Penn Medicine
Hospital of the University of Pennsylvania

MONTHLY MULTI-INSTITUTIONS HEMATOPATHOLOGY INTERESTING CASE CONFERENCE

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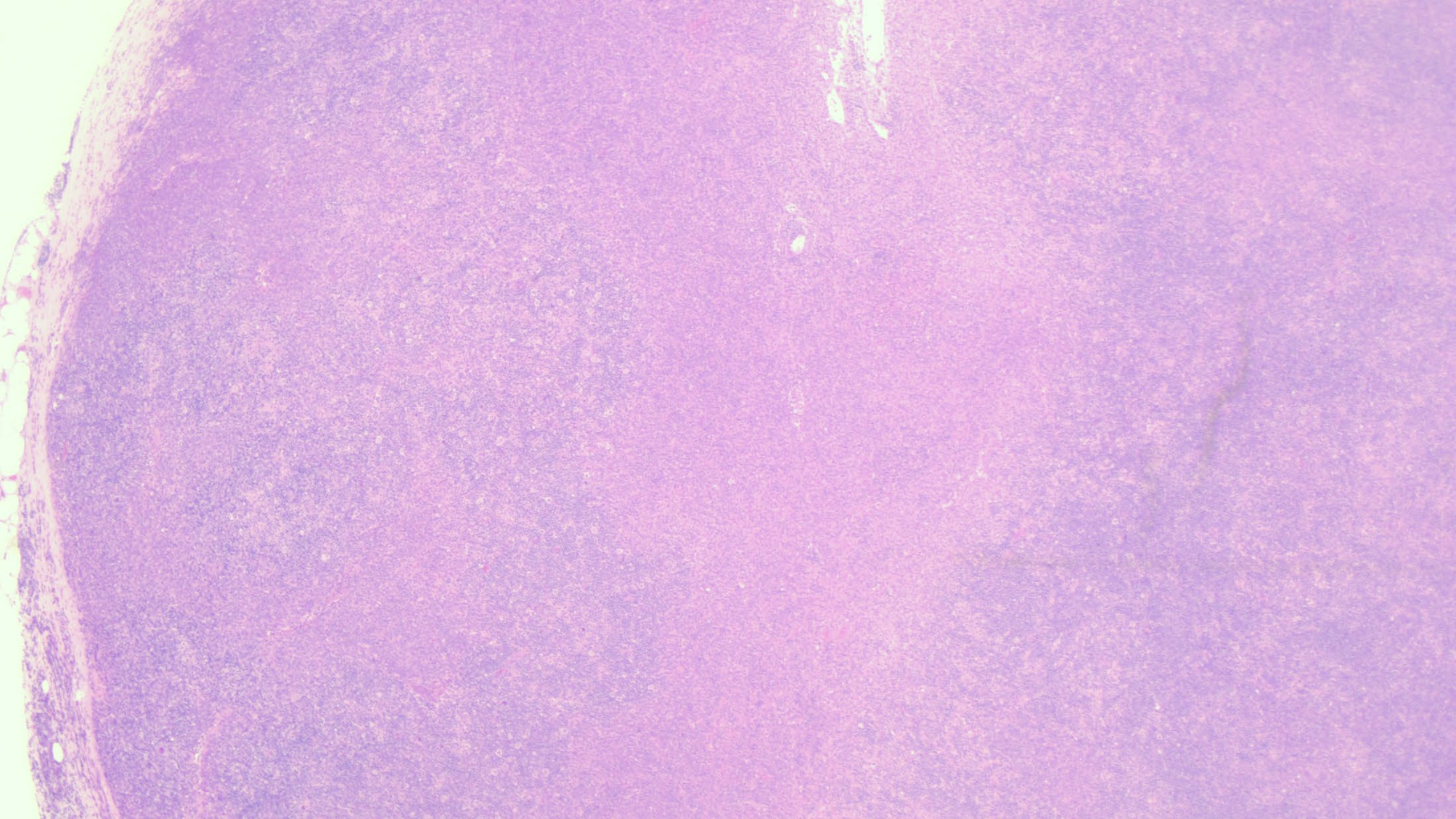
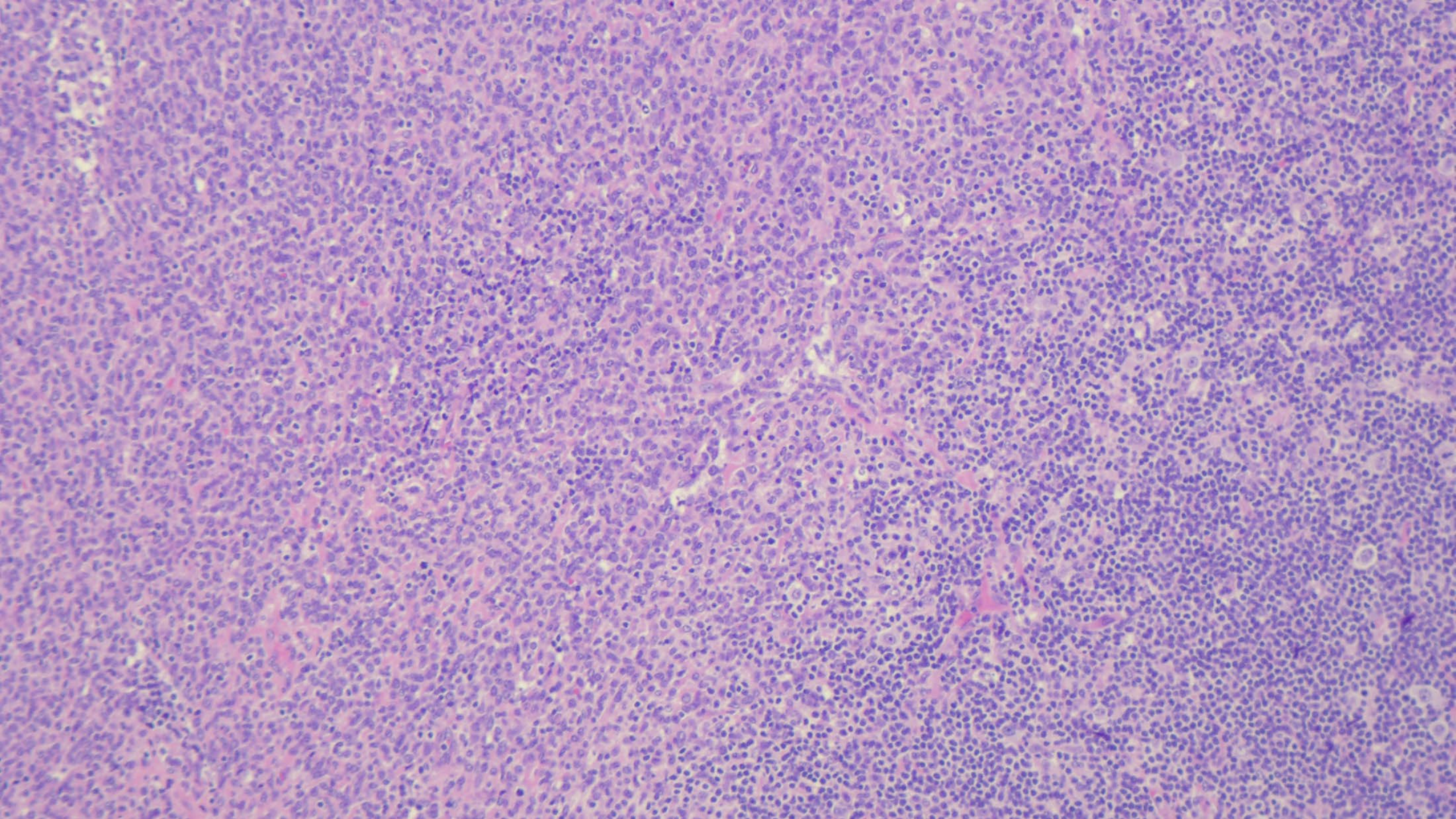
Clinical Presentation of 72 y/o M

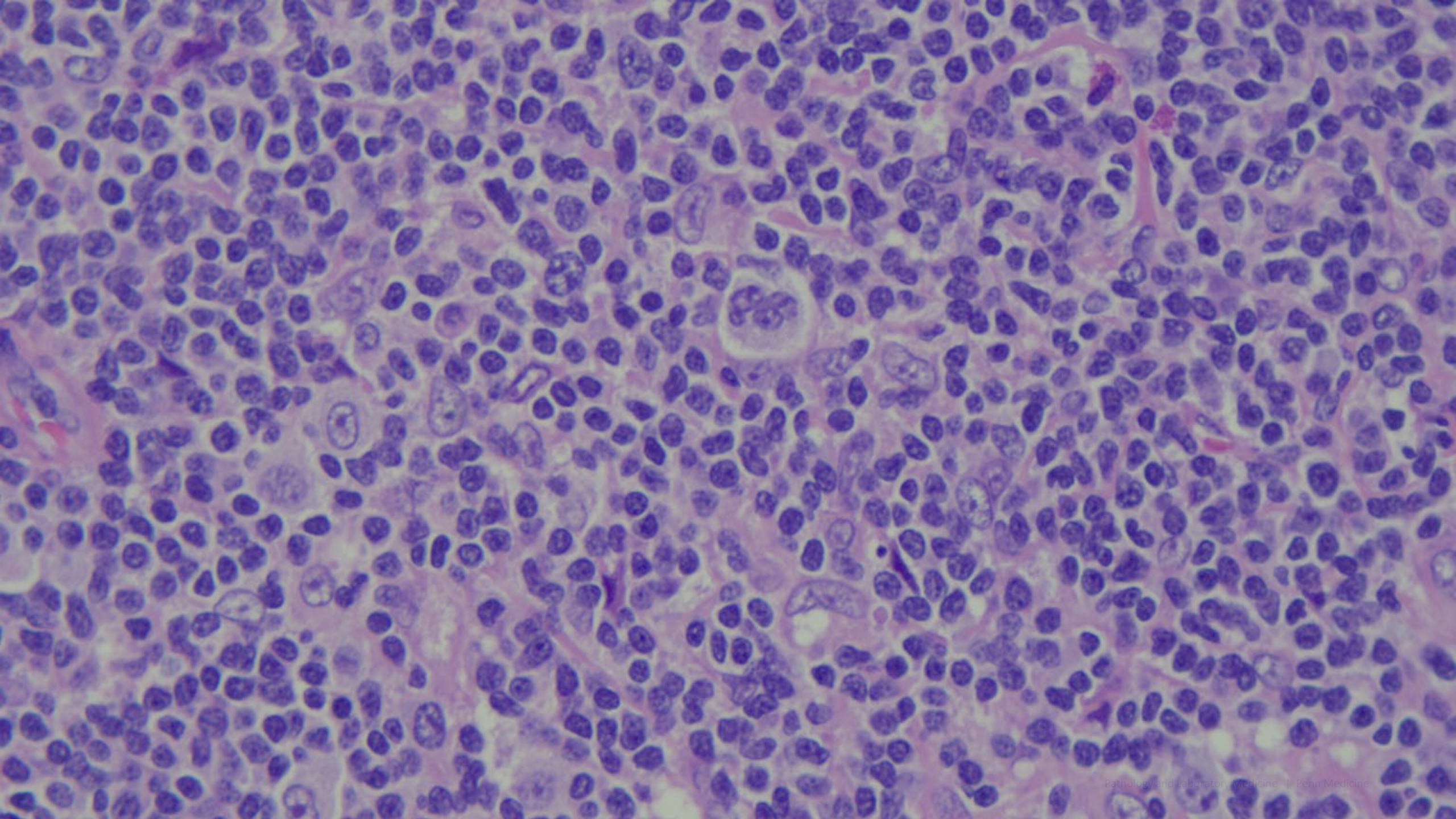
- **72 y/o male patient with h/o D.M. hyperlipidemia, and HTN**
- **Onset (April/25):** Fatigue, anorexia, unintentional weight loss
- **ED Presentation (Late July/25):**
  - Presyncope, left-sided neck mass
  - Episodes of diaphoresis and “sense of impending doom” with minimal exertion
  - **Labs:** Hb 8.6 g/dL, K^+ 2.9 mmol/L, WBC: absolute monocytosis
  - **CXR:** No consolidation/effusion

CT Neck with IV Contrast

LEFT CERVICAL LYMPHADENOPATHY WITH THE DOMINANT LYMPH NODE MEASURING 4.3 × 4.5 CM





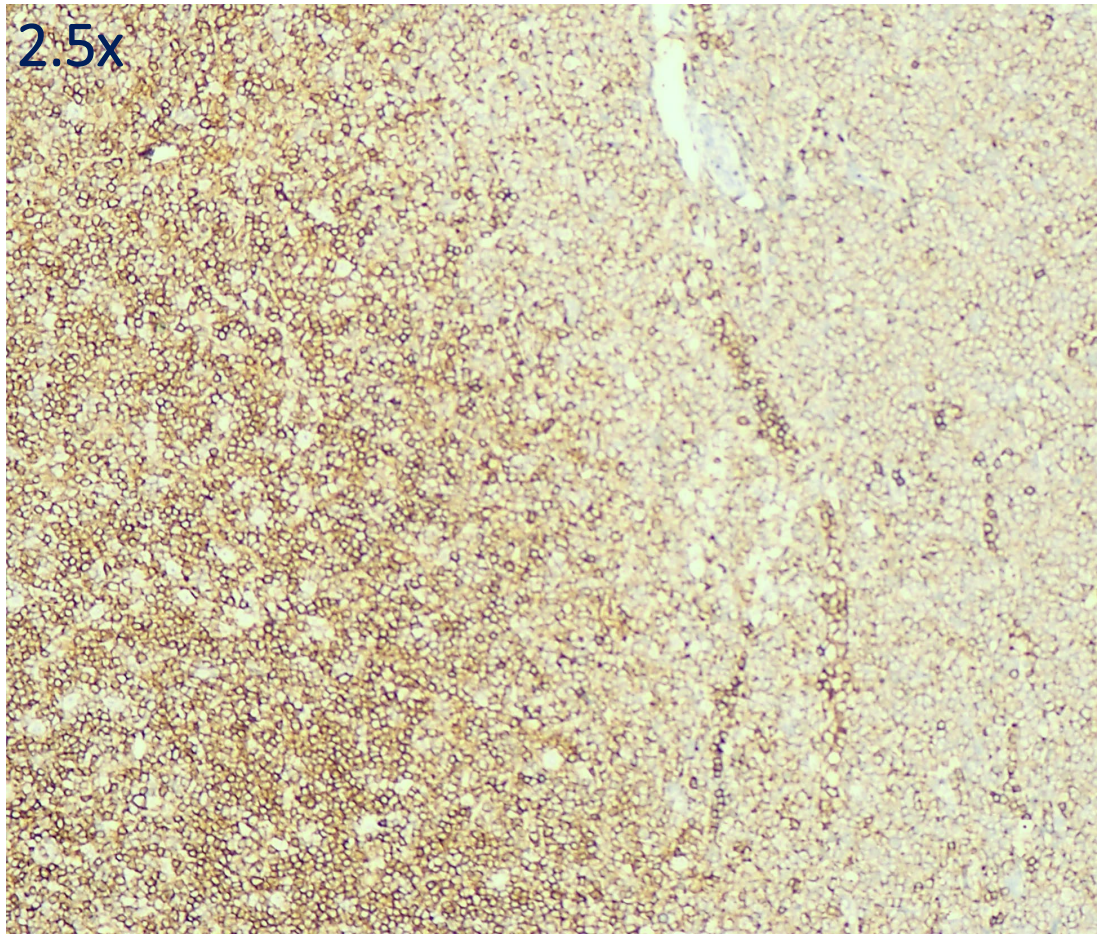


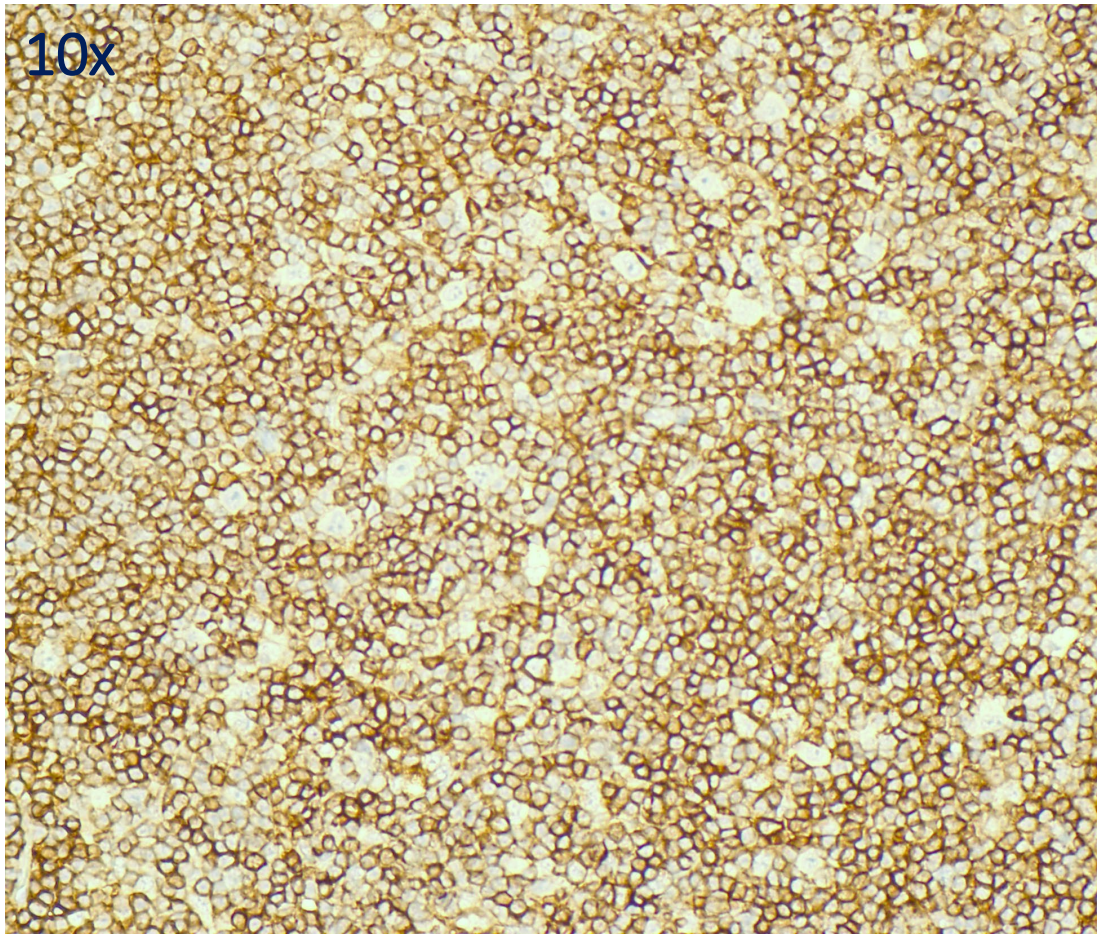
LN Flow Cytometry

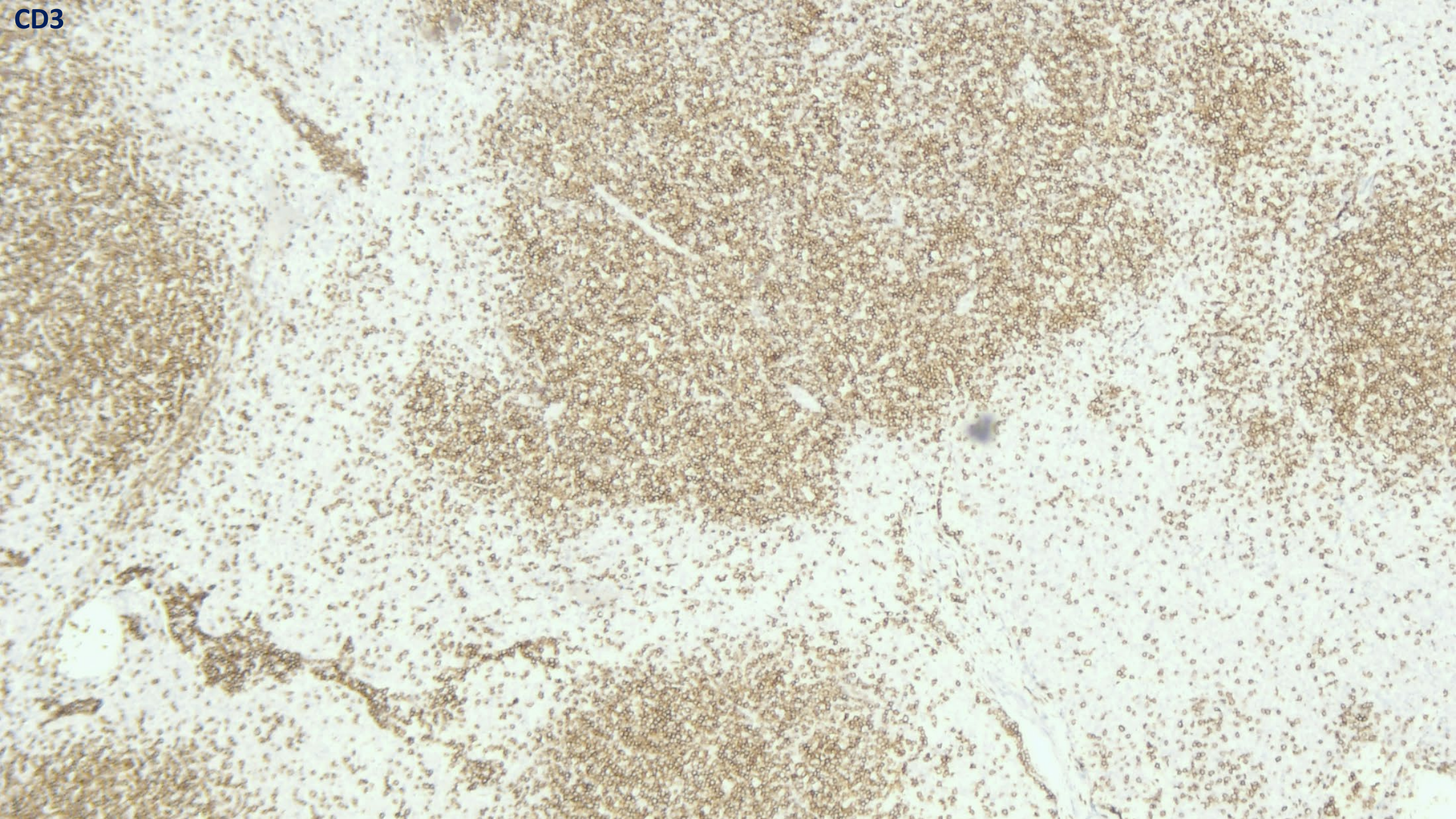
- Flow cytometry **did not detect an overt B- or T-cell Hodgkin lymphoma population**
- Limitations: Flow may miss CHL, some large cell lymphomas, or non-hematopoietic tumors due to processing
- **21.3 % atypical/immature monocytic population**
- Aberrant phenotype: **↓ CD13, ↓ CD14, CD56+**

Recommendation at the time: Correlation with morphology and bone marrow studies

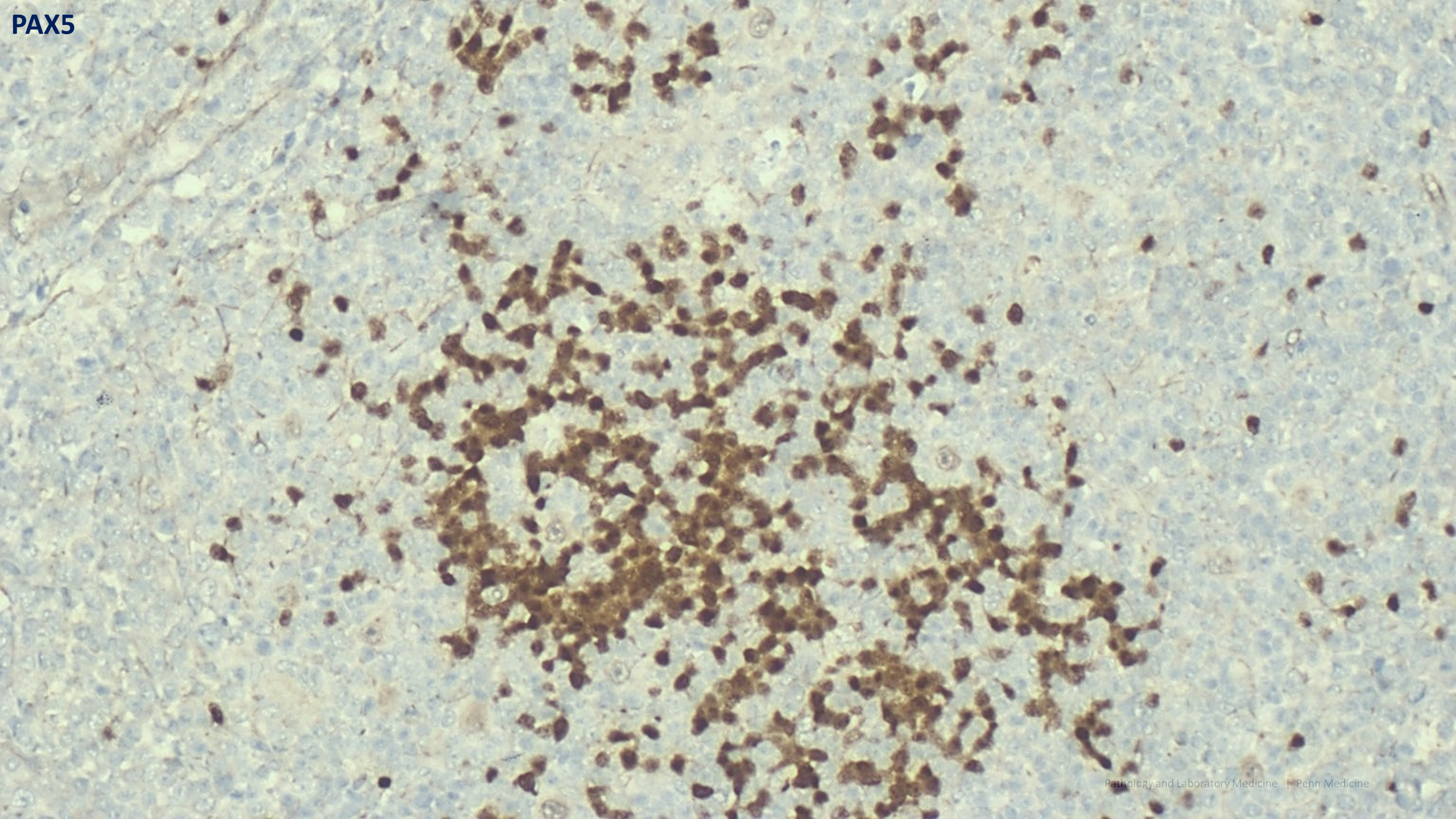
CD45

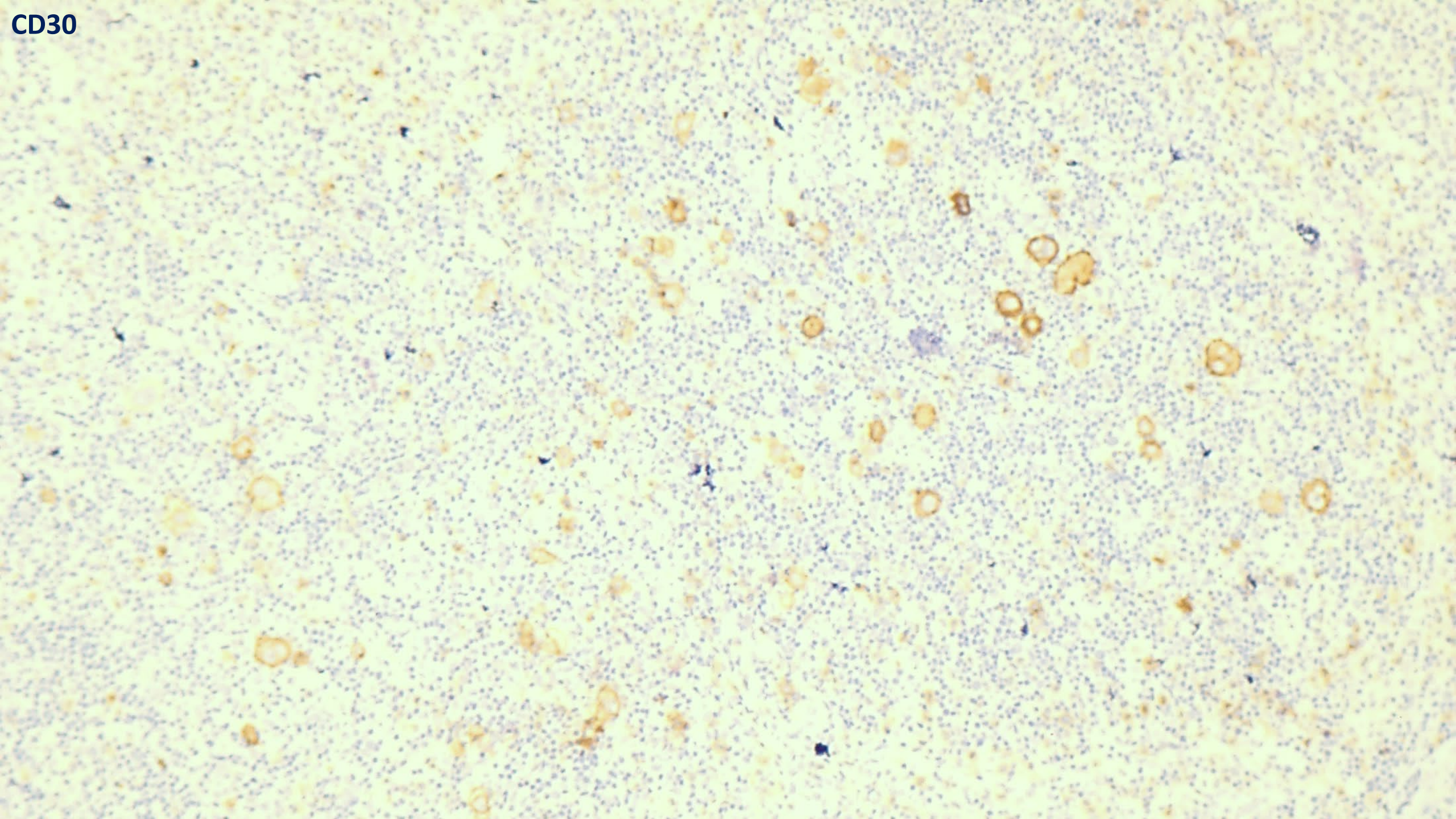


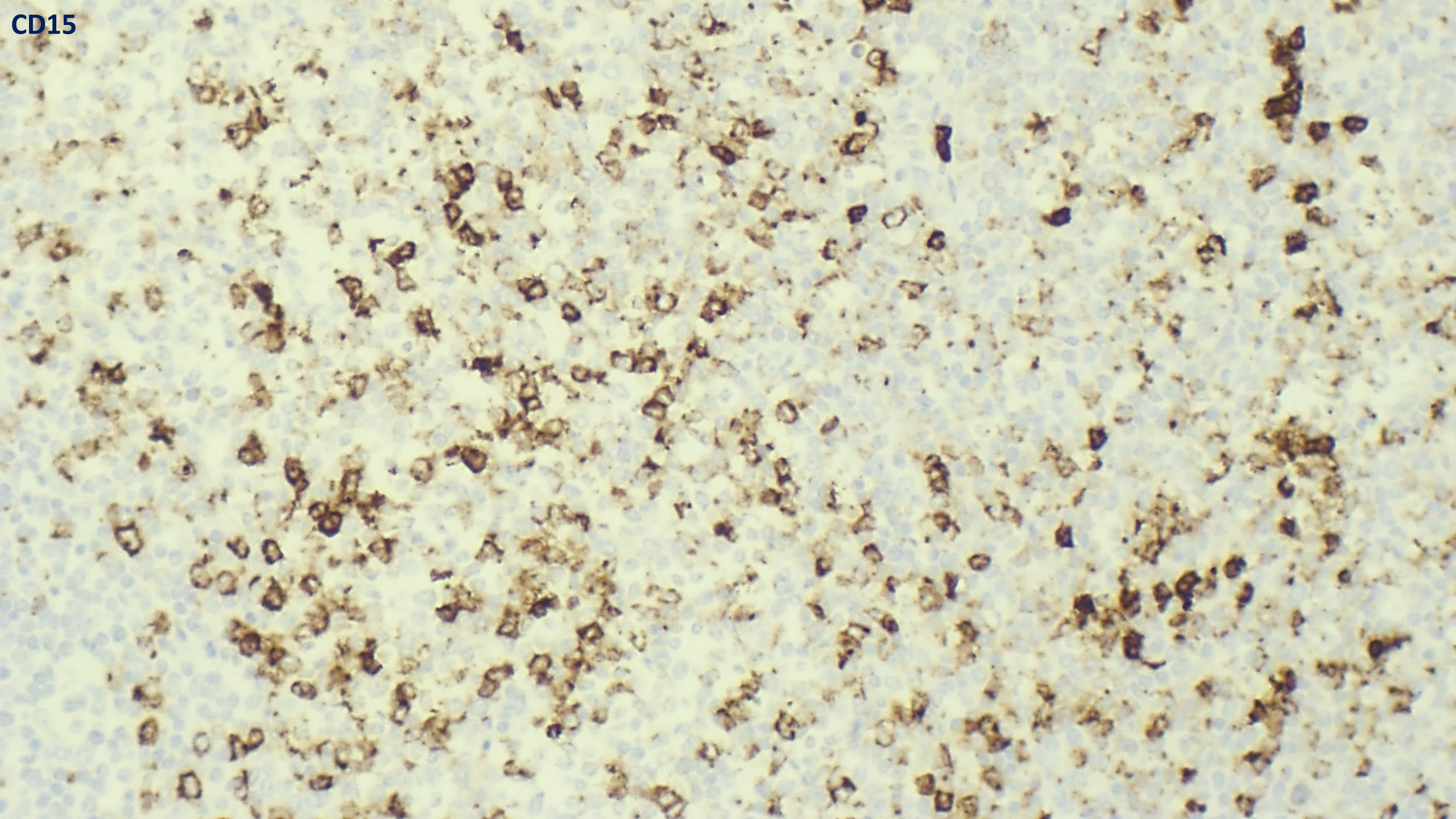



CD3

PAX5




CD30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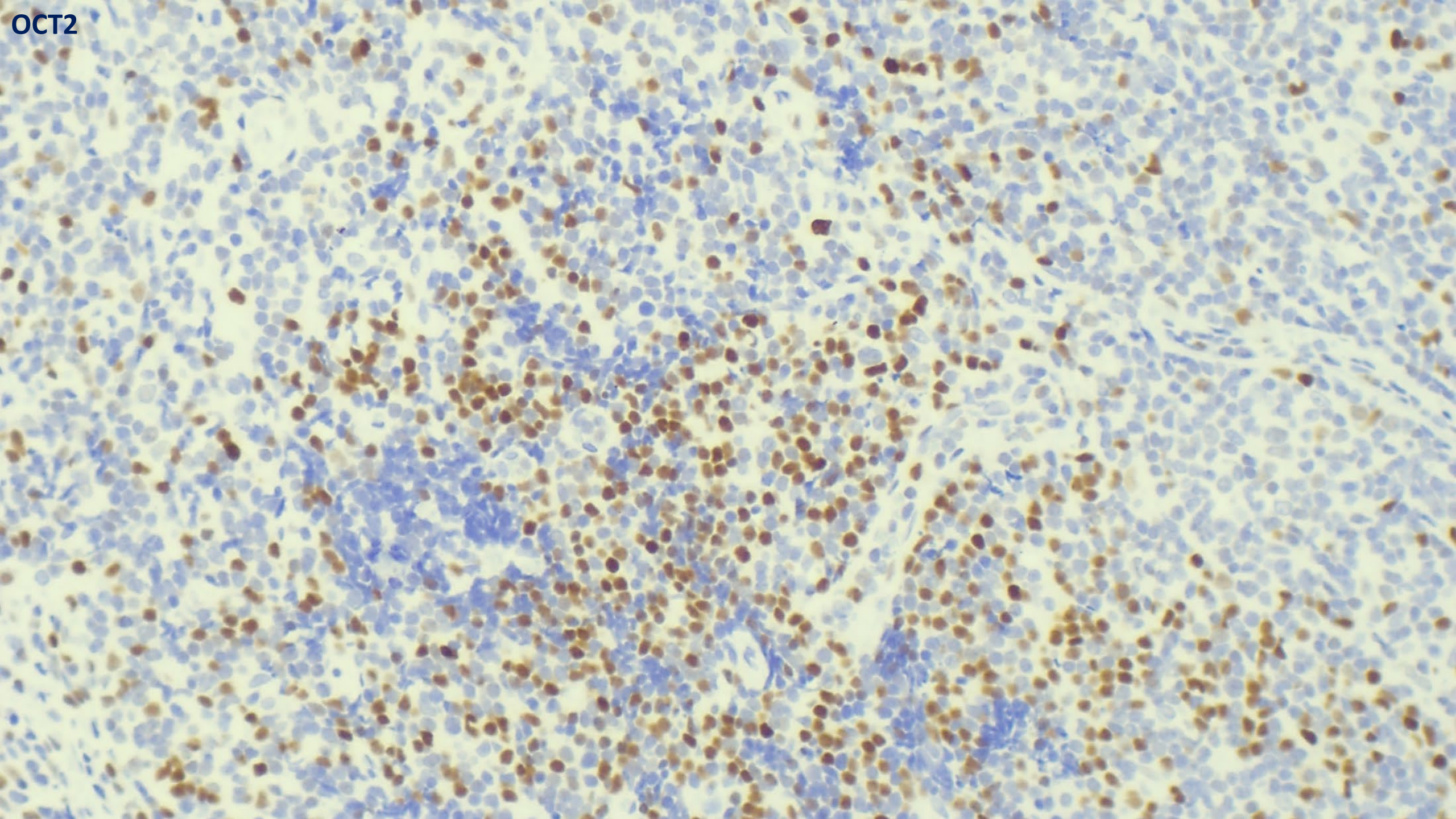
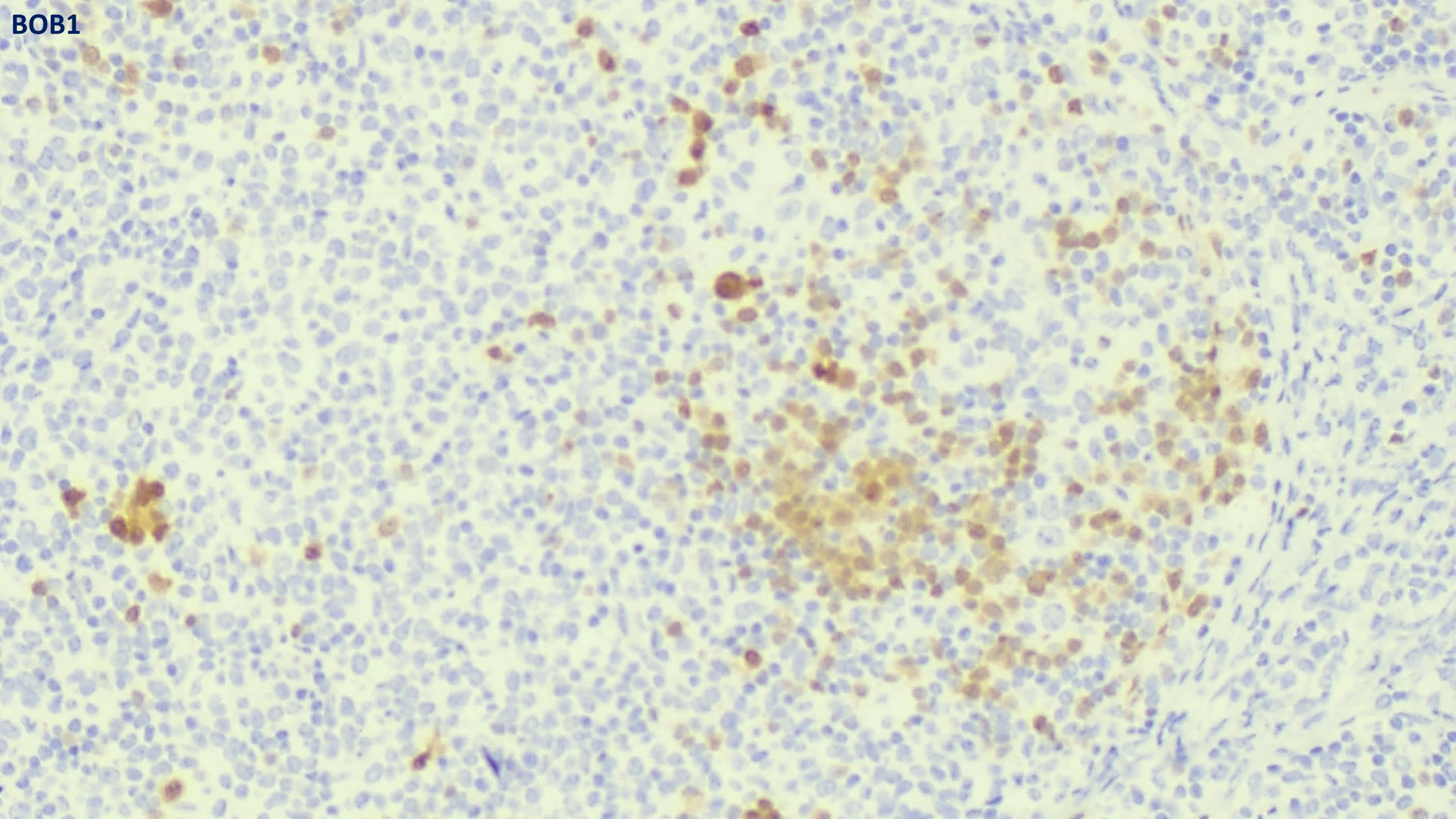
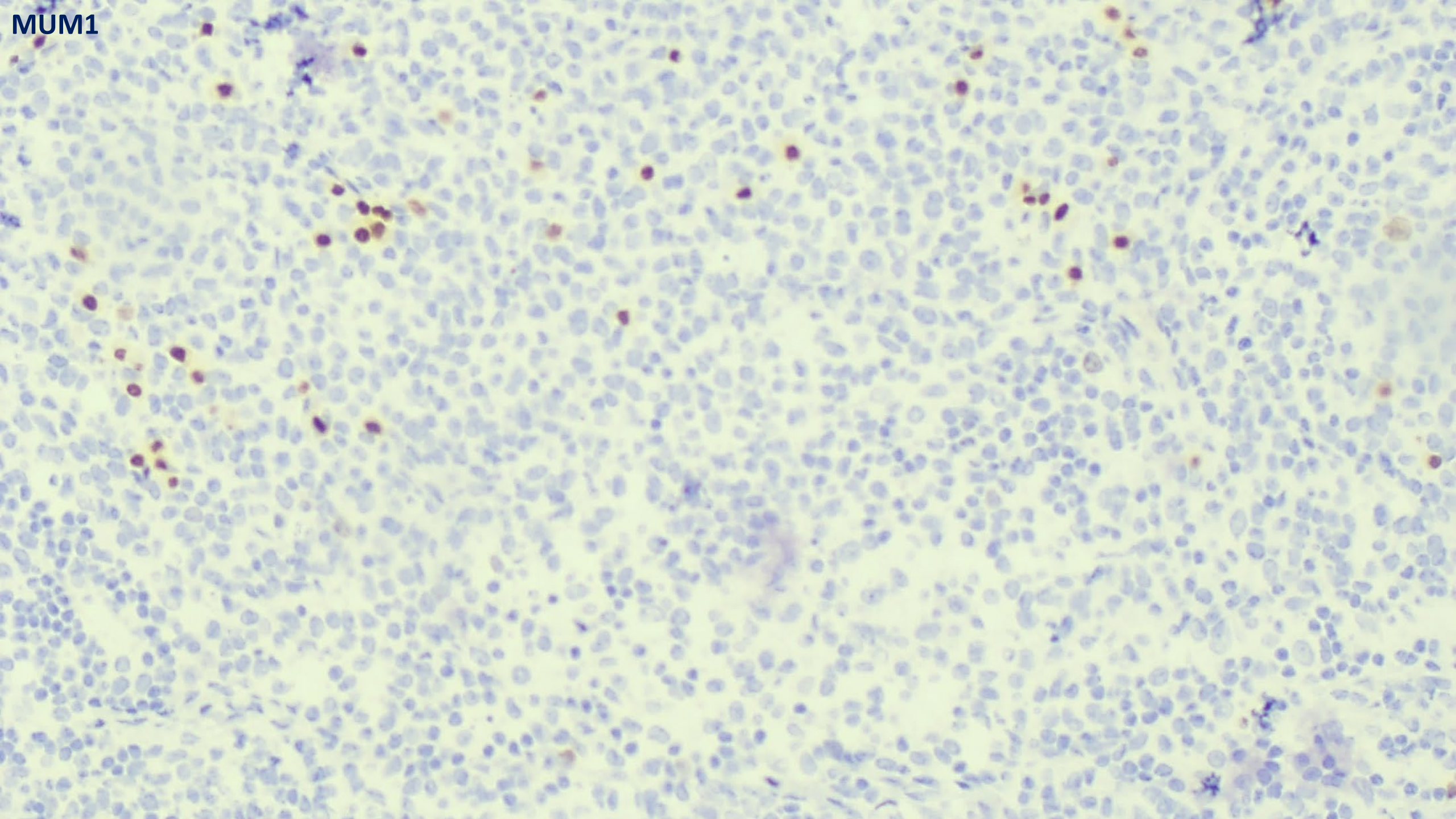
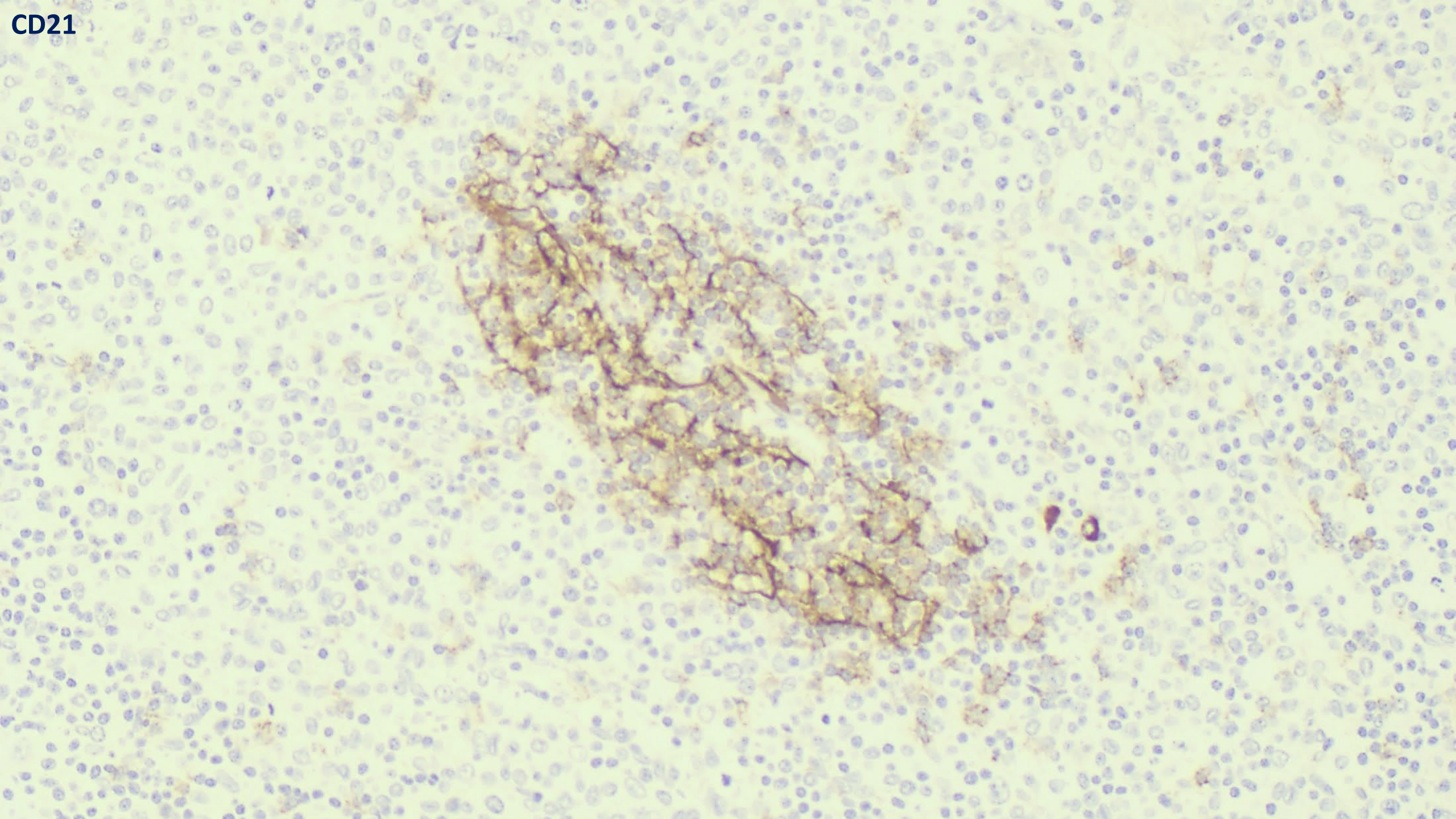
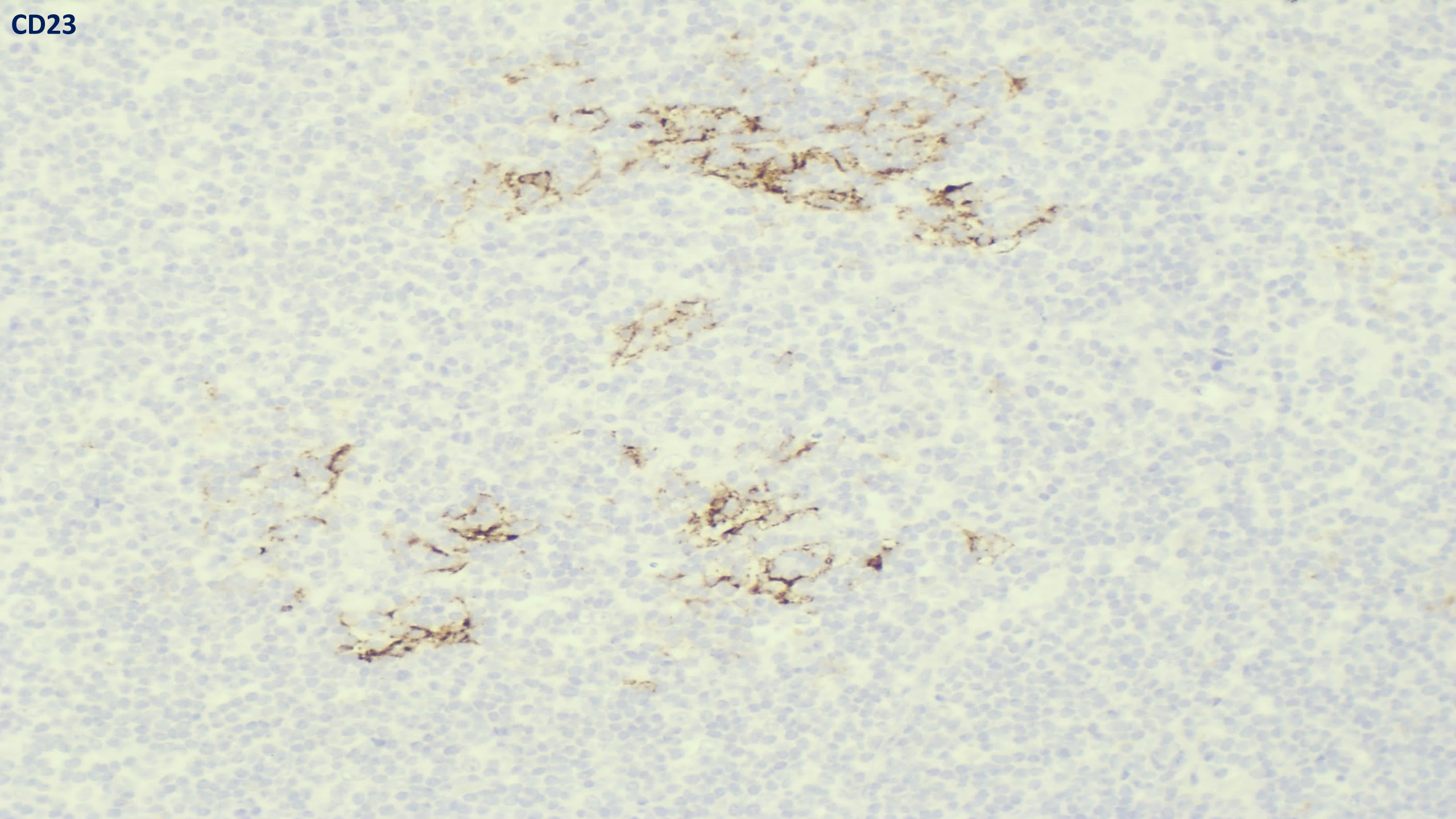

OCT2


BOB1


MUM1


CD21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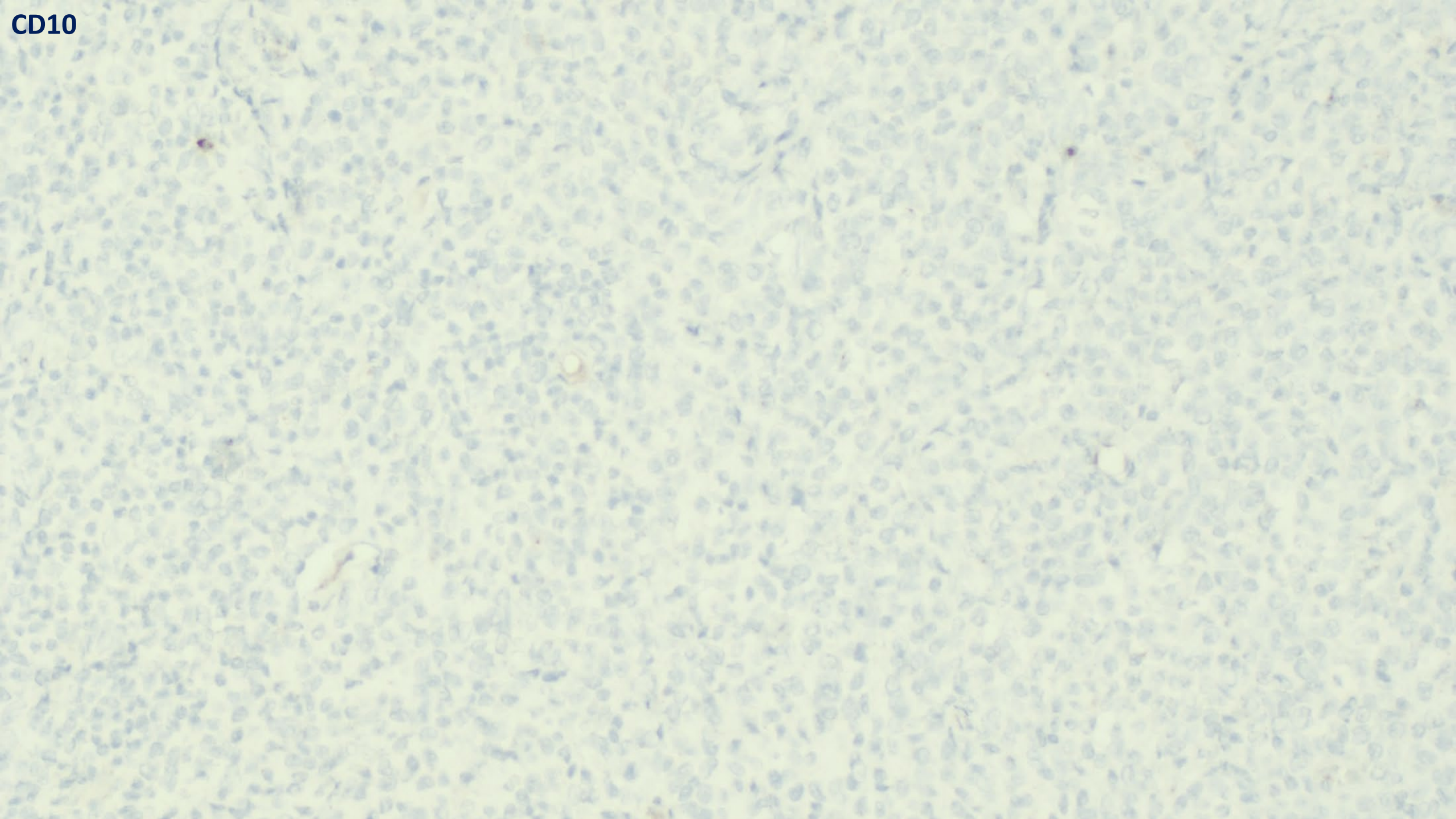
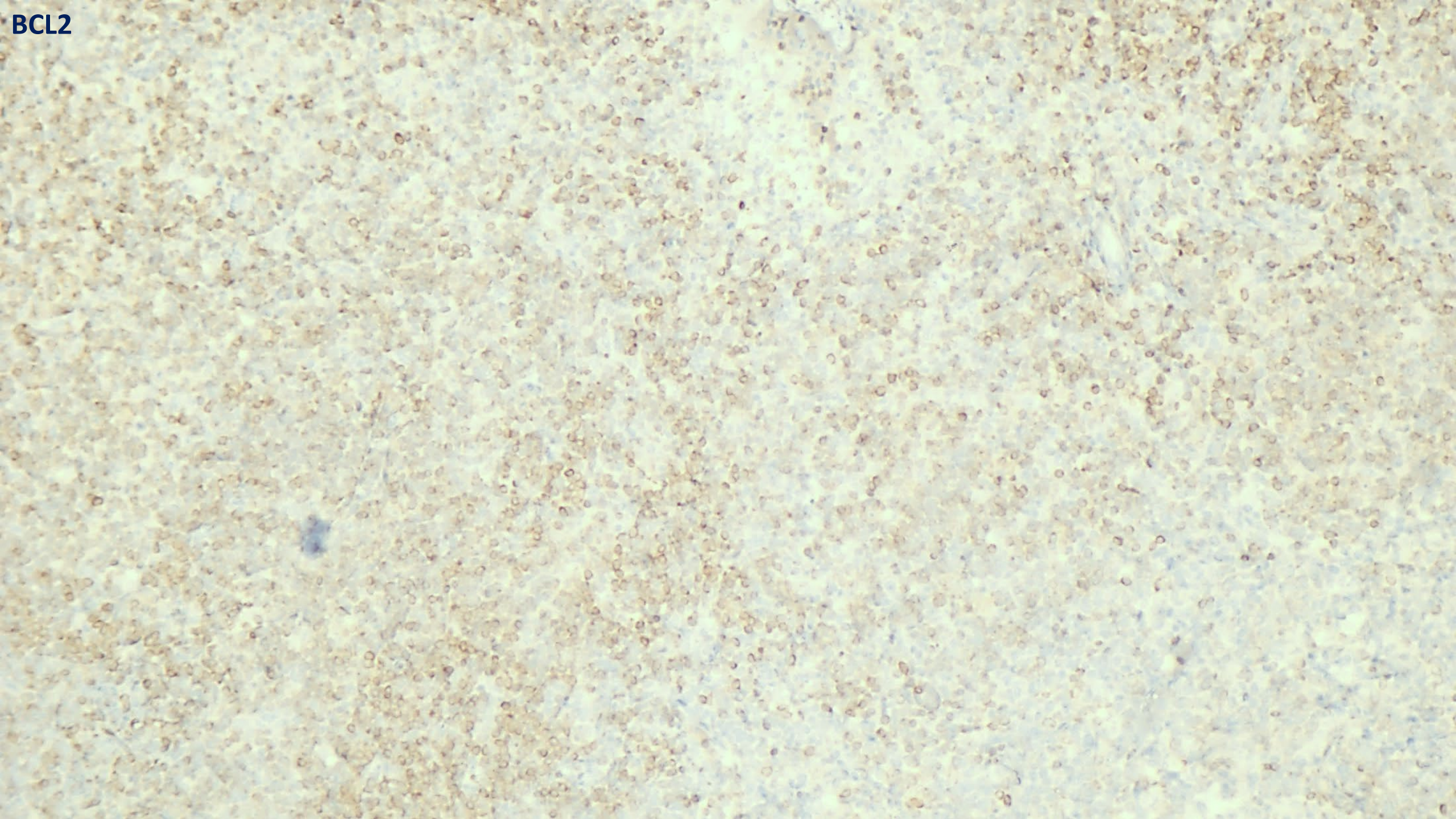
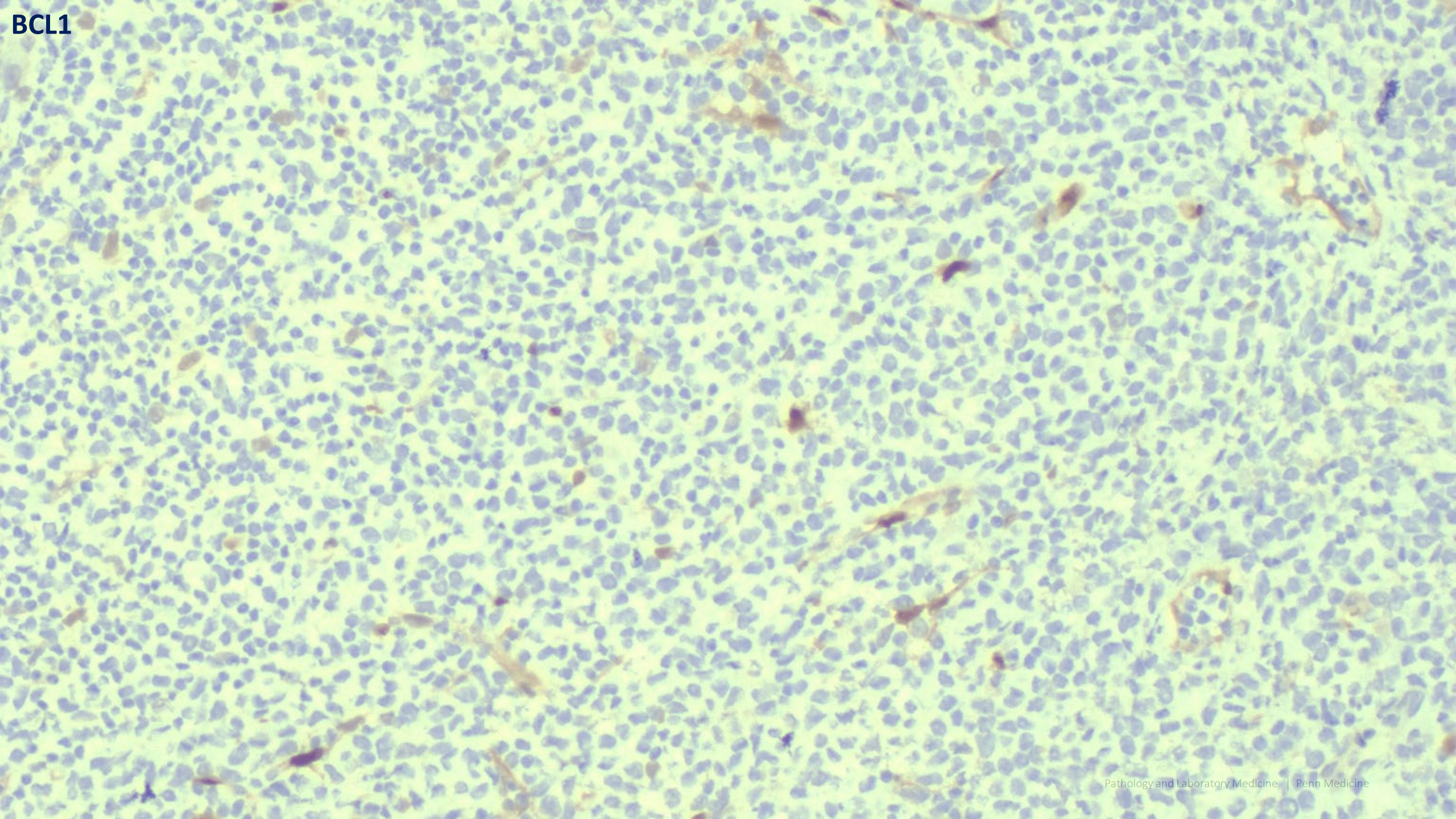
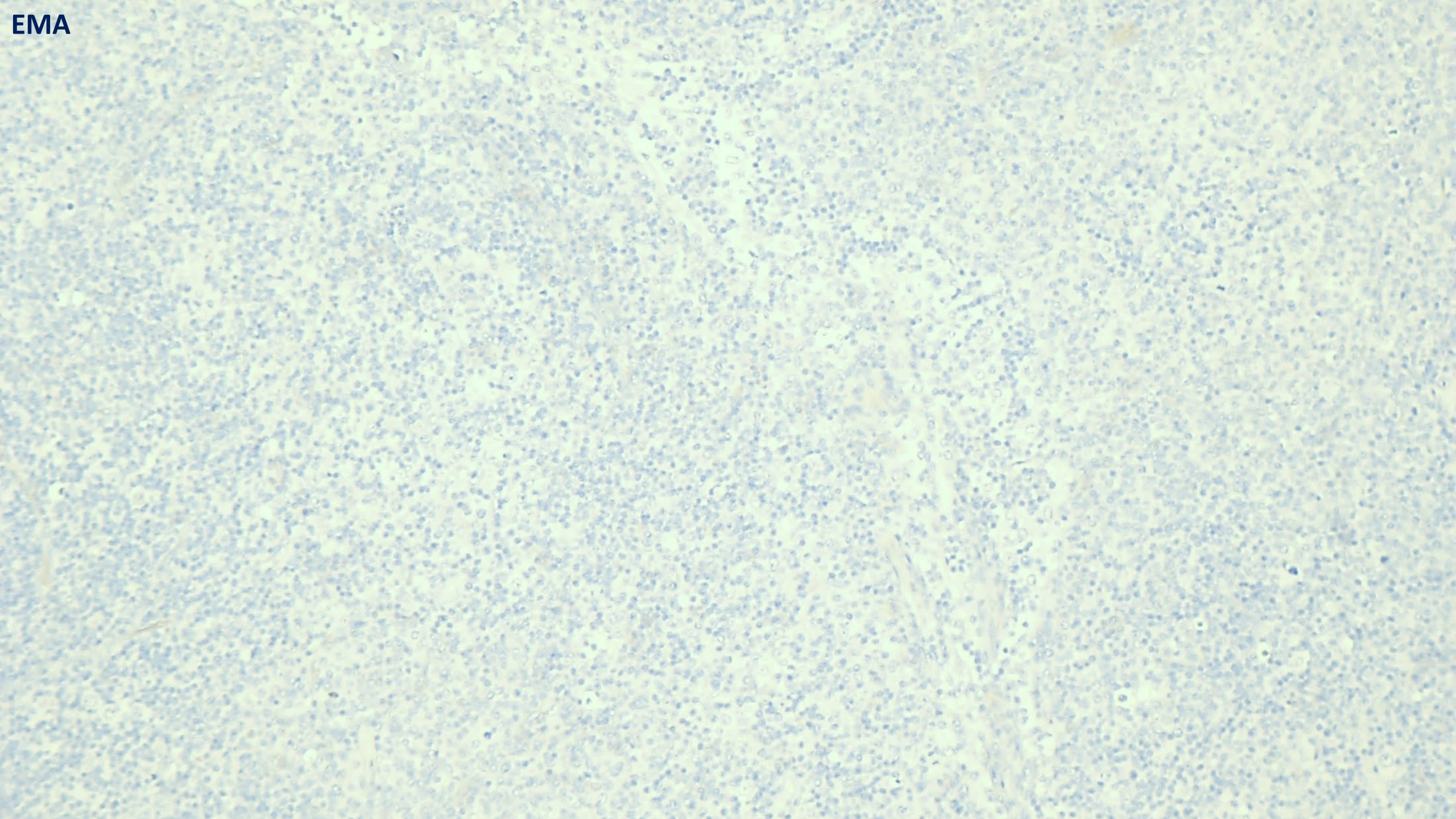
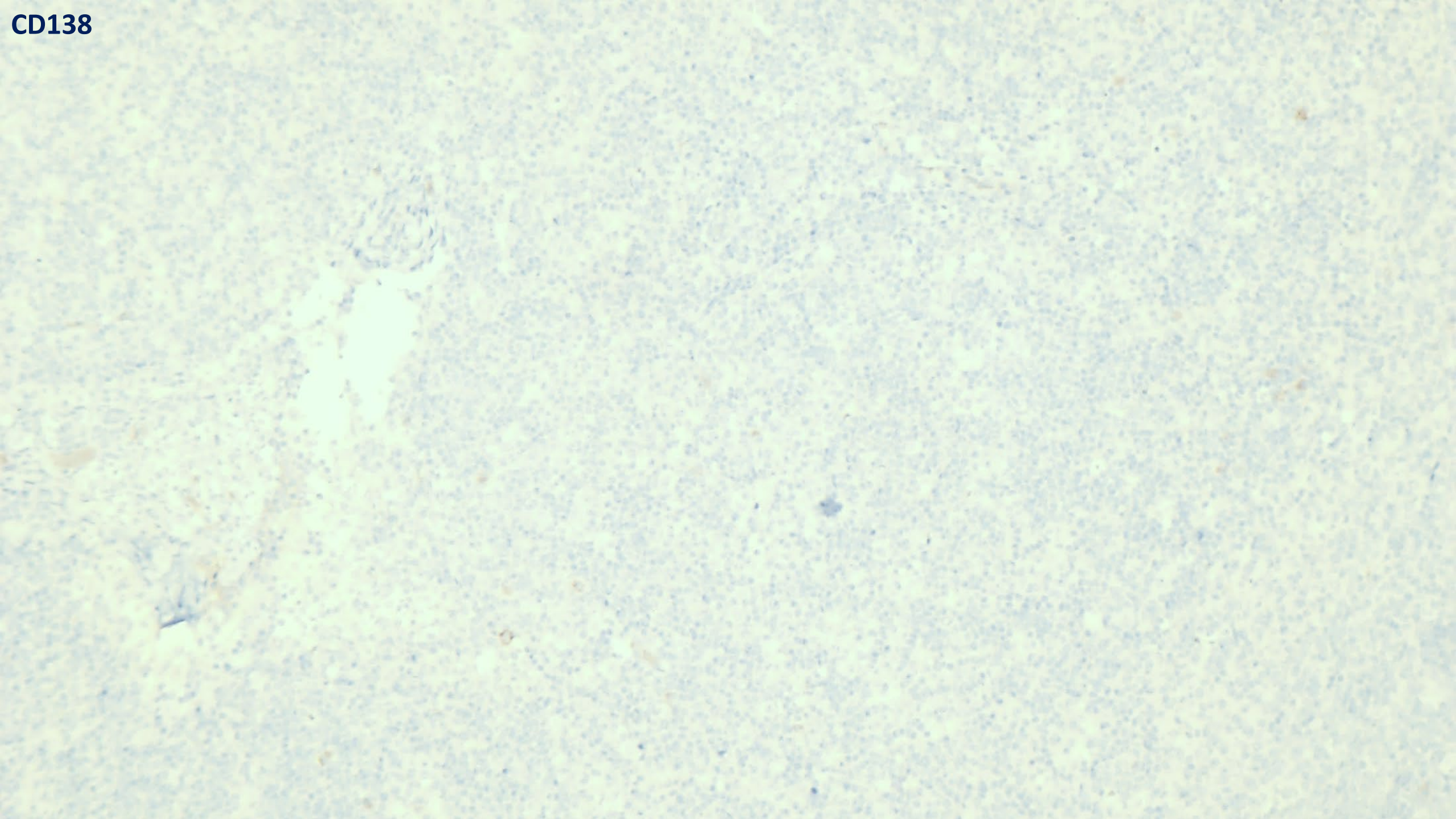

CD10

BCL6

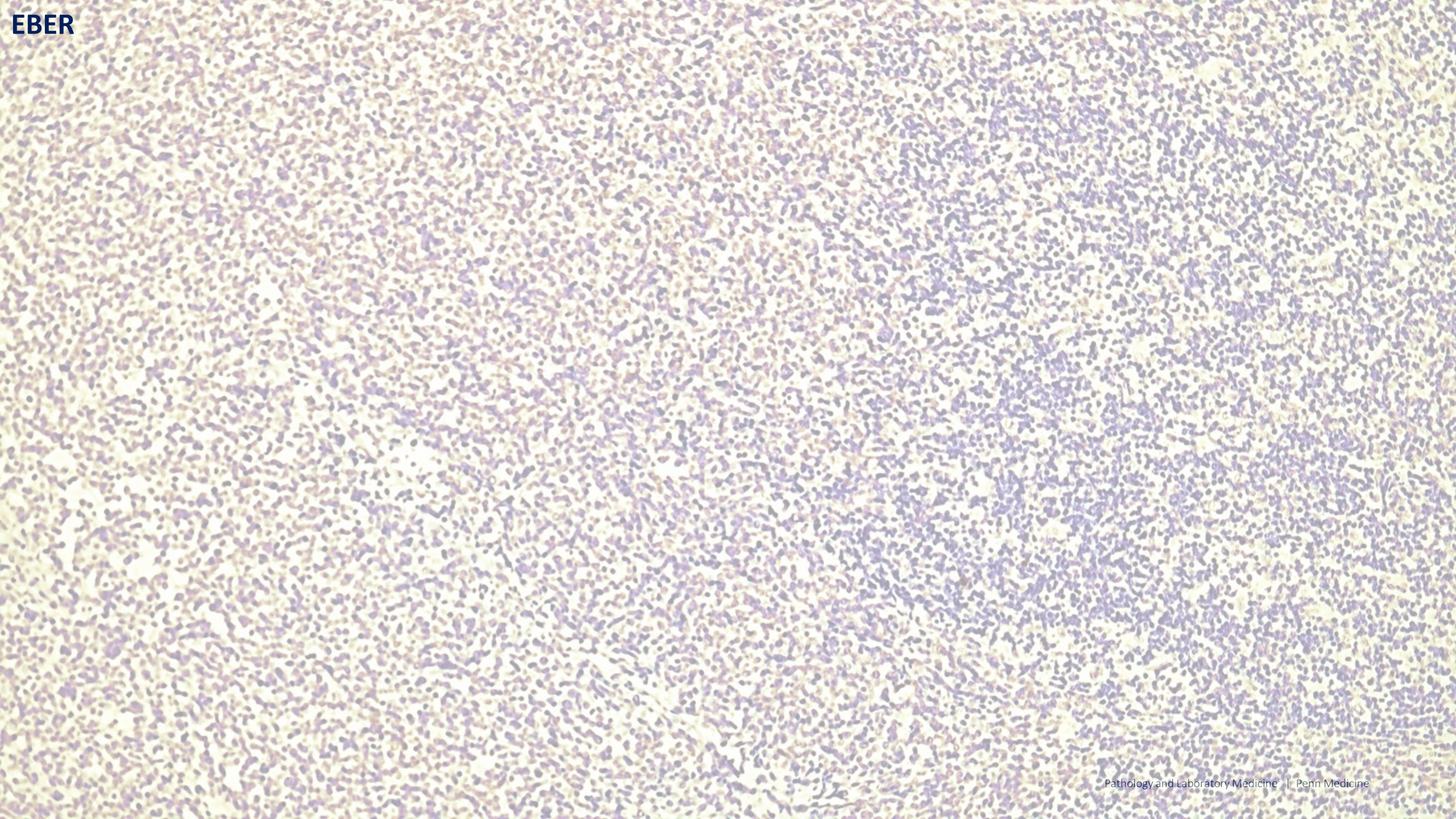

BCL2


BCL1

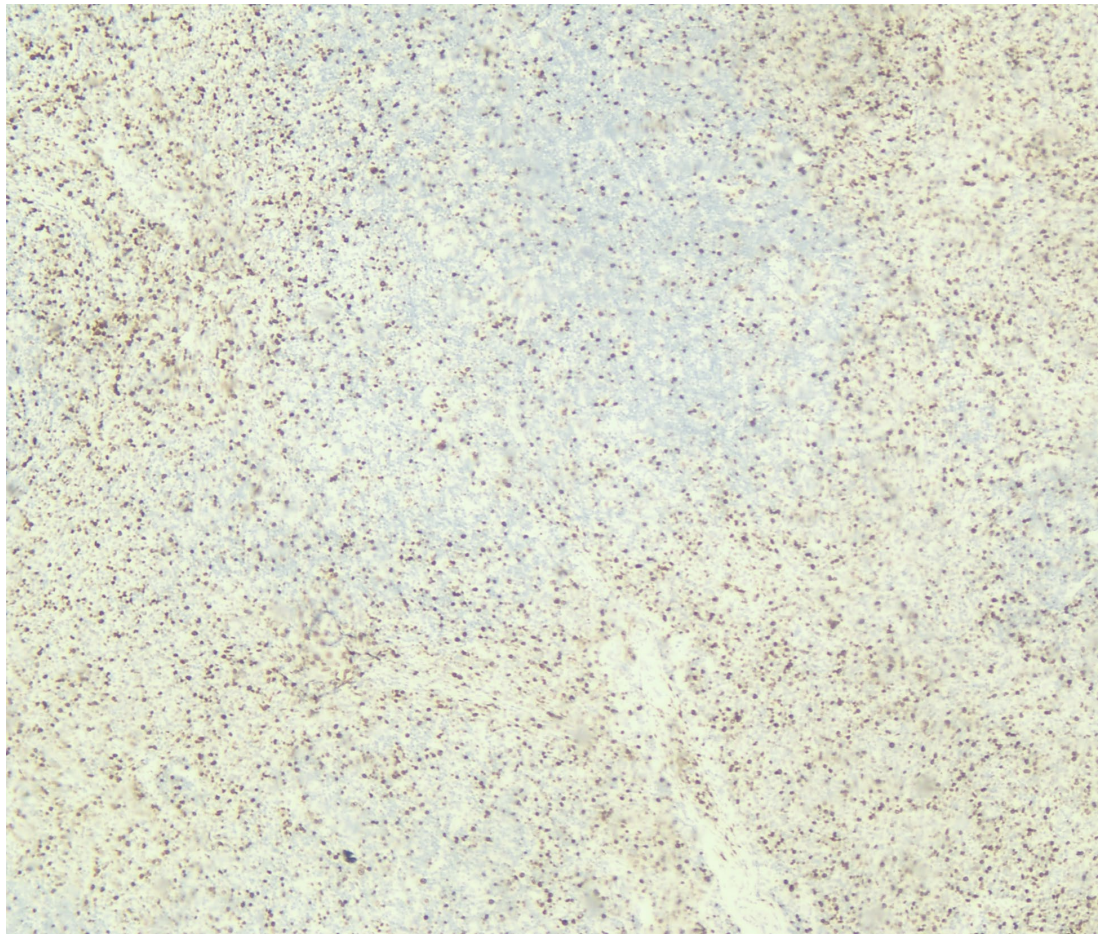

EMA

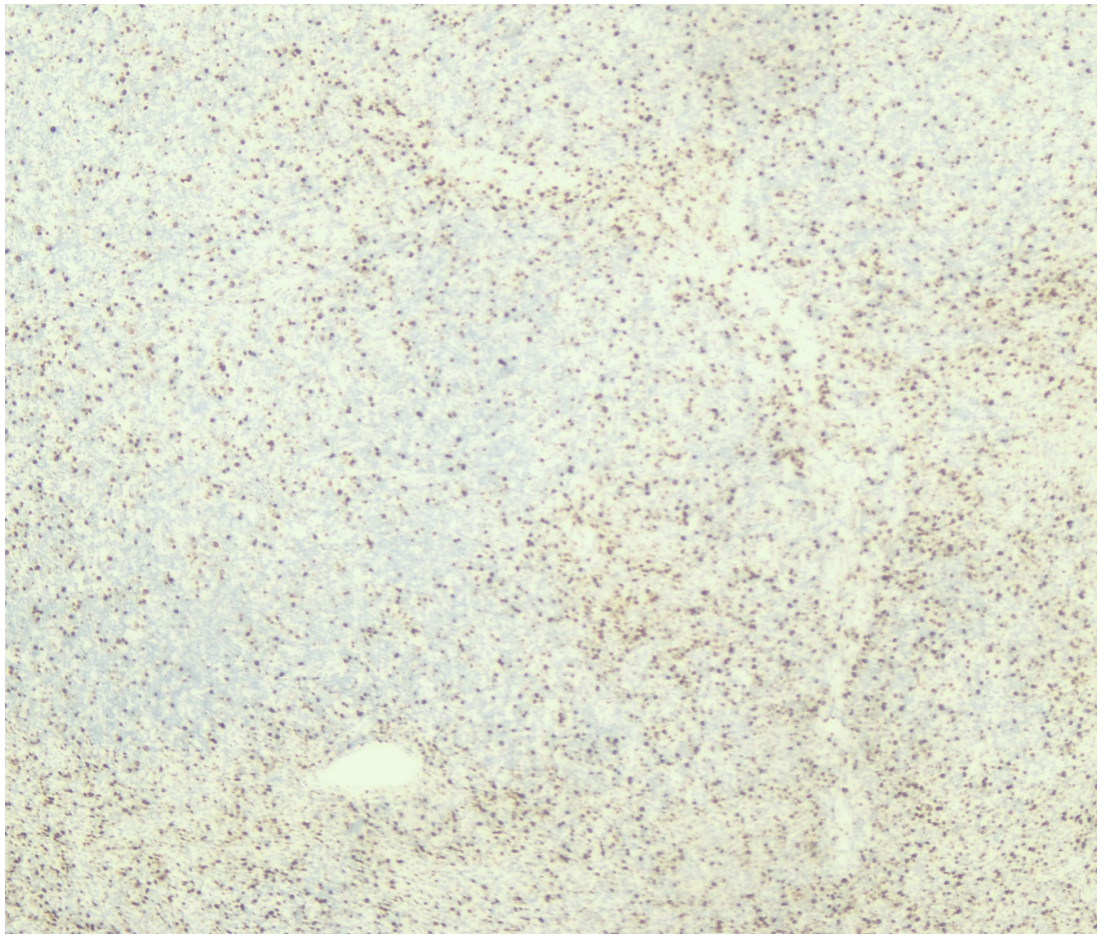

CD138

EBER



KI-67





Diagnosis

(July/28) Lymph node, Left Neck, Excisional Biopsy:

- Classic Hodgkin Lymphoma

Disclaimer: a diagnosis re-visit has been issued later

Clinically staged as IIB.

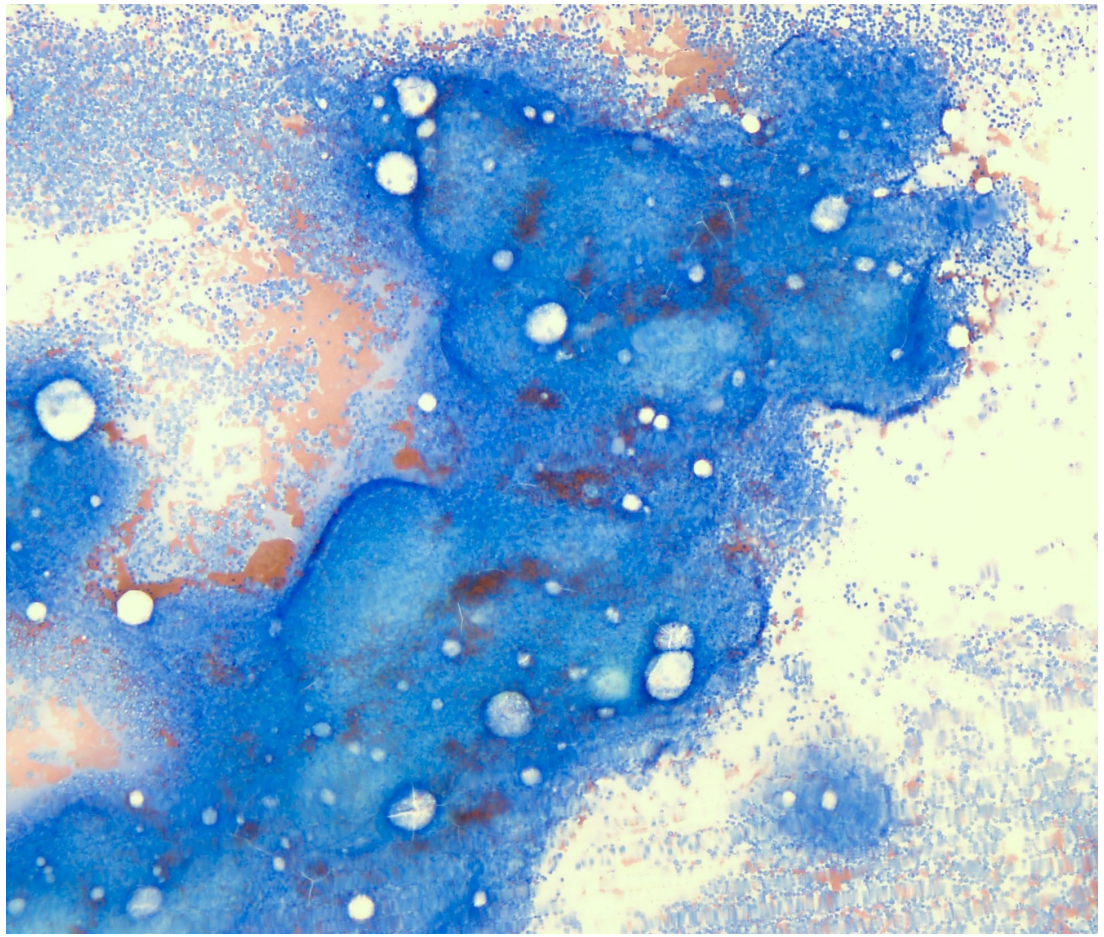
Interim Course – August 1, 2025

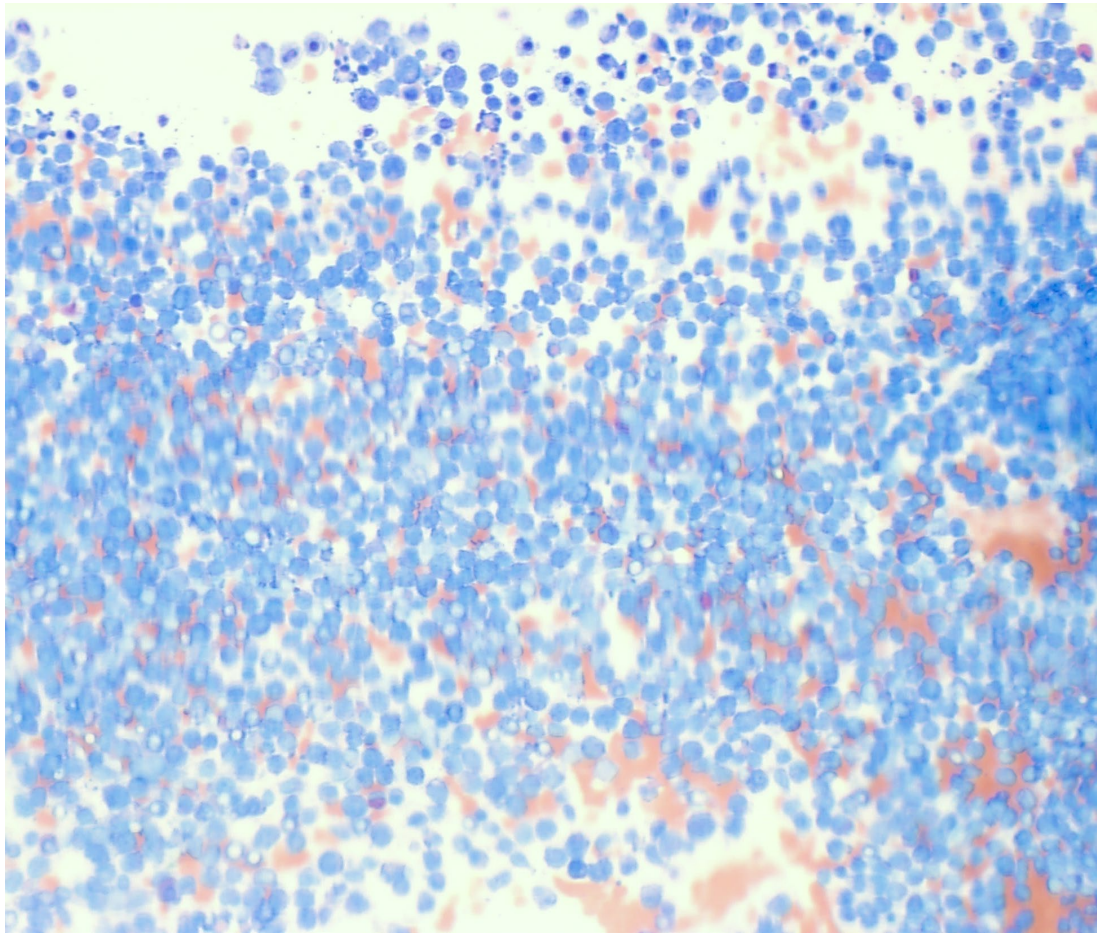
- **Symptoms:** Severe fatigue, anorexia, lightheadedness, nausea
- **Labs:** Hgb decline from 11 g/dL (6/2025) → 8 g/dL; pending results from 7/29
- **Review of systems:** No bleeding, no fever; continued weight loss
- **Oncologist's assessment/plan:**
  - **Plan:** initiate **ABVD chemotherapy**; ECHO EF normal
  - Port placement ordered
  - Noted **macrocytosis** (unclear etiology; B12 and Folate WNL → BM biopsy planned)
  - Considered **AIHA** (labs not supportive: bili & T&S WNL)

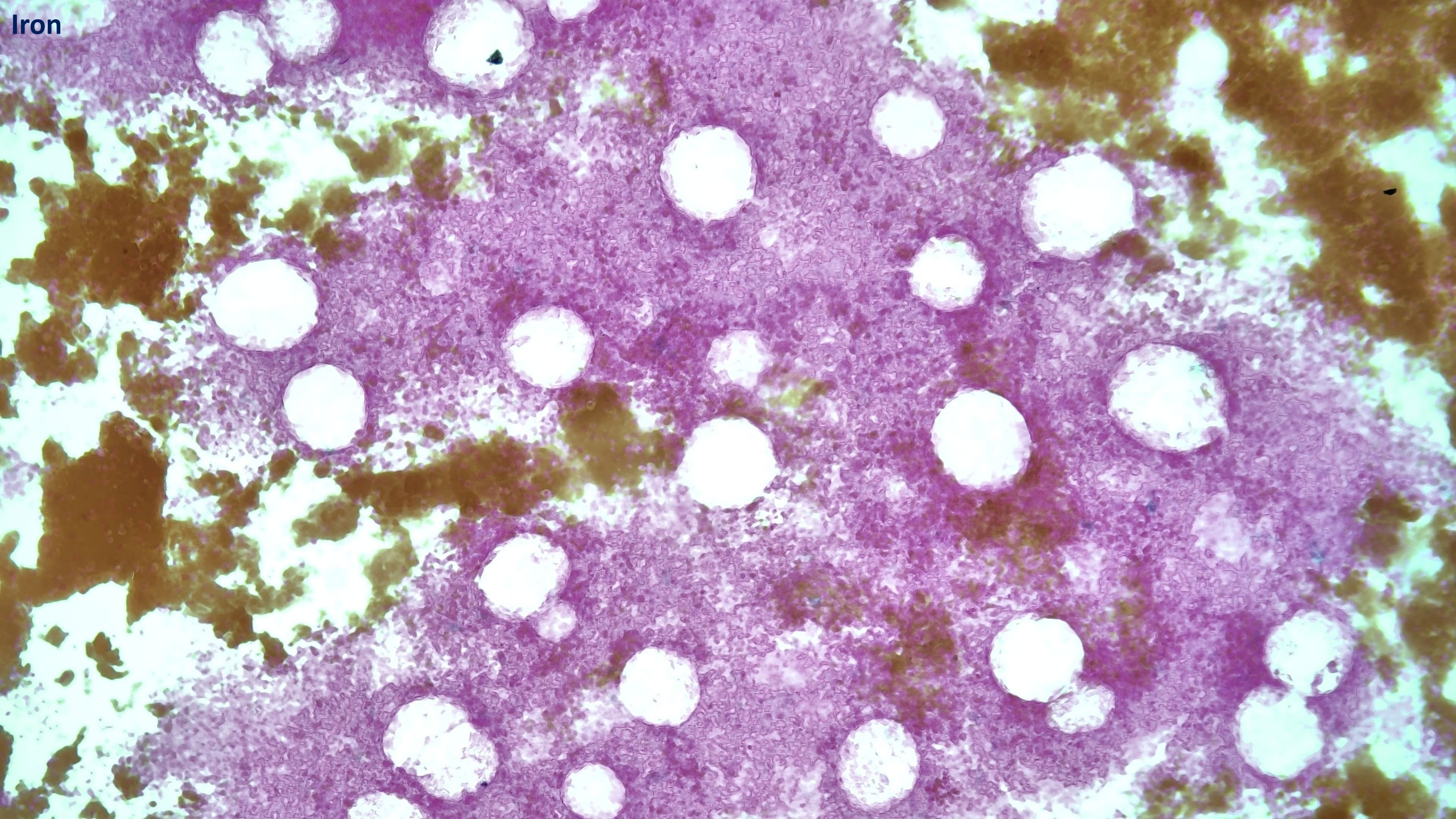
Interim Course – Cont’

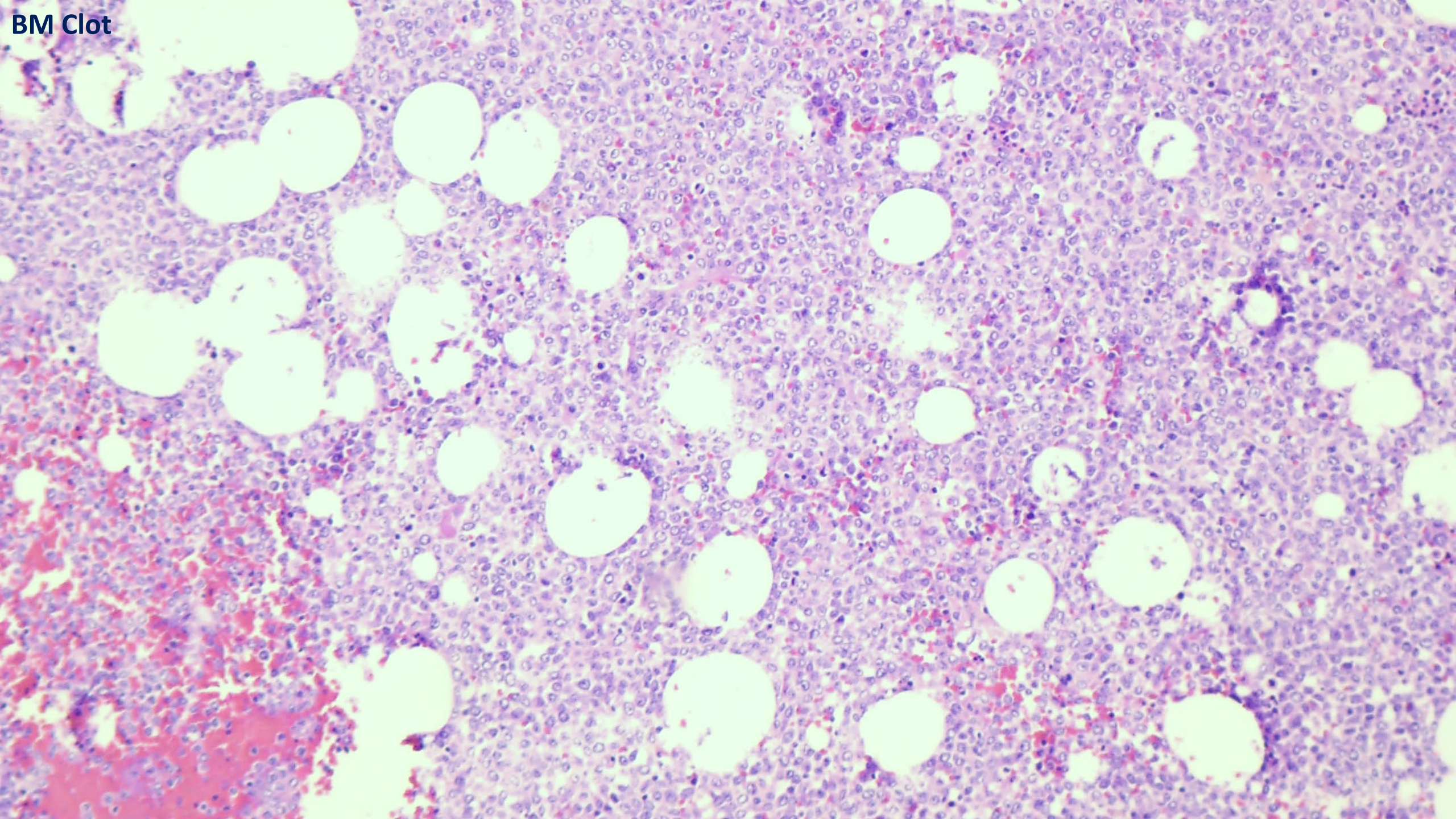
- Admitted for port placement for Hodgkin-directed therapy, but needs to decide between ABVD or a regimen incorporating immunotx
- During the hospitalization, the patient developed AKI, hypotension, anemia, hypoxic respiratory failure, and was treated for pneumonia
- CBC: WBC 69.0 × 10^9/L, RBC 2.12; Hb 7.1 g/dL, Plt 183 × 10^9/L, **40% circulating blasts**

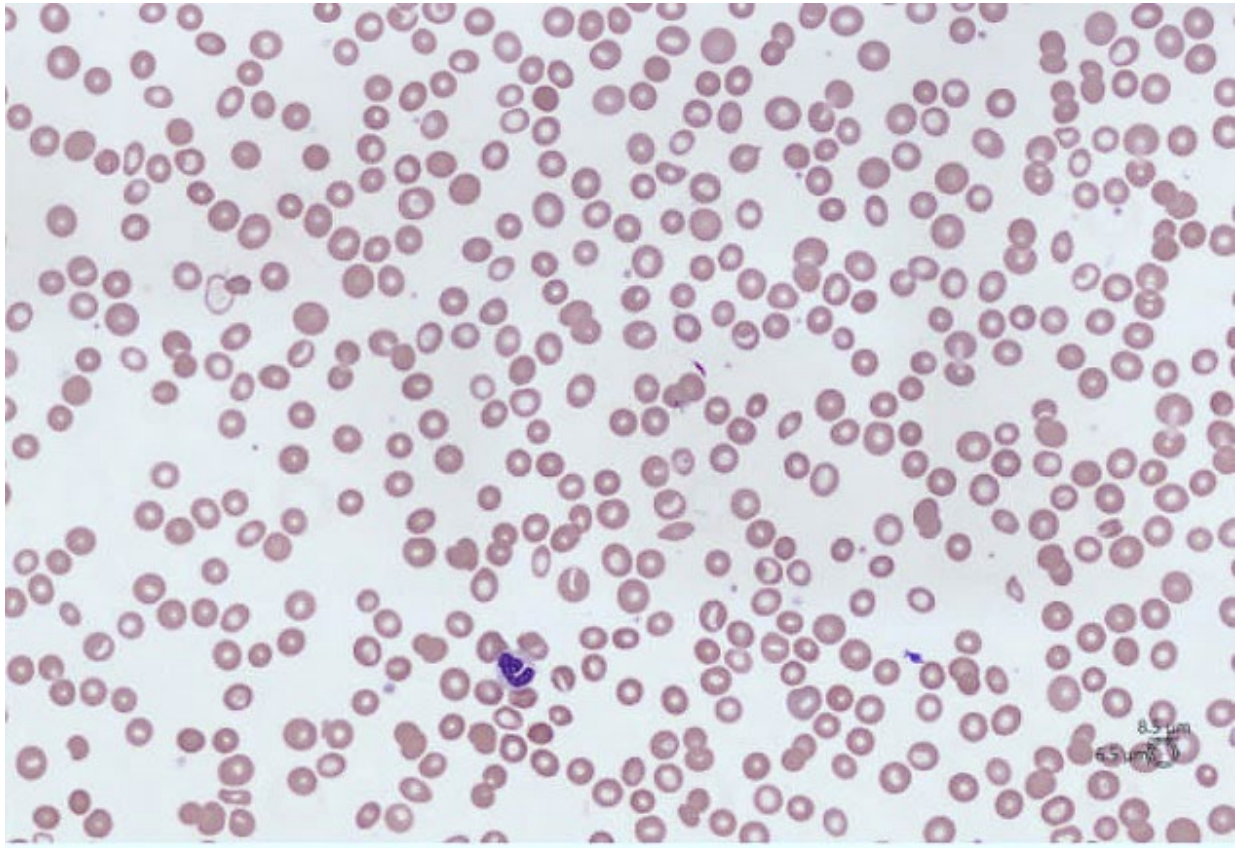
Outside Aspirate

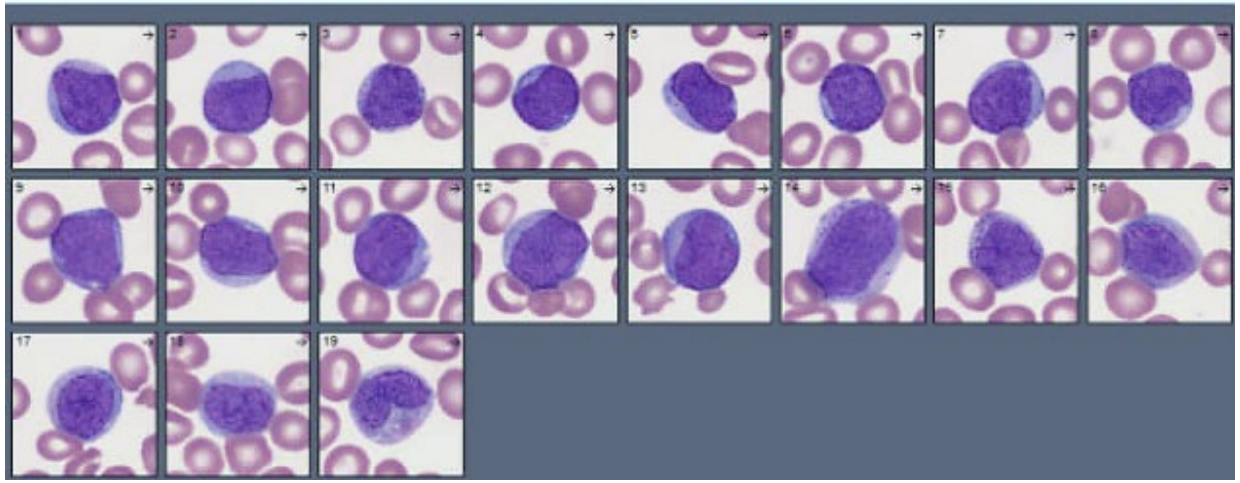





Iron

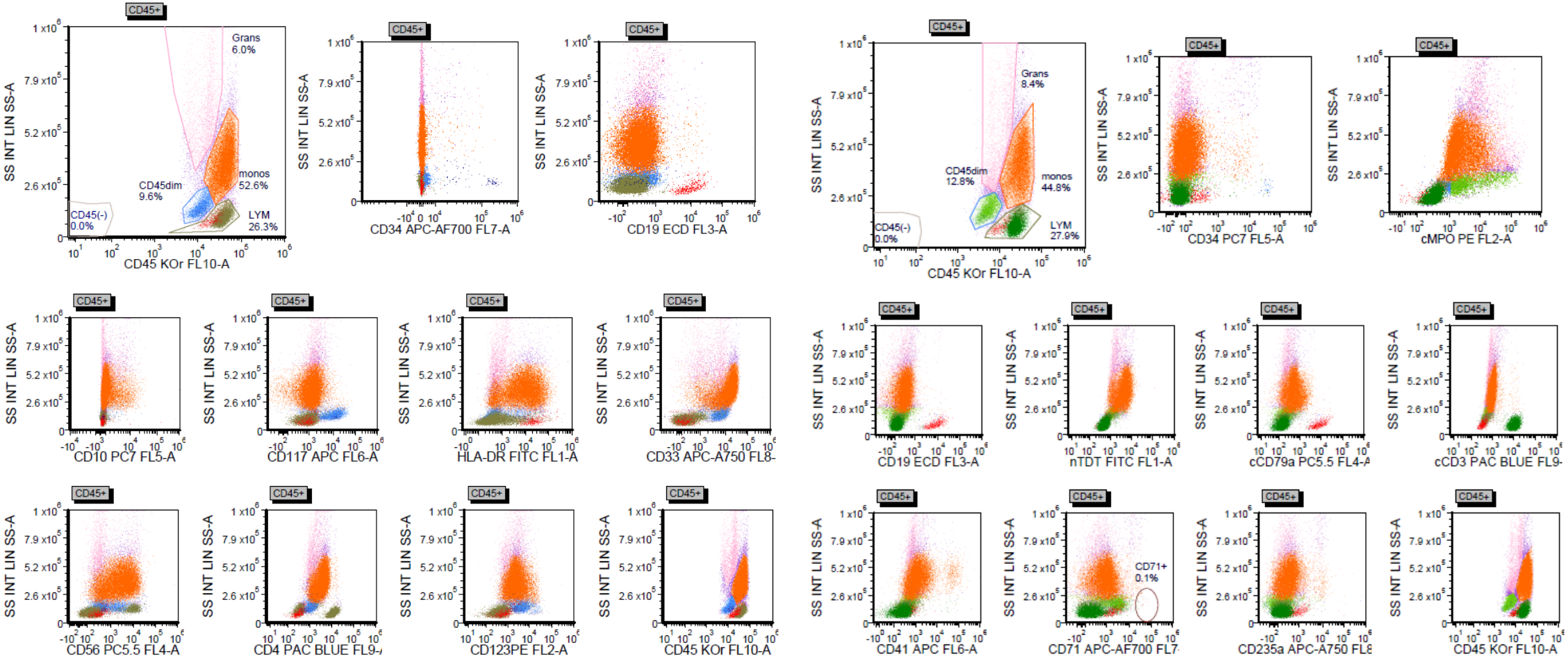

BM Clot





- **RBCs**: microcytic, polychromic, no dacrocytes, Occasional schistocytes (<1-2 per hpf)
- **WBCs**: **~10-15% large basophilic cells with a large N: C ratio and prominent nucleoli, no cytoplasmic granulocytes/auer rods.** lymphocytes appear normal in number and morphology
- **Platelets**: No platelet clumping, no giant platelets, Normal in number

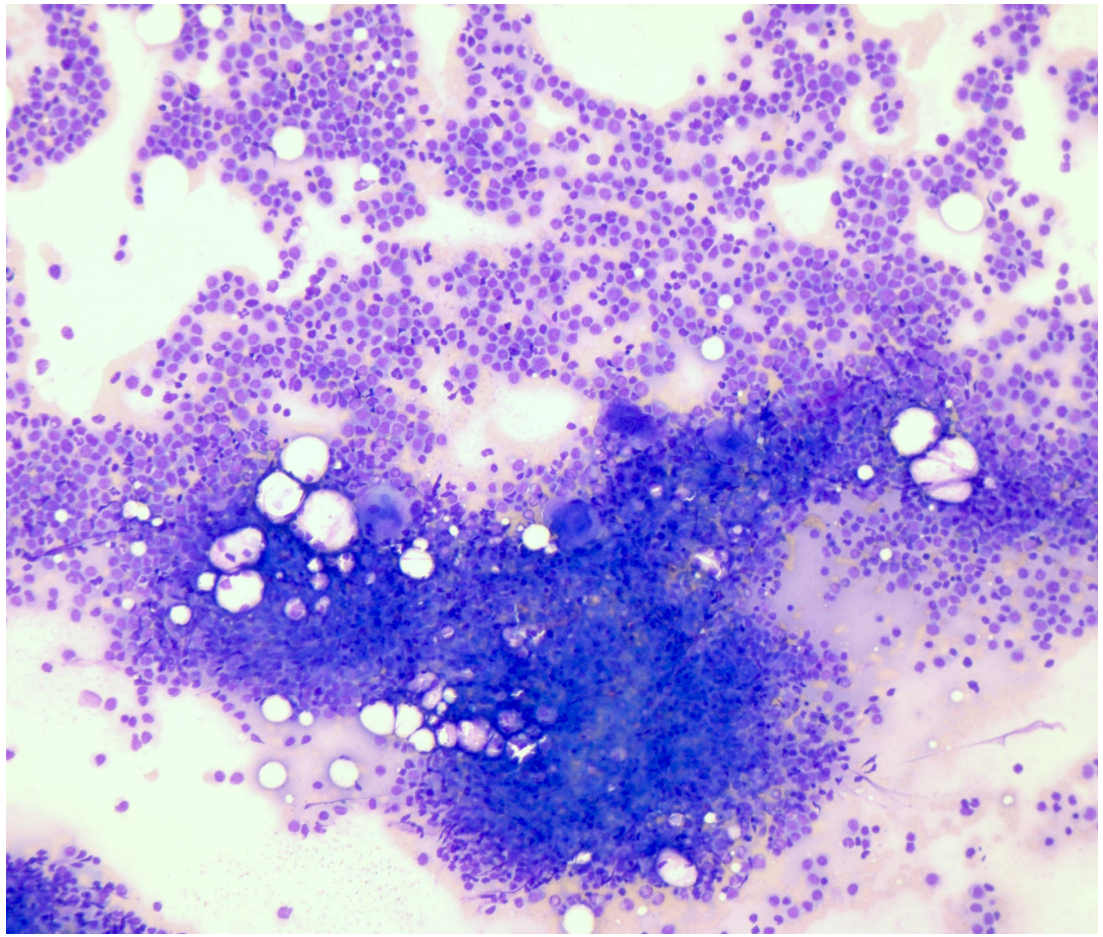
Peripheral Blood Flow Cytometry

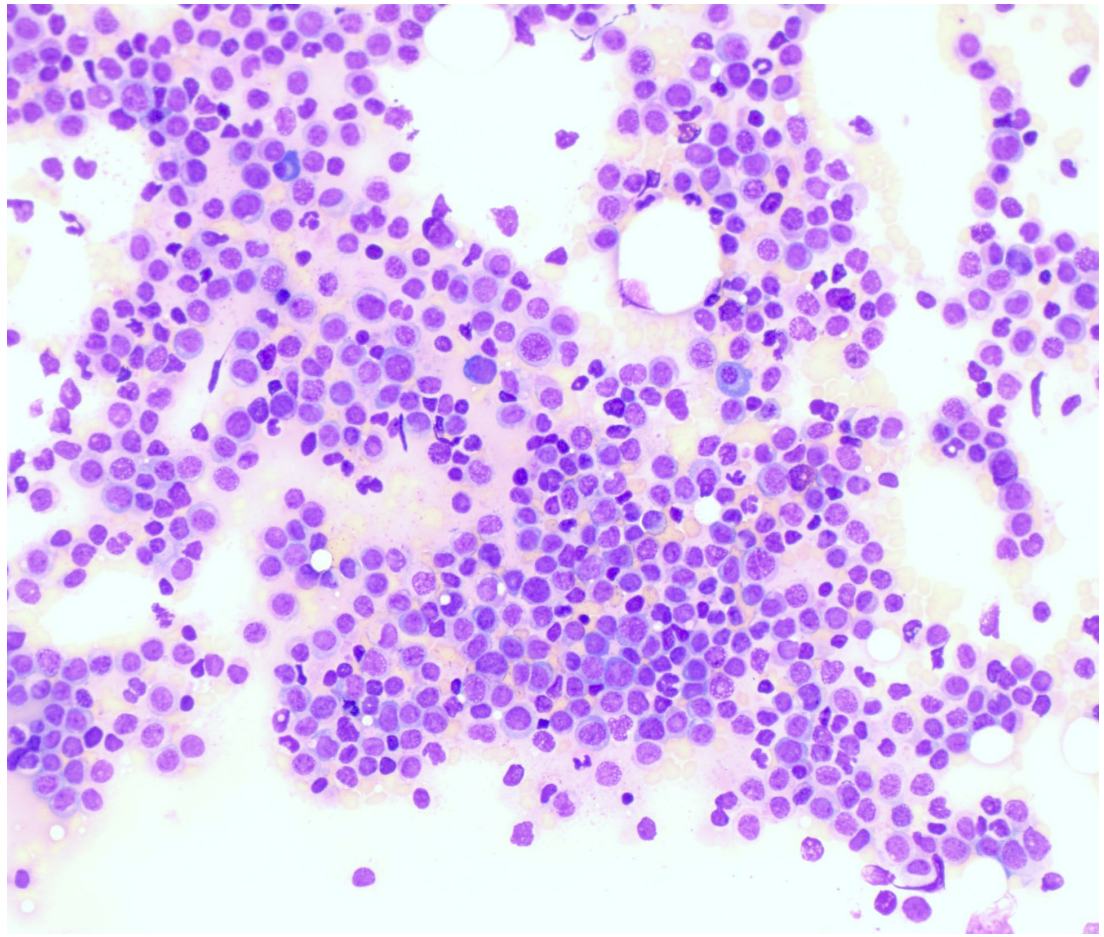


Peripheral Blood Flow Cytometry

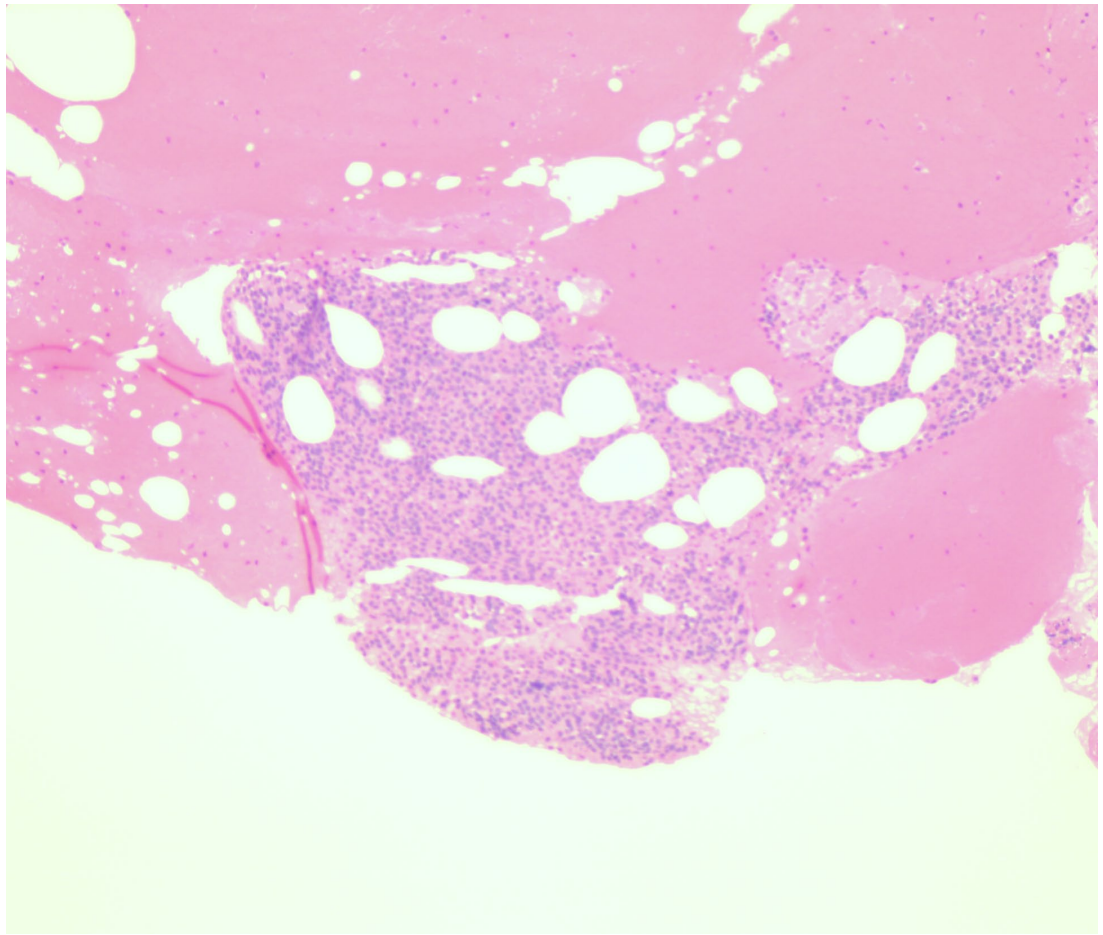
- Cellularity (by CD45/SSC):
  - 9% CD45^dim immature precursors
  - 26% lymphocytes
  - 53% monocytes (expanded, aberrant phenotype)
  - 9% granulocytes
- Immature precursor population (CD45^dim):
  CD34–, CD117+, HLA-DR–,
  cMPO+, CD33+, CD13(dim+), CD15–,
  CD123(dim+), CD4(dim+), CD14–, CD64–, CD11b–,
  CD56(subset+), TdT–, CD71–
  - Consistent with acute myeloid leukemia with monocytic differentiation
- Monocyte region:
  - Expanded with aberrant profile: ↓ CD14, ↓ HLA-DR, ↓ CD15, ↓ CD13
  - Aberrant gain: ↑ CD16, major subset CD56+
- Lymphocyte region:
  - 6.9% polytypic CD19+ B cells (κ:λ = 1.1)
  - 76.2% CD3+ T cells (CD4:CD8 = 5.1)
  - 14.7% NK cells

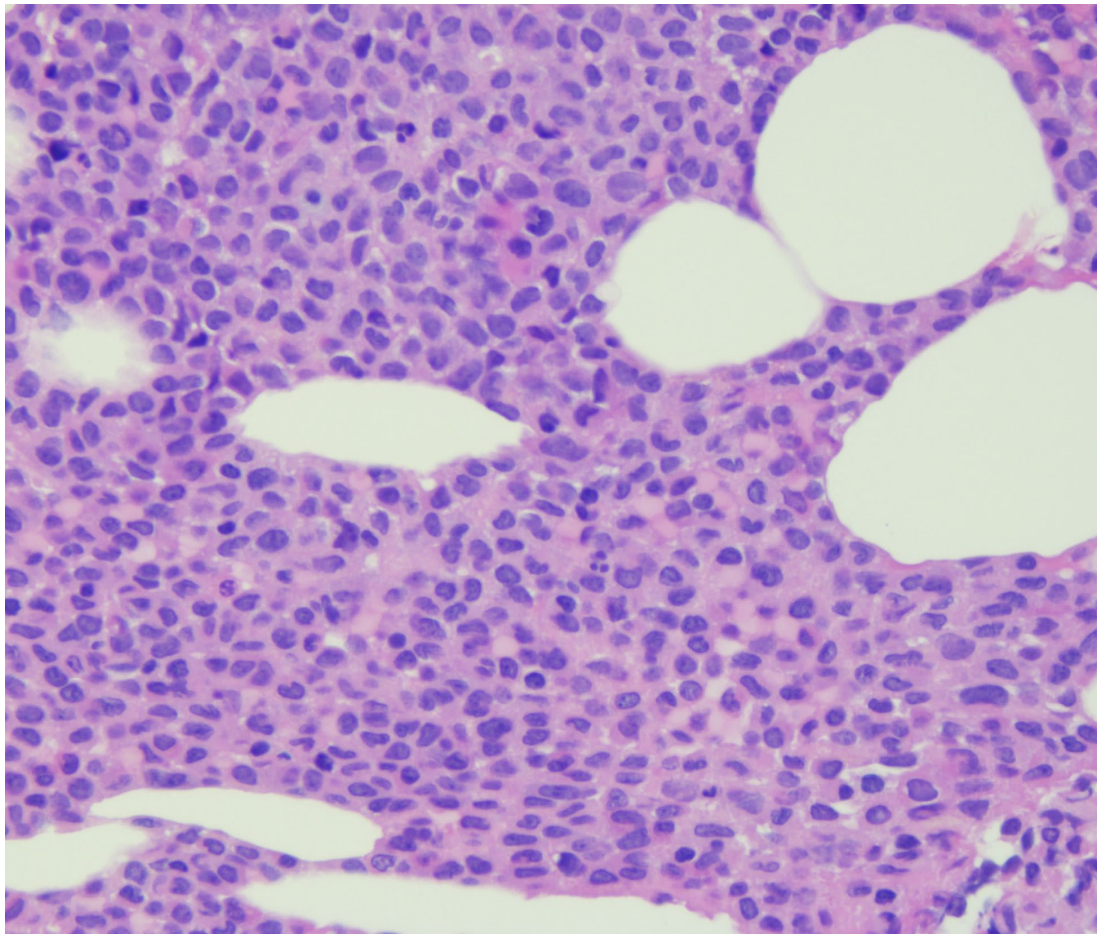
Penn Aspirate



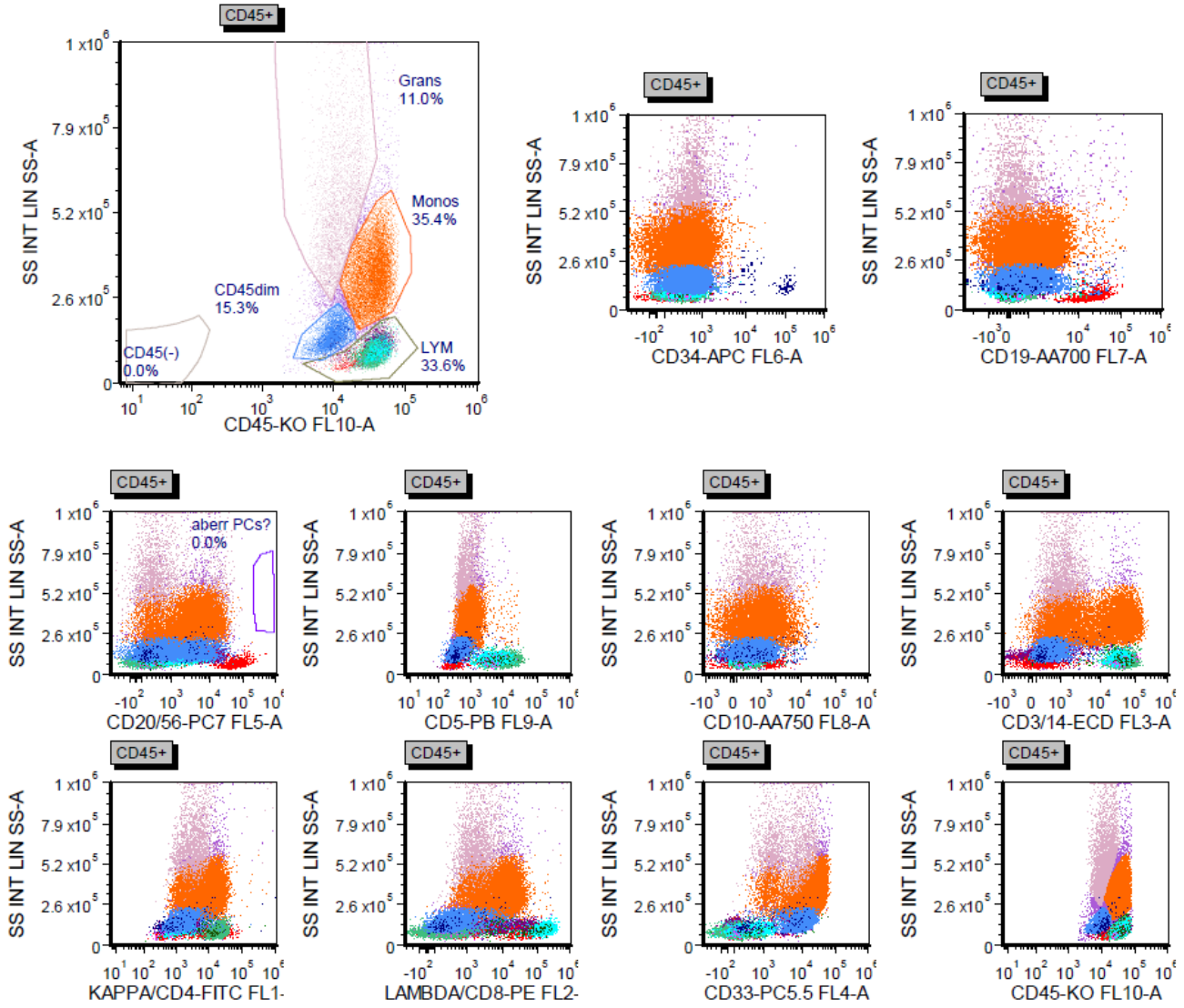


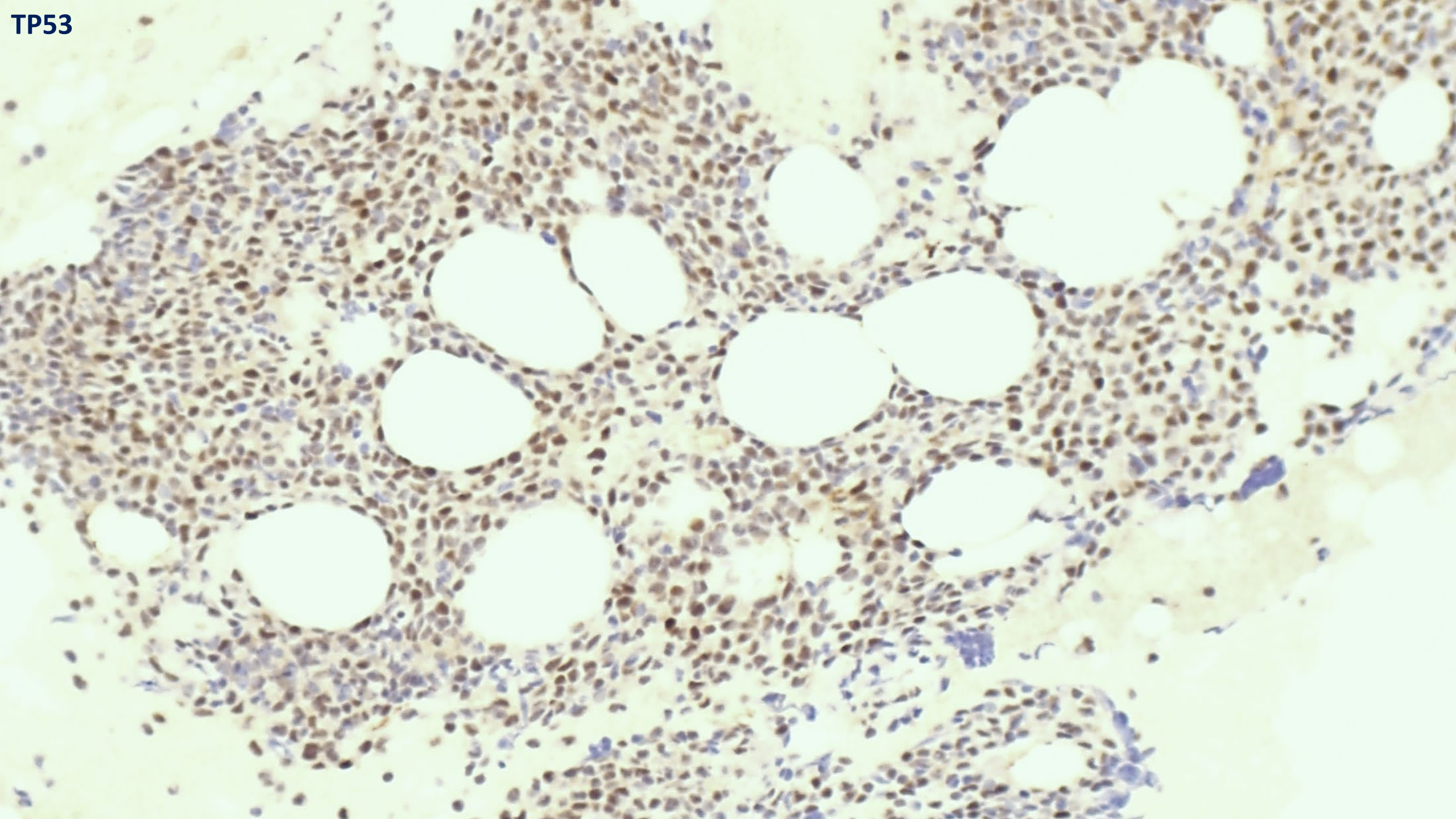
Penn BM Biopsy

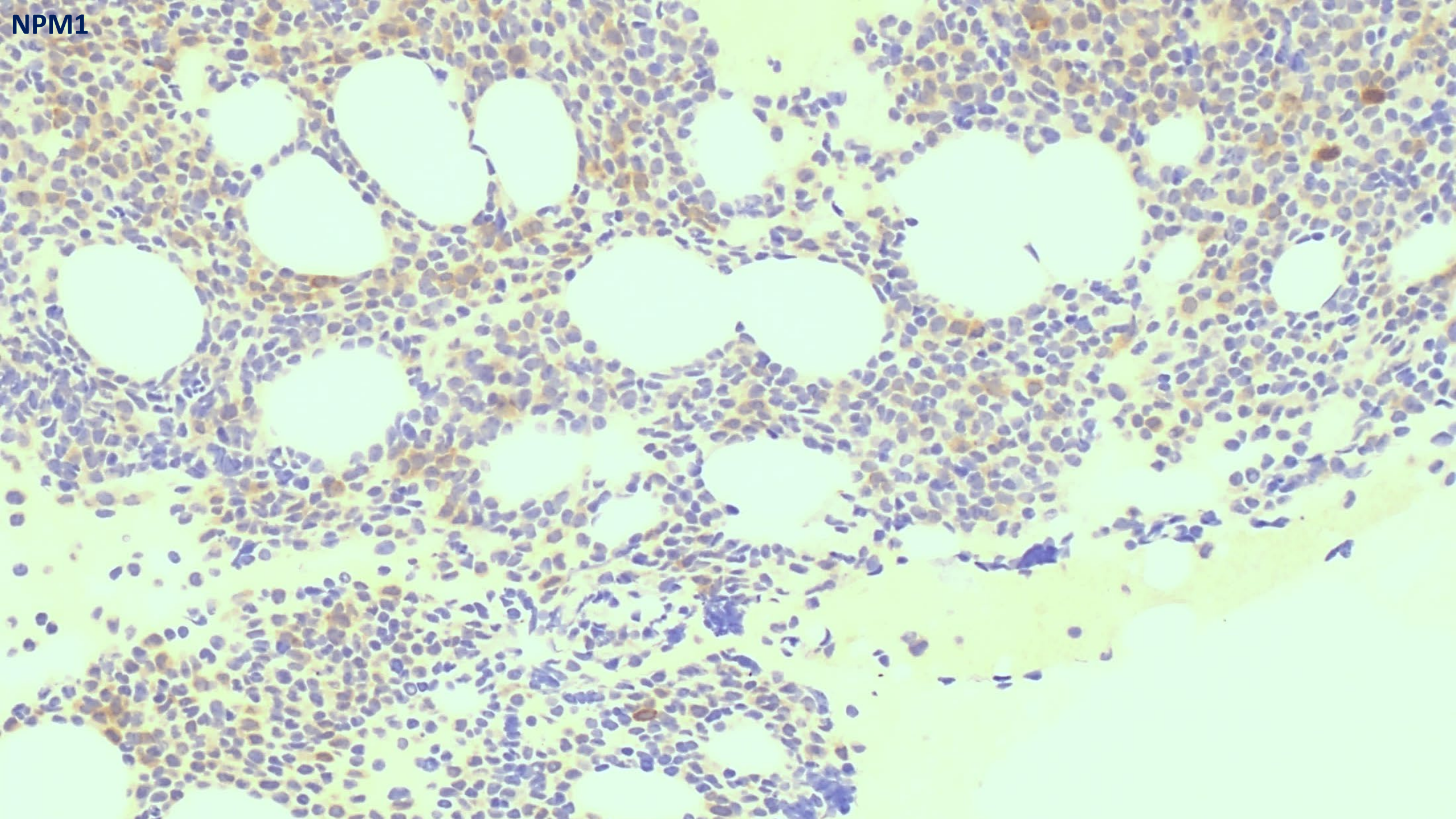




Bone Marrow Flow Cytometry




TP53


NPM1

FISH

Probe: **5p15/5q31 (XL del(5)(q31))**

Number of Cells Analyzed: 200

WITHIN NORMAL LIMITS**: NOT DETECTED**

Probe: **7q31/7cen (CL 7q31(D7S486))**

Number of Cells Analyzed: 200

WITHIN NORMAL LIMITS: **NOT DETECTED**

Probe: **RUNX1/RUNX1T1 (XL t(8;21) plus)**

Number of Cells Analyzed: 200

WITHIN NORMAL LIMITS: **NOT DETECTED**

Probe**: 11q23 (XL MLL plus) [(KMT2A, BA)]**

Number of Cells Analyzed: 200

WITHIN NORMAL LIMITS: **NOT DETECTED**

Probe: **16q22 (XL CBFB)**

Number of Cells Analyzed: 200

WITHIN NORMAL LIMITS: **NOT DETECTED**

Probe: **17p13/17q11.2 (XL TP53 / NF1)**

Number of Cells Analyzed: 200

WITHIN NORMAL LIMITS: **NOT DETECTED**

Molecular RT-PCR

NPM1:	Detected

PML::*RARA*:	Not Detected
RUNX::*RUNX1T1*:	Not Detected
CBFB::*MYH11*:	Not Detected

BCR::*ABL1*:	Not Detected

IDH1:	Not Detected
IDH2:	Not Detected

FLT3 ITD:	Not Detected
FLT3 D835:	Not Detected

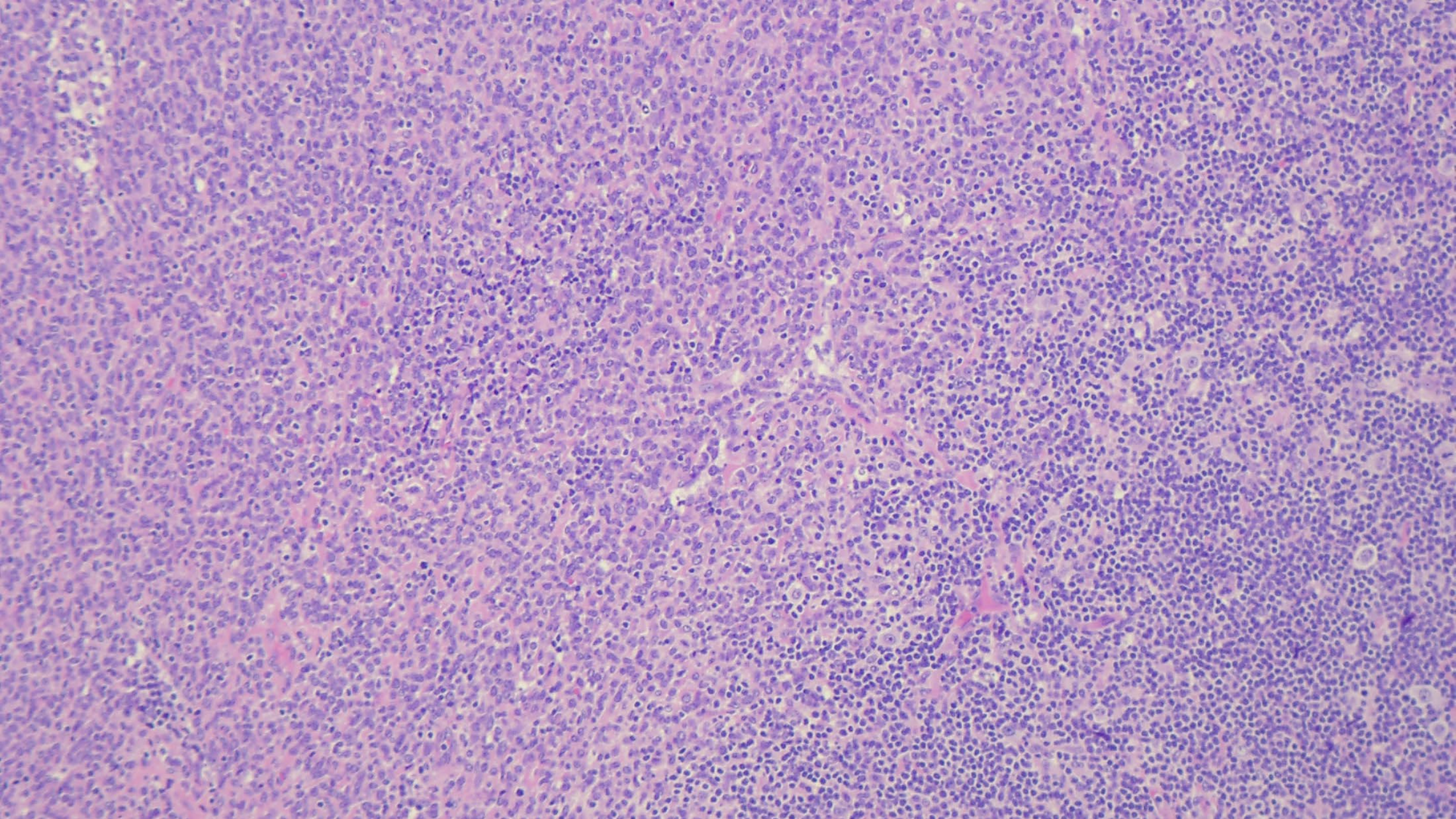
Final Diagnosis

Lymph node, Left Neck, Excisional Biopsy:

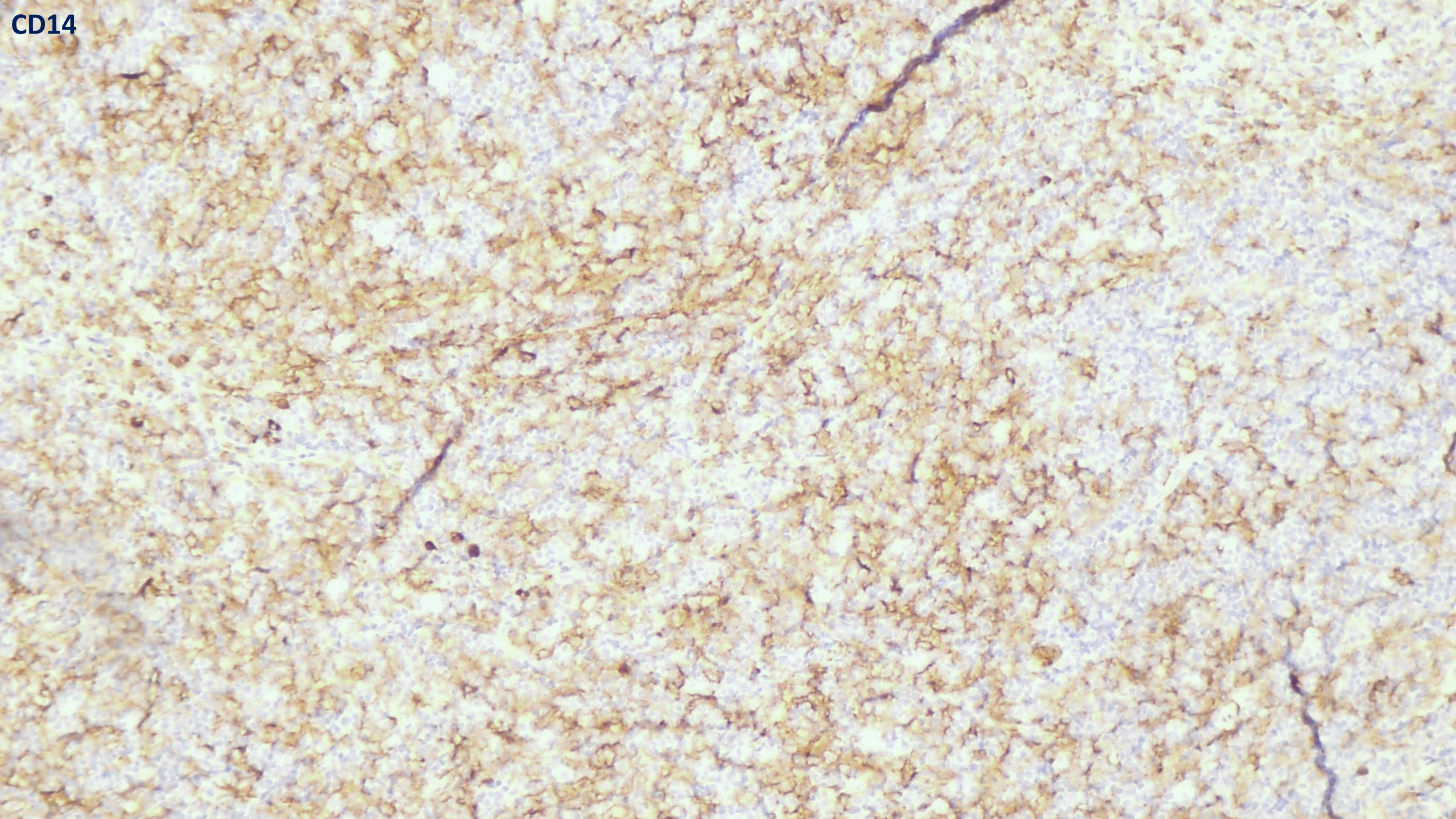
- Classic Hodgkin Lymphoma
- Myeloid Sarcoma (extramedullary AML) with Mutated *NPM1*

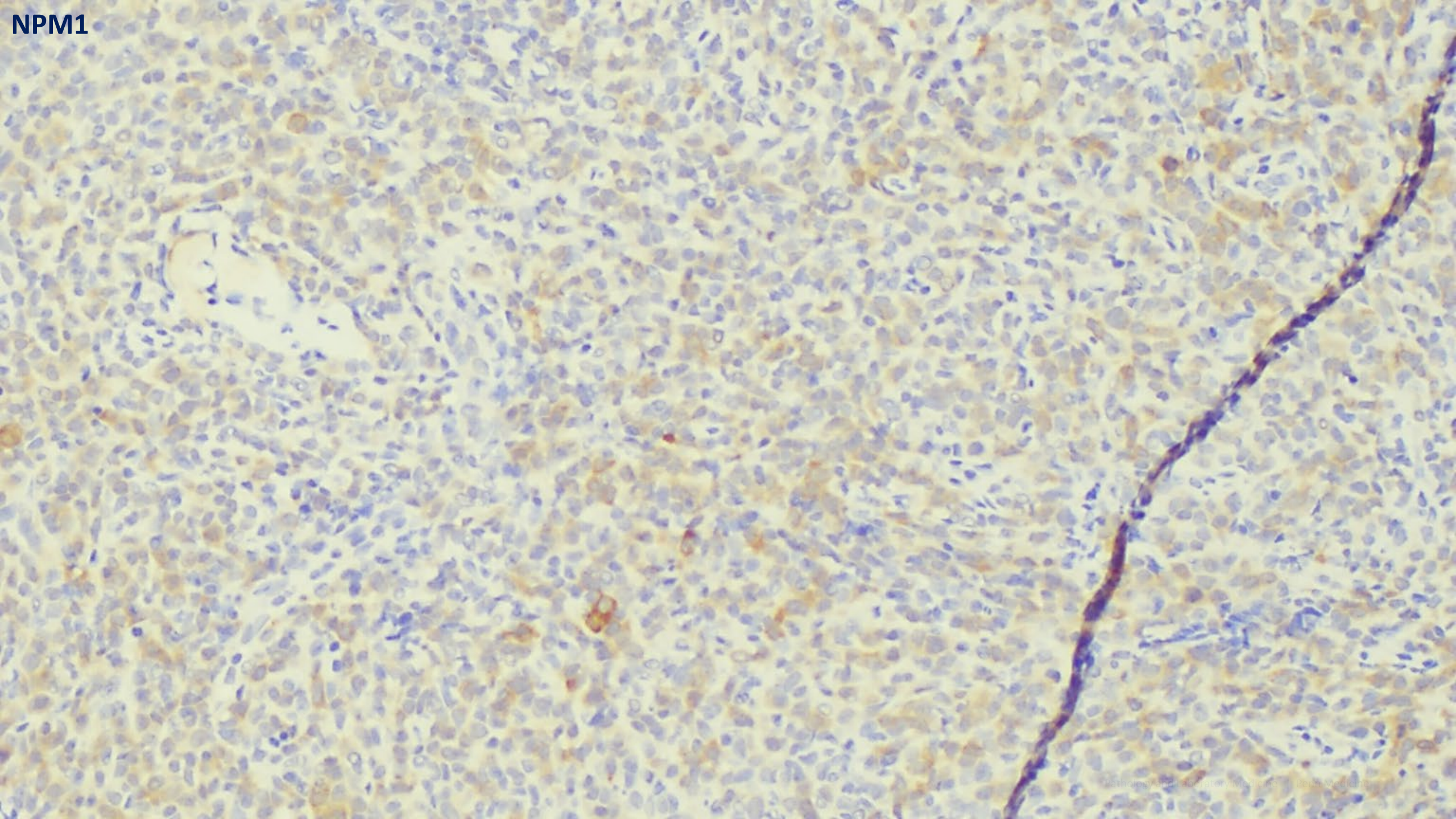
Bone Marrow Aspirate Smear, Clot, and Biopsy:

- Acute Myeloid Leukemia




IBA1


CD14


NPM1

Treatment & Follow-Up

Induction: Azacitidine + Venetoclax (initiated 8/2025)

Course:

- No tumor lysis syndrome
- Febrile neutropenia and hypoxia → managed with cefepime + dexamethasone

By Sept/25: now in remission, with the latest **BM findings** showing:

- Hypercellular marrow (50%) with erythroid-predominant hematopoiesis; **no overt evidence of residual/recurrent acute leukemia**

Literature Context: Rare Coexistence of HL and Myeloid Sarcoma/AML

Reference	What is similar	What is different
Relapsed nodular sclerosis Hodgkin lymphoma and therapy-related myeloid sarcoma in a mediastinal mass — Paessler et al.	Concurrent Hodgkin lymphoma relapse + myeloid sarcoma in the same biopsy. Diagnostic overlap.	Therapy-related (after chemo + radiation), and not exactly first diagnosed CHL with later AML Doesn't include NPM1 mutation
Myeloid Sarcoma: Experience from a Tertiary Care Center — Murugan et al.	Cases of MS presenting in lymph nodes; some treated as if lymphoma initially; diagnostic delays; use of IHC / molecular.	Again, no Hodgkin lymphoma + AML + NPM1 + retrospective LN MS in identical fashion.
Hodgkin's Disease Coexisting With Myelodysplastic Syndrome — Elghetany et al.	Rare coexistence of Hodgkin lymphoma with a myeloid stem cell disorder (MDS → AML); shows malignant myeloid disease in Hodgkin patients.	But the timeline is different; myeloid disease (MDS) preceding or in coexistence, but not the same presentation with missed myeloid sarcoma in lymph node then overt AML.

Discussion Points: Diagnosis, Prognosis, and Treatment Challenges

- **Rare coexistence:** Classic Hodgkin lymphoma with concurrent myeloid sarcoma/acute myeloid leukemia

- **Prognosis:**
  - NPM1-mutated AML is typically favorable
  - Complicated by presence of **CHL + extramedullary disease**

- **Therapeutic dilemma:**
  - Biggest challenge = **dual diagnosis of AML and CHL at presentation**
  - Limited precedent → no established guidelines for concurrent management

References

Arber DA, et al. WHO Classification of Haematolymphoid Tumours, 5th Edition. IARC, 2022.

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