Spindle Cell Conundrums in the Chest
2019 Anatomic Pathology Update
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Why a Lecture on Spindle Cell Lesions?

- Frequent problem
- Challenge on small biopsies
- Wide spectrum of possibilities
- Treatment variable
- IHC triage necessary
What do we mean by spindle cells?

- Elongate cytoplasm
- Indistinct cell borders
- Variable amounts of cytoplasm, but frequently minimal
- Cytology often deceptively bland or low grade
Outline

• Neoplastic vs. non neoplastic
• Low grade pulmonary lesions
• Metastatic lesions
• High grade pleuropulmonary neoplasms
• Approach with IHC
Are the Spindle Cells Neoplastic or Not?
Organizing Pneumonia
# CT Findings in Organizing Pneumonia

<table>
<thead>
<tr>
<th>Pattern</th>
<th>Percent (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consolidation</td>
<td>80</td>
</tr>
<tr>
<td>Bilateral</td>
<td>74</td>
</tr>
<tr>
<td>Migratory</td>
<td>12</td>
</tr>
<tr>
<td>Diffuse reticular</td>
<td>10</td>
</tr>
<tr>
<td>Mass-like</td>
<td>8</td>
</tr>
<tr>
<td>Cavitary</td>
<td>2</td>
</tr>
</tbody>
</table>

Drakopanagiotakis F et al. Chest 2011;139:893-900
Mass-like Organizing Pneumonia

- Asymptomatic – 62%
- H/O malignancy or smoking ~25%
- Contrast enhancement on CT and PET positive
- 90% idiopathic, 10% post infectious

Aspiration without Food or Particulate Matter

Histology

<table>
<thead>
<tr>
<th>Pattern</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organizing pneumonia</td>
<td>40</td>
</tr>
<tr>
<td>Diffuse alveolar damage</td>
<td>30</td>
</tr>
<tr>
<td>Chronic bronchiolitis</td>
<td>30</td>
</tr>
</tbody>
</table>

Yousem SY and Faber C. Am J Surg Pathol 2011;35:426-431
37 year old man with solitary lung mass
Non Neoplastic Inflammatory “Pseudotumor”

My Diagnosis: OP with prominent lymphoplasmacytic infiltrates

Keratin, CD34, alk negative
14 year old boy with solitary lung mass
“Neoplastic Inflammatory Pseudotumor”
Inflammatory Myofibroblastic Tumor

Alk
Inflammatory Pseudotumors

• Non-Neoplastic variants
  – Plasma cell granuloma
  – Lymphoplasmacytic/plasma cell type
  – Organizing pneumonia type
  – IgG4-related
Inflammatory Pseudotumors

- Non-Neoplastic variants
  - Plasma cell granuloma
  - Lymphoplasmacytic/plasma cell type
  - Organizing pneumonia type
  - IgG4-related
Inflammatory Pseudotumors

- Neoplastic- inflammatory myofibroblastic tumor
  - Fibrous histiocytoma
  - Inflammatory fibrosarcoma
  - Plasma cell granuloma
  - Inflammatory fibromyxoid tumor
Inflammatory Pseudotumors

• Neoplastic
  – Inflammatory myofibroblastic tumor
  – Fibrous histiocytoma
  – Inflammatory fibrosarcoma
  – Plasma cell granuloma
  – Inflammatory fibromyxoid tumor

Metastasis!
Inflammatory Pseudotumors

- Neoplastic variants more common in children
  - alk rearranged in 40-60%
- Adult pulmonary tumors
  - alk rearranged in 30-50%
- Specificity limited
- ROS-1, RET, ETV-6

IgG4-Related Disease

• Major criteria- 2/3 needed for dx
  – Dense lymphoplasmacytic infiltrate
  – Fibrosis, focally storiform
  – Obliterative phlebitis

• Additional characteristic features
  – Phlebitis without obliteration
  – Increased tissue eosinophils

• Exceptions exist in lung, LN, minor salivary and lacrimal glands (fibrosis and phlebitis may be absent)
IgG4-related Disease

Radiologic Patterns of Lung Involvement

- Solitary nodule (+/- ground glass opacity)
- Consolidation, unilateral or bilateral
- Interstitial lung disease
IgG 4-related Disease
Quantitation

- Serum IgG4 concentrations normal-40%
- IgG4 + cells/IgG plasma cells > 40% mandatory
- > 20-50 IgG4 + cells/hpf (3- 40x fields)

Deshpande V et al. Modern Pathol 2012; 1-12
History

49 year old man with posterior flank pain
## Solitary Fibrous Tumor

<table>
<thead>
<tr>
<th>IHC stain</th>
<th>% Positive</th>
</tr>
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<tbody>
<tr>
<td>Stat 6 nuclear</td>
<td>98</td>
</tr>
<tr>
<td>Stat 6 cytoplasmic</td>
<td>96</td>
</tr>
<tr>
<td>Bcl 2</td>
<td>95</td>
</tr>
<tr>
<td>CD34</td>
<td>93</td>
</tr>
<tr>
<td>𝛽 catenin</td>
<td>88</td>
</tr>
<tr>
<td>TLE</td>
<td>14</td>
</tr>
<tr>
<td>S100</td>
<td>7</td>
</tr>
<tr>
<td>PanKeratin</td>
<td>3</td>
</tr>
<tr>
<td>CAM 5.3</td>
<td>3</td>
</tr>
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</table>
## Predicting Recurrence in SFT

<table>
<thead>
<tr>
<th>Feature</th>
<th>Points</th>
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</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td></td>
</tr>
<tr>
<td>&lt; 55</td>
<td>0</td>
</tr>
<tr>
<td>≥ 55</td>
<td>1</td>
</tr>
<tr>
<td>Size (cm)</td>
<td></td>
</tr>
<tr>
<td>&lt; 5</td>
<td>0</td>
</tr>
<tr>
<td>5 to &lt; 10</td>
<td>1</td>
</tr>
<tr>
<td>10 to &lt; 15</td>
<td>2</td>
</tr>
<tr>
<td>≥ 15</td>
<td>3</td>
</tr>
<tr>
<td>Tumor necrosis (%)</td>
<td></td>
</tr>
<tr>
<td>&lt; 10</td>
<td>0</td>
</tr>
<tr>
<td>≥ 10</td>
<td>1</td>
</tr>
<tr>
<td>Mitoses/10hpf</td>
<td></td>
</tr>
<tr>
<td>&lt; 4</td>
<td>0</td>
</tr>
<tr>
<td>≥ 4</td>
<td>1</td>
</tr>
</tbody>
</table>

Low risk 0-3, Intermediate risk 4-5, High risk 6-7

Demicco EG et al Mod Pathol 2017:30: 1433-1442
Malignant SFT

Inc. cellularity

Necrosis

Mitoses
**Predicting Recurrence in SFT**

<table>
<thead>
<tr>
<th>Risk of metastasis at # years (%)</th>
<th>y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>0, 10 y</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>10, 10 y</td>
</tr>
<tr>
<td>High risk</td>
<td>73, 5 y</td>
</tr>
</tbody>
</table>
History

• A 73-year-old woman presented with a dominant lung mass

• Needle biopsy had been performed and diagnosed as “most consistent with epithelioid hemangioendothelioma”…but CD31 was negative
Diagnosis?

Most consistent with Metastatic Endometrial Stromal Sarcoma

Estrogen Receptor Protein
Uterus removed 20 years previously
Challenges in Dx of Metastatic ESS

• Unknown or misdiagnosis of uterine ESS
• Long tumor-free interval
• Unusual symptoms or radiologic presentation
  – Pneumothorax
  – Solitary nodule
  – Cystic lesions
  – Bilateral infiltrates mimicking interstitial ds
Metastatic ESS

• Histology parallels uterine primary
  – Spindle cells, ± smooth muscle or sex cord differentiation, hyaline fibrosis

• Immunohistochemistry
  – ER/PR/vimentin: ~ 100%
  – Actin/desmin/keratin/CD10: ~ 50%
  – Rarely positive: Inhibin, CAM 5.2, Chromogranin, HMB-45, CD34
Marked Interstitial Growth
Biphasic Appearance
Cysts: Macro
Cysts: Micro

CD10

ER
Metastatic ESS

Differential Diagnosis

• Epithelioid hemangioendothelioma
• Other metastatic spindle cell tumors (dermatofibroma, DFSP, other sarcomas, PEComa)
• Solitary fibrous tumor
• Synovial sarcoma
Epithelioid Hemangioendothelioma
Epithelioid Hemangioendothelioma

Ker

CD31
Metastatic Cellular Dermatofibroma
Metastatic Cellular Dermatofibroma

Factor XIIIa
Outline

• Neoplastic vs. non neoplastic
• Low grade pulmonary lesions
• Metastatic lesions
• High grade pleuropulmonary neoplasms
• Approach with IHC
Inflammatory Sarcomatoid Carcinoma

- Variant of Sa Ca with deceptively bland morphology
- Mimics
  - Inflammatory process
  - Lymphoma, incl HD
  - Inflammatory myofibroblastic tumor
  - Fibrous histiocytoma

Wick MR et al Hum Pathol 1995; 26:1014
Inflammatory Sarcomatoid Ca
Inflammatory Sa Ca with vascular invasion

Keratin
Inflammatory Sa Ca

- Occur in cigarette smokers
- Key features
  - Relatively bland spindle cells arranged in fascicles, haphazard configurations or storiform arrays
  - Assoc inflammatory infiltrate
  - Keloid-like fibrosis
  - Vascular invasion
  - Focal ordinary bronchogenic ca

Wick MR et al Hum Pathol 1995; 26:1014
Sarcomatoid Carcinoma
Differential Diagnosis

- Organizing pneumonia
- Inflammatory myofibroblastic tumor
- IgG 4-related sclerosing disease
- Lymphoma, particularly Hodgkin L.
- Malignant mesothelioma
Case History

- A 78 yr old man has a recurrent right pleural effusion for which he had talc pleurodesis.
- 1 yr later developed recurrent pleural effusion with nodularity.
- He undergoes VATS biopsy.
The single best IHC stain to order on this block is:

a. Ber EP4
b. CEA
c. CK7
d. MOC-31
e. Pan keratin
The diagnosis is:

a. Atypical/suspicious for malignancy
b. Desmoplastic mesothelioma
c. Fibrous pleurisy
d. Pleomorphic lung carcinoma
e. Solitary fibrous tumor
Sarcomatoid Mesothelioma-WHO

“Mesenchymal or spindle cell morphologic appearance.”
Sarcomatous Mesothelioma
Non-Desmoplastic Type

- No zonation
- Cellular
- Frankly malignant cytology
- May merge with epithelioid foci
- Identification of invasion not always necessary for diagnosis
Desmoplastic Mesothelioma

WHO

Dense collagenized tissue separated by malignant mesothelial cells arranged in a storiform or so-called patternless pattern, which must be present in at least 50% of the tumor.
Desmoplastic Mesothelioma

- No zonation
- Paucicellular
- Atypical cells hard to find
- Capillaries hard to find
- Invasion typically necessary
- Abrupt transitions to frankly cellular foci
- Bland infarct-like necrosis
Desmoplastic Mesothelioma

No atypia
No capillaries
Desmoplastic Mesothelioma - Invasion

Keratin
Desmoplastic Meso - invasion

Pl elastica
Desmo’ic Meso- abrupt ↑ cellularity
Bland Infarct-like Necrosis
## IHC: Sarcomatous Mesothelioma (%)

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Spindle Cell Carcinoma</th>
<th>Sarcomatous Mesothelioma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keratin (broad sp)</td>
<td>88</td>
<td>89</td>
</tr>
<tr>
<td>Calretenin</td>
<td>37</td>
<td>54</td>
</tr>
<tr>
<td>D2-40</td>
<td>20</td>
<td>74</td>
</tr>
<tr>
<td>WT-1</td>
<td>31</td>
<td>45</td>
</tr>
<tr>
<td>CK 5/6</td>
<td>0</td>
<td>26</td>
</tr>
<tr>
<td>TTF-1</td>
<td>~17</td>
<td>4.6</td>
</tr>
<tr>
<td>GATA-3</td>
<td>15 focal wk</td>
<td>100 strong diffuse</td>
</tr>
</tbody>
</table>

Stains not useful in most cases: CEA, CD15, MOC 31, etc.

Marchevsky AM Hum Pathol 2017;67:160-168
Spindle Cell Ca

Ker

orig. TTF-1

repeat TTF-1
Inconclusive Immunostains?

- When the immunostains don’t fit or are inconclusive, revert to gross/radiologic findings and H&E
- Some cases are insoluble: “Malignant tumor, carcinoma favored over mesothelioma”
Sarcomatous Meso vs. Other Sarcomatous Neoplasms

• Most sarcomatous mesos ker +
• Meso specific markers not very helpful
• Other tumor specific markers may be helpful- CD31, Fli-1, Erg
• May have to rely on imaging to distinguish from sarcomatoid ca
Monophasic Synovial Sarcoma

Keratin
First Round IHC

• Keratin-broad spectrum AE1/3, OSCAR, CAM 5.2
• NOT CK7/20
• Consider TTF-1
  – Primary site
  – Architecture- Is it invading lung?
Keratin – Benign/low grade
Sarcomatoid Ca (lung, kidney)
Mesothelioma
Carcinoid
Thymoma
Organizing Pn
IMT
Met ESS, DF, DFSP
SFT
Desmoid
Melanoma
Infectious Pseudoneoplasms
Keratin – High grade
Angiosarcoma
Synovial Sarcoma
EHE
Infectious Pseudoneoplasm
Questions?