EBUS-TBNA of hilar and mediastinal lymphadenopathy in extrathoracic malignancy

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Introduction

- Lung cancer accounts for the majority of mediastinal LAP

- The mediastinum: one of the most frequent sites for malignant metastasis

- Spreading of malignancy
  - May be occurred by lymphatic or hematogeneous routes

- Mediastinal LN is a frequent diagnostic dilemma
Introduction

- In patients with concurrent or previously diagnosed extrathoracic malignancy
- Intrathoracic hilar and/or mediastinal nodal enlargement is a common finding
  - CT of thorax
  - PET-CT
- Up to 30% of extrathoracic malignancy cases could metastasize to the mediastinum
- Early identification of metastasis is important for the treatment strategy and prognosis
Clinical scenarios

- Screening lungs
- As a initial procedure
  - Diagnosing
  - Staging
  - Affects treatment option and prognosis
- After a curative treatment
  - May imply relapse
  - May be from primary intrathoracic malignancy
  - May be from granulomatous diseases

EBUS-TBNA also can be used for molecular analysis
- Breast carcinoma
- Renal cell carcinoma
- Colorectal carcinoma
- Melanoma
- Others
Presentation of the mediastinal metastasis

- Symptoms and signs of the primary site
  - Respiratory symptoms and signs
    - Dyspnea
    - Hoarseness
    - Dysphagia
    - Chest pain
    - Cough
  - Radiologic findings
    - Chest X-Ray
    - Computed tomography of thorax
- PET
- **Tissue Confirmation**
- Attributing radiographic findings such as mediastinal lymphadenopathy without tissue confirmation as cancer recurrence can lead to unnecessary and toxic therapy.

Histopathologic confirmation is mandatory.
▪ In the past: mediastinoscopy was the only diagnostic procedure
  ▪ General anesthesia
  ▪ Hospitalization
  ▪ Difficulty after radiation therapy or chemotherapy
  ▪ Higher complication rate
  ▪ Only paratracheal and anterior subcarinal LNs

▪ Today cTBNA, EBUS and EUS are mostly used techniques
  ▪ EBUS-TBNA is a minimally invasive outpatient procedure
- 153 patients were evaluated for mediastinal enlarged LNs
- Non caseating granuloma was identified by EBUS-TBNA in 17 pts.
  - 9 patients of these 17, had prior history of cancer and none had prior history of granulomatous diseases
CONCLUSIONS

- All mediastinal adenopathy is not due to cancer recurrence

- "local sarcoid reactions" and "sarcoid like lymphadenopathy" have been described in patients with cancer

- Tb adenitis may occur in cancer patient
• Retrospectif multicenter study
• Patients with an active or previous diagnosed of extrathoracic malignancy
• Enlarged intrathoracic lymphadenopathy
• Who underwent EBUS-TBNA
• 161 patients with 196 LN
• Median size 25 mm
• Median pass 4

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>87 %</td>
<td>73 %</td>
<td>88%</td>
</tr>
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</table>
Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration for the Diagnosis of Intrathoracic Lymphadenopathy in Patients with Extrathoracic Malignancy: A Multicenter Study

Neal Navani, MD; Matthew Nankivell, MSc; Ian Woolhouse, MD; Richard N. Harrison,

J Thorac Oncol. 2011 September; 6(9): 1505–1509.

161 patients with extra-thoracic malignancy and intrathoracic lymphadenopathy

EBUS-TBNA (n=161)

- Metastasis from extra-thoracic malignancy (n=71)
- New lung cancer (n=20)
- Carcinoma of unknown primary (n=5)
- Sarcoidosis (n=14)
- Reactive lymph node (n=42)
- Inadequate or no sample (n=9)

Mediastinoscopy (n=9) and/or 6 months clinical follow-up
• 40% cases were diagnosed as a benign LNs in this study

• Only lymph node size found significantly associated with malignancy

• Every increase in lymph node size of 1 mm, the probability of the lymph node being malignant increases by 4%.
- 92 patients with extrathoracic malignancy
- EBUS-TBNA provided;

Sensitivity: 85%
NPV: 76%

EBUS prevented invasive procedure 61%
- 78 LN were sampled in 48 patients with extrathoracic malignancy
- At least three aspirations were performed for each LN

**Table 1: The distribution of previously diagnosed malignancies in patients with newly arising mediastinal and/or hilar lymph nodes**

<table>
<thead>
<tr>
<th>Malignancy</th>
<th>Frequency (n)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast carcinoma</td>
<td>22</td>
<td>45.8</td>
</tr>
<tr>
<td>Colon carcinoma</td>
<td>7</td>
<td>14.5</td>
</tr>
<tr>
<td>Cervix carcinoma</td>
<td>4</td>
<td>8.3</td>
</tr>
<tr>
<td>Gastric carcinoma</td>
<td>3</td>
<td>6.2</td>
</tr>
<tr>
<td>Renal cell carcinoma</td>
<td>4</td>
<td>8.3</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>2</td>
<td>4.2</td>
</tr>
<tr>
<td>Endometrium carcinoma</td>
<td>2</td>
<td>4.2</td>
</tr>
<tr>
<td>Malignant melanoma</td>
<td>2</td>
<td>4.2</td>
</tr>
<tr>
<td>Laryngeal carcinoma</td>
<td>2</td>
<td>4.2</td>
</tr>
<tr>
<td>Thyroid carcinoma</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td>Pancreatic carcinoma</td>
<td>1</td>
<td>2.1</td>
</tr>
</tbody>
</table>
Table 3: Comparison of EBUS-TBNA results and final diagnosis in patients with known extrathoracic malignancies

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Final diagnosis</th>
<th>EBUS-TBNA</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Malignancy</td>
<td>18</td>
<td>37.5</td>
</tr>
<tr>
<td>Breast</td>
<td>10</td>
<td>20.8</td>
</tr>
<tr>
<td>Colon</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td>Gastric</td>
<td>2</td>
<td>4.2</td>
</tr>
<tr>
<td>Renal</td>
<td>2</td>
<td>4.2</td>
</tr>
<tr>
<td>Endometrium</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td>Malignant melanoma</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>6</td>
<td>12.5</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>4</td>
<td>8.3</td>
</tr>
<tr>
<td>Reactive adenitis</td>
<td>20</td>
<td>41.6</td>
</tr>
</tbody>
</table>

14 of 33 benign cases underwent m.copy
The rest were followed radiologically.
Of 48 cases, only 18 (37.5%) were found to have a malignancy.

The majority of the cases were diagnosed with granulomatous diseases or benign conditions (62.4%)
- granulomatous diseases (20.8%)
- other benign conditions (41.6%)

The sensitivity of EBUS-TBNA for malignancy was 83.3%

The negative predictive value for malignancy was 90.9%

Procedure-related complications were minor bleeding in two cases and slight reversible oxygen desaturation in one case.
6 studies with 533 patients were included
Our study was in placed in this meta-analysis

- Pooled estimated sensitivity 85%
- Pooled estimated specificity 99%
- Lymph node size ranged from 2 to 50 mm.
- The target lymph node was punctured one to six times
- 21 or 22 gauge needle were used

**Conclusion:** EBUS-TBNA has high degree of diagnostic accuracy for diagnosing intrathoracic lymph node metastases in patients with extrathoracic malignancies
<table>
<thead>
<tr>
<th>Author</th>
<th>Case</th>
<th>Rate of metastasis</th>
<th>Granuloma</th>
<th>Second primary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jae-Uk Song (2011)</td>
<td>57</td>
<td>61.9%</td>
<td>8.7%</td>
<td></td>
</tr>
<tr>
<td>Neal Navani (2014)</td>
<td>161</td>
<td>52.1%</td>
<td>9%</td>
<td>16.1%</td>
</tr>
<tr>
<td>Jinkyeong Park (2011)</td>
<td>57</td>
<td>61.4%</td>
<td></td>
<td>3.5%</td>
</tr>
<tr>
<td>Marcus P Kennedy (2008)</td>
<td>115</td>
<td>50.4%</td>
<td>7.8%</td>
<td></td>
</tr>
<tr>
<td>Jose Sanz-Santos (2013)</td>
<td>117</td>
<td>43.5%</td>
<td>5.1%</td>
<td>28.2%</td>
</tr>
<tr>
<td>Torun E. (2012)</td>
<td>48</td>
<td>37.5%</td>
<td>20.8%</td>
<td></td>
</tr>
<tr>
<td>K. G. Tournoy (2010)</td>
<td>92</td>
<td>53.2%</td>
<td>5.4%</td>
<td>13%</td>
</tr>
</tbody>
</table>
Case 1

- 52 year old woman
- Nonsmoker
- She was operated with diagnosis of breast cancer in 2010
- After chemotherapy, she had followed by CT
- Mediastinal LNs enlargement was detected on CT in 2015
- Increased FDG uptake of lymph nodes were also present
Case 1

- **Clinical scenarios**
  - Mediastinal LN metastasis from breast cancer?
  - New malignancy with unknown origin?
  - Granulomatous lymphadenitis?
  - Reactive lymph adenitis?
Case 1
Case 1

Questions
- Best treatment option?
- Prognosis?
- Estrogen and progesterone status are the determinants of prognosis
- If estrogen and progesterone are negative, recurrences are more likely
- Estrogen and progesterone status can be identified by EBUS-TBNA

![Images of estrogen and progesterone staining]

**Estrogen**

**Progesterone**
Case 2

- 65 y.o male
- Smoker
- He had submandibular mass lesion
- FNA was resulted with squamous Ca
- Mediastinal LN enlargement was seen at 4R
- High FDG affinity was seen
Case 2

- Clinical scenarios
  - Mediastinal LN metastasis from submandibuler cancer?
  - New malignancy with unknown origin?
  - Granulomatous lymphadenitis?
  - Reactive lymph adenitis?
Case 3

- 50 y.o male
- Exsmoker
- He has been suffered from non Hodgkin lymphoma since 2000
- Recurrence in 2007
- Mediastinal LN enlargement was seen at 4R on CT of thorax
Case 3

Clinical scenarios

• Recurrence of lymphoma?
• New malignancy with unknown origin?
• Granulomatous lymphadenitis?
• Reactive lymph adenitis?

Adeno carcinoma of the lung
Case 4

- 75 y.o man
- Prostate cancer, 5 years ago (RT)
- He has been suffered from SOB, cough for 3 months
- He has been diagnosed as sarcoidosis without biopsy and received systemic corticosteroid
- He was admitted with SOB, cough
Case 4

Clinical scenarios
- Prostate cancer metastasis?
- Sarcoidosis?
- Tuberculosis?
- Secondary cancer?
Case 4

- EBUS TBNA was performed and 4R was sampled

Squamous ca (primary lung carcinoma)
Case 5

- 44 y.o. Male
- He has been suffered from seminoma since 2015
- He was operated and
- Treated with RT in 2015
- Metabolically active subcarinal lymph node discovered in 2017 Feb.
- No other LN or metastasis
- SUV was measured as 12.4
- EBUS-TBNA was performed in our center

Metastasis of germ cell tumor
Case 6

- 53 years old, female
- No pulmonary symptom
- Medical history: gastric cancer (3 years ago)
  - Total gastrectomy
  - Signet-ring cell adenocarcinoma
    - After 2 years follow up period CEA level increased
    - No local relapse was detected
- Nonsmoker
- No additional disease history
Atypical cells with clear or foamy cytoplasm were observed in signet-ring cell morphology.
Take Home Messages

- Differentiation between metastasis and development of secondary malignancy is important

- Lymphadenopathy can be tuberculosis, sarcoidosis or reactive lymphadenitis

- Tissue confirmation is mandatory for defining prognosis and treatment plan

- EBUS-TBNA can be used as a first step minimally invasive technique for tissue confirmation

- EBUS-TBNA can be used for molecular tests

- If EBUS-TBNA is negative, mediastinoscopy should be used as needed procedure
Thank you..

ευχαριστώ...