Classical Hodgkin Lymphoma and Its Mimickers

A Diagnostic Journey

Case presentation.

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Hospital Raja Perempuan Zainab 2

Case 1

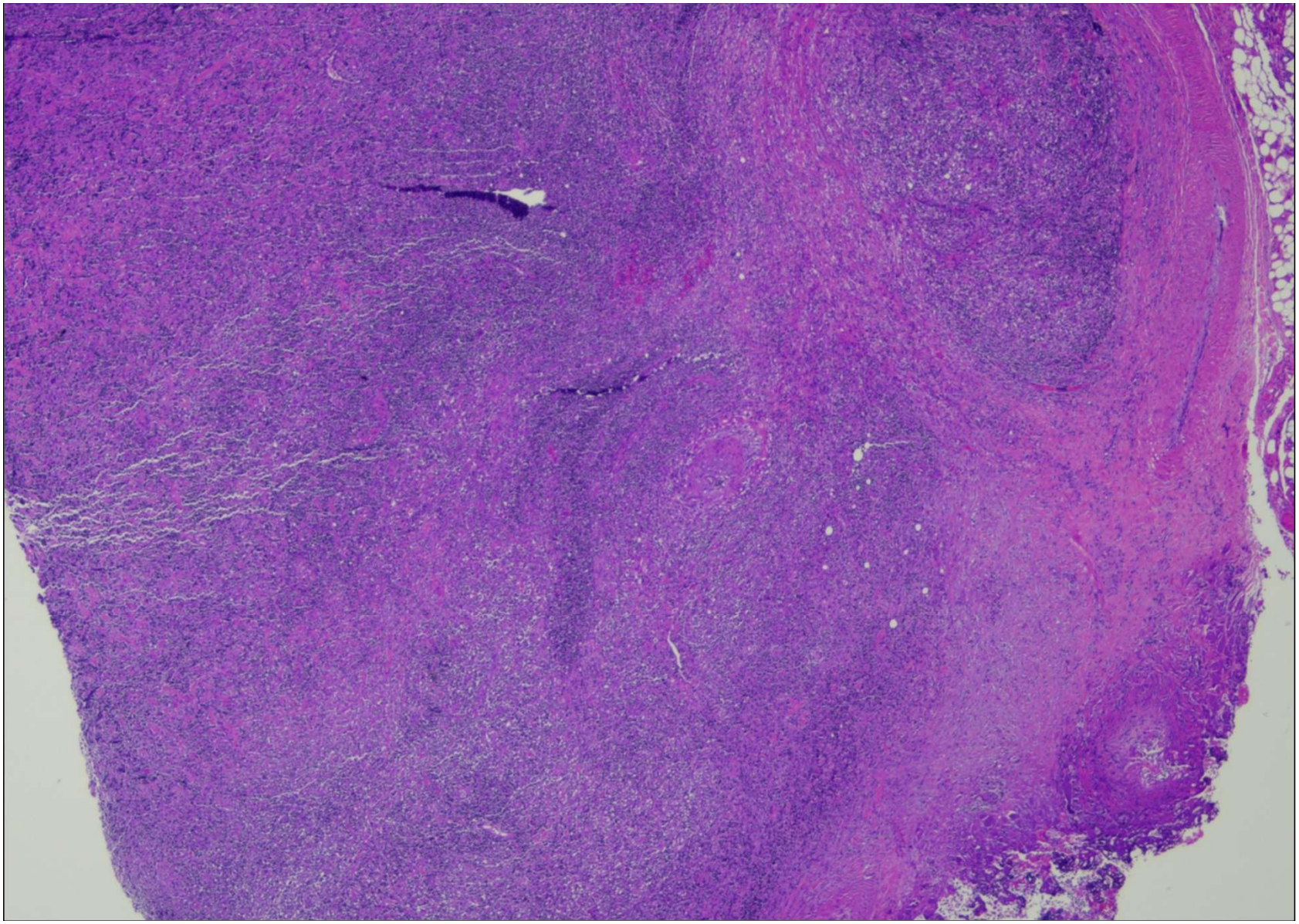
25 years old

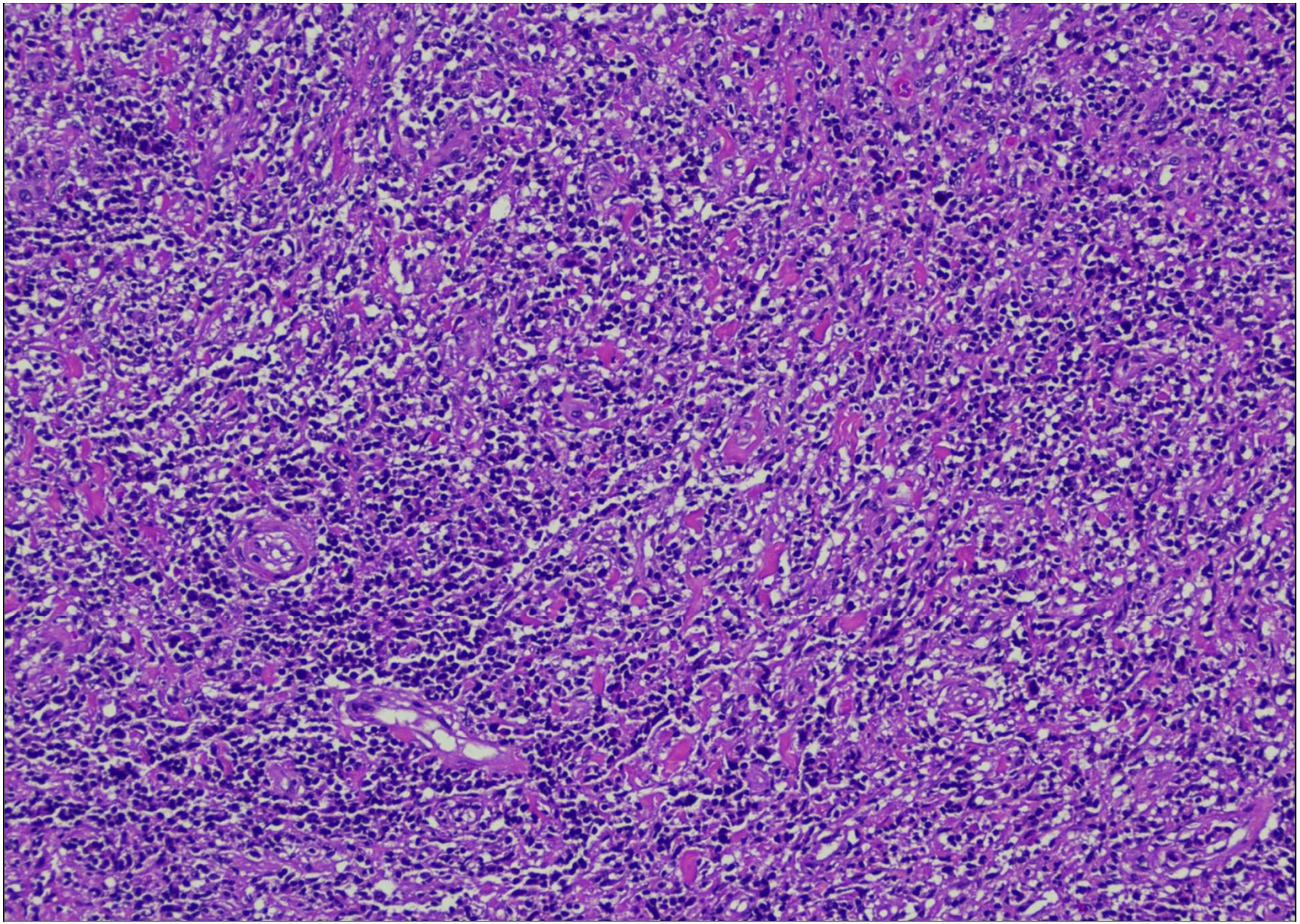
Female

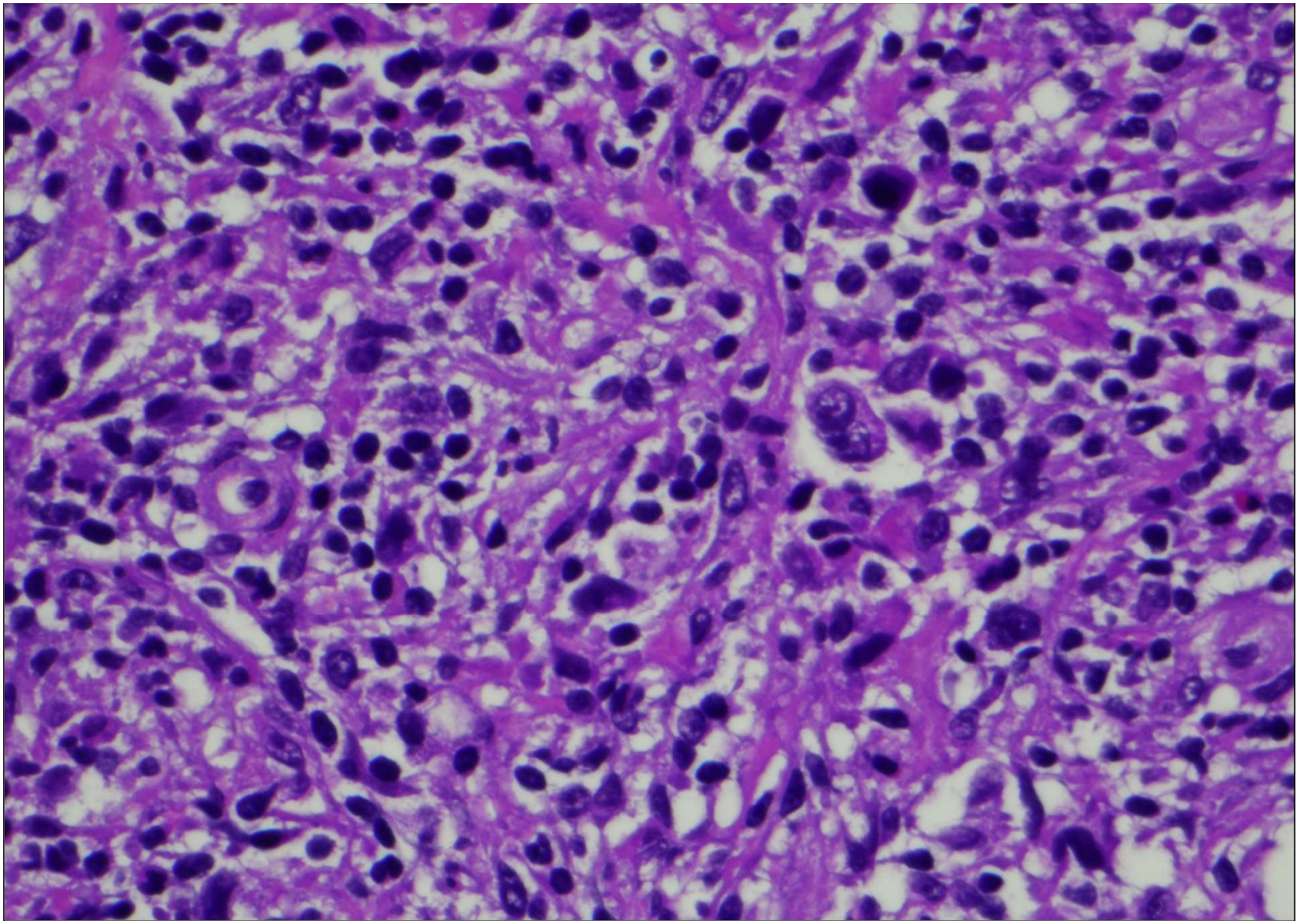
Left neck swelling for 9 months

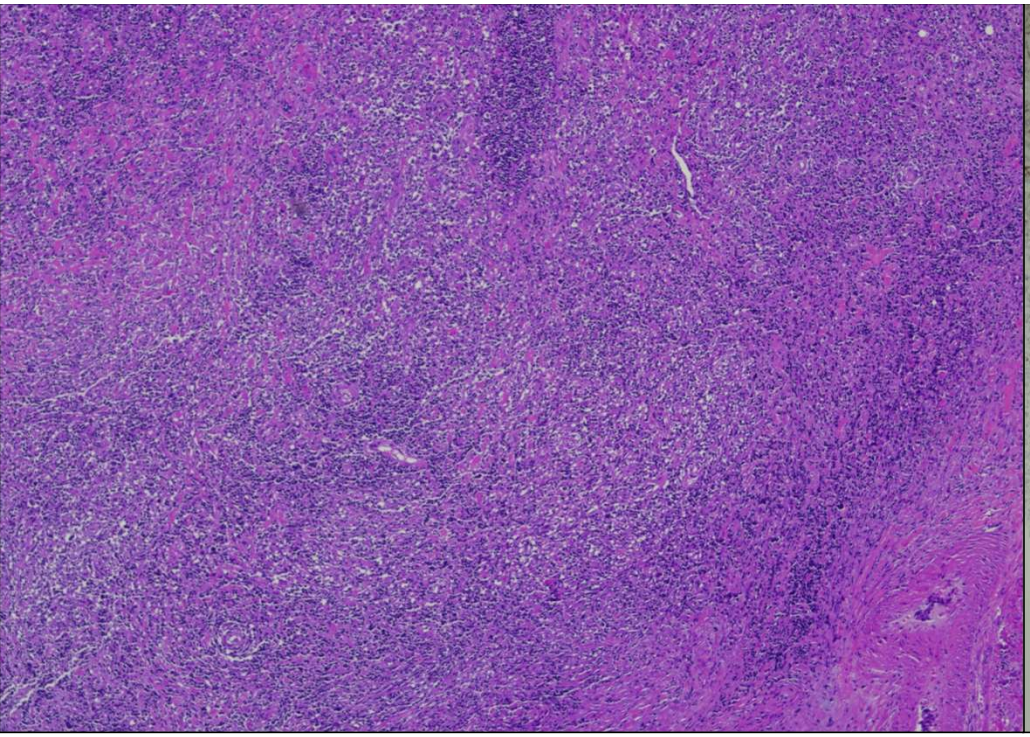
Chest X-Ray

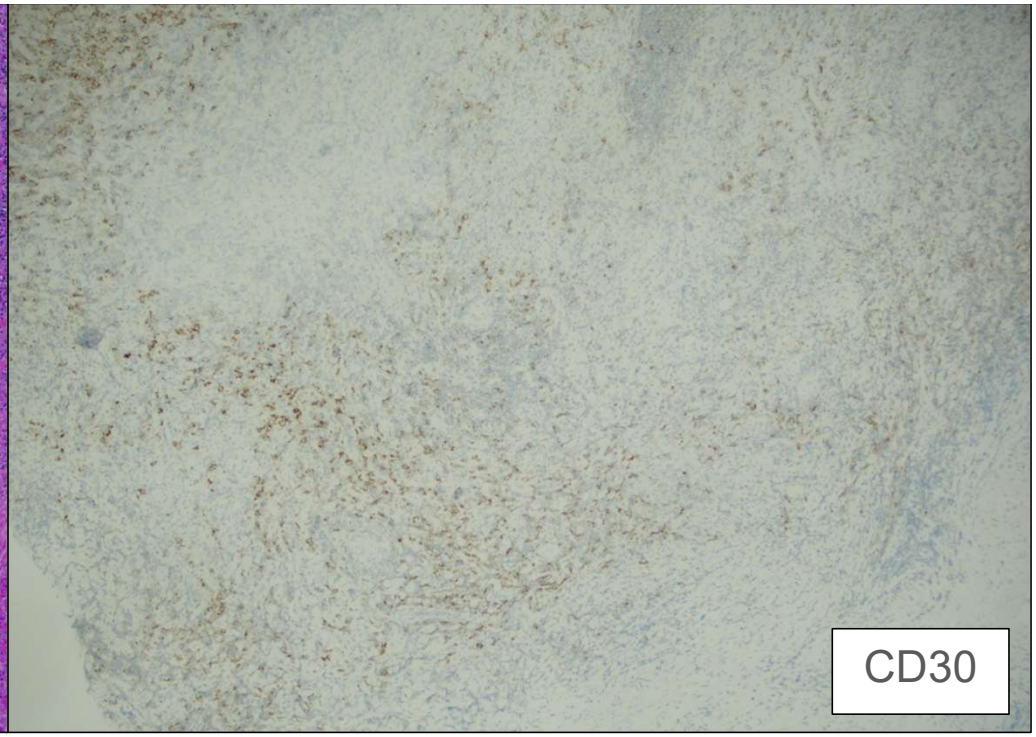
Widened mediastinum

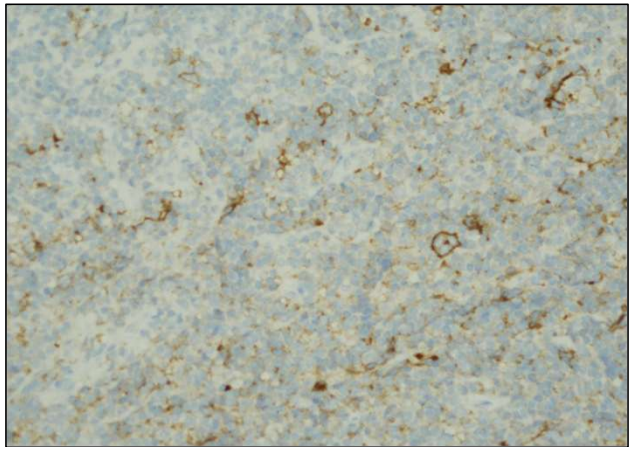


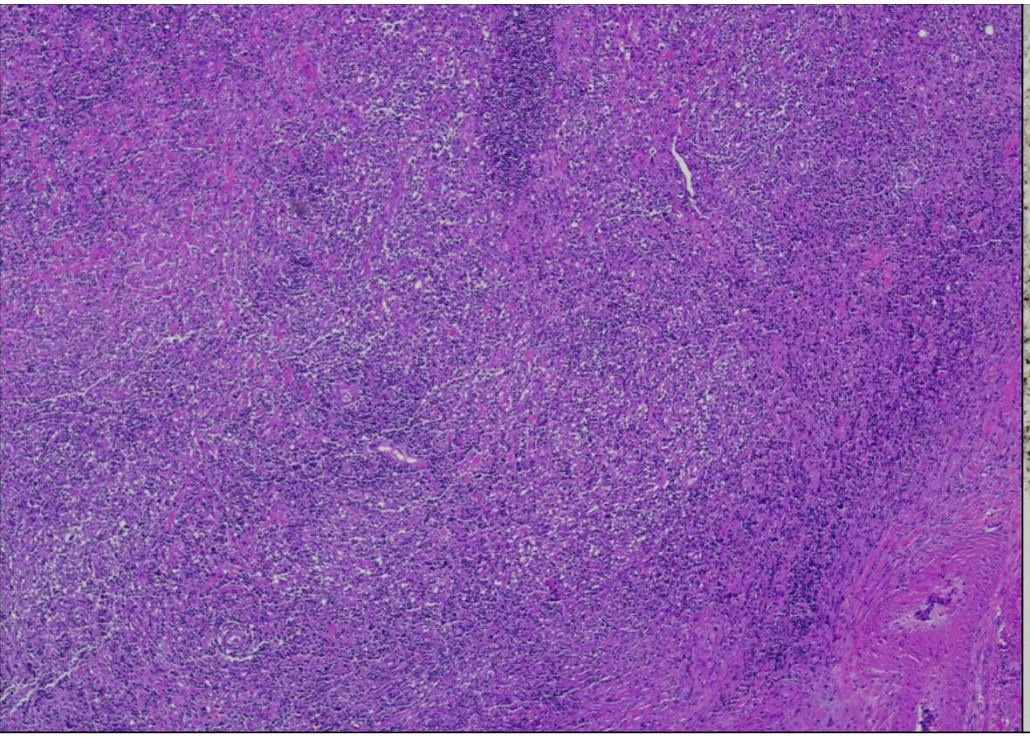


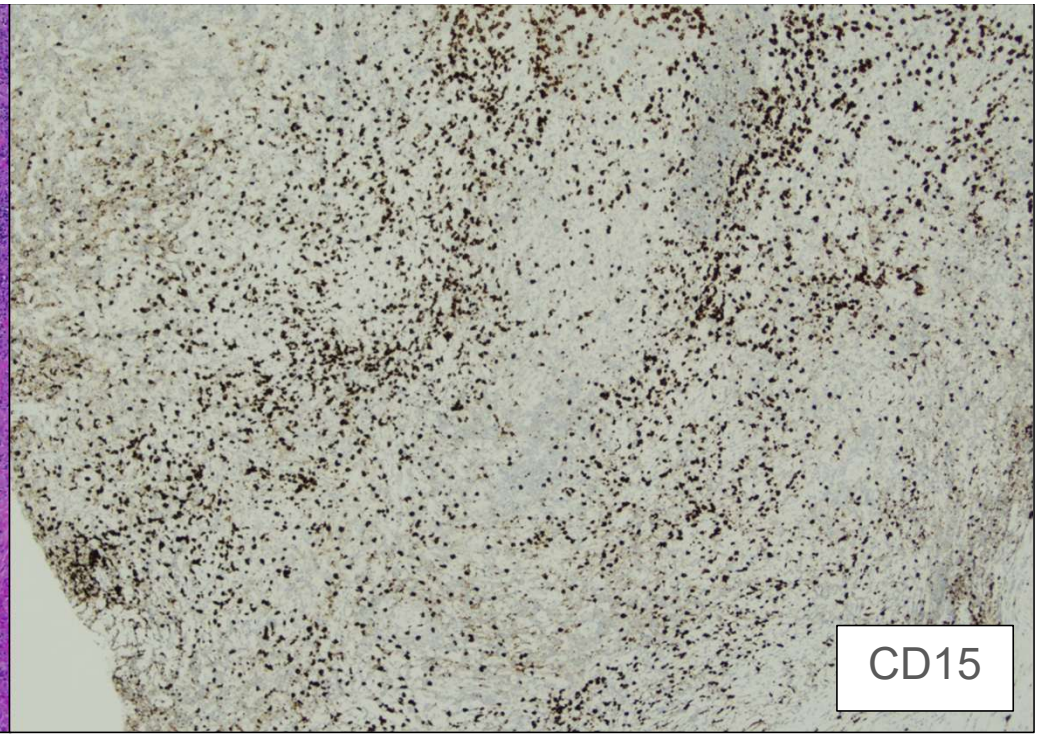





CD30



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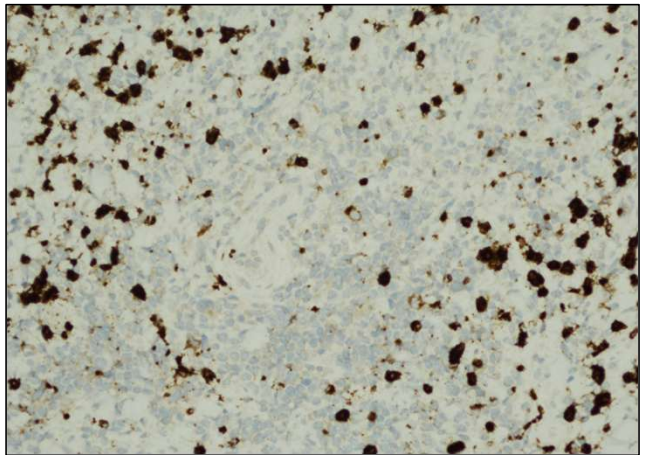
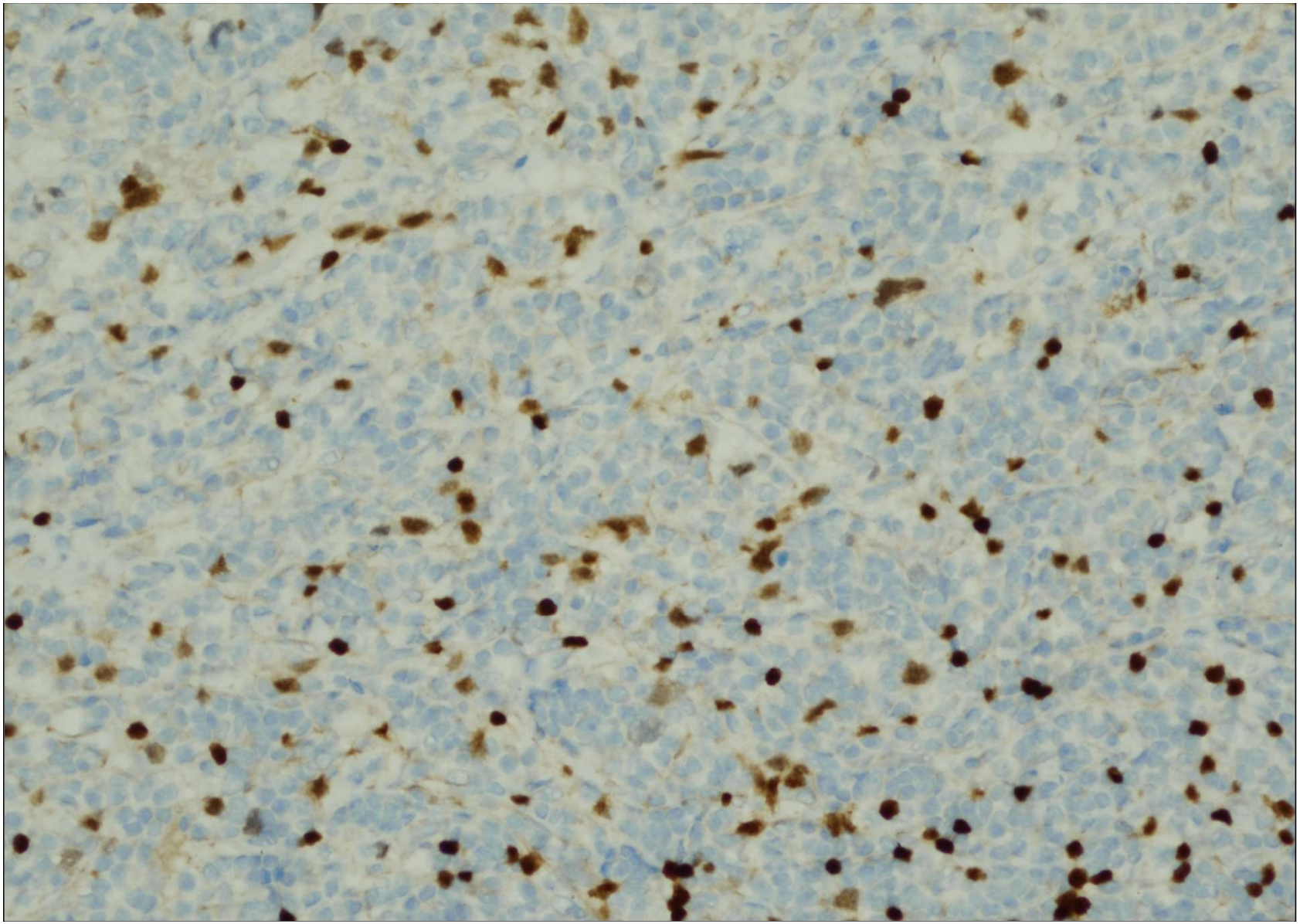
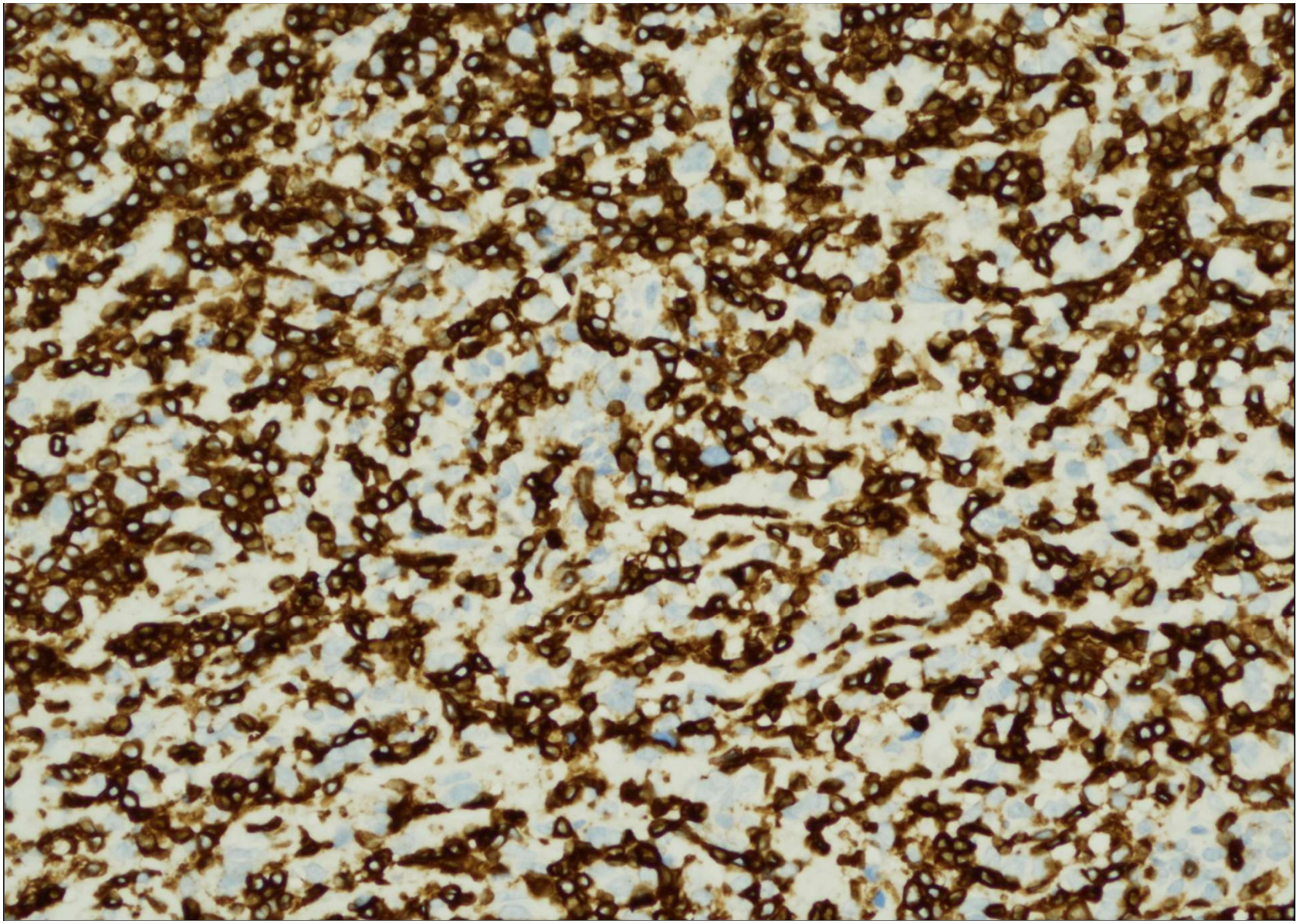




PAX5



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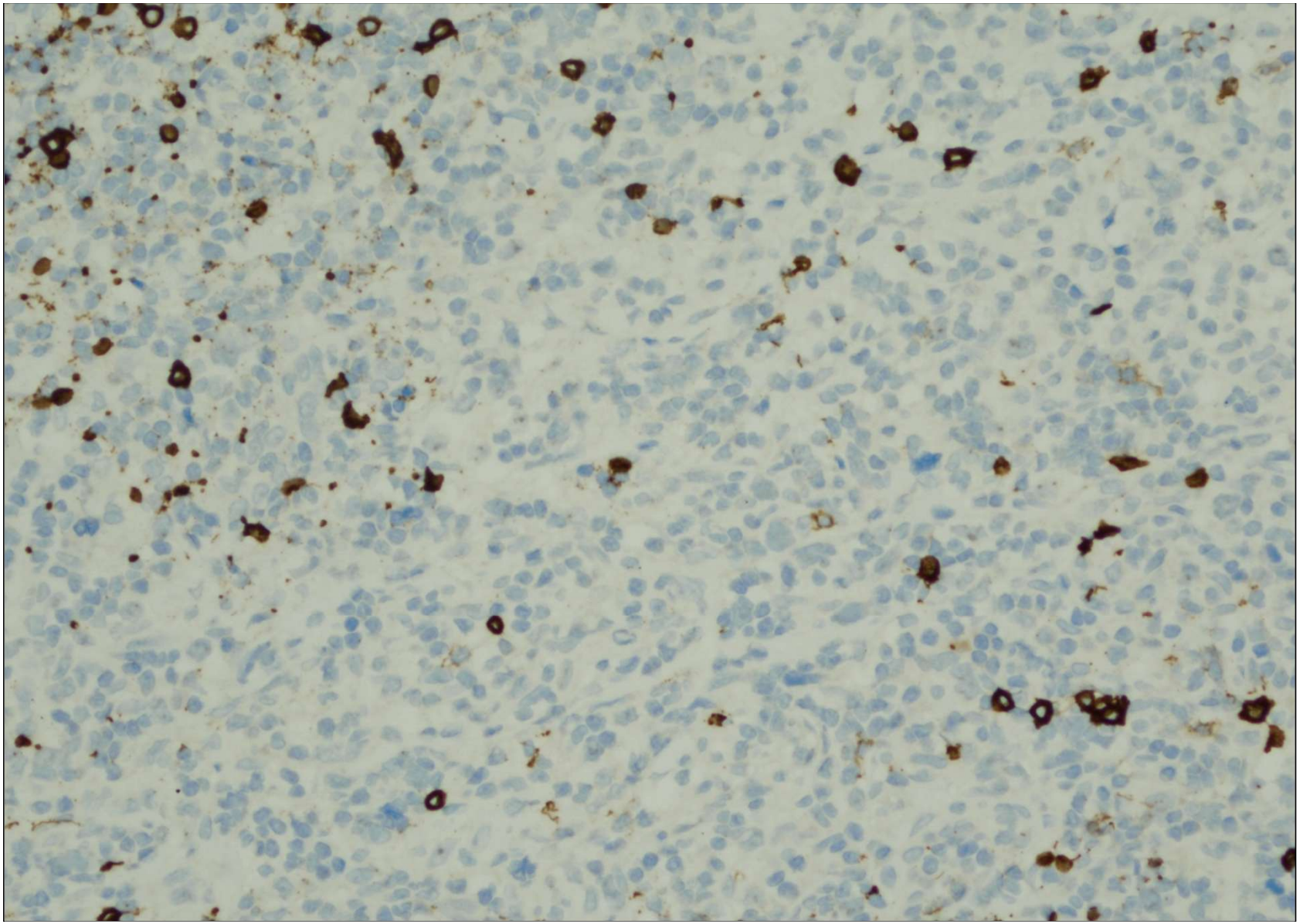


CD20

Diagnostic Report

Interpretation

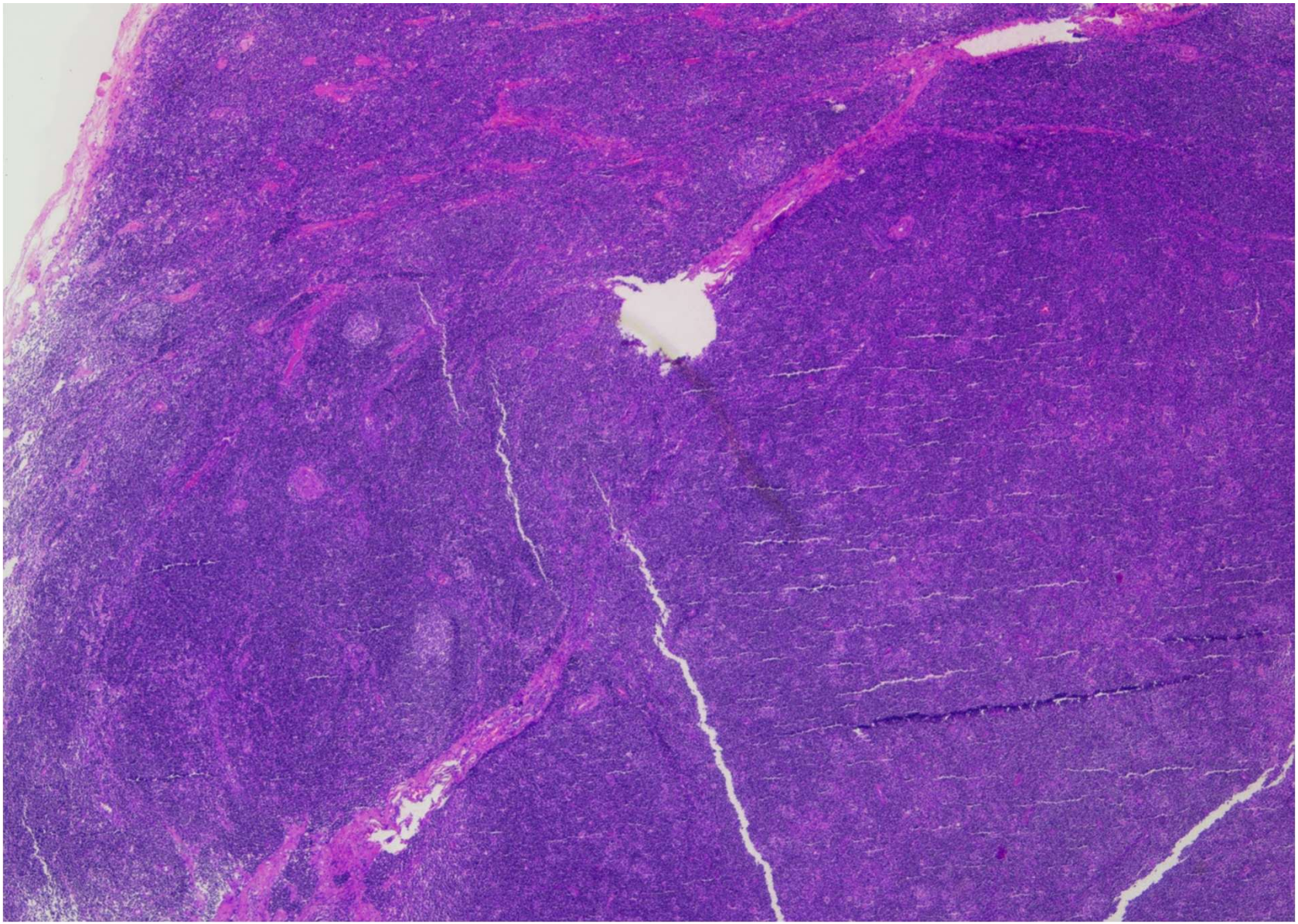
Classic Hodgkin Lymphoma, nodular sclerosis

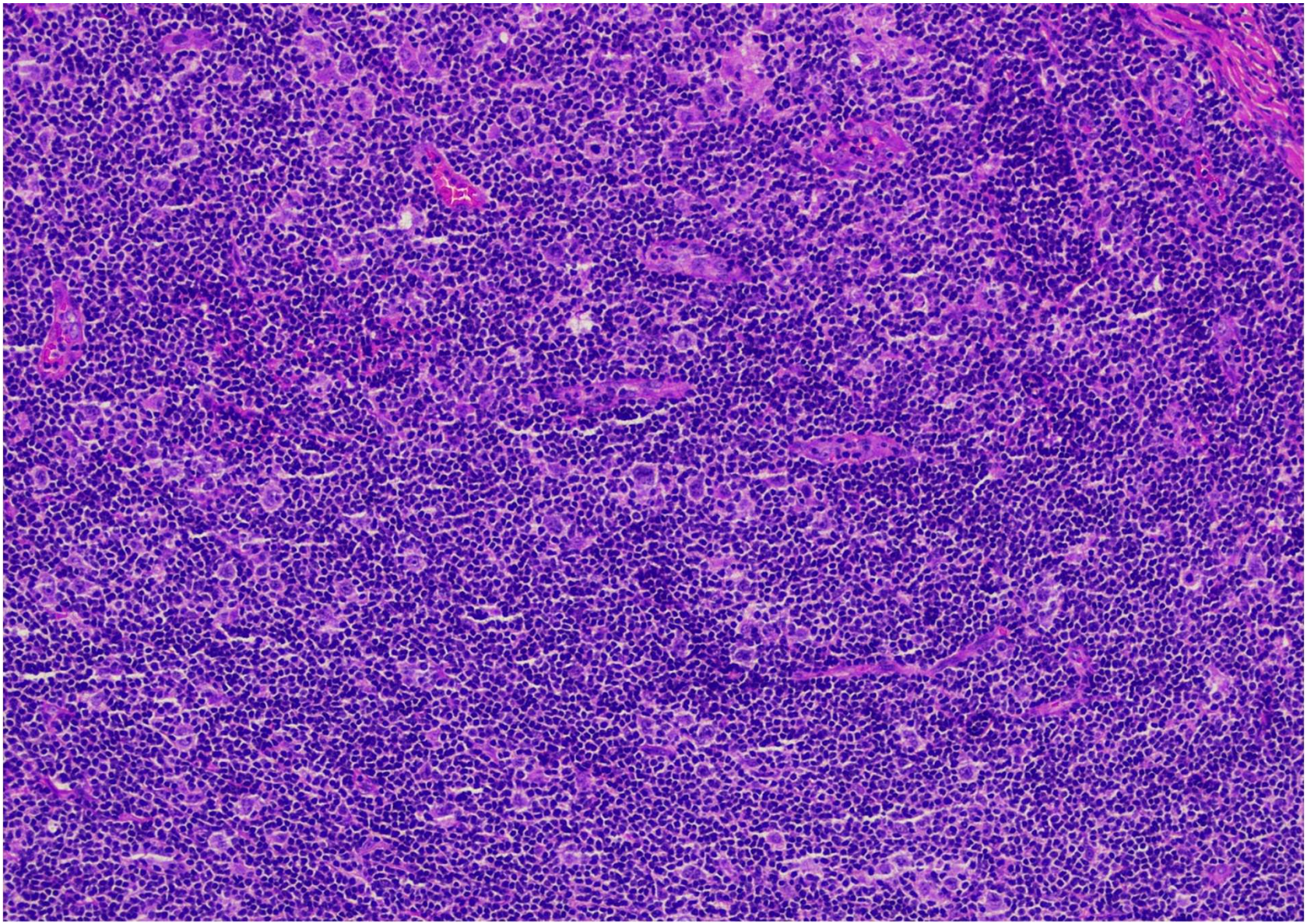
Case 2

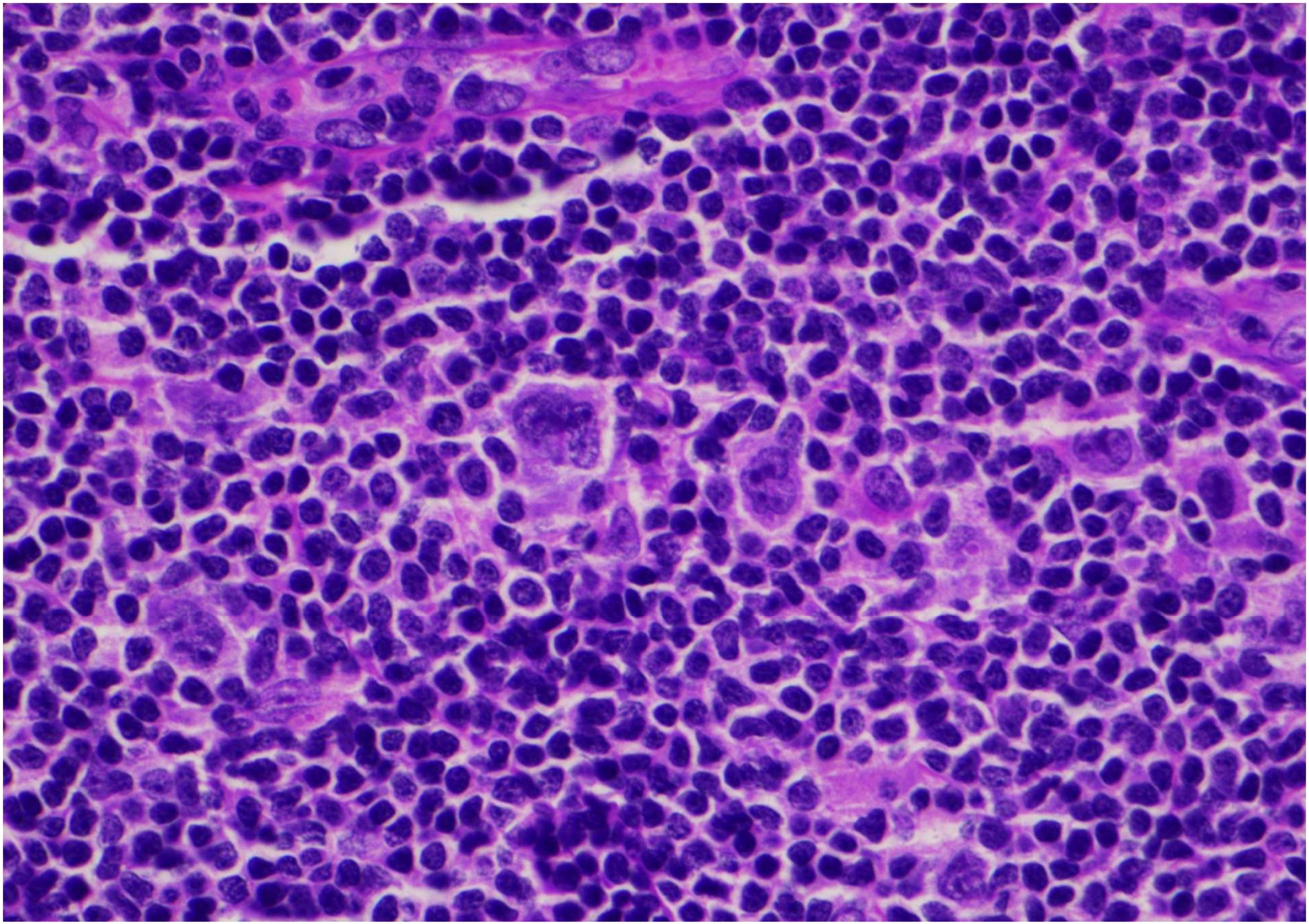
15 years old, female
NKMI

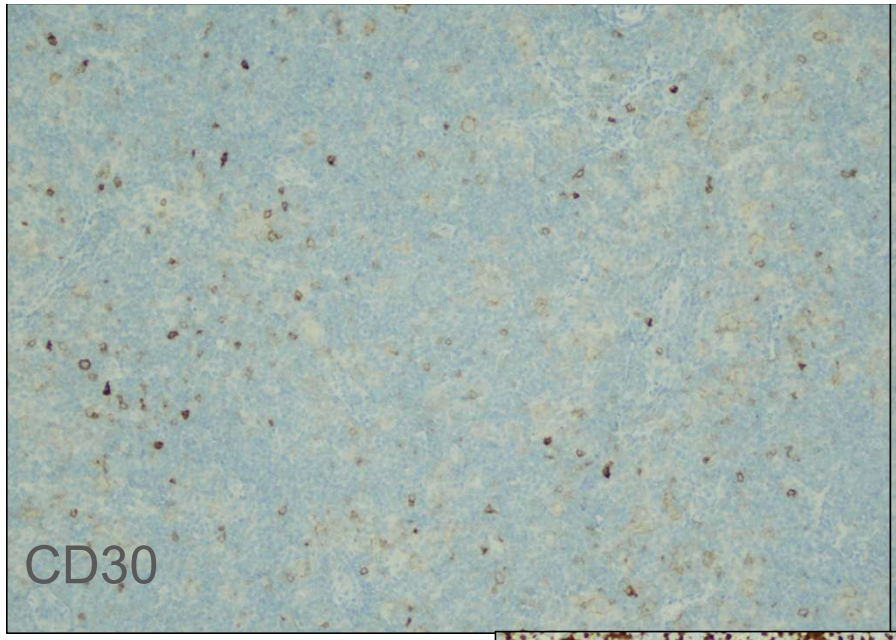
- Right neck swelling for 1 year, not increasing in size.

Location	Size
Right level V	2 x 2 cm





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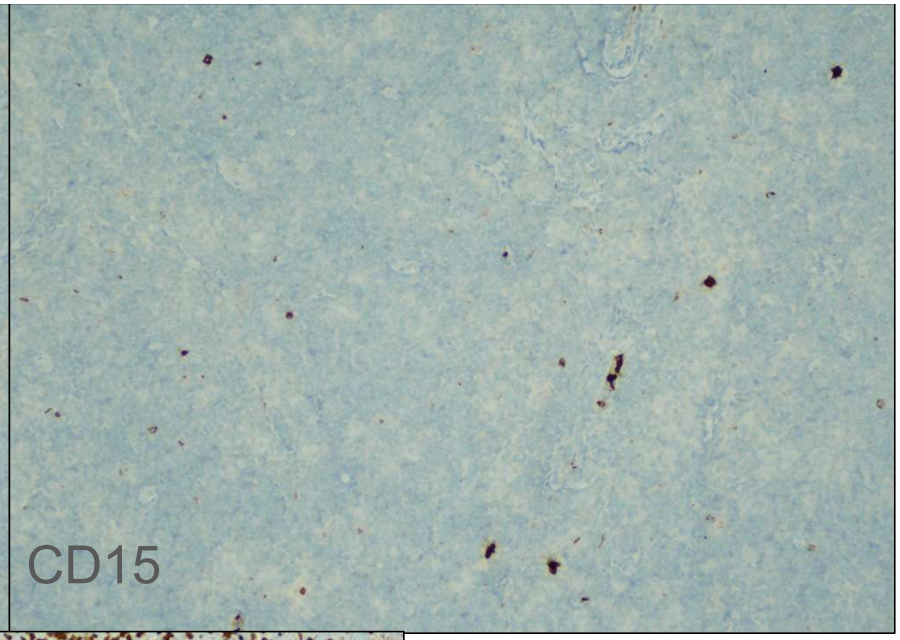
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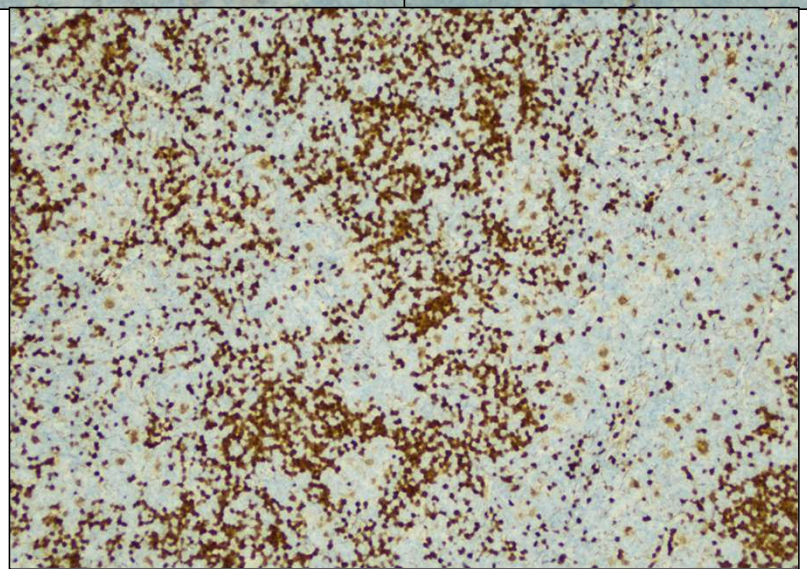
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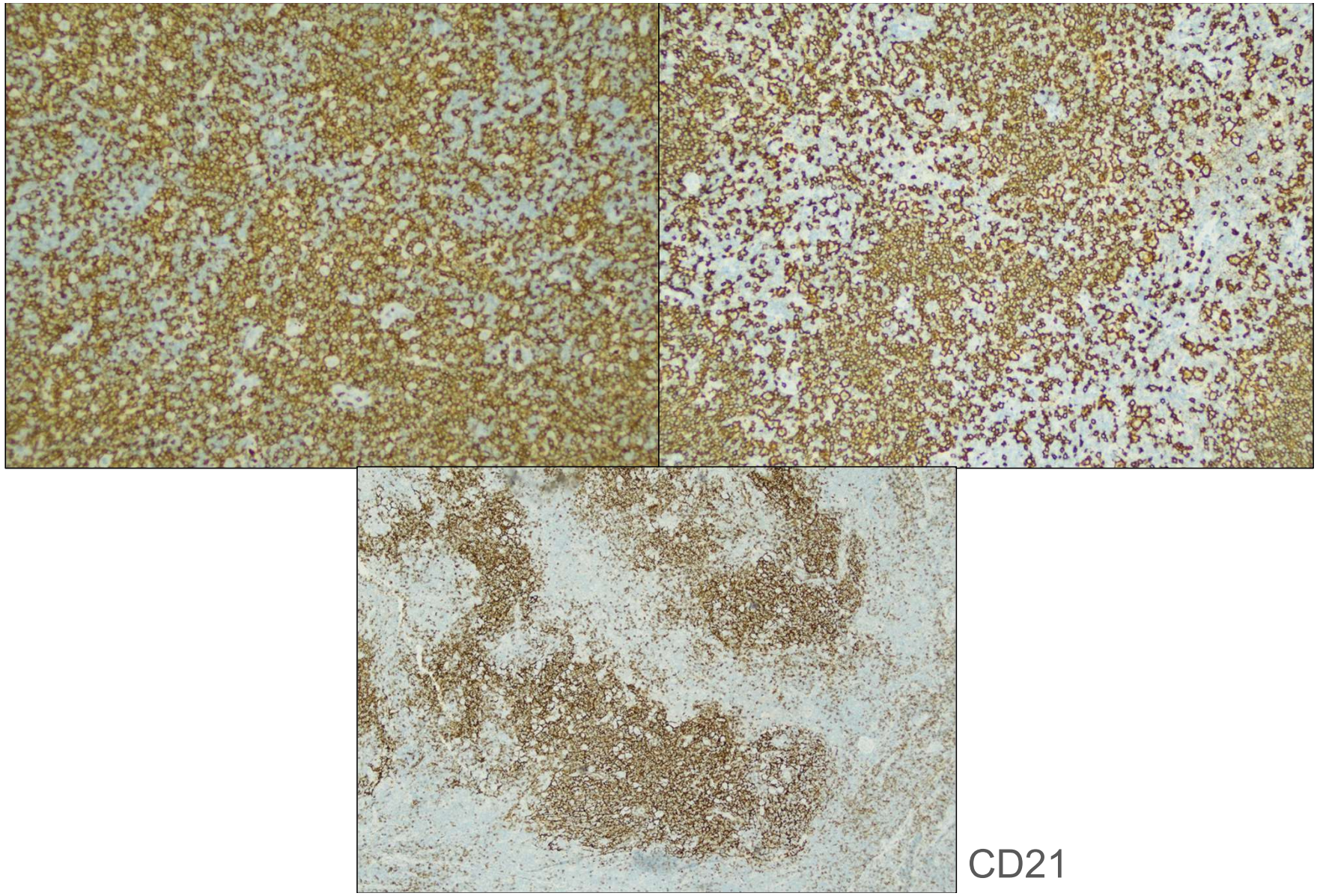
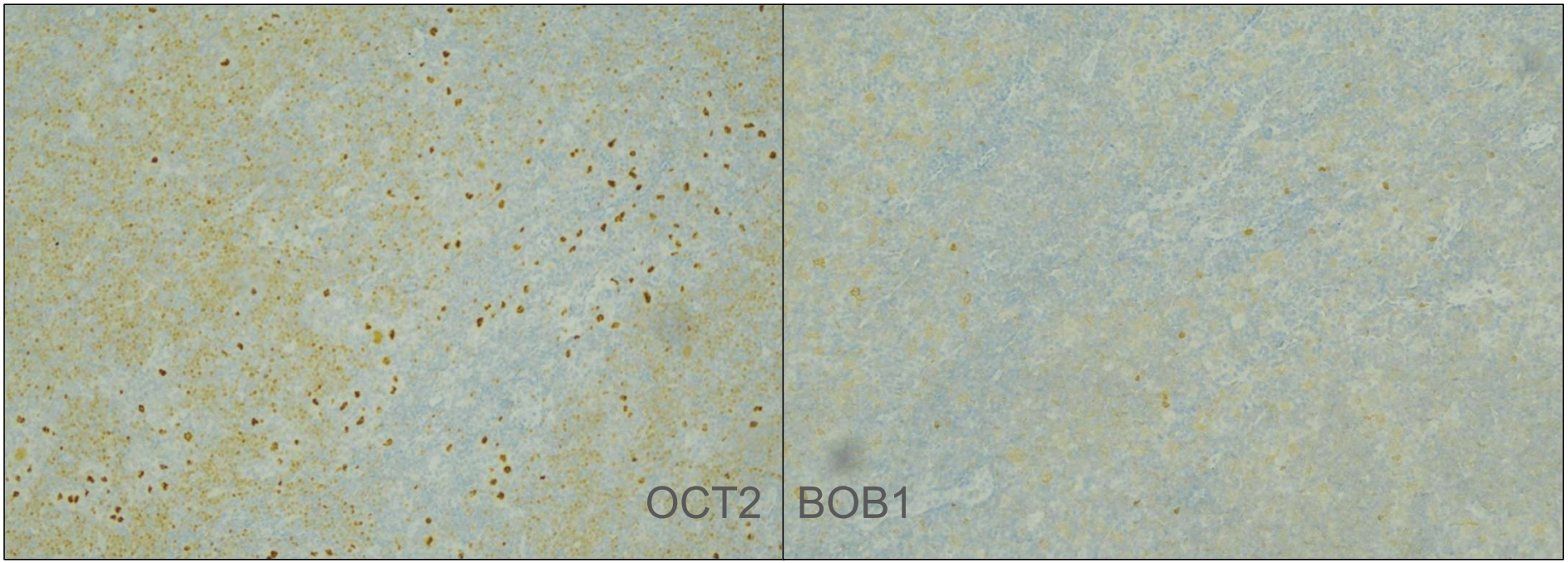

CD3
CD20
CD21


OCT2
BOB1

Diagnostic Report

Interpretation

Nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL).

Diagnostic Comparison

CHL vs. NLPHL Key Features

Classic Hodgkin Lymphoma (CHL)

Immunophenotype

CD30+, weak PAX5, CD20−/weak

- **HRS cells** scattered within inflammatory background
- **Immune evasion** frequently associated with PD-L1 overexpression
- Usually lacks intact FDC nodules

Nodular Lymphocyte-Predominant (NLPHL)

Immunophenotype

CD20+, strong PAX5, OCT2+, BOB1+

- **LP ("popcorn") cells** within nodules
- **TFH-cell rosettes** (PD-1, CD57, CXCL13) are characteristic
- Retains mature B-cell phenotype
- Expanded CD21/CD23-positive FDC meshworks

Clinical Outcome
Case 2

NLPHL

Staging

Stage IA

CT scan reveals subscentimeter cervical lymph nodes.

0Progression

Stage IIA

1 Year Later

Repeat scan indicates disease progression to Stage IIa.

Treatment

R-ABVD

Initiated targeted chemotherapy regimen.

Outcome

Complete Response

June 2026

PET scan confirms complete metabolic response.

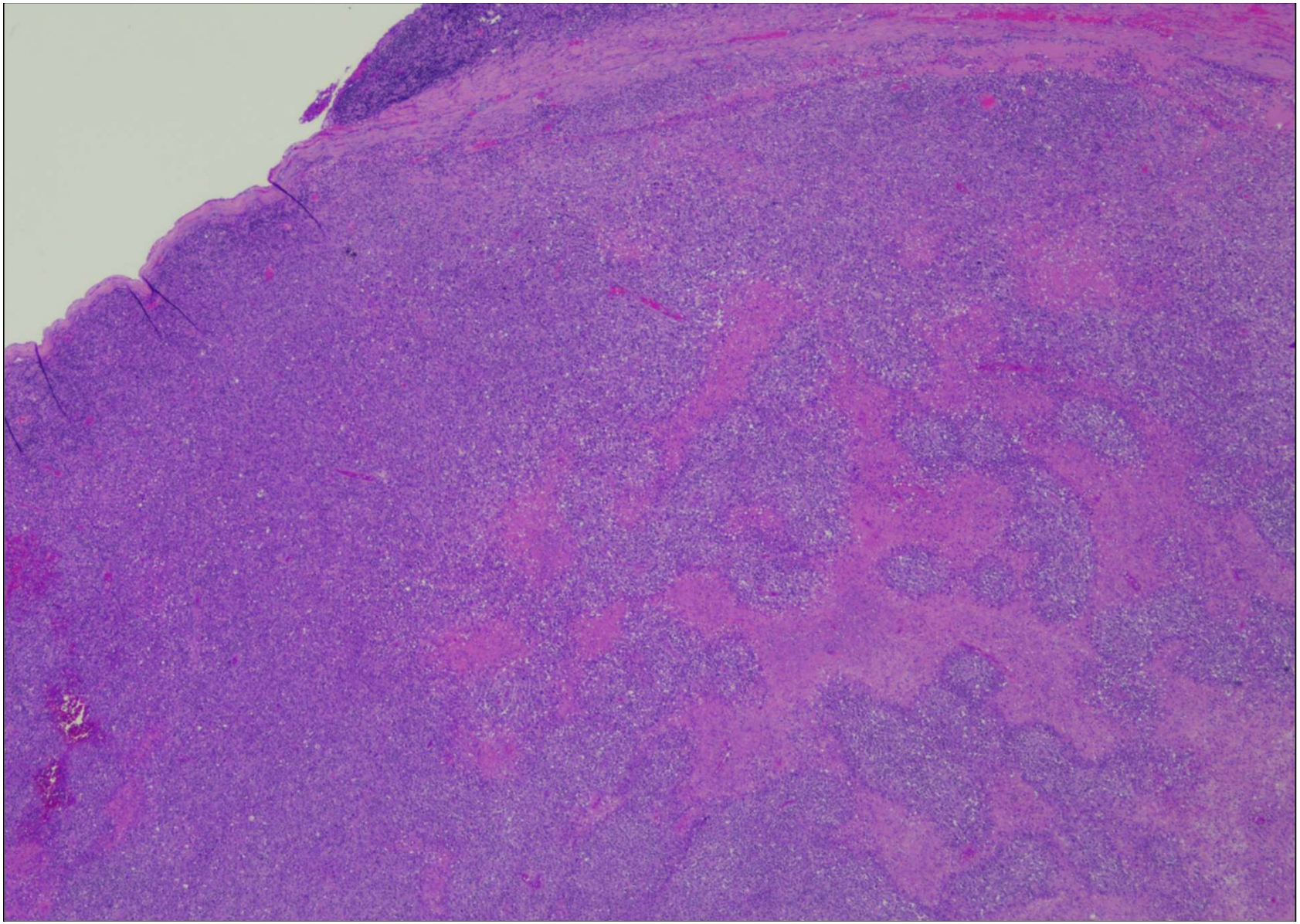
Case 3

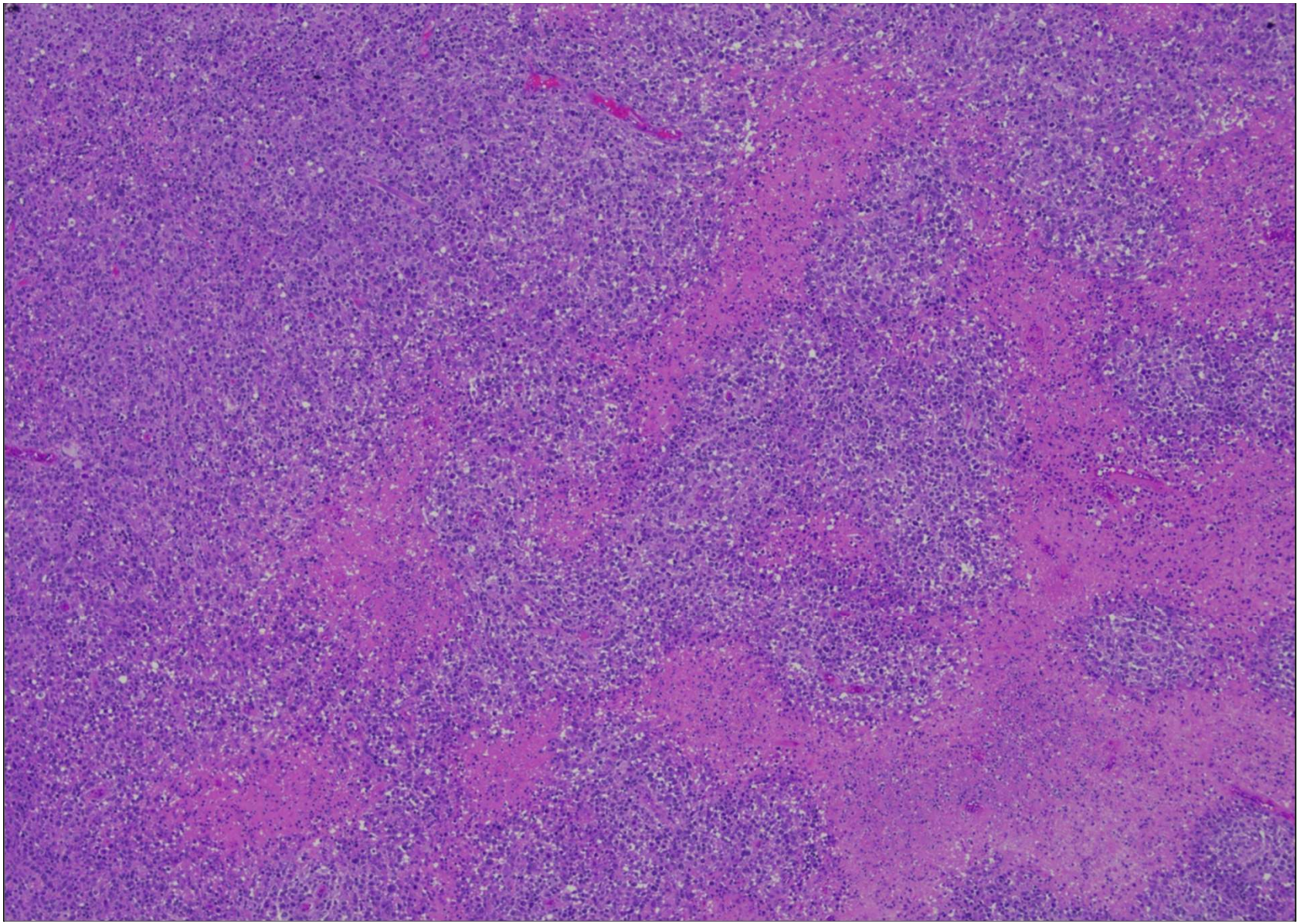
21 years old, man
NKMI

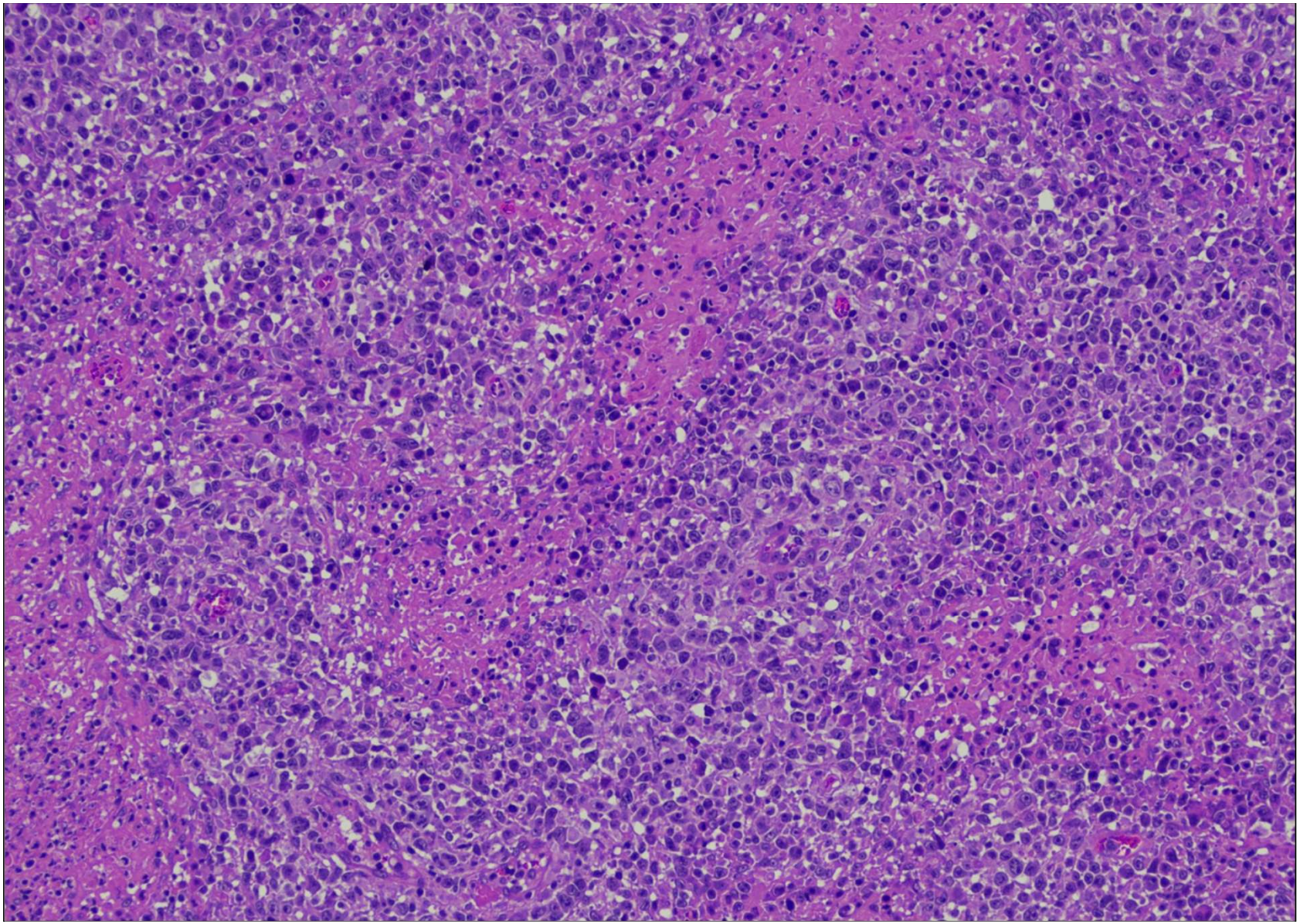
- SOB, fever, & constitutional symptoms
  Duration: 7 months

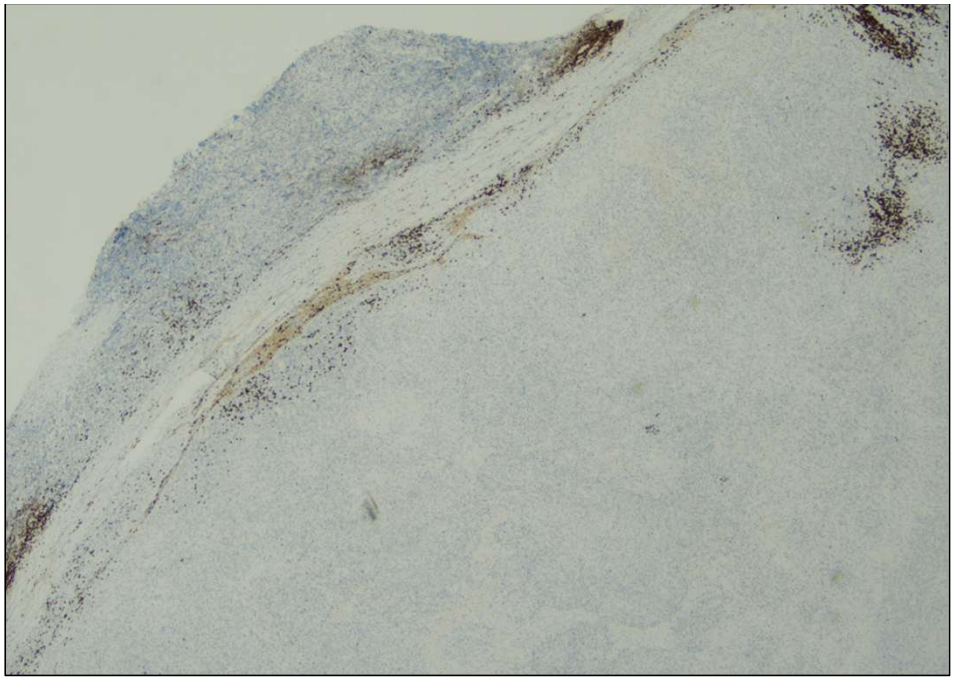
CXR left middle zone consolidation ? mass, widened mediastinum.

Location	Size
Left Cervical	2 x 1 cm
Right Anterior Cervical	3 x 2 cm









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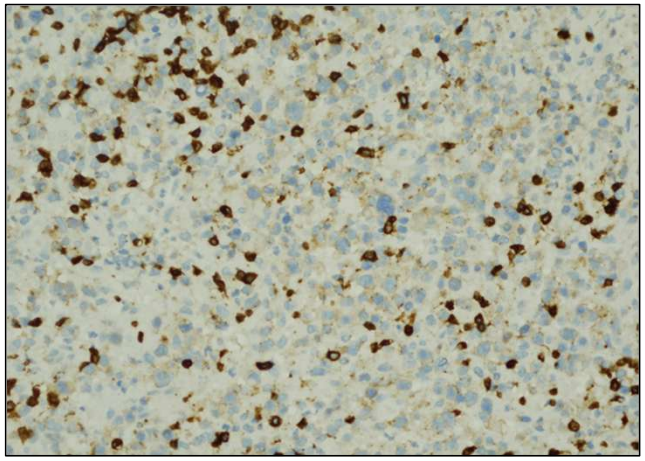
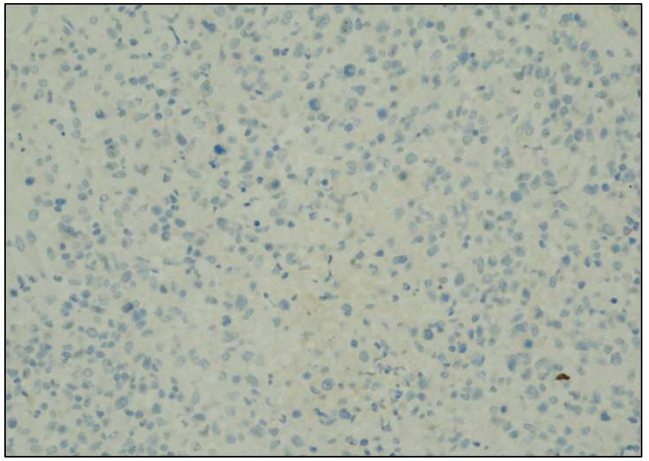
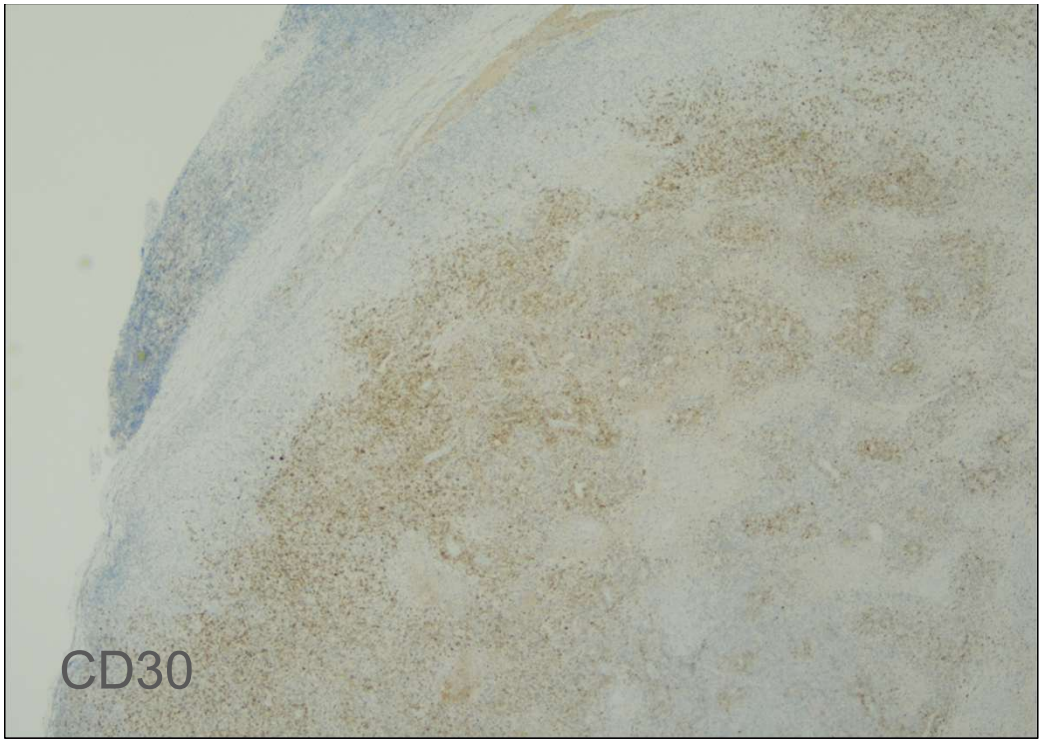
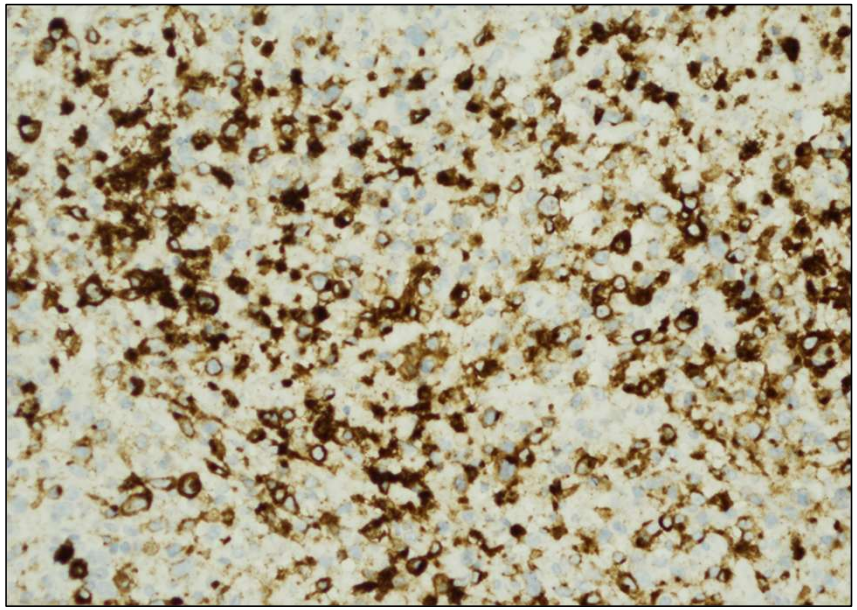


CD20







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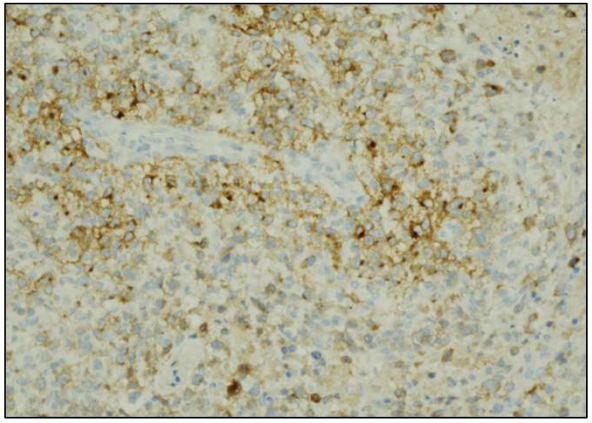
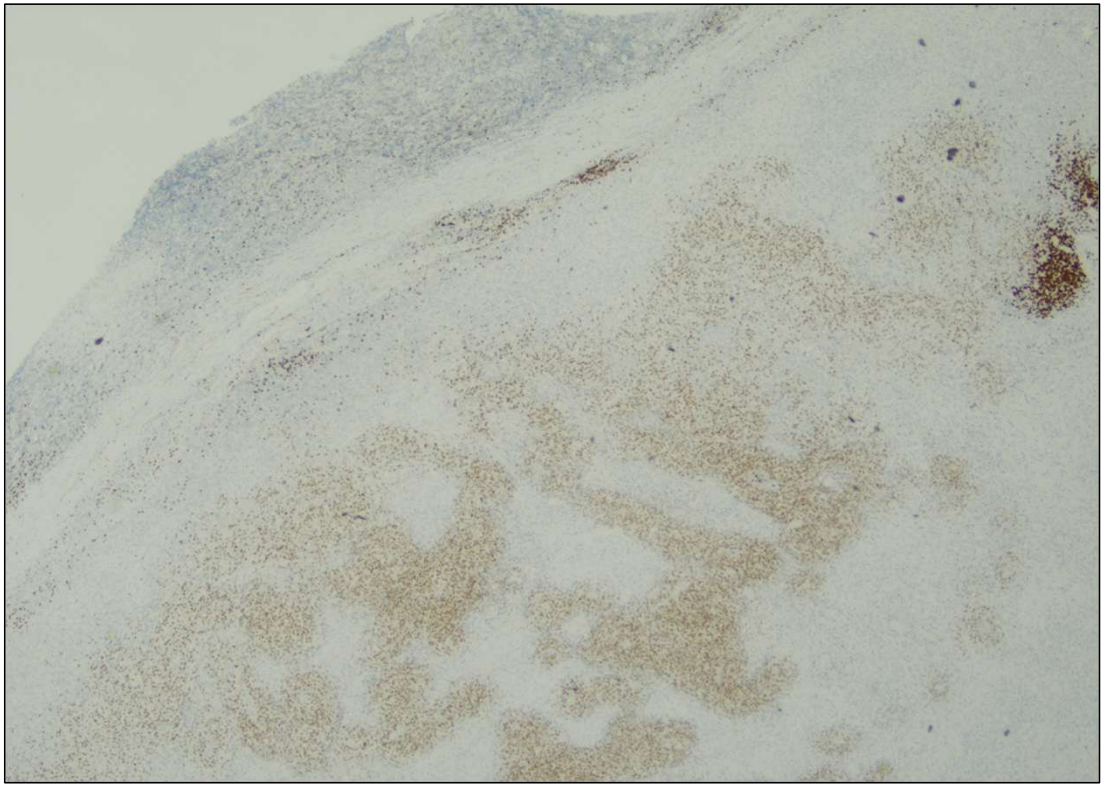
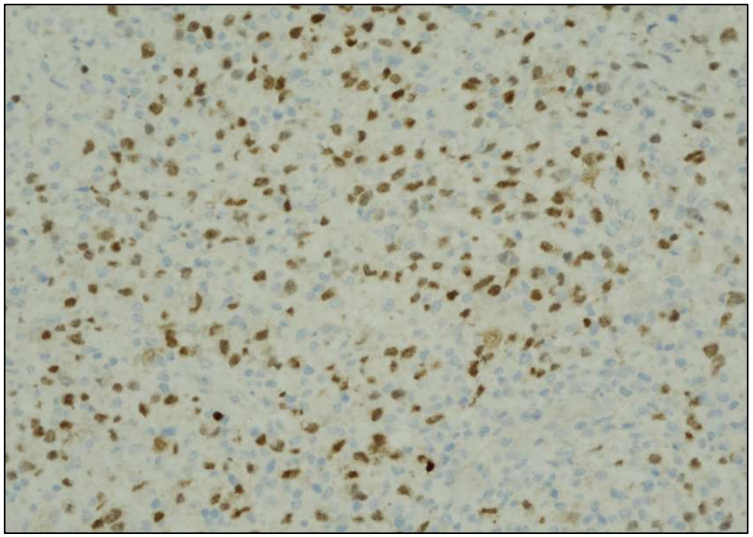
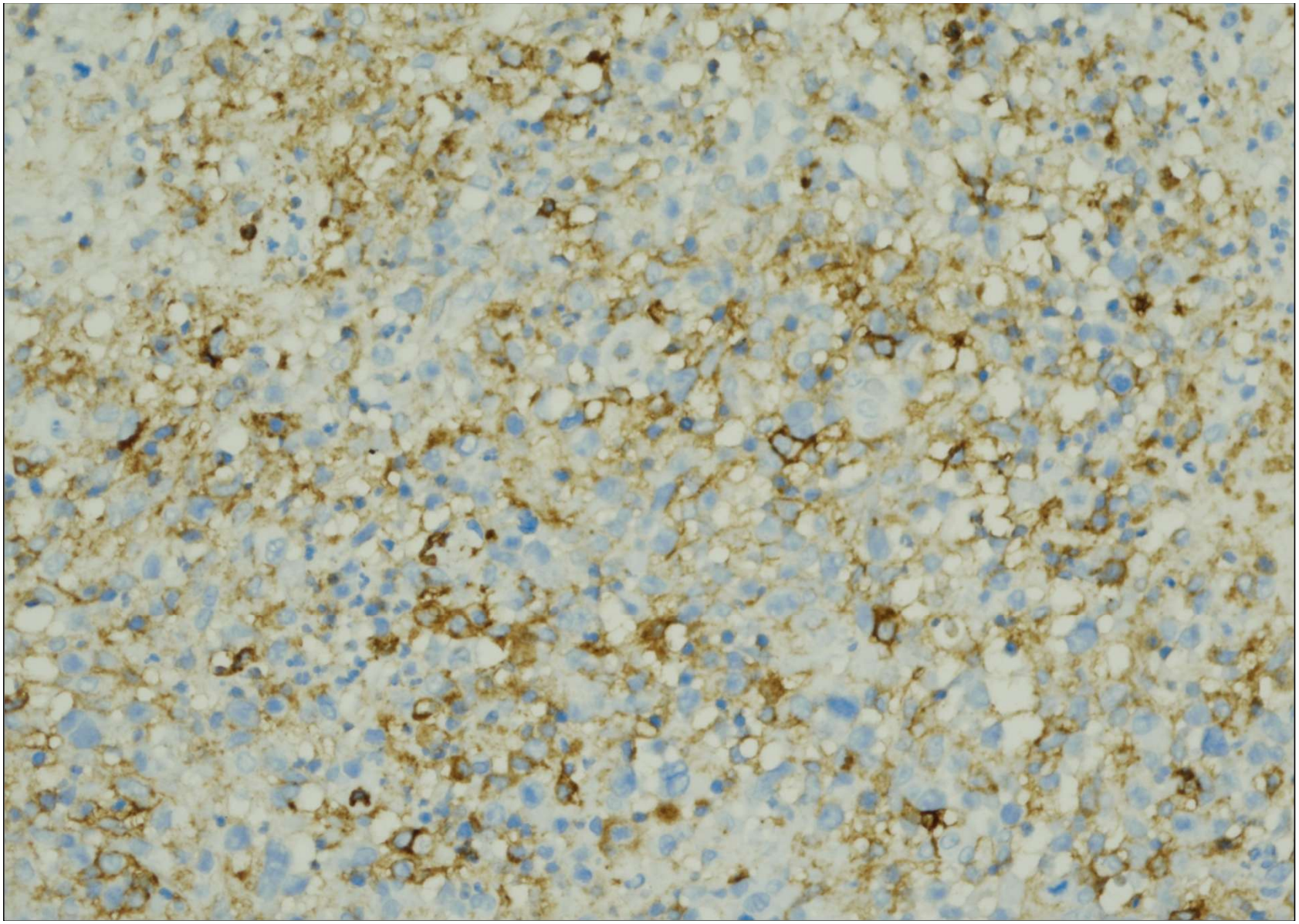




PAX5





LCA

Diagnostic Report

Interpretation

Classic Hodgkin Lymphoma, syncytial variant.

Clinical Outcome

Case 3

DIAGNOSIS

CHL

CECT THORAX

- **Anterior mediastinal mass** with extension into the left anterior chest wall
- **Bony involvement** & pericardial infiltration
- **Multiple enlarged nodes** in the mediastinum causing vascular and airway compression

TREATMENT & COURSE

BEACOCP

First-line chemotherapy regimen initiated.

OUTCOME

Uneventful

Tolerated well without major complications.

Syncytial Variant of NS-CHL

Morphological Features

- Morphological variant of **nodular sclerosis classical Hodgkin lymphoma (NSCHL)**
- Broad **cohesive (syncytial) sheets** of lacunar/HRS cells
- Often associated with **necrosis** and a less conspicuous inflammatory background

Diagnostic Significance

May closely mimic:

- Poorly differentiated carcinoma
- ALK-negative ALCL
- PMBCL / Mediastinal grey zone lymphoma
- Germ cell tumour (mediastinum)

Particularly challenging in **small biopsy specimens**

Practical Pearls

- **Immunophenotype remains typical of CHL** (CD30+, weak PAX5, CD15 variable)
- **Recognition prevents misclassification as a more aggressive malignancy**

Think of syncytial variant CHL when a CD30-positive mediastinal tumour forms cohesive sheets but retains the characteristic immunophenotype of classical Hodgkin lymphoma.

References: Wang & Medeiros, *Hum Pathol* 2021; Zhang *et al.*, *Hum Pathol* 2022.

Case 4

22 years old

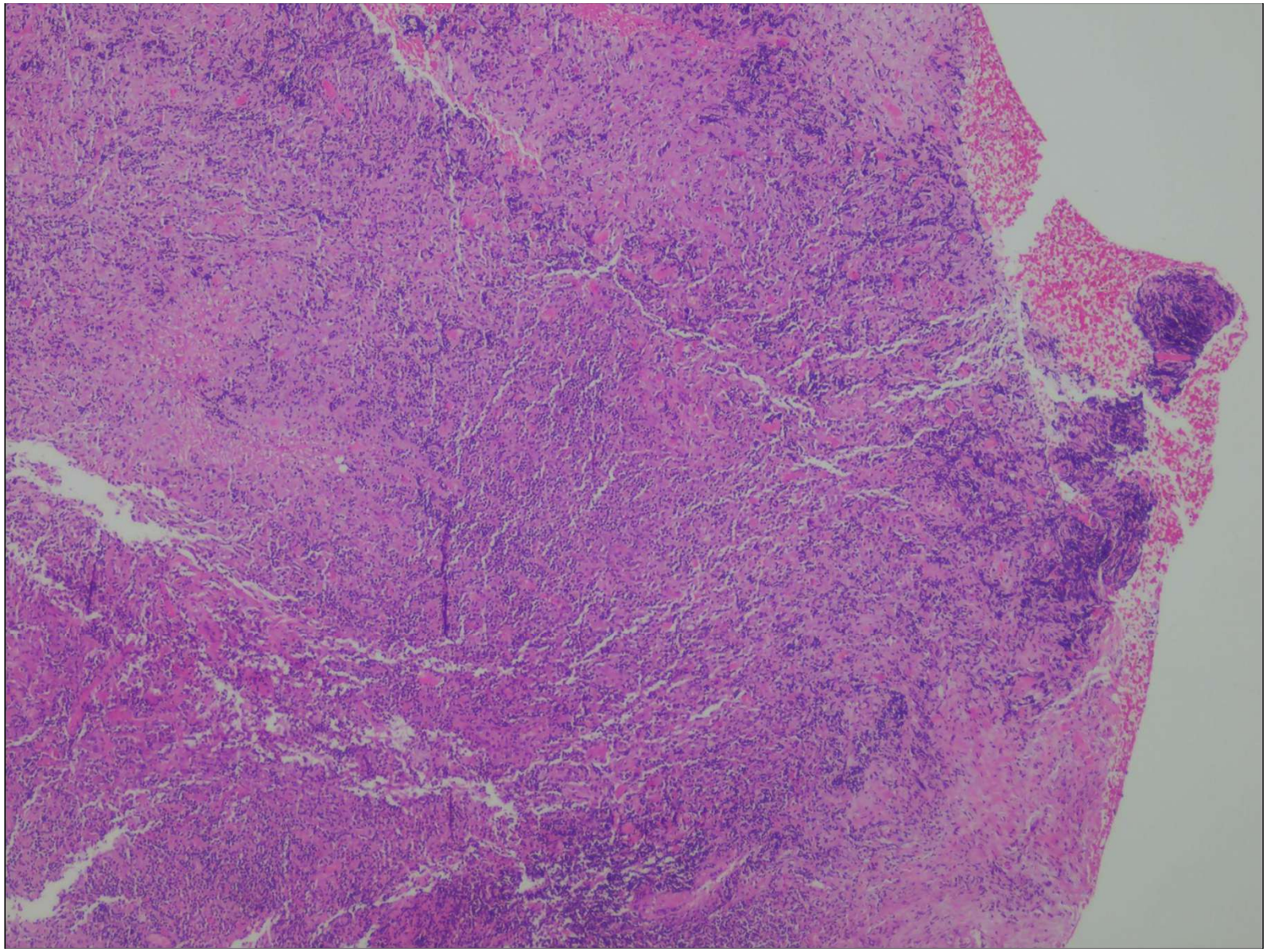
Female

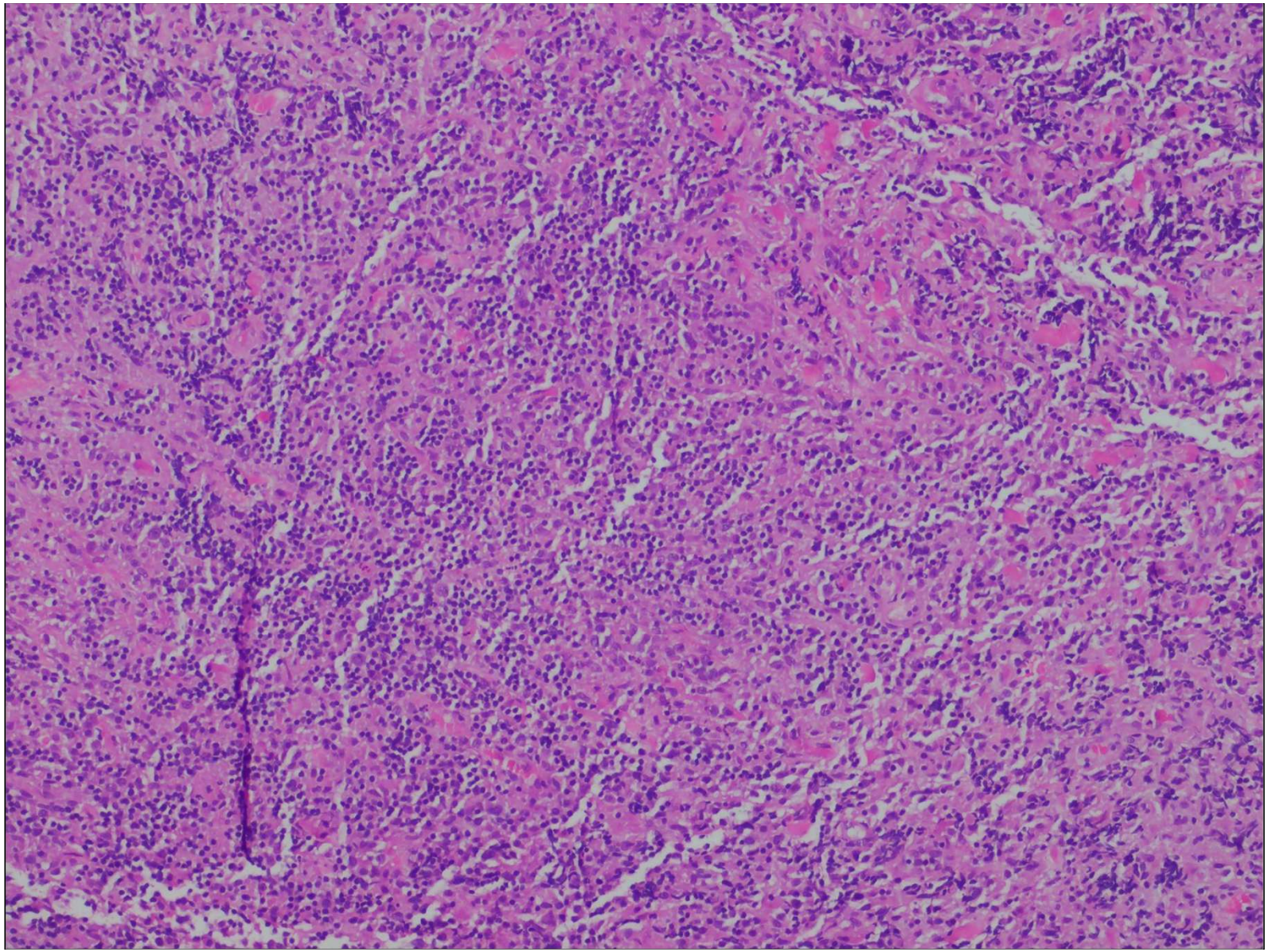
Right neck swelling for 6 months

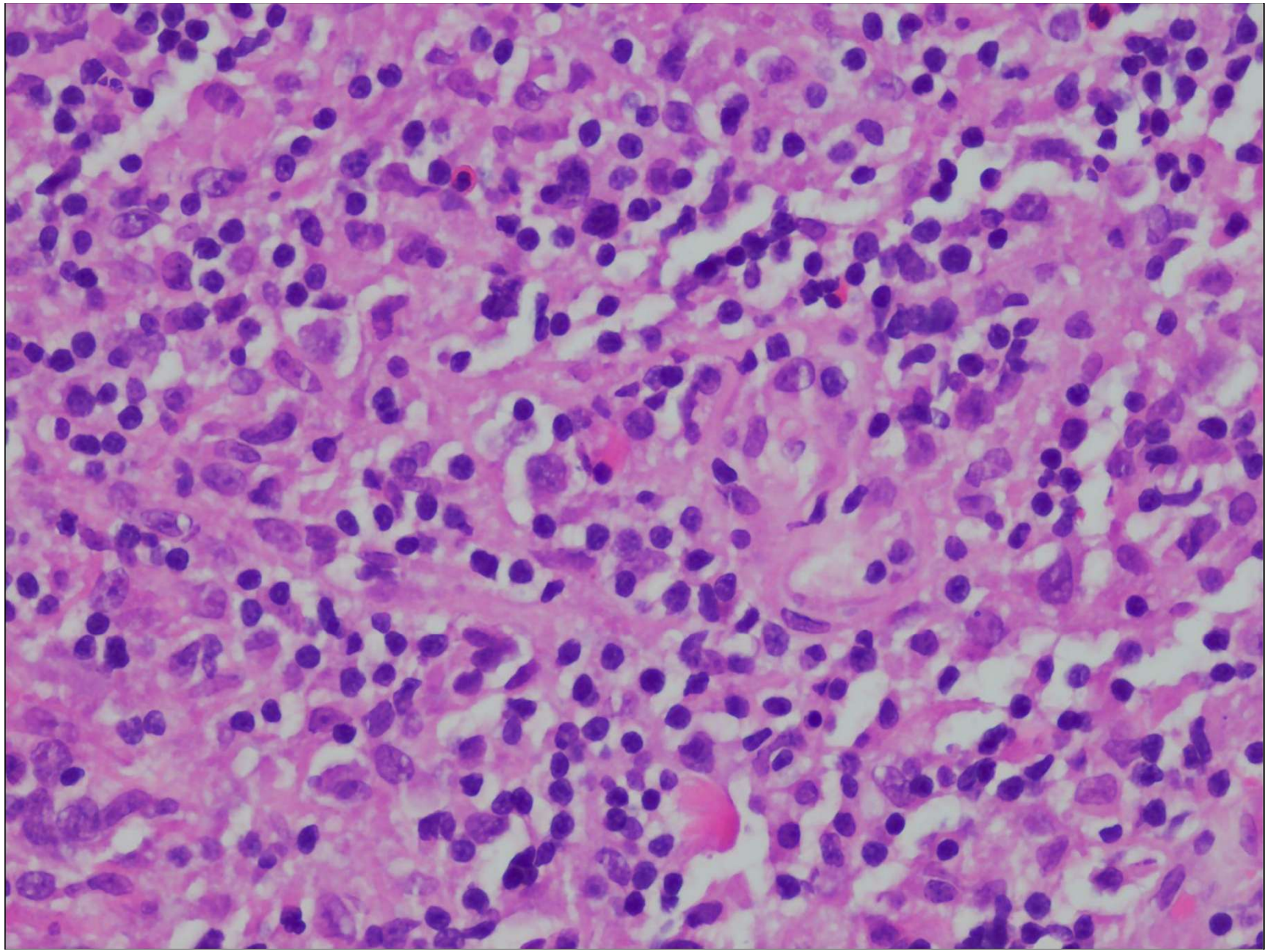
Clinical findings

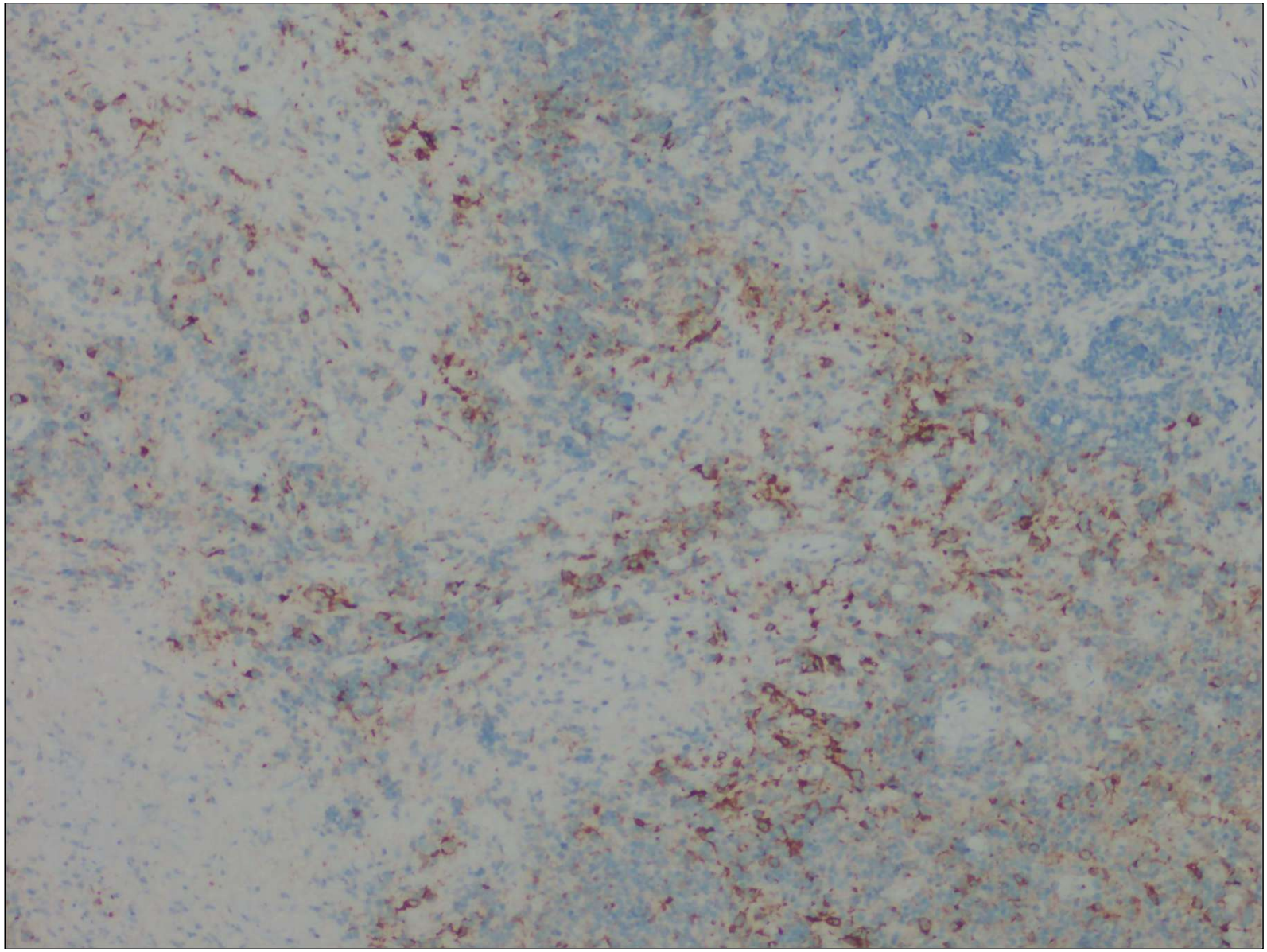
Right supraclavicular lymph node,

8 x 4 cm

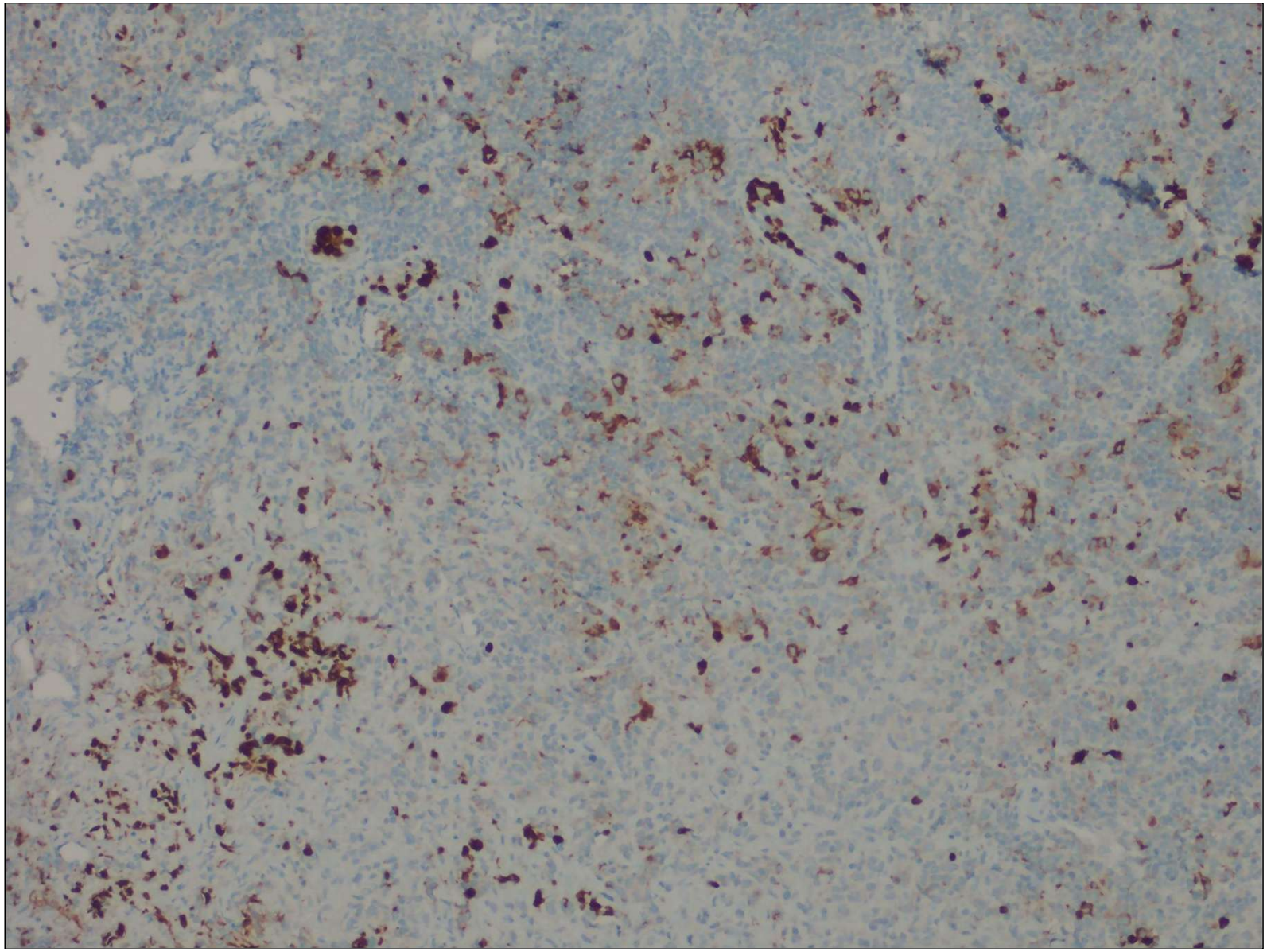








CD30



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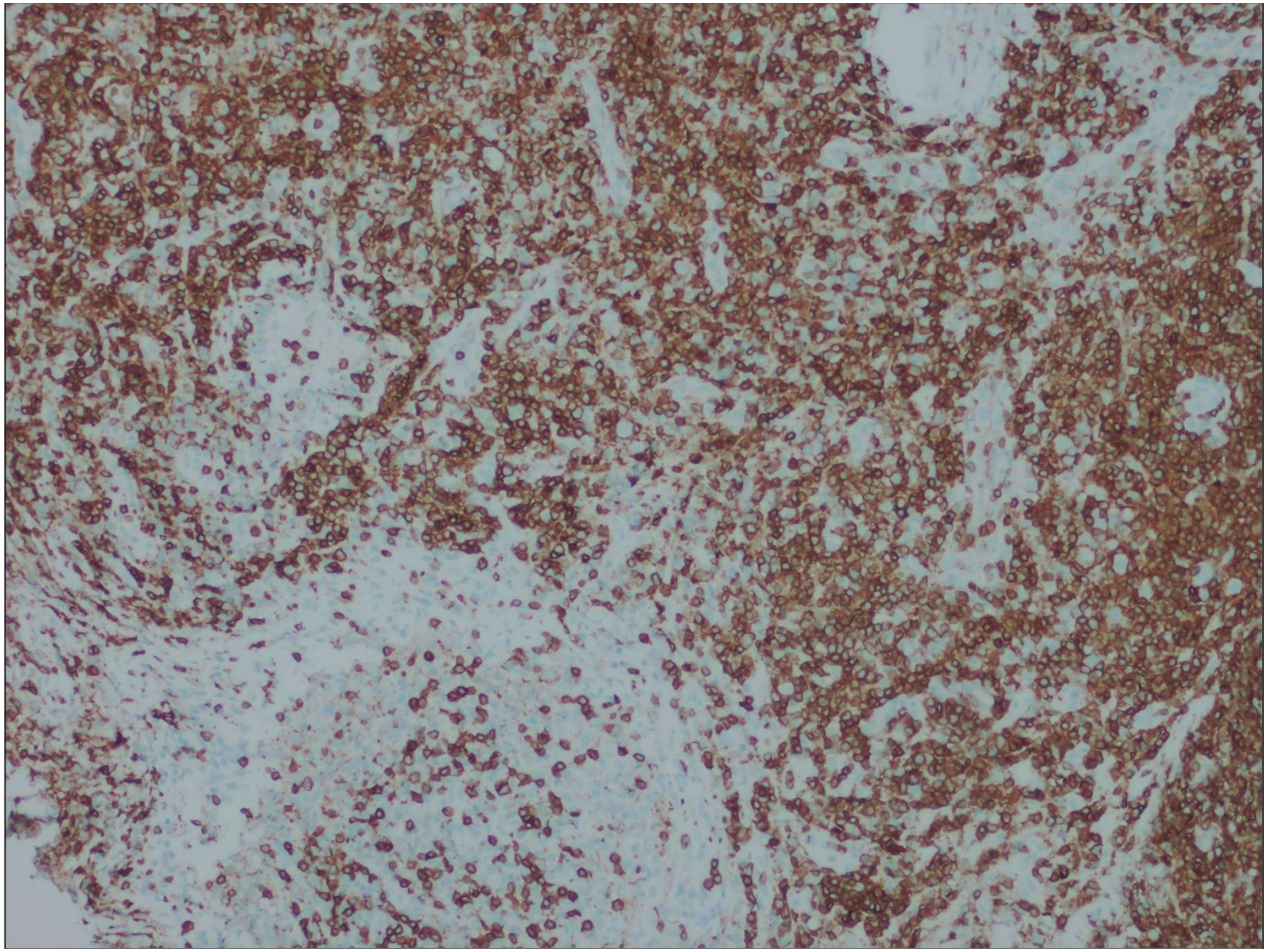
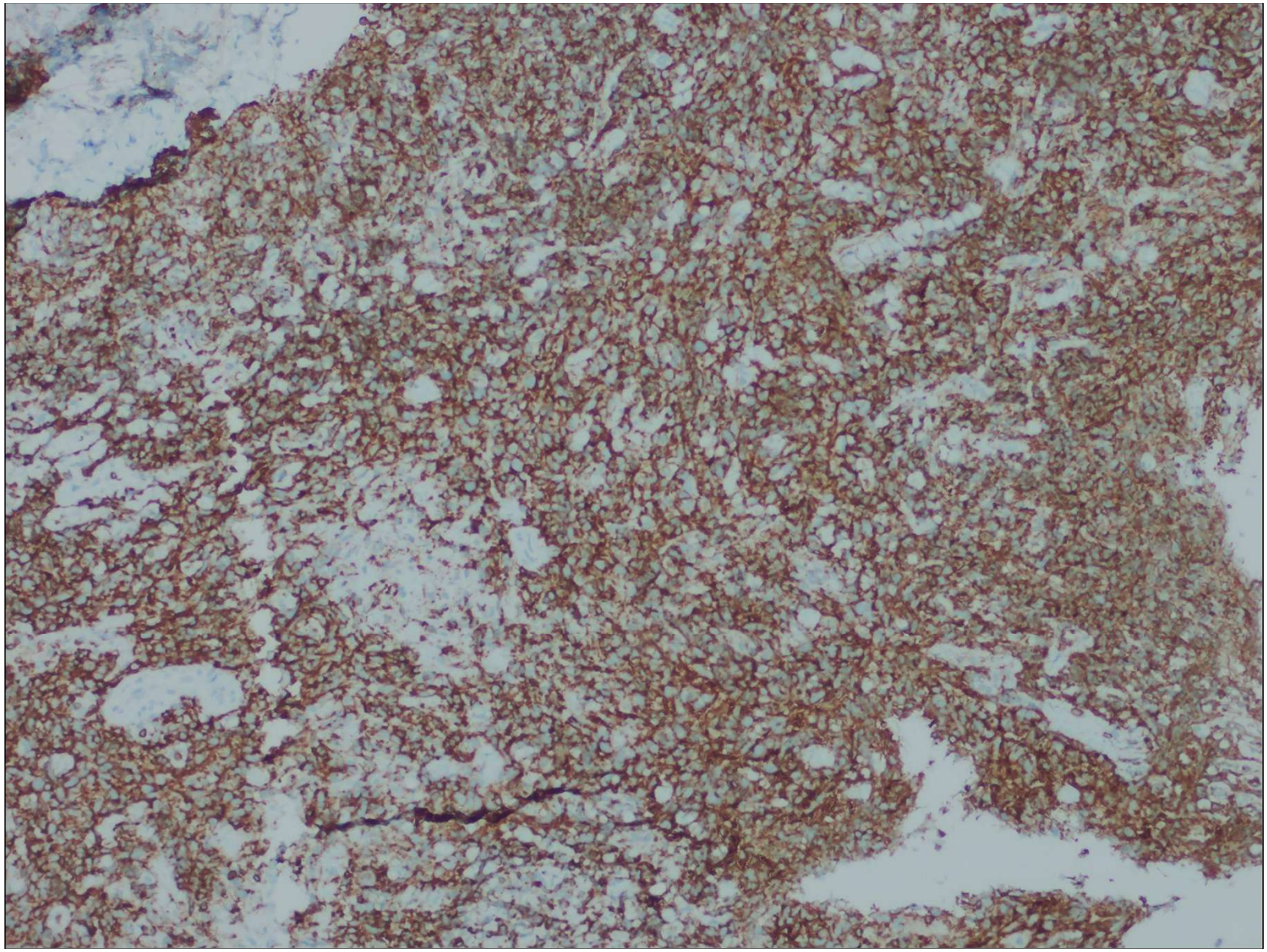


CD3



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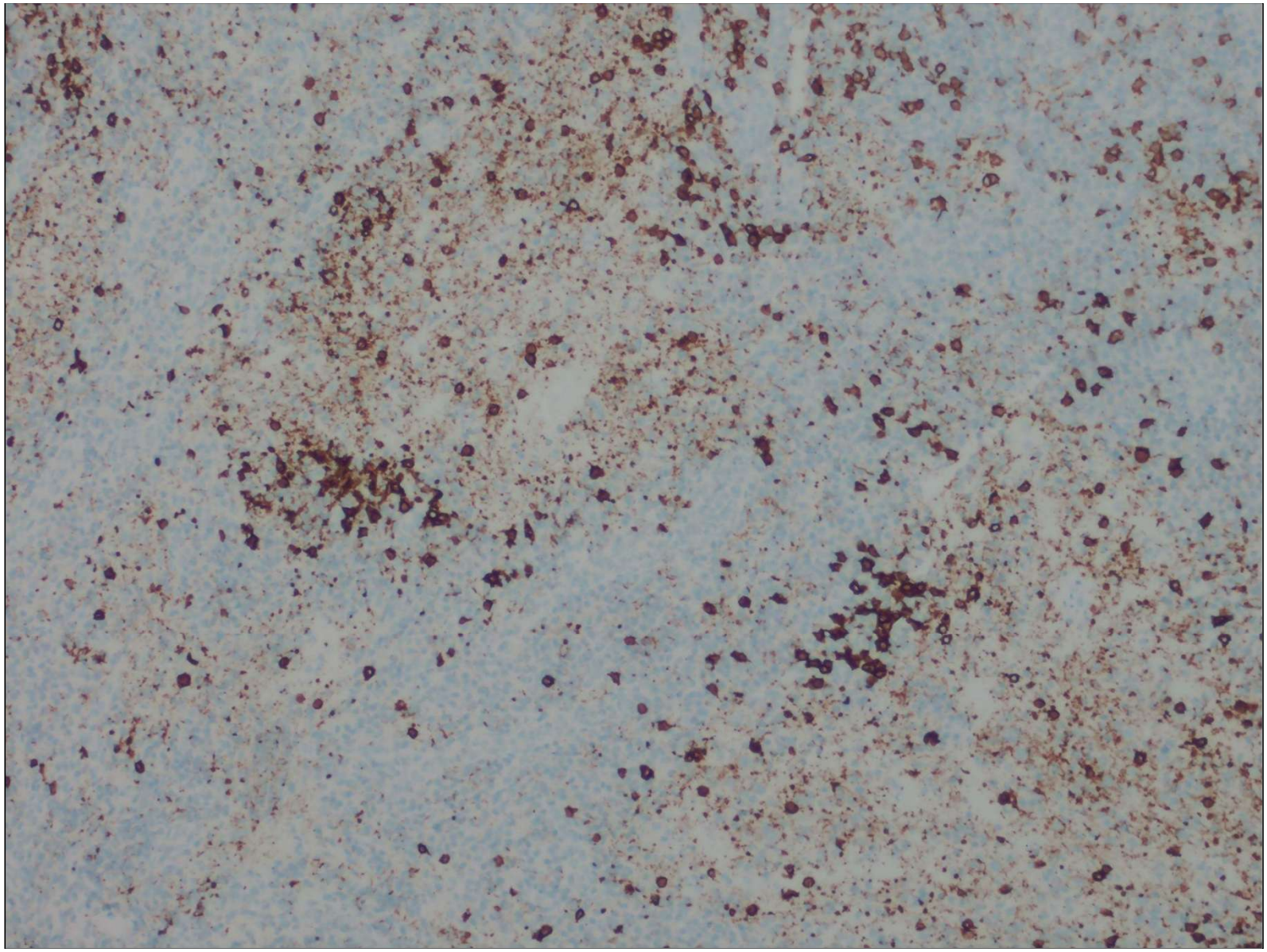

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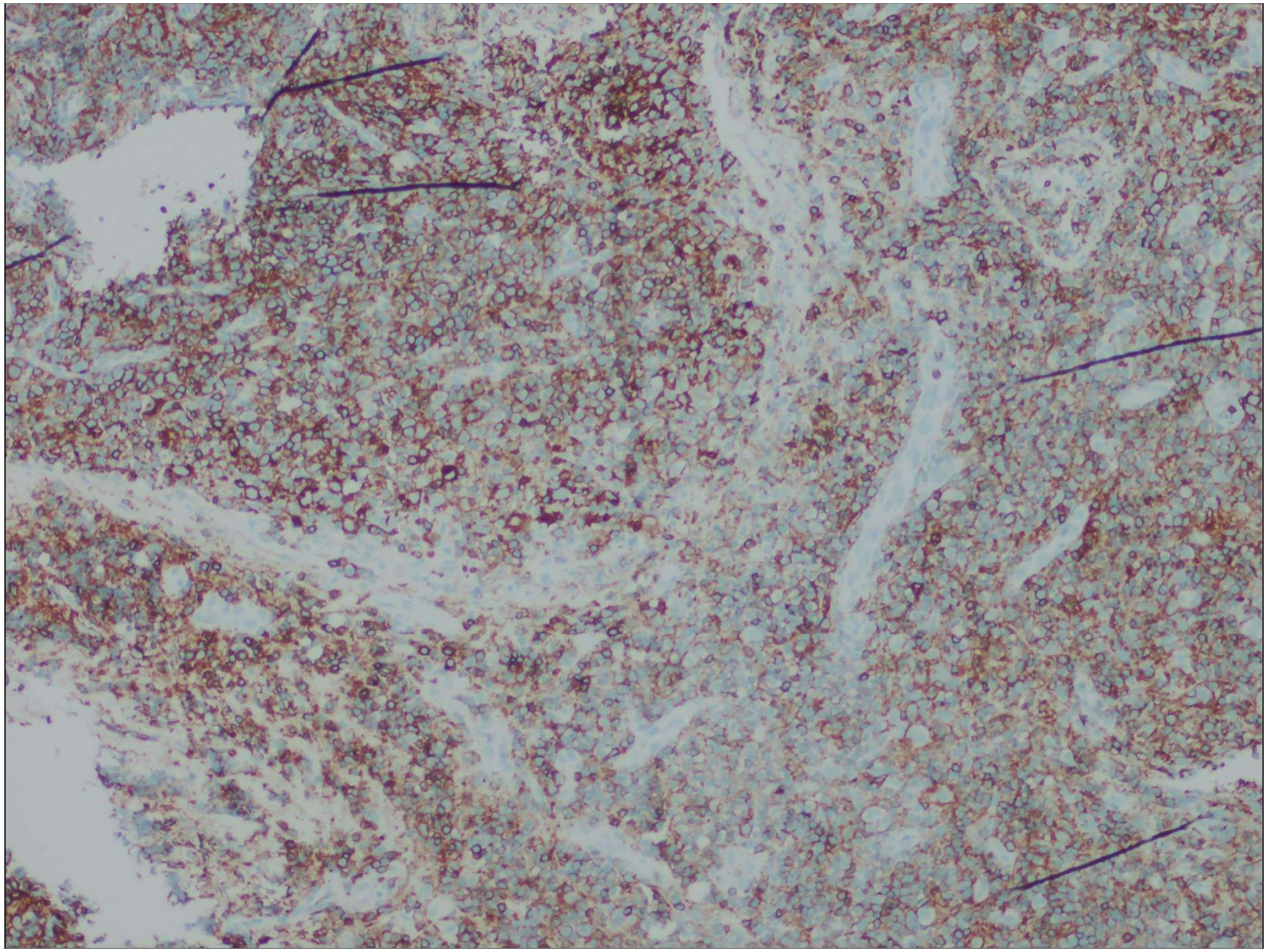


LCA

Further Information

CECT TAP

Primary Finding

Mediastinal Mass

An isodense mass insinuating in between the major vascular structures.

Mass Dimensions

7.2 × 15.5 × 11.1cm

Secondary Findings

Lymphadenopathy

Right Supraclavicular

Right Lower Cervical

Further IHC

T-Cell Markers

CD2+ / CD4+
CD7- / CD8-

B-Cell Markers

CD79a-
PAX5 (Inconclusive)

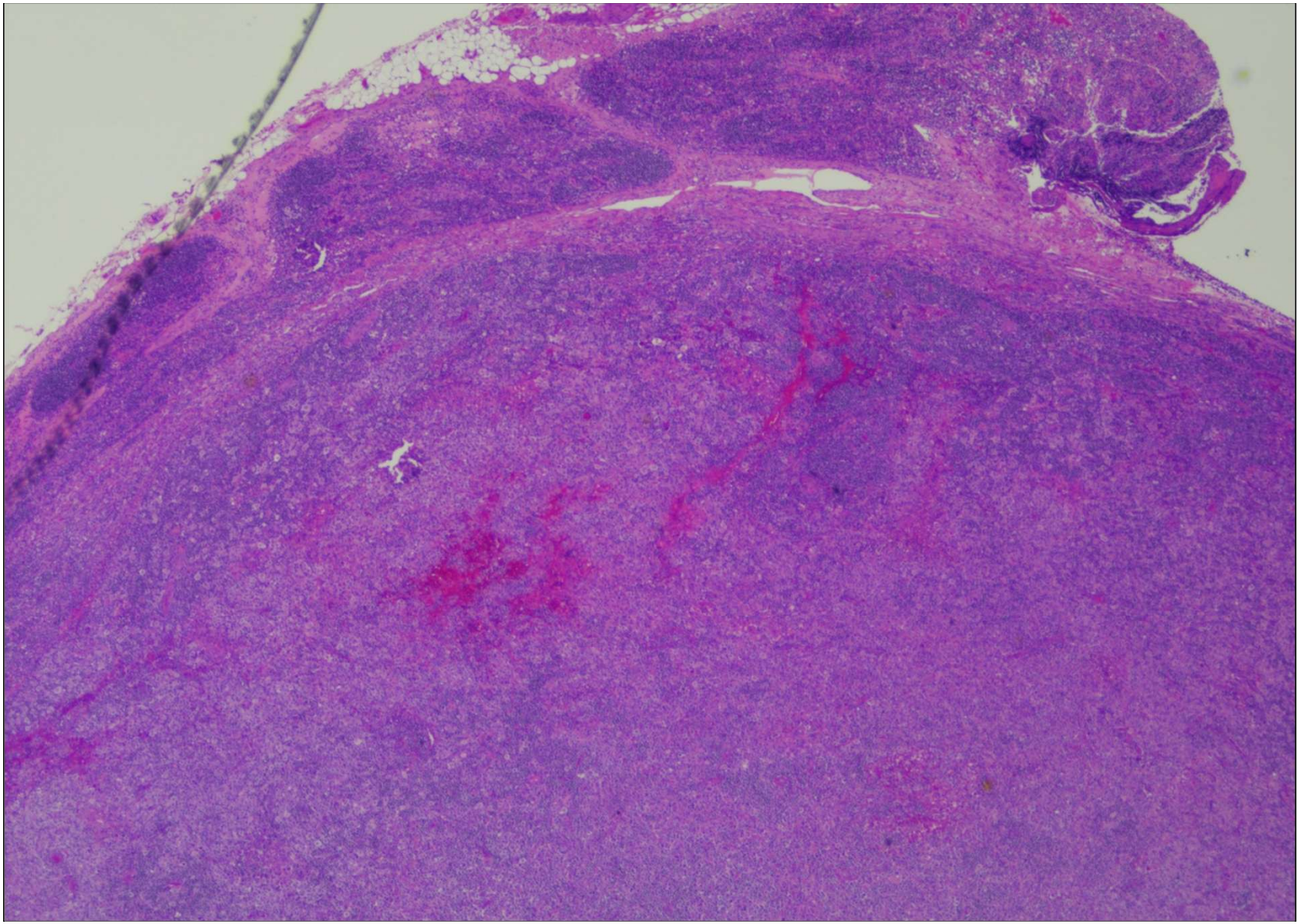
CD21 Expression

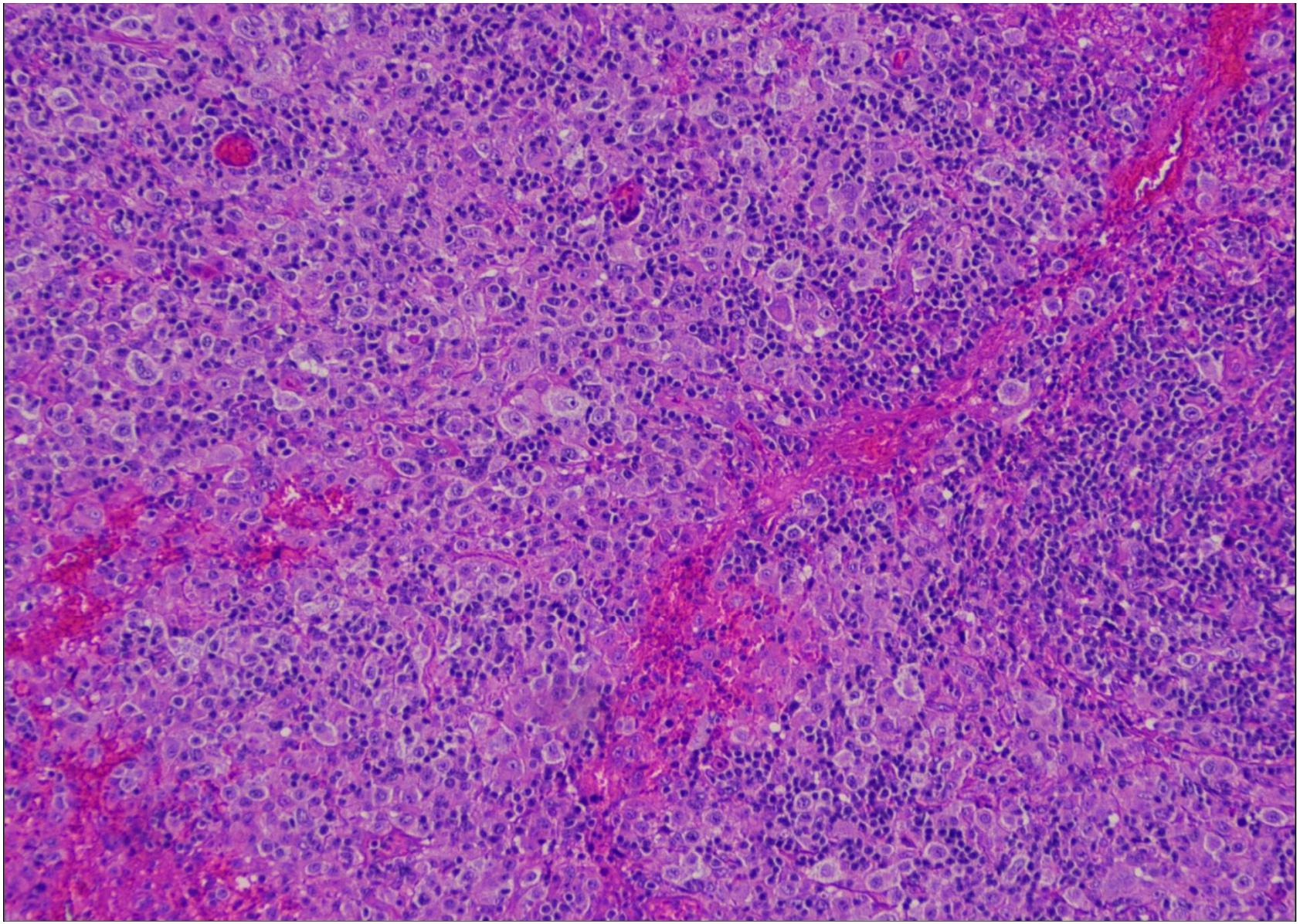
CD21 highlights a few disrupted FDC meshworks that are overrun by the neoplastic cells.

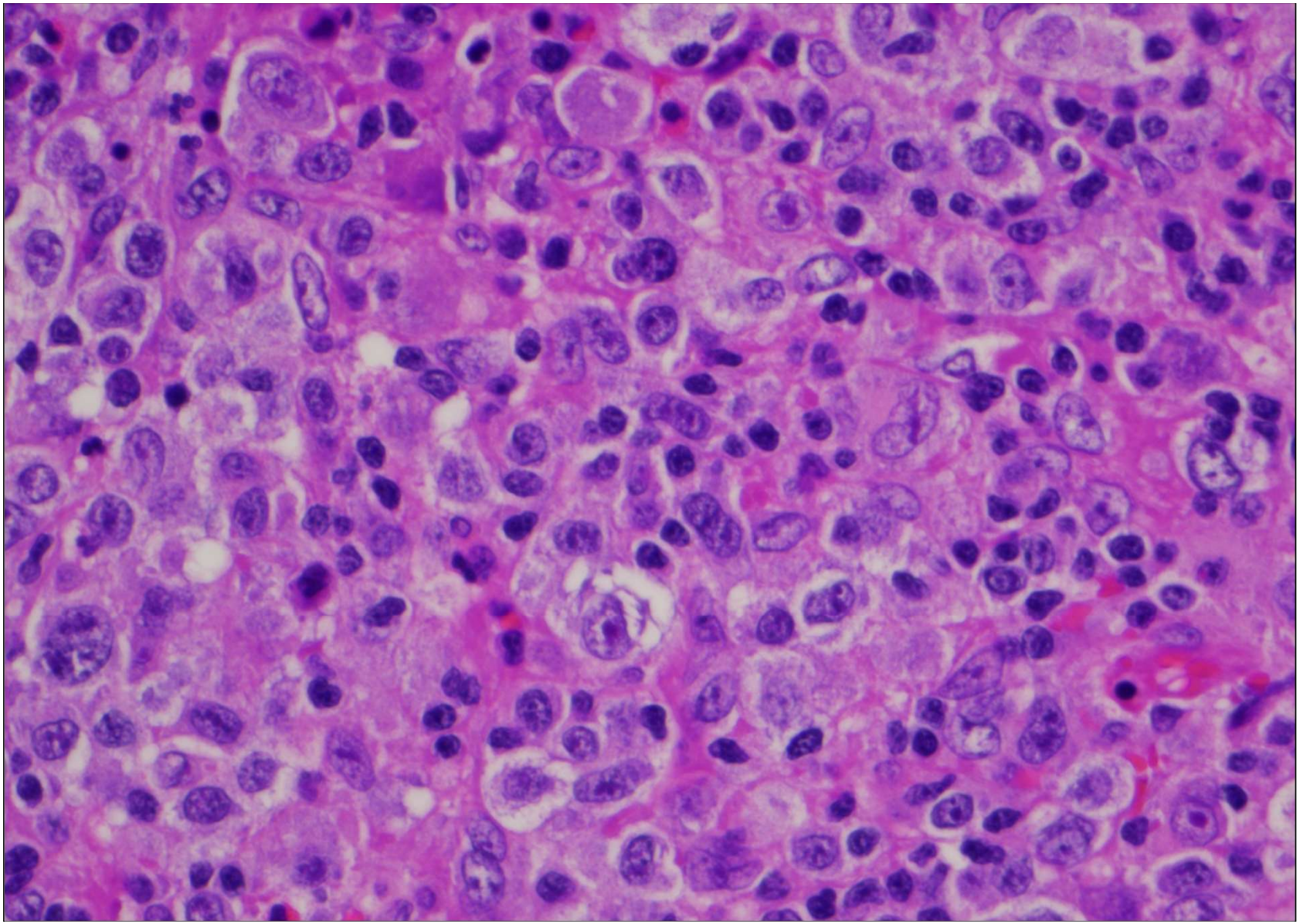
Diagnostic Report

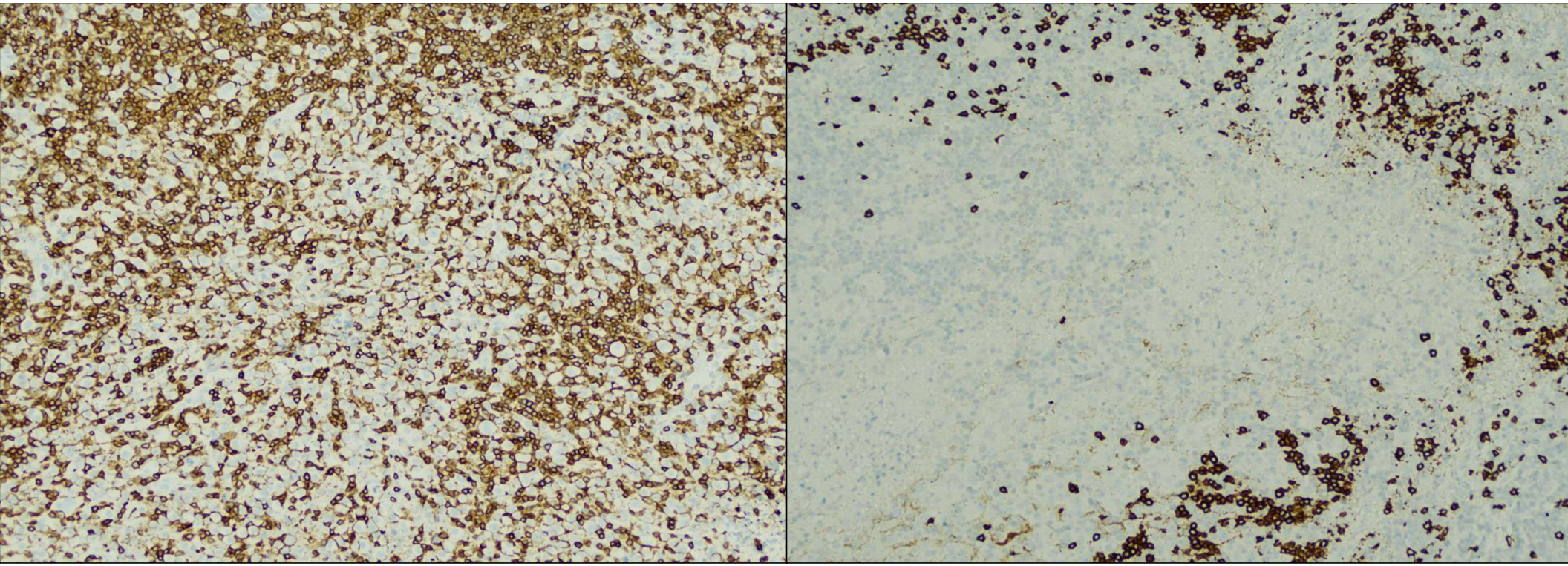
Interpretation

Fragmented lymph node tissue, suspicious for a lymphoproliferative disorder. A repeat biopsy, is recommended.



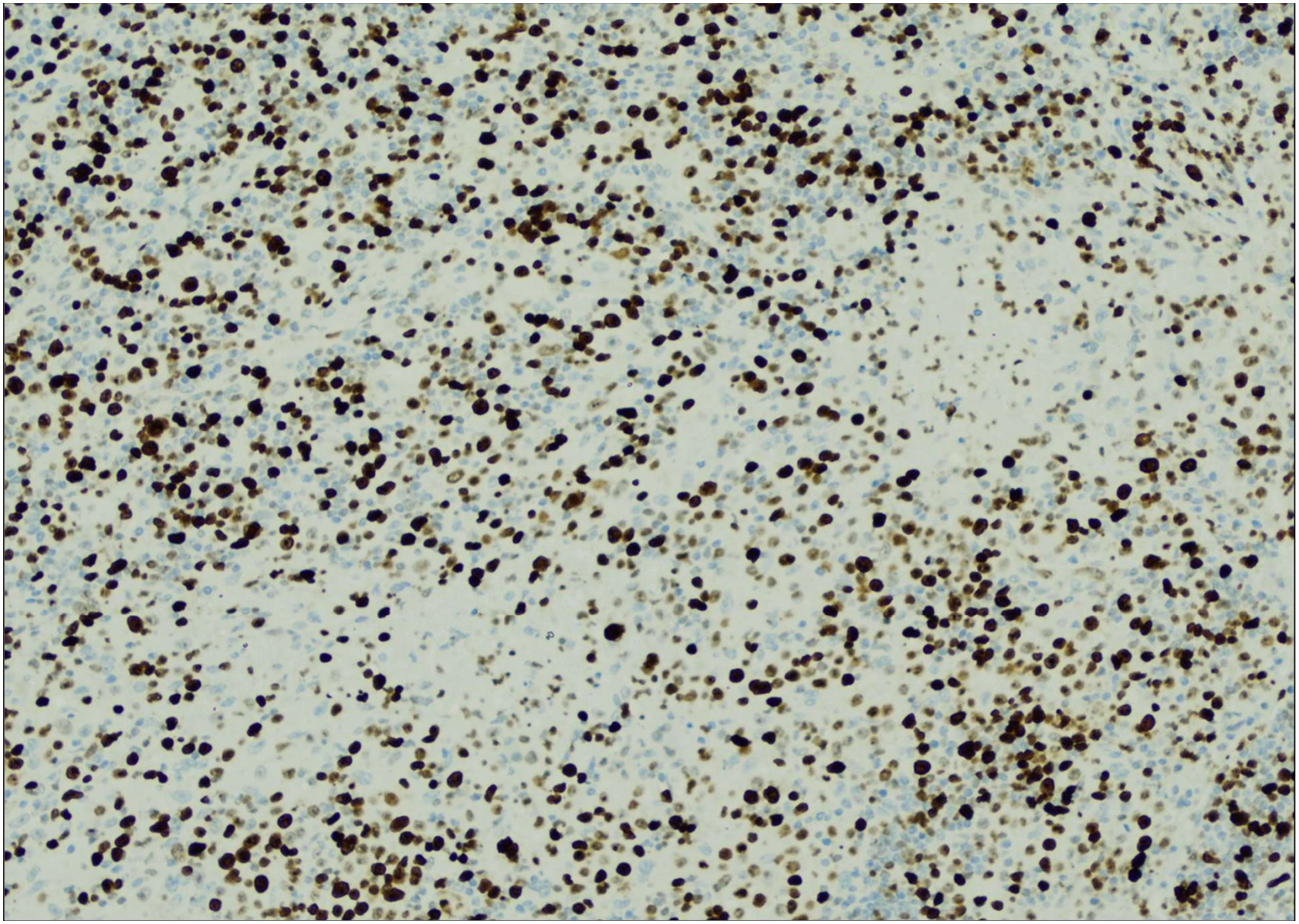




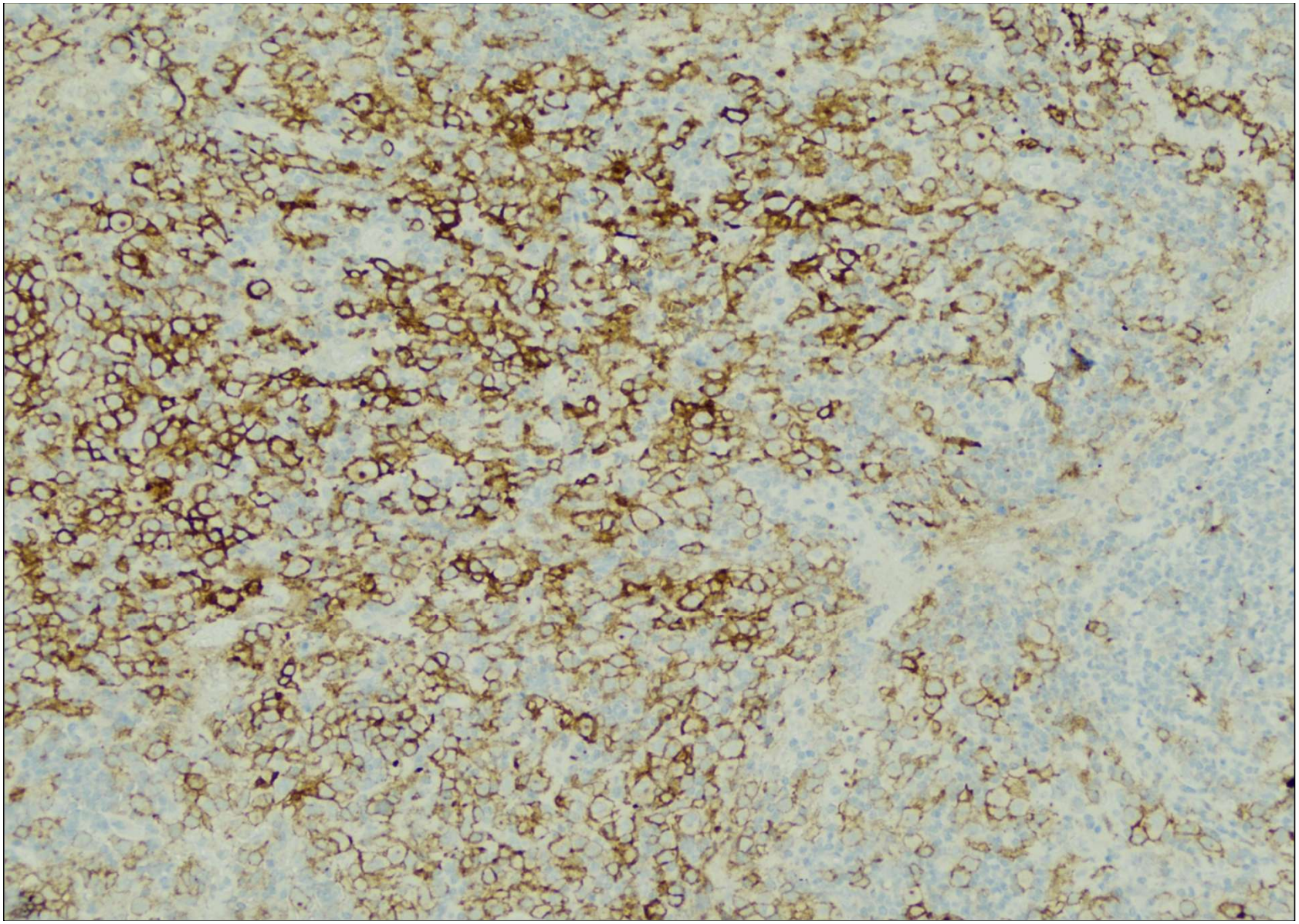


CD3

CD20



Ki67



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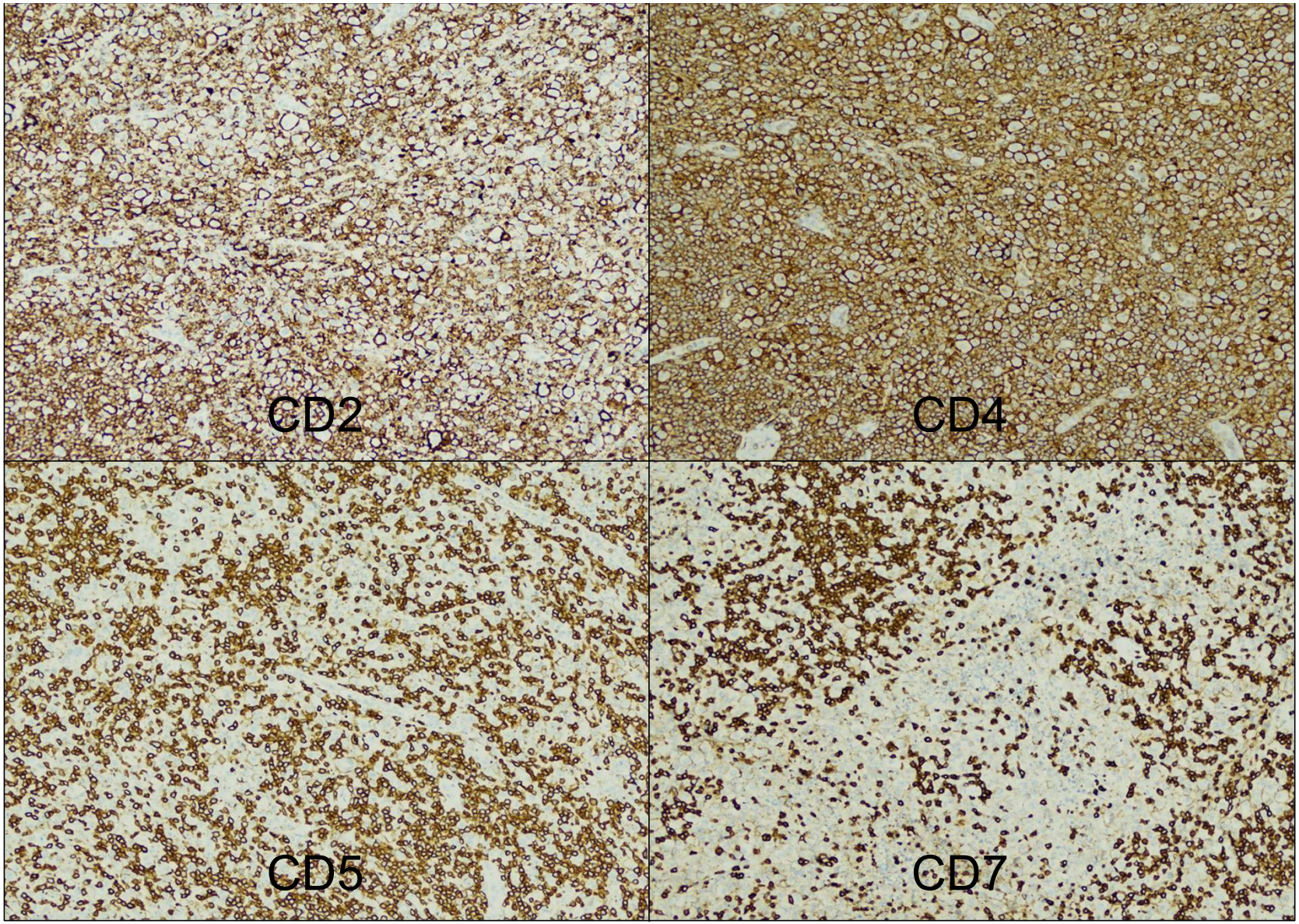
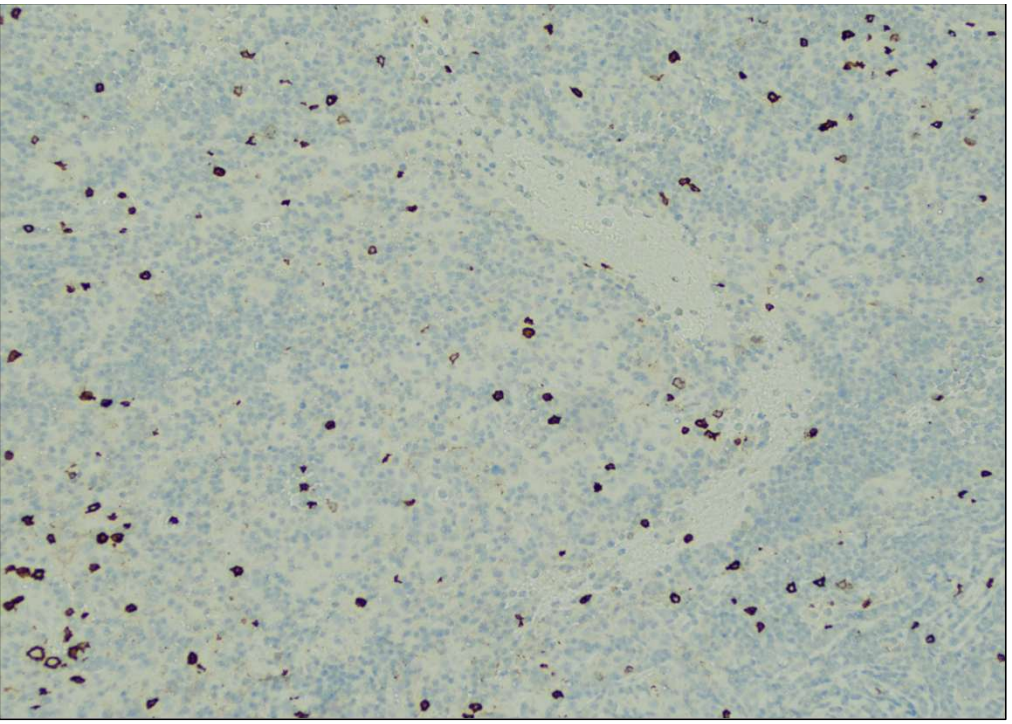

CD2
CD4
CD5
CD7



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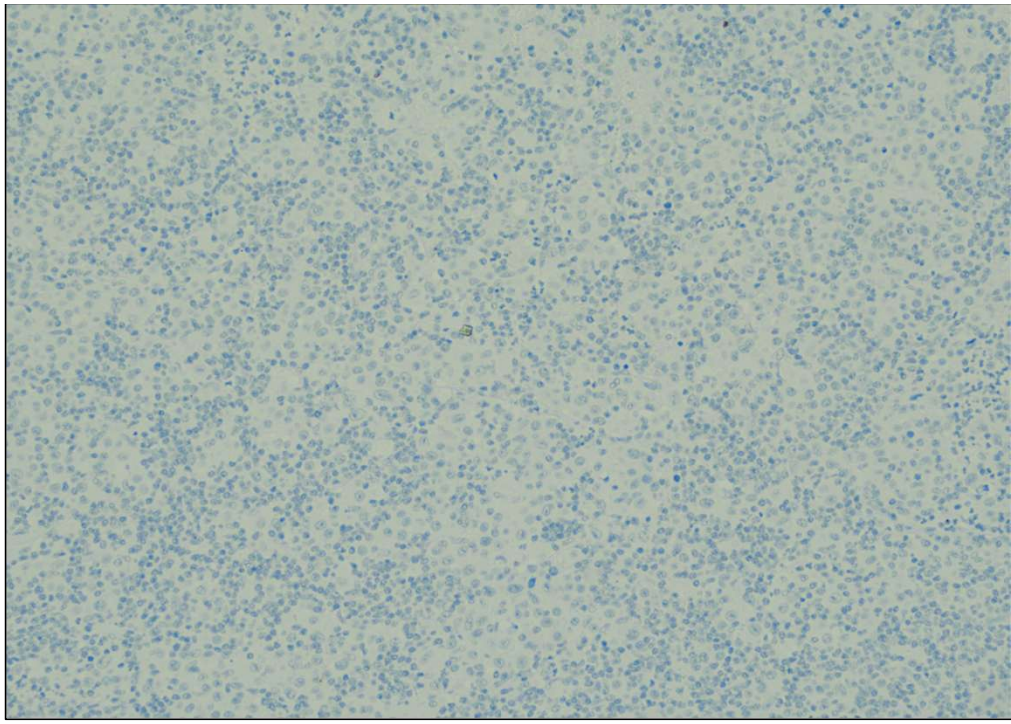
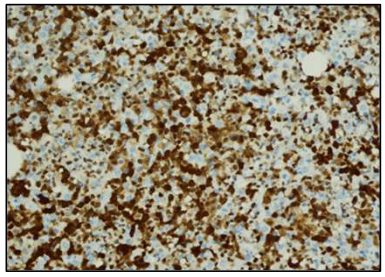


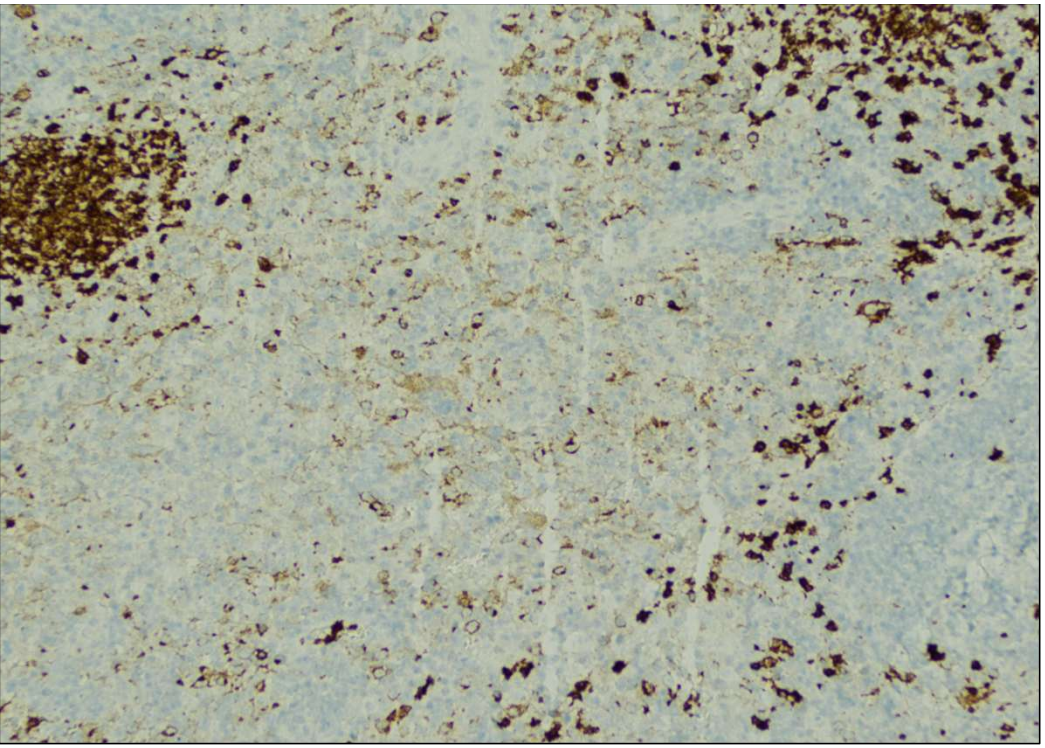
ALK



ALK positive control

Further History

The patient was travelling back and forth from her hometown.



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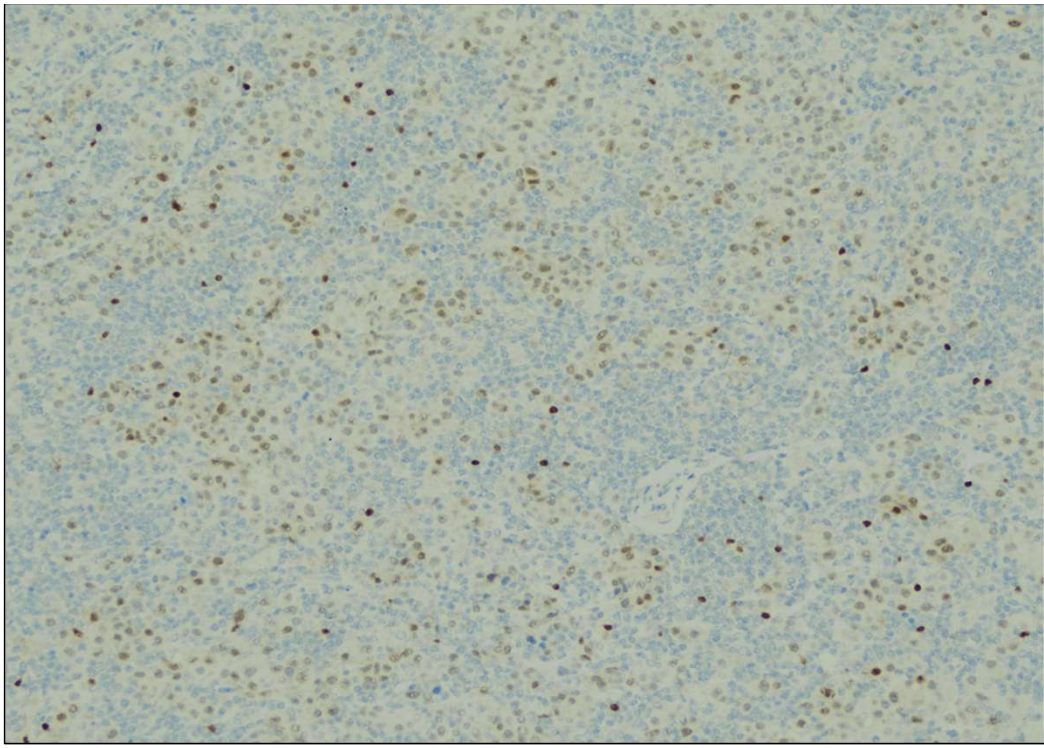


PAX5

Diagnostic Report

Interpretation

Classic Hodgkin Lymphoma

with aberrant expression of T-cell antigens

Classical Hodgkin Lymphoma with Aberrant T-cell Antigen Expression

Rare Phenomenon

Recognised occurrence in 2–5% of cases

Reported in approximately **2–5%** of all Classical Hodgkin Lymphoma (CHL) cases.

Expressed T-cell markers

CD2 CD3 CD4 CD5 CD7 CD8 (rare)

Lineage Check

Does NOT indicate T-cell lineage

Reflects aberrant antigen expression by HRS cells rather than actual T-cell lineage.

Does not alter the diagnosis when morphology and remaining immunophenotype are typical.

Pitfall Avoidance

Avoid Diagnostic Pitfalls

Never let a single aberrant marker outweigh the overall pattern.

Always integrate:

- Morphology & Inflammatory background
- PAX5 intensity & Immunophenotype
- Clinical findings

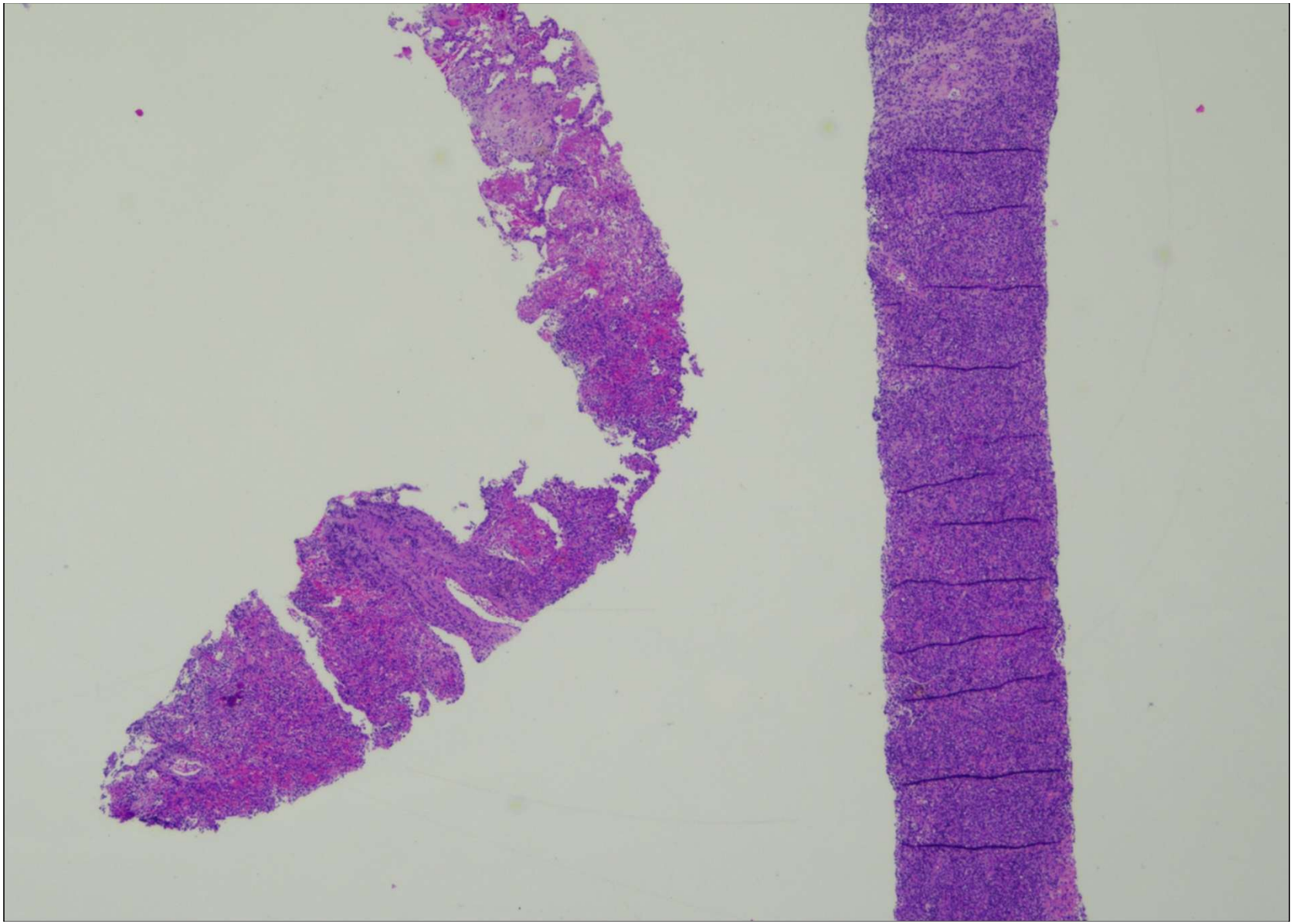
Morphology remains the cornerstone of diagnosing classical Hodgkin lymphoma.

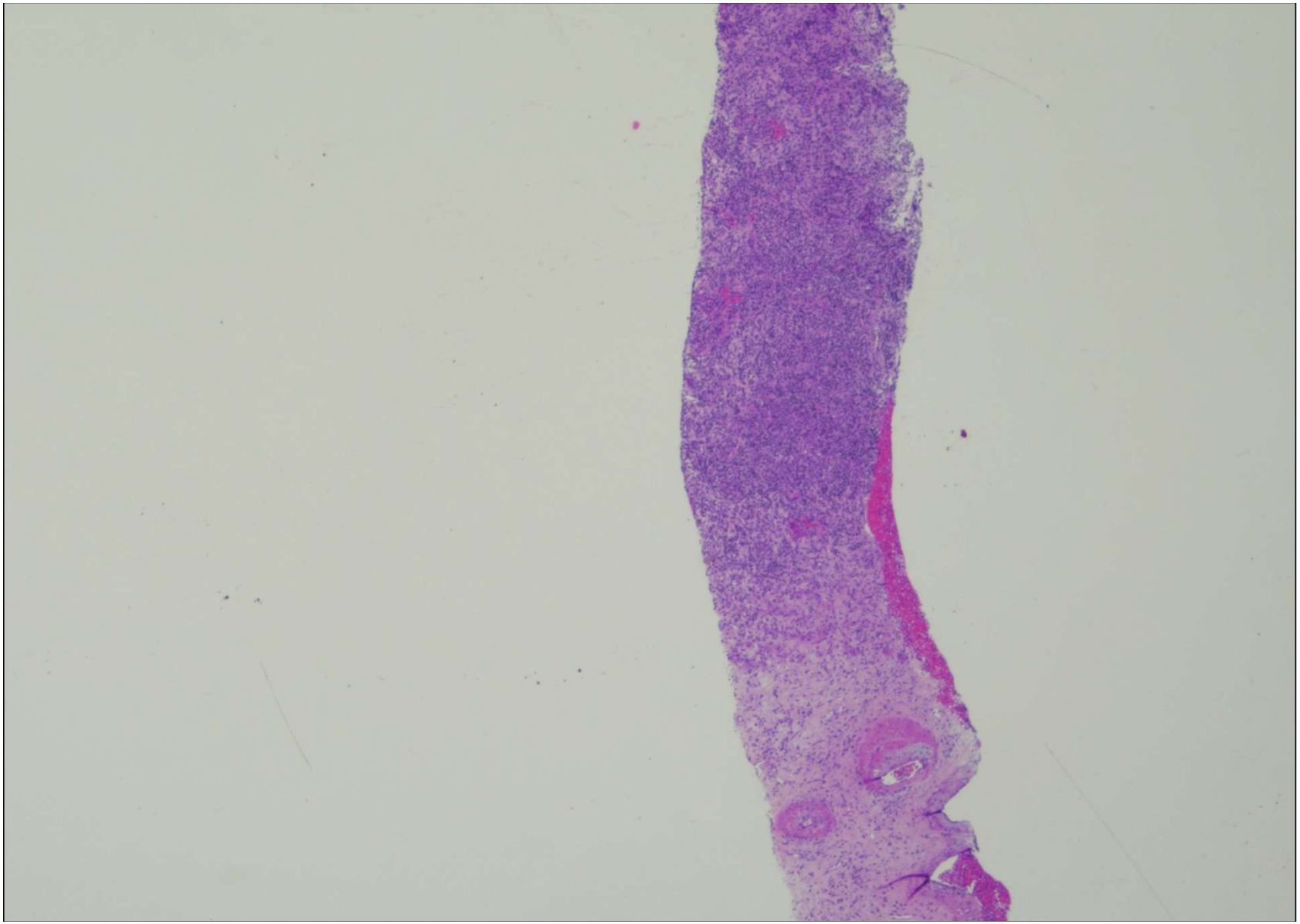
Tzankov A, Bourgau C, Kaiser A, et al. Rare expression of T-cell markers in classical Hodgkin's lymphoma. *Modern Pathology*. 2005;18:1542–1549.
Asano N, et al. Aberrant T-cell antigen expression in classical Hodgkin lymphoma is associated with decreased event-free survival and overall survival. *Blood*. 2013;121:1795–1804.
WHO Classification of Tumours Editorial Board. *WHO Classification of Tumours: Haematolymphoid Tumours*. 5th ed. IARC; 2022.

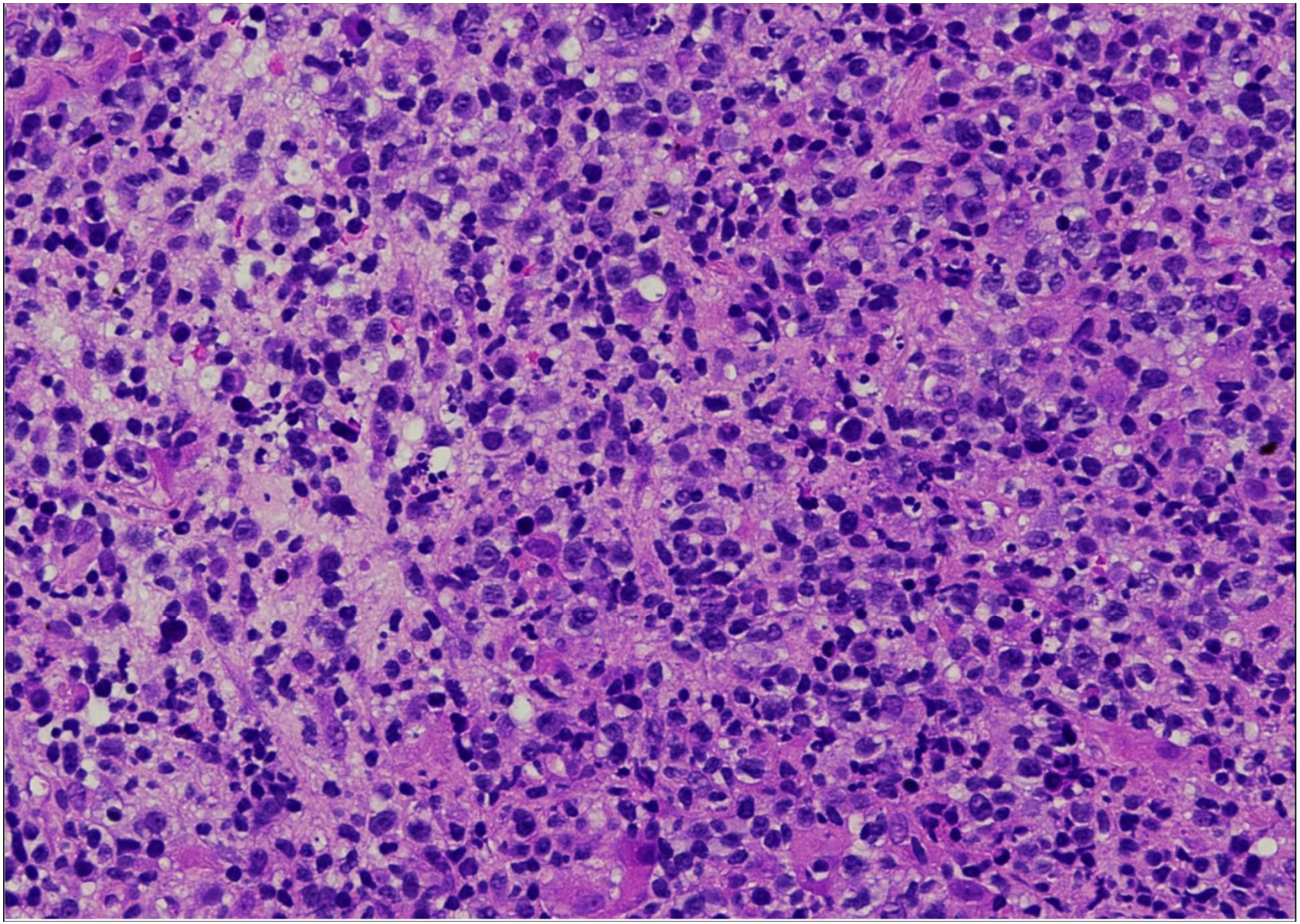
Case 5

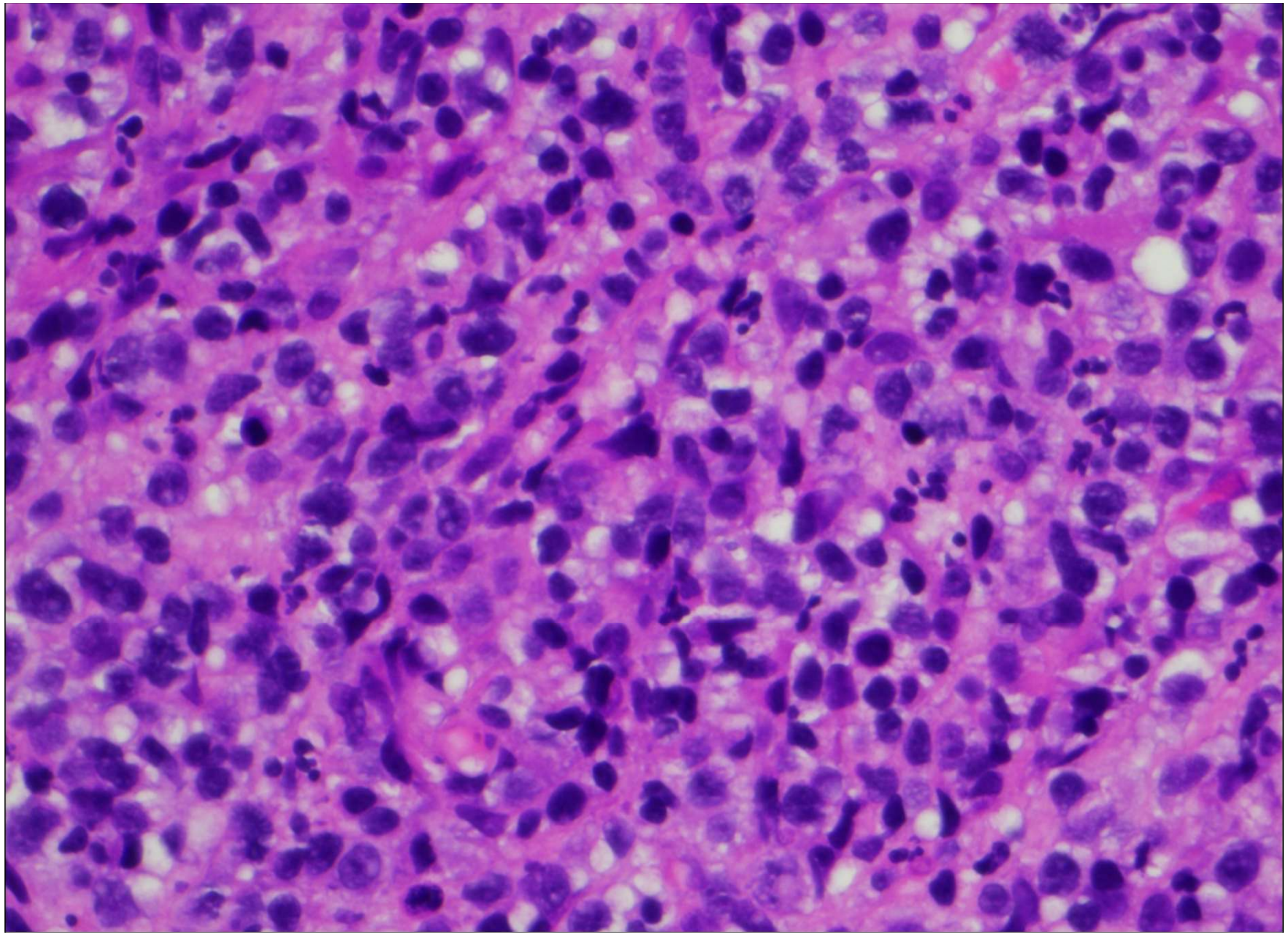
62 years old

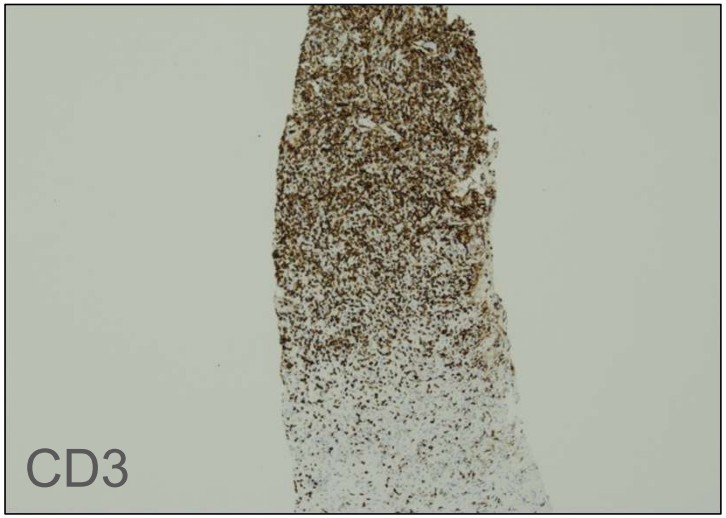
Male, multiple lung masses and nodules.







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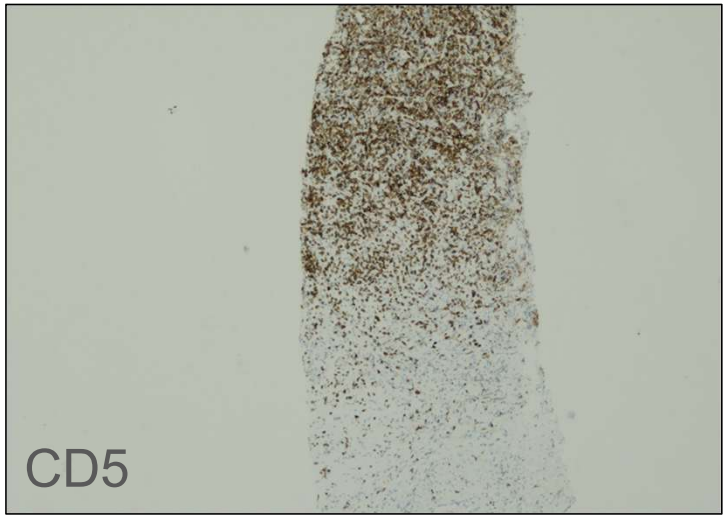
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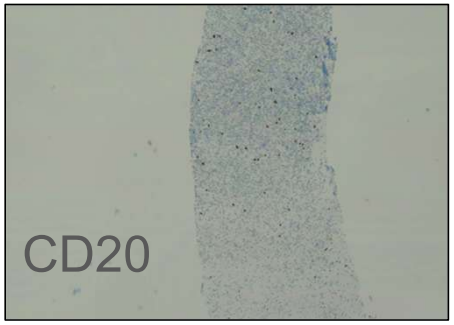
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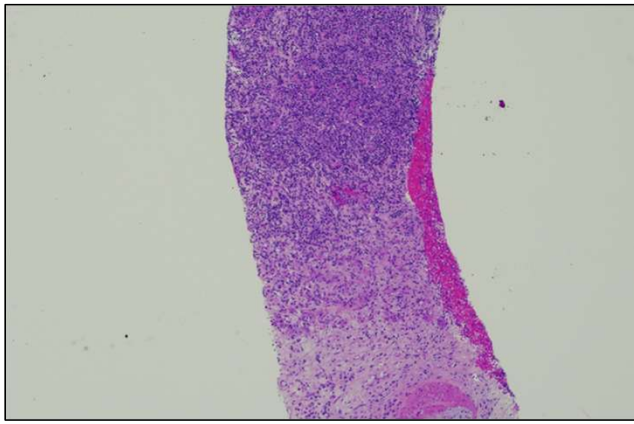

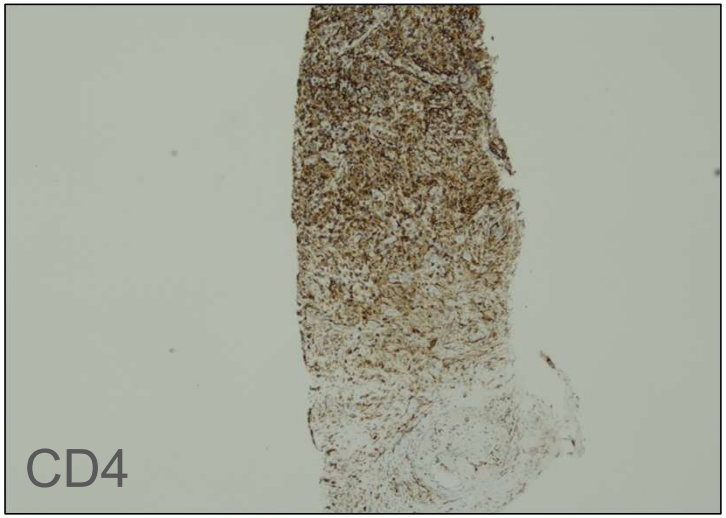
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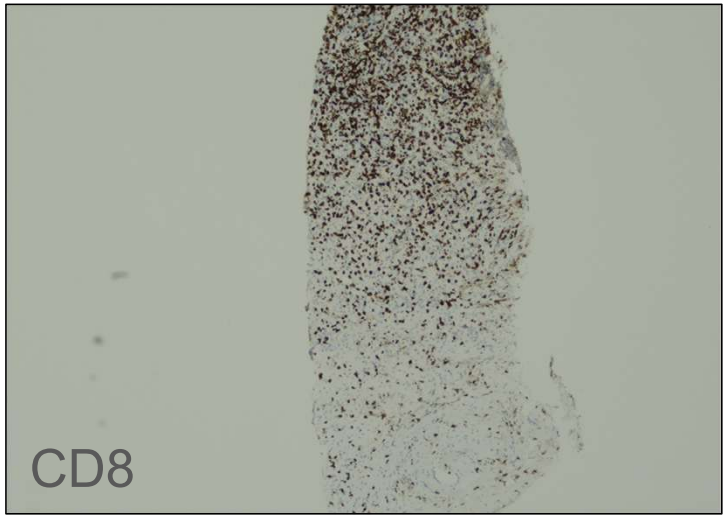
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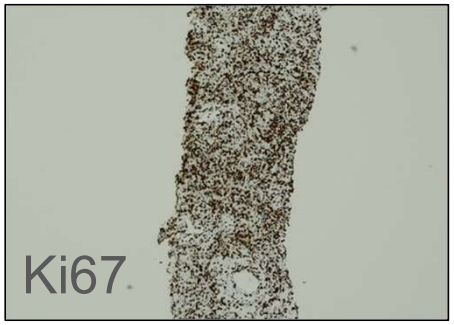
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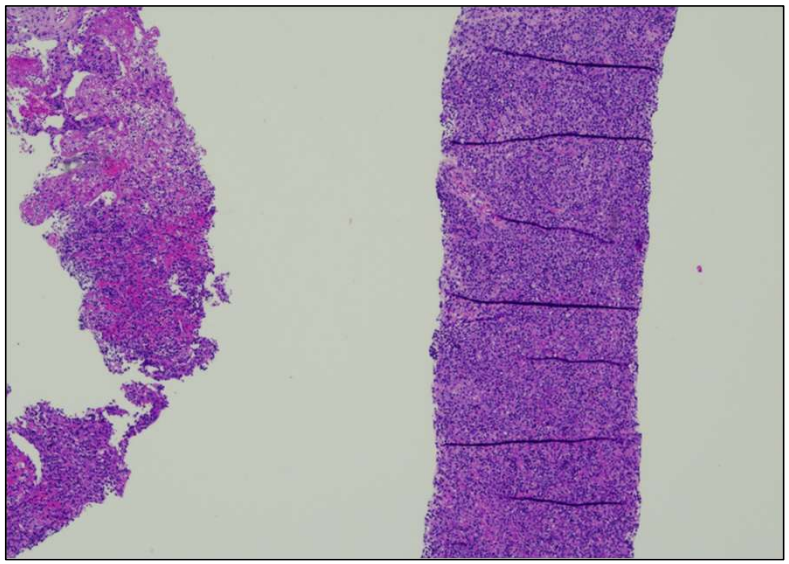

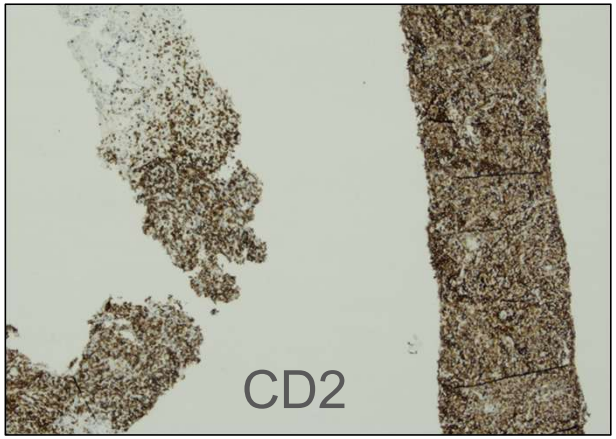
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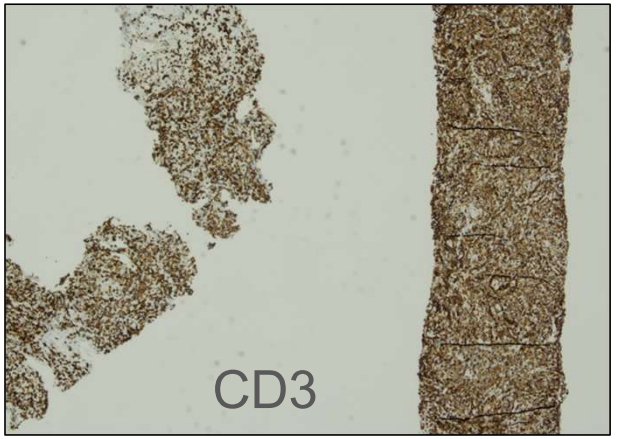
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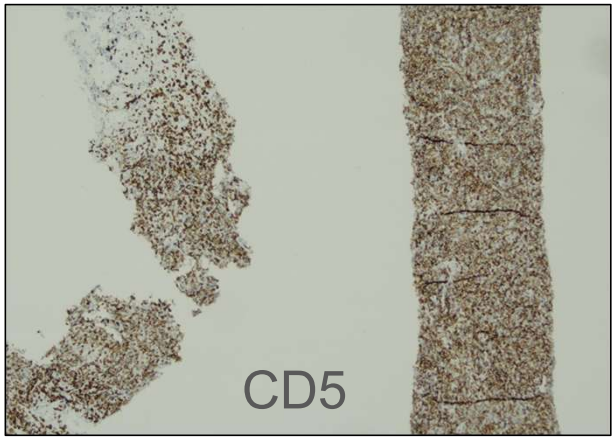
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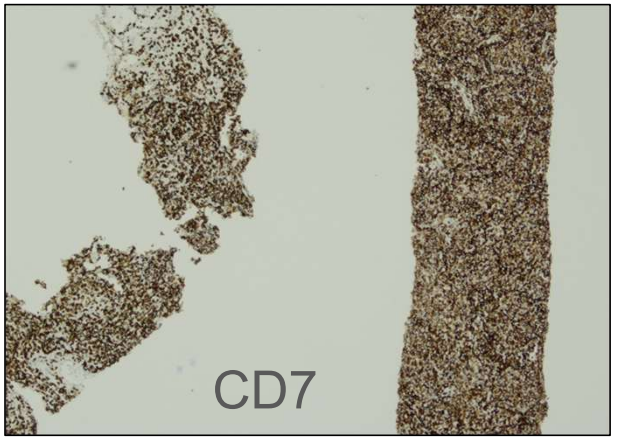
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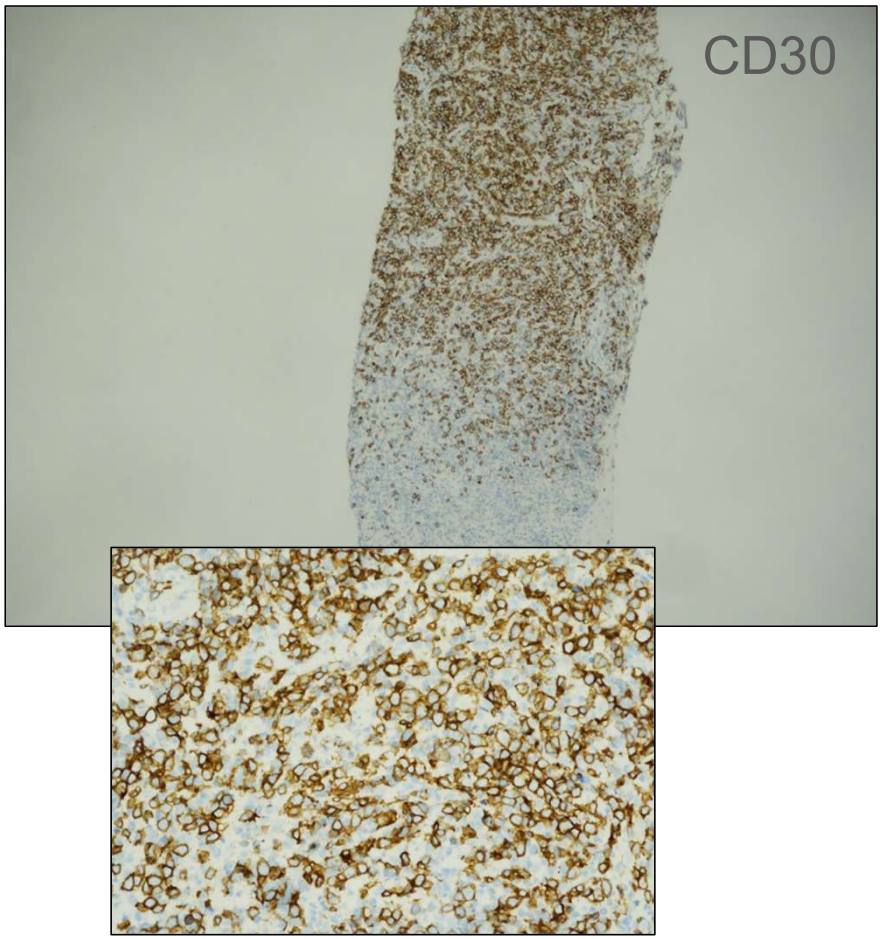
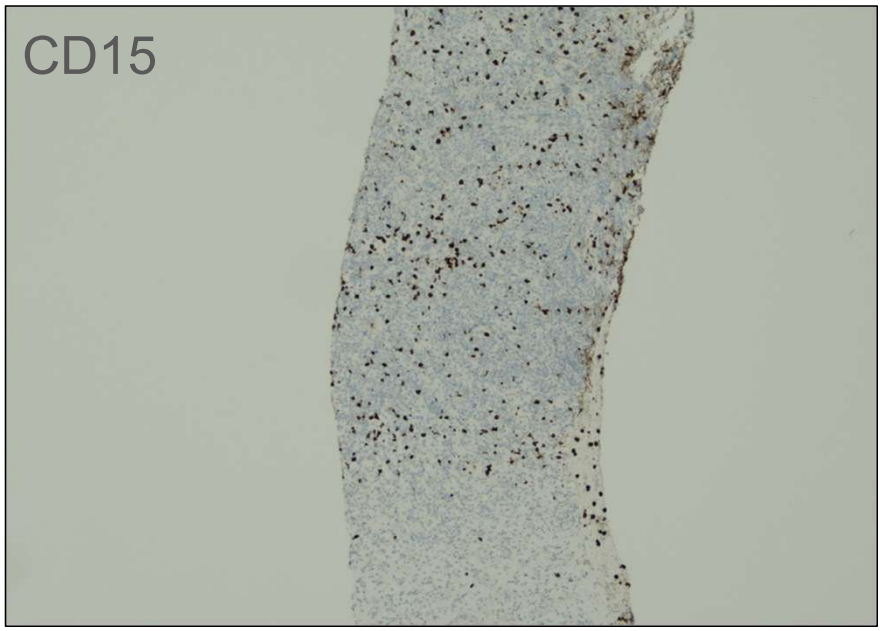
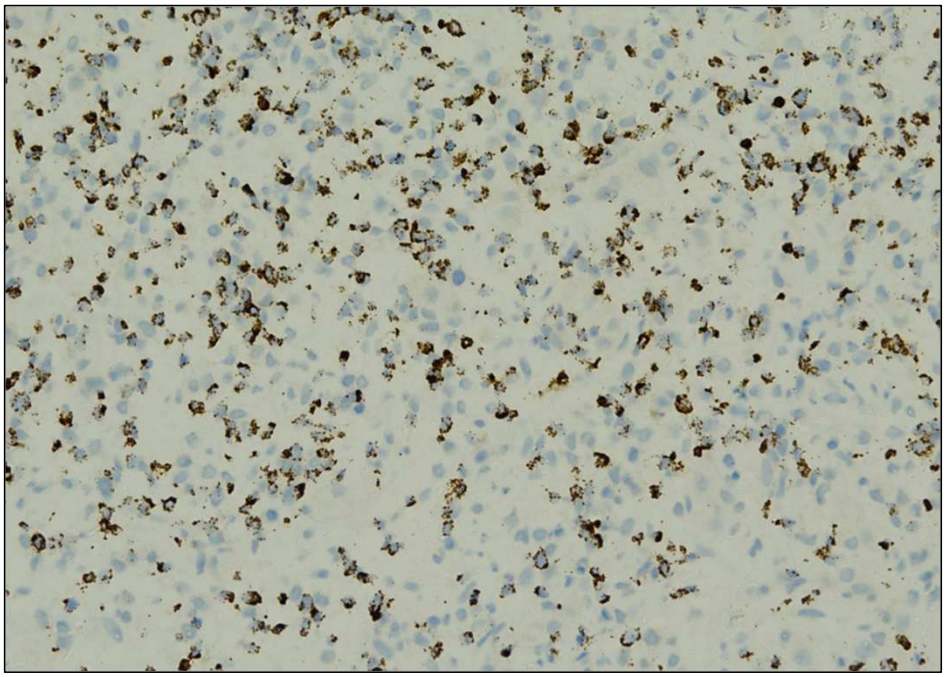
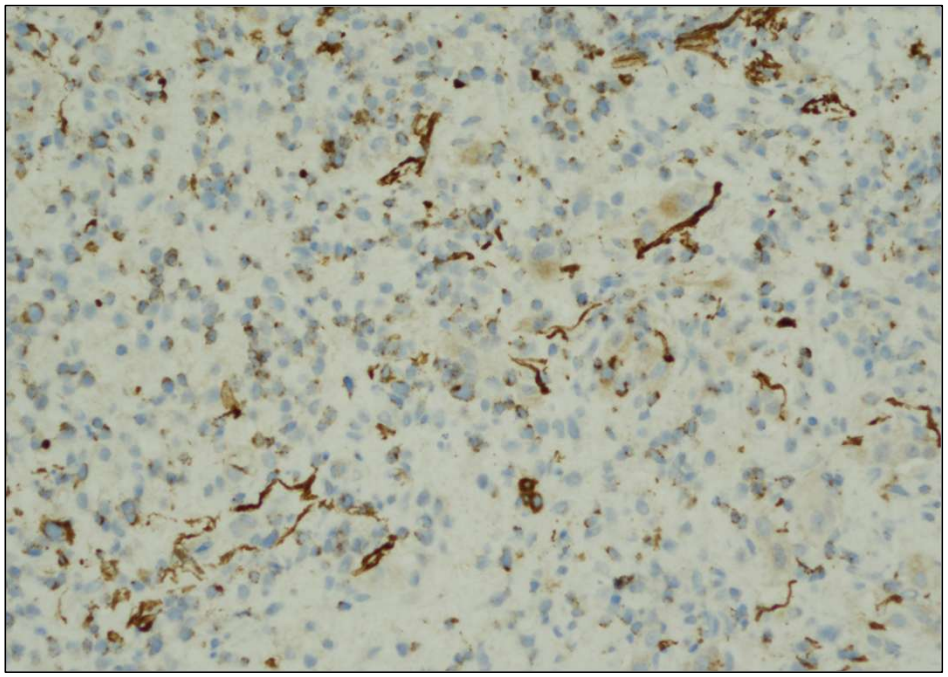




ALK -
CD56 -



TIA1



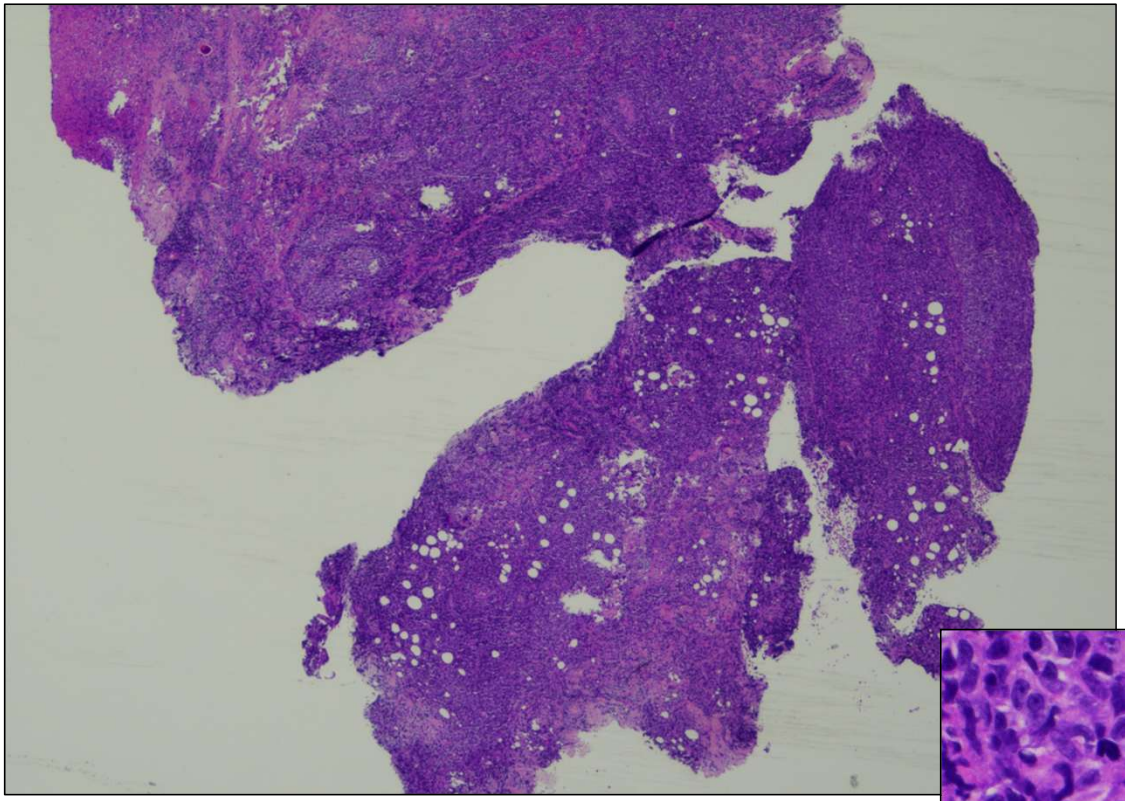
Granzyme B

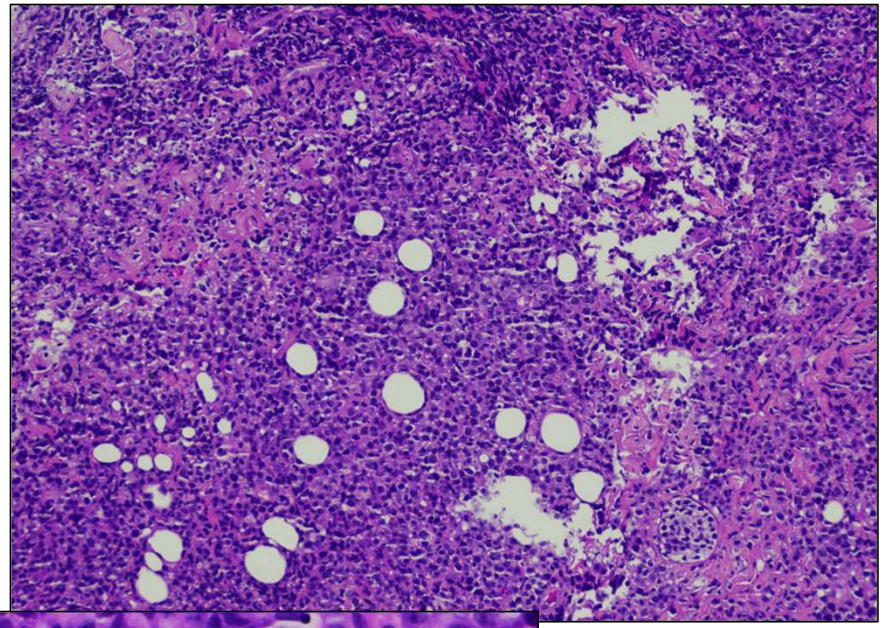
FINAL DIAGNOSIS?

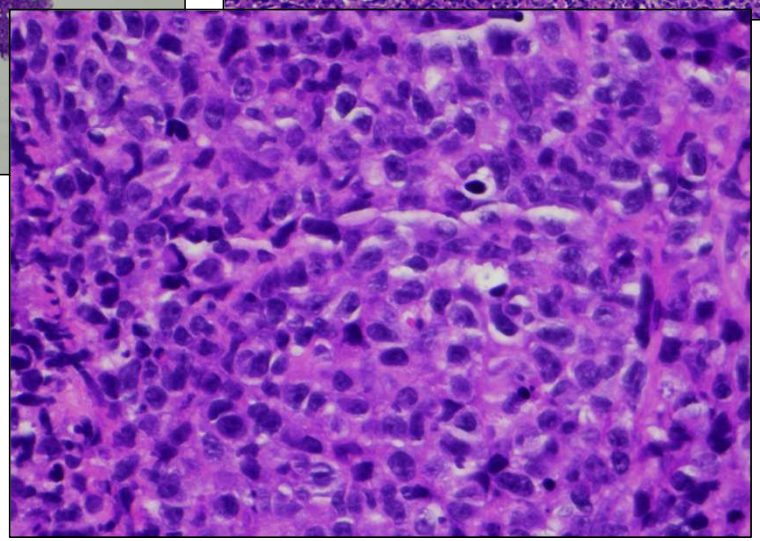
Should we add more IHC?

Further History

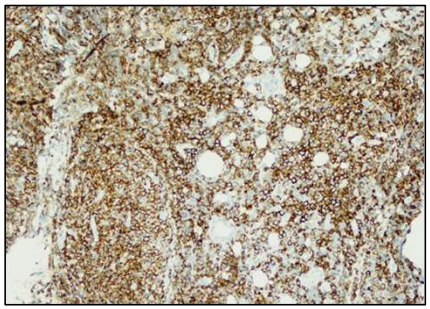
The patient has a cheek swelling with hard palate mass.

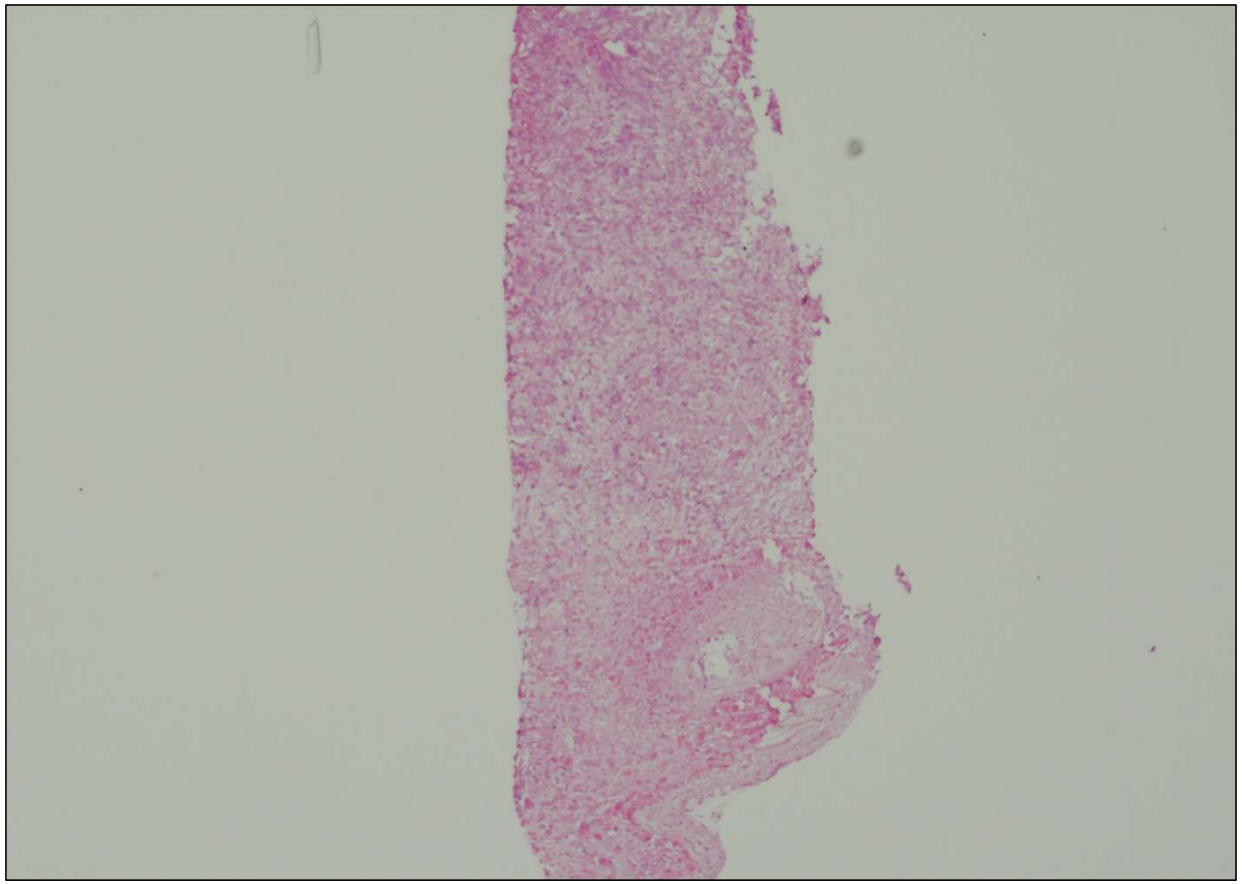




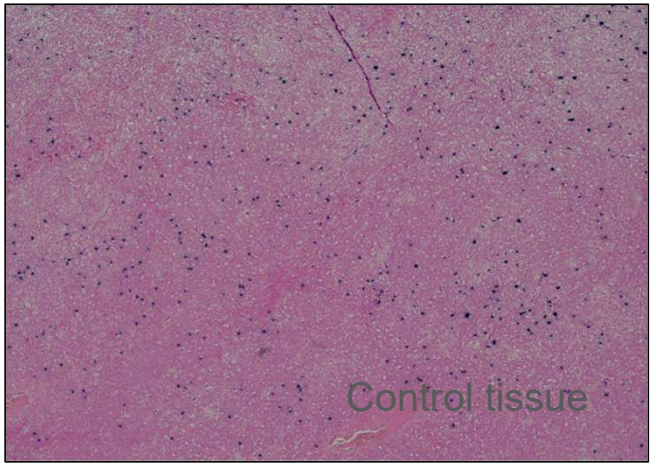


CD30





EBER-ISH negative



Diagnostic Report

Interpretation

ALK negative ALCL

Why Perform EBER-ISH?

Hard palate / upper aerodigestive tract is a classic site for **EBV-associated lymphomas**

Helps exclude:

- Extranodal NK/T-cell lymphoma
- EBV-positive diffuse large B-cell lymphoma
- EBV positive mucocutaneous ulcer(EBVMCU)

Negative EBER, together with morphology and immunophenotype, supports **ALK-negative ALCL**

In CD30-positive lymphomas arising in the upper aerodigestive tract, EBER should be performed routinely to exclude EBV-associated mimics.

WHO HAEM5, 2022; Jaffe et al. *Hematopathology*, 3rd ed.

Clinical Outcome

Case 5

Confirmed Diagnosis

ALK-negative ALCL

CT Thorax Findings

Irregular, heterogeneously enhancing lung mass

Size: 5.3cm x 5.1cm x 5.5cm with spiculated margin at the apical segment of the right upper lobe.

Treatment & Response

Initiation of mini-CHOP

Chemotherapy started promptly with mini-CHOP

- **Day 14 post chemo : Cheek swelling resolved.**

Case 6

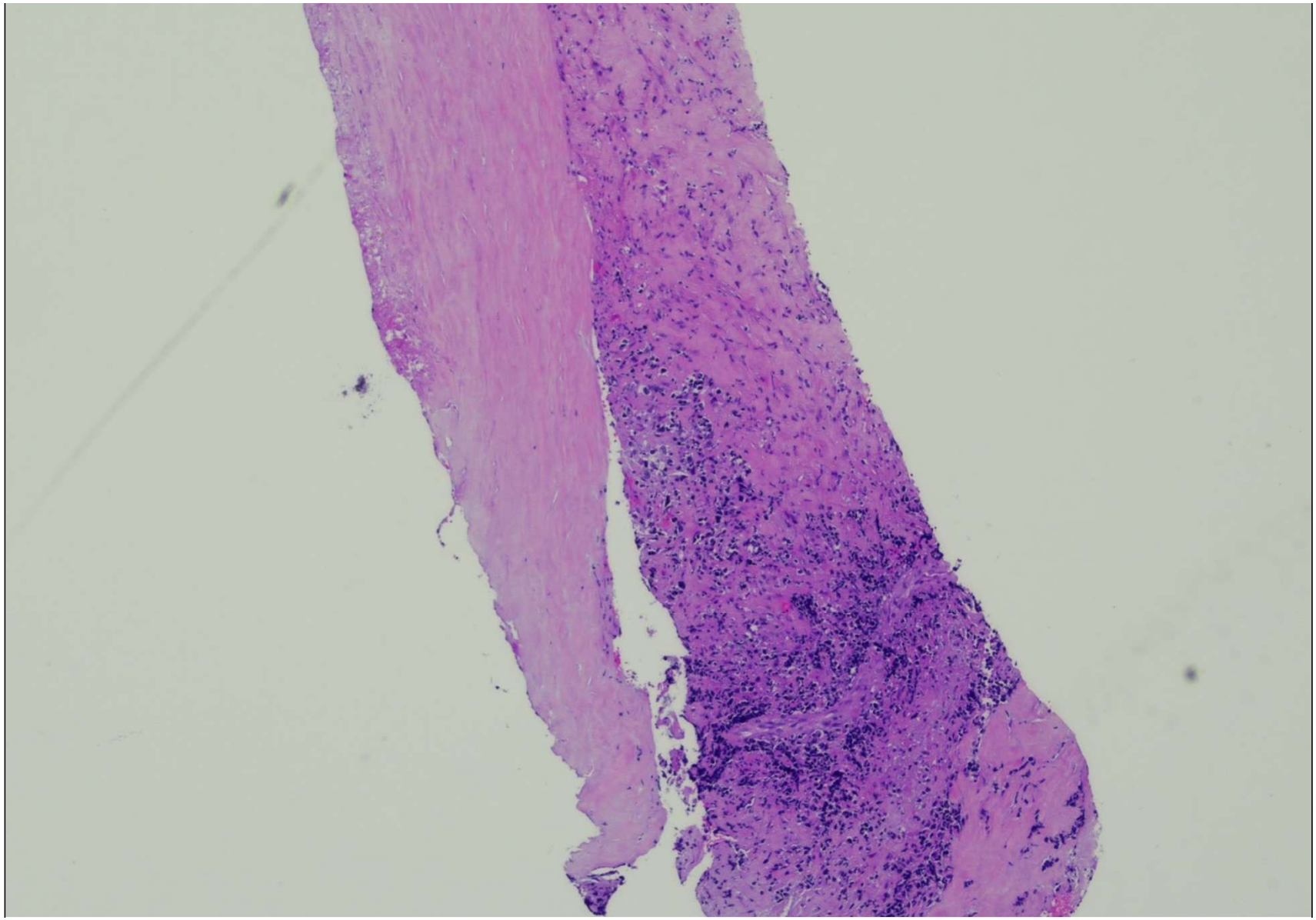
35 years old

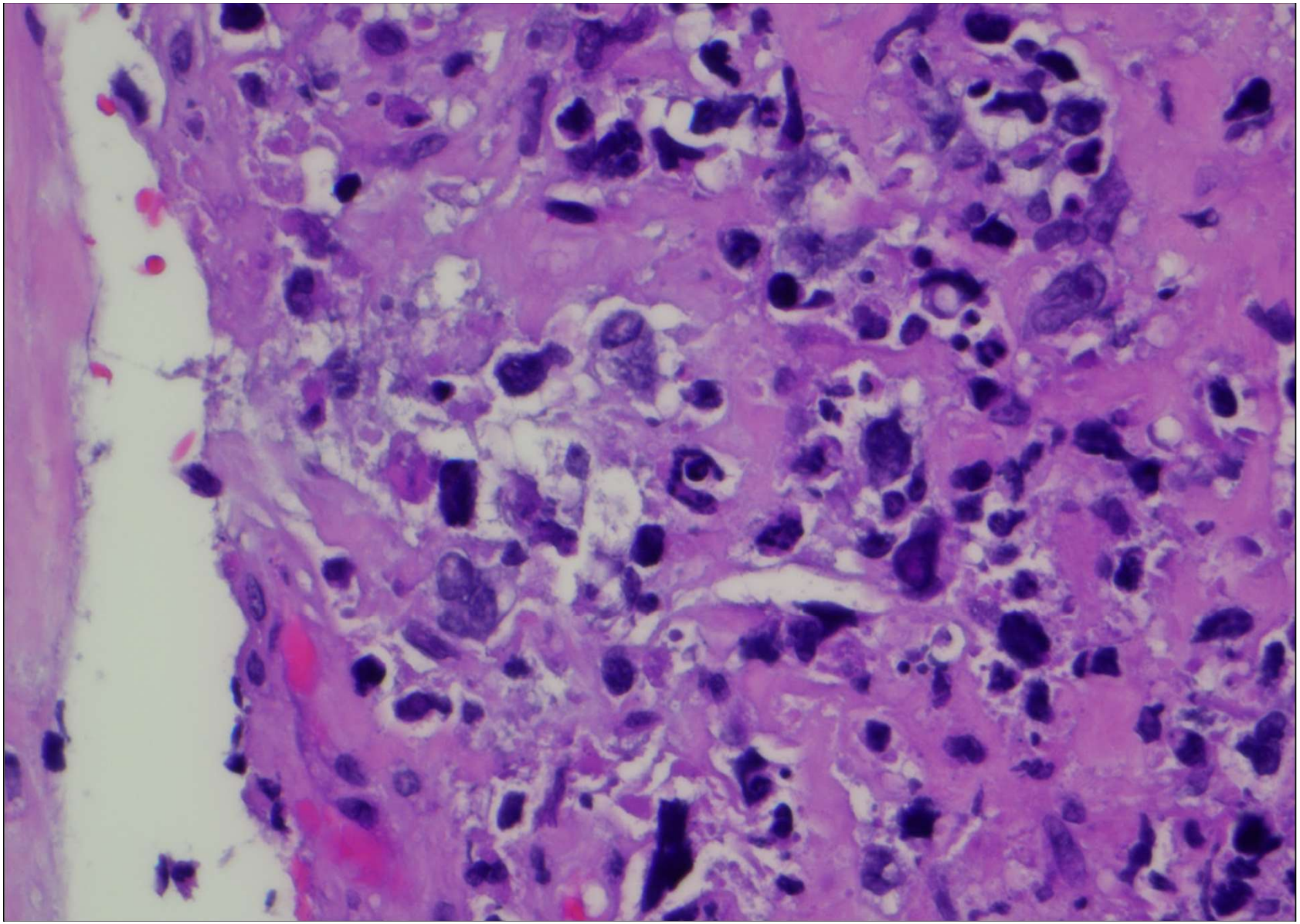
Female, NKMI, presented with SOB, LOA, LOW.

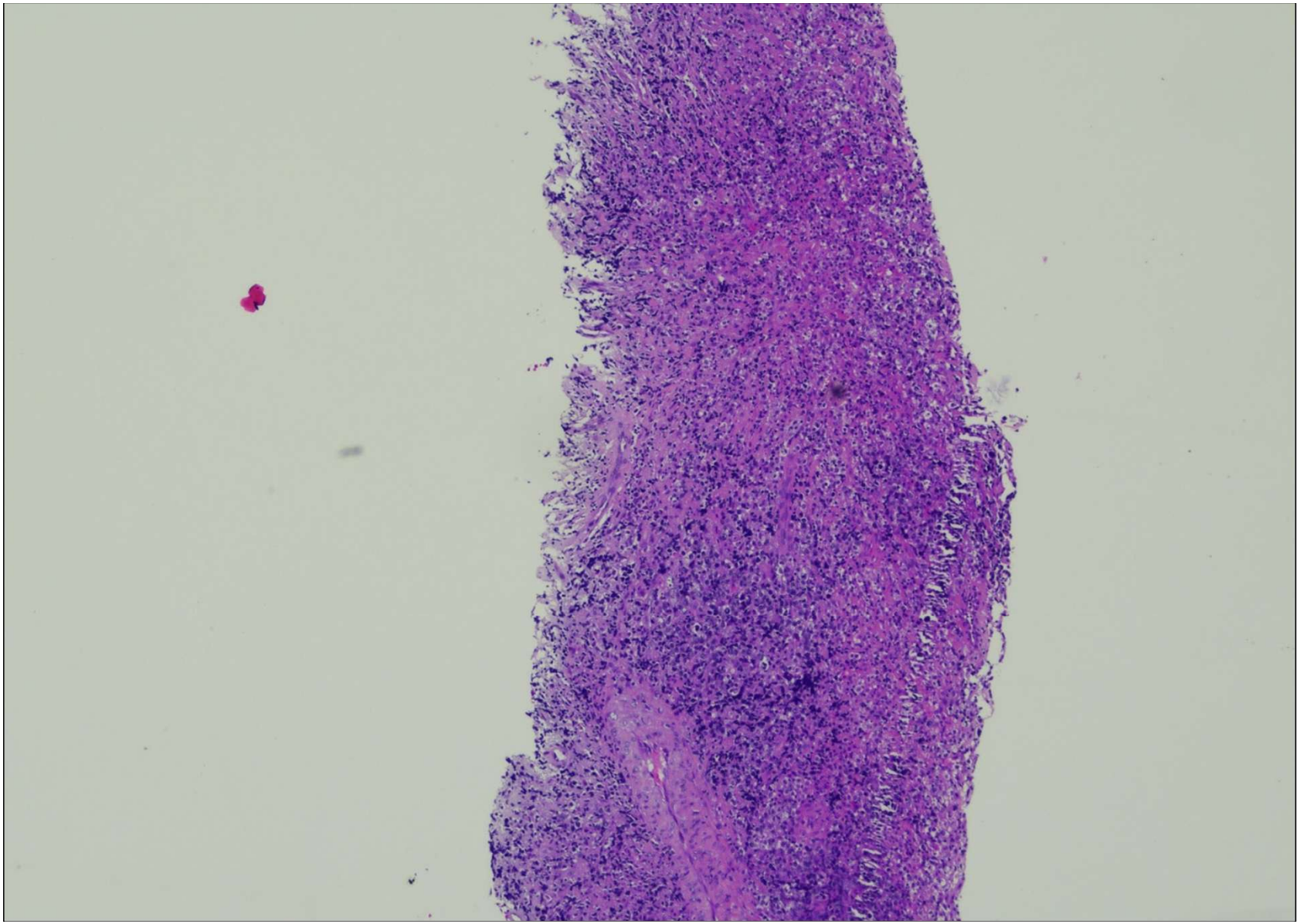
CT thorax :

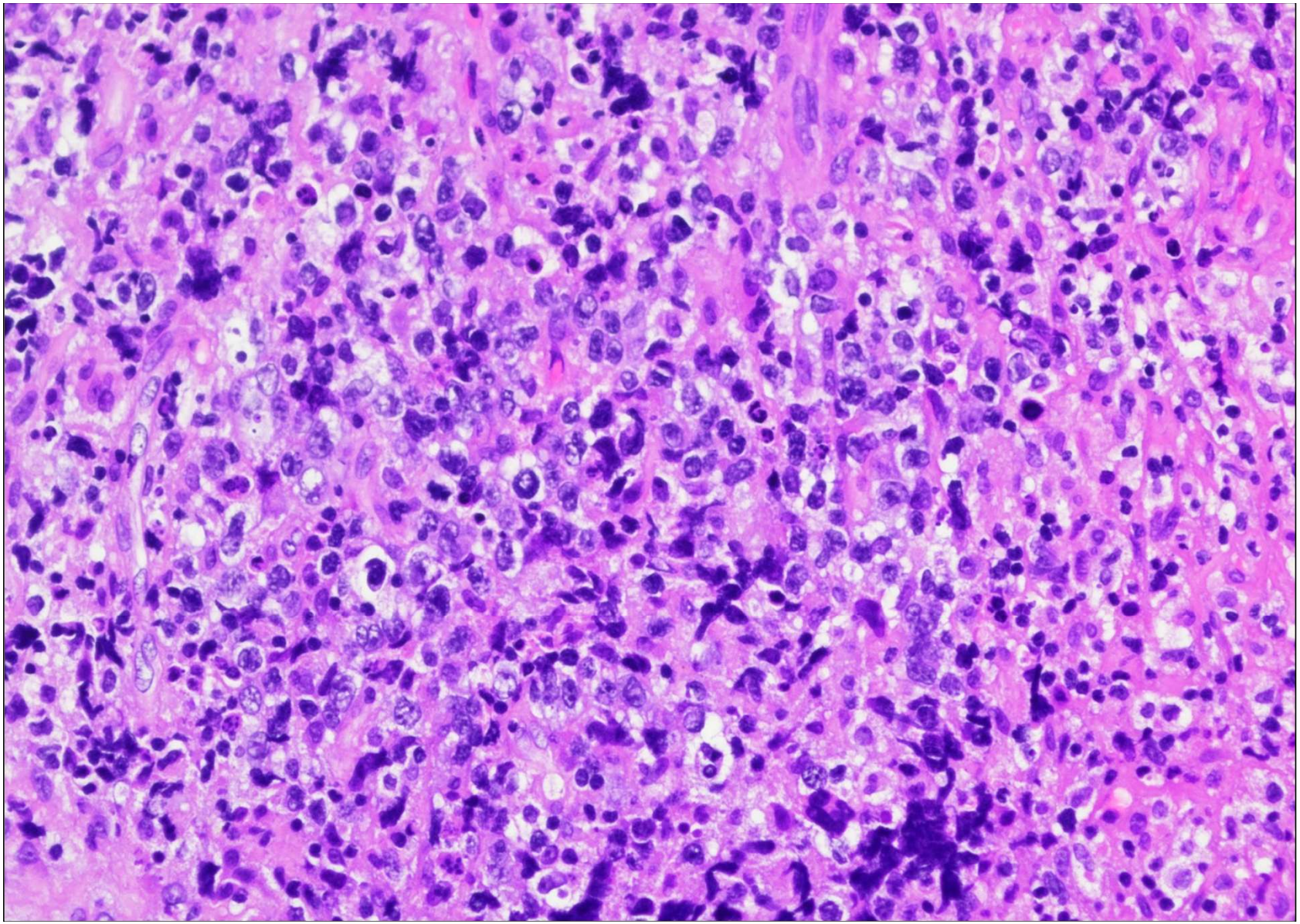
Anterior mediastinal mass.

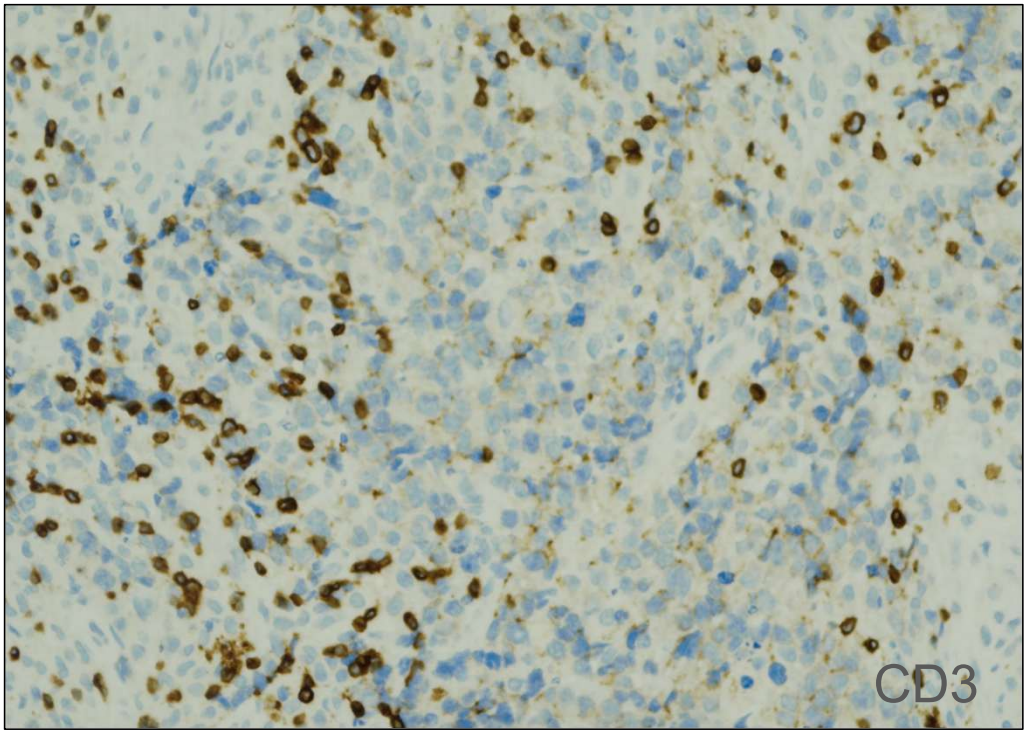
Clinical impression: **Anterior mediastinal mass with svco and pericardial effusion.**

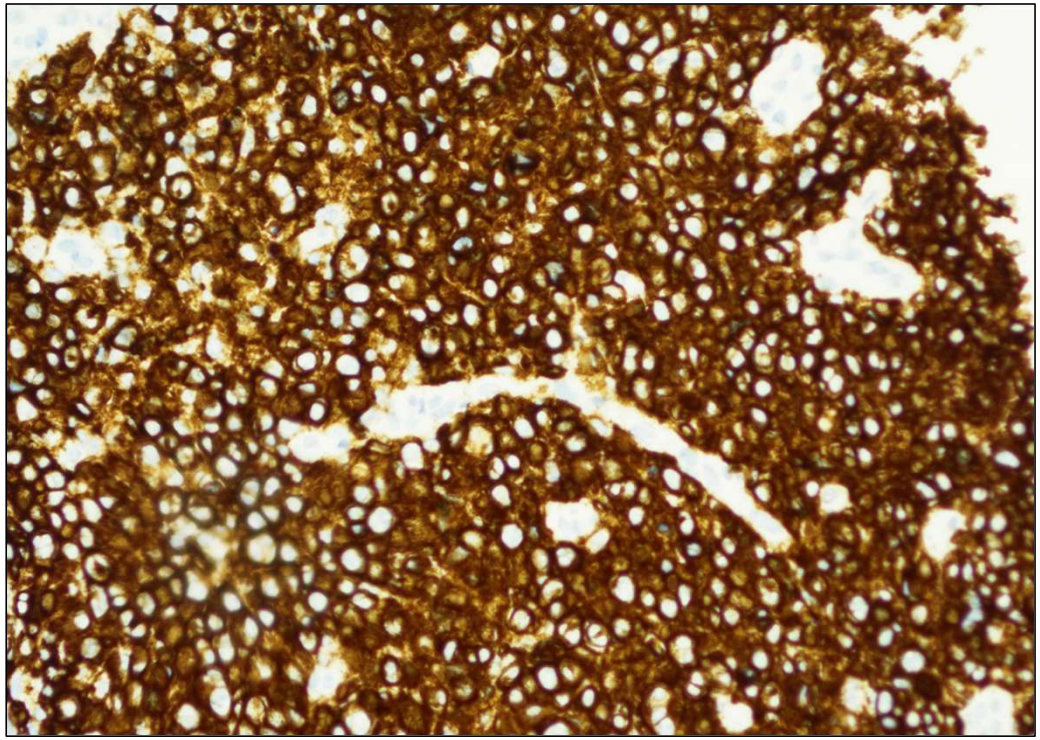












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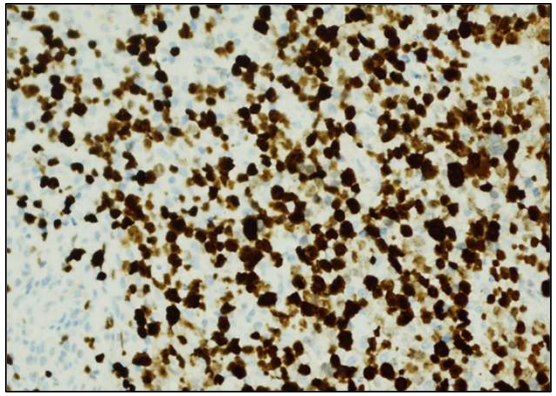

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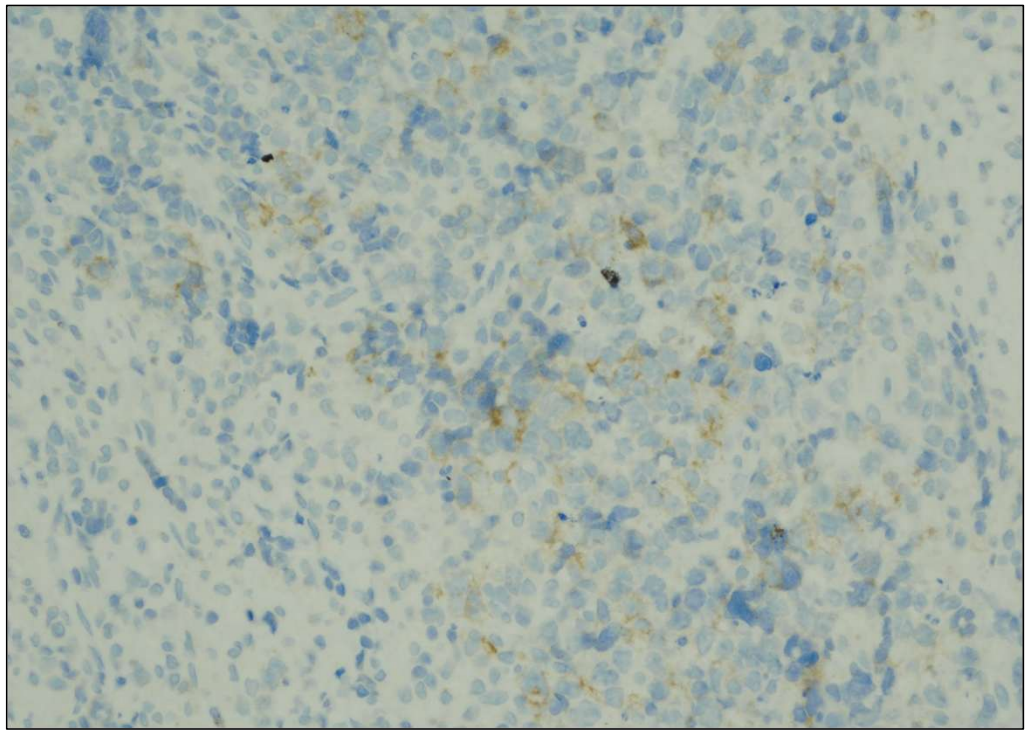

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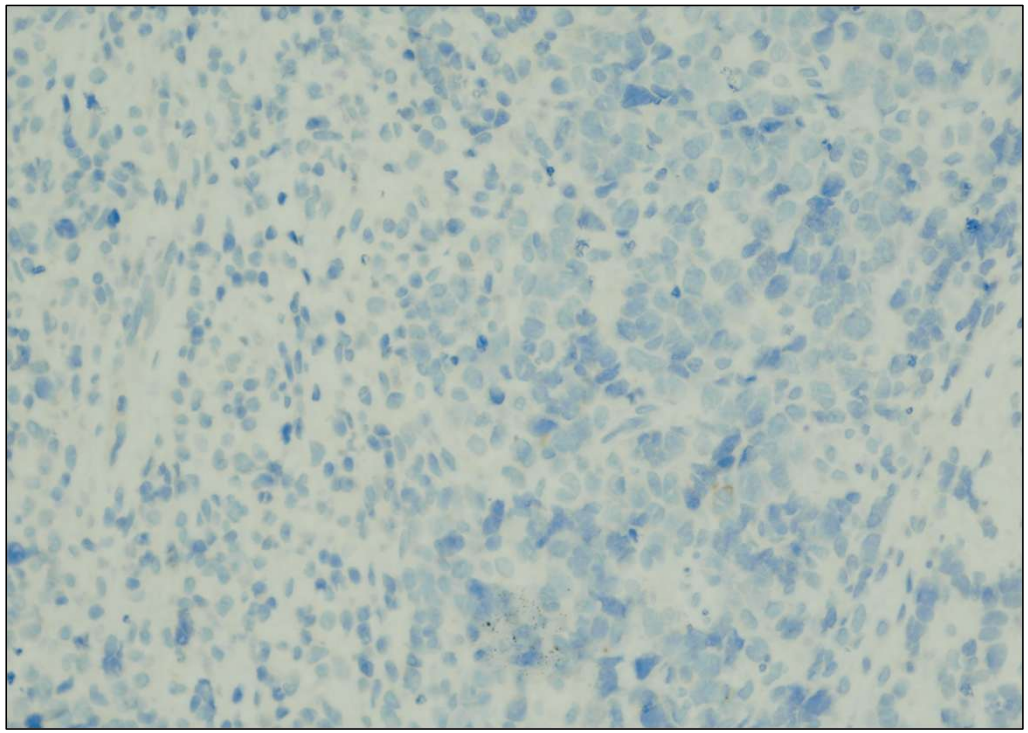


CD23

Diagnostic Report

Interpretation

High grade B-cell lymphoma, favouring a primary mediastinal large B-cell lymphoma.

Feature	PMBCL	DLBCL, NOS
Age	Young adults	Older adults
Site	Anterior mediastinum	Nodal/extranodal
Fibrosis	Common	Uncommon
CD23	Frequently positive	Usually negative
CD30	Variable (often weak)	Usually negative
PD-L1	Frequently positive	Usually negative

WHO HAEM5, 2022; Jaffe et al. *Hematopathology*, 3rd ed.

Clinical Outcome

Case 6

Diagnosis

PMBCL

Regimen & Current Status

Received RCVP

Day 21 resolving pericardial effusion.

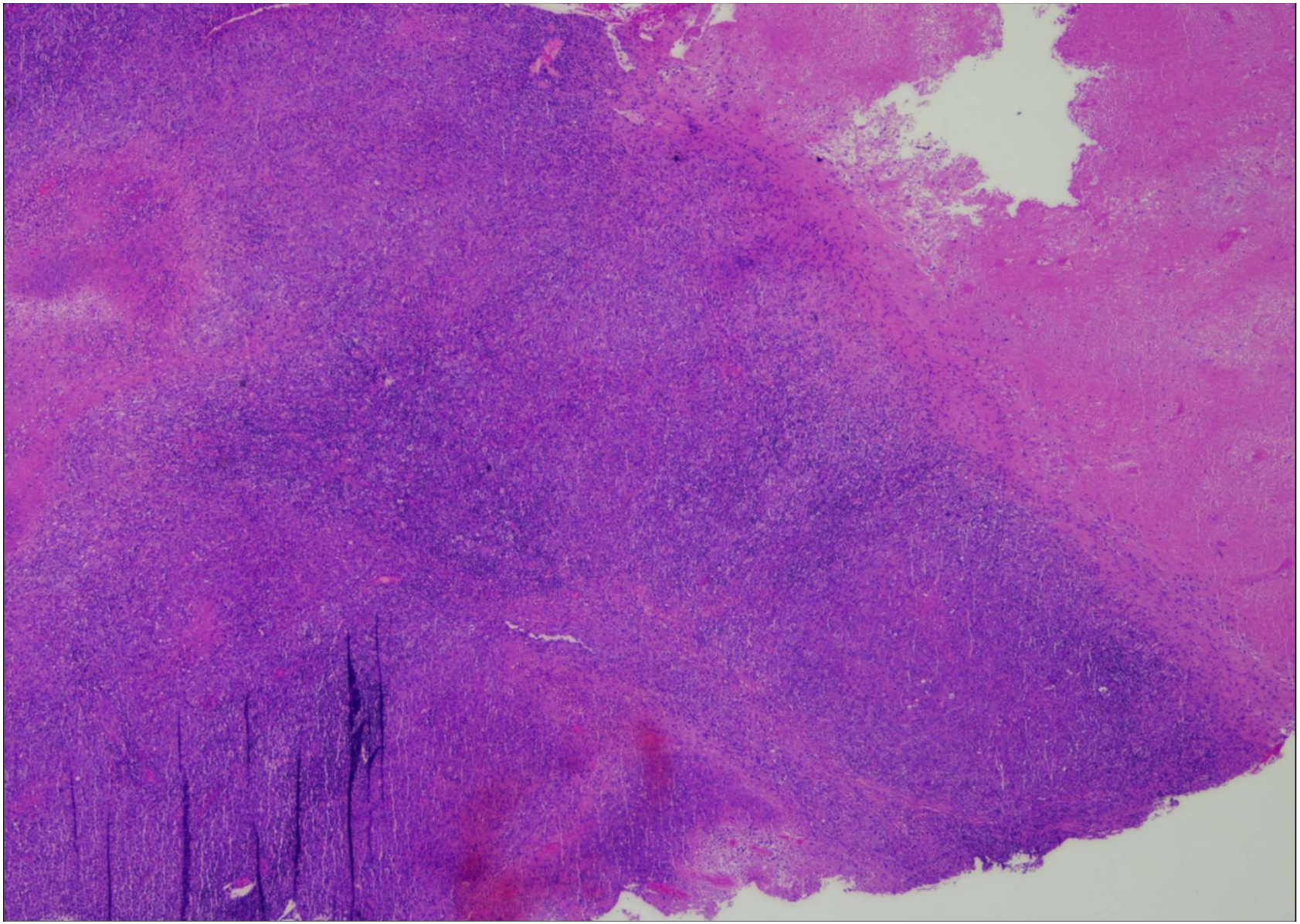
Case 7

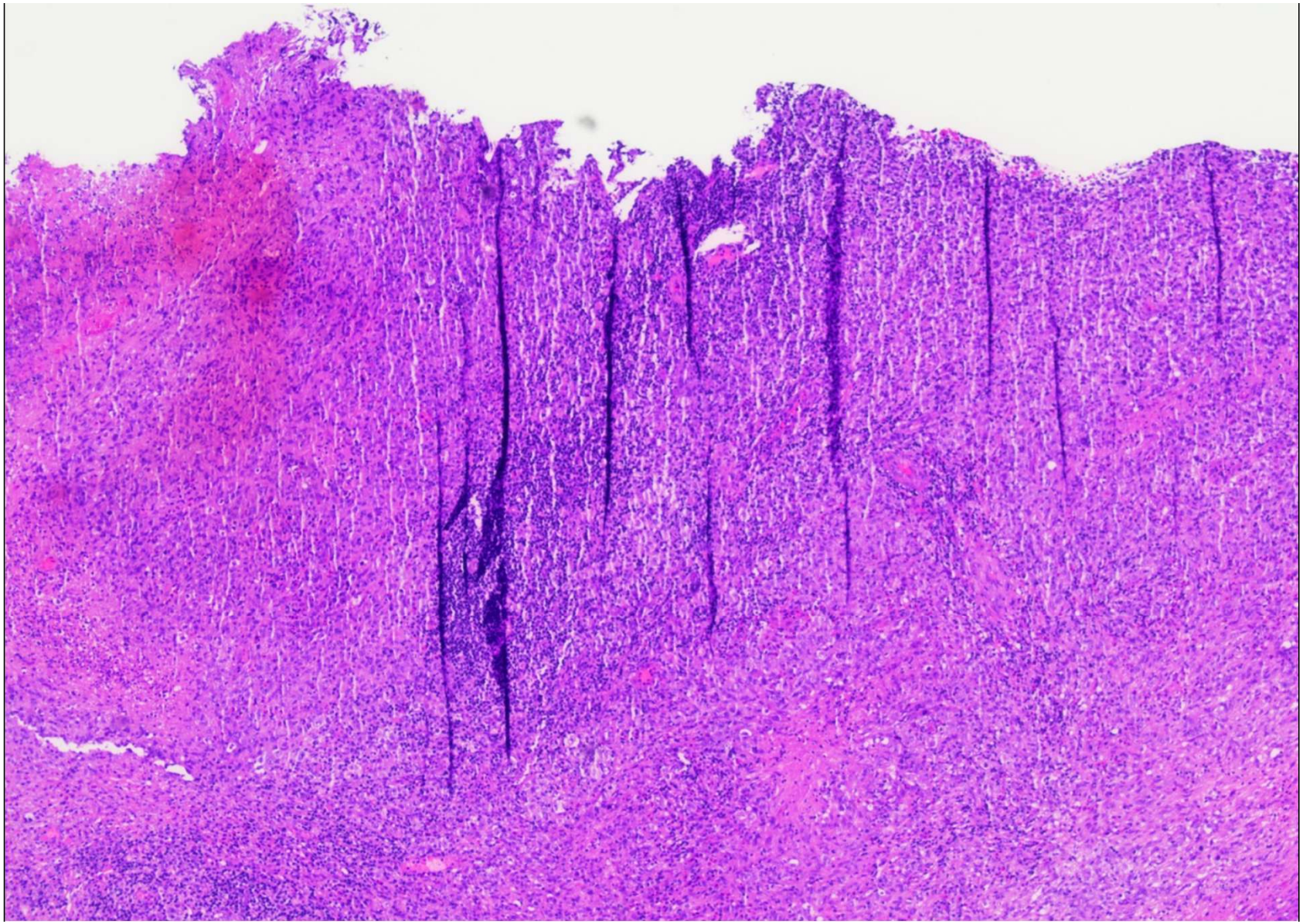
23 years old

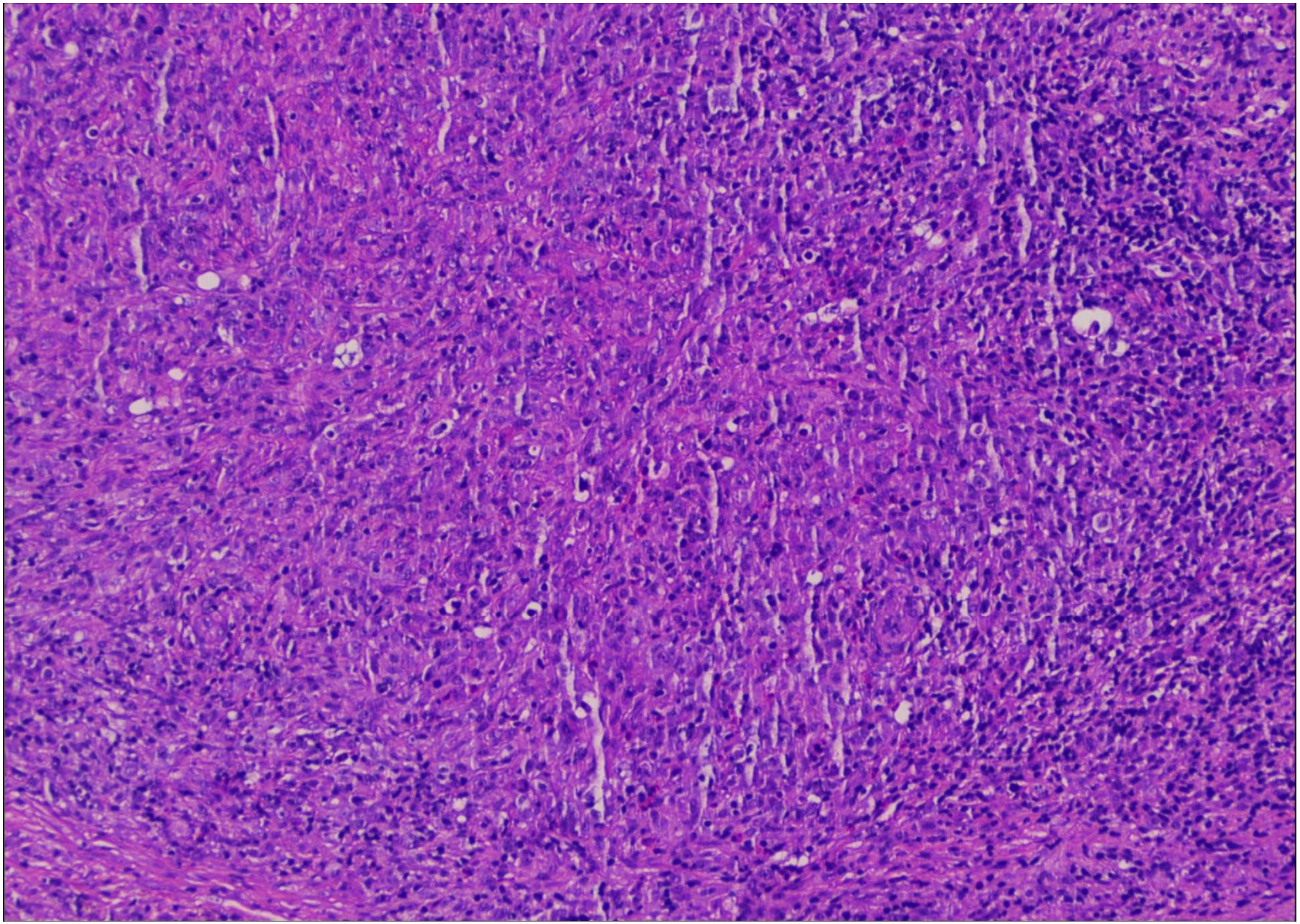
Female, presented with fever, cough x 2/52, LOW.

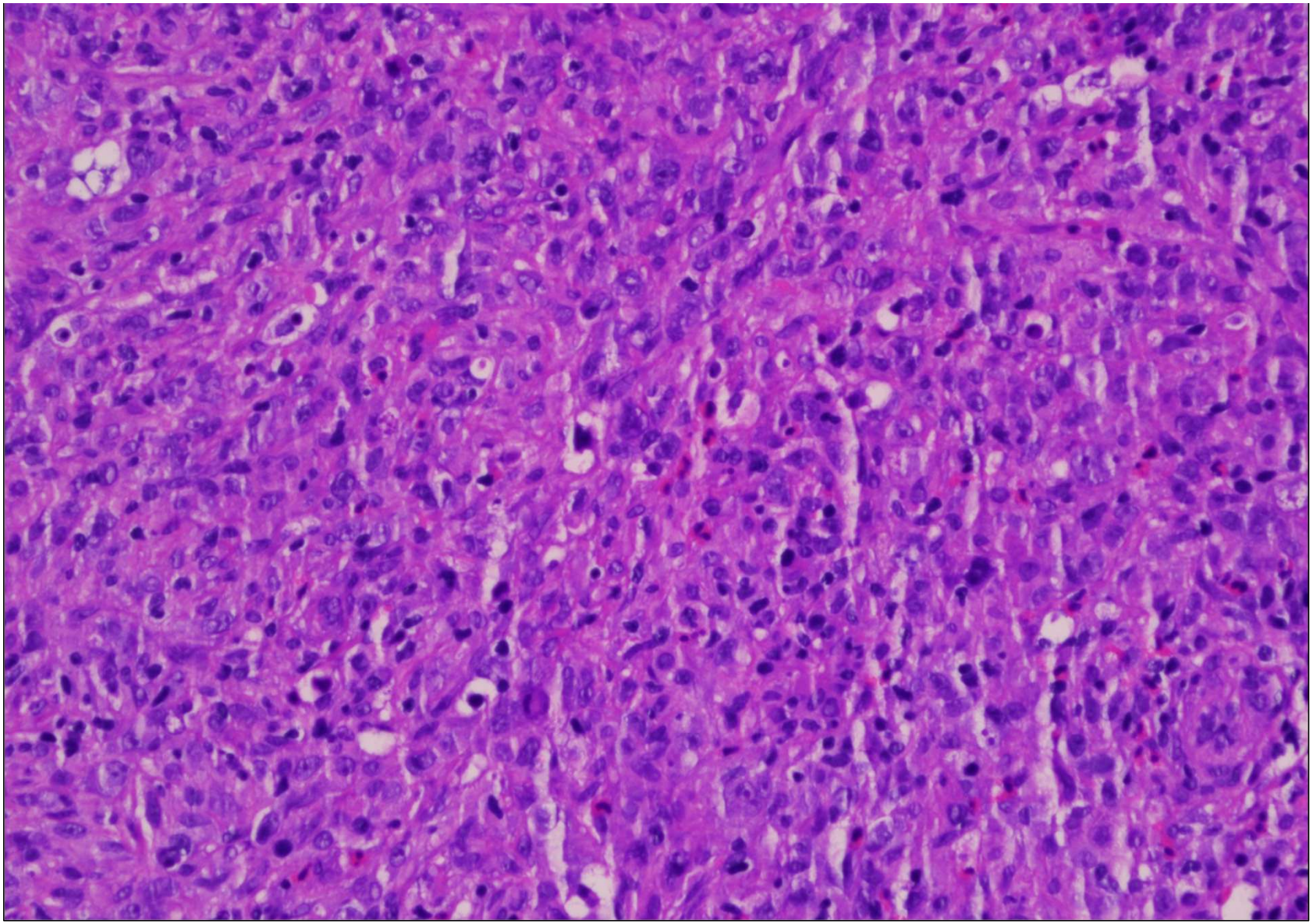
Further history from the clinician:

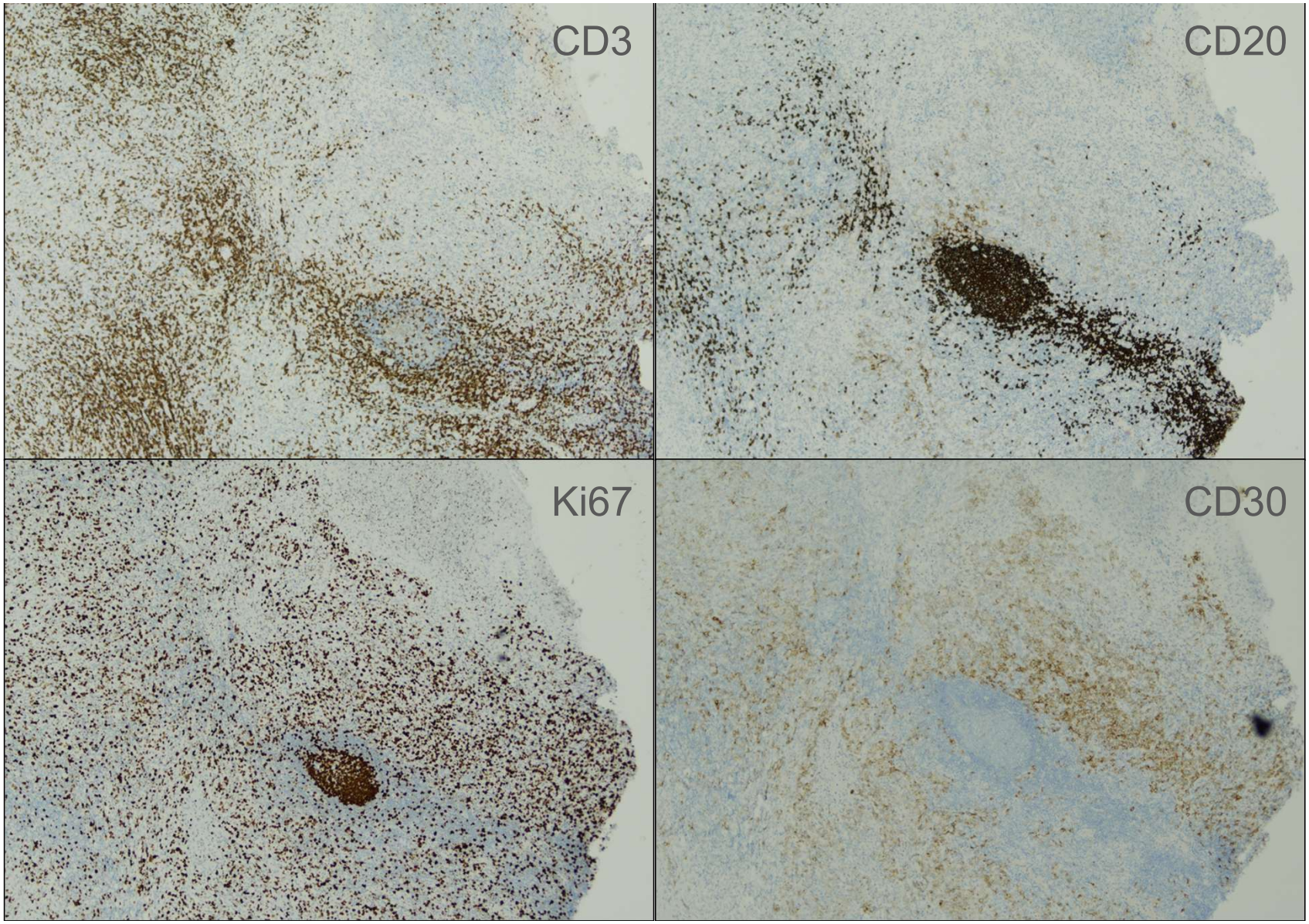
Huge mediastinal mass.

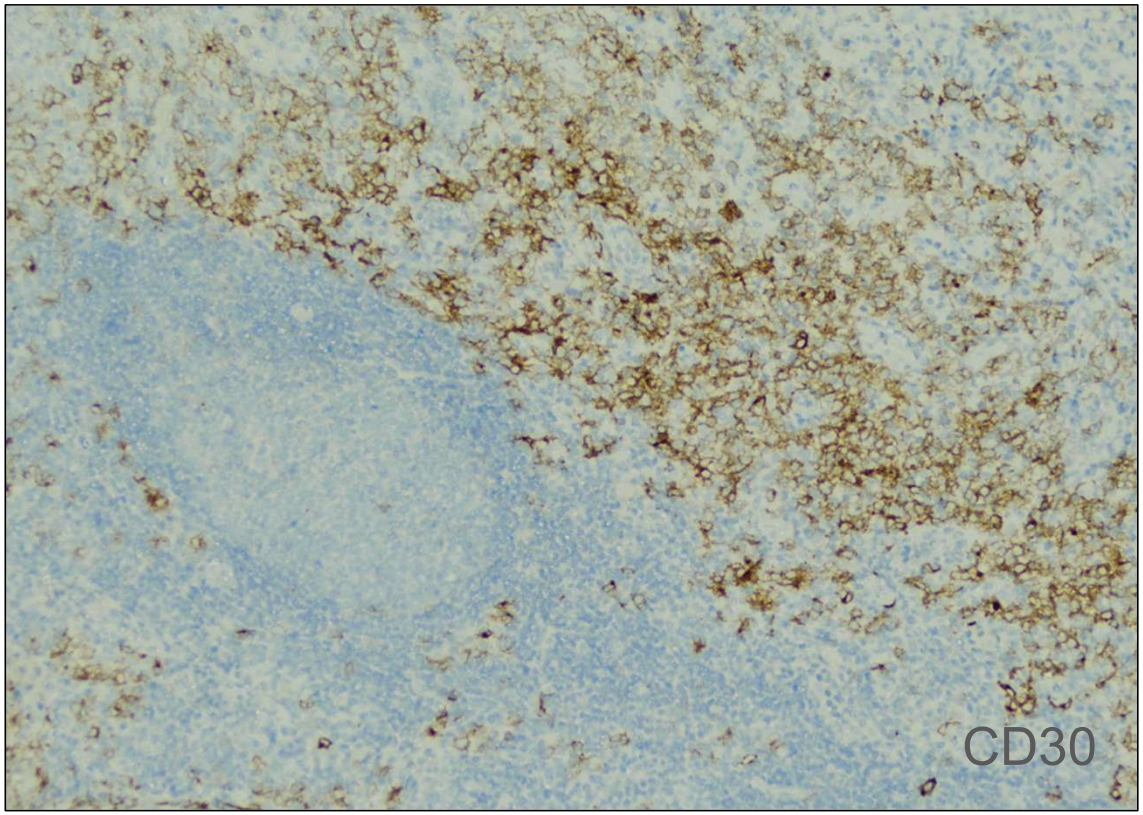


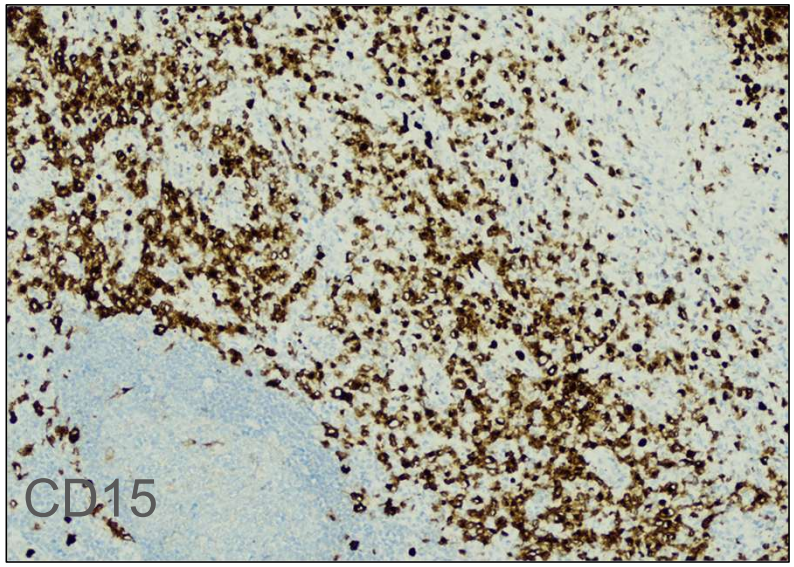


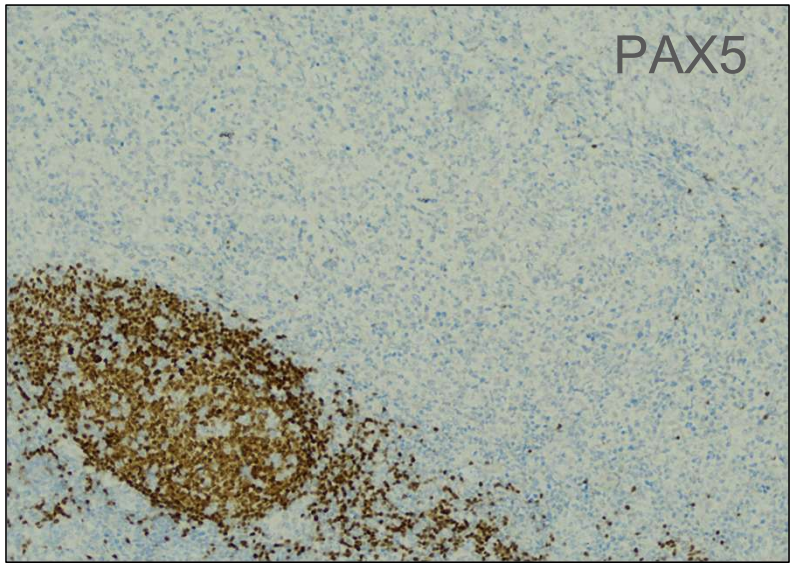





CD3
CD20
Ki67
CD30







ALK-
BOB1-
OCT2-
LCA-

Diagnostic Report

Interpretation

Mediastinal grey zone lymphoma, PMBCL-like

Disease	First-line Treatment
CHL	ABVD or BV-AVD (stage-dependent)
PMBCL	Dose-adjusted EPOCH-R (DA-EPOCH-R) or R-CHOP ± radiotherapy
Mediastinal Grey Zone Lymphoma (MGZL)	Treated more like aggressive B-cell lymphoma (most commonly DA-EPOCH-R); outcomes generally poorer than CHL or PMBCL

Misdiagnosing mediastinal grey zone lymphoma as CHL may lead to suboptimal initial therapy, increasing the risk of refractory disease or early relapse.

WHO Classification of Haematolymphoid Tumours (WHO HAEM5), 2022.
Wilson WH, Pittaluga S, Nicolae A, et al. *Blood*. 2014;124:1563–1569.

Clinical Outcome

Case 7

Diagnosis

Mediastinal grey zone lymphoma

Staging & Imaging

CT TAP: No evidence of intra-abdominal or pelvic involvement or metastasis

Discharge Plan

Discharged and electively admitted for chemotherapy

Current Status & Treatment

Completed Level 4 DA-EPOCH

Planned for 6 cycles of DA-EPOCH chemotherapy. Currently admitted for HAP.

Thank you.