EBUS-guided FNA of Lung and Lymph Nodes: From Adequacy to Final Diagnosis

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Learning Objectives

• Review modified Giemsa-stained endoscopic transbronchial ultrasound-guided (EBUS) fine needle aspiration (FNA) slides to render an adequacy interpretation.
• Identify situations in which specimen triage is critical during EBUS-guided FNA rapid on-site evaluations, and select appropriate triage options.
• Use appropriate ancillary studies to arrive at definitive diagnoses of EBUS-guided lung and lymph node FNA specimens.

Introduction

• Endobronchial ultrasound-guided FNA (EBUS)
  • Minimally-invasive technique for evaluating the mediastinum, staging lung carcinoma, diagnosing lung nodules and lymph nodes in patients with mediastinal lymphadenopathy
  • PPV 95% and NPV 100% with experienced operators
• Electromagnetic Navigational Bronchoscopy (ENB)
  • Image-guided localization to sample peripheral and subpleural lung lesions
  • Diagnostic yields of 77-94%

Laboratory Practices in Respiratory Cytology

• 2013 survey on respiratory cytology practices to labs enrolled in CAP NGC Interlaboratory Comparison Program
• 880/2074 labs (42%) responded with 778 evaluating respiratory samples
• ~95% bronchial washings/brushings
• 43% EBUS-guided FNA
• 14% ENB specimens
• 55% modified Giemsa-stained direct smears, 22% rapid H&E, 13% rapid Pap, 10% other stains

Polling Question 1. I am a...

• Cytotechnology student
• Cytotechnologist
• Pathology resident
• Cytopathology fellow
• Practicing pathologist

Sample Processing at Cleveland Clinic

Polling Question 2
Did you review the virtual whole slide images prior to today?
• No
• Yes
• A little bit, but I am not used to reviewing virtual slides

Case 1

Clinical Presentation
• 51-year-old female with history of left breast moderately-differentiated invasive ductal carcinoma 2 years ago
• New 3.5 cm right suprahilar mass
• EBUS-guided FNA of station 11R lymph node

Modified Giemsa-Stained Slide – Case 1
Polling Question 3
What is your adequacy assessment for Case 1?
- Non-diagnostic
- Atypical cells present
- Suspicious for malignancy
- Positive for malignancy

Pap-stained Slide – Case 1

Cell Block – Case 1

Immunostains on Cell Block – Case 1

GATA-3
TTF-1

Differential Diagnosis
- Poorly-differentiated lung adenocarcinoma
- Metastatic adenocarcinoma
- Malignant melanoma

Discussion and Follow-up – Case 1
- If suspected breast carcinoma, ensure specimen fixation is compatible with ER/PR/HER2 testing guidelines
- IHC positive for CK7, GATA-3, and GCDFP-15
- IHC negative for TTF-1 and Napsin-A
- ER/PR negative
- HER2 FISH positive
- Right lung and hilar radiation for metastatic breast carcinoma
- Doing well 5 ½ years post-treatment
Clinical Presentation

- 76-year-old male non-smoker with a history of basal cell carcinomas
- Bilateral scattered rounded lung nodules up to 13 mm in greatest dimension, inflammatory vs. metastatic
- EBUS-guided FNA of right upper lobe lung lesion

Polling Question 4
What is your adequacy assessment for Case 2?

- Non-diagnostic
- Atypical cells present
- Suspicious for malignancy
- Positive for malignancy
Differential Diagnosis

- Well-differentiated lung adenocarcinoma
- Metastatic adenocarcinoma (papillary thyroid carcinoma)

Discussion and Follow-up – Case 2

- IHC positive for TTF-1, thyroglobulin and PAX-8, confirming thyroid origin
- Total thyroidectomy and central neck dissection performed
  - 2.2 cm papillary thyroid carcinoma with 4/6 positive lymph nodes
- Radioactive iodine given and patient was refractory to treatment
- Patient deceased approximately 5 years post-diagnosis

Case 3

Clinical Presentation

- 56-year-old male non-smoker with 3-week history of lower back and RUQ abdominal pain
- Confluent 3.0 cm left parahilar mass, adenopathy, lytic osseous metastatic lesions and hepatic lesion
- EBUS-guided FNA of left upper lobe parahilar lesion

Modified Giemsa-stained slide – Case 3

Polling Question 5
For case 3, you ask the pulmonologist for additional material for...

- Culture
- Flow cytometric analysis
- Molecular testing
Case 3

**Pap-stained Slide and Cell Block**

**Differential Diagnosis**
- Lung adenocarcinoma
- Metastatic adenocarcinoma
- Poorly-differentiated squamous cell carcinoma

**Discussion and Follow-up**
- L858R EGFR mutation in Exon 21 – treated with tyrosine kinase inhibitor therapy
- EGFR mutated lung adenocarcinomas more likely to retain glandular and/or papillary architecture and have vacuolated cytoplasm than KRAS mutated tumors
- Palliative radiation to cervical spine
- Follow-up at outside facility, but deceased 2 years post-diagnosis

Case 4

**Clinical Presentation**
- 44-year-old female never-smoker admitted through ED with pleuritic chest pain; no history of immunocompromised state
- 1.8 cm right lower lobe mass and 2 pleural-based wedge-shaped masses in right middle lobe
- EBUS-guided FNA of right lower lobe mass

**Modified Giemsa-stained Slide**
Polling Question 6
For Case 4, you ask the pulmonologist to collect additional material for...

- Culture
- Flow cytometric analysis
- Molecular testing

Differential Diagnosis

- Granulomatous process (sarcoid, infectious)
- “Sarcoid-like” reaction
  - Granulomas associated with a neoplastic process
    - Hodgkin lymphoma
    - Squamous cell carcinoma

Discussion and Follow-up – Case 4

- Granulomas from various infectious agents appear similar
- Lung cultures positive for *Cryptococcus neoformans*
- 5-20 μm with thick mucopolysaccharide capsule
- Organisms stain with GMS but capsule does not
- Capsule stains positive for mucicarmine, Alcian blue/PAS
- Single teardrop-shaped budding
- Possible exposure to pigeons roosting on her neighbor’s home
- Patient improved significantly with antifungal therapy

Case 5
Clinical Presentation
- 66-year-old male never smoker presented with persistent productive cough
- 7.4 x 5.7 cm left hilar soft tissue mass and PET positive lymphadenopathy
- EBUS-guided FNA of 2L lymph node

Polling Question 7
What is your adequacy assessment for Case 5?
- Lymphoid sample with granulomas
- Atypical cells present
- Suspicious for malignancy
- Positive for malignancy

Surgical Excision of 2L lymph node

Stains on 2L Lymph node excision – Case 5
- Sarcoid-like Reaction
- Reed-Sternberg Cells
- CD30
- EBER CISH
Differential Diagnosis

- Granulomatous process (sarcoid, infection)
- "Sarcoid-like" reaction
  - Granulomas associated with a neoplastic process
    - Classical Hodgkin lymphoma
    - Squamous cell carcinoma

Discussion and Follow-up — Case 5

- Atypical lymphoid cells at ROSE were few in number and missed
- Discussion with pulmonologist at ROSE revealed sarcoidosis and infection unlikely clinically
- Surgical excision important to confirm diagnosis
- Diagnosed with bulky 2A Classical Hodgkin disease
- Received 6 cycles of chemotherapy
- Currently 9 years post-diagnosis and in remission

Case 6

Clinical Presentation

- 63-year-old male with history of right upper arm melanoma 2 years prior
- Large right upper lobe mass with mediastinal and hilar adenopathy
- EBUS-guided FNA of 2R lymph node

Polling Question 8
What additional testing should be performed for this case?

- ALK
- BRAF
- EGFR
- PD-L1

Modified Giemsa-stained Slide — Case 6
Pap-stained Slide – Case 6

Cell block Slide – Case 6

Immunostains – Case 6

Differential Diagnosis

• Poorly-differentiated non-small cell carcinoma
• Malignant melanoma
• Anaplastic large cell lymphoma

Discussion and Follow-up – Case 6

• Classical melanoma cytologic features
  • Plasmacytoid shape
  • Large cells with bi- or multi-nucleation
  • Macronucleoli
  • Intranuclear inclusions
• IHC positive for Melan-A, S-100 protein, MITF
• IHC negative for TTF-1 and cytokeratin AE1/3
• Molecular testing positive for BRAF V600E mutation
• Treated with ipilimumab
• Deceased 5 months after diagnosis

Case 7
Clinical Presentation

- 59-year-old male smoker with history of liver transplant 5 years ago
- 2.3 cm right upper lobe hilar lesion
- EBUS-guided FNA of right upper lobe lung lesion

Polling Question 9
What is your adequacy assessment for Case 7?
- Non-diagnostic
- Atypical cells present
- Suspicious for malignancy
- Positive for malignancy

Differential Diagnosis

- Squamous cell carcinoma in situ
- Invasive squamous cell carcinoma
- Atypical keratinizing metaplasia
- Cavitary infectious process
Discussion and Follow-up – Case 7

- Classic squamous cell carcinoma morphology
  - Large thick syncytial clusters with spindled cells
- Right upper lobectomy - 2.5 cm invasive poorly-differentiated squamous cell carcinoma
- All nodes negative
- Patient doing well 6 years after diagnosis, quit smoking in January 2020 after 44 years

Clinical Presentation

- 66-year-old male with recent outside diagnosis of squamous cell carcinoma, here for nodal staging
- 9.2 x 8.7 cm right upper lobe mass with right hilar lymphadenopathy
- EBUS-guided FNA of 11R lymph node

Polling Question 10
What is your adequacy assessment for Case 8?

- Non-diagnostic
- Atypical cells present
- Suspicious for malignancy
- Positive for malignancy
Immunostains – Case 8

Differential Diagnosis

- Squamous cell carcinoma with pseudoglandular morphology
- Poorly-differentiated adenocarcinoma
- Adenosquamous carcinoma

Discussion and Follow-up – Case 8

- Best to render diagnosis of non-small cell carcinoma with ambiguous morphology so molecular testing can be performed
- Both adenocarcinoma and squamous cell carcinoma components seen in the lymph node
  - p63 and p40 positive in some areas of tumor
  - TTF-1 and Napsin A positive in other areas of tumor
- Molecular testing positive for ALK (2p63) translocation
- Progressed on chemotherapy with adrenal and brain metastases
- Palliative radiation to chest wall/RUL mass
- Patient transferred to hospice

Summary

- Review pertinent clinical history and imaging prior to EBUS procedure
- Important to determine specimen adequacy and triage specimens for additional appropriate testing (i.e. culture, flow cytometric analysis, molecular testing) during rapid on-site evaluation of EBUS-guided FNA
- Ancillary studies may be necessary for definitive diagnosis
- Surgical excision may be required for definitive diagnosis is selected cases

Thank you for attending!

Questions? boothc1@ccf.org