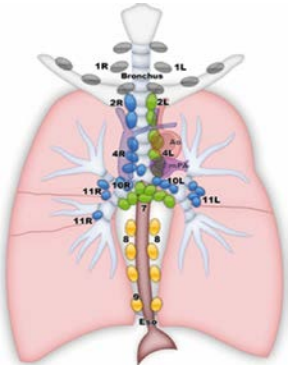
SELECTED DILEMMAS IN RESPIRATORY CYTOPATHOLOGY (2 CASES)

Dr. Mariamma Joseph
Professor of Pathology
Division Head – Cytopathology
Department of Pathology and Laboratory Medicine
LHSC and Western University



Objectives

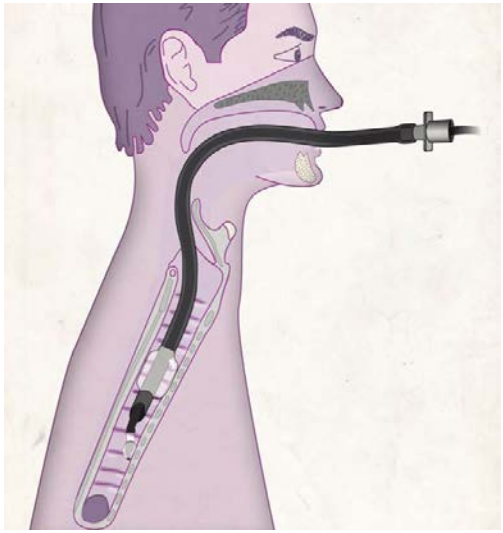
1) An Interesting EBUS FNA Lung Case
   - Unusual cytomorphology
   - How to optimize samples for molecular tests, LHSC experience
2) A Challenging Effusion Case
   - Patterns and pitfalls in effusion cytology

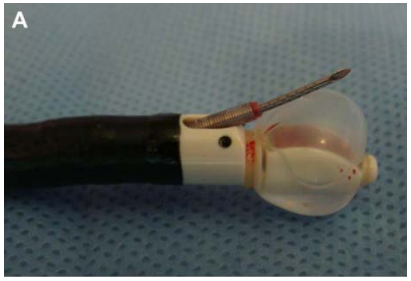
Case 1

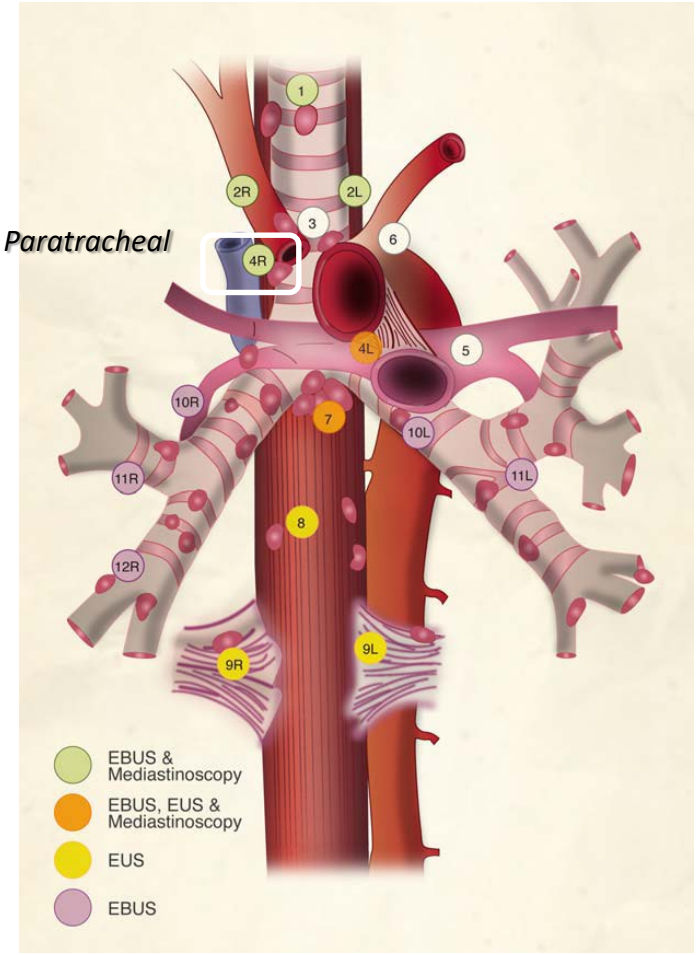
- 60 F, 40 pack year smoker
- Productive cough, un resolving pneumonia
- CT: RUL mass (9x6x5cm)
- Mediastinal adenopathy, adrenal & brain Met
- Stage 1V disease

Diagnostic Modality
EBUS FNA Biopsy, 4R lymph Node

Olymbus bronchoscope
US probe with transducer
Needle (22g)

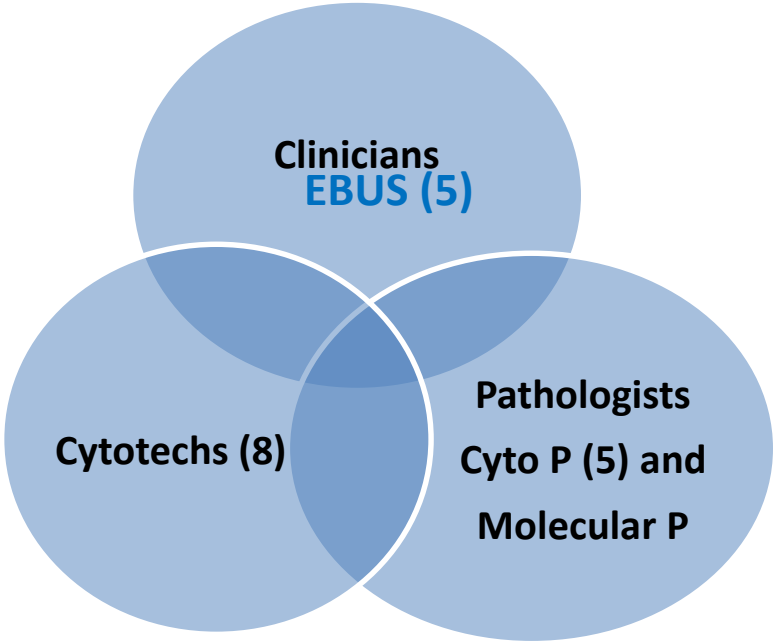




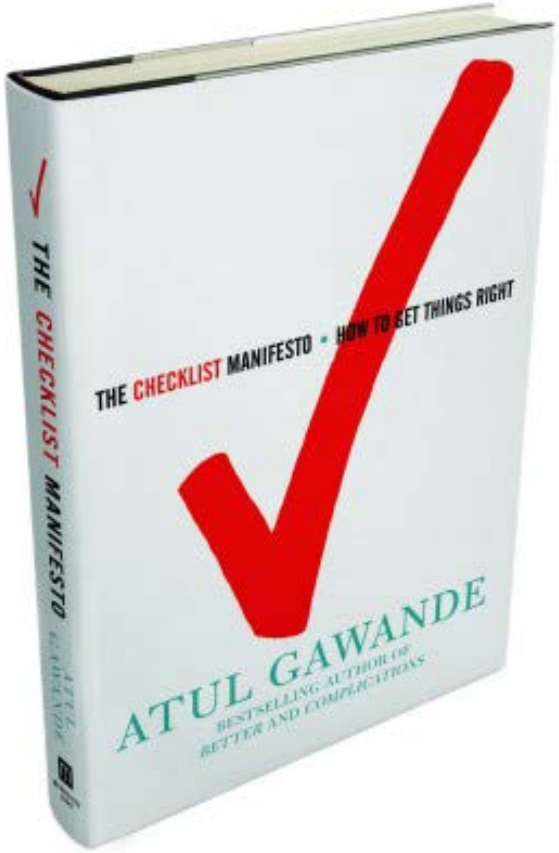


LHSC EBUS – FNA Service
N=340 cases/yr

- Success of EBUS-FNAB service depends on the combined skill and competency of the pulmonologists, cytotechnologists and cytopathologists – Total health care team



CHECK LIST Manifesto: Dr. Atul Gawande



Professor at Harvard
Surgeon at Bringham H

ROSE Form

APPROVED

PaLM
Pathology and Laboratory Medicine

CYTOPATHOLOGY LABORATORY
FNAB SERVICE WORKSHEET
for Cytotechnologists

University Hospital: Ext. 32956
Victoria Hospital: Ext. 55410, Pager 17227
St. Joseph's Hospital: Ext. 64314, Pager 10498

Label

❒ VH ❒ SJHC ❒ UH

❒ EUS ❒ EBUS ❒ H&N US Thyroid FNAB ❒ H&N ❒ CT ❒ US ❒ OTHER: _____

Physician Name DM

Radiologist Name _____

Time in 9:00
Time out 9: 35
CY initials RH

Diff quik slide # 1
Pap stain slide # 1
❒ Thin prep aliquot X

❒ Flow aliquot
❒ Touch prep # _____
❒ Cores in formalin # 3 size __

❒ Thyroglobulin test
❒ Calcitonin test
❒ PTH test

❒ **Pancreatic Cyst Protocol**
- ❒ 2 Air dried slides
- ❒ 1 Pap stain slide
- ❒ 1 DiffQuik stain slide

❒ **Extra Passes for Cell Block**

Case Comment

CP1 -	CSUFF	CINS	CLOWC	CIFC	CLP	CSLNS*	RINSE	FLOW
CP2 -	CSUFF	CINS	CLOWC	CIFC	CLP	CSLNS*	RINSE	FLOW
CP3 -	CSUFF	CINS	CLOWC	CIFC	CLP	CSLNS*	RINSE	FLOW
CP4 -	CSUFF	CINS	CLOWC	CIFC	CLP	CSLNS*	RINSE	FLOW
CP5 -	CSUFF	CINS	CLOWC	CIFC	CLP	CSLNS*	RINSE	FLOW
CP6 -	CSUFF	CINS	CLOWC	CIFC	CLP	CSLNS*	RINSE	FLOW

*CSLNS – sufficient lymph node sampling: abundant lymphocytes (≥100 cells/LPF X 5 fields) or abundant histiocytes with carbon pigment and scant respiratory cells (EBUS).

Patient Identifiers Confirmed

❒ Armband
❒ Patient verbal
❒ Double - witnessed visual recognition by (choose two persons)
❒ Physician ❒ Nurse ❒ Technician/Technologist ❒ Other _____ (specify)
❒ Physician only _____ (name)
❒ Not able to verify patient ID. Give reason _____
Other Information _____

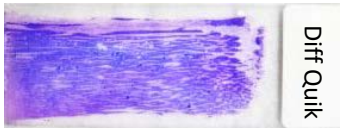
FLOW CHART for EBUS at LHSC

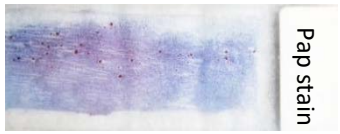
For suspected lymphoma, place a sample in Flow medium

FNAB + Needle Rinses

ROSE: 1 or 2 Passes

No ROSE: remaining Passes x 2-3





ROSE needle rinses in CytoLyt

CytoLyt

Place tissue cores & needle rinses in Formalin

Formalin

Cytology Lab

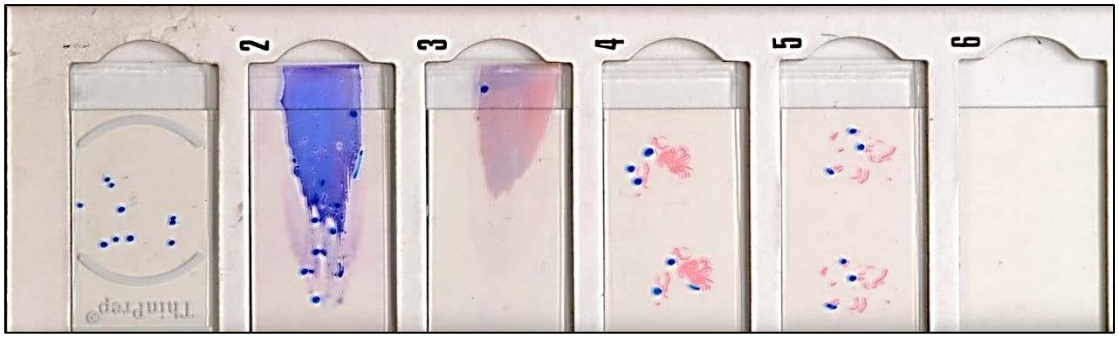
Thin Prep

CytoLyt Cell Block - CCB

Cytology Lab

Formalin Cell Block FCBC, FCBP (Histogel)

Strategies to Optimize EBUS Samples for Molecular Tests



Save sample for molecular testing

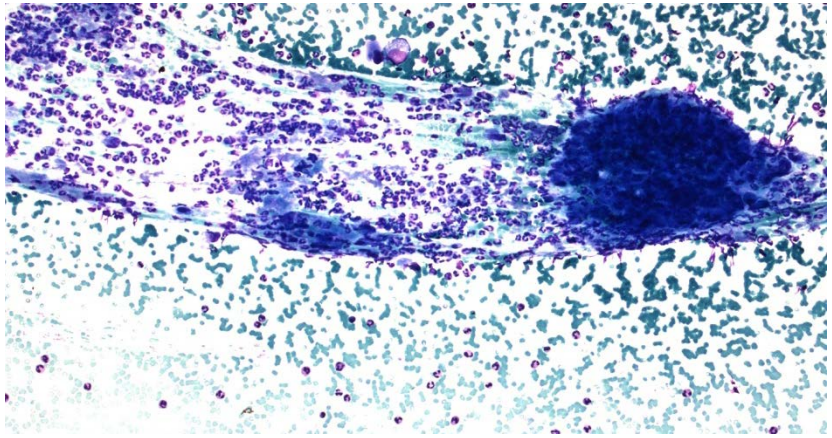
- ROSE by cytotechs
- Formalin fixation – high quality CBs
- Do not trim sign for CB
- Semi quantitation of malignant cells
- Judicious use of immuno-markers for cell typing (P40 and TTF-1)
- **Aim: maximize sample for ALK,EGFR, PD-L1…..**

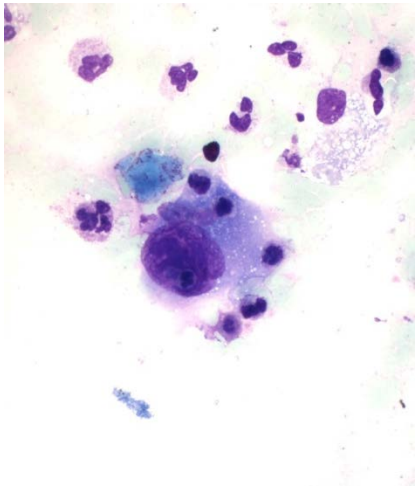
Number of Abnormal Cells	Cell Block Quality
<10	Scanty
10 – 50	Low
50 – 100	Moderate
>100	High

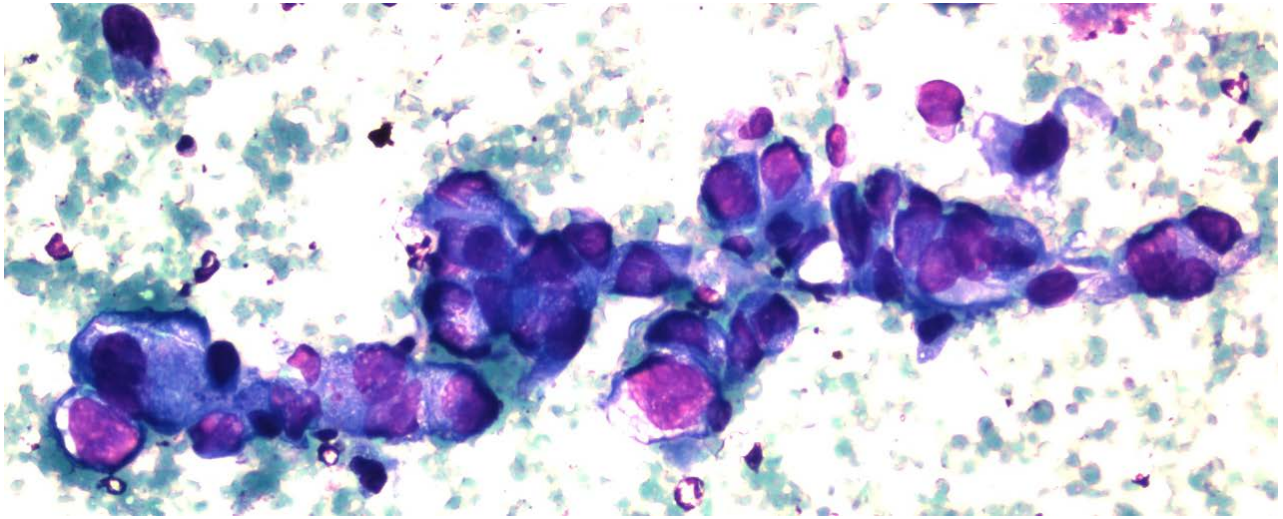
Ref: Arch Pathol Lab Med 2017;141:402-409

Current Case: ROSE

Diff Quik stain







ADEQUATE: Lesional cells present

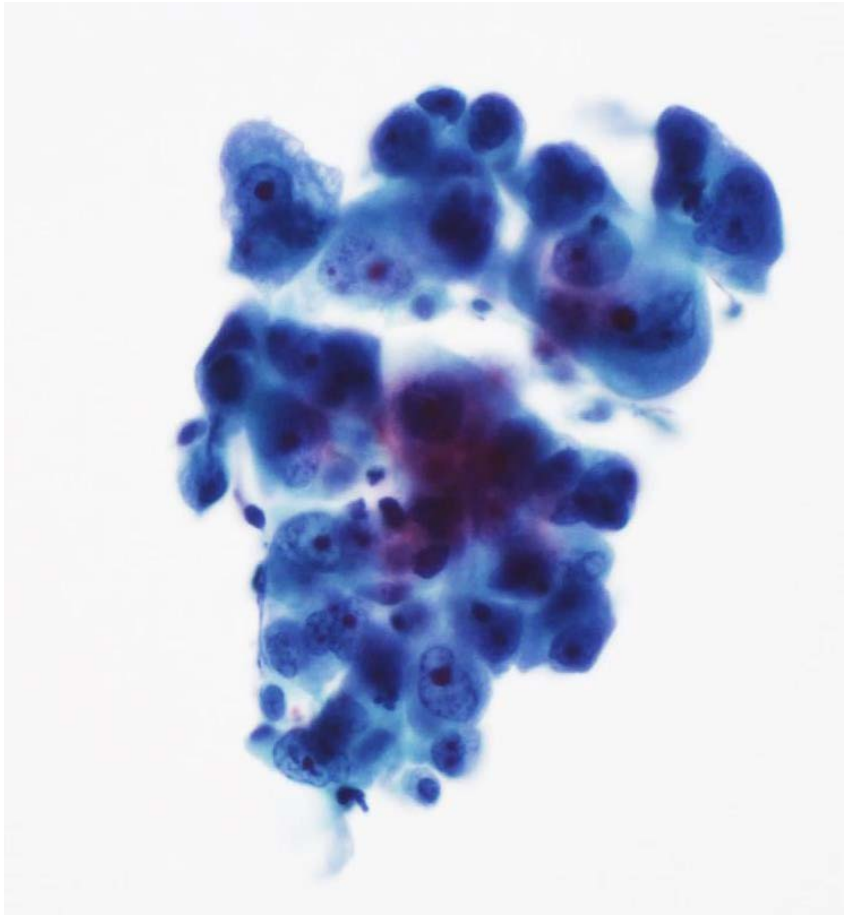
Obtain more material (additional passes in formalin)

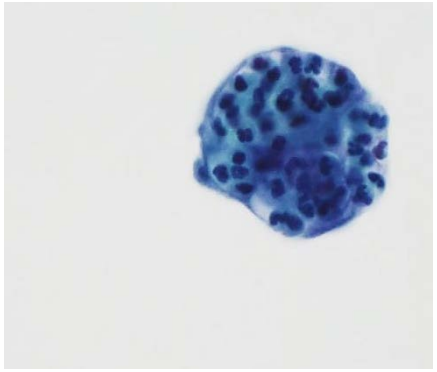
☑Cell block

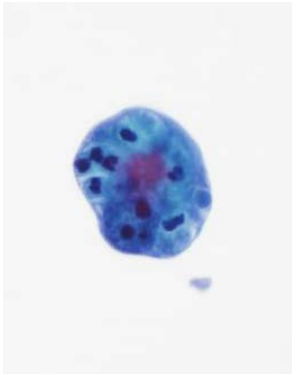
FCM: No

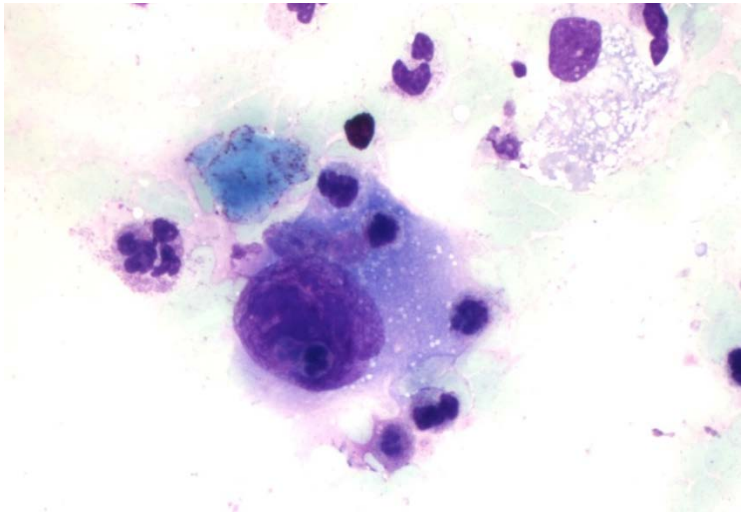
Microbiology: No

Cytomorphology
Emperipolesis

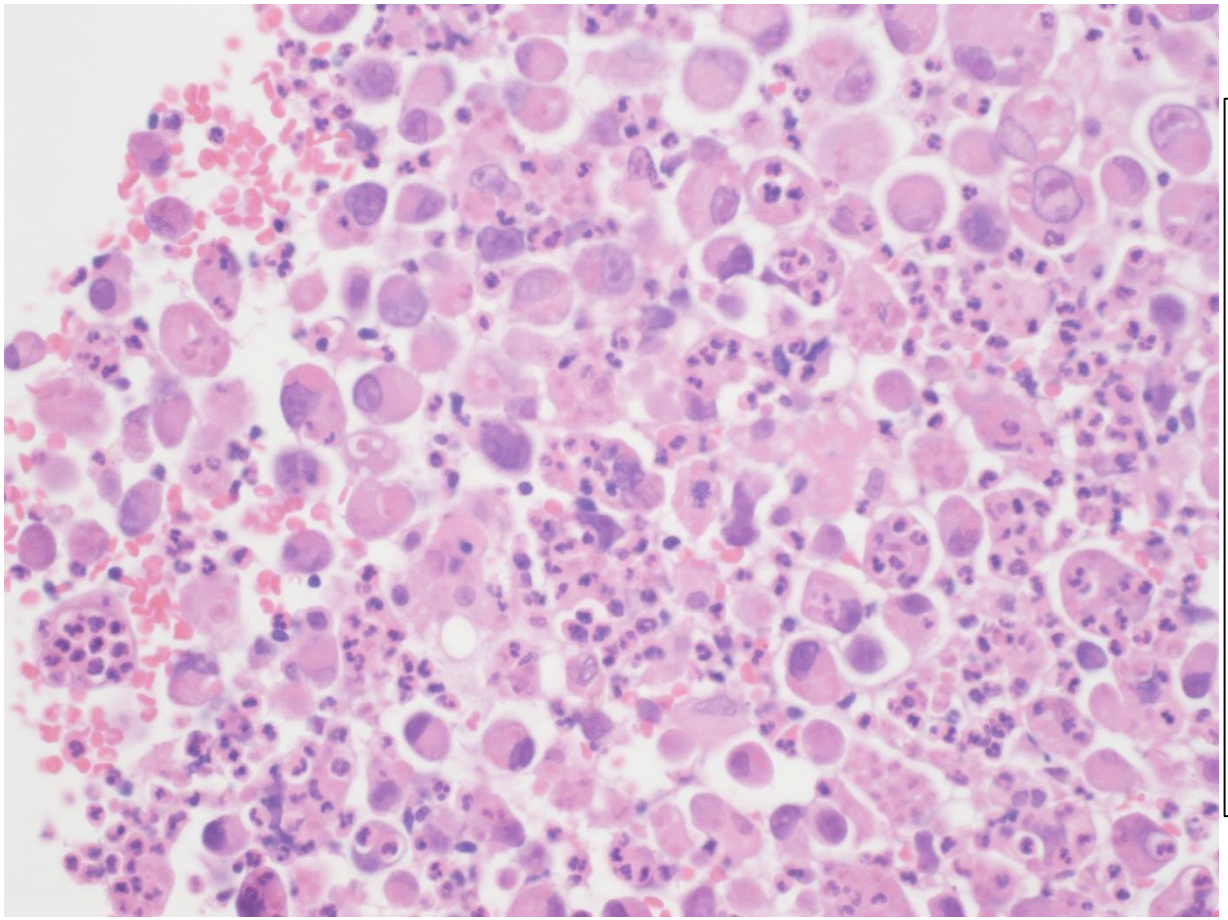








Cell Block: Emperipolesis



High cellularity >100 cells, PASD: Negative

Immuno:

Positive: CK7

Negative: P40, &TTF-1

Molecular:

Negative: EGFR and ALK

PD-L1 – not requested

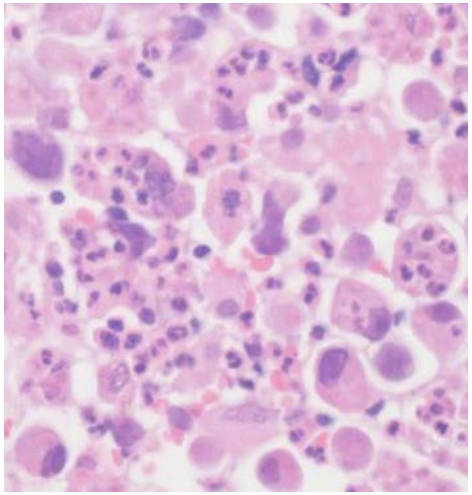
Diagnosis

Non-small cell carcinoma.
Morphological features favour **Giant Cell Carcinoma**.

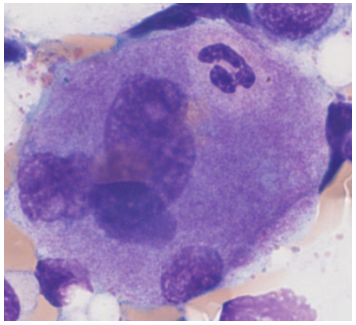
Comment: Definite diagnosis of this subtype may only be made on the resected specimen

Giant Cell Carcinoma Lung

- Rare subtype of non small cell carcinoma
  - <1% of all lung cancers, > male (5:1)
- Aggressive, present with advanced disease
- WHO: Pleomorphic (spindle/giant cell) ca
- Cytomorphology: emperipolesis



Emperipolesis

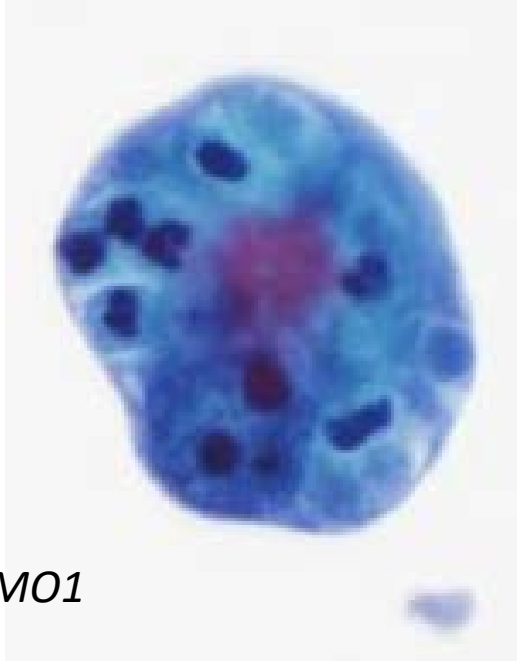


Physiological:

- Megakaryocytes: Increased expression of P- selectin (a cell adhesion molecule) on the surface of megakaryocytes promote increased neutrophil-megakaryocyte interaction

Pathological:

- Rosai-Dorfman disease
- Carcinoma: Giant cell carcinoma
  - Oral squamous cell ca
- Hemato-lymphoid disorders
- Neuroblastoma, rhabdomyosarcoma

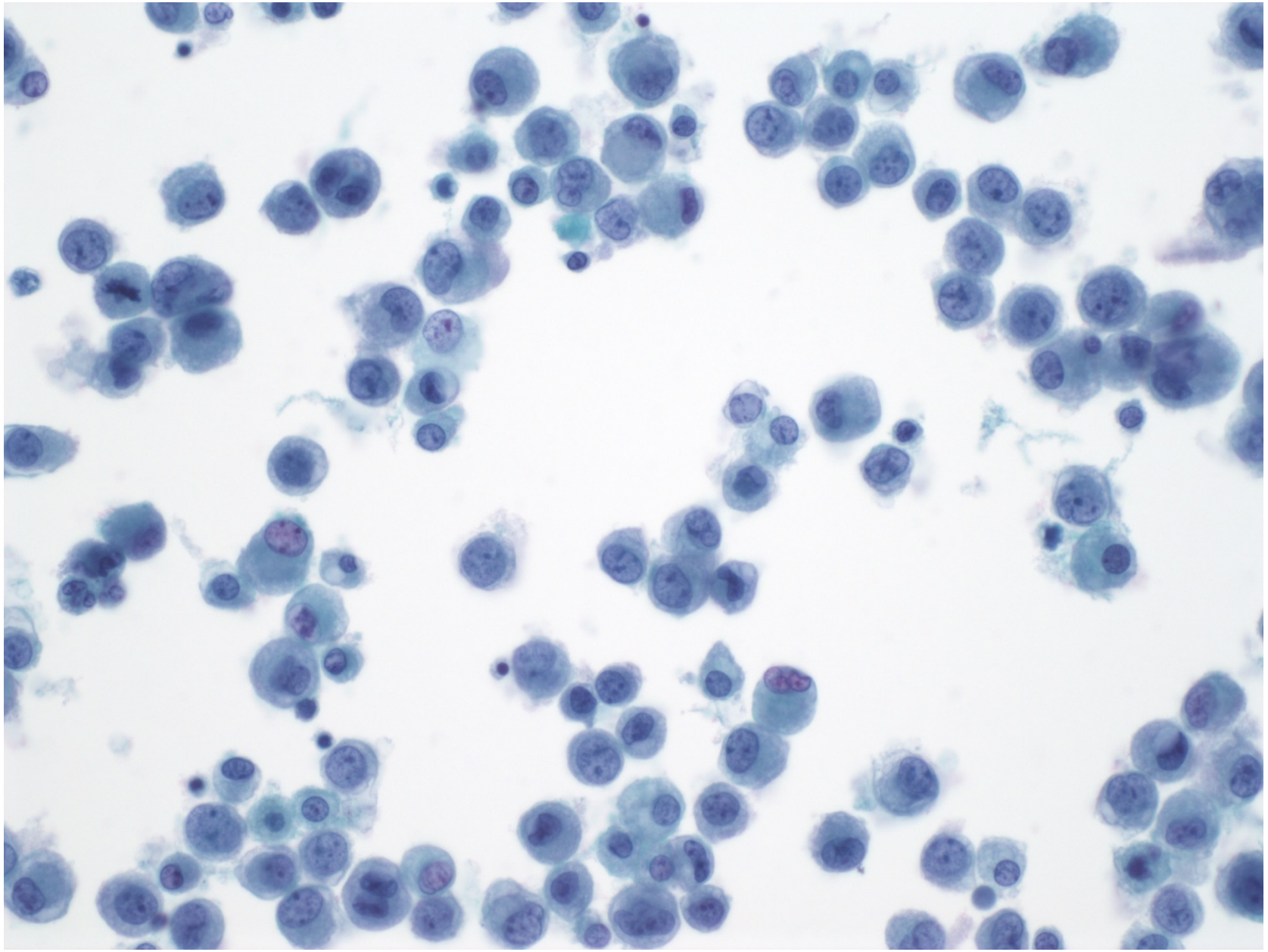


Journal of Clinical and Diagnostic Research 2014 Vol8 (12): ZMO1

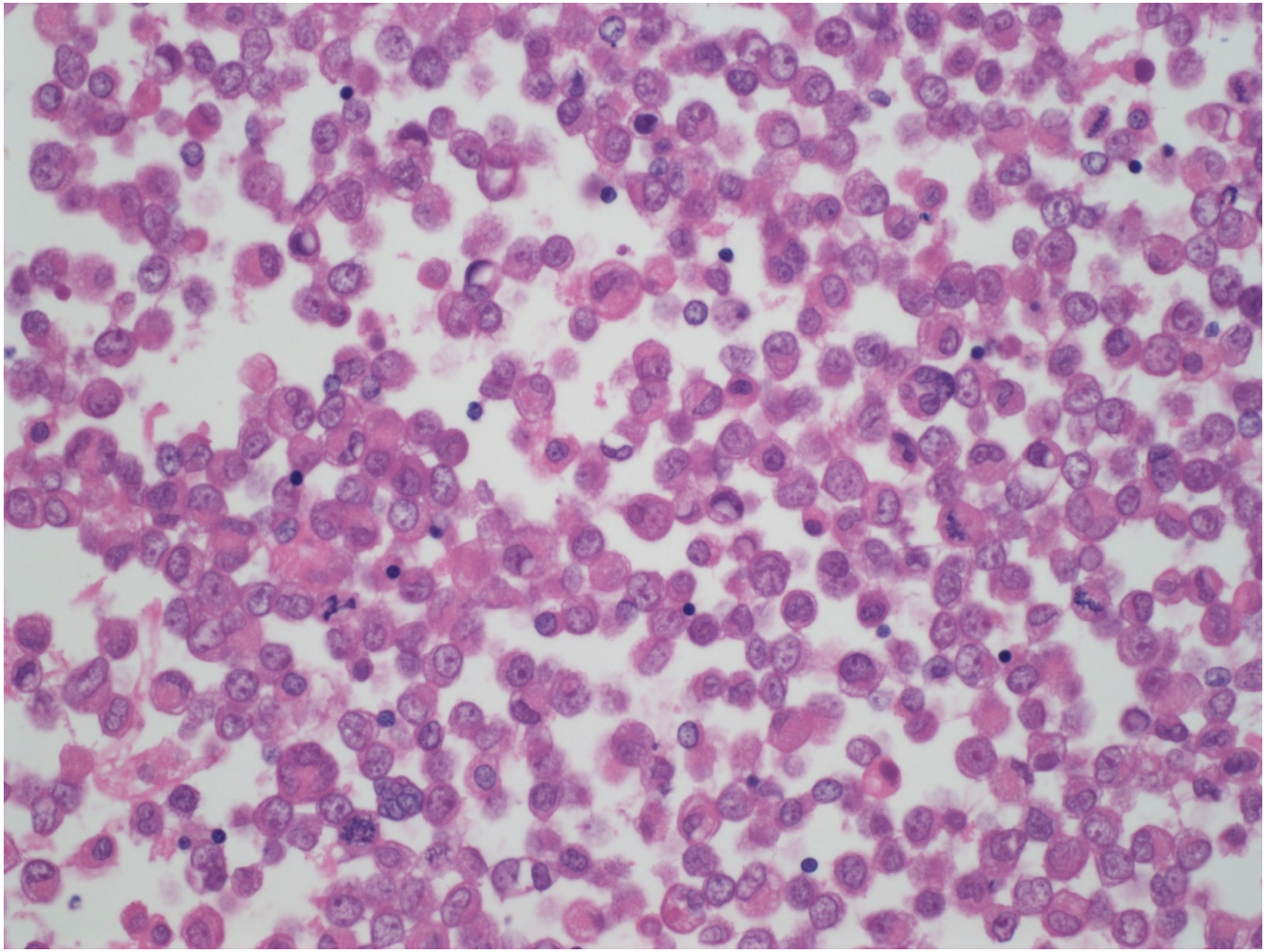
Munnar Resort, Kerala

Case 2

- 74-year-old male smoker
- (R) pleural effusion
- Diagnostic sample: Pleural fluid cytology



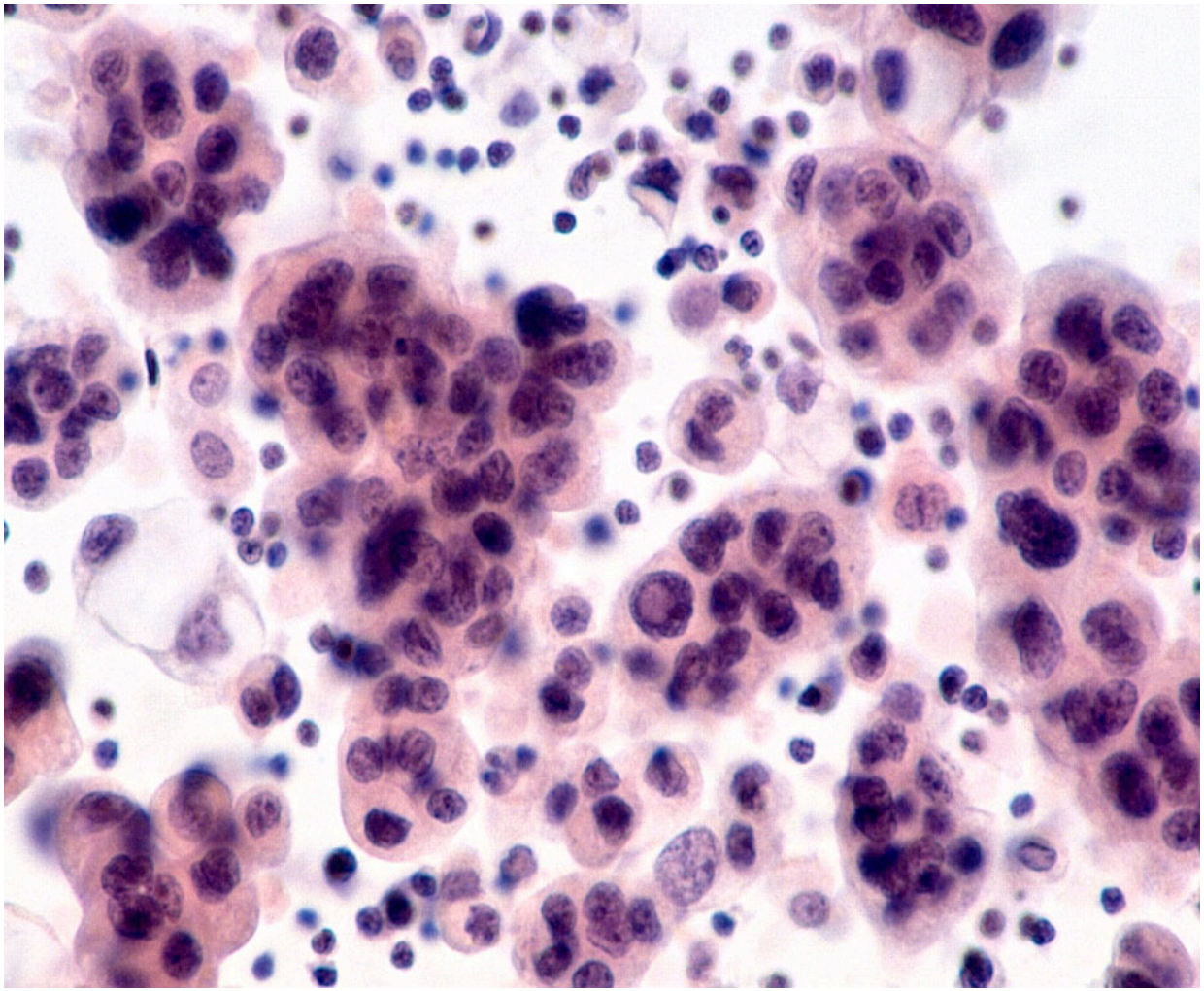
Cell Block

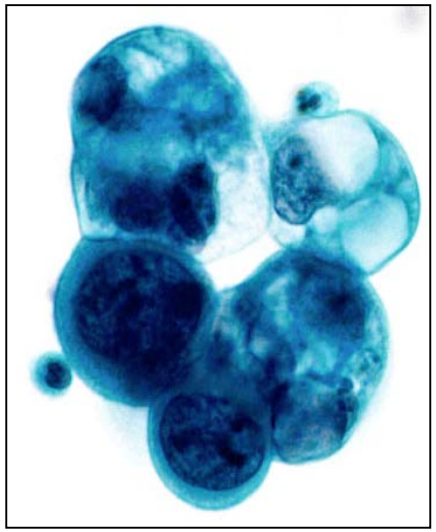


Adenocarcinoma
4 Cytologic Patterns

- Classic Dual Cell (two-cell) Pattern
- Cell Balls/Proliferation Spheres
- Papillary Pattern
- Single cell Pattern (rare)

Pattern 1: Dual Cell (Two Cell) Pattern

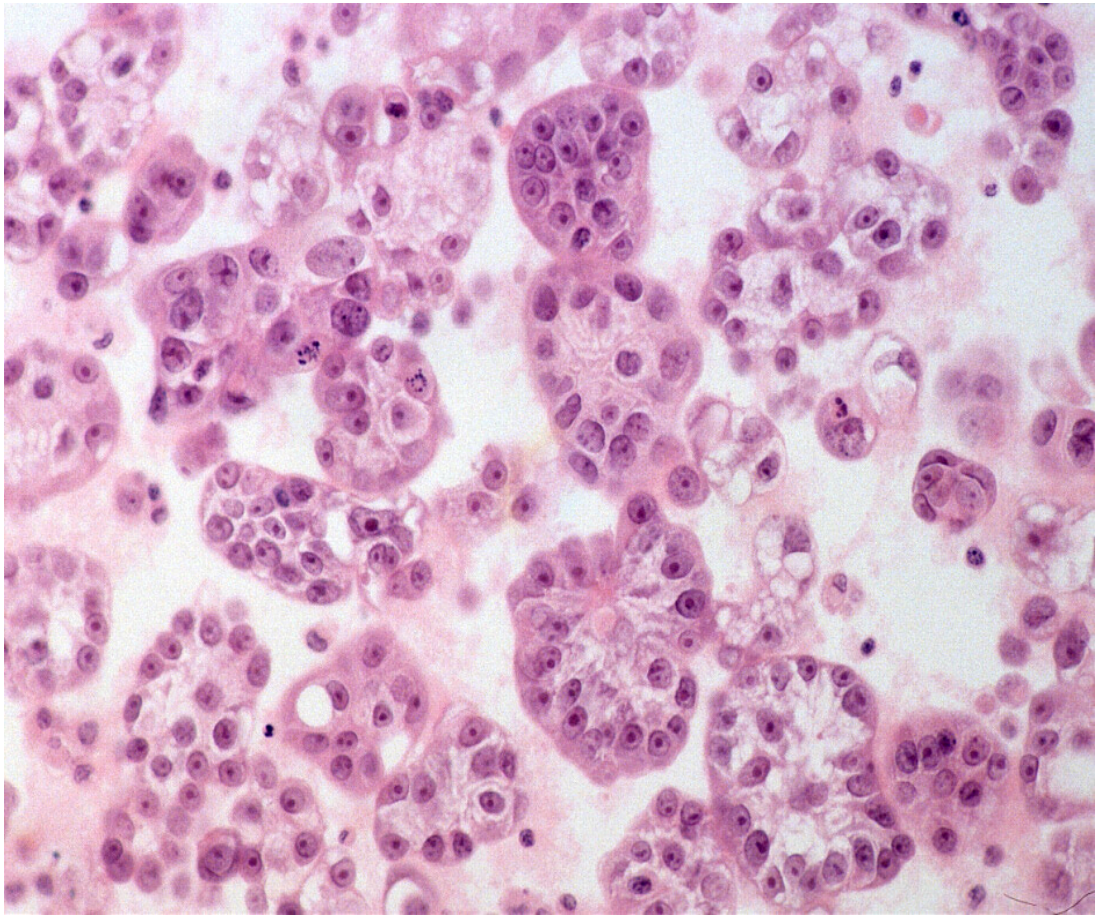




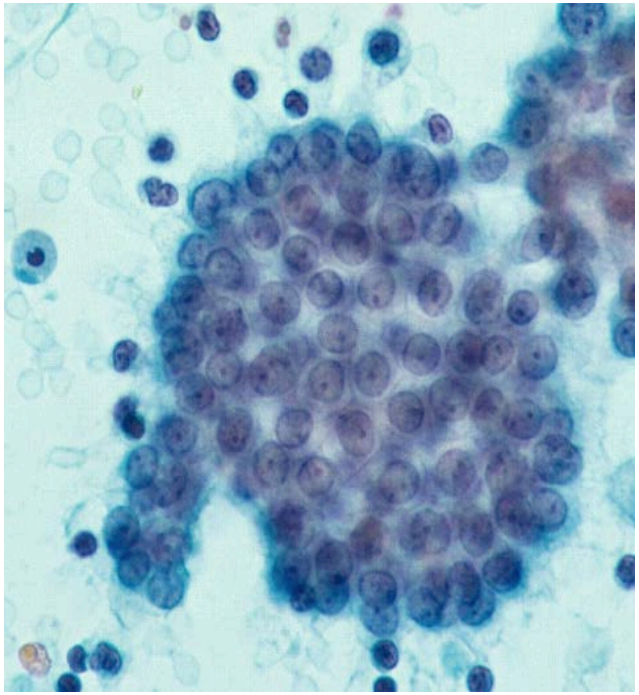
Proved to be Lung primary

Clusters of adenocarcinoma cells, **severe** nuclear atypia
Reactive mesothelial cells in background

Pattern1: Dual Cell Pattern

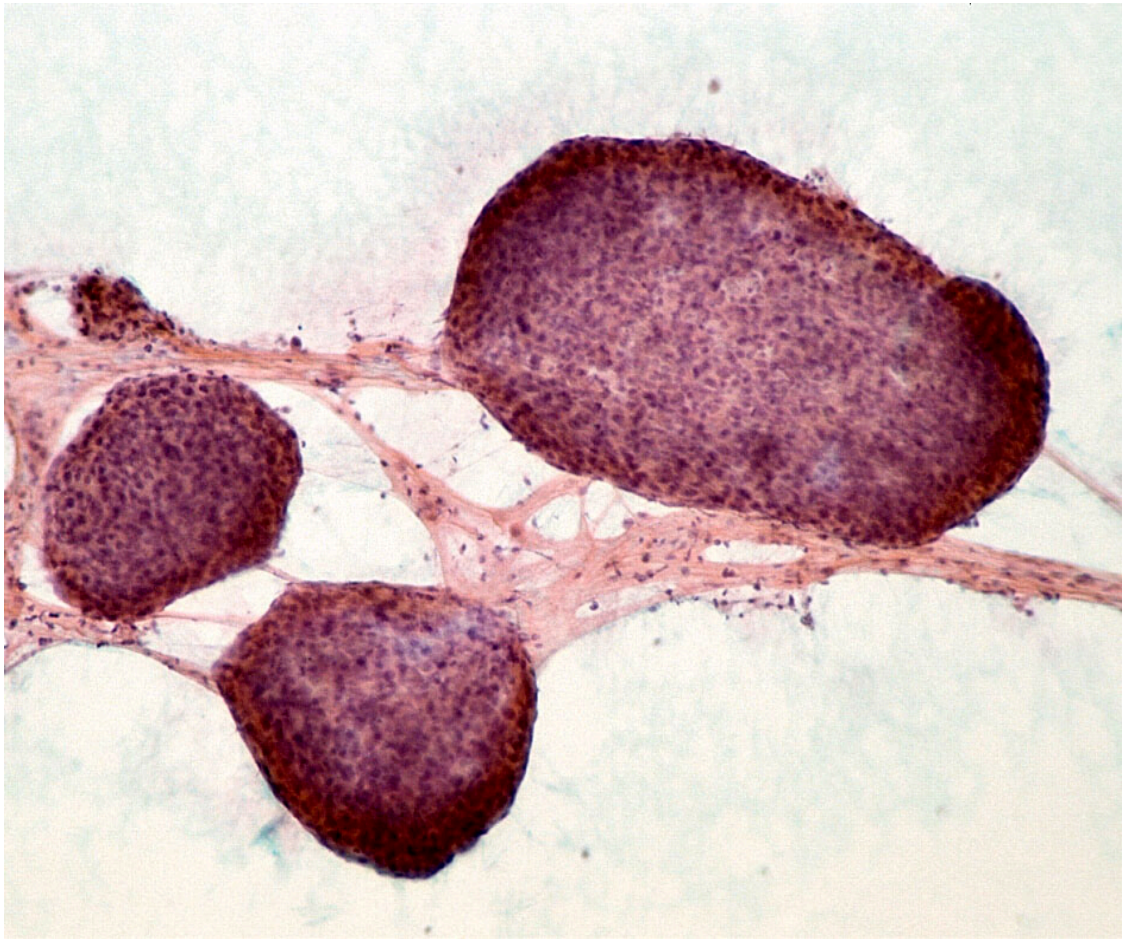


Clusters of adenocarcinoma cells, **moderate** nuclear atypia



Proved to be Lung primary

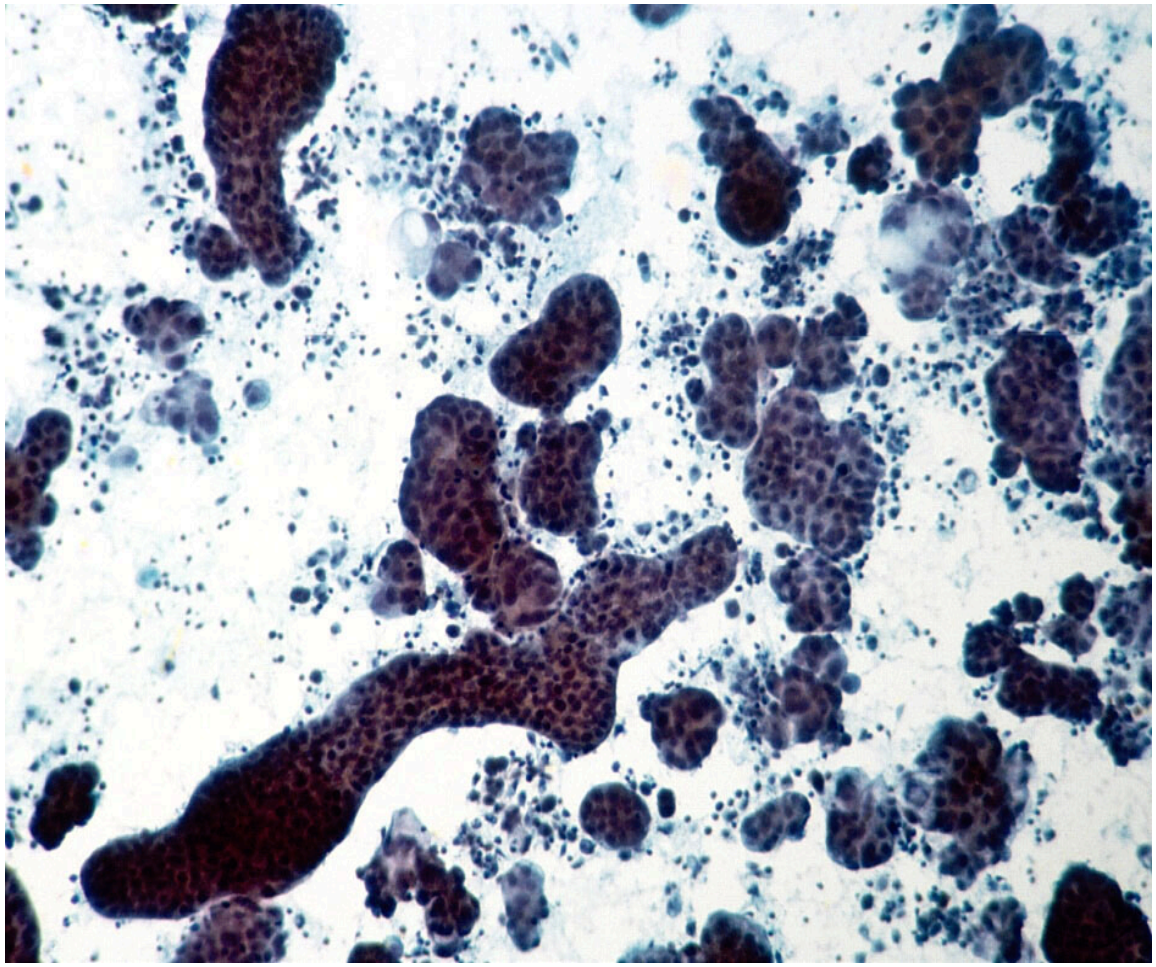
Pattern 2: Cell Balls/Proliferation Spheres

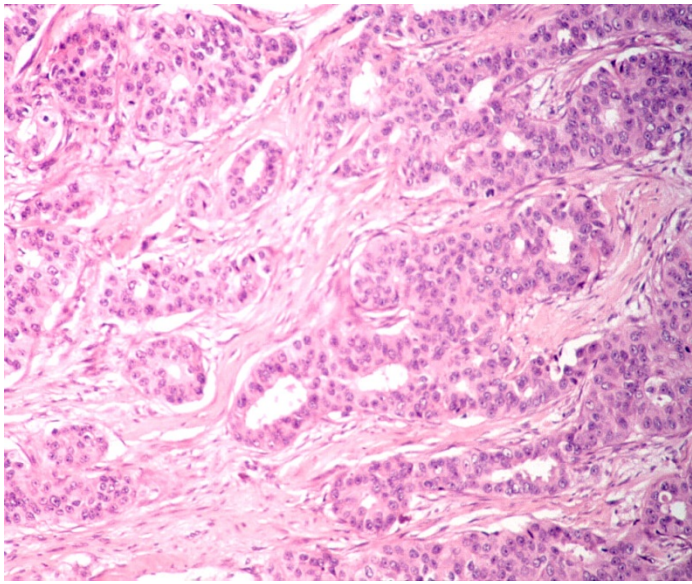


Proved to be
Breast primary

Tightly cohesive uniform cancer cells with smooth community border

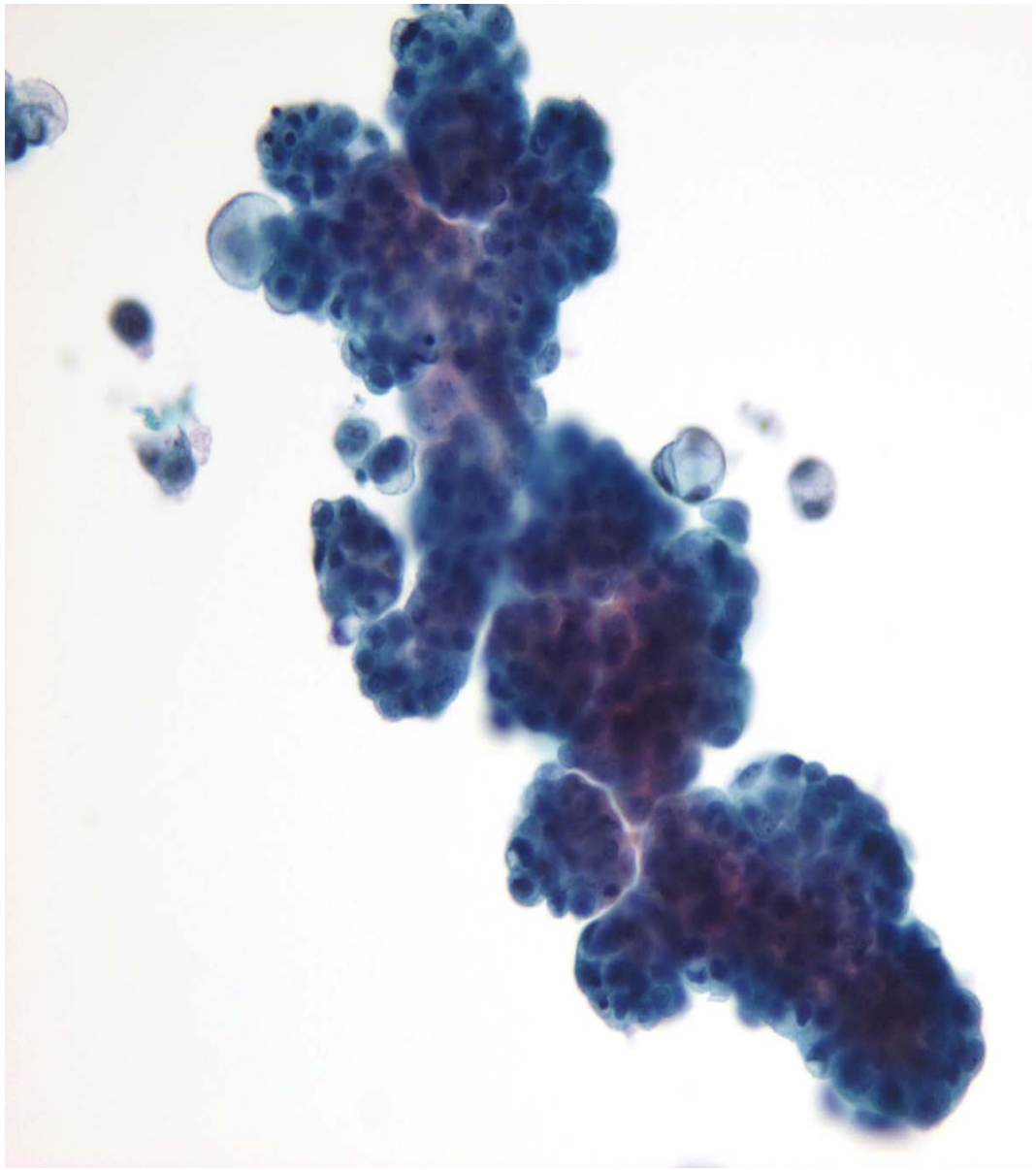
Pattern 2: Cell Balls and Large Elongated Proliferation Cylinders

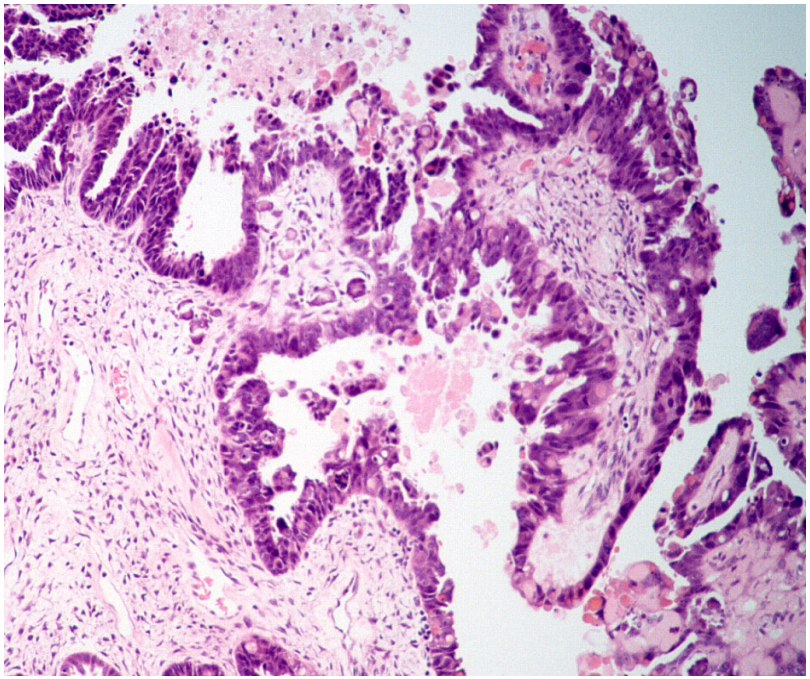




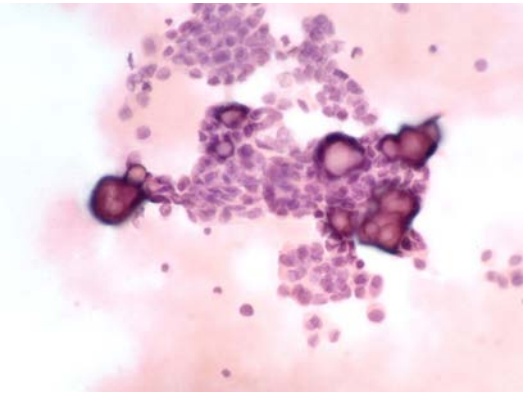
Proved to be Breast primary

Pattern 3: Papillary Pattern (Peritoneal Fluid, Female)

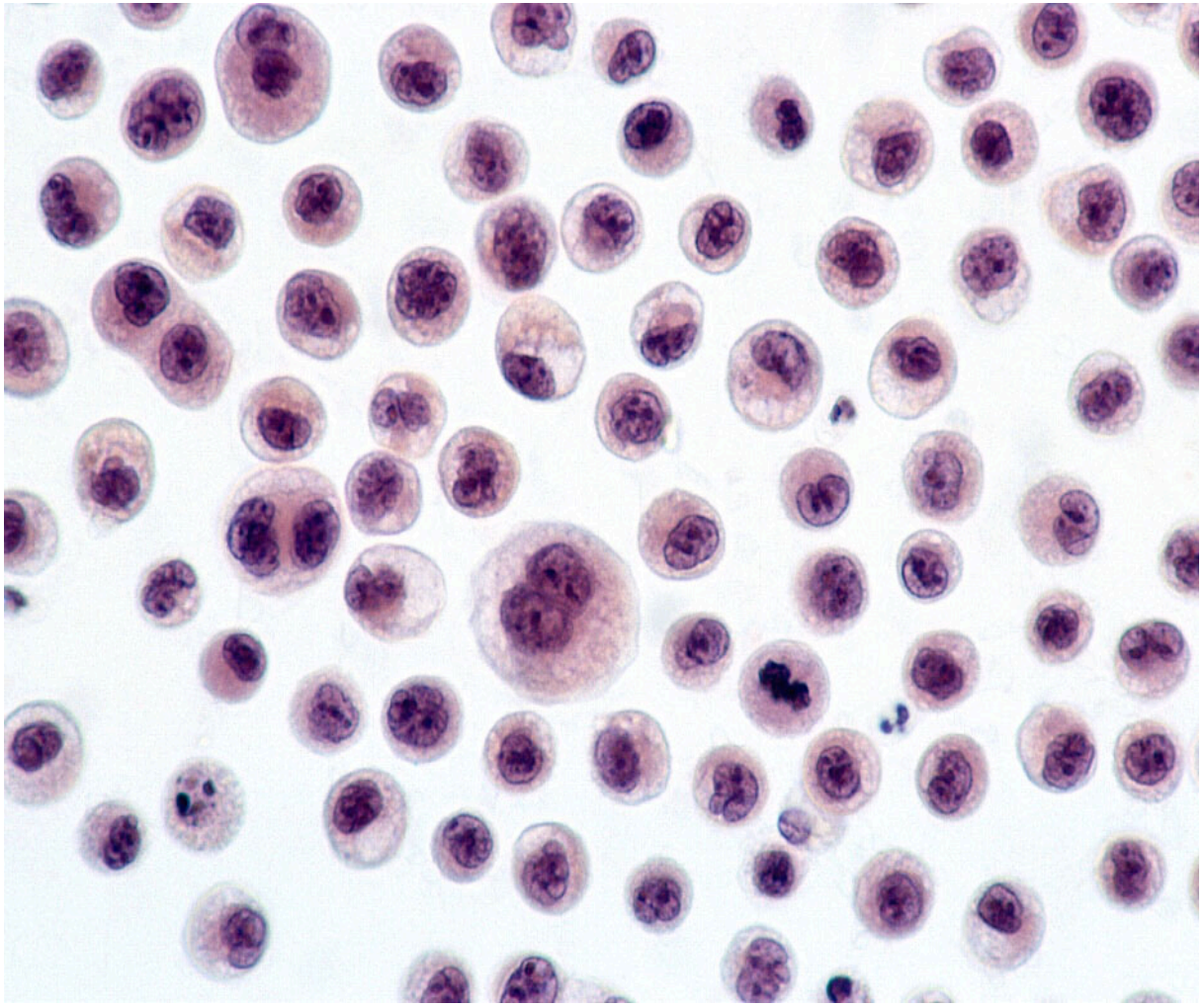




Primary Ovary



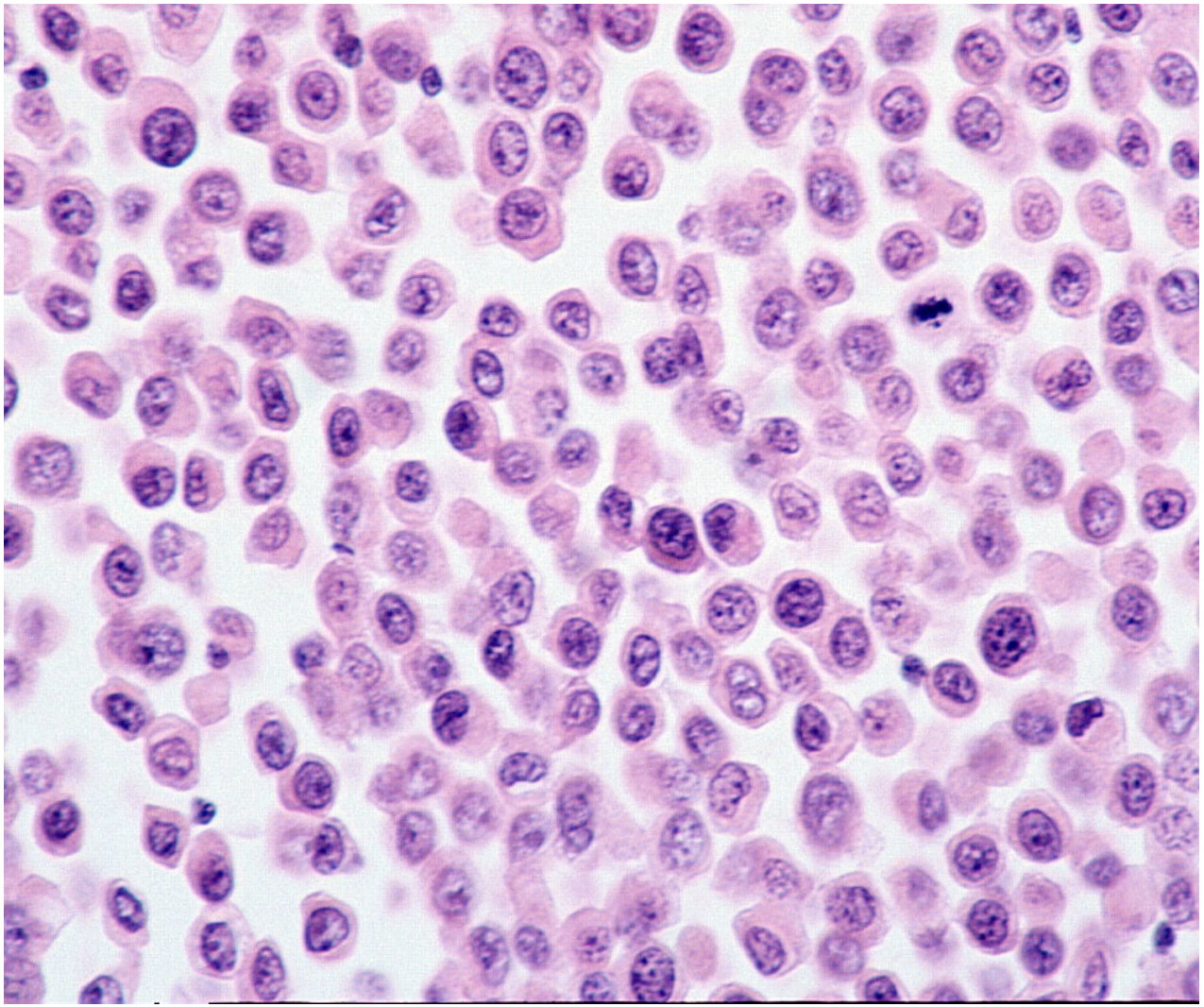
Pattern 4: Single Cell Pattern



Marked nuclear atypia

Proved to be
Lung primary

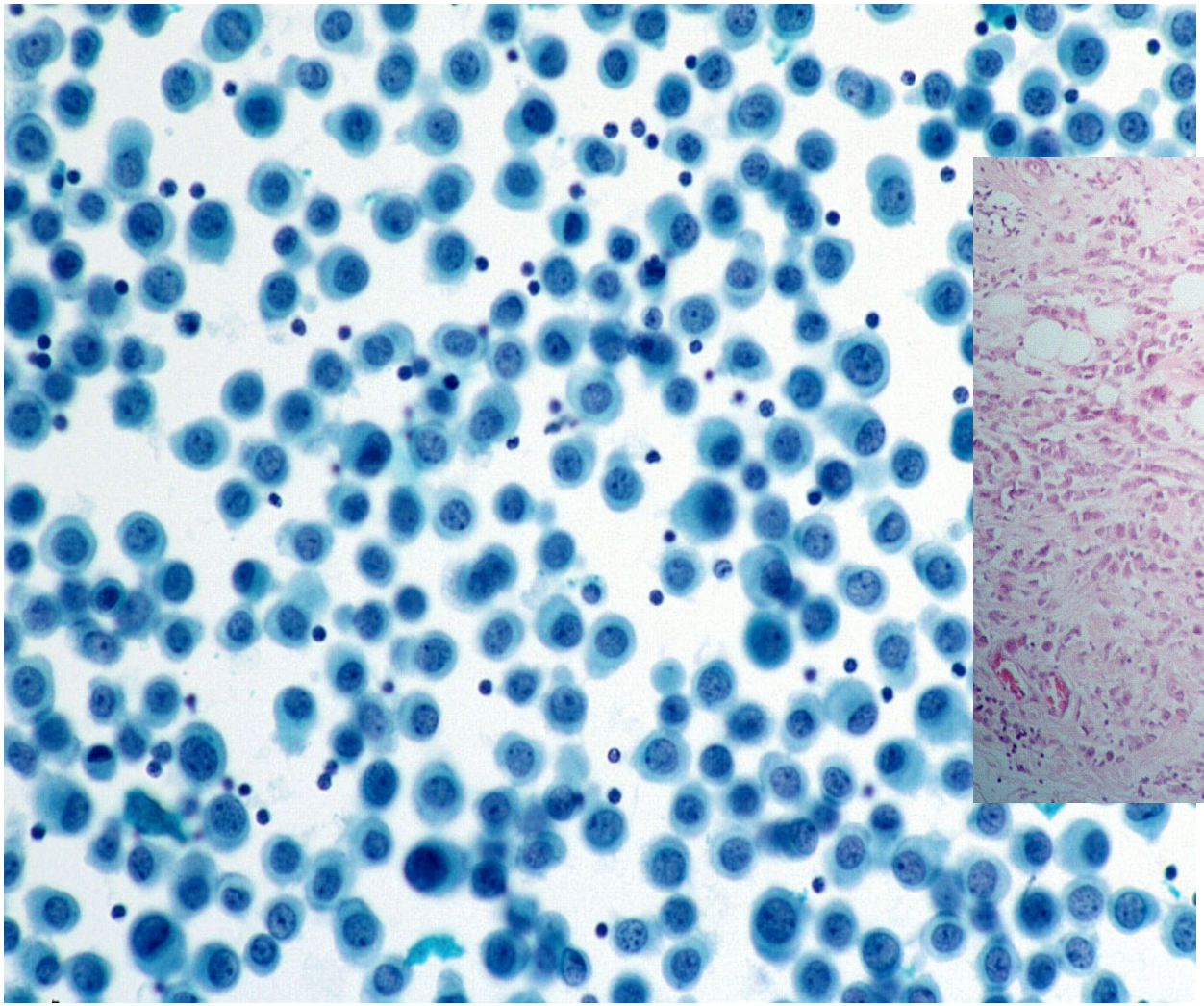
Pattern 4: Single Cell Pattern

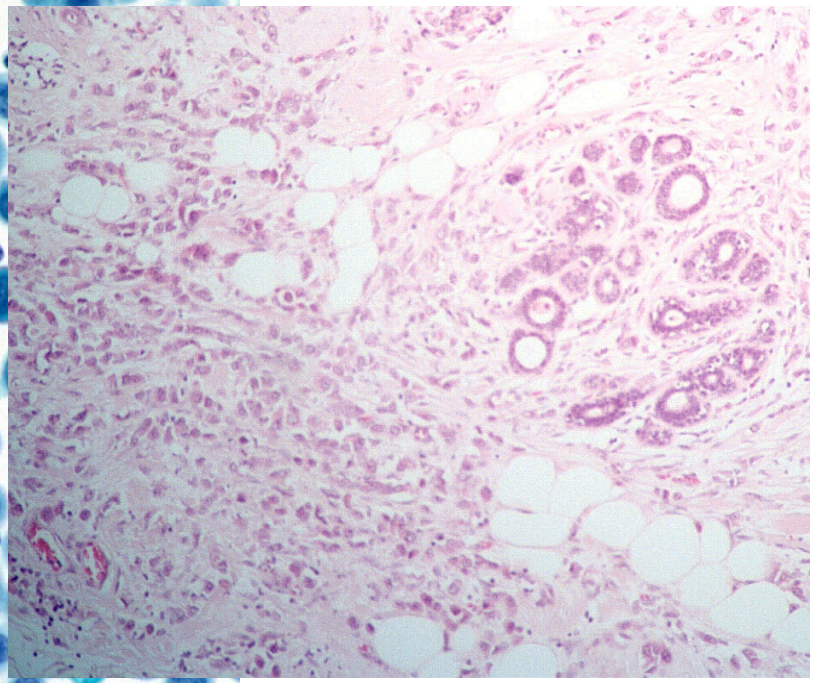


Moderate nuclear atypia

Proved to be
Colon primary

Pattern 4: Single Cell Pattern



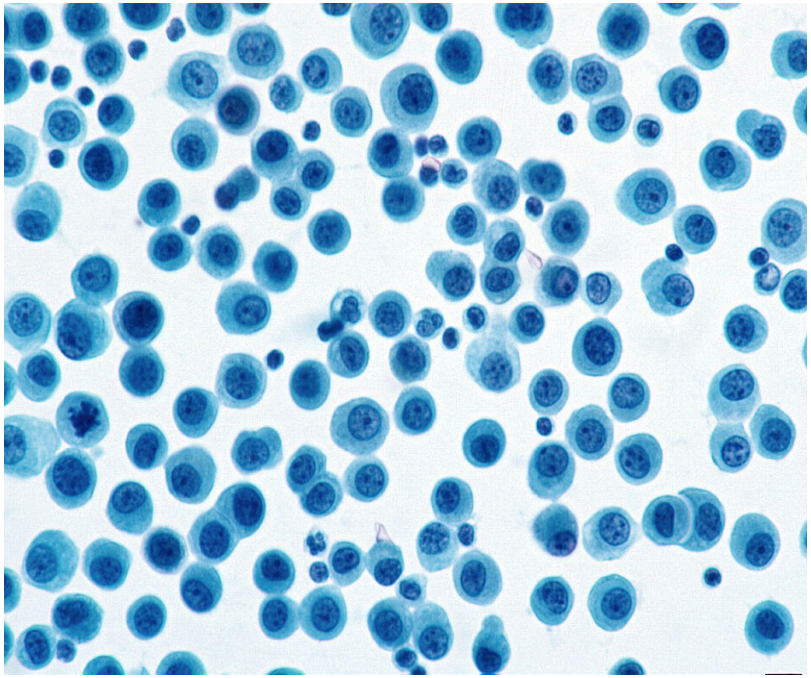


Breast primary

Minimal atypia, resemble reactive mesothelial cells

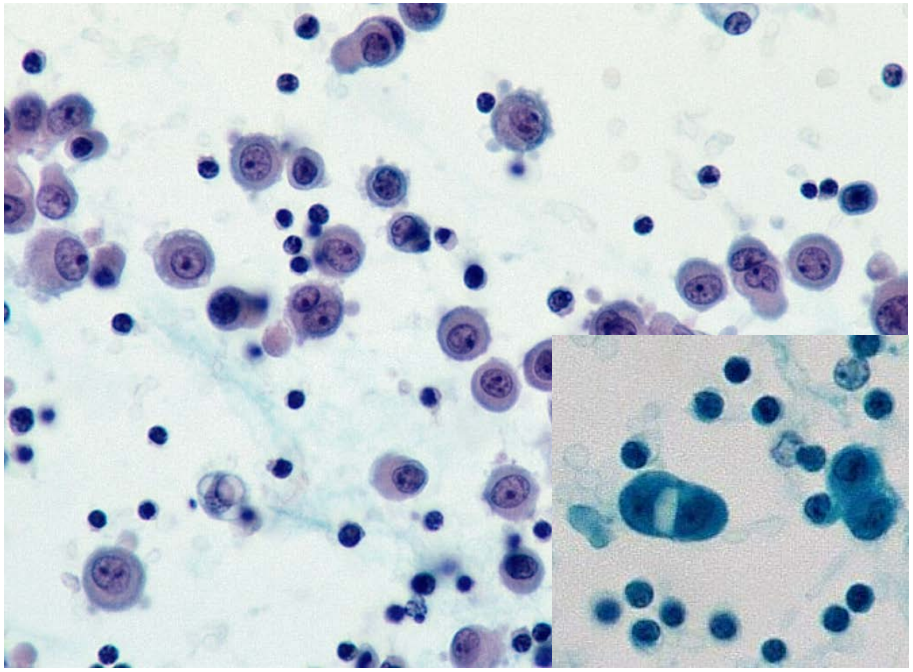
Immuno Essential for Dx

Single Cell Adenoca



Abundant single cells, clean background
Monomorphic population
Nuclear atypia variable, can be mild
DDx: Lymphoma, melanoma, Sarcoma

Atypical Mesothelial cells

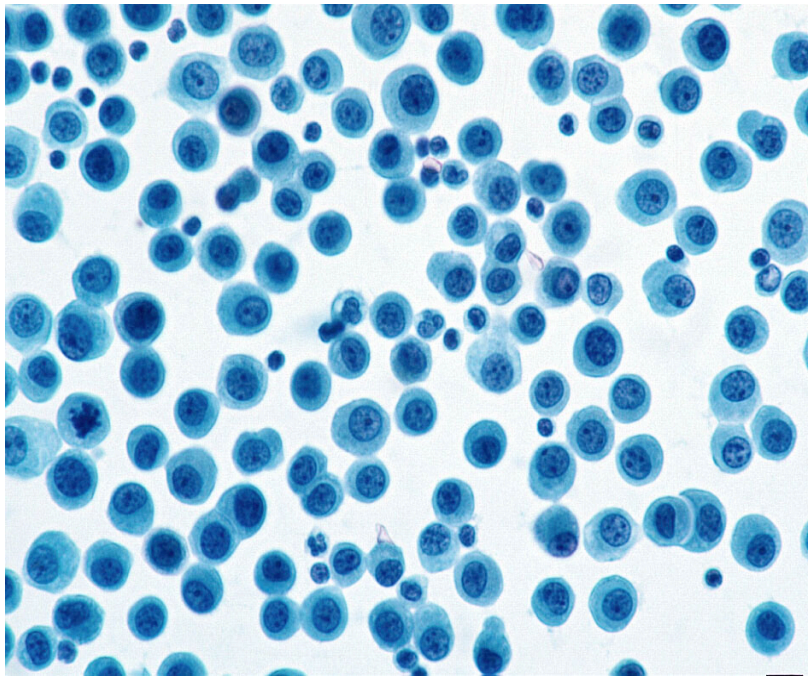


Inflammatory background
Dense/ two toned cytoplasm
Blebs, microvilli (lacy skirt), windows
Nuclear atypia mild, nucleoli

Adenoca vs Atypical Mesothelial Cells

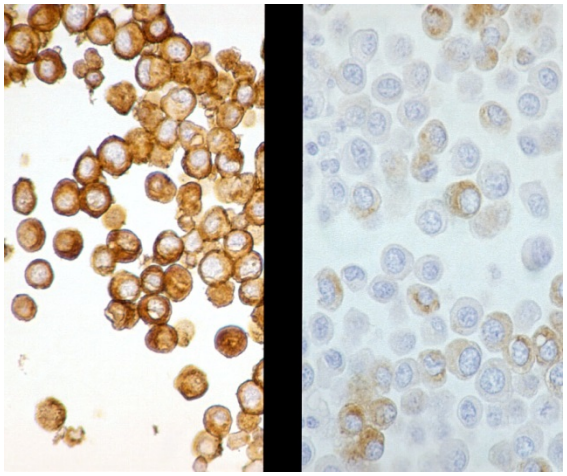
- Adenoca markers
  - MOC 31
  - BER EP4
  - TTF-1
  - CEA (polyclonal)
  - BRST-3 (B72.3)
- Mesothelial cell markers
  - Calretinin
  - CK 5/6
  - WT1 (not commonly used in cytology)

Single cell malignant effusion

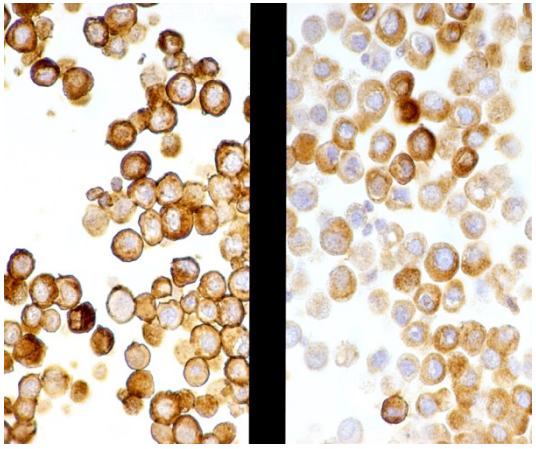


Breast Primary

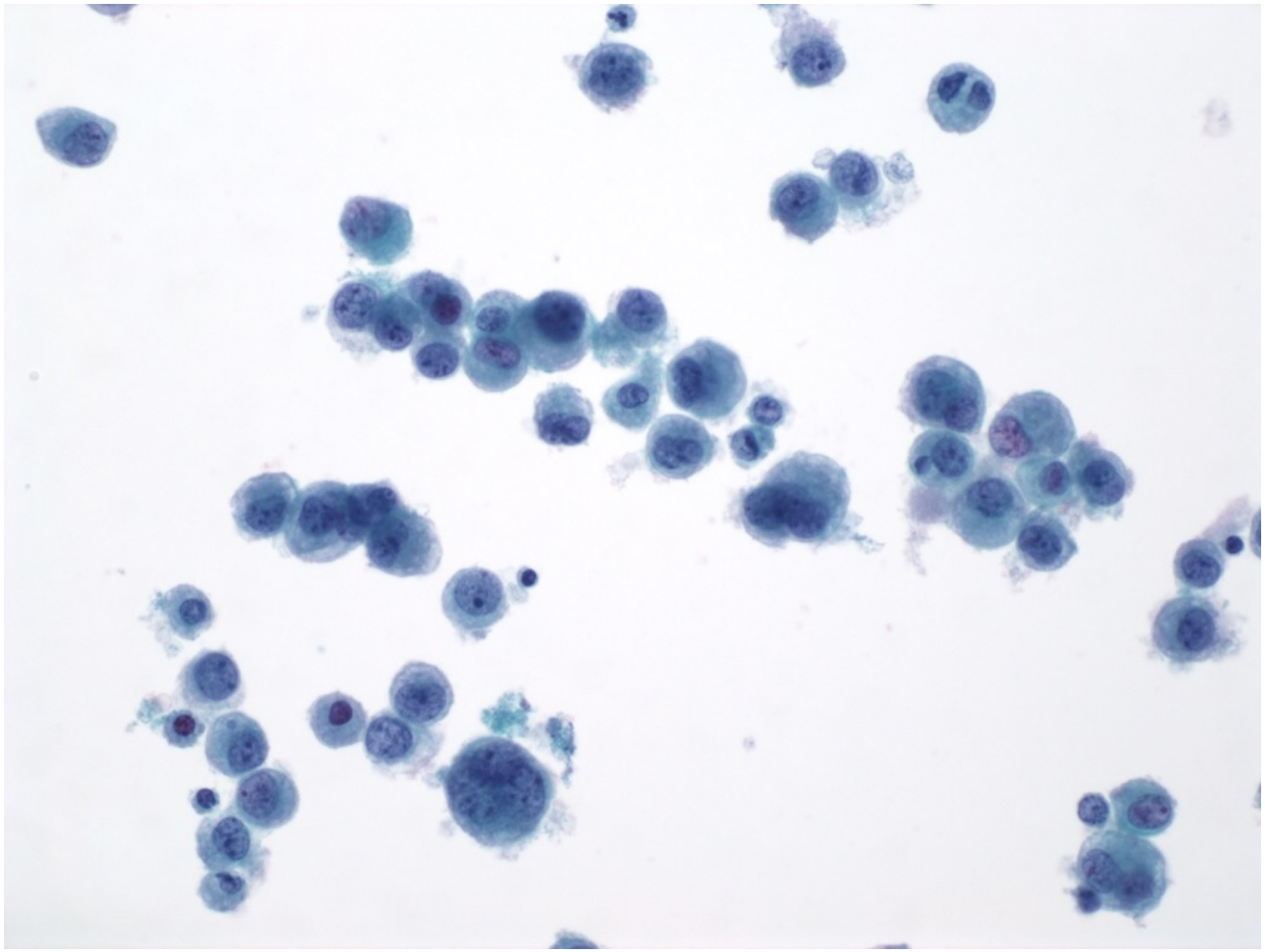
MOC31 **CEA**

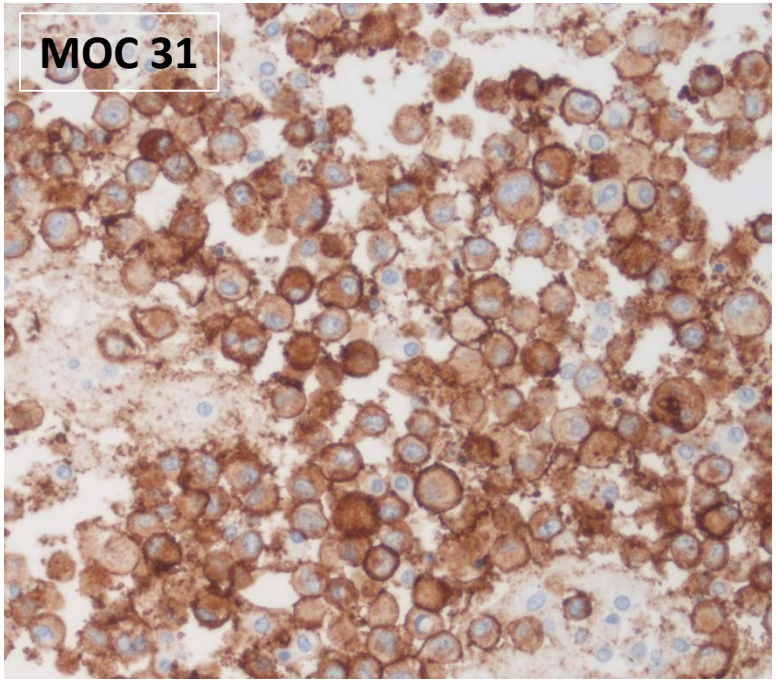


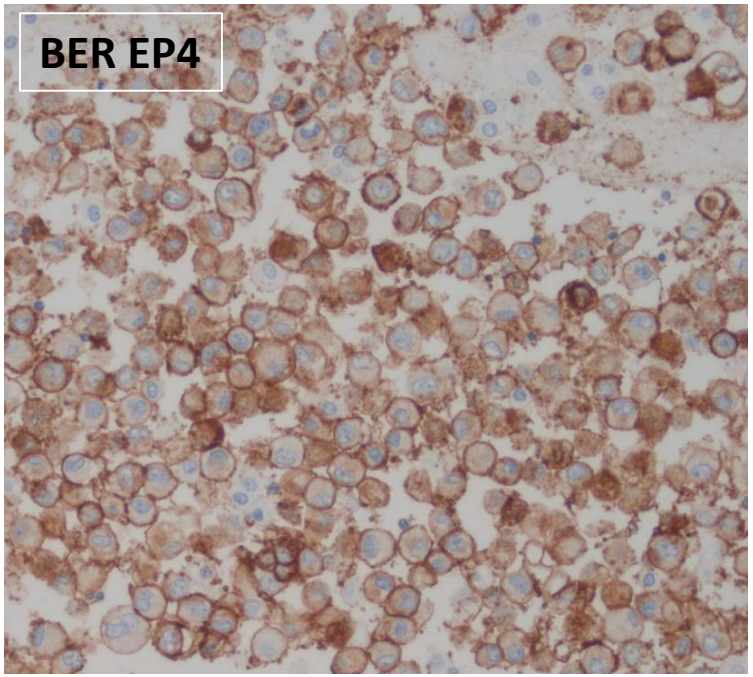
B72.3 Ber EP4

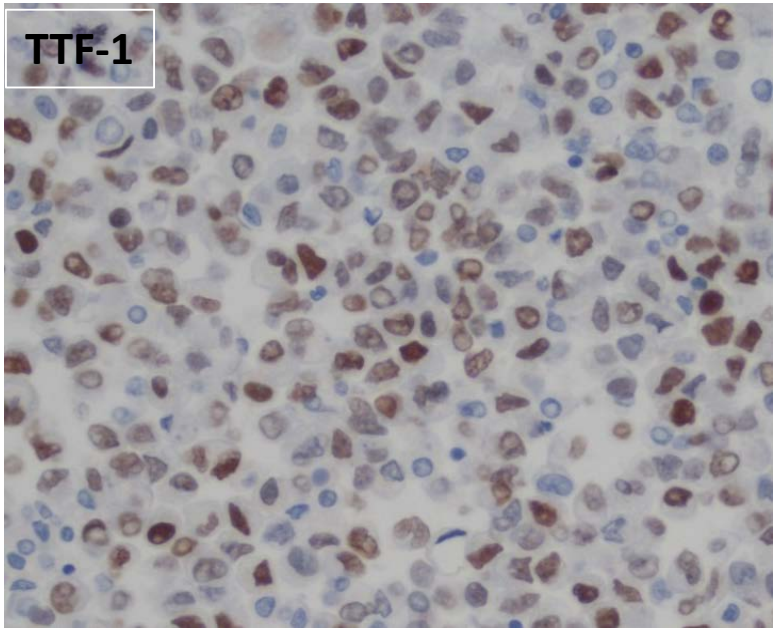


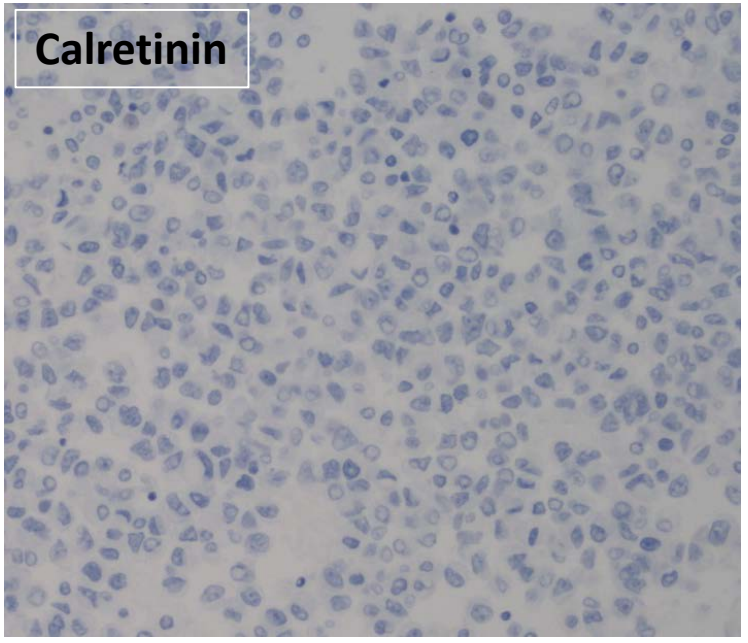
Current Case




MOC 31


BER EP4


TTF-1


Calretinin

Diagnosis

Pleural fluid: Adenocarcinoma
consistent with lung primary

Take Home Message

- Effusion fluid is a diagnostic sample, precise diagnosis is feasible
- Be aware of single cell malignant effusion
- Utilize CB for ancillary studies
- Molecular testing is feasible on pleural fluid (requires high cellularity and formalin fixation)

Thank you