

Lung Cytopathology: Interactive Unknown Cases

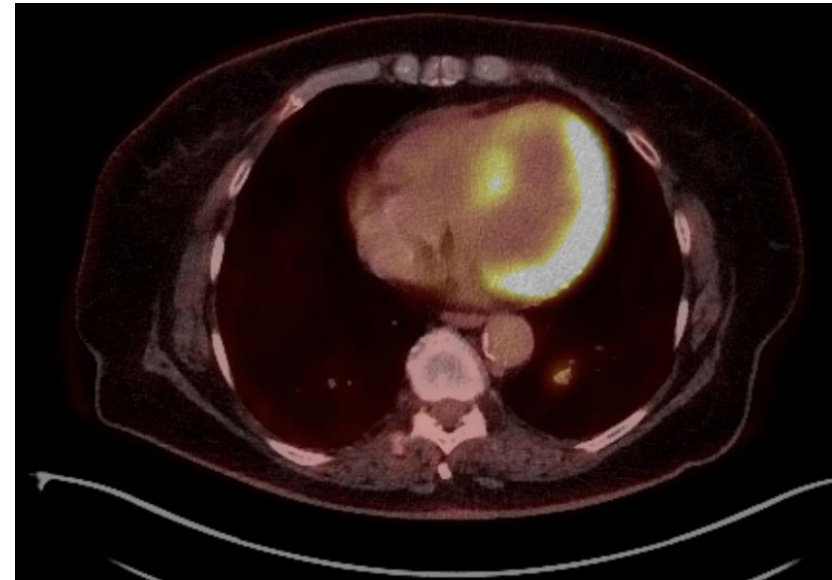
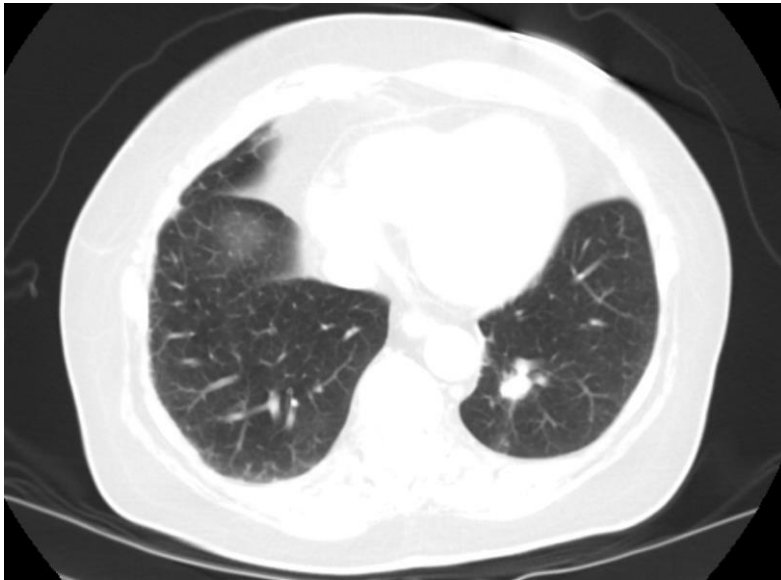
Guoping Cai, MD

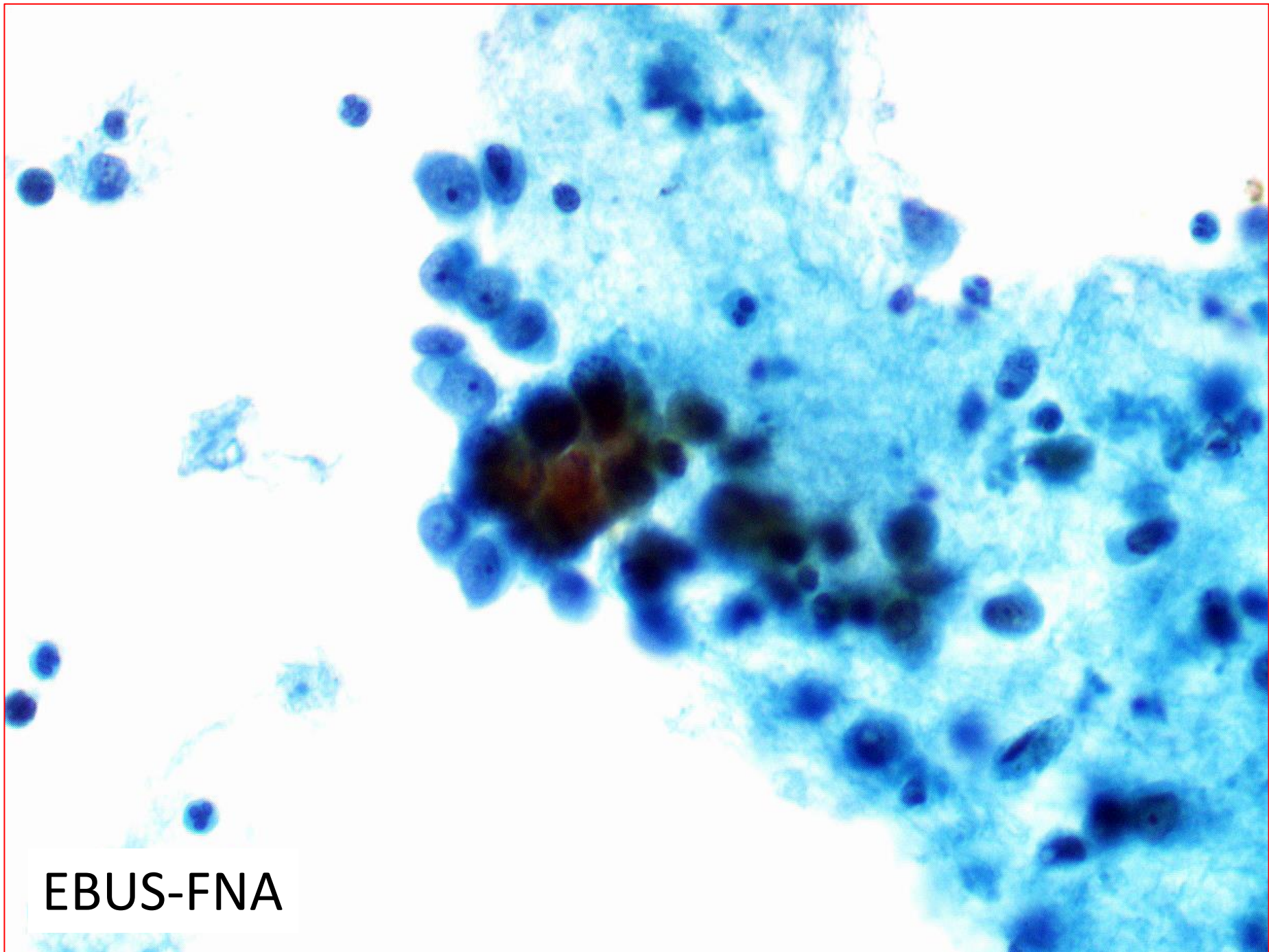
Yale University School of Medicine



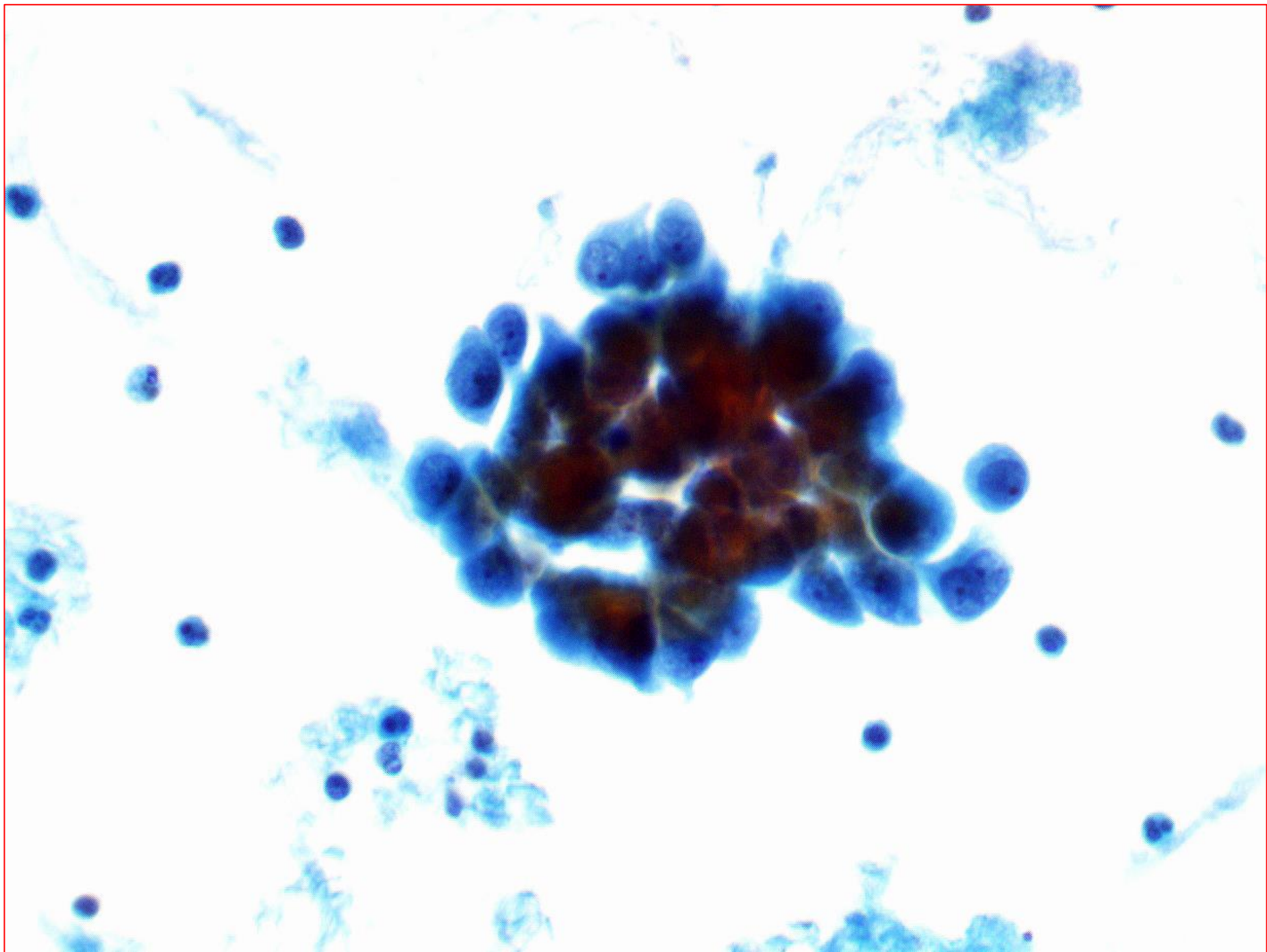
Case #1

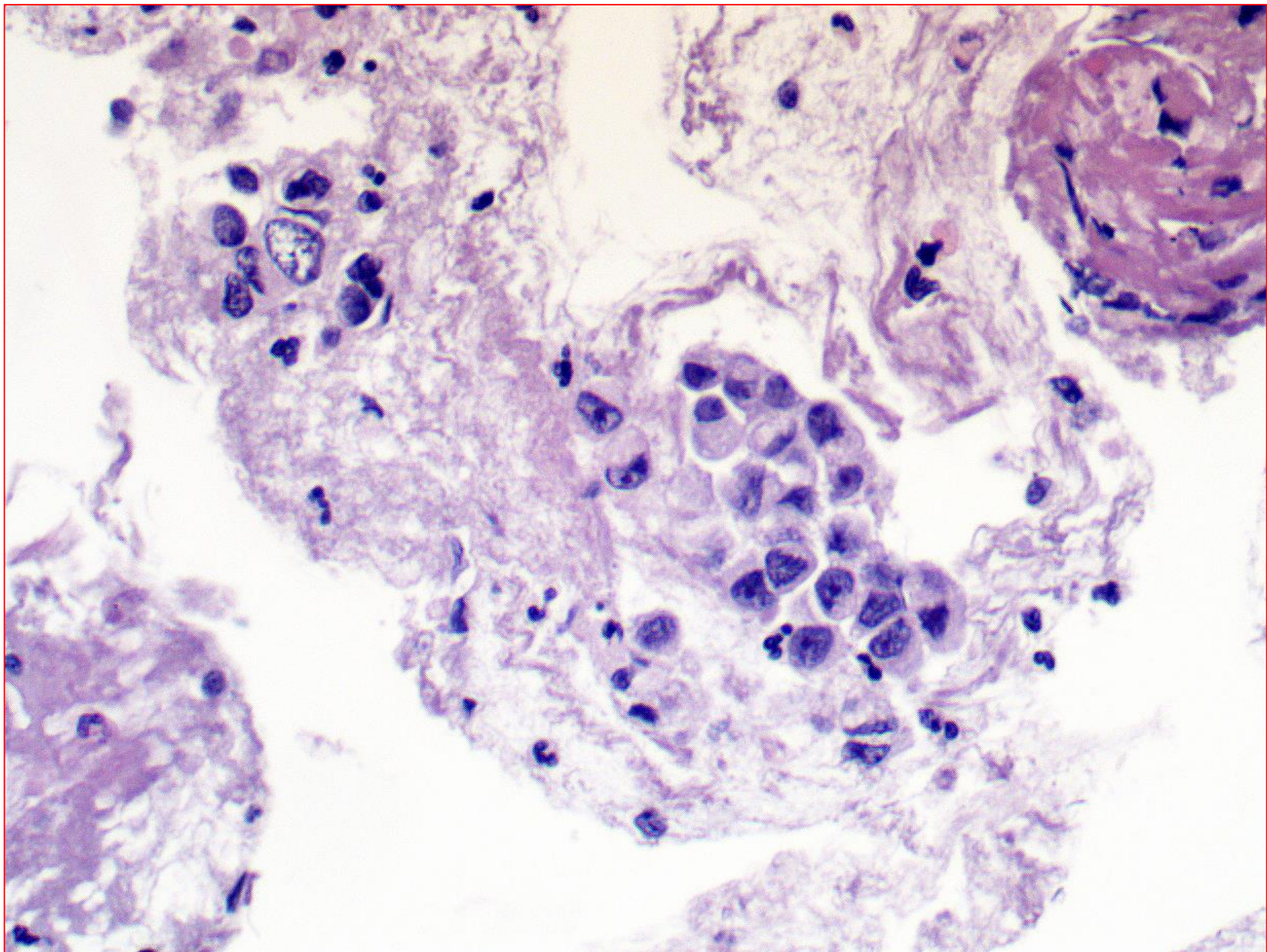
- 72/F, h/o coronary artery disease
- A 1.4-cm spiculated, moderately PET-avid nodule in the left lower lower, increased from 0.8 cm with 6 months

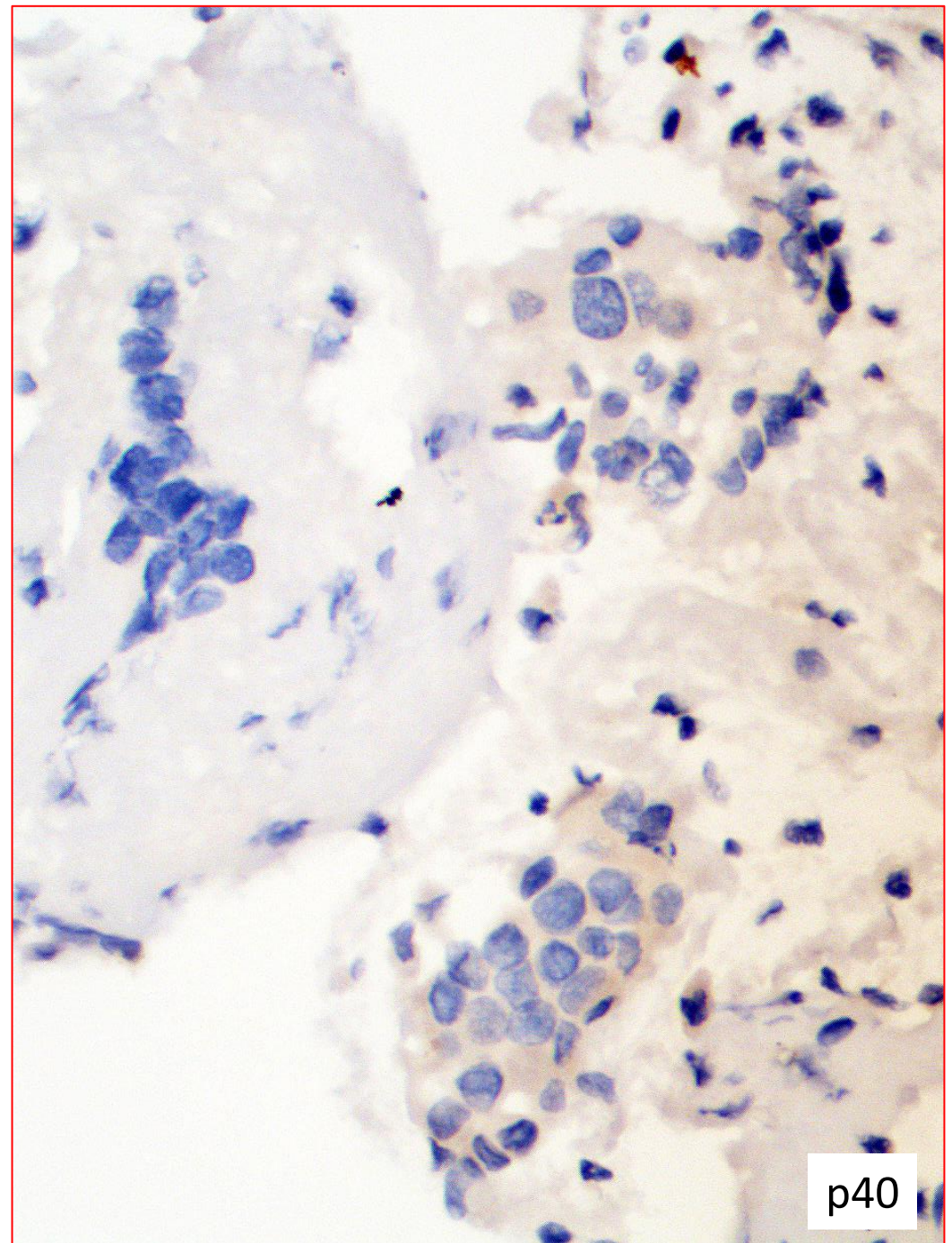
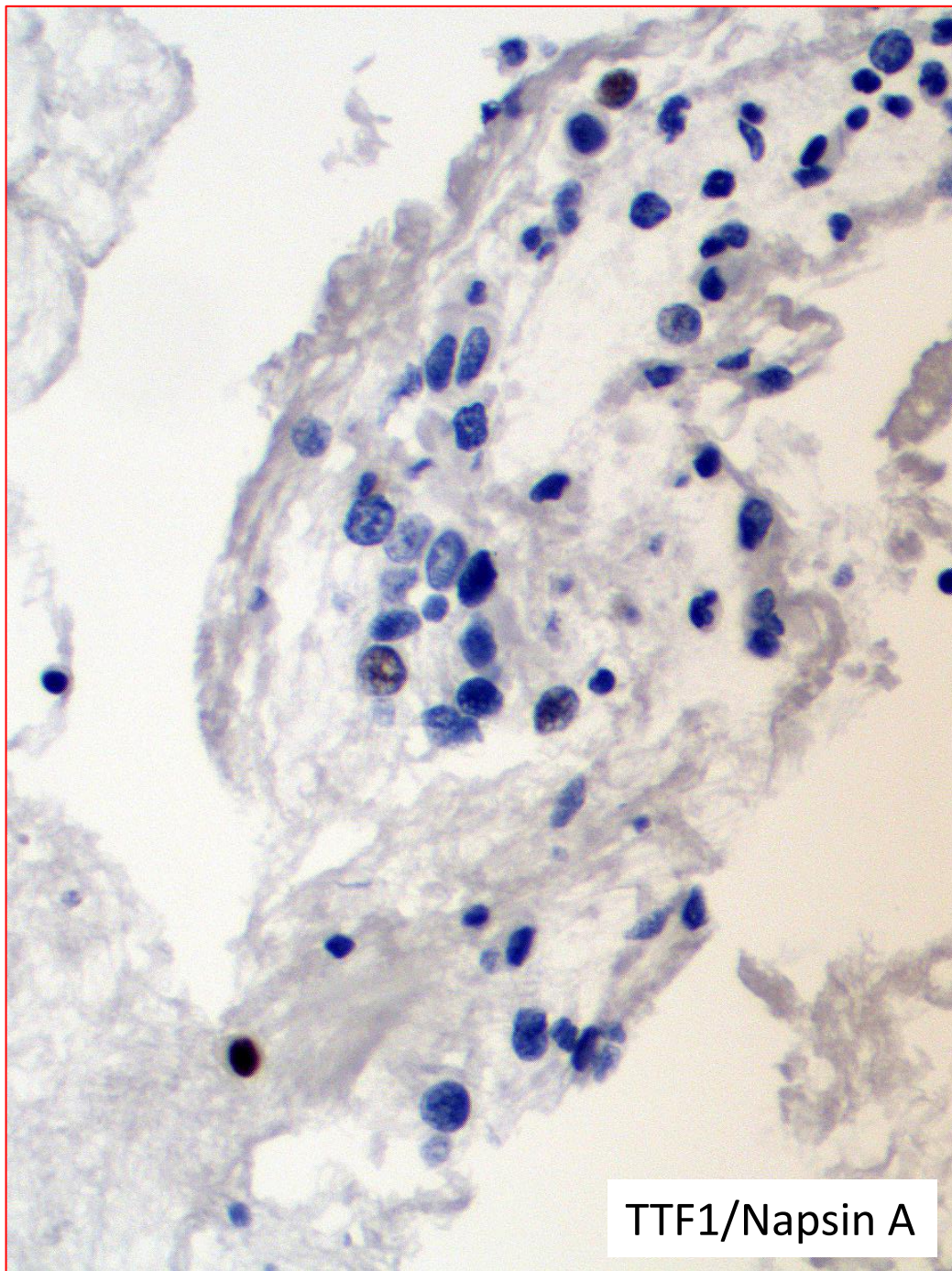




EBUS-FNA

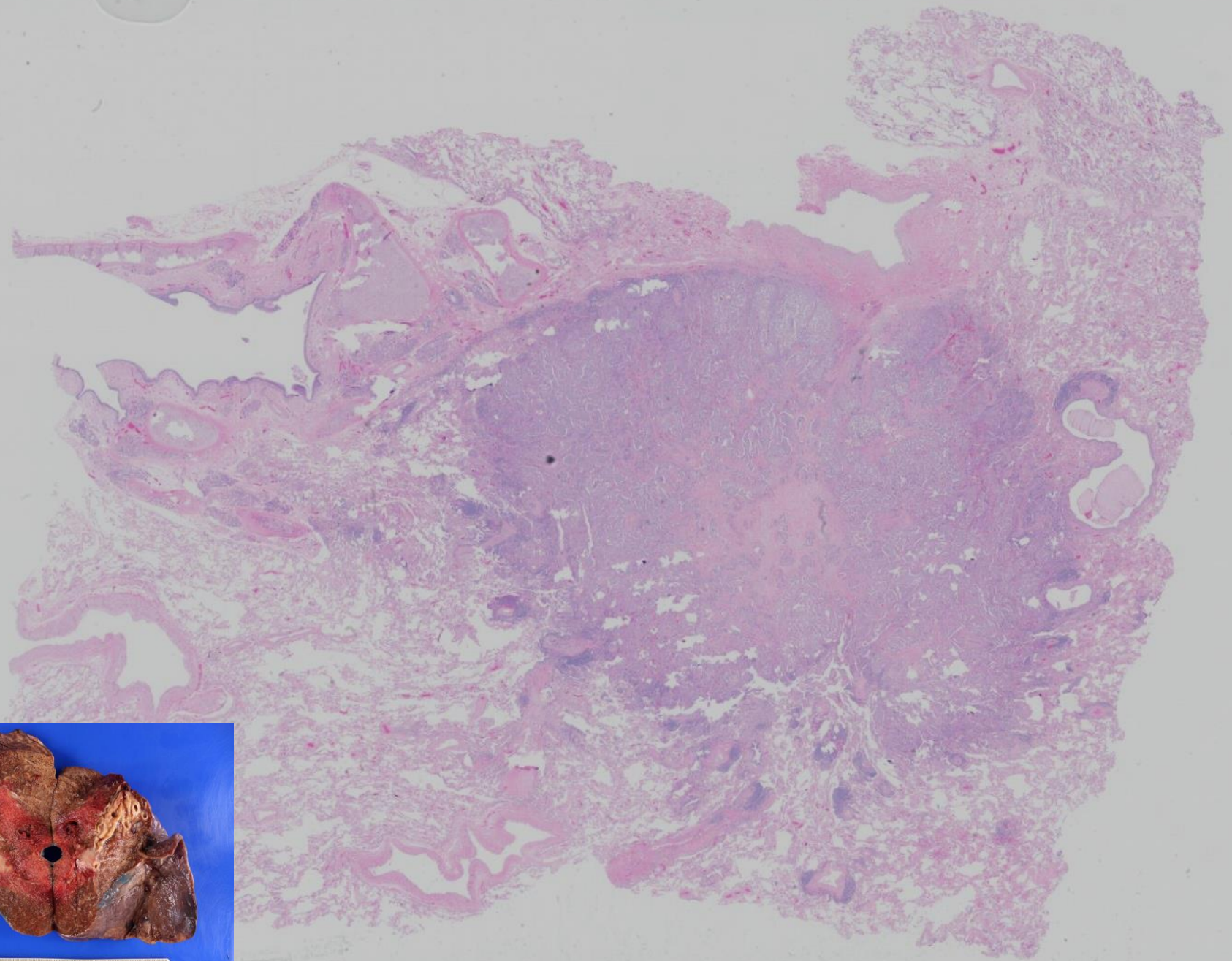


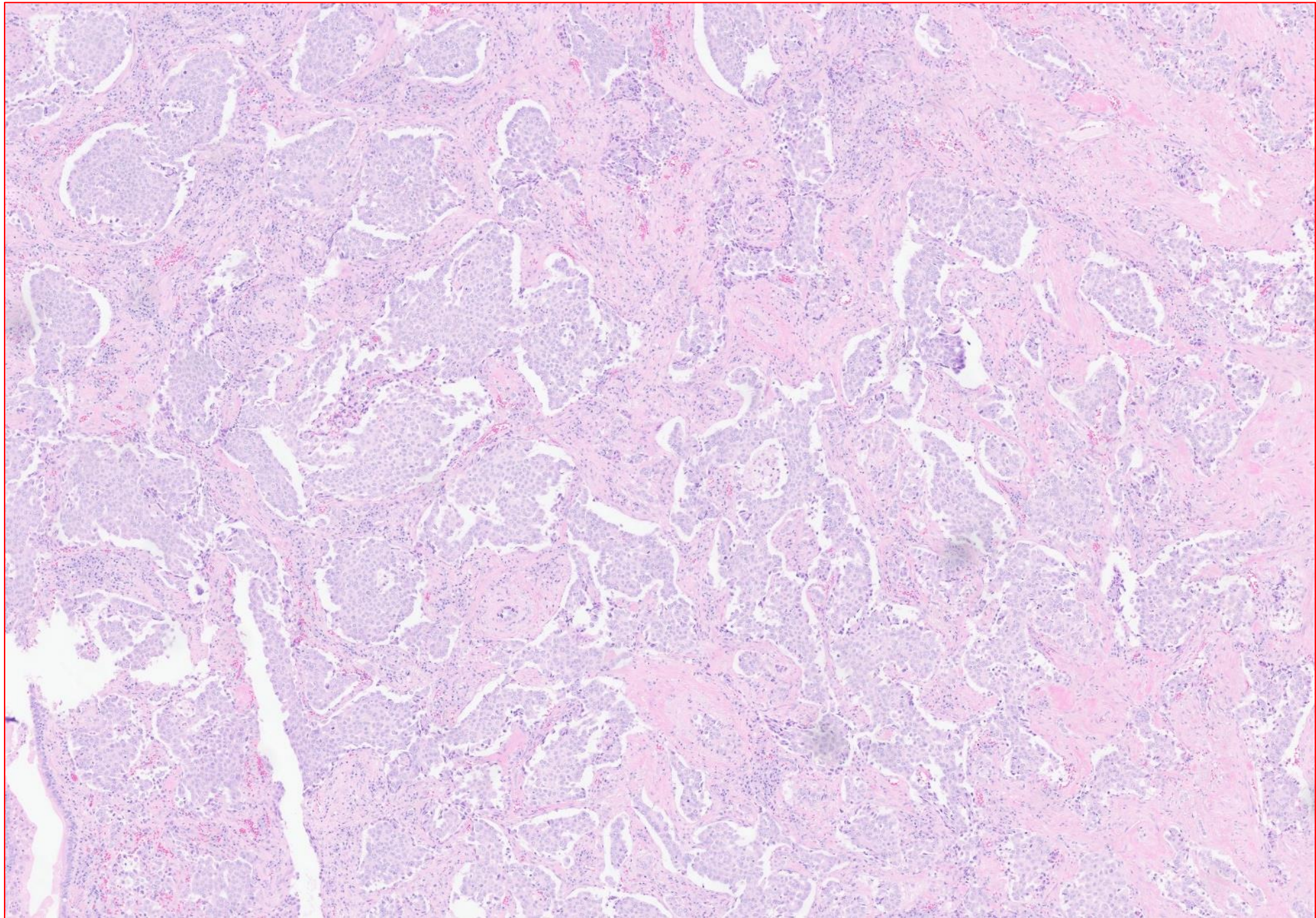


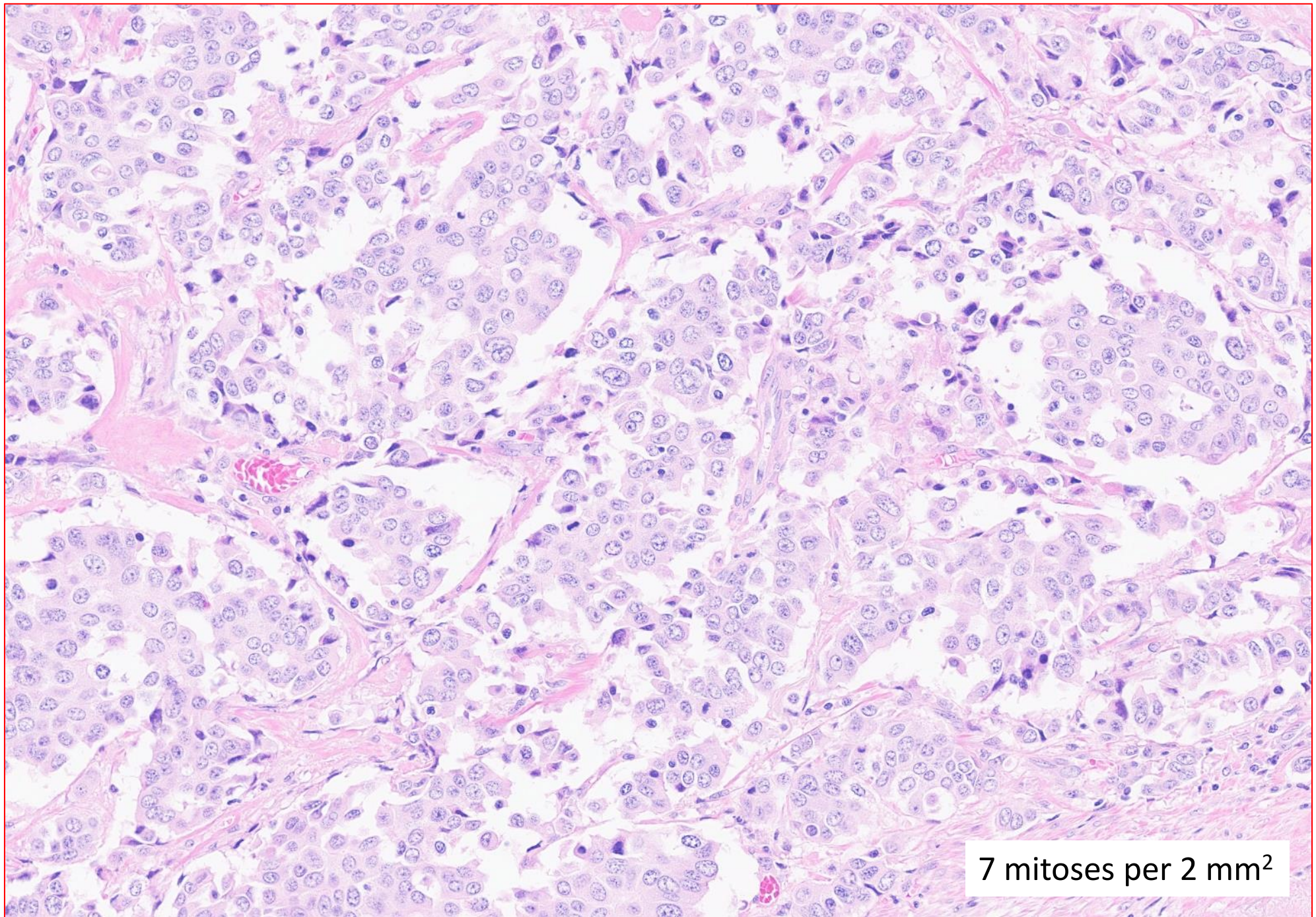


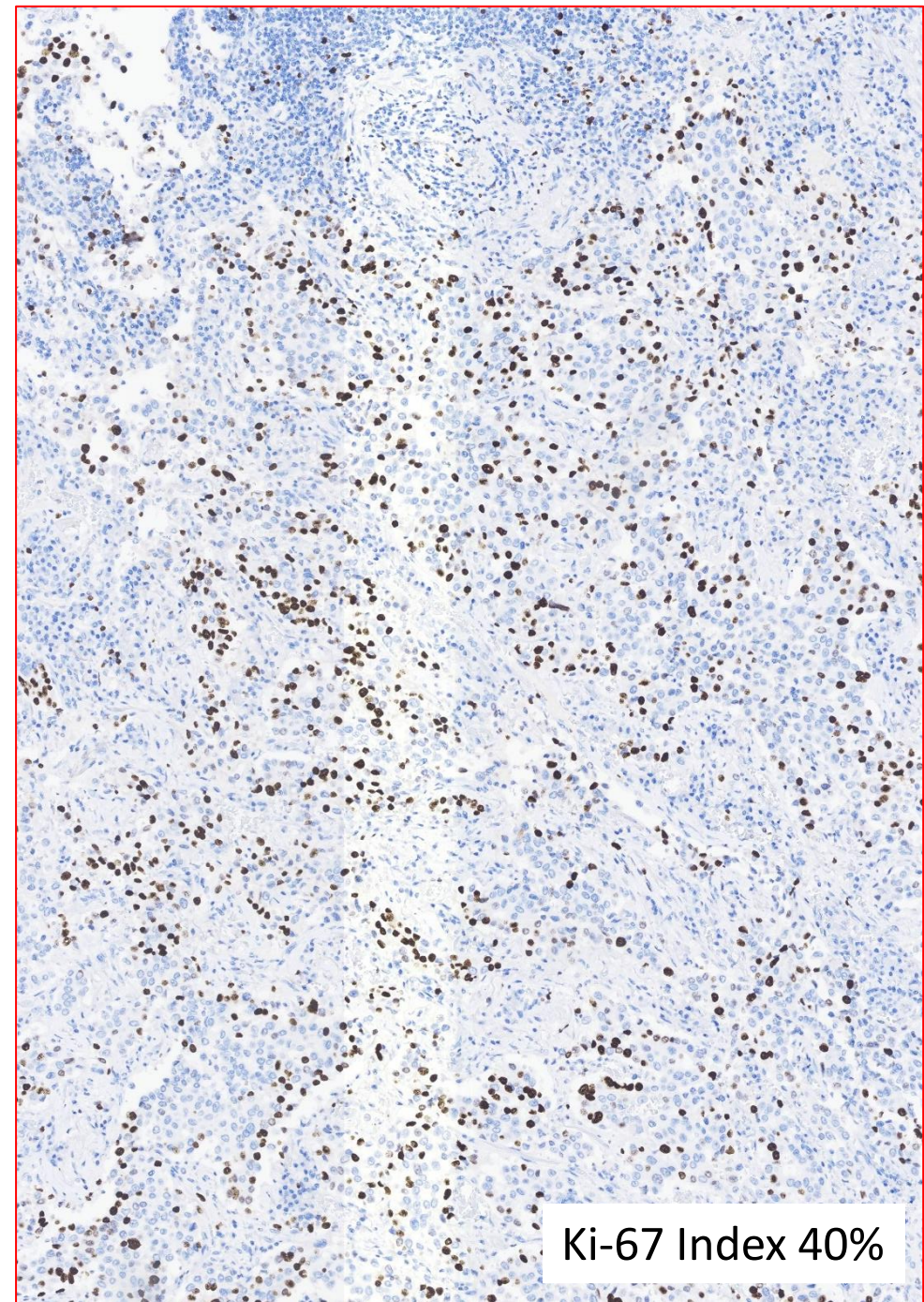
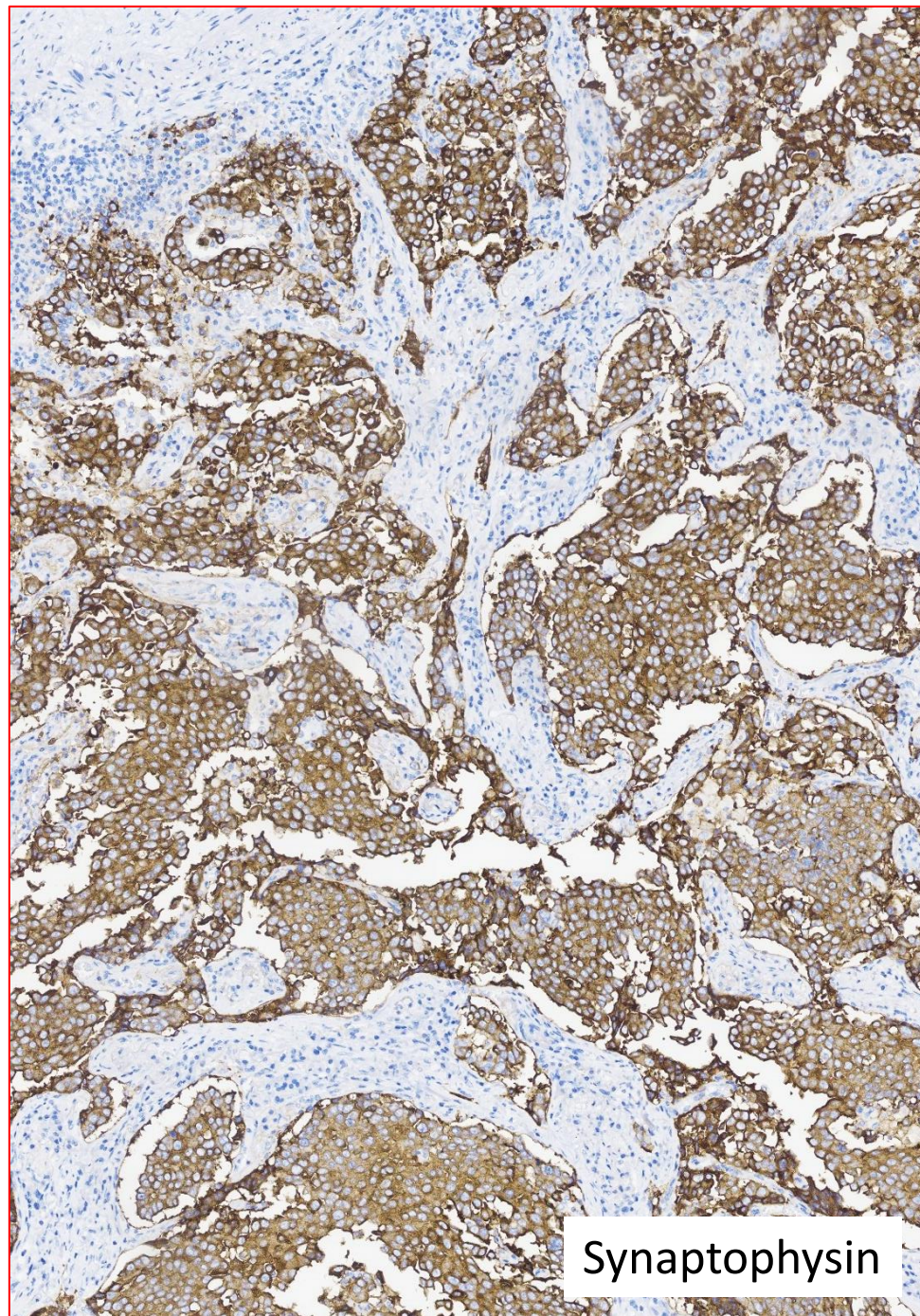
Diagnosis?

- Adenocarcinoma
- Squamous cell carcinoma
- Non-small cell carcinoma
- Others









Final Diagnosis

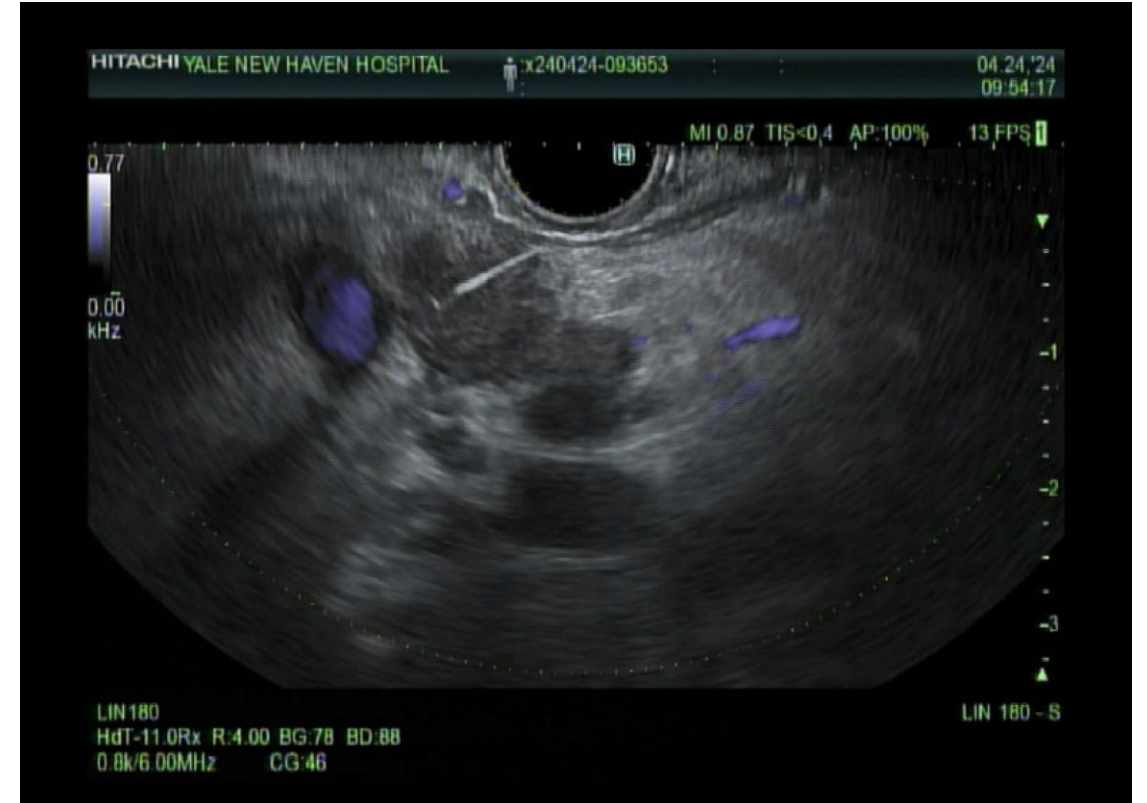
Atypical Carcinoid/Carcinoid with Increase Proliferation Rate

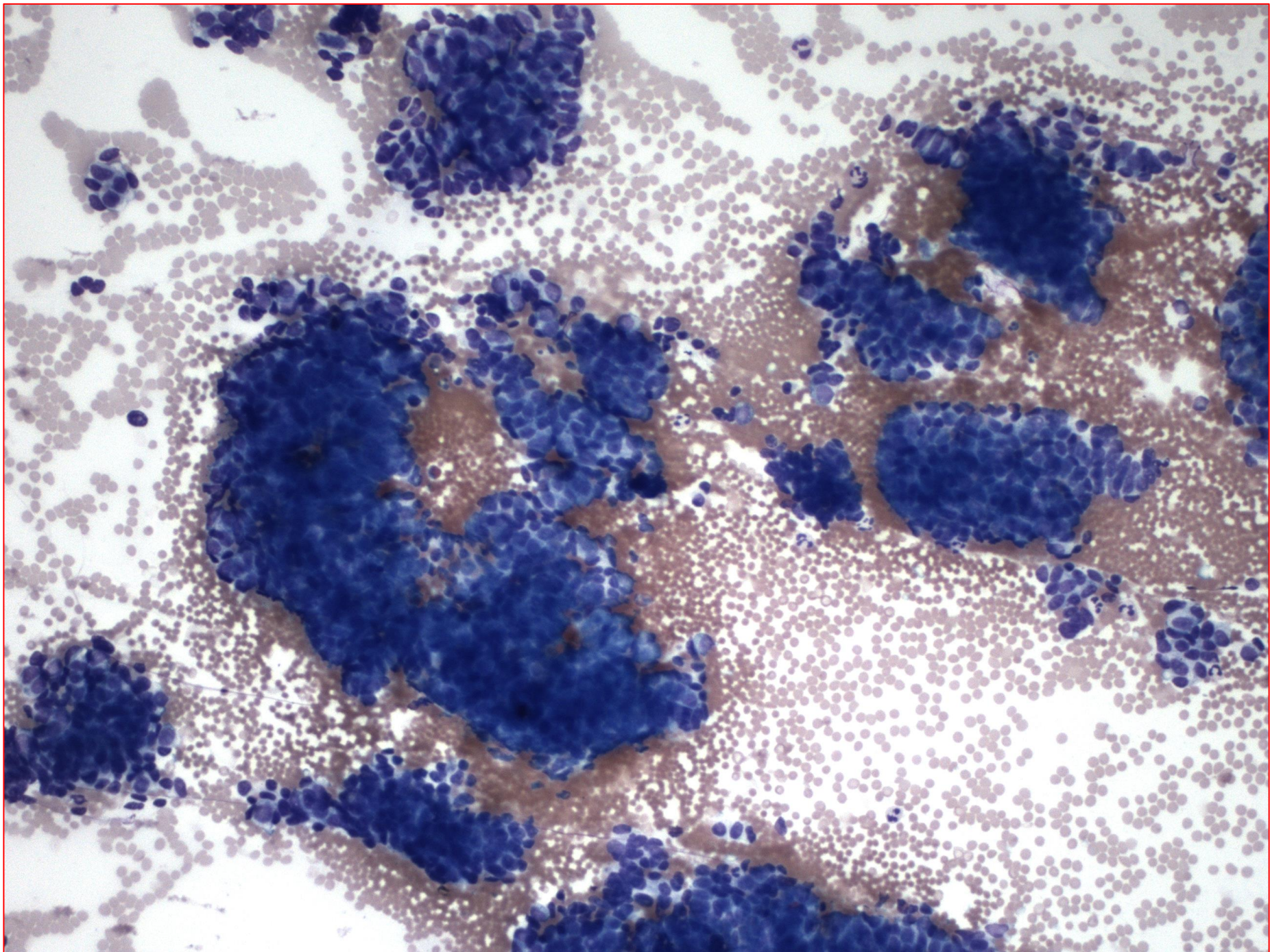
Somatic variants detected in the tumor: (Oncomine Assay)

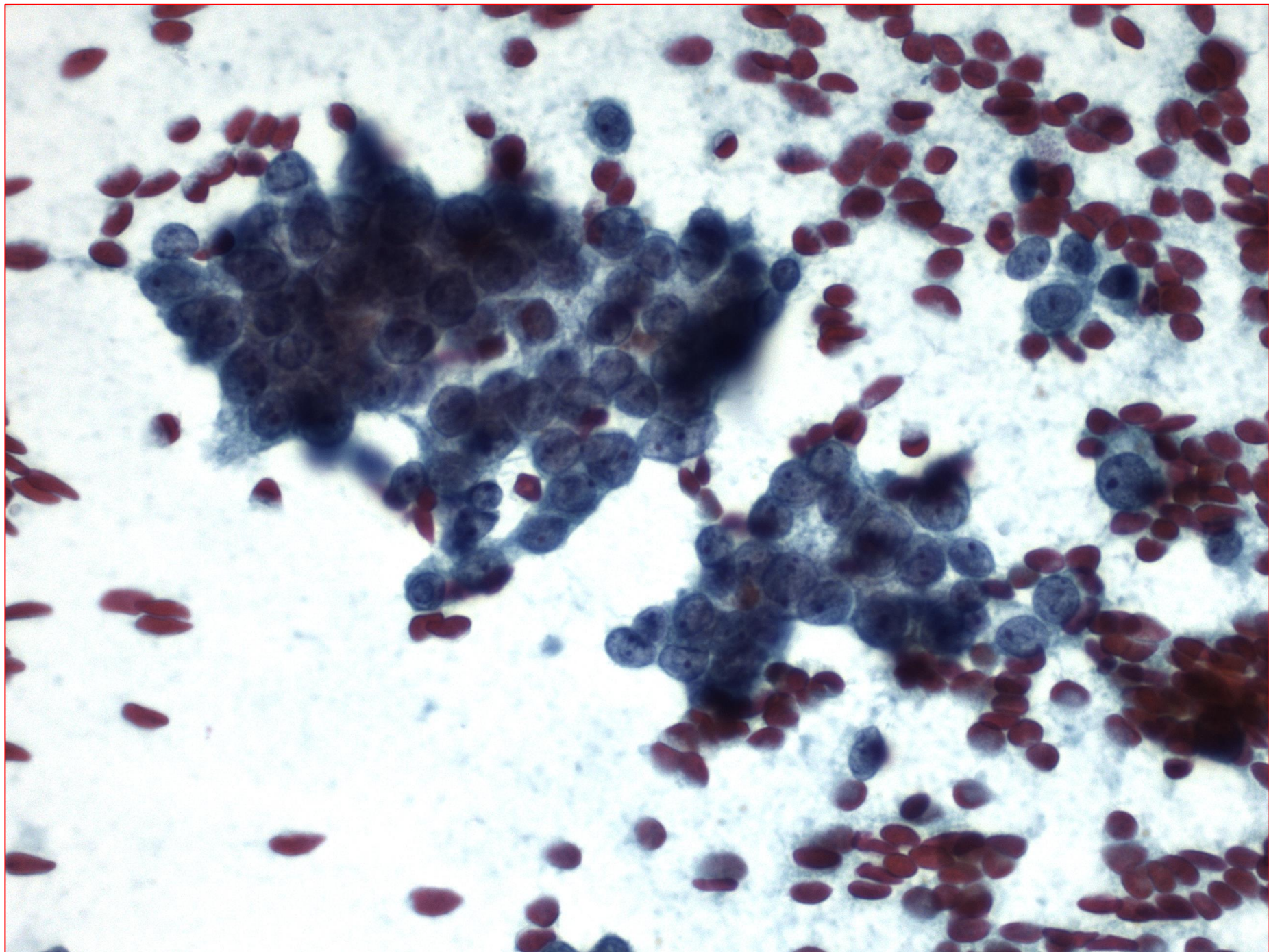
| <u>Variant</u> | <u>Allelic Fraction</u> |
|------------------------------|-------------------------|
| <i>KRAS</i> G12V | 58% |
| <i>SETD2</i> N1693fs | 31% |
| <i>SETD2</i> G1717Ter | 25% |
| <i>KNSTRN</i> D10Y | 23% |
| <i>CDKN2A</i> D125N | 21% |
| <i>NOTCH1</i> Q1527H | 19% |

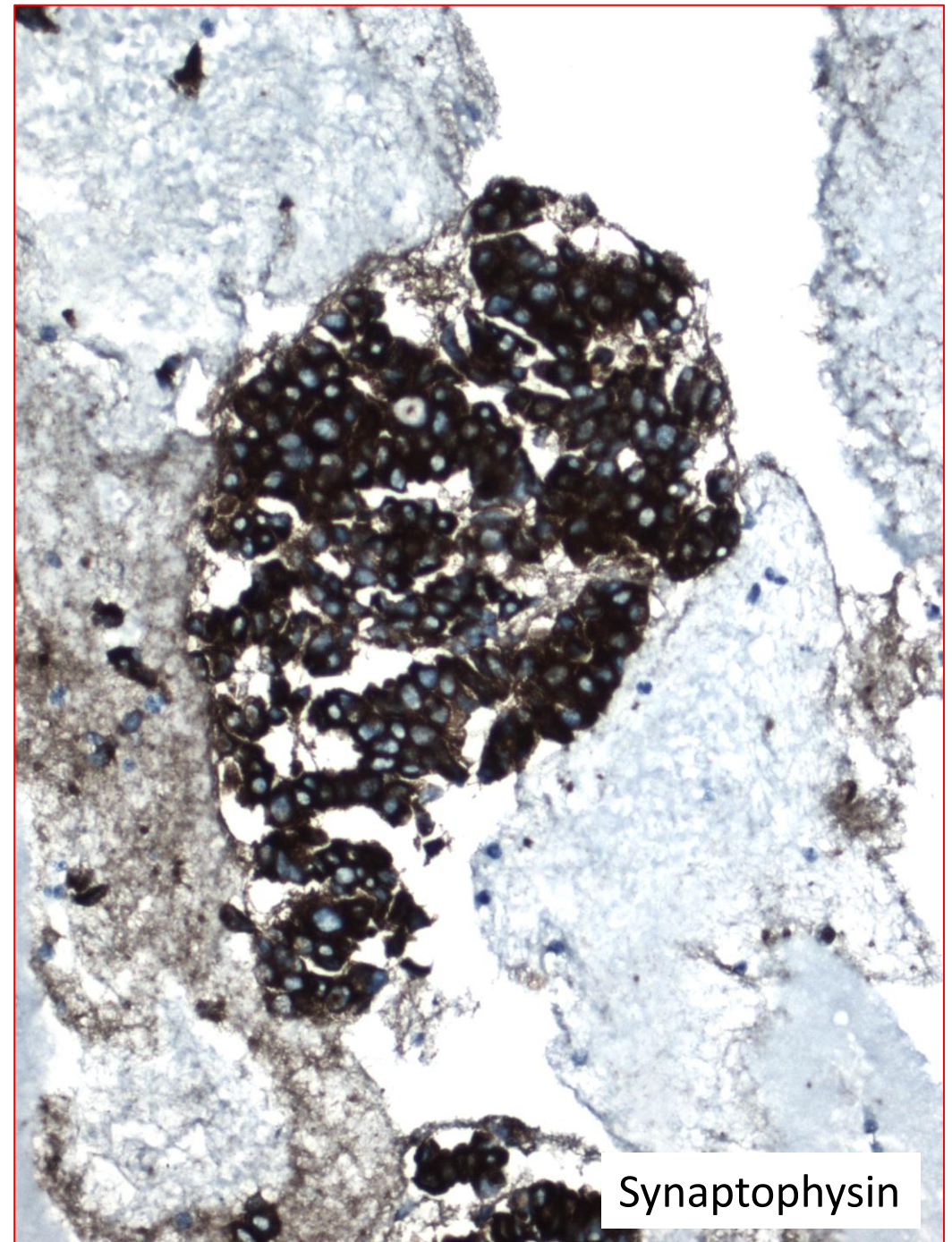
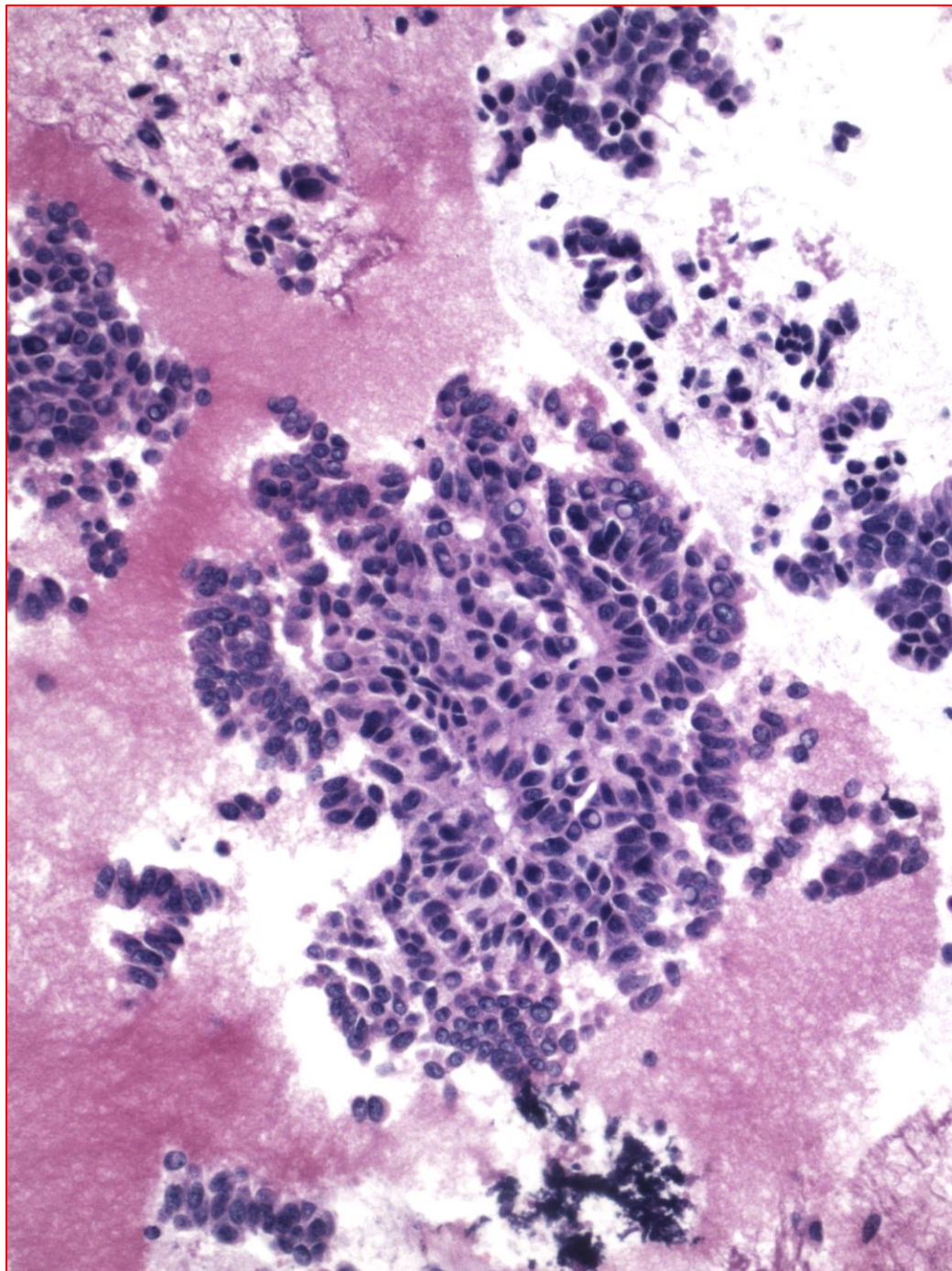
Endoscopic Ultrasound of the Pancreas

- Two irregular masses, 16 and 10 mm, with well-defined borders, in close proximity in the pancreatic body









Synaptophysin

FINAL DIAGNOSIS

1&2) PANCREAS BODY MASS, FINE NEEDLE ASPIRATION/WASH:

- SPECIMEN IS ADEQUATE FOR INTERPRETATION.
- **POSITIVE FOR PANCREATIC NEUROENDOCRINE TUMOR.**

Procedure/Addenda

MOLECULAR DIAGNOSTIC TESTING - PCR Pathologist:

Status: Signed Out

Ordered:

Reported:

Findings (Results)

KRAS genotyping has been performed on [redacted] using polymerase chain reaction (PCR) with exon 2 flanking primers followed by single-strand conformational polymorphism (SSCP) analysis. Mutations are detected as shifts in bands seen when the PCR products are separated by SSCP gel electrophoresis.

Bandshifts compatible with a GTT mutation in codon 12 of *KRAS* are **detected**.

Analytic specific reagent (ASR) is used. This test was developed and its performance characteristics determined by the Yale Pathology Molecular Diagnostics Laboratory. The test has not been cleared or approved by the U.S. Food and Drug Administration. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88) as qualified to perform high complexity clinical laboratory testing.

Interpretation

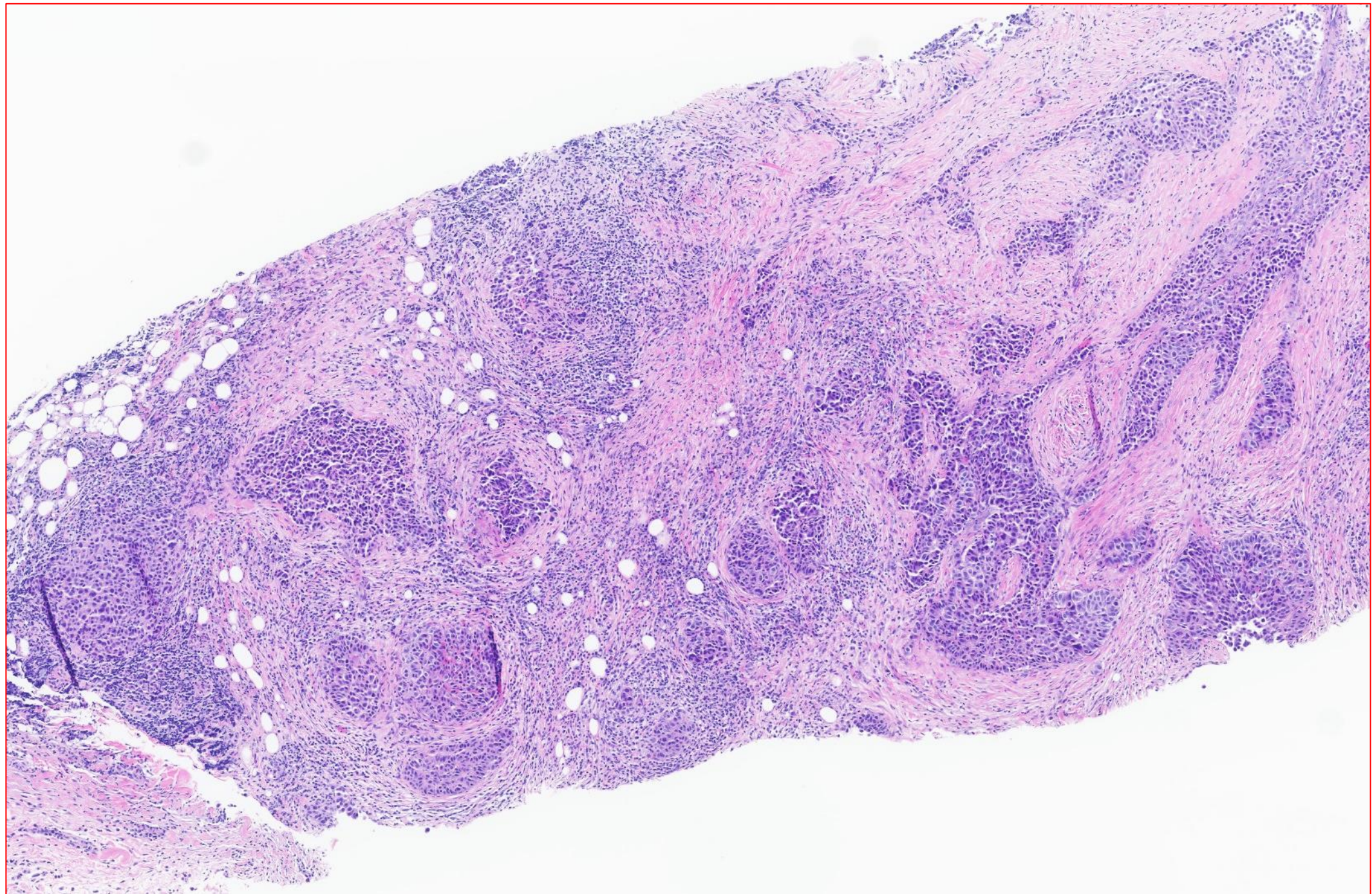
Mutation detected in the *KRAS* gene.

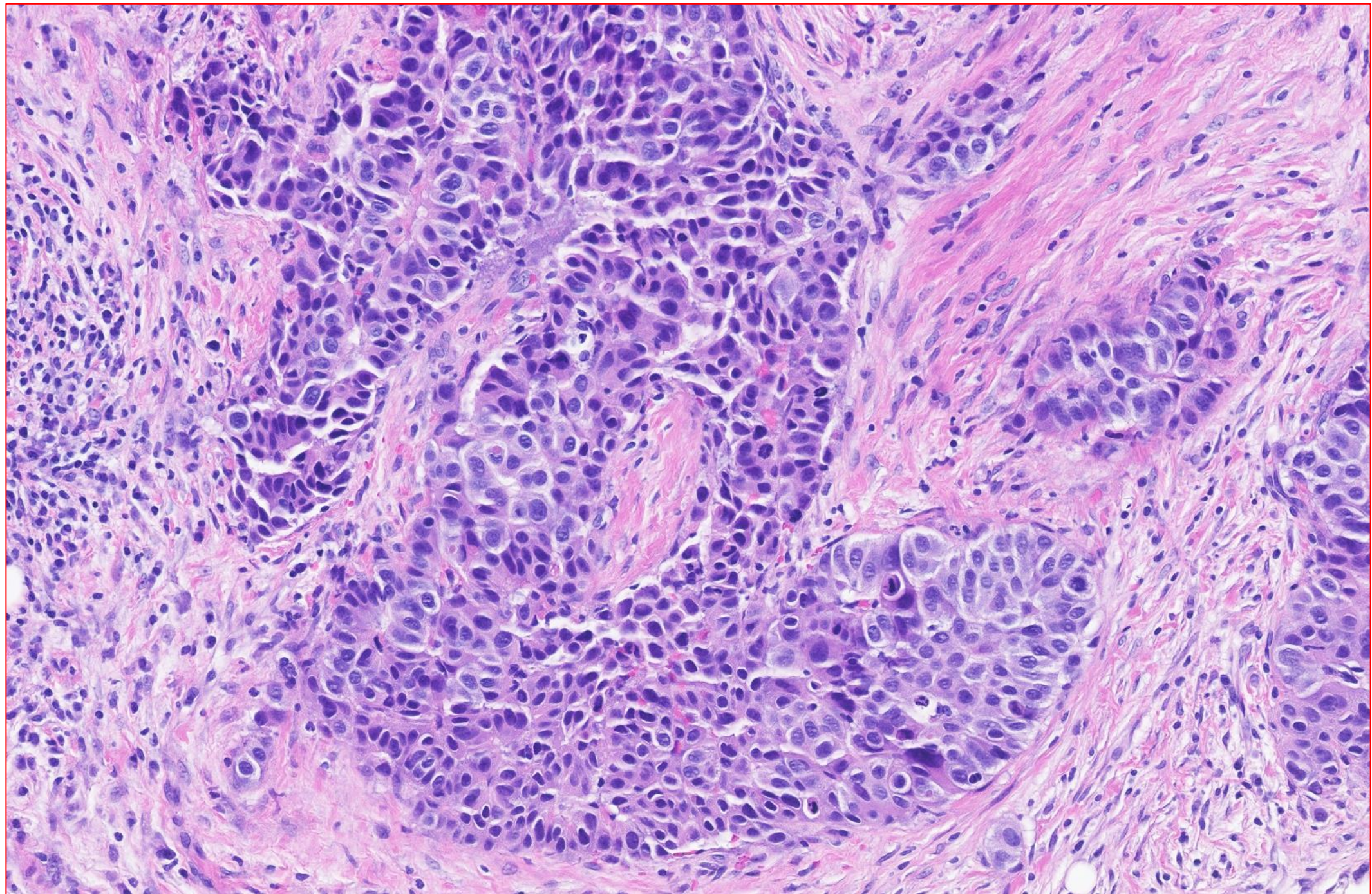


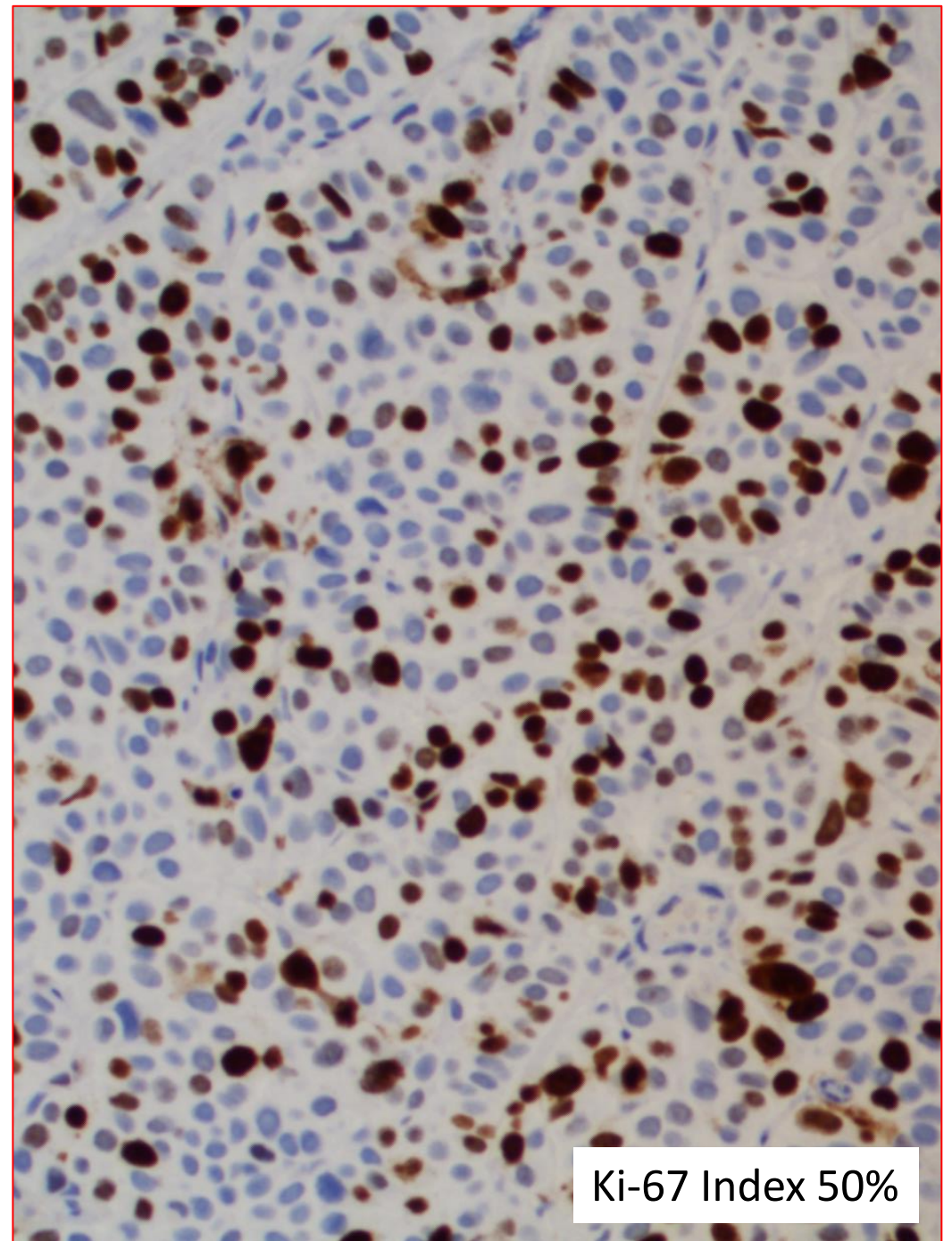
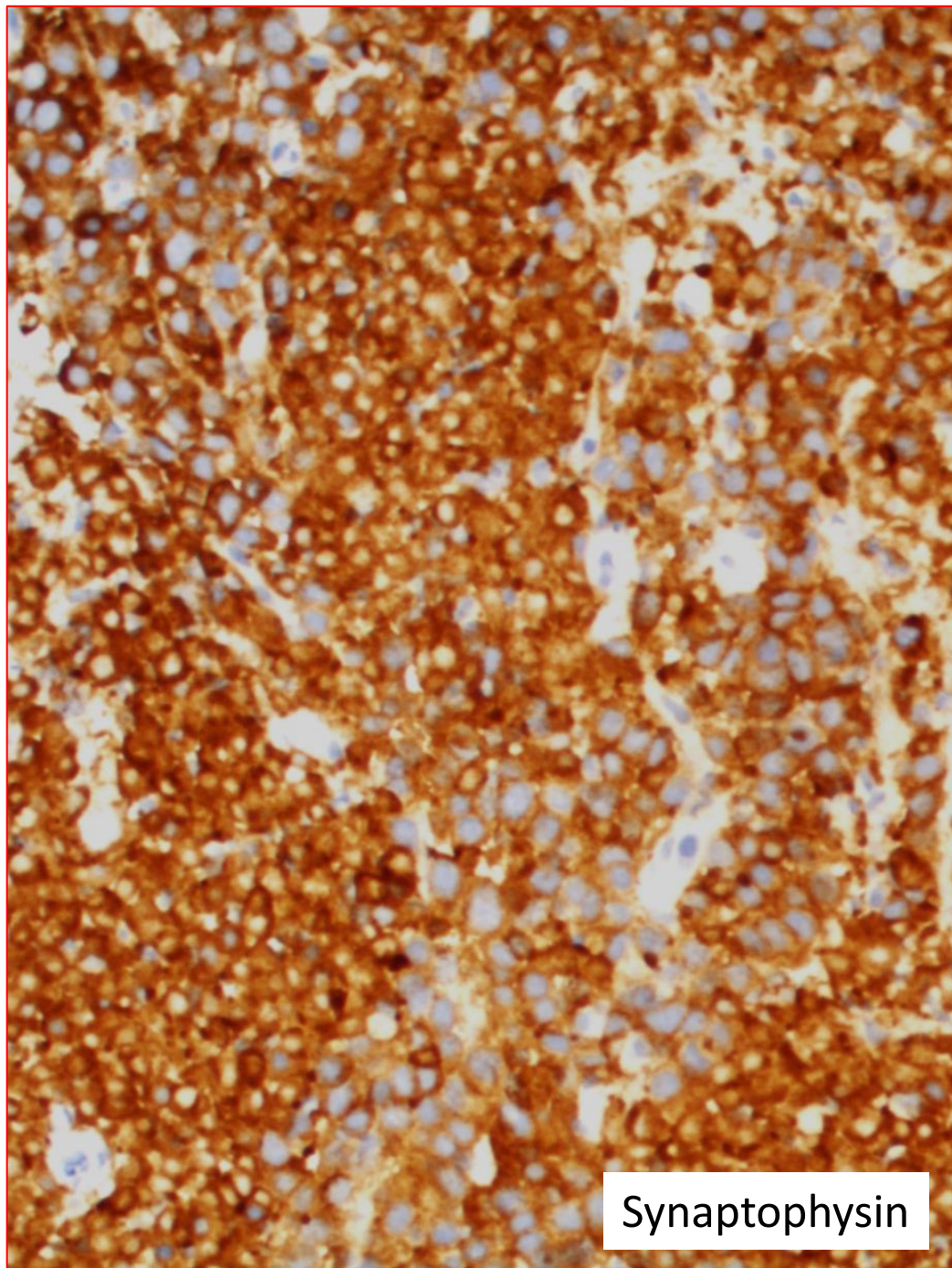
KRAS^{G12V}

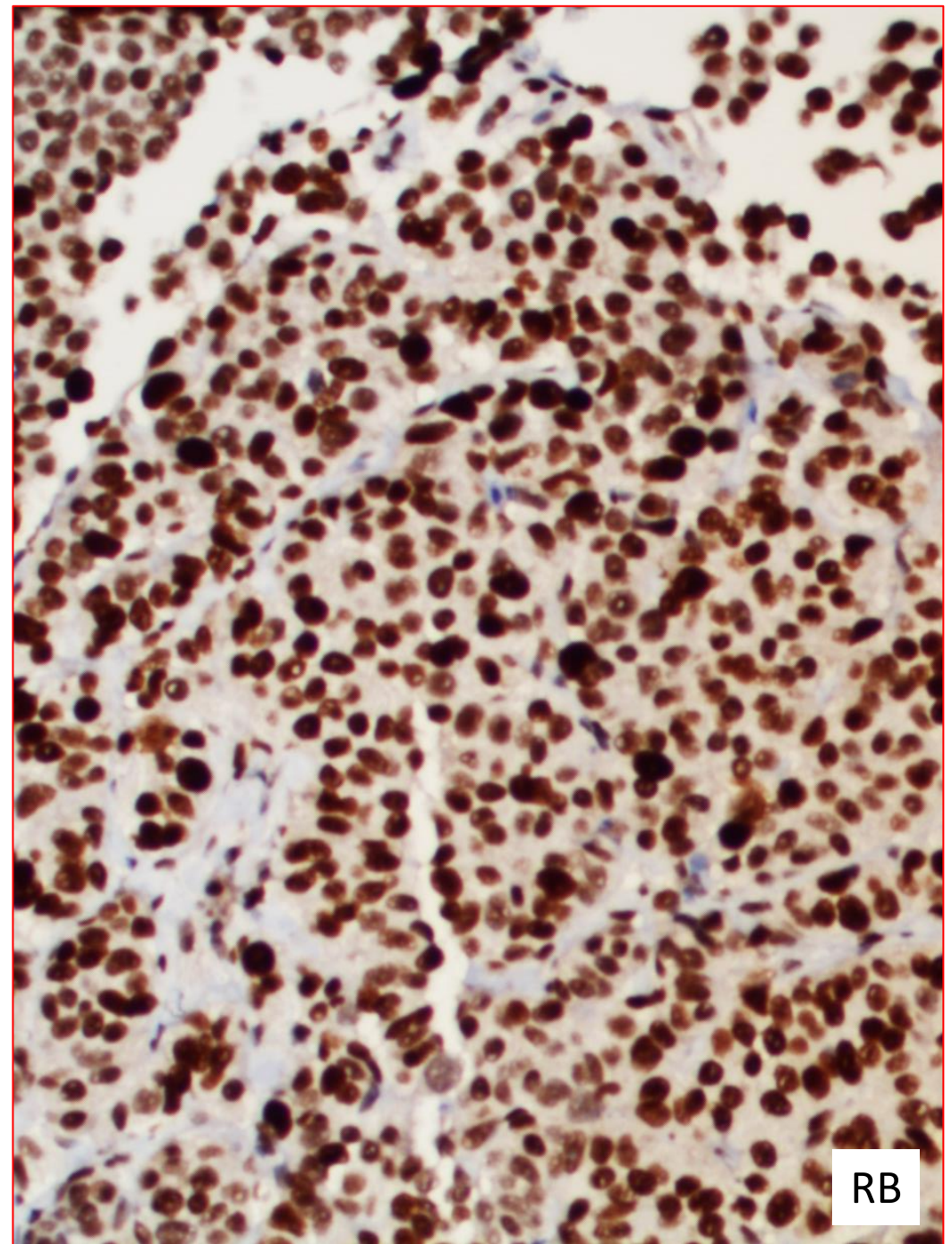
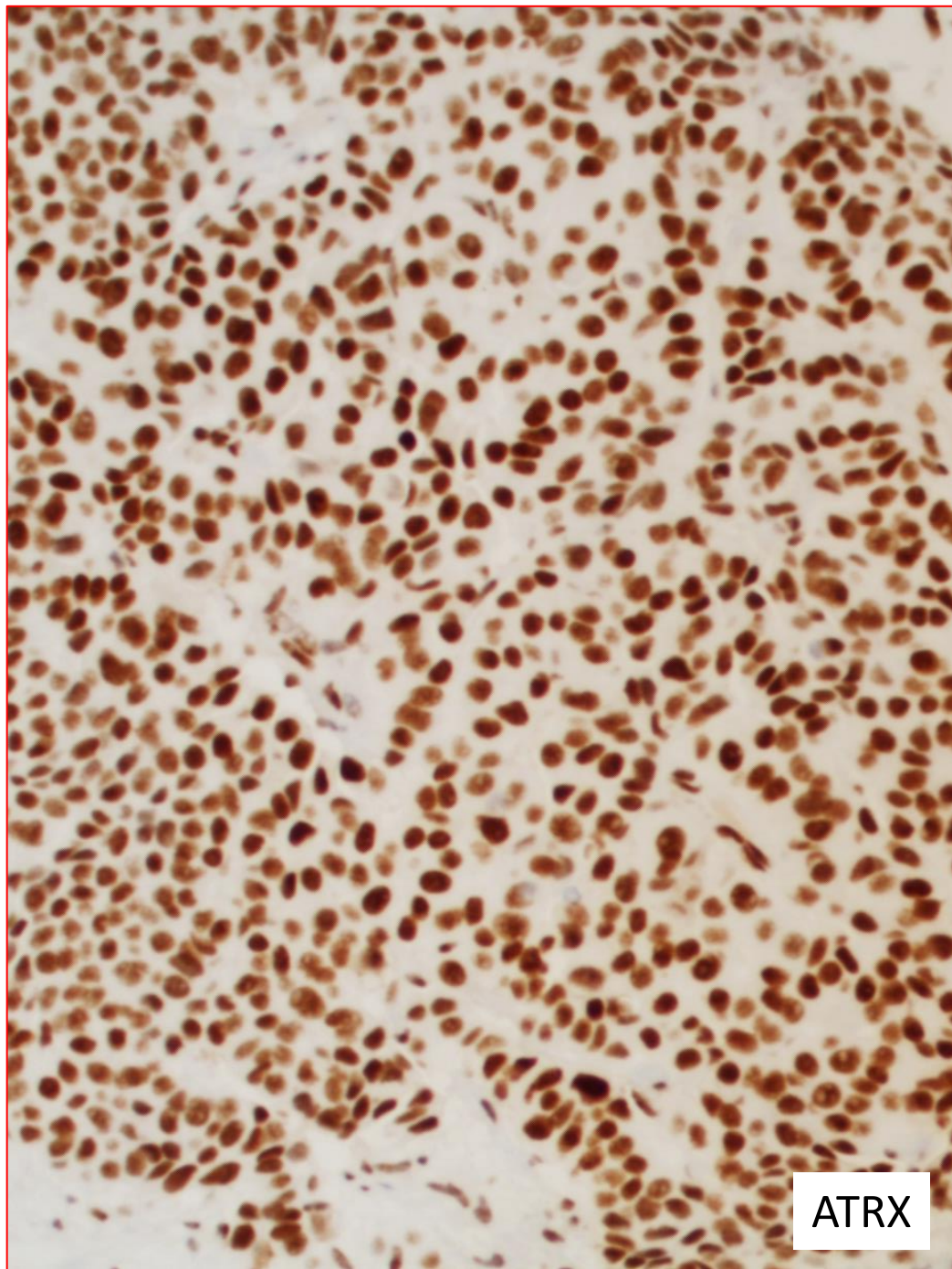
Left Breast Core Needle Biopsy











Diagnosis

- Breast, Left, Core Needle Biopsy
 - Metastatic well-differentiated neuroendocrine tumor/carcinoid
- Oncomine Assay

Somatic variants detected in the tumor (See note):

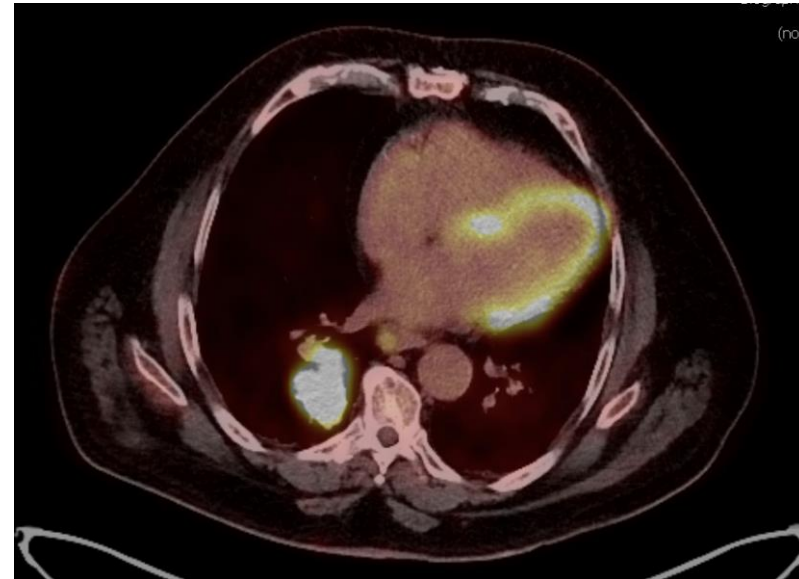
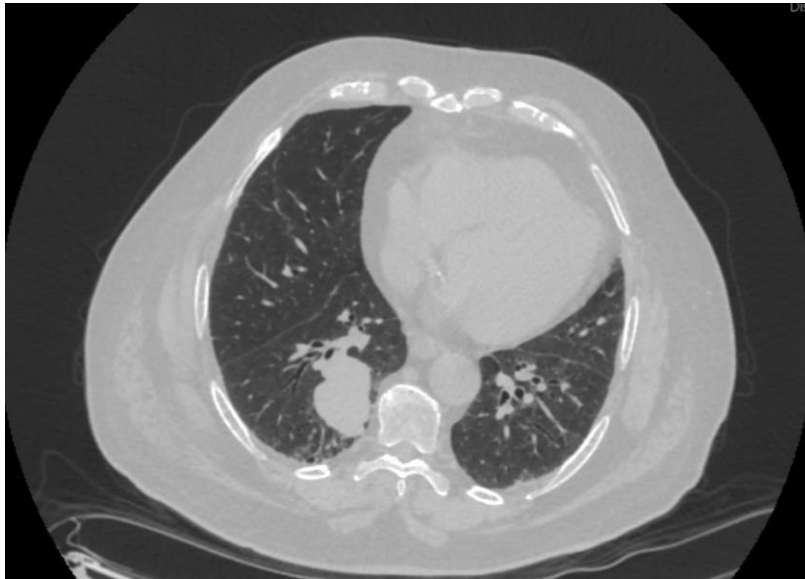
| <u>Variant</u> | <u>Allelic Fraction</u> |
|------------------------------|-------------------------|
| <i>KRAS</i> G12V | 38% |
| <i>SETD2</i> G1717Ter | 22% |
| <i>NOTCH1</i> Q1527H | 20% |
| <i>SETD2</i> R1297C | 11% |
| <i>CDKN2A</i> D125N | 9% |

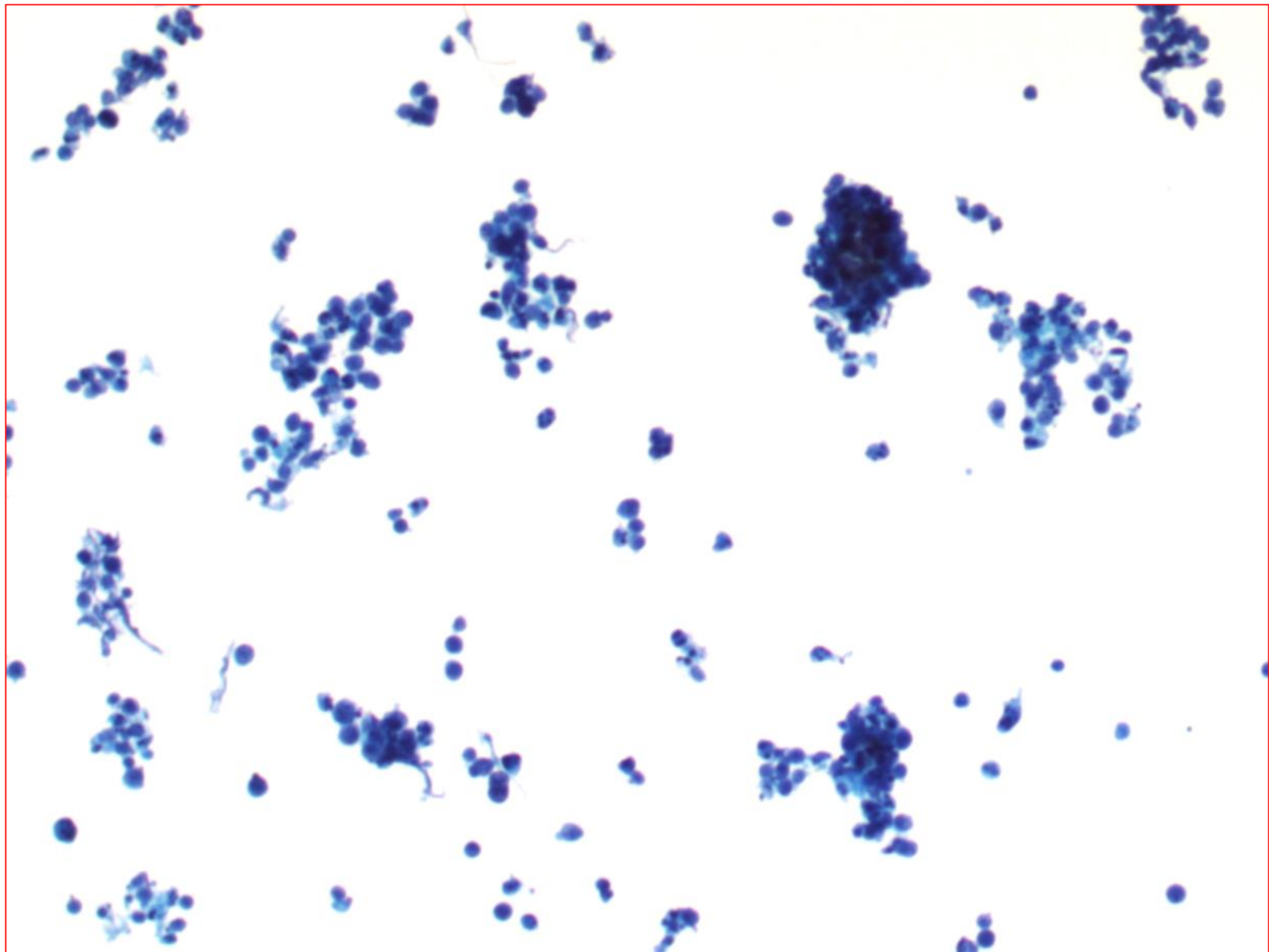
Learning Points

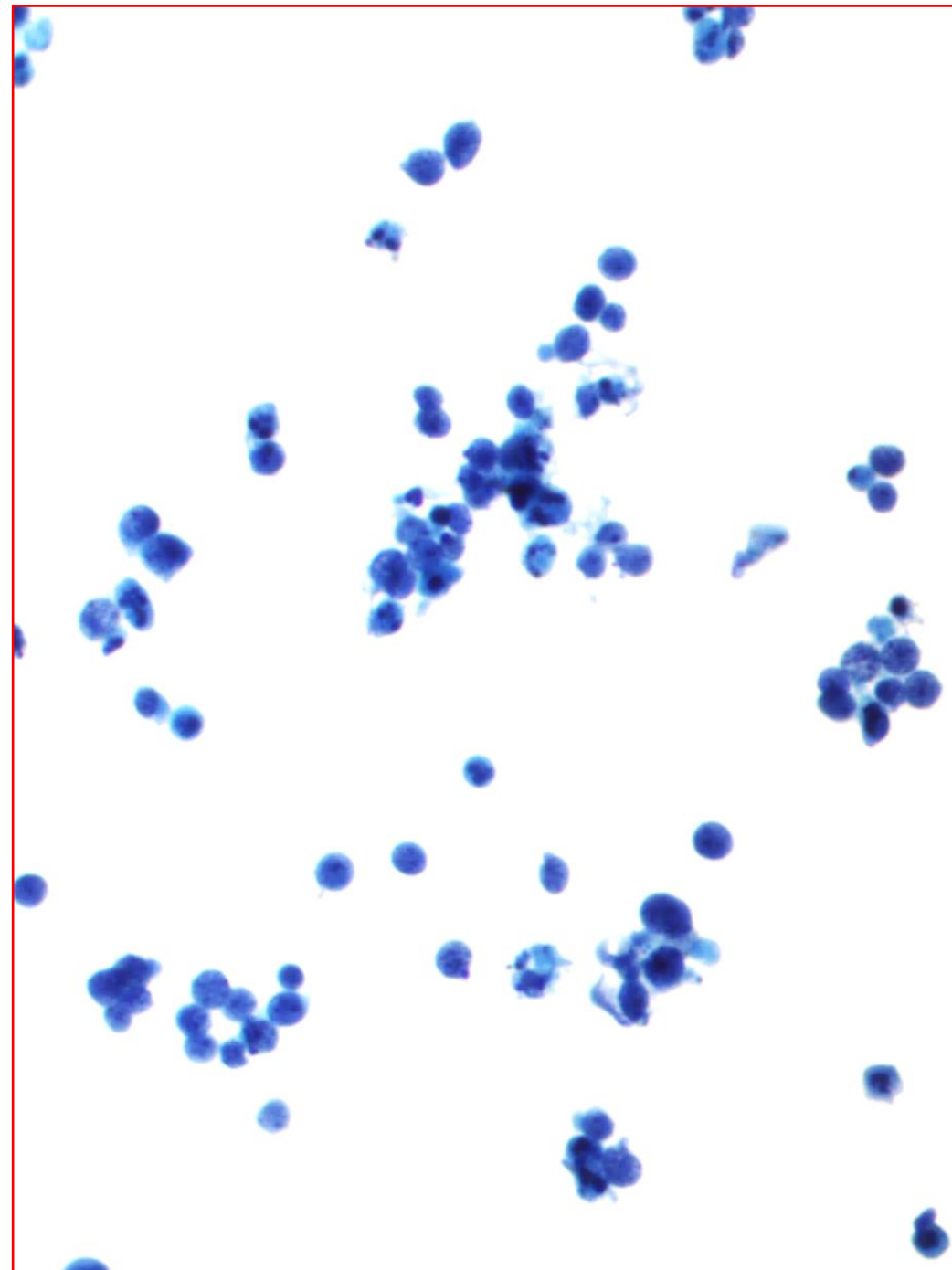
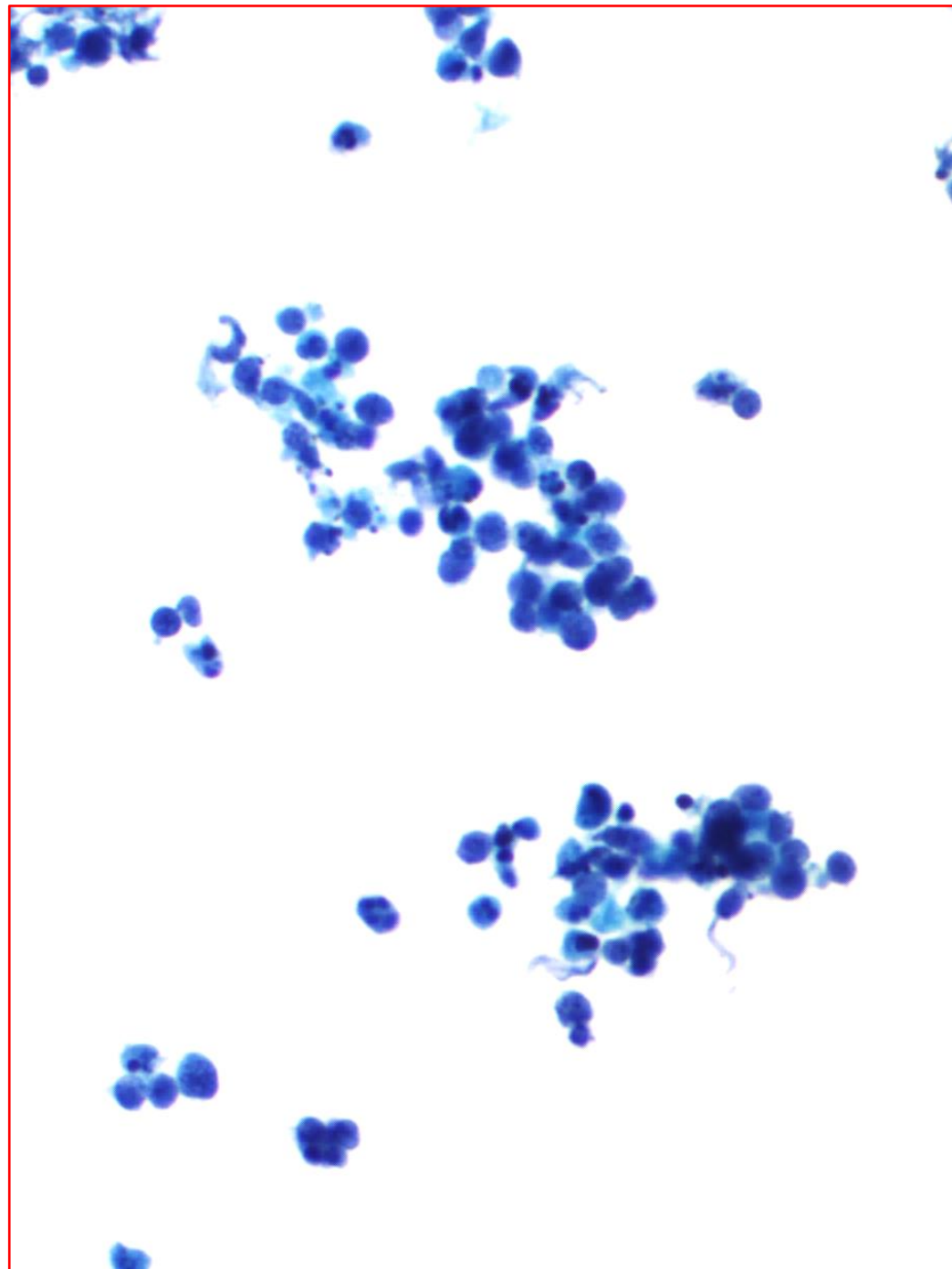
- Carcinoid tumors can mimic non-small cell carcinoma, especially in cytology specimens.
- Not all carcinoid tumors have an indolent clinical course.
- Clinical correlation is always recommended for identification of tumor origin.

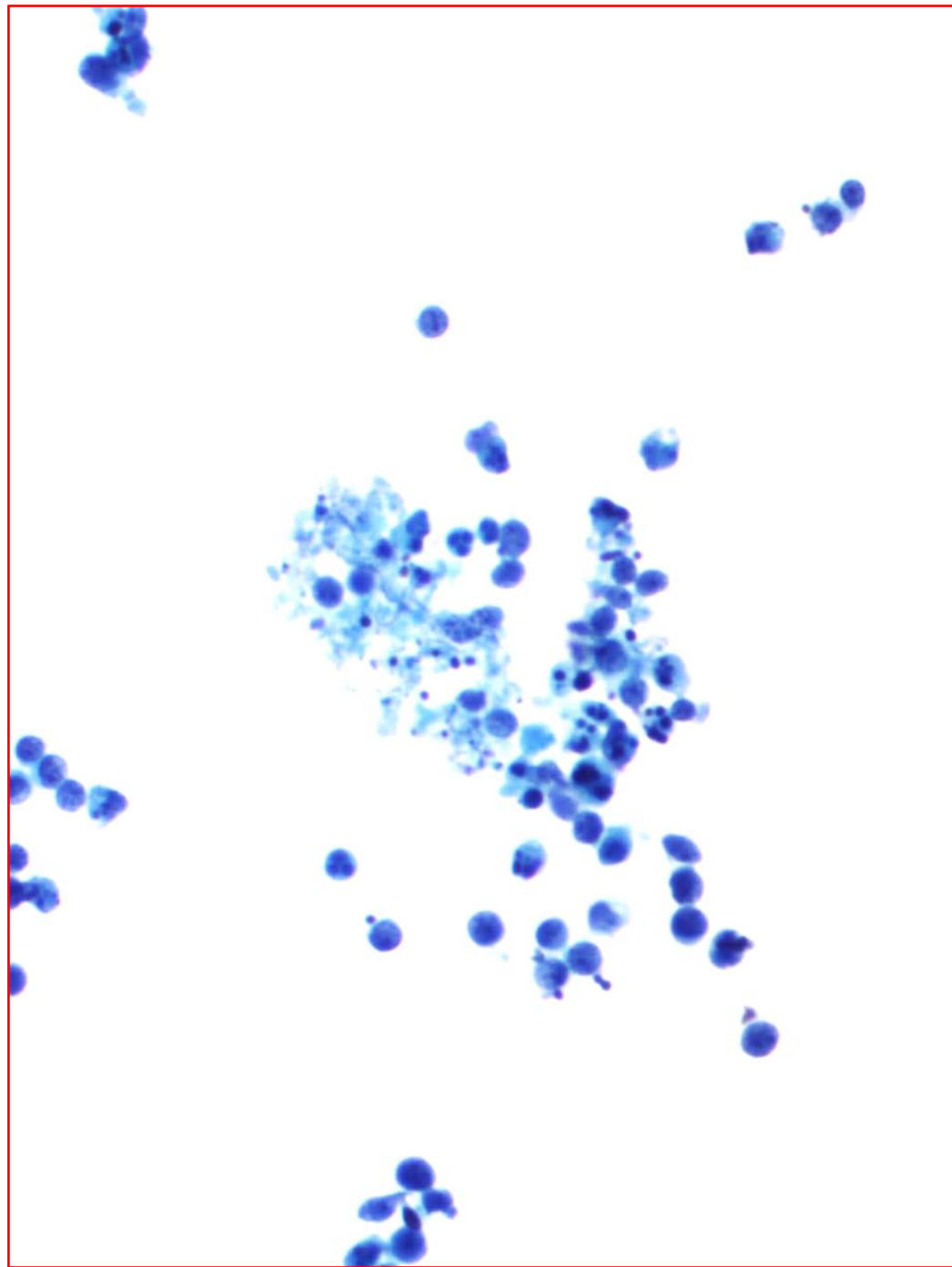
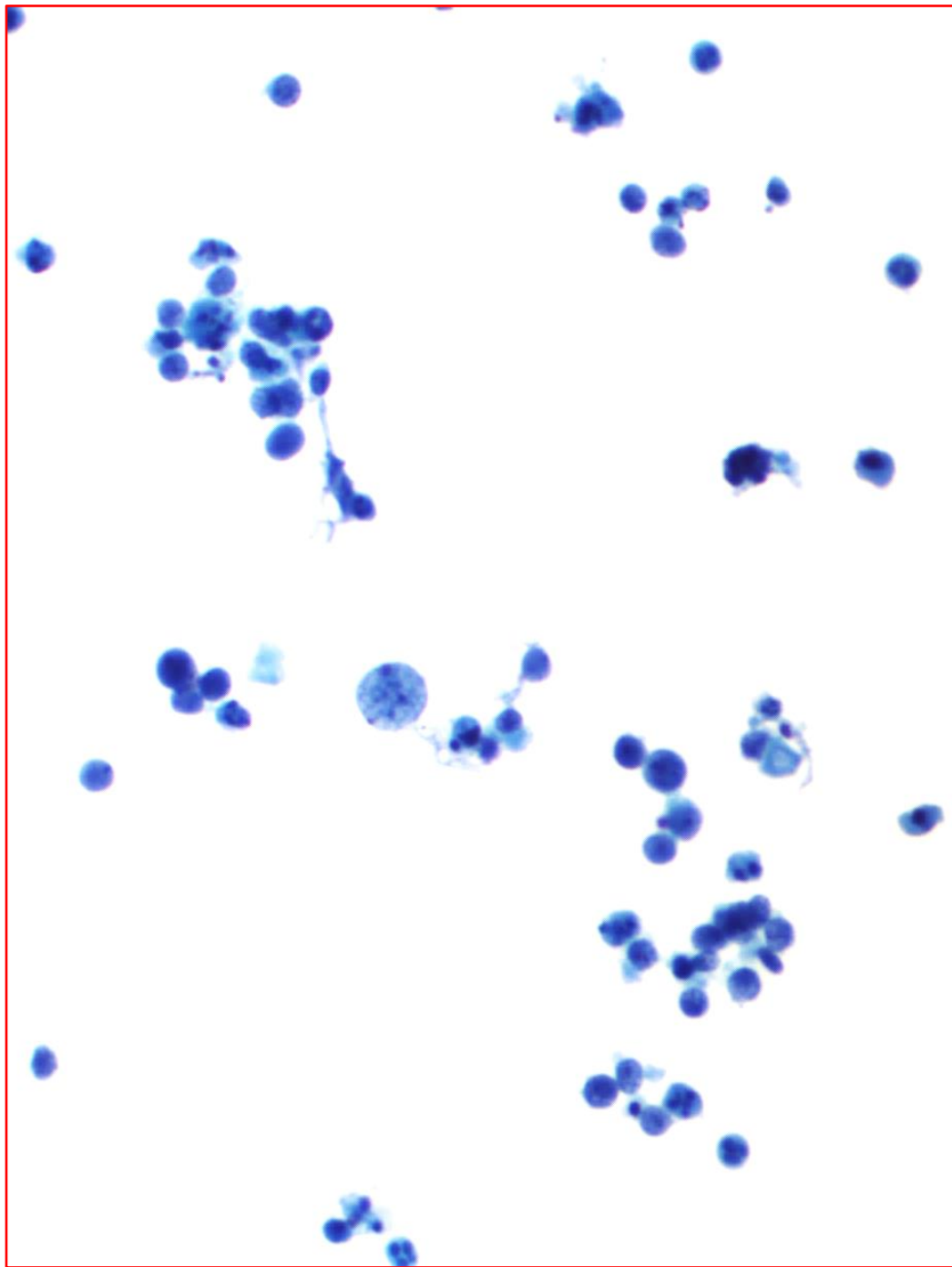
Case #2

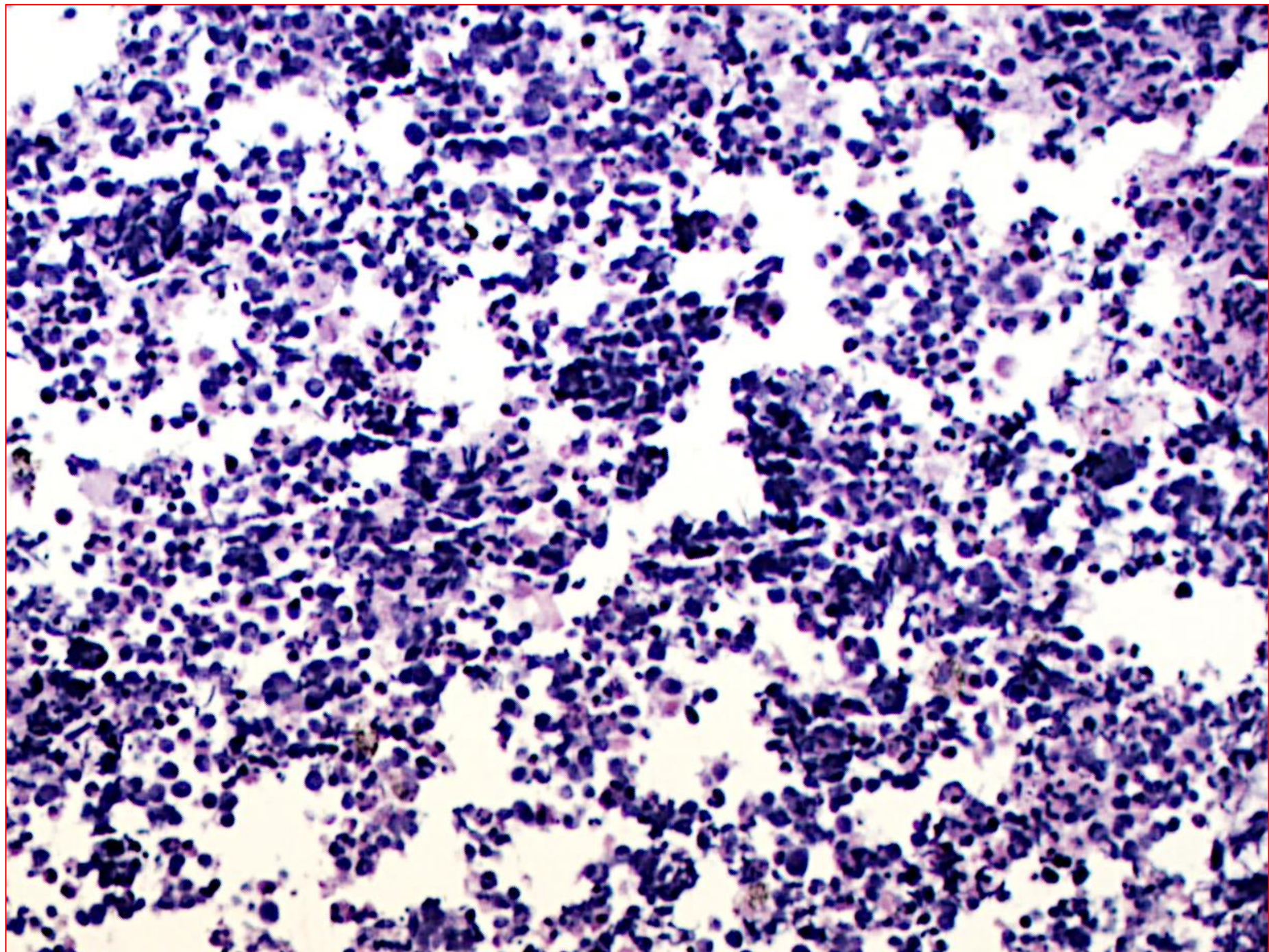
- 77/M, h/o cardiac disease
- A 4.4-cm PET-avid mass in the right lower lobe mass with PET-avid enlarged mediastinal lymph nodes including subcarinal lymph node

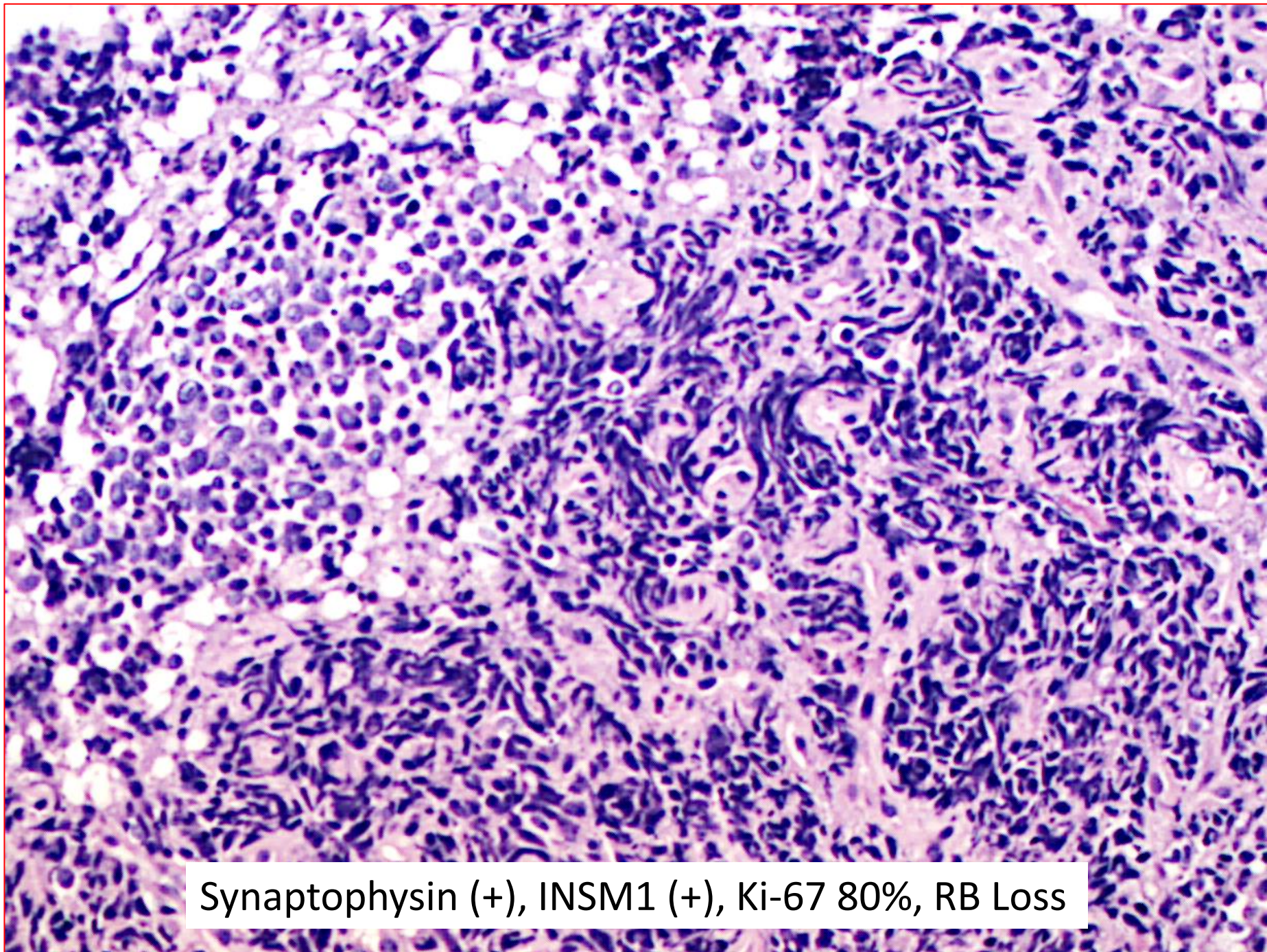








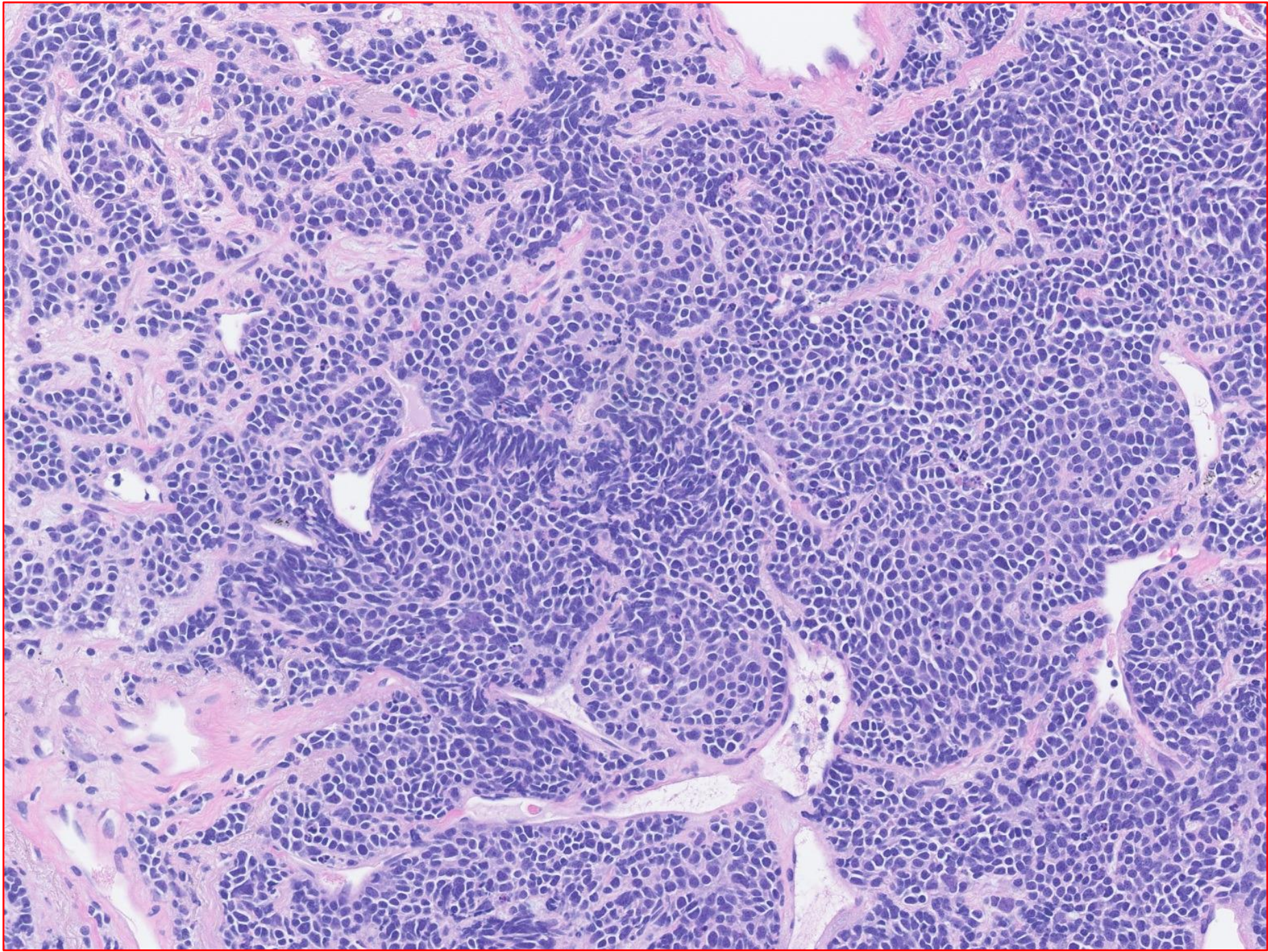


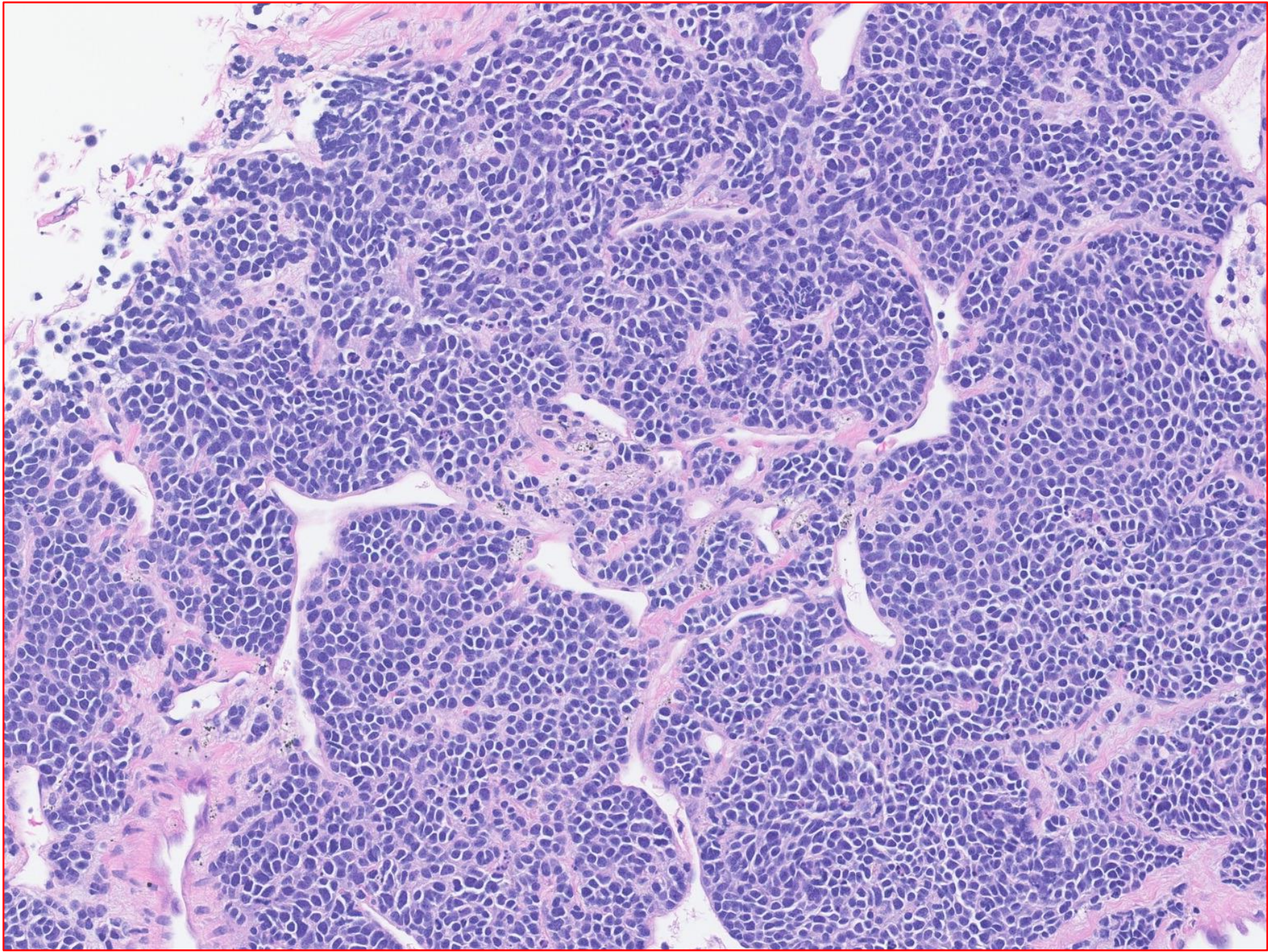


Synaptophysin (+), INSM1 (+), Ki-67 80%, RB Loss

Diagnosis?

- Small cell carcinoma
- Large neuroendocrine cell carcinoma
- Mixed small and large cell neuroendocrine carcinoma
- High-grade neuroendocrine carcinoma







Favor Large Cell Neuroendocrine Carcinoma???

Diagnosis

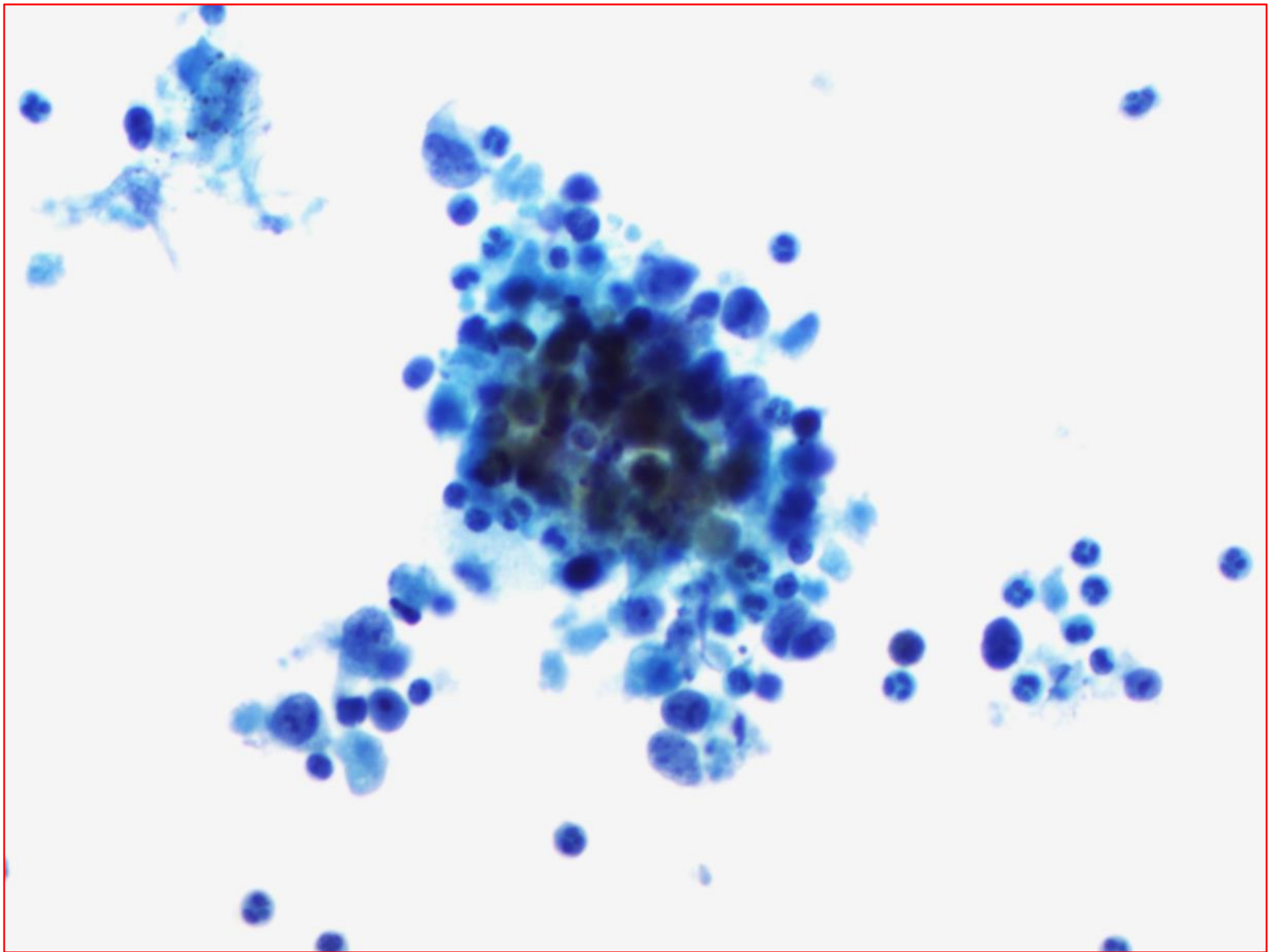
- High-grade neuroendocrine carcinoma, favor small cell carcinoma

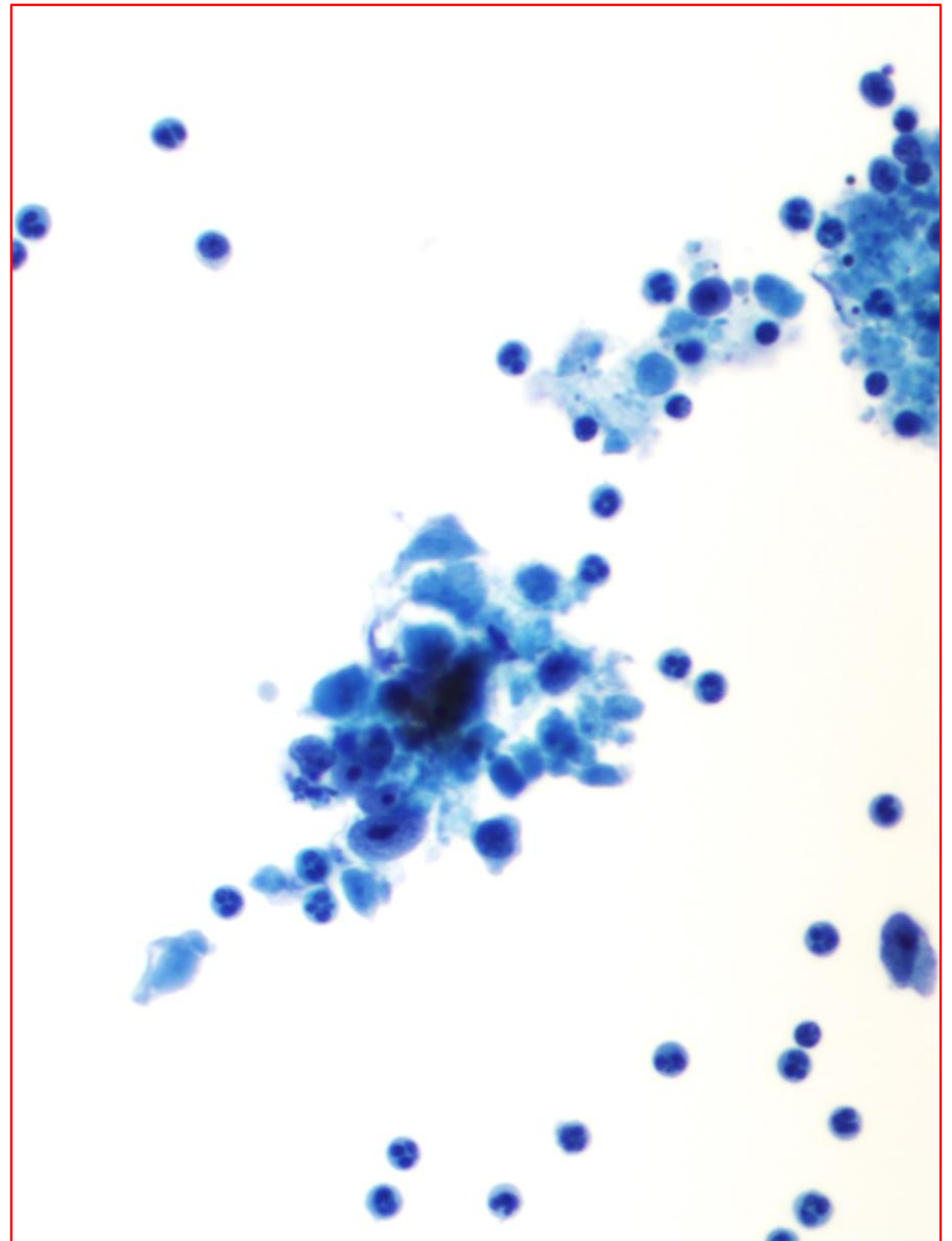
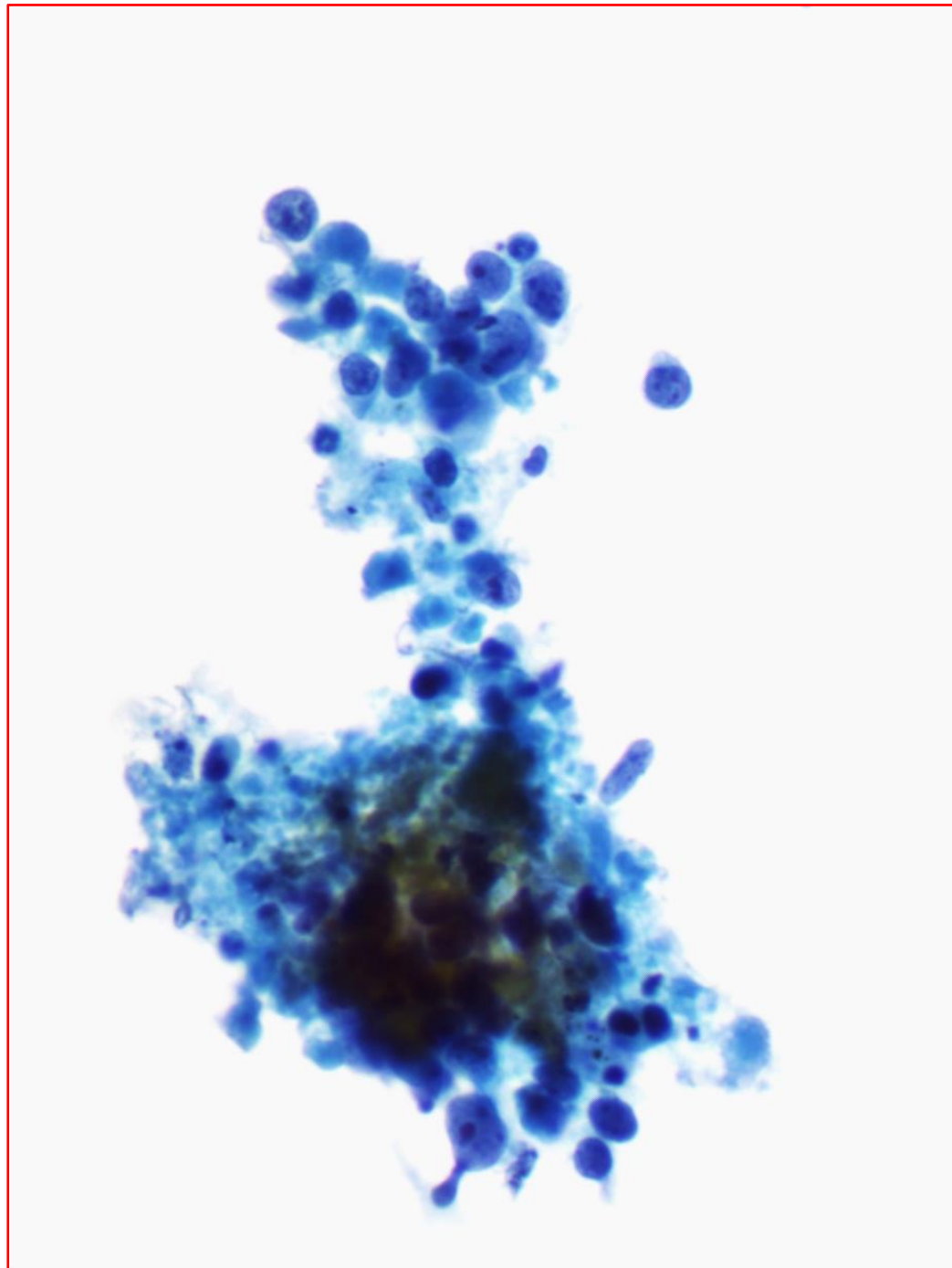
Learning Points

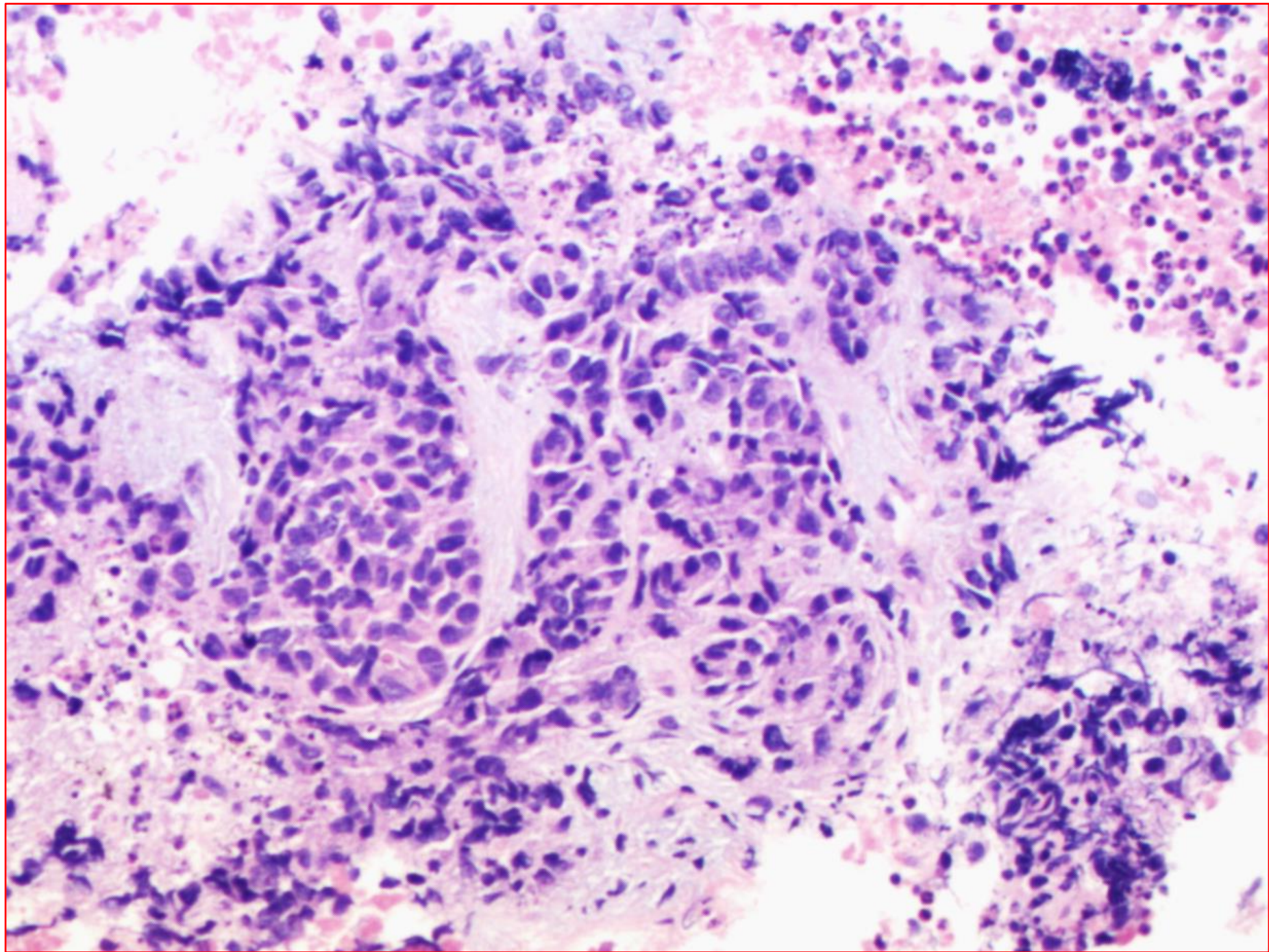
- Cell size is not the only deciding factor to class tumor as small cell carcinoma vs large cell neuroendocrine carcinoma.
- Small cell carcinoma can have large tumor cells but show scant cytoplasm and inconspicuous nucleoli.

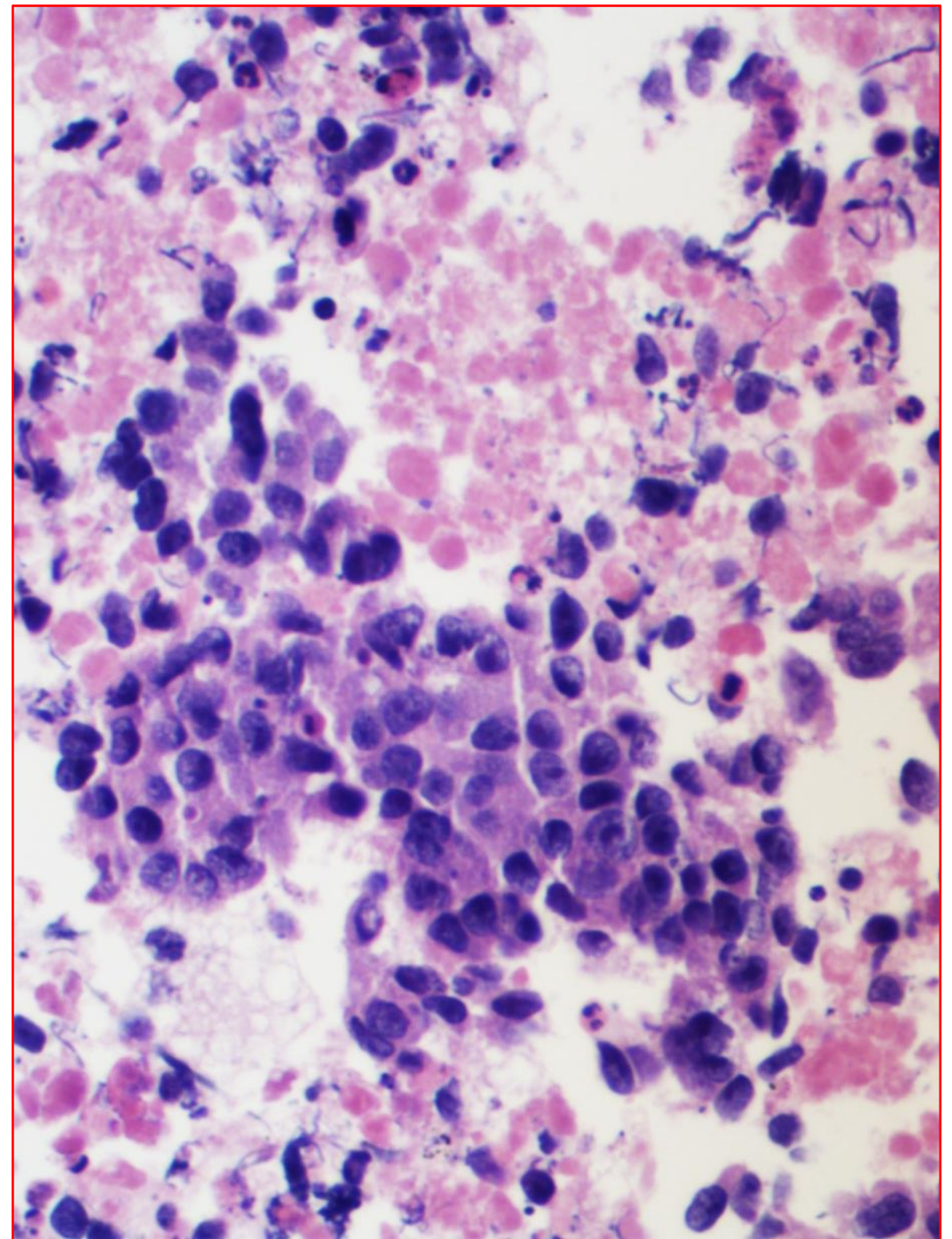
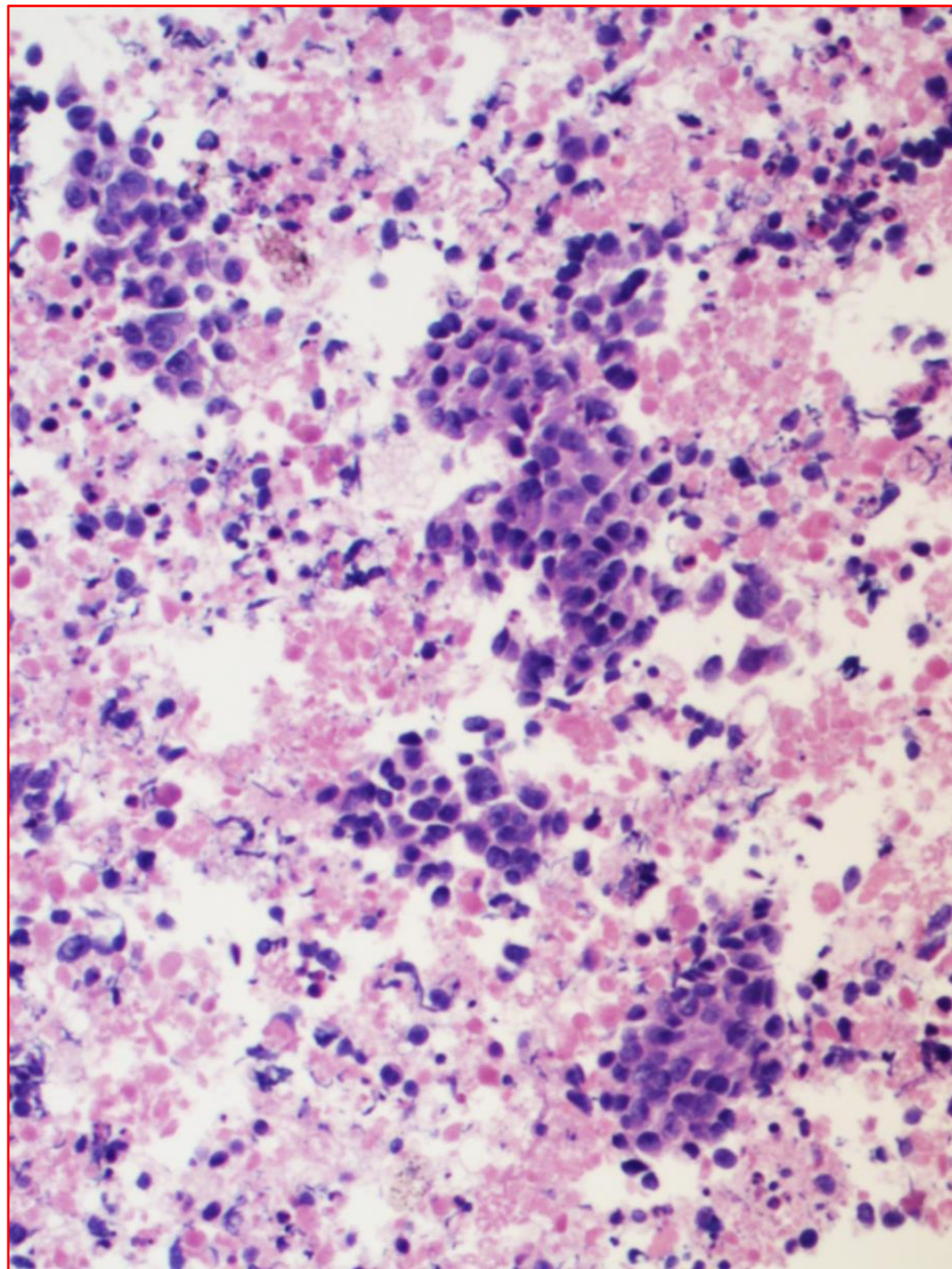
Case #3

- 62/F, h/o endometrial carcinoma, s/p hysterectomy
- Large ill-defined right lung mass measuring up to 8.4 cm, with mediastinal extension and lymphangitic carcinomatosis.
- Enlarged mediastinal and upper abdominal retroperitoneal lymph nodes, presumably metastatic.





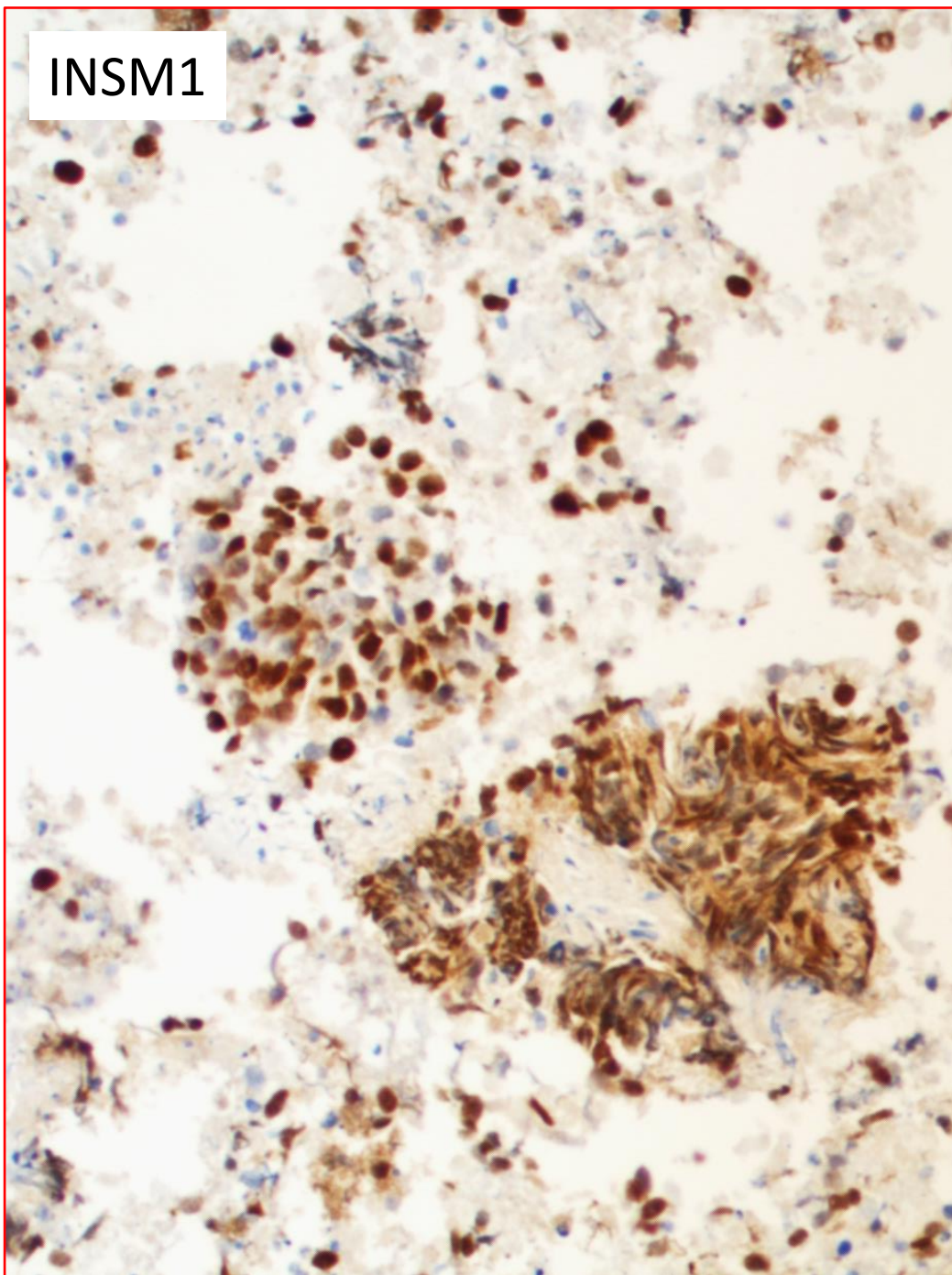




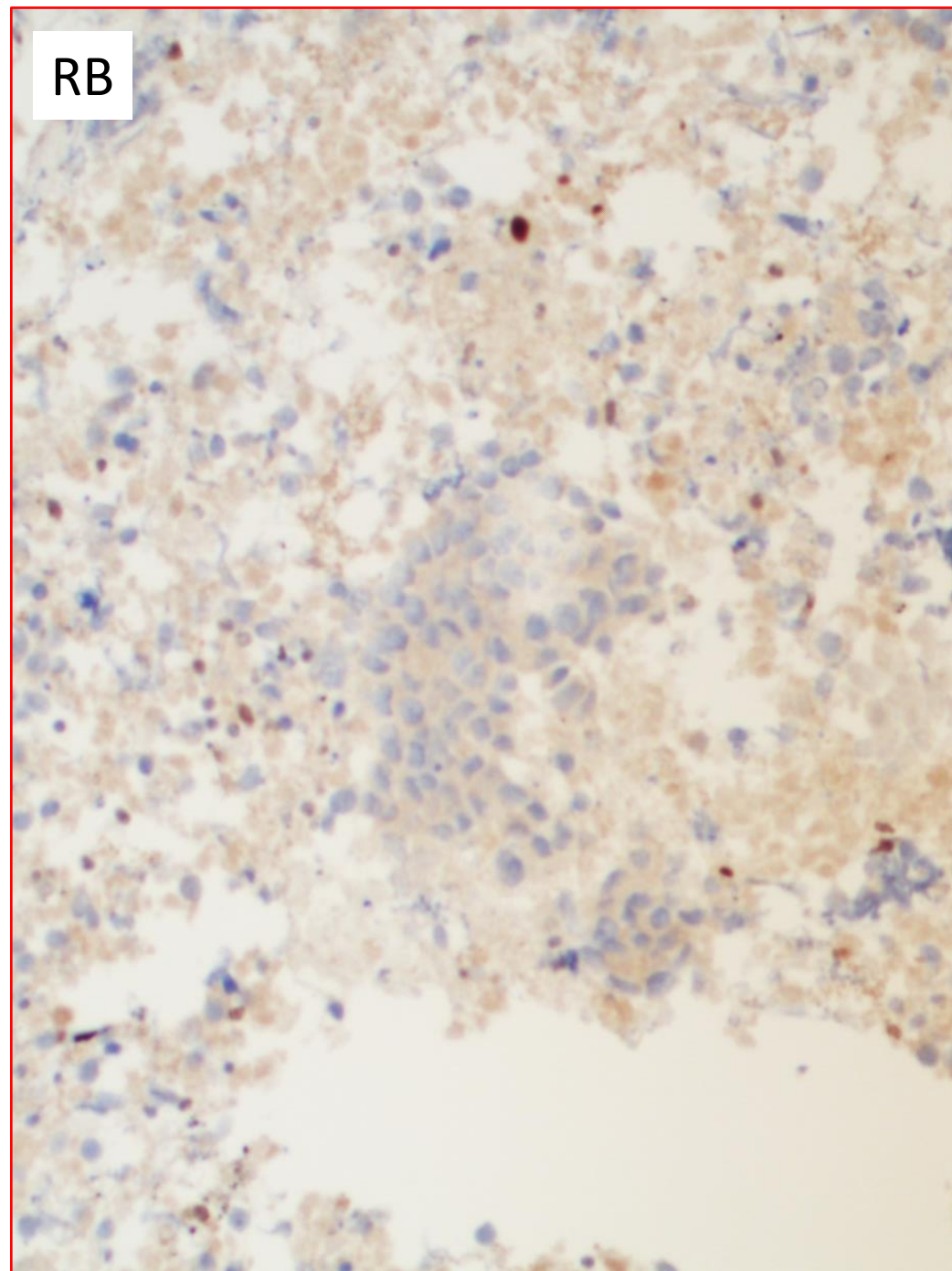
Diagnosis?

- Non-small cell carcinoma
- Squamous cell carcinoma
- Large neuroendocrine cell carcinoma
- Metastatic endometrial carcinoma

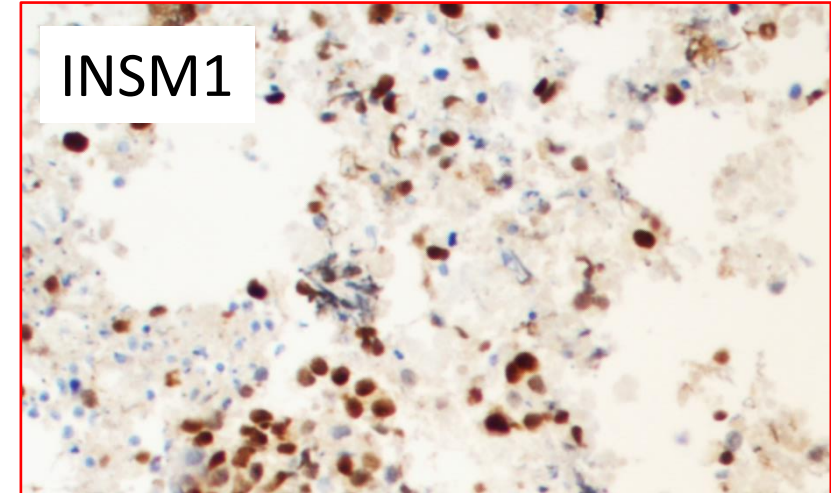
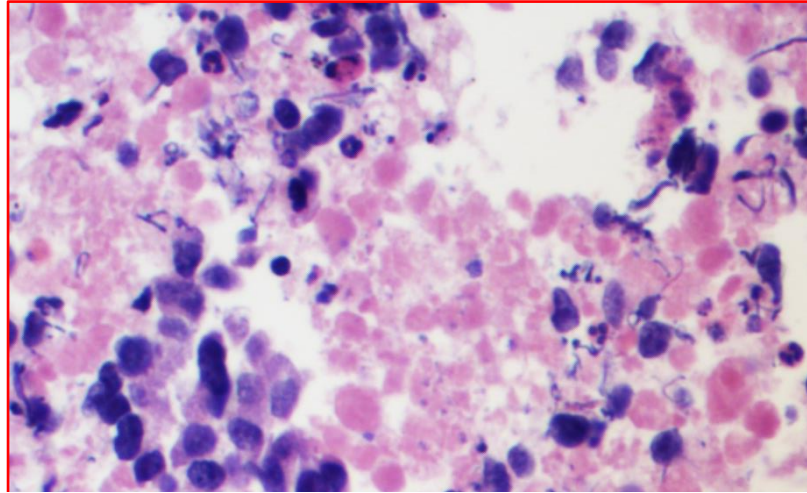
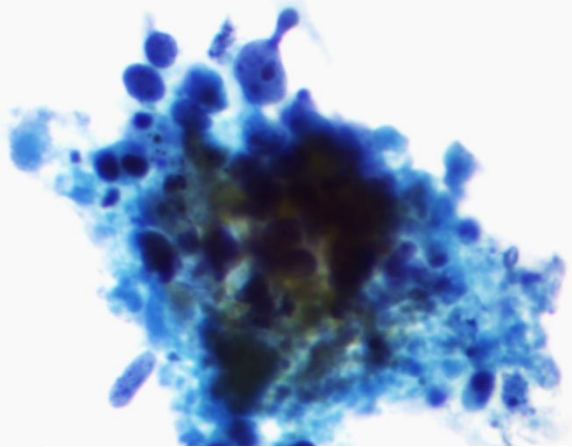
INSM1



RB

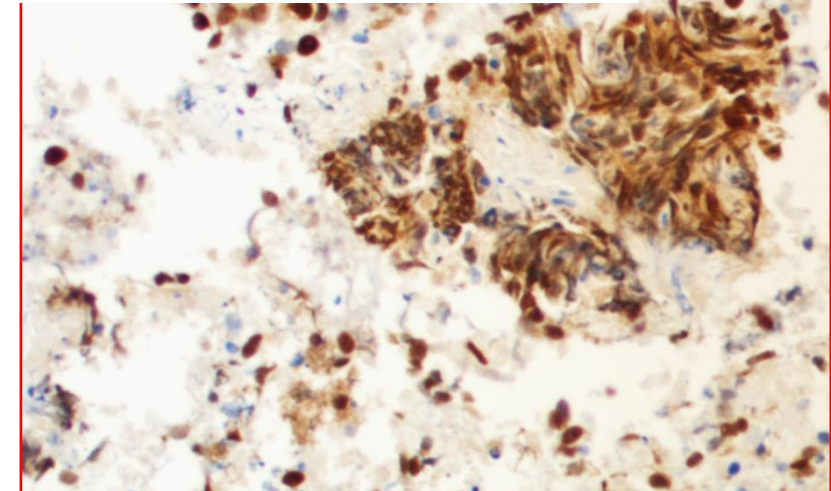
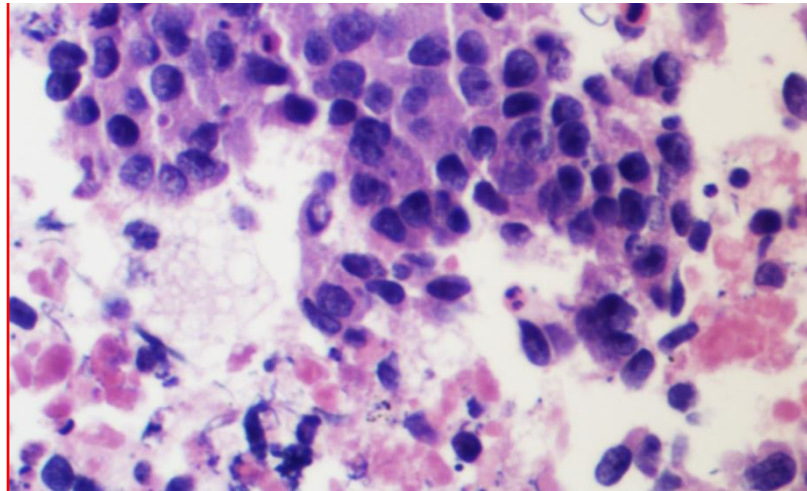
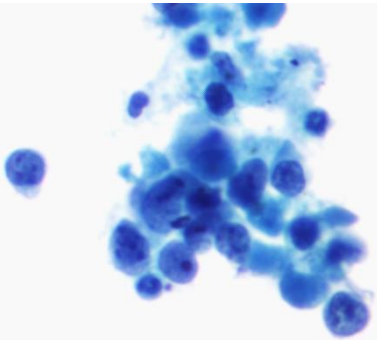


Diagnosis



INSM1

Non-small Cell Carcinoma, Suggestive of Large Cell Neuroendocrine Carcinoma

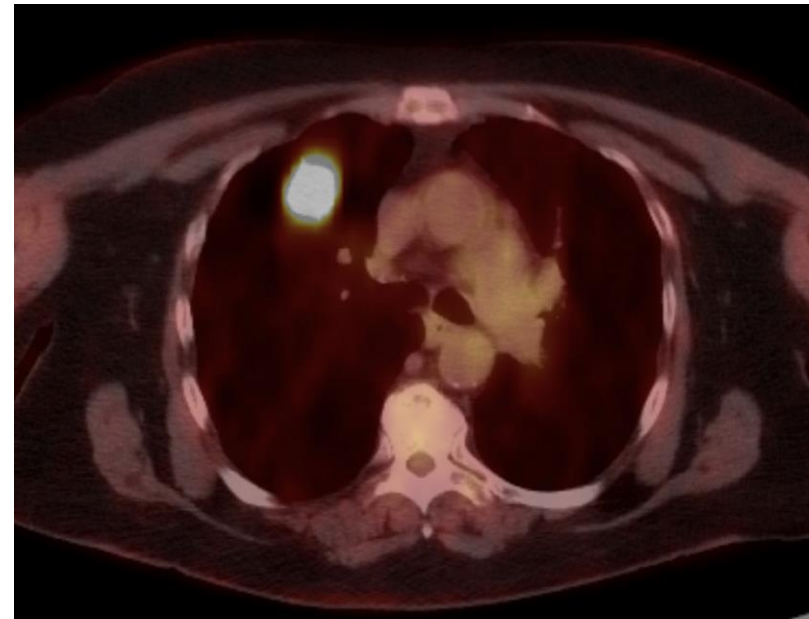
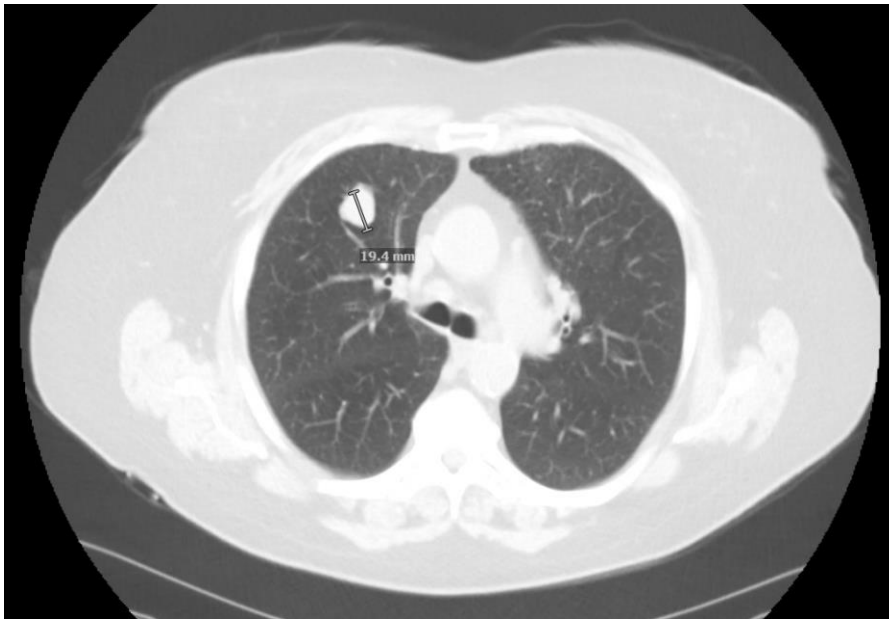


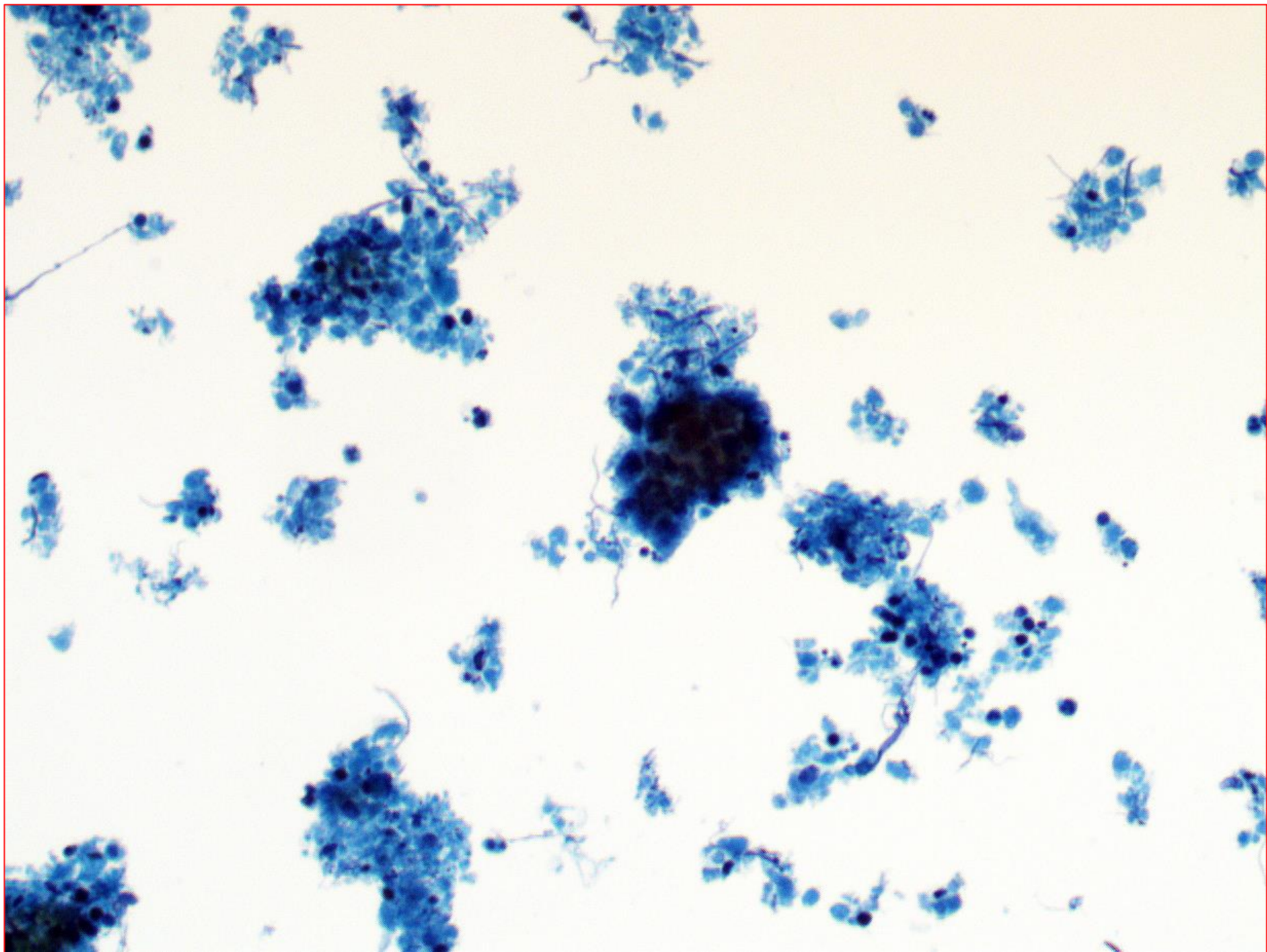
Learning Points

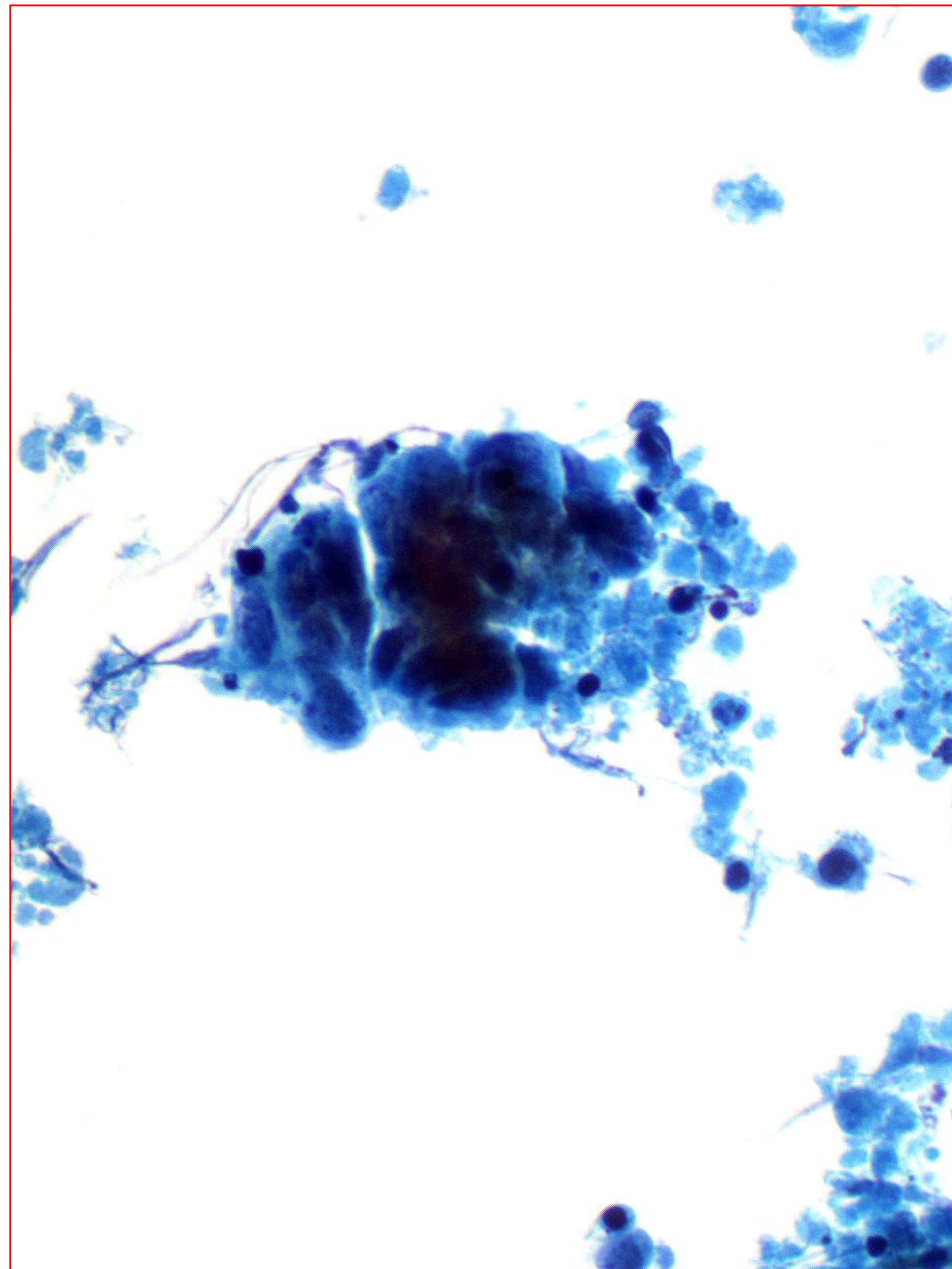
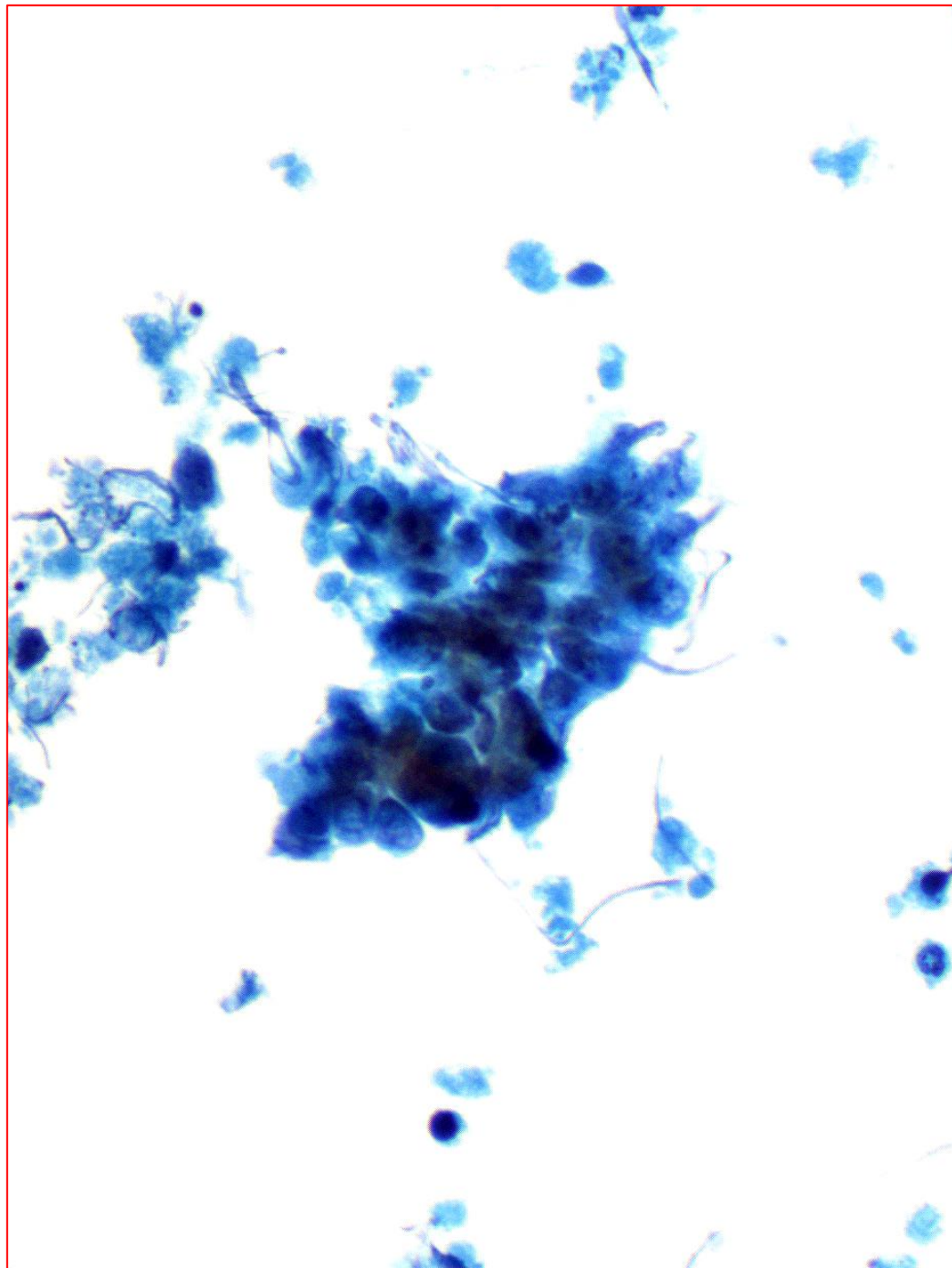
- Large cell neuroendocrine carcinoma may lack typical cytomorphic features of neuroendocrine tumors.
- Relatively uniform tumor with necrosis may raise suspicion for large cell neuroendocrine carcinoma.
- Ancillary immunostains may be helpful for rendering an accurate diagnosis.

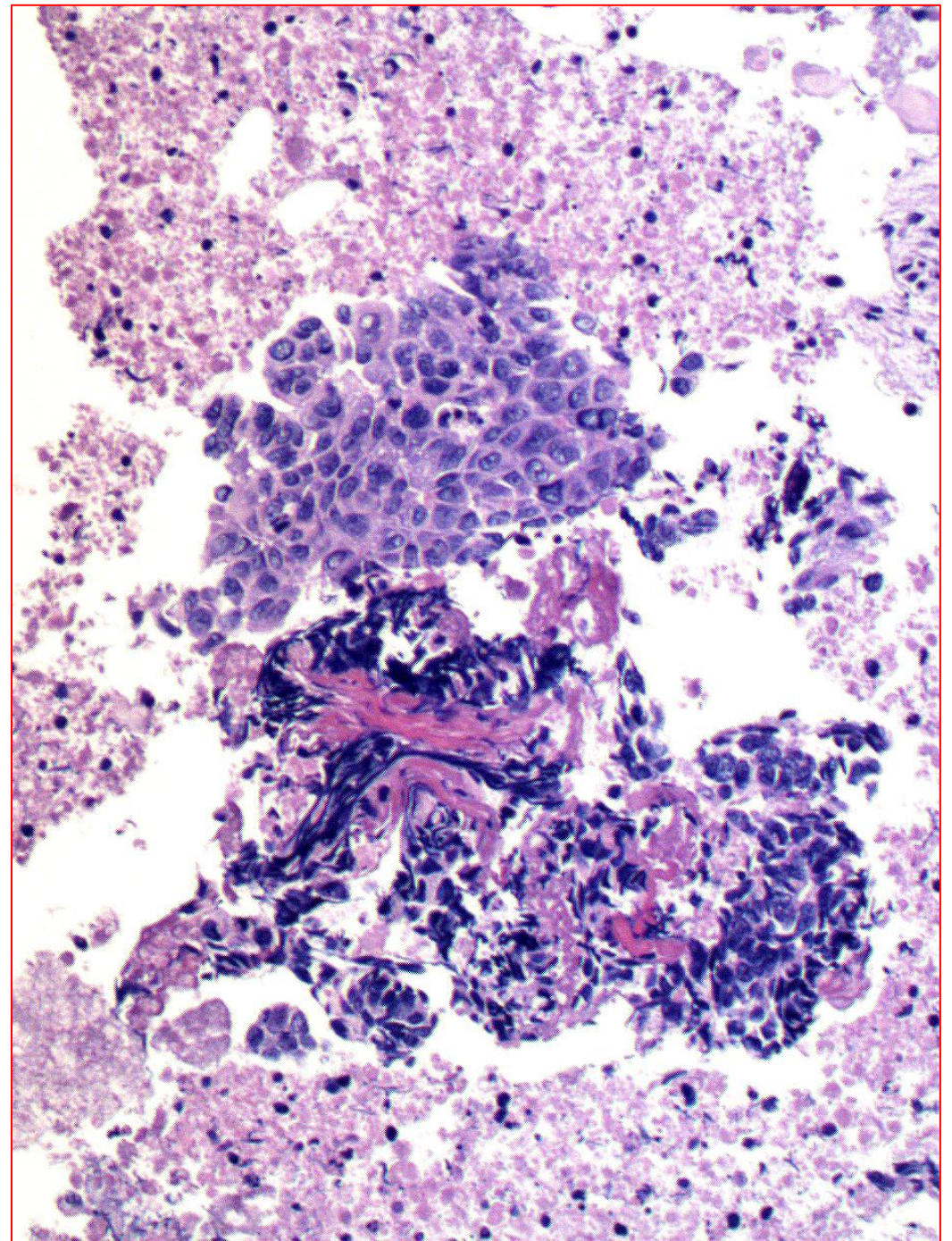
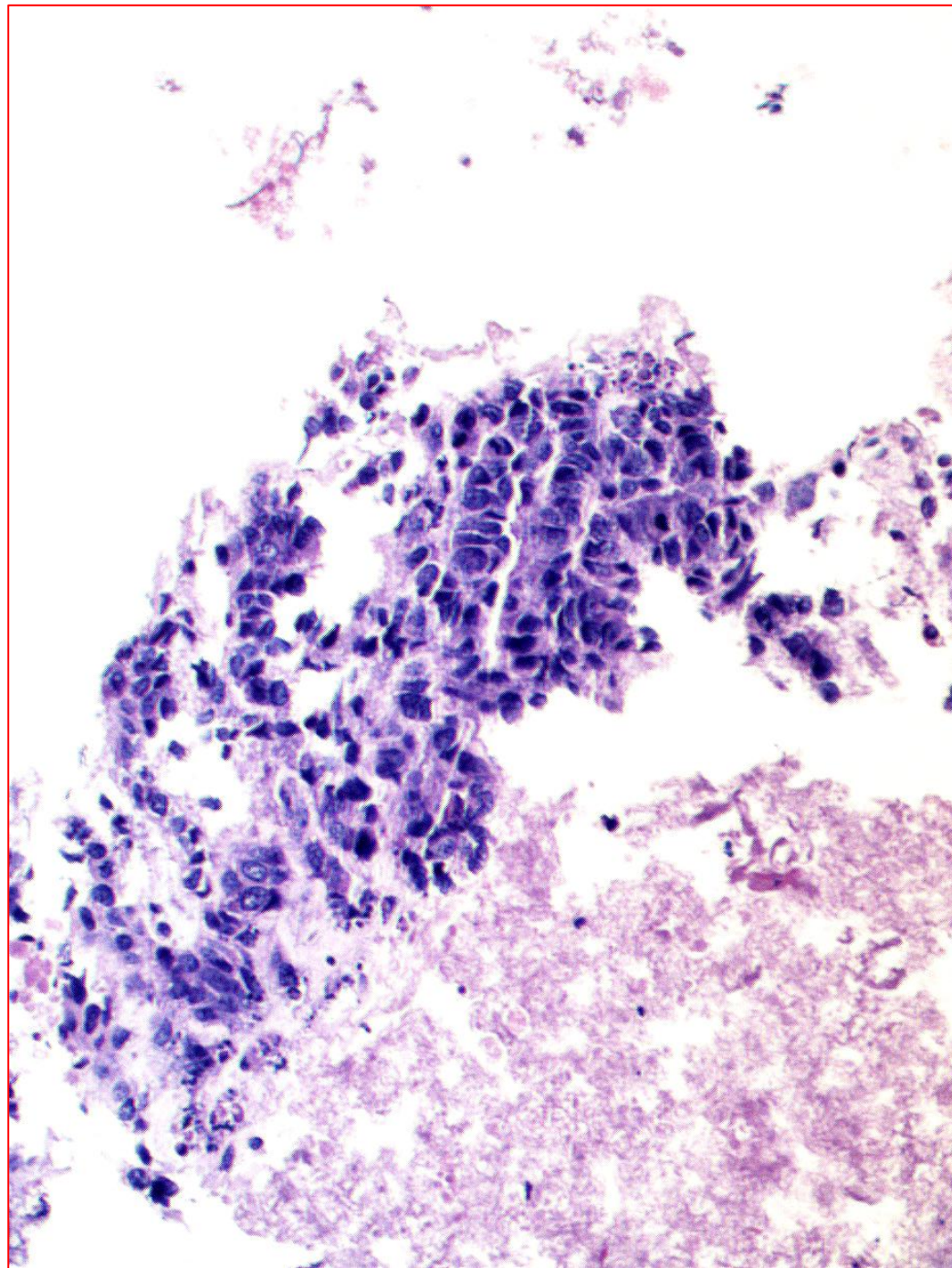
Case #4

- 71/F, h/o presumed right middle lobe NSCLC, s/p SBRT
- A solitary PET-avid nodule within right upper lobe currently 2.2 cm, previously 7 mm





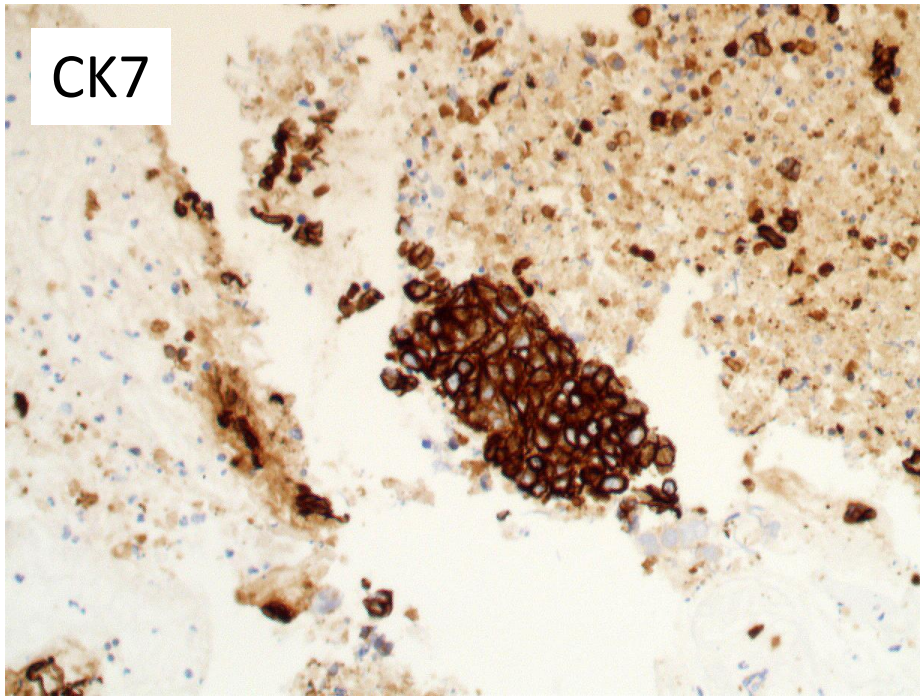




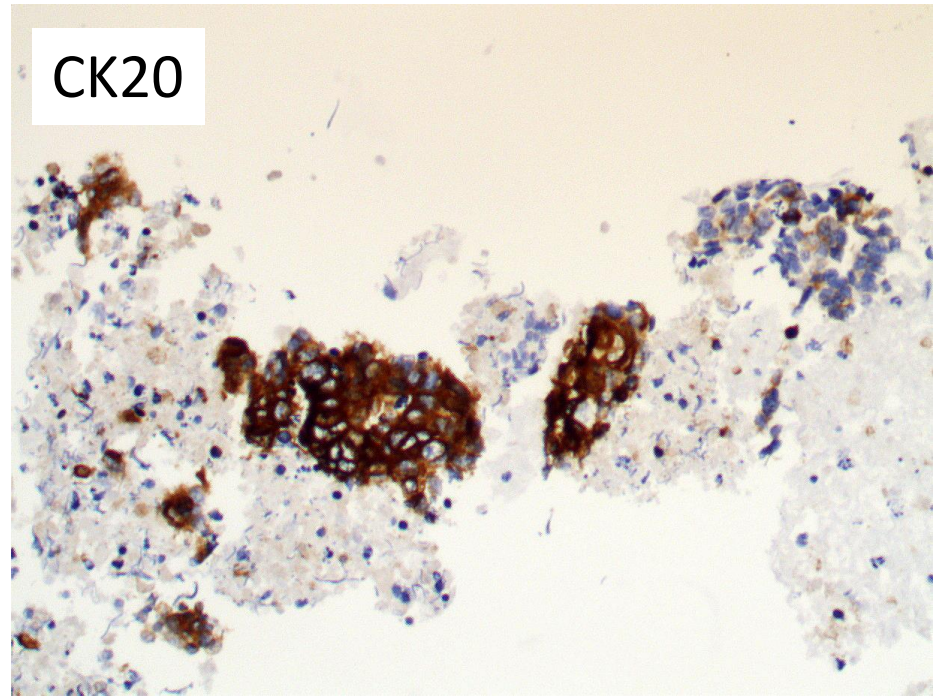
Diagnosis?

- Lung adenocarcinoma
- Squamous cell carcinoma
- Large neuroendocrine cell carcinoma
- Others

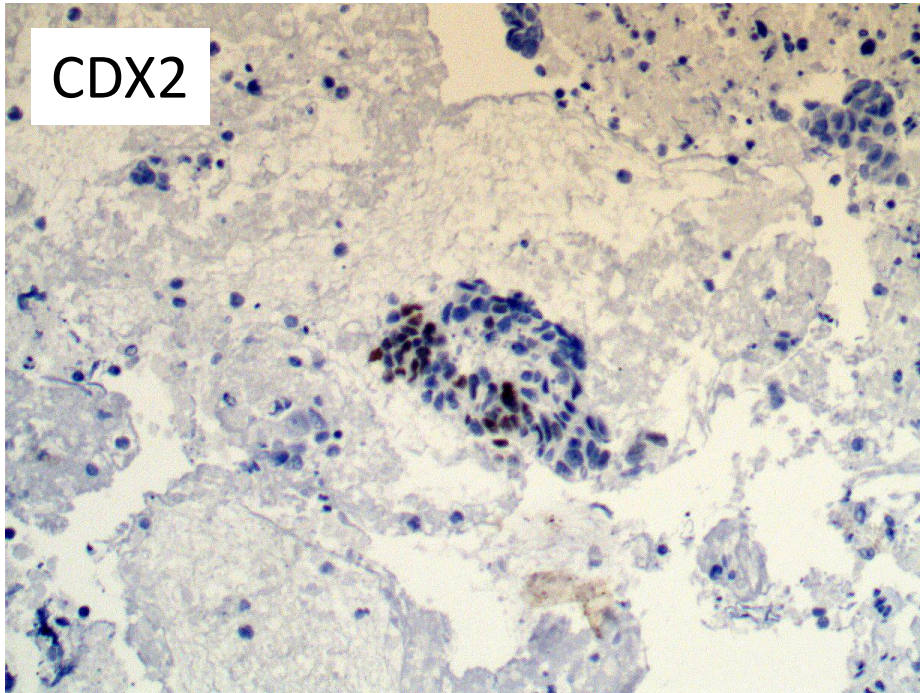
CK7



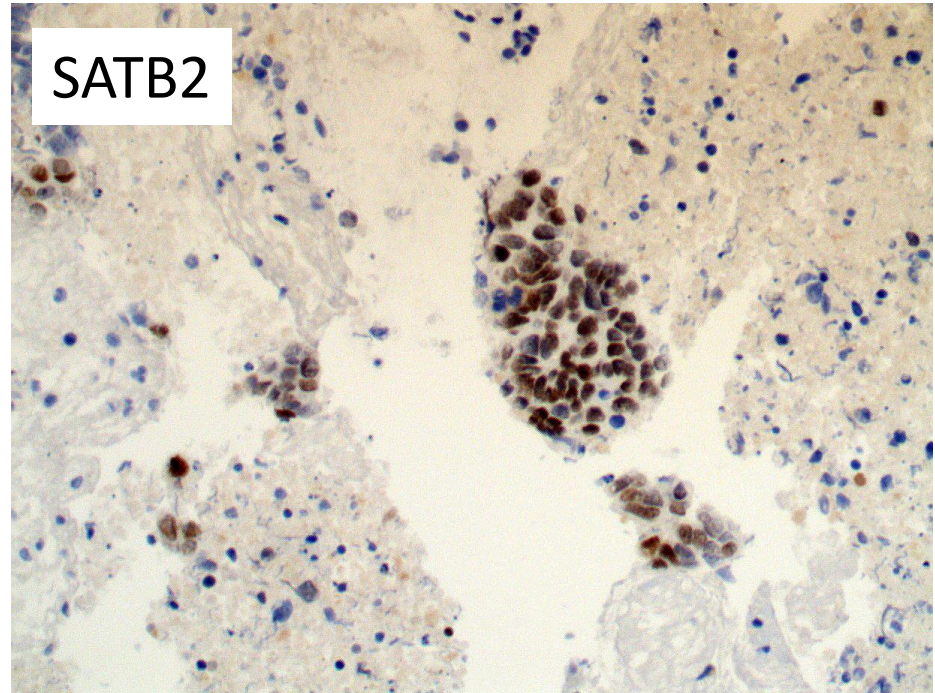
CK20

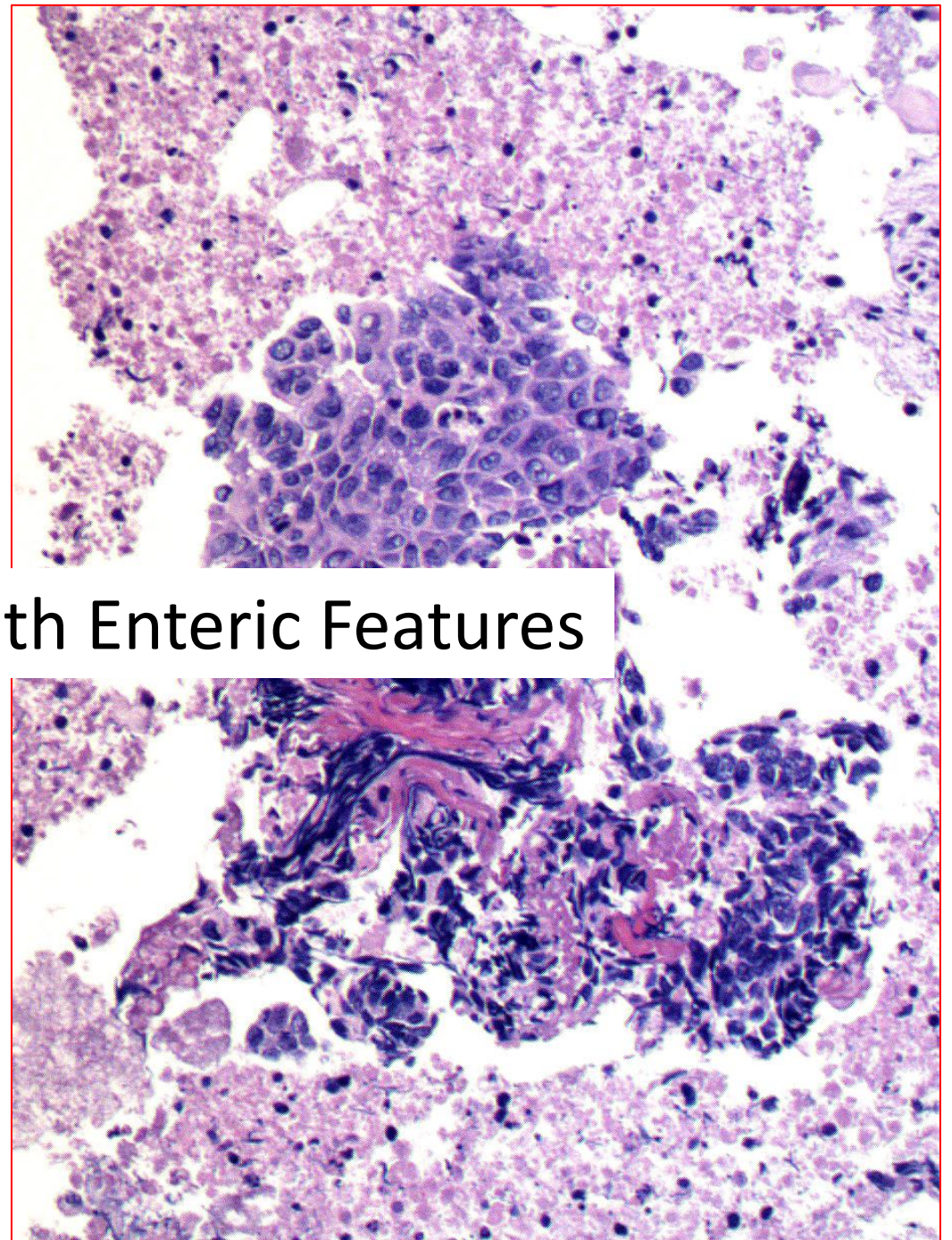
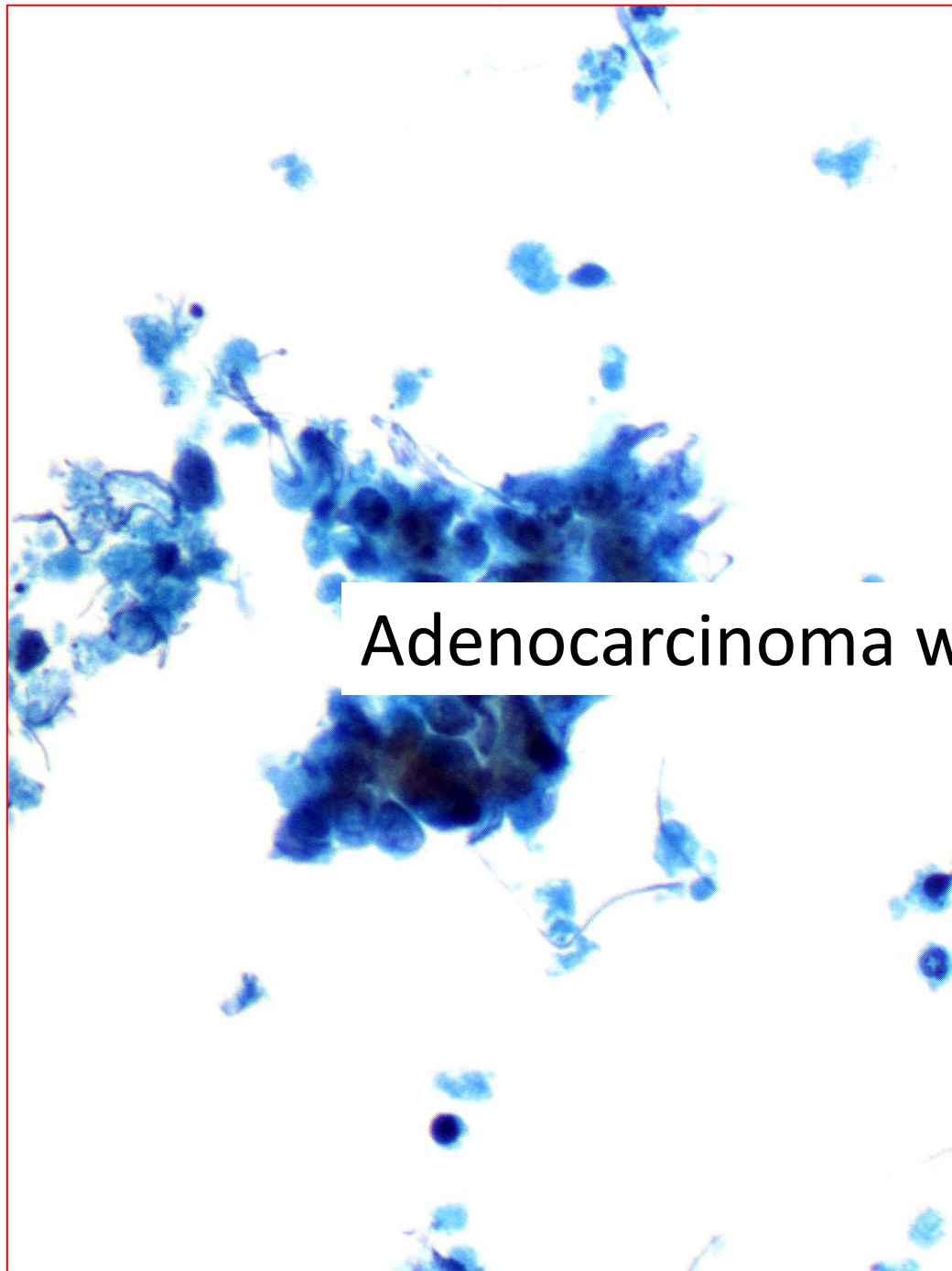


CDX2



SATB2





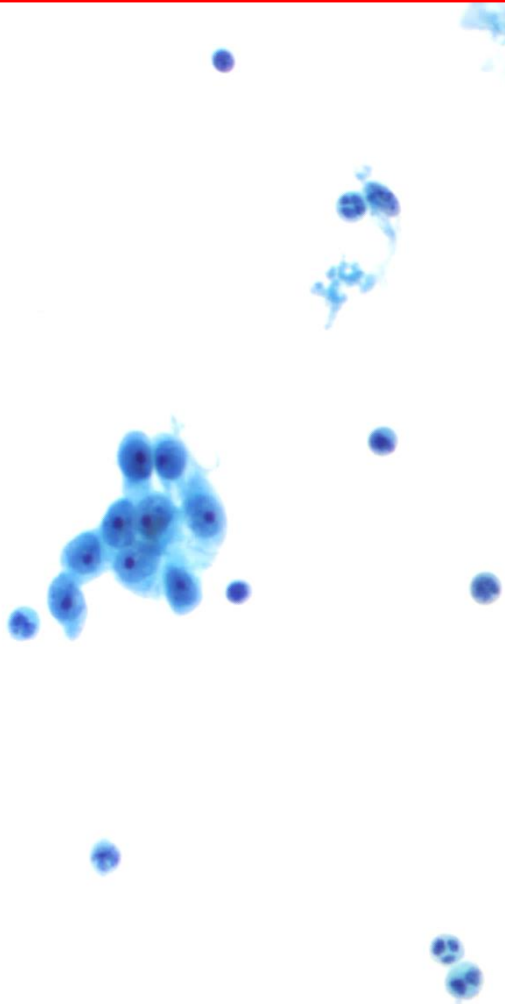
Adenocarcinoma with Enteric Features

Learning Points

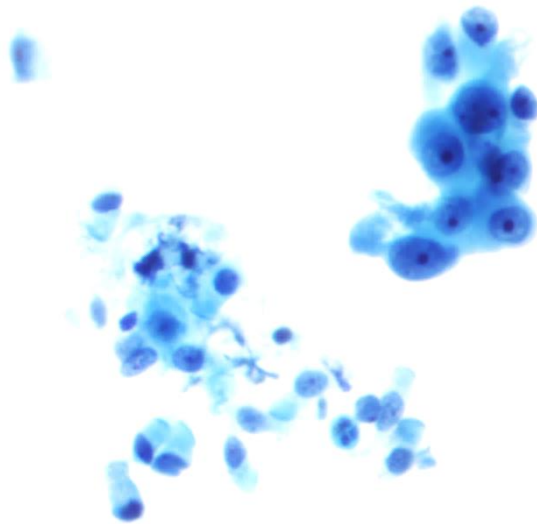
- Lung adenocarcinoma can show enteric features, both morphologically and immunophenotypically, mimicking colon cancer.
- Clinical history and imaging/colonoscopy findings important to exclude the possibility of metastatic colon cancer.

Cases 5-7

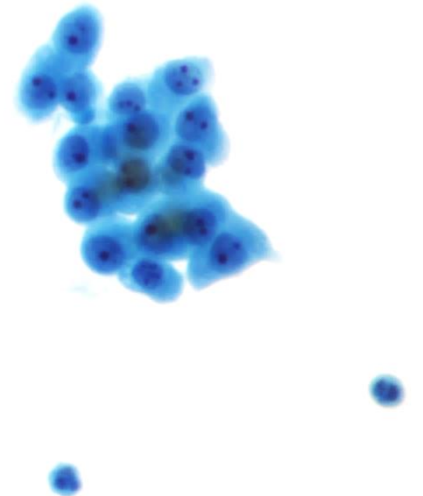
#5



#6

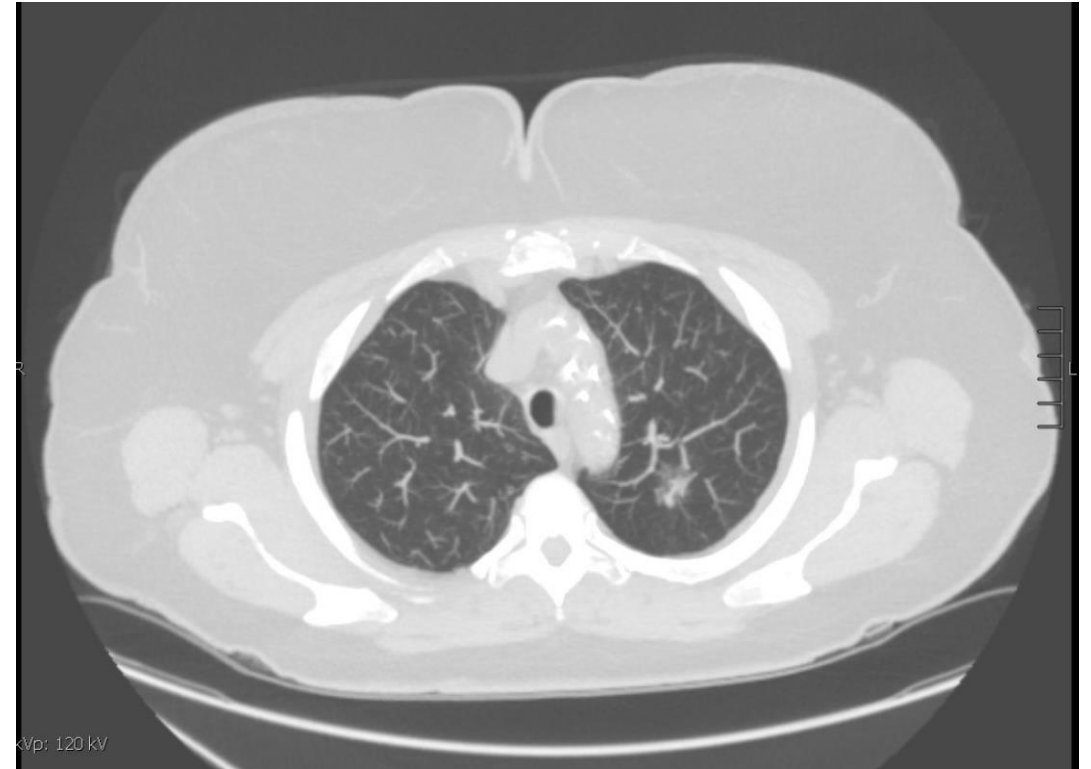


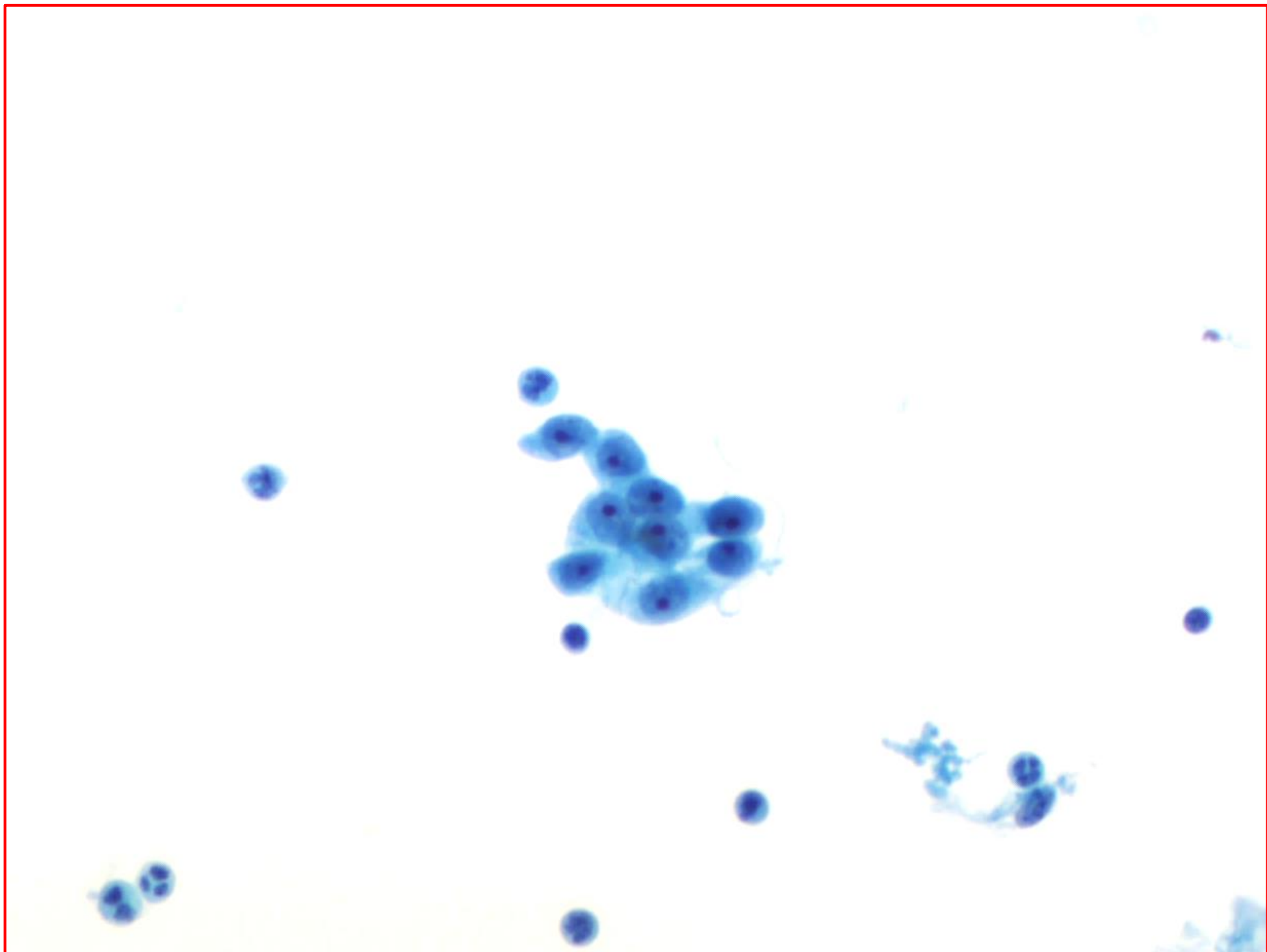
#7

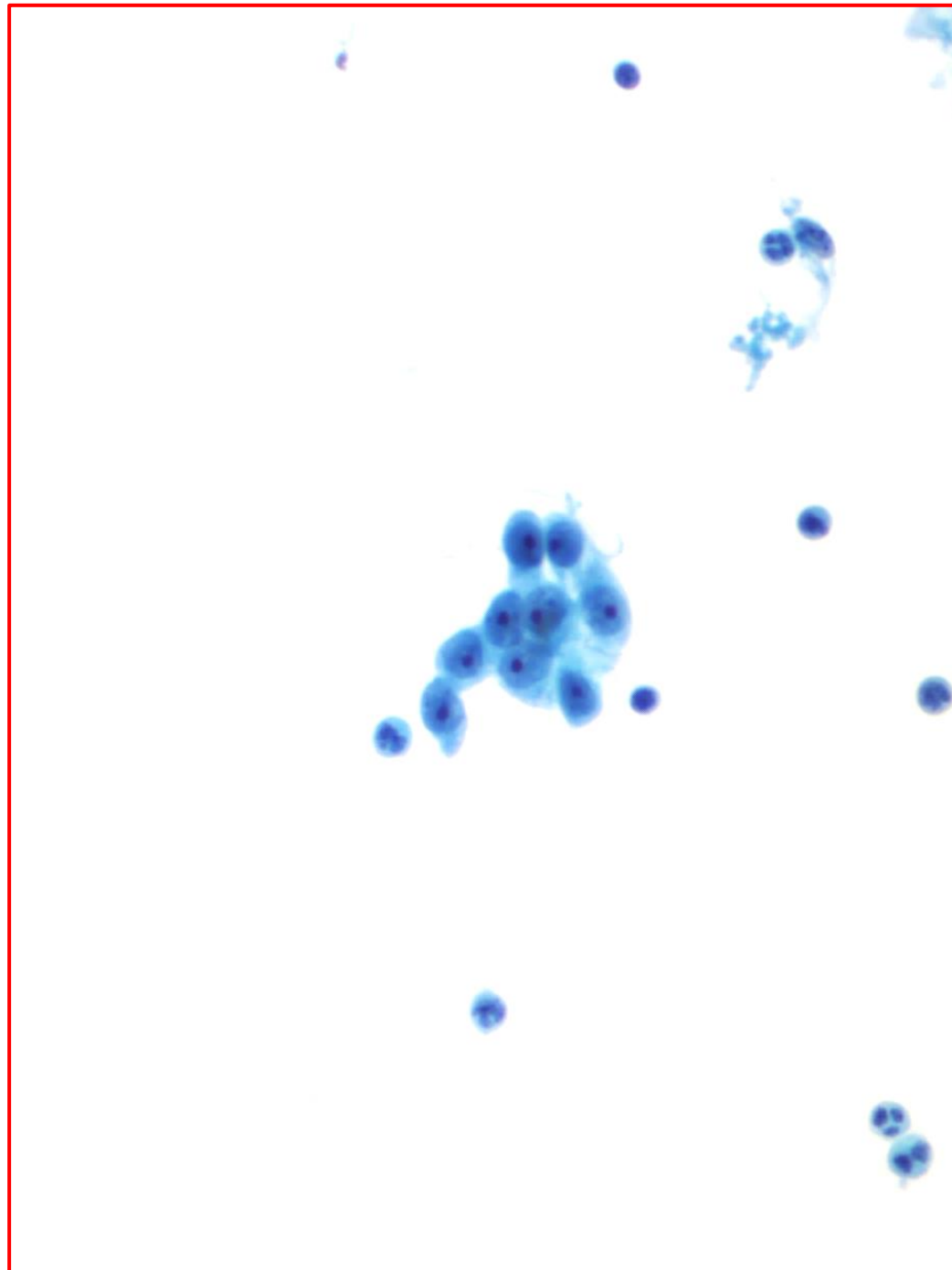
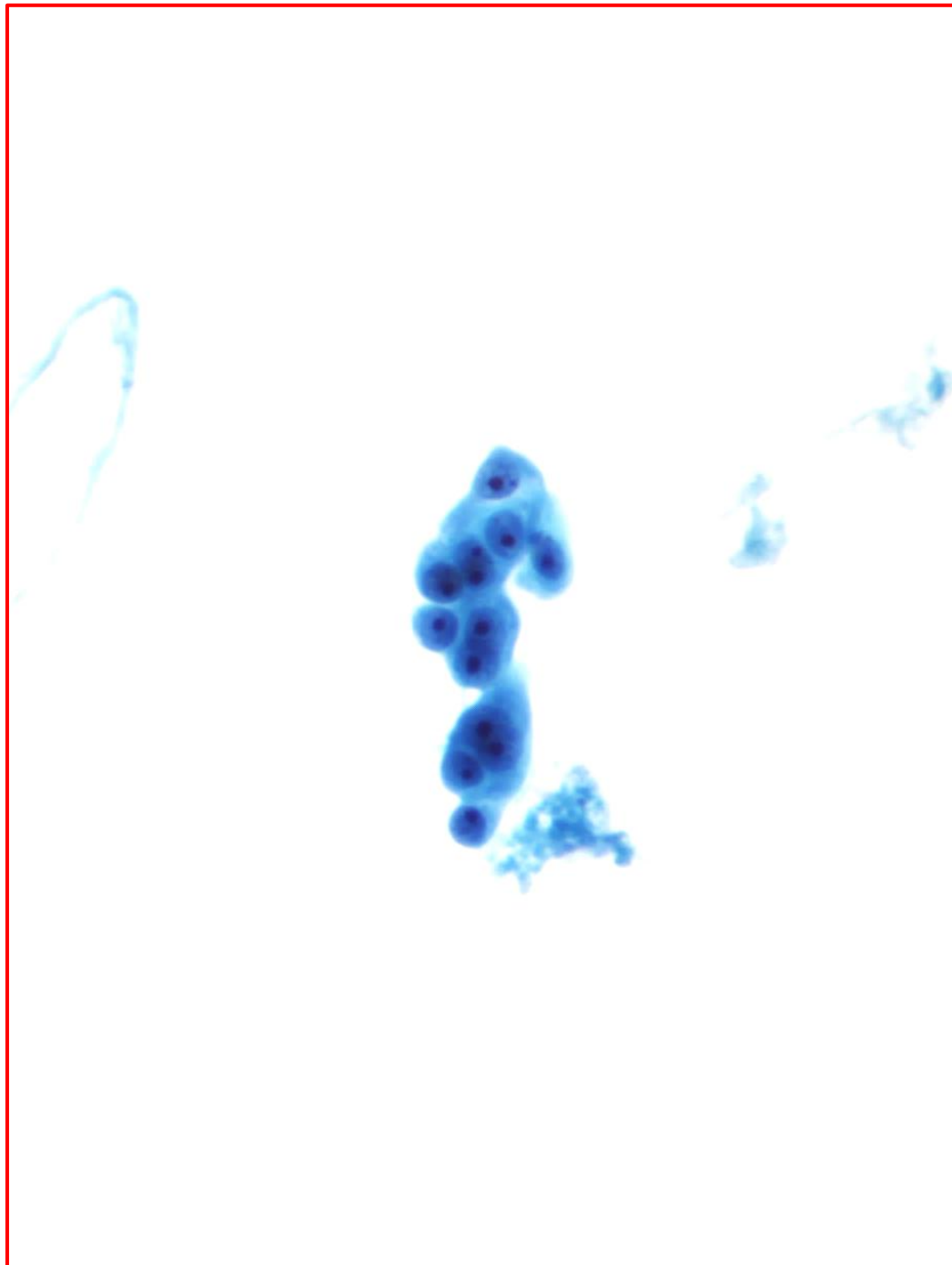


Case #5

- 74/F, former smoker, h/o asthma
- A 1.7-cm mild PET-avid semi-solid nodule in the left upper lobe, concerning for malignancy



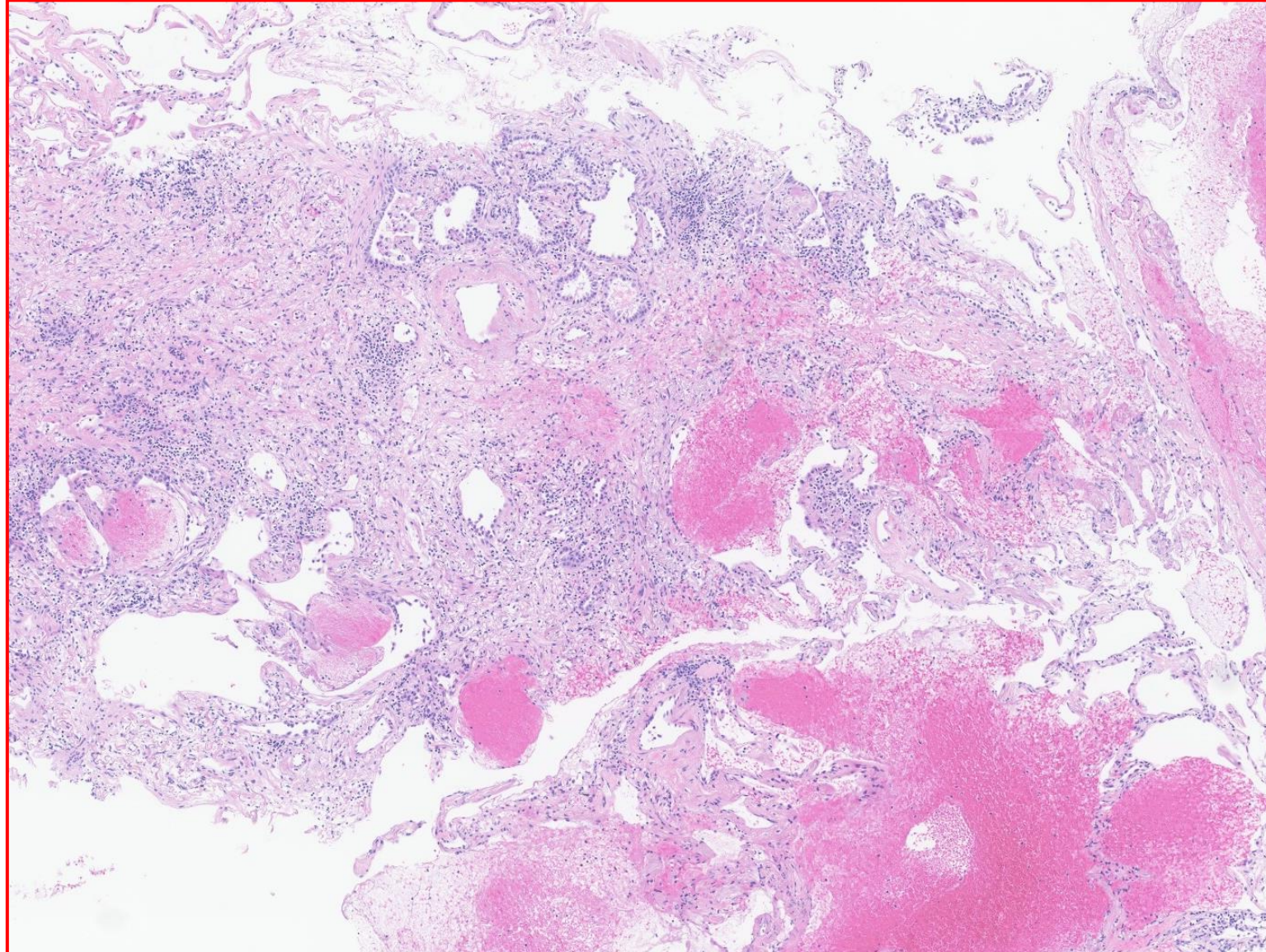


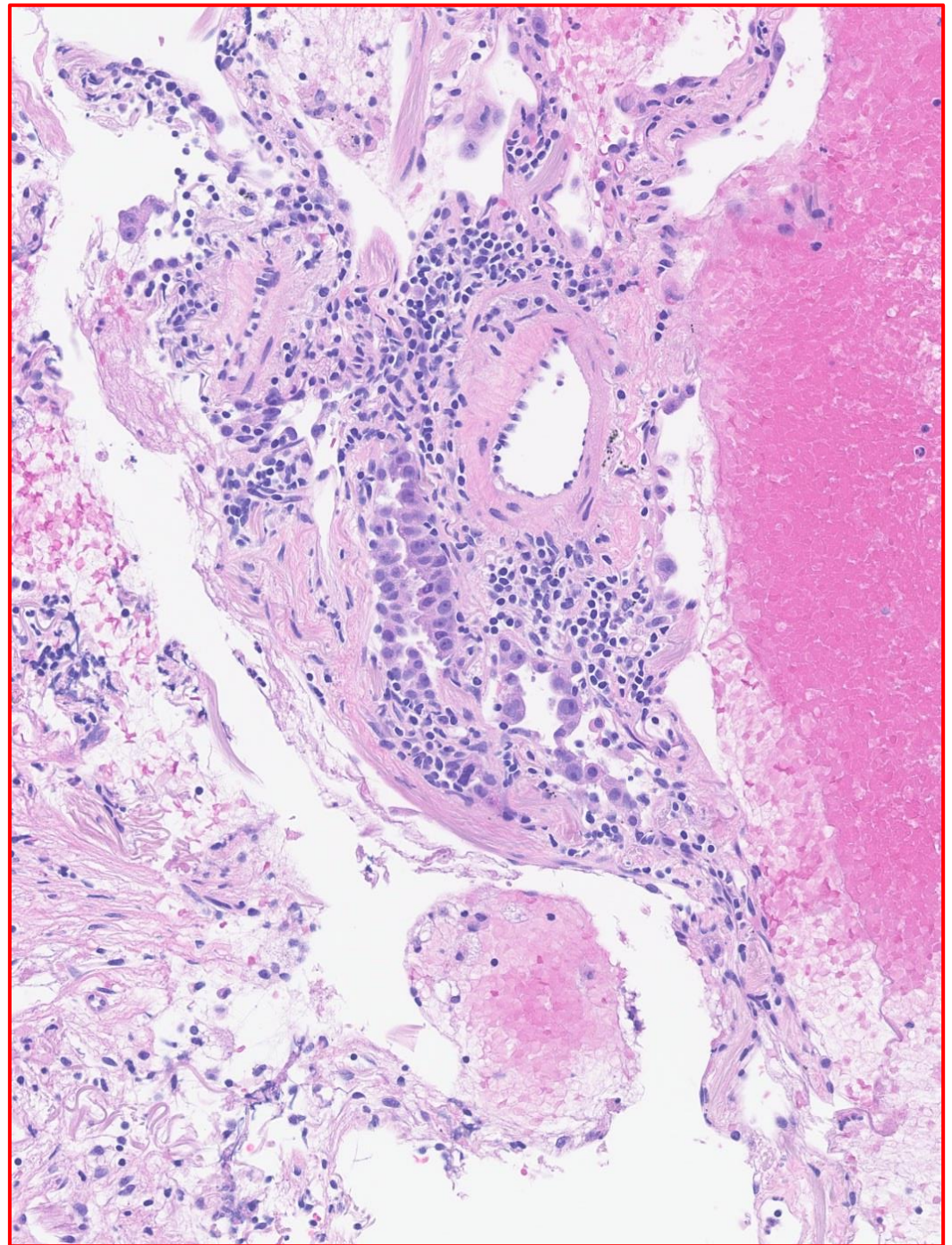
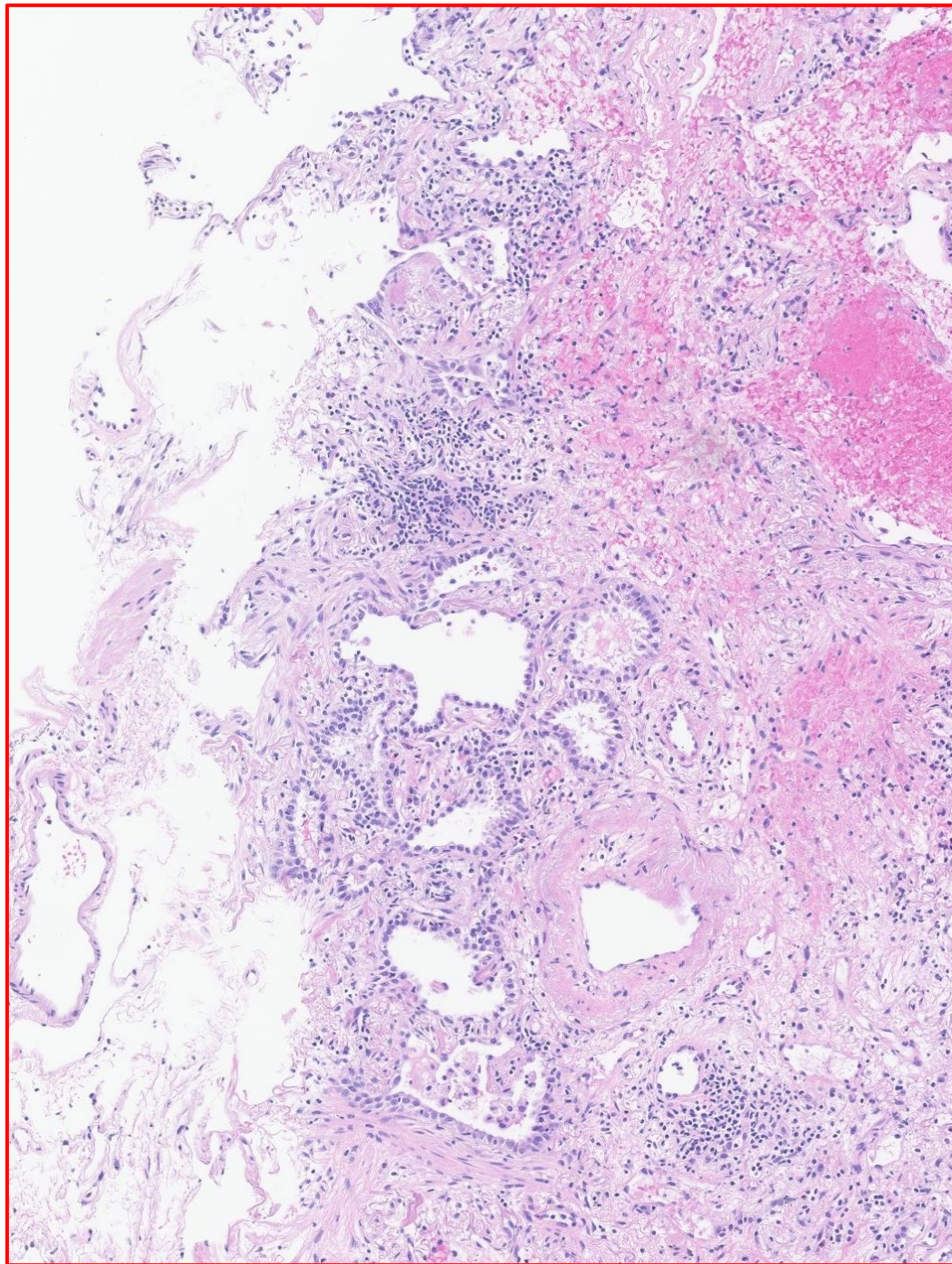


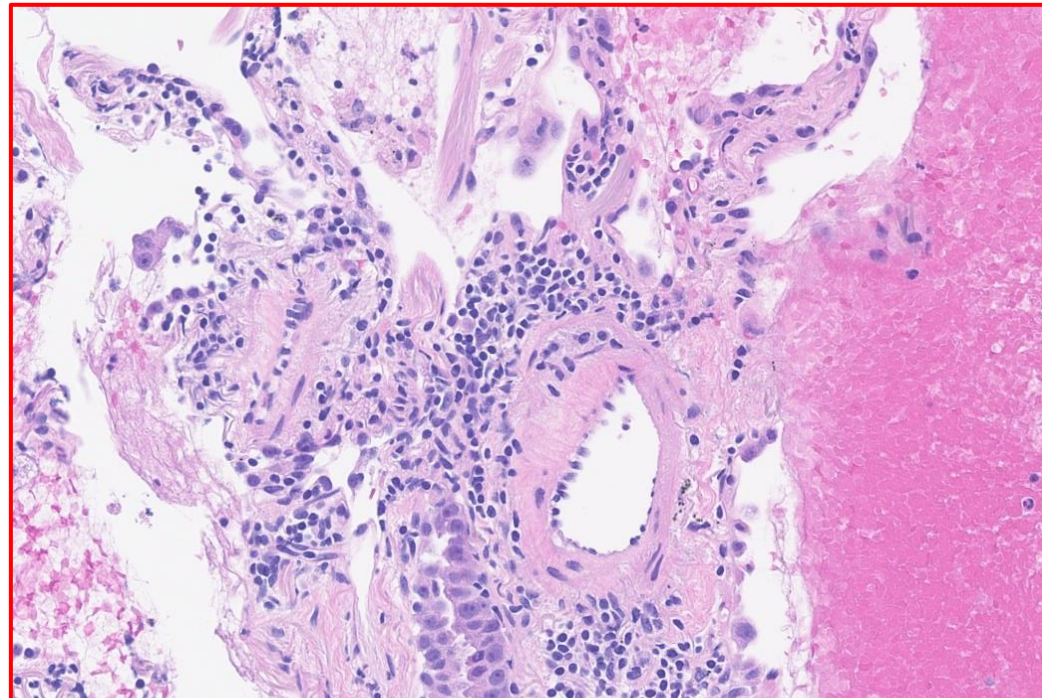
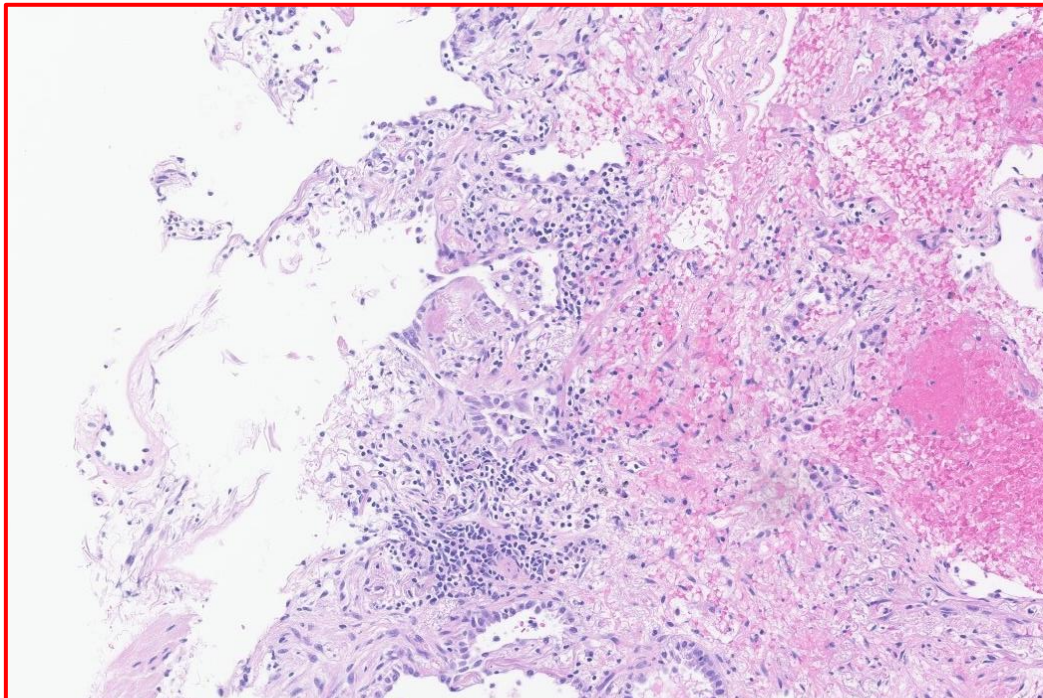
Diagnostic Considerations

- Benign
- Atypical
- Suspicious
- Malignant

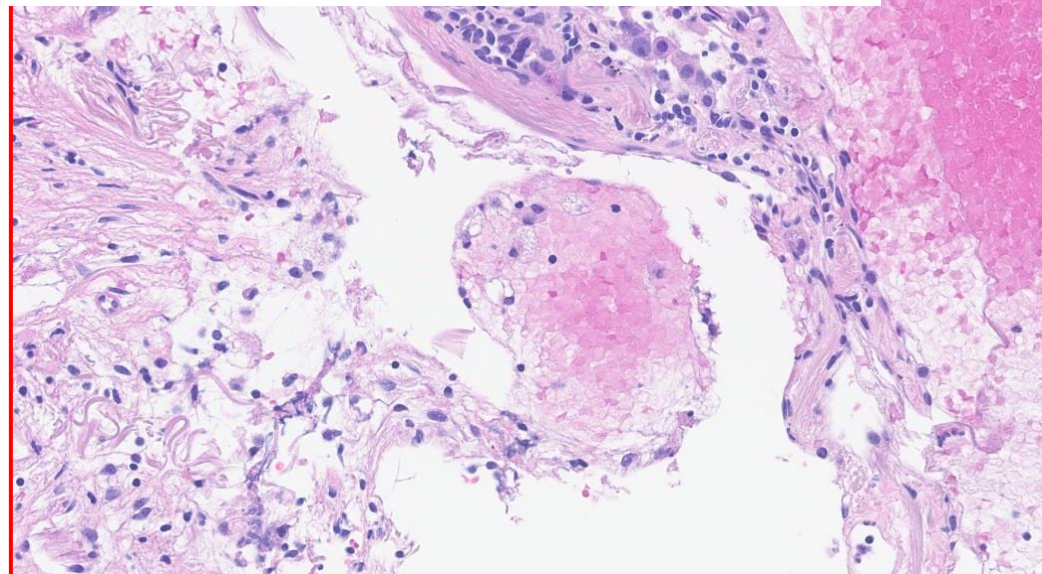
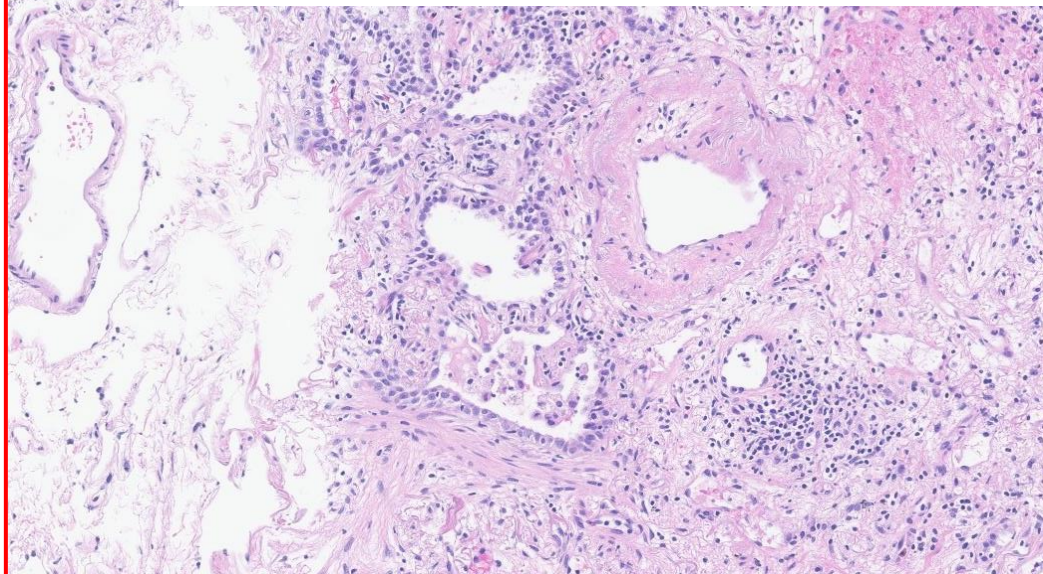
Concurrent Biopsy







Pulmonary Apical Cap with Reactive Pneumocytes



Follow-up

- The left upper lobe nodule has decreased in size to 1.2 cm (initially 1.7 cm) in 4 months.



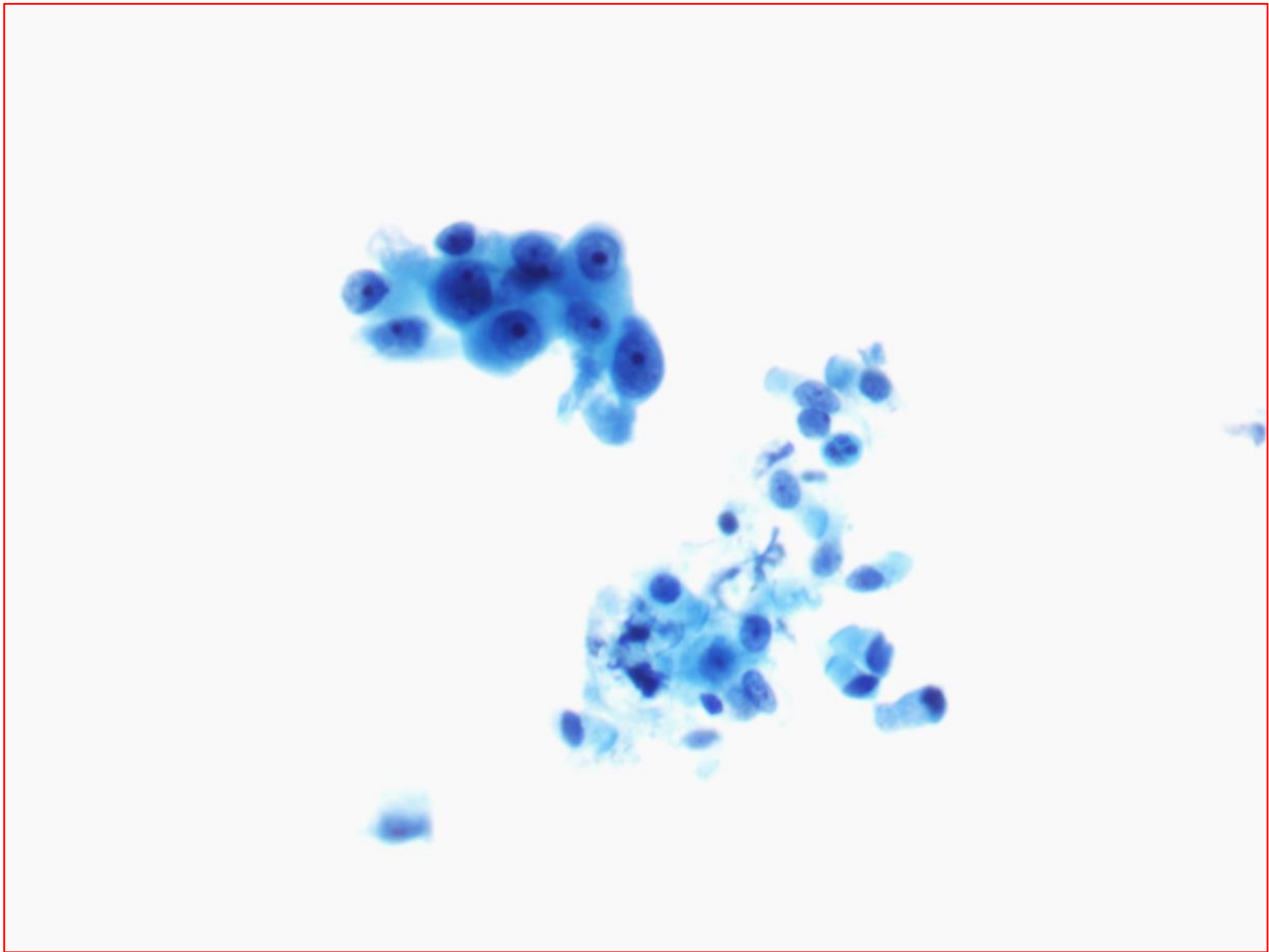
Learning Points

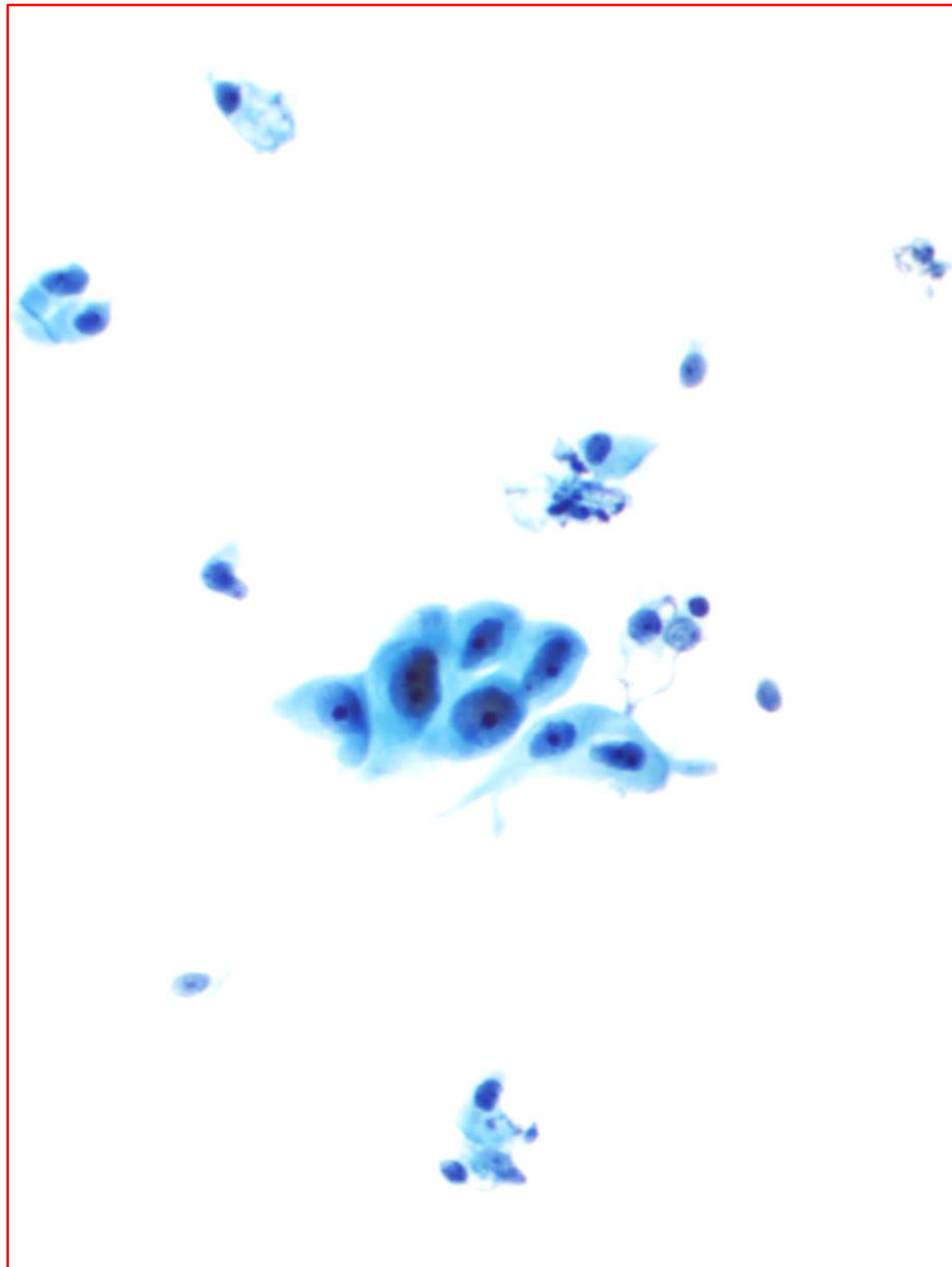
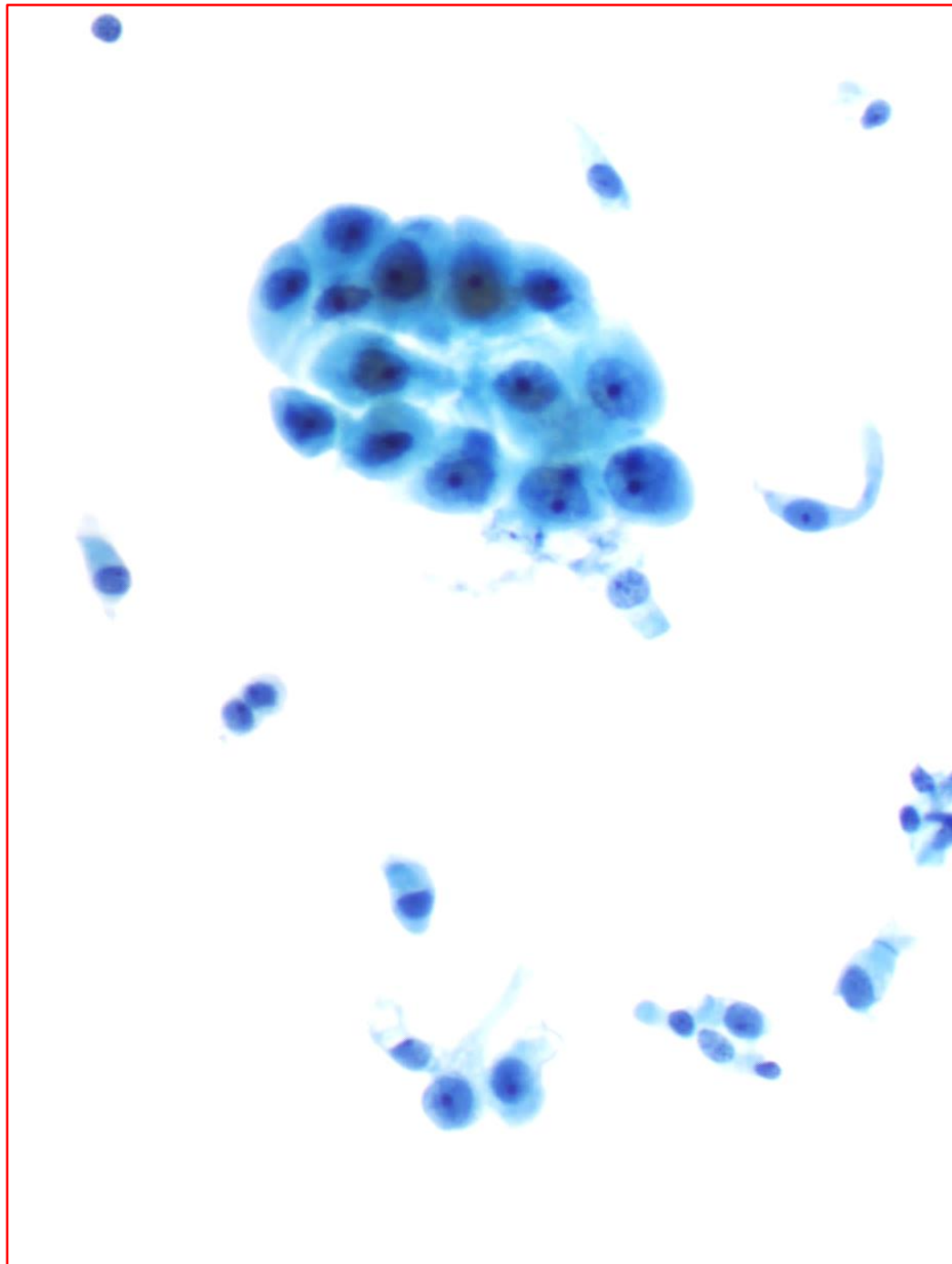
- It should be cautious to render a malignant diagnosis for the lung nodule close to the apex.
- The pneumocytes in the pulmonary apical cap (PAC) can show significant cytological atypia.

Case #6

- 76/M, h/o COPD, NSCLC, prostate cancer, s/p chemotherapy
- An irregular semisolid nodule in the right upper nodule



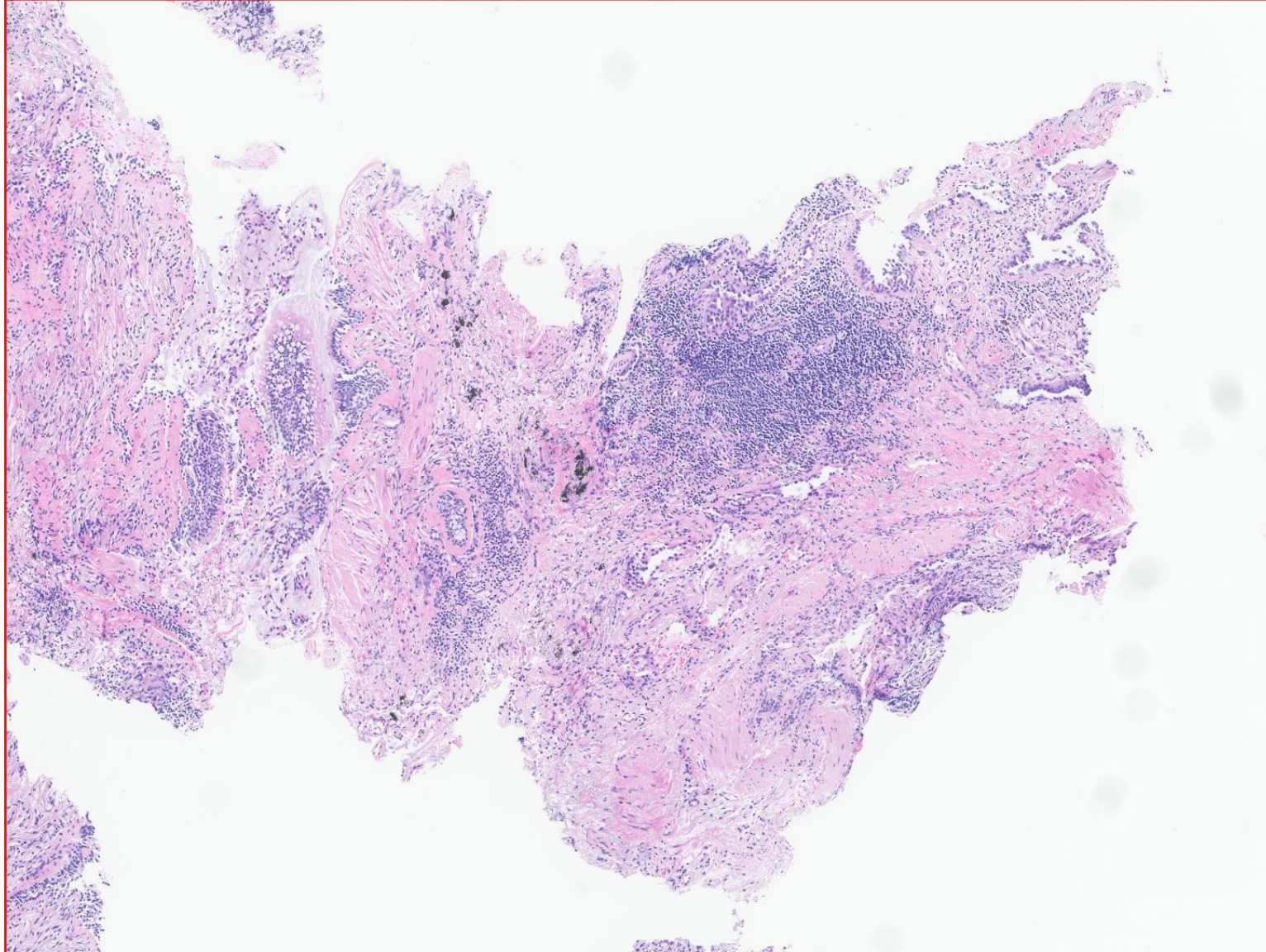


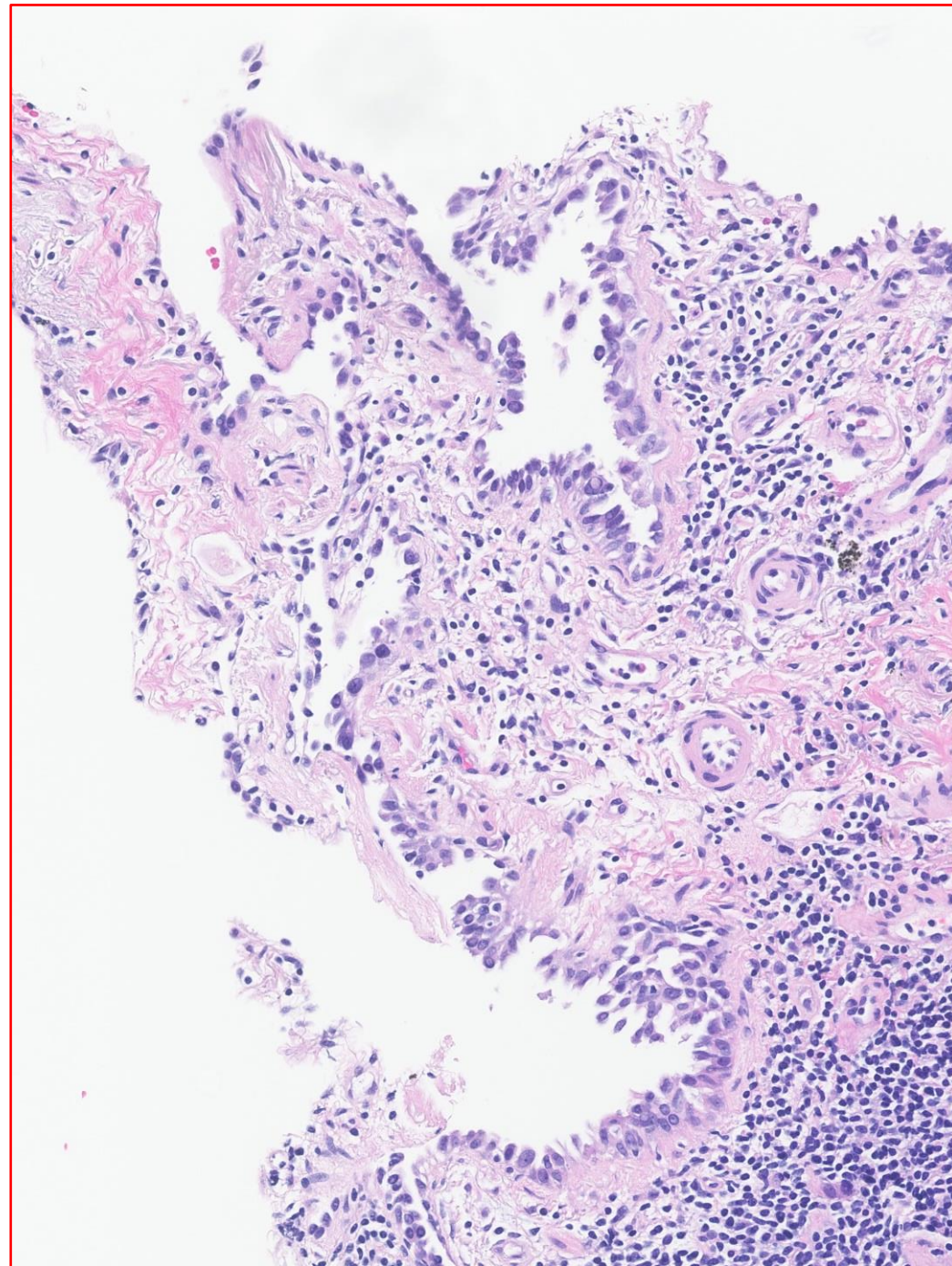
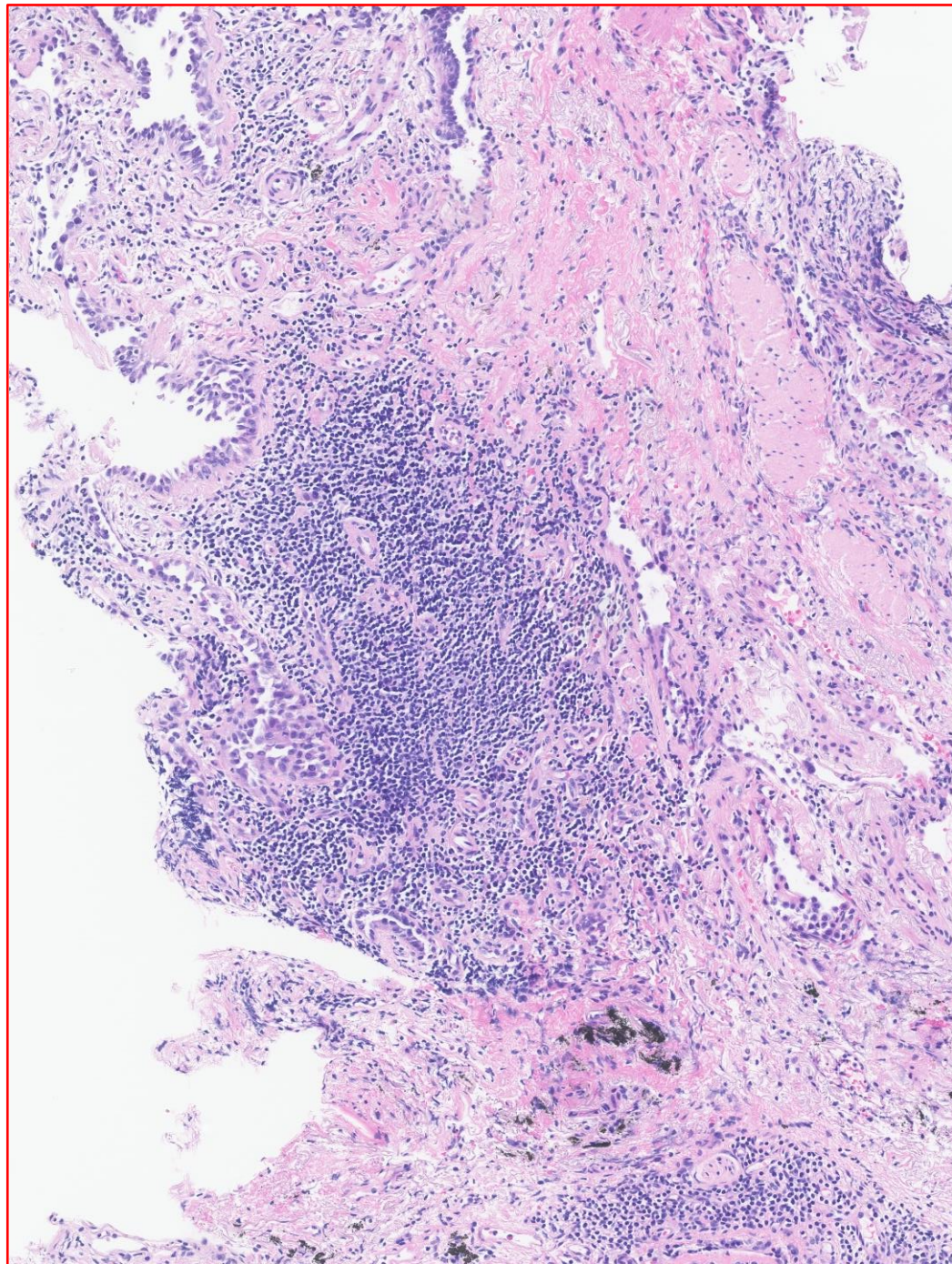


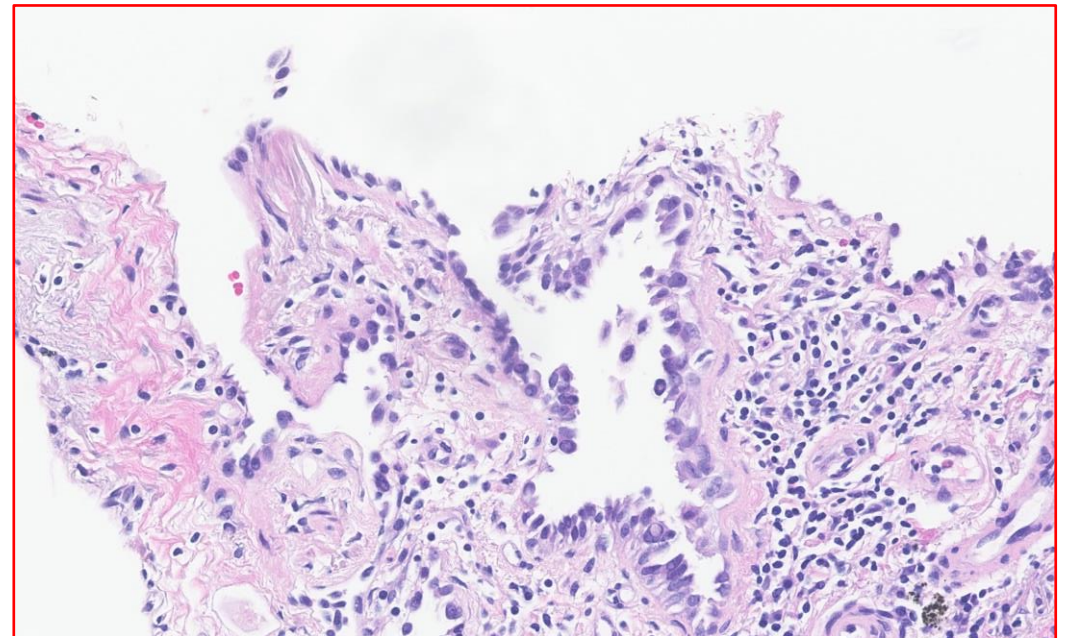
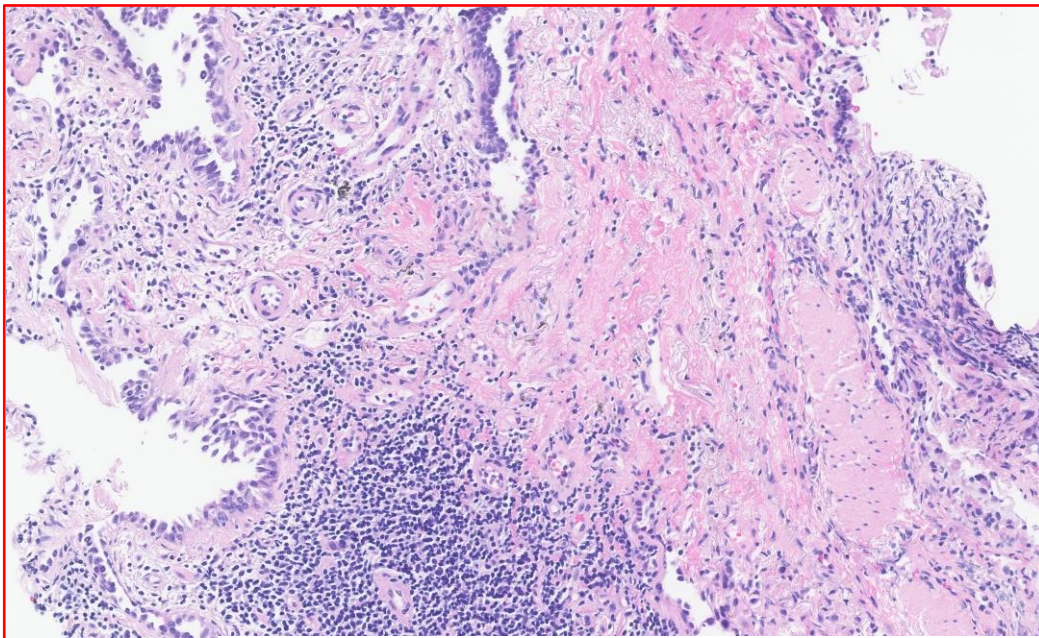
Diagnostic Considerations

- Benign
- Atypical
- Suspicious
- Malignant

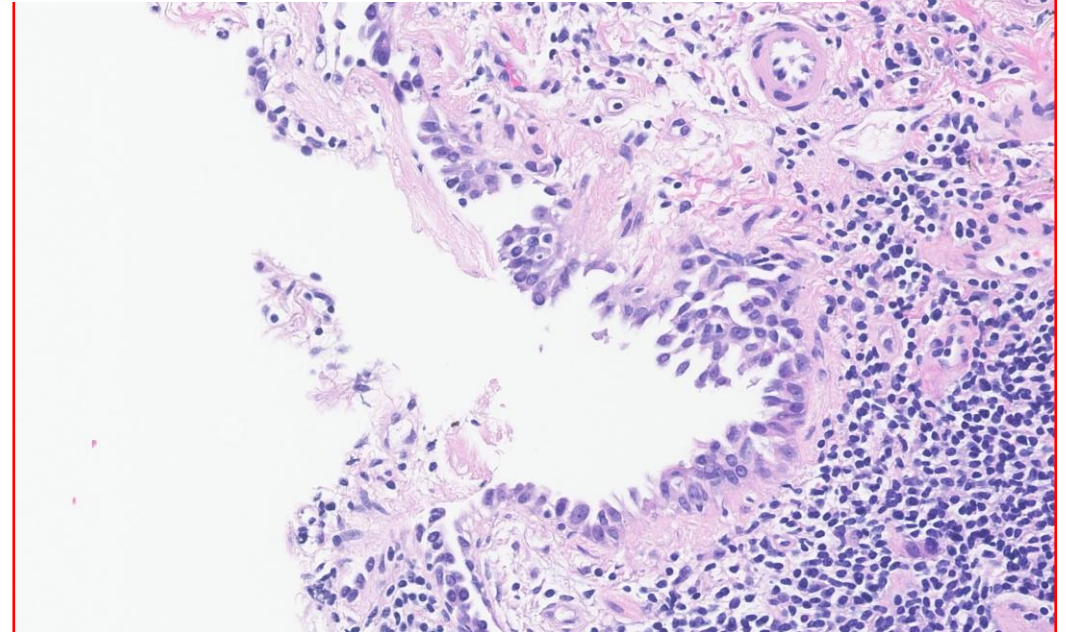
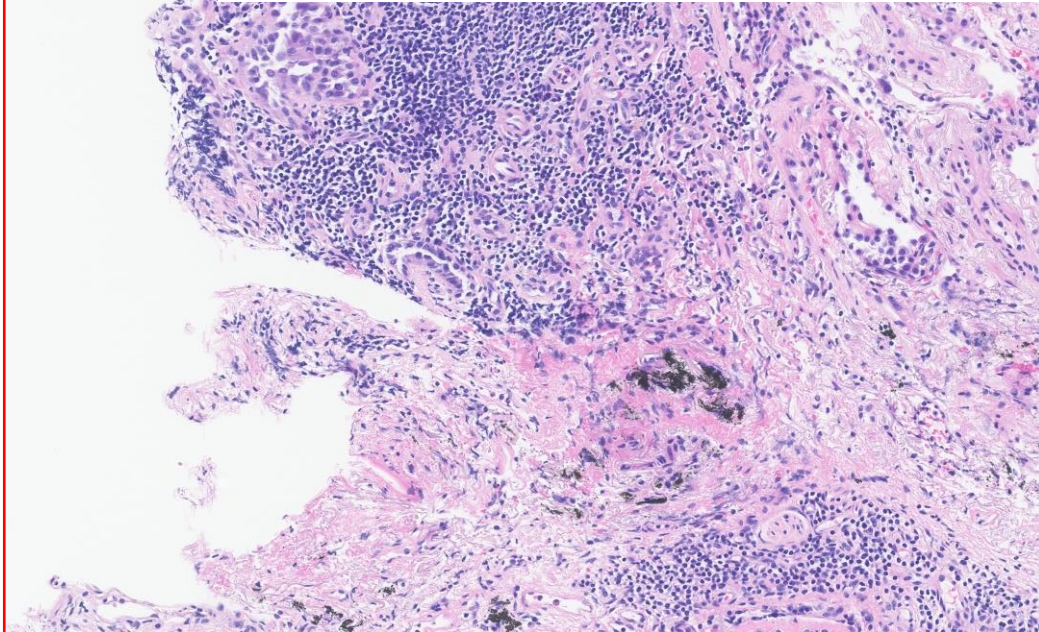
Concurrent Biopsy







Scar with Atypical Pneumocytes, Favor Reactive

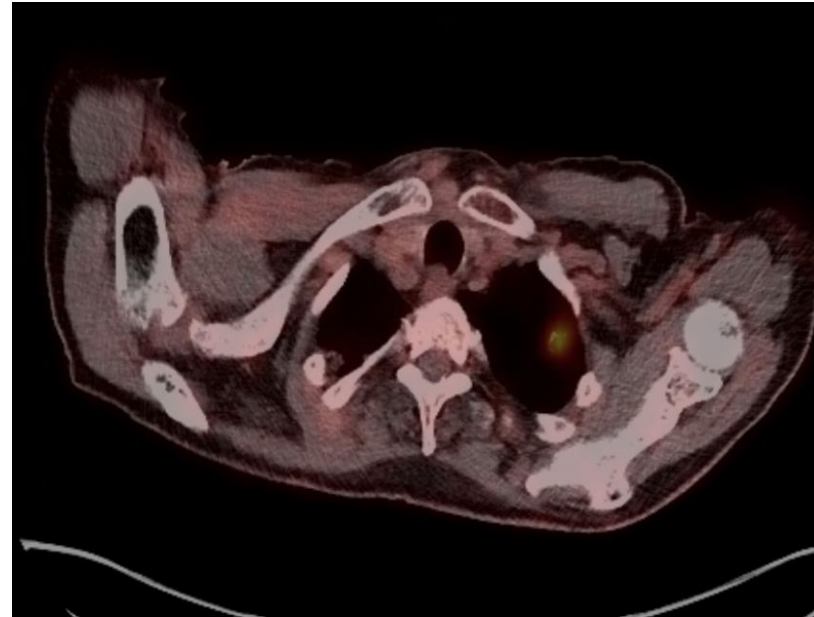
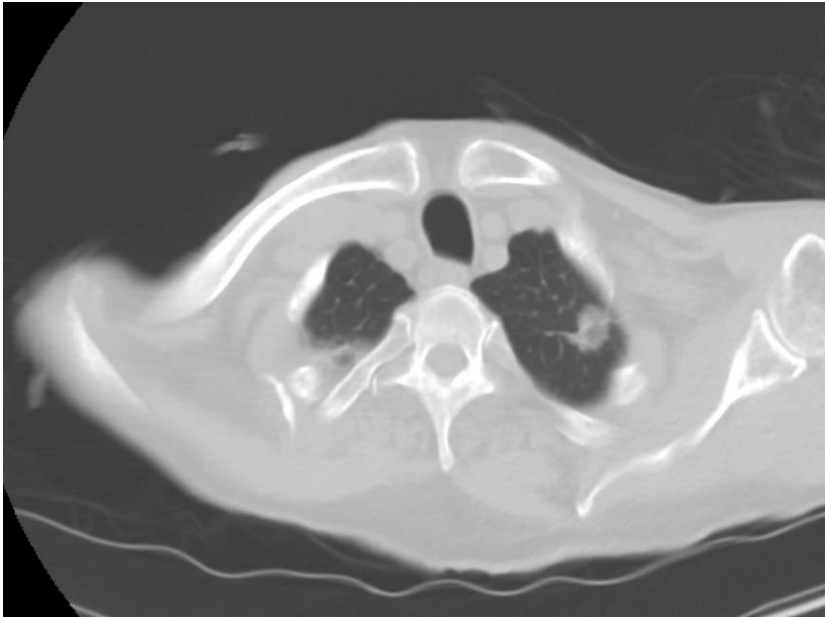


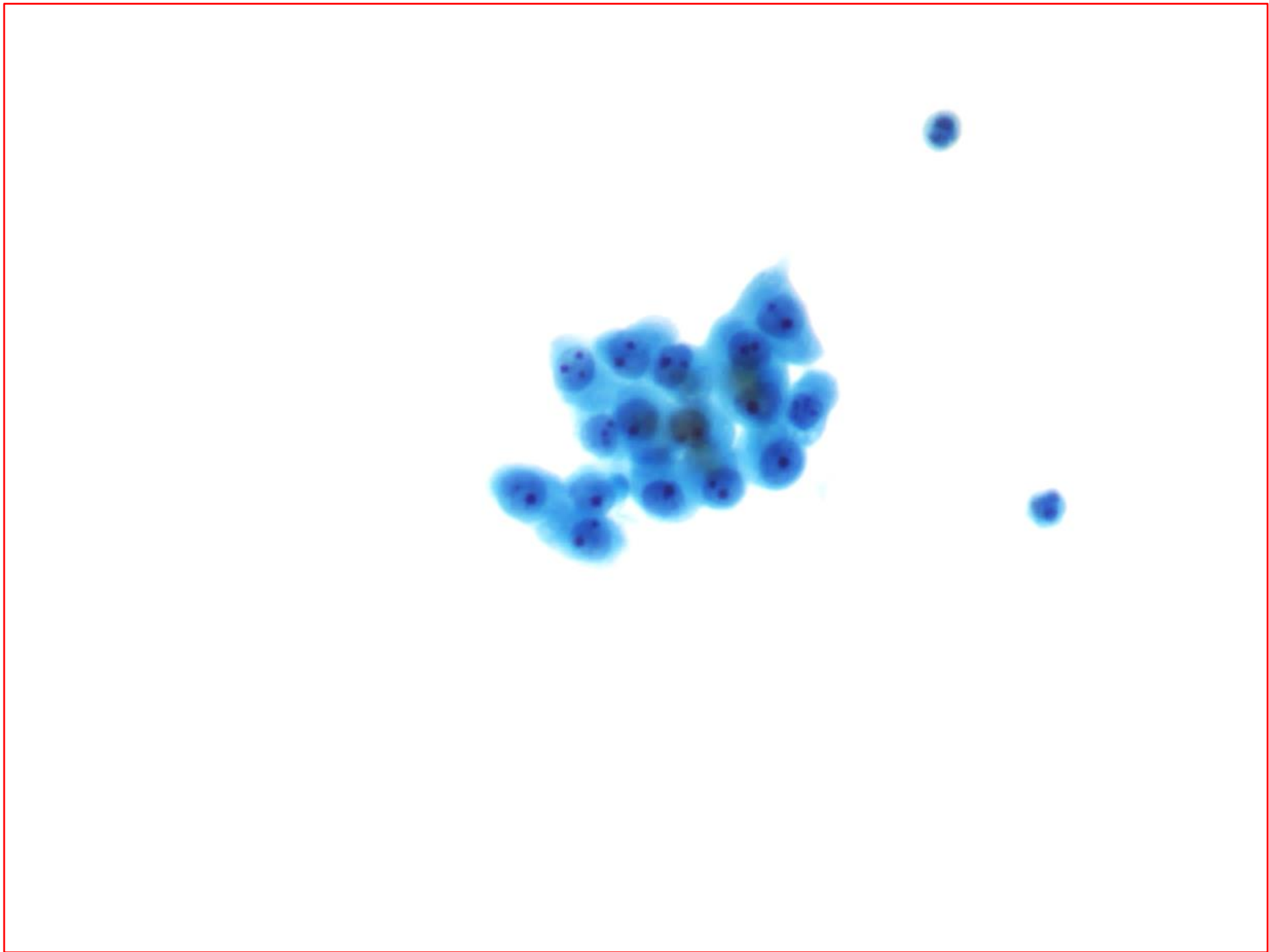
Learning Points

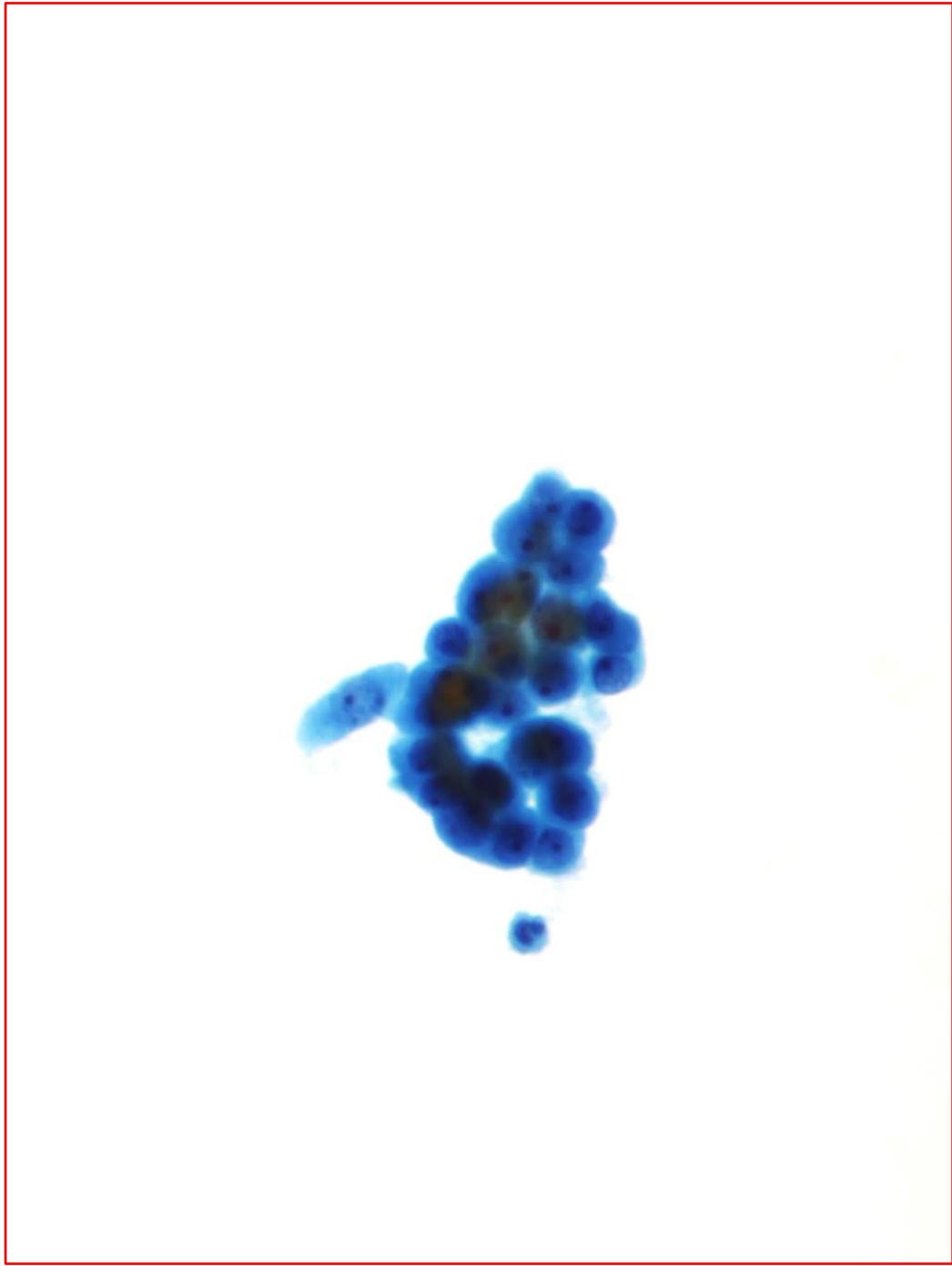
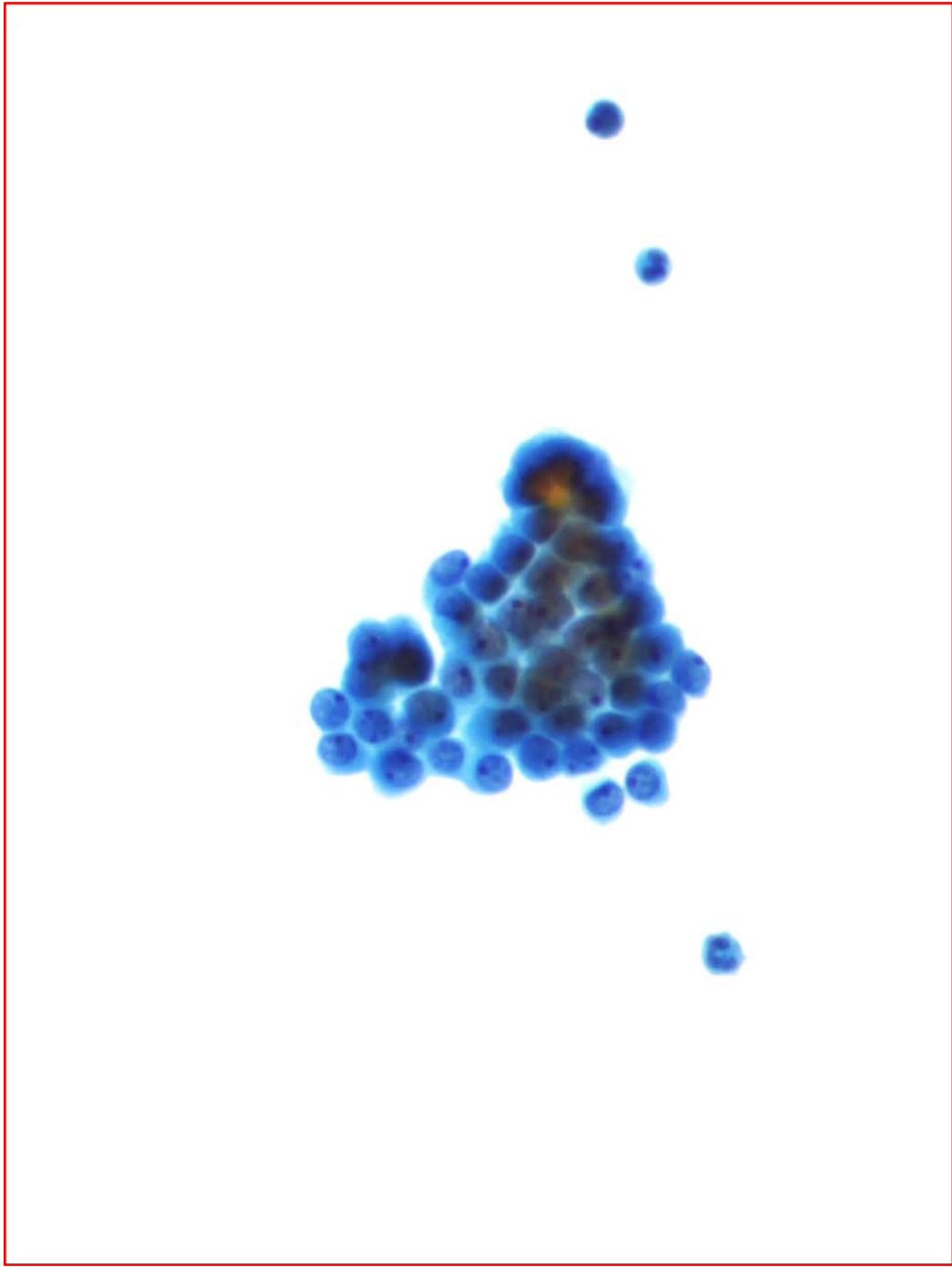
- It should be cautious to render a malignant diagnosis for the lung nodule with prior chemo/radiation therapies.
- Reactive pneumocytes can show significant cytological atypia in the setting of s/p therapies, mimicking malignancy.

Case #7

- 89/M, former smoker
- A partial solid 2.5-cm moderately PET-avid nodule in the left upper lobe



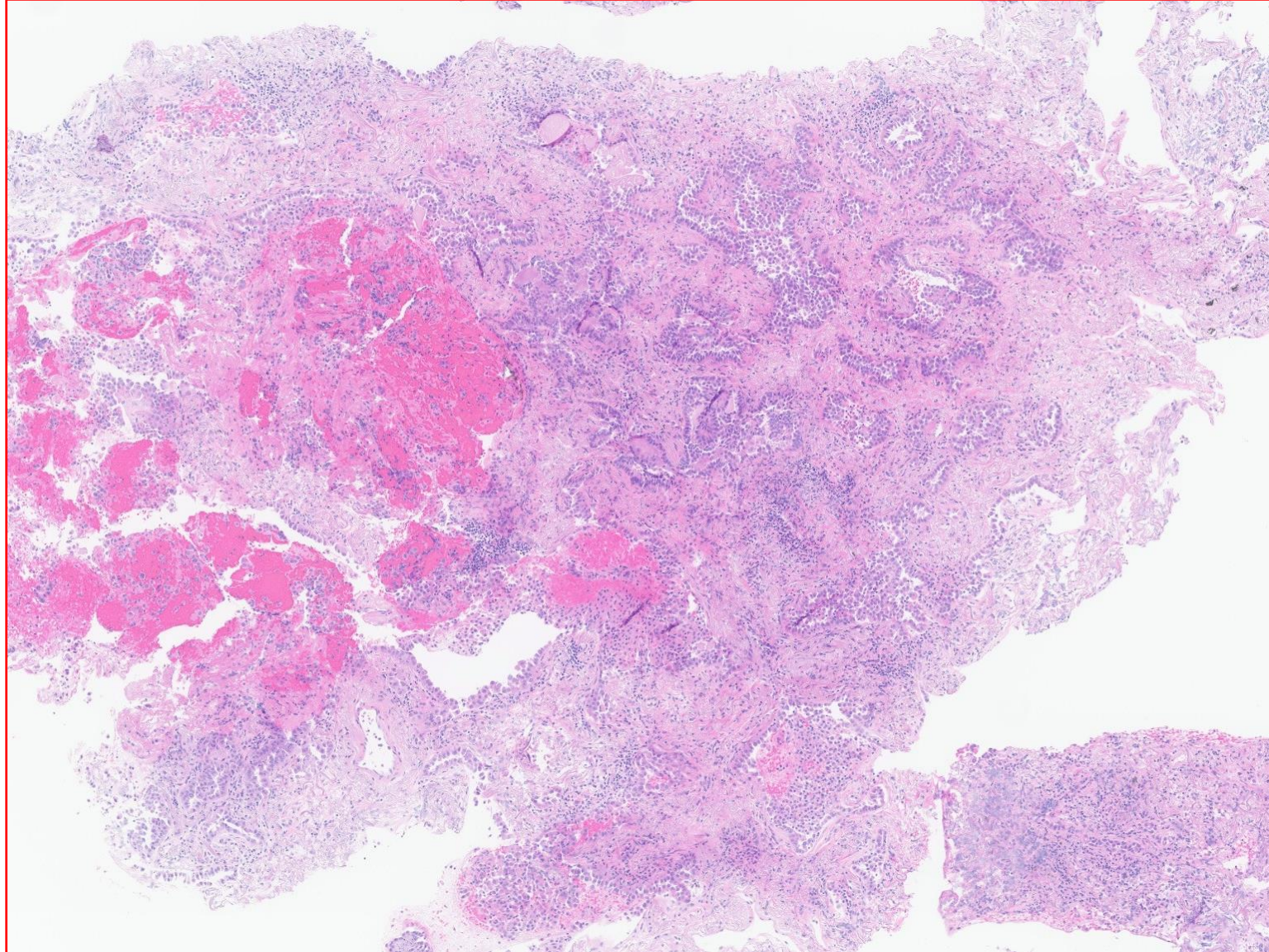


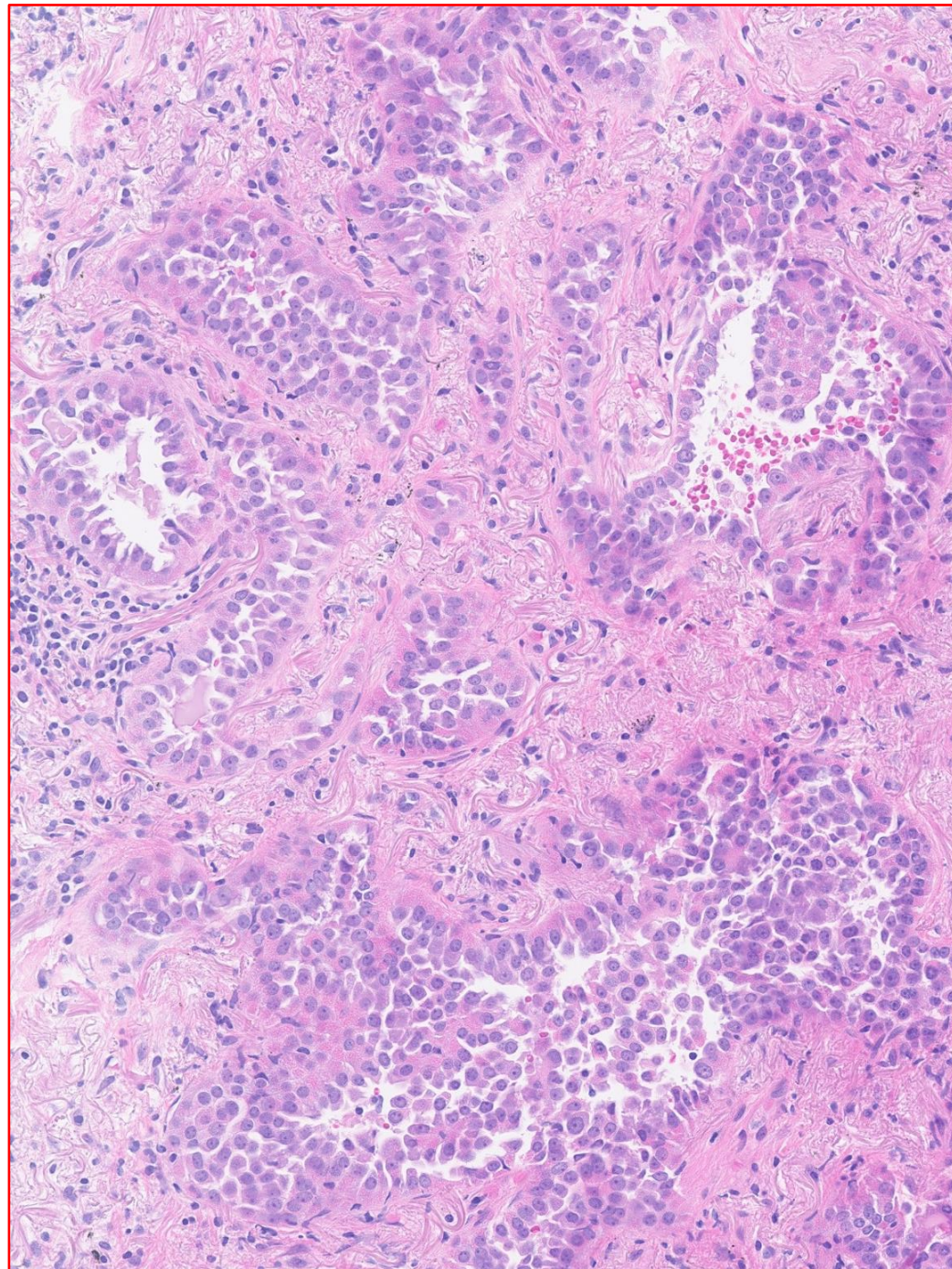
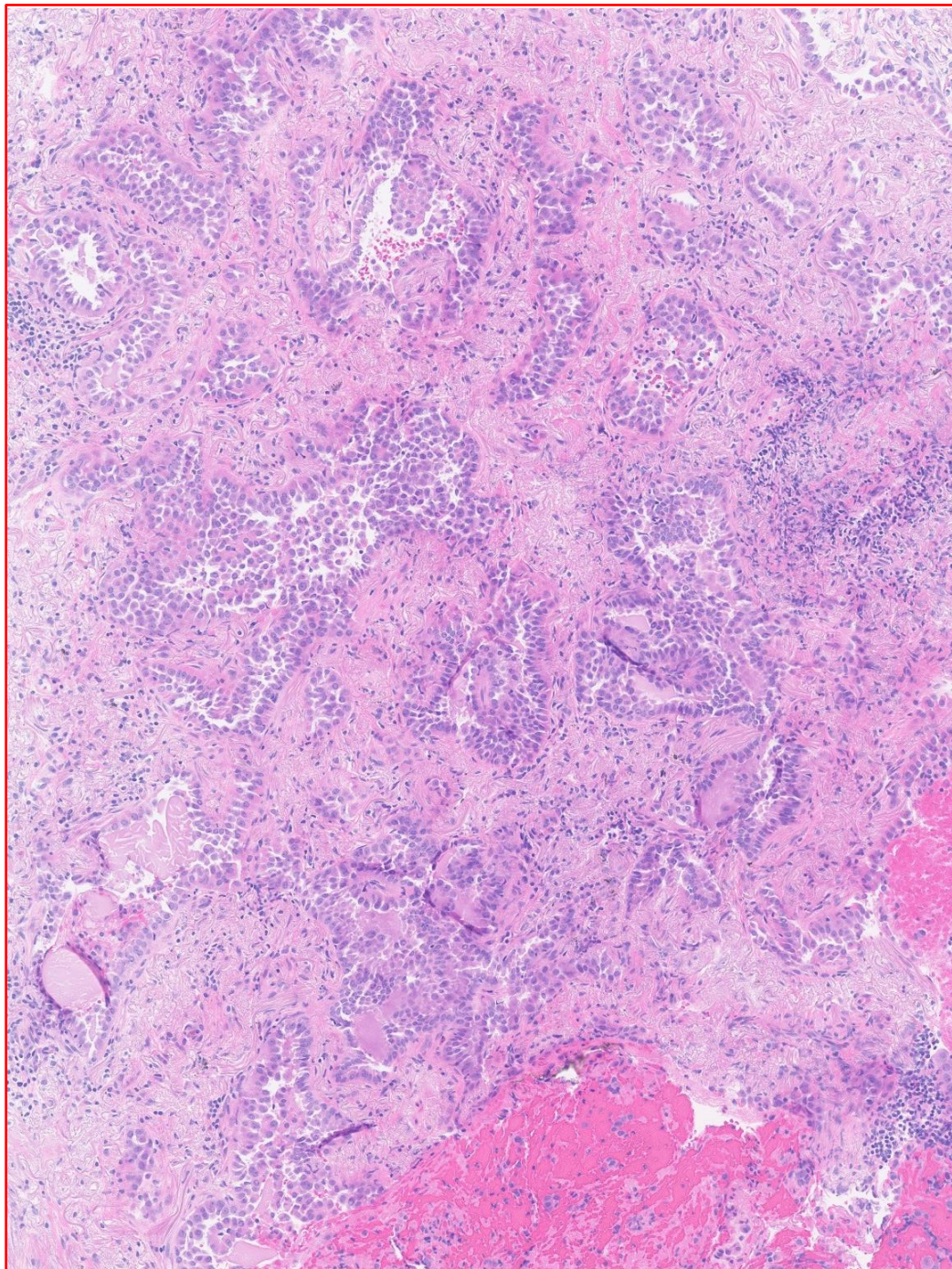


Diagnostic Considerations

- Benign
- Atypical
- Suspicious
- Malignant

Concurrent Biopsy





The image consists of four panels of histological sections, each showing a different field of view of the same tissue. The tissue is stained with hematoxylin and eosin (H&E), resulting in pink cytoplasm and extracellular matrix, and purple nuclei. The panels show a dense population of cells arranged in irregular, glandular or acinar structures. These acini are lined by a single layer of cuboidal to columnar cells with hyperchromatic, enlarged nuclei. The surrounding stroma is fibrous and contains scattered inflammatory cells. In the bottom-left panel, there is a prominent area of hemorrhage, appearing as a bright red, amorphous mass. The overall architecture is characteristic of an adenocarcinoma with an acinar growth pattern.

Adenocarcinoma, Acinar Predominant

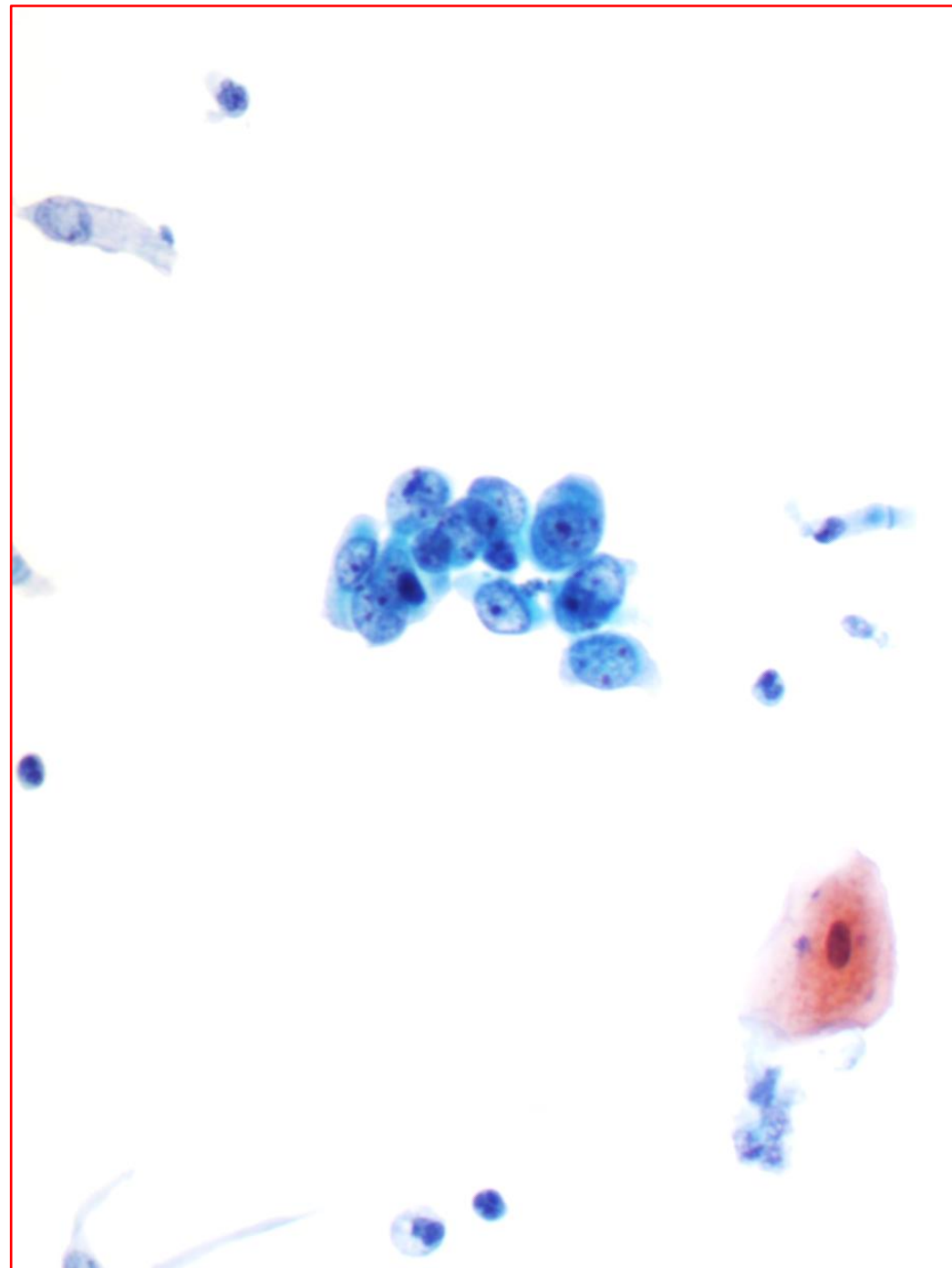
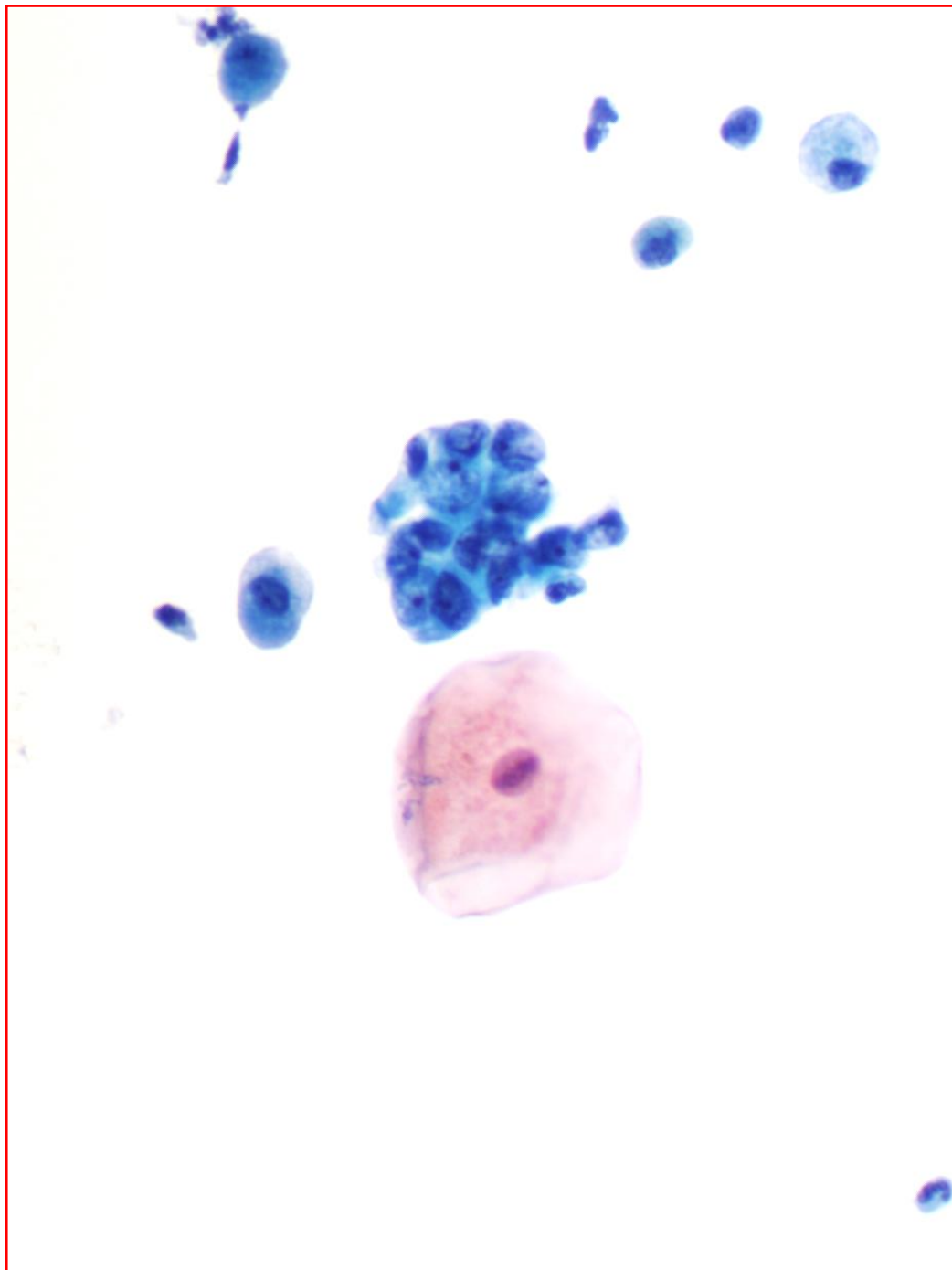
Learning Points

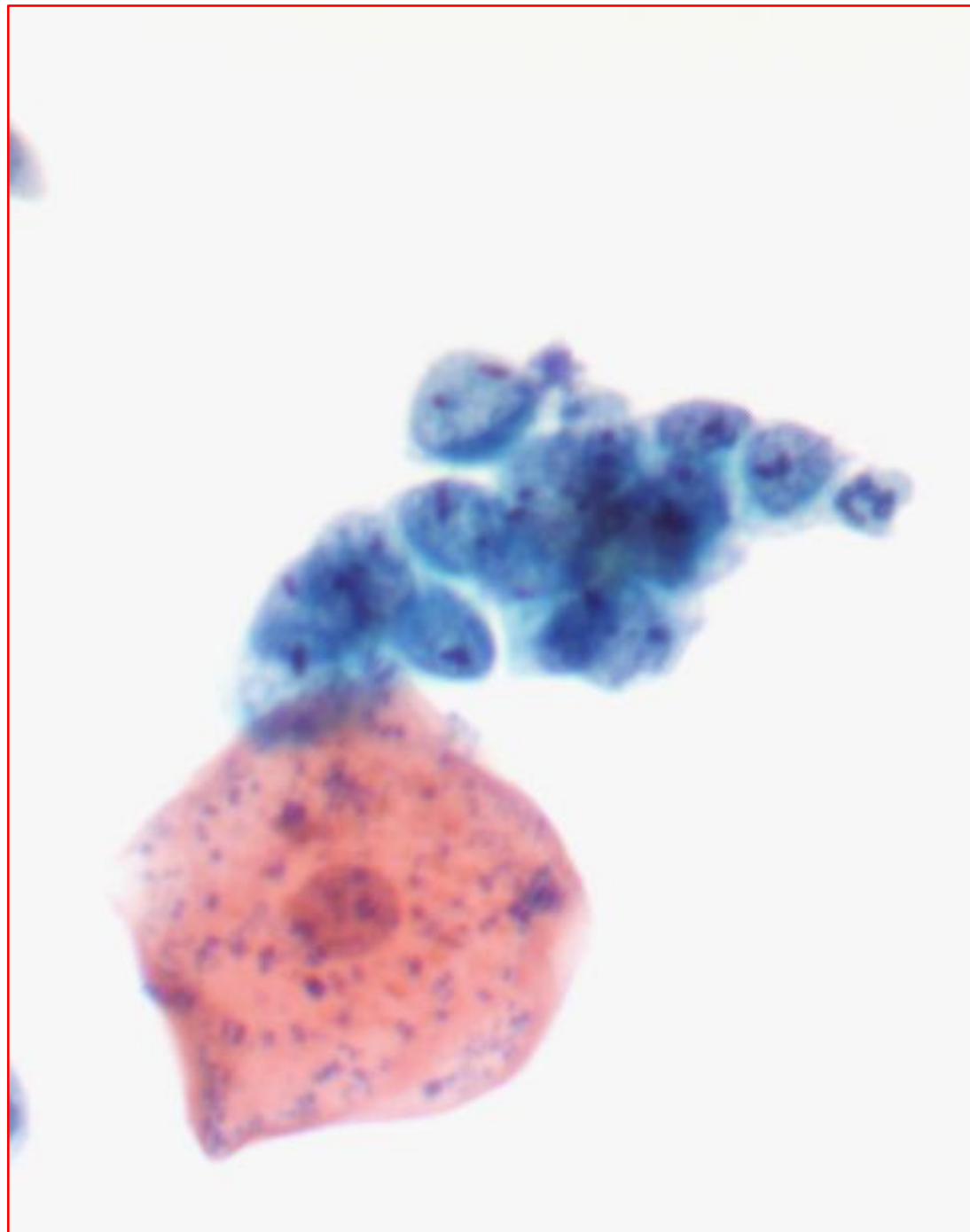
- Lung adenocarcinoma may have cytomorphologic features overlapping with reactive changes/benign mimics.
- Correlation with concurrent biopsy specimens may help avoid pitfalls.

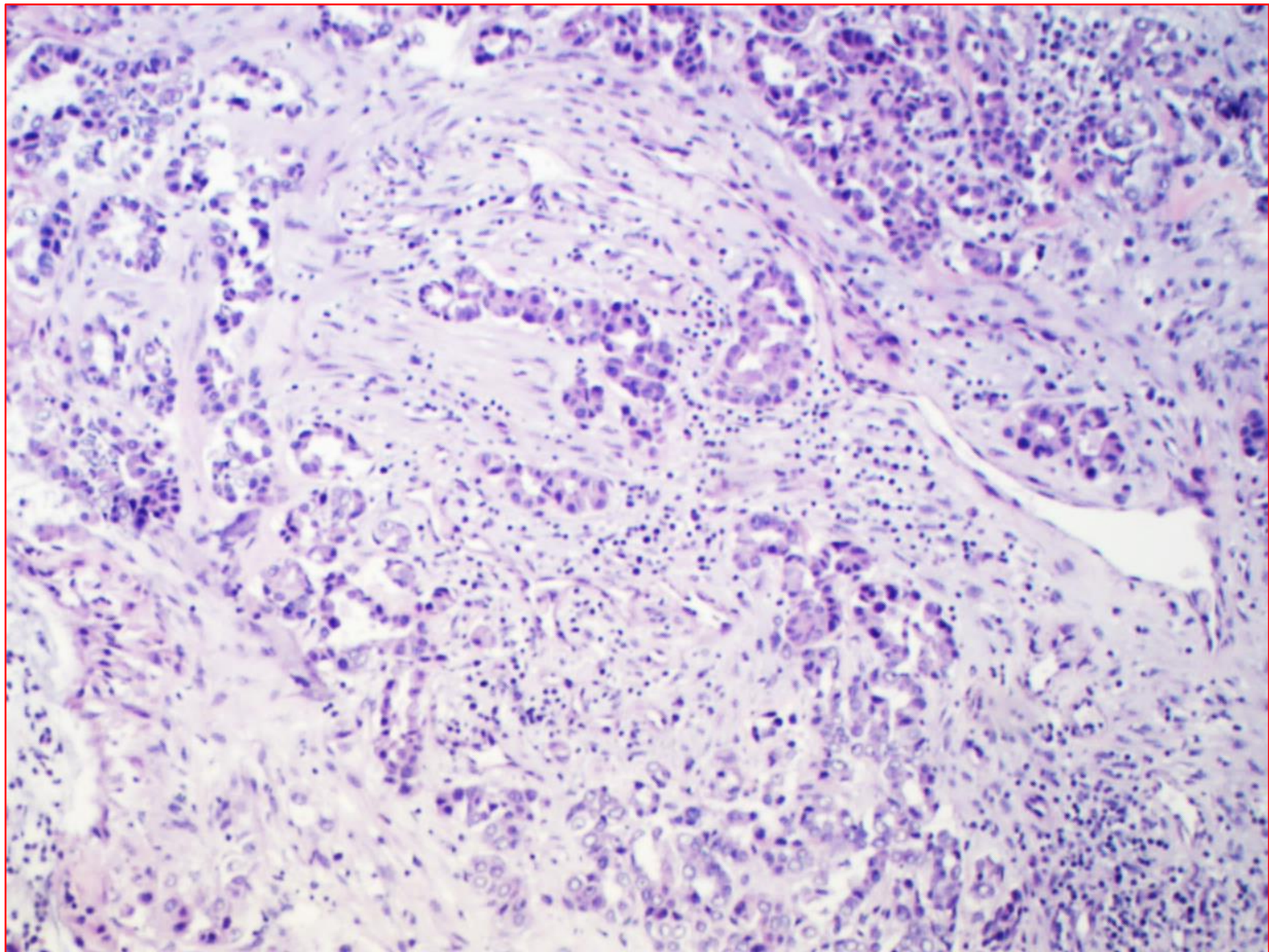
Case #8

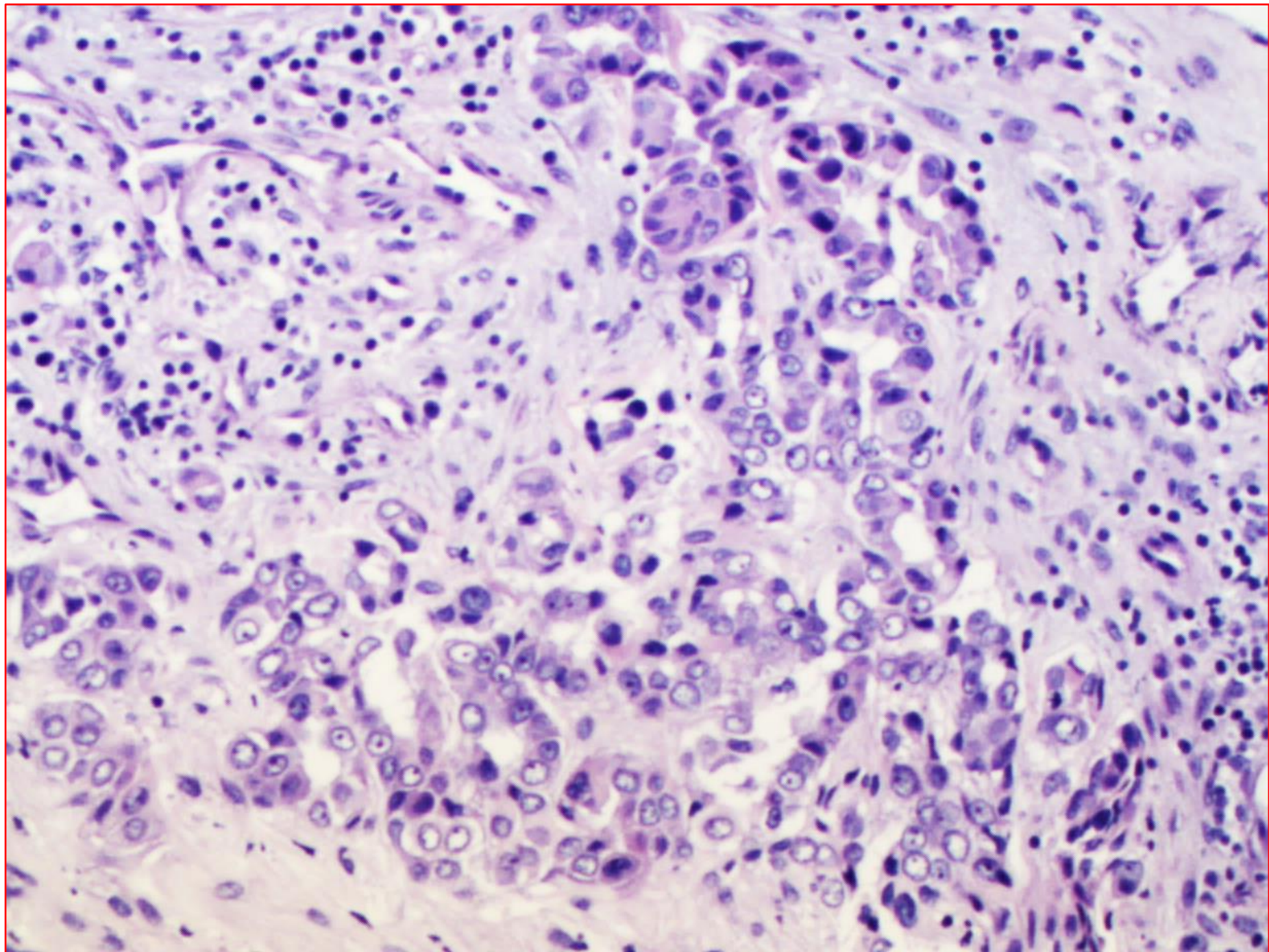
- 78/M, h/o mesothelioma, s/p pleurectomy and radiation therapy
- Persistent mucus plug of right middle lobe and right lung consolidation
- Endobronchial polypoid lesion, bronchial wash







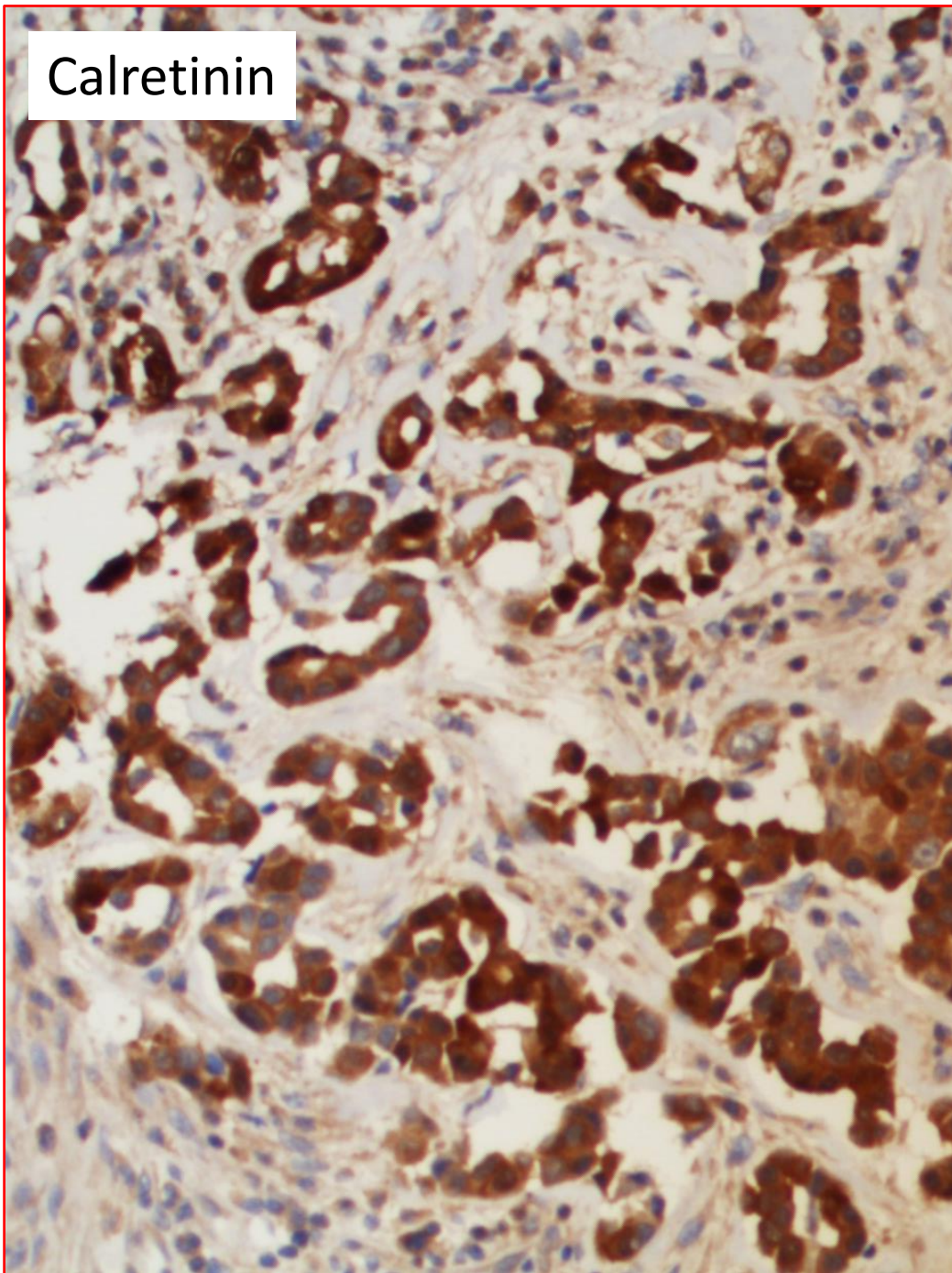




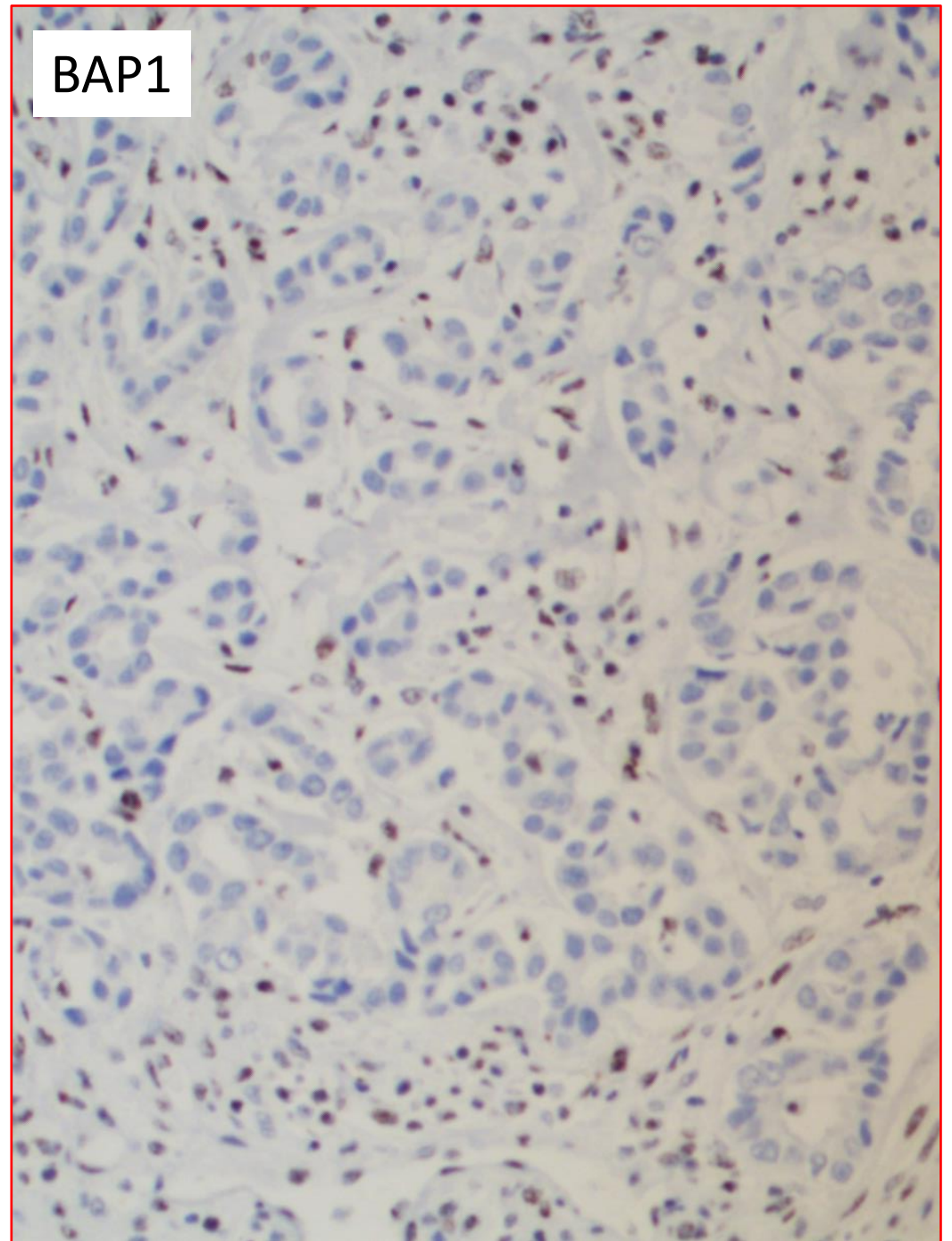
Diagnosis?

- Non-small cell carcinoma
- Adenocarcinoma
- Mesothelioma
- Others

Calretinin



BAP1



The image is a composite of four microscopic views of tissue. The left column shows two panels of a tissue section with a prominent, dark blue, irregularly shaped mass, likely representing a tumor. The right column shows two panels of a tissue section with a dense population of small, round, blue-stained cells, characteristic of a high-grade malignancy. A central white box with black text reads "Metastatic Mesothelioma". A small white box with black text in the bottom right corner reads "BAP1".

Metastatic Mesothelioma

BAP1

Learning Points

- Metastatic mesothelioma can be seen at an unusual location with an unusual presentation (like endobronchial lesion).
- Clinical history and ancillary immunocytochemistry help render an accurate diagnosis.



*Thank
you*



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