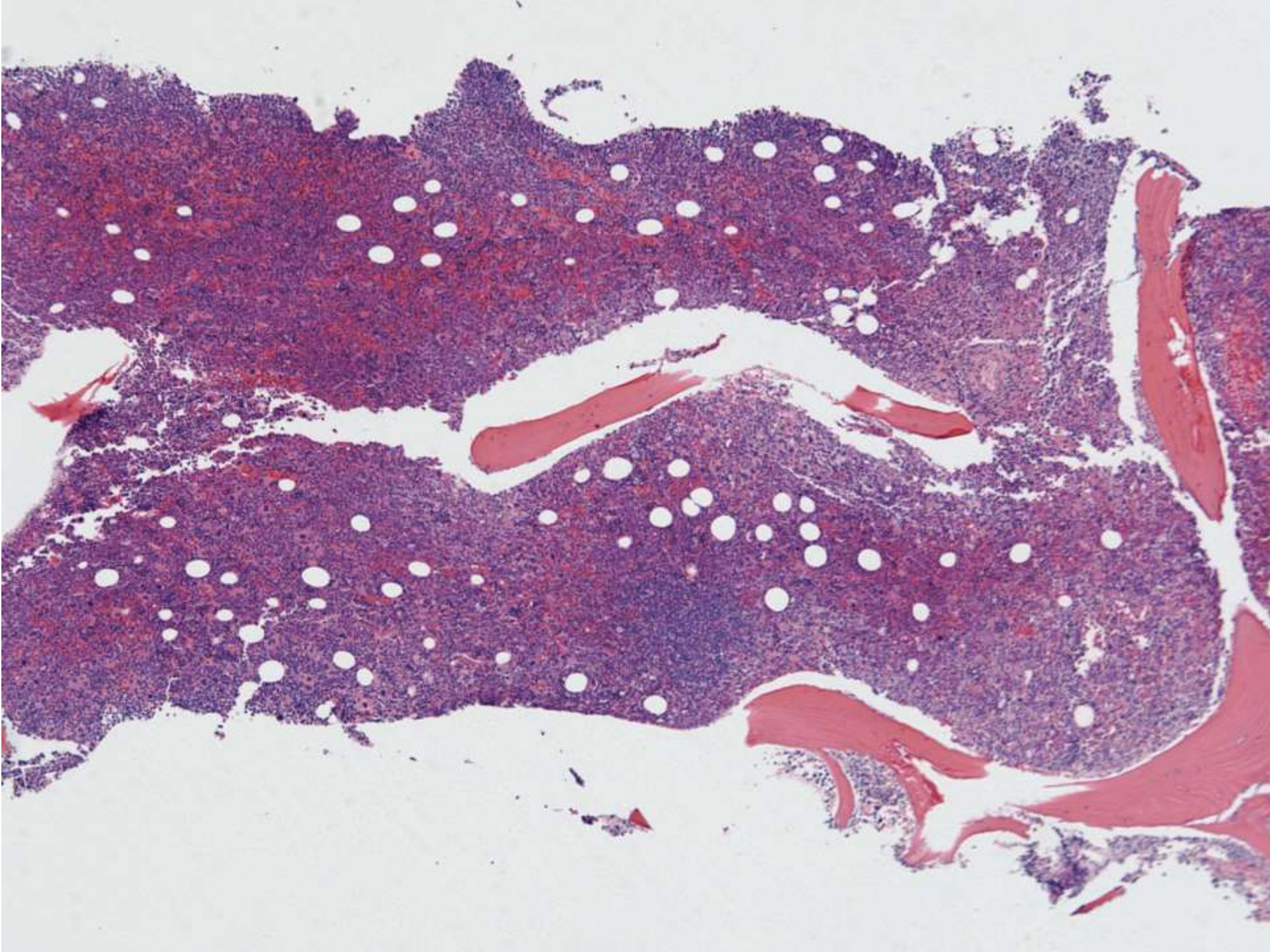


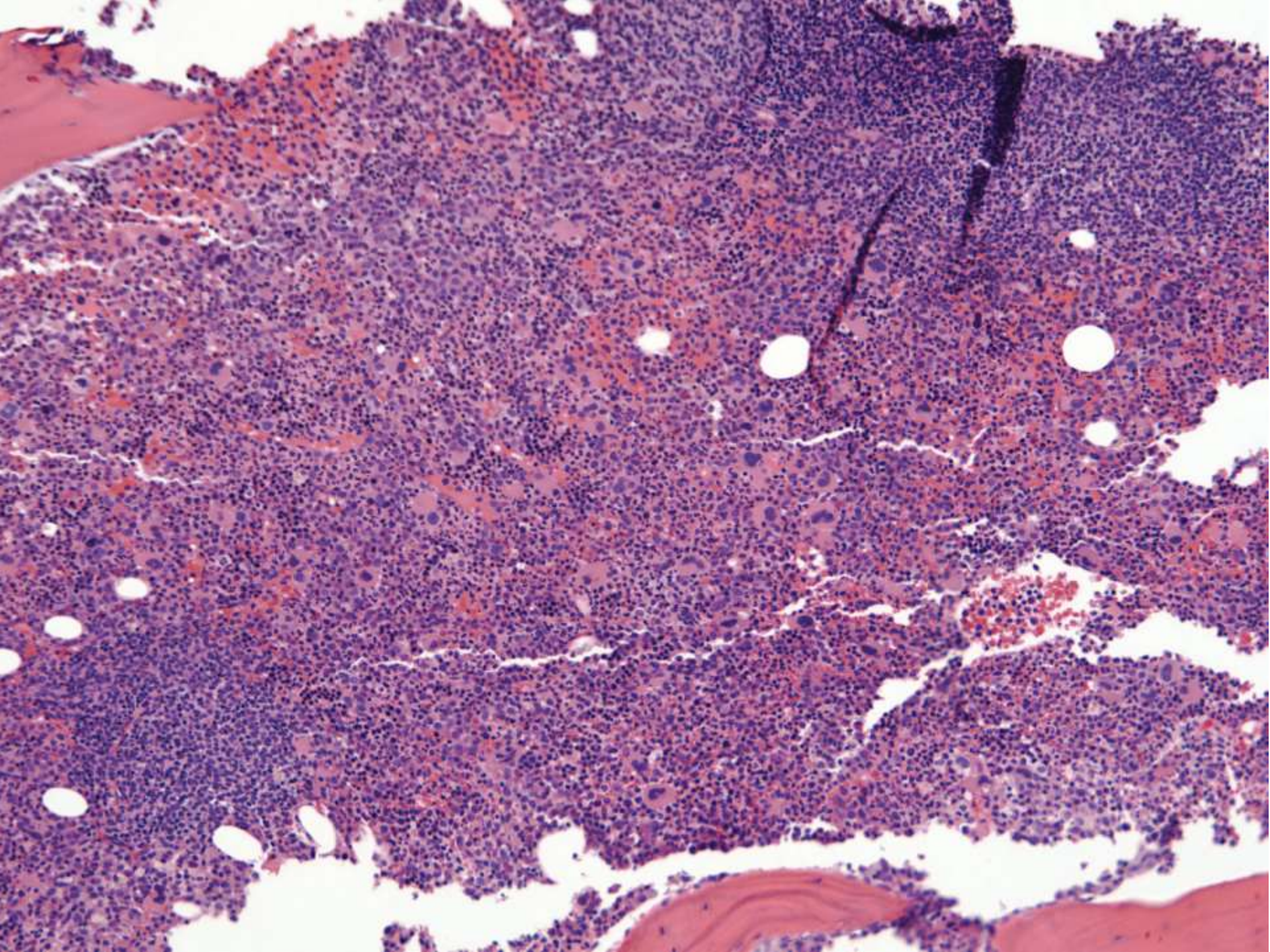


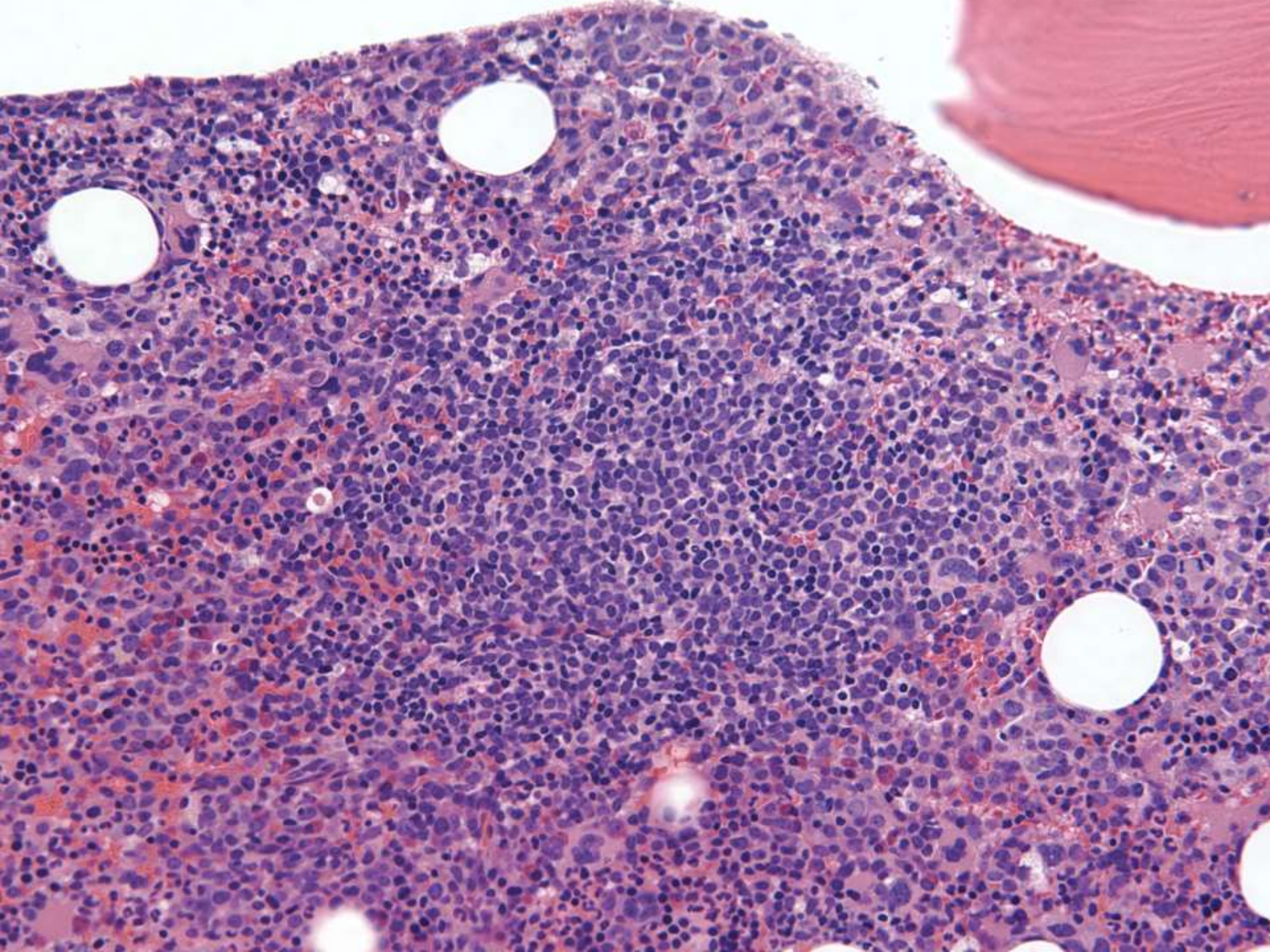
Bone marrow aspirate summary

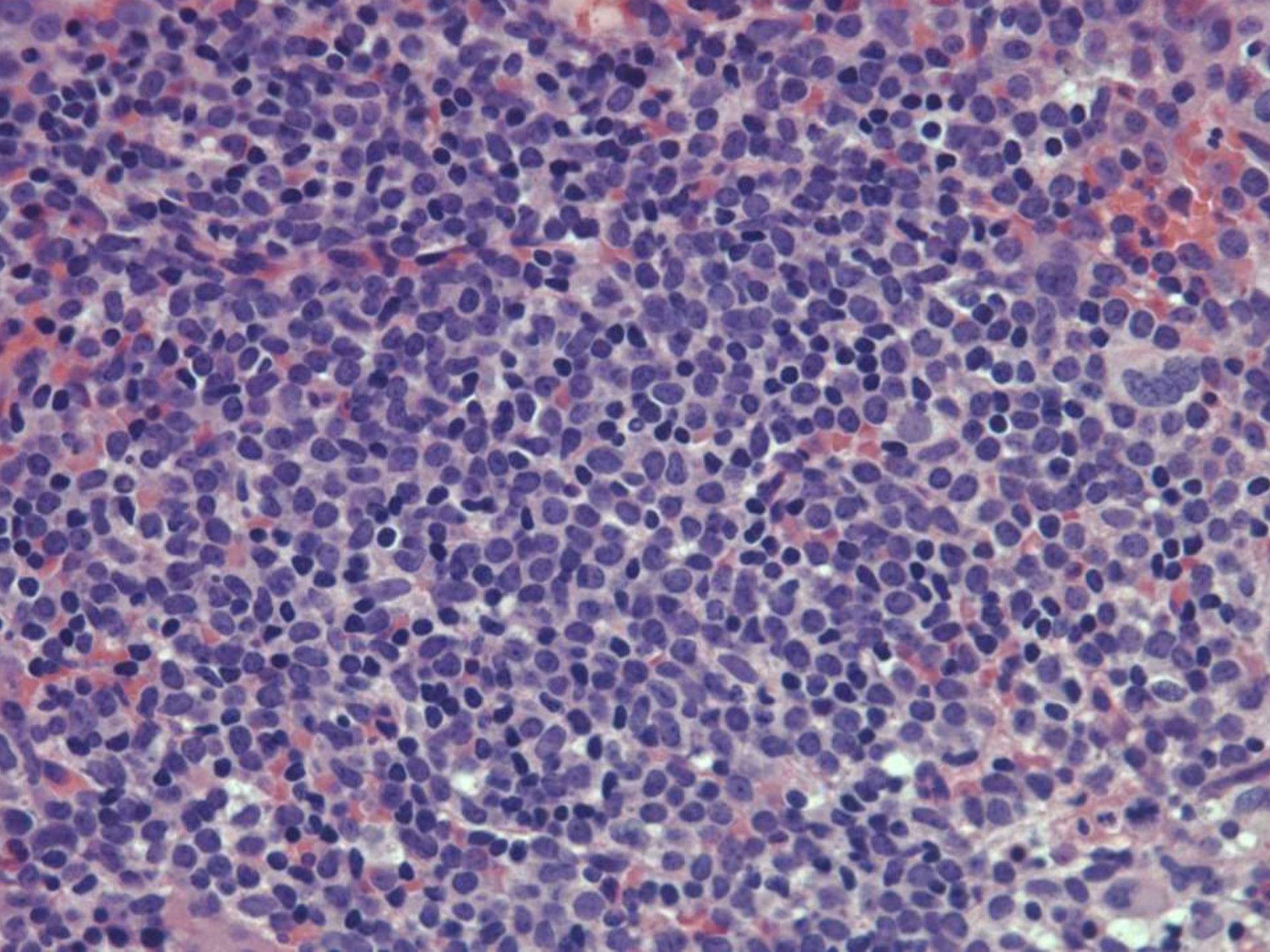
- Blasts 10.5% on 500 cell differential
- Megakaryocytic dysplasia
- Qualitative erythroid irregularities

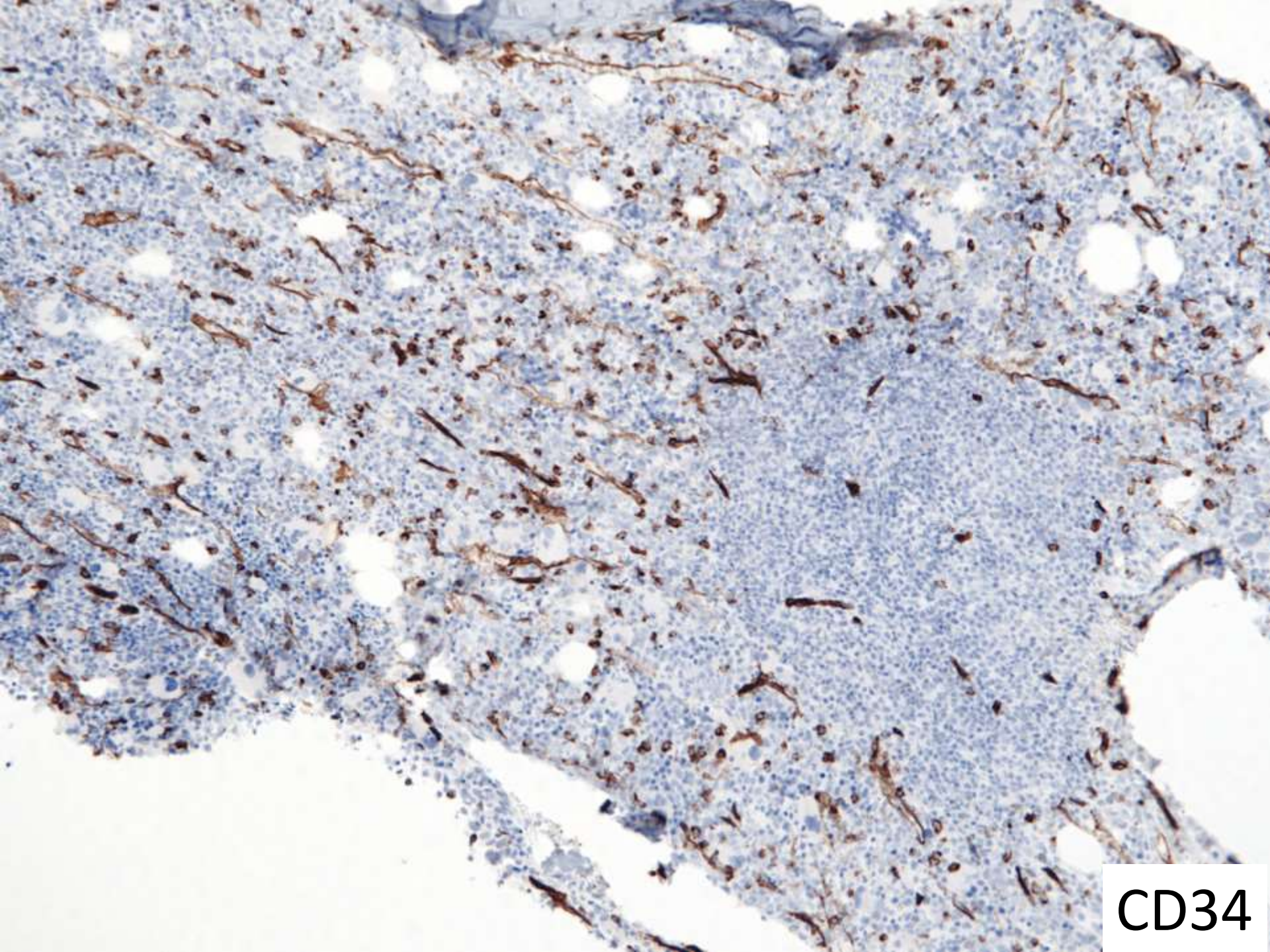


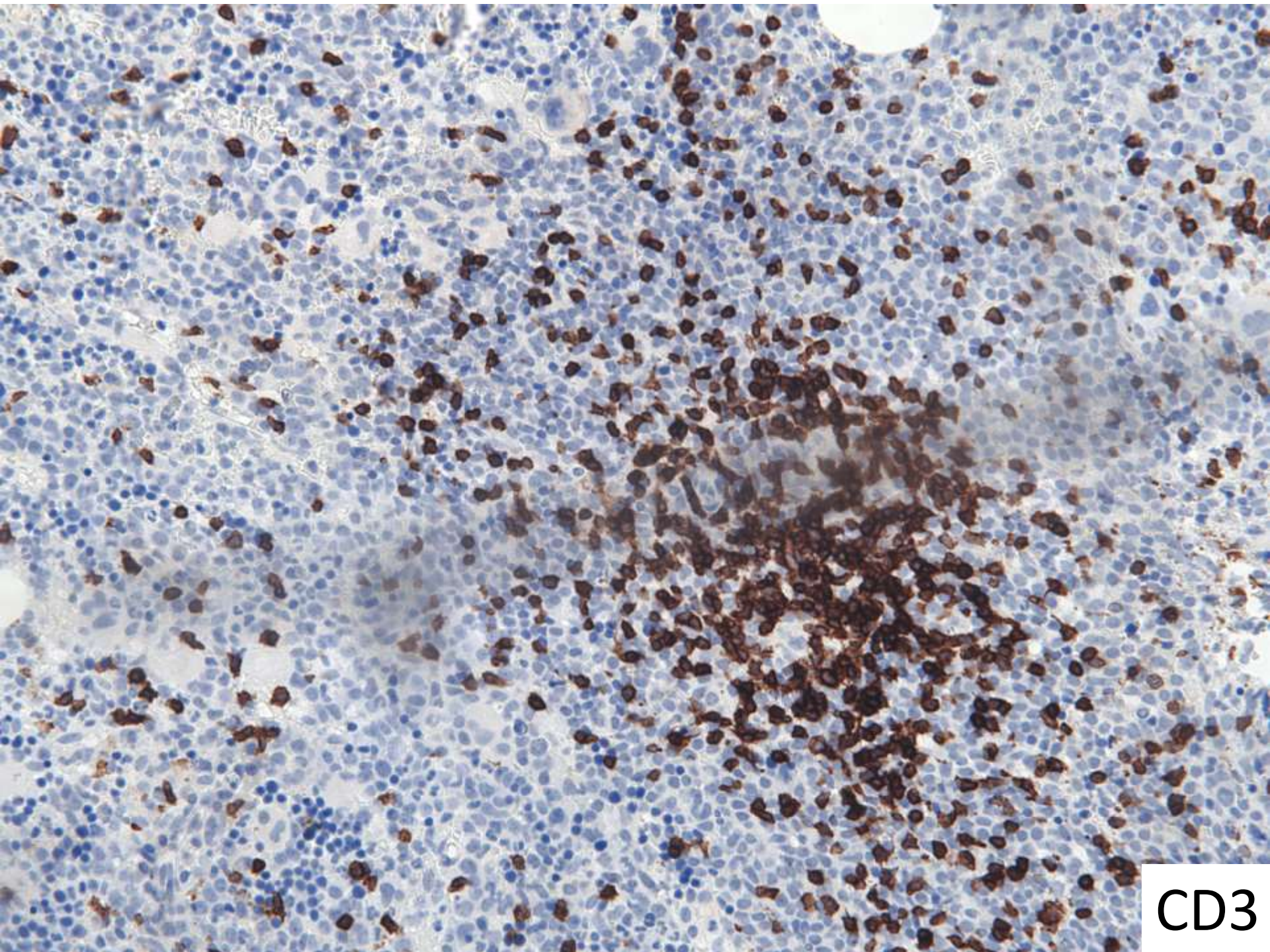


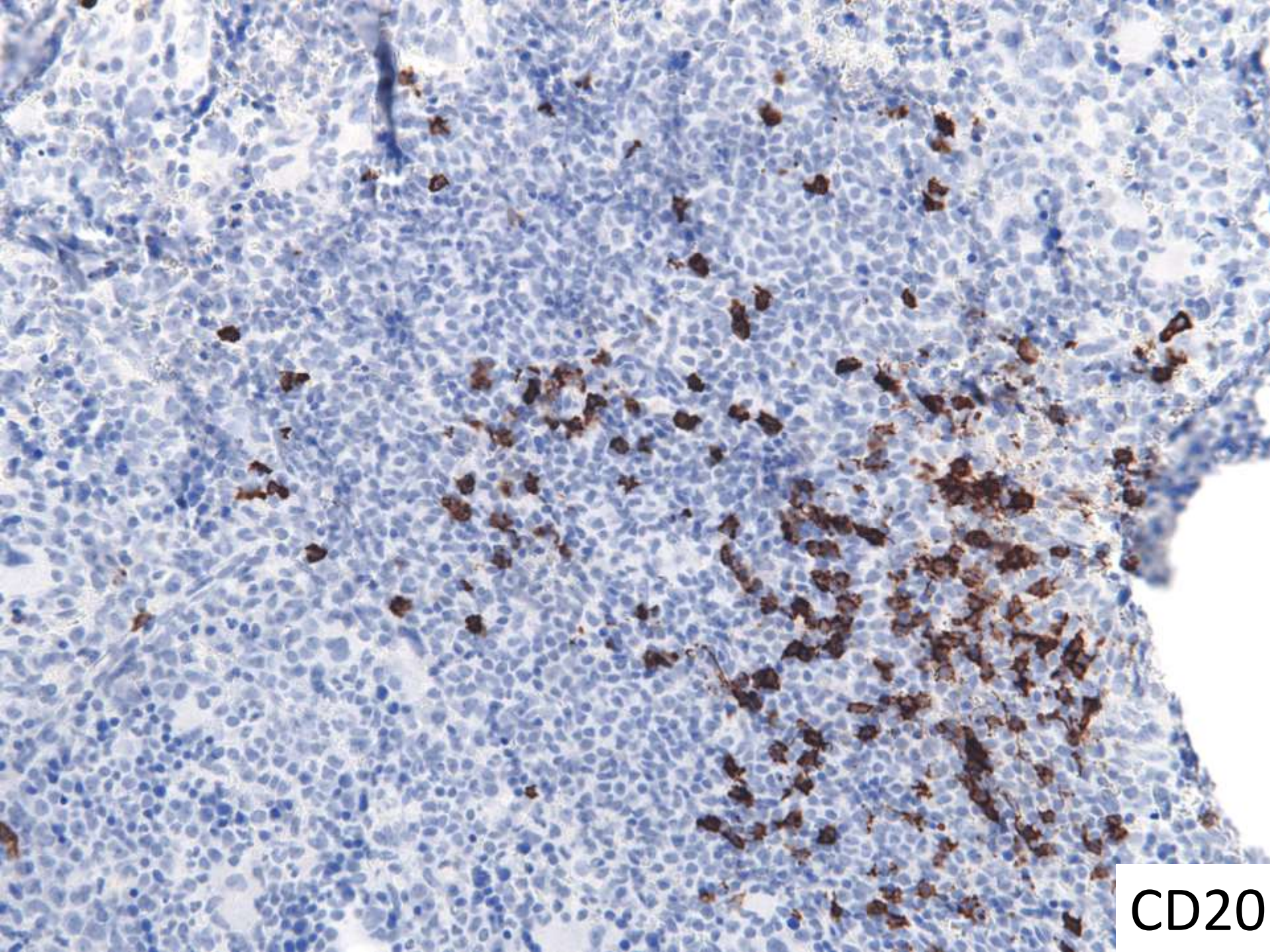


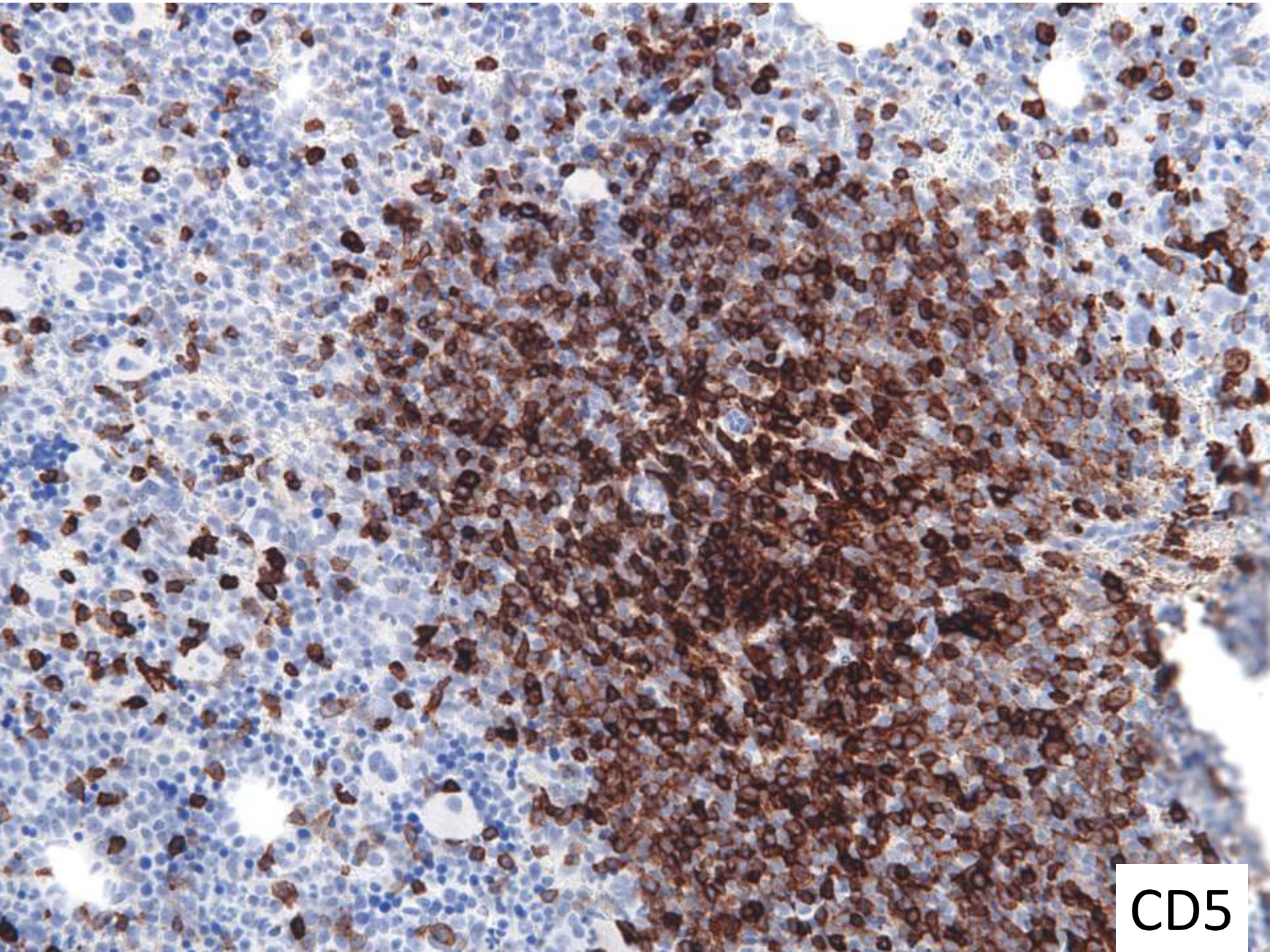


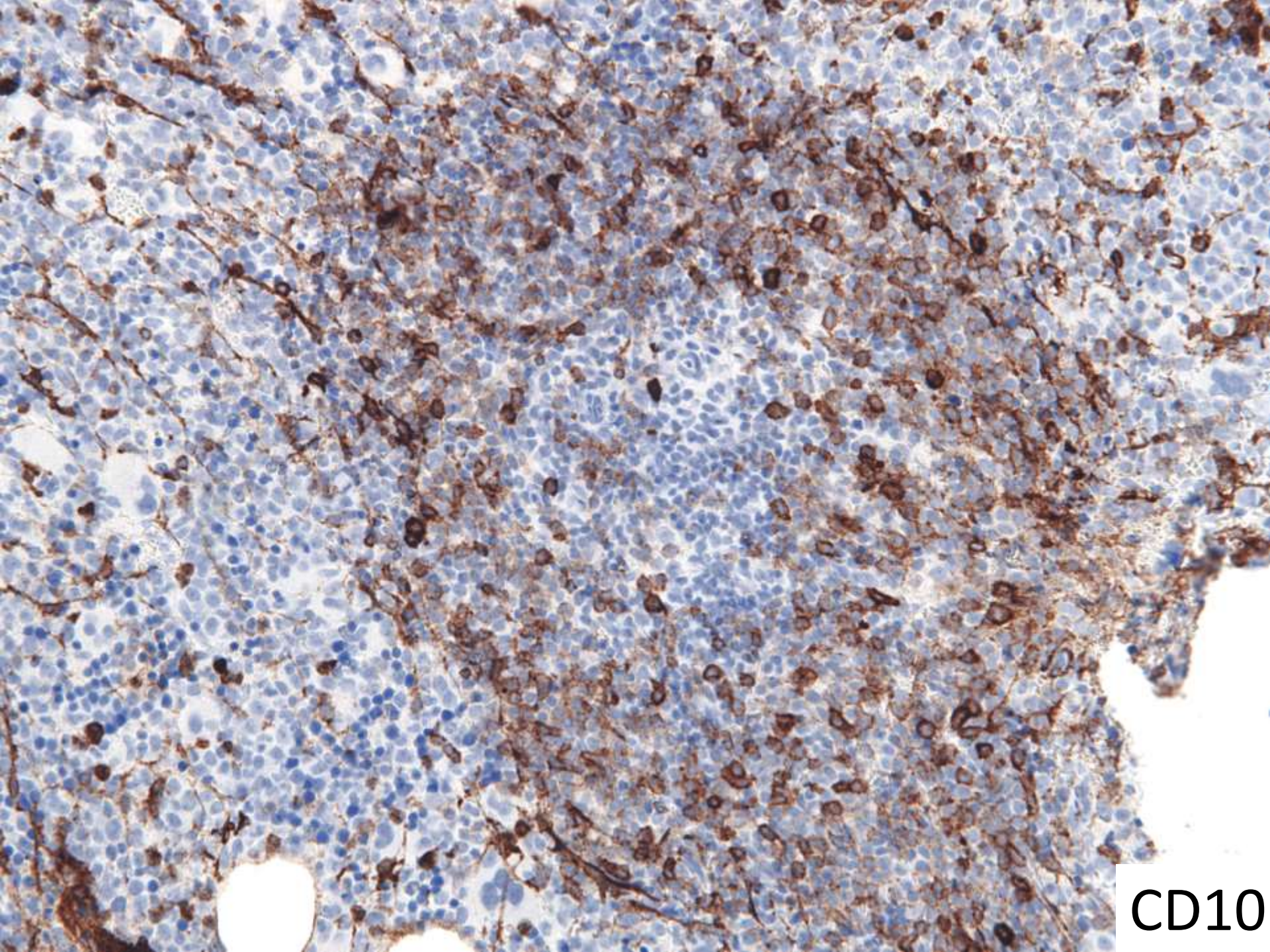



CD34


CD3


CD20


CD5


CD10

Flow cytometry

- Abnormal blast population (5% of total events) that expresses CD45, CD4, CD5, CD34, CD117, CD13, CD33, CD38, CD123, CD11c, and HLA-DR and lacks CD10, CD15, CD64, CD14, CD36, CD64, CD56, CD61, CD235, CD16, and MPO

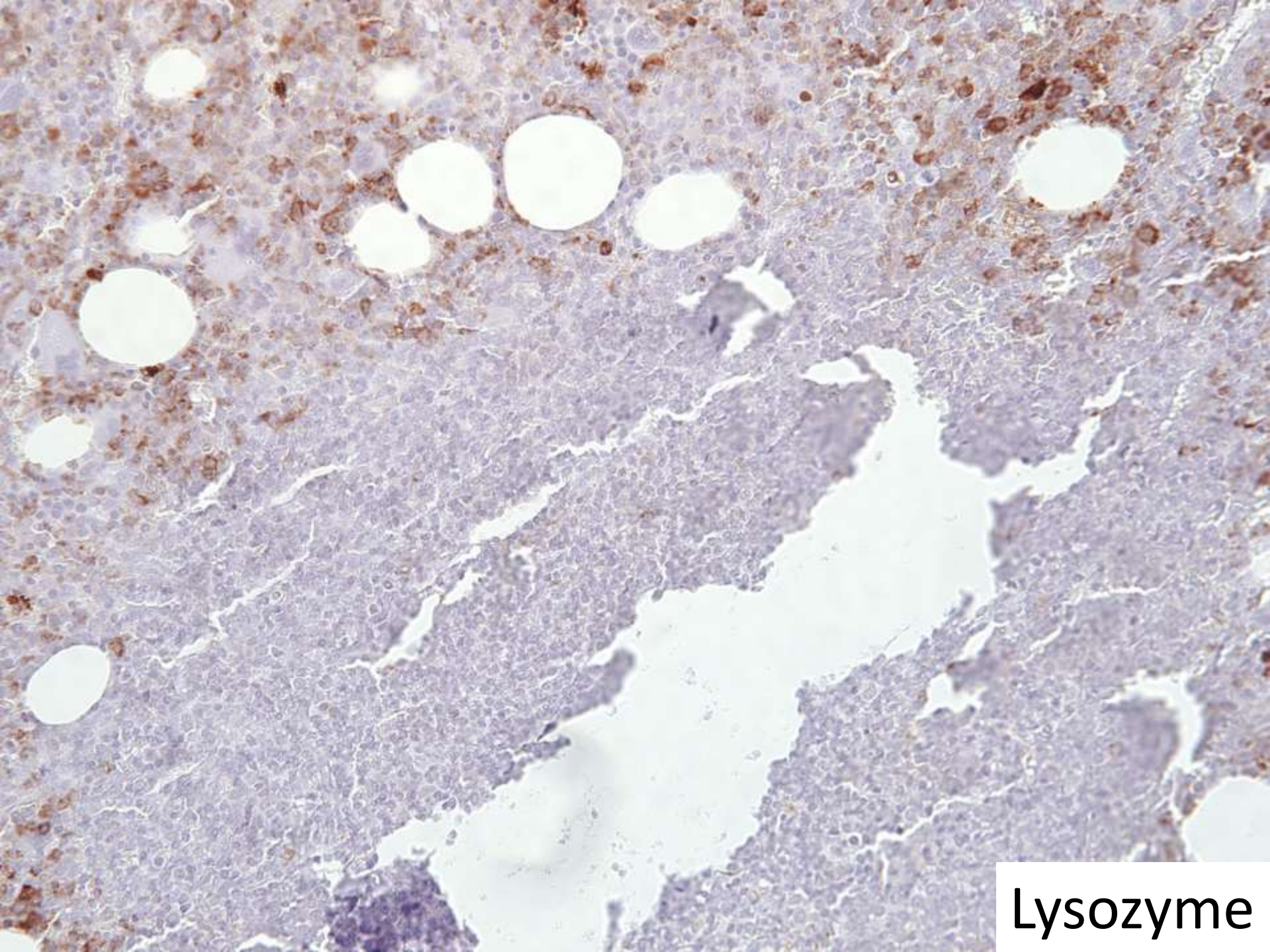
DIAGNOSIS?

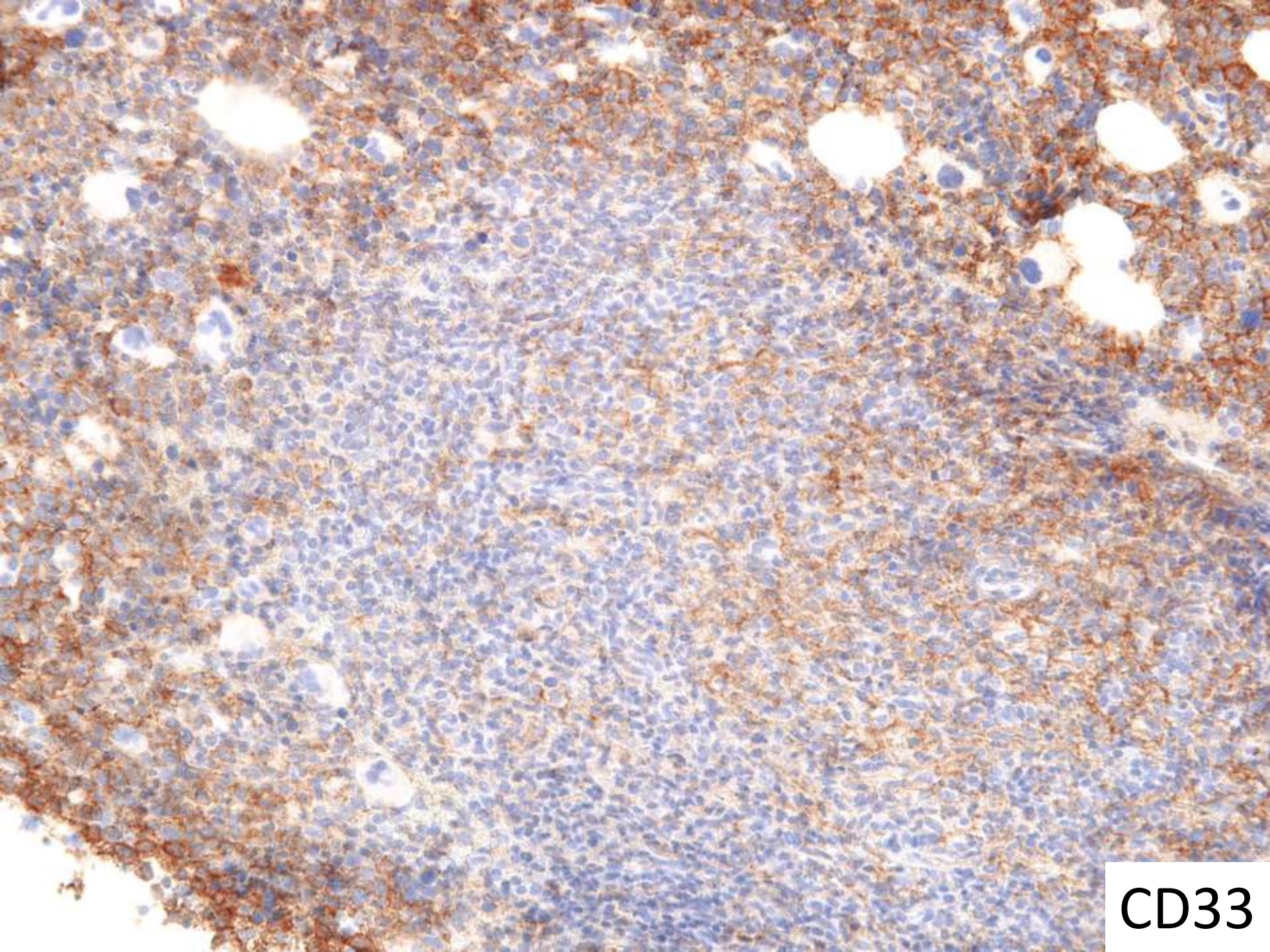
South Bay Case Part 2

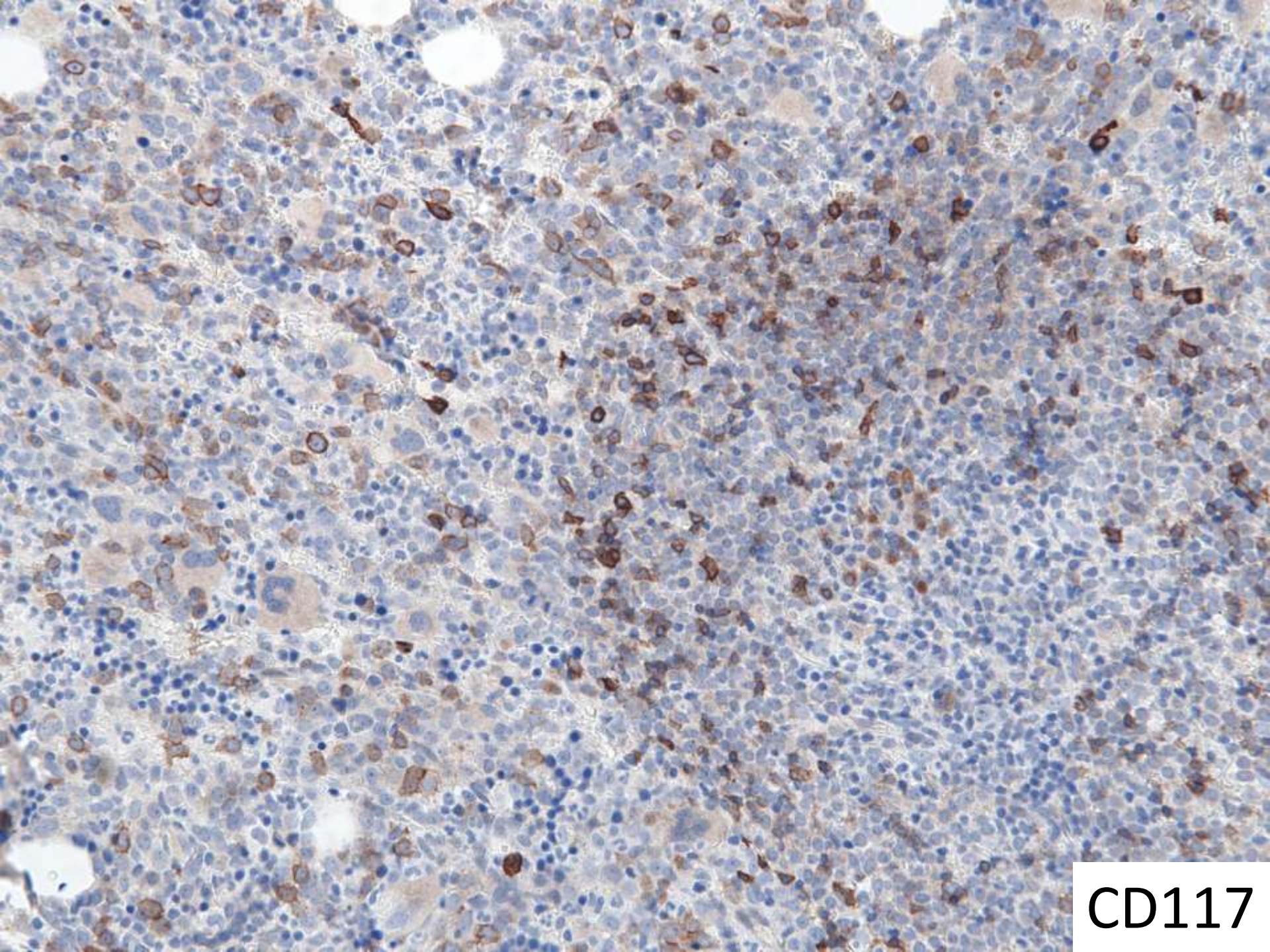
Joshua Menke

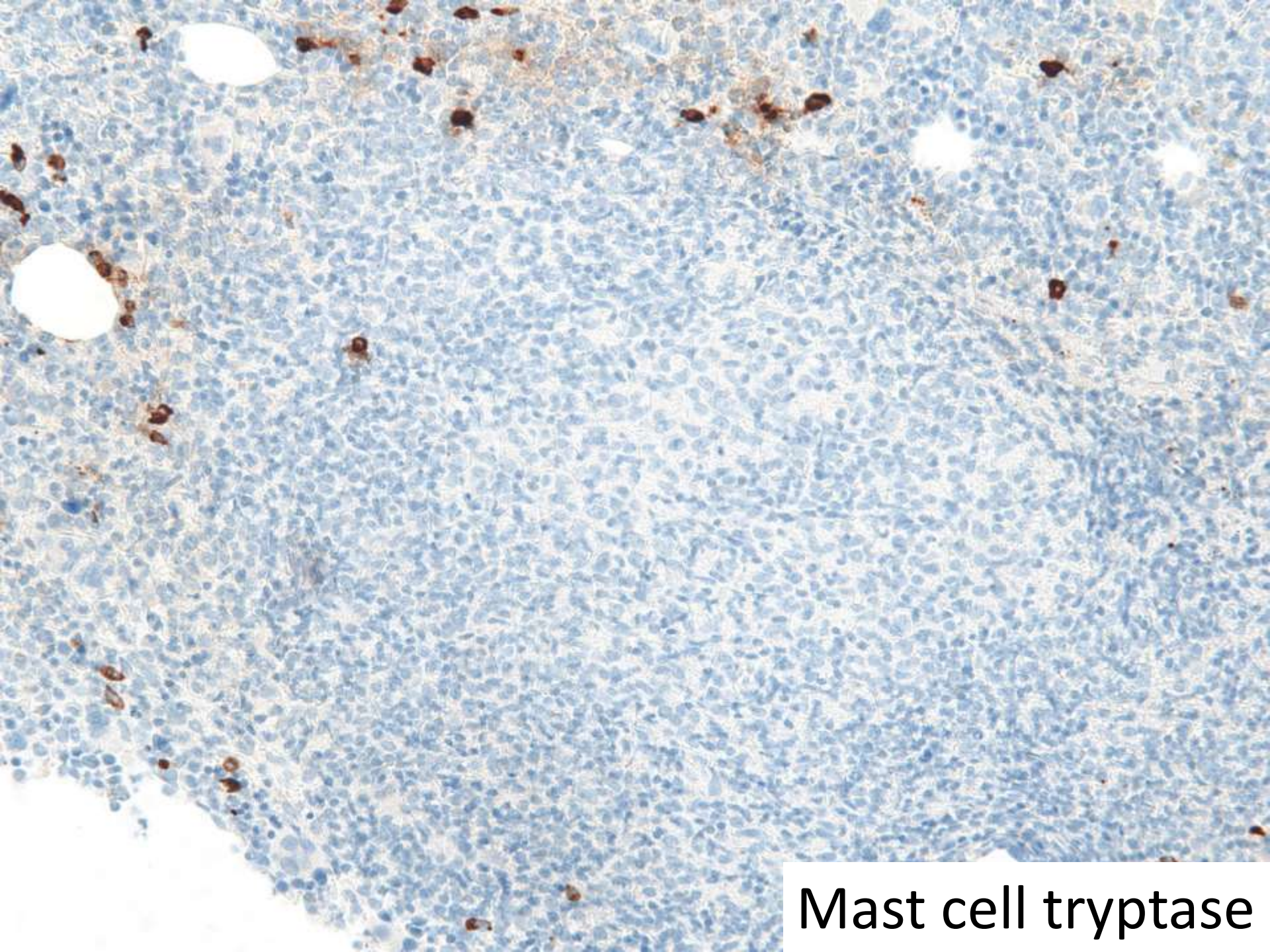
Brent Tan

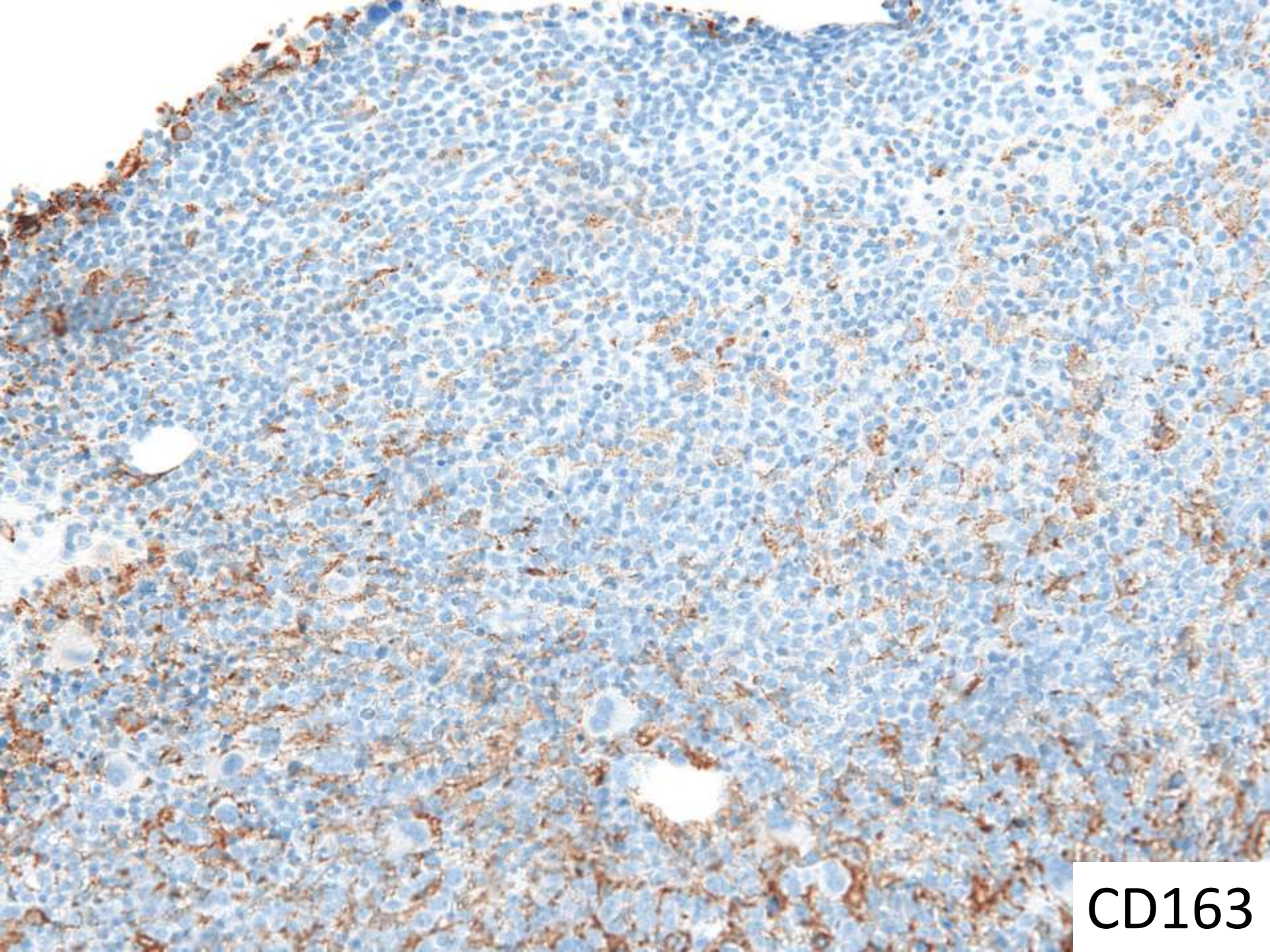
Stanford University

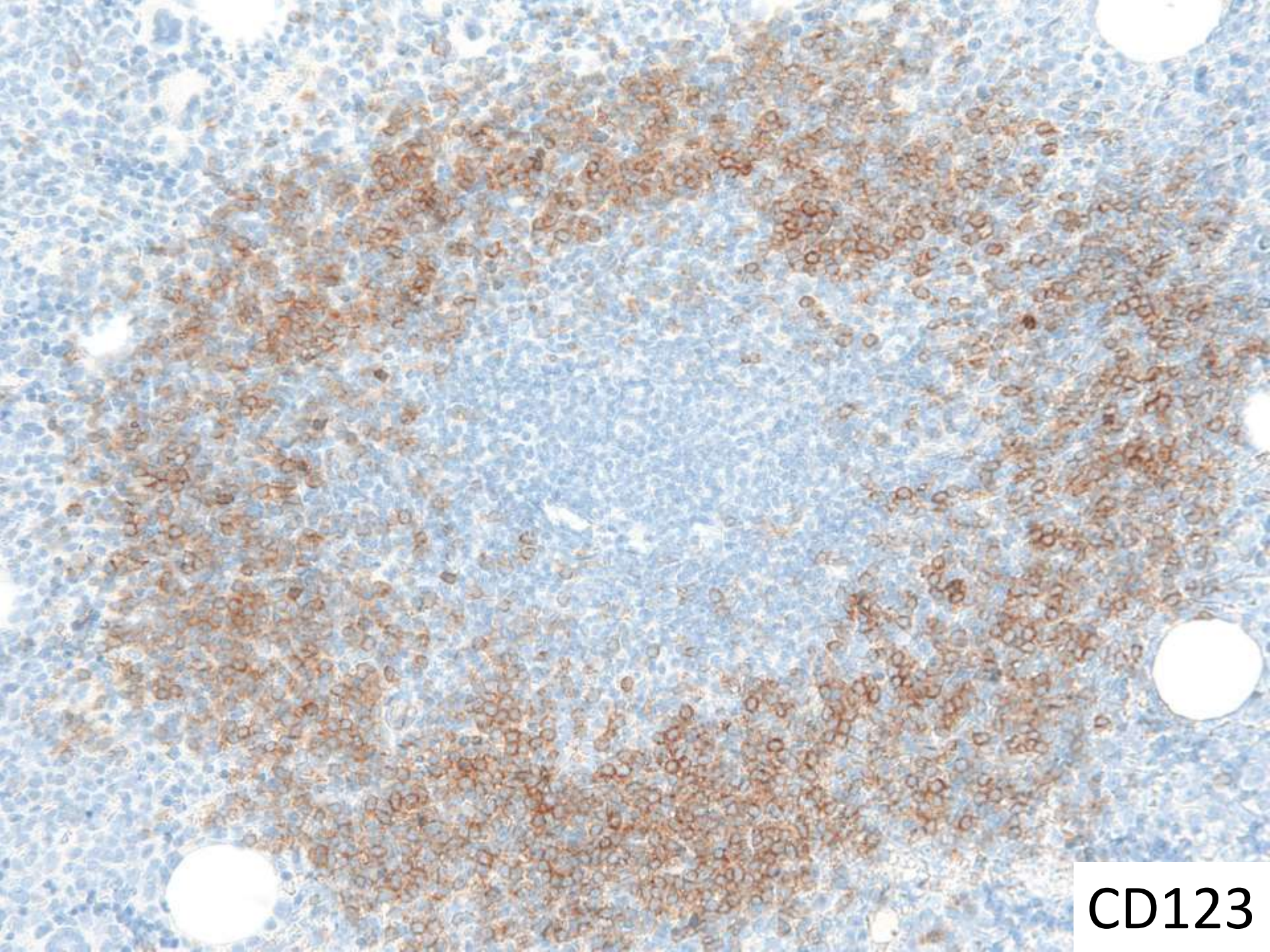

Lysozyme

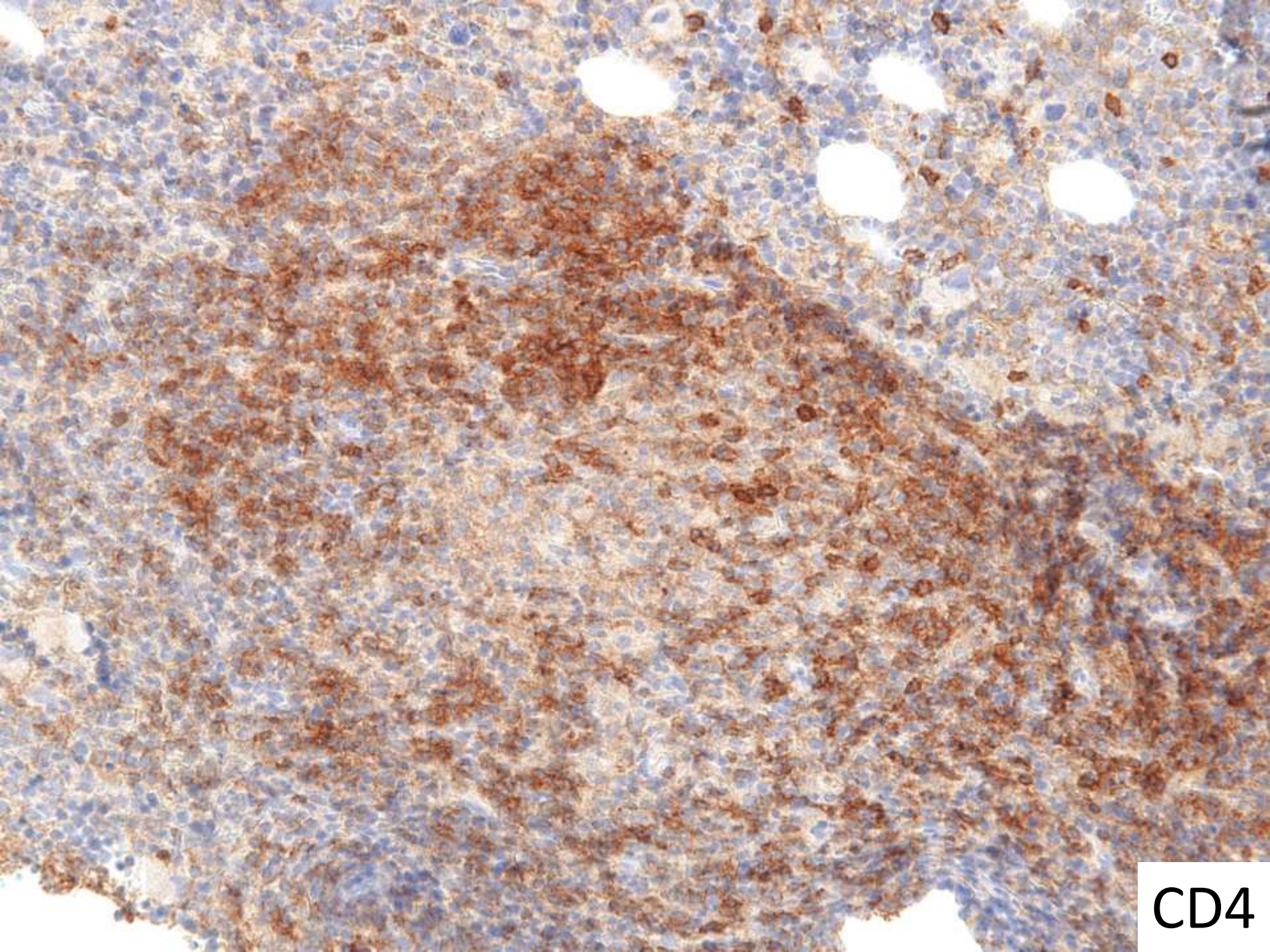

CD33

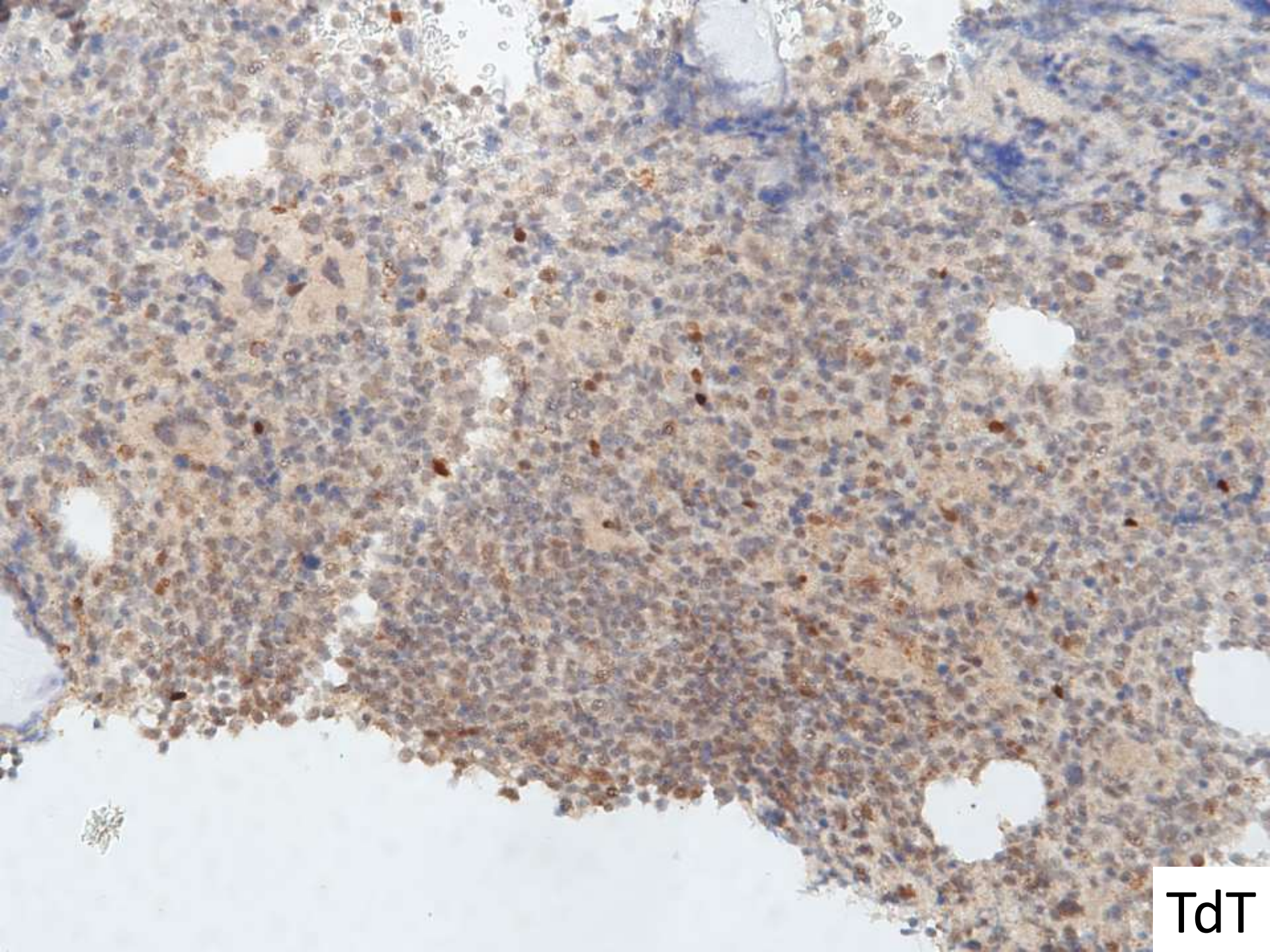

CD117

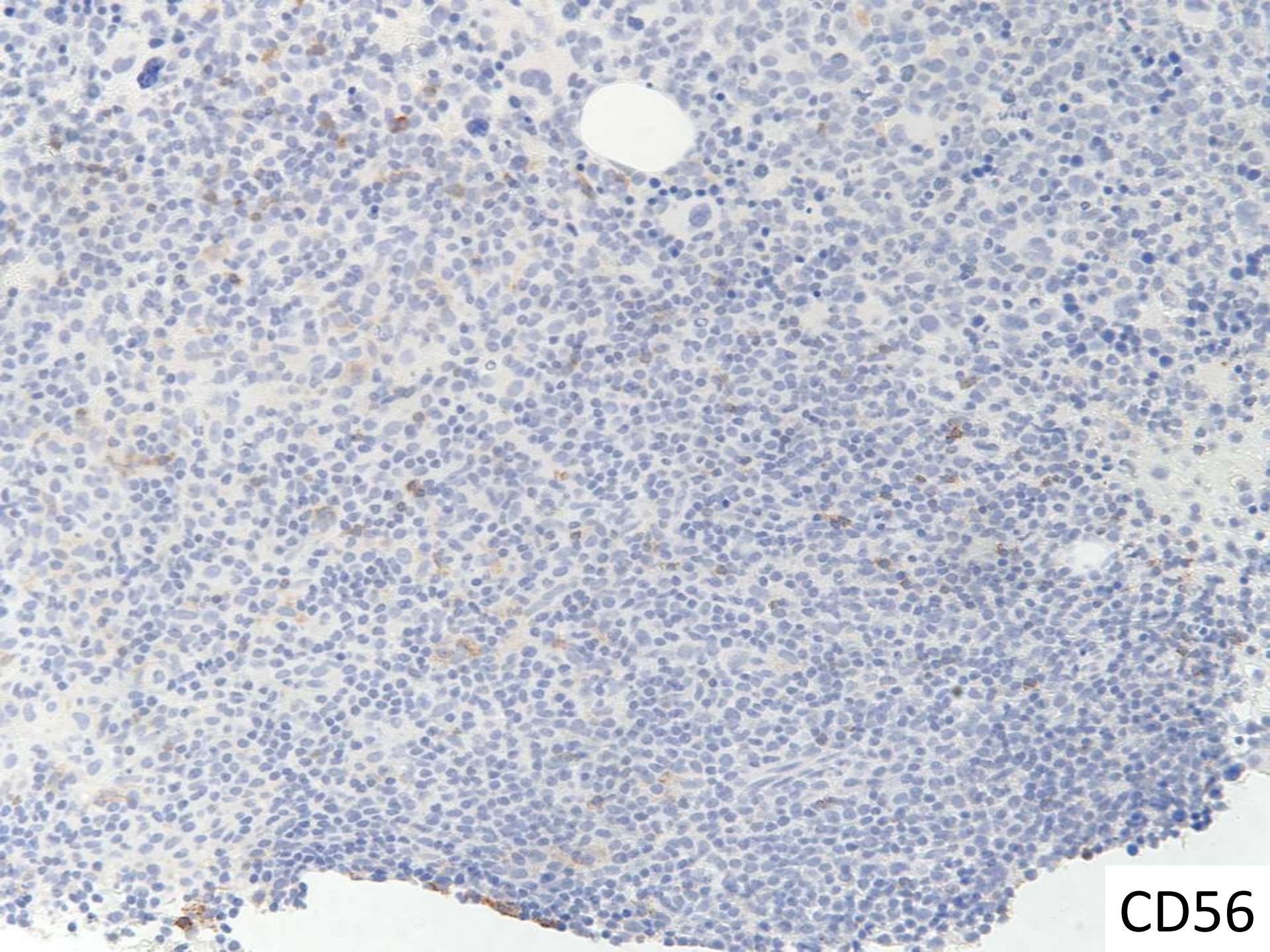

Mast cell tryptase

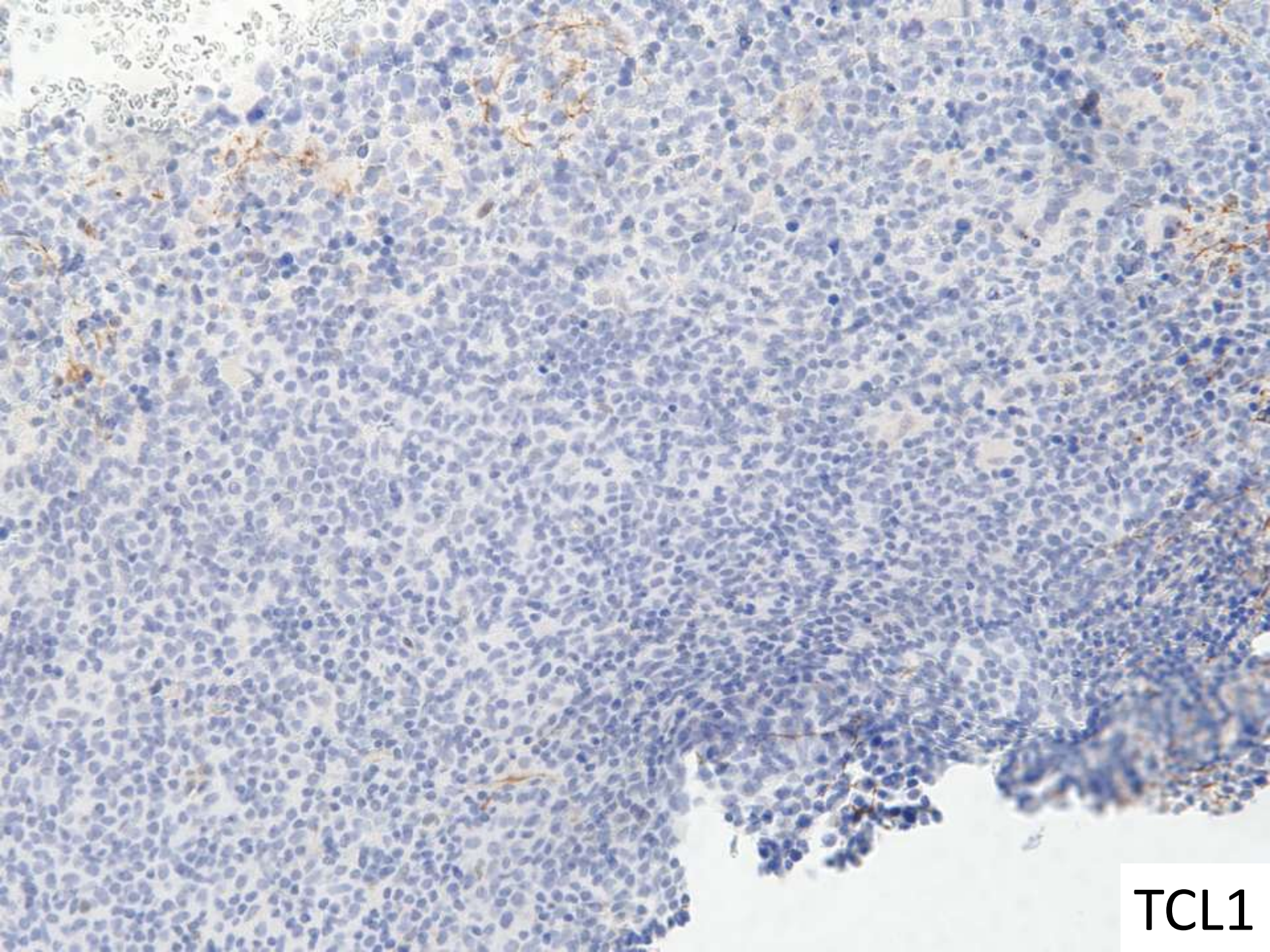

CD163

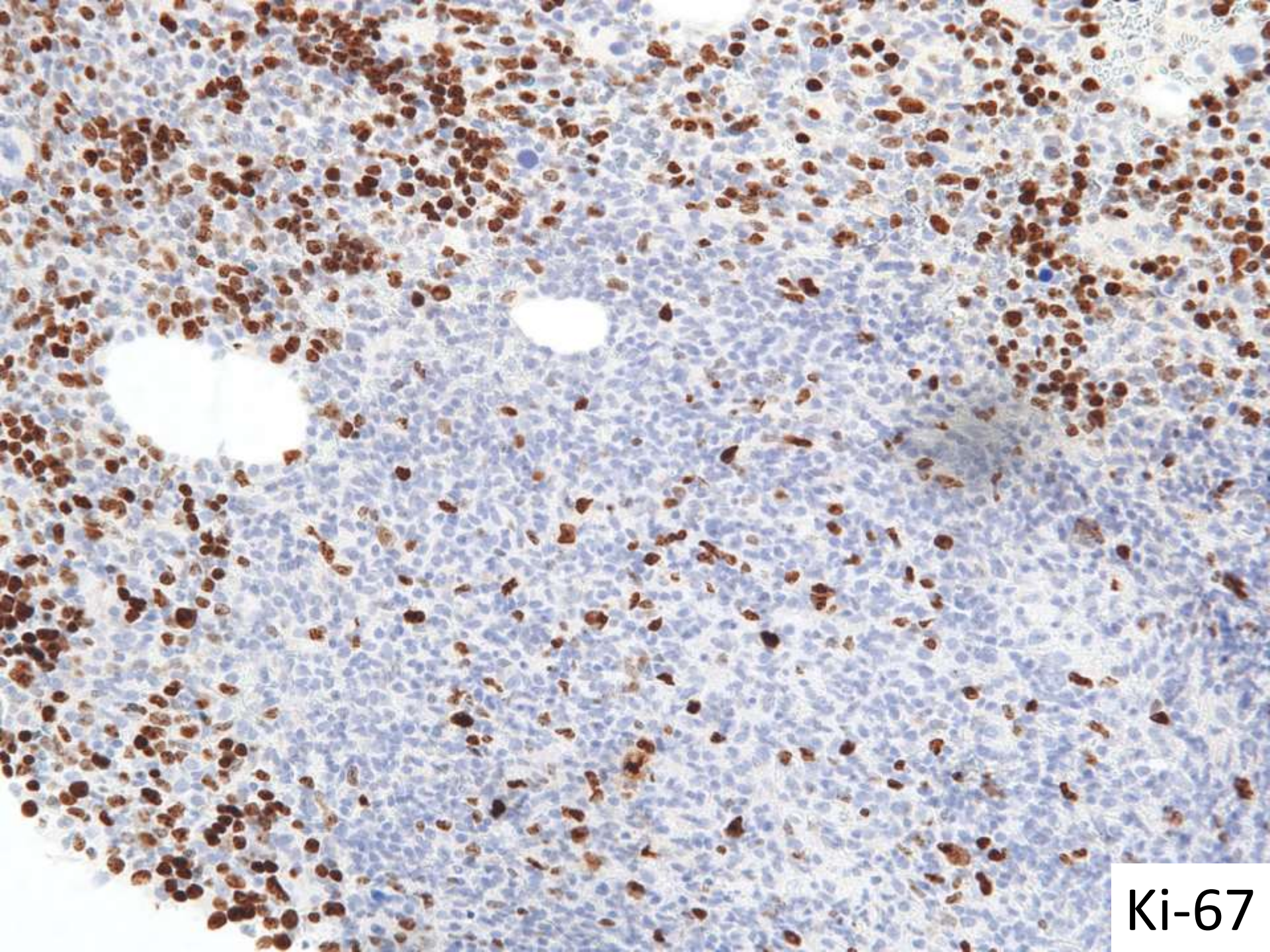

CD123

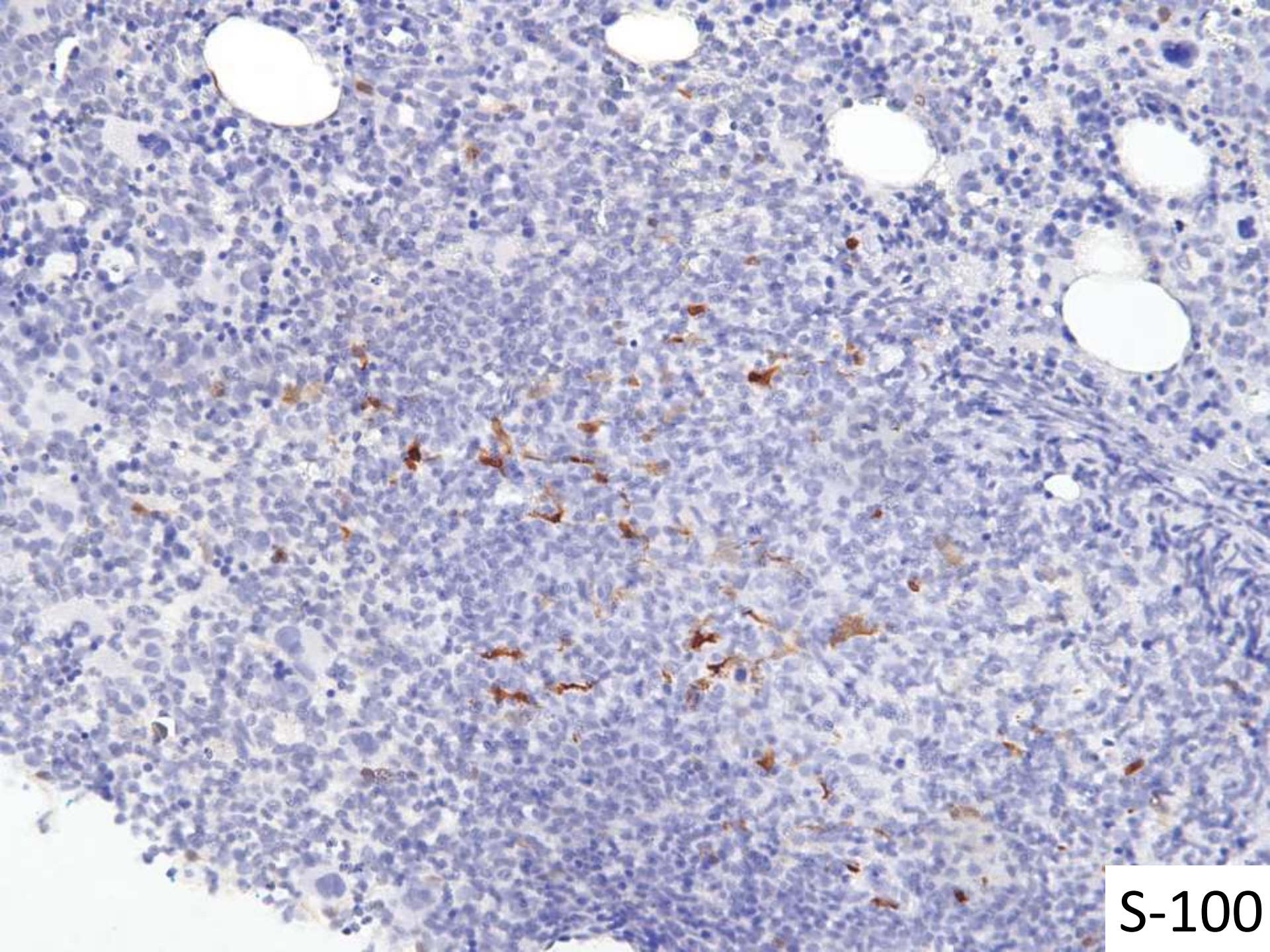

CD4


TdT


CD56


TCL1


Ki-67


S-100

Differential Diagnosis

- Blastic plasmacytoid dendritic cell neoplasm
  - In one large study, only 1/54 cases of BPDCN lacked CD56 expression, the majority had TdT expression, and Ki-67 proliferation rate was greater than 30% in all cases
- Atypical myeloid blast aggregates
  - CD117, CD34, and CD33, which are expressed on the patient's blasts by flow, are negative by immunohistochemistry in the PDC aggregates

Jegalian AG, Adv Anat Pathol, 2009.

Diagnosis: Myeloid neoplasm with atypical plasmacytoid dendritic cell (PDC) proliferation

- Clonal PDC proliferations have been associated with chronic myelomonocytic leukemia and myeloid neoplasms with monocytic differentiation
  - Clonally related to associated myeloid disorder in many cases (e.g. monosomy 7 in both by FISH)
- Form compact, sharply demarcated nodules
- Accumulate in lymph nodes, skin, spleen, marrow
- Prognosis driven by underlying myeloid neoplasm

Vermi W, Am J Surg Pathol 2004;
Jegalian AG, Adv Anat Pathol, 2009.

Comparison of PDC proliferations

Marker	Normal PDCs	"Tumor forming" PDCs	Blastic plasmacytoid dendritic cell neoplasm
CD123	Positive	Positive	Positive
TCL1	Positive	Negative/Positive*	Positive
CD4	Positive	Positive	Positive
CD56	Negative	Negative	Positive
TdT	Negative	Negative	Positive/negative
Ki-67	< 5%	< 10%	> 30%

- "Tumor forming" PDCs may also express aberrant CD2, CD5, CD7, CD10, CD14, or CD15

Modified from Jegalian AG, Adv Anat Pathol, 2009.

References

1. Jegalian AG, Facchetti F, Jaffe ES. Plasmacytoid dendritic cells: physiologic roles and pathologic states. Adv Anat Pathol. 2009 Nov;16(6):392-404. doi:10.1097/PAP.0b013e3181bb6bc2. Review. PubMed PMID: 19851130.

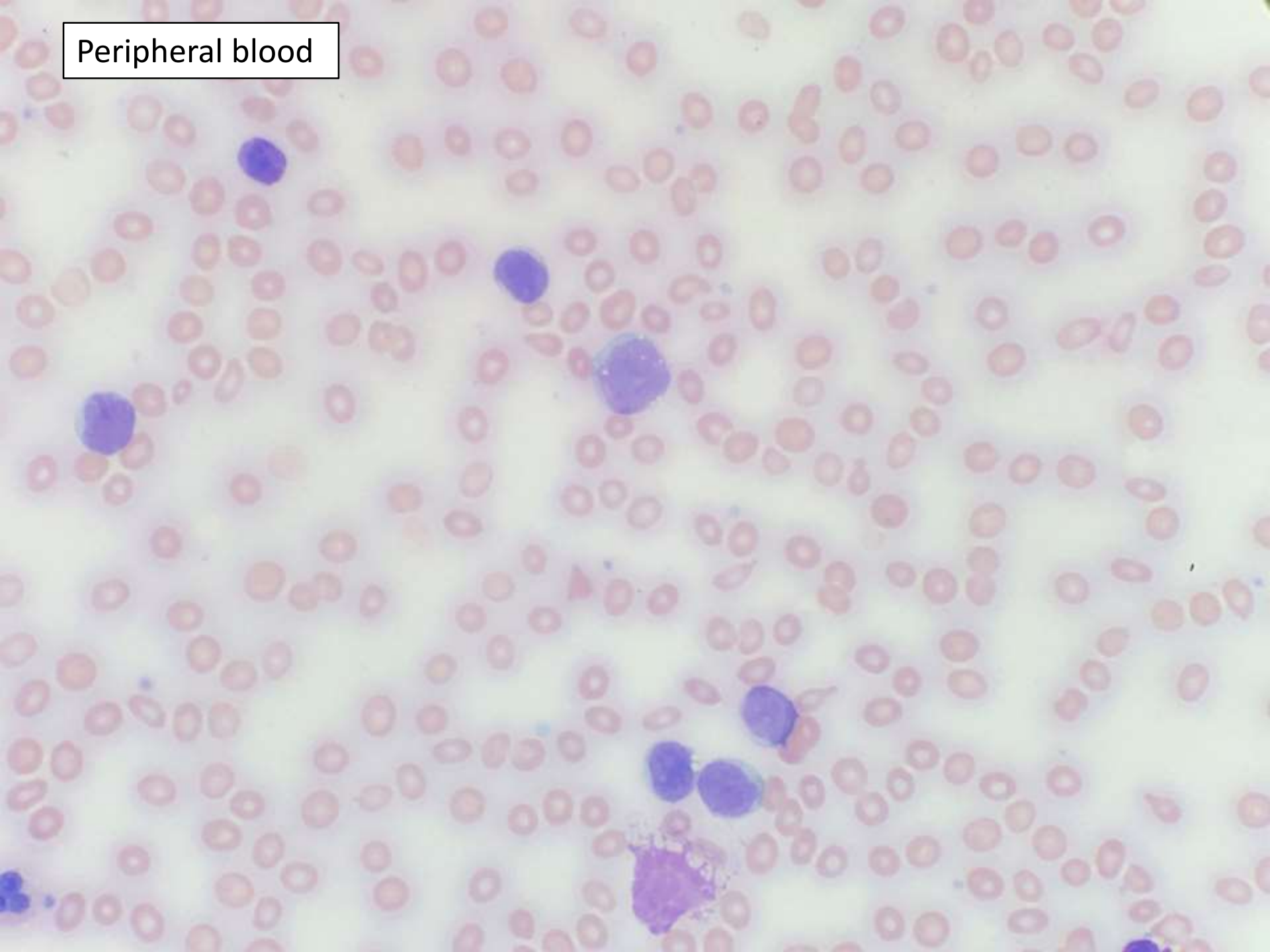
2. Vermi W, Facchetti F, Rosati S, Vergoni F, Rossi E, Festa S, Remotti D, Grigolato P, Massarelli G, Frizzera G. Nodal and extranodal tumor-forming accumulation of plasmacytoid monocytes/interferon-producing cells associated with myeloid disorders. Am J Surg Pathol. 2004 May;28(5):585-95. PubMed PMID: 15105645.

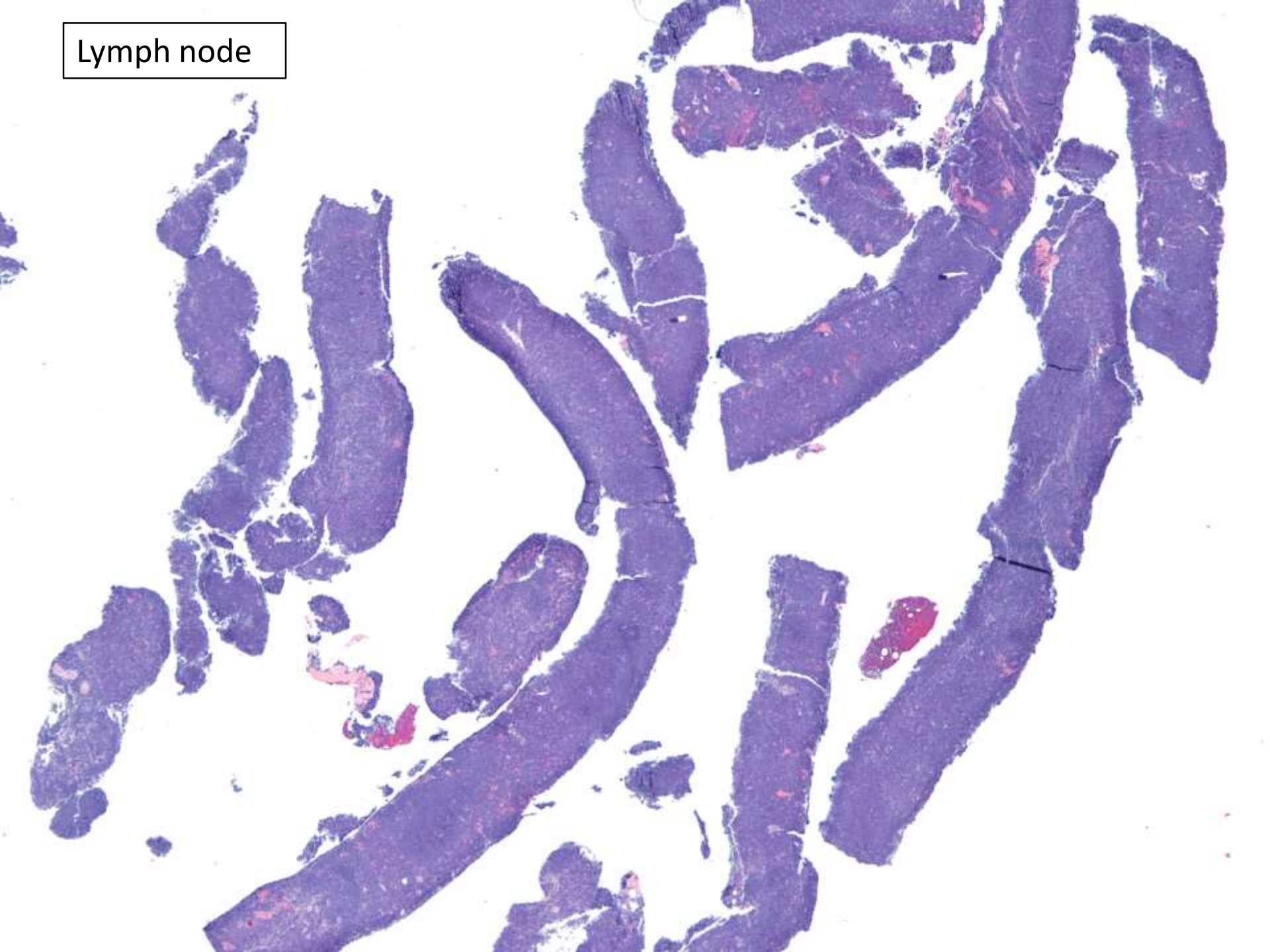
SB 6306

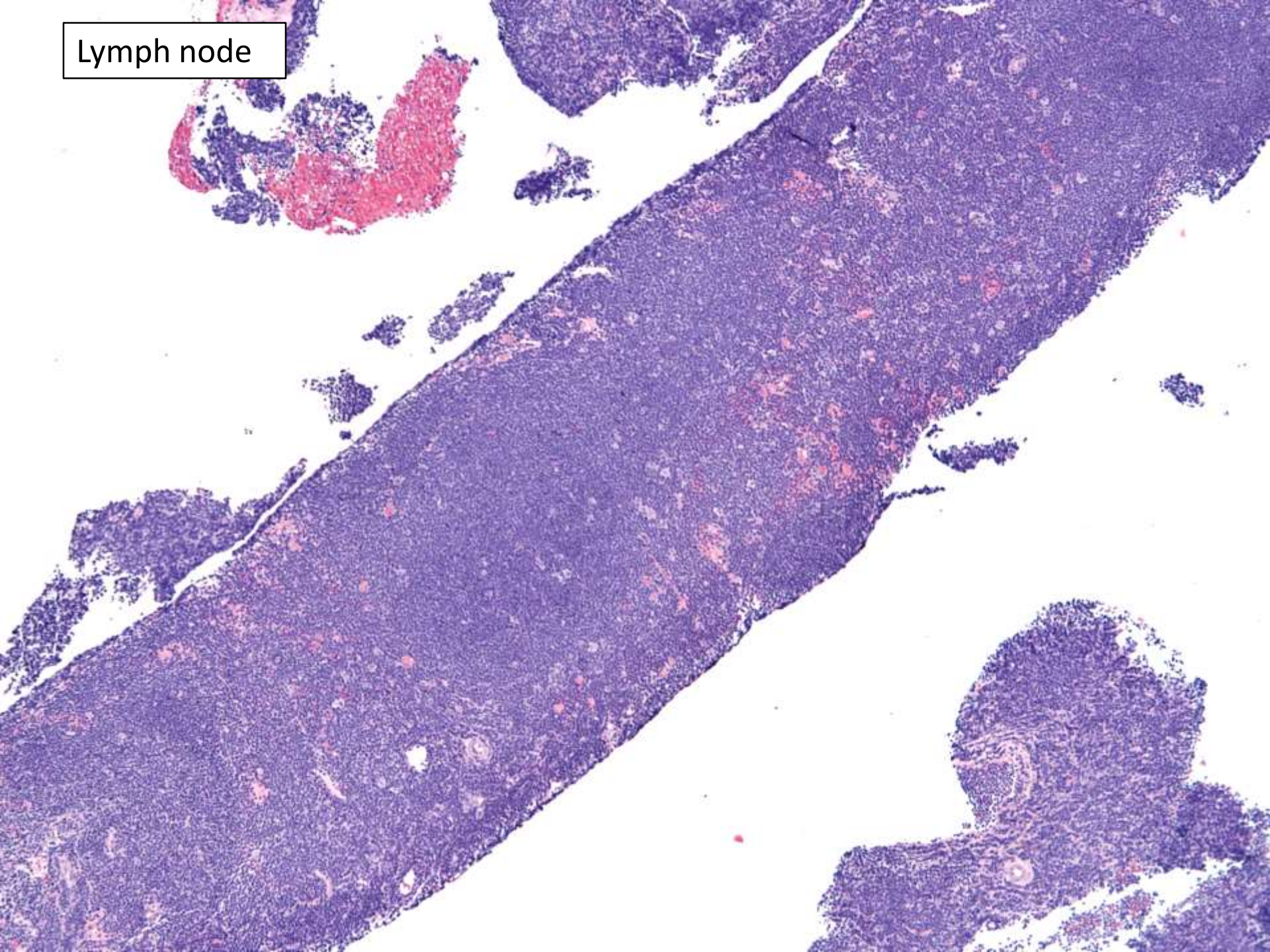
Lhara Lezama/Dita Gratzinger; Stanford

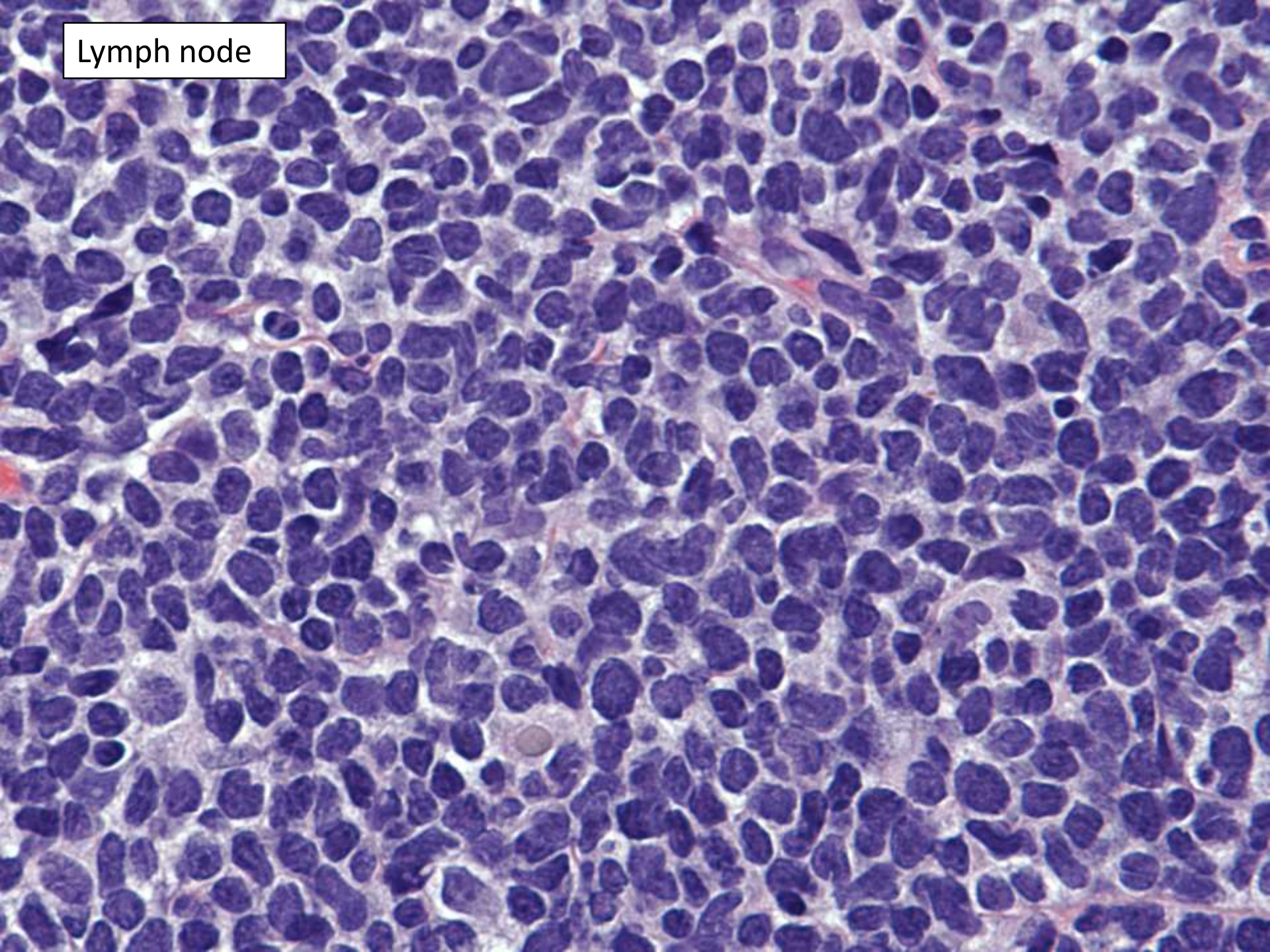
69-year-old male with large left axillary mass. Lymph node and peripheral blood submitted.


Peripheral blood

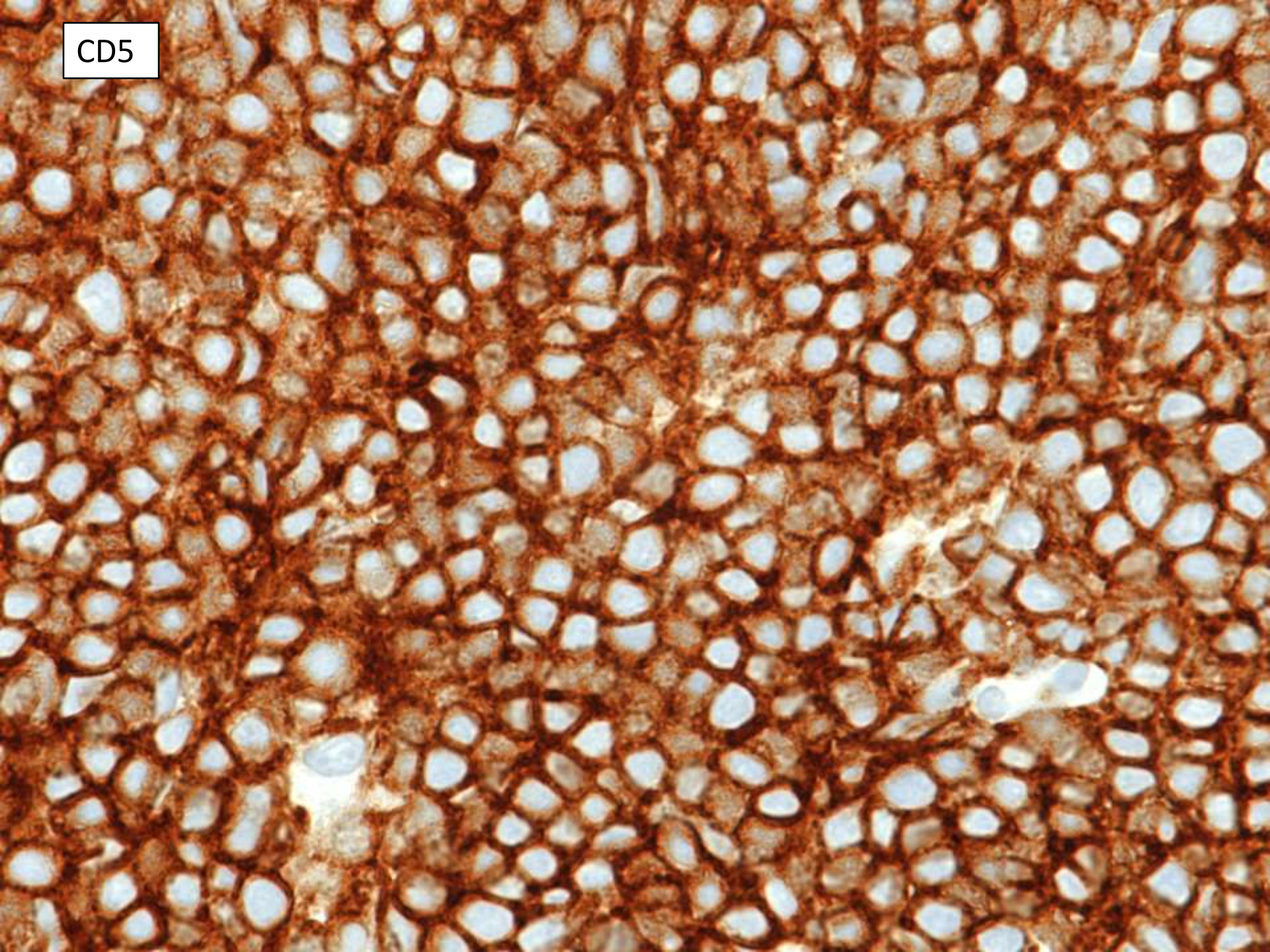

Peripheral blood


Lymph node

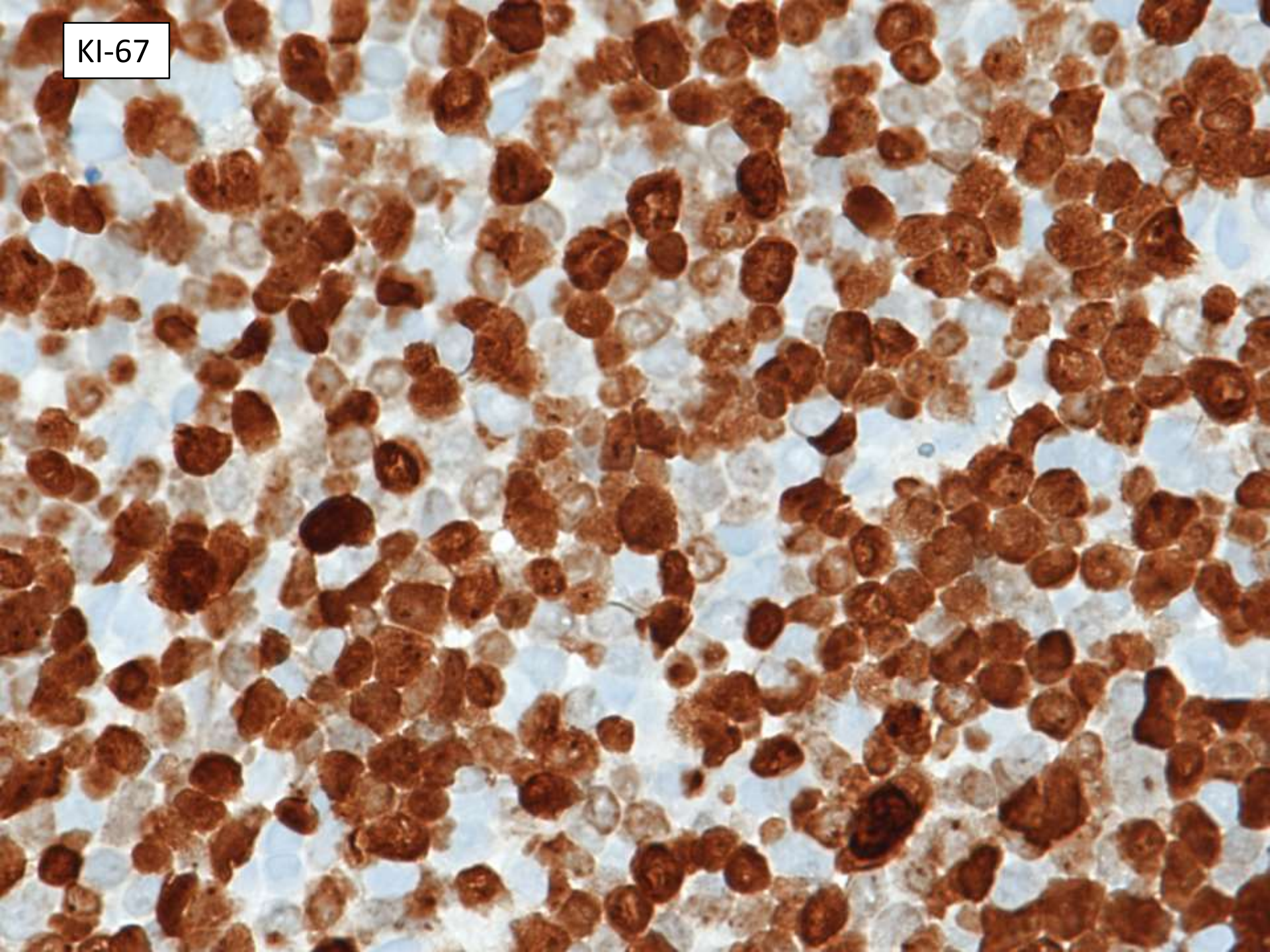

Lymph node


Lymph node


CD20


CD5


SOX11


KI-67

DIAGNOSIS?

SB 6306

September 2018

Lhara Lezama MD (PGY-5)

Stanford MEDICINE

Diagnosis:

Blastoid variant of mantle cell lymphoma

Flow cytometric findings

The peripheral blood show an atypical kappa-restricted B-cell population that ***expresses CD5, CD10 (bright), CD19, CD20, CD22 (dim), CD79a (variable), partial CD38, and kappa light chains,*** and do not express CD3, CD8 , CD4, CD16, CD13, CD56, CD34, HLA-DR, CD117, CD15, TdT, or MPO.

Immunohistochemistry

IHC study	Result
CD20	Positive
BCL2	Positive
CD5	Positive
SOX11	Positive
BCL1	Negative
BCL6	Negative
CD23	Negative
CD10	Negative
Ki-67	90-95%

Blastoid variant of mantle cell lymphoma

- Characterized by a monotonous population of medium-sized lymphocytes with scant cytoplasm, round nuclei with finely dispersed chromatin, and inconspicuous nucleoli.
- May resemble lymphoblastic lymphoma or nodal involvement by acute myeloid leukemias.
- Immunophenotyping may display CD23 and CD10 positivity and CD5 negativity in a subset.
- Genetic analysis demonstrates an increased number of complex genetic alterations.
- Responds poorly to conventional chemotherapy and has a short duration of response.

Case follow-up

6/21/2018 Hospitalization with tumor lysis syndrome and possible GI bleed that has since resolved, with hospital course complicated by neutropenic fevers, rash, acute kidney injury.

7/5/2018 Skin biopsy showed interface dermatitis and mantle cell lymphoma in dermis.

7/17/2018 Status post palliative treatment of lymphoma complicated by tumor lysis syndrome and on-going rash. Discharged to home with hospice.

Take-home Points

- The *proliferative activity* is the most important prognostic parameter in MCL.
- Cases with *complex karyotypes* have a more aggressive course.
- Blastoid variants are associated with other parameters related to poor prognosis, such as ***high proliferative activity, increased cytogenetic alterations, and molecular alterations in tumor suppressor genes.***

References

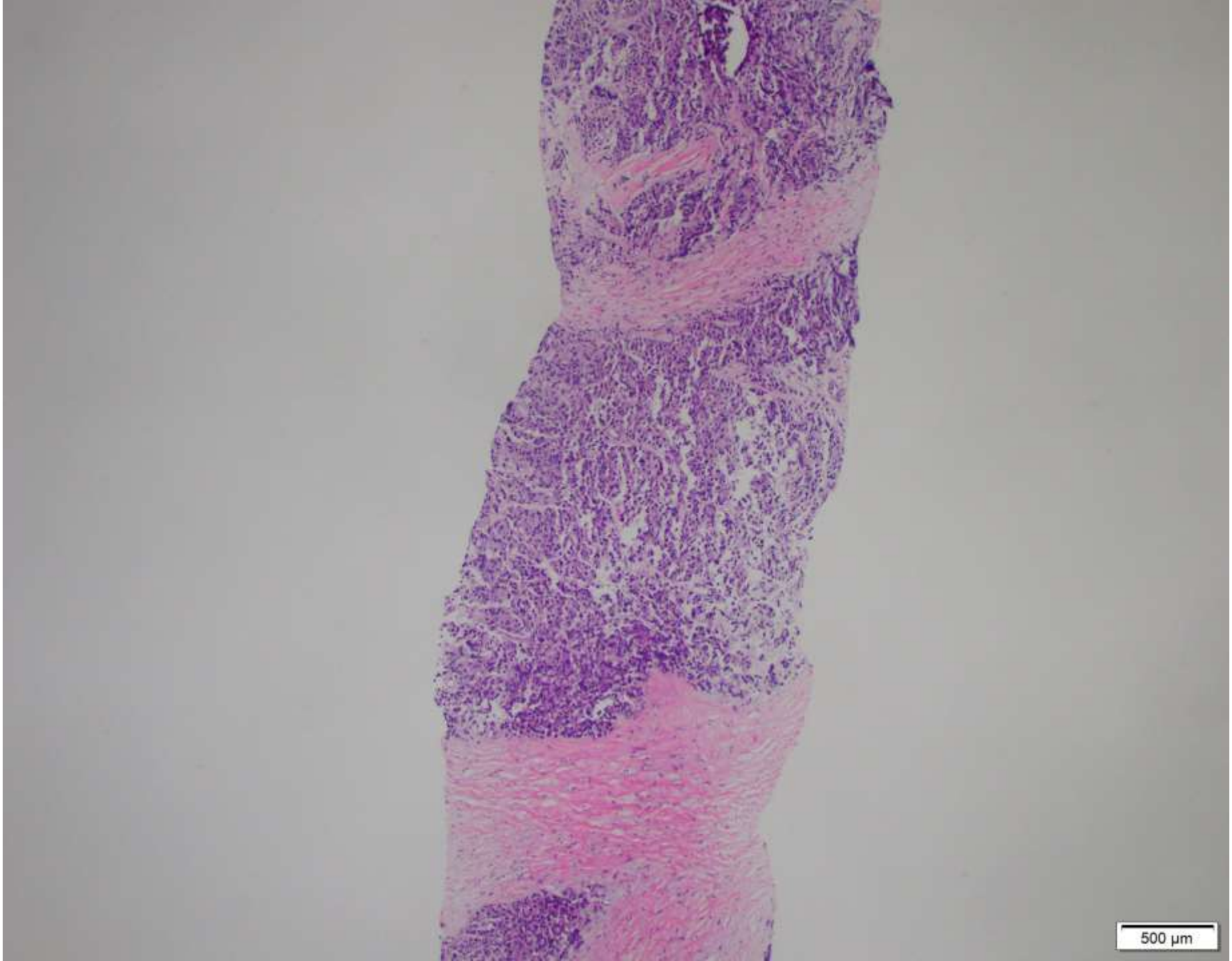
1. Bhatt, V. R. et al. Clinicopathologic features, management and outcomes of blastoid variant of mantle cell lymphoma: a Nebraska Lymphoma Study Group Experience. *Leuk. Lymphoma* **57**, 1327–1334 (2016).

2. Shrestha, R., Bhatt, V. R., Guru Murthy, G. S. & Armitage, J. O. Clinicopathologic features and management of blastoid variant of mantle cell lymphoma. *Leuk. Lymphoma* **56**, 2759–2767 (2015).

SB 6307

Jim Mathews; Kaiser Antioch

Adult male with mediastinal mass biopsy.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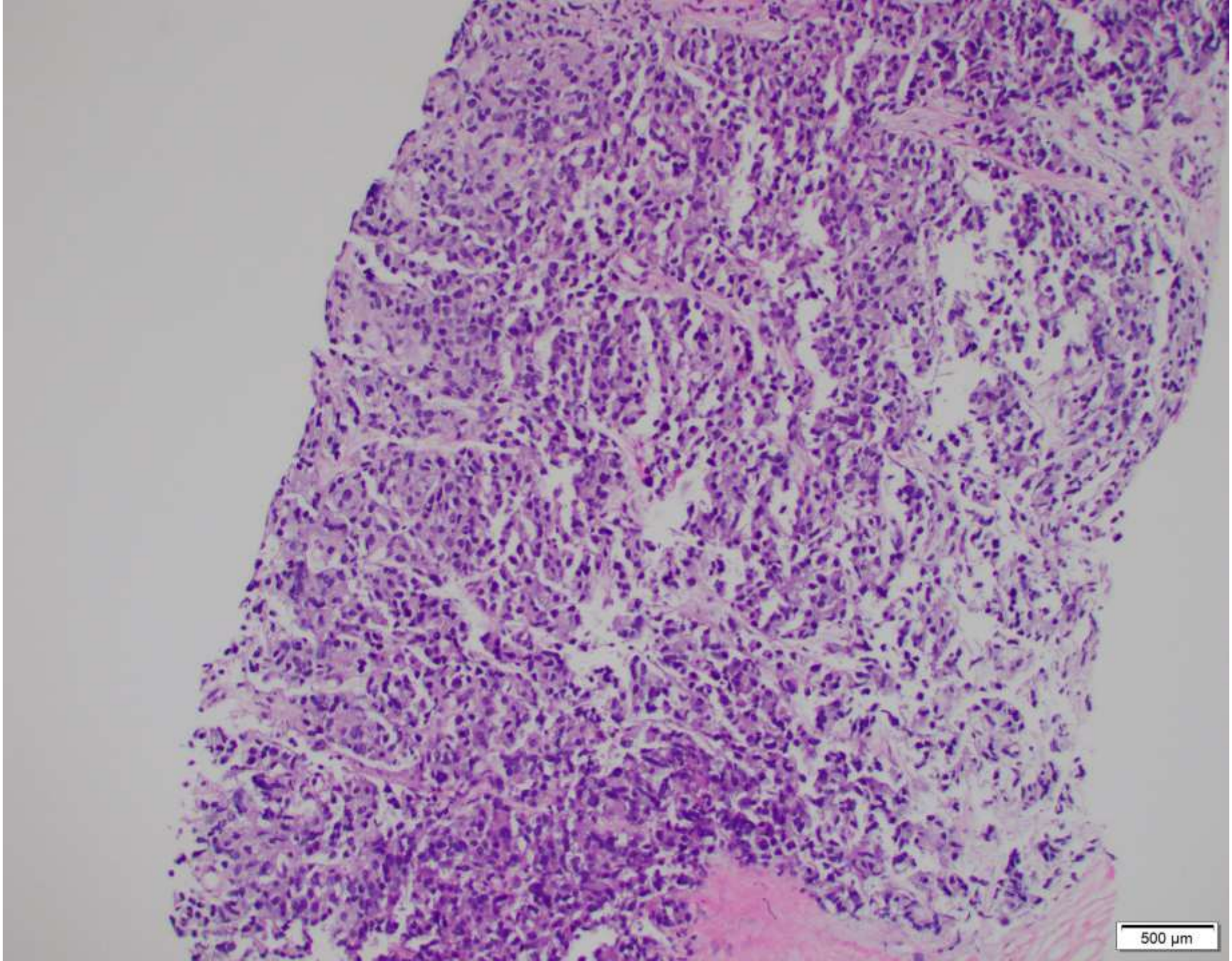
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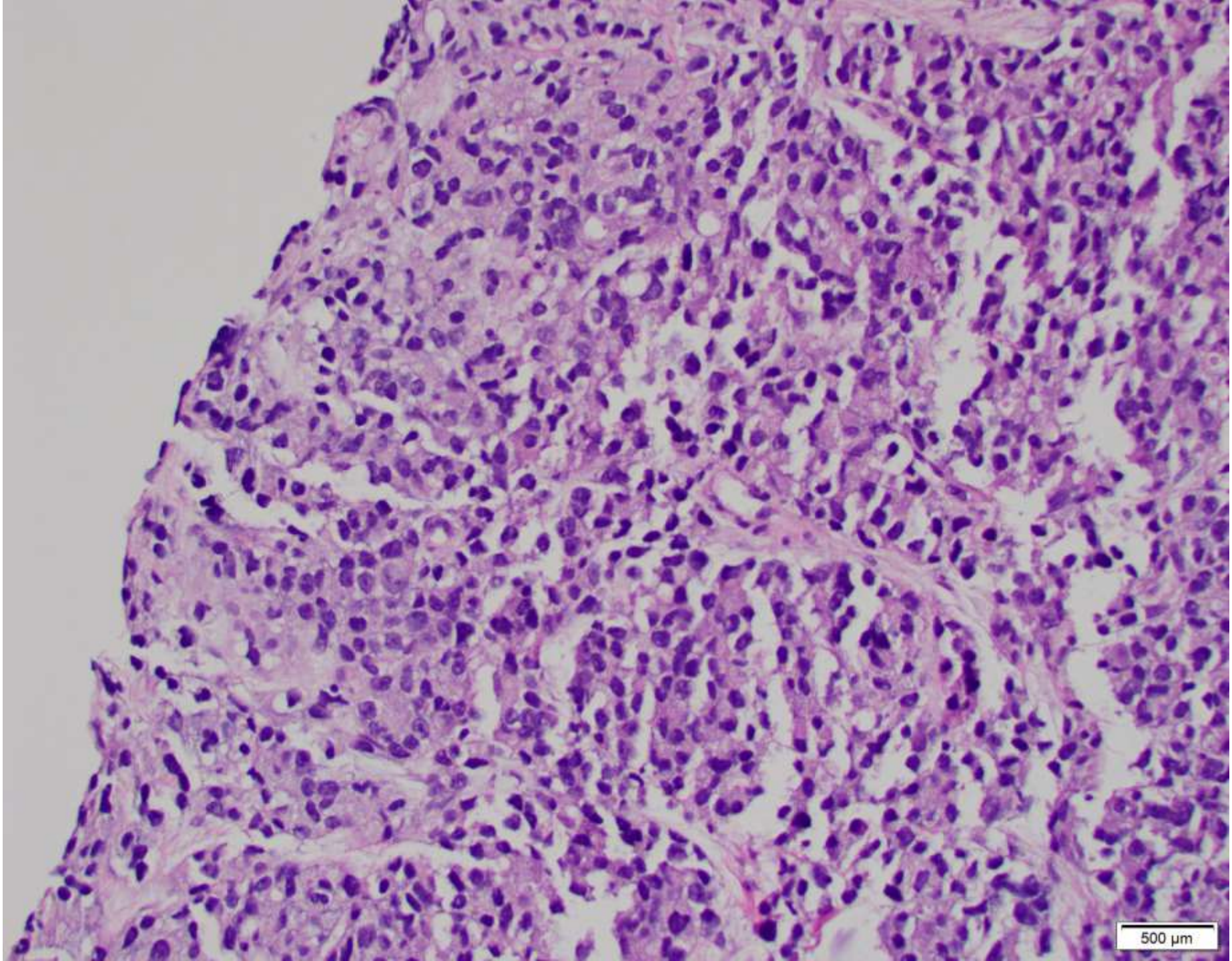
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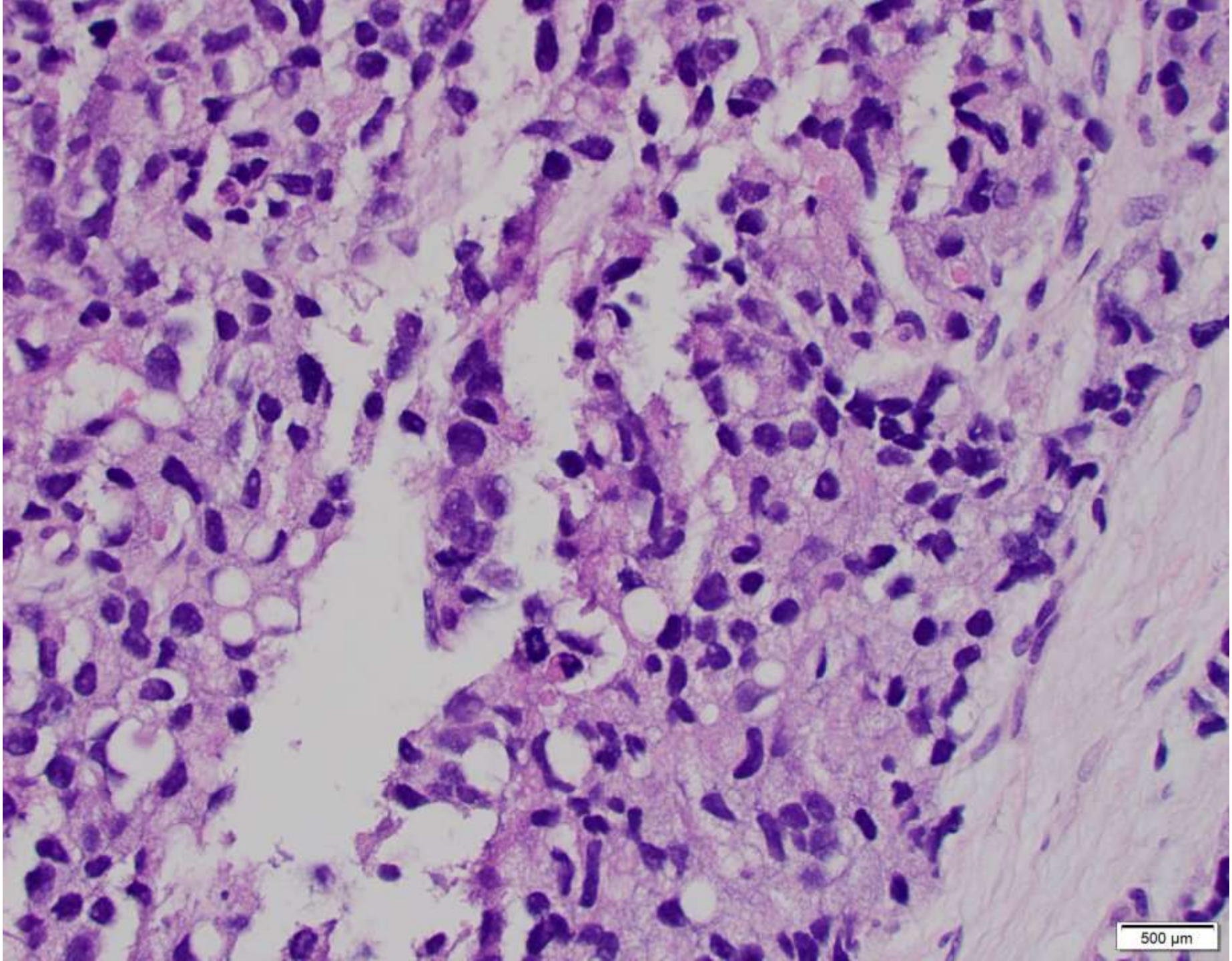

500 µm

DIAGNOSIS?

80 year old man with an a 6.0 cm anterior mediastinal mass with associated lymphadenopaty

Differential Diagnosis for Mediastinal Tumors

Anterior Mediastinum

- Thymic tumor/hyperplasia
- Teratoma/Germ cell tumor
- Thyroid tissue
- [Terrible] Lymphoma

Posterior Mediastinum

- Neural tumors
- Meningocele
- Spinal lesions

Stains performed

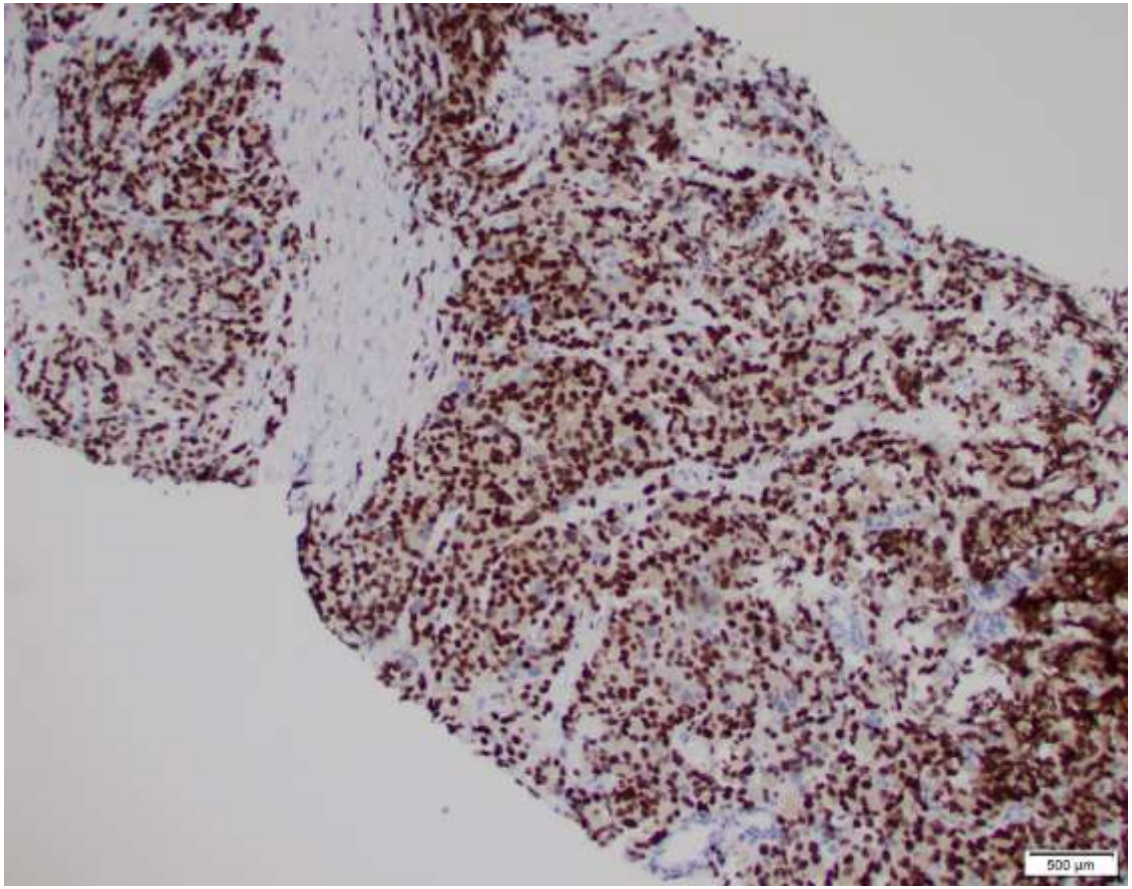
Anterior Mediastinum ddx

- Thymic tumor/hyperplasia
- Teratoma/Germ cell tumor
- Thyroid tissue
- [Terrible] Lymphoma

Negative stains

- Pancytokeratin, CK7, CK20
- SALL4
- TTF1
- CD45
- Plus a host of other stains

NKX3.1



Additional Patient History

- Treatment performed at OSH
  - Radical prostatectomy 25 years ago
  - Pelvic XRT for rising PSA 12 years ago
- Multiple bone mets seen in post biopsy bone scan

Common sites of prostate metastasis

- Bone
  - Characteristically osteoblastic
  - Lumbar spine, sacrum and pelvis most common
- Lymph nodes
  - Pelvic lymph nodes most common
    - Rarely a supraclavicular lymph node or mediastinal lymph node is the first manifestation of disease
  - May be present in perirectal lymph nodes removed during LAR for rectal carcinoma

Uncommon sites of metastasis

- Lung
- Pleura
- Penis
- Testis
- CNS
- Ureter
- Kidneys
- Paranasal sinus
- Breast
- Surgical sites
- GI tract
- Liver
- Omentum
- Skin

Detection of prostate carcinoma metastasis

Sensitivity of NKX3.1, PSA and PSAP for Metastatic Prostate Carcinoma

	NKX3.1	PSA	PSAP
Lymph Node	59/59 (100%)	58/59 (98.3%)	59/59 (100%)
Distant	9/10 (90%)	7/10 (70%)	9/10 (90%)
Overall	68/69 (98.6%)	65/69 (94.2%)	68/69 (98.6%)

Specificity: 99.7%

Gurel B, et al. Am J Surg Pathol. 2010 Aug;34(8):1097-105.

Table 1

Detection rates of prostate markers in prostate cancer metastases.

Marker	Detection Rate (%)	Mean IRS	Number of Cases
PSA	80.8	6.3	52
PSAP	66.0	3.5	53
PSMA	84.3	6.0	51
Prostein	59.6	4.2	52
Androgen receptor (AR)	98.1	6.7	53
ERG	50.0	2.6	52
NKX3.1	100.0	8.0	50
HOXB13	60.4	4.7	53

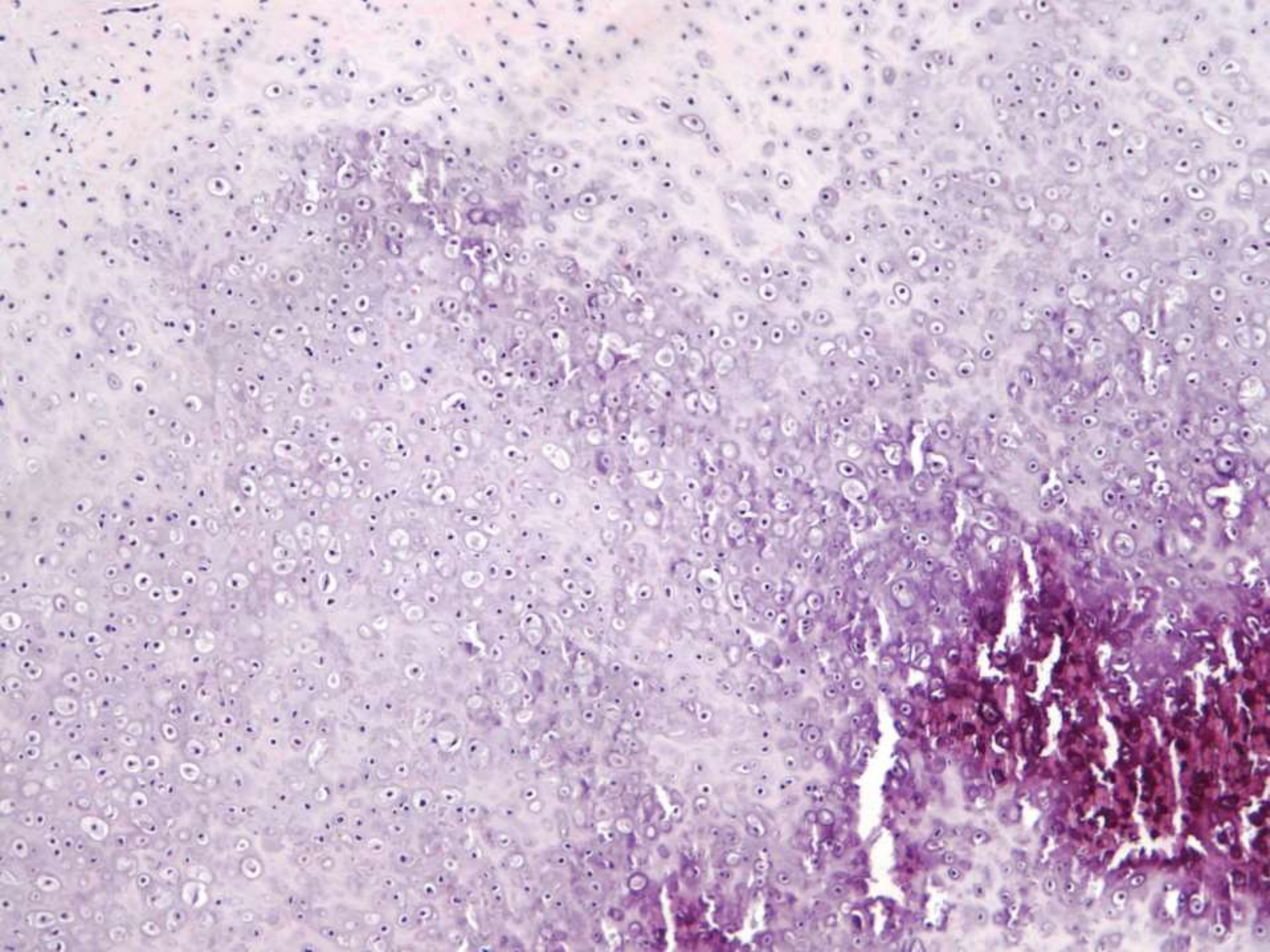
Abbreviations: IRS = immunoreactive Score according to Remmele.

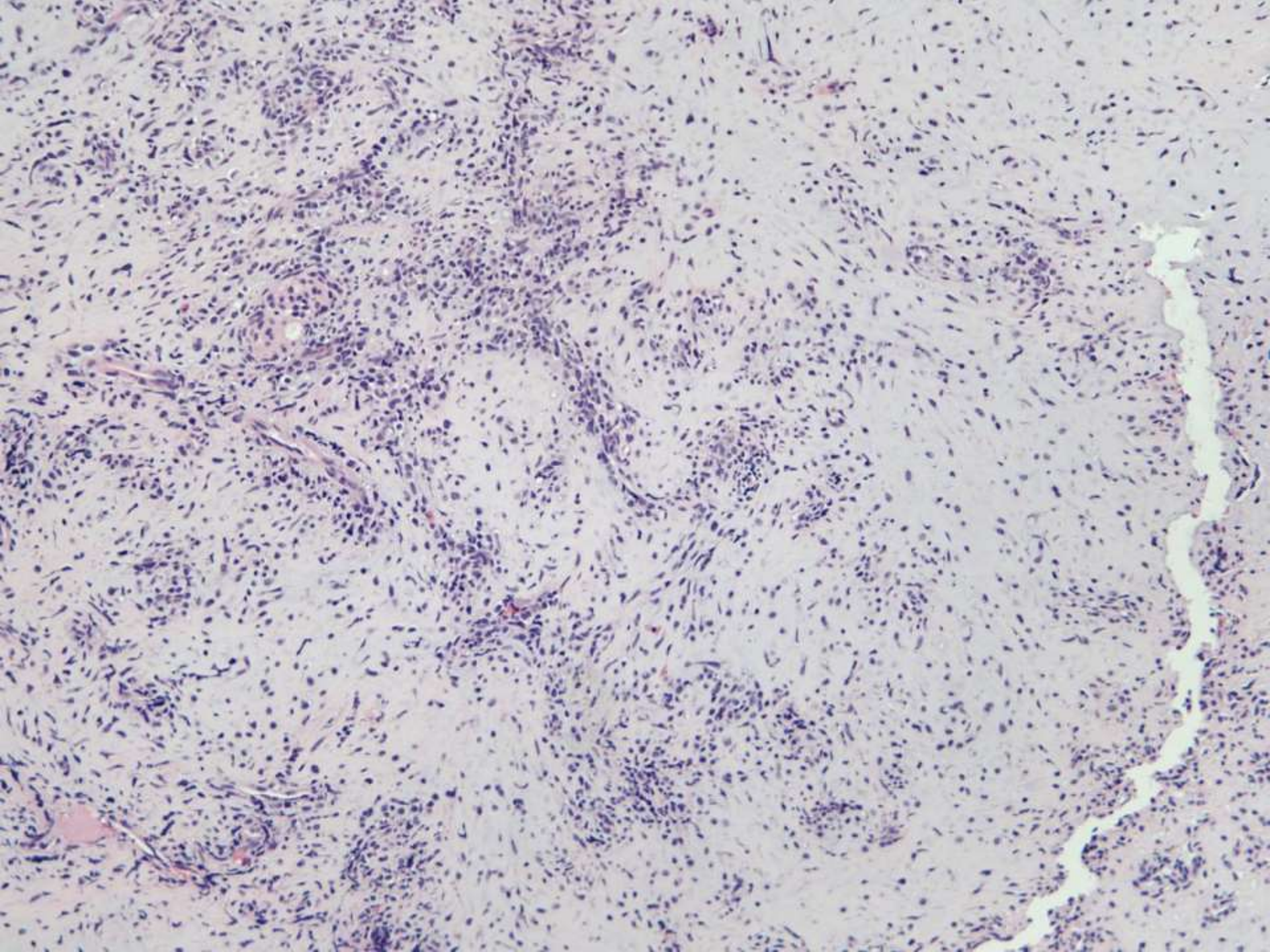
Kristiansen I, et al. Int J Mol Sci. 2017 May 29;18(6).

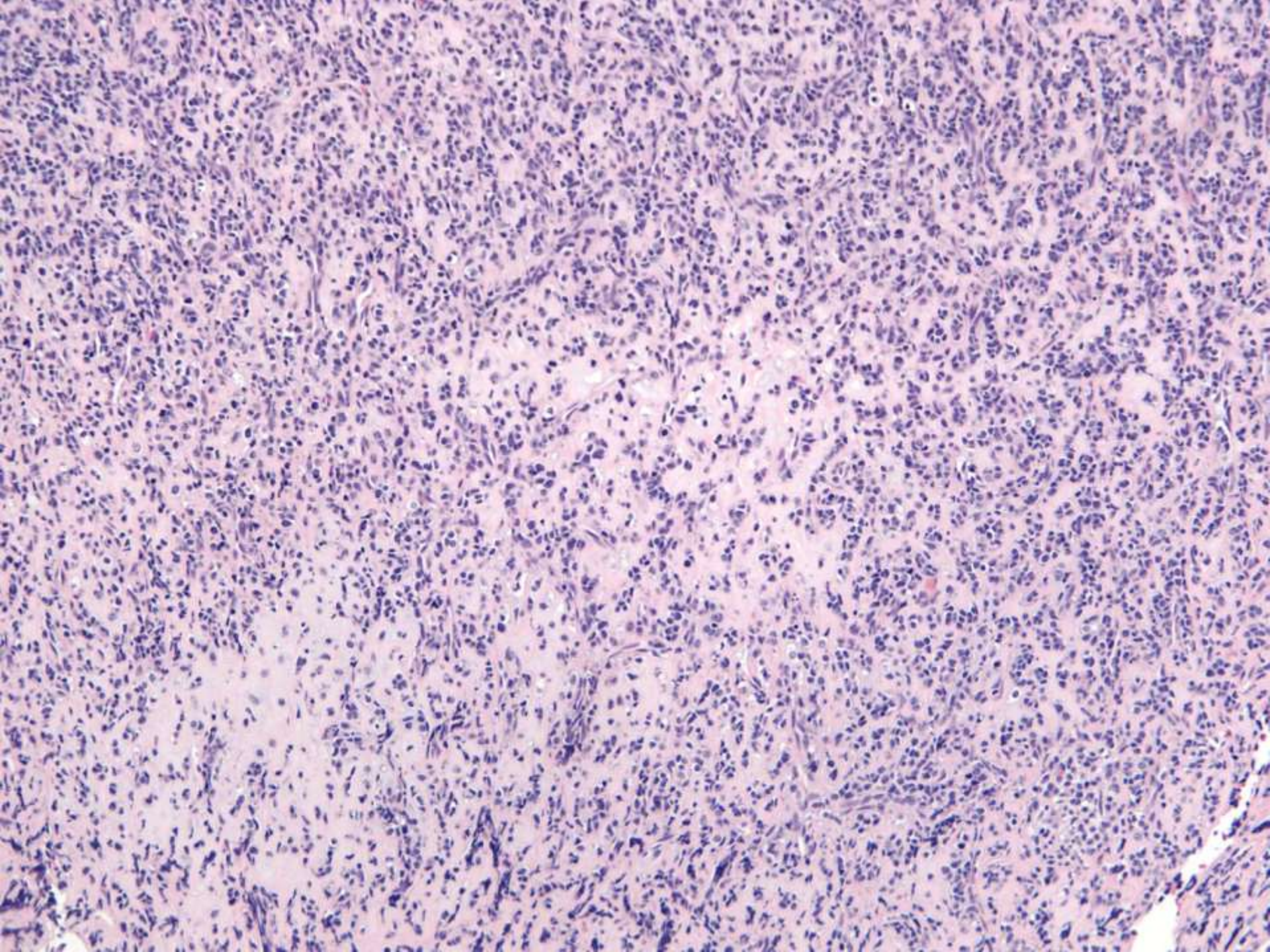
SB 6308

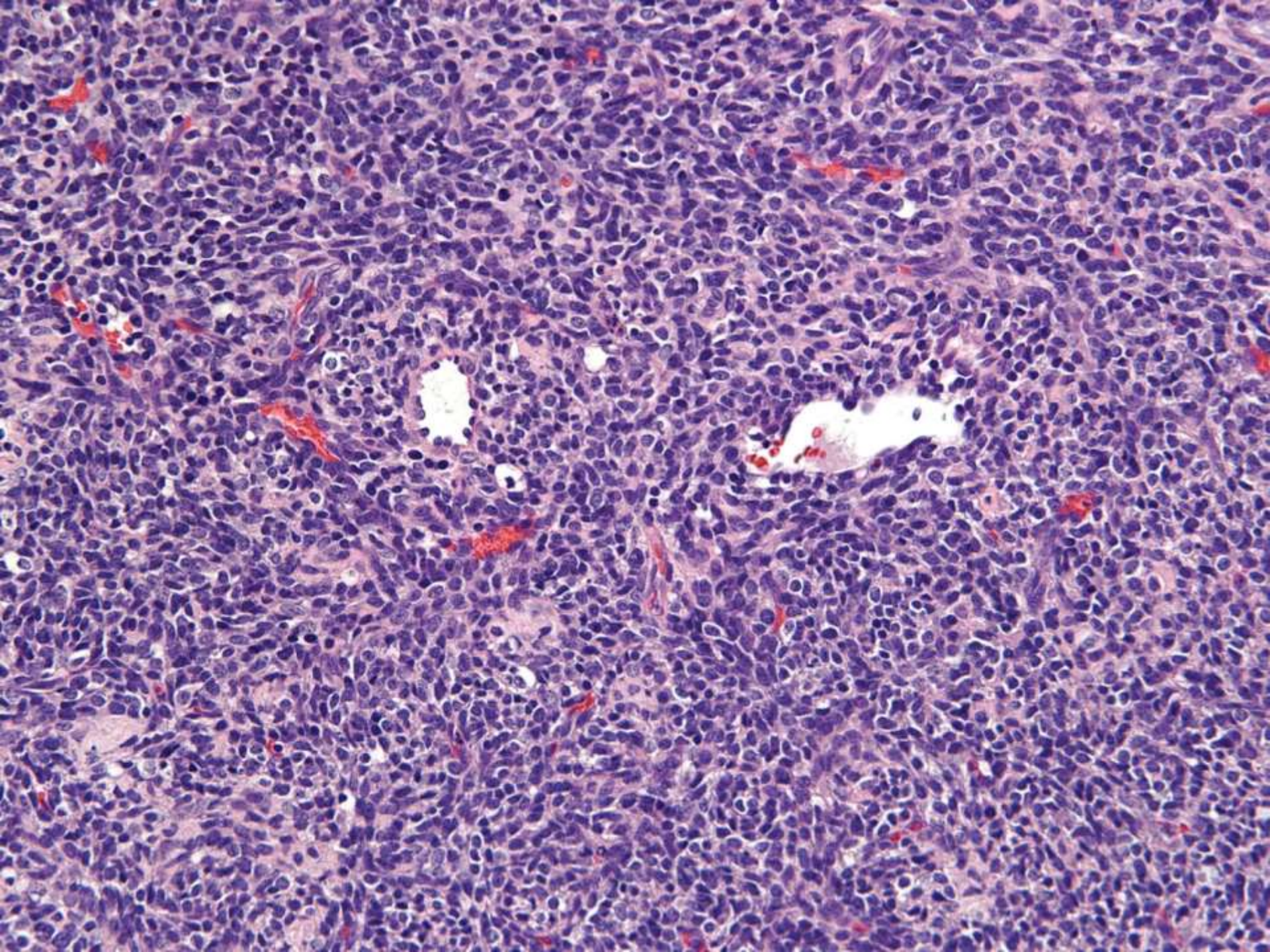
Jonathan Lavezo/Donald Born; Stanford

22-year-old female with headaches and nausea. MRI shows multi-lobulated extra-axial enhancing mass along the falx.









DIAGNOSIS?

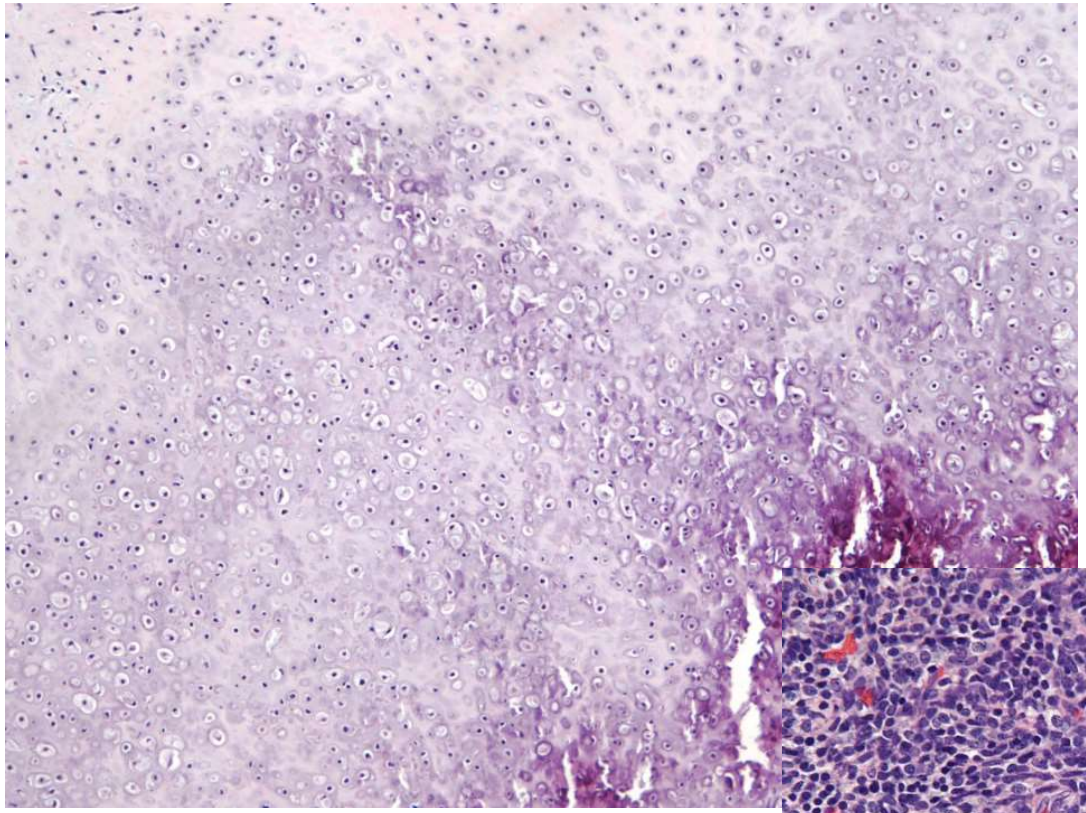
SB 6308

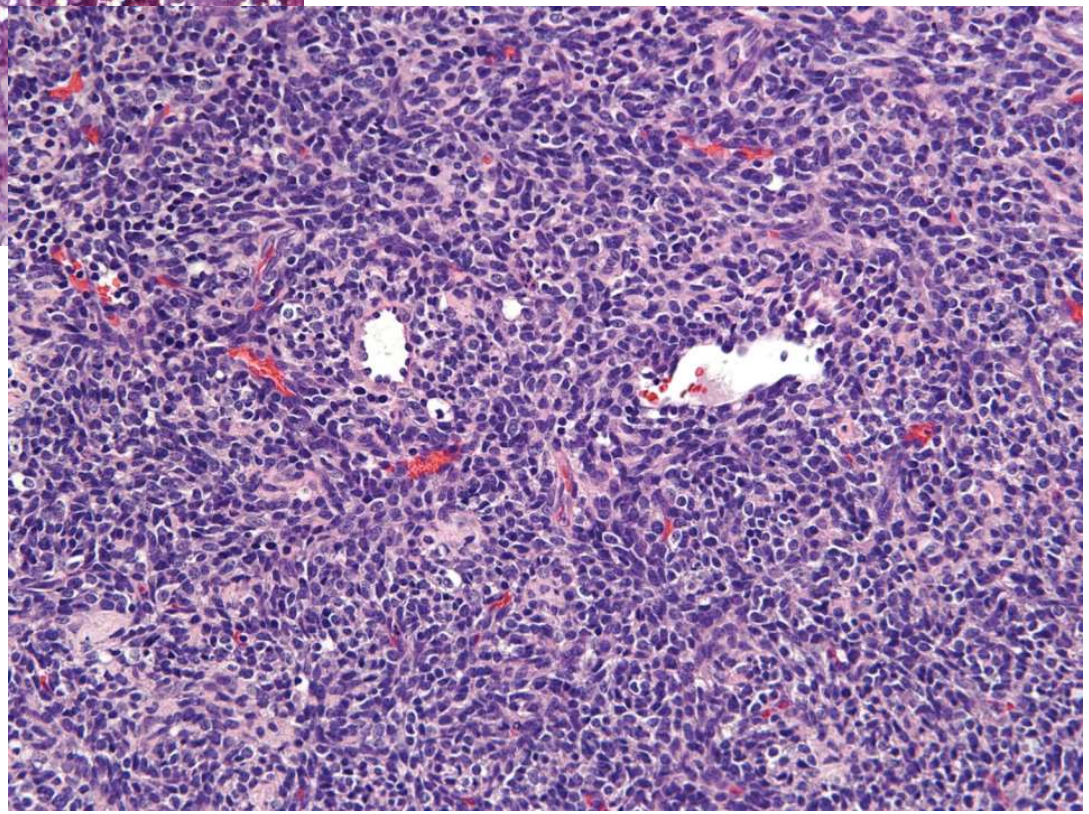
Jonathan Lavezo/Donald Born; Stanford

22 year-old woman with headaches and nausea. MRI shows a multi-lobulated extra-axial enhancing mass along the falx.

Differential diagnosis

- Chondrosarcoma
- Ewing Sarcoma
- Synovial Sarcoma
- Hemangiopericytoma/SFT
- MPNST with heterologous cartilage
- Atypical teratoid rhabdoid tumor
- Sclerosing rhabdomyosarcoma





Mesenchymal Chondrosarcoma

- <3% of all primary chondrosarcomas
- Peak incidence during the 2nd and 3rd decades of life (M=F)
- Most common sites include craniofacial bones, ribs, ilium, and vertebra
- 1/5 to 1/3 affect soft tissues with meninges being one of the most common sites of extraskeletal involvement
- Meningial MCs <0.2% of all intracranial neoplasms

Clinical and Imaging

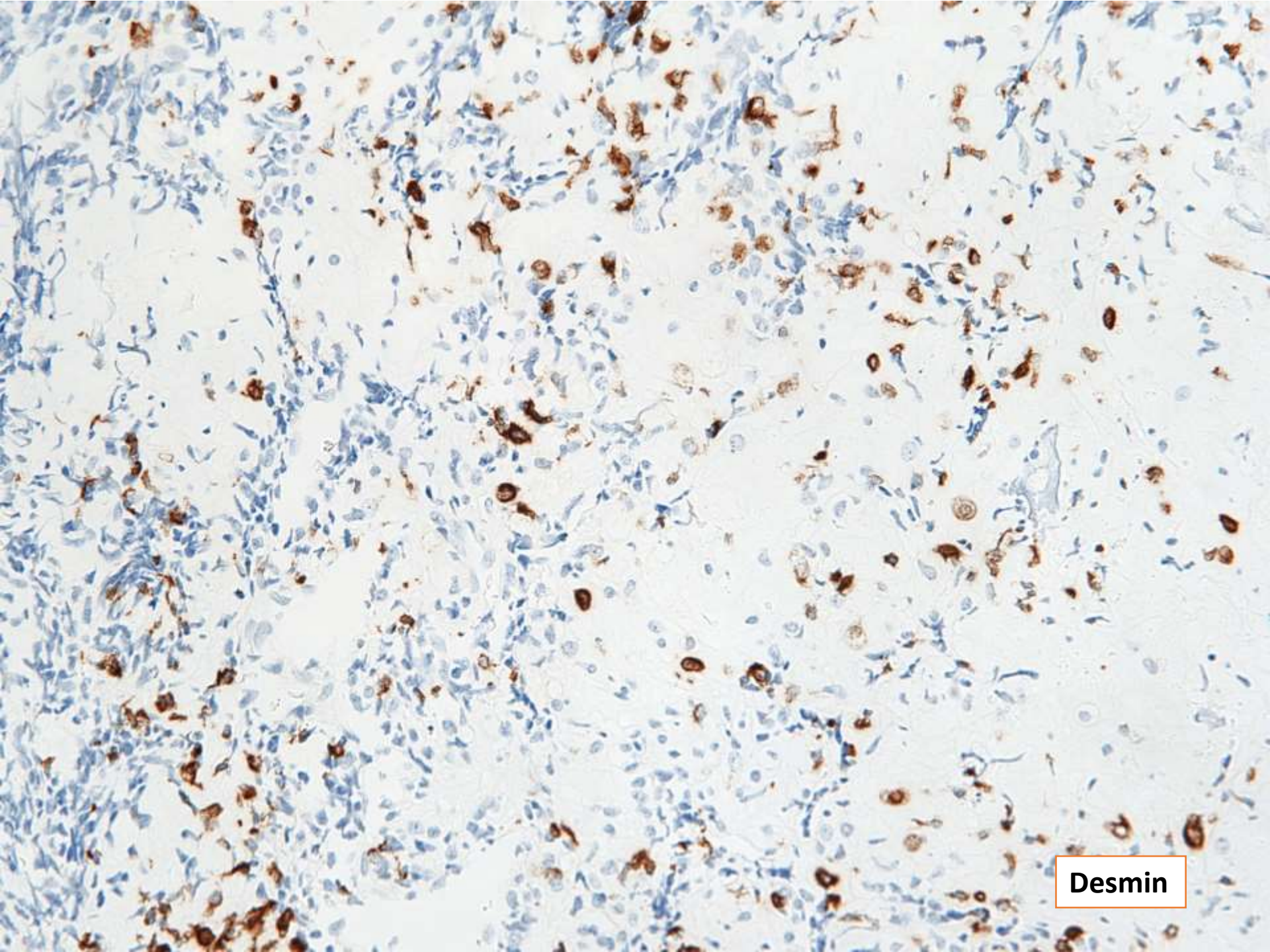
- Skeletal MCs
  - Present with pain and swelling
  - Symptoms range from lasting years to only days
  - Skeletal lesions are lytic, destructive, and have poor margins, similar to conventional chondrosarcoma
  - Cortical breakthrough with extra-osseous extension is common
- Extra-skeletal MCs
  - Often show lobulated growth with calcifications and moderate contrast enhancement

Pathology and Genetics

- Biphasic pattern composed of poorly differentiated small round to oval cells with scant cytoplasm admixed with islands of hyaline cartilage
- Amount of cartilage is variable
- Round cell component may be distinct from cartilage or blend gradually together
- Round cell areas often show myopericytoma-like vascular pattern
- Occasionally cells are spindled
- Recurrent *HEY1-NCOA2* fusion present

IHC Pitfalls

- Small cell component often express CD99 and desmin
- Has been show to also express Myogenin and MyoD1
- Can present diagnostic challenge on biopsy specimens containing mostly/only round cell component


Desmin

Treatment

- Intracranial extraskeletal mesenchymal chondrosarcomas should undergo complete resection
- Use of chemotherapy/radiotherapy in meningeal MCs is controversial

Prognosis

- Intracranial meningeal MCs neoplasms have varied outcomes
- In general, MCs are more likely to recur than conventional chondrosarcomas
  - 63% vs 16% recurrence rate, respectively
- Aggressive neoplasm with late (>20 year) distant metastases
- Protracted clinical course requires long-term follow-up

Prognosis Cont.

- No correlation between histologic appearance and prognosis
- Children, adolescents, and young adults have a slightly better outcome
- Involvement of jaw bones appear more indolent

Patient Follow-up

- 1st surgery was terminated due to blood loss from the tumor
- 2nd surgery one week later with gross total resection
- Completed final round of radiation therapy to resection cavity

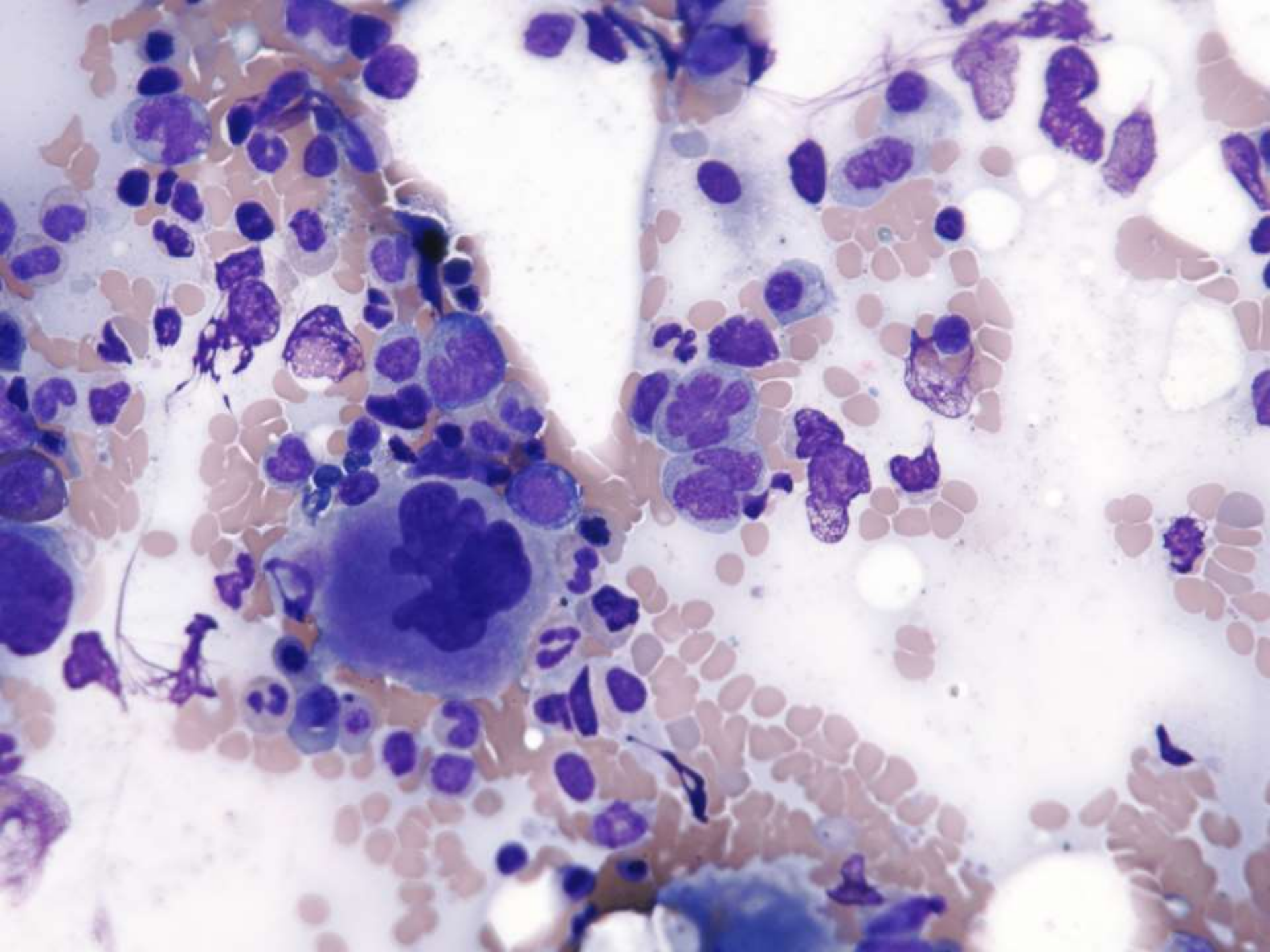
References

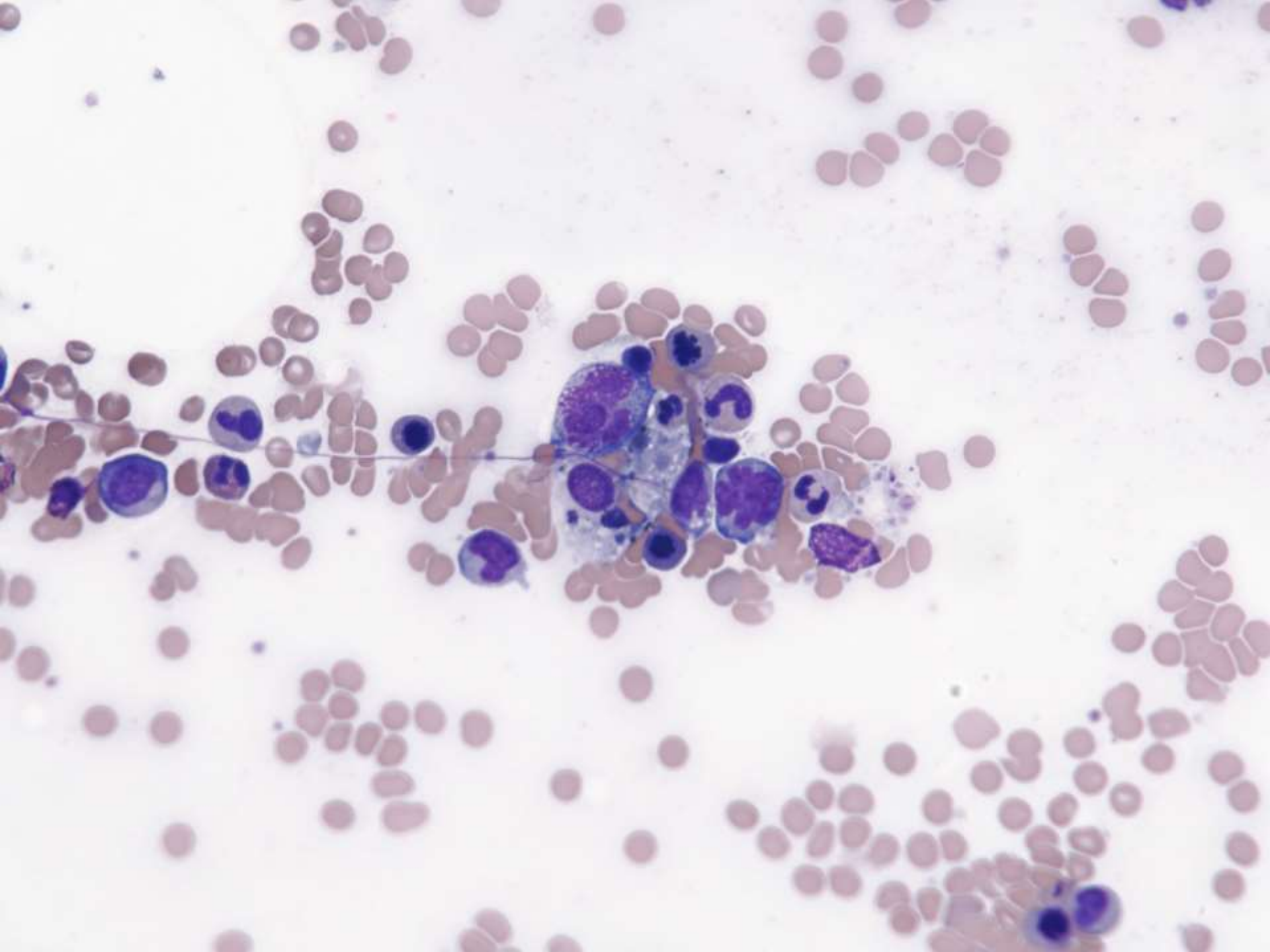
- Folpe, AL, et al. Mesenchymal chondrosarcomas showing immunohistochemical evidence of rhabdomyoblastic differentiation: a potential diagnostic pitfall. *Hum Pathol*.2018 Jul;77:28-34.
- Sadashiva, N. et al. Intracranial Extraskeletal Mesenchymal Chondrosarcoma. *World Neurosurg*. 2016 Nov;95:618.
- World Health Organization - Classification of bone and soft tissue tumours

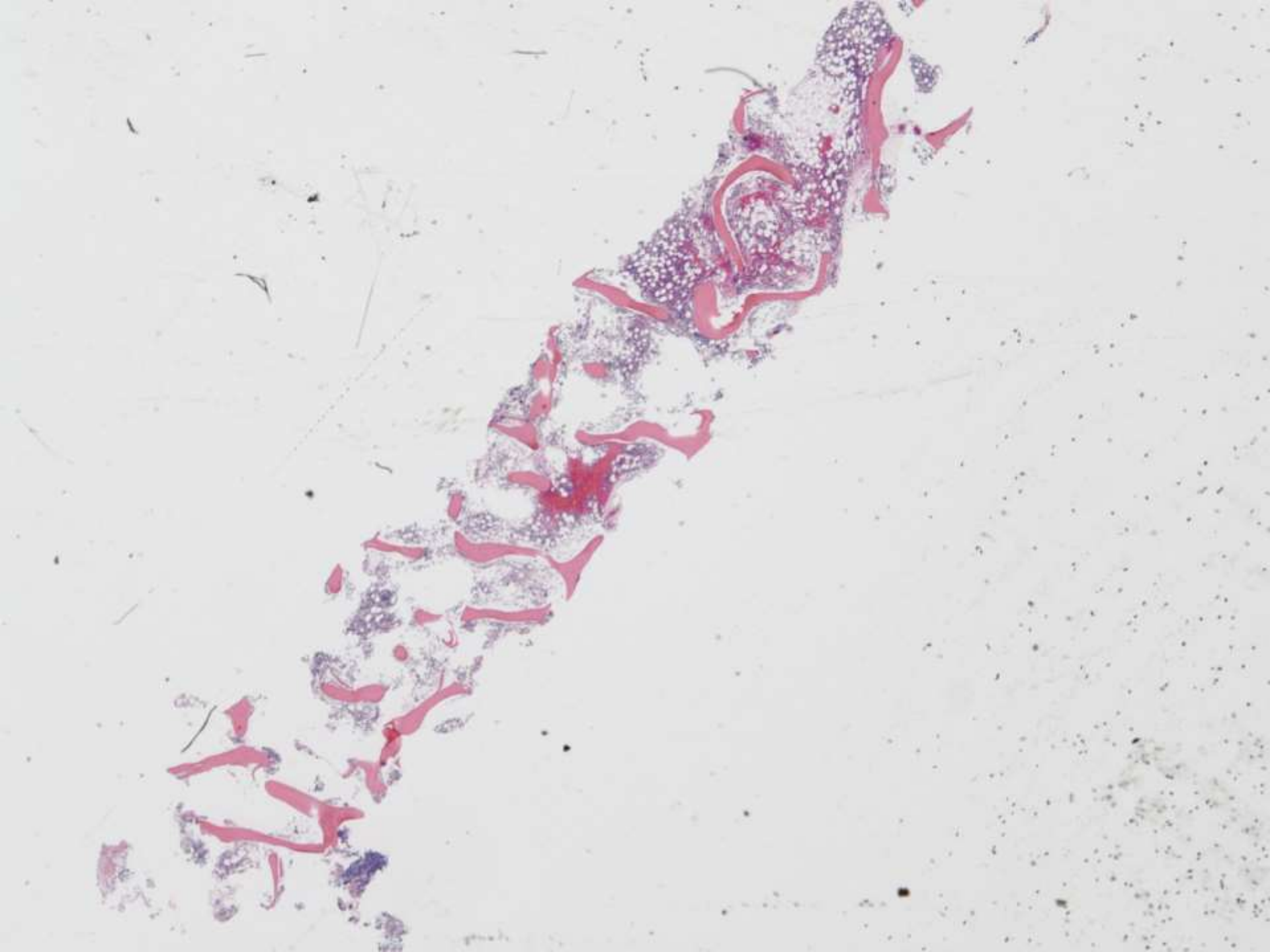
SB 6309

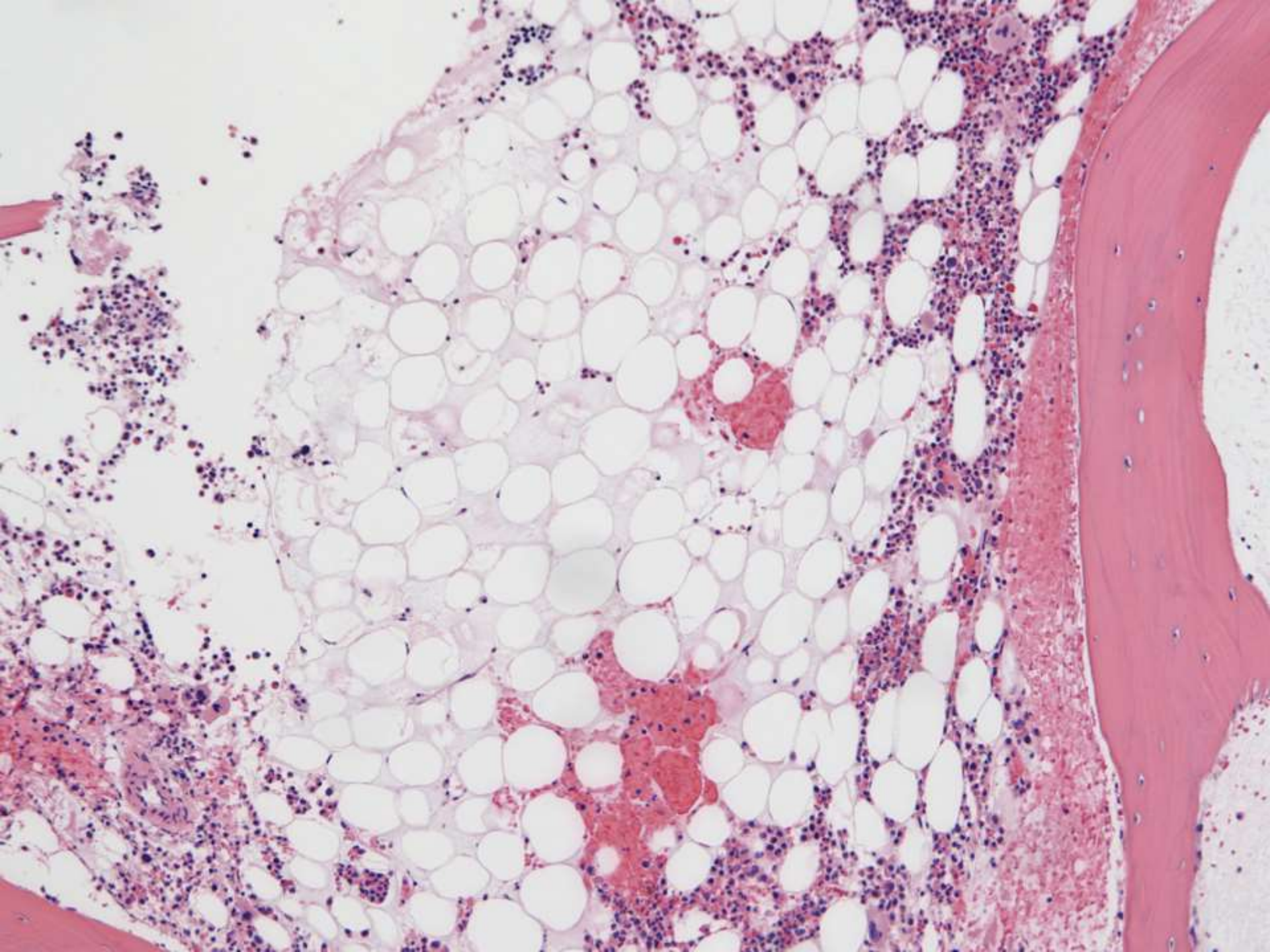
Sebastian Fernandez-Pol/Dita Gratzinger; Stanford

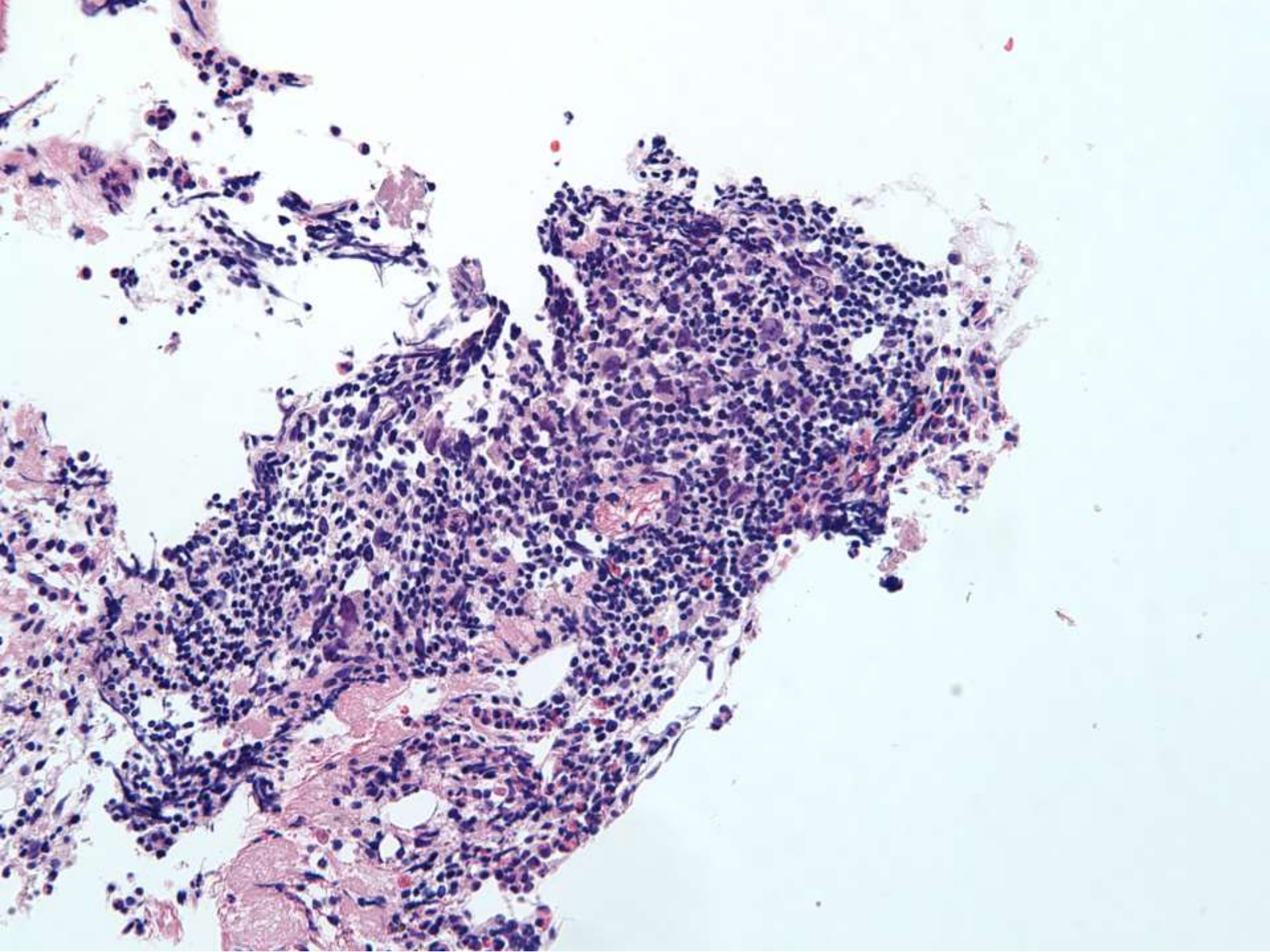
50-year-old male with experience weight loss, night sweats, and abdominal pain. CT/PET showed widespread lymphadenopathy in the neck, chest, and abdomen with moderate bilateral pleural effusions and large ascites.

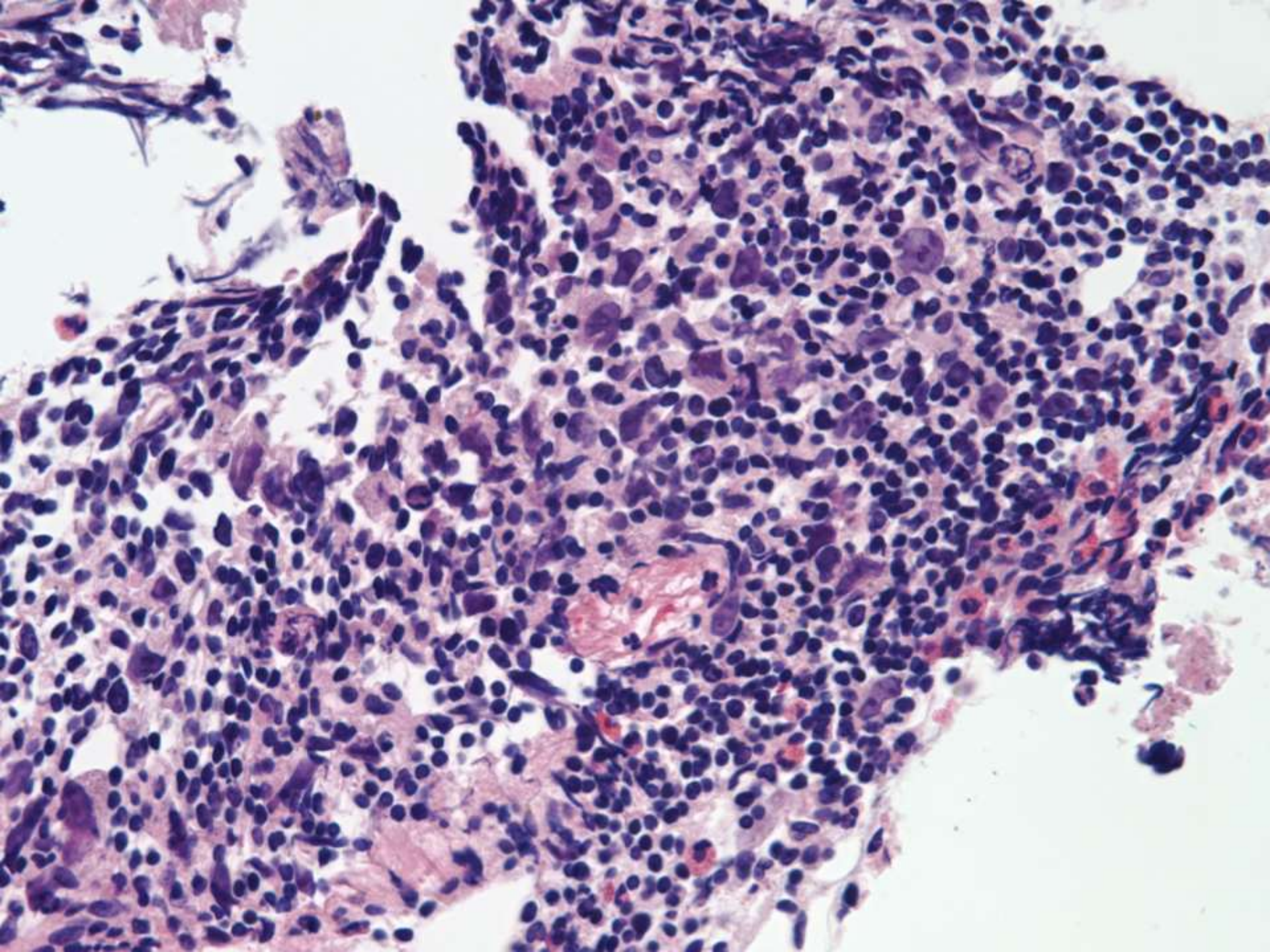




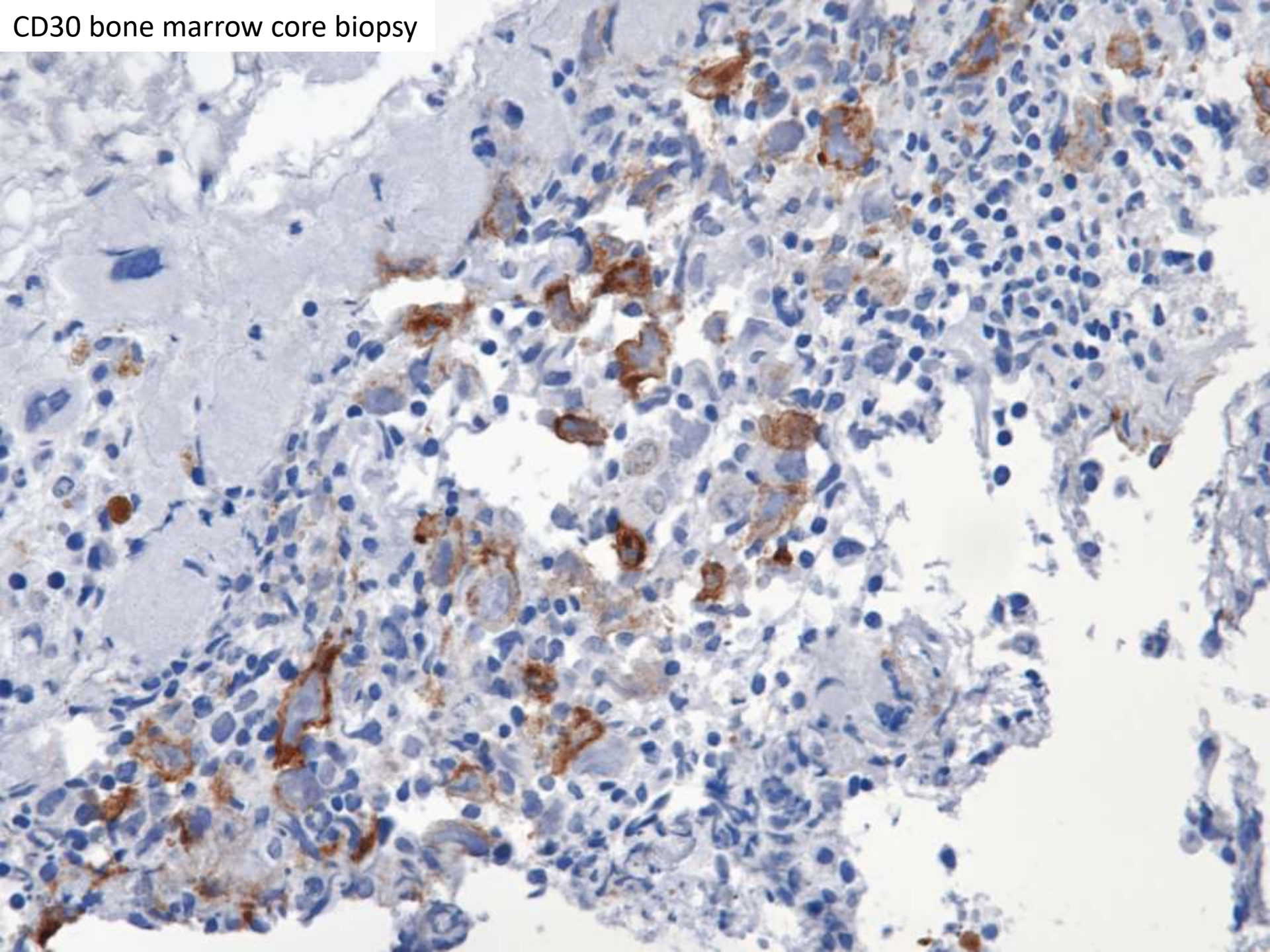


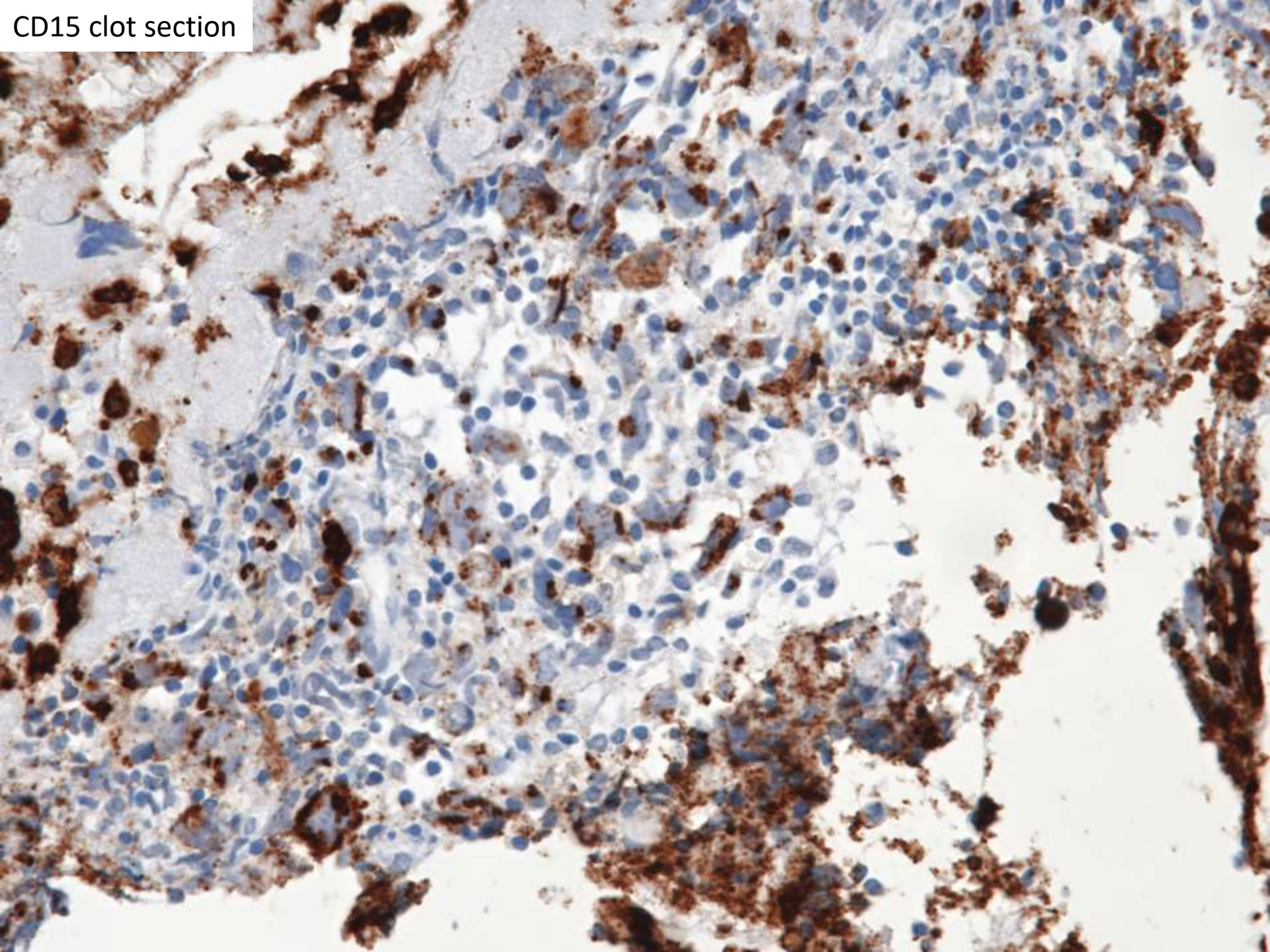


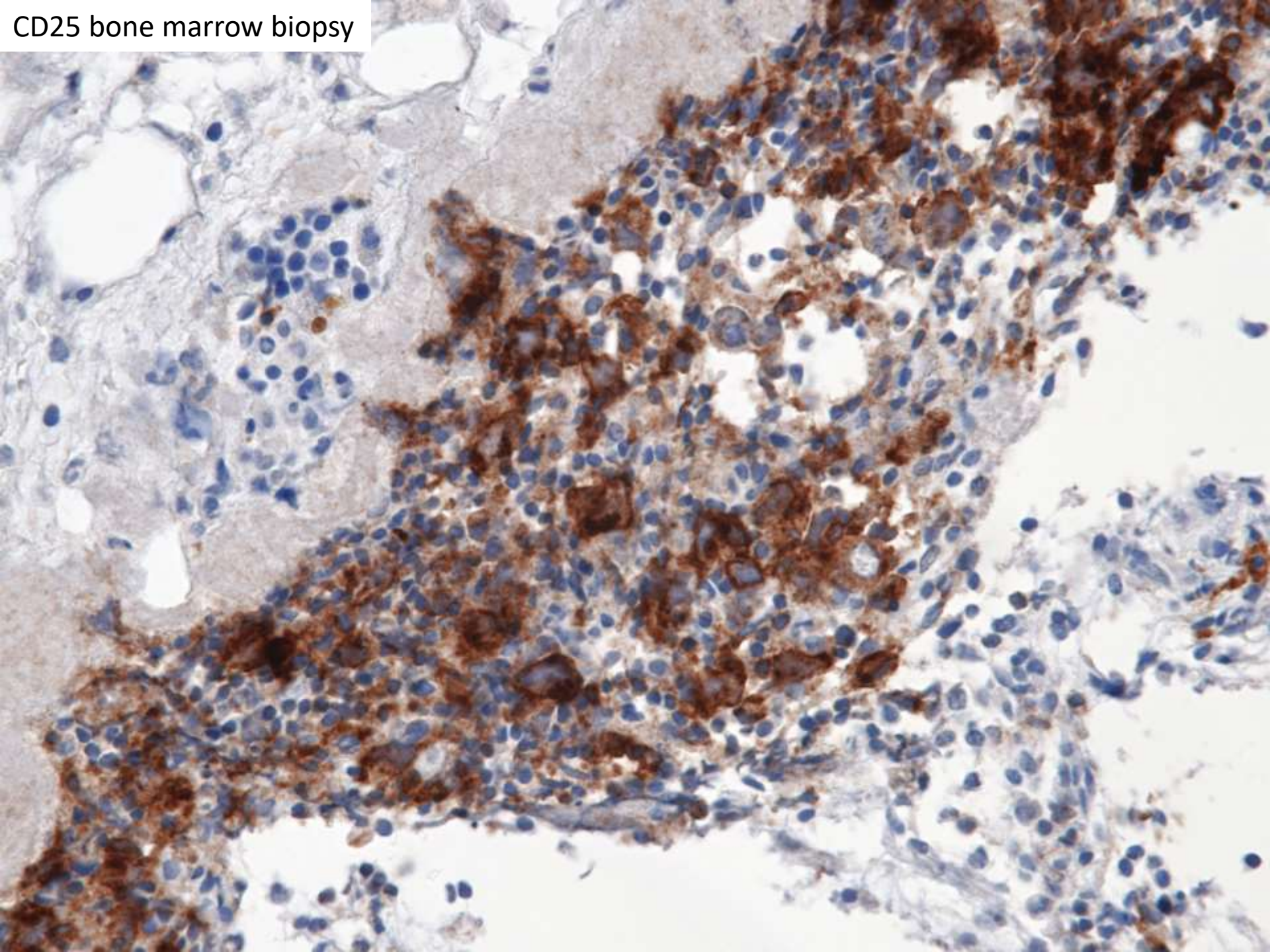


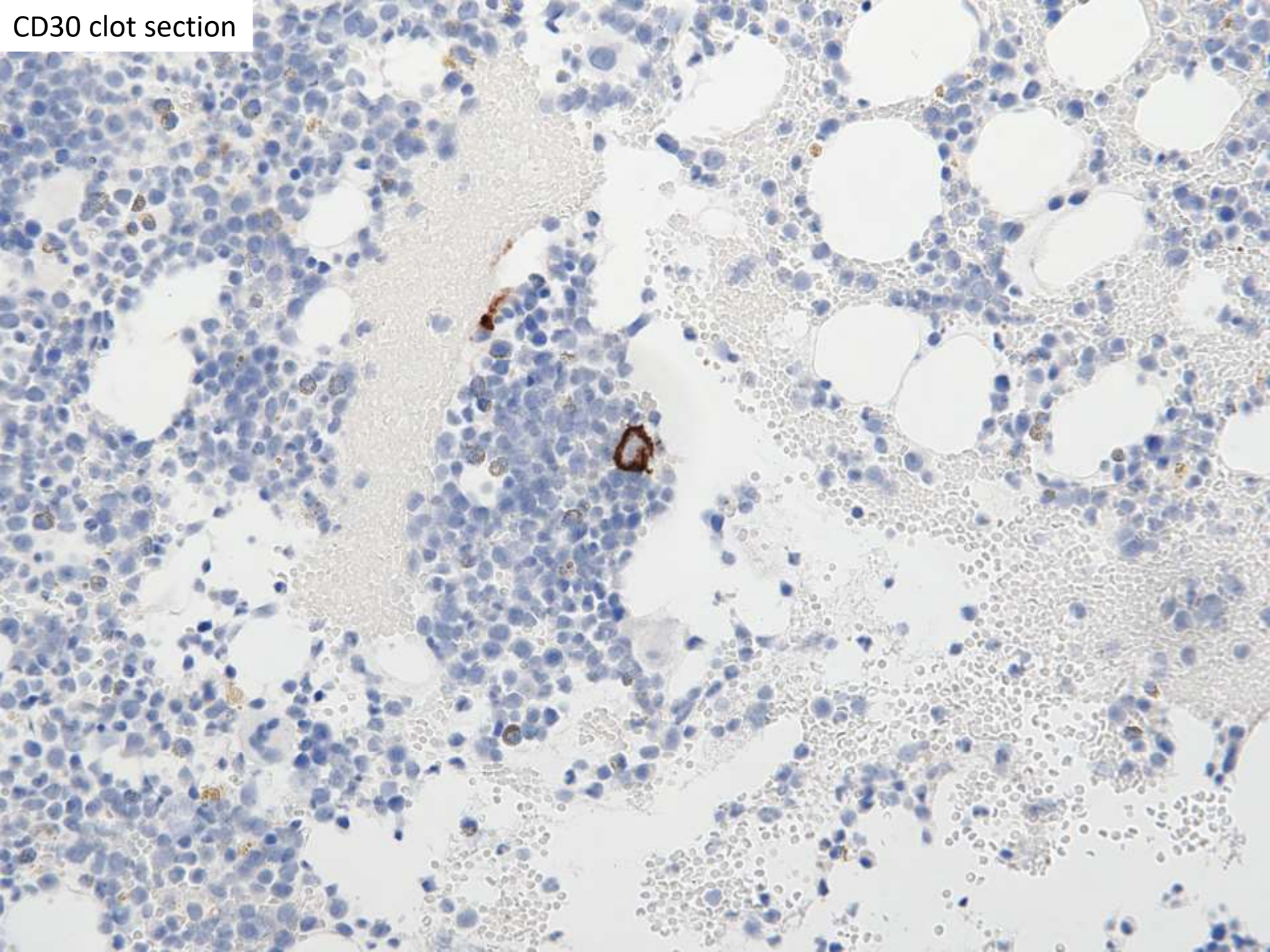


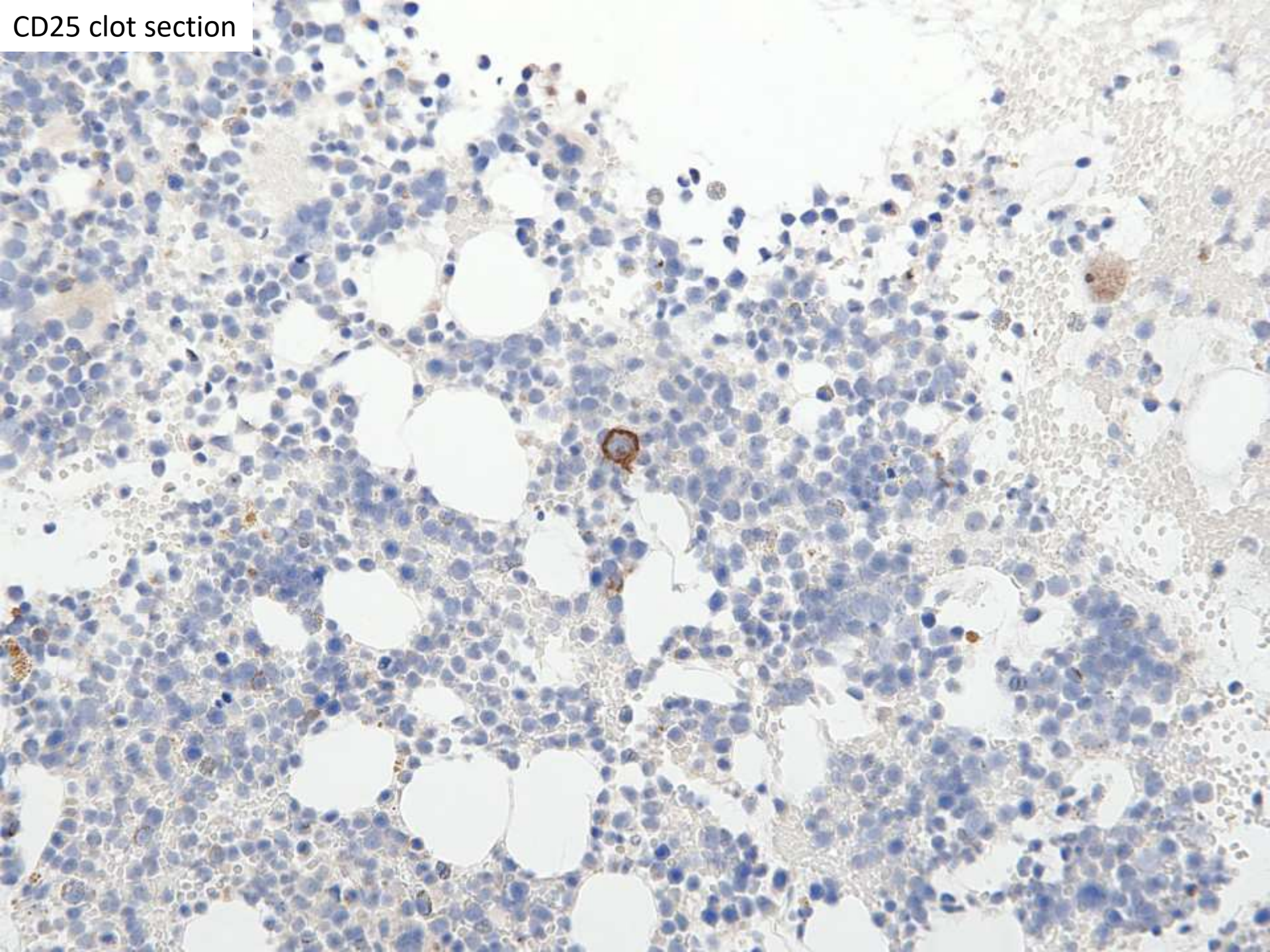
CD30 bone marrow core biopsy

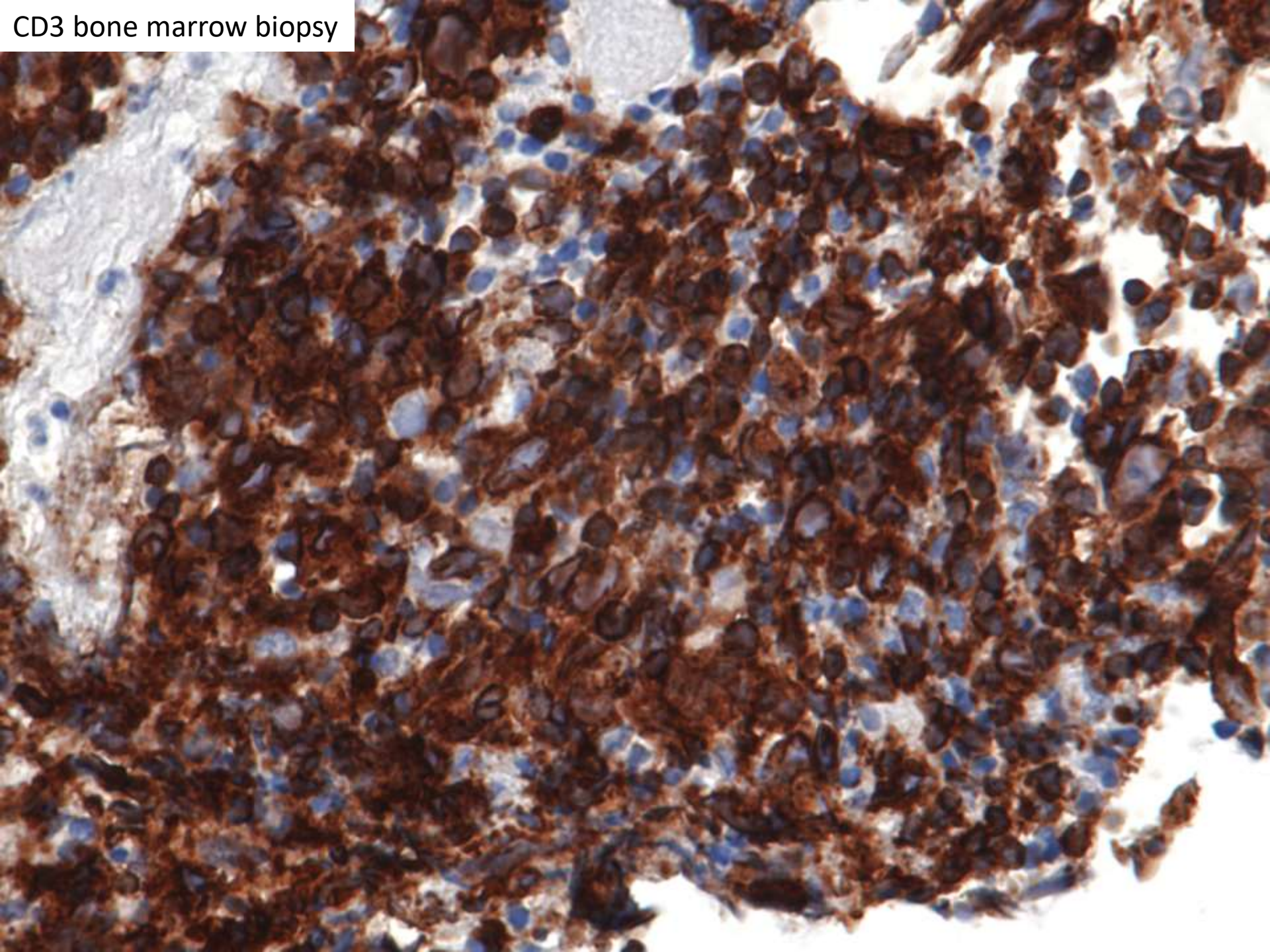


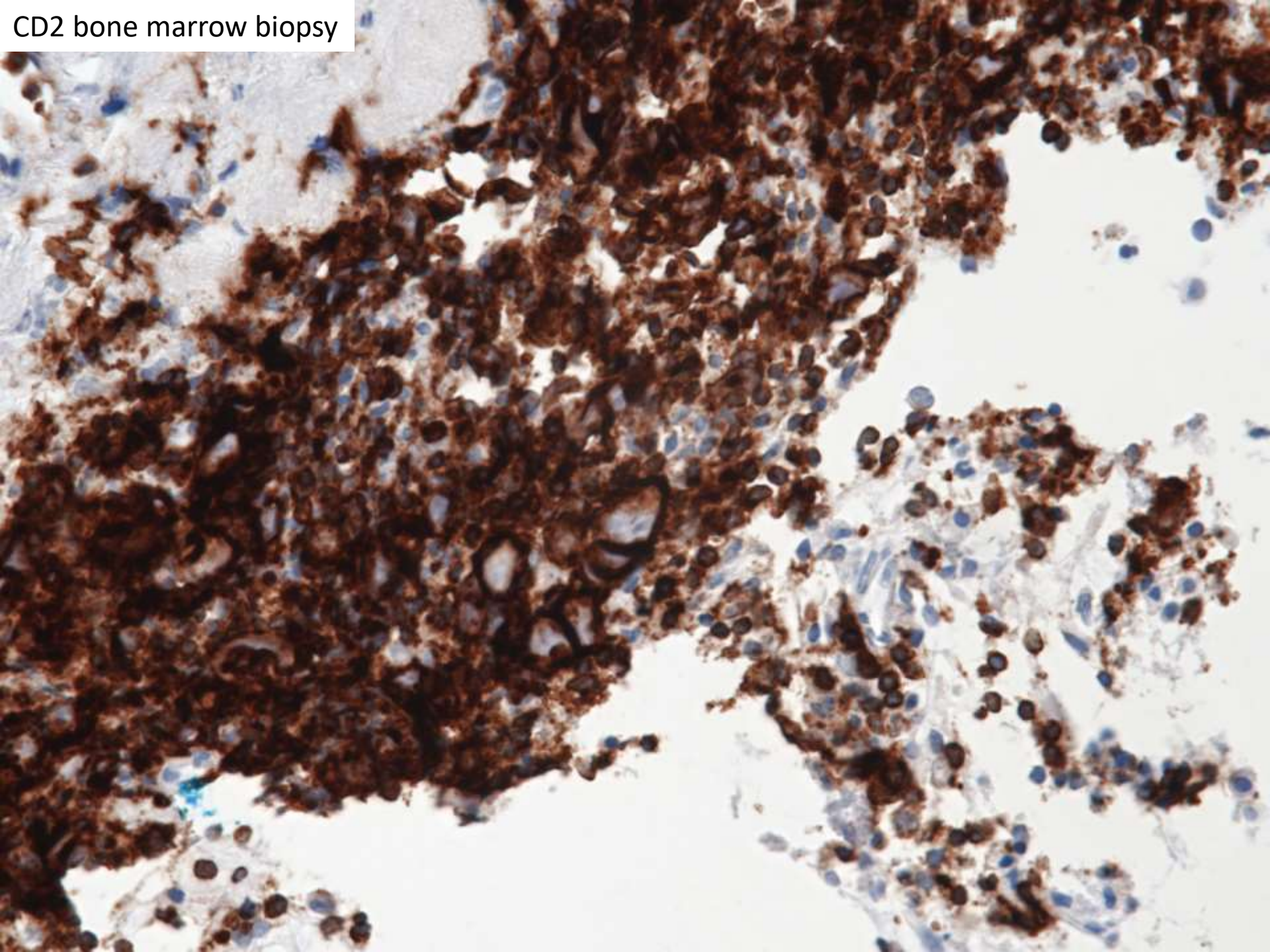

CD15 clot section

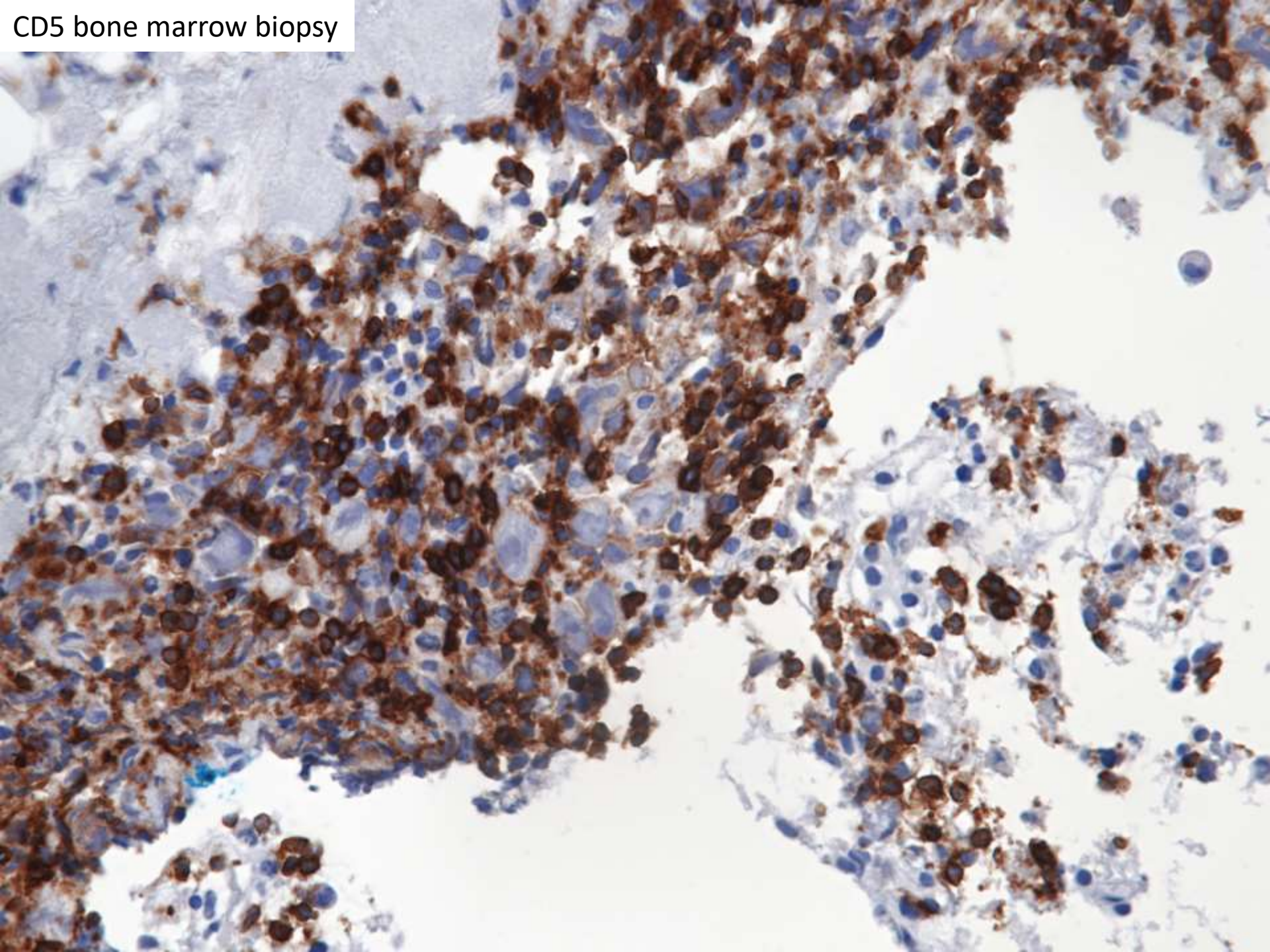

CD25 bone marrow biopsy

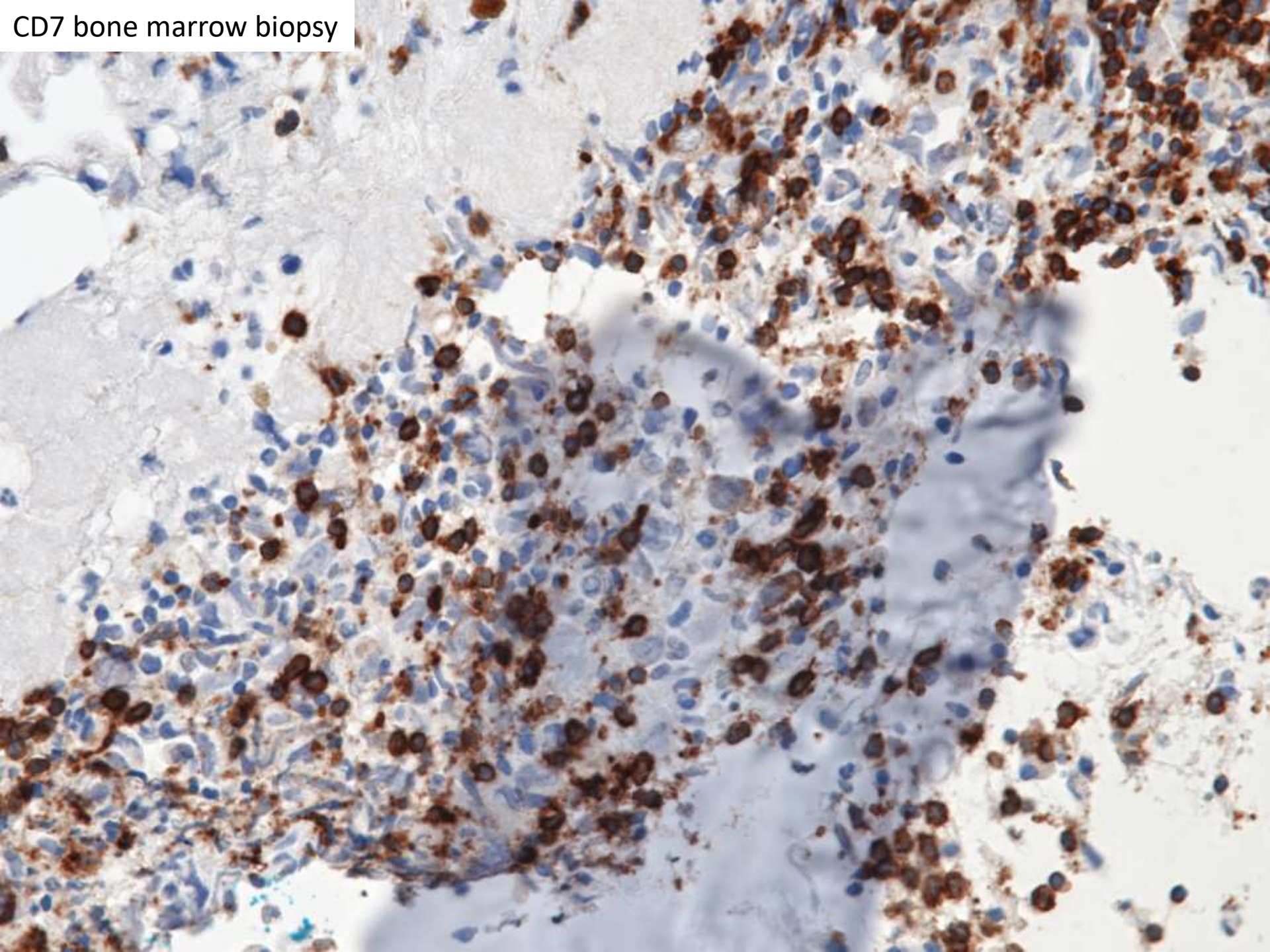

CD30 clot section

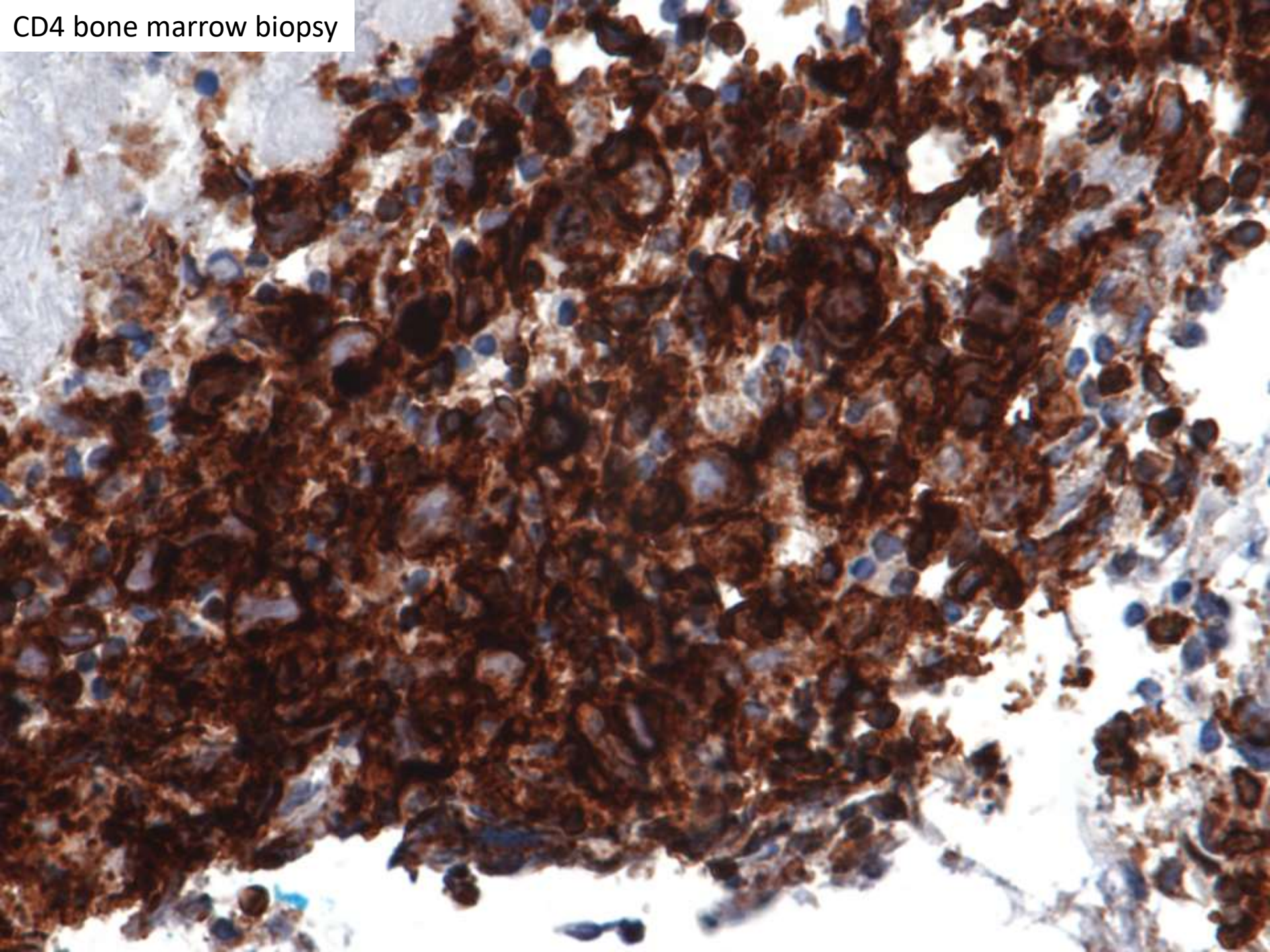

CD25 clot section

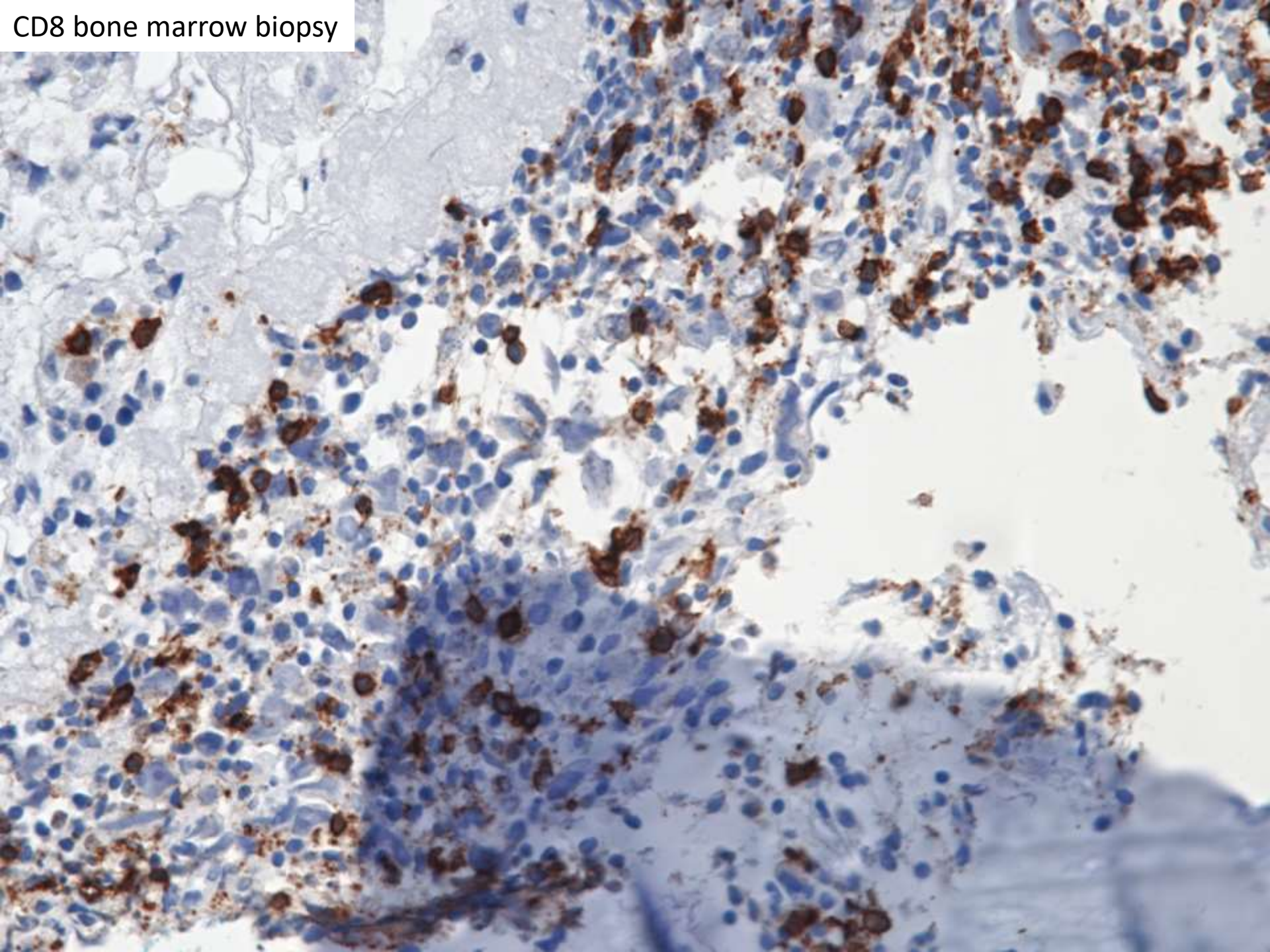

CD3 bone marrow biopsy


CD2 bone marrow biopsy


CD5 bone marrow biopsy


CD7 bone marrow biopsy


CD4 bone marrow biopsy


CD8 bone marrow biopsy

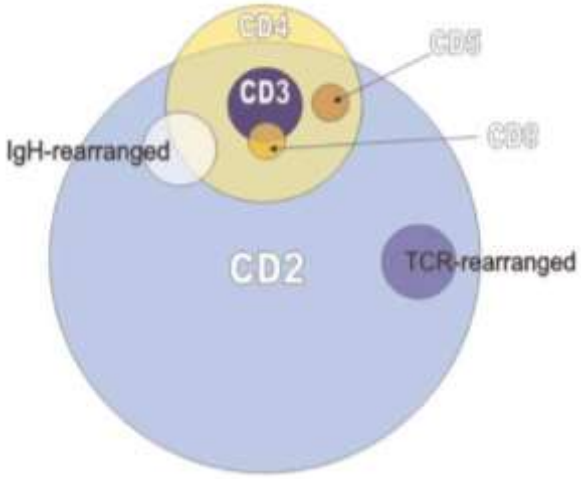
DIAGNOSIS?

Differential diagnosis

- Classic Hodgkin lymphoma with expression of T-cell antigens
  - Seen in 5% of cases
  - Can express up to four T-cell markers

- T-cell lymphomas associated with CD30-positive cells
  - Peripheral T-cell lymphoma, NOS (PTCL)
  - Anaplastic large cell lymphoma (ALCL)
  - Angioimmunoblastic T-cell lymphoma (AITL)
  - Adult T-cell leukemia/lymphoma (ATLL)

Most common T-cell antigens expressed in classic Hodgkin lymphoma



Two populations of cells

Large atypical cells (Hodgkin-like)

- Positive for:
  - CD30
  - CD15
  - CD2
  - CD4
  - CD25
- Negative for:
  - CD5
  - CD7
  - CD8
  - EBV (EBER)

Small/medium cells (abnormal T-cells)

- Positive for:
  - CD3
  - CD2
  - CD4
  - CD25 (minor subset)
- Negative for:
  - CD5 (partial loss)
  - CD7 (partial loss)
  - CD8

Additional studies

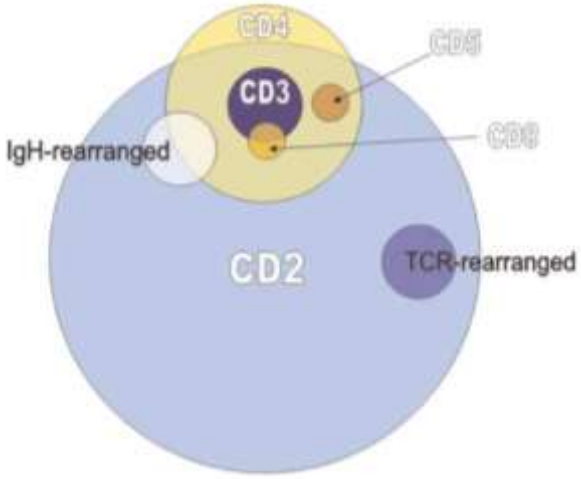
- HTLV AB Screen was repeatedly positive
- ELISA and western blot studies for HTLV were also positive

Differential diagnosis

- Classic Hodgkin lymphoma with expression of T-cell antigens
  - Seen in 5% of cases
  - Can express up to 4 T-cell markers

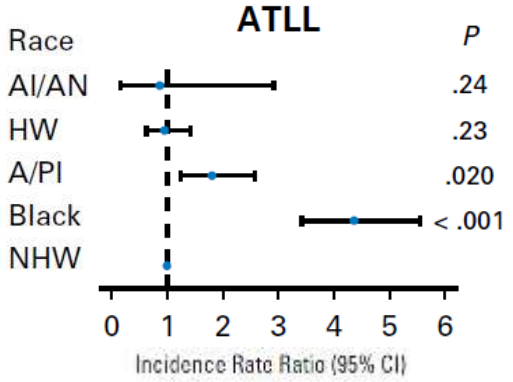
- T-cell lymphomas associated with CD30-positive cells
  - Peripheral T-cell lymphoma, not otherwise specified
  - Anaplastic large cell lymphoma
  - Angioimmunoblastic T-cell lymphoma
  - **Adult T-cell leukemia/lymphoma**

Most common T-cell antigens expressed in classic Hodgkin lymphoma



Adult T-cell leukemia/lymphoma (ATLL)

- ATLL is endemic in several regions of the world
  - Southwestern Japan
  - Caribbean basin
  - Parts of central Africa
  - Iran
- In the US, the incidence of ATLL is higher among blacks, Asians/Pacific Islanders, and Japanese Americans than among non-Hispanic whites
  - Corresponds to a higher prevalence of HTLV-1 in these populations
- Lifetime ATLL risk of approximately 2.5% in infected individuals



Four main clinical forms of ATLL

Feature	Smoldering	Chronic	Acute	Lymphomatous
Lymphocytosis	No	Mildly increased, $>4 \times 10^9$/L	Increased	No
T-cell receptor PCR	Sometimes monoclonal	Monoclonal	Monoclonal	Monoclonal
Elevated LDH	No	Minimal	Yes	Yes
Hypercalcemia	No	No	Yes	Variable
Skin lesions	Erythematous rash	Rash, papules	Variable, >50%	Variable, >50%
Lymphadenopathy	No	Mild	Usually present	Yes
Hepatosplenomegaly	No	Mild	Usually present	Often present
Bone marrow infiltration	No	No	May be present	No
Median survival (yr)	>2	2	<1	<1
Morphology	Small lymphocytes Minimal atypia	Mild atypia Flower cells sometimes seen	Marked atypia Polylobated and blastic forms	Marked atypia Polylobated and blastic forms

LDH, lactate dehydrogenase; *PCR*, polymerase chain reaction.

CD30 expression in ATLL

- Rare
- Can be on the neoplastic cells
- Can also have Hodgkin/Reed-Sternberg-like cells intermixed
  - Can be EBV-positive

Follow up 6 months after bone marrow biopsy

- CHOP x1
- CHOEP x5 with CR
- Haploidentical stem cell transplant 07/03
- 8/15 Skin biopsies positive for disease
- 8/15 Peripheral blood flow cytometry showed ATLL accounting for 45% of all cells (6 K/uL)
- Looking for hospice care

Take home points

- CD30 and CD15 co-expressing cells can be seen in T-cell lymphomas in addition to B-cell lymphomas
  - Classic Hodgkin lymphoma
  - Chronic lymphocytic leukemia with Hodgkin/Reed-Sternberg-like cells
  - Peripheral T-cell lymphomas, NOS
  - Angioimmunoblastic T-cell lymphoma
  - Anaplastic large cell lymphoma
  - Adult T-cell leukemia/lymphoma

- Immunophenotype of the smaller cells in the background can help

- Definitive diagnosis of adult T-cell leukemia lymphoma requires demonstration of HTLV-1 infection

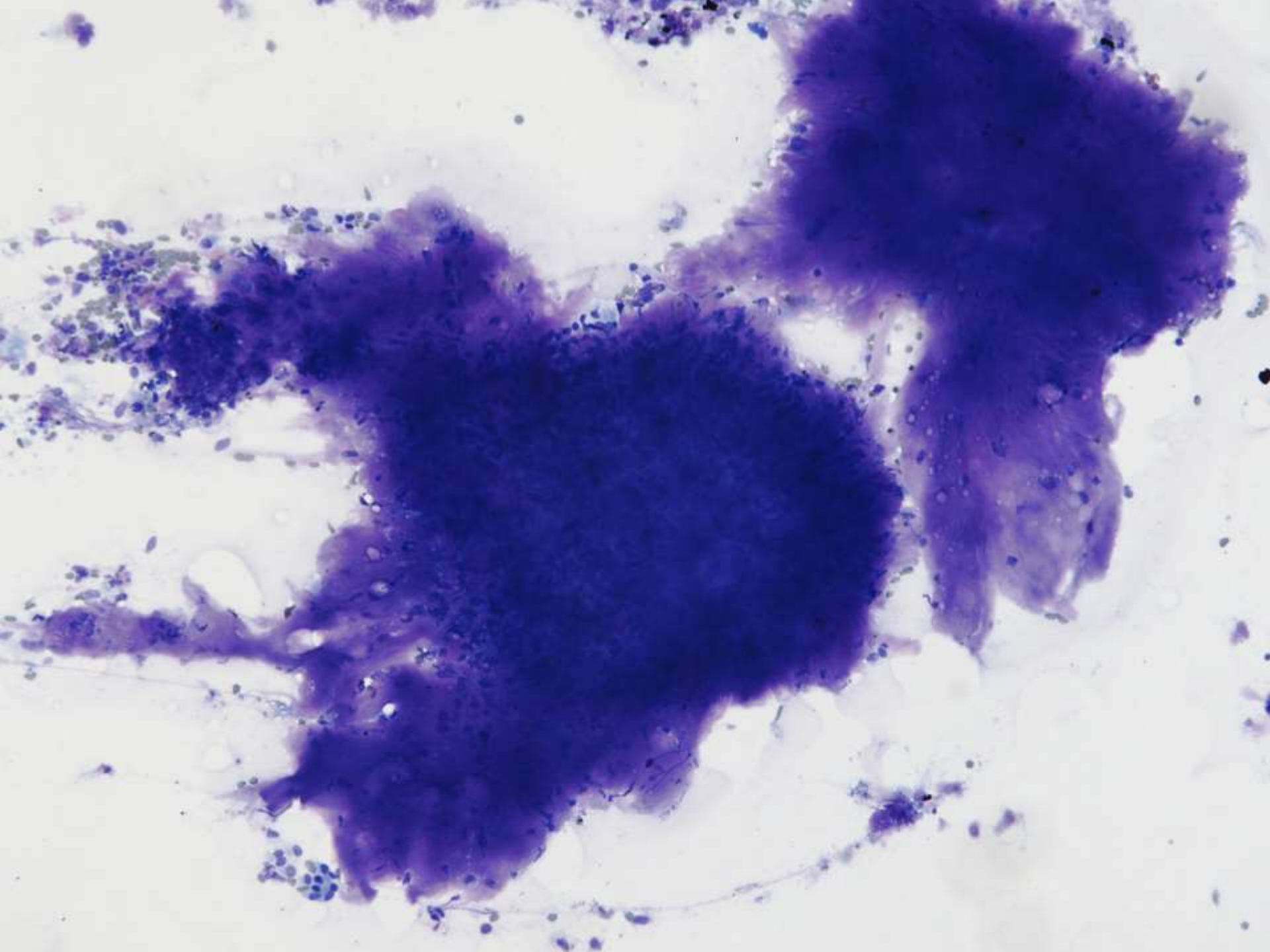
References

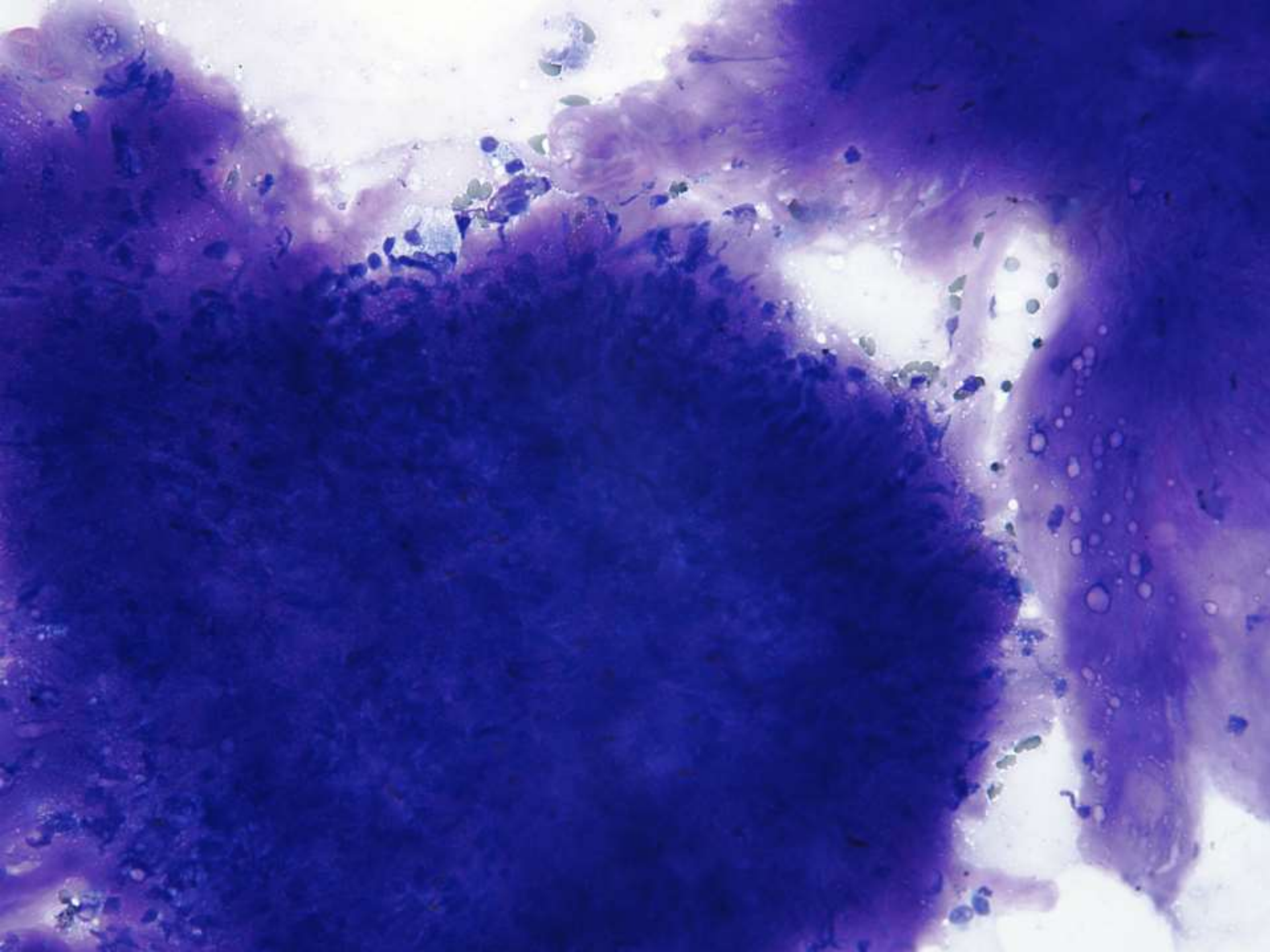
- Tzankov A, Bourgau C, Kaiser A, et al. Rare expression of T-cell markers in classical Hodgkin's lymphoma. Mod Pathol 2005;18(12):1542-1549.
- Venkataraman G, Song JY, Tzankov A., et al. Aberrant T-cell antigen expression in classical Hodgkin lymphoma is associated with decreased event-free survival and overall survival. Blood. 2013;12110:1795–1804.
- Adams S.V., Newcomb P.A., Shustov A.R. Racial patterns of peripheral T-cell lymphoma incidence and survival in the United States. J. Clin. Oncol. 2016;34:963–971.
- Venkataraman G, Berkowitz J, Morris JC, et al. Adult T-cell leukemia/lymphoma with Epstein-Barr virus-positive Hodgkin-like cells. Hum Pathol. 2011;42:1042–1046.
- Ohtsuka E, Kikuchi H, Nasu M, et al. Clinicopathological features of adult T-cell leukemia with CD30 antigen expression. Leuk Lymphoma 1994;15:303-10.

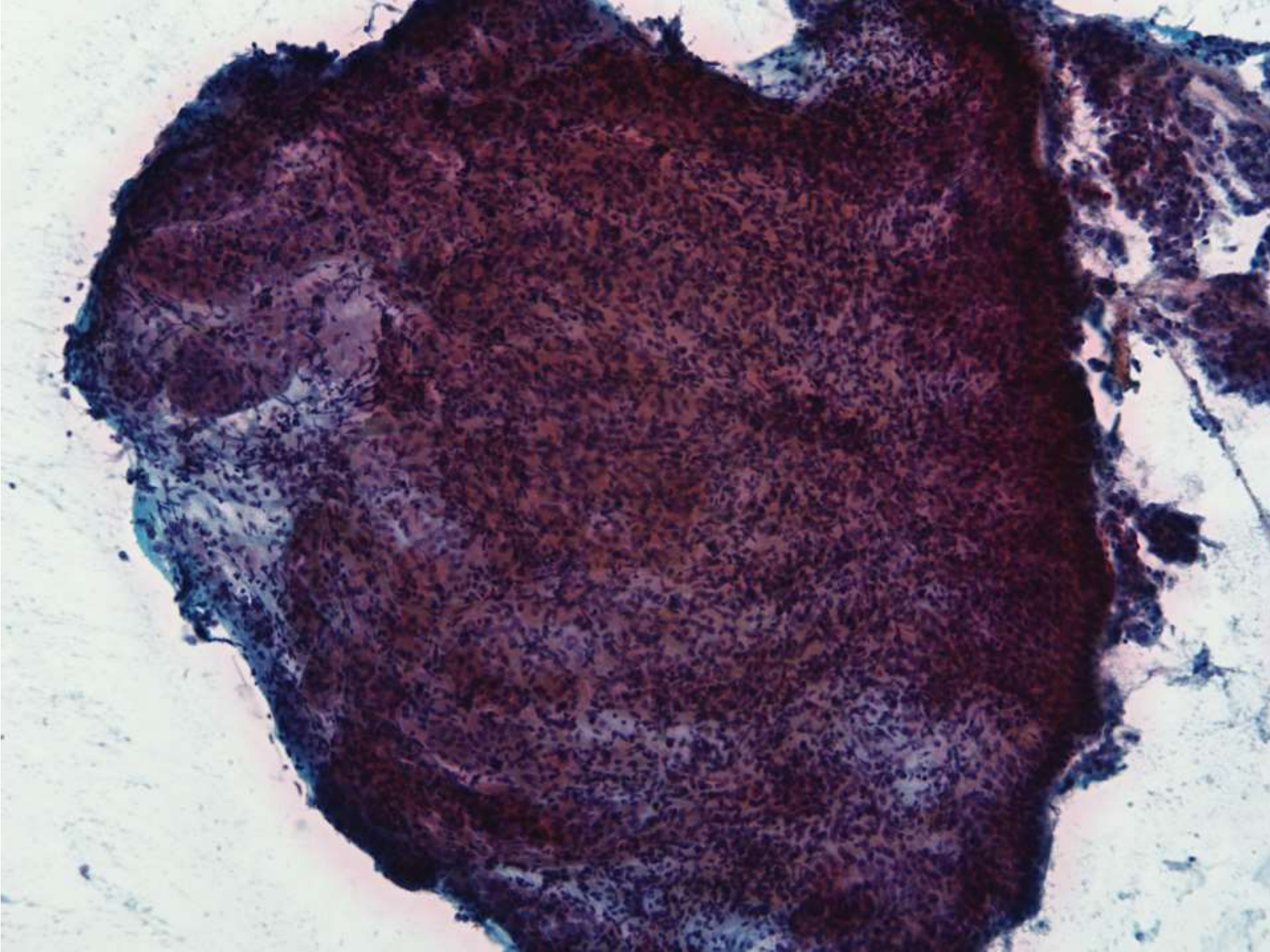
SB 6310

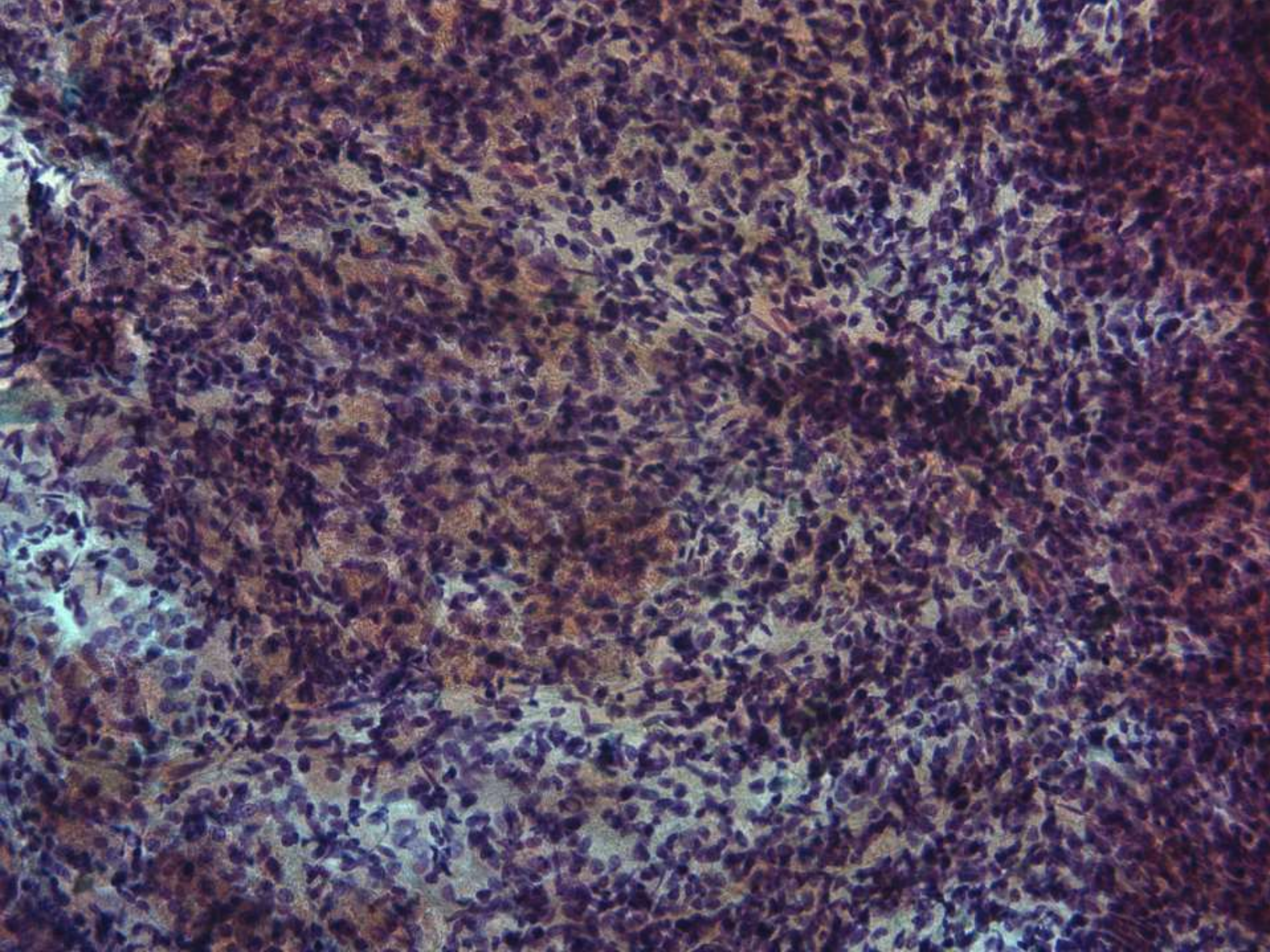
Erna Forgo/Eduardo Zambrano/Brittany Holmes; Stanford

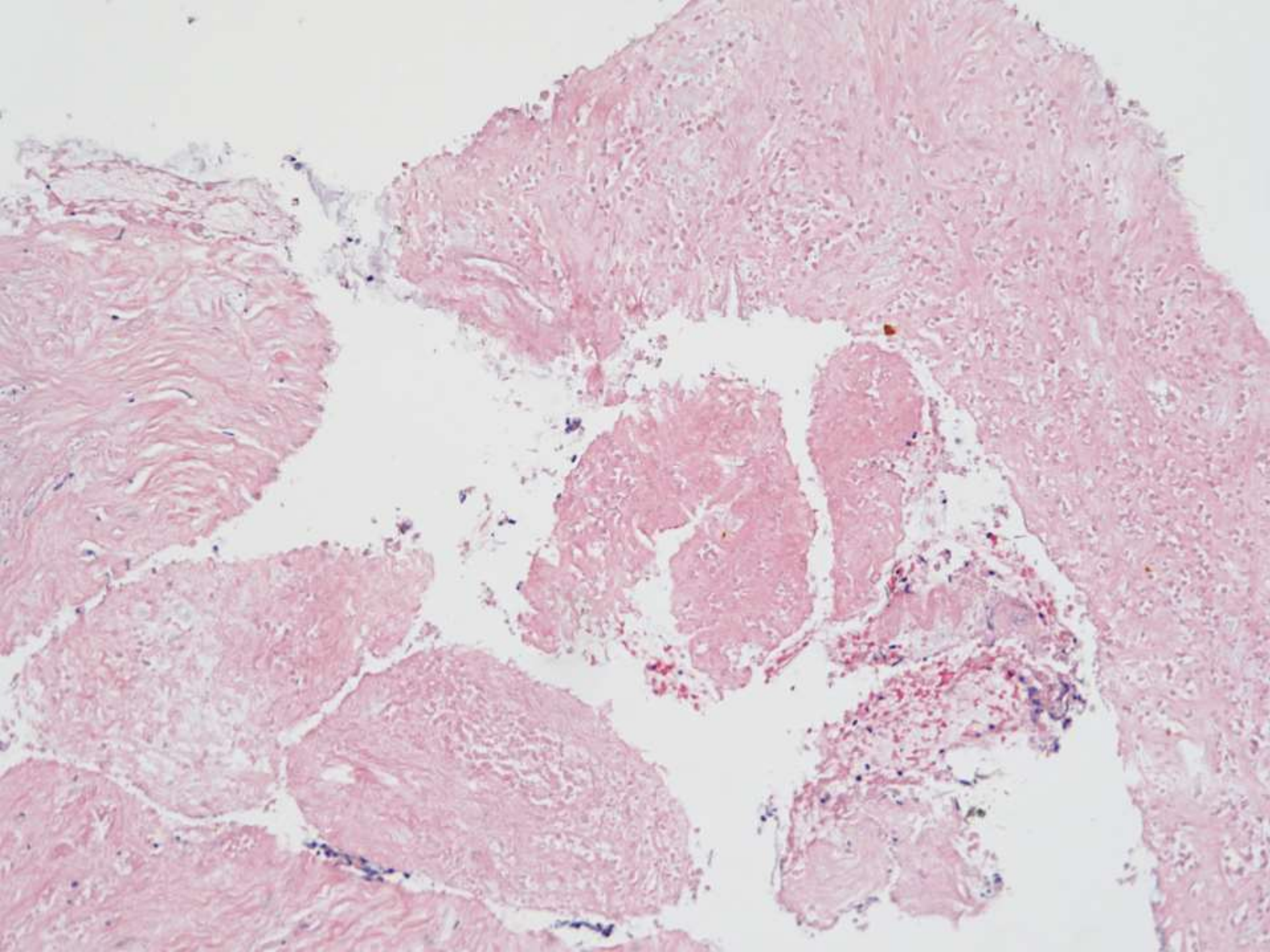
73-year-old male with h/o of low grade fibromyxoid sarcoma, currently on anti-PDGFRa chemotherapy, now presenting with severe abdominal pain c/w pancreatitis (drug-induced vs autoimmune). PET/CT shows diffuse pancreatic enlargement with FDG avidity. FNA pancreas submitted.

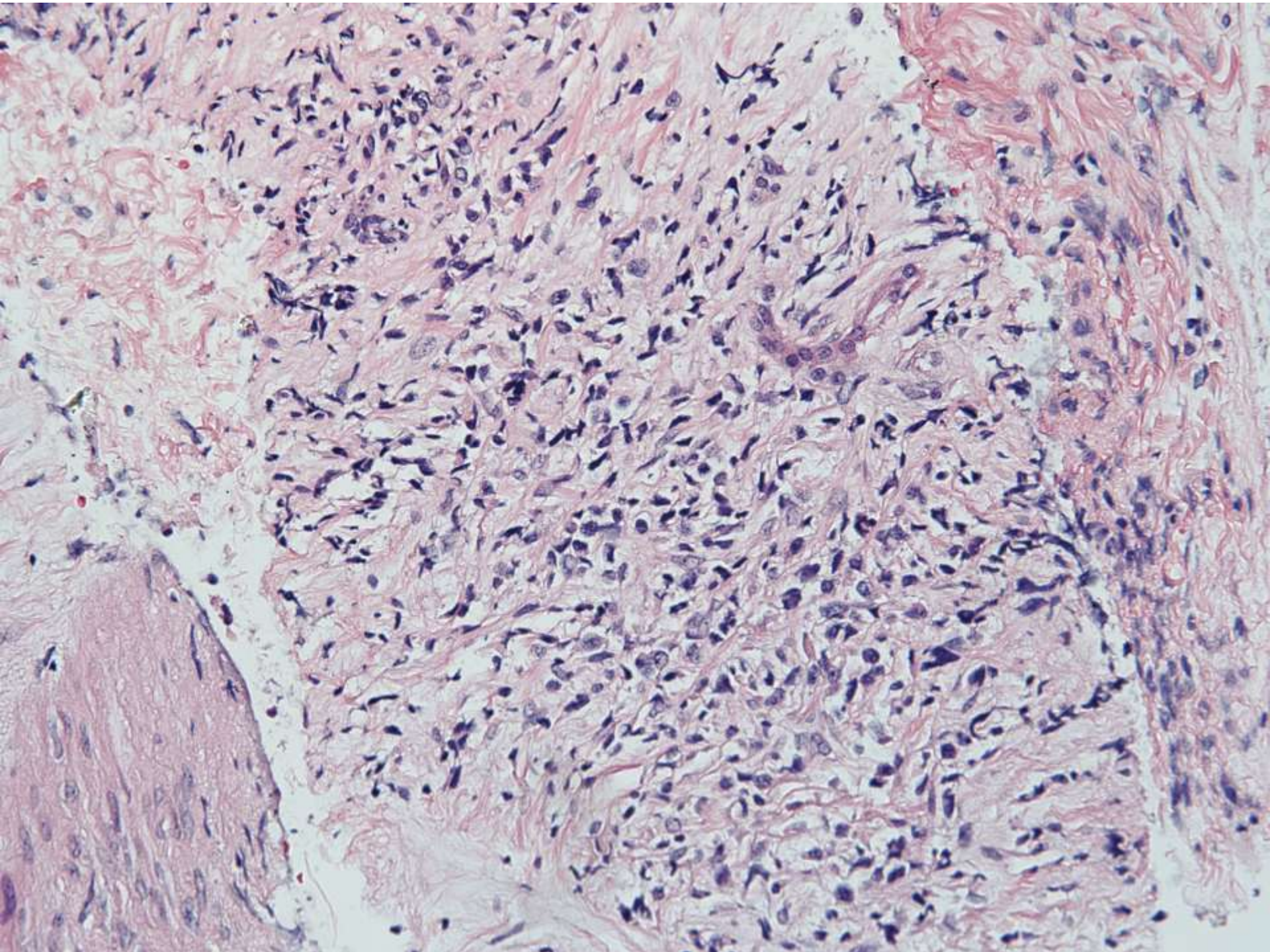


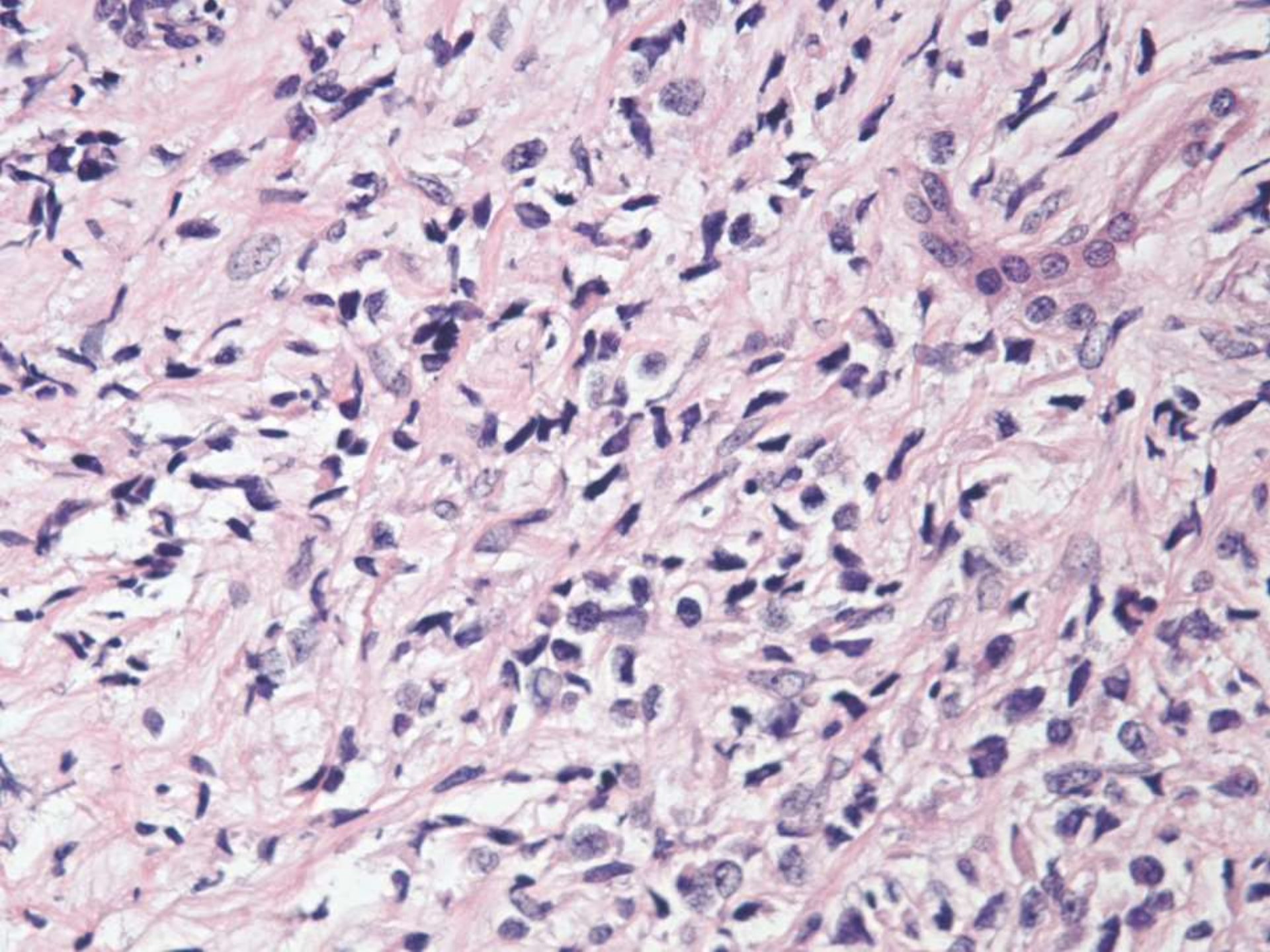




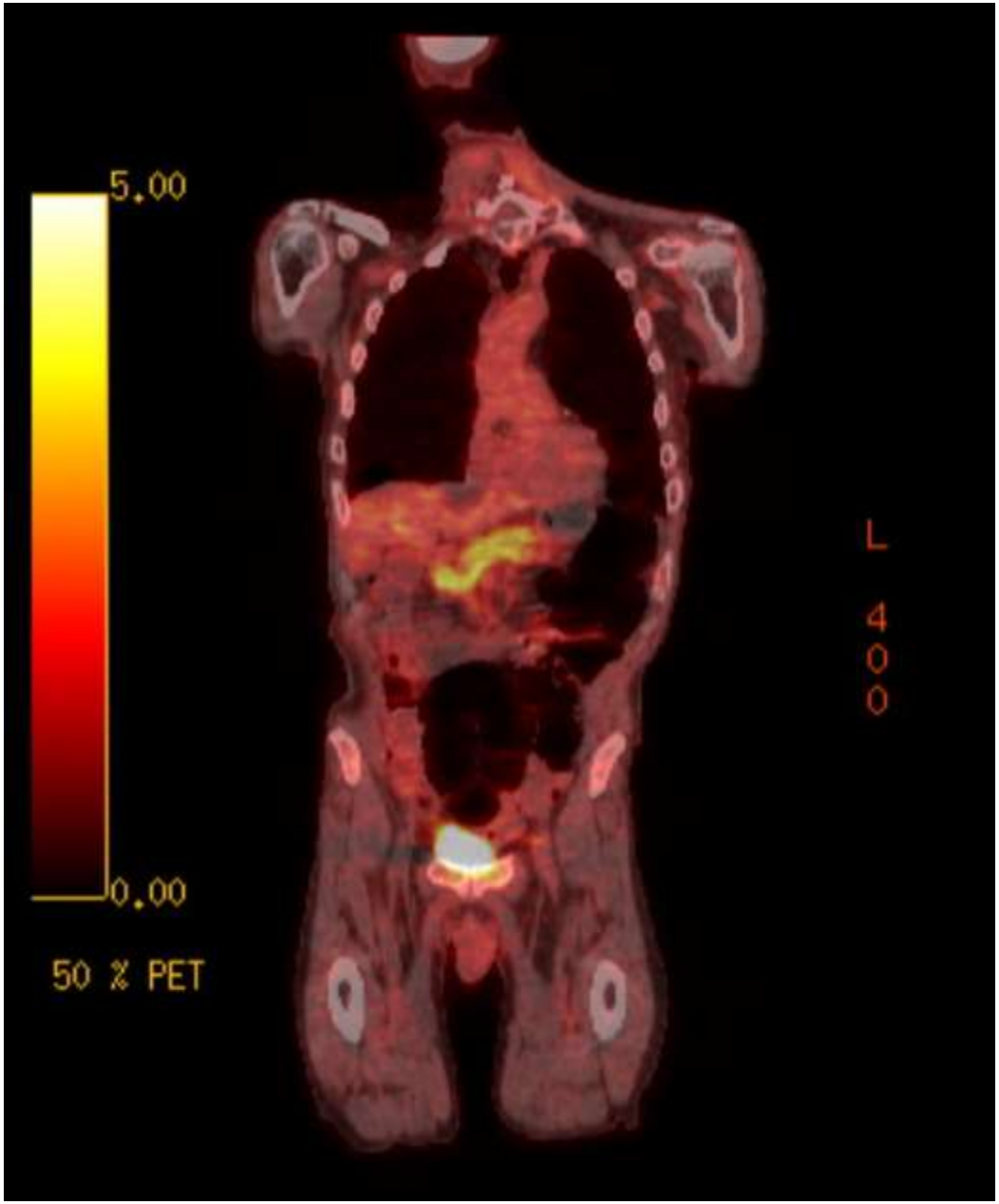








DIAGNOSIS?


5.00
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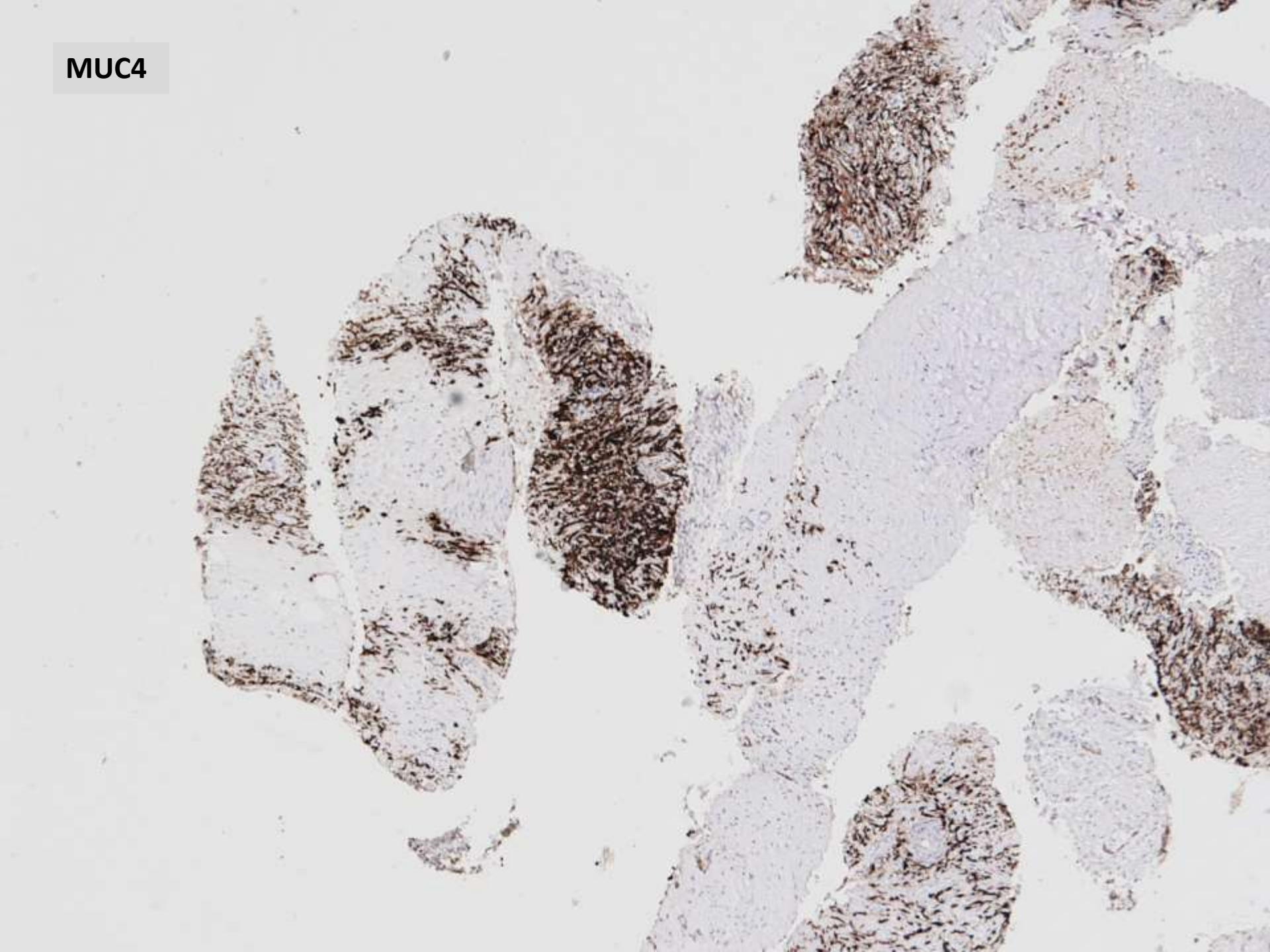
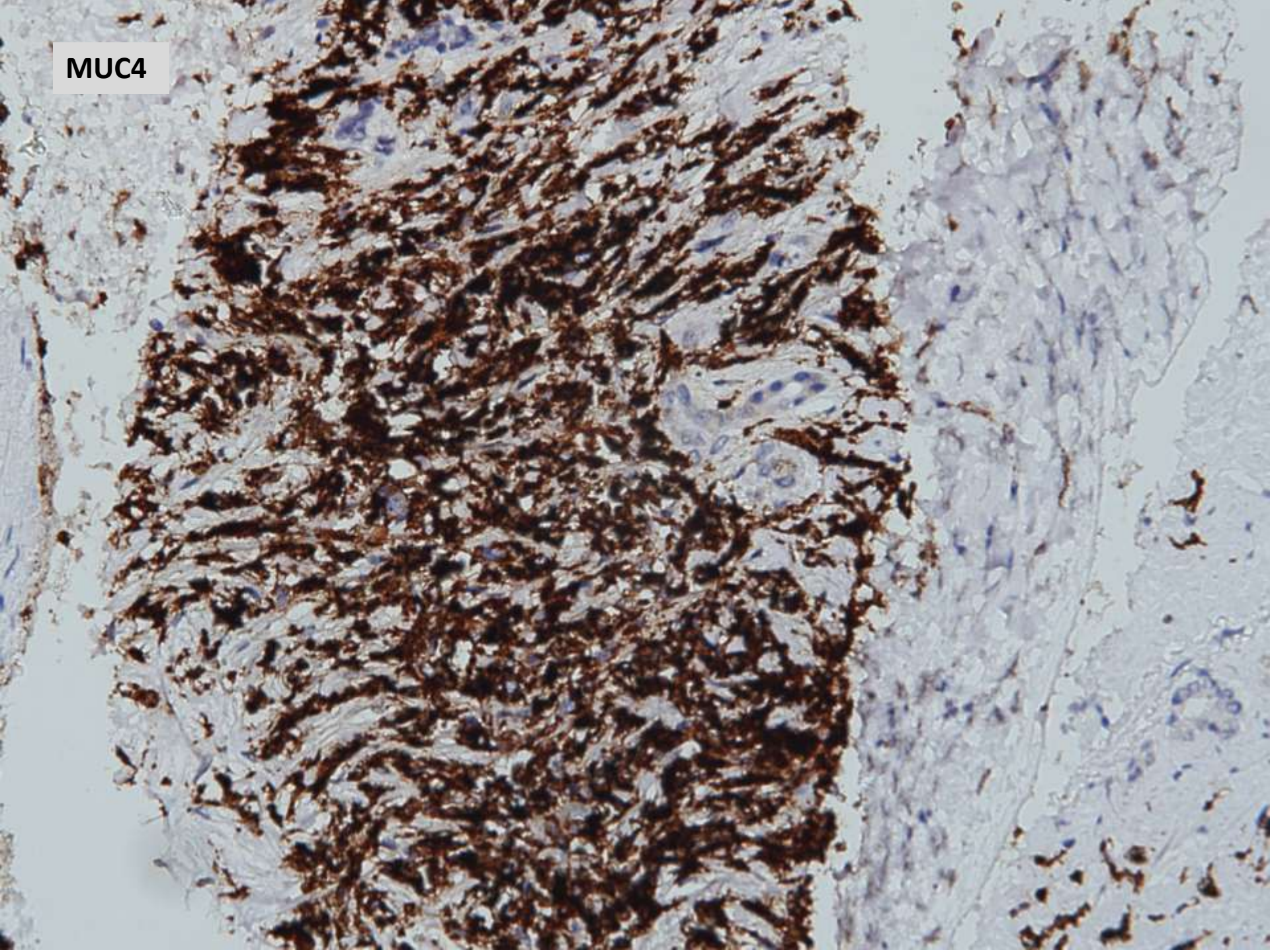
Differential Diagnosis

- Pancreatitis
- Drug inducted (chemotherapy)
- Autoimmune pancreatitis
- Metastatic infiltration
- Primary malignancy


MUC4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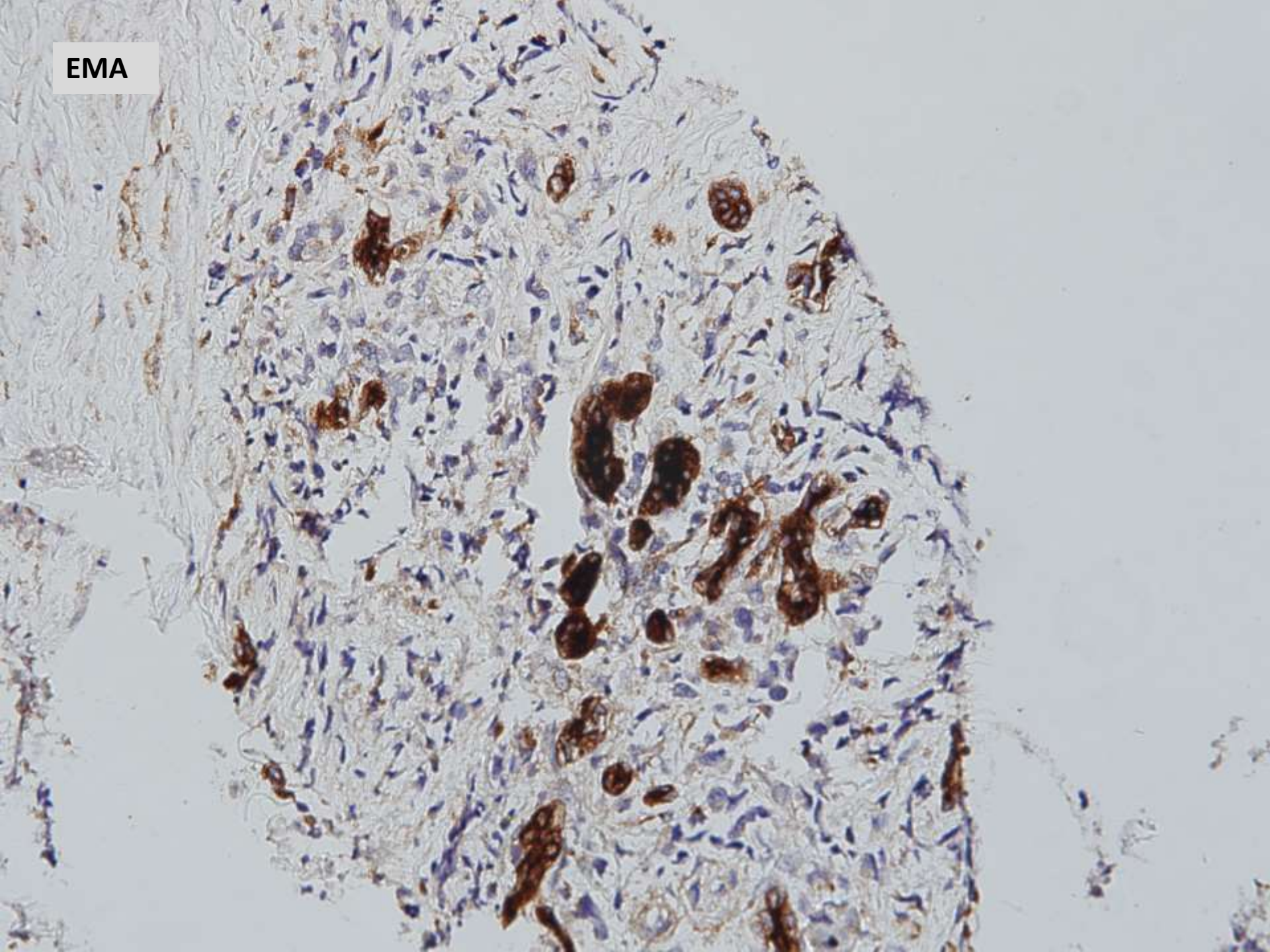
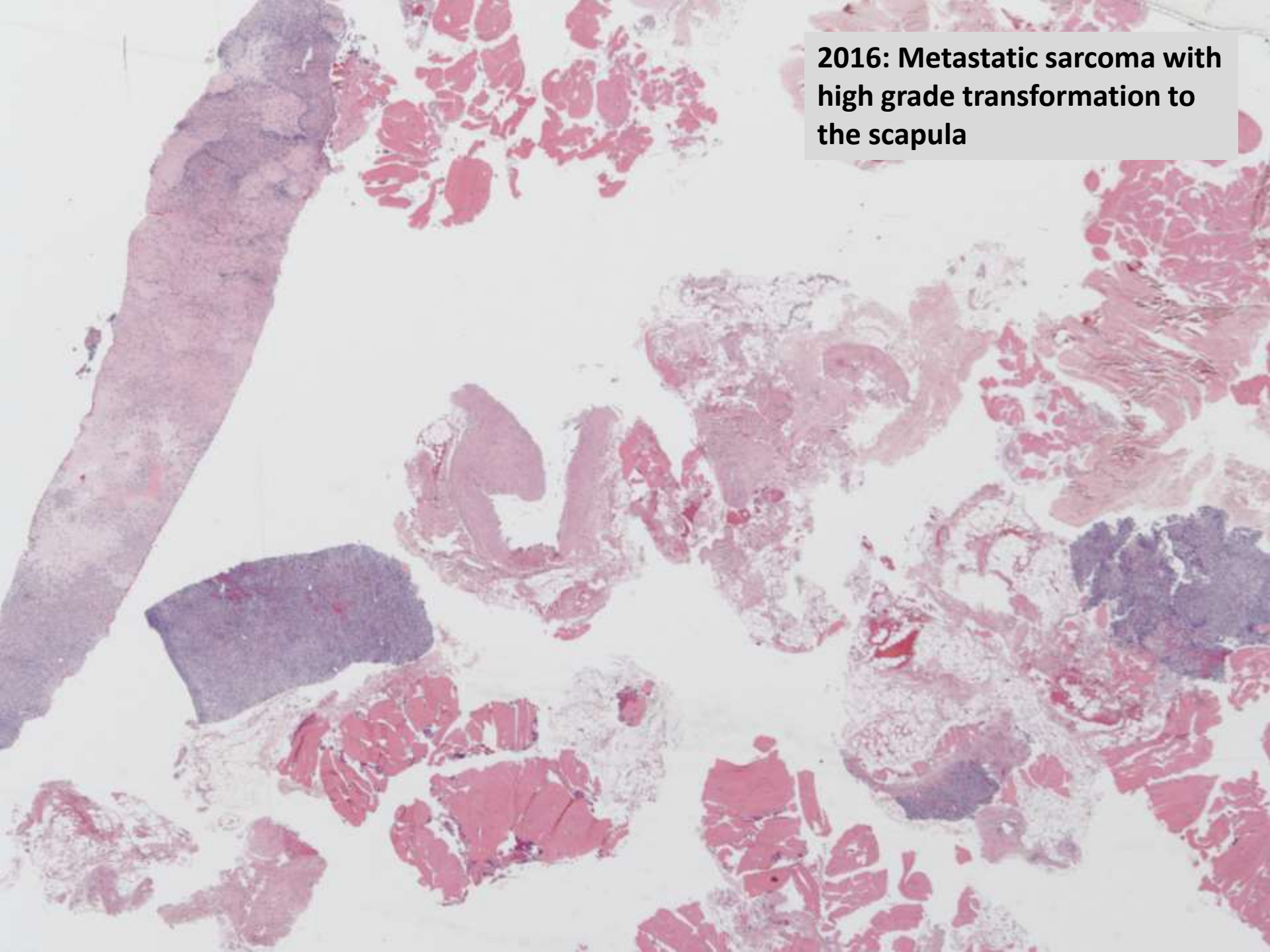
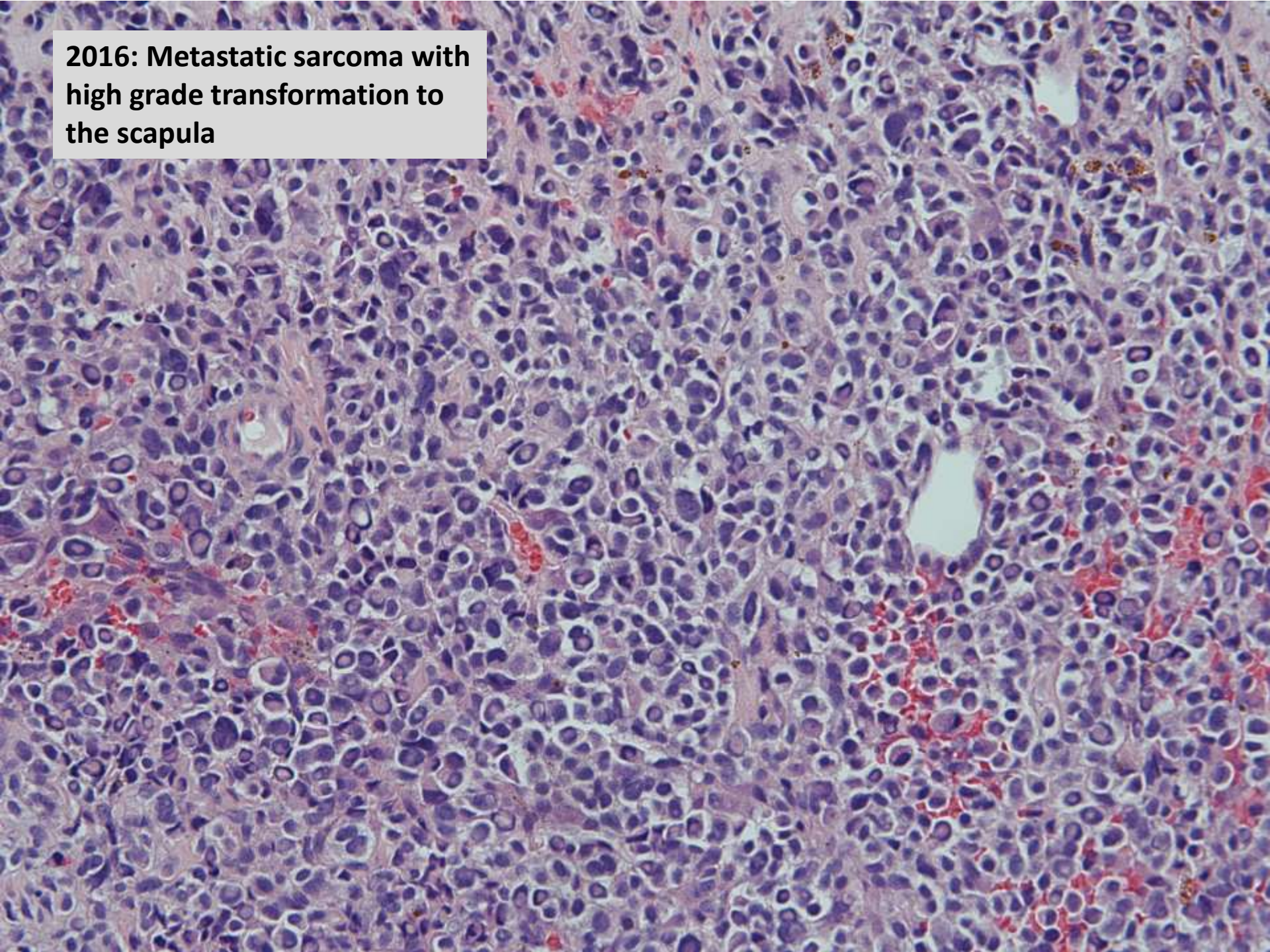

EMA

Additional IHC work-up

- CD3 and CD20 highlighted background mixed T and B cells
- CD163 highlighted background macrophages
- IgG, IgG4 was negative


2016: Metastatic sarcoma with high grade transformation to the scapula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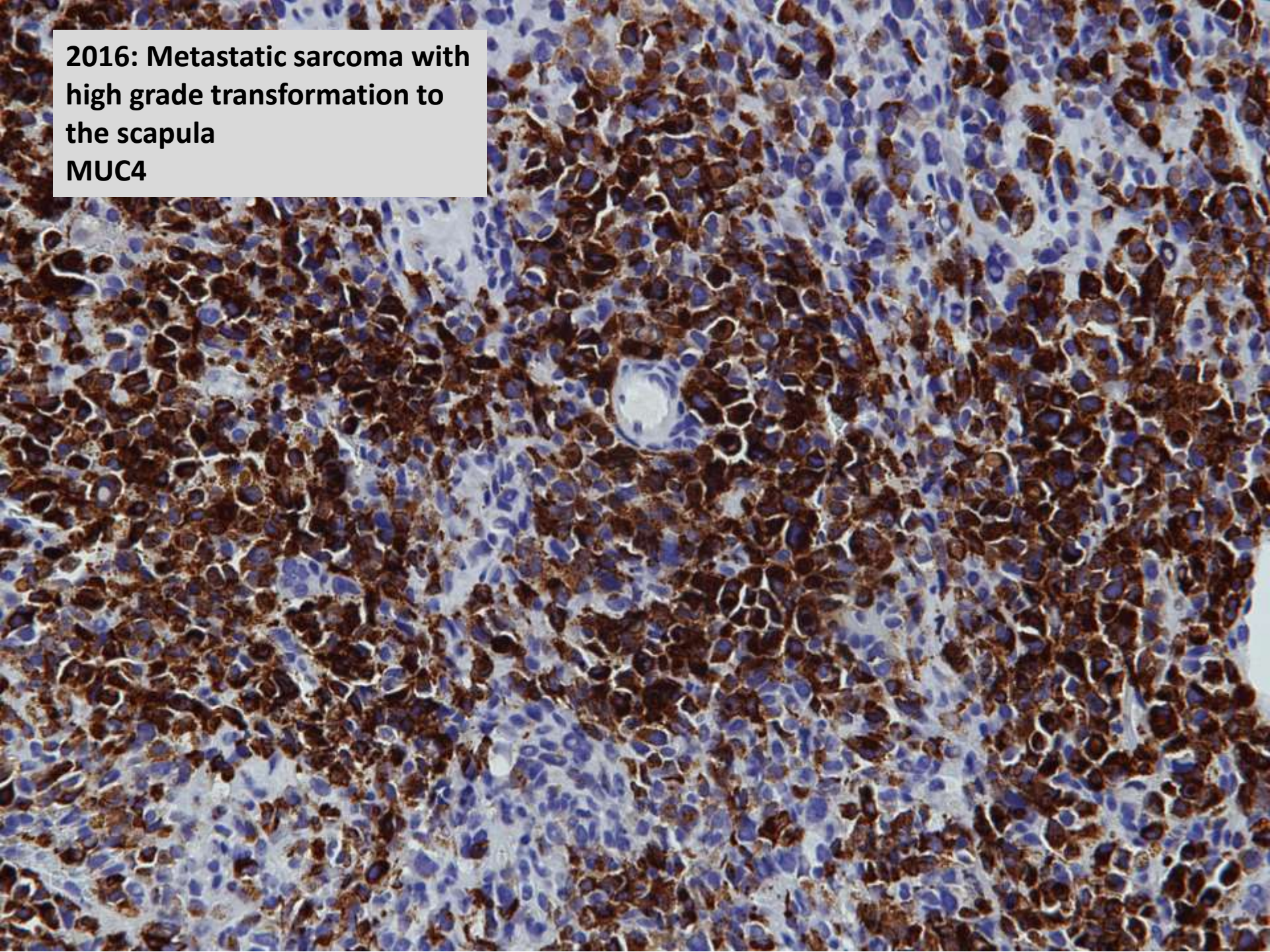
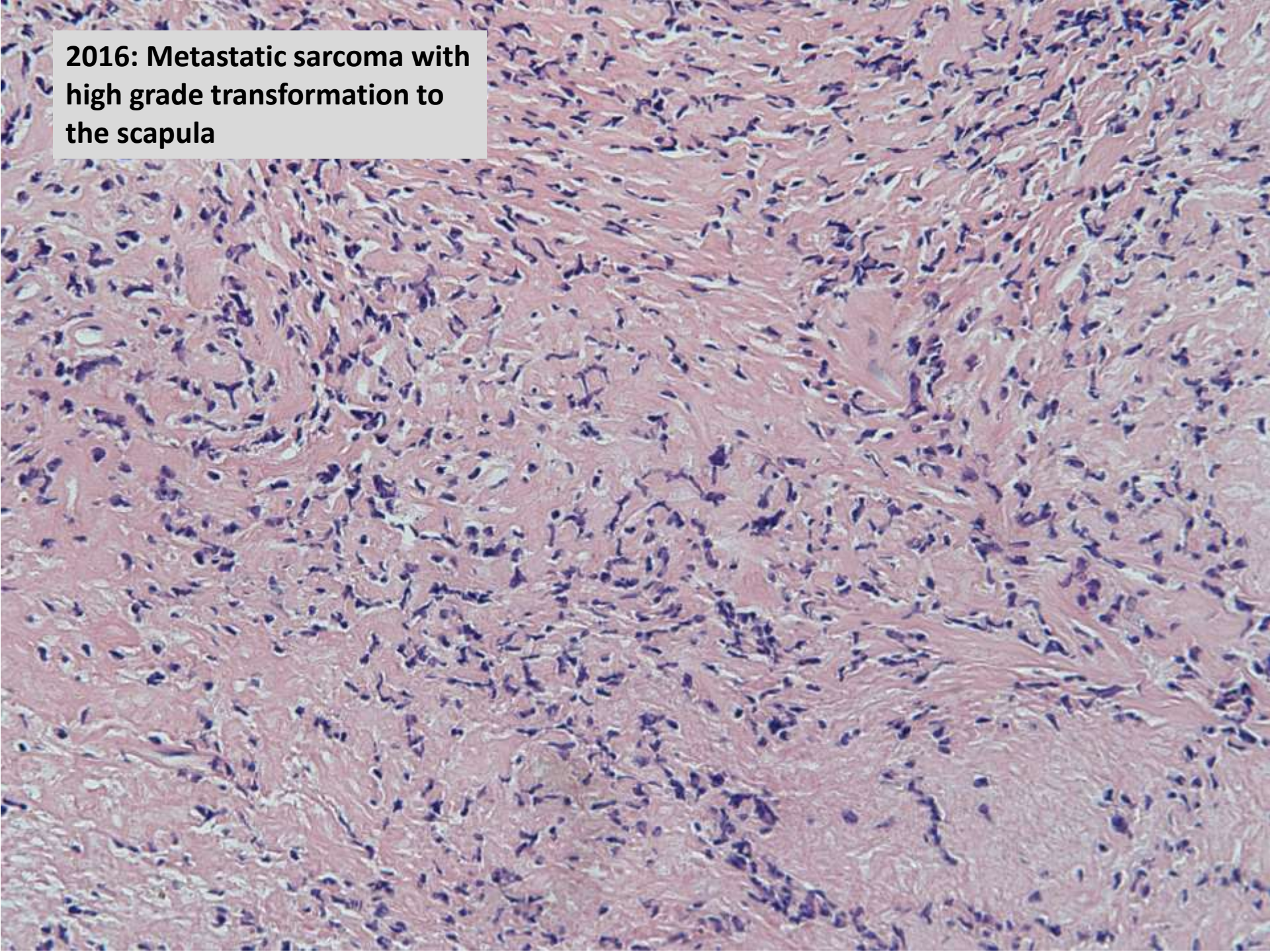
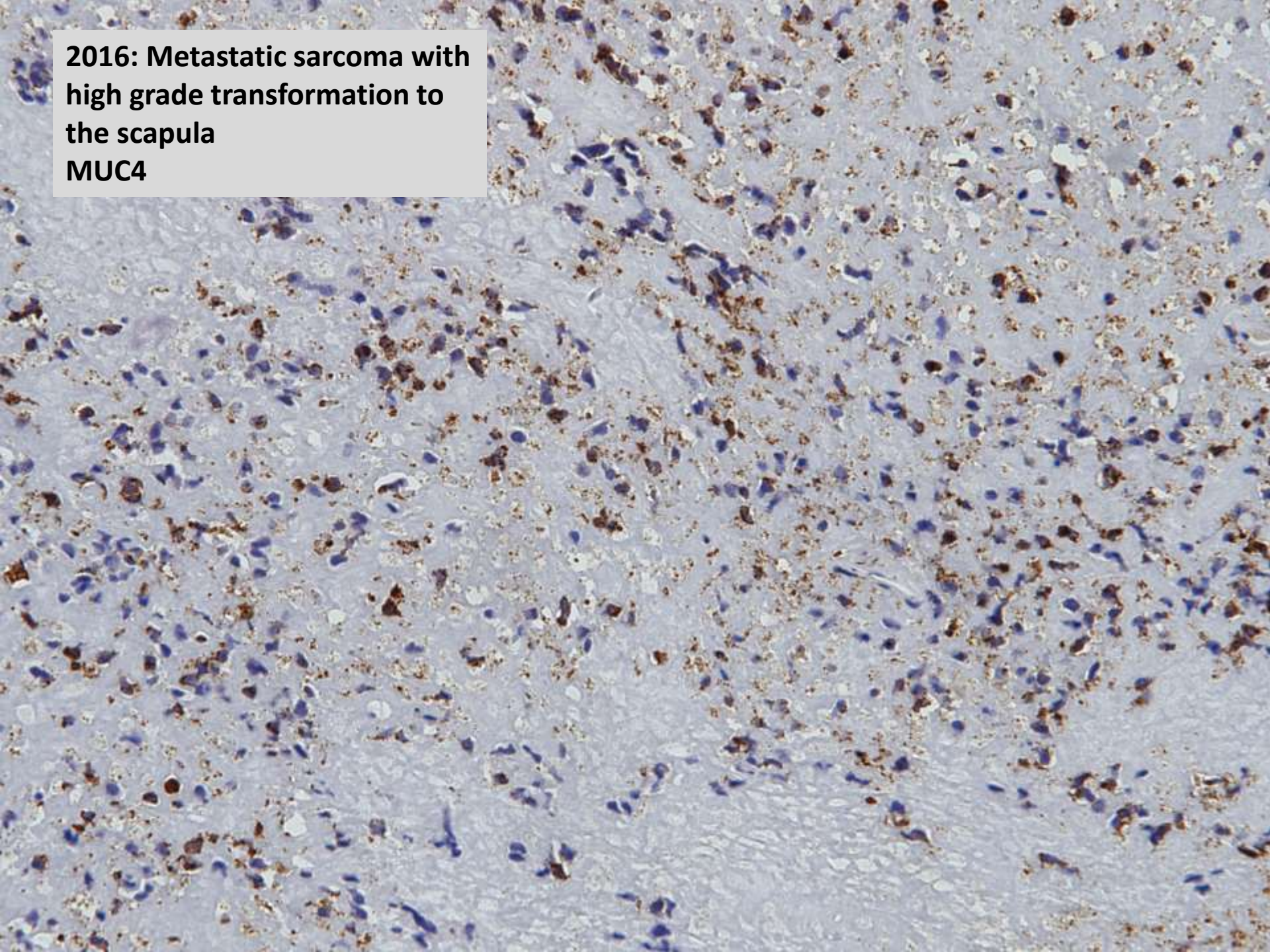

2016: Metastatic sarcoma with high grade transformation to the scapula
MUC4


2016: Metastatic sarcoma with high grade transformation to the scapula


2016: Metastatic sarcoma with high grade transformation to the scapula
MUC4

MUC4 staining in the Pancreas

Table 2. Pattern of mucin (MUC) expression

	Pancreatic cancer		Chronic pancreatitis		Normal pancreas	
MUC	Positive staining (%)	Quickscore, median (IQR)	Positive staining (%)	Quickscore, median (IQR)	Positive staining (%)	Quickscore, median (IQR)
MUC1	100	300 (270–300)	100	270 (270–270)*	100	260 (200–280)*
MUC2	25	0 (0–15)	39	2 (0–30)	15	0 (0–0)
MUC3	56	15 (0–60)	97†	100 (70–160)*	92†	70 (50–140)*
MUC4	91	150 (80–210)	85	120 (60–180)	65	80 (20–150)
MUC5AC	86	180 (90–270)	85	50 (30–90)*	65	20 (10–60)*
MUC6	64	30 (3–120)	100	180 (150–240)*	88	120 (100–180)*

IQR, Interquartile range.
*Mann–Whitney *U*-test $P < 0.001$ as compared with pancreatic ductal cell adenocarcinoma.
†Chi-square test $P < 0.001$ as compared with pancreatic ductal cell adenocarcinoma.

Sierzega M et al. *Histopathology*. 2016 Oct;69(4):582-91

Diagnosis

- 2017 FNA of pancreas – FISH for FUS negative

- DIAGNOSIS:
  - -- ATYPICAL (SEE COMMENT)
  - -- FISH NEGATIVE FOR FUS GENE REARRANGEMENT

“While the findings could be consistent with chronic pancreatitis, the necrosis and atypia are unusual, and involvement by the patient’s known sarcoma cannot be entirely excluded.”

Additional FISH work up

- 2016 metastatic sarcoma – FUS negative

Am J Surg Pathol. 2013 May;37(5):734-8. doi: 10.1097/PAS.0b013e31827560f8.

EWSR1-CREB3L1 gene fusion: a novel alternative molecular aberration of low-grade fibromyxoid sarcoma.

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Abstract

Low-grade fibromyxoid sarcoma (LGFMS) is an uncommon sarcoma with a deceptively bland-looking morphology that disguises its malignant clinical behavior. It shows distinctive chromosomal translocations resulting in fusion of FUS with the CREB3L2 gene in most cases and CREB3L1 in rare cases. Thus molecular studies are particularly helpful in the diagnosis of this bland-looking sarcoma. We report 2 cases of LGFMS serendipitously found to harbor a novel alternative EWSR1-CREB3L1 gene fusion, as confirmed by DNA sequencing of reverse transcriptase-polymerase chain reaction products and fluorescence in situ hybridization. One patient was a child who presented with a subcutaneous nodule on the lower leg, and the other was a middle-aged woman who had a mass lesion over the proximal thigh. Morphologically, one case showed a spindle cell tumor with hyalinization and giant rosettes, whereas the other showed classical histology of LGFMS with focal metaplastic bone formation. Immunostaining for MUC4 showed extensive positive staining. Our findings therefore expand the spectrum of gene fusions that characterize LGFMS and suggest that the EWSR1 gene may substitute for the function of FUS in gene fusions of sarcoma.

Additional FISH work up

- 2016 metastatic sarcoma – FUS negative
- 2016 metastatic sarcoma – EWSR1 **positive**!
- 2017 FNA of pancreas – EWSR1 **positive**!

Follow up

- Celiac plexus block - 12/11/2017, 12/28/2017, 1/18/2018
- Prednisone, methadone, dilaudid, Lyrica

- Referred to local Radiation Oncology for urgent radiation
- Prednisone taper started (was still on 70mg of daily)
- Admitted to Hospice care on 2/19/2018 and passed away on 2/22/2018

Low-Grade Fibromyxoid Sarcoma

- Deceptively bland malignant fibroblastic neoplasm composed of spindle cells in variable collagenous to myxoid matrix
- Proximal extremities and trunk, deep soft tissue
- Treatment: Wide surgical excision
- Generally indolent clinical course
  - Higher rates of recurrence and metastatic disease with longer clinical follow-up
  - Most common to lung, pleura, and chest wall

Chromosomal Translocations

- t(7;16)(q33;p11) is most common (75%)
  - Results in *FUS-CREB3L2* fusion
- t(11;16)(p11;p11)
  - Results in *FUS-CREB3L1* fusion

- Very rare tumors reported with *EWSR1-CREB3L1* fusion

Take home points

- MUC4 staining in normal pancreas and chronic pancreatitis
- Rare EWSR1 gene rearrangements in LGFMS
- Sarcomas can metastasize to the pancreas