SELECTED DILEMMAS IN RESPIRATORY CYTOPATHOLOGY (2 CASES)

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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

Olympus 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 Brigham H
FLOW CHART for EBUS at LHSC

FNAB + Needle Rinses

ROSE: 1 or 2 Passes

ROSE needle rinses in CytoLyt

Place tissue cores & needle rinses in Formalin

No ROSE: remaining Passes x 2-3

For suspected lymphoma, place a sample in Flow medium

Cytology Lab

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 cytotechnics
  - 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.....

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

**ADEQUATE:** Lesional cells present

Obtain more material (additional passes in formalin)

- Cell block

FCM: No

Microbiology: No
Cytomorphology
Emperipolesis
Cell Block: Emperiploesis

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

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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

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

Proved to be Lung primary
Pattern 1: Dual Cell Pattern

Clusters of adenocarcinoma cells, moderate nuclear atypia

Proved to be Lung primary
Tightly cohesive uniform cancer cells with smooth community border

Proved to be Breast primary
Pattern 2: Cell Balls and Large Elongated Proliferation Cylinders
Pattern 3: Papillary Pattern (Peritoneal Fluid, Female)
Pattern 4: Single Cell Pattern

Marked nuclear atypia

Proved to be Lung primary
Pattern 4: Single Cell Pattern

Proved to be Colon primary

Moderate nuclear atypia
Pattern 4: Single Cell Pattern

Minimal atypia, resemble reactive mesothelial cells
**Immuno Essential for Dx**

**Single Cell Adenocarcinoma**
- 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
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