

Difficulties in Lymphoma Diagnosis

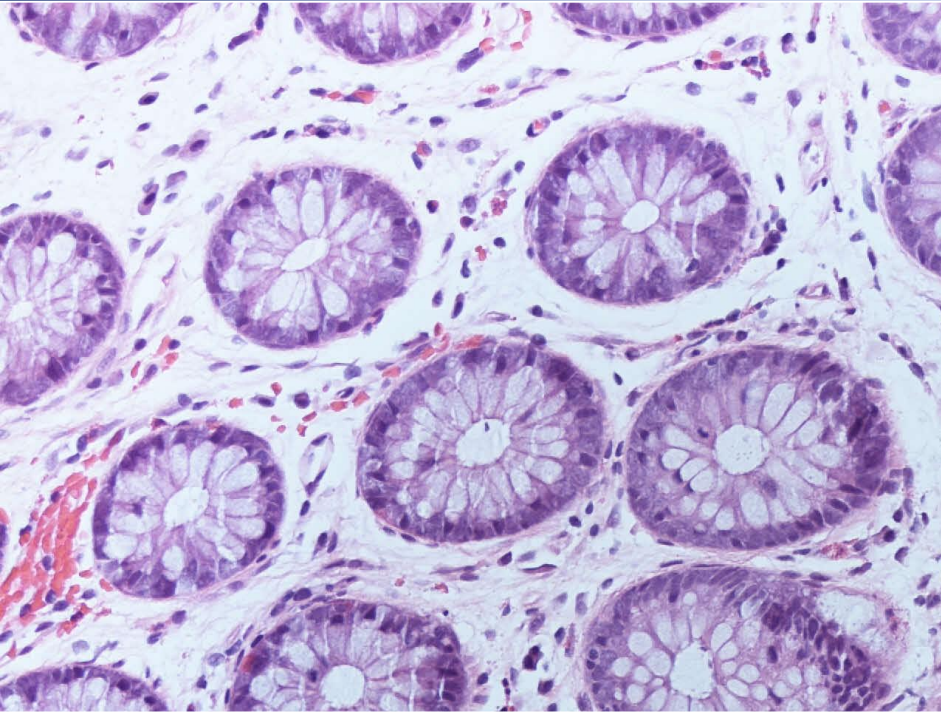
Dr Sarah Liptrot

2019

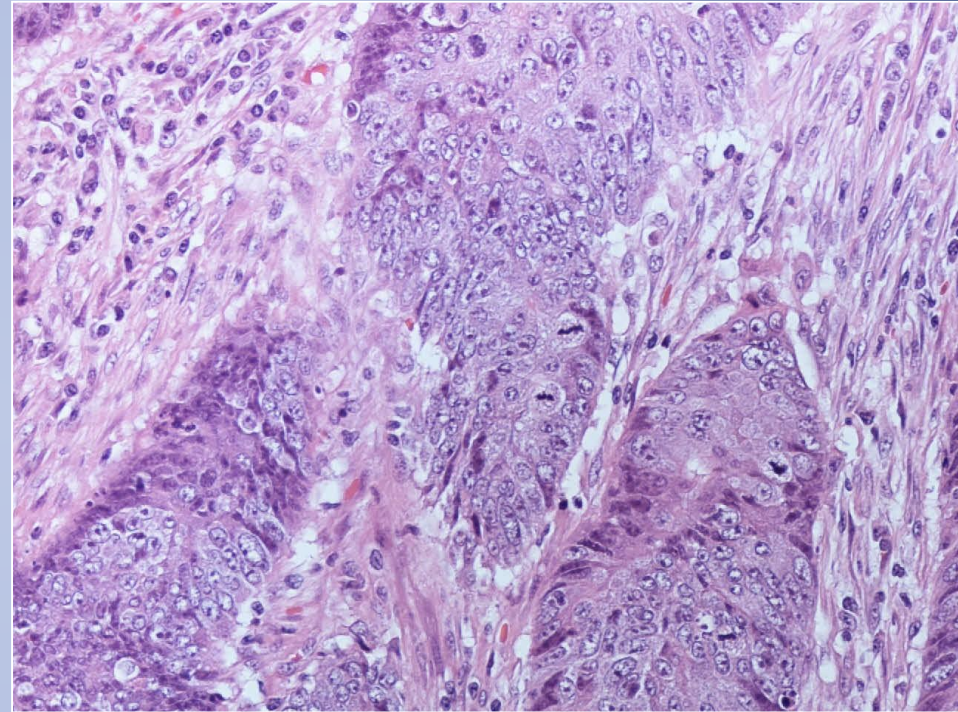
Diagnosis of malignancy

- Based on morphology
- Microscopic appearances help us to differentiate between benign and malignant tissues/cells
- This is the mainstay of pathology ie being able to recognise patterns and decide whether or not they are benign or malignant
- ICC is an adjunct

Epithelial Pathology

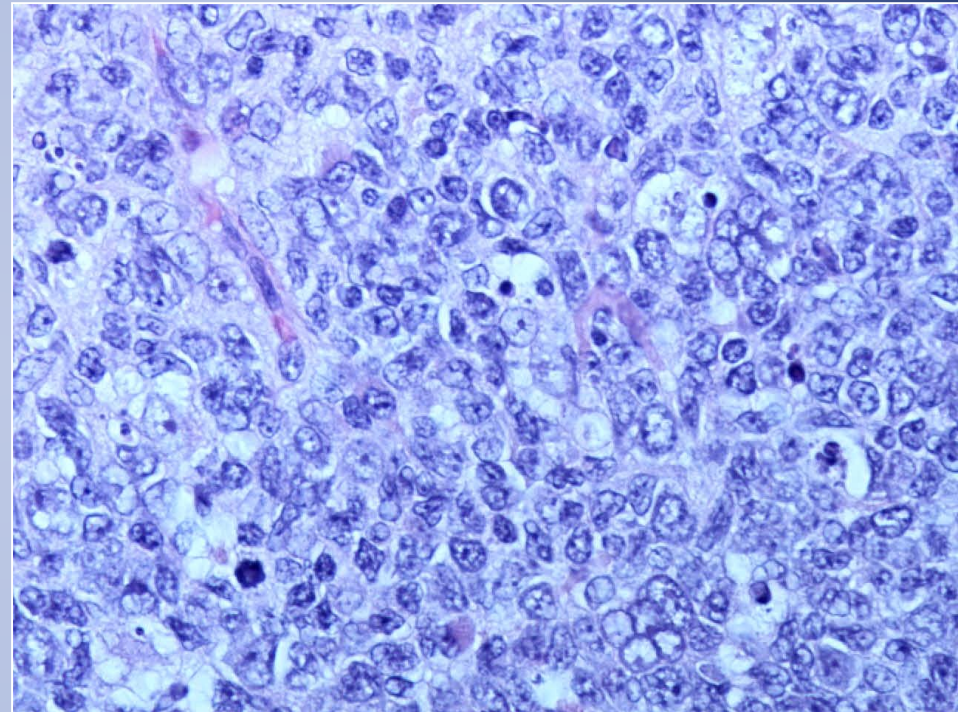
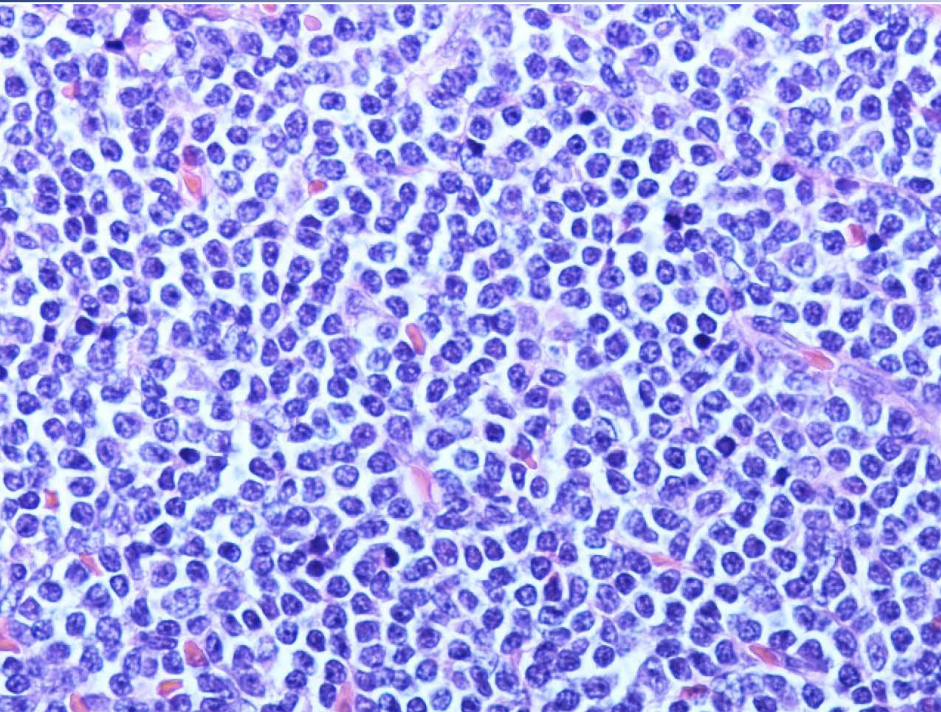


Benign



Malignant

Lymphoid Pathology



How do we recognize lymphoma?

- Morphology is very important in the recognition of lymphoma
- It can be more subtle than solid organ malignancies, no mets, no mass lesion
- Its often confined to lymph nodes
- Imaging is very important
- Site and number and size of nodes
- Sometimes only an isolated group of nodes

size of sample

- Excision biopsy of node submitted to lab (fresh or fixed)
- Targeted Core biopsy
- Fine Needle aspirate

Lymphoma Diagnosis

- Morphological (appearance of cells under a microscope)
- High grade or low grade?
- B cell or T cell
- Determines which panel of immunohistochemical stains
- Tissue limited

Lymphoma Diagnosis

- Morphological (appearance of cells under a microscope).
- Immunophenotypical (cell differentiation – by cd expression)
- Molecular genetic features (classical Cytogenetics, FISH, PCR).
- Clinical features.

What might be the problems
reaching the diagnosis?

Necrosis

Tissue limitation

Complex
morphology

Poor Fixation

Immunocytochemistry
interpretation

Bad processing

Difficulties

Atypical
immunophenotype

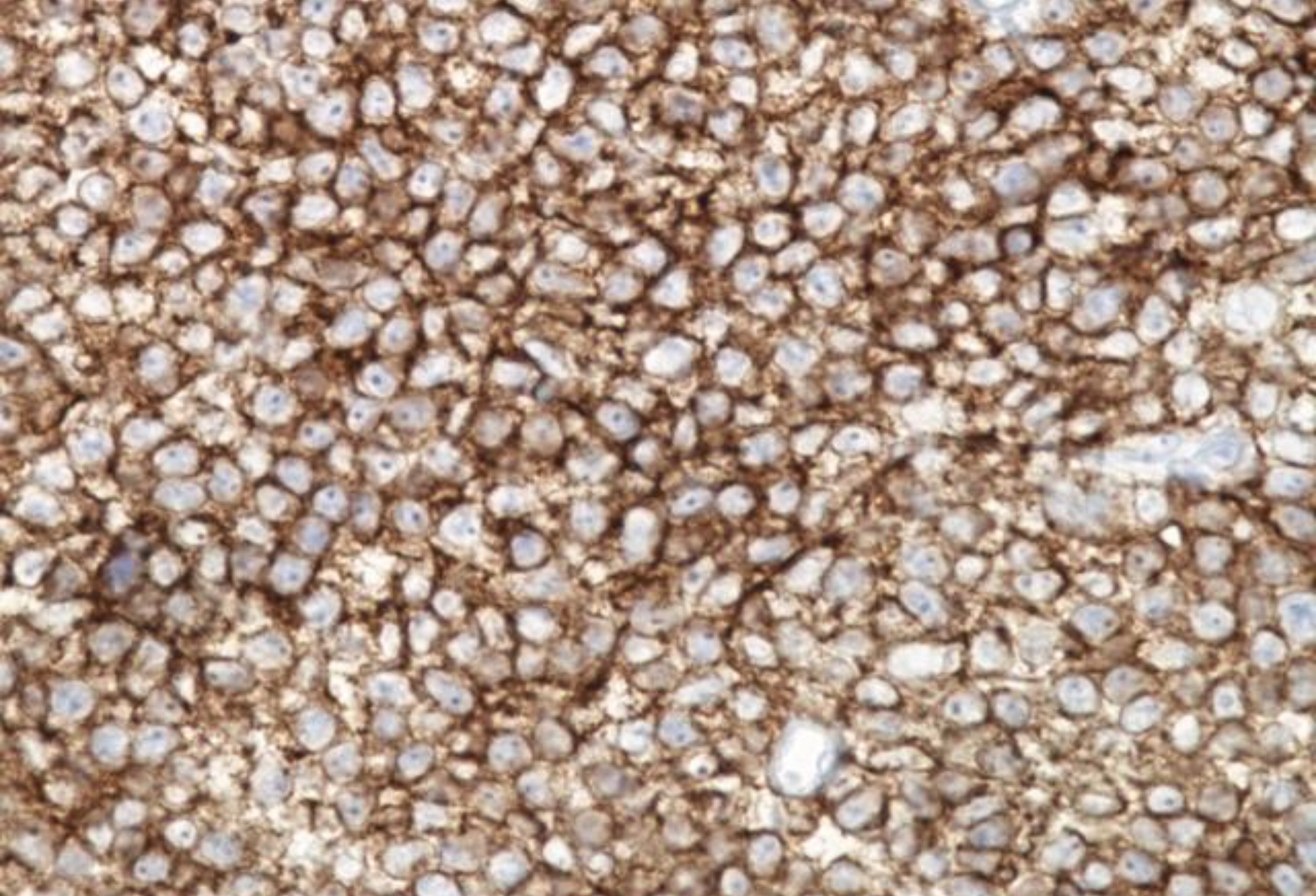
Observer
issues
(Pathologist)

Molecular

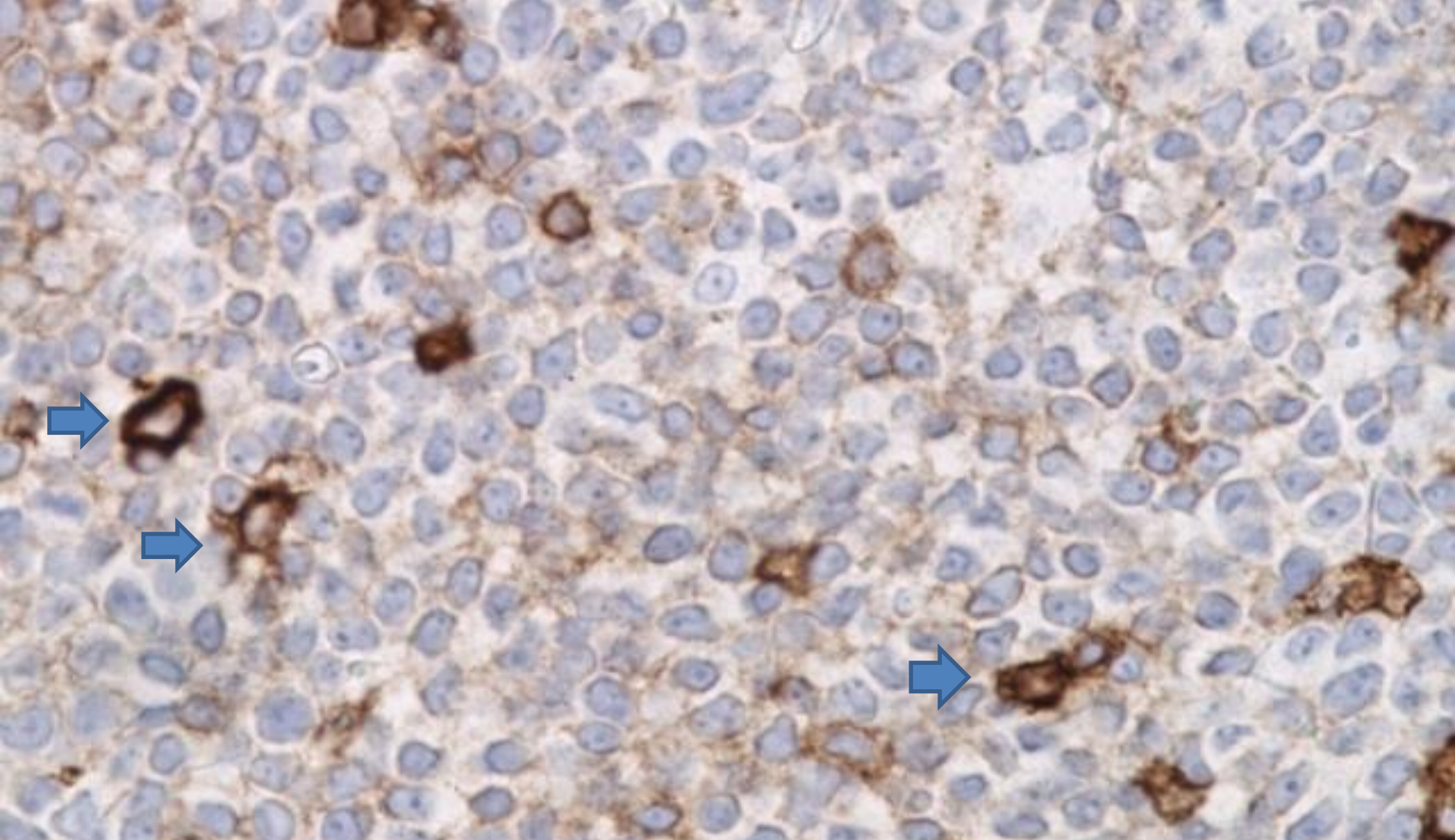
Grey Zone
lymphoma

Problems in immunocytochemistry

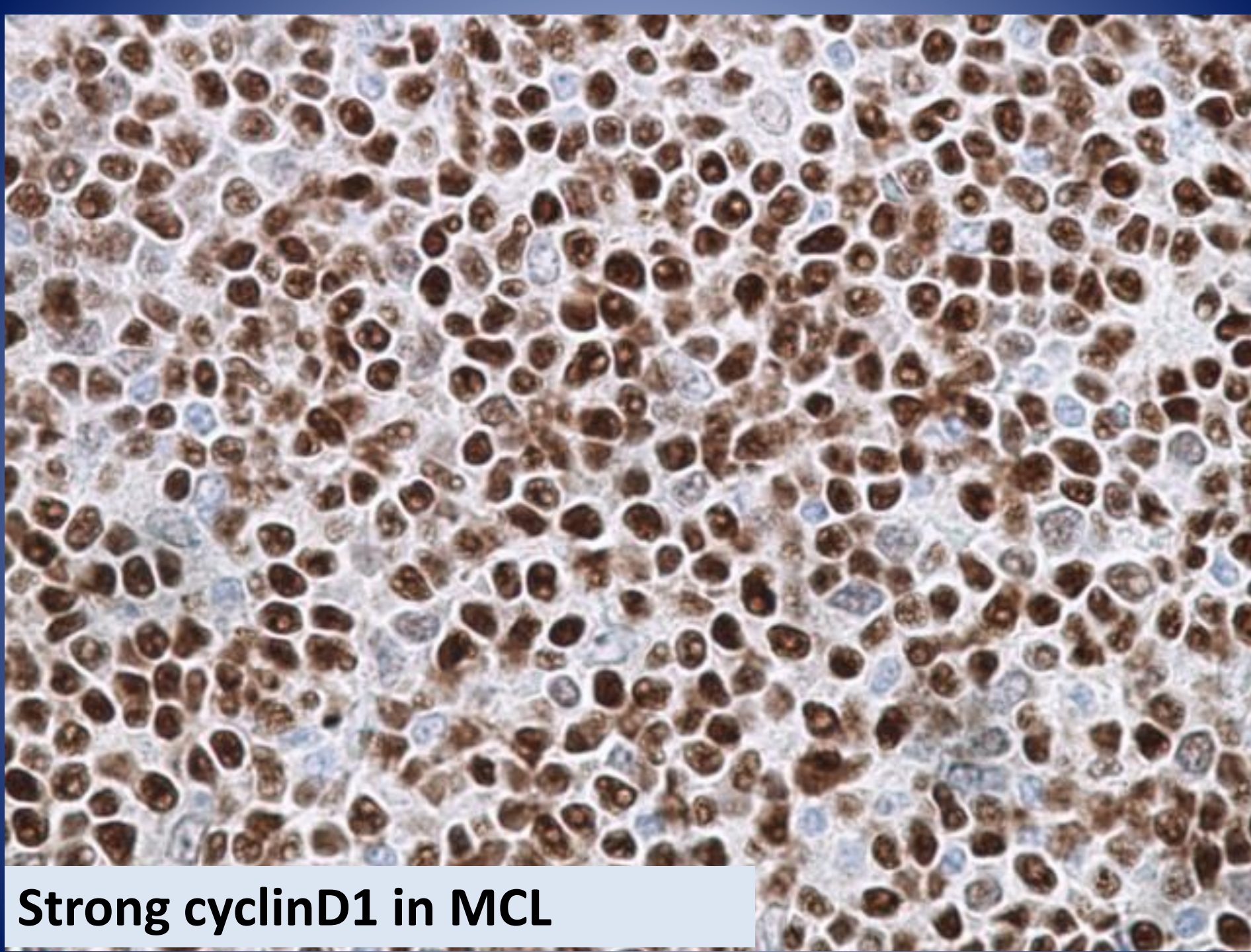
- ICC can be fantastic however, this is not always the case
- Issues causing ICC to fail include
 - Poor fixation
 - Tissue limitation (cutting out)
 - Poor processing
 - Poor interpretation



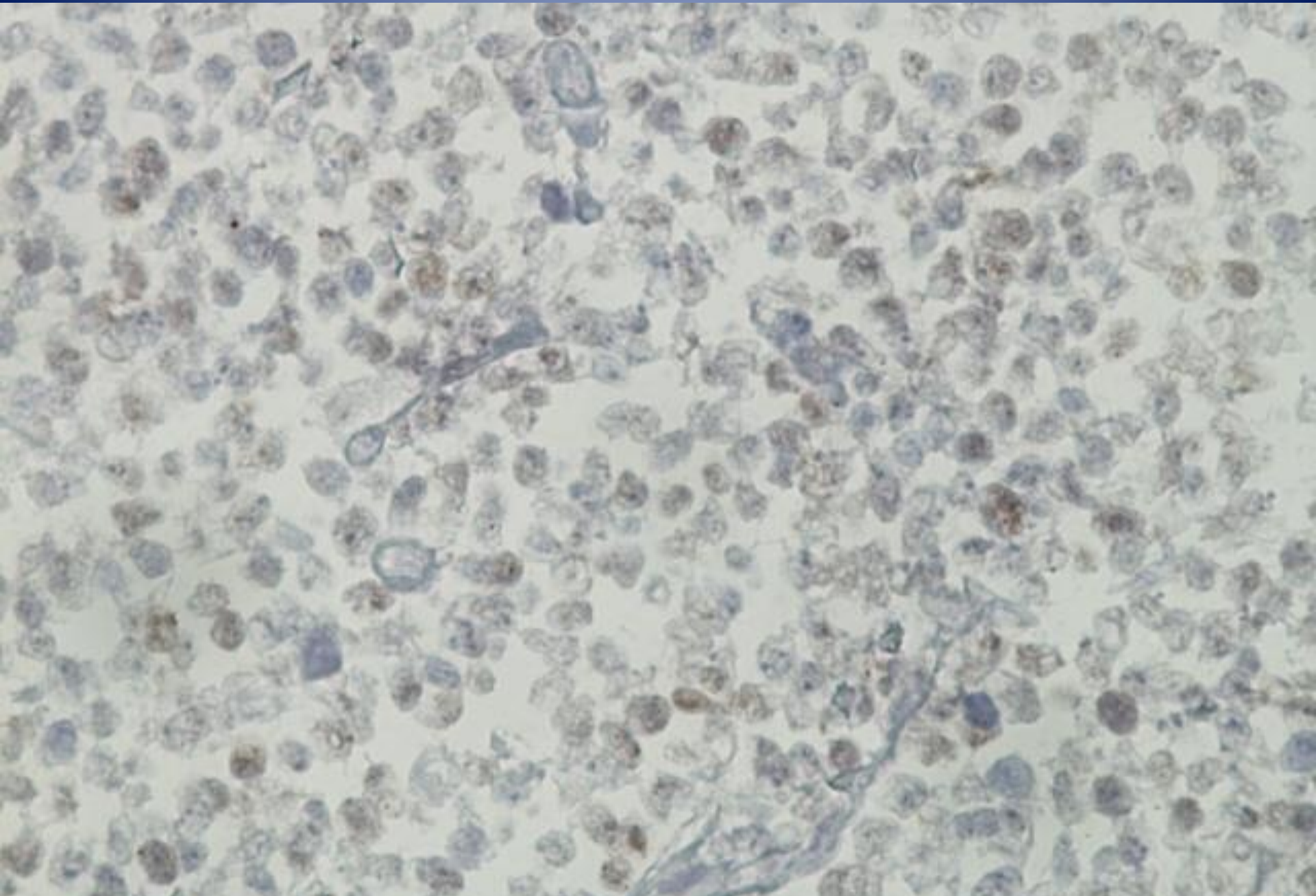
CD5 expression in Mantle cell lymphoma



Weak CD5 expression in Mantle cell lymphoma (T cells arrowed)



Strong cyclinD1 in MCL



Weak Cyclin D1 in MCL

Immunocytochemistry

- The intensity of immunocytochemistry varies due to
- Delay in fixation
- Length of fixation in formalin
- Type of antigen retrieval
- Age of antibody
- Presence of necrosis
- Individual nature of tumour.

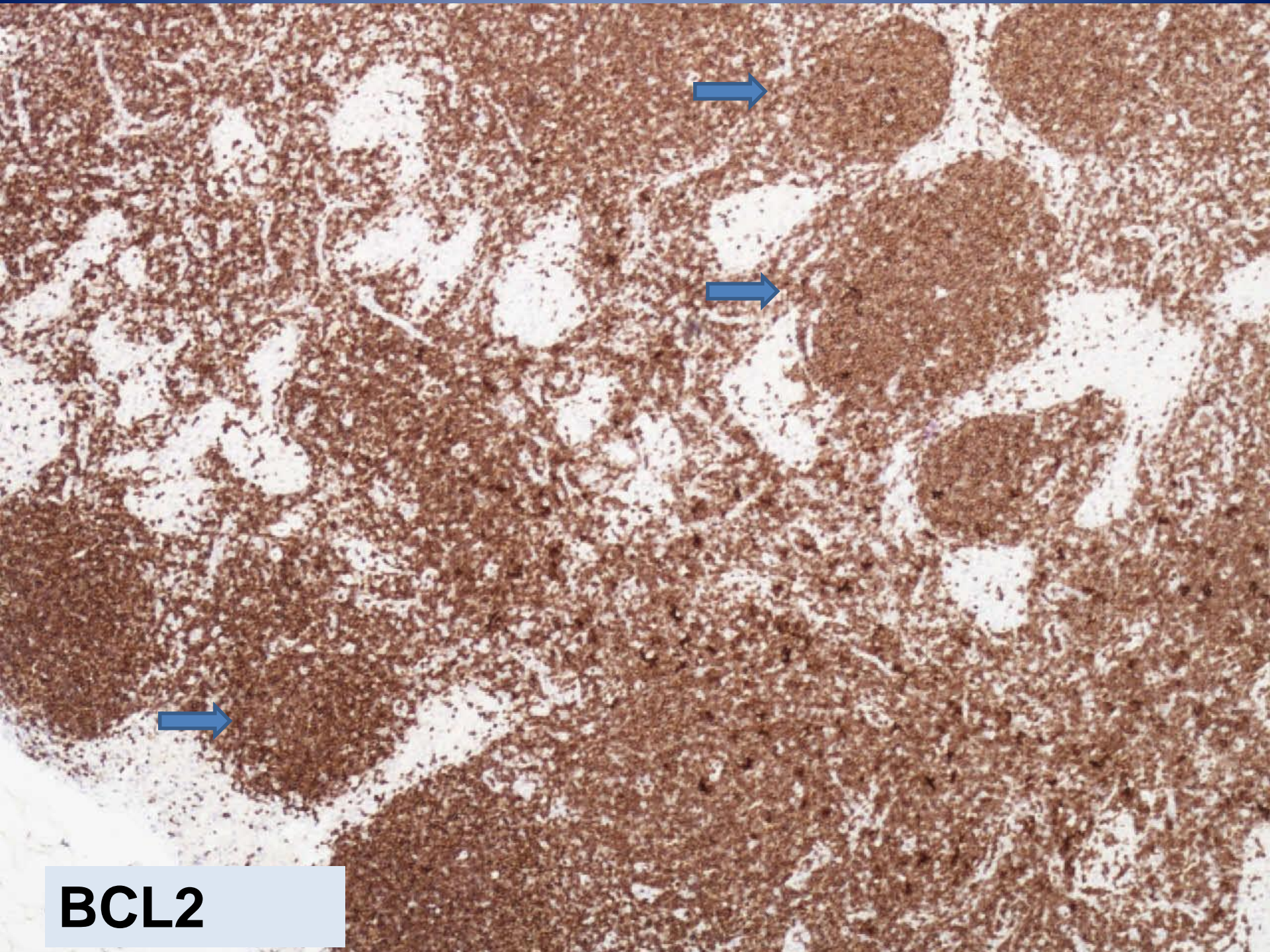
Main pitfalls in diagnosing lymphoma

- Reactive lesions mimicking lymphoma such as follicular hyperplasia
- Malignant Lymphoma diagnosed as reactive eg AITCL
- Error in classification of lymphoma (commonest problem)

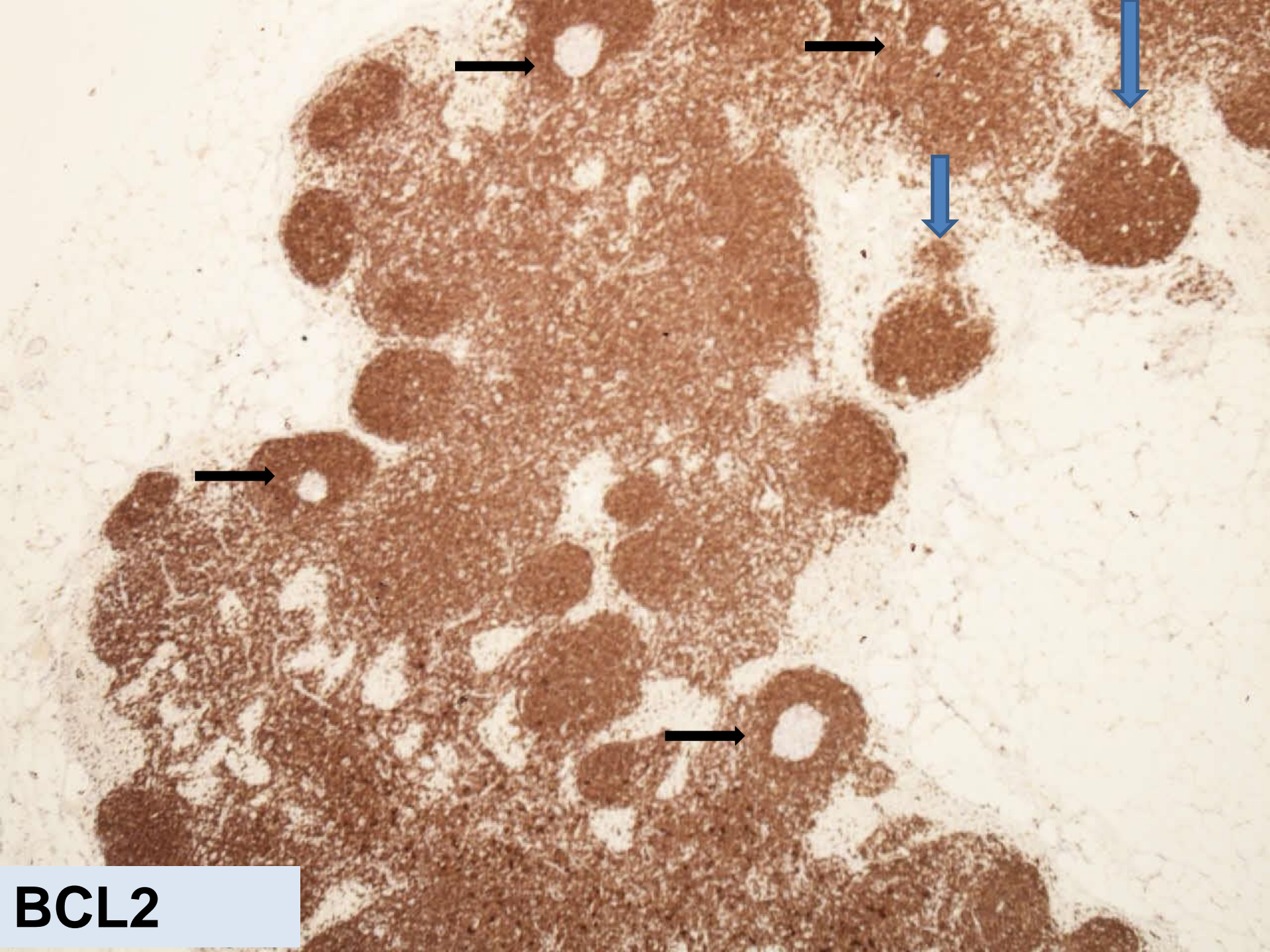
All Wales Audit. Management changed in 8% of cases following specialist review.

Case 1 Male 40

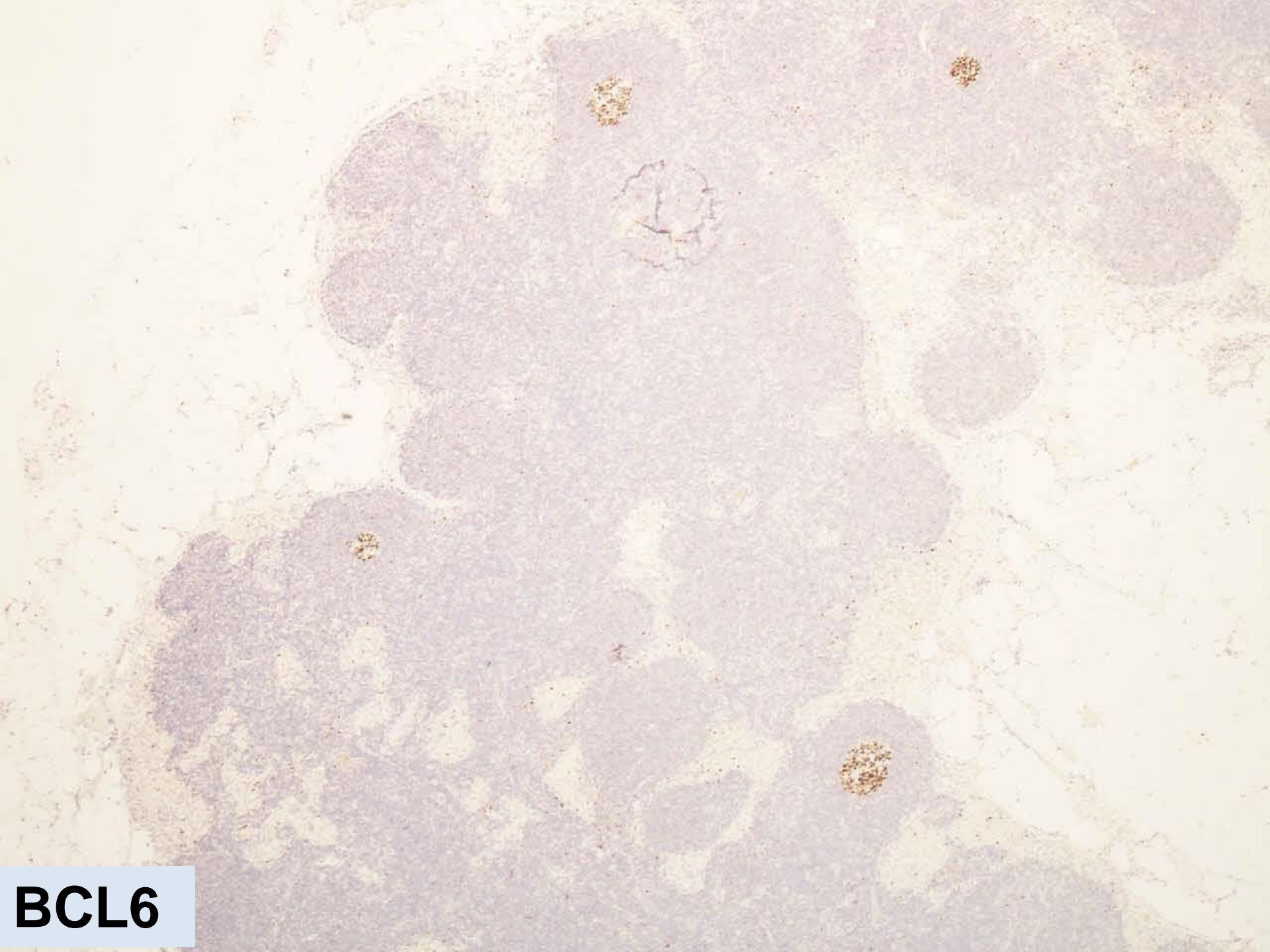
- Lymph node excision
- Slight enlargement
- ?lymphoma



BCL2



BCL2



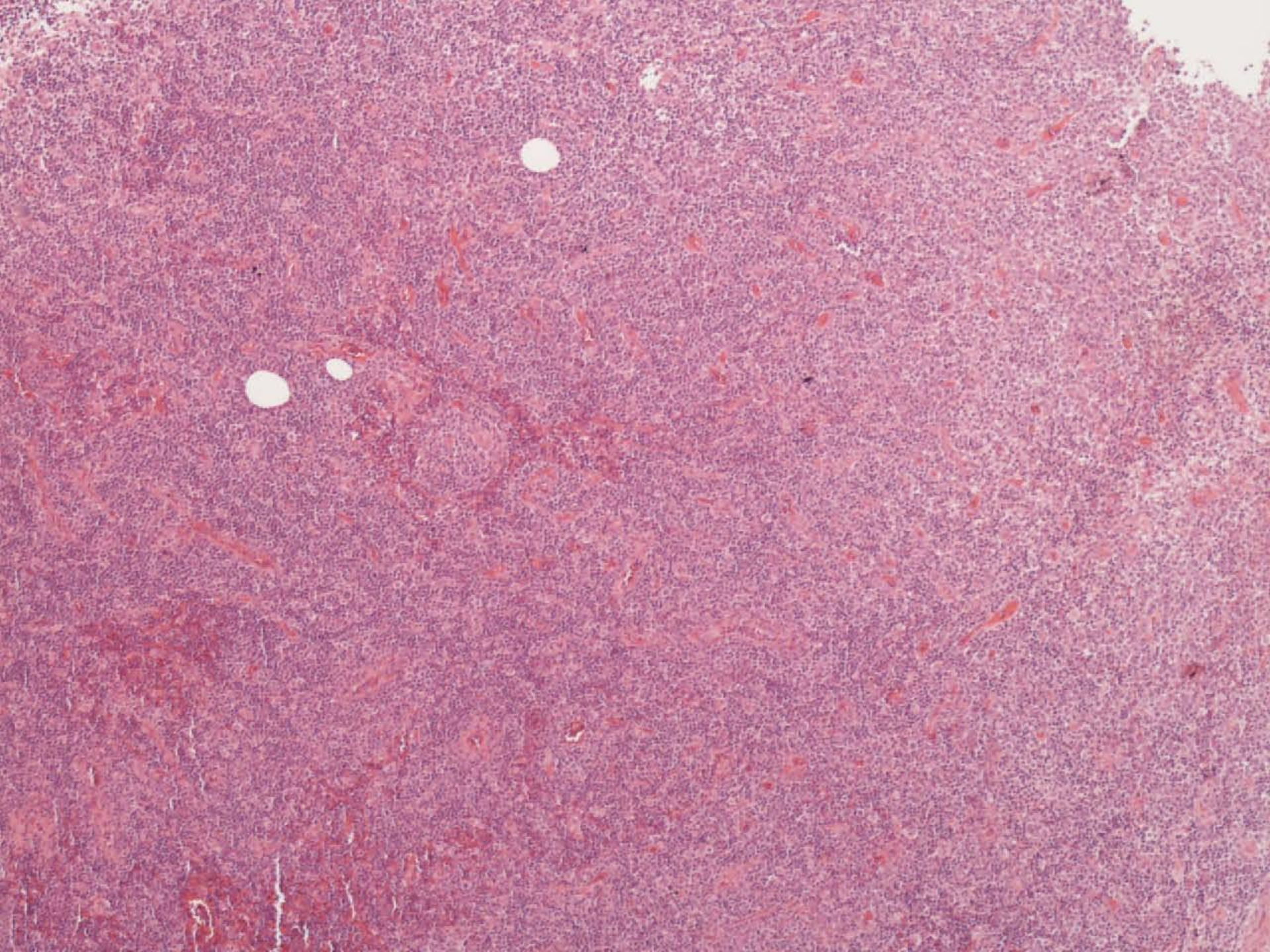
BCL6

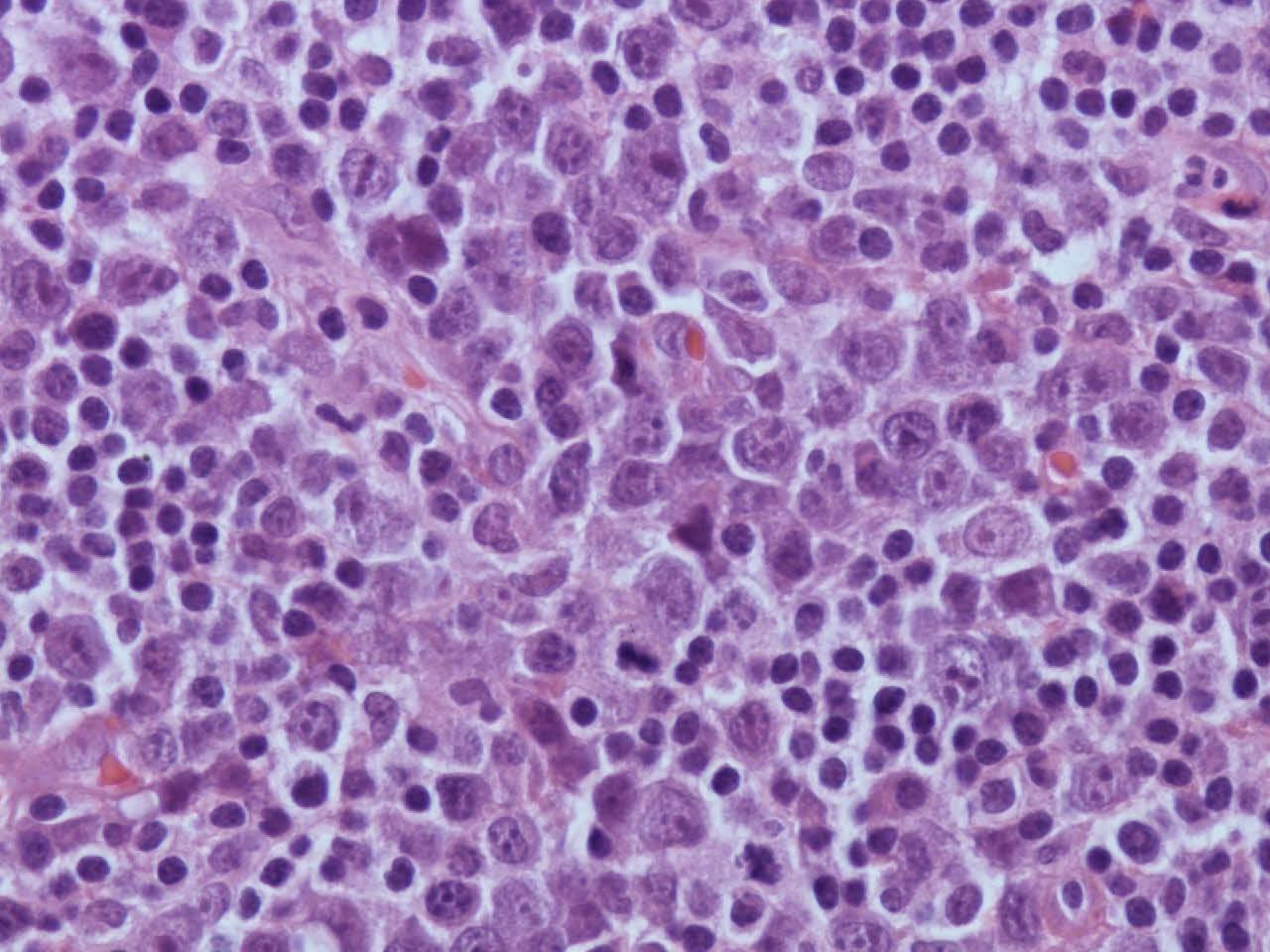
Case 1

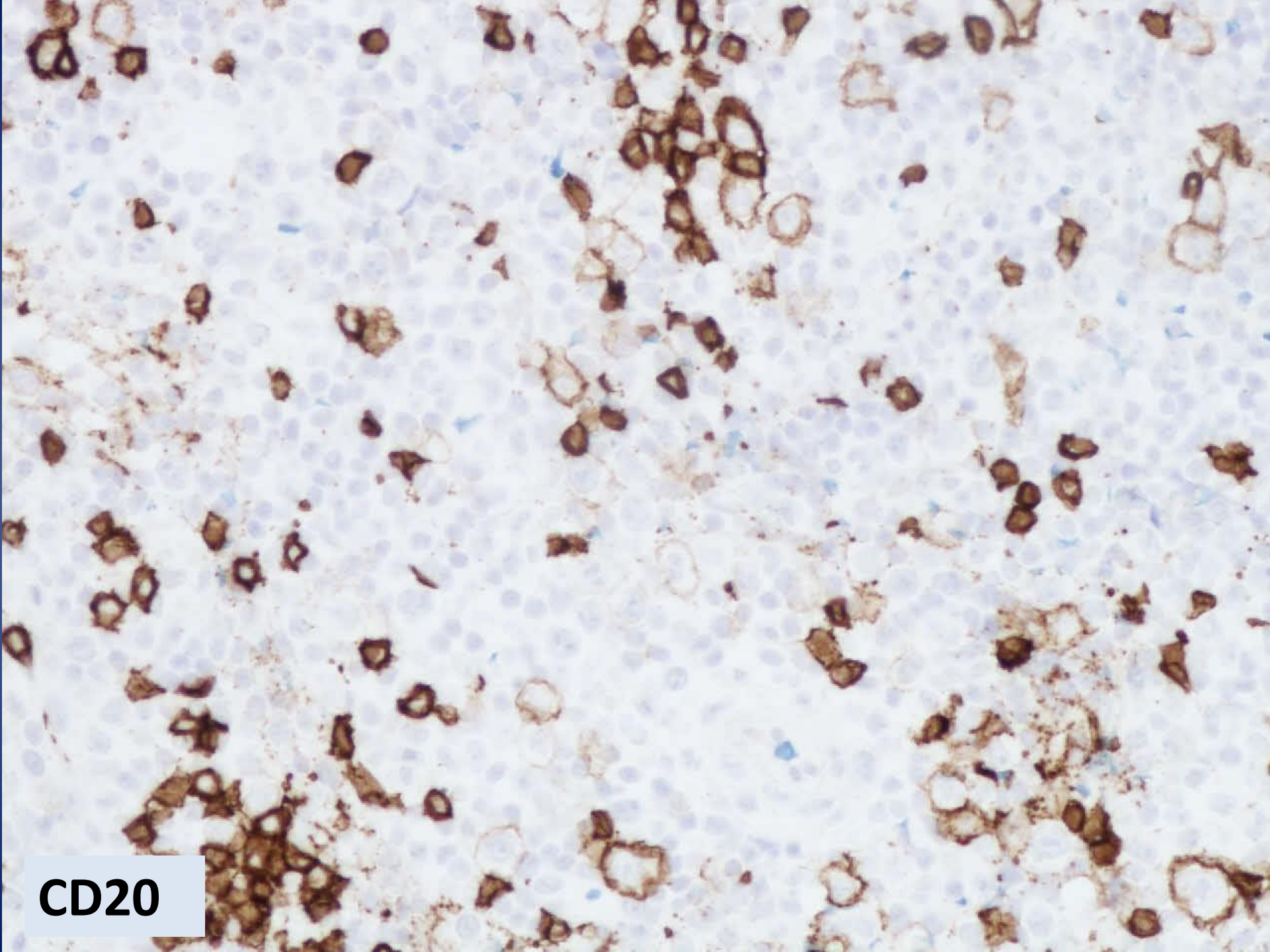
- Primary follicles in Lymph node
- Don't mistake bcl2+ primary follicles for neoplastic follicles
- Inadvertent dx of Malignancy in reactive node

Case 2

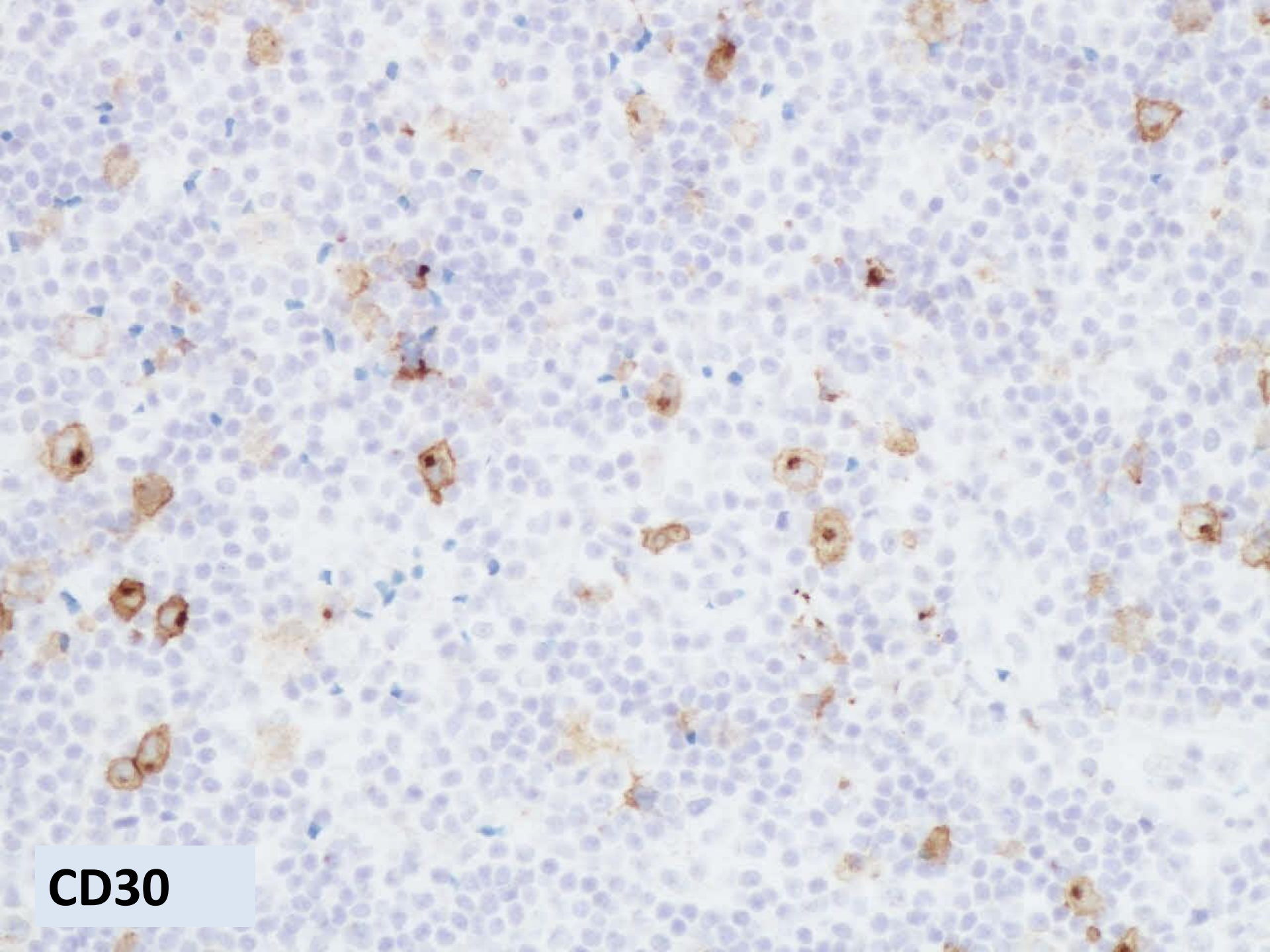
- Female 36
- ?femoral hernia
- Excision biopsy of groin lymph node







CD20



CD30



Kappa

This image shows a microscopic view of tissue stained for Kappa immunoglobulin. The tissue is densely populated with cells, many of which exhibit brown staining, indicating a positive result for Kappa chains. The background is a light blue/purple color, likely due to a counterstain like hematoxylin.



Lambda

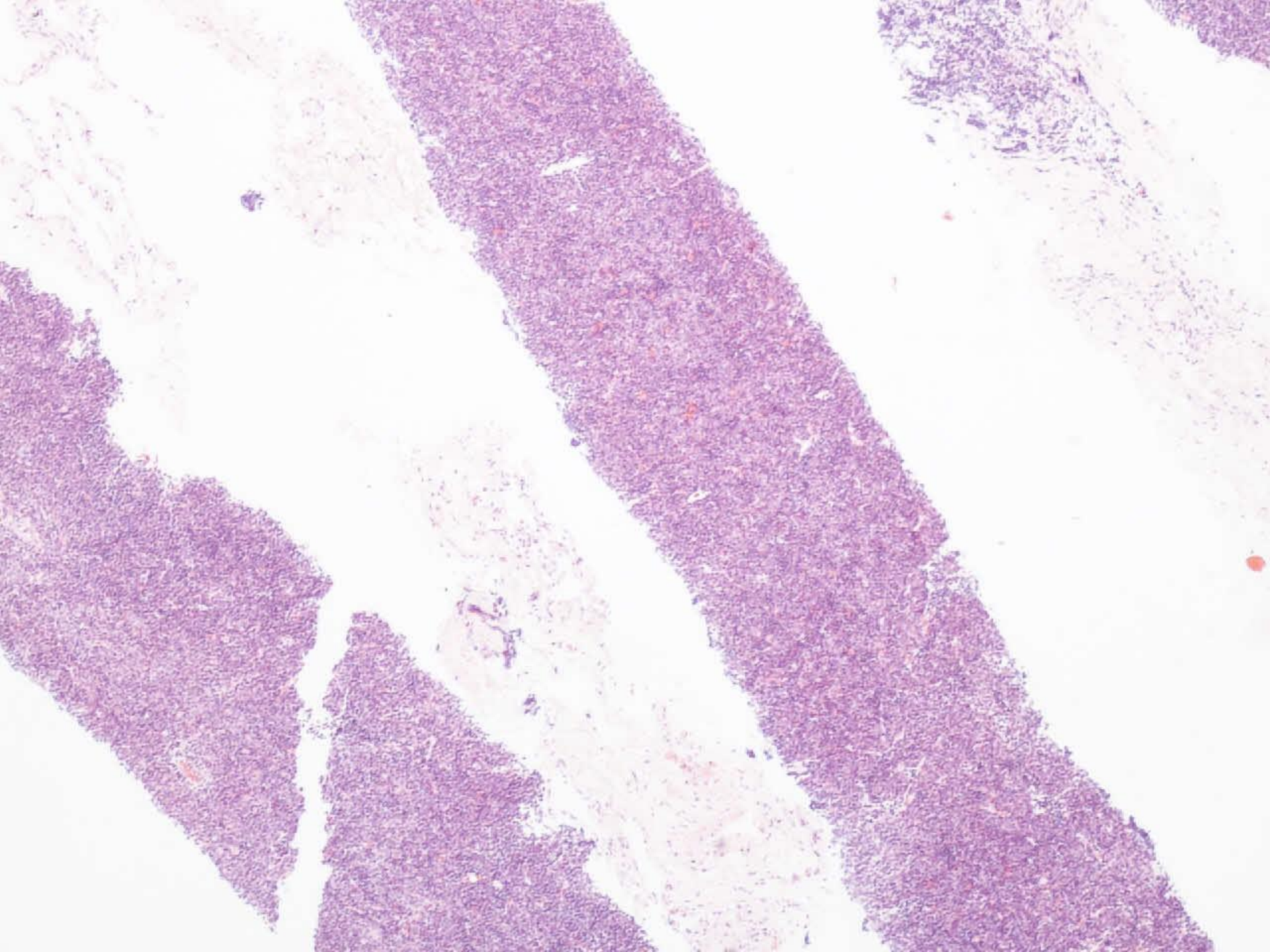
This image shows a microscopic view of tissue stained for Lambda immunoglobulin. The tissue is densely populated with cells, many of which exhibit brown staining, indicating a positive result for Lambda chains. The background is a light blue/purple color, likely due to a counterstain like hematoxylin.

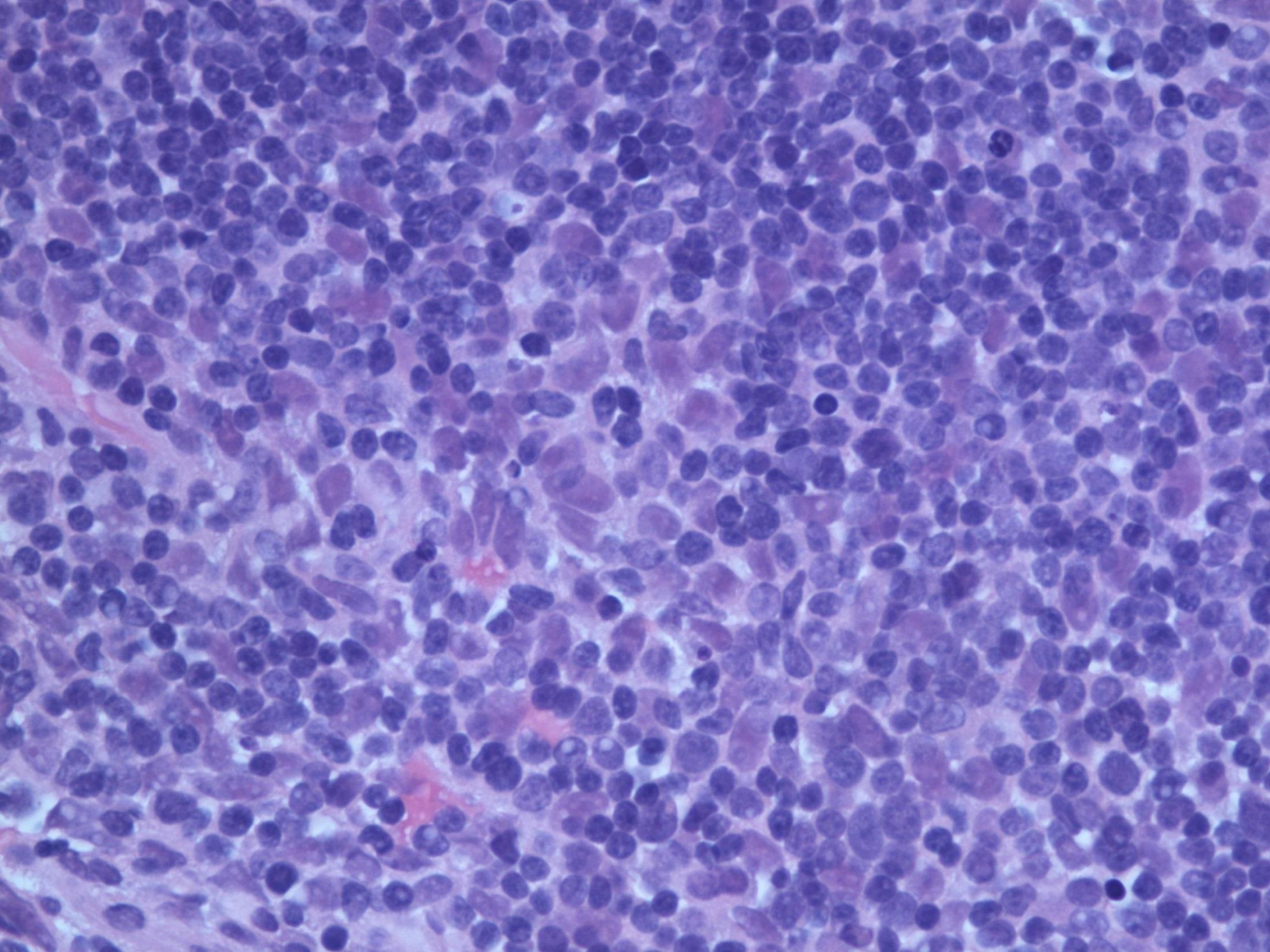
Immunoblastic reaction

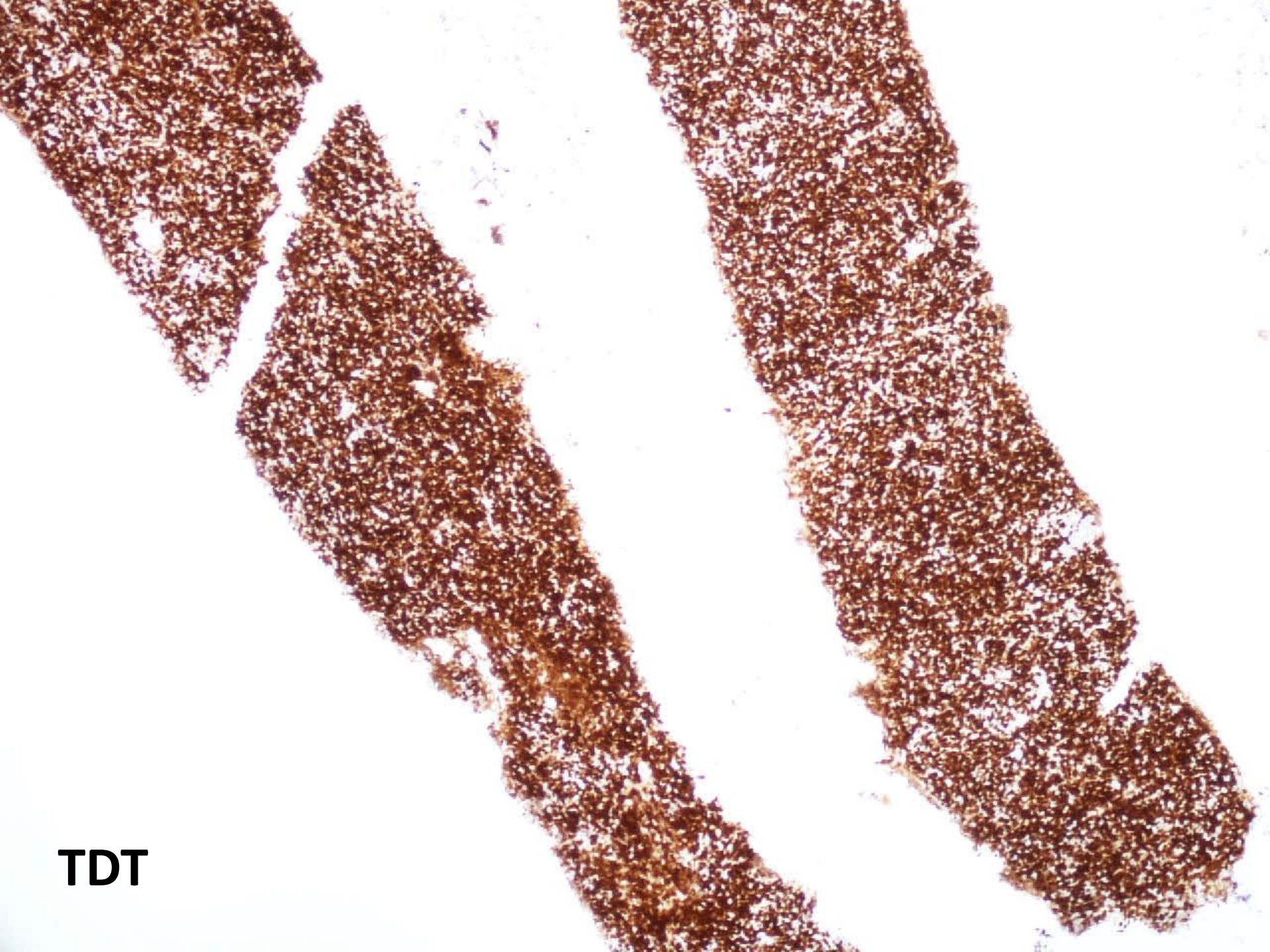
- Highly pleomorphic immunoblasts may resemble Reed Sternberg cells or ALCL
- They are strongly positive for CD30
- Negative for CD15
- Usually positive for CD20 and light chain
- **Inadvertent diagnosis of classical Hodgkin Lymphoma in reactive node**

Case 3 Mediastinal Mass F 28y/o

- ?Lymphoma







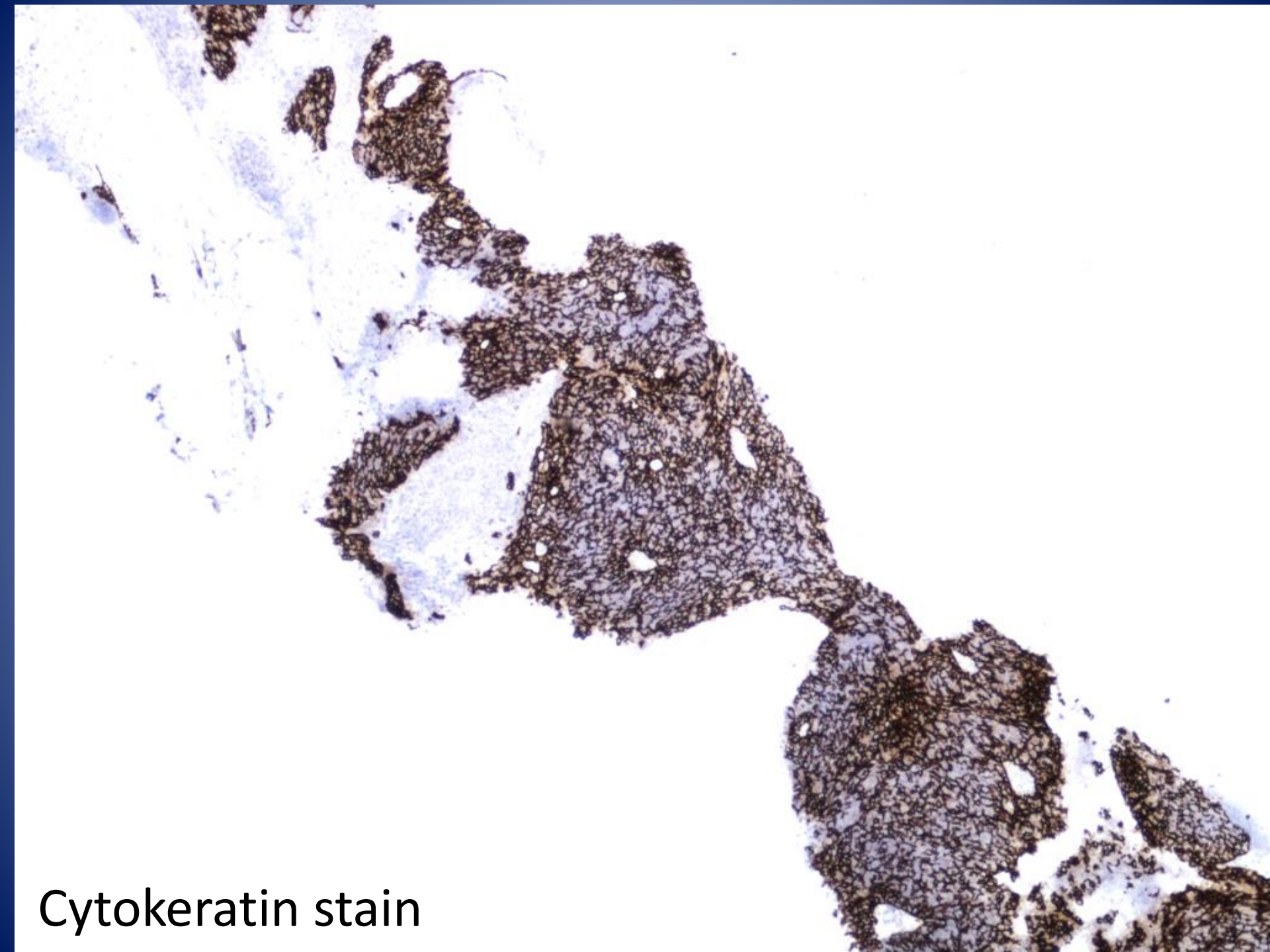
TDT

CD3

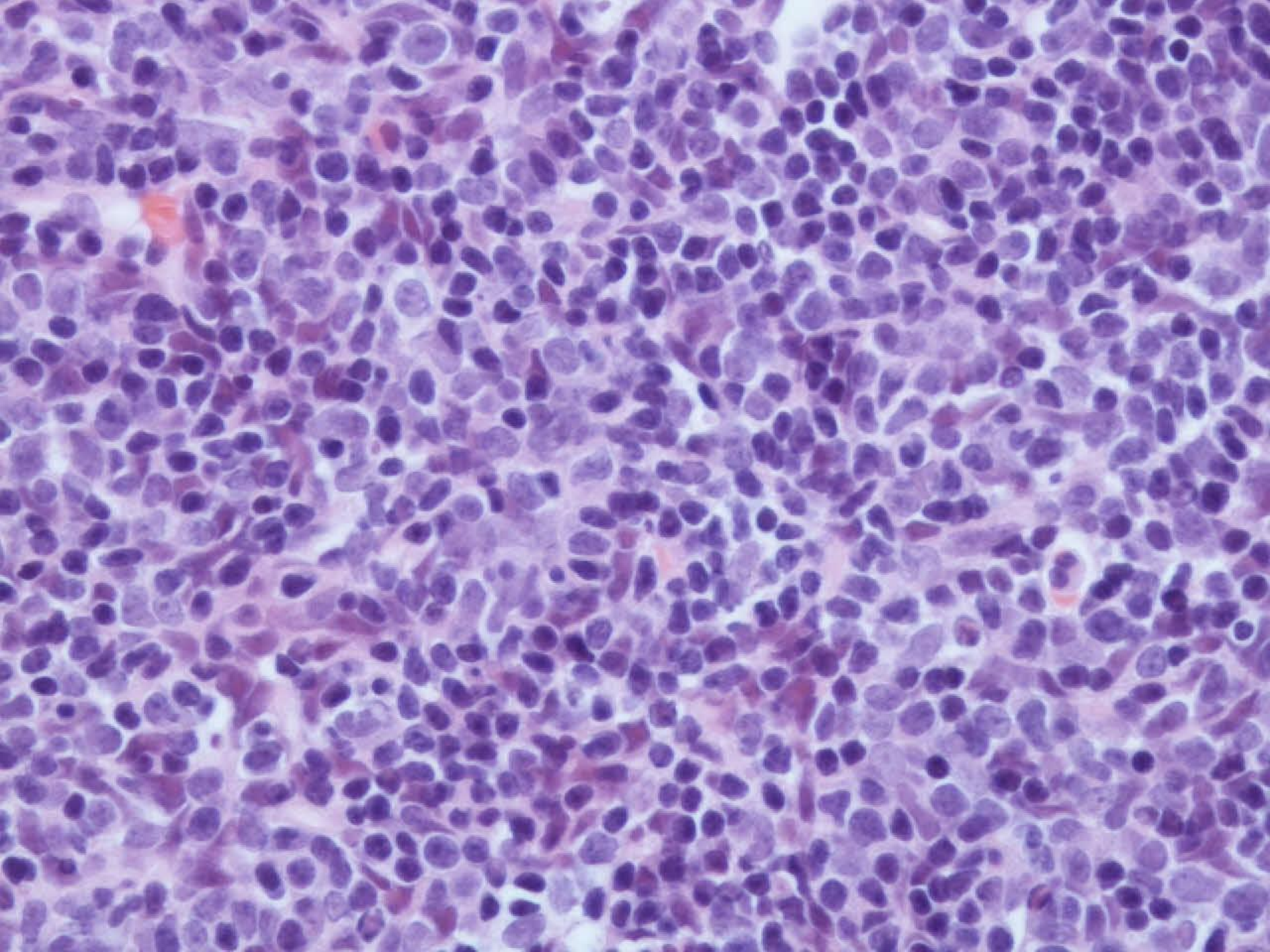


Diagnosis

- T cell Acute Lymphoblastic Lymphoma.



Cytokeratin stain

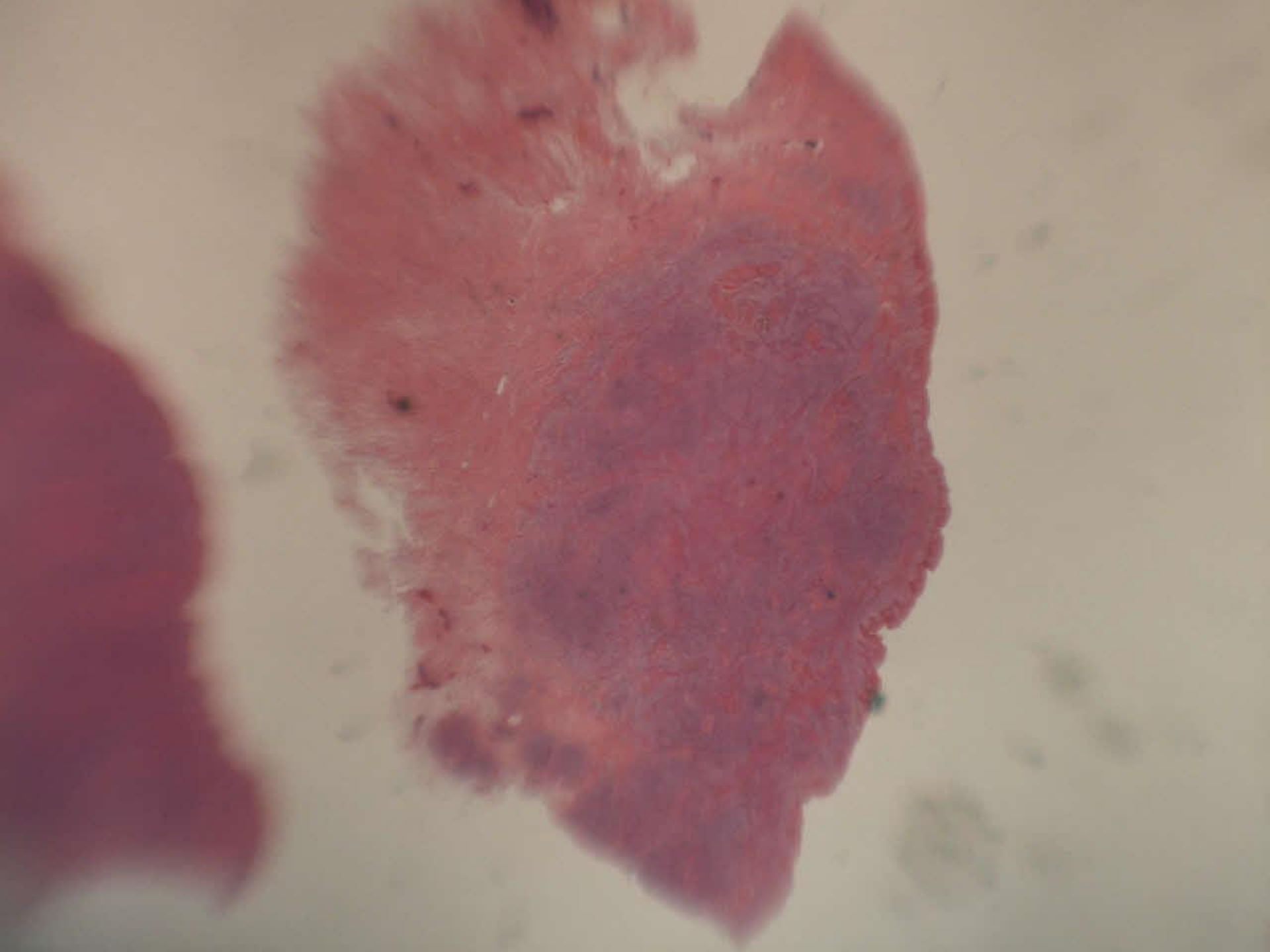


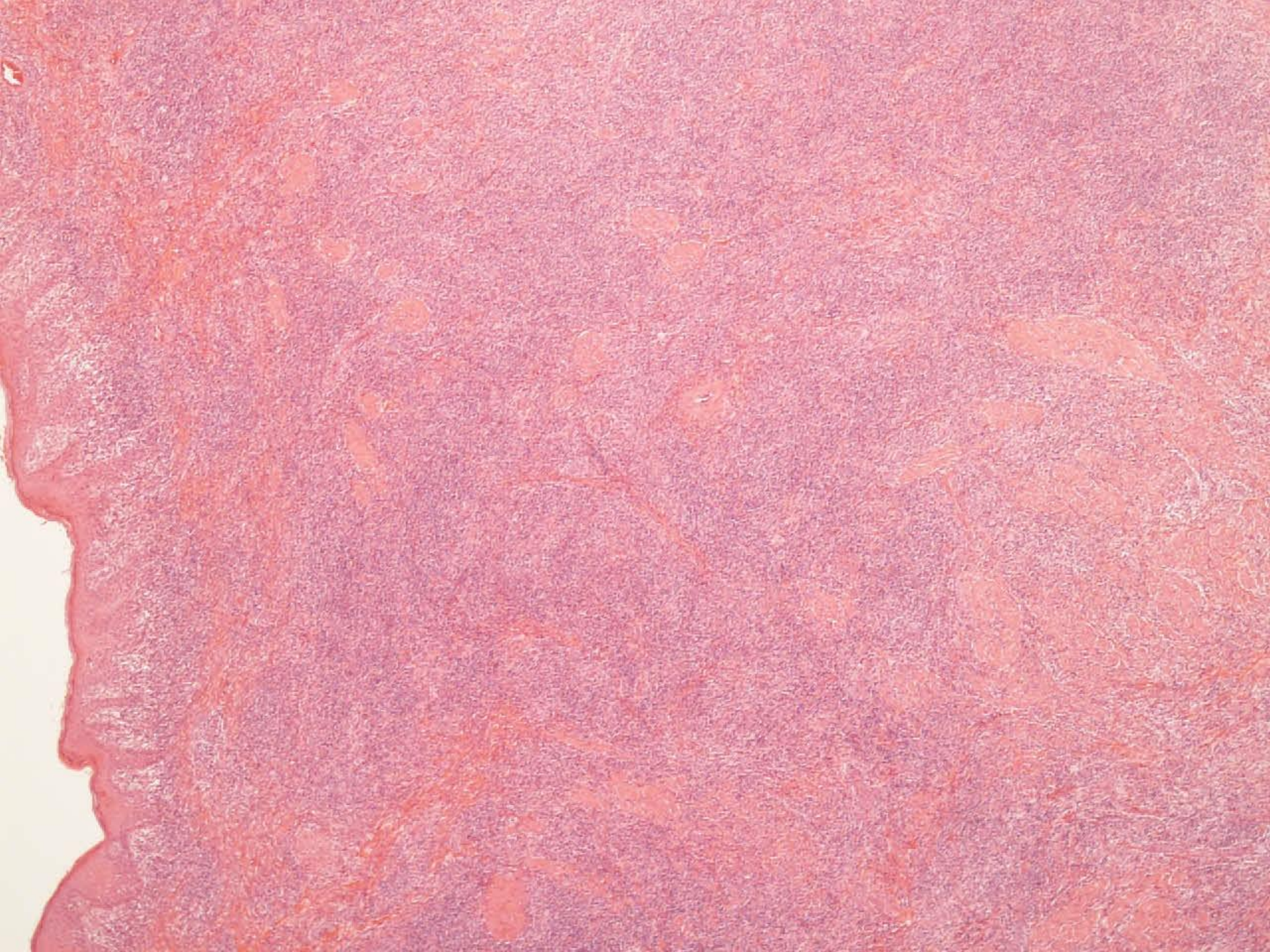
Final diagnosis Thymoma B1

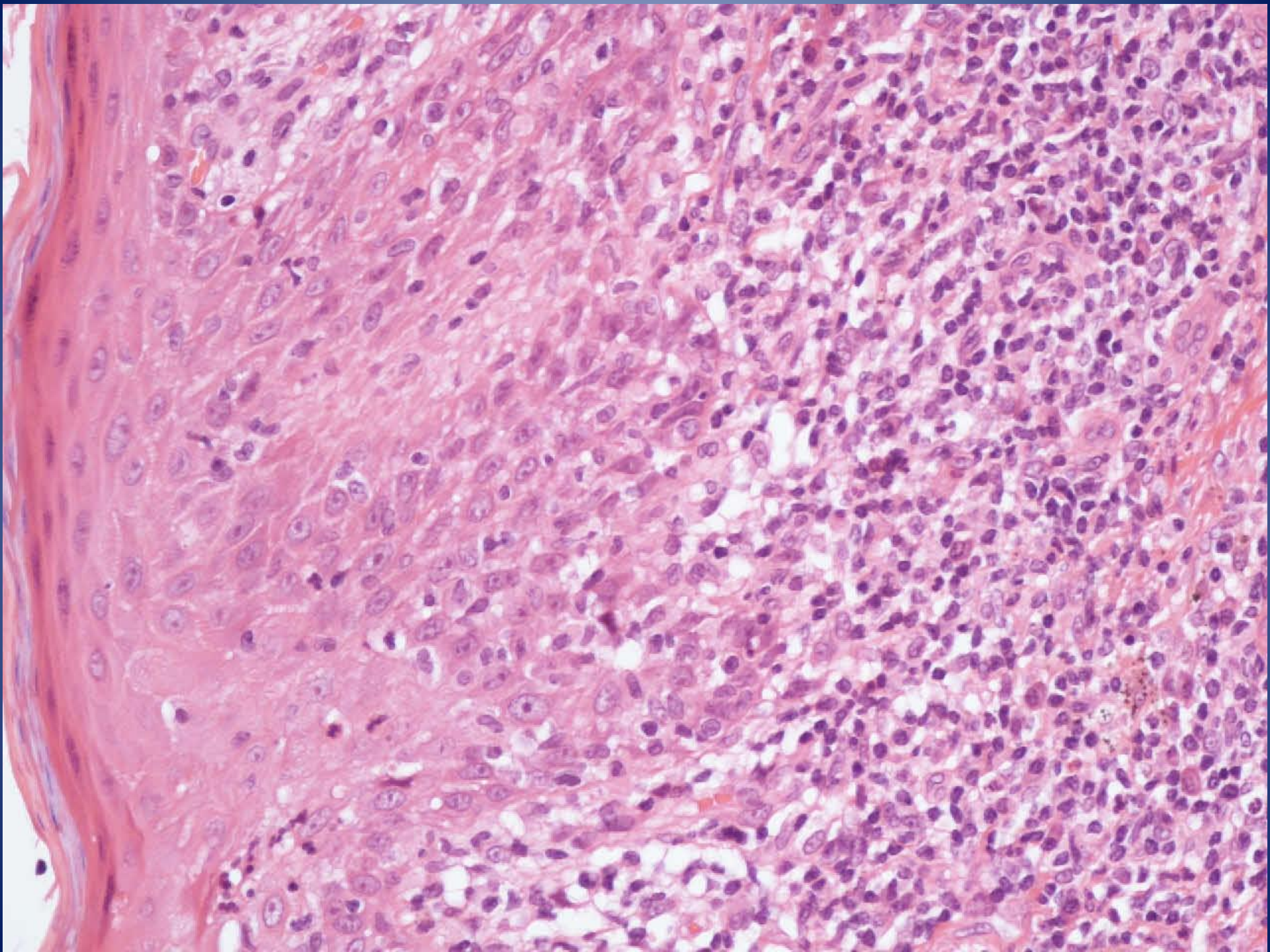
- Do not mistake thymoma for T lymphoblastic leukaemia
- Always do a cytokeratin stain in mediastinal biopsies.
- Inappropriate dx of malignancy in benign condition

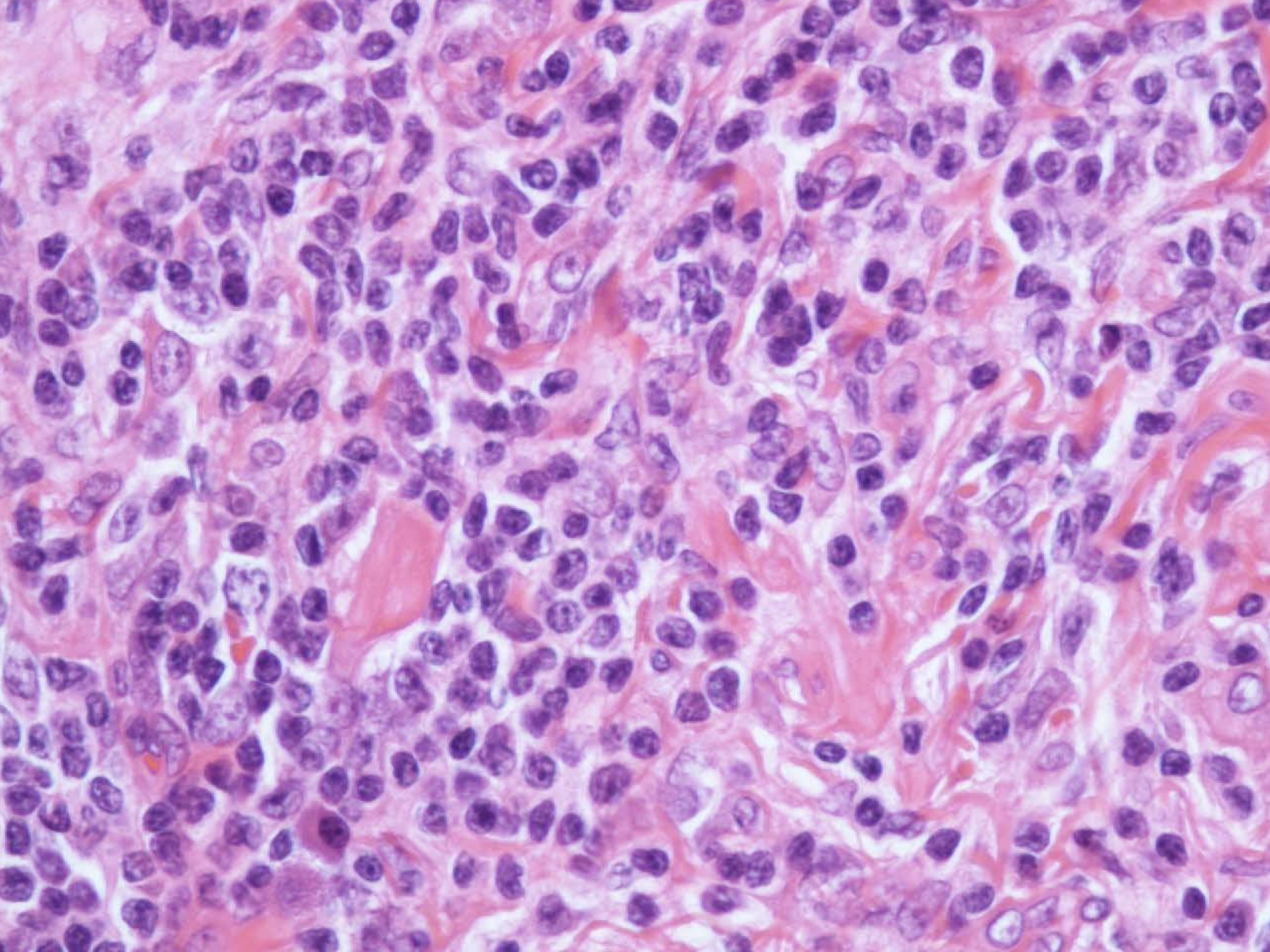
Case 4

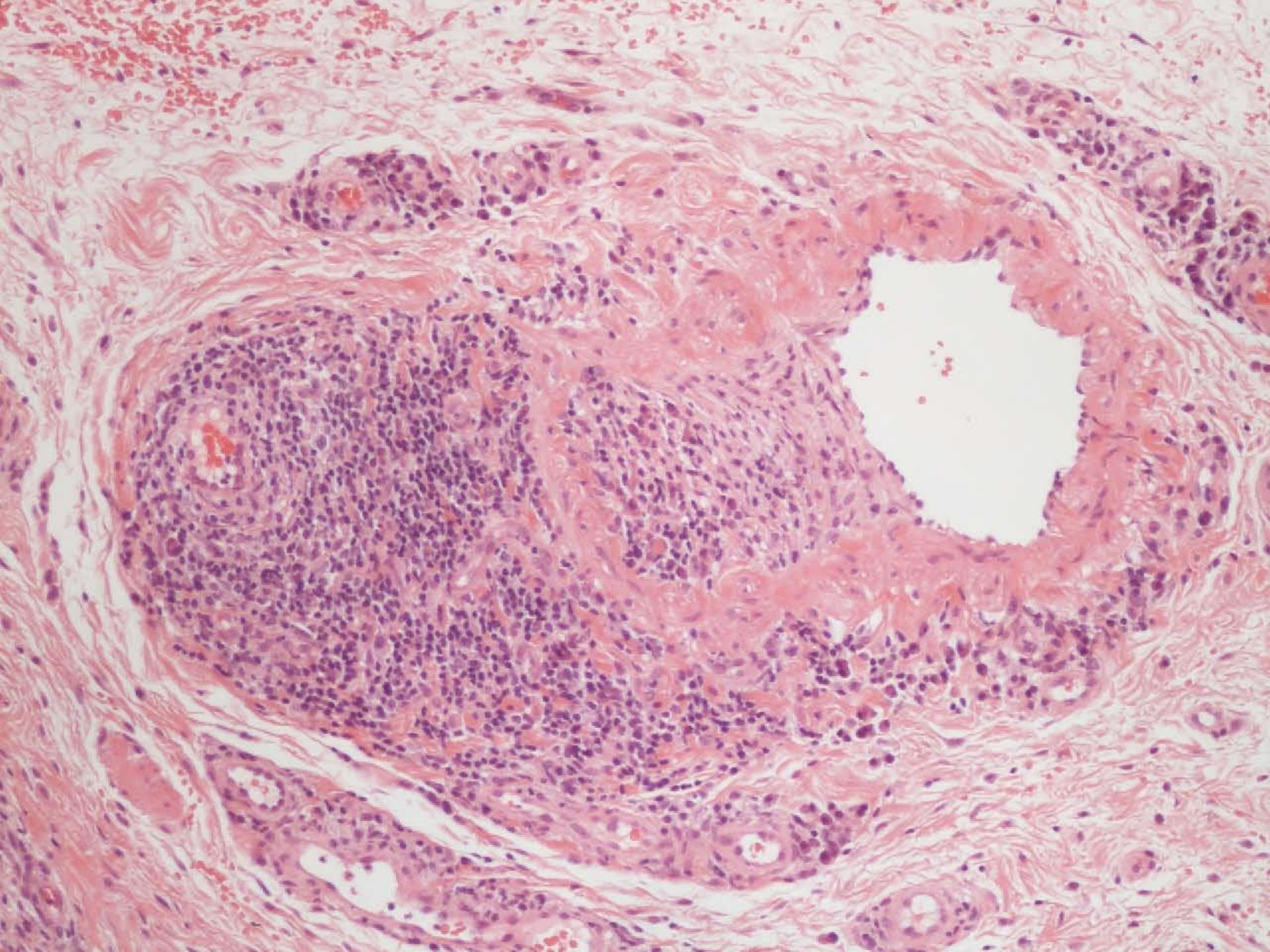
- Male 52
- 2cm red lump on penis for 6 weeks
- referred to Urologist
- Incisional biopsy taken(very generous)

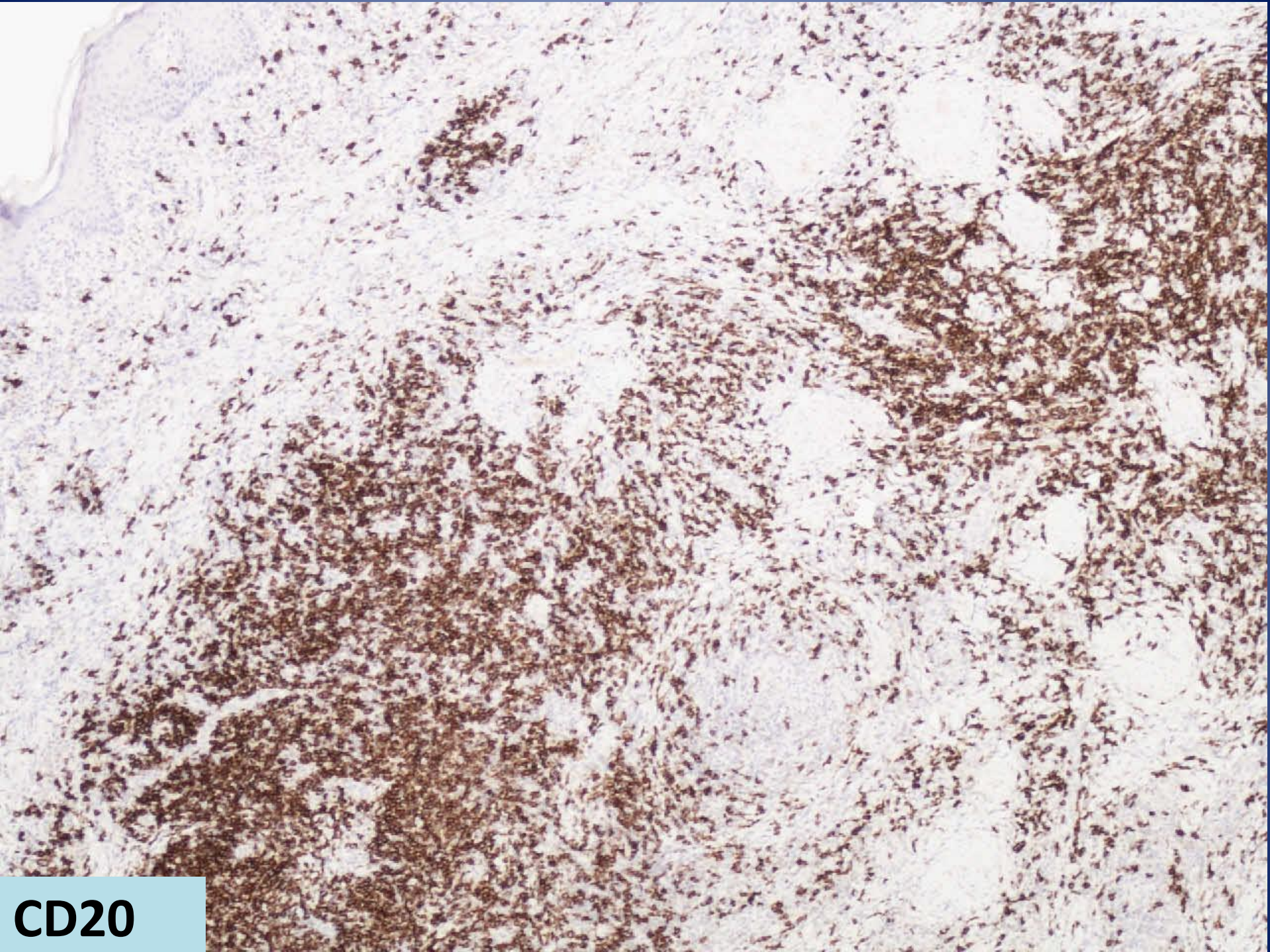




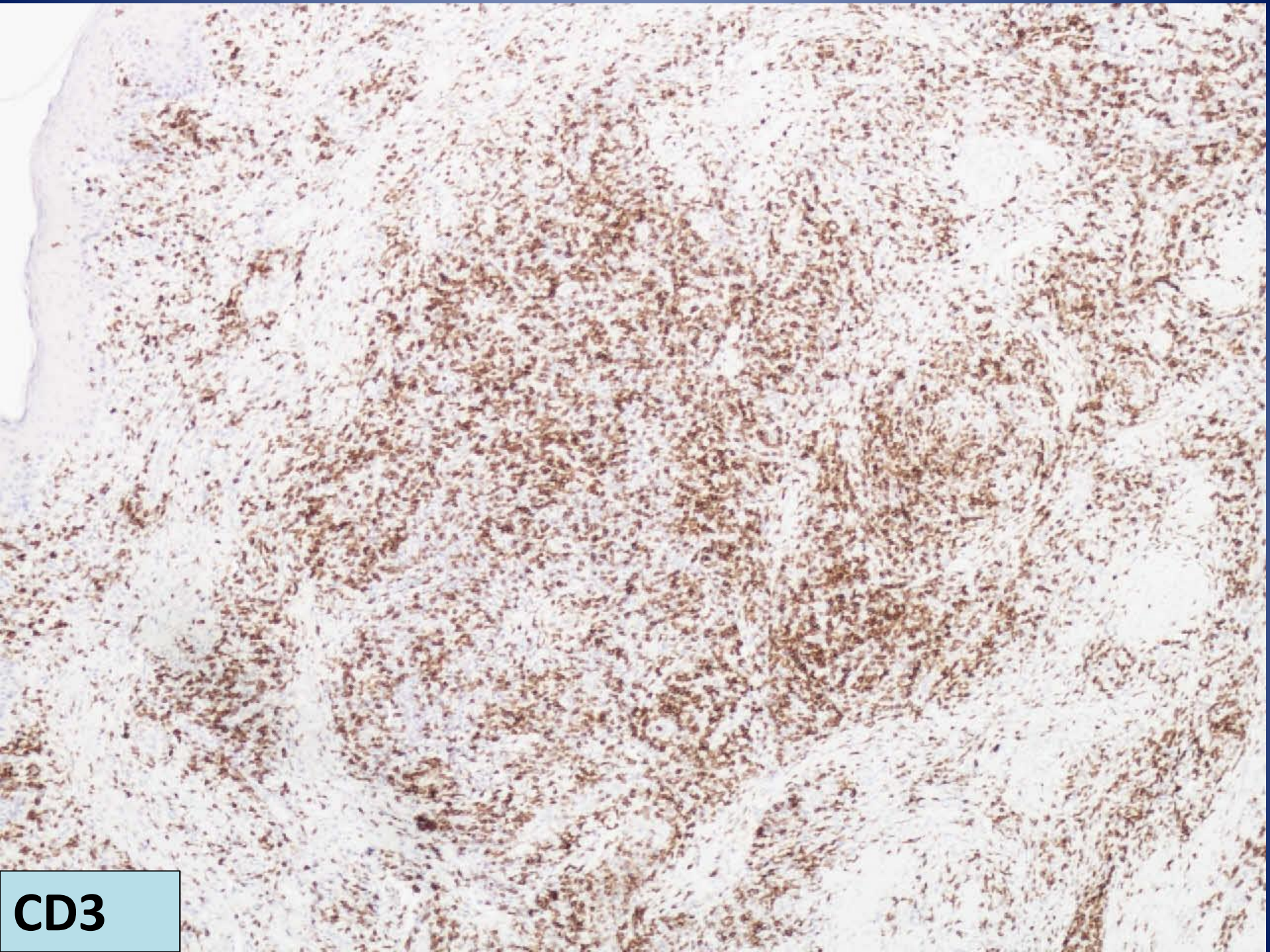








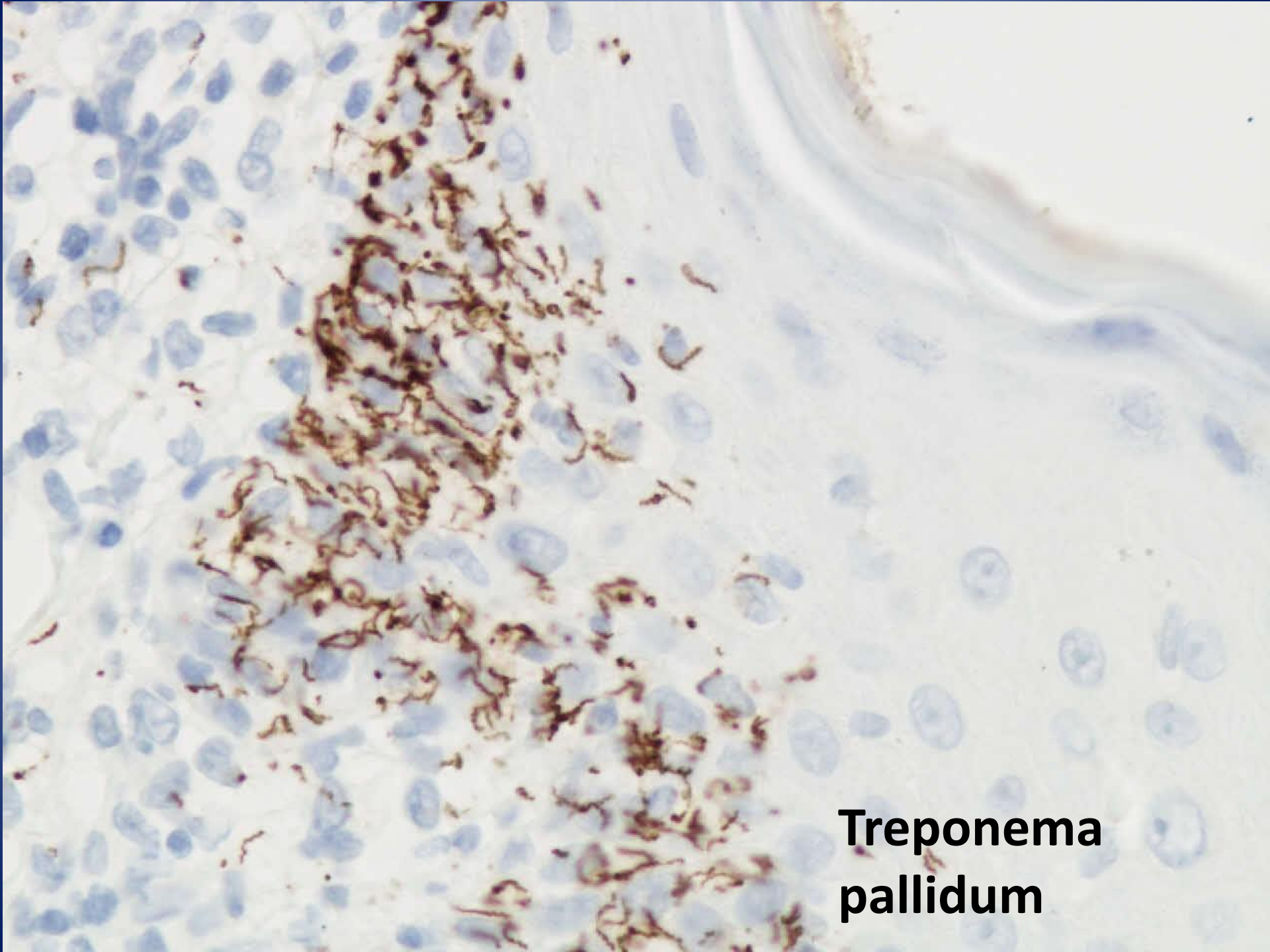
CD20



CD3

Diagnosis

- B cell lymphoma
- T cell Lymphoma
- Pseudolymphoma



**Treponema
pallidum**

Final diagnosis

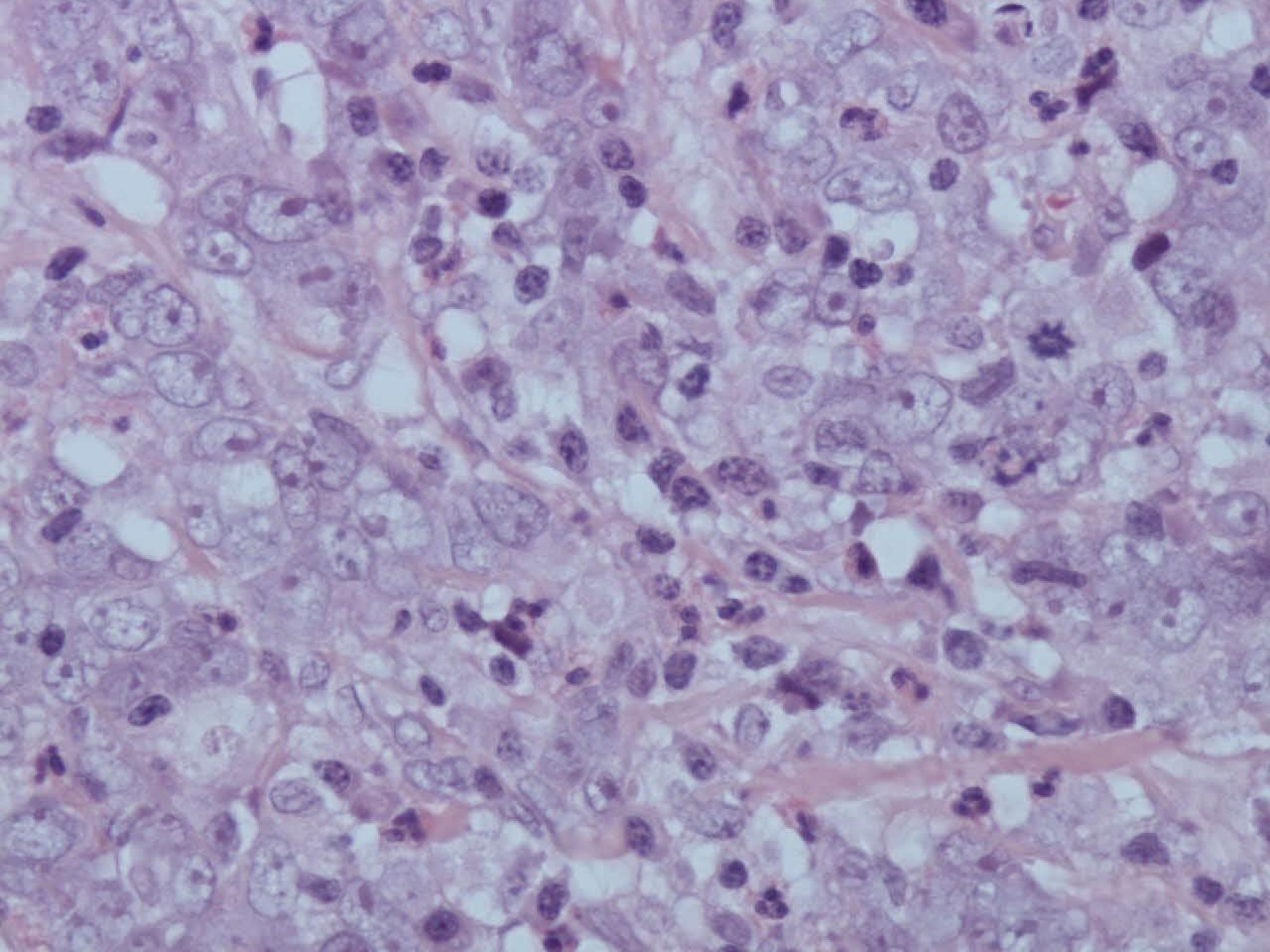
- Syphilis – secondary
- The great mimicker!
- *Borrellia Burgdorferi* can cause lymphocytic infiltrates in skin –both lymphoma and pseudolymphoma

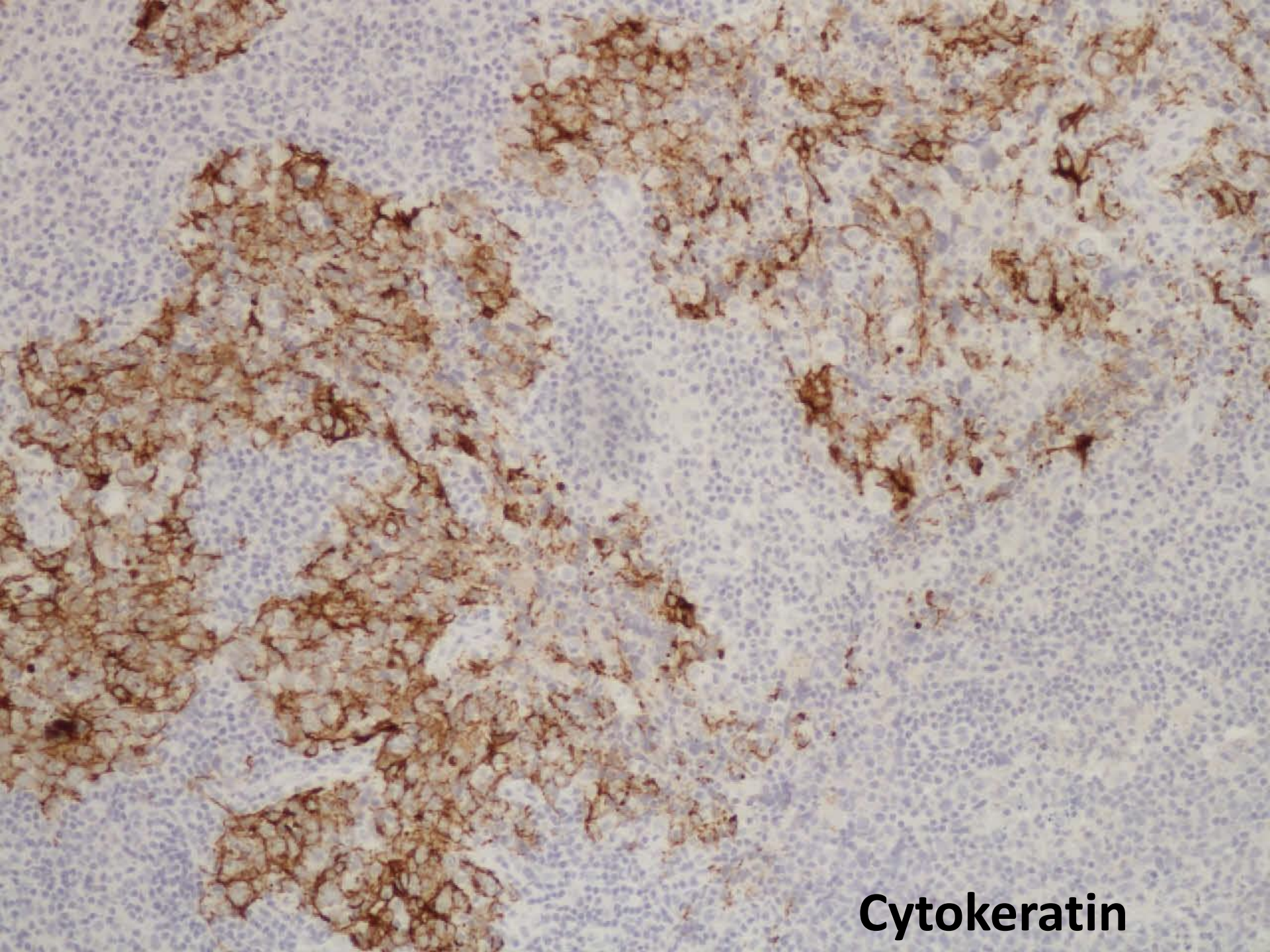
Reactive lesions misdiagnosed as lymphoma

- Immunoblastic reaction
- Kikuchi
- Inf Mono
- Pseudolymphoma
 - Borrelia (Tick bite)
 - Syphilis, Lymphogranuloma venereum
 - Drug reaction
 - Tattoo reaction
 - Vaccination reaction
 - Actinic reticuloid

Case 5

- Male 36
- L node enlarged in cervical region





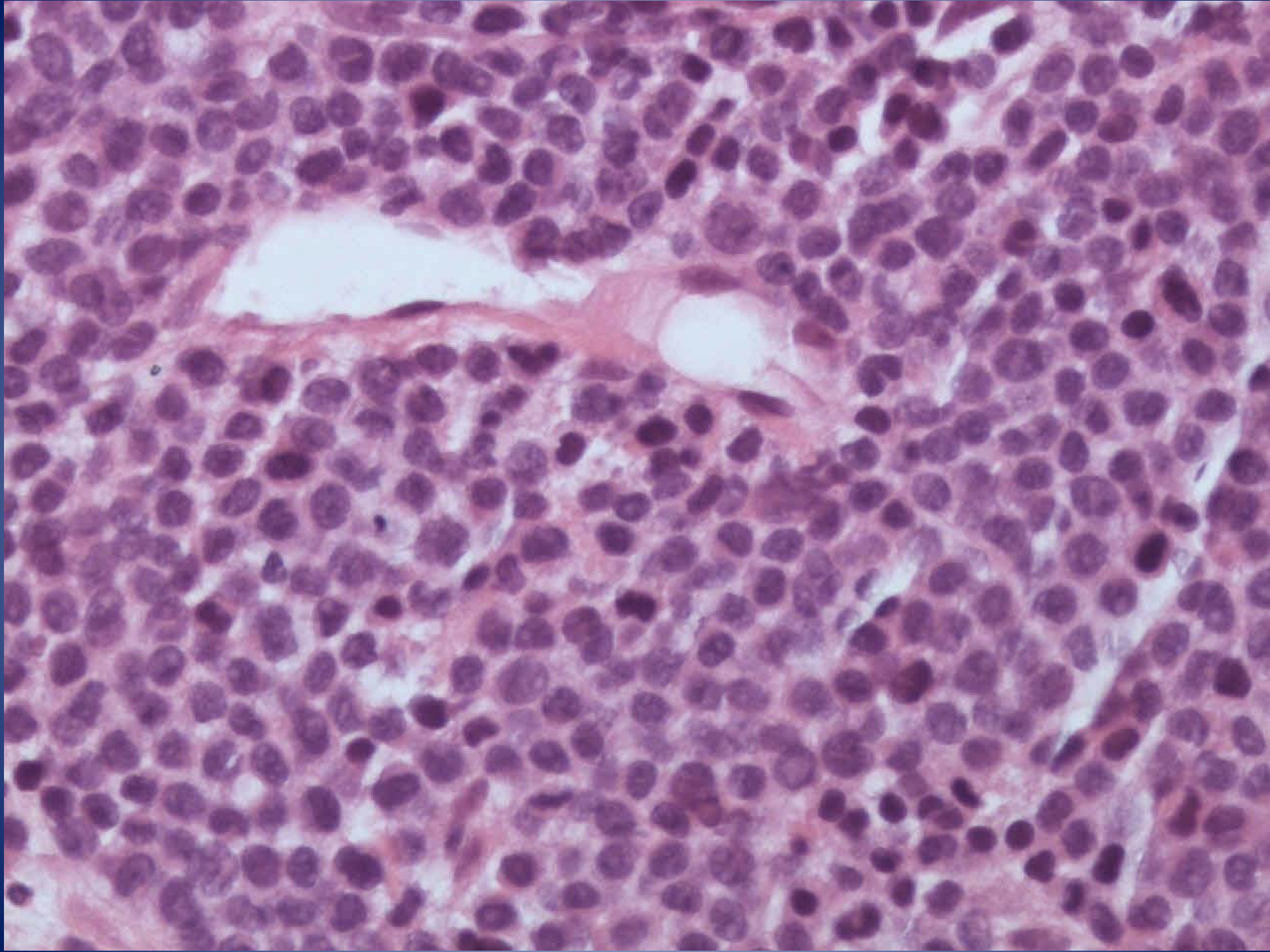
Cytokeratin

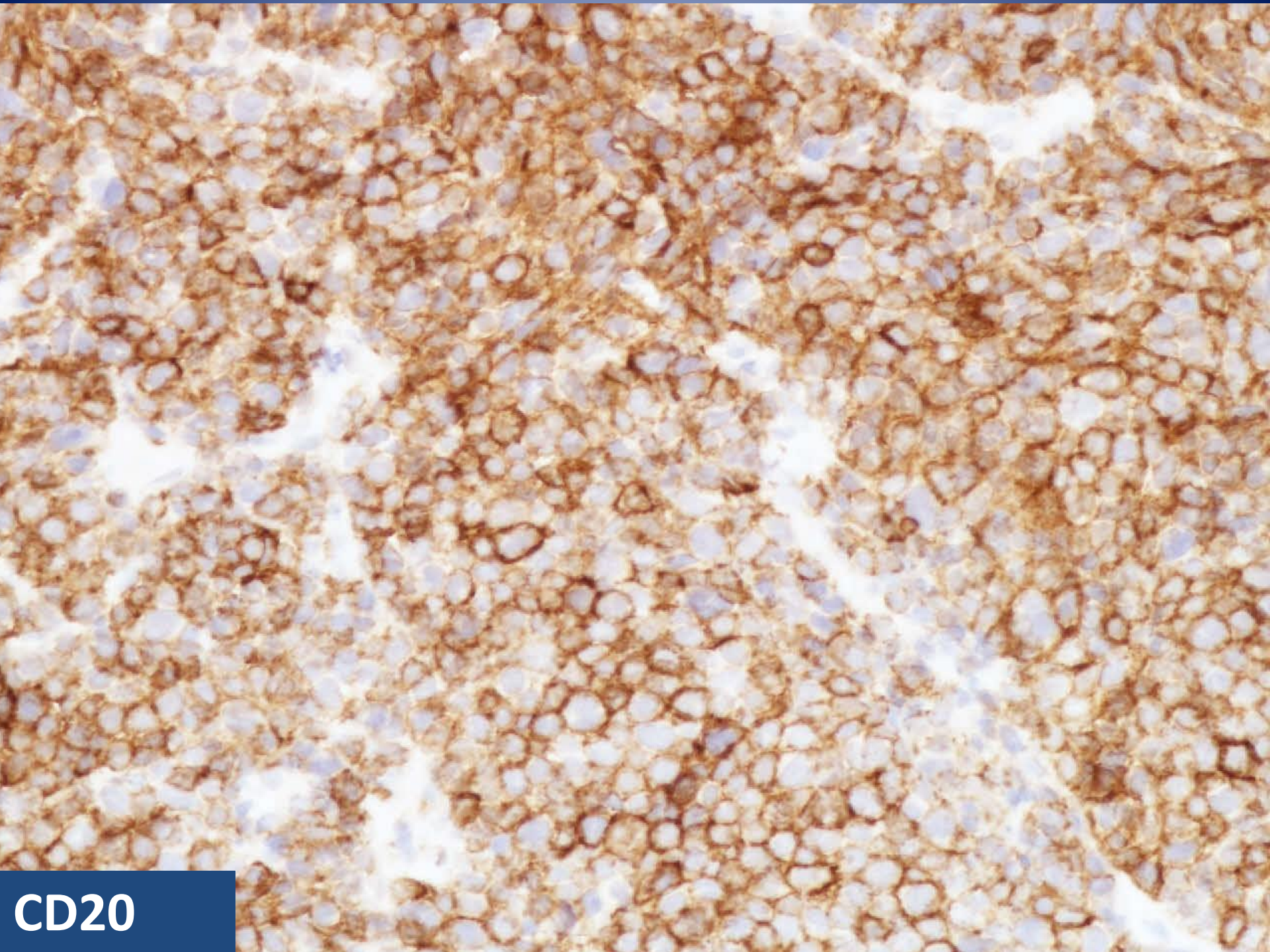
Diagnosis

- Metastatic Nasopharyngeal carcinoma
- Urgent request for diagnosis based on H&E may result in incorrect initial diagnosis!!
- And visa versa – Called Carcinoma when it is Lymphoma

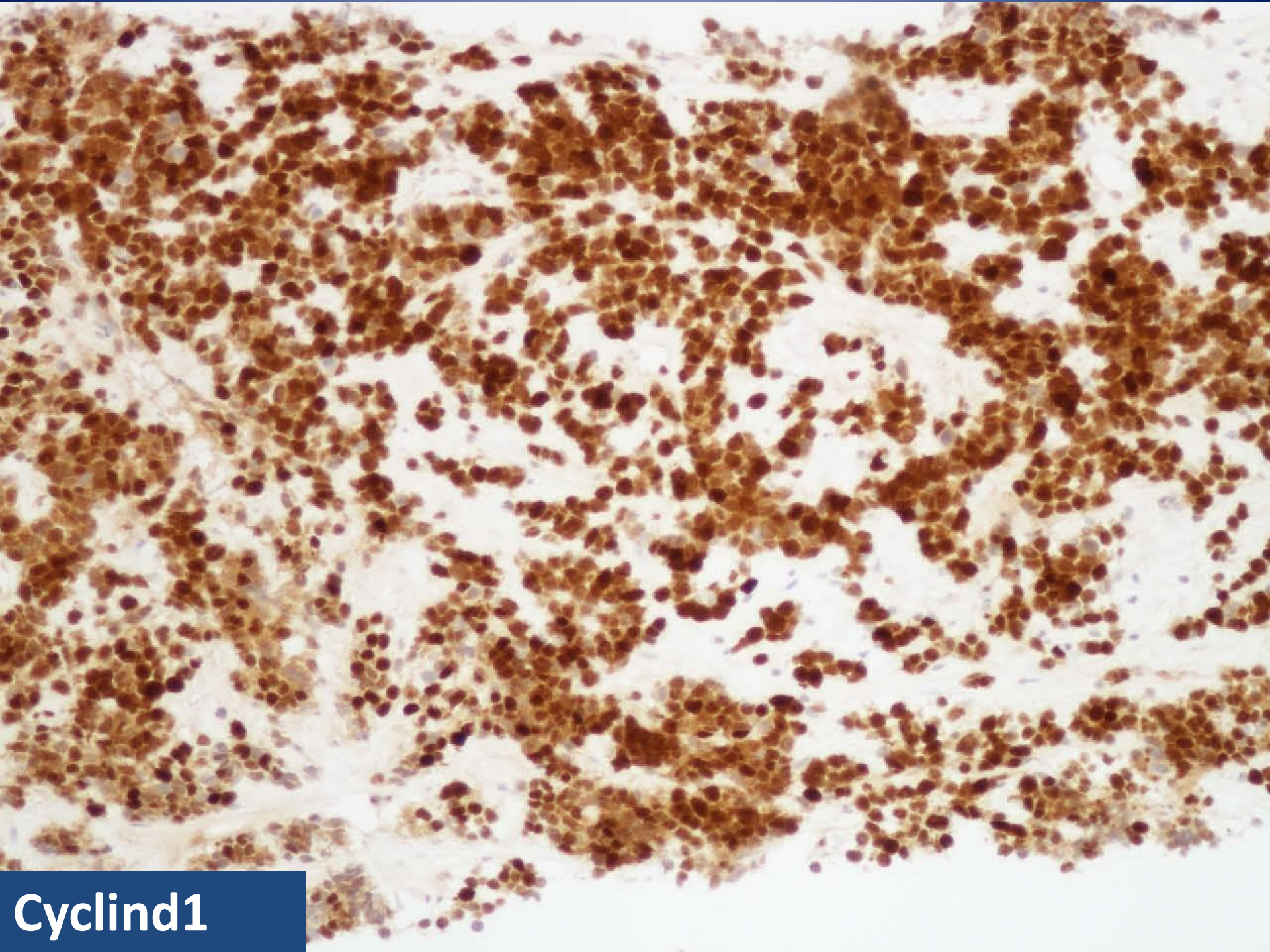
Case 6

- 67 y/o female
- Nasopharyngeal mass





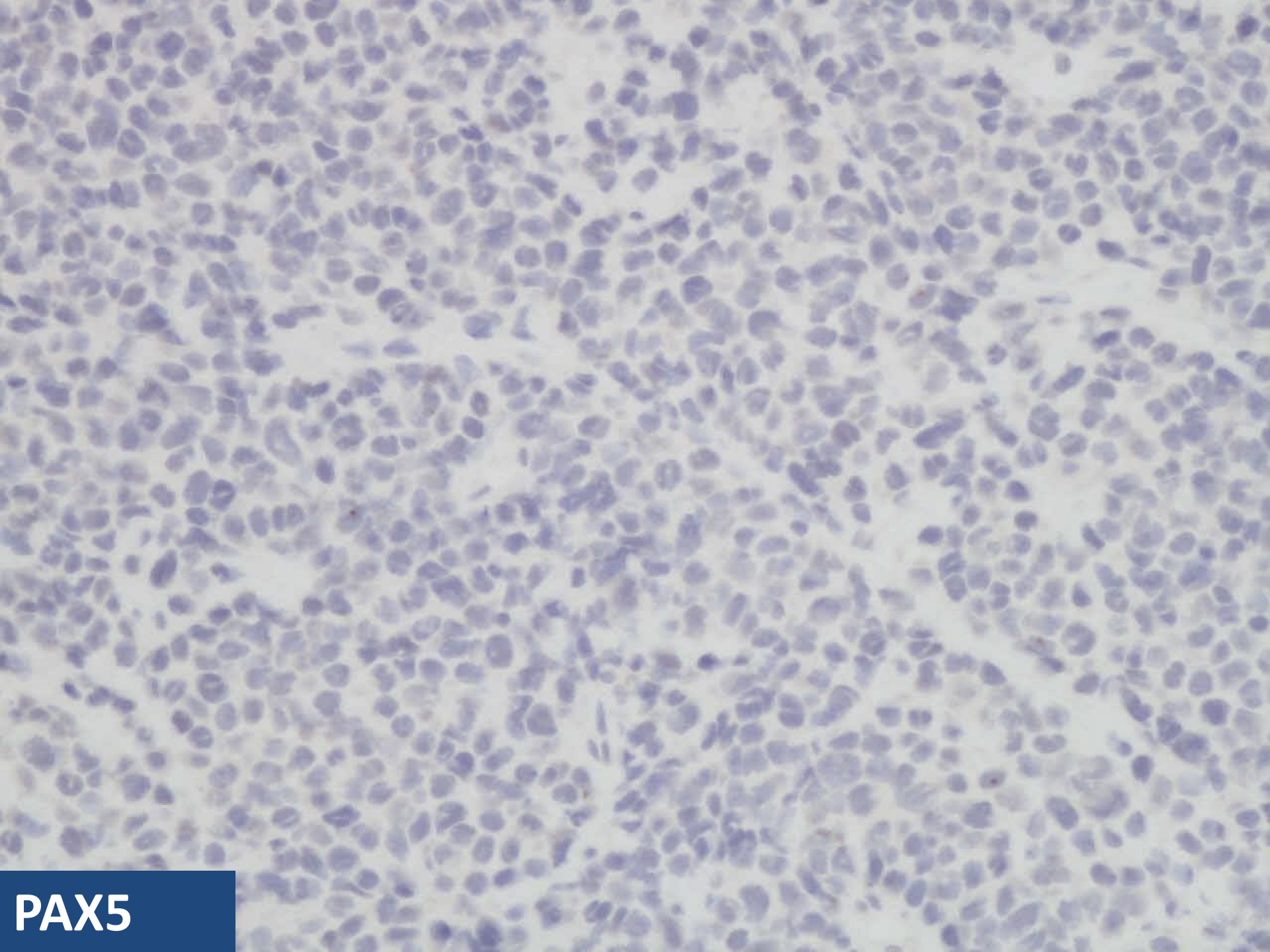
CD20



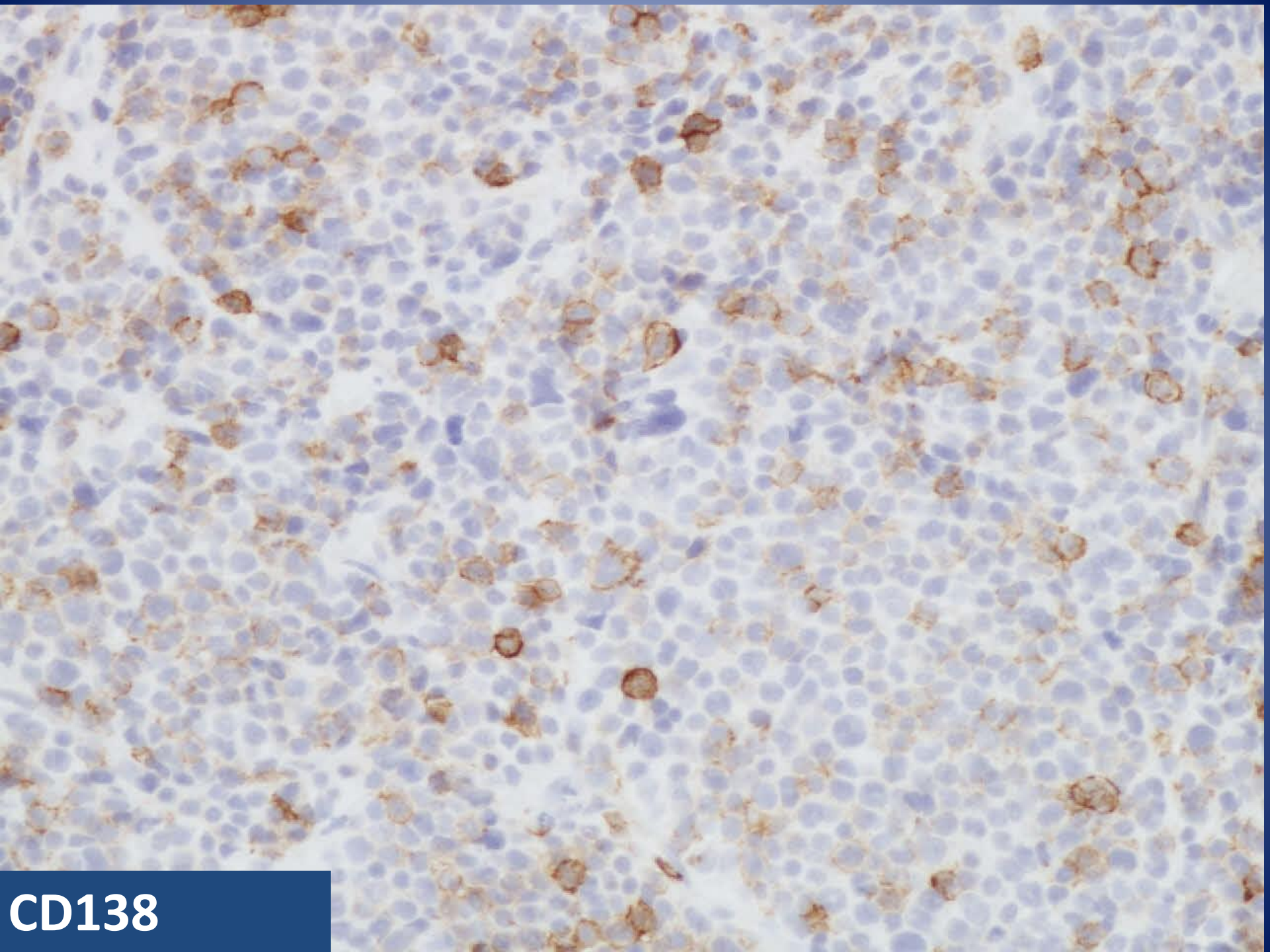
Cyclind1

Diagnosis

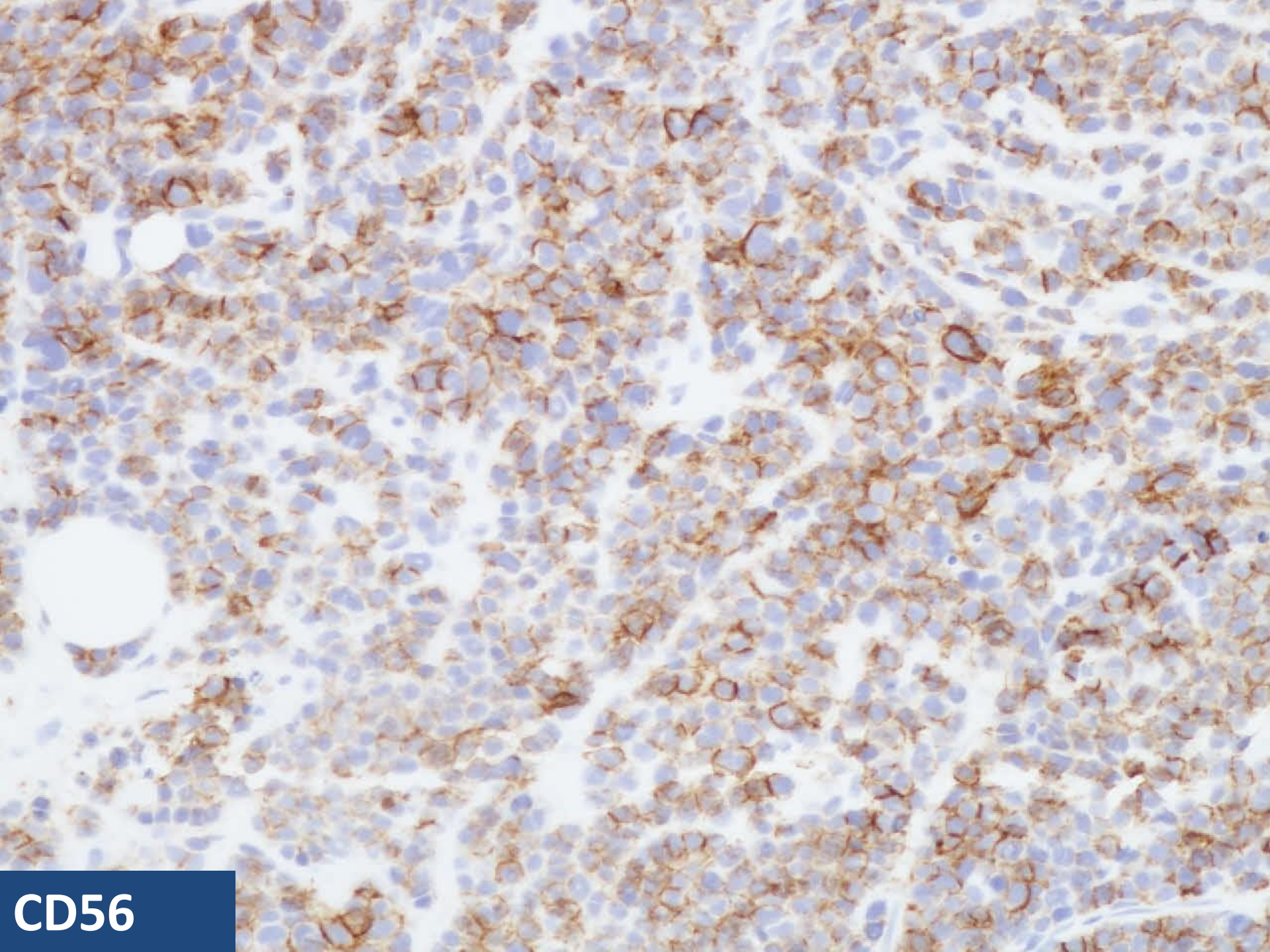
- Mantle Cell Lymphoma



PAX5



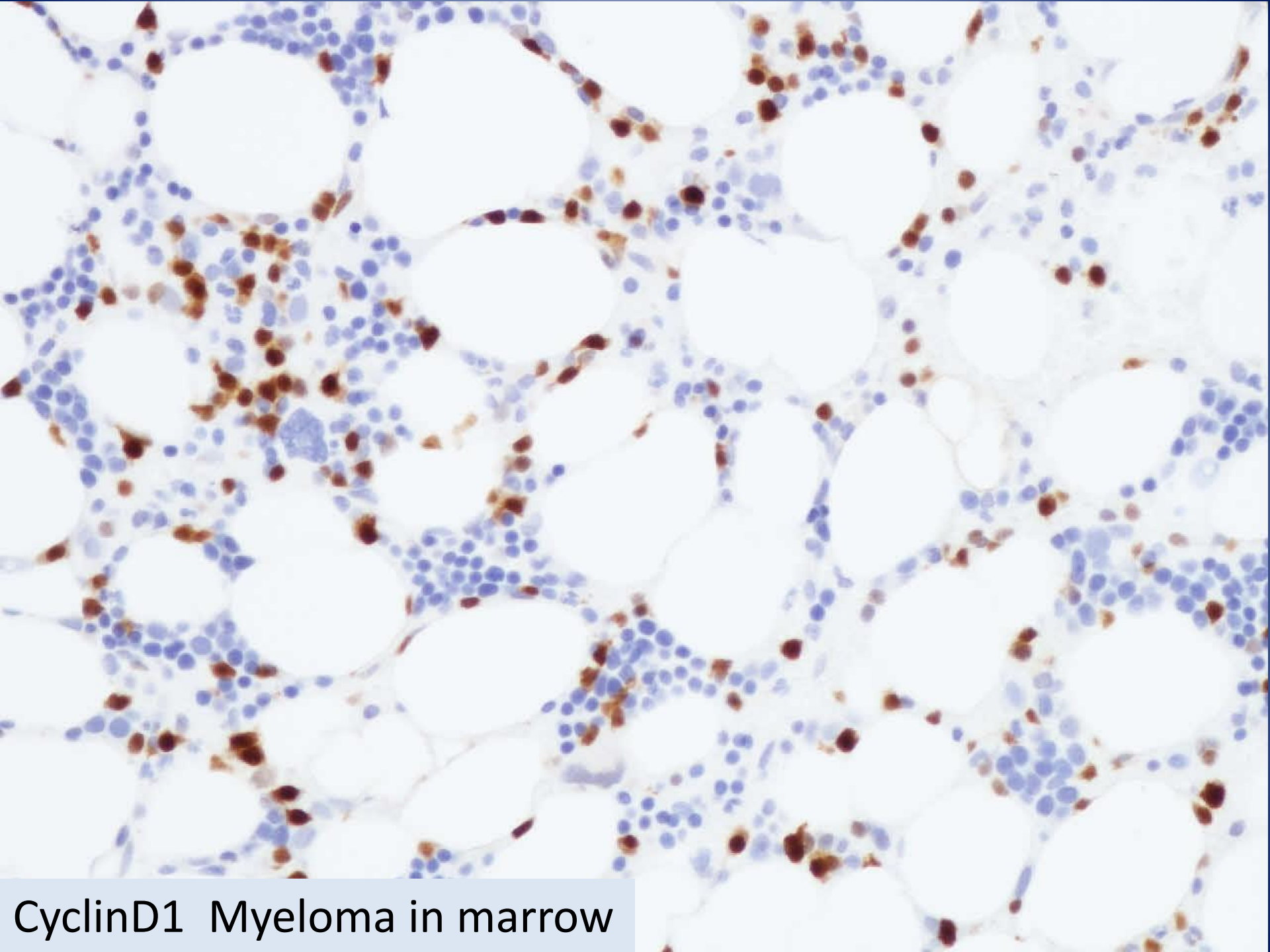
CD138



CD56

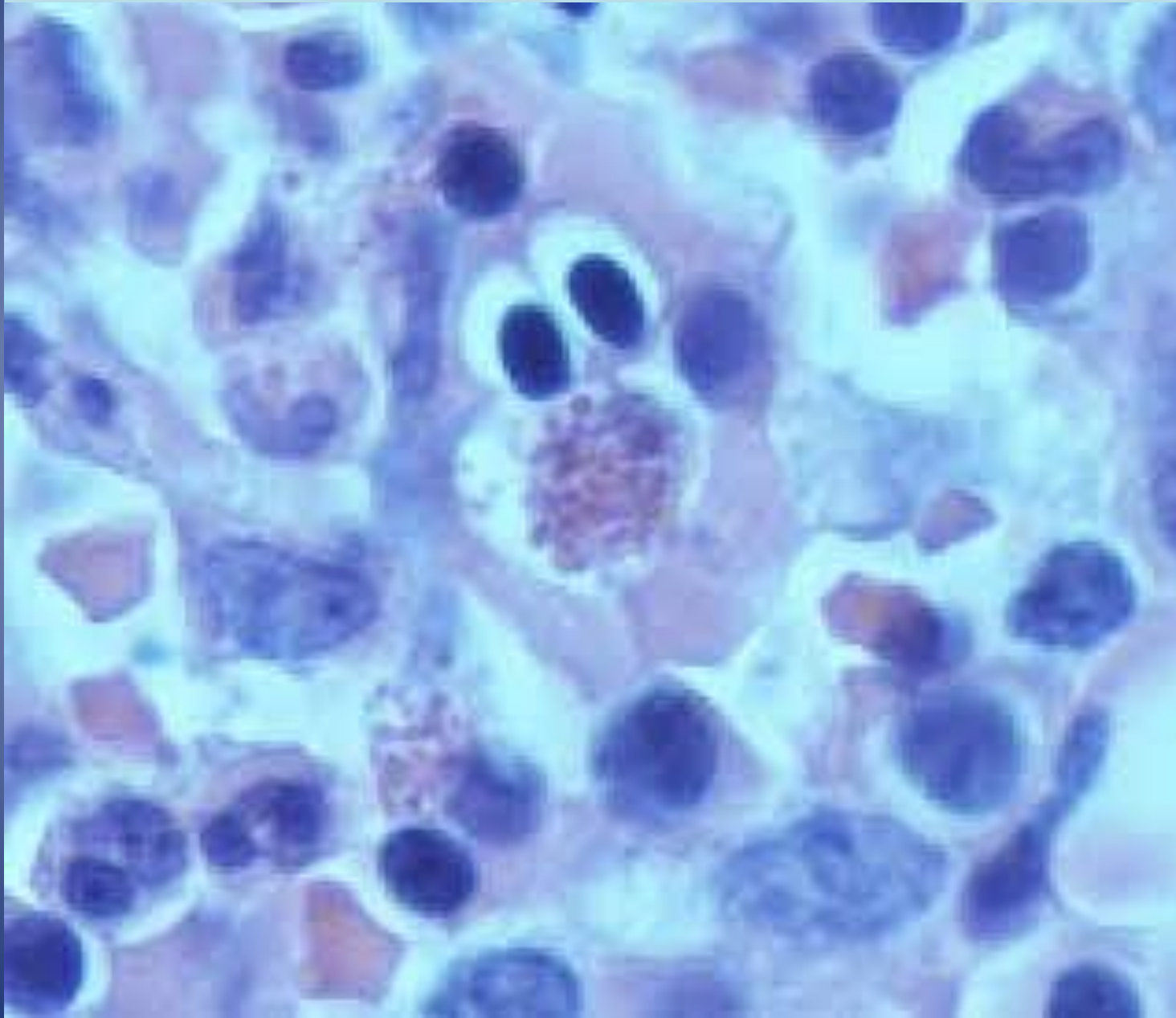
Case 6 Diagnosis

- Plasmacytoma/myeloma
- CyclinD1 is positive in
 - MCL
 - Myeloma (10%)
 - Hairy cell Leukaemia
 - Normal and neoplastic epithelia
 - Endothelial cells



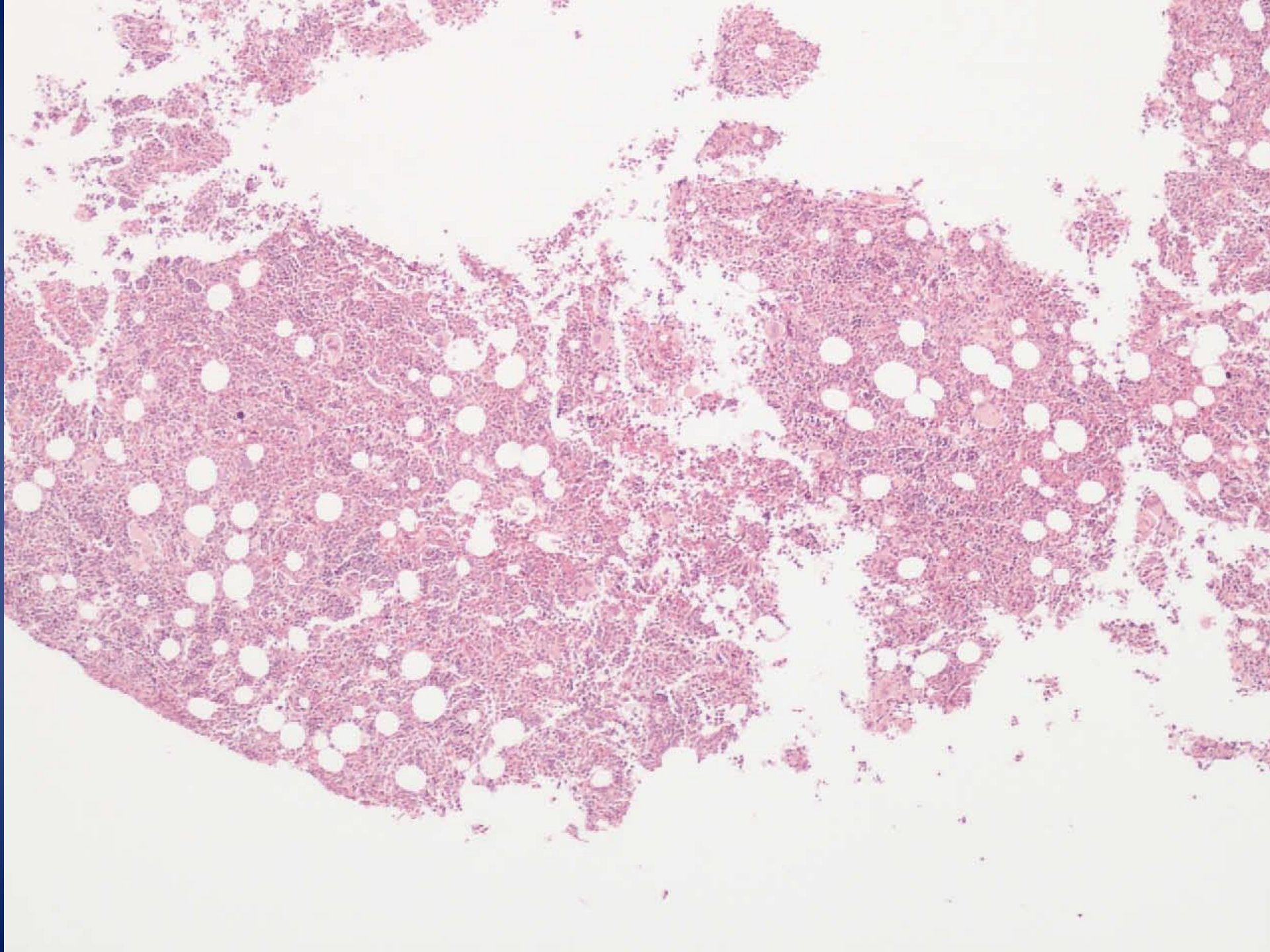
CyclinD1 Myeloma in marrow

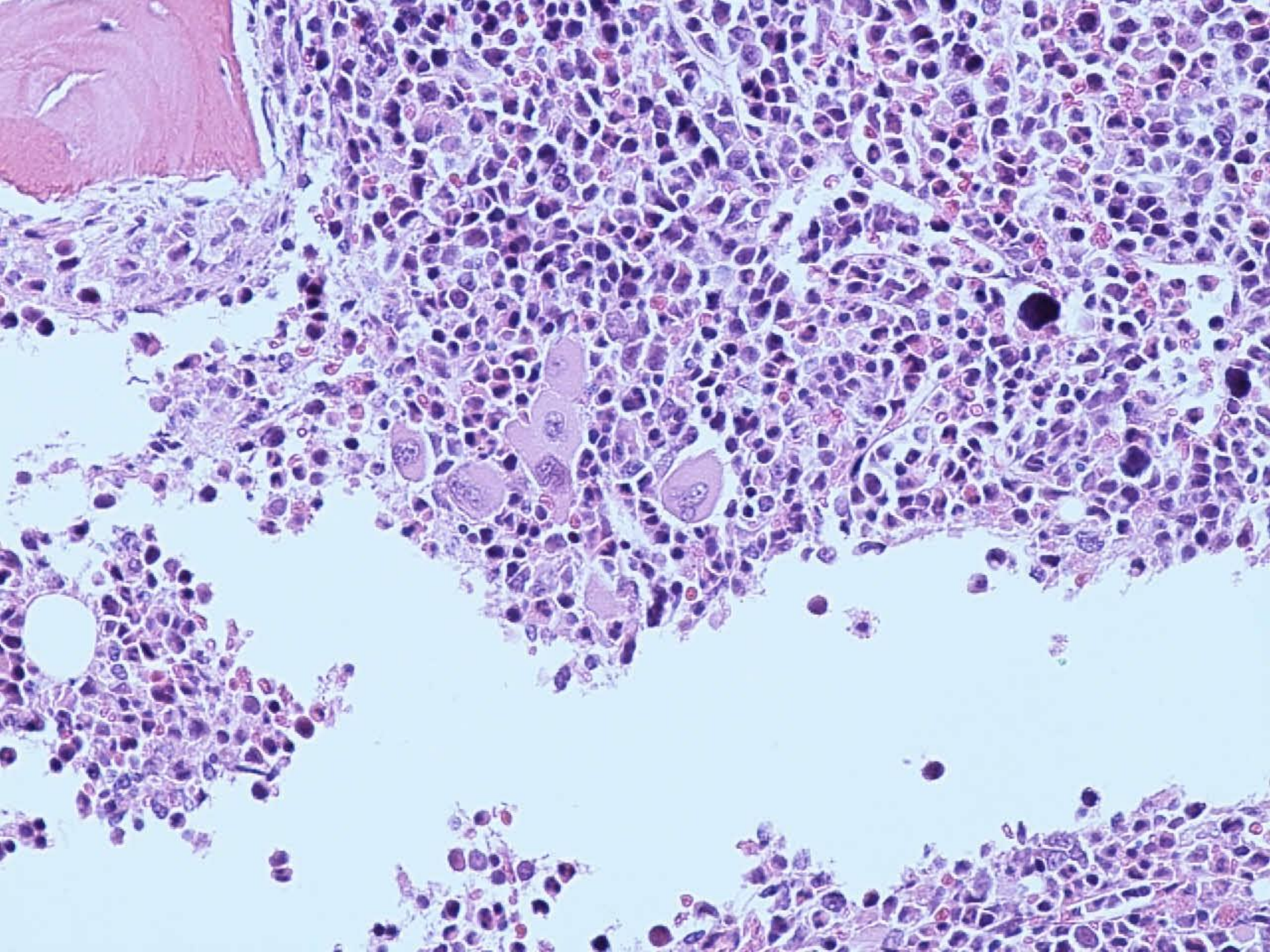
bone marrow and lymphoma

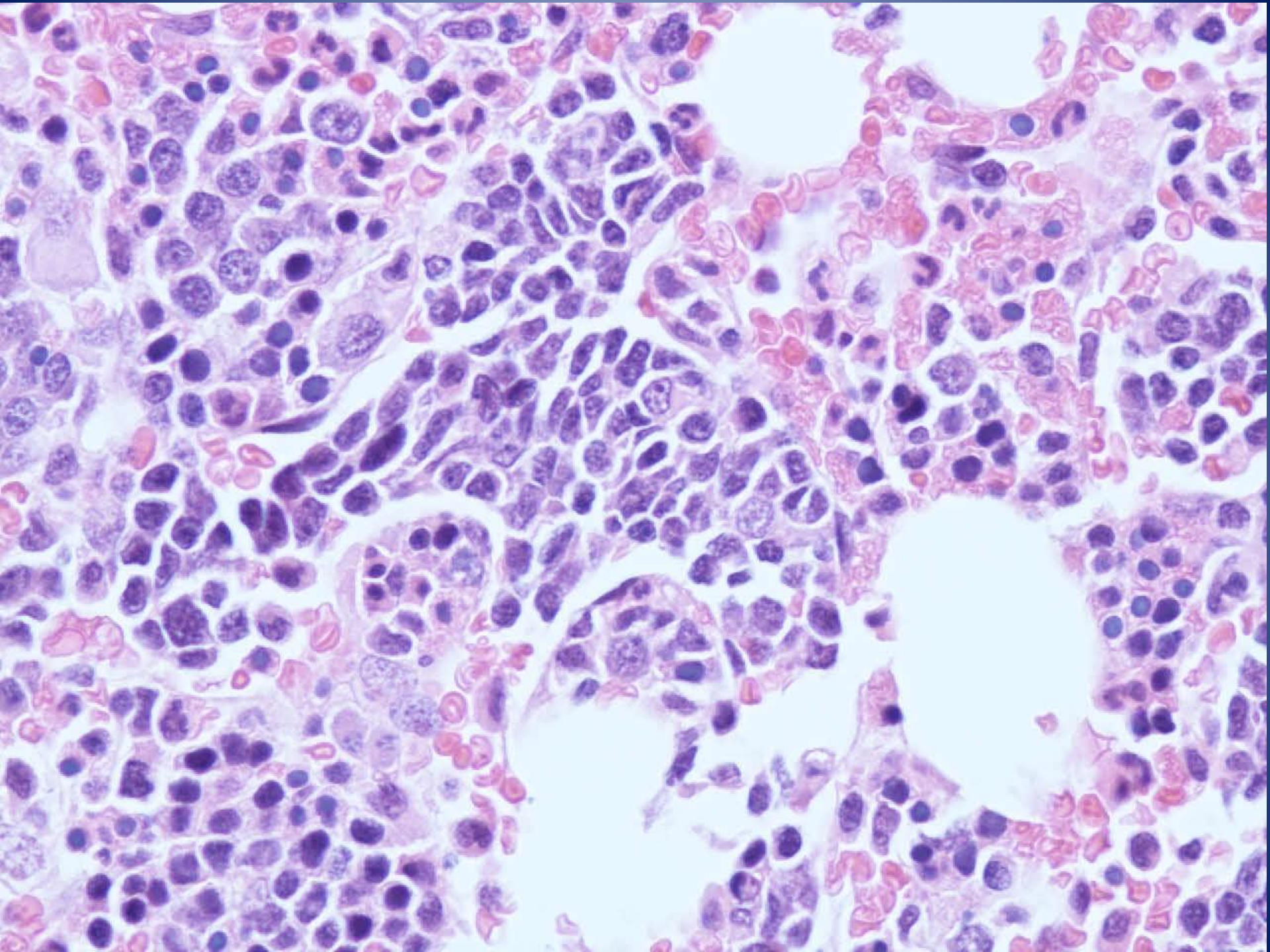


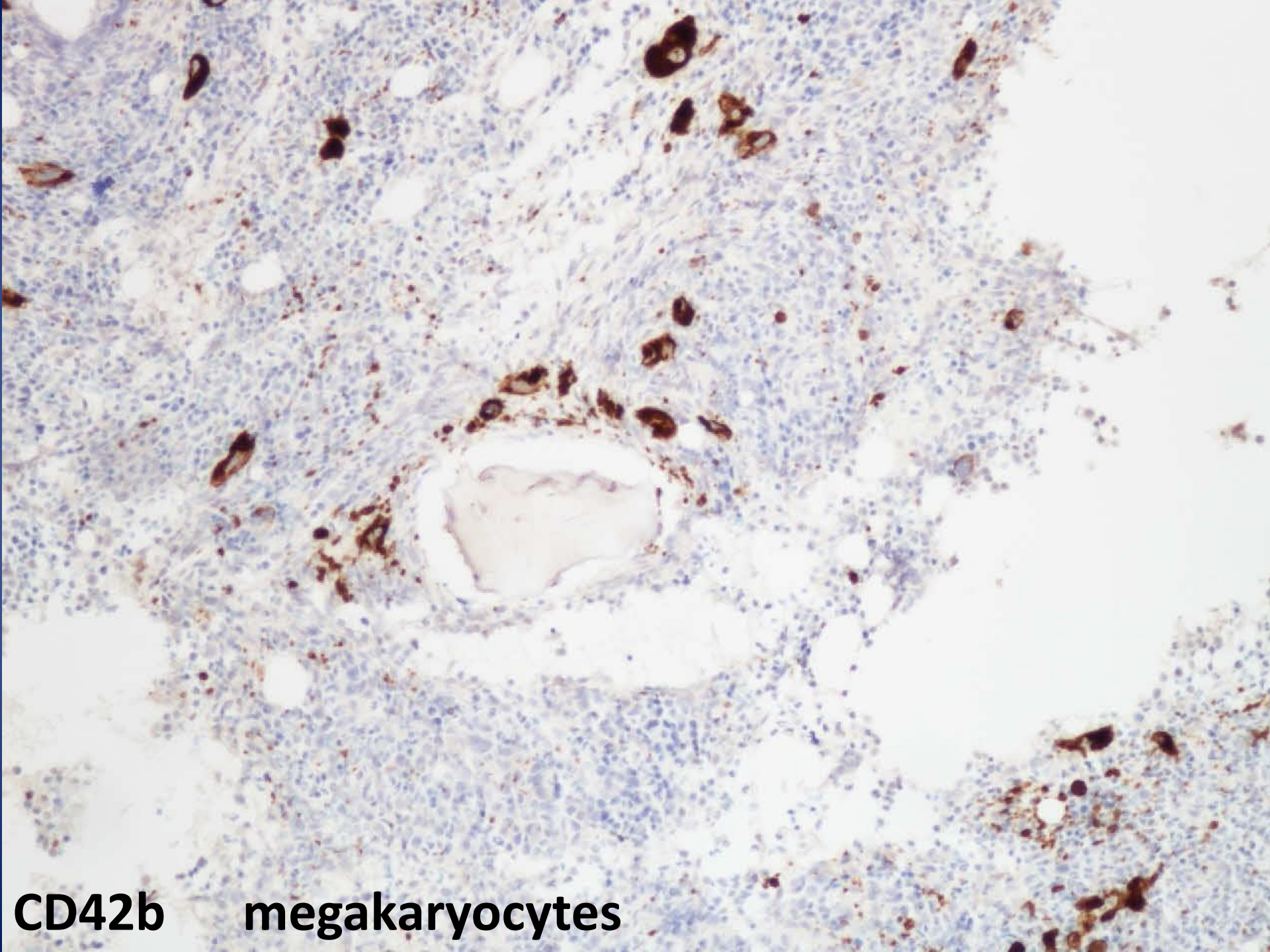
Case 7

- Female 75
- Known Myeloproliferative disorder
- Jak2+
- Sudden deterioration in counts
- ?blast transformation

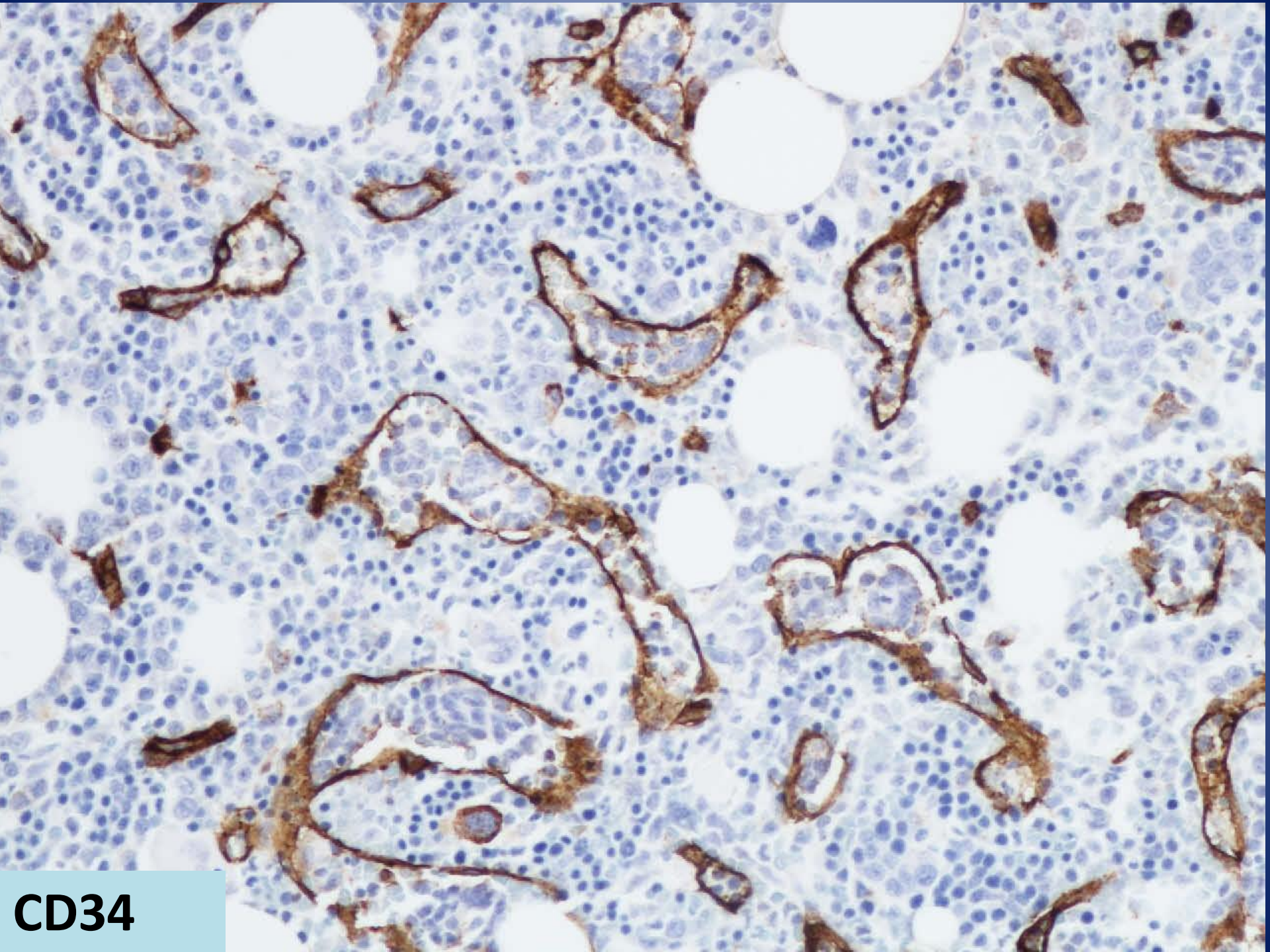




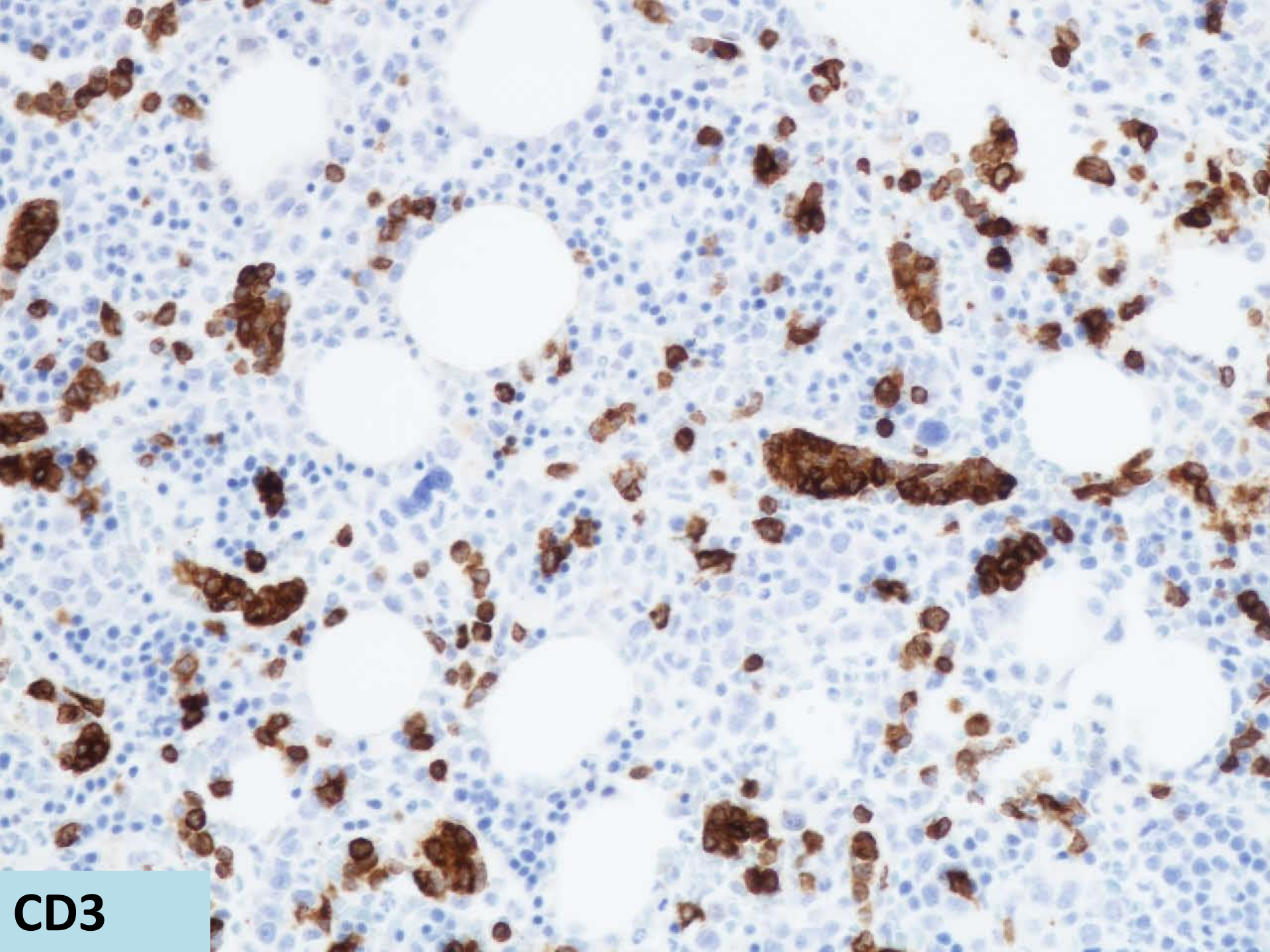




CD42b **megakaryocytes**



CD34



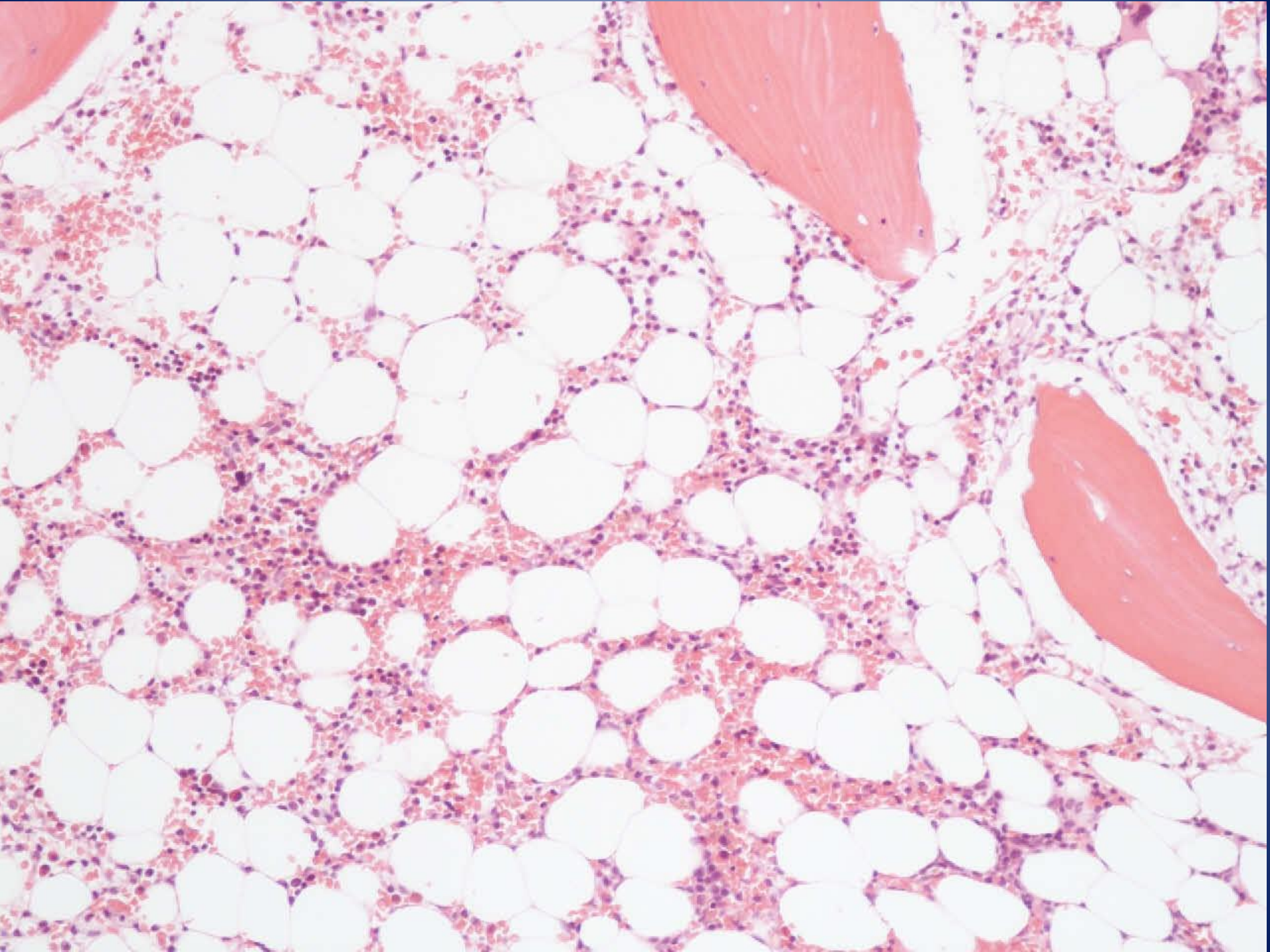
CD3

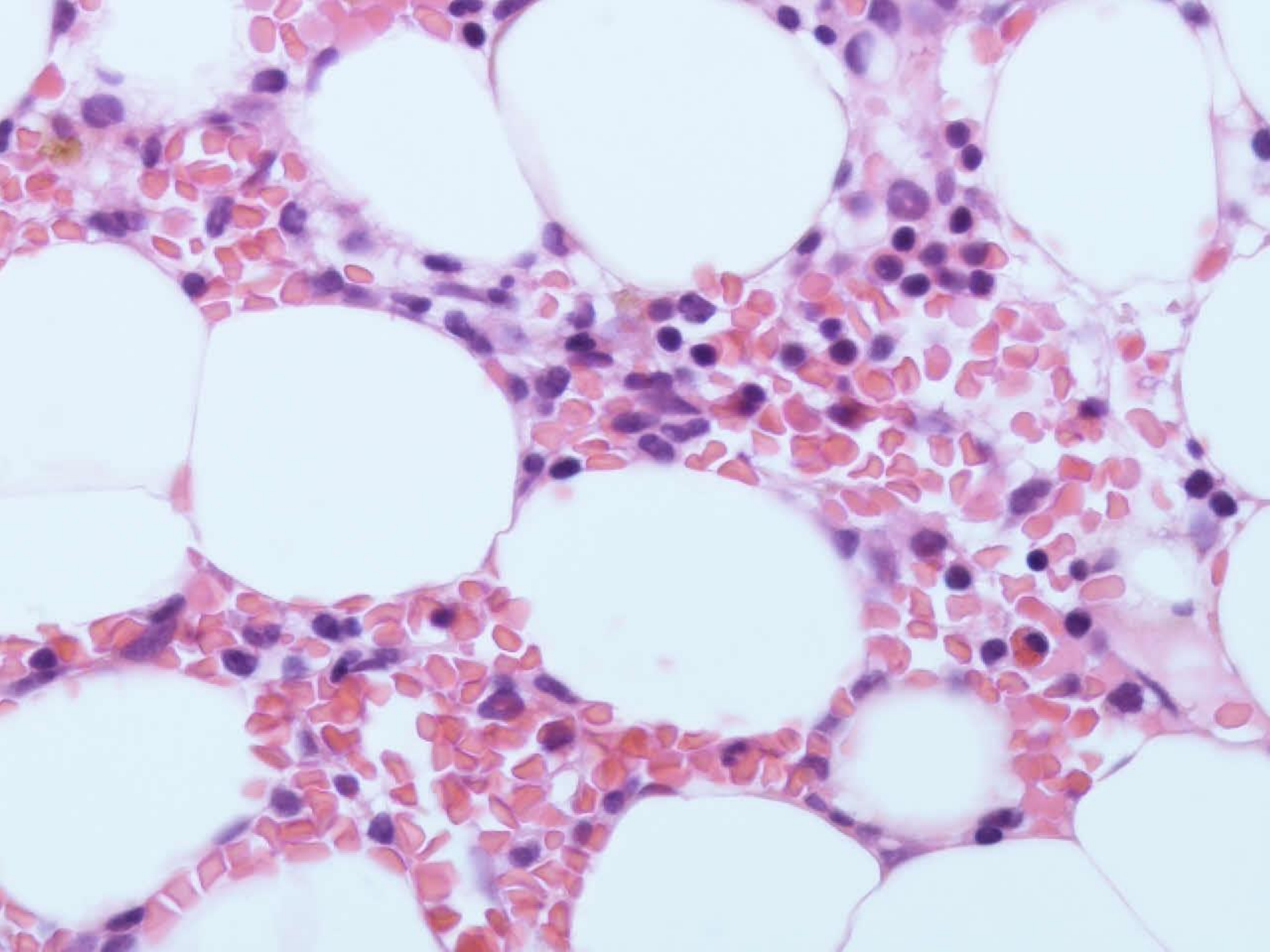
Final diagnosis

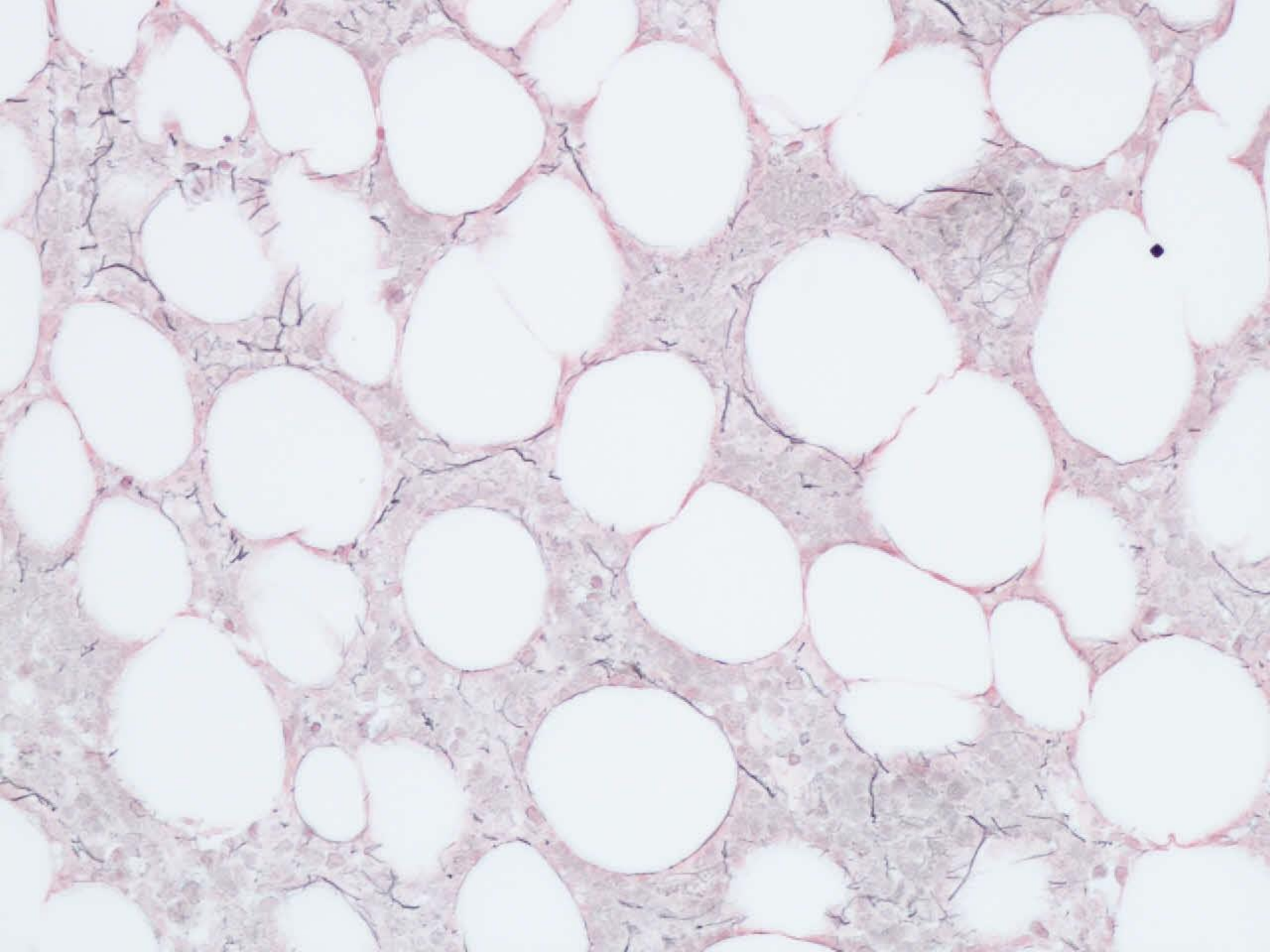
- Hepato Splenic Gamma/Delta T cell Lymphoma
- + MPD
- NB. Always include basic lymphoid markers in assessment of marrow when there is a significant clinical change

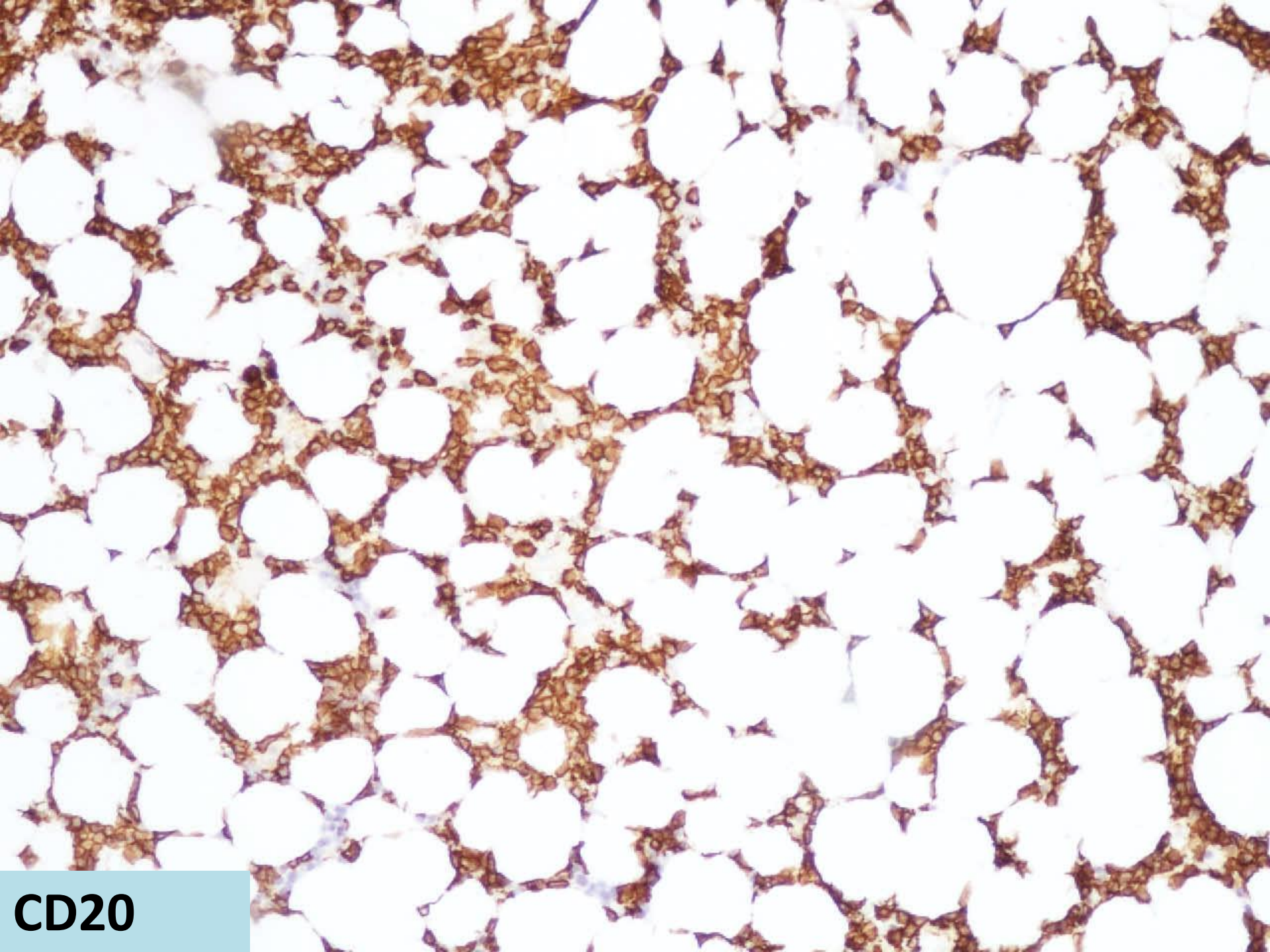
Case 8

- Male 60
- Mild thrombocytopaenia and anaemia
- ?MDS

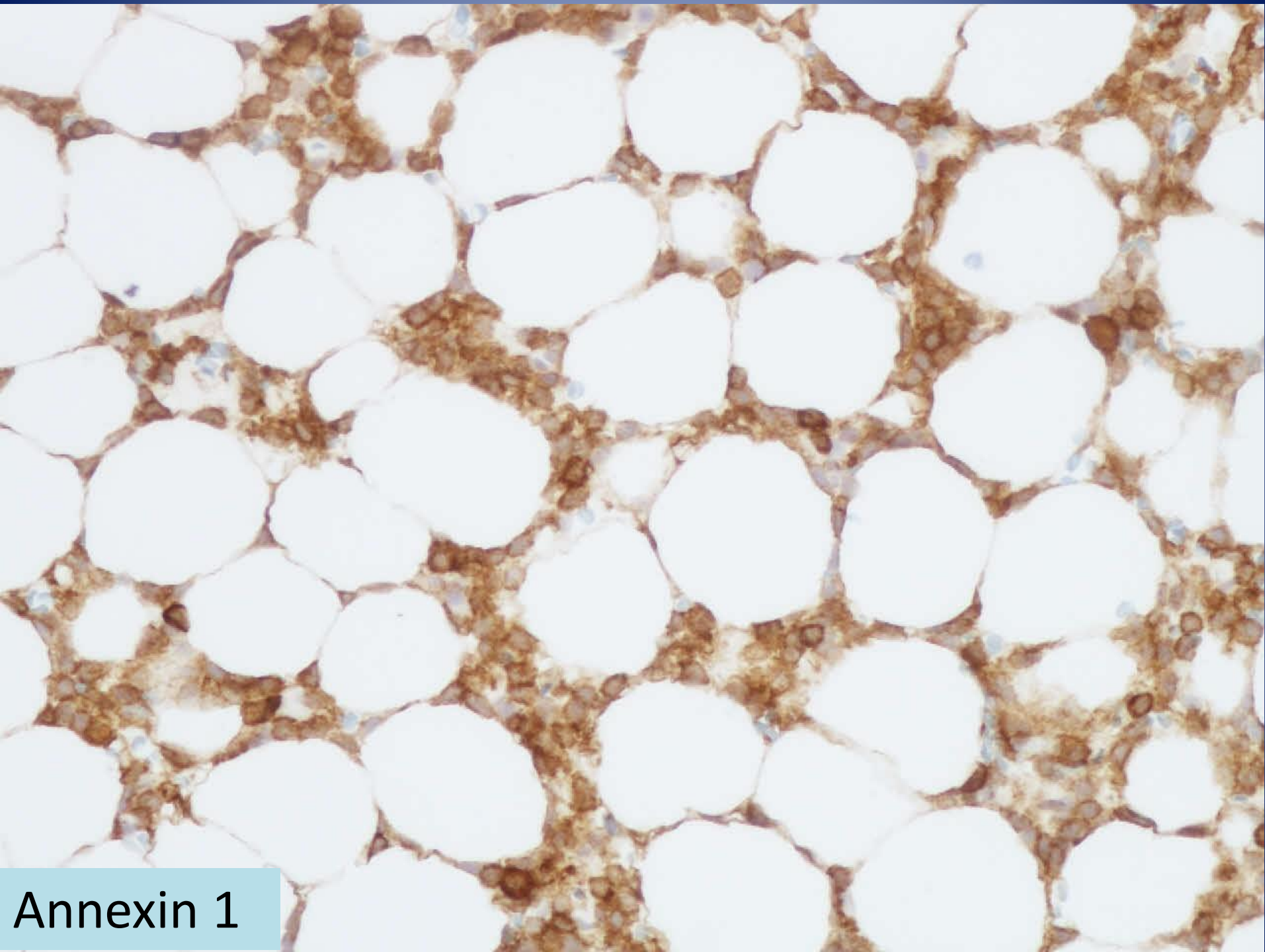








CD20



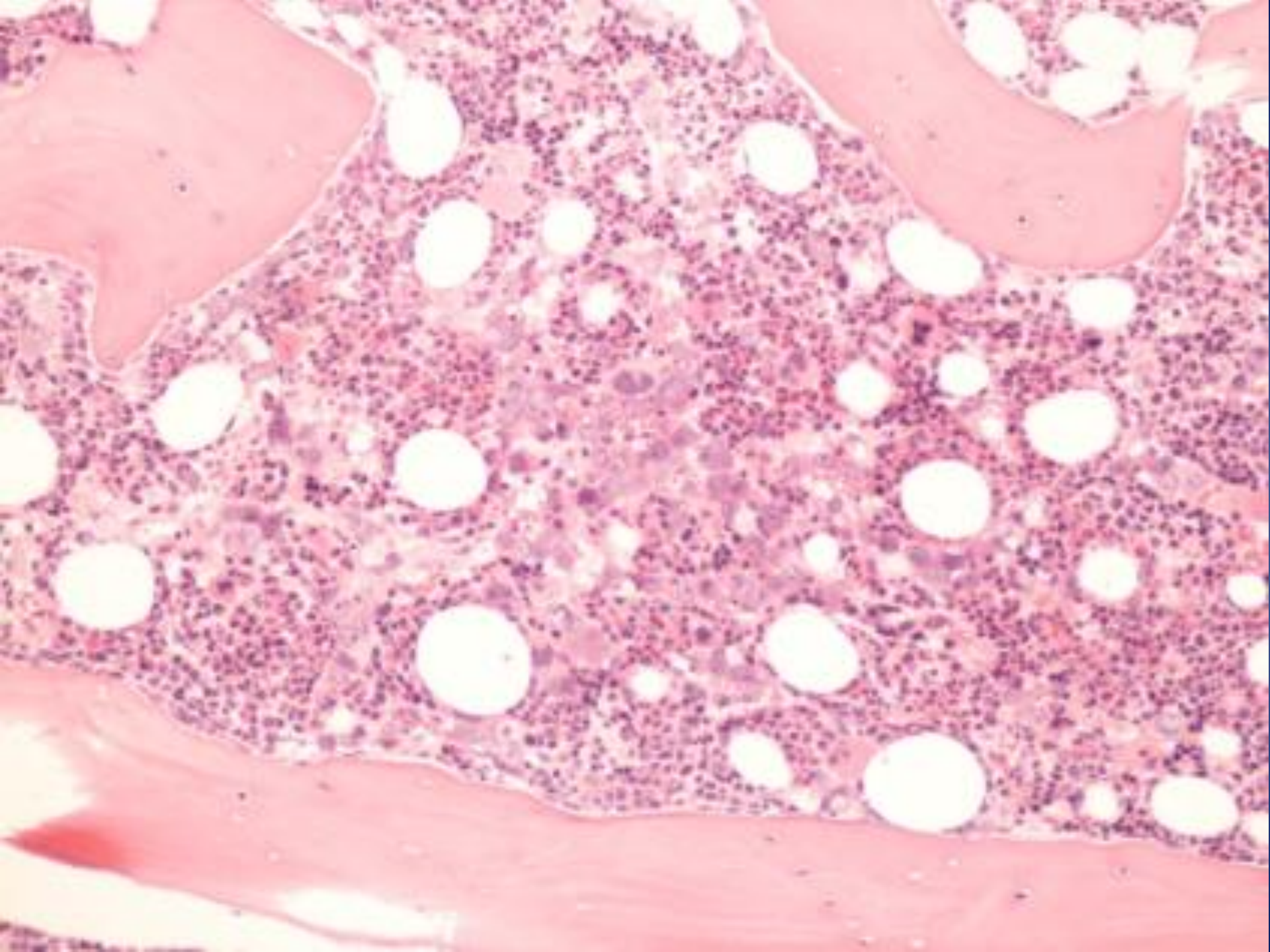
Annexin 1

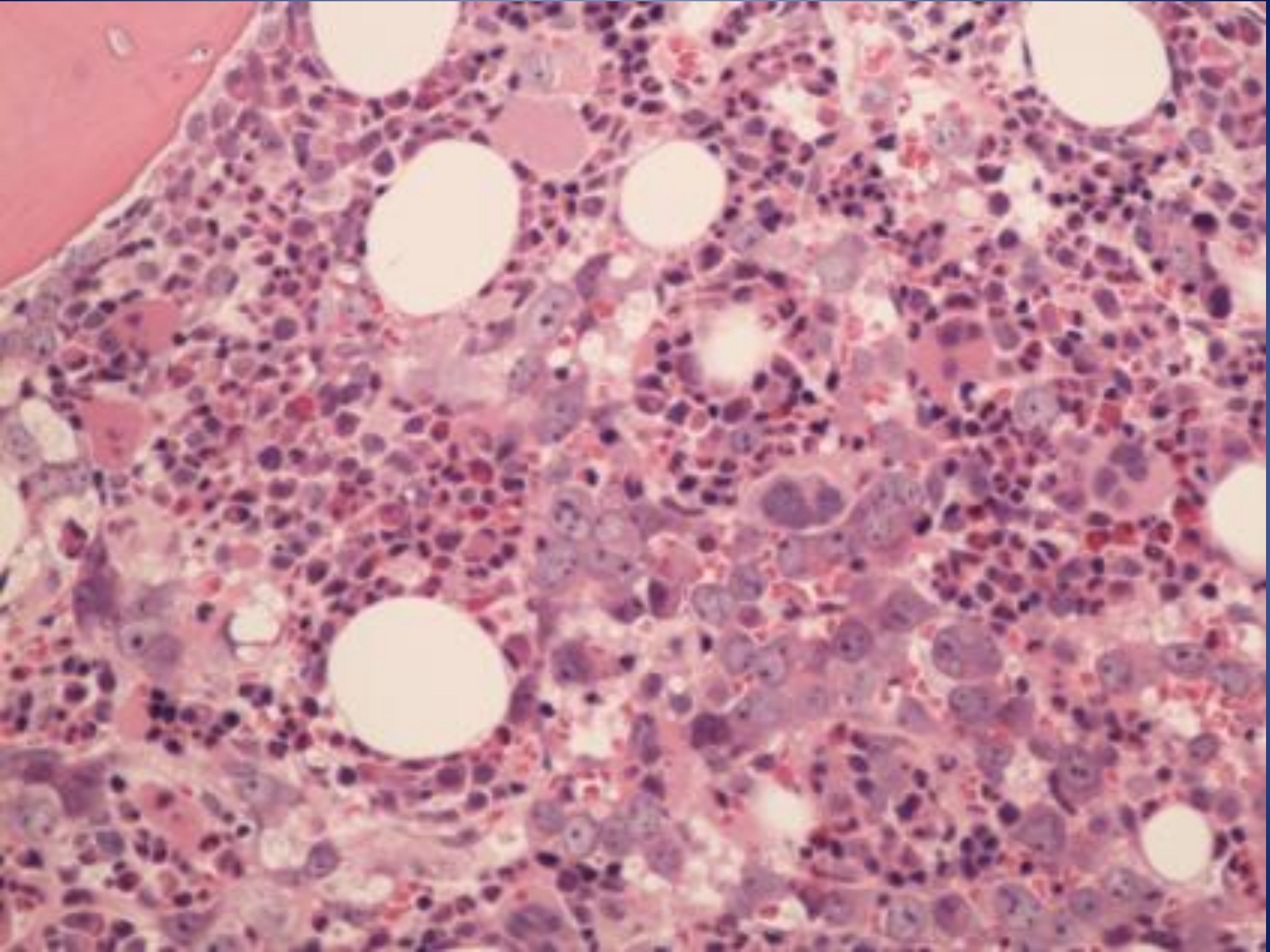
Final Diagnosis

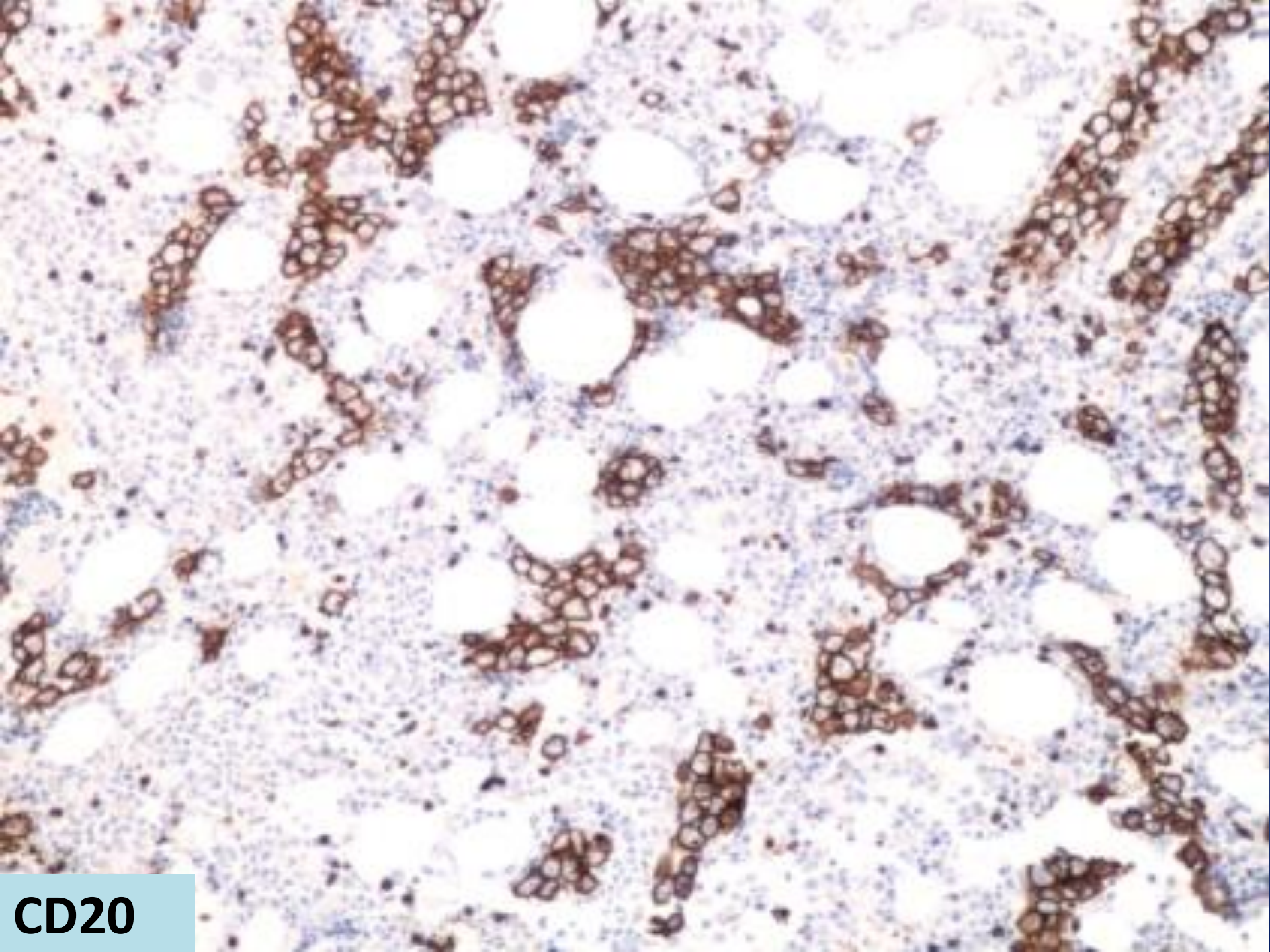
- Hairy cell Leukaemia (“invisible on H&E” variant)
- Always include **T and B cell markers** in your ICC panel when investigating MDS.
- (CD34,CD117,CD42b,MPO,GlycophorinC,CD3,CD20)

Case 9

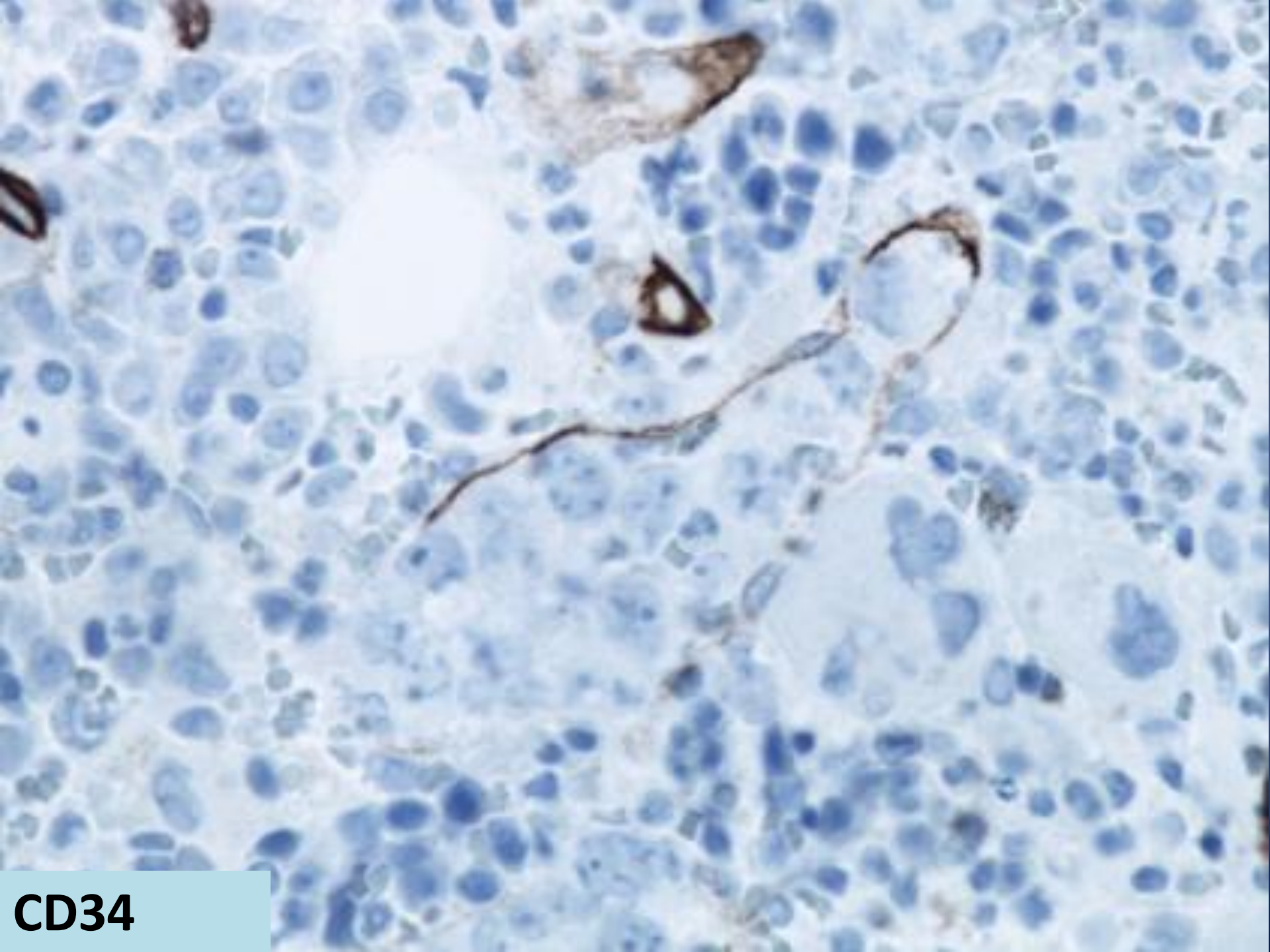
- Pancytopenia
- Confusion







CD20



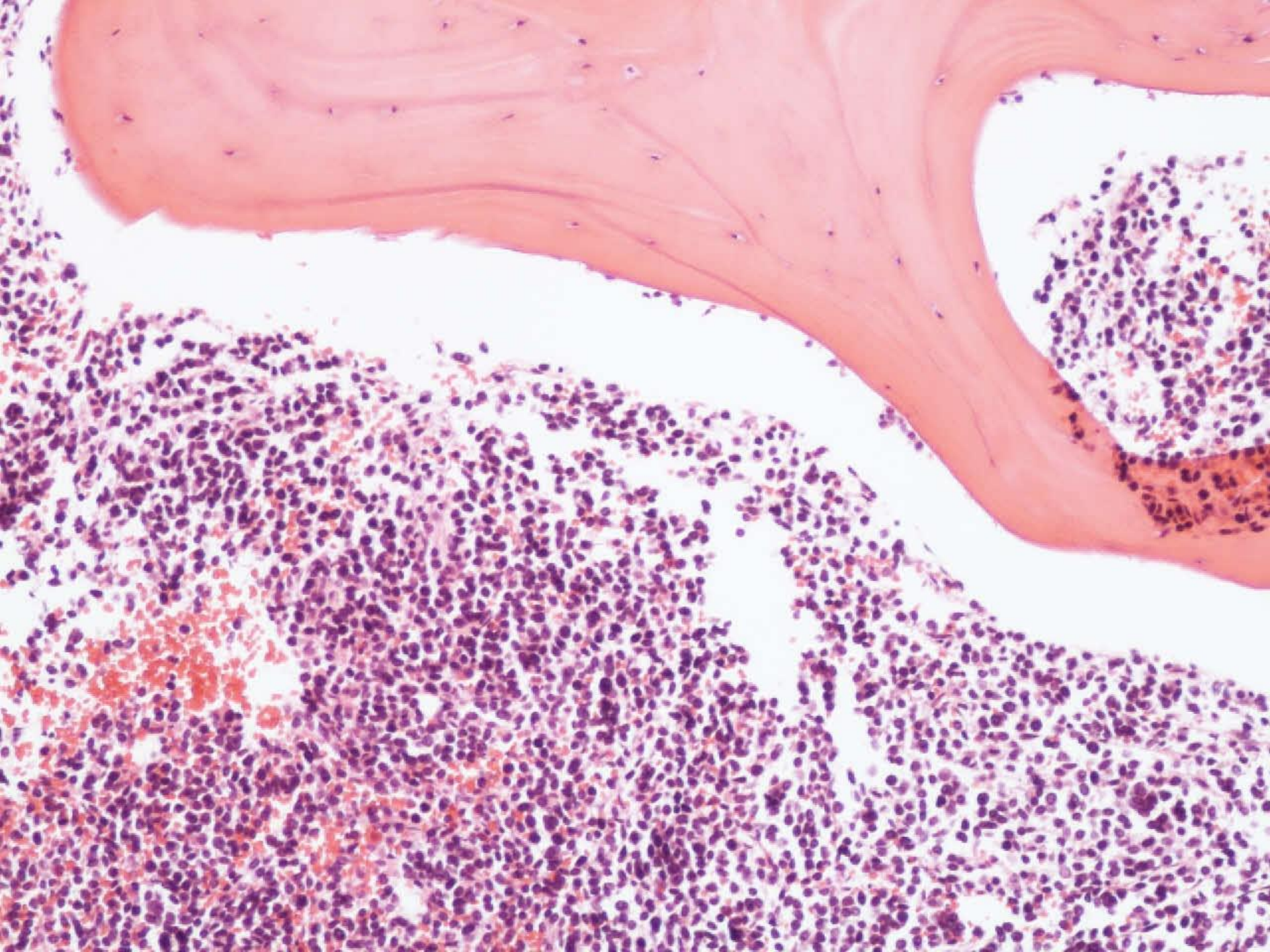
CD34

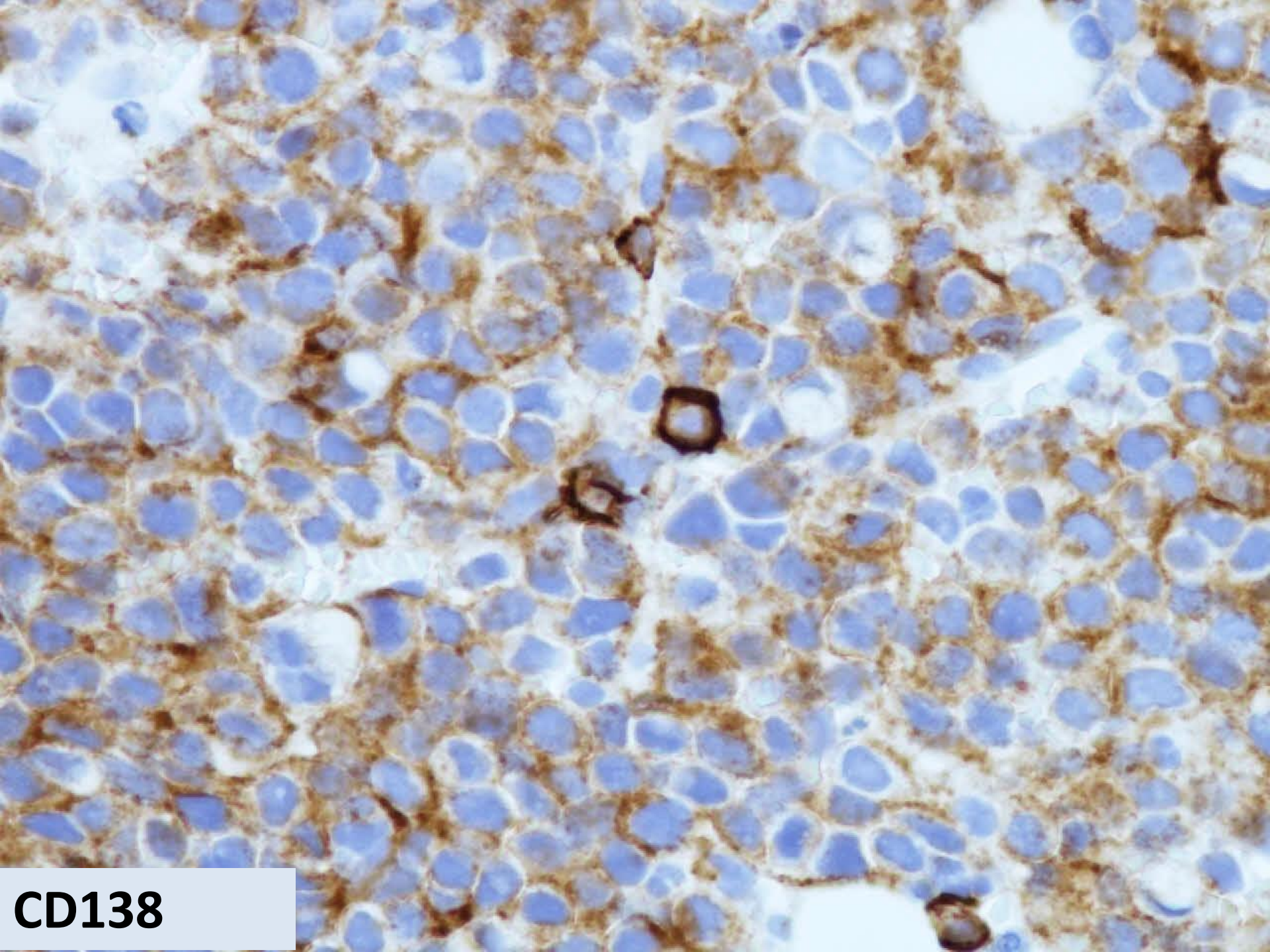
Case 9

- Intravascular large B cell lymphoma

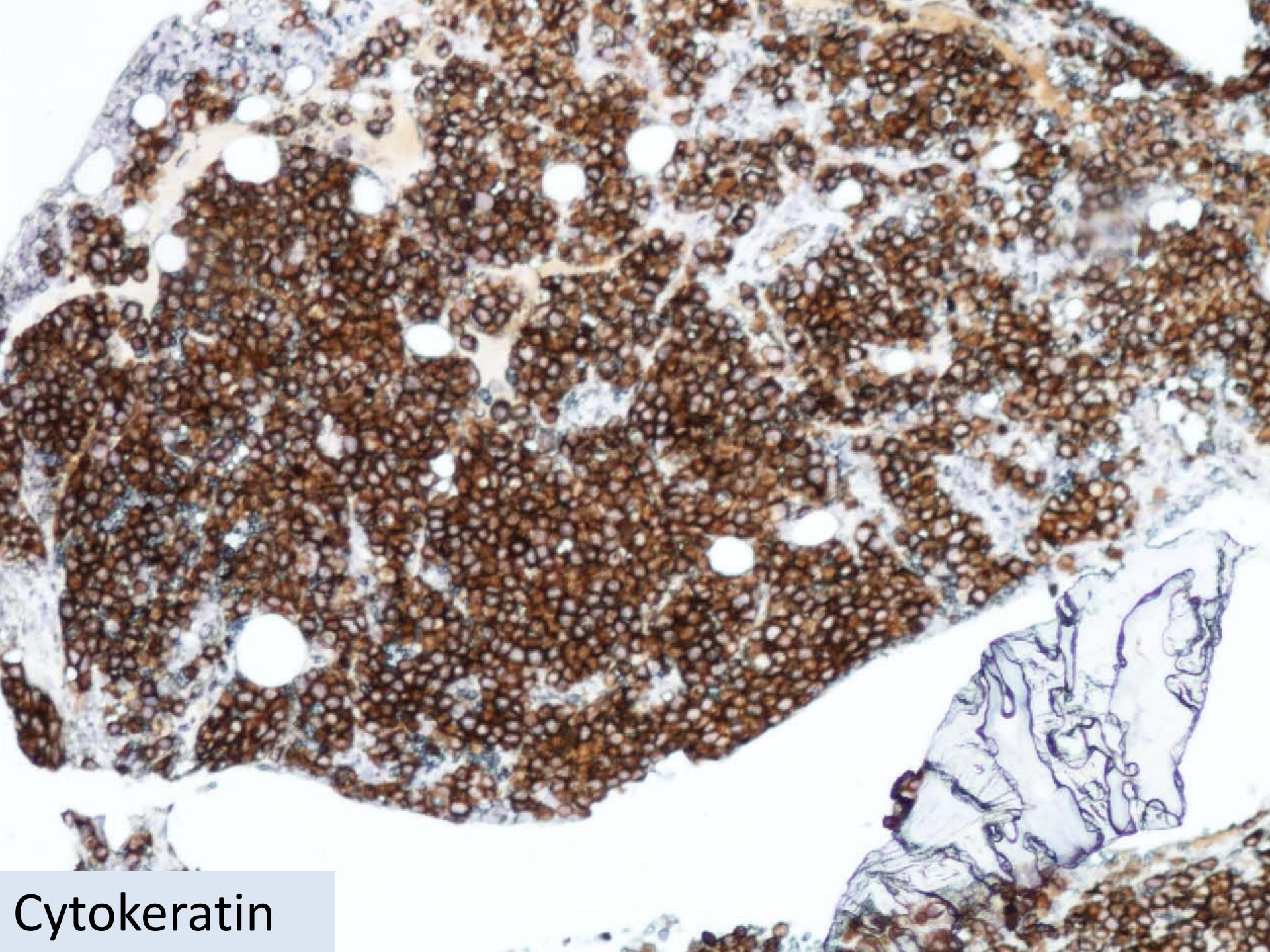
Case 10

- Male 72
- Multiple lytic lesions in bone
- ?myeloma ?other
- Trephine bx

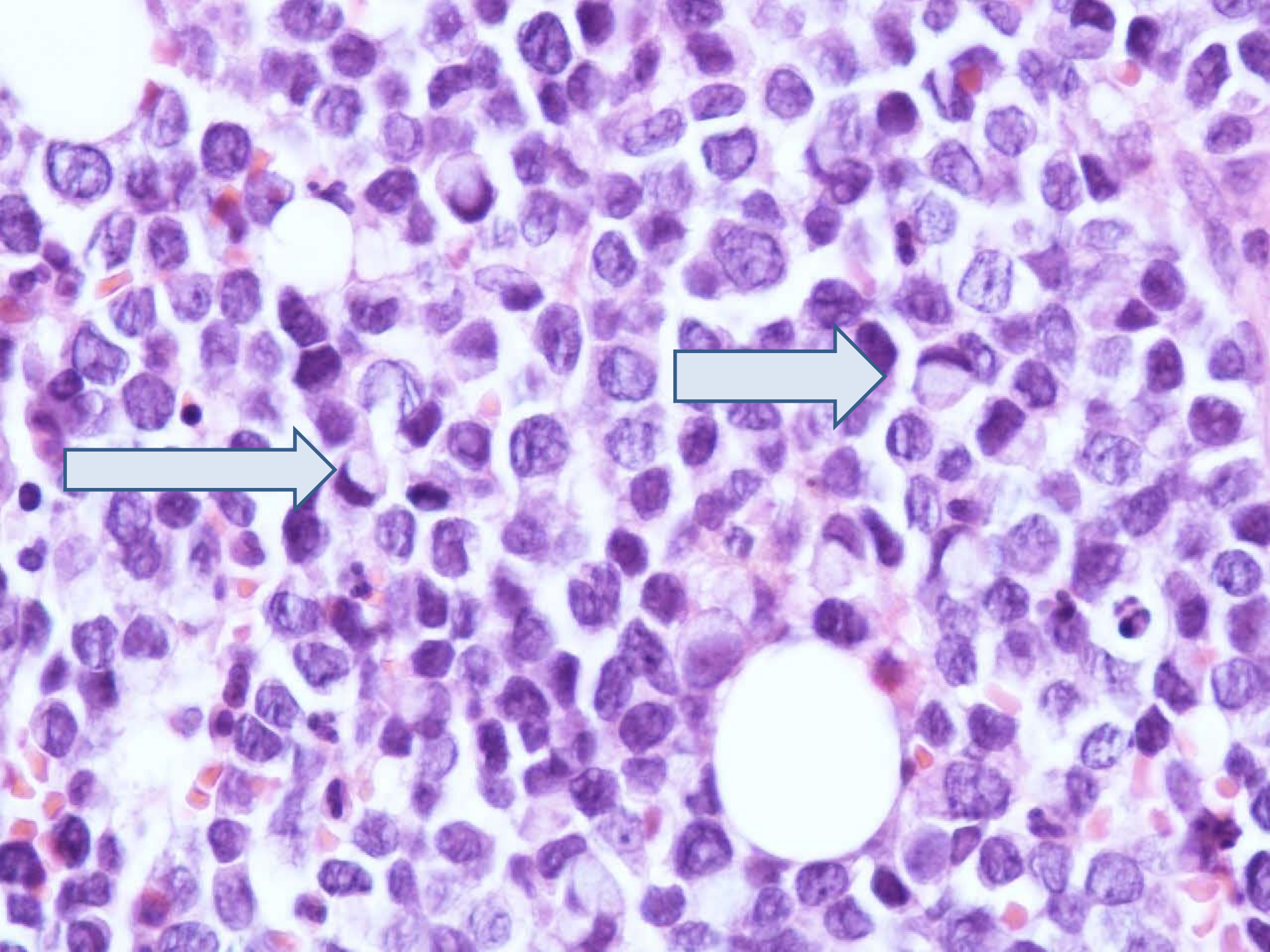




CD138



Cytokeratin

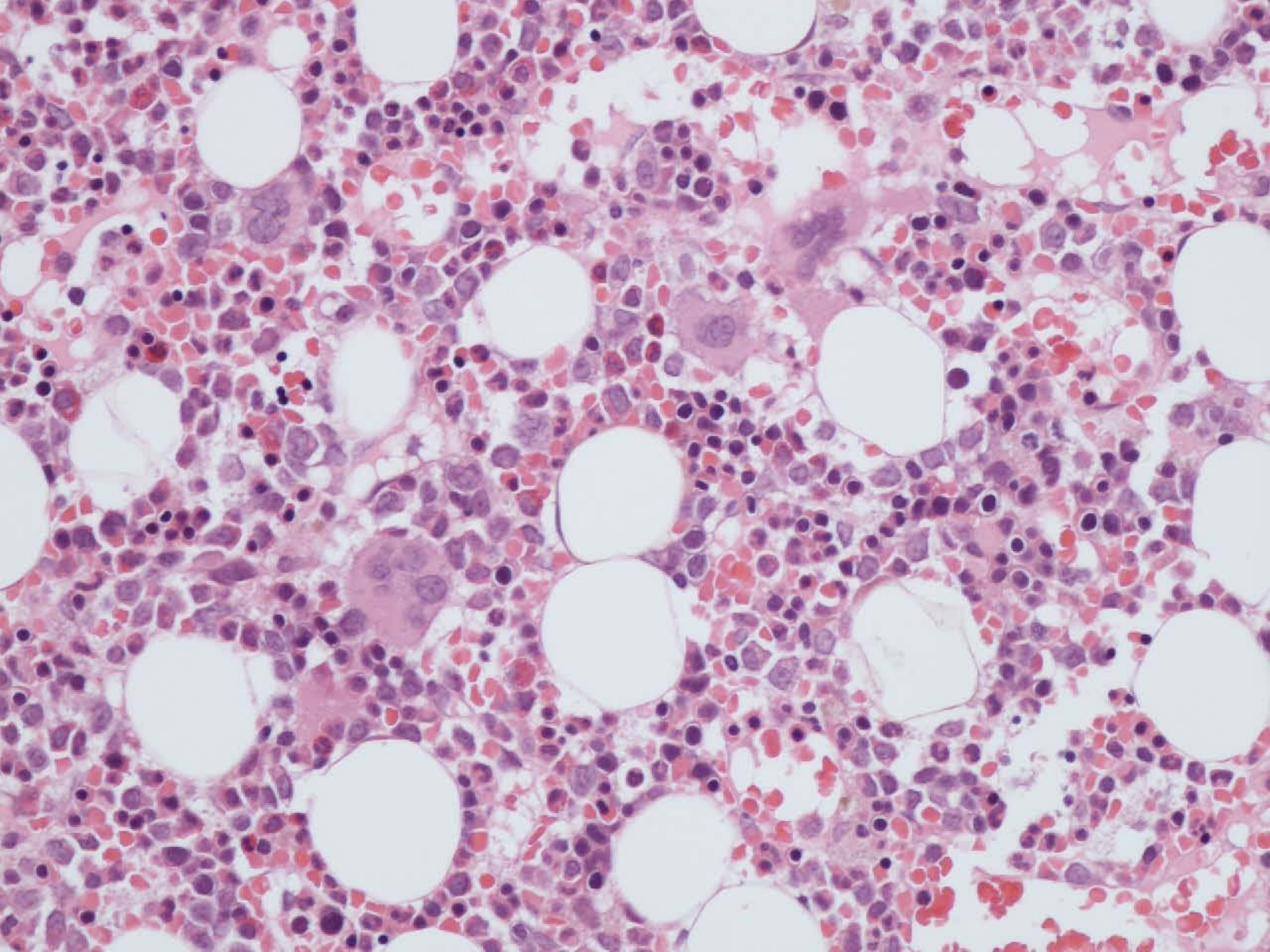


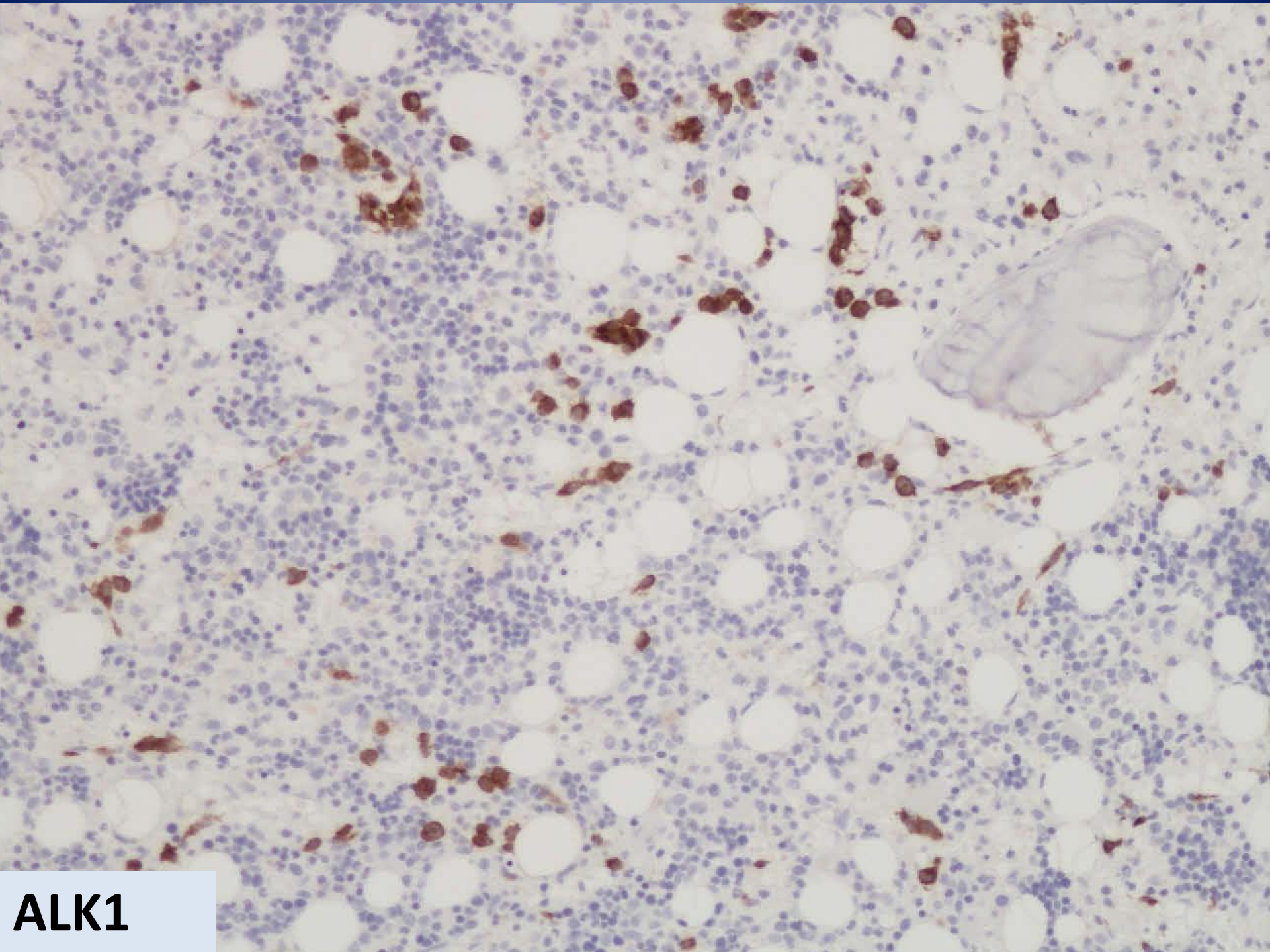
Diagnosis

- Metastatic poorly differentiated adenocarcinoma with signet ring morphology
- CD138 is **not** lineage specific.
 - Positive in carcinoma
 - Positive in **Melanoma**

Case 11

- Staging Marrow for ALCL ALK1 positive



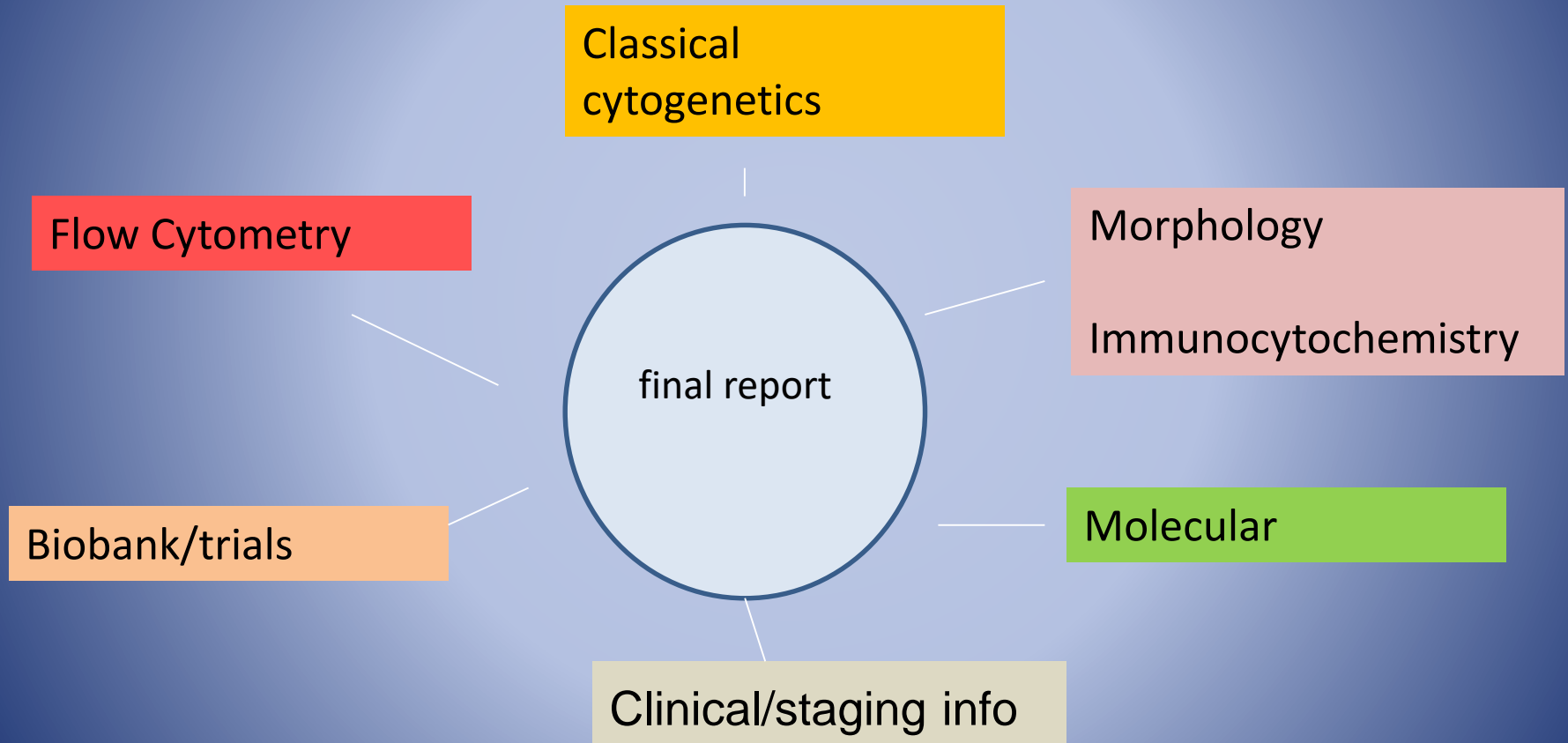


ALK1

Diagnosis

- Marrow involvement by ALCL ALK+
- Always do appropriate stain for staging purposes
 - Eg ALK1 for ALCL ALK+
 - CD30 for cHL
 - CD20 for NLPHL
 - SOX11 for Mantle
 - CD20 for DLBCL
 - PAX5 for post Rituximab assessment
 - No need for a large panel

Integrated service required to avoid error



- Thank you