Serous Effusion: Unknown Case Interactive session

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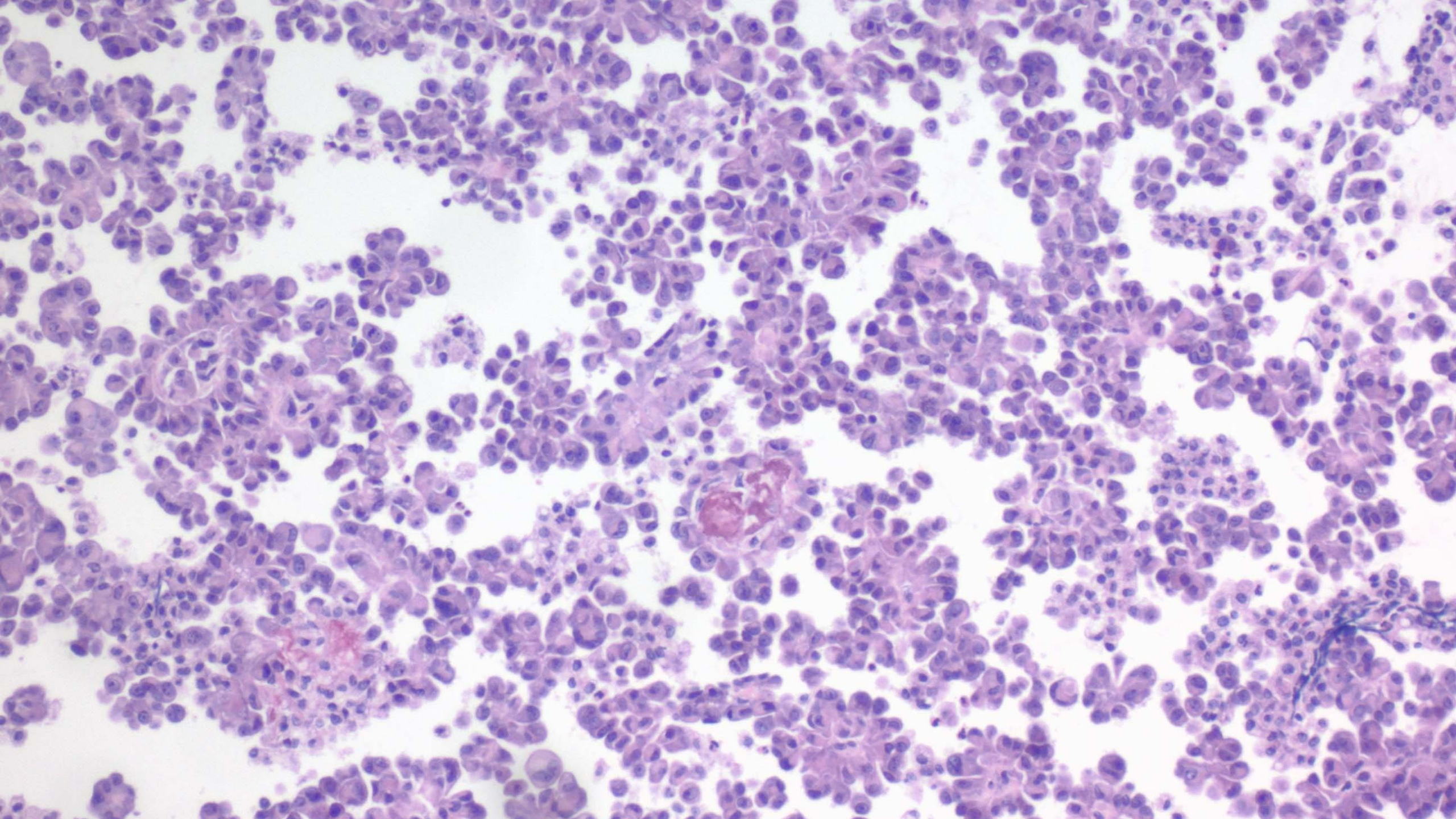
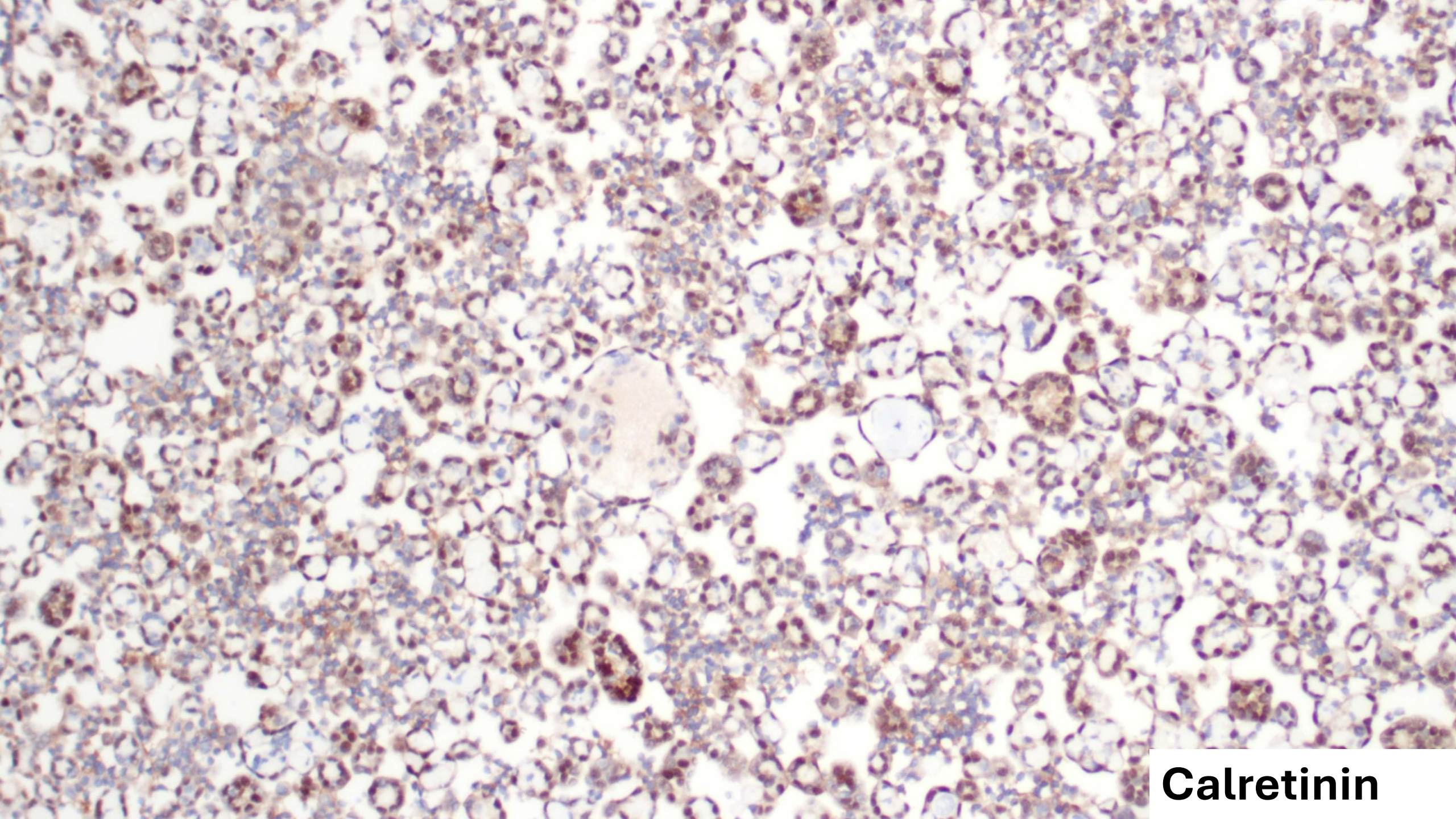
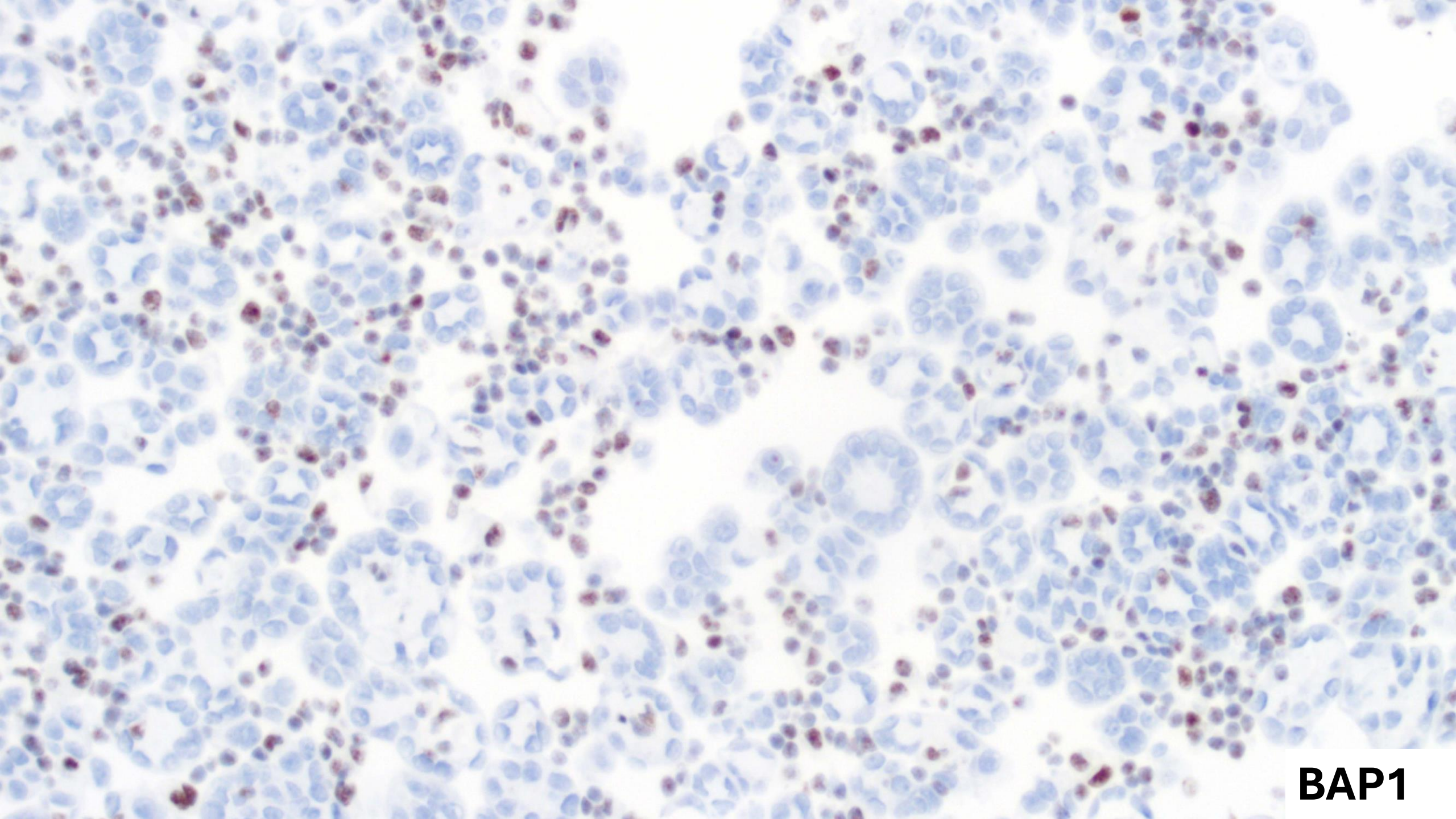
Case 1

- 67 yr old female presented with shortness of breath and large volume right pleural effusion
- Also had moderate ascites of unknown etiology
- CT scan showed multiple nodules on diaphragm




Calretinin

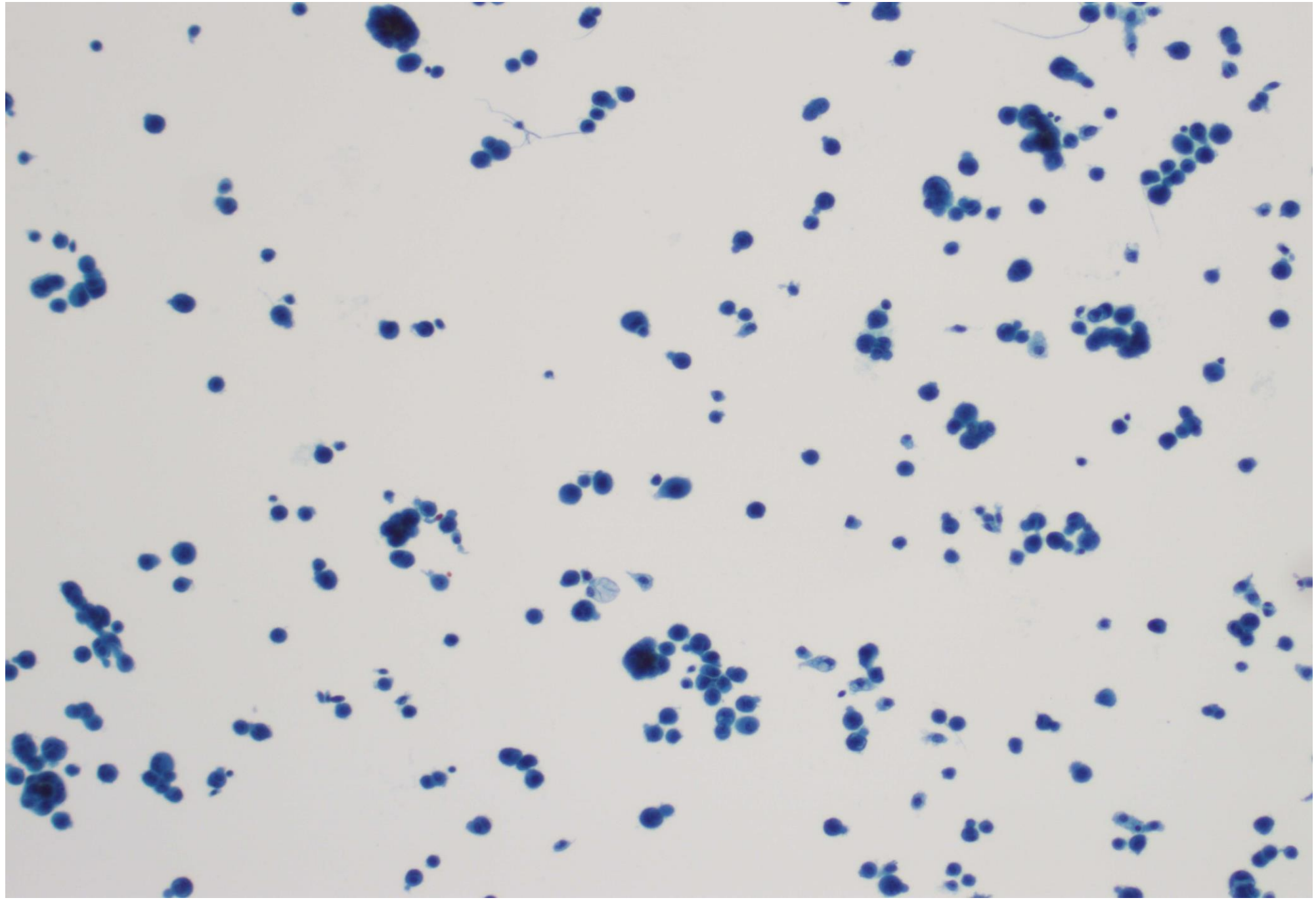

BAP1

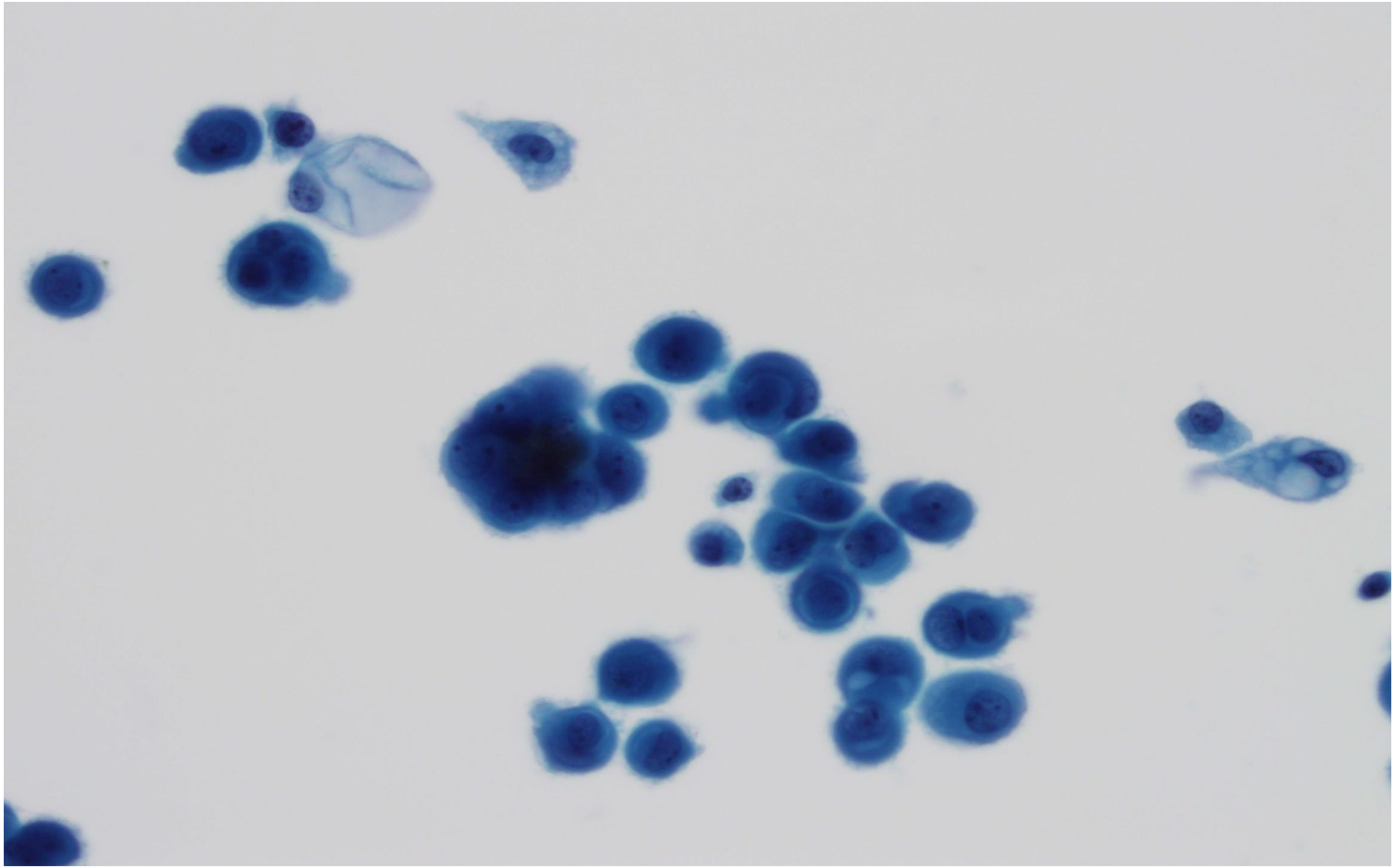
#1
What is the Diagnosis?

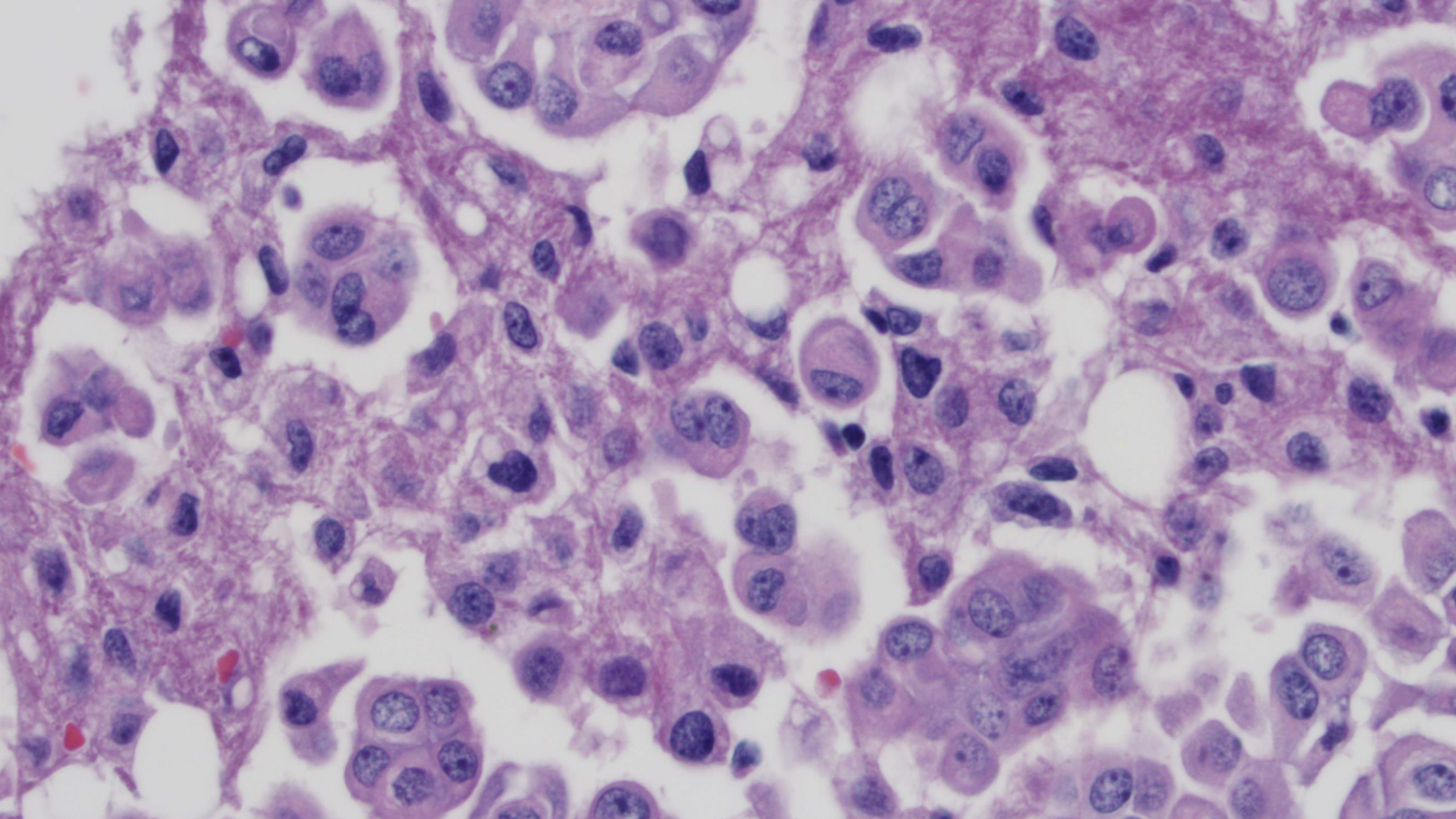
- A. Reactive mesothelial proliferation
- B. Adenocarcinoma
- C. Mesothelioma
- D. Endometriosis

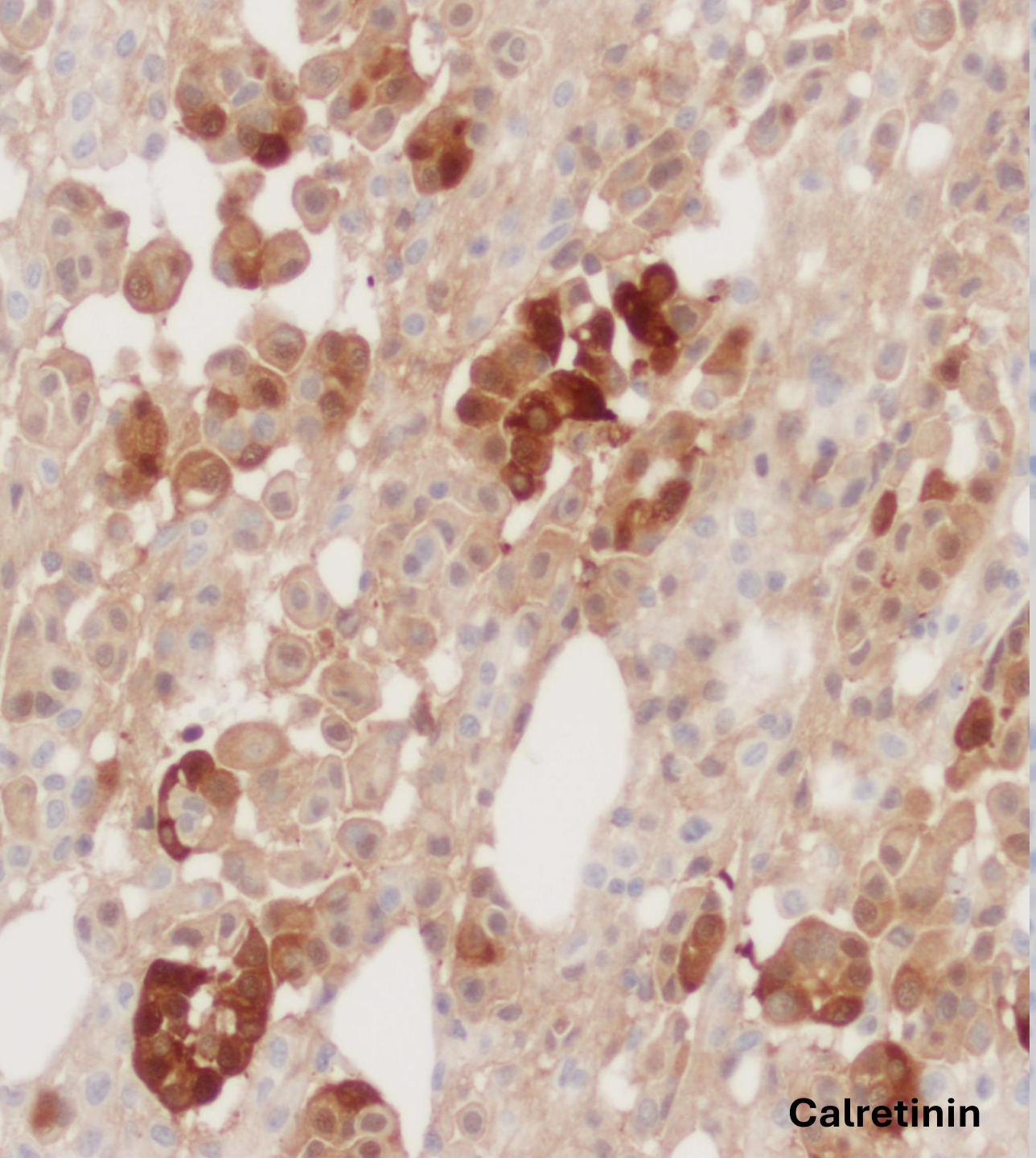
Case 2

- 74 yr old male presented with shortness of breath and bilateral pleural effusion
- CT scan showed multiple nodules on pleura bilaterally





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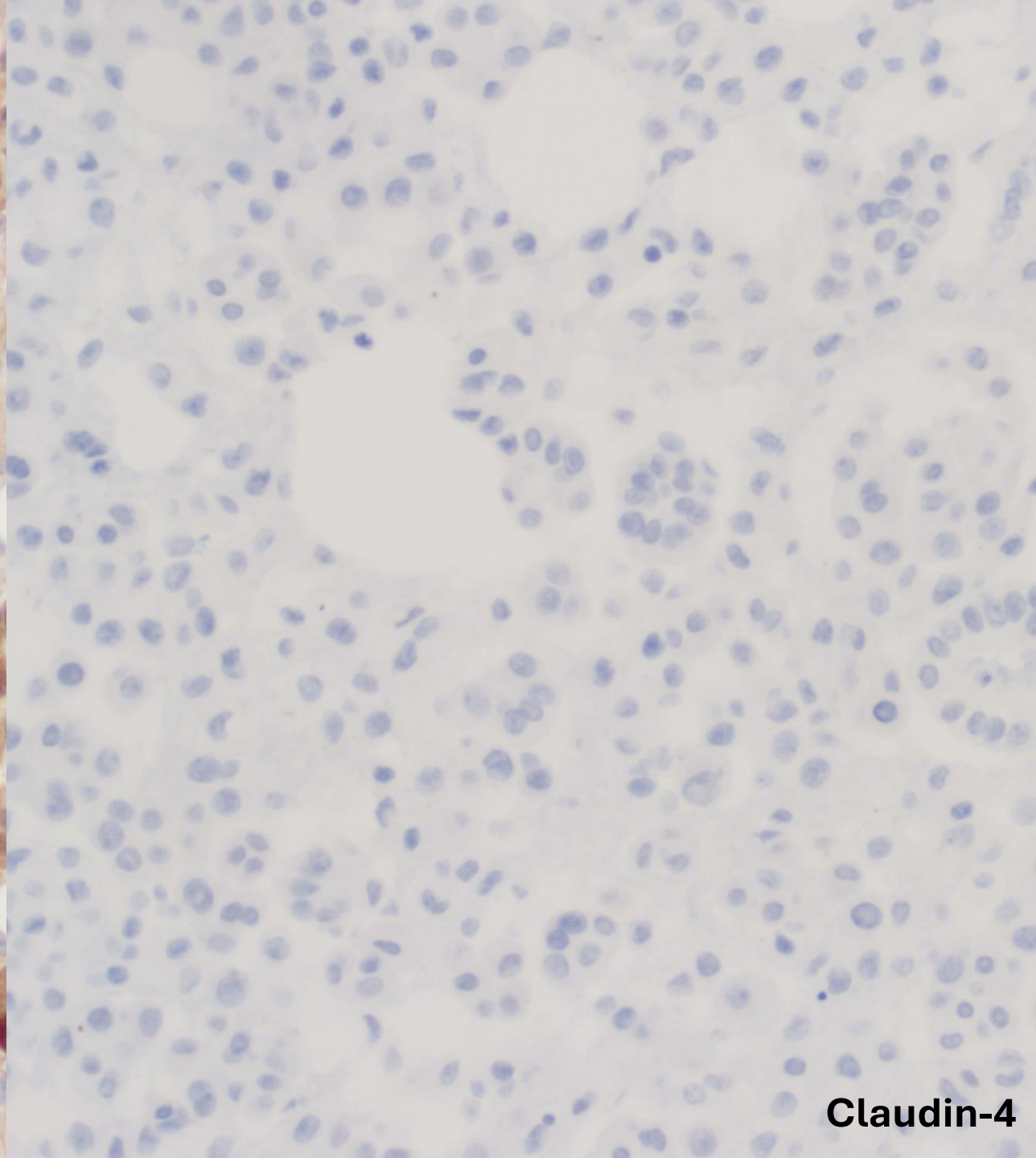
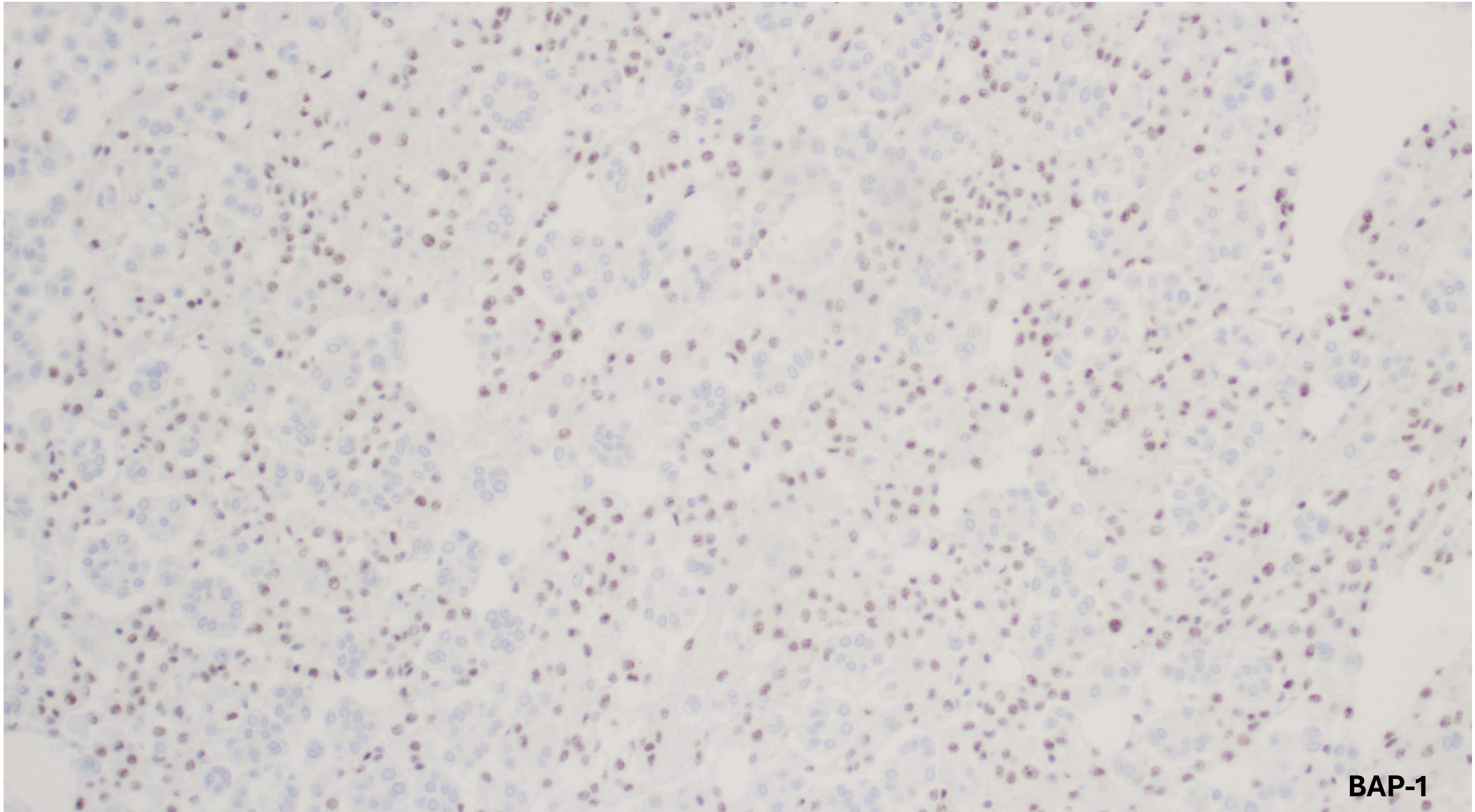

Claudin-4


BAP-1

#2
What is the Diagnosis?

- A. Reactive mesothelial proliferation
- B. Adenocarcinoma
- C. Mesothelioma
- D. Endometriosis

Malignant-Primary (Mesothelioma) Definitive criteria

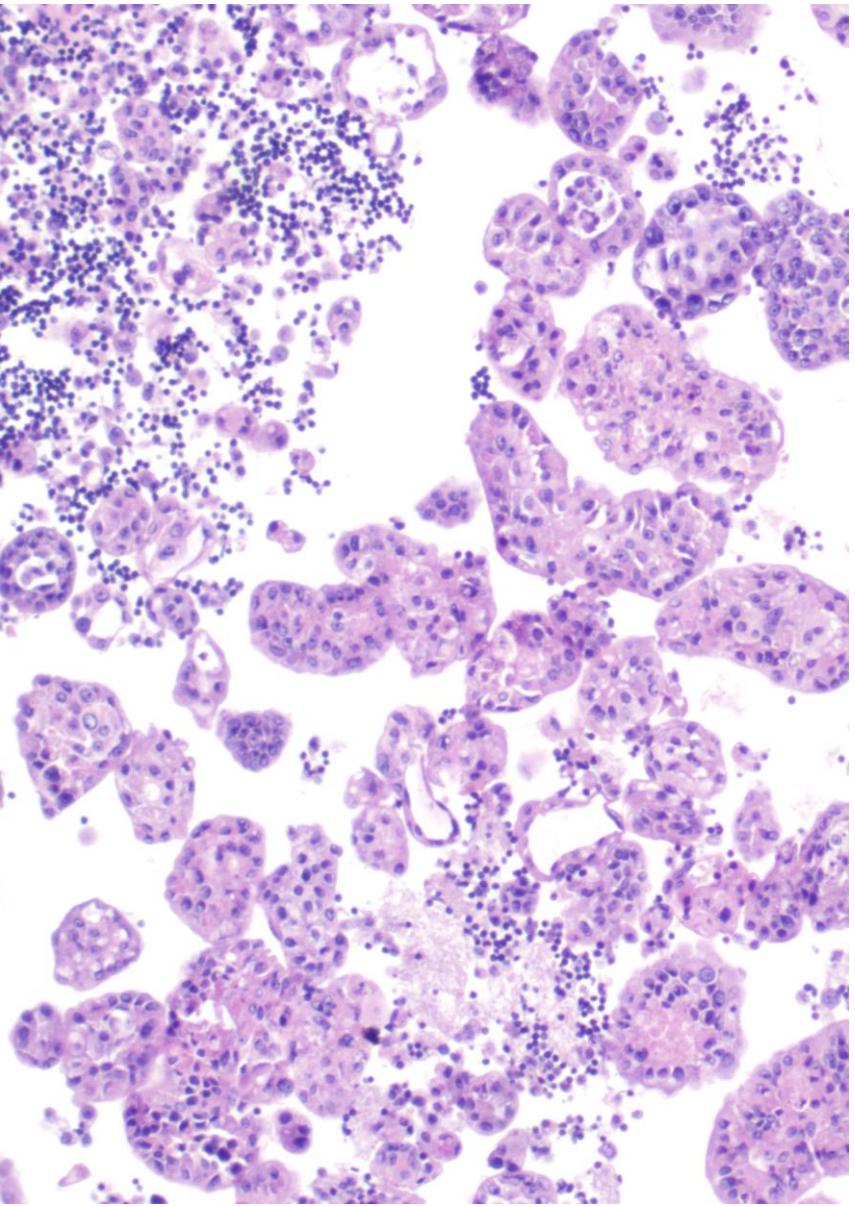
- Hypercellularity
- Numerous cellular spheres, papillary tissue fragments, berry-like morules, single cells or a mixture
- Malignant features identified by either:
  - Overt nuclear abnormalities diagnostic of malignancy (nuclear enlargement, irregular nuclear membranes, macronucleoli, frequent binucleation, and multinucleation, cellular pleomorphism, atypical mitoses)
  - Numerous large tissue fragments and cellular clusters

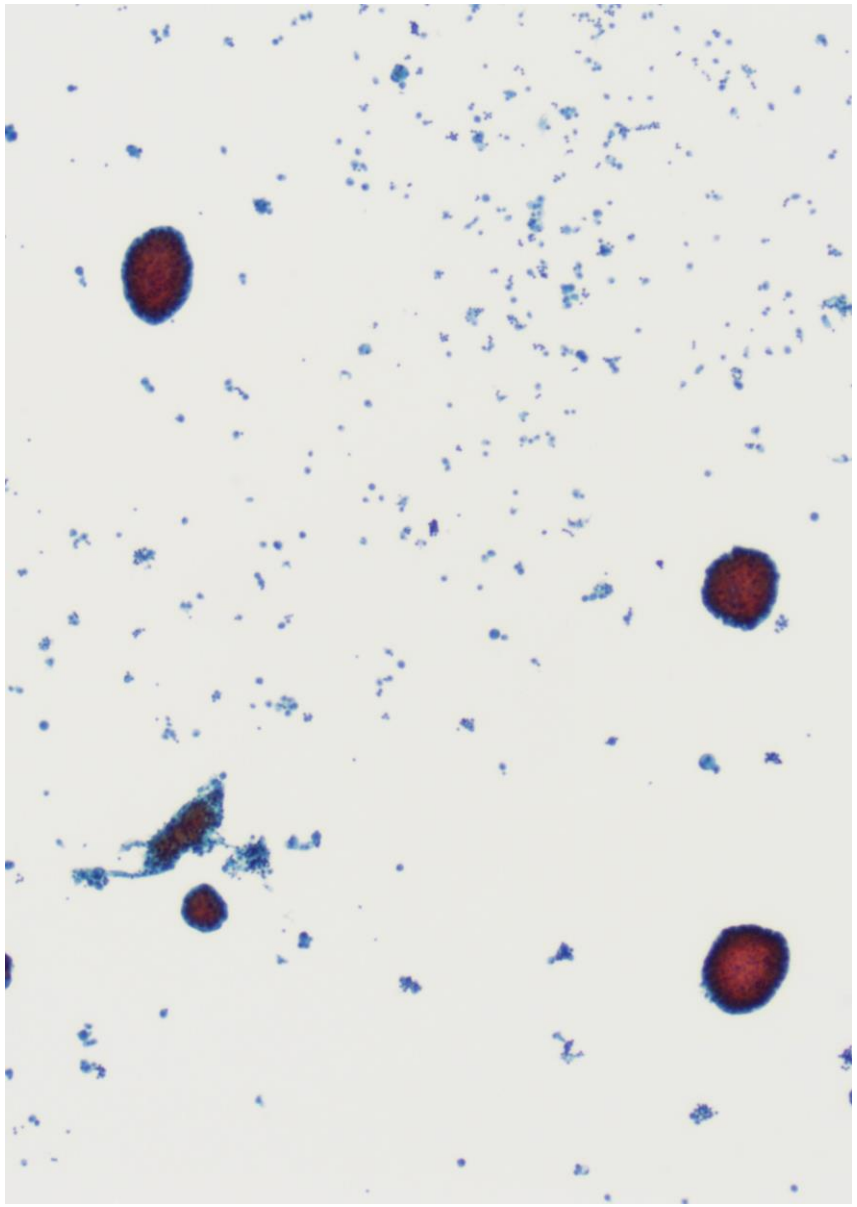
Malignant-Primary (Mesothelioma) Supportive criteria

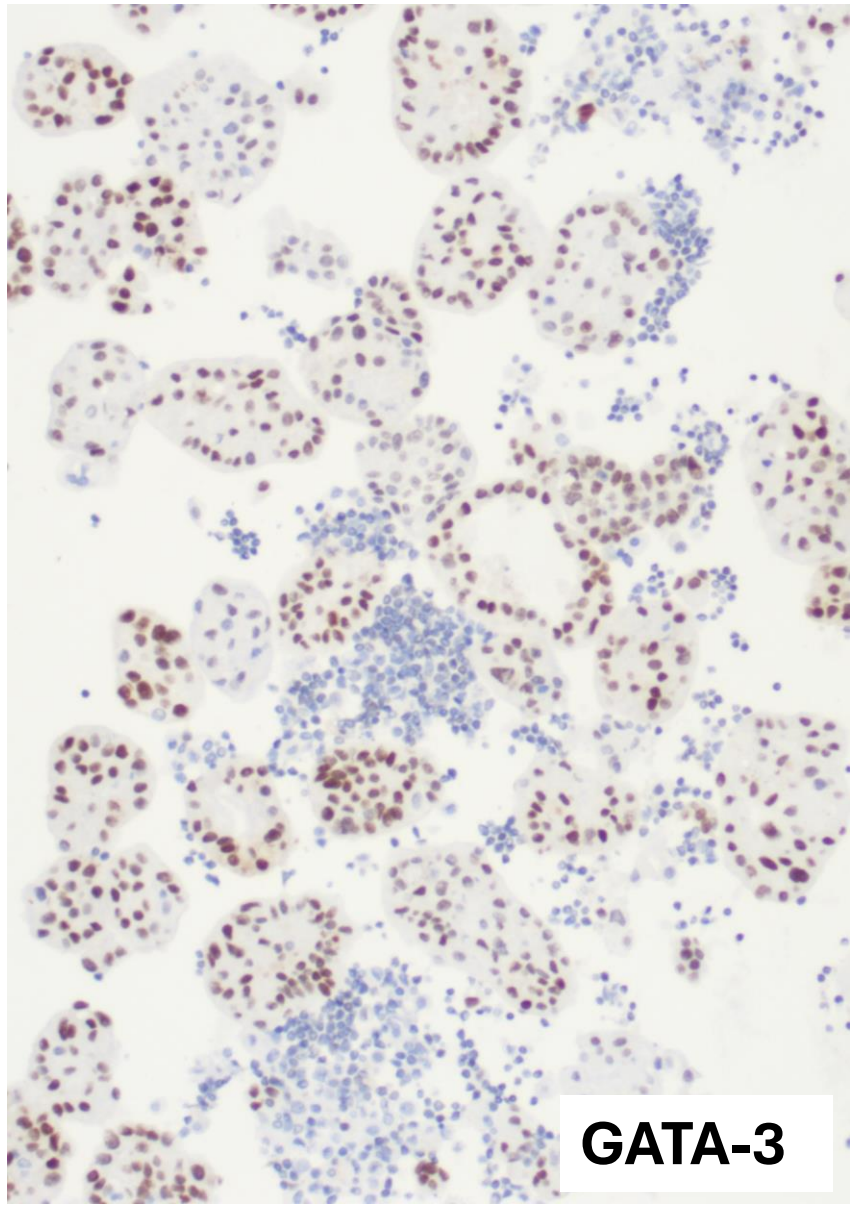
- Significantly enlarged mesothelial cells with abundant cytoplasm
- Large nuclei with subtle atypia
- Prominent nucleoli, often variable in size and number
- Wide variation in cellular size
- Numerous multinucleated cells
- Tissue fragments or papillary groups with collagen or basement membrane cores
- Pseudokeratotic cells
- Large clusters with scalloped (“knobby”) edges
- Giant mesothelial cells, including binucleated and multinucleated forms
- Cellular clasping and “cell within cell” appearance

Case 3

- 72 yr old female presented with bilateral pleural effusion
- History of ovarian serous carcinoma, lung adenocarcinoma and infiltrating ductal carcinoma of right breast







PAX-8 Negative; TTF-1/Napsin-A Negative

#3
What is the Diagnosis?

- A. Metastatic serous papillary carcinoma
- B. Metastatic lung adenocarcinoma
- C. Mesothelioma
- D. Metastatic breast carcinoma

Key diagnostic features of Adenocarcinoma

- Cellular sample with 2-cell population
- 3-D cell groups with common cell border
- Numerous large clusters
- Eccentric nuclei with marked hyperchromasia and prominent irregular nucleoli
- Homogeneous delicate cytoplasm with large randomly distributed secretory vacuoles
- Lacunae (cell block sections)

When to use Immunohistochemistry for effusions

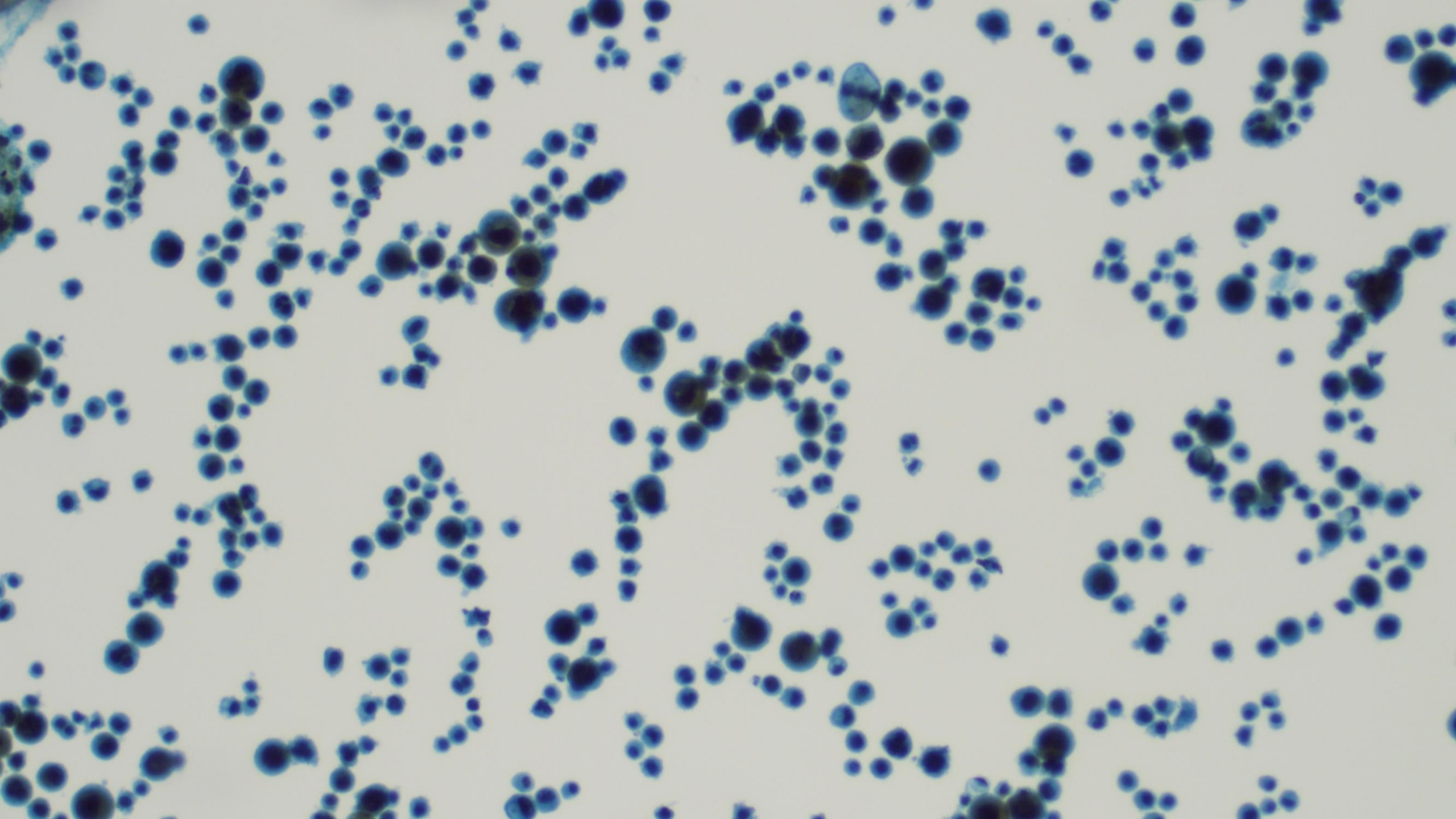
- Confirming malignancy when morphology alone is equivocal
- Distinguishing adenocarcinoma from mesothelioma
- Screening an effusion for lobular breast cancer
- Establishing the primary site of a malignant effusion
  - Occult primary
  - Multiple primaries
- Establishing vulnerability of advanced lung and other cancers to targeted therapy and immunotherapy
- Assessing receptor status (e.g., HER2) for patients with breast and gastric cancers

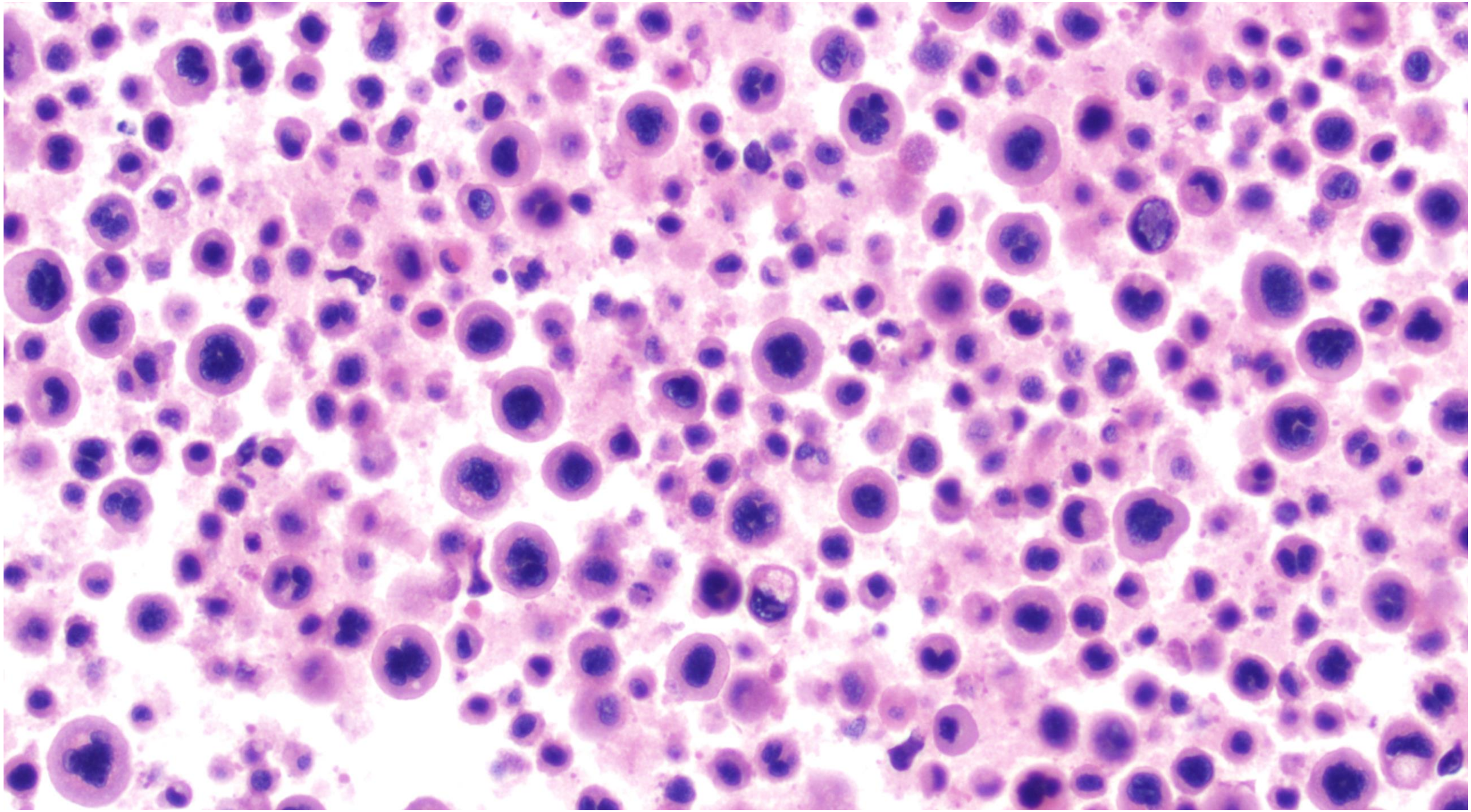
Pitfalls in body cavity fluids

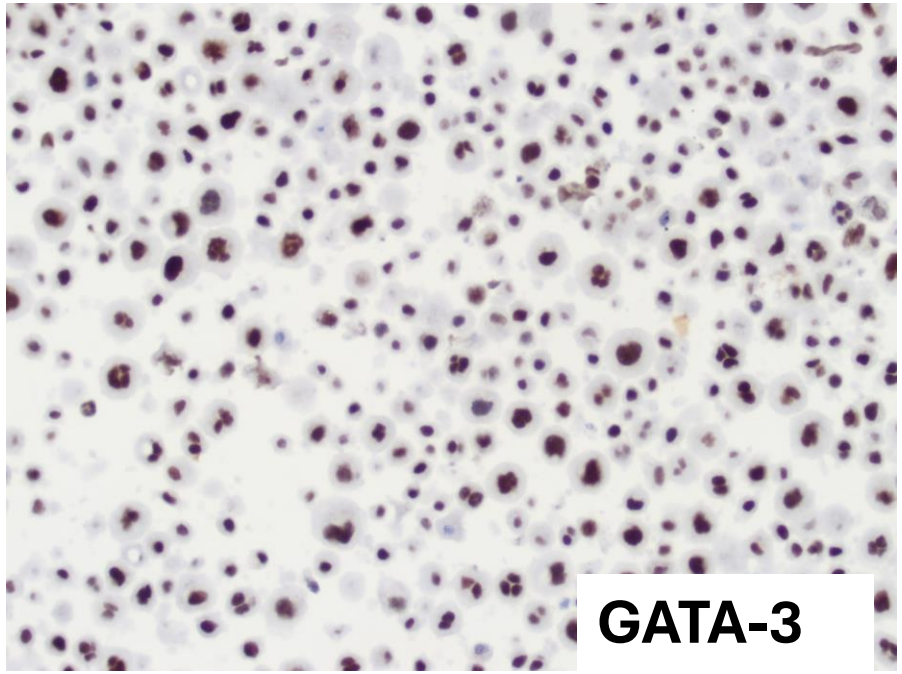
- Single malignant cells
- Uniform population of tumor cells with virtually no mesothelial cells
- Reactive atypia

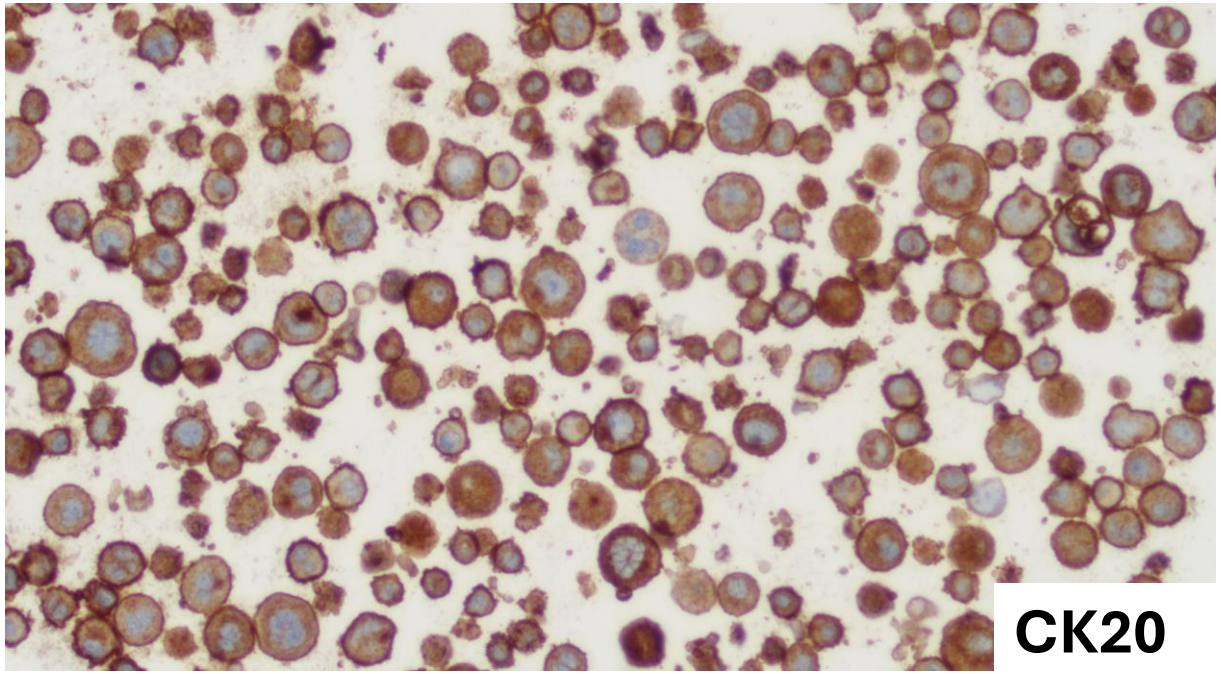
Case 4

- 84 yr old male presented with bilateral pleural effusion
- History of gastric adenocarcinoma, high grade urothelial carcinoma and melanoma






GATA-3


CK20

Immunohistochemistry

- GATA-3 +
- SOX10 –
- HMB45 –
- CK7 +
- CK20 +
- CDX2 –

#4
What is the Diagnosis?

- A. Metastatic melanoma
- B. Metastatic high grade urothelial carcinoma
- C. Mesothelioma
- D. Metastatic gastric adenocarcinoma

Clues to identifying single malignant cells

- Intracytoplasmic mucin may be a distinct, well-defined vacuole i.e. target-like, or may be multiple, small, fine vacuoles
- High nuclear/cytoplasmic ratio (N/C) cells
- History – breast (lobular), gastric or other GI primaries are especially notorious for producing dispersed malignant cells
- Always look for the lurking, hiding malignant cells

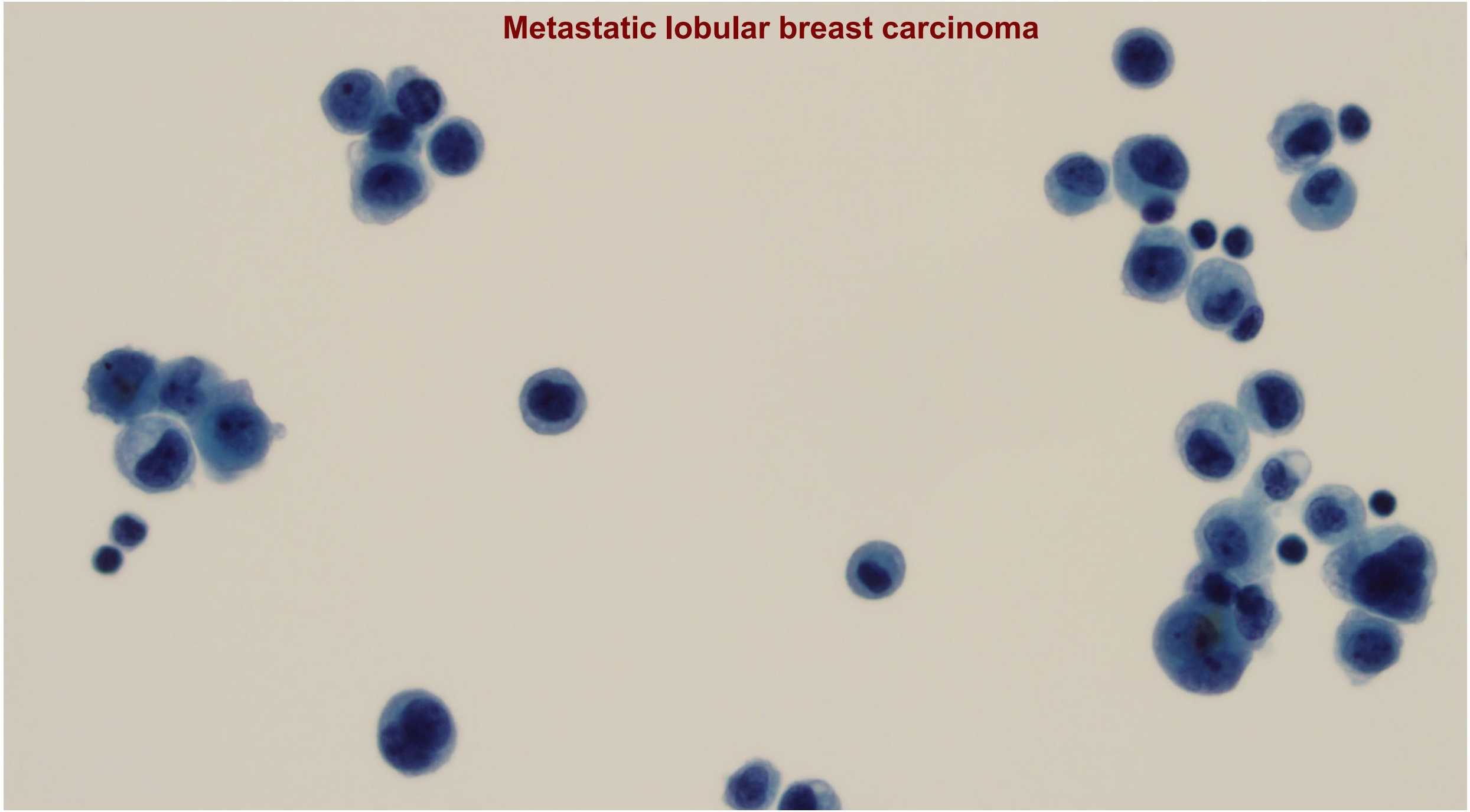
Differential diagnosis of overtly malignant single cells

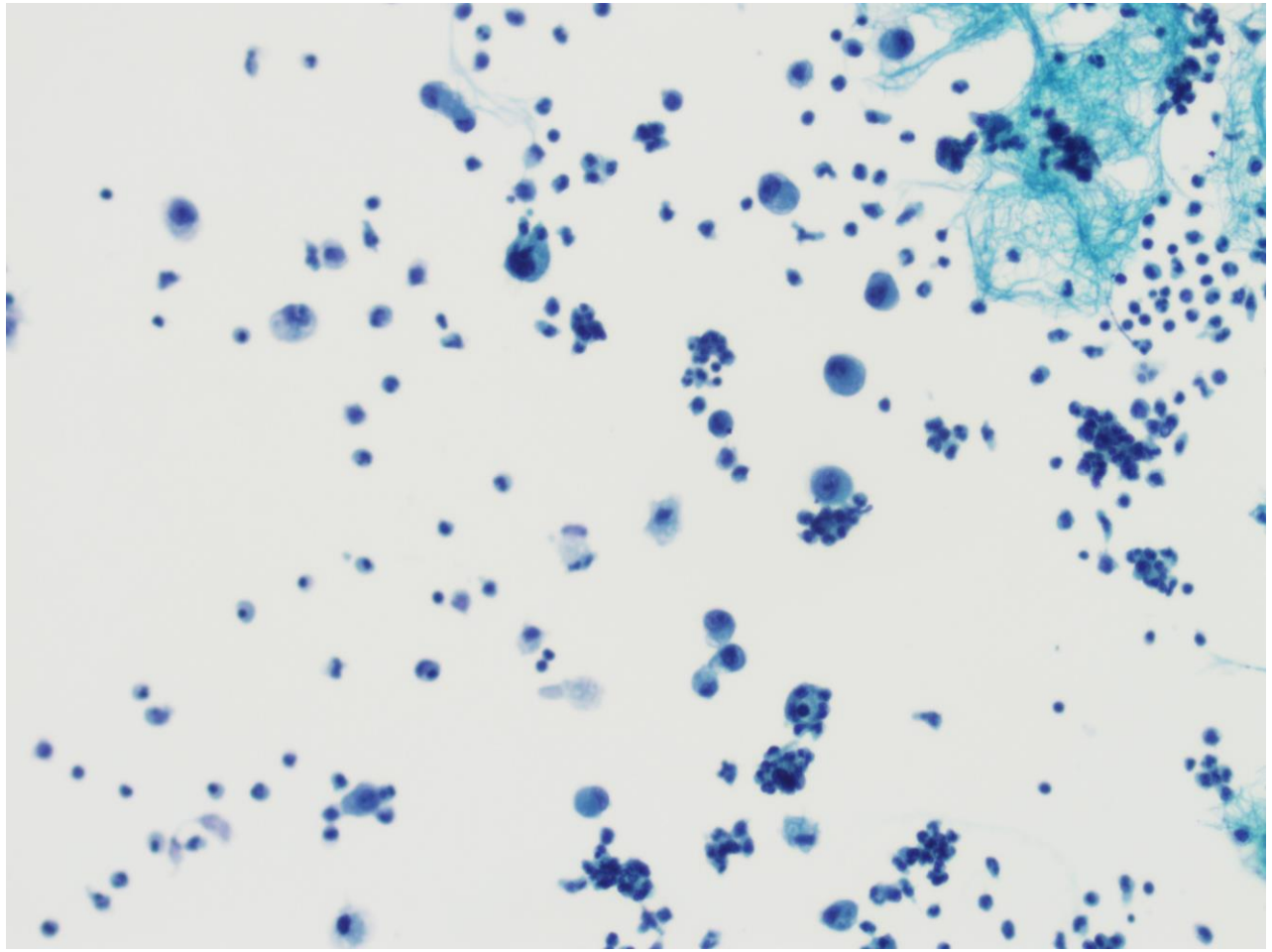
1. Carcinoma
2. Large cell lymphoma
3. Acute leukemia
4. Melanoma
5. Malignant mesothelioma
6. Sarcoma

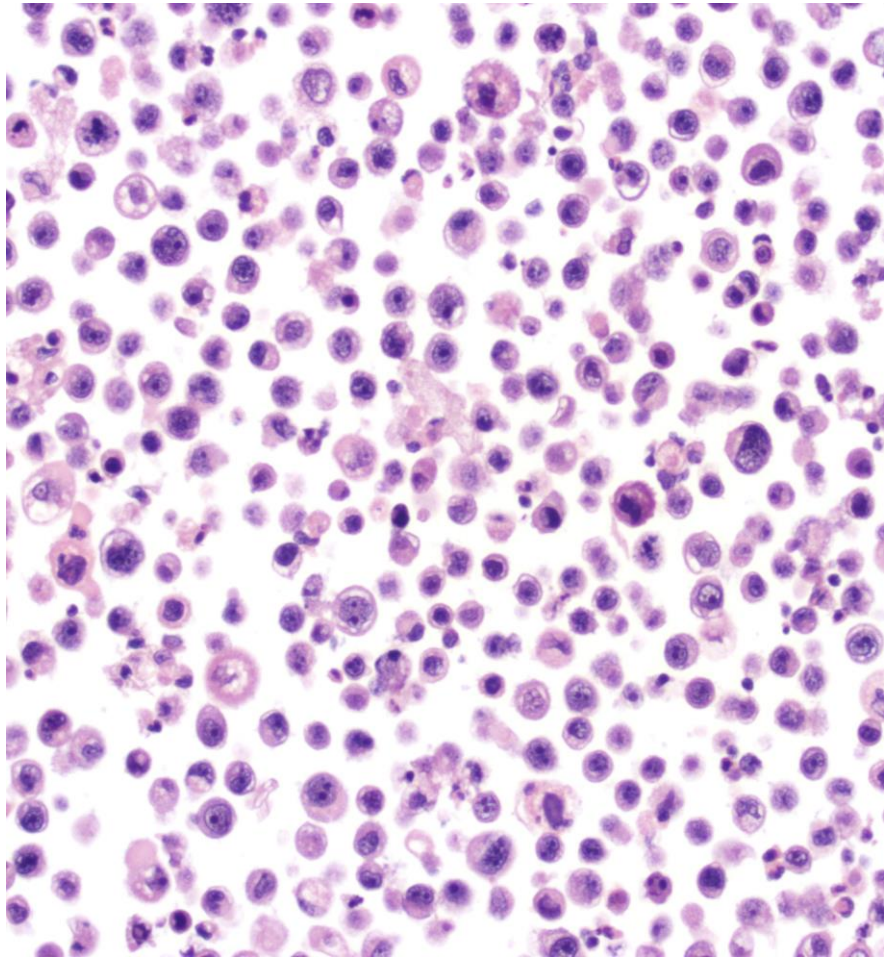
Basic immunohistochemistry panel

- Pancytokeratin
- LCA
- CD20
- CD30
- S-100
- Melanoma cocktail (or HMB-45 or Melan-A or SOX-10)

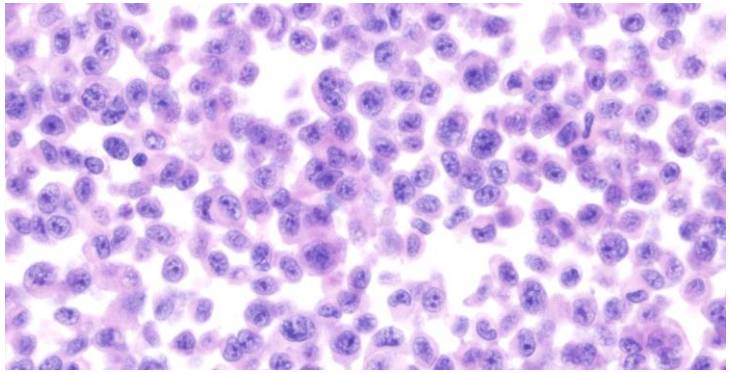
Metastatic lobular breast carcinoma

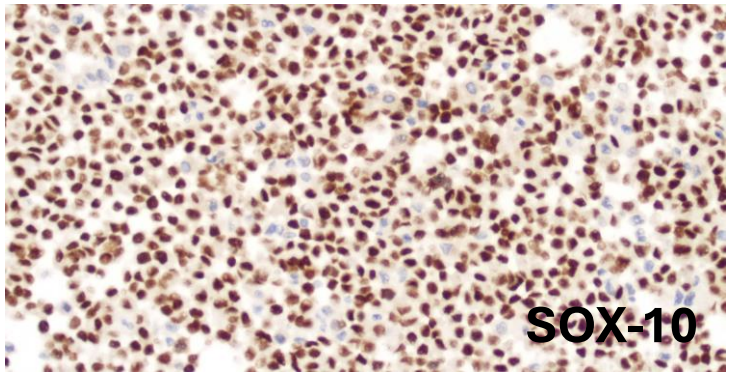


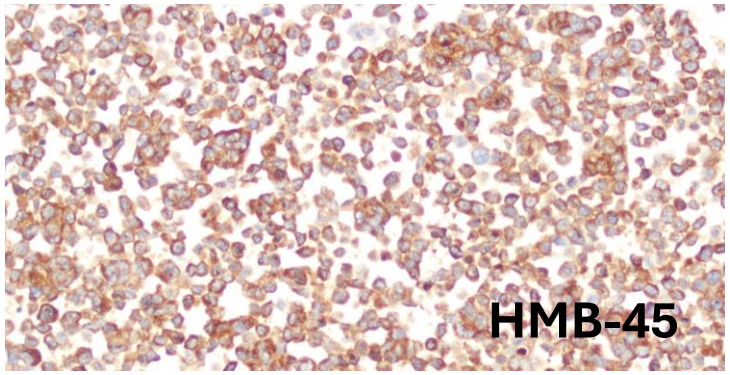


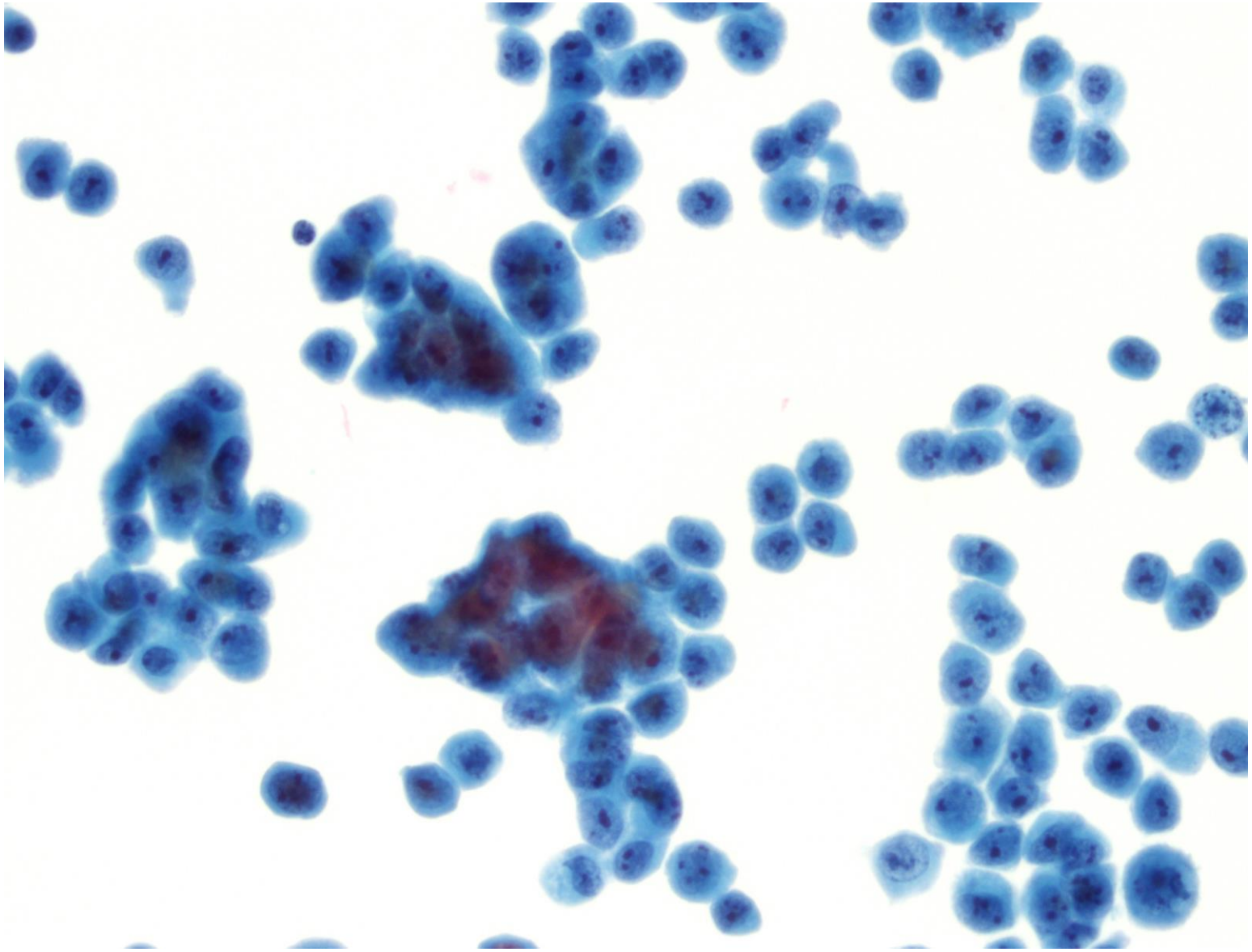


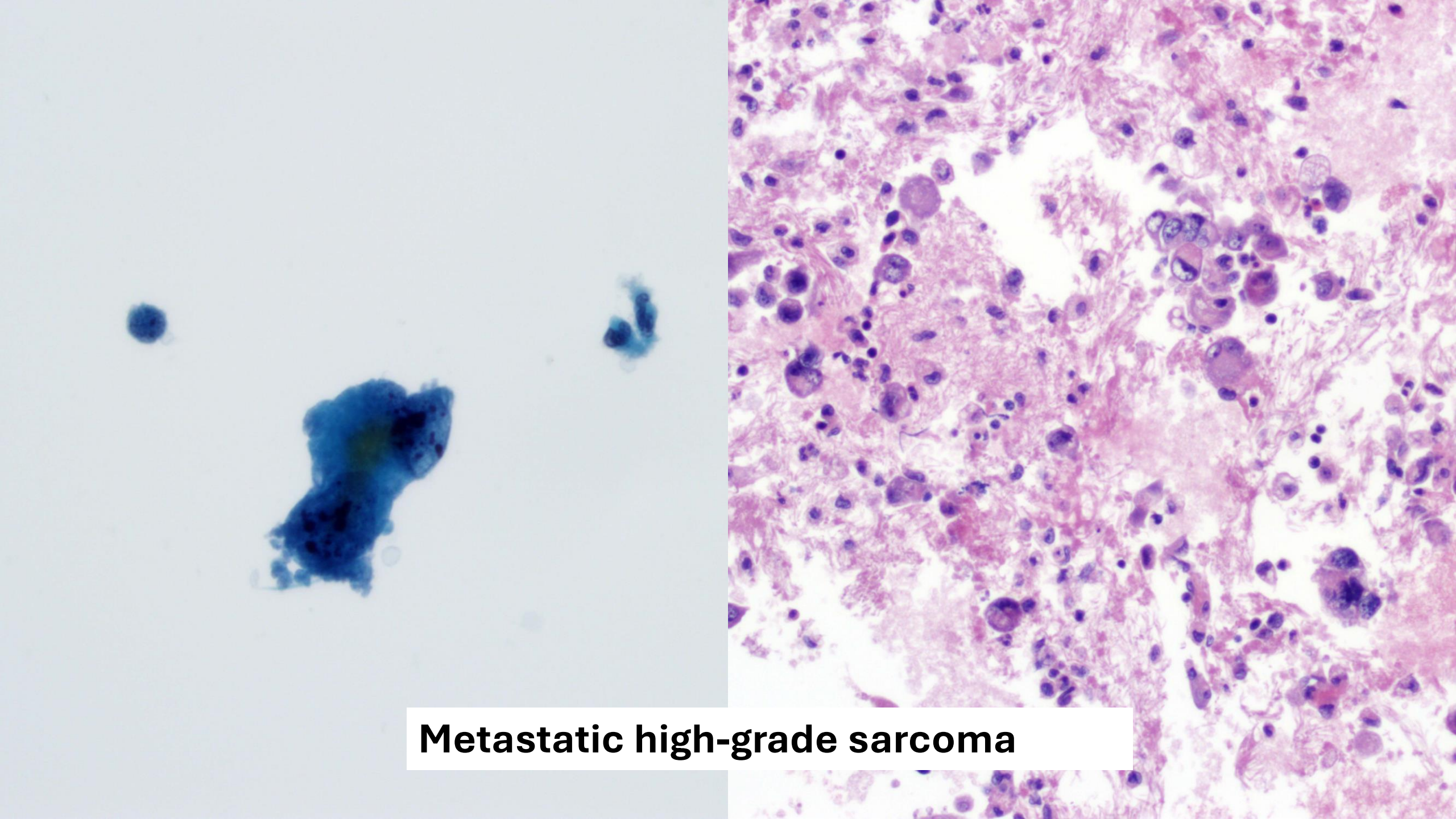
Gastric adenocarcinoma




SOX-10


HMB-45





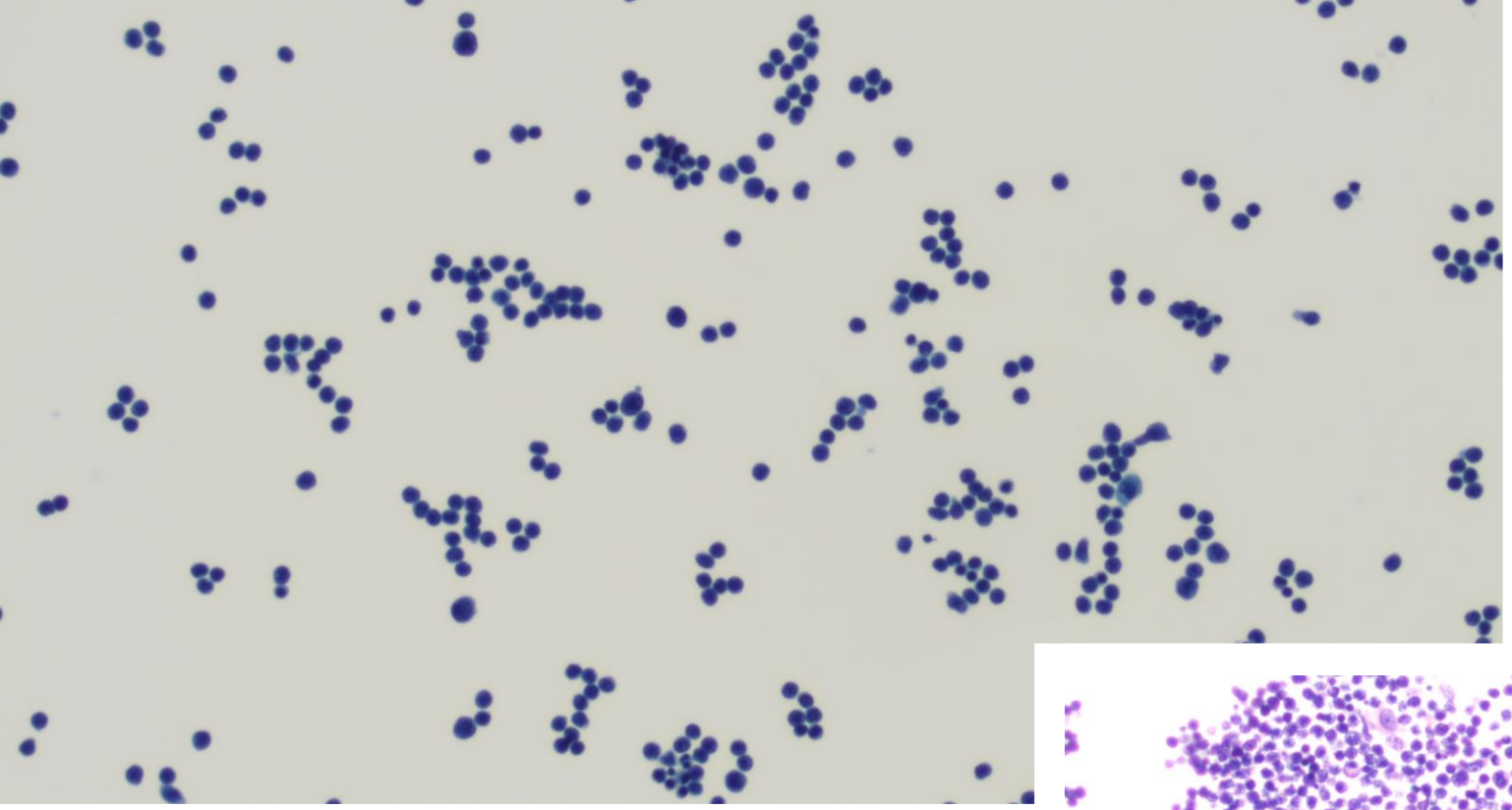
Metastatic high-grade sarcoma

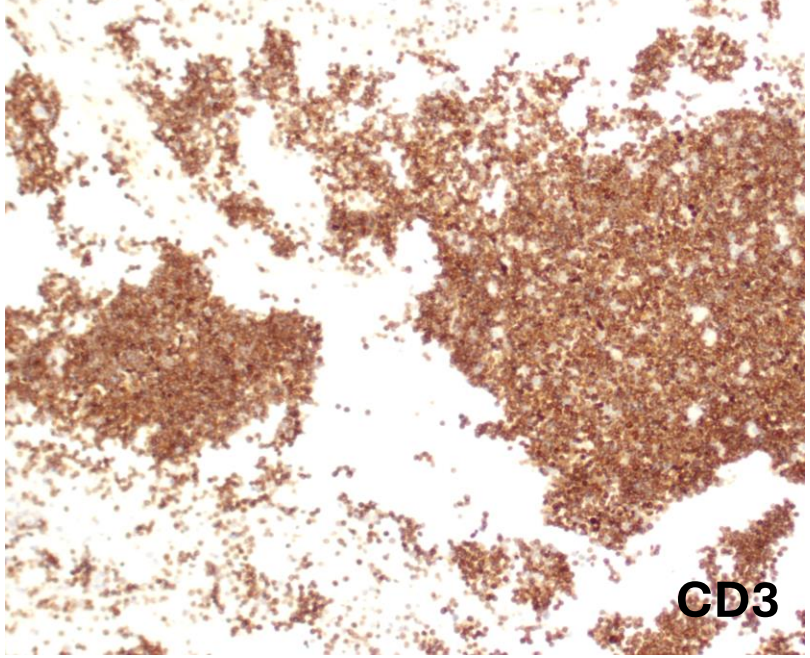
Lymphocytic effusions

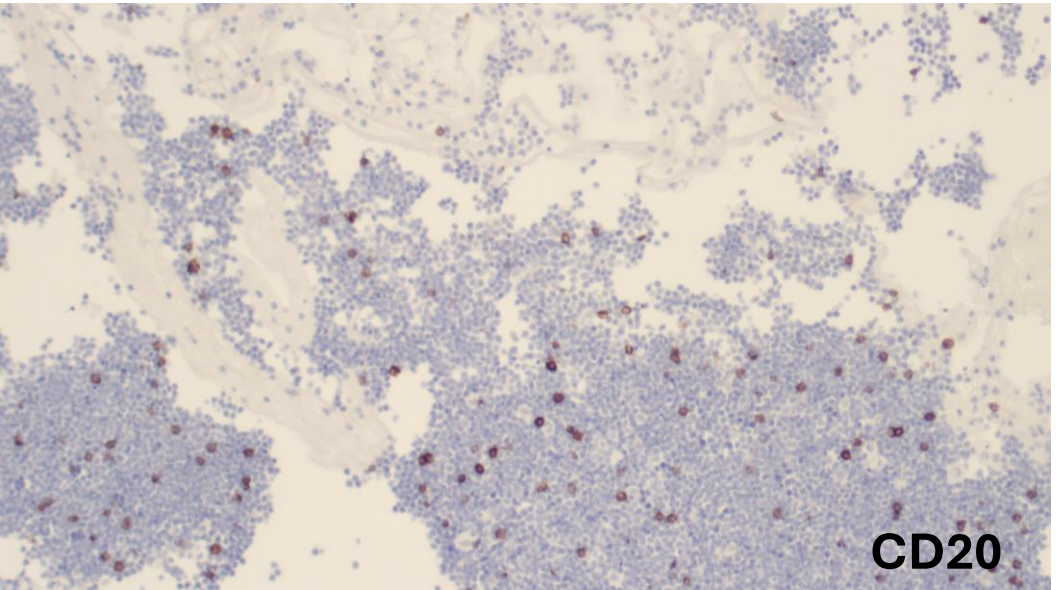
- Relatively common but nonspecific finding
- High cellular preparations composed almost exclusively of dispersed small lymphocytes
- Mesothelial cells conspicuously absent or scant
- Common causes:
  - Malignancy
    - Pleural malignancy: Evoke a peritumoral lymphocytic response
    - Lung malignancy: Obstruct lymphatic outflow
    - Lymphoid malignancy: Rarely the initial manifestation
  - Tuberculosis
  - Status post coronary artery bypass graft

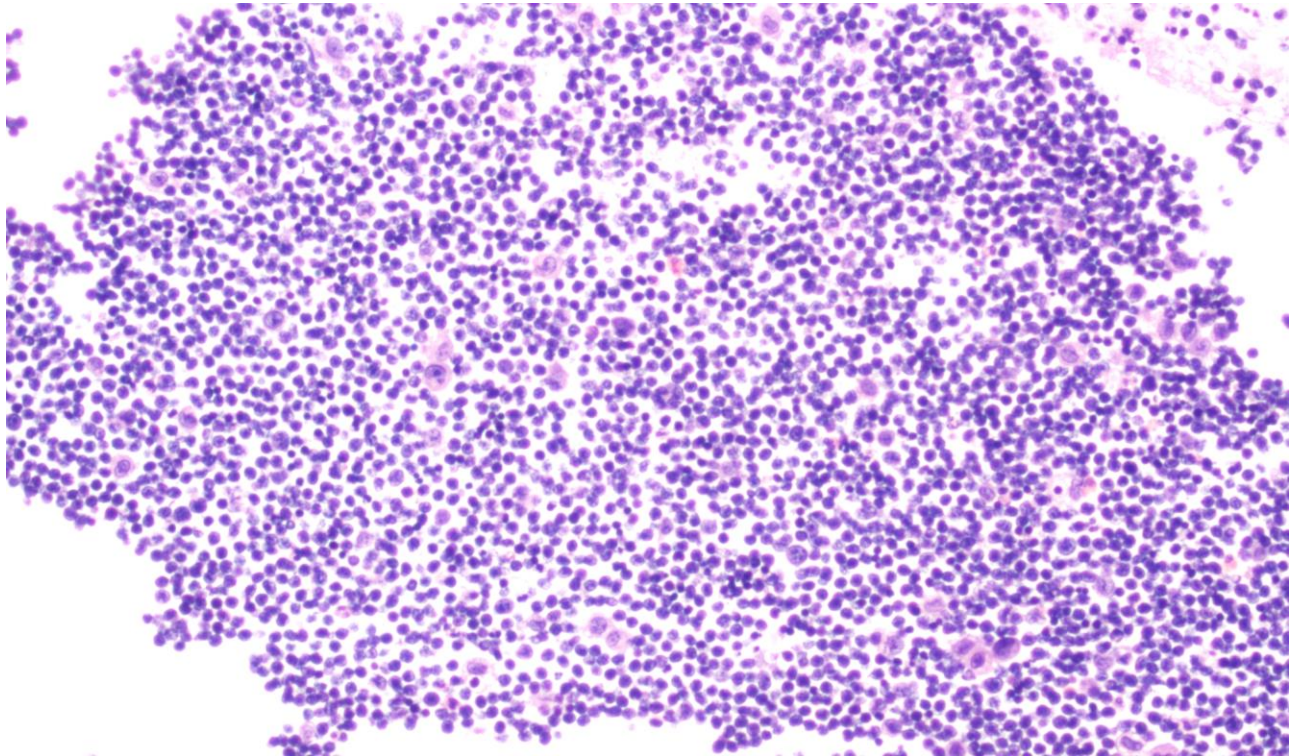
Effusions containing a mixed population of lymphoid cells

- Need surface markers for diagnosis
  - Kappa κ
  - Lambda λ
  - CD3
  - CD20




CD3


CD20

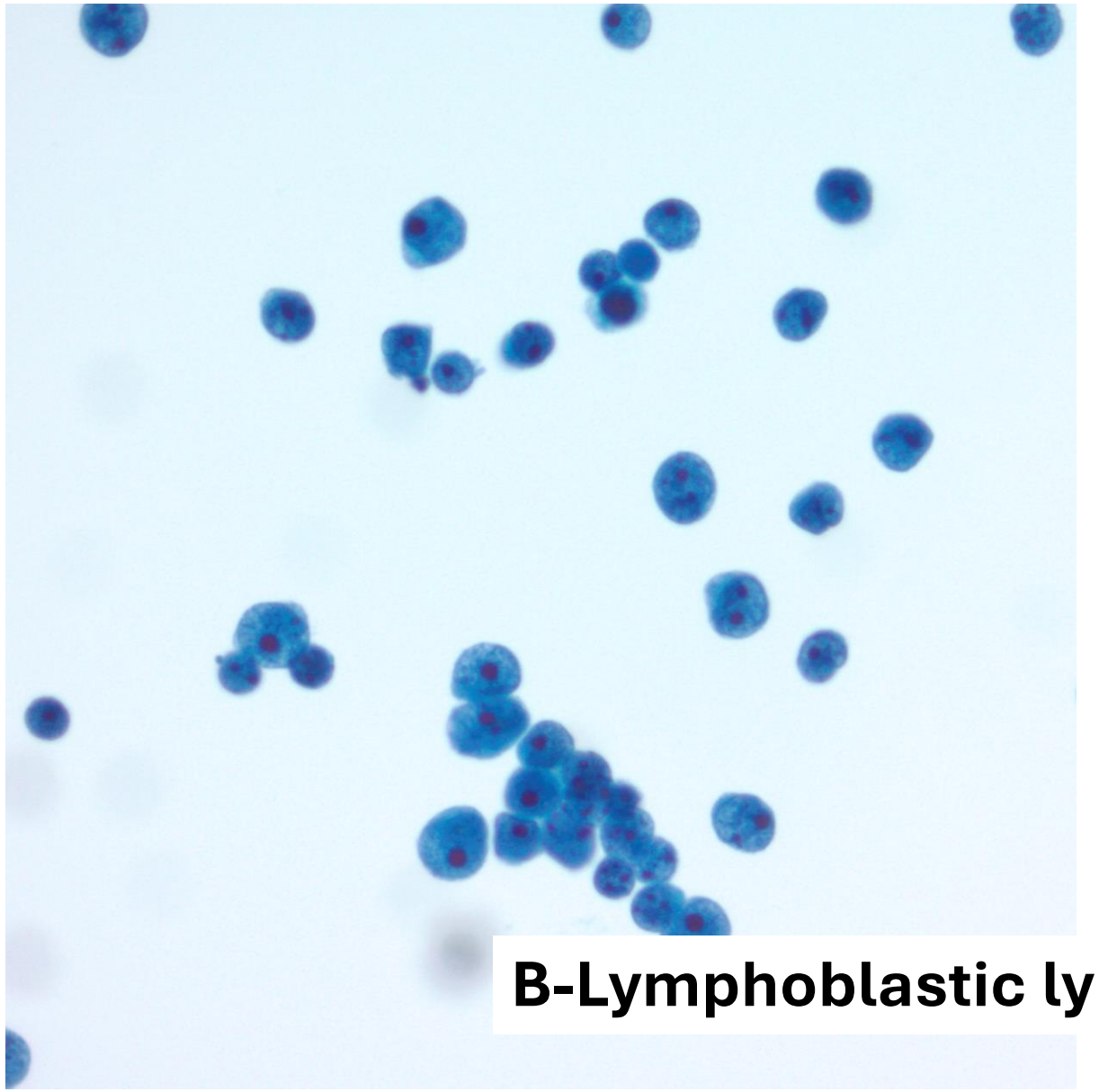


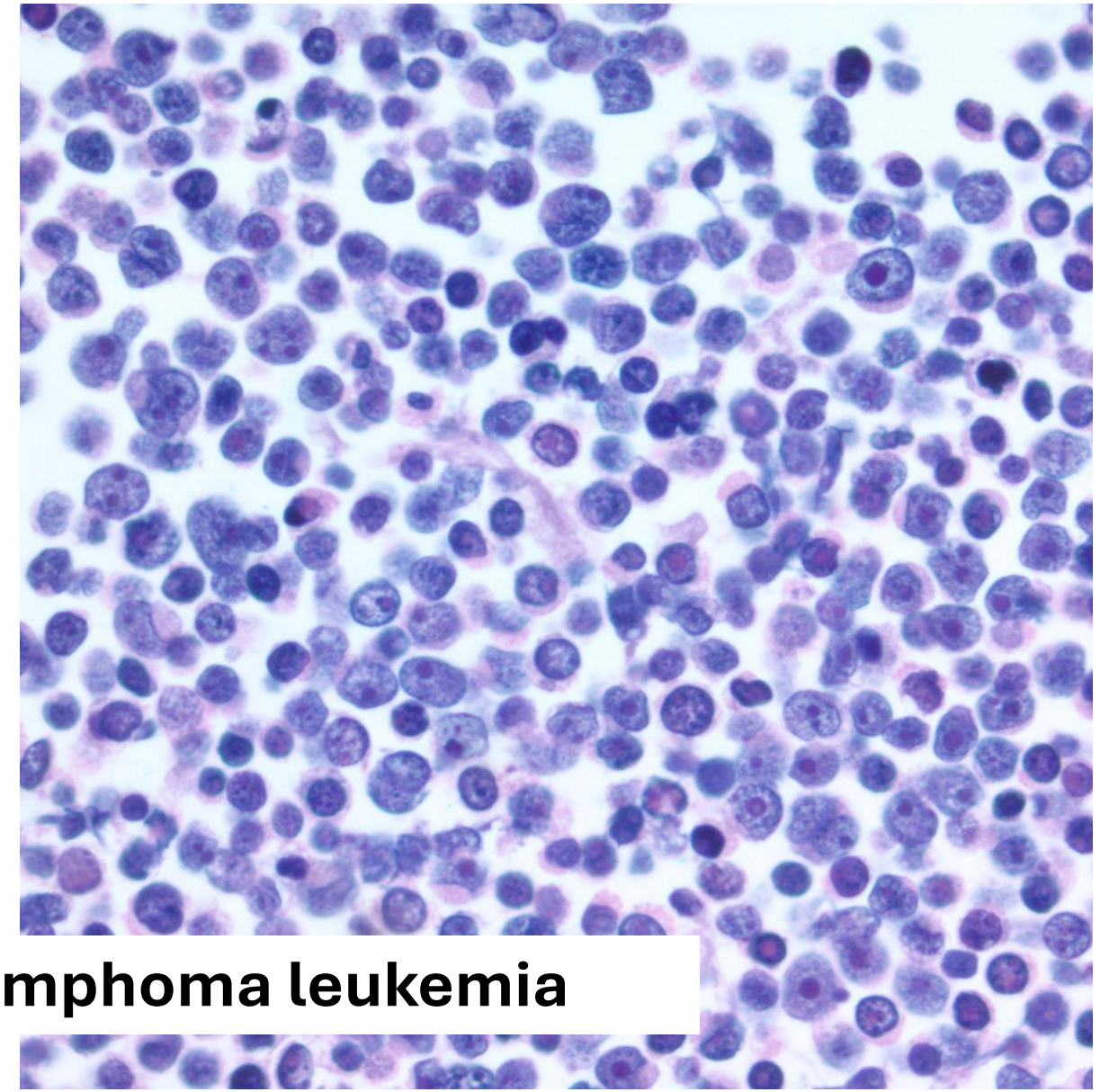
Effusions with lymphoid cells and other hematologic cells

- Lymphomas and leukemias that commonly produce malignant effusions are high grade lymphomas and acute leukemias
- The lymphoma/leukemic cells are large and cytologically abnormal

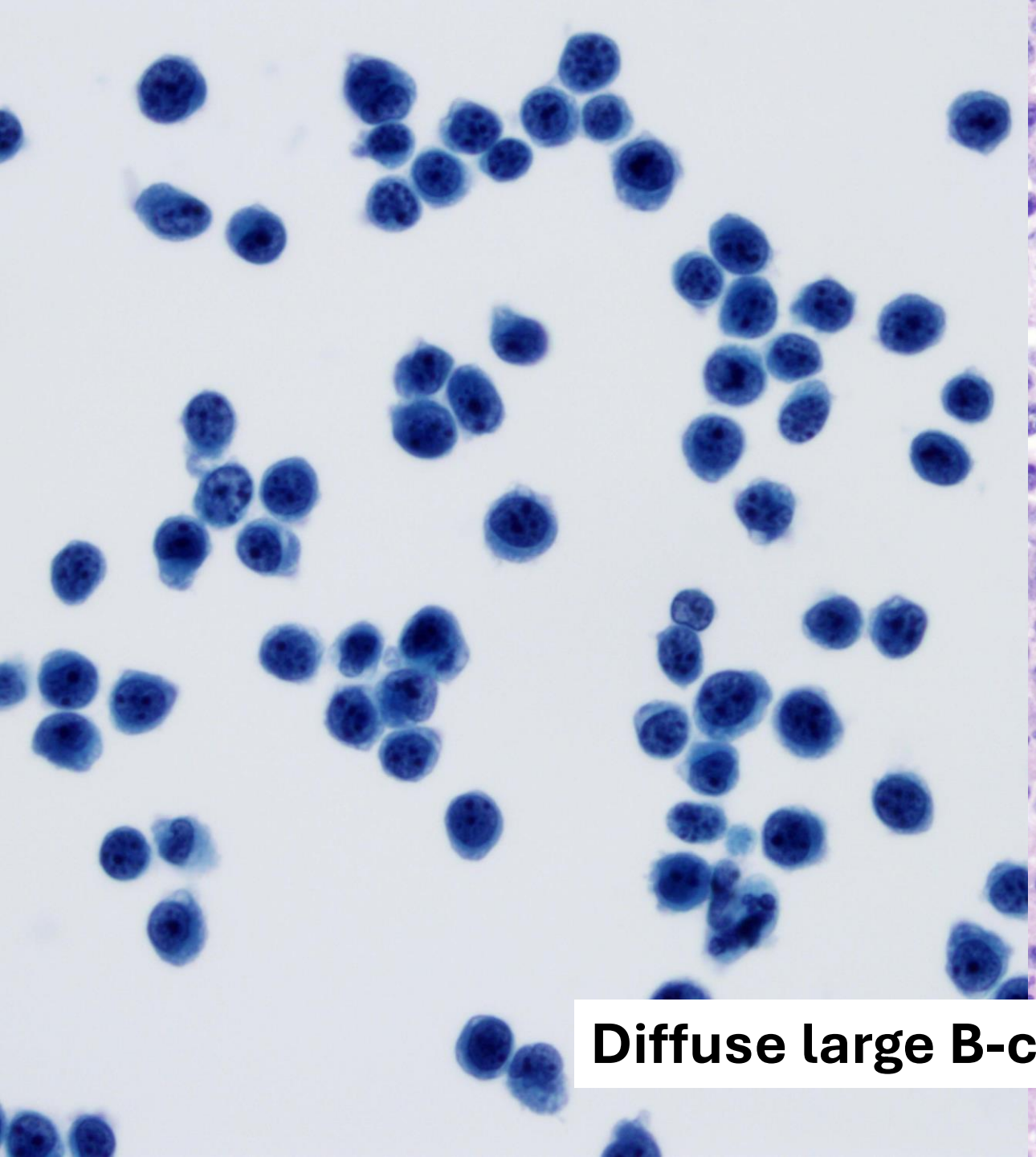
Examples of hematologic malignancies in effusion

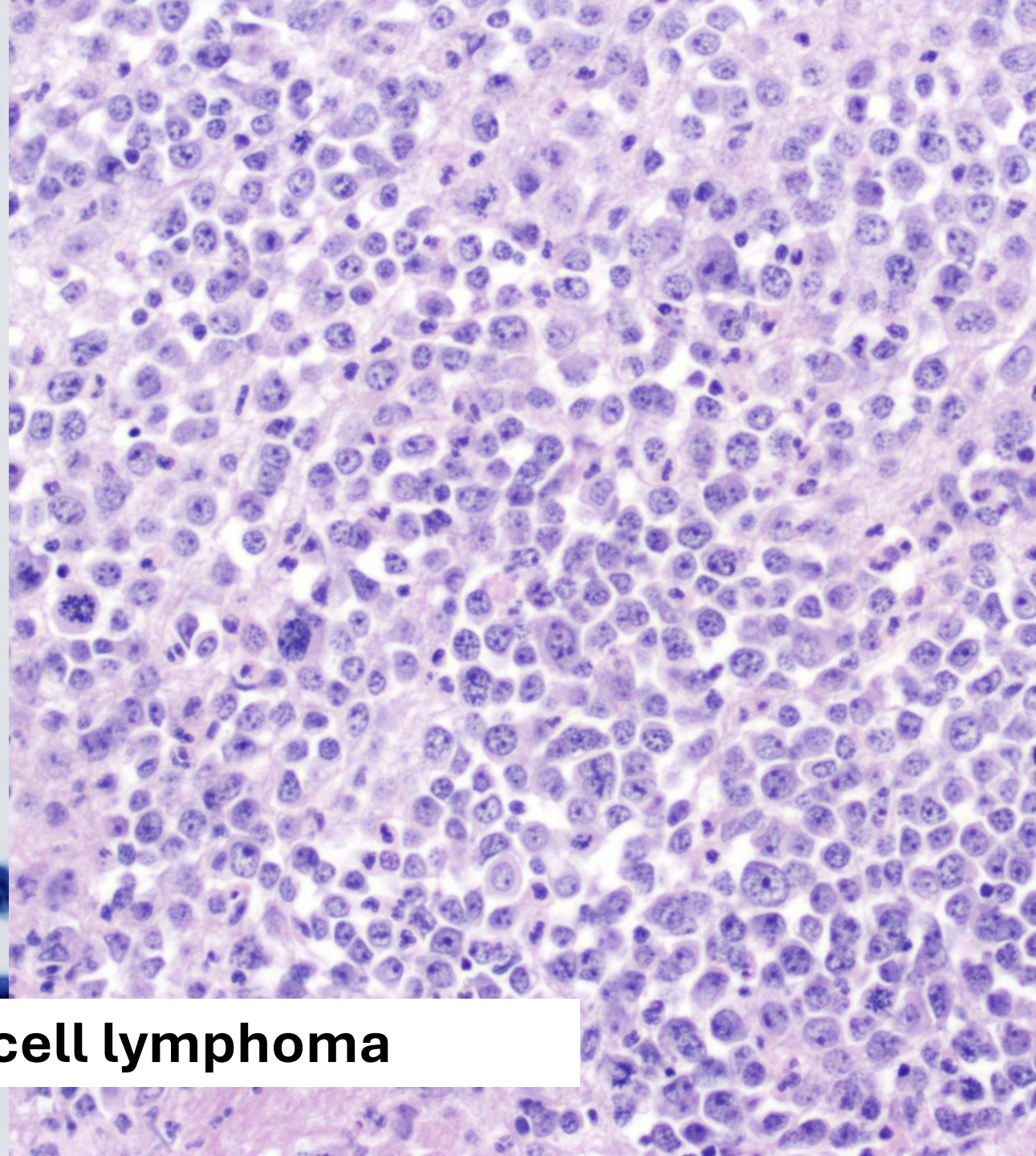
- Primary effusion lymphoma
- Anaplastic large cell lymphoma
- Diffuse large B cell lymphoma
- Burkitt lymphoma
- Acute myeloid leukemia
- Acute lymphocytic leukemia
- Blast crisis of chronic myelogenous leukemia
- T-cell lymphomas (rare involvement of body cavities)
- Plasma cell neoplasm (rare)



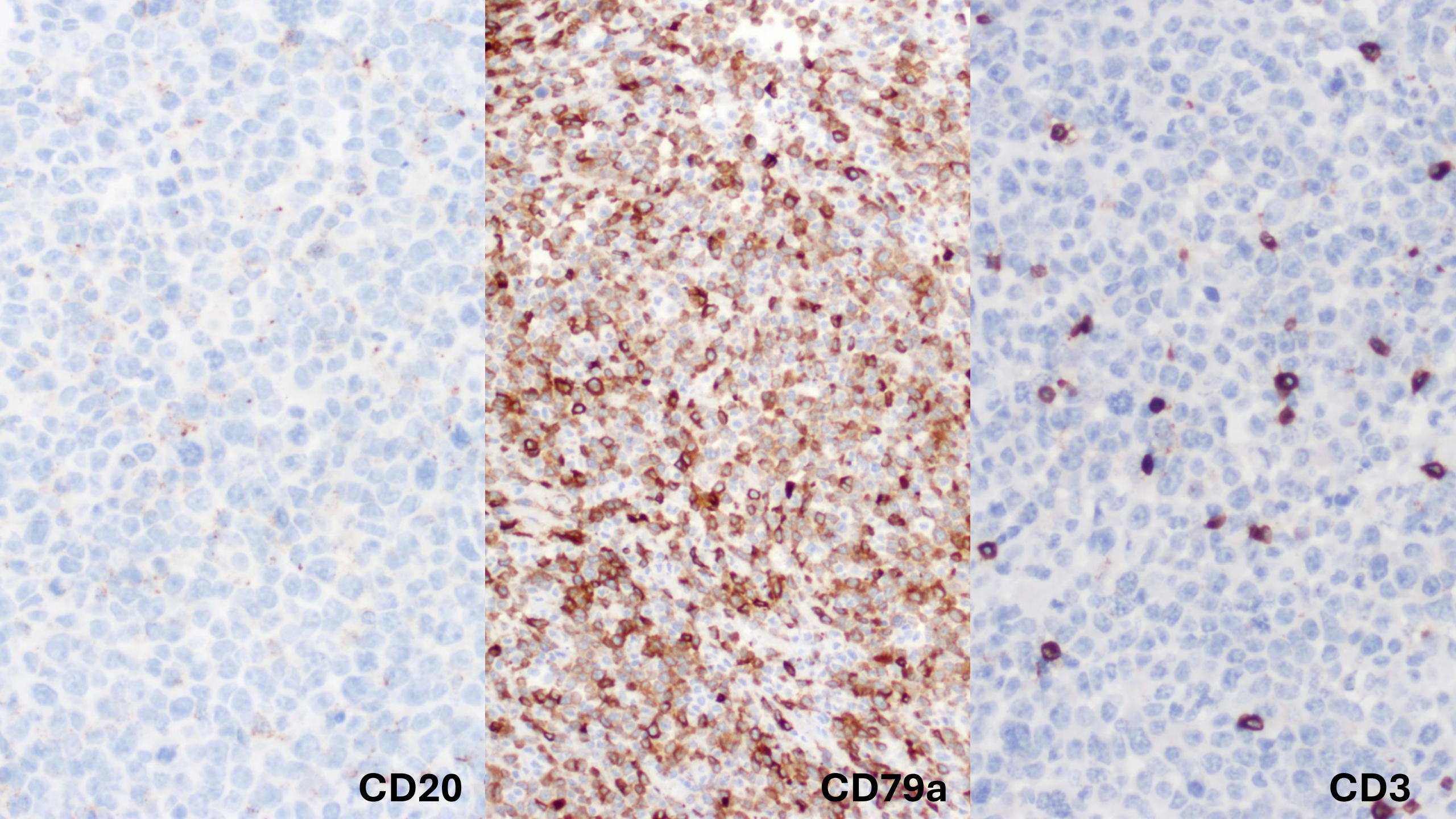


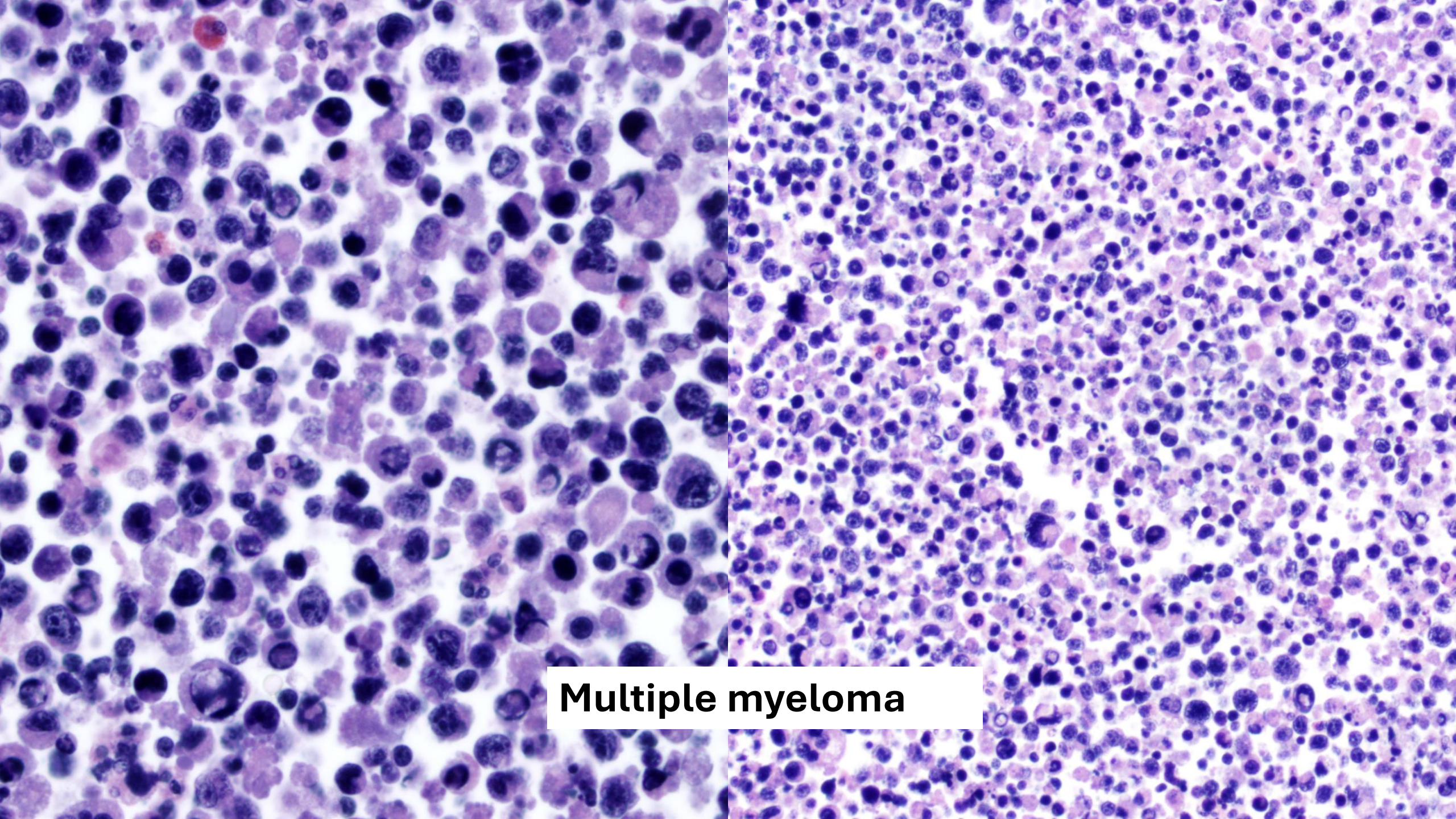
B-Lymphoblastic lymphoma leukemia

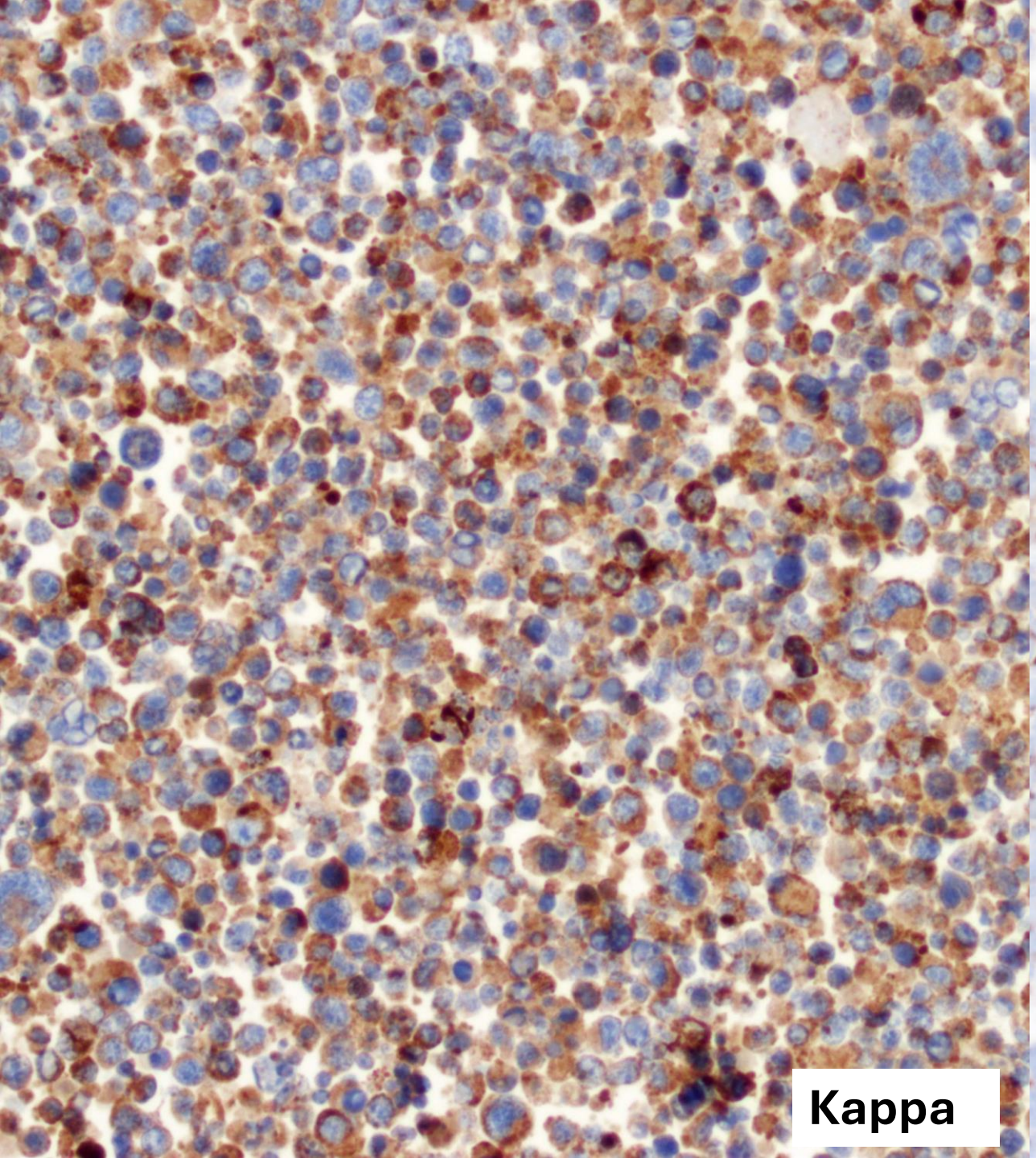


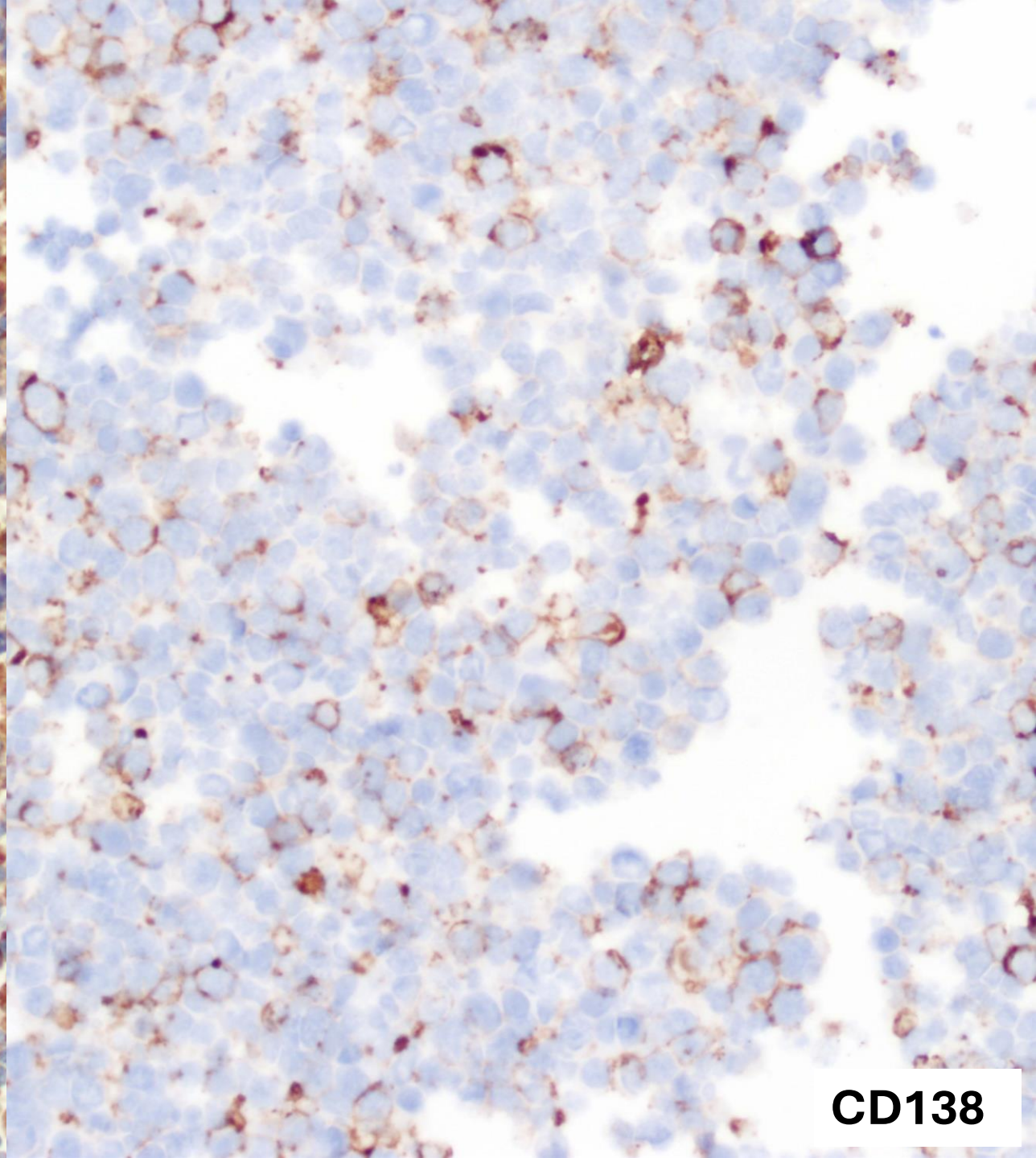


Diffuse large B-cell lymphoma


CD20
CD79a
CD3

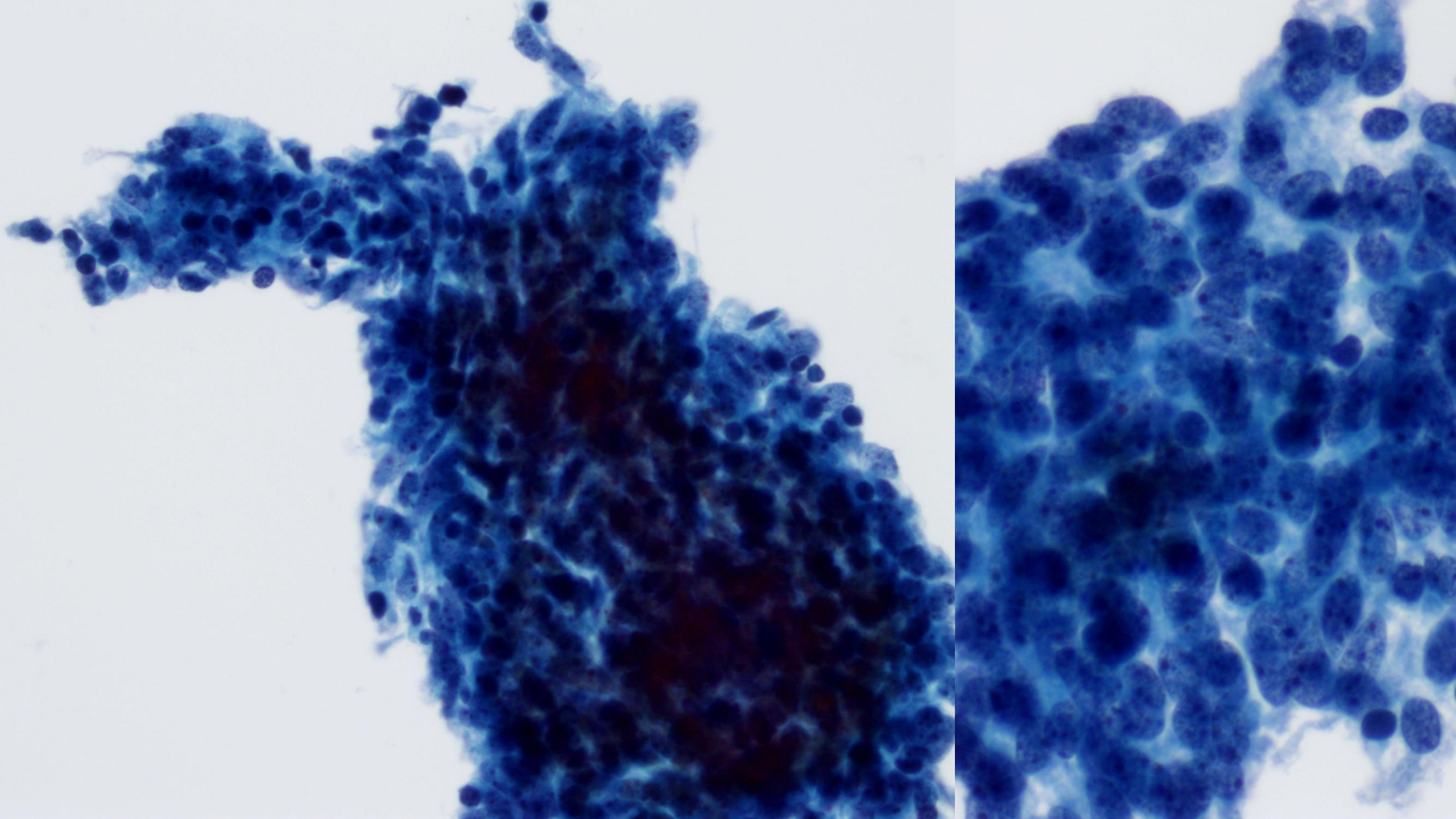

Multiple myeloma

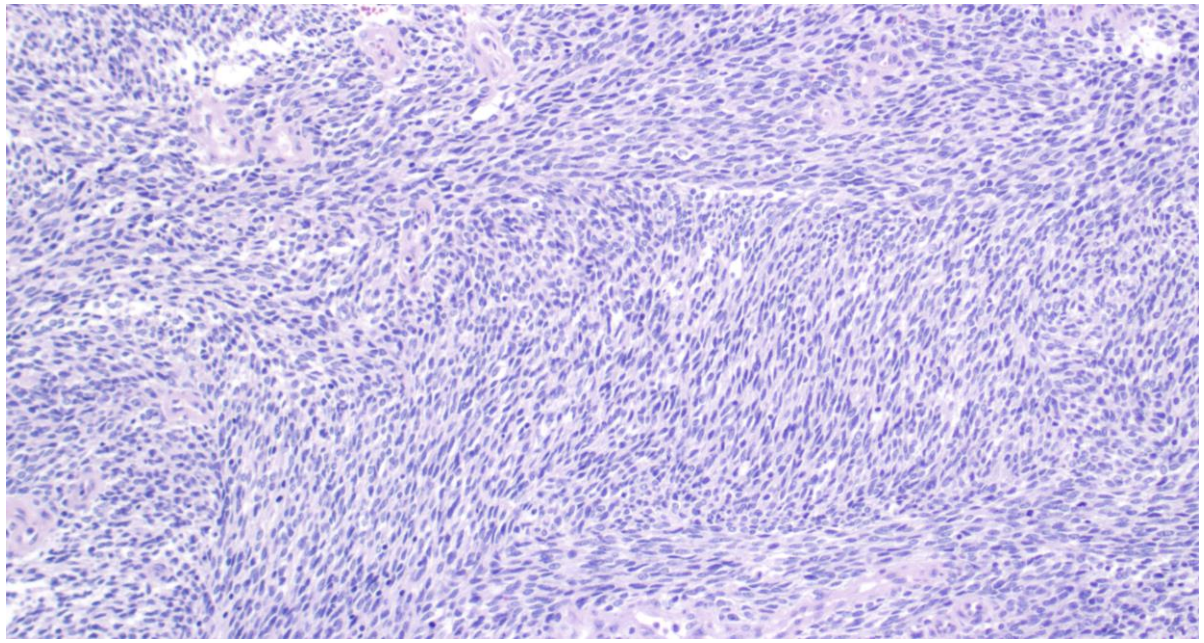

Kappa

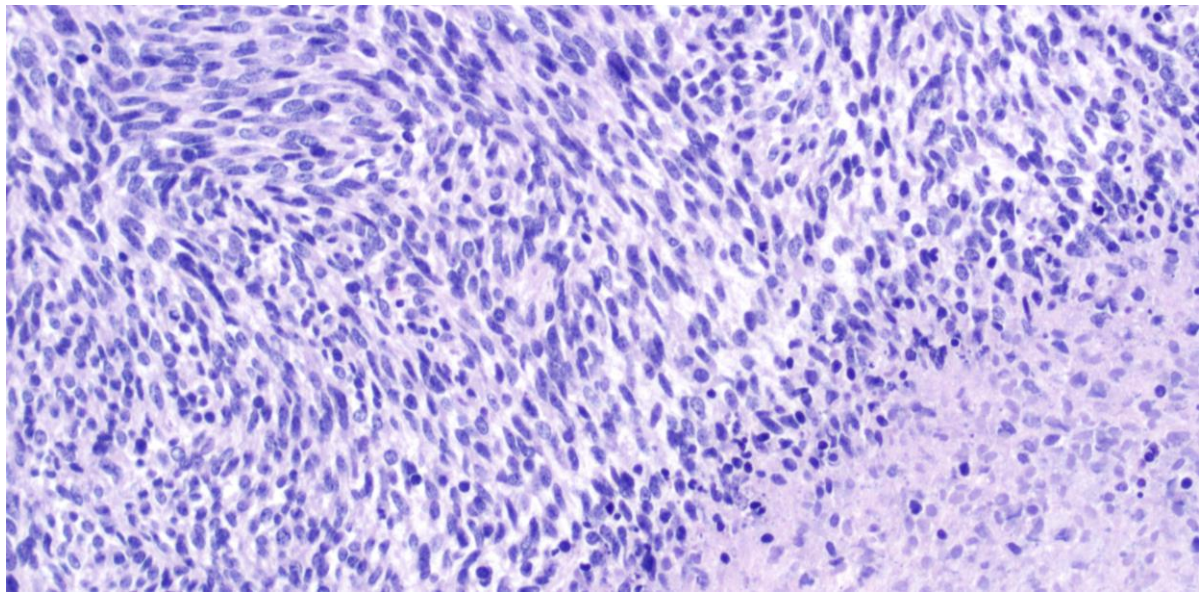

CD138

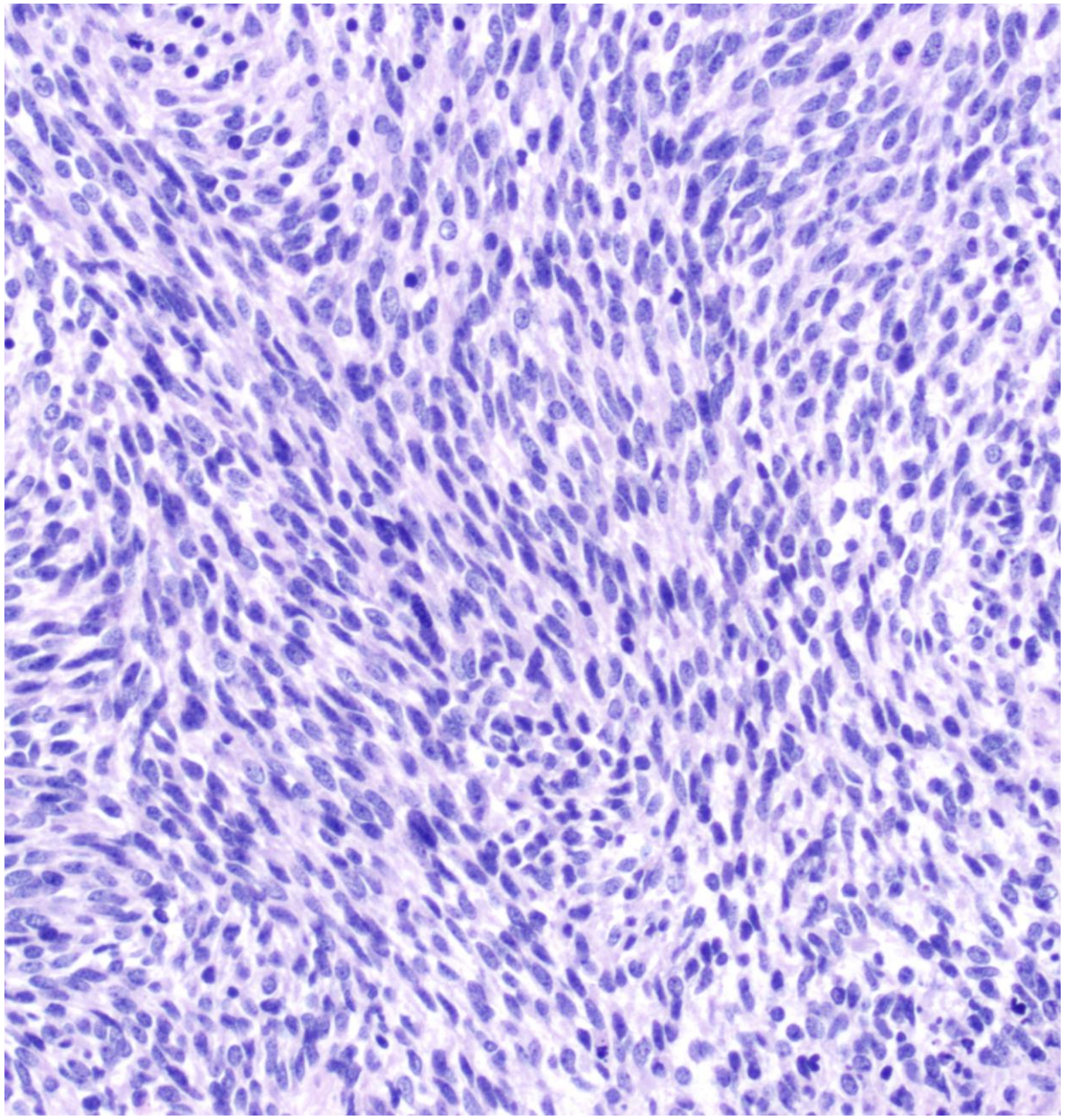
Case 5

- 33 yr old male presented with worsening shortness of breath
- History of left forearm swelling of several months duration









Ancillary studies

- EMA +
- CD99 +
- BCL2 +
- CD34 –
- STAT6 –
- Calretinin –
- t(X;18) by FISH

#5
What is the Diagnosis?

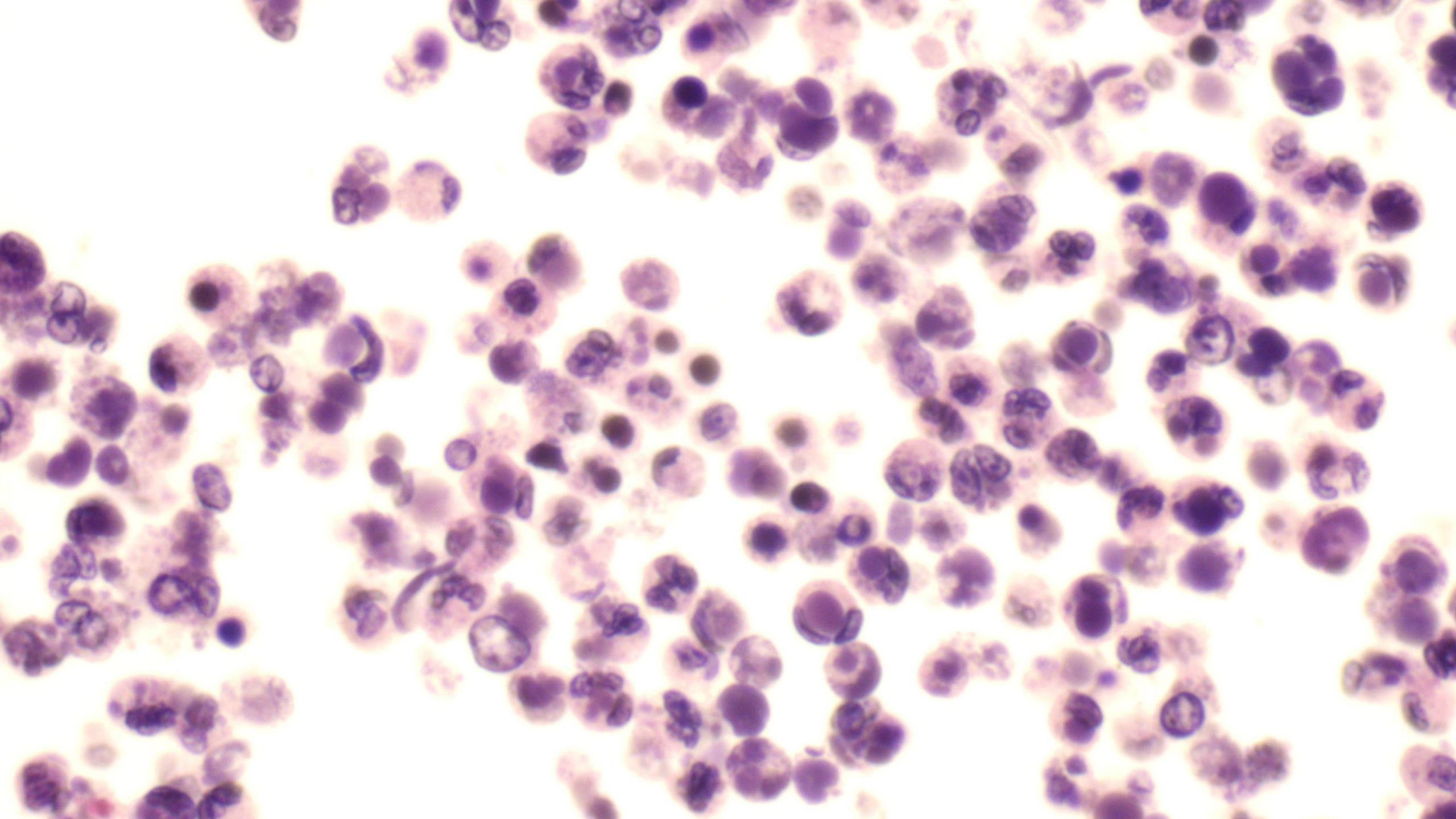
- A. Metastatic synovial sarcoma
- B. Solitary fibrous tumor
- C. Sarcomatoid mesothelioma
- D. Metastatic sarcomatoid carcinoma

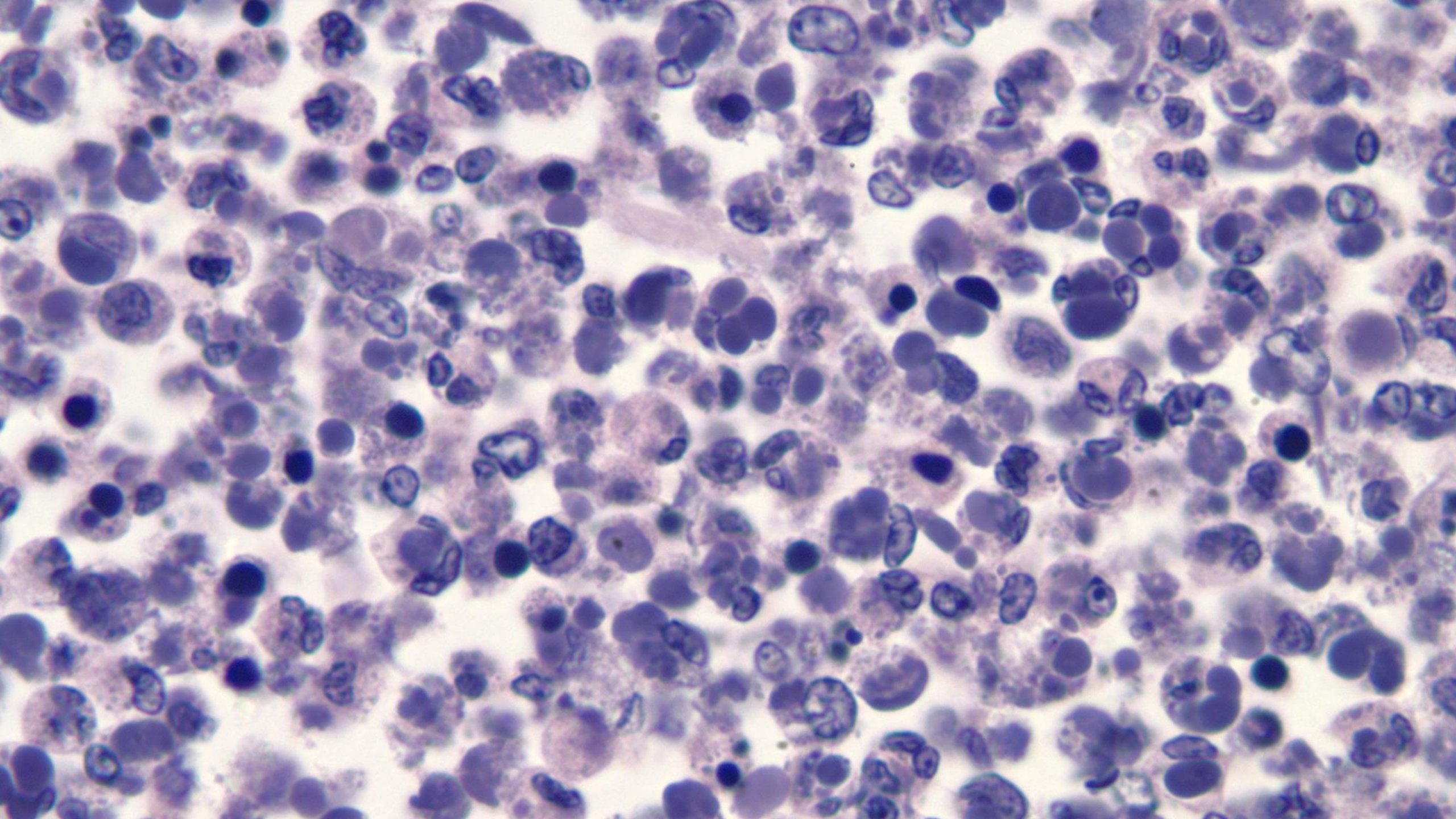
Sarcomas in effusions

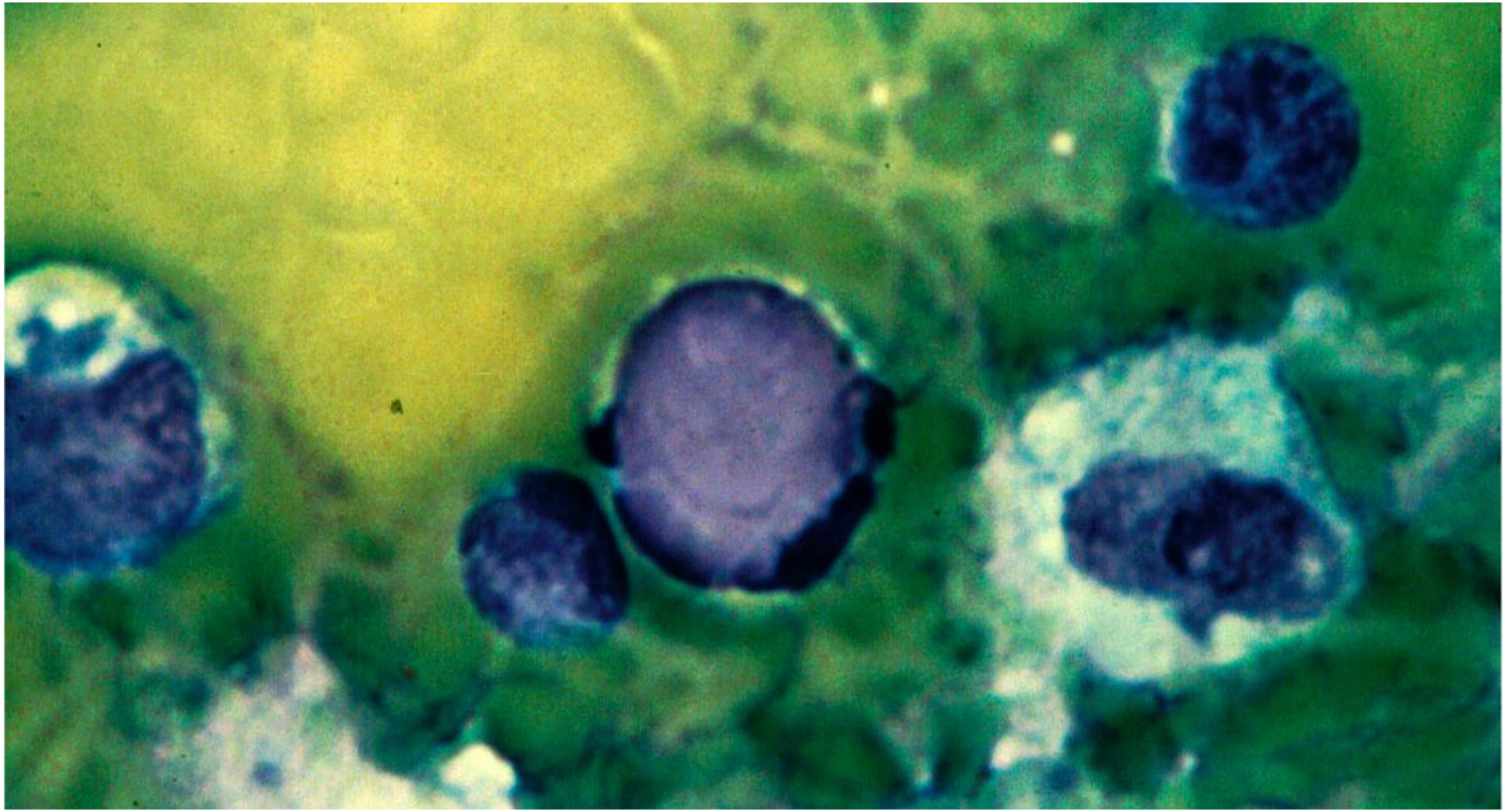
- Less frequent than other tumors
- Characterization only possible with adequate clinical history, comparative evaluation of the primary sarcoma and ancillary studies.

Case 6

- 45 yr old female presented with chest pain, exertional dyspnea and orthopnea
- ESR 55mm/hr
- ANA 1:2560
- Anti-dsDNA 1:3150
- Rh factor 75 IU/mL
- CT scan revealed bilateral pleural effusion







#6

The characteristic cells depicted in the images are best described as:

- A. Tart cells
- B. Lupus erythematosus (LE) cells
- C. Cells with cytomegalovirus inclusion
- D. Cells with intracytoplasmic mucin secretion

Lupus Pleuritis

- Characteristic cell is the LE cell
- Neutrophil or macrophage that has phagocytized the denatured nuclear material of another cell
- The denatured material is an absorbed hematoxylin body, which has a glassy, homogeneous appearance
- Should be differentiated from other possible cytoplasmic inclusions: ingested cellular debris, apoptotic material, RBCs, hemosiderin, melanin, mucus

Negative for malignancy

- Specimen composed of only benign or reactive cellular components
- No malignant tumor cells or cells concerning for malignancy
- Mostly mesothelial cells as single cells, small clusters, or flat sheets
- Rare mesothelial binucleation or multinucleation
- Variable histiocytes, giant cells, lymphocytes, and neutrophils
- No or minimal cellular atypia
- May include other benign components (e.g. Psammoma bodies, collagen balls, asbestos bodies, organisms)
- Distribution of predominately one cell type
- Risk of malignancy: ~21%

Causes and key cytologic features of Non-neoplastic effusions

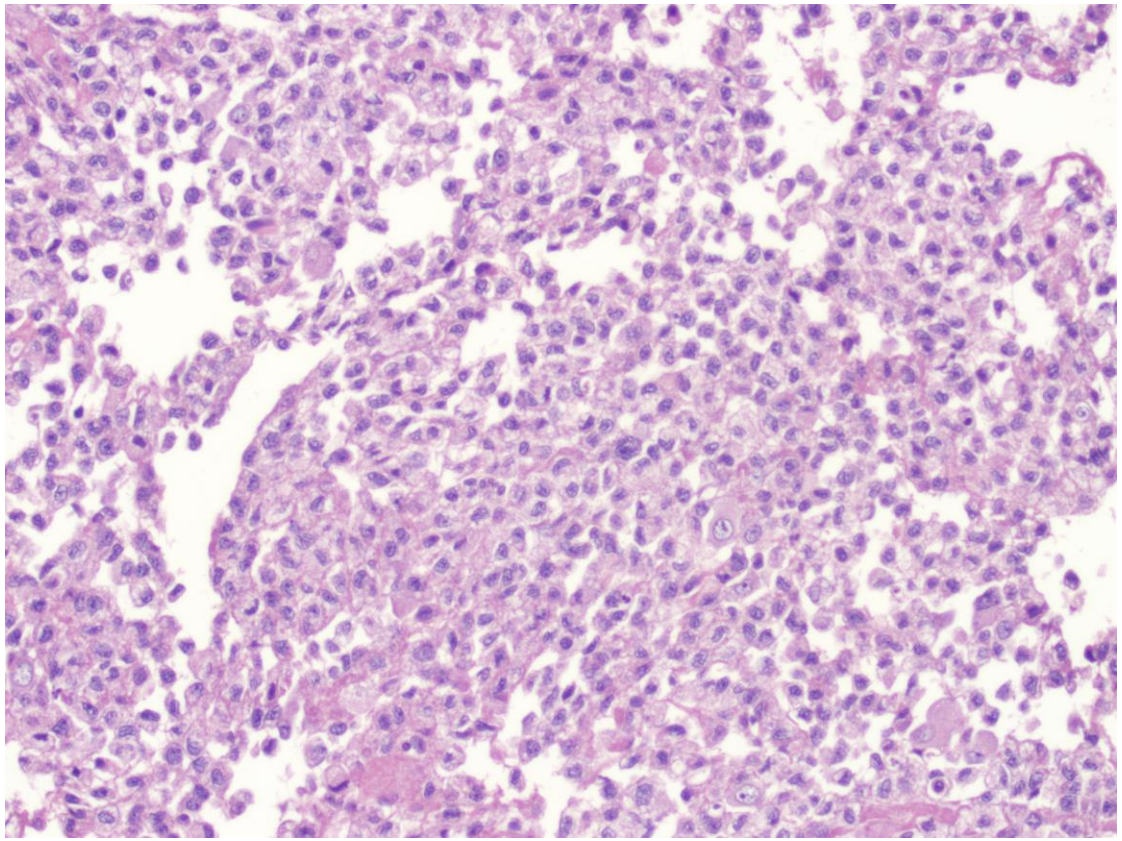
- Congestive heart failure
  - Occasional hemosiderophages
- Pulmonary infarction
  - Non-specific mixed inflammation
- Pneumonia
  - Inflammatory cells of various types depending on the nature and duration of pneumonia
- Chemotherapy and Radiation pneumonitis
  - No consistent and distinctive changes
- Autoimmune serositis (e.g. SLE)
  - Characteristic LE cells and moderate amount of neutrophils
- Rheumatoid pleuritis
  - Abundant clumps of granular debris and macrophages
- Tuberculosis
  - High proportion of lymphocytes and few mesothelial cells
- Others: Hypothyroidism, Nephrotic syndrome, Cirrhosis

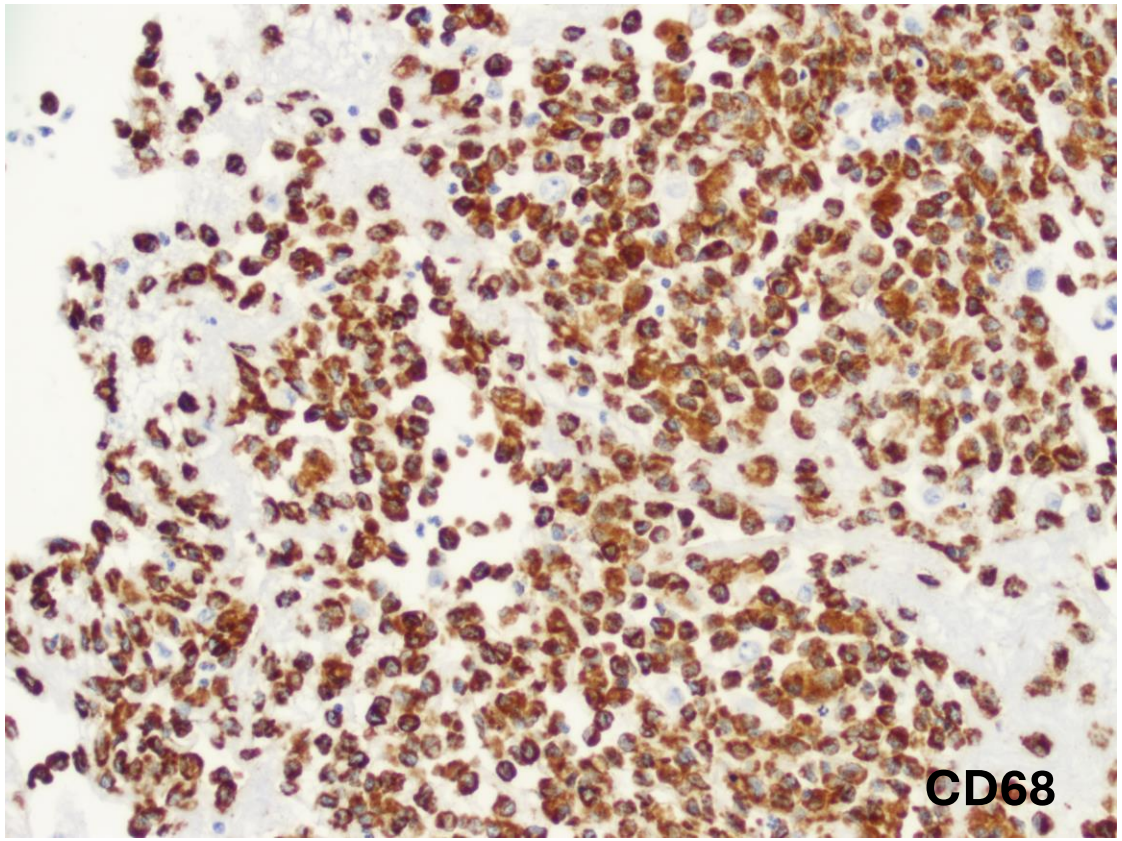
Rheumatoid effusion

- **Classic triad** – necrotic granular debris, epithelioid histiocytes and multinucleated giant cells.
- The epithelioid histiocytes are spindled or carrot-shaped cells that are frequently degenerated, with pyknotic nuclei and dense blue to pink to orangiophilic cytoplasm, which can mimic keratinizing SCC

Cytomorphology of histiocytes

- Smaller nucleus than that of mesothelial cells
- Nucleus often folded
- Cytoplasm granular or vacuolated
- No “windows” between adjacent cells
- Dense aggregates (in cell block sections)




CD68

THANK YOU!