A Practical Approach to Mediastinal Biopsies

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Mediastinal Pathology Made Ridiculously Simple
Facts

- The most common tumor in the mediastinum is Lymphoma; however, the most popular is Thymoma.
- Because we do not see mediastinal (thymic) tumors often, we feel uncomfortable and if we add the controversial issues regarding classifications schemas – we do not like to deal with it.
- The lack of knowledge regarding IHC in normal thymus often leads to incorrect interpretations.
- Generally, these are small biopsy material.
Mediastinum

• Biopsy material is commonly obtained in two forms:
  – Mediastinoscopic biopsy (core biopsy) – more common
  – Open thoracoscopic biopsy
• Cytology FNA.
Let us start with Normal Histology
IHC of Normal Thymus

- Pan Keratin
- Keratin 5/6
- P40
- P63
- CD10
- MIC2 (O13)
- Nerve growth factor
- Epidermal growth factor
- S-100 protein
- CD45
- CD20
- CD1a
- CD8
- CD4
- CD23
- Tdt
- XIAP (X-linked inhibitor of apoptosis protein)
Role of IHC

• It should be used as an aid to the diagnosis.
• The interpretation of the IHC results should be within the context of the morphology of the tumor.
• The best approach is to perform a panel rather than just one or two stains.
• Even though the use of IHC may highly suggest a particular entity, it should not be viewed as “pathognomonic.”
Two Distinct Approaches

- Clinical
  - Gender
  - Age
  - Associated Medical Condition

- Histological
  - Mixed population (lymphocytes and epithelial cells) or one predominates over the other.
  - Spindle cells
Clinical Approach

• Man < 35 years
  – Germ cell tumor
  – Mediastinal Lymphoma
  – Gray zone lymphoma
  – Hodgkin Lymphoma
    • If history of MEN
      – NEC

• Man > 35 years
  – Thymoma/Thymic Carcinoma
  – Lymphoma, large B-cell
  – Hodgkin Lymphoma
Clinical Approach

• Woman <35 years
  – PMBCL (ML sclerosis/Clear cell lymphoma)
  – Hodgkin lymphoma
  – If history of Collagen vascular disease (Sjogren’s syndrome)
    • MALT lymphoma

• Woman > 35 years
  – Thymoma/Thymic carcinoma
  – NEC
  – Hodgkin lymphoma
Histological Approach

• Biphasic cellular proliferation
  – Normal thymus
  – Thymic hyperplasia
  – Thymoma/Carcinoma
  – MTC

• Spindle cells
  – Thymoma
  – Thymic carcinoma
  – Sarcoma
What to do?

• Practical approach:
  – Depending on the type of material obtained in the biopsy, one should be able to lead not only the morphological approach but also the immunohistochemical panel that most likely will provide the desirable result.
  – The most common markers will include: epithelial and lymphoid markers.
IHC

**Thymoma**
- All epithelial and lymphoid markers commonly used for thymoma will also show positive staining in normal thymus

**Normal thymus / thymic hyperplasia**
- All epithelial and lymphoid markers staining normal thymus may also show positive staining in thymomas with lymphoid component.
Differential Diagnosis

- Any mediastinal tumor with spindle cell morphology should raise the following possibilities:
  - Spindle cell thymoma
  - Spindle cell carcinoid tumor
  - Solitary fibrous tumor
  - Spindle cell sarcoma
    - Monophasic synovial sarcoma
Differential Diagnosis

Spindle cell carcinoid

Spindle cell thymoma
**IHC**

<table>
<thead>
<tr>
<th>Spindle cell carcinoid</th>
<th>Spindle cell thymoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Keratin +</td>
<td>• Keratin +</td>
</tr>
<tr>
<td>• Keratin 5/6 –</td>
<td>• Keratin 5/6 +</td>
</tr>
<tr>
<td>• <strong>Chromogranin</strong> +</td>
<td>• Chromogranin –</td>
</tr>
<tr>
<td>• <strong>Synaptophysin</strong> +</td>
<td>• Synaptophysin -/+</td>
</tr>
<tr>
<td>• CD-56 +</td>
<td>• CD-56 –</td>
</tr>
<tr>
<td>• EMA +</td>
<td>• EMA –</td>
</tr>
<tr>
<td>• TTF-1 + (about 40-50%)</td>
<td>• TTF-1 -/+ (few cases)</td>
</tr>
<tr>
<td>• Bcl-2 -</td>
<td>• Bcl-2 -/+ (few cases)</td>
</tr>
</tbody>
</table>
Differential Diagnosis

Spindle cell thymoma

Solitary fibrous tumor
IHC

Spindle cell thymoma
• Keratin +
• Keratin 5/6 +
• EMA –
• TTF-1 -/+ (few cases)
• Bcl-2 -/+ (few cases)
• CD-34 –
• STAT6 -

Solitary fibrous tumor
• Keratin –
• Keratin 5/6 –
• EMA –
• TTF-1 –
• Bcl-2 +
• CD-34 +
• STAT6 +
Differential Diagnosis

Monophasic synovial sarcoma

Spindle cell thymoma
IHC

**Monophasic synovial sarcoma**
- Keratin + (focal)
- Keratin 5/6 –
- EMA + (focal)
- TTF-1 –
- Bcl-2 +
- CD-34 + (in some cases)

**Spindle cell thymoma**
- Keratin +
- Keratin 5/6 +
- EMA –
- TTF-1 -/+ (few cases)
- Bcl-2 -/+ (few cases)
- CD-34 –
Differential Diagnosis

• Atypical thymoma should be distinguished from the following:
  – Thymic carcinoma – keratinizing and non-keratinizing.
  – Seminoma
IHC

**Atypical thymoma**
- Pan keratin +
- Keratin 5/6 +
- CD-5 + (about 50-60%)
- P63 +
- P40 +
- EMA +
- CD117 – (in a few cases focally+)
- Tdt +
  - Plasma cell absent

**Thymic carcinoma**
- Pan keratin +
- Keratin 5/6 +
- CD-5 +
- P63 +
- P40 +
- EMA +
- CD117 +
- Tdt –
  - Plasma cells present
Conclusions

• Mediastinal Pathology is very diverse and can harbor tumor of different lineages.
• Mediastinoscopic biopsies should be properly addressed on morphology and a panel of immunohistochemistry.
• Most important is to determine that the lesion is indeed in the mediastinum.
• Proper imaging and clinical correlations are important in arriving at a more accurate diagnosis.
Thank you