

Spindle Cell Conundrums in the Chest

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University of Utah
Park City, Utah

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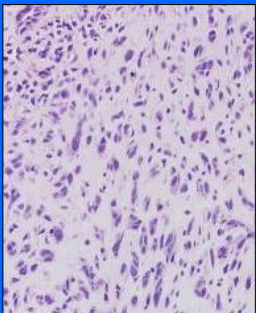


Why a Lecture on Spindle Cell Lesions?

- Frequent problem
- Challenge on small biopsies
- Wide spectrum of possibilities
- Treatment variable
- IHC triage necessary

What do we mean by spindle cells?

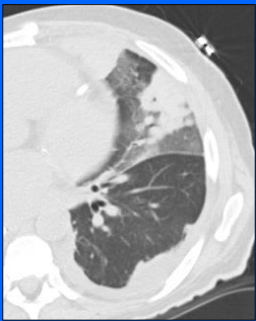
- Elongate cytoplasm
- Indistinct cell borders
- Variable amounts of cytoplasm, but frequently minimal
- Cytology often deceptively bland or low grade

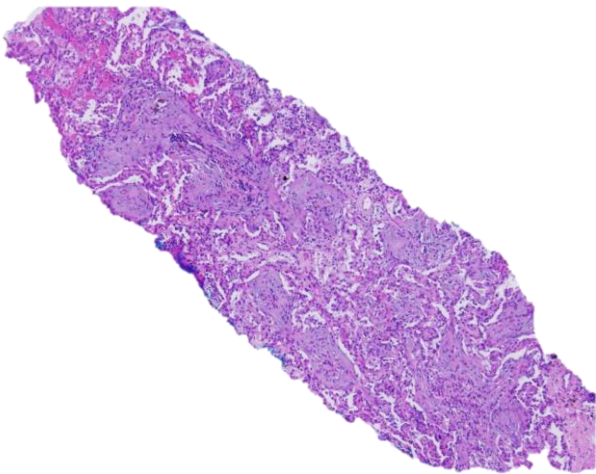


Outline

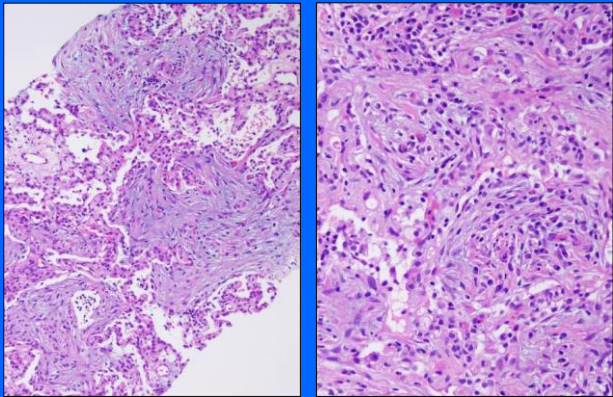
- Neoplastic vs. non neoplastic
- Low grade pulmonary lesions
- Metastatic lesions
- High grade pleuropulmonary neoplasms
- Approach with IHC

**Are the Spindle Cells
Neoplastic or Not?**





Organizing Pneumonia



CT Findings in Organizing Pneumonia

Pattern	Percent (n = 50)
Consolidation	80
Bilateral	74
Migratory	12
Diffuse reticular	10
→ Mass-like	8
Cavitary	2

Drakopanagiotakis F et al. Chest 2011;139:893-900

Mass-like Organizing Pneumonia

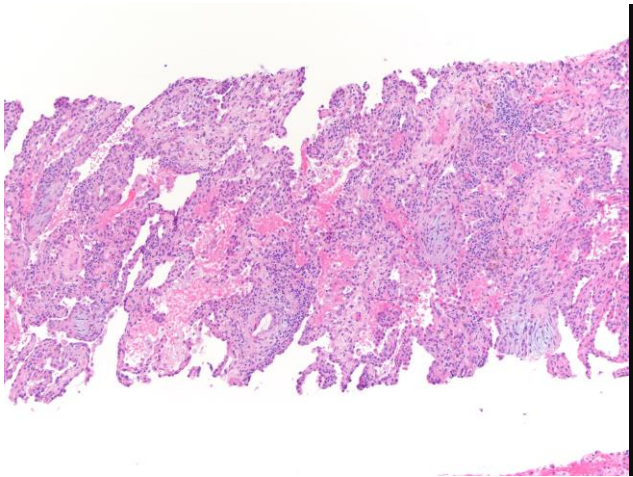
- Asymptomatic – 62%
- H/O malignancy or smoking ~25%
- Contrast enhancement on CT and PET positive
- 90% idiopathic, 10% post infectious

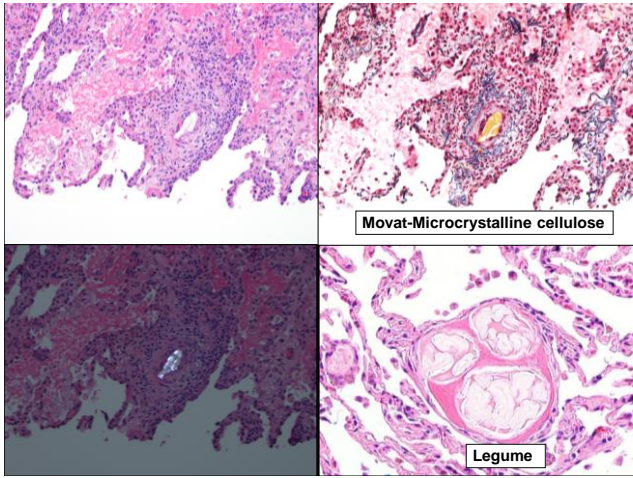
Maldonado F et al. Chest 2007;132:1579-1583

**Aspiration without
Food or Particulate Matter
Histology**

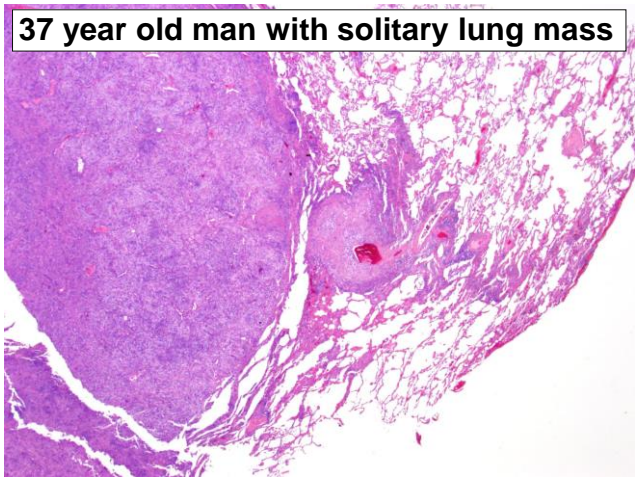
Pattern	Percent
Organizing pneumonia	40
Diffuse alveolar damage	30
Chronic bronchiolitis	30

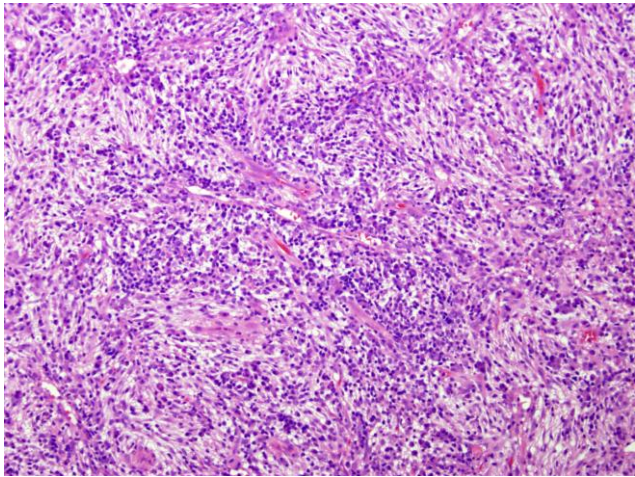
Yousem SY and Faber C. Am J Surg Pathol 2011;35:426-431





37 year old man with solitary lung mass

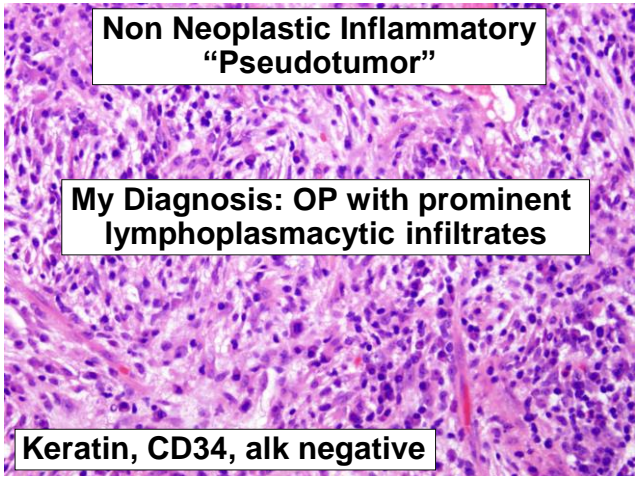




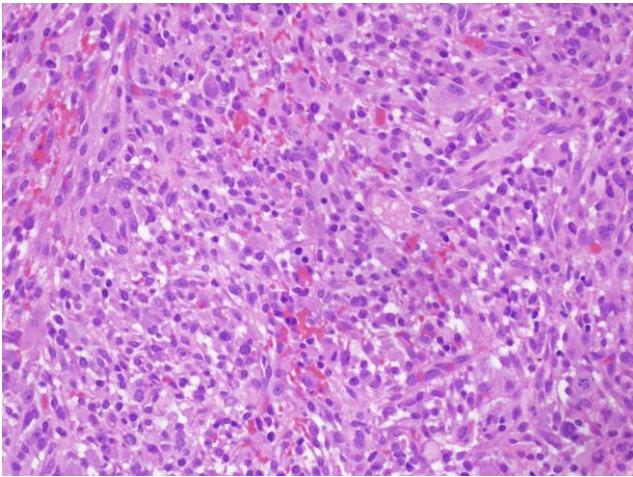
**Non Neoplastic Inflammatory
“Pseudotumor”**

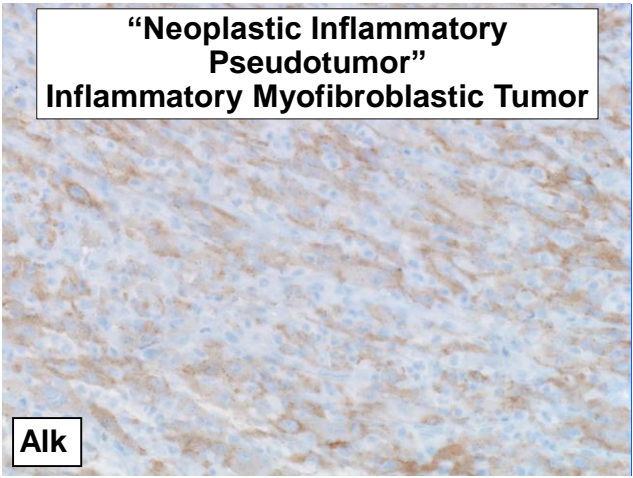
**My Diagnosis: OP with prominent
lymphoplasmacytic infiltrates**

Keratin, CD34, alk negative









Inflammatory Pseudotumors

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

Inflammatory Pseudotumors

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 - Organizing pneumonia type
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Inflammatory Pseudotumors

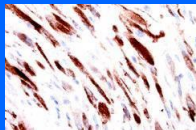
- Neoplastic- inflammatory myofibroblastic tumor
 - Fibrous histiocytoma
 - Inflammatory fibrosarcoma
 - Plasma cell granuloma
 - Inflammatory fibromyxoid tumor

Inflammatory Pseudotumors

- Neoplastic
 - Inflammatory myofibroblastic tumor
 - Fibrous histiocytoma **Metastasis!**
 - Inflammatory fibrosarcoma
 - Plasma cell granuloma
 - Inflammatory fibromyxoid tumor

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



Yi E et al. Arch Pathol Lab Med 2012; 114: 417-426

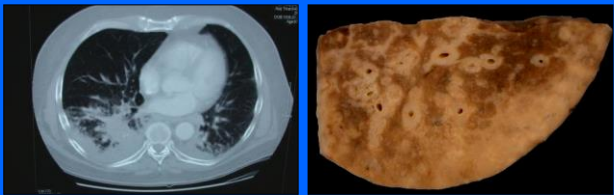
IgG4-Related Disease

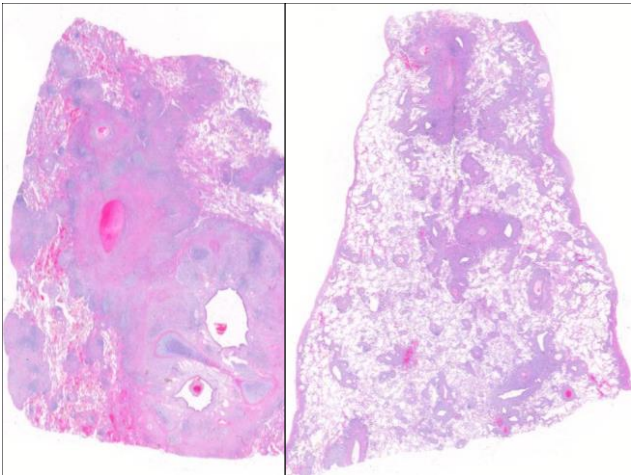
- Major criteria- 2/3 needed for dx
 - Dense lymphoplasmacytic infiltrate
 - Fibrosis, focally storiform
 - Obliterative phlebitis
- Additional characteristic features
 - Phlebitis without obliteration
 - Increased tissue eosinophils
- Exceptions exist in lung, LN, minor salivary and lacrimal glands (fibrosis and phlebitis may be absent)

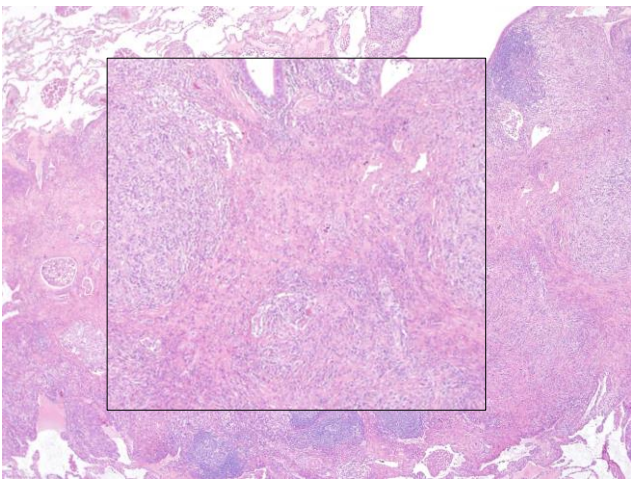
IgG4-related Disease

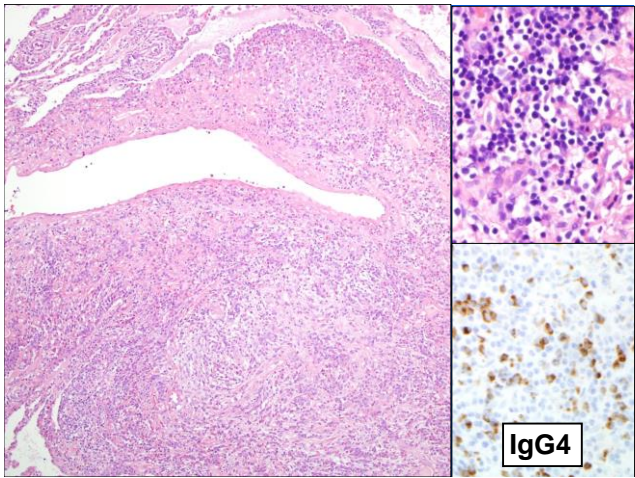
Radiologic Patterns of Lung Involvement

- Solitary nodule (+/- ground glass opacity)
- Consolidation, unilateral or bilateral
- Interstitial lung disease









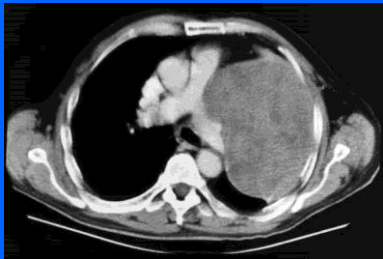
IgG 4-related Disease
Quantitation

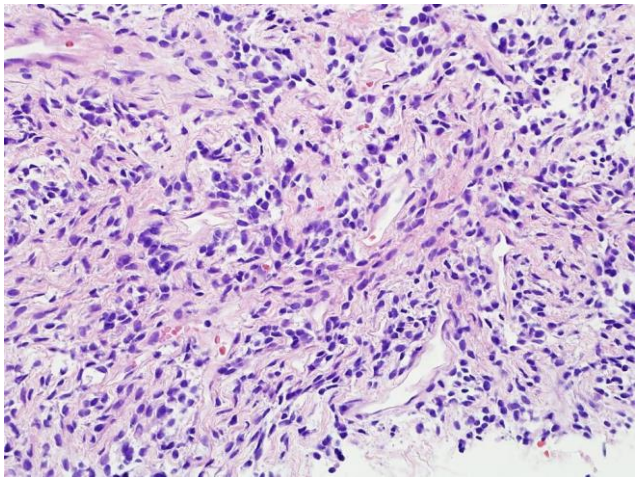
- Serum IgG4 concentrations normal-40%
- IgG4 + cells/IgG plasma cells > 40% mandatory
- > 20-50 IgG4 + cells/hpf (3- 40x fields)

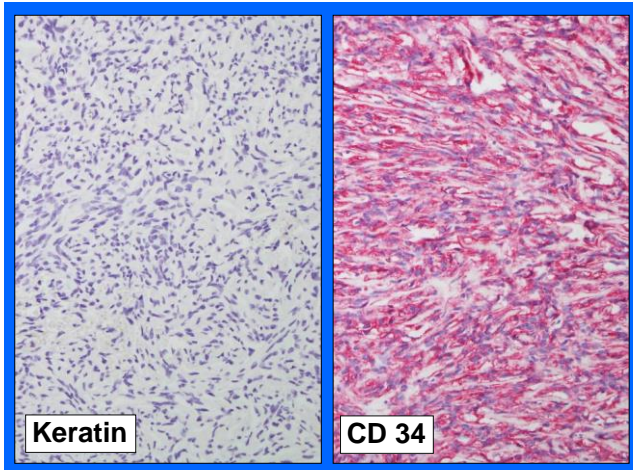
Deshpande V et al. Modern Pathol 2012; 1-12

History

49 year old man with posterior flank pain







Solitary Fibrous Tumor

IHC stain	% Positive
Stat 6 nuclear	98
Stat 6 cytoplasmic	96
Bcl 2	95
CD34	93
β catenin	88
TLE	14
S100	7
PanKeratin	3
CAM 5.3	3

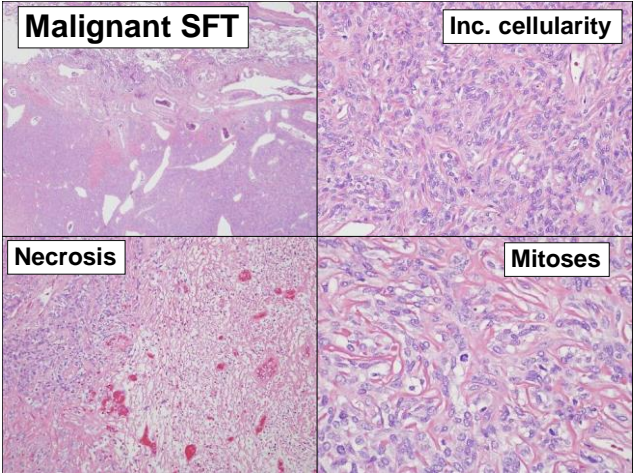
Immunocytochemistry®

Predicting Recurrence in SFT

	Feature	Points
Age (yrs)	< 55	0
	≥ 55	1
Size (cm)	< 5	0
	5 to < 10	1
	10 to < 15	2
	≥ 15	3
Tumor necrosis (%)	< 10	0
	≥ 10	1
Mitoses/10hpf	< 4	0
	≥ 4	1

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

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



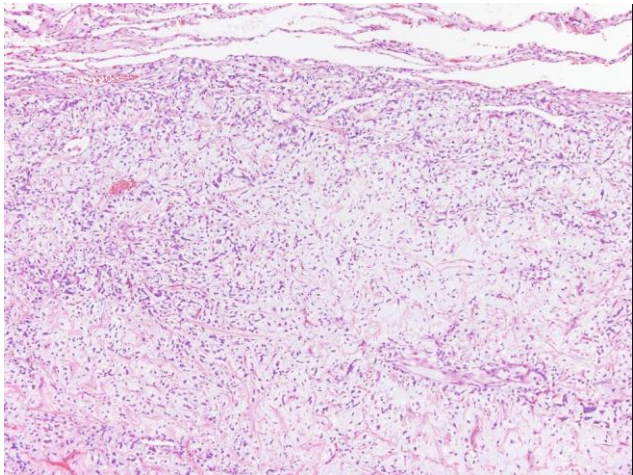
Predicting Recurrence in SFT

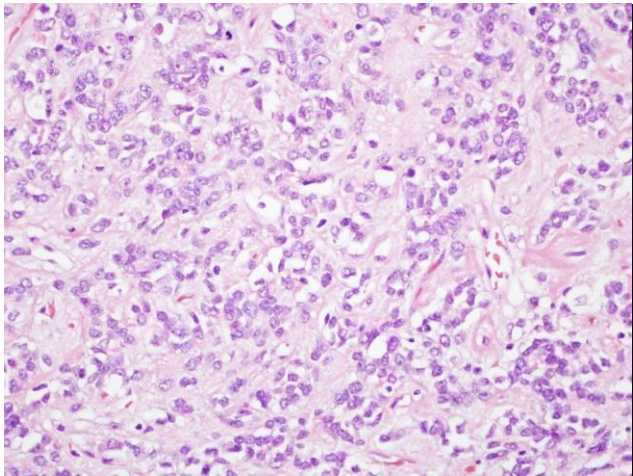
Risk of metastasis at # years (% , y)

Low risk	0, 10 y
Intermediate risk	10, 10 y
High risk	73, 5 y

History

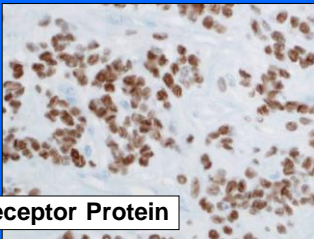
- A 73-year-old woman presented with a dominant lung mass
- Needle biopsy had been performed and diagnosed as “most consistent with epithelioid hemangioendothelioma”...but CD31 was negative





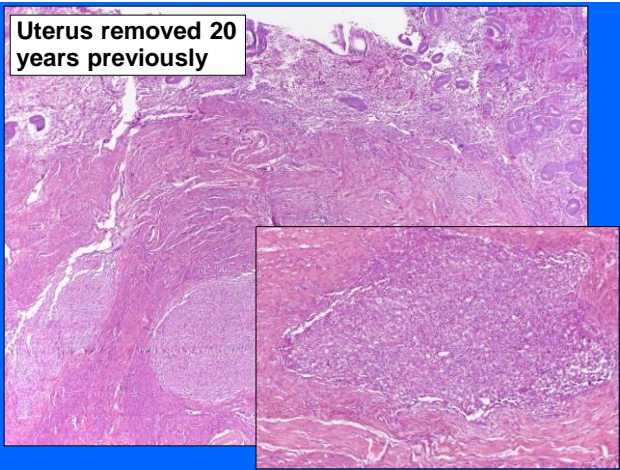
Diagnosis?

Most consistent with Metastatic Endometrial Stromal Sarcoma



Estrogen Receptor Protein

Uterus removed 20 years previously

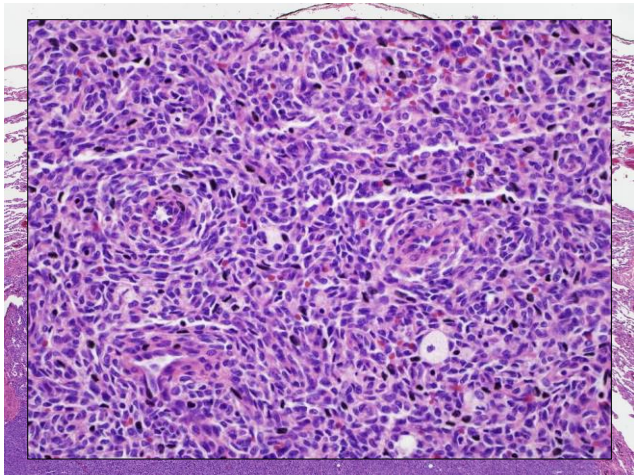


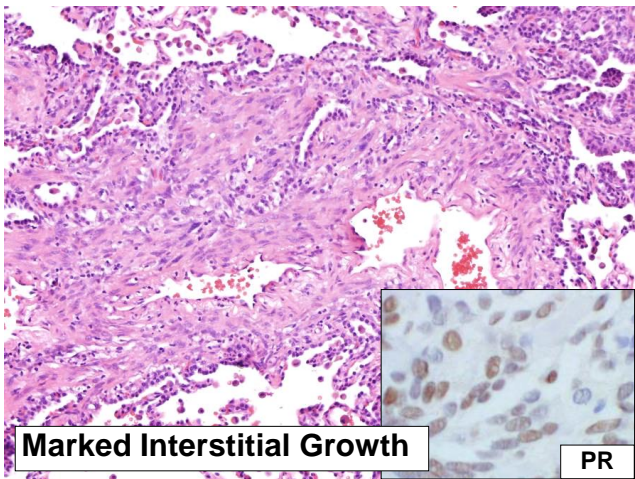
Challenges in Dx of Metastatic ESS

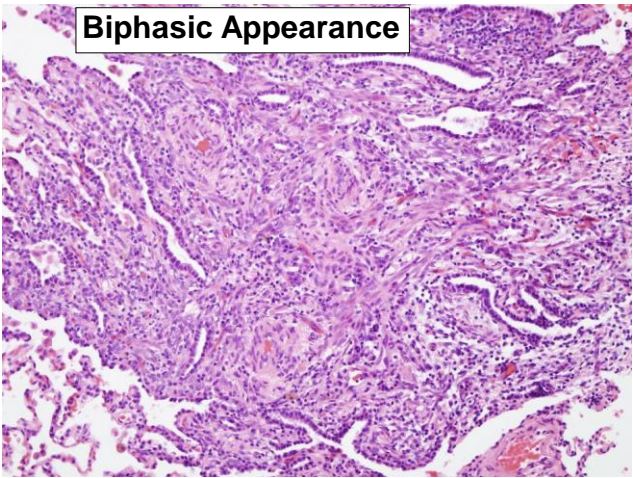
- Unknown or misdiagnosis of uterine ESS
- Long tumor-free interval
- Unusual symptoms or radiologic presentation
 - Pneumothorax
 - Solitary nodule
 - Cystic lesions
 - Bilateral infiltrates mimicking interstitial ds

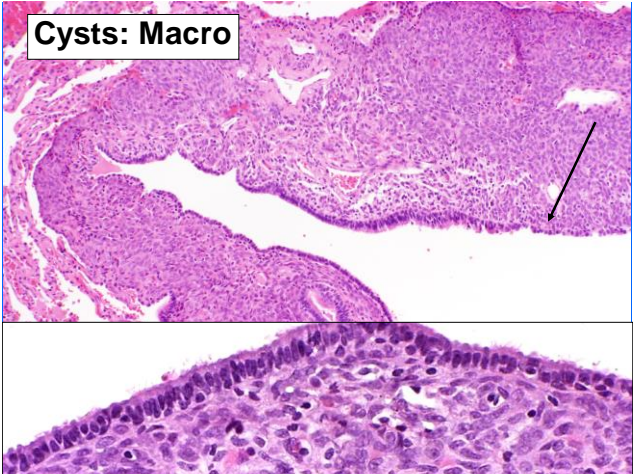
Metastatic ESS

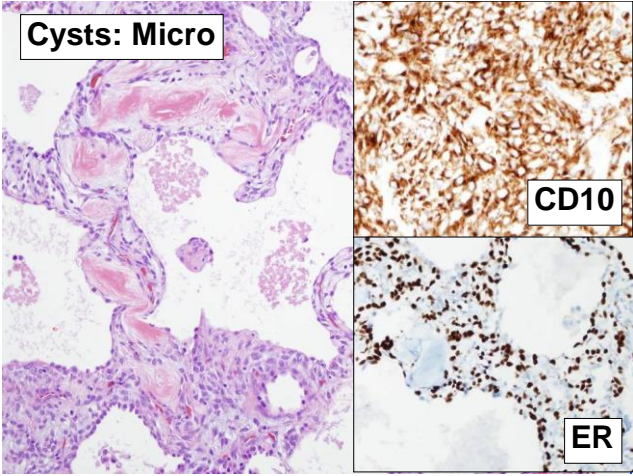
- Histology parallels uterine primary
 - Spindle cells, ± smooth muscle or sex cord differentiation, hyaline fibrosis
- Immunohistochemistry
 - ER/PR/vimentin: ~ 100%
 - Actin/desmin/keratin/CD10: ~ 50%
 - Rarely positive: Inhibin, CAM 5.2, Chromogranin, HMB-45, CD34





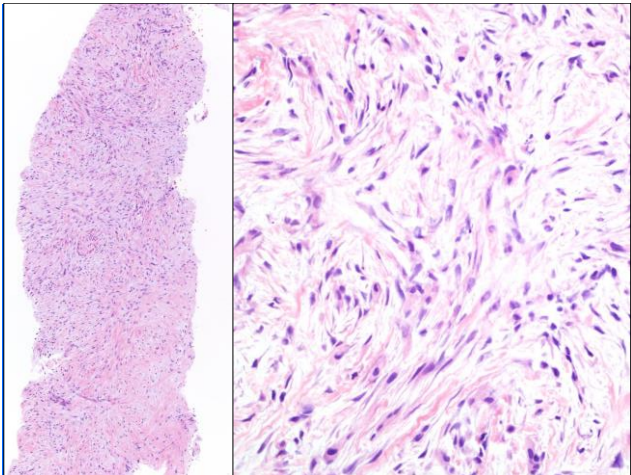


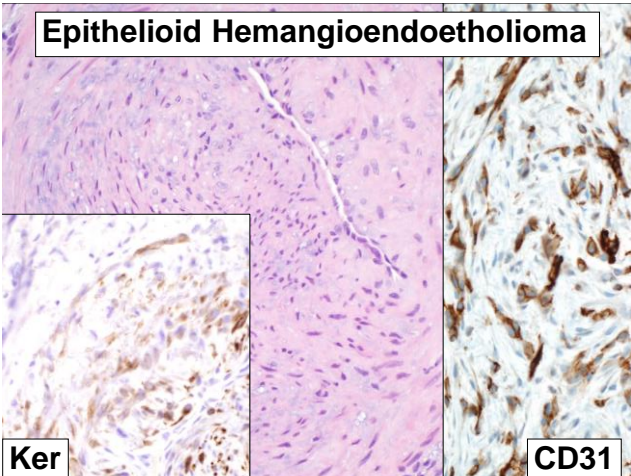


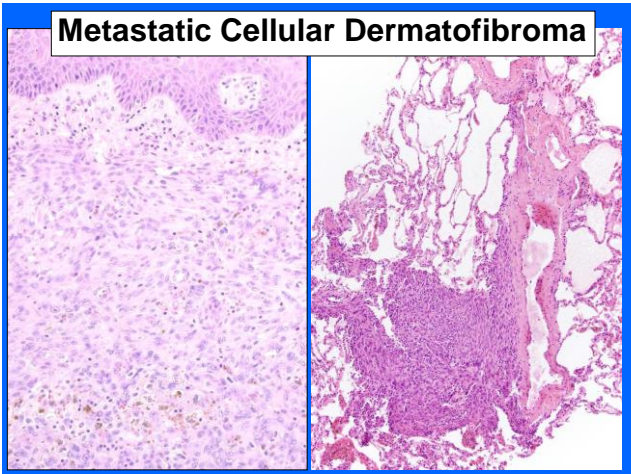


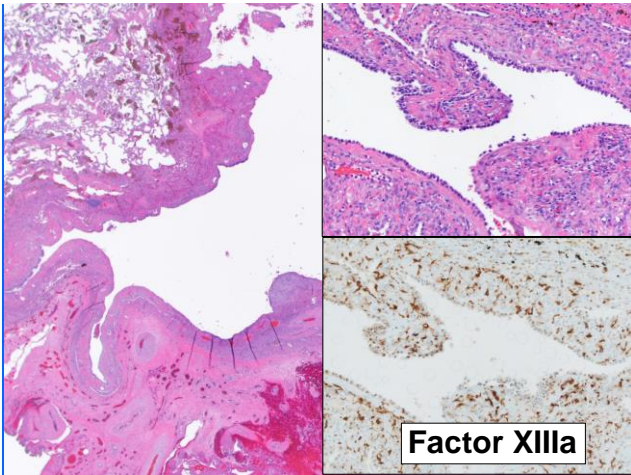
Metastatic ESS
Differential Diagnosis

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









Outline

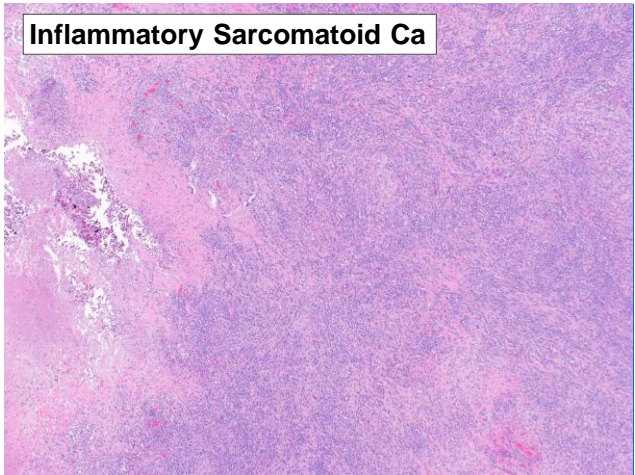
- Neoplastic vs. non neoplastic
- Low grade pulmonary lesions
- Metastatic lesions
- ➔ • High grade pleuropulmonary neoplasms
- Approach with IHC

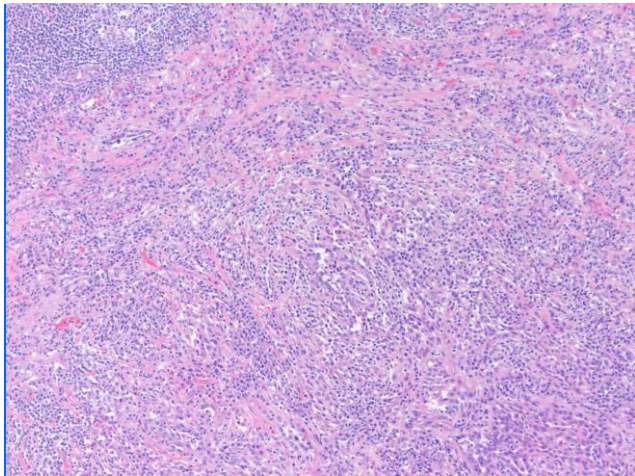
Inflammatory Sarcomatoid Carcinoma

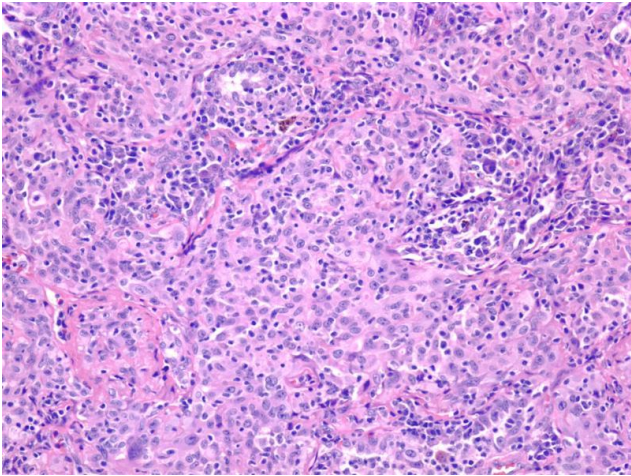
- Variant of Sa Ca with deceptively bland morphology
- Mimics
 - Inflammatory process
 - Lymphoma, incl HD
 - Inflammatory myofibroblastic tumor
 - Fibrous histiocytoma

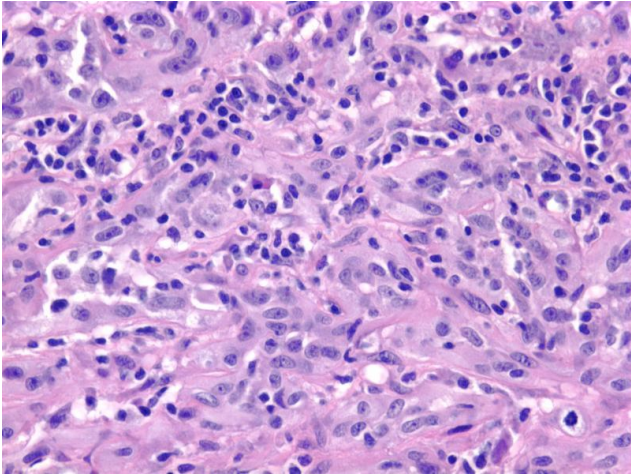
Wick MR et al Hum Pathol 1995; 26:1014

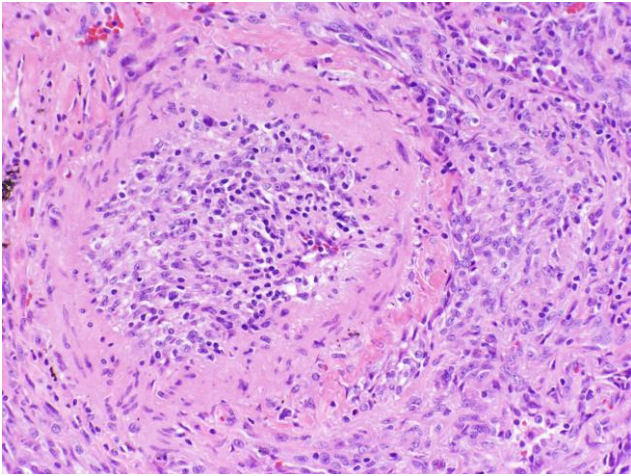
Inflammatory Sarcomatoid Ca

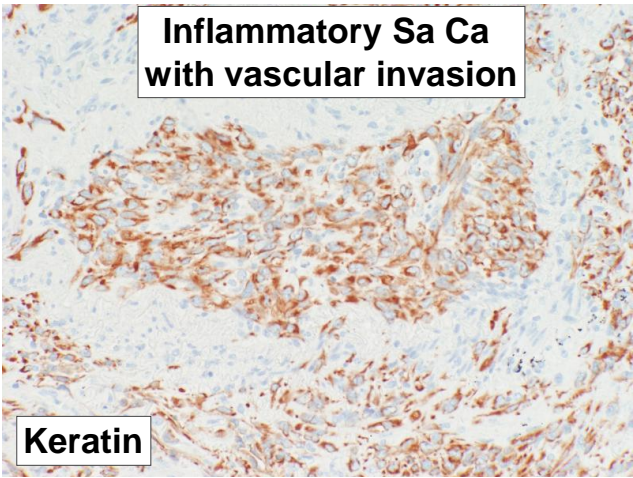












Inflammatory Sa Ca

- 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

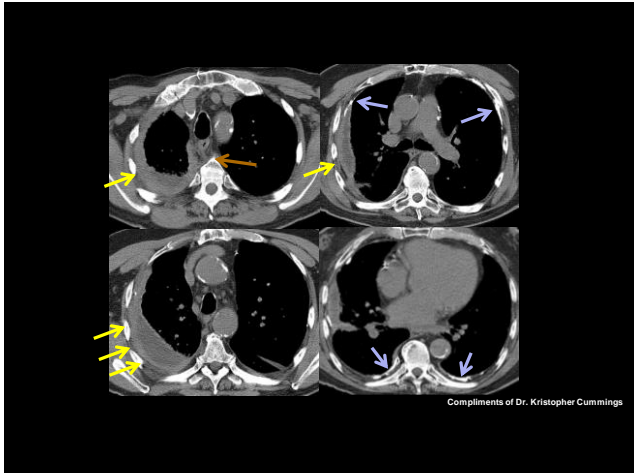
Wick MR et al Hum Pathol 1995; 26:1014

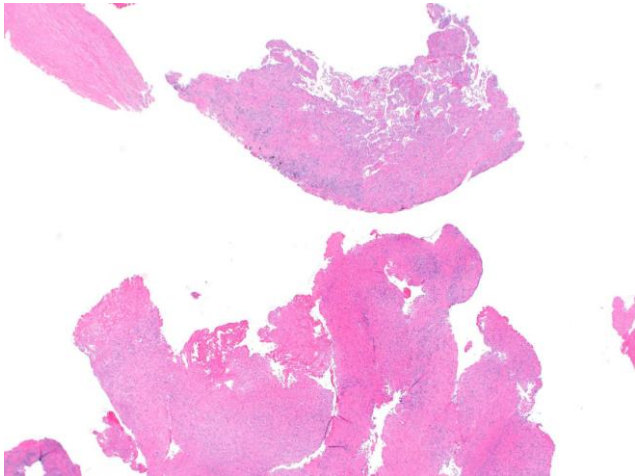
**Sarcomatoid Carcinoma
Differential Diagnosis**

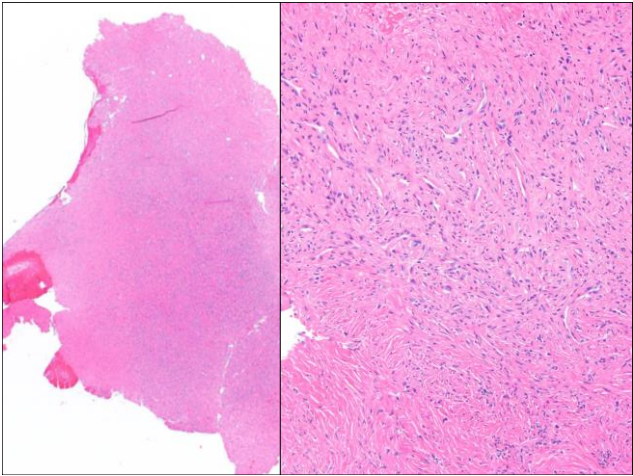
- Organizing pneumonia
- Inflammatory myofibroblastic tumor
- IgG 4-related sclerosing disease
- Lymphoma, particularly Hodgkin L.
- Malignant mesothelioma

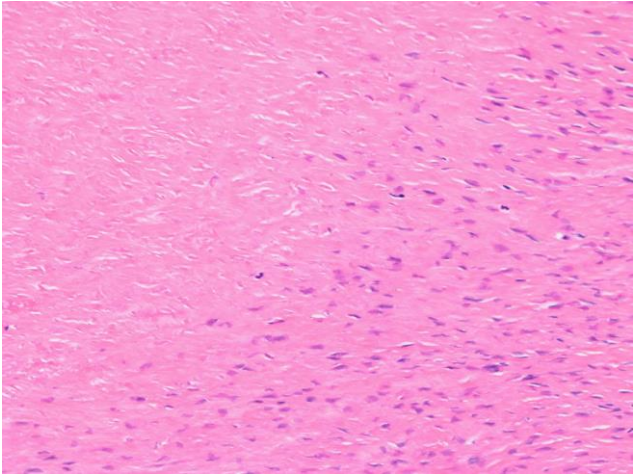
Case History

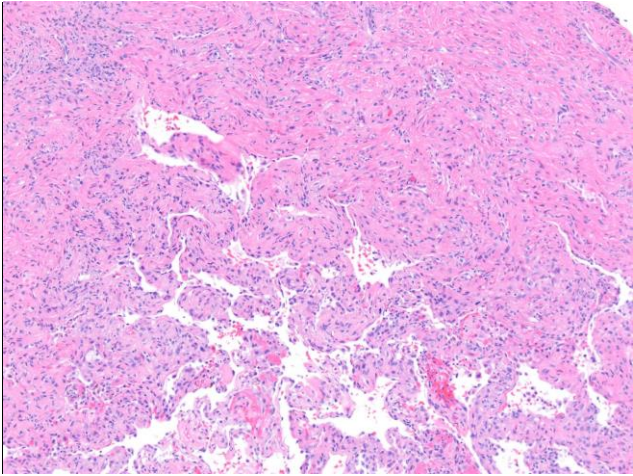
- A 78 yr old man has a recurrent R pleural effusion for which he had talc pleurodesis.
- 1 yr later developed recurrent pleural effusion with nodularity.
- He undergoes VATS biopsy.

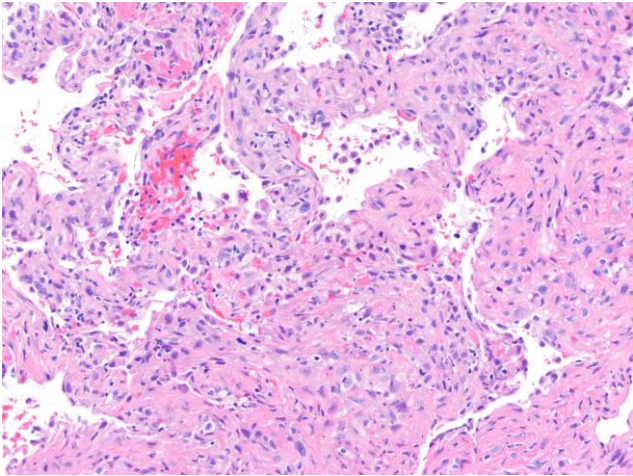


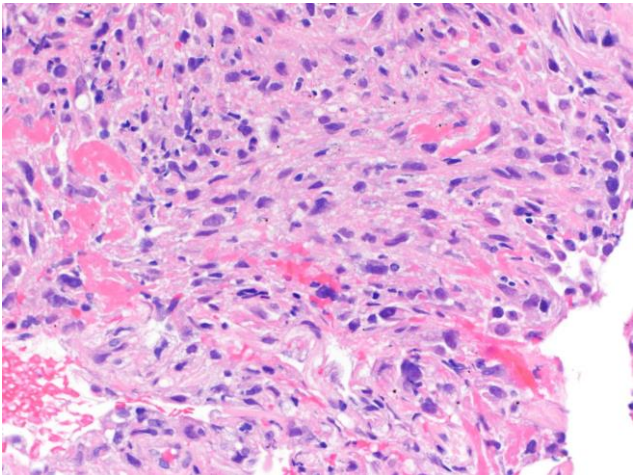






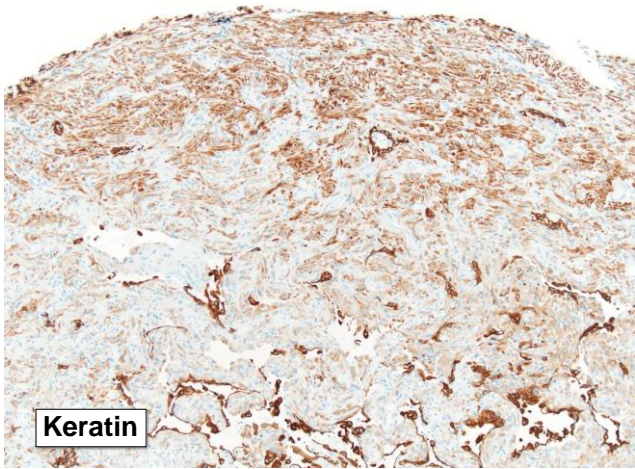


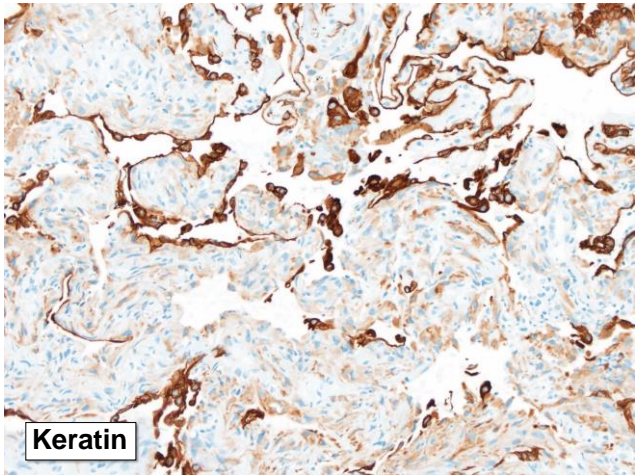


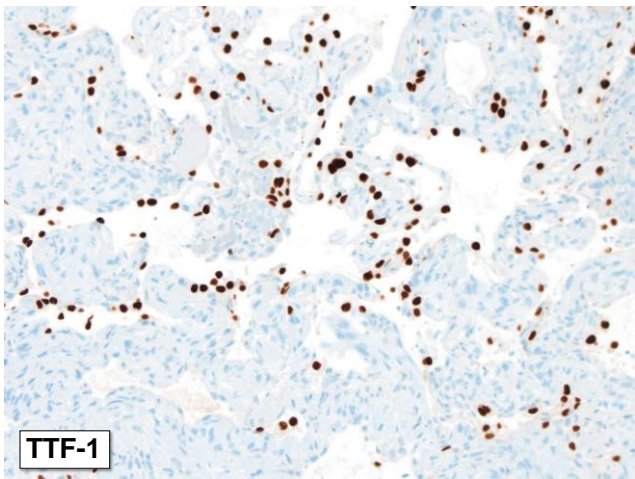


The single best IHC stain to order on this block is:

- a. Ber EP4
- b. CEA
- c. CK7
- d. MOC-31
- e. Pan keratin





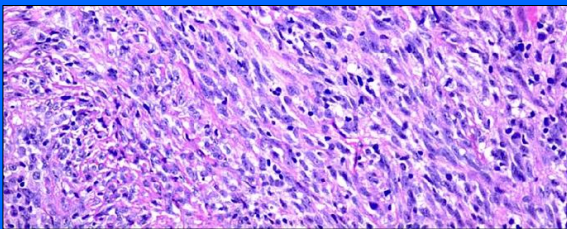


The diagnosis is:

- 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

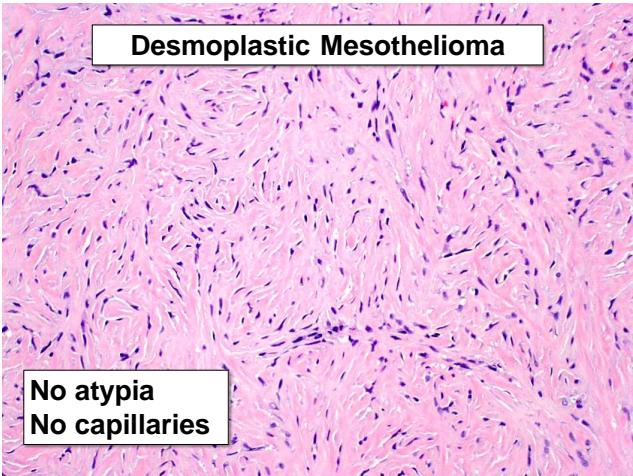
- No zonation
- Cellular
- Frankly malignant cytology
- May merge with epithelioid foci
- Identification of invasion not always necessary for diagnosis

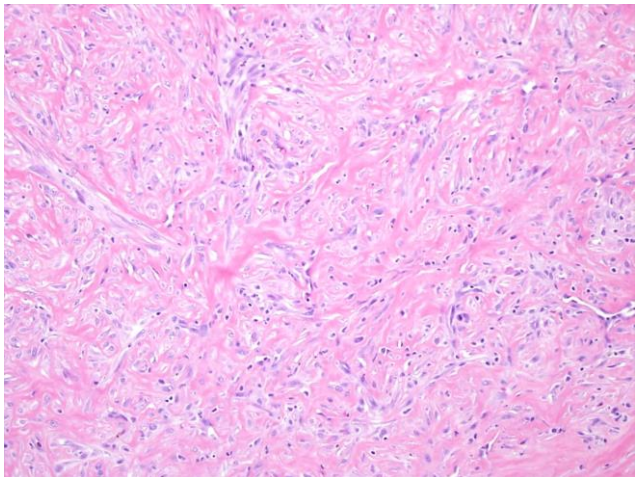
Desmoplastic Mesothelioma
WHO

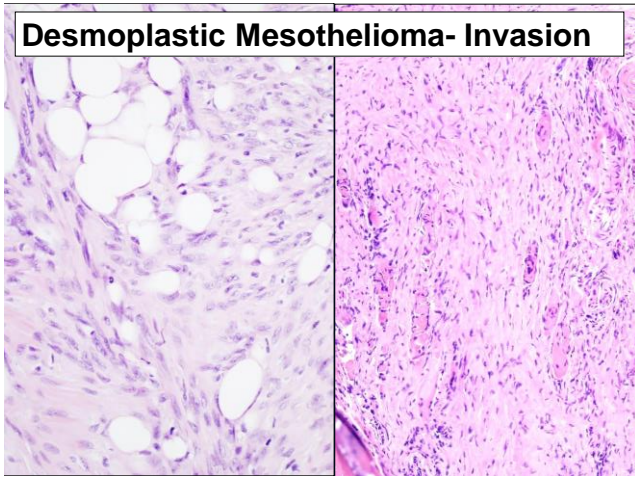
Dense collagenized tissue
separated by malignant
mesothelial cells arranged in a
storiform or so-called patternless
pattern, which must be present
in at least 50% of the tumor.

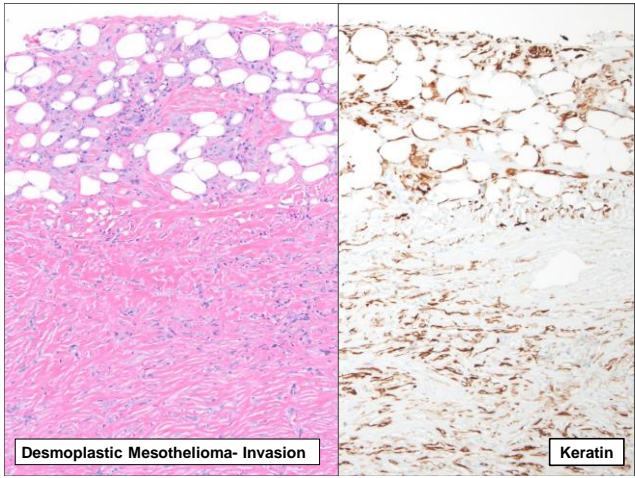
Desmoplastic Mesothelioma

- 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

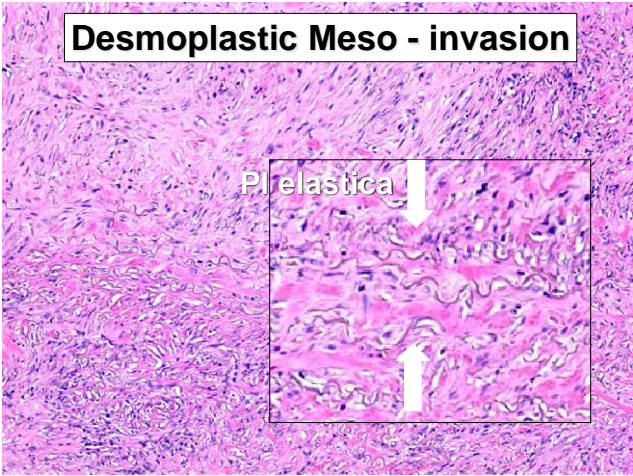




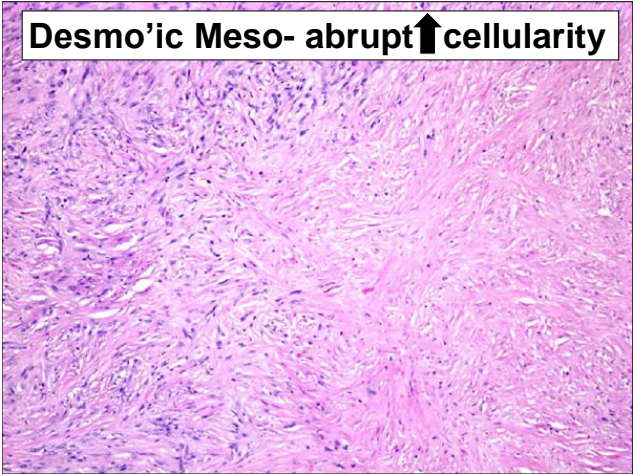




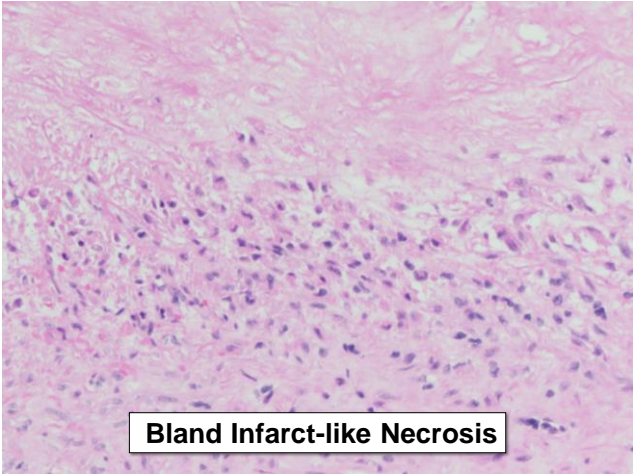
Desmoplastic Meso - invasion

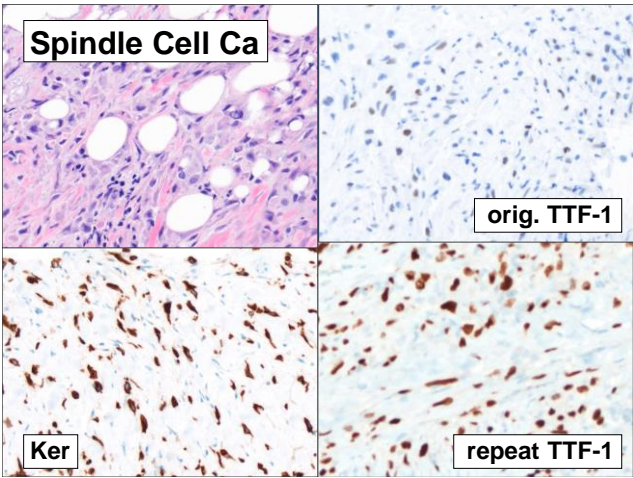


Desmo'ic Meso- abrupt↑cellularity



Bland Infarct-like Necrosis



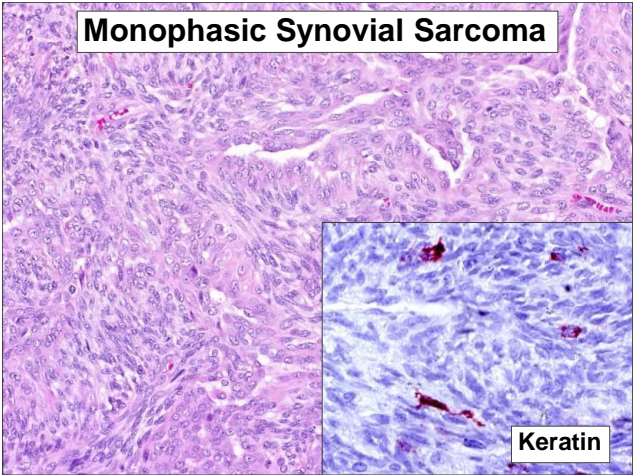


Inconclusive Immunostains ?

- 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



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

Organizing Pn

IMT

Met ESS, DF,

Mesothelioma

Synovial Sarcoma

EHE

Angiosarcoma

Infectious

Pseudoneoplasm

Benign/low grade

Organizing Pn

Met ESS, DF, SF

Desm

Melan

Infect. Pseudoneoplasm

Locally +

Sarcoma

oma

oma

in -

grade

arcoma

-T

arcoma