Update: Morphologic Considerations in Mesothelioma within the Pleural and Peritoneal Cavities

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Objectives

* Review Historical Features associated with prognosis
* Present and describe the histologic subtypes
* Discuss the reproducibility and impact on prognosis of histologic subtypes
Based on a 1994 workshop by the International Association for the Study of Lung Cancer (IASLC), a staging system for pleural mesothelioma was instituted in the 6th (2006) and 7th (2010) AJCC system.

Validation of staging system was studied in 2012:
- 3101 patients were studied
- No evidence based recommendations could be made based on a lack of granular data
- 15 centers
Follow-up group from 29 centers was attempted to analyze the staging system

2460 patients were able to be analyzed

827 patients had pre-treatment info; 830 had post surgical data; 803 had both data elements

Limited ability to influence staging parameters
AJCC Histologic Type (Pleural)

- Epithelioid
- Biphasic (at least 10% of either element)
- Sarcomatoid
- Desmoplastic
Pleural Mesothelioma

**STAGE I**
Cancer is Localized in the Pleura

**STAGE II**
Cancer has spread to a single lung and lymph nodes

**STAGE III**
Tumor is extensive, spreading to the lungs, chest wall, abdomen, and cardiac cavity.

**STAGE IV**
Cancer has metastasized throughout the chest, abdomen, neck, and bones.
Peritoneal Mesothelioma

- Plaque
- Asbestos Fiber
- Mesothelioma Cell
- Peritoneum (Thin Layer That Covers the Abdominal Organs)
- Plaque
Historical Publications

* Distinguishing malignant vs benign

* Distinguishing metastasis vs mesothelioma

* Limited work separating out prognosis based on morphologic features
Pathologic parameters
(choose one option then delete the other option and delete this line)
- Depth of invasion: Superficially invasive (≤0.5 mm) / Deeply invasive (>0.5mm)
- Prominent desmoplasia: Yes / No
- Mitotic count: ≤5/50 hpf / >5/50hpf
- Nuclear grade: Low / High
- Lymph node metastases: Yes / No
- Sarcomatoid component: Yes / No
(Assessment of CDKN2A/p16 and NF2 by FISH, and BAP1 and PD-L1 by immunohistochemistry are pending; the results will follow in an addendum)
Nuclear grade (Cerruto et al)
### Table 4. Histologic Subtypes and Patterns of Malignant Mesothelioma

<table>
<thead>
<tr>
<th>Subtype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelioid mesothelioma</td>
</tr>
<tr>
<td>Tubulopapillary</td>
</tr>
<tr>
<td>Micropapillary</td>
</tr>
<tr>
<td>Trabecular</td>
</tr>
<tr>
<td>Acinar</td>
</tr>
<tr>
<td>Adenomatoid</td>
</tr>
<tr>
<td>Solid</td>
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<tr>
<td>Clear cell</td>
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<tr>
<td>Deciduoid</td>
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<tr>
<td>Adenoid cystic</td>
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<tr>
<td>Signet ring cell</td>
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<tr>
<td>Small cell</td>
</tr>
<tr>
<td>Rhabdoid</td>
</tr>
<tr>
<td>Pleomorphic</td>
</tr>
<tr>
<td>Sarcomatoid mesothelioma</td>
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<tr>
<td>Conventional, spindle cell</td>
</tr>
<tr>
<td>Desmoplastic</td>
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<tr>
<td>Heterologous differentiation (osteosarcomatous, chondrosarcomatous, etc)</td>
</tr>
<tr>
<td>Lymphohistiocytoid (may also be classified as epithelioid)</td>
</tr>
<tr>
<td>Biphasic/mixed</td>
</tr>
</tbody>
</table>

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Subtype must be given in the diagnosis, but histologic pattern, epithelioid or sarcomatous, may be described in a comment or microscopic description.
Reproducibility Studies for Epithelioid Subtypes

Pleural Reproducibility
- Acinar
- Adenomatoid
- Micropapillary
- Solid
- Tubulopapillary
- Trabecular

Peritoneal Reproducibility
- Tubulopapillary
- Micropapillary
- Trabecular
- Solid
- Pleomorphic
  - Papillary
  - Tubular
Epithelioid Subtypes – in pictures

Figure 1. Histological growth patterns of epithelioid malignant peritoneal mesothelioma (haematoxylin and eosin). A. Tubulopapillary growth pattern with varying combinations of tubules and papillary structures. B. Micropapillary growth pattern with small tufts of papillary structures lacking central fibrovascular cores. C. The trabecular pattern was only seen focally as a few cells infiltrating as cords (arrows). D. Solid growth pattern with sheets of tumour cells. E. Papillary growth pattern containing papillary structures with central fibrovascular cores. F. Tubular growth pattern with pure tubules and acini.
Definitions of papillary lesions have overlapping descriptions
Epithelioid Subtype – Decisions?
“Pure” Epithelioid Patterns rarely observed (19% in one study)
Most frequently (41%) observe three epithelioid morphologies
Solid subtype was most reproducible among four reviewers
Prognosis - Peritoneal

- Epithelioid Solid subtype associated with a shorter overall survival compared to tubulopapillary and micropapillary
- Mitotic index (>5/50 per high power field) associated with a poor survival
- Small study size (84 cases)
63 yo male who presented with abdominal pain and shortness of breath

Diagnosed with malignant mesothelioma

Treated with cisplatin and Alimta
Lymphocytic Response - Peritoneal

- Grade of lymphocytic host response
  - None-mild
  - Moderate
  - Severe
- May be relevant; reproducibility studies need to be performed/Image analysis

Diagram showing survival rates over time with different severity levels.
Epithelioid subtype mesothelioma frequently shows multiple morphologic patterns. Some morphologic patterns are associated with a lower survival. Lack of reproducibility and low case series to evaluate limit the ability to study the significance of epithelioid subtype morphology. Changing treatment paradigms will further complicate the assessment of epithelioid subtypes.
6. www.mesothelioma.com