An Update on EBUS Cytopathology

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Real-time endobronchial ultrasound guided transbronchial needle aspiration for sampling mediastinal lymph nodes

Endobronchial Ultrasound (EBUS) Diagnosis for Lung...
health.ucsd.edu/specialties/pulmonary/procedures/.../endobronchial.aspx
Endobronchial ultrasound (EBUS) is a relatively new procedure used in the diagnosis of lung cancer, infections, and other diseases causing enlarged lymph...
OUTLINE

1. Why EBUS?: Dx of Mediastinal/Lung Lesions
   - Approach to Diagnosis of Mediastinal Lesions
   - EBUS/EUS FNA
   - Clinical Perspective

2. Cytology Perspective
   - Rapid On-Site Evaluation (ROSE)
   - Adequacy Assessment

3. Case-Based Discussion (DDx & Pitfalls)
   - Cases

4. Conclusions
Mediastinal Mass: DDx

Non-neoplastic
- RLH
  - Granulomatous
    - Sarcoidosis
    - Infectious
  - Other

Neoplastic
- Lymphoma
  - NHL
  - HL
- Primary
- Metastases
  - Lung Ca
  - Other

5T’s
Imaging & Diagnosis of Mediastinal/Lung Lesions

- Imaging Modalities
  - Chest Xray
  - CT Scan
  - PET CT Scan

- Diagnostic Modalities
  - Sputum/BAL/BB/BW/PI FI
  - CT-Guided FNA
  - Transbronchial FNA (Wang Bx)
  - Mediastinoscopy/Thoracoscopy
  - EBUS & EUS guided FNA
EBUS/EUS FNA

- 1st available in 2004-2005
- Minimally invasive
- Real-time image guidance

Indications:
- Staging
- Dx of lung or mediastinal mass
- Dx of +CT/PET findings

Among patients with clinical stage IIIA, 40% of patients were down-staged with EBUS-FNA
Gilbert S et al. JTCVS 2009
EBUS/EUS FNA

**Advantages:**
- Minimally invasive
- Image guidance
- Tissue confirmation of +PET/CT findings & evaluation of LNs <1 cm
- Broad sampling capability
- On-site evaluation → triage

**Disadvantages:**
- Inability to access all LNs
- Not universally available
- Time requirement
- Experience
- Non-diagnostic specimens

Varela-Lema L et al., *Eur Repir J*, 2009
EBUS/EUS: Special Situations

- Restaging
- Small LNs < 1 cm
- Poor Operative Candidates
- Non-Surgical Diseases
Cost of EBUS/EUS FNA

EBUS/EUS-FNA
Cost = $2,000

Mediastinoscopy
Cost = $8,000

Thoracotomy
Cost = $26,000

Cut cost

RISKS
Clinical Algorithm

Suspected Mediastinal Lymphadenopathy

CT or CT/PET scan

LN size > 1 cm
PET positive
EBUS
Diagnostic
Positive
Specific Diagnosis (e.g.: sarcoid)
LN tissue negative for cancer
Surgical LN biopsy
Treatment

LN size < 1 cm
PET negative
EBUS
Non-Diagnostic
Negative
LN tissue negative for cancer
Specific Diagnosis (e.g.: sarcoid)
Surgical LN biopsy
Treatment

Non-Diagnostic
Positive
Specific Diagnosis (e.g.: sarcoid)
LN tissue negative for cancer
Surgical LN biopsy
Treatment

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Gilbert S et al. JTCVS 2009
<table>
<thead>
<tr>
<th>Study</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>Khazai L et al</td>
<td>69% (histological follow-up)</td>
<td>99% (histological follow-up)</td>
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<tr>
<td>Cytojournal 2011</td>
<td>95-97% (clinical &amp; histological follow-up)</td>
<td>99% (clinical &amp; histological follow-up)</td>
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<tr>
<td>Sun W et al</td>
<td>89% (histological follow-up)</td>
<td>96% (histological follow-up)</td>
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<tr>
<td>Diag Cytopath 2010</td>
<td></td>
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<tr>
<td>Gilbert S et al</td>
<td>88% (histological follow-up)</td>
<td>100% (histological follow-up)</td>
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<tr>
<td>Ann Thorac Surg 2009</td>
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<tr>
<td>Feller-Kopman D et al</td>
<td>85% (histological follow-up)</td>
<td>100% (histological follow-up)</td>
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<tr>
<td>Cancer Cytopathology 2009</td>
<td>95% (clinical &amp; histological follow-up)</td>
<td></td>
</tr>
<tr>
<td>Alsharif M et al</td>
<td>86% (histological follow-up)</td>
<td>100% (histological follow-up)</td>
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</table>
EBUS FNA & EUS FNA
for Mediastinal Masses

**EBUS FNA**
- USG thru **bronchus**
- **Anterior** mediastinum
- **Limitation:**
  - Inability to access posterior & inferior
- Sen generally >80%
- Spec generally >98%

**EUS FNA**
- USG thru **esophagus**
- **Posterior** mediastinum
- **Limitation:**
  - Inability to access anterior & superior
- Sen generally >80%
- Spec generally >98%
Sampling techniques and their diagnostic reach of mediastinal and hilar lymph node stations (1, highest mediastinal; 2, upper paratracheal; 4, lower paratracheal; 5, subaortic; 7, subcarinal; 8, paraesophageal; 9, pulmonary ligament; 10, hilar; 11, interlobar; and 12, lobar)

EBUS/EUS FNA

LN Stations

EBUS-TBNA and Mediastinoscopy
EBUS-TBNA
EUS-FNA

Yasufuku K et al. Chest 2006; 130: 710-18
EBUS FNA: Technical Aspects

- **Location:**
  - Bronchoscopy lab (conscious sedation)
  - Operating room (general anesthesia)

- **Equipment:**
  - Olympus bronchoscope + US probe + 22G FNA needle

- **Target:**
  - Identify with PET-CT
  - Confirm with real-time US guidance
EBUS Procedure

Subcarinal (Level 7)

A

B

C

D

Herth FJF et al. J Bronchol 2006; 13(2): 84-91
EBUS FNA: Technical Aspects

Courtesy of Dr. David Wilson, Department of Pulmonary Medicine, University of Pittsburgh Medical Center
EBUS/EUS: Clinical Perspective

- **Cancer vs. No Cancer**

- Adequacy of specimen: Need more passes?

- Adequate/sufficient for ancillary studies?

- More tissue needed: mediastinoscopy

- Communication: surgeon and cytology team
1. Why EBUS?: Dx of Mediastinal/Lung Lesions
   - Approach to Diagnosis of Mediastinal Lesions
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2. Cytology Perspective
   - Rapid On-Site Evaluation (ROSE)
   - Adequacy Assessment

3. Case-Based Discussion (DDx & Pitfalls)
   - Cases 1-12
   - Additional Cases (static images)
   - Additional Cases (virtual cases)

4. Conclusions
Cytology Perspective
EBUS/EUS FNA

Evaluation by Cytopathology

? Mediastinoscopy
Why Rapid On-Site Evaluation (ROSE)?

1. Immediate feedback
2. Assessment of adequacy
3. High-quality smears/CB
4. Triage: Flow Cytometry, Cultures, etc
5. Rapid Diagnosis: Management
Patient with enlarged & palpable mass

FNAB performed

ALWAYS

Smears

RPMI

Sterile Tube

Cell Block Material

Flow Cytometry

Microbiology

FISH Cytogenetics

IHC

? Infexn

? Lymphoma

? Ancillary Studies

? Infexn

? Ancillary Studies
EBUS FNA: Inadequate/NonDx

EBUS FNA: Adequate/Positive
Benign bronchial cells

Lesional cells
Benign Components in EBUS-FNA

- Lymphocytes
- Bronchial Cells
- Cartilage
- Anthracotic Pigment Laden Macrophages
- Mucus
- Squamous cells
Issues in Implementation of EBUS/EUS Service

- **Time requirement**  
  (longer at start; # days coverage)

- **Where will you go?**  
  (OR vs. Bronch Lab)

- **What will you use?**  
  (cart, FS room, own space; light; masks)

- **Who will go?**  
  (cytotech, fellow, pathologist)

- **How to collect specimen?**  
  (formalin, Thin Prep, other media)

- **ROSE? Telecytology?**
Issues in Implementation of EBUS/EUS Service

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- **ROSE? Telecytology?**

**STAGGERING STATIONS**

1\textsuperscript{st} pass LN#1

1\textsuperscript{st} pass LN#2

1\textsuperscript{st} pass LN#3

2\textsuperscript{nd} pass LN#1

2\textsuperscript{nd} pass LN#2

2\textsuperscript{nd} pass LN#3
Issues in Implementation of EBUS/EUS Service

- **Billing** (documentation per pass)
- **Reporting** (preliminary, final)

**INTRAPROCEDURAL RESULTS:**

**TIME:** 12:20, 12:22 PM
FNA OF: LYMPH NODE, SUBCARINAL, EBUS-GUIDED FNA
PART: 1
PASSES: 1,2
   A. LESS THAN OPTIMAL-MATERIAL COLLECTED FOR ANCILLARY STUDIES
   B. DEFER
   C. SUSPICIOUS FOR METASTATIC CARCINOMA

**TIME:** 12:25 PM
FNA OF: LYMPH NODE, SUBCARINAL, EBUS-GUIDED FNA
PART: 1
PASS: 3
   A. ADEQUATE-MATERIAL COLLECTED FOR ANCILLARY STUDIES
   B. POSITIVE FOR MALIGNANT CELLS
   C. METASTATIC ADENOCARCINOMA

PASSES 4,5 COLLECTED ENTIRELY FOR CELL BLOCK
OUTLINE

1. Why EBUS?: Dx of Mediastinal/Lung Lesions

2. Cytology Perspective

3. Case-Based Discussion (DDx & Pitfalls)
   - Adequacy
   - Granulomas
   - Bland-appearing neoplasms
   - Non-small cell carcinoma
   - Neuroendocrine tumors
   - Lymphoma
   - Background material

4. Conclusions
Case 1: EBUS FNA

- 69/F with NSCLC and mediastinal LAD.
- EBUS FNA of Rt hilar LN.
Case 1

Diagnosis

"LN", Right hilar, EBUS FNA:

- Unsatisfactory for evaluation.
- Non-diagnostic specimen.
  - Insufficient lymphoid cells.
**Diagnosis**

- LN, Subcarinal, EBUS FNA:
  - Adequate.
  - Negative for malignant cells.
Spectrum of Diagnoses in EBUS-FNA

- Unsatisfactory
- Satisfactory - Negative
- Satisfactory - Positive
EBUS FNA Adequacy

- Usually 3-5 passes

- Adequate if:
  - Malignant lesion is identified
  - Lesional material (e.g. granulomas)
  - Sufficient nodal tissue is obtained
    - Numerous lymphocytes
    - Anthracotic pigment-laden macrophages
    - Germinal center fragments
Anthracotic Pigment Laden Macrophages
How many lymphocytes do I need to see? 

- <40 hpf
- 40 hpf
- >40 hpf

hpf = 40x objective (x400 magnification)
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>UNSAT Cases # (%)</th>
<th>LTO Cases # (%)</th>
<th>Total # (%)</th>
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<tbody>
<tr>
<td><strong>BENIGN</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Benign lymphoid tissue</td>
<td>16 (53.3%)</td>
<td>32 (58.2%)</td>
<td>48 (56.5%)</td>
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<tr>
<td>Benign lymph node with scar/fibrosis</td>
<td>1 (3.3%)</td>
<td>0 (0%)</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Non-necrotizing granulomas</td>
<td>0 (0%)</td>
<td>5 (9.1%)</td>
<td>5 (5.9%)</td>
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<tr>
<td>Granulomas with hyalinization/fibrosis</td>
<td>5 (16.7%)</td>
<td>6 (11%)</td>
<td>11 (12.9%)</td>
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<tr>
<td>Necrotizing granulomas</td>
<td>1 (3.3%)</td>
<td>1 (1.8%)</td>
<td>2 (2.3%)</td>
</tr>
<tr>
<td><strong>MALIGNANT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>0 (0%)</td>
<td>1 (1.8%)</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma with fibrosis</td>
<td>3 (10%)</td>
<td>1 (1.8%)</td>
<td>4 (4.7%)</td>
</tr>
<tr>
<td>Classical Hodgkin lymphoma</td>
<td>3 (10%)</td>
<td>6 (10.9%)</td>
<td>9 (10.6%)</td>
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<tr>
<td>Squamous cell carcinoma</td>
<td>0 (0%)</td>
<td>1 (1.8%)</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>0 (0%)</td>
<td>1 (1.8%)</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Necrotic tumor</td>
<td>1 (3.3%)</td>
<td>1 (1.8%)</td>
<td>2 (2.4%)</td>
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<tr>
<td><strong>Total cases with follow-up</strong></td>
<td>30</td>
<td>55</td>
<td>85</td>
</tr>
</tbody>
</table>
• Cohesion;
• Low N/C ratio
• No nuclear enlargement, x2
• No significant pleomorphism
• Only reactive/degenerative atypia
38/M with mediastinal LAD

- **Diagnosis**
  - LN, Subcarinal, EBUS FNA:
    - Non-necrotizing granulomatous inflammation
    - Clinically compatible with sarcoidosis
**Diagnosis**

- Lymph node, Mediastinal.
  - EUS FNA:
    - Positive for malignant cells.
    - Malignant NHL, high-grade.

**Pitfall:** Tumor with granulomas

**Dx:**

Metastatic Seminoma.

68/M with mediastinal LAD. EUS FNA performed of LN.
71/F with mediastinal LNs and a lung mass. EBUS of precarinal LN.

**Diagnosis**

- LN, Precarinal, EBUS FNA:
  - Positive for malignant cells.
  - Metastatic Adenocarcinoma.
60/M with multiple FDG-avid lung nodules. EUS FNA: PTC
83/M with Hx of prostate ca and melanoma. EBUS of subcarinal LN
58/M with a large anterior mediastinal mass
Mediastinal Mass, Anterior, FNA:

- Thymic neoplasm

Pitfall of epithelial cells with lymphoid cells. Remember the 5T’s
Conclusions

- EBUS/EUS FNA have changed the way that thoracic & mediastinal lesions are approached

- The EBUS/EUS FNA diagnoses can be difficult & challenging
  - Be aware of pitfalls
  - Consider the wide spectrum of conditions in the mediastinum
  - Cytomorphology & ancillary studies can help to make a definitive dx in most cases
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Q & A