Biopsy Interpretation of Spindle cell proliferations of the Serosa

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Spindle cell proliferations - Pleura

INFLAMMATORY
- Acute/Chronic Fibrous Pleuritis
- Specialised Forms of Pleuritis – TB, Xanthomatous, Eosinophilic

NEOPLASTIC
- Malignant Mesothelioma, sarcomatoid type
- Epithelial Tumors - Sarcomatoid Carcinoma, Thymomas
- Soft Tissue Tumors (various)
  - Solitary Fibrous Tumor
  - Synovial Sarcoma
  - Vascular sarcoma
  - Desmoplastic tumor/Fibromatosas
  - Calcifying Fibrous Pseudotumor
- Metastatic Tumors (various)

Spindle cell proliferations - Peritoneum

INFLAMMATORY
- Acute Difuse Peritonitis
- Specialised Forms of Peritonitis – Granulomatous peritonitis
- Peritoneal Adhesions
- Sclerosing Peritonitis - peritoneal dialysis, liver cirrhosis, long-standing shunt, thecomas, CVD
- Polyserositis
- Sclerosing Mesenteritis – Mesenteric Pancreatitis
Spindle cell proliferations - Peritoneum
Neoplasms & Tumor-like Lesions
• Malignant peritoneal mesothelioma, sarcomatoid type
• Metastatic Sarcomatoid Carcinoma
• Mesenchymal Tumors – Solitary Fibrous Tumor
  Omental – Mesenteric Fibromatosis
  Inflammatory Myofibroblastic Tumor
  Vascular Tumors
  Synovial Sarcoma
eGIST
  Calcifying Fibrous Pseudotumor

Spindle cell proliferations - Peritoneum
Tumor-like Lesions
• Leiomyomatosis Peritonealis Disseminata
• Gliomatosis Peritonei
• Serosal Deciduosis

Spindle cell Proliferations - Pericardium
INFLAMMATORY
• Acute Pericarditis
• Granulomatous Pericarditis
• Chronic Constrictive Pericarditis
NEOPLASTIC
• Pericardial Mesothelioma
• Sarcoma

Spindle cell Proliferations - Tunica
INFLAMMATORY
• Hydrocoele
• Nodular fibrous periorchitis
• Inflammatory pseudotumor
NEOPLASTIC
• Malignant mesothelioma
• Mesenchymal - Sarcoma

Spindle Cell Proliferations
Reactive vs Neoplastic Pathology
1st vs 2nd Spindle Cell Neoplasms

W.H.O. Classification
Tumor Histology (%)

- Conventional sarcomatoid MM of NOS subtype: 44%
- Sarcomatoid with desmoplastic areas: 21%
- Desmoplastic: 34%
- Osteosarcomatous and/or chondrosarcomatous: 1%
- Lymphohistiocytoid: 1%

Immunohistochemistry

**Mesothelial Markers**

- Calretinin
- CK 5/6
- WT 1
- D2–40
- Thrombomodulin
- Mesothelin

**Epithelial/Carcinoma Markers**

- CEA
- CD 15
- AUA - 1
- Ber - EP4
- MOC – 31
- TTF - 1

No marker is wholly specific or sensitive for any given tumour.

In Sarcomatoid Neoplasms, immunohistochemistry very limited.

Malignant Mesothelioma: Desmoplastic Variant

- 7% of all mesotheliomas.
- Extensively pleural tumours.
- Tumour diagnosis requires:
  - > 50% tumour composed of paucicellular collagen
  - Sarcomatoid component
  - Bland necrosis
  - Chest wall / visceral invasion
- Immunohistochemistry limited use.
- Differential diagnoses: reactive fibrous pleuritis.

Serosal Proliferations

Reactive v Neoplastic
Is the spindle cell proliferation benign or malignant?

- Frankly sarcomatous areas
- Foci of bland necrosis
- Invasion of adipose tissue, skeletal muscle or lung.
- Distant metastases.
  

- Immunohistochemistry: CK highlight invasion

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**PRESENTATION TITLE**

**DESMOPLASTIC MESOTHELIOMA**

**EXPANSILE NODULE FORMATION**

**BIOPSY**

Reactive Serositis vs Desmoplastic mesothelioma

- Gross features – important

- Factors favouring benign process
  - Cellular zonation – superficial cellularity
  - Angiogenic pattern – perpendicular to surface
The Fake Fat Phenomenon in Organizing Pleuritis: A Source of Confusion With Desmoplastic Malignant Mesotheliomas

Andres Chang, MD,* Philip Cagle, MD† Thomas V. Collins, MD; Joseph M. Carson, MD‡
Alice R. Gibbs, MD; Samuel Haemmer, MD; Nelson Oudard, MD; Victor L. Regis, MD;*†
Henry D. Vezijn, MD; William D. Pevale, MD;† Mark W. Wirtz, MD;‡ and
from the US-Canadian Mesothelioma Reference Panel

Experience has shown that morphology frequently fails, immunoreactivity is of no real use in this setting, ... even experts in the field often disagree about a given case.

What is needed is a molecular marker, and thus far, no such marker has been described.

Arch. Pathol. Lab. Med. 2005; 129; 1405 - 1406

Homozygous p16 deletion = adverse prognostic marker
~80% sarcomatoid MM
40% epithelioid MM

P16 deletion by FISH seen in 80% Sarcomatous/Desmoplastic Mesotheliomas
P16 deletion by FISH seen in 27% Sarcomatoid Carcinomas
BAP-1 loss by IHC seen in 15% Sarcomatoid/Desmoplastic Mesotheliomas
BAP-1 loss NOT seen in any Sarcomatoid Carcinomas


Vascular Sarcomas
CD31, CD34, VWF, ERG, FLI1+
CK+, WT-1+, D2-40+, T+ (+1:3) WWTR1-CAMTA1

Arch. Pathol. Lab. Med. 2013; 137; 632 - 636

Molecular Markers in Mesothelioma – p16 deletion

Prognostic Marker for Mesothelioma
Homozygous p16 deletion = adverse prognostic marker
~80% sarcomatoid MM
40% epithelioid MM

Predictive Marker of Malignancy
Homozygous p16 deletion not seen in benign/reactive mesothelial processes
= Marker of Benign vs Malignant

Arch. Pathol. Lab. Med. 2016; 137; 632 - 636
CONCLUSIONS

- Spindle cell proliferations of serosa – difficult, esp. peritoneum
- Overall, benign v malignant - morphology, CK, p16 FISH
- Overall, molecular diagnostics useful in confirming various soft tissue NG
- Problem - Sarcomatoid MM vs CA – Clinical, morphology +/-, p16 + BAP-1
- What is the Gold Standard for Diffuse Serosal Sarcomatoid NG?
  - Clinical AND/OR Pathology? – Clinical provides a Default diagnosis of MM