

# **Spindle Cell Conundrums in the Chest**

## **2019 Anatomic Pathology Update**

### **University of Utah**

#### **Park City, Utah**

**Henry D. Tazelaar, M.D.**  
**Chair and Geraldine Zeiler**  
**Colby Professor of**  
**Cytopathology**

**Department of Laboratory**  
**Medicine and Pathology**  
**Alix College of Medicine and**  
**Science**  
**Mayo Clinic Arizona**

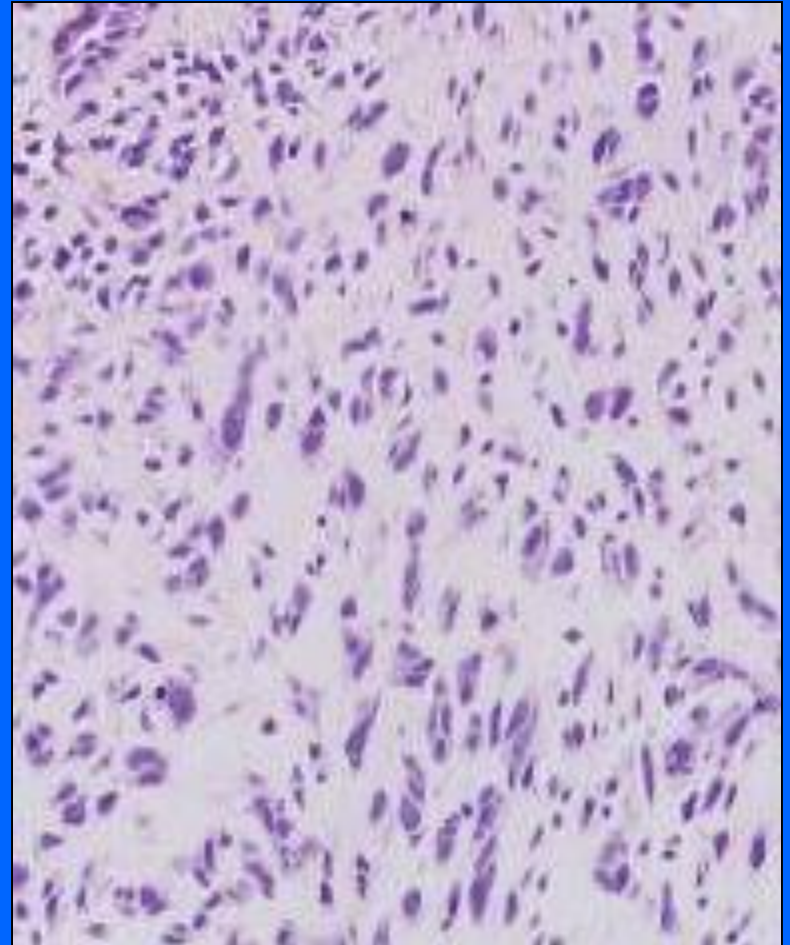


# **Why a Lecture on Spindle Cell Lesions?**

- **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

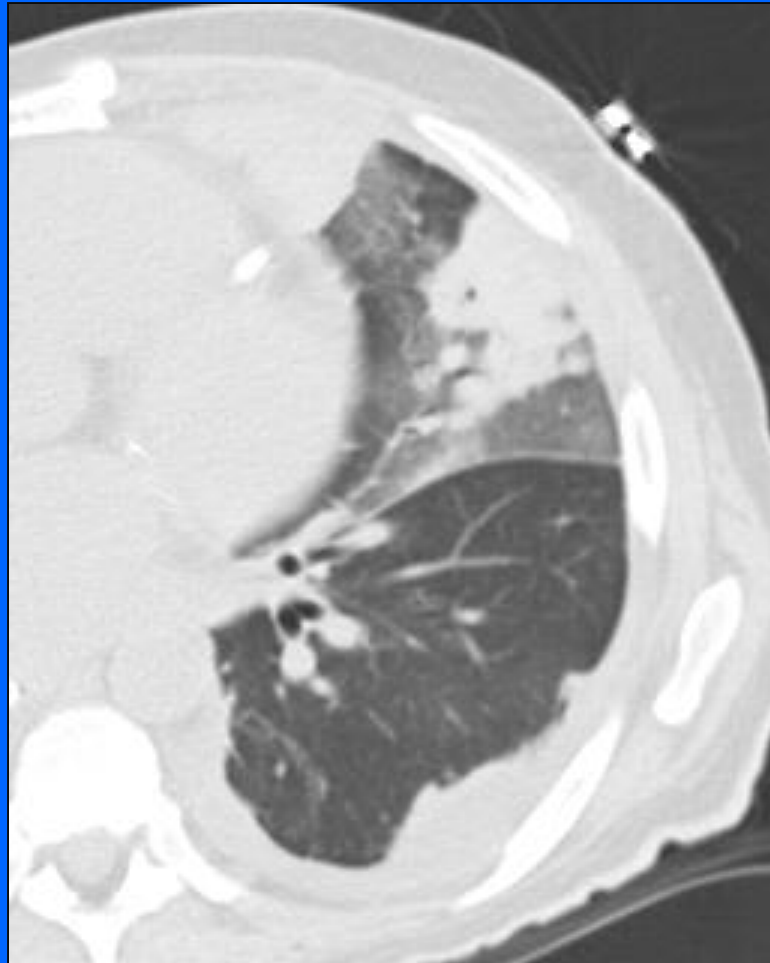


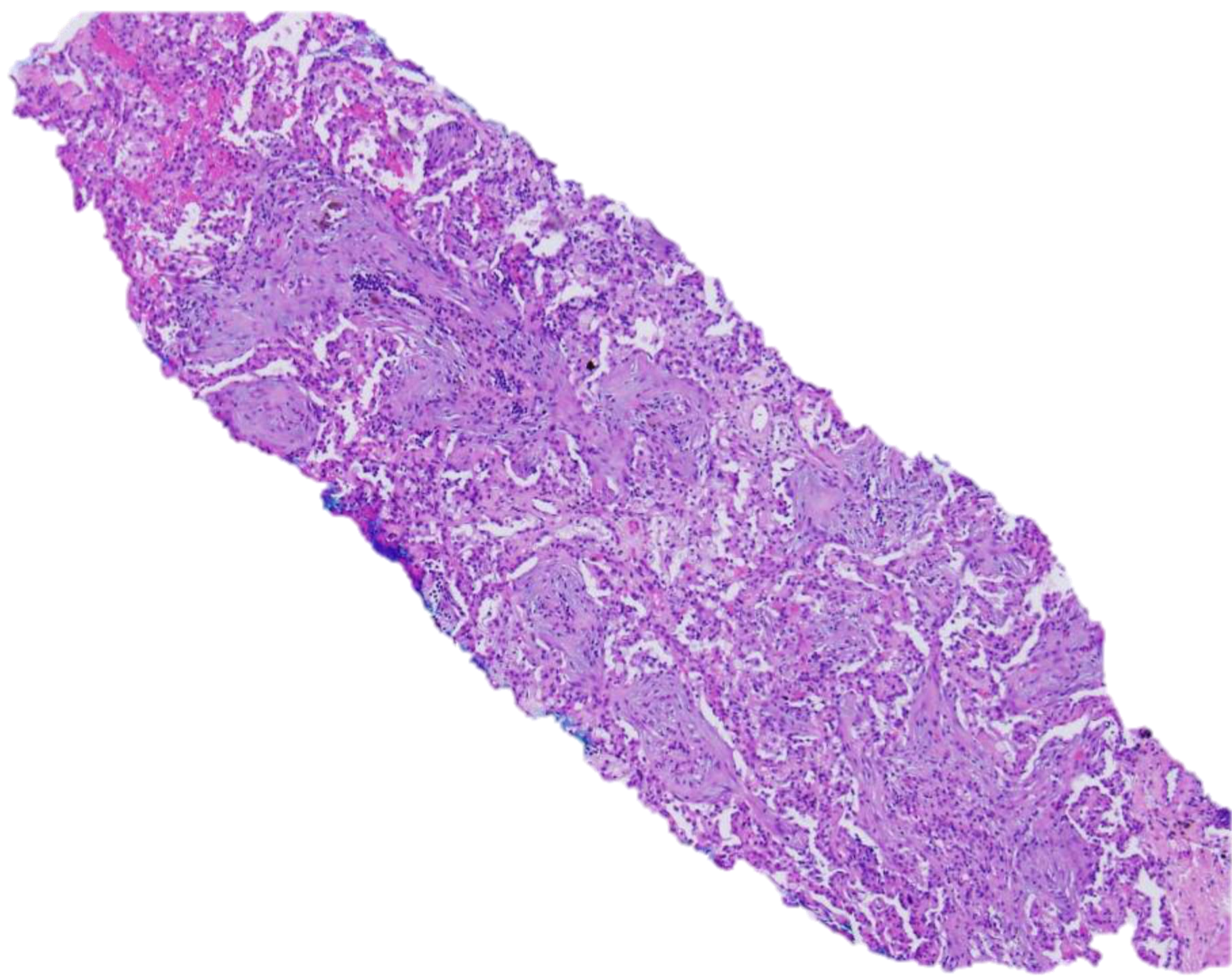
# Outline

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



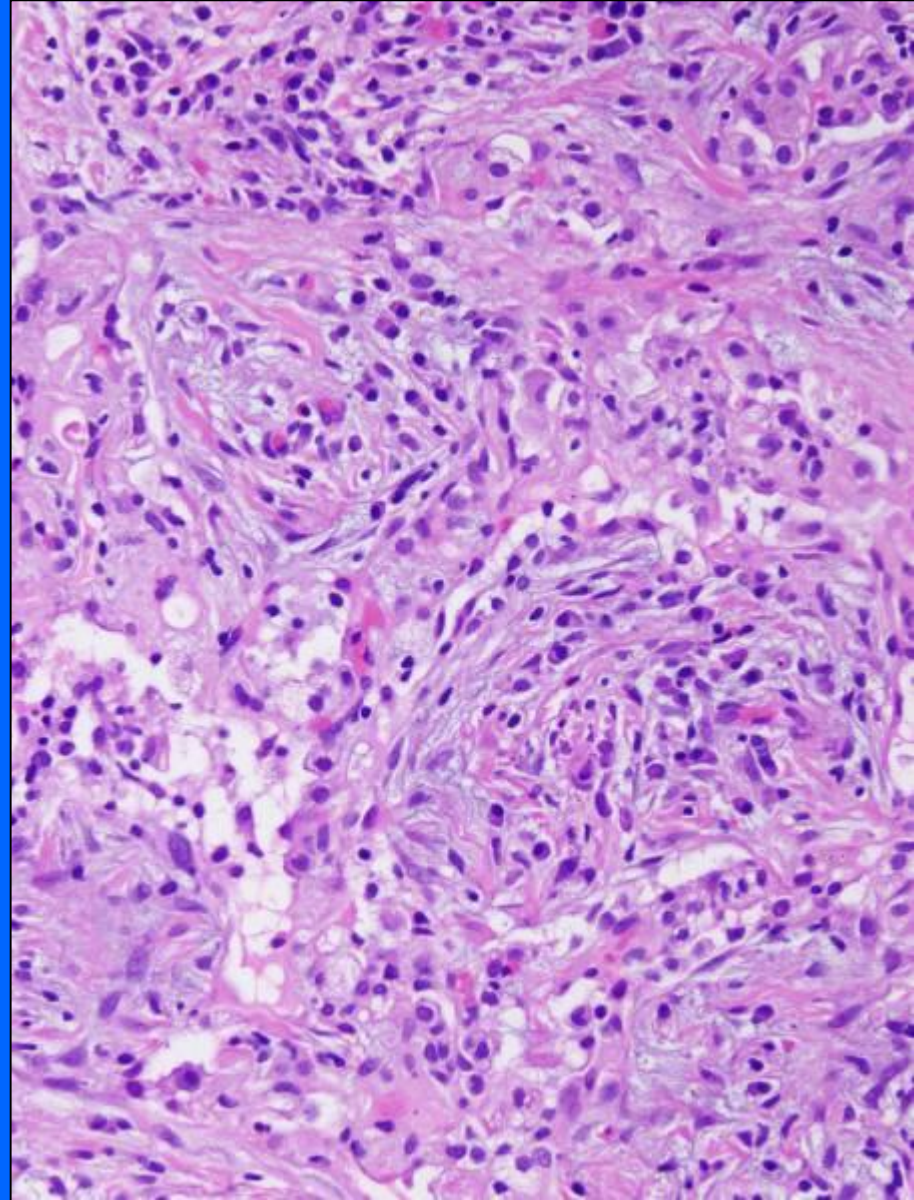
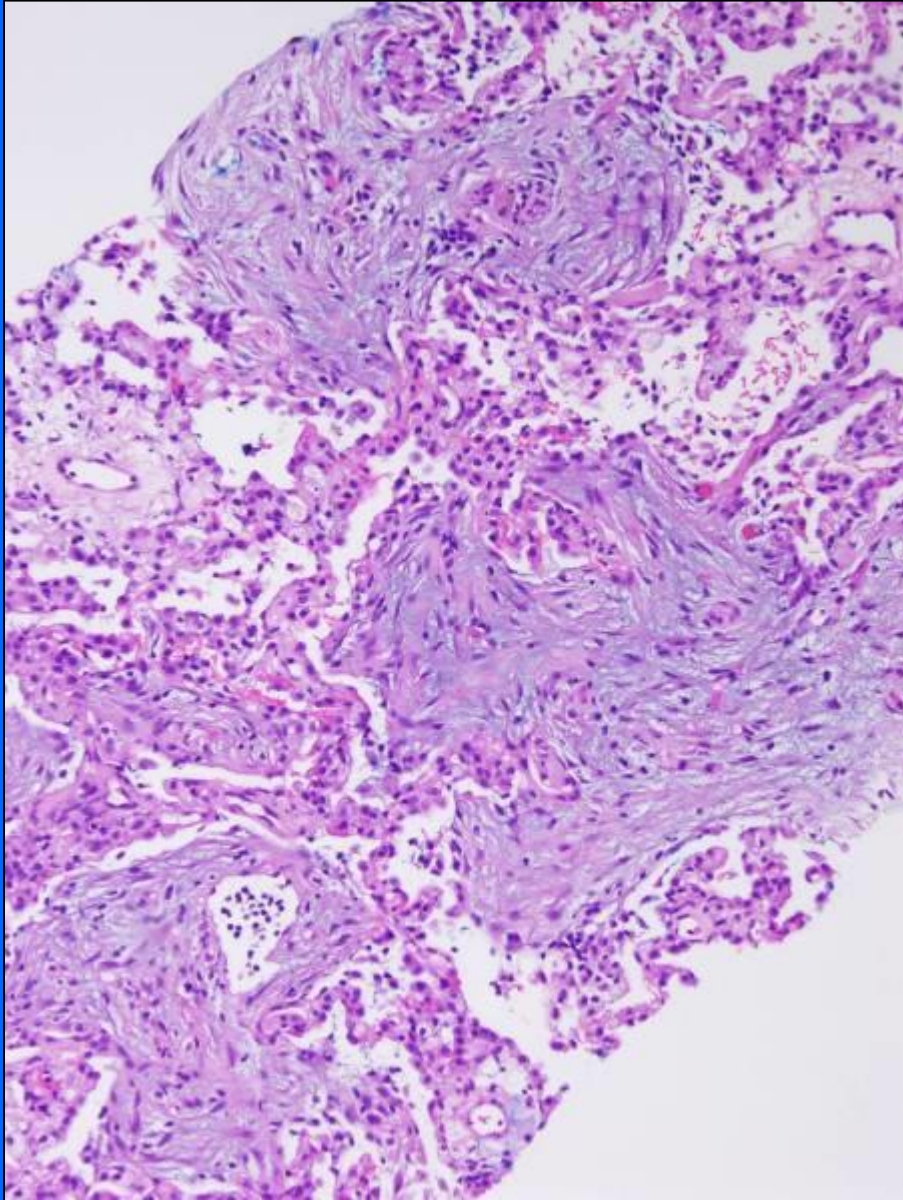
# Are the Spindle Cells Neoplastic or Not?







# 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

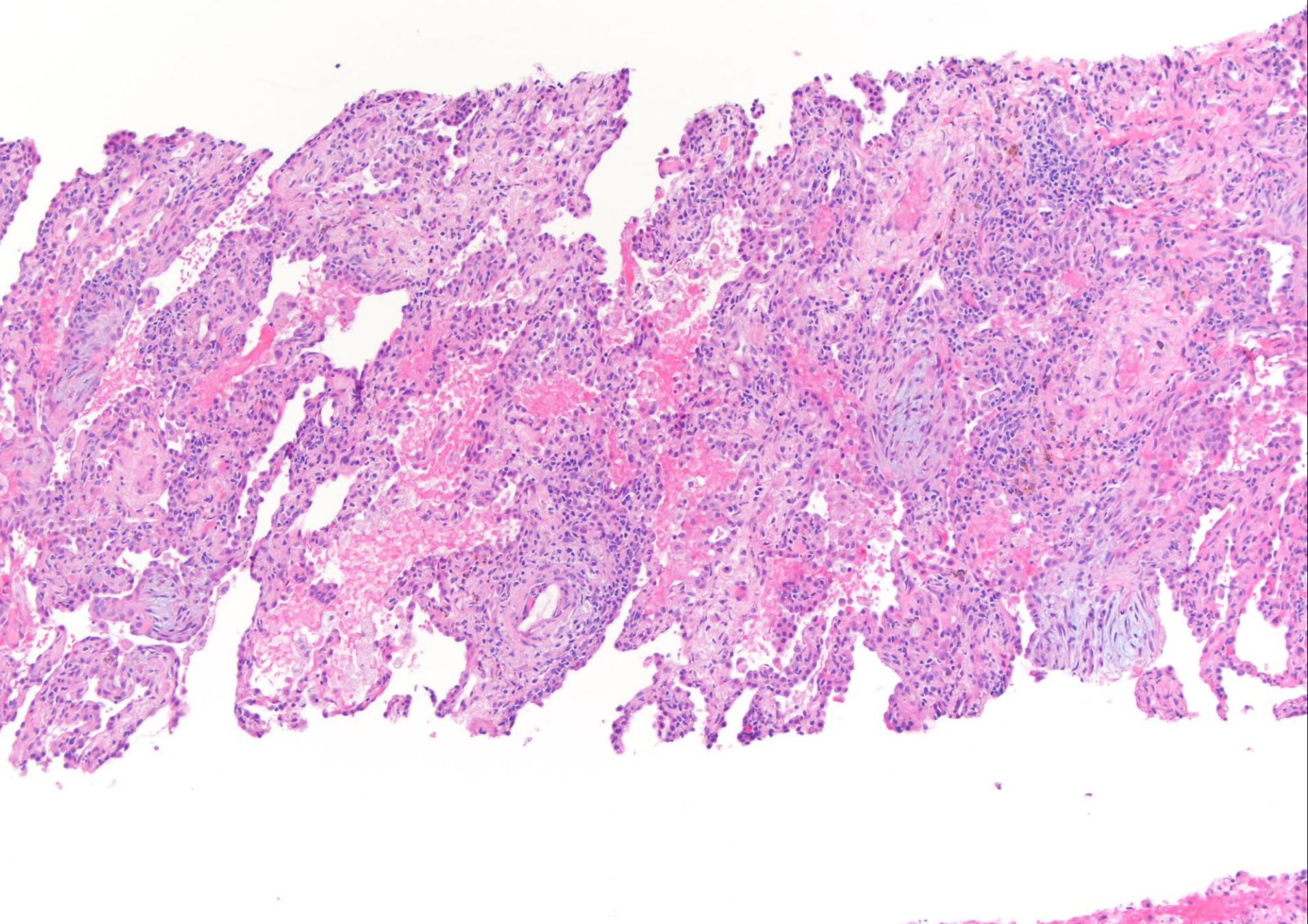


# Mass-like Organizing Pneumonia

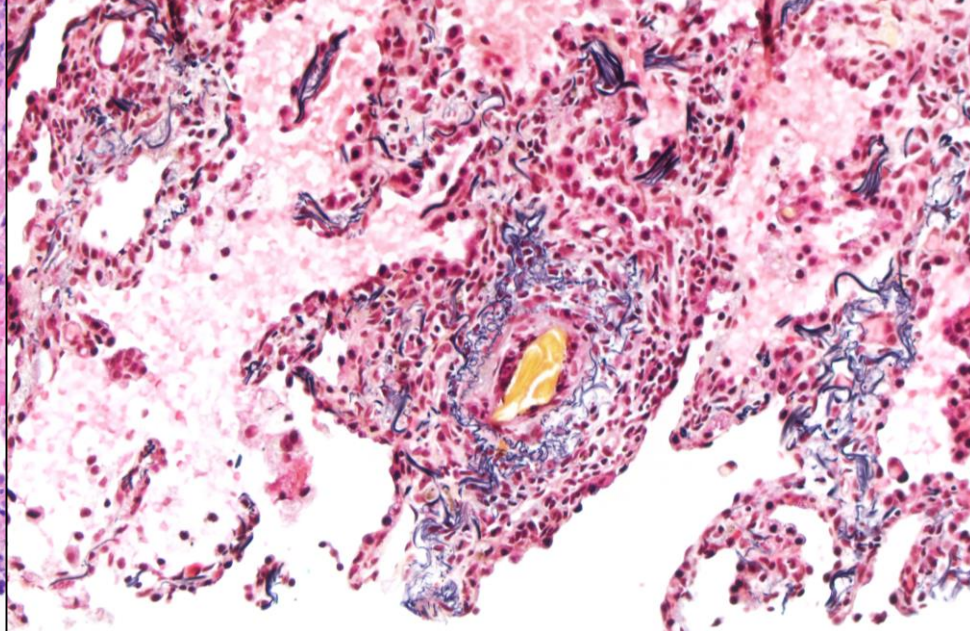
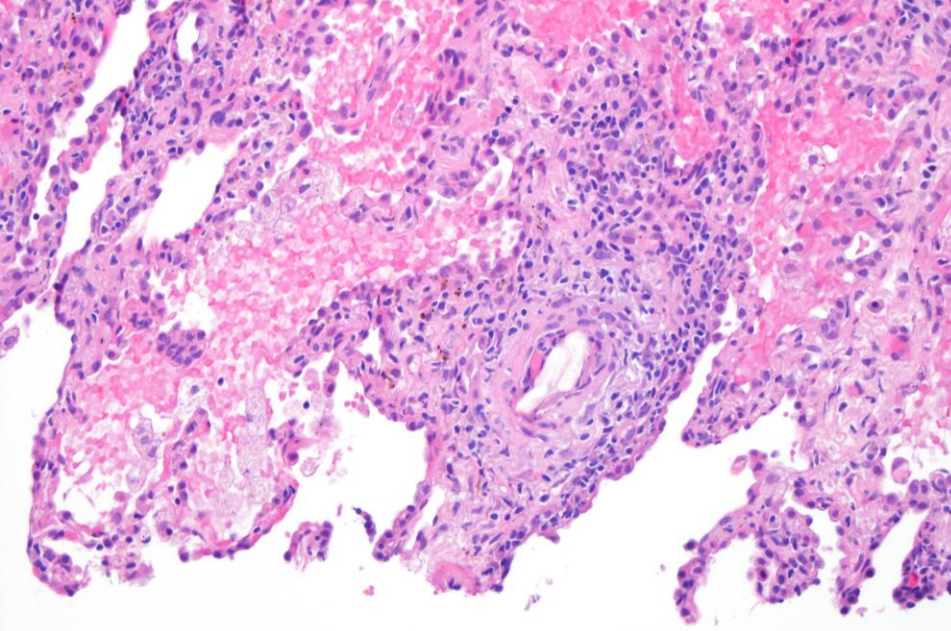
- Asymptomatic – 62%
- H/O malignancy or smoking ~25%
- Contrast enhancement on CT and PET positive
- 90% idiopathic, 10% post infectious

# **Aspiration without Food or Particulate Matter Histology**

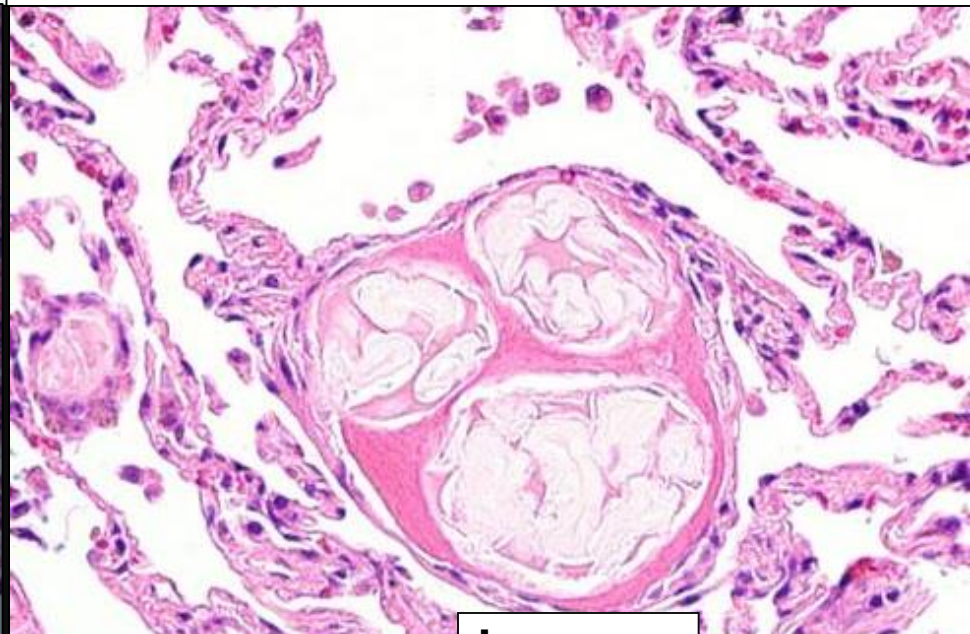
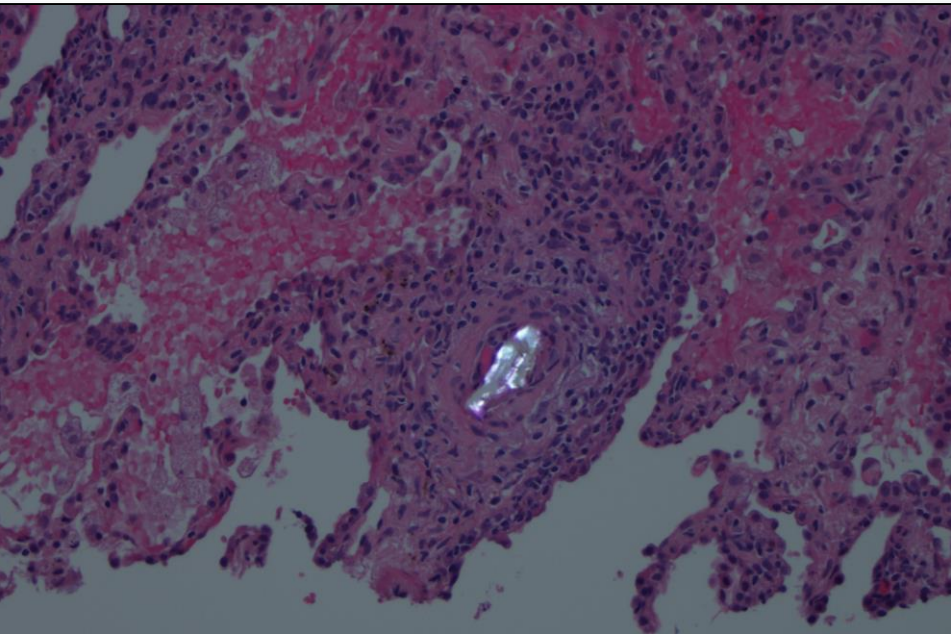
<b>Pattern</b>	<b>Percent</b>
<b>Organizing pneumonia</b>	<b>40</b>
<b>Diffuse alveolar damage</b>	<b>30</b>
<b>Chronic bronchiolitis</b>	<b>30</b>







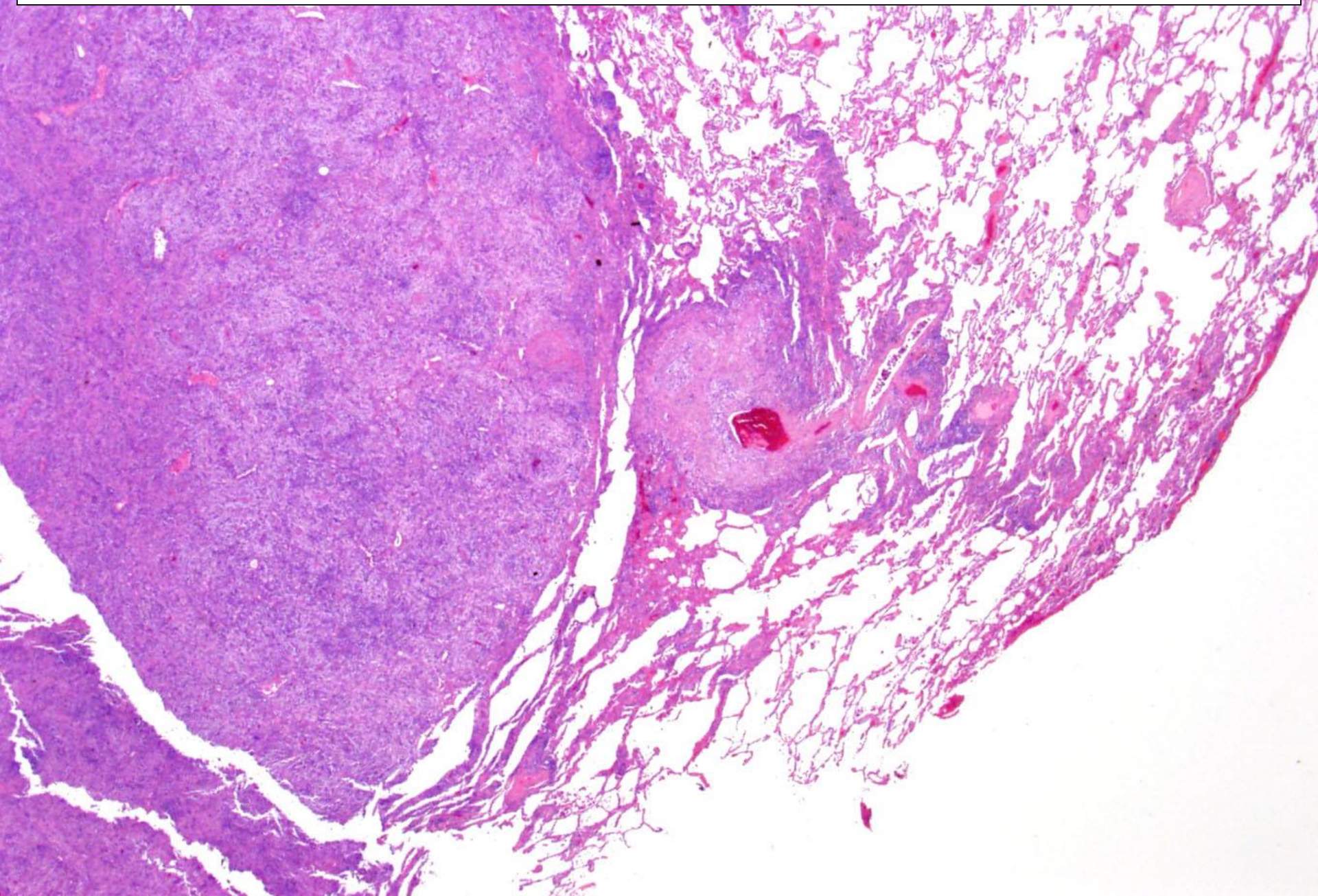
**Movat-Microcrystalline cellulose**



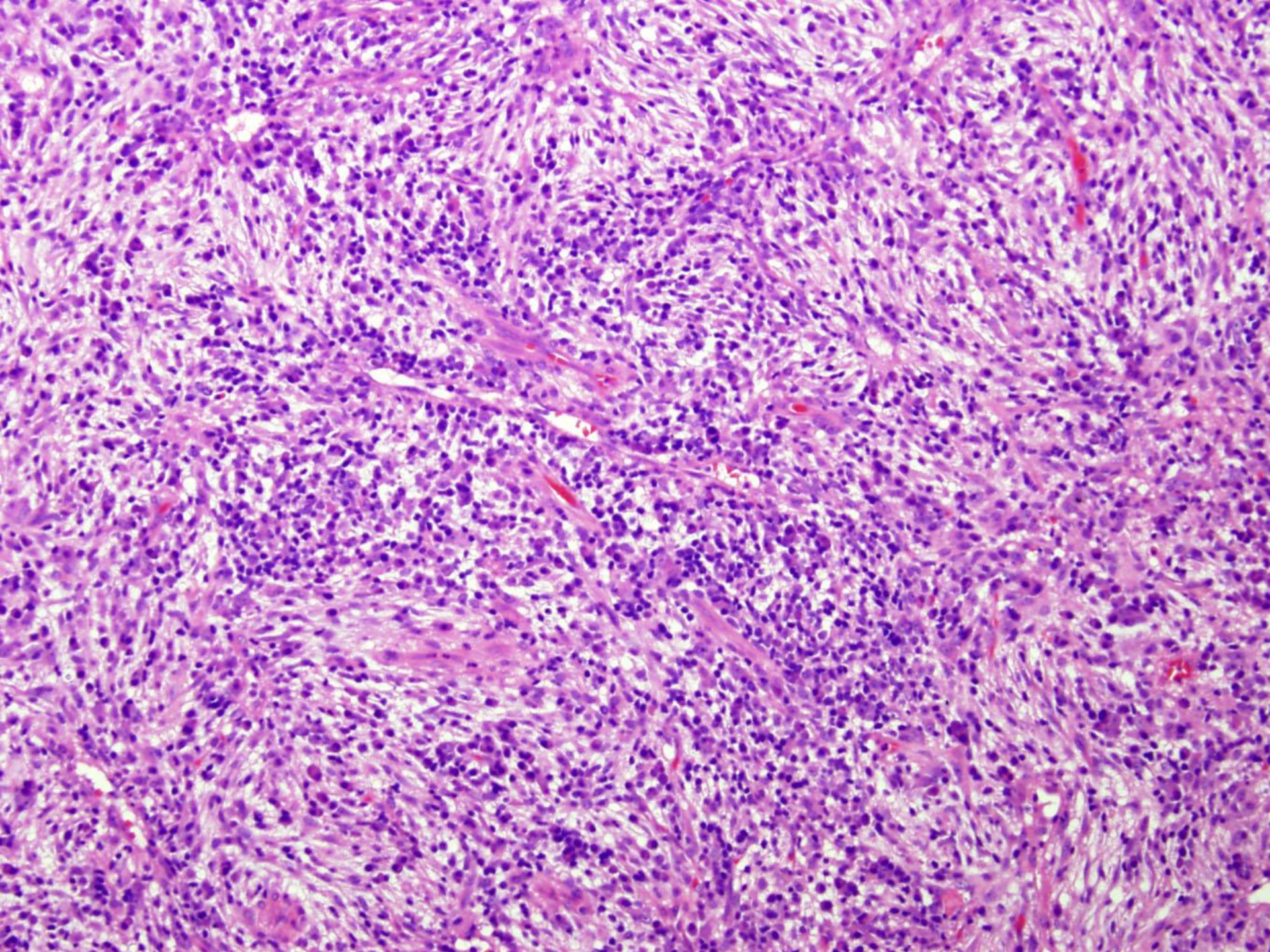
**Legume**



# 37 year old man with solitary lung mass











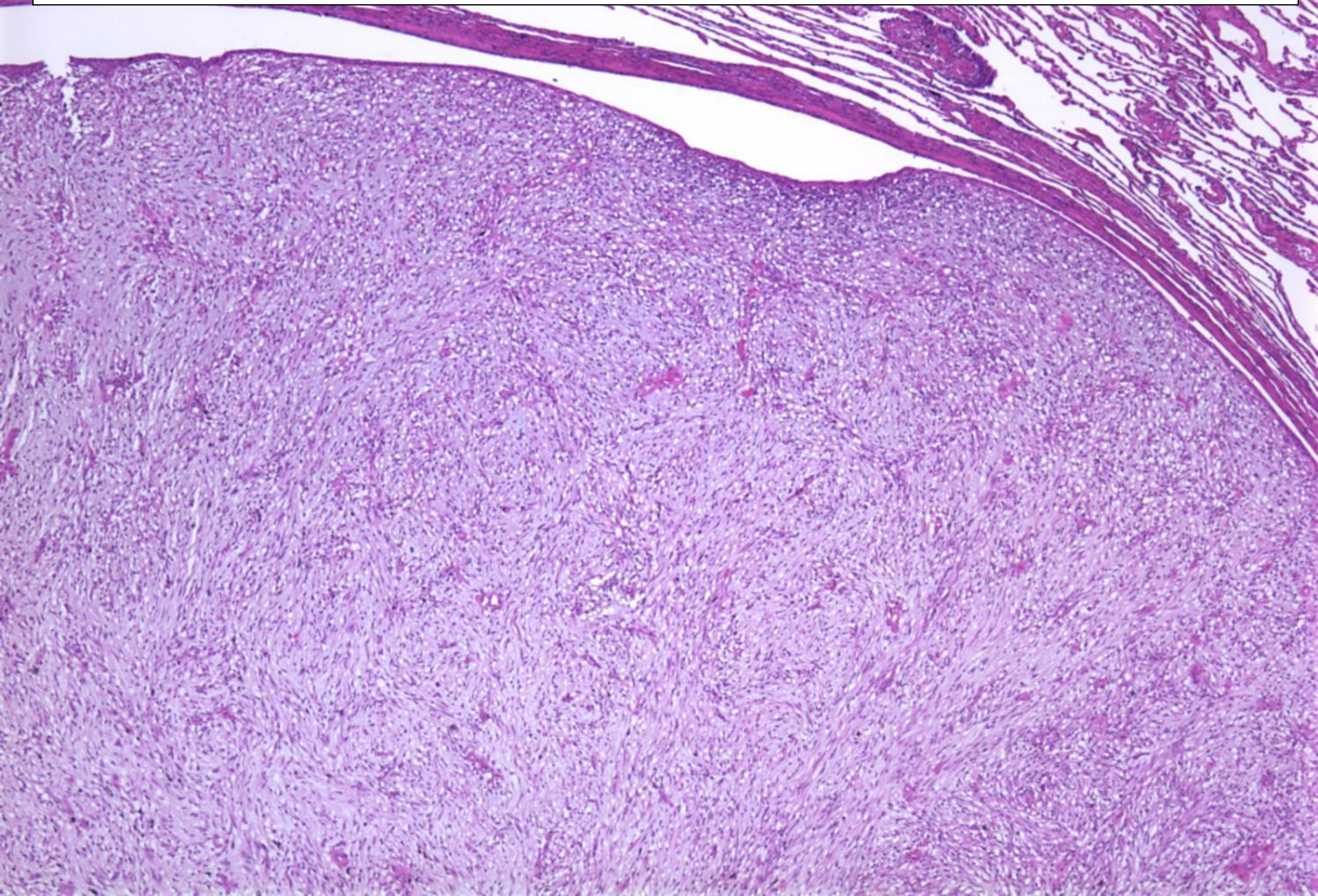
# **Non Neoplastic Inflammatory “Pseudotumor”**

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

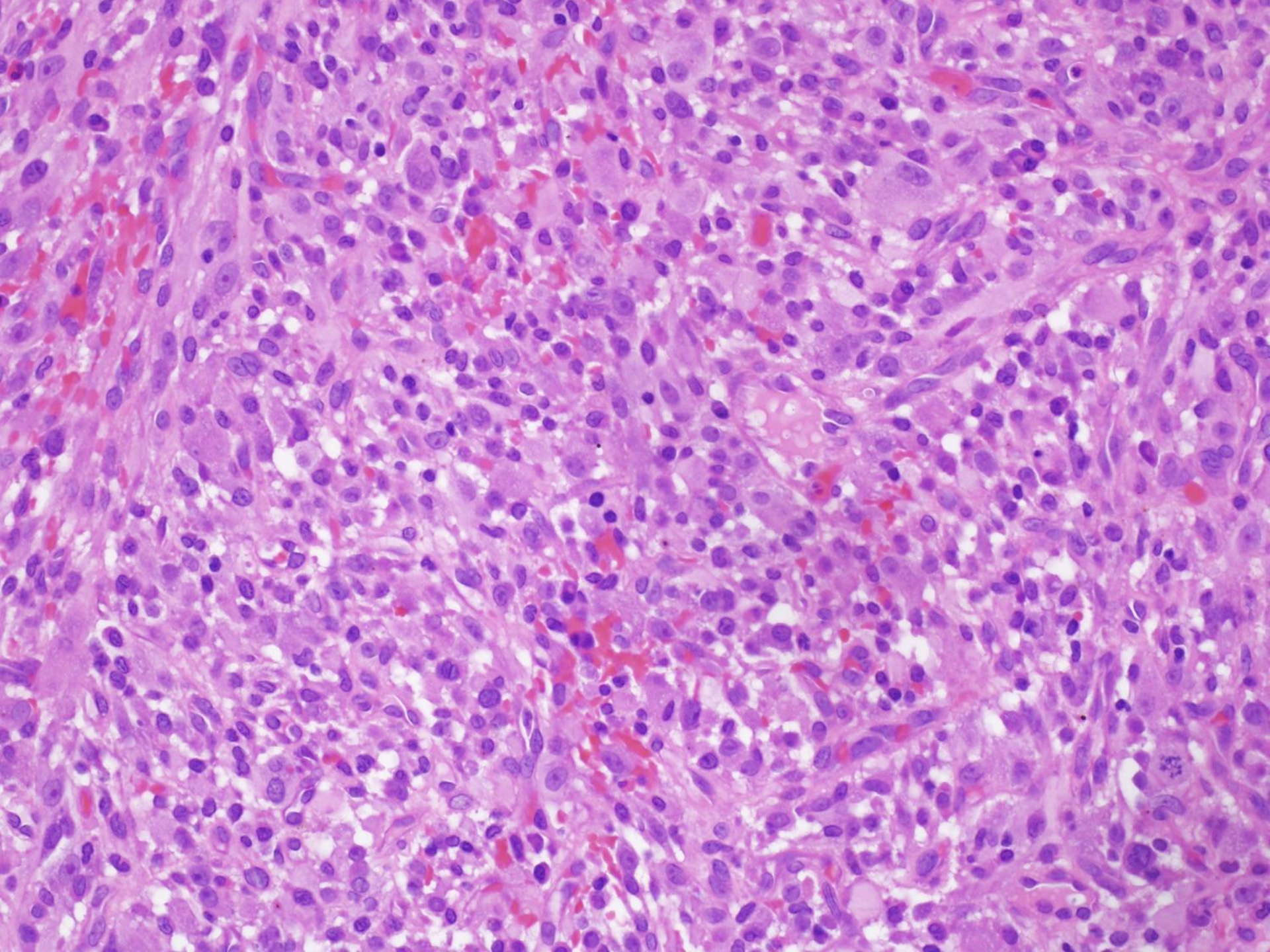
**Keratin, CD34, alk negative**



# 14 year old boy with solitary lung mass

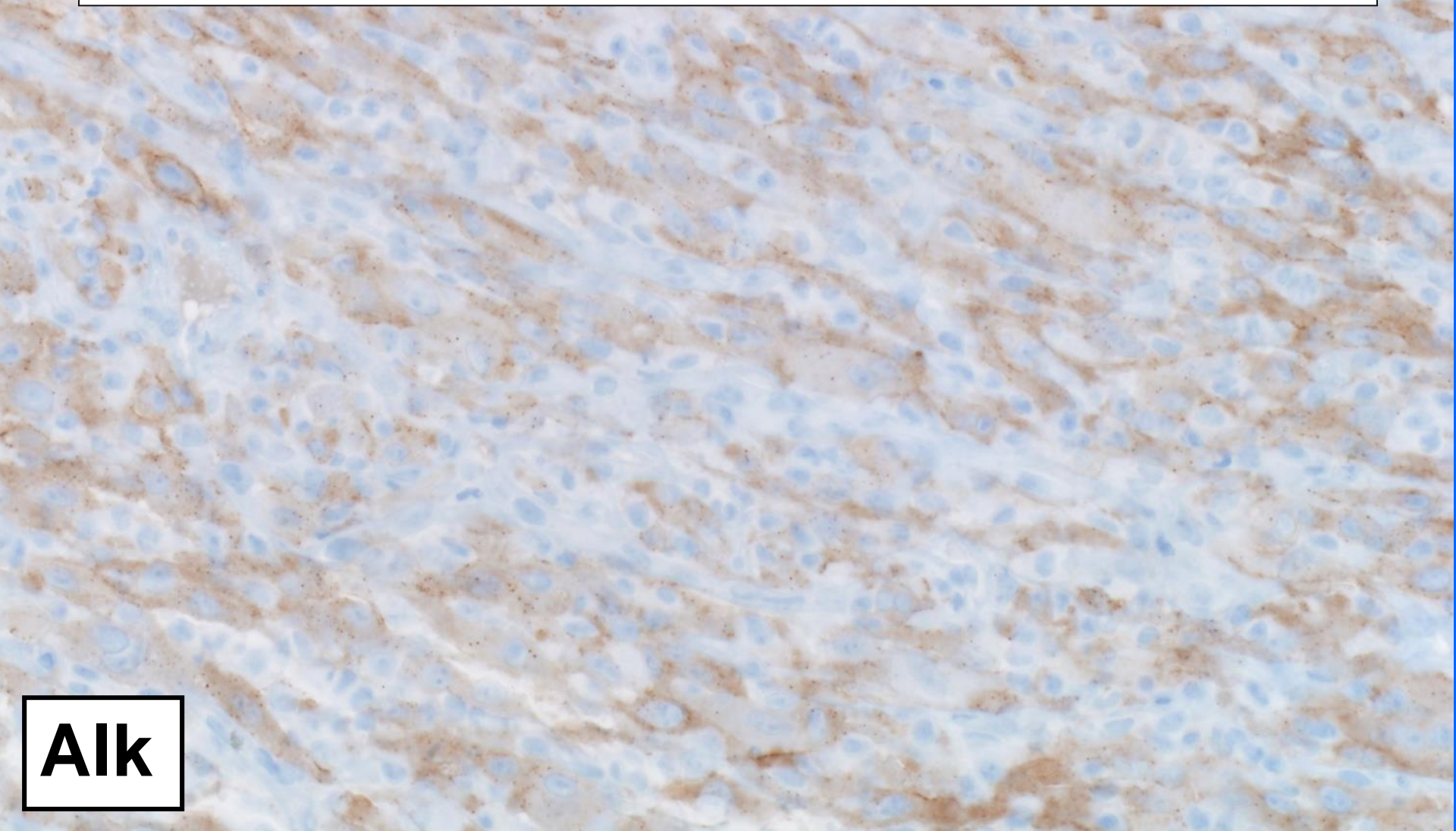








# **“Neoplastic Inflammatory Pseudotumor” Inflammatory Myofibroblastic Tumor**



**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

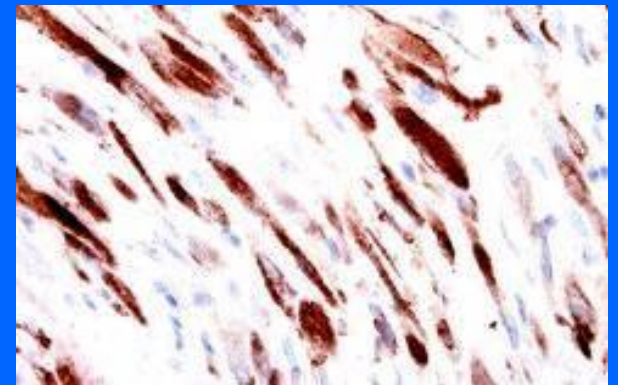
# Inflammatory Pseudotumors

- Neoplastic
  - Inflammatory myofibroblastic tumor
  - Fibrous histiocyoma **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



# **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)**

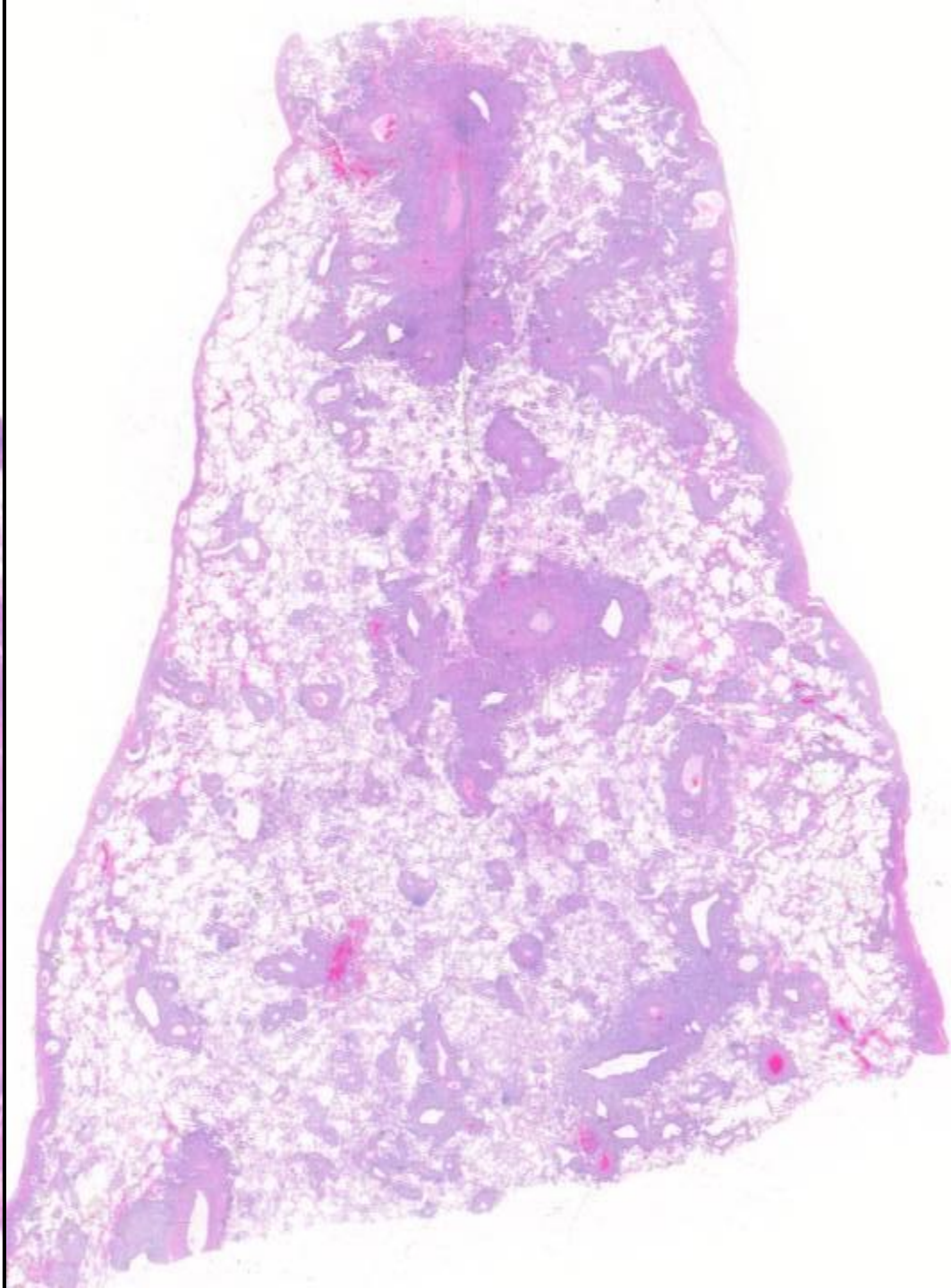
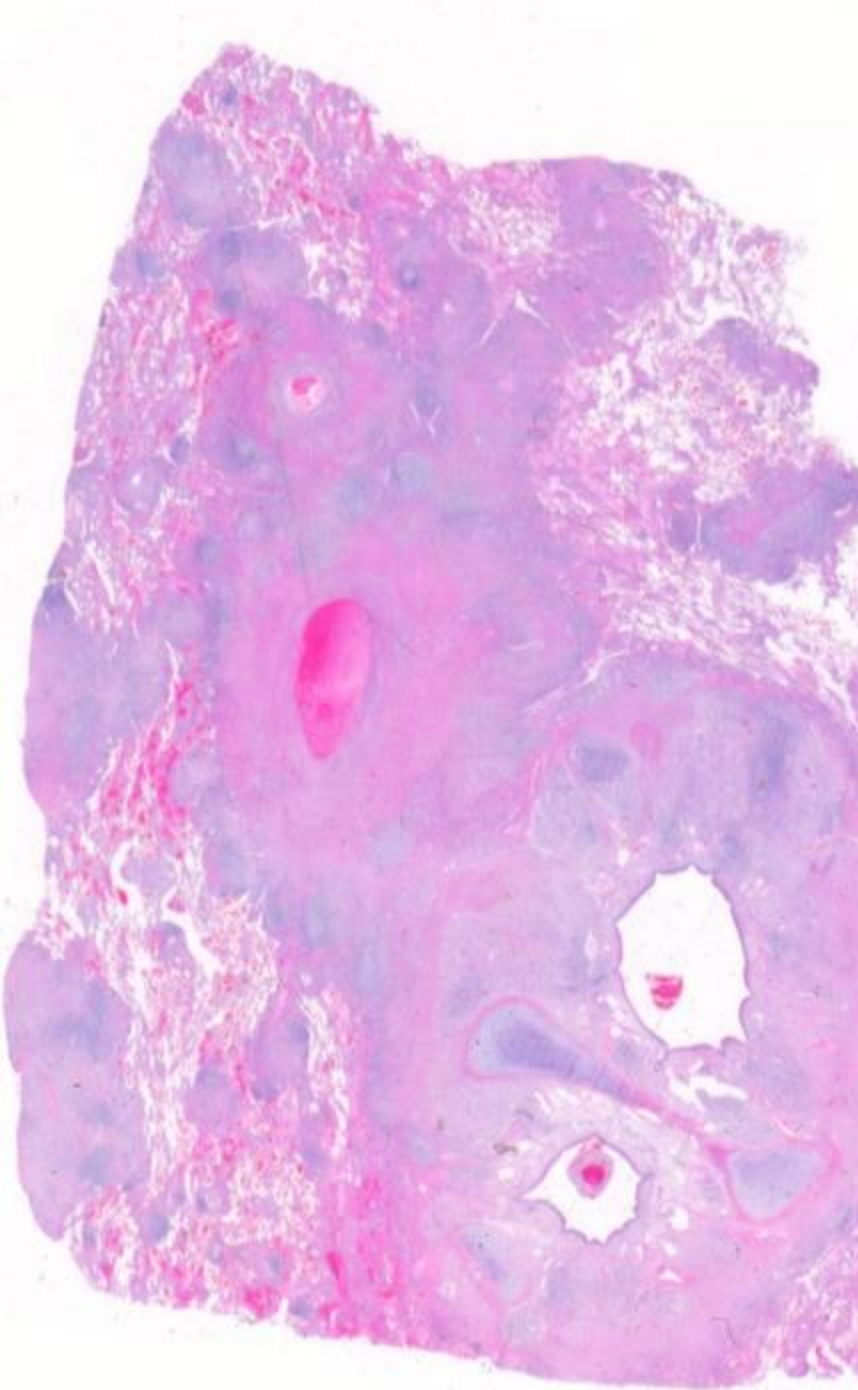


# IgG4-related Disease

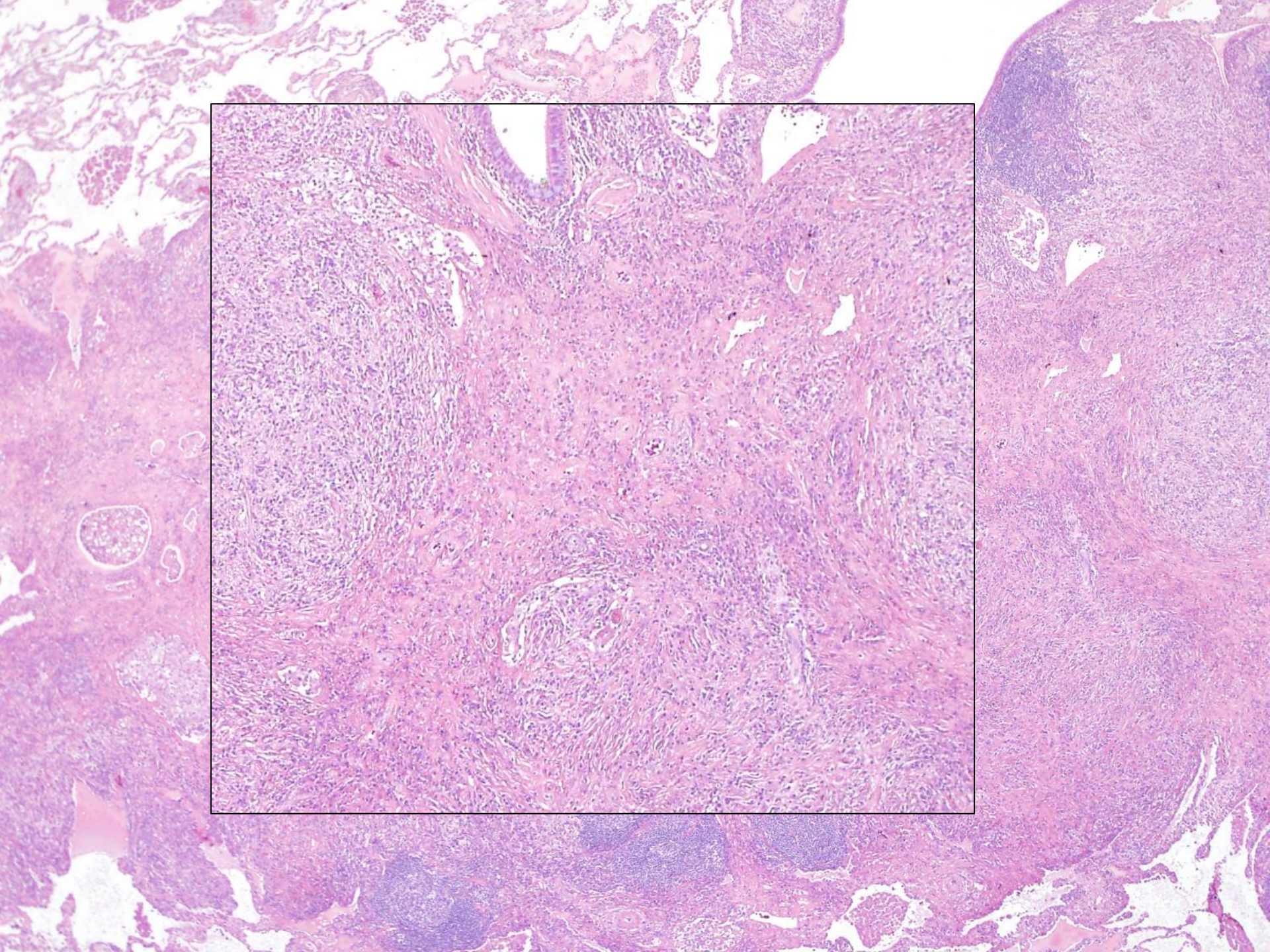
## Radiologic Patterns of Lung Involvement

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

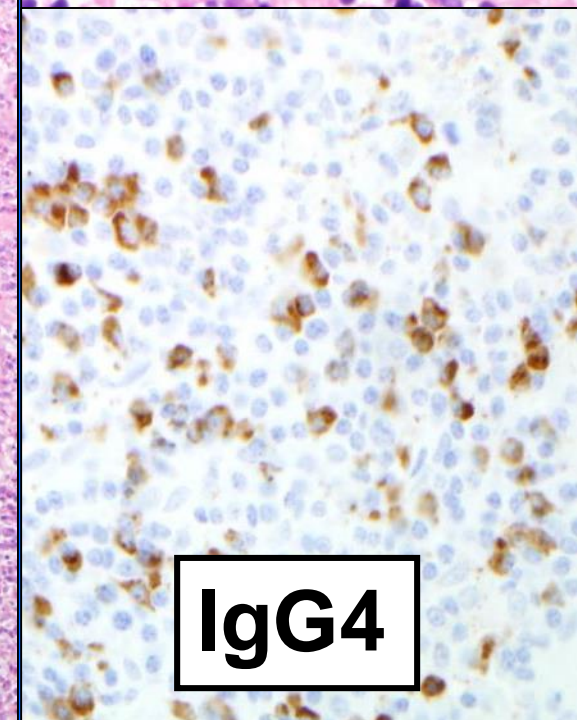
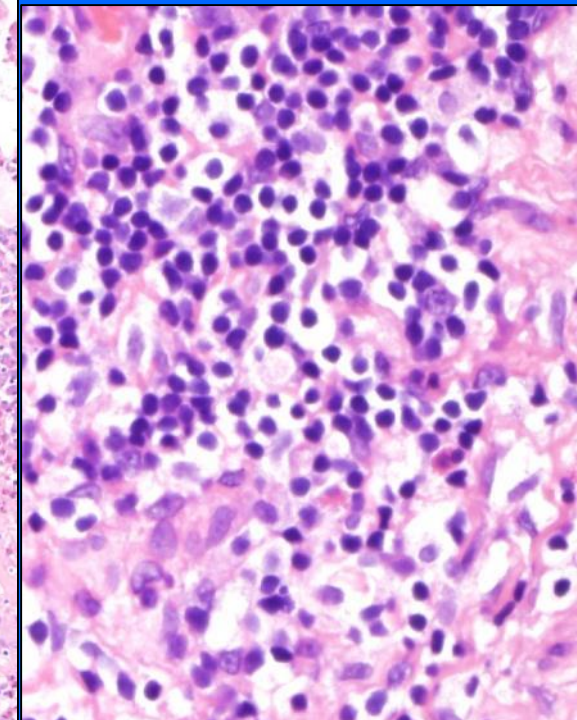
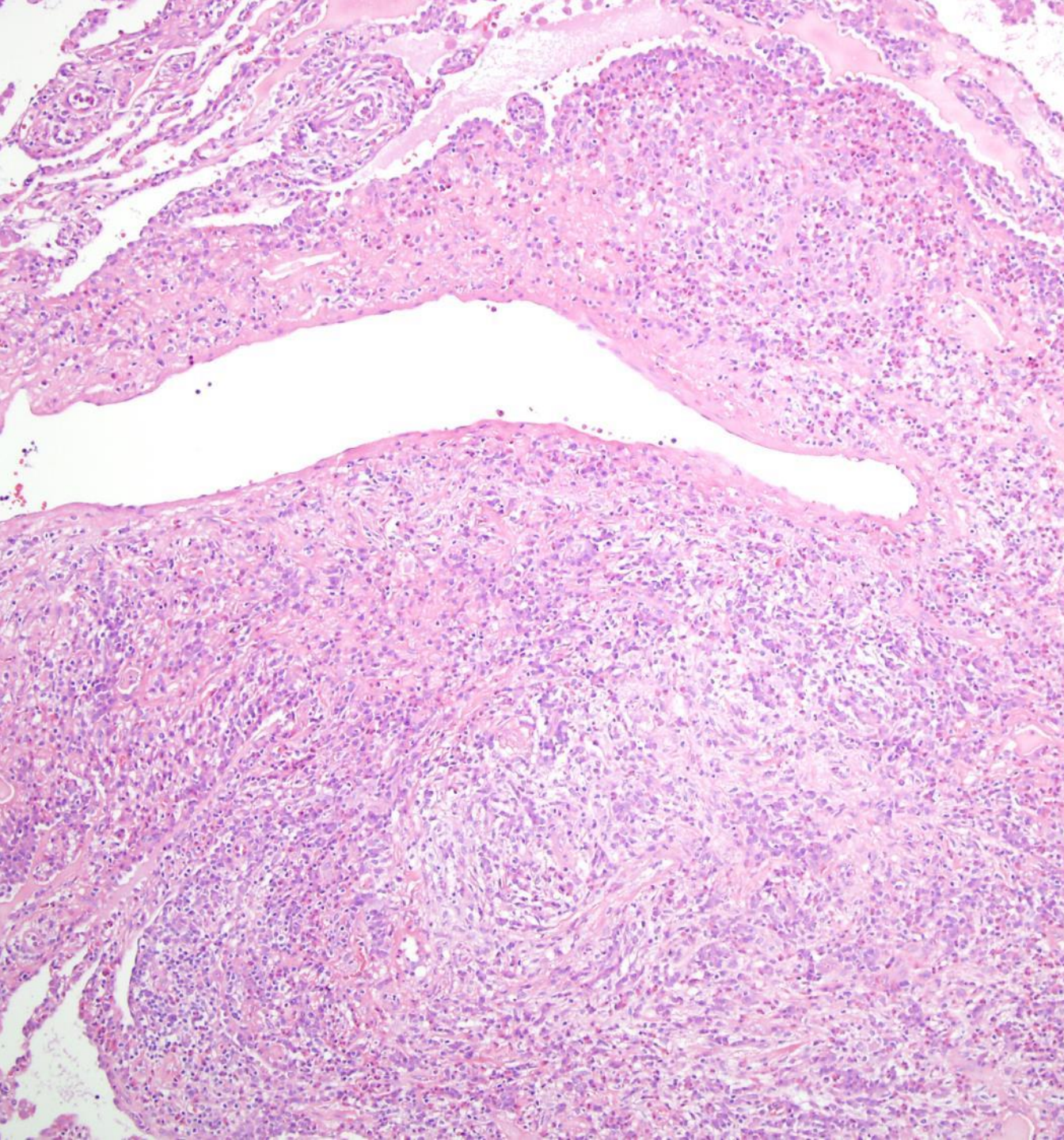












**IgG4**



# **IgG 4-related Disease**

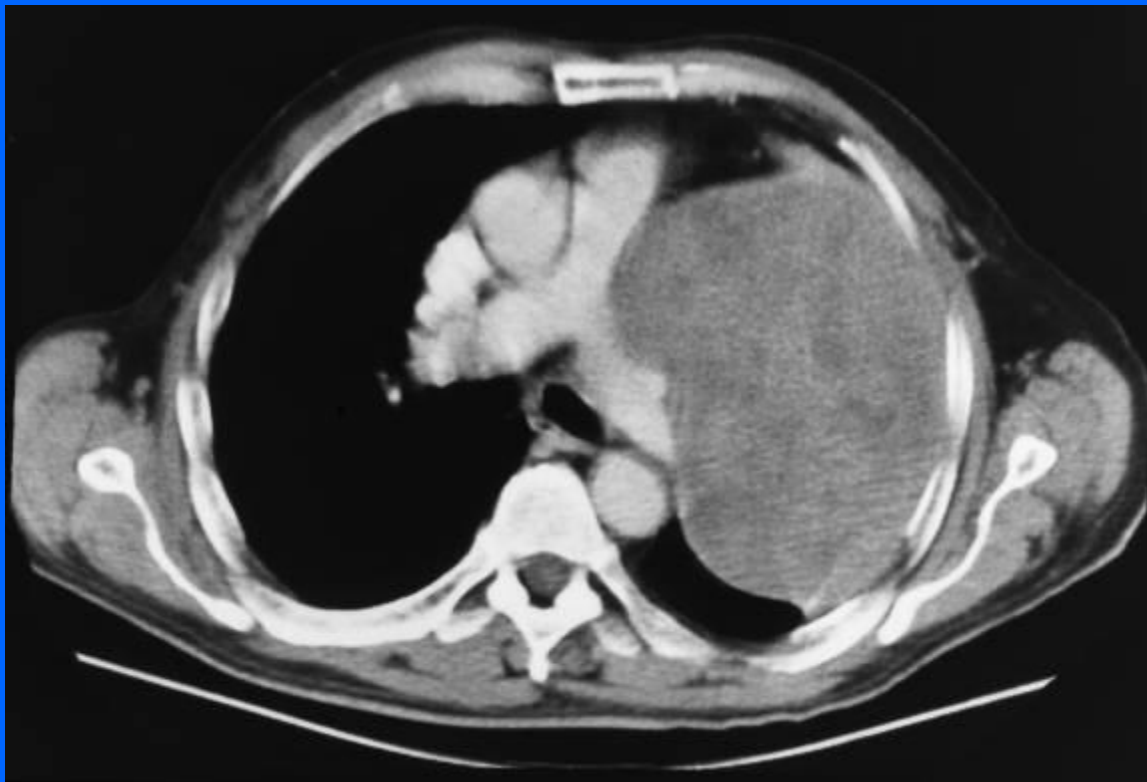
## **Quantitation**

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

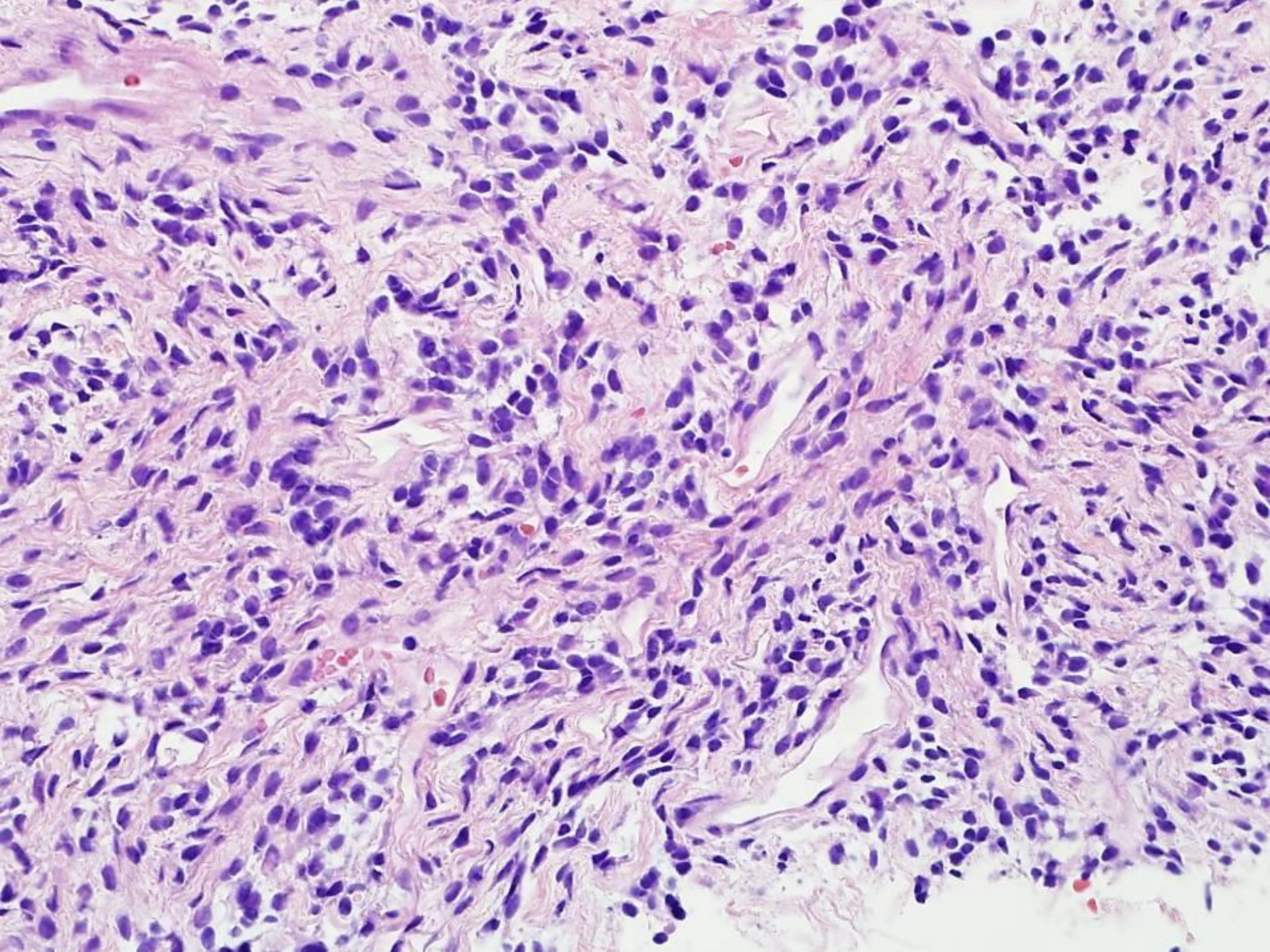


# History

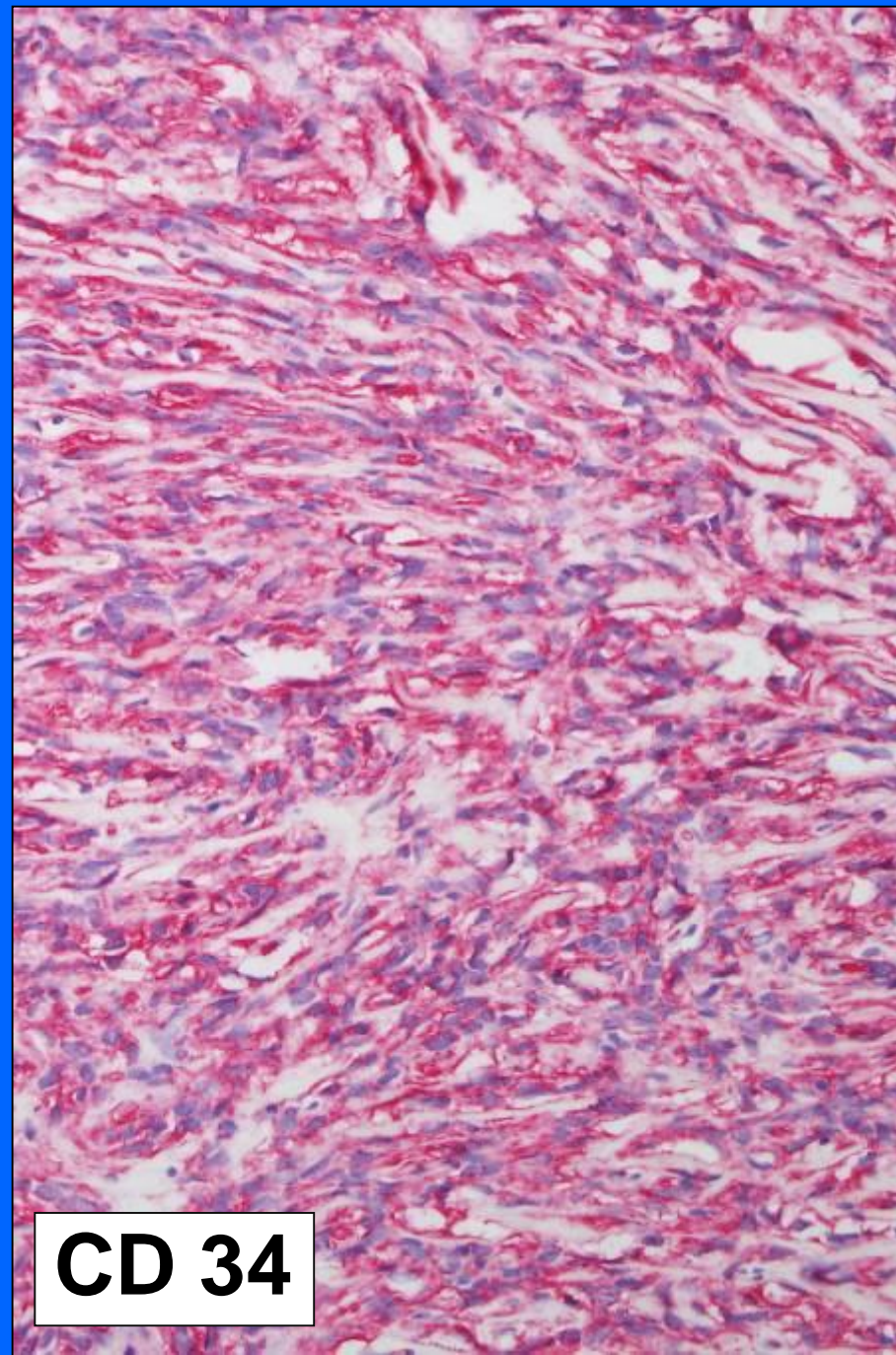
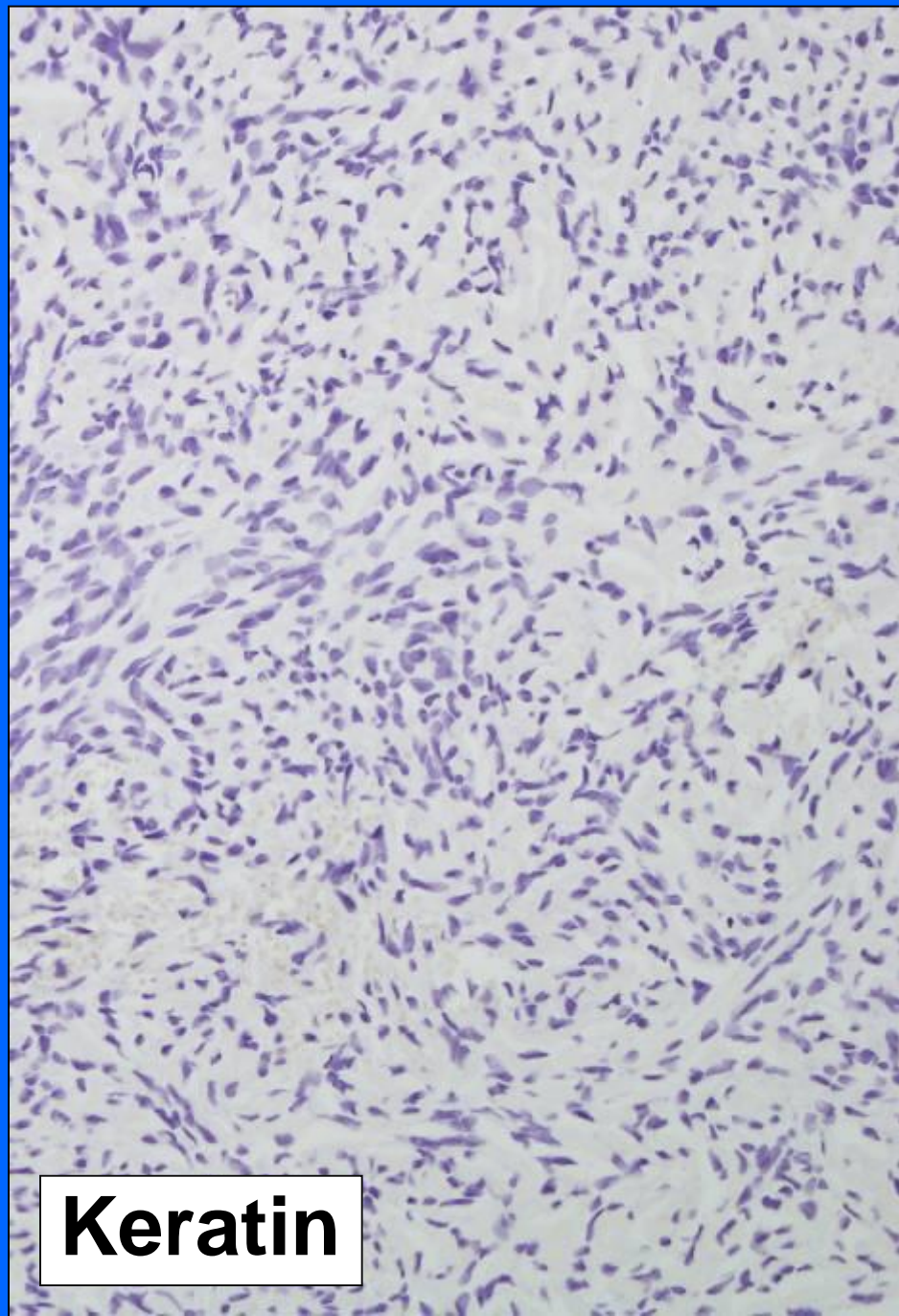
49 year old man with posterior  
flank pain











# Solitary Fibrous Tumor

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



# Predicting Recurrence in SFT

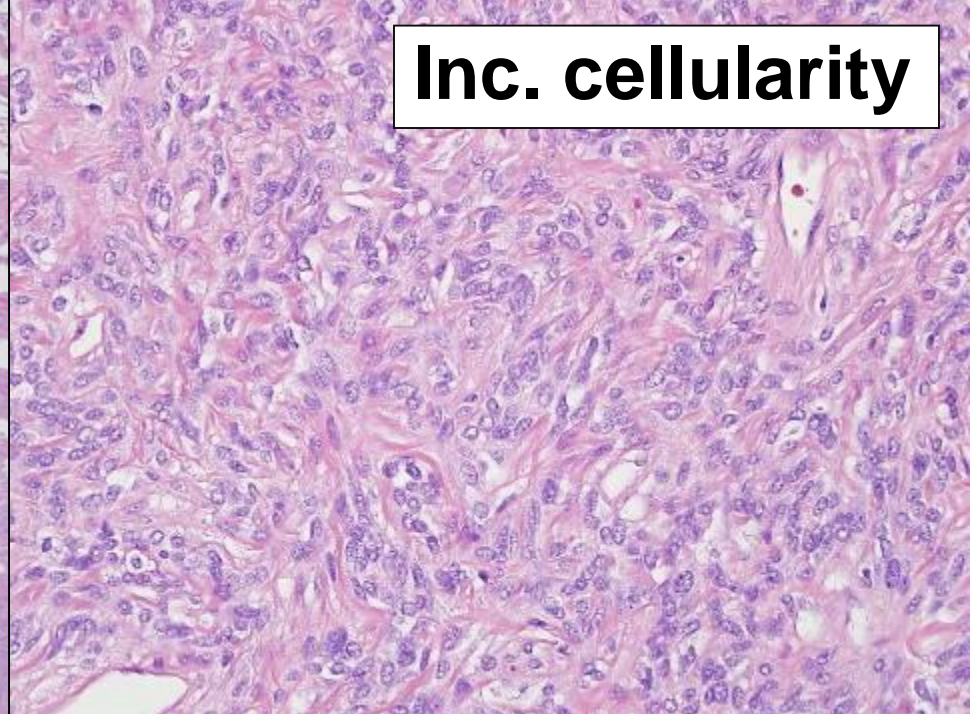
	Feature	Points
Age (yrs)	< 55	0
	$\geq 55$	1
Size (cm)	< 5	0
	5 to < 10	1
	10 to < 15	2
	$\geq 15$	3
Tumor necrosis (%)	< 10	0
	$\geq 10$	1
Mitoses/10hpf	< 4	0
	$\geq 4$	1

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

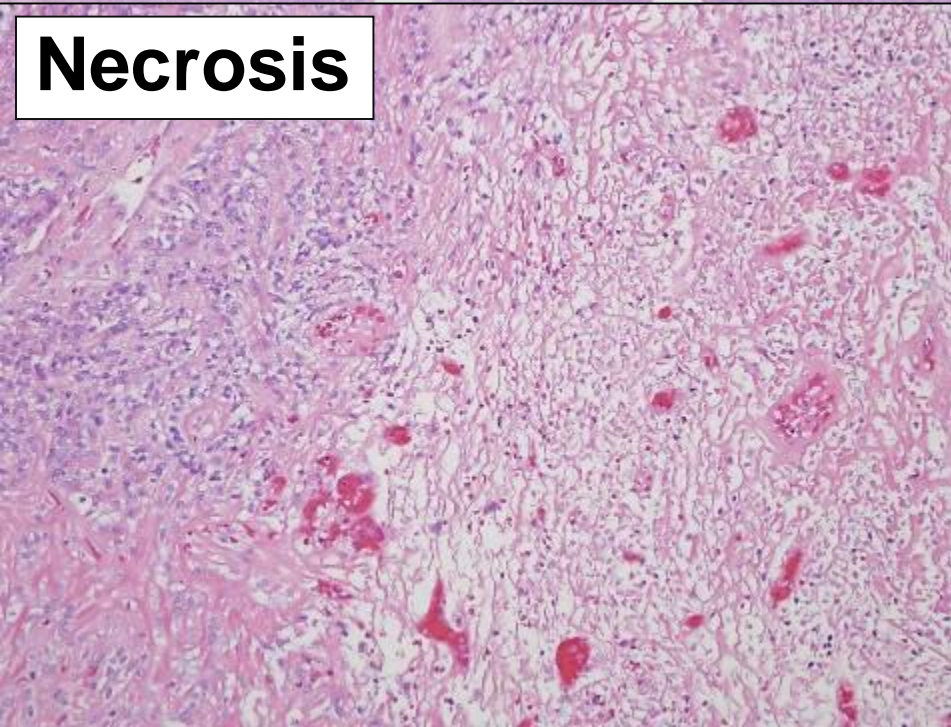
# Malignant SFT



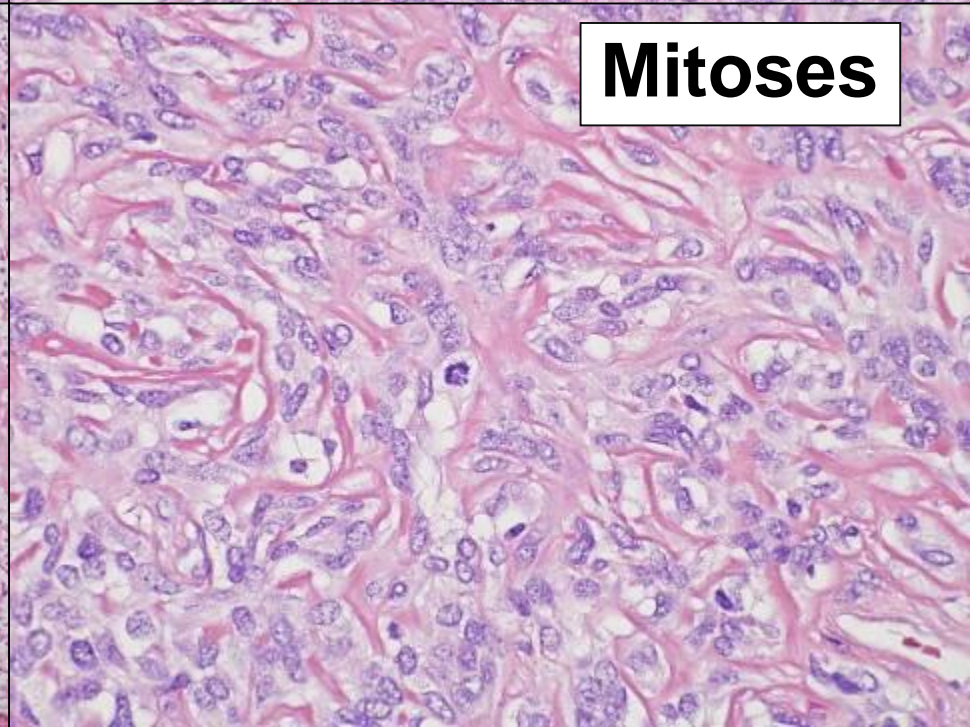
**Inc. cellularity**



**Necrosis**



**Mitoses**





# Predicting Recurrence in SFT

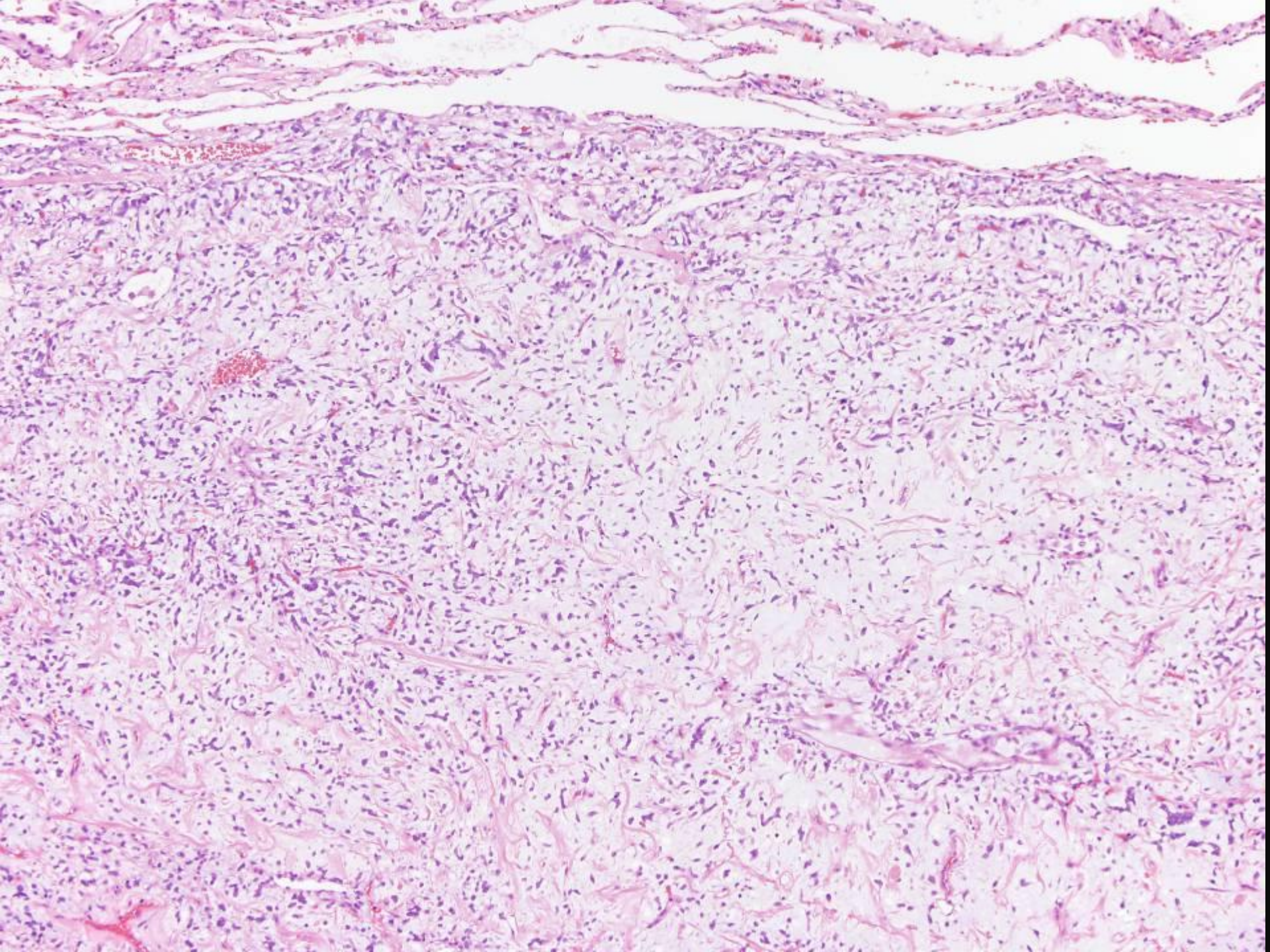
Risk of metastasis at # years (% , y)

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

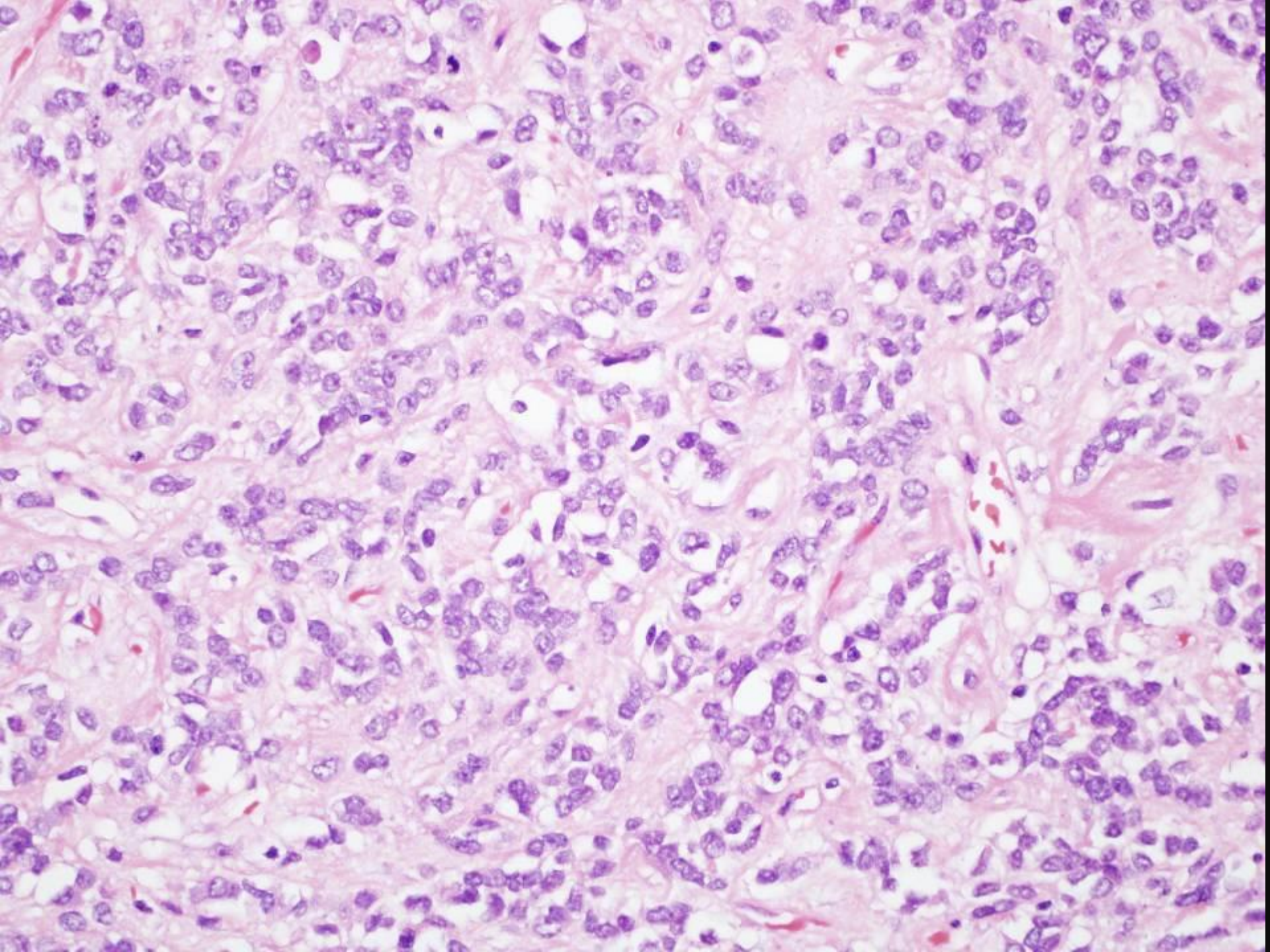
# History

- 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





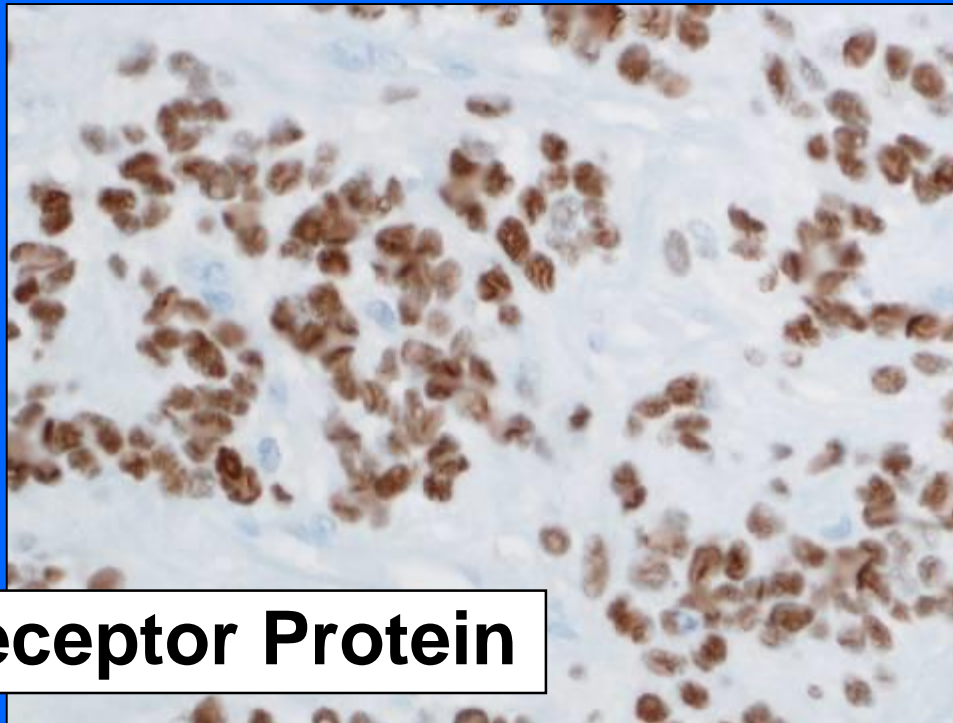






# Diagnosis?

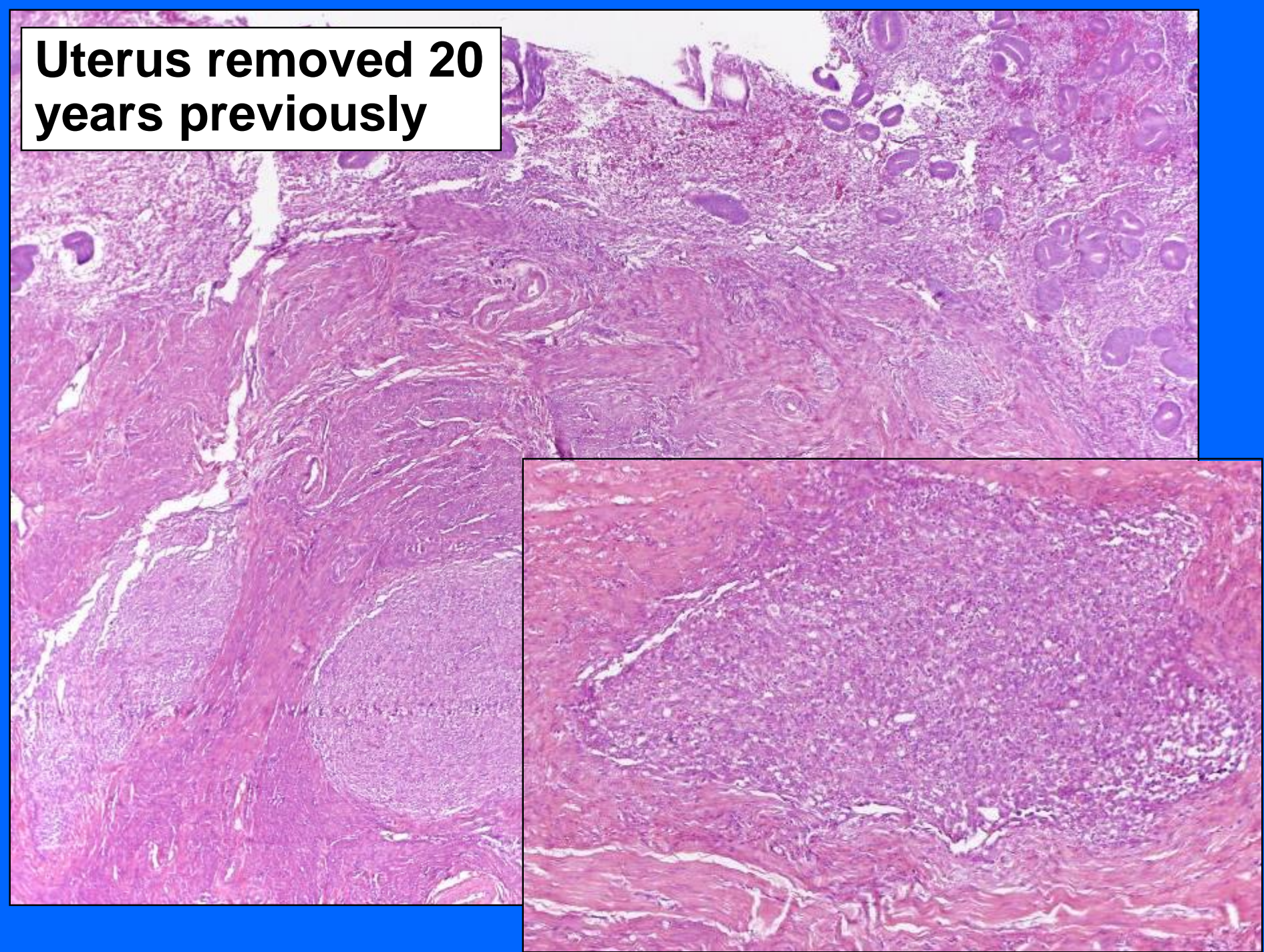
**Most consistent with Metastatic  
Endometrial Stromal Sarcoma**



**Estrogen Receptor Protein**



**Uterus removed 20  
years previously**





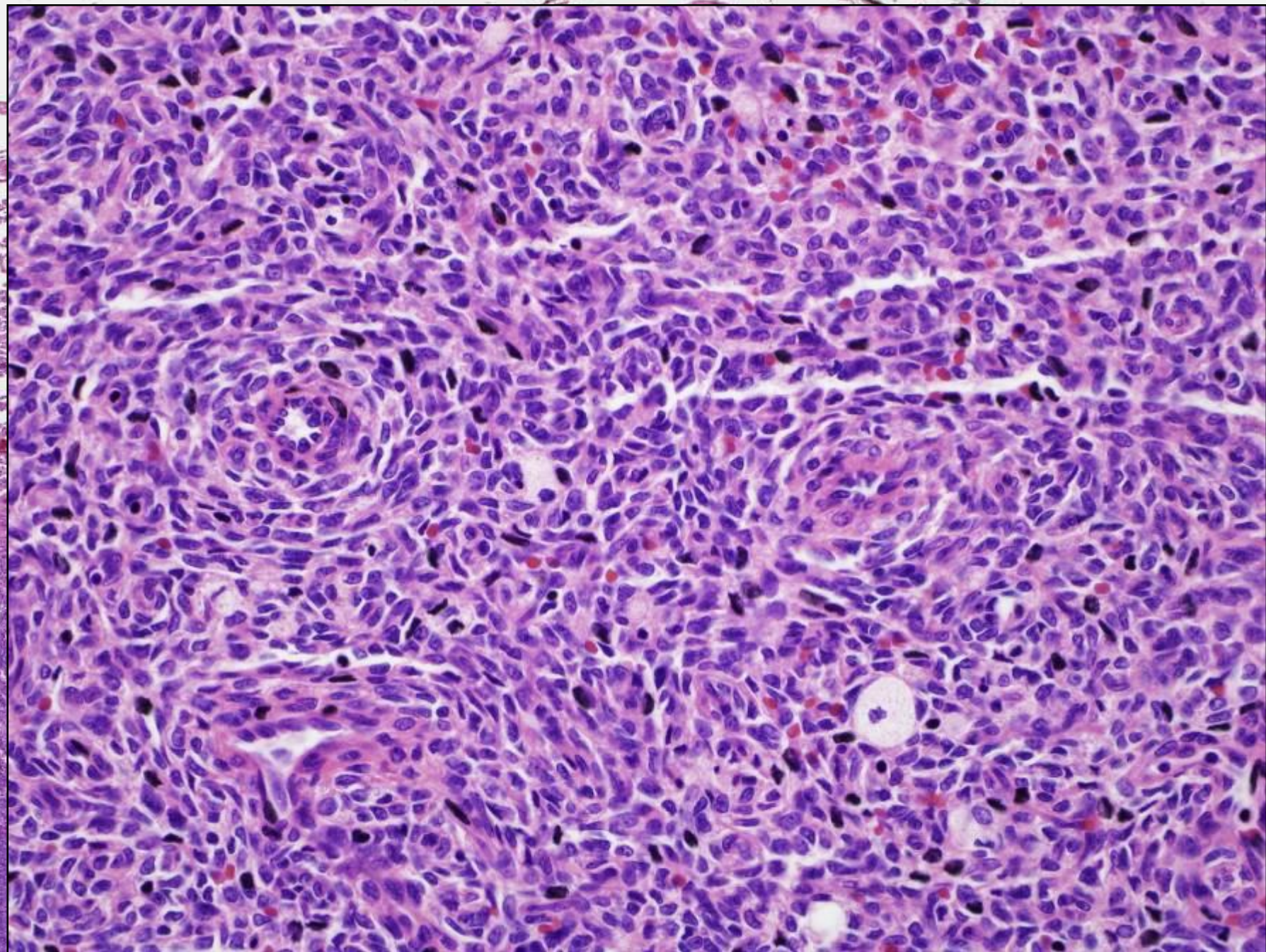
# Challenges in Dx of Metastatic ESS

- 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

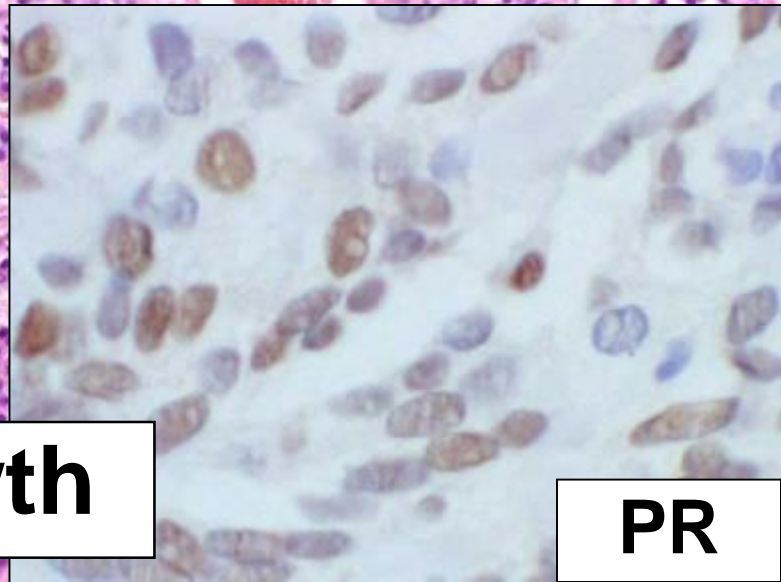
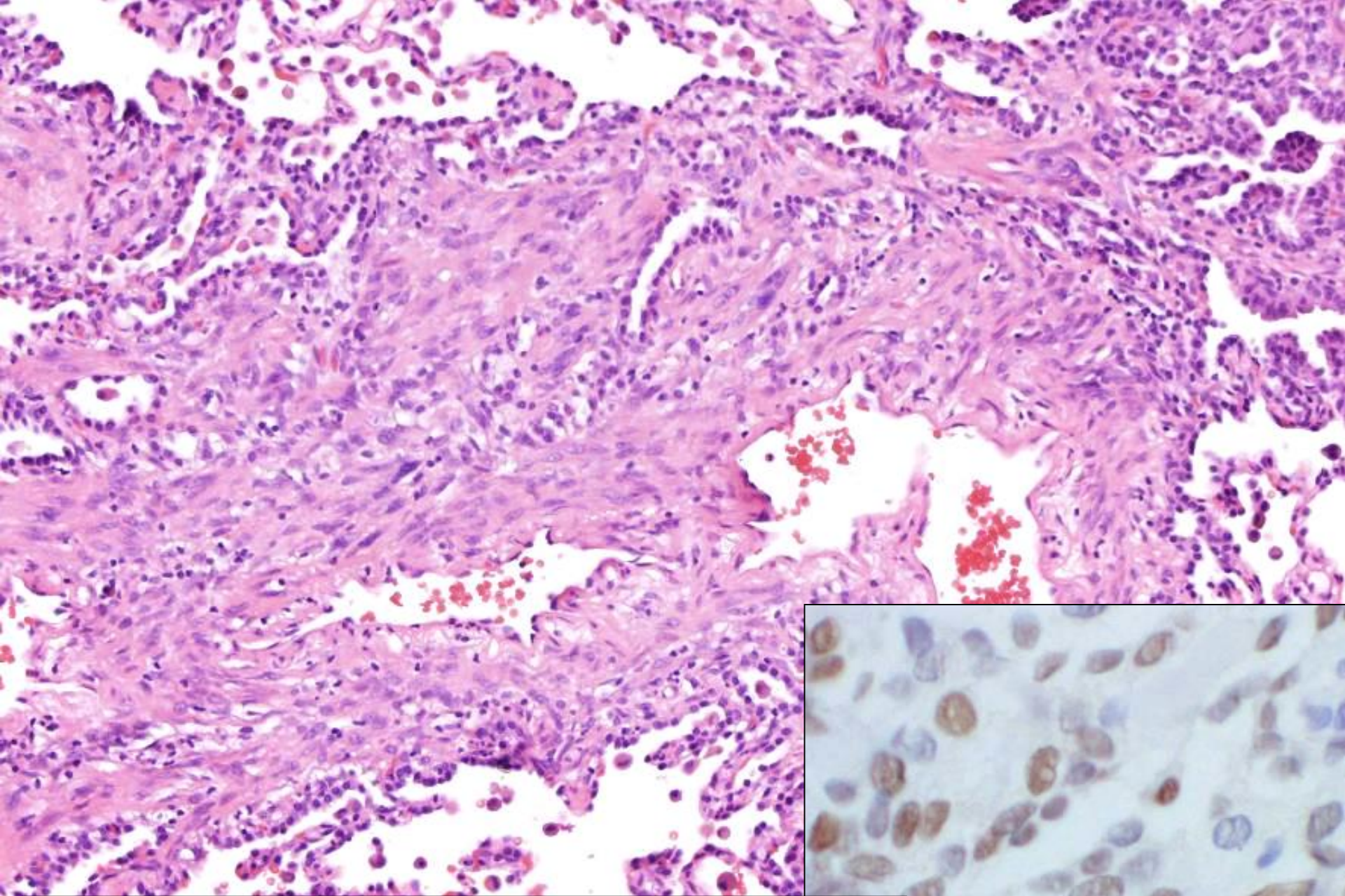
# Metastatic ESS

- Histology parallels uterine primary
  - Spindle cells,  $\pm$  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







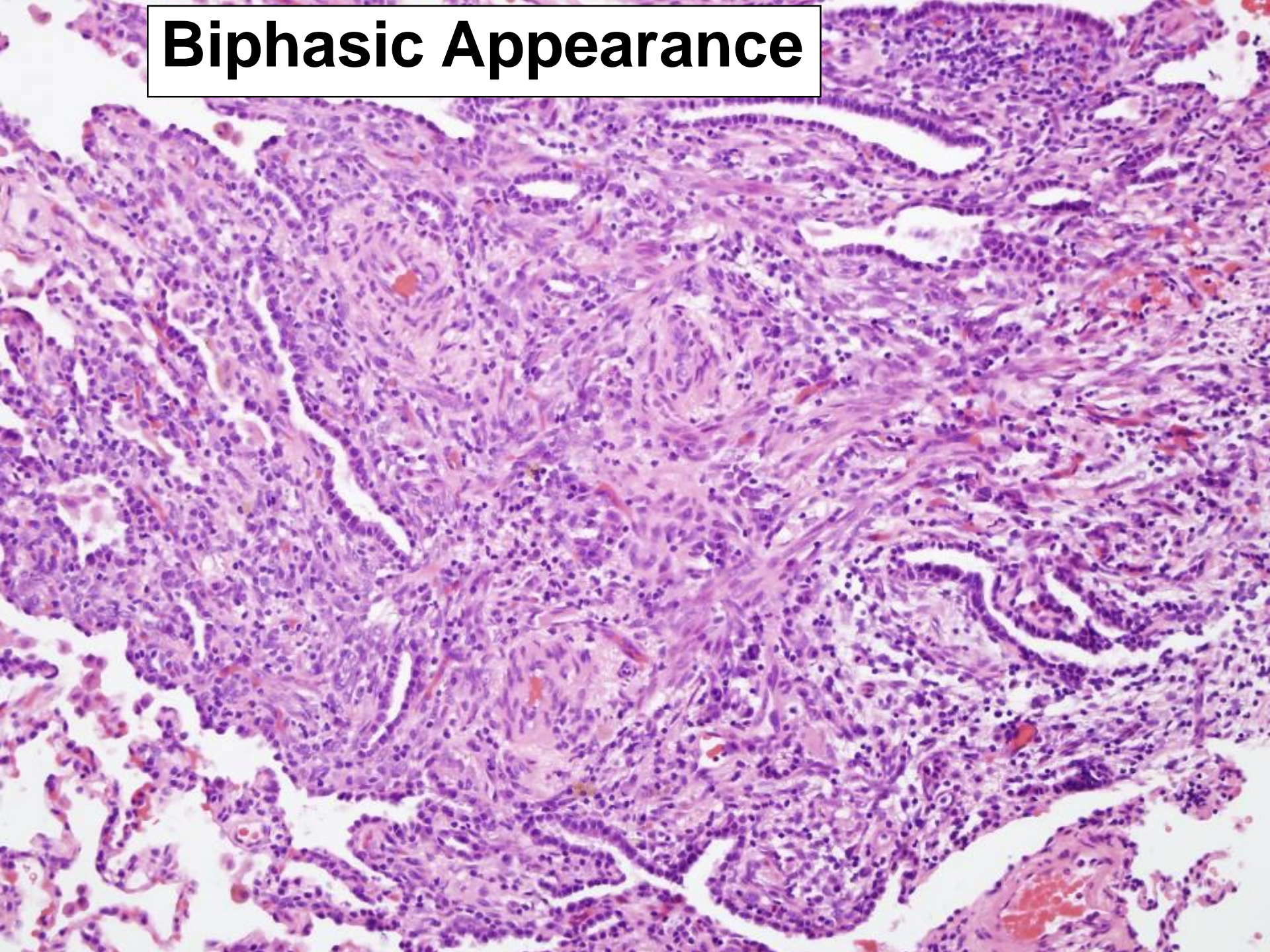


**Marked Interstitial Growth**

**PR**

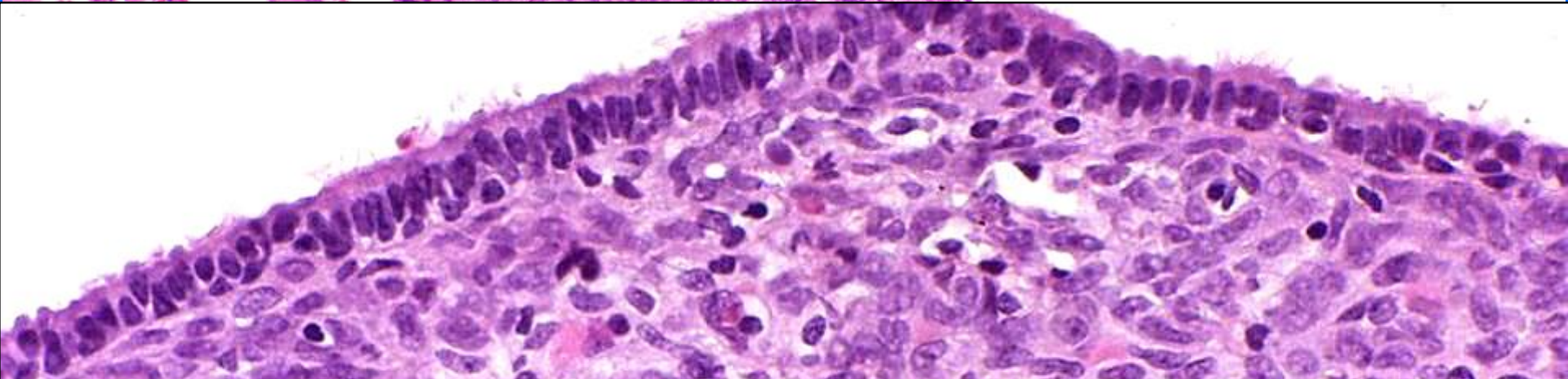
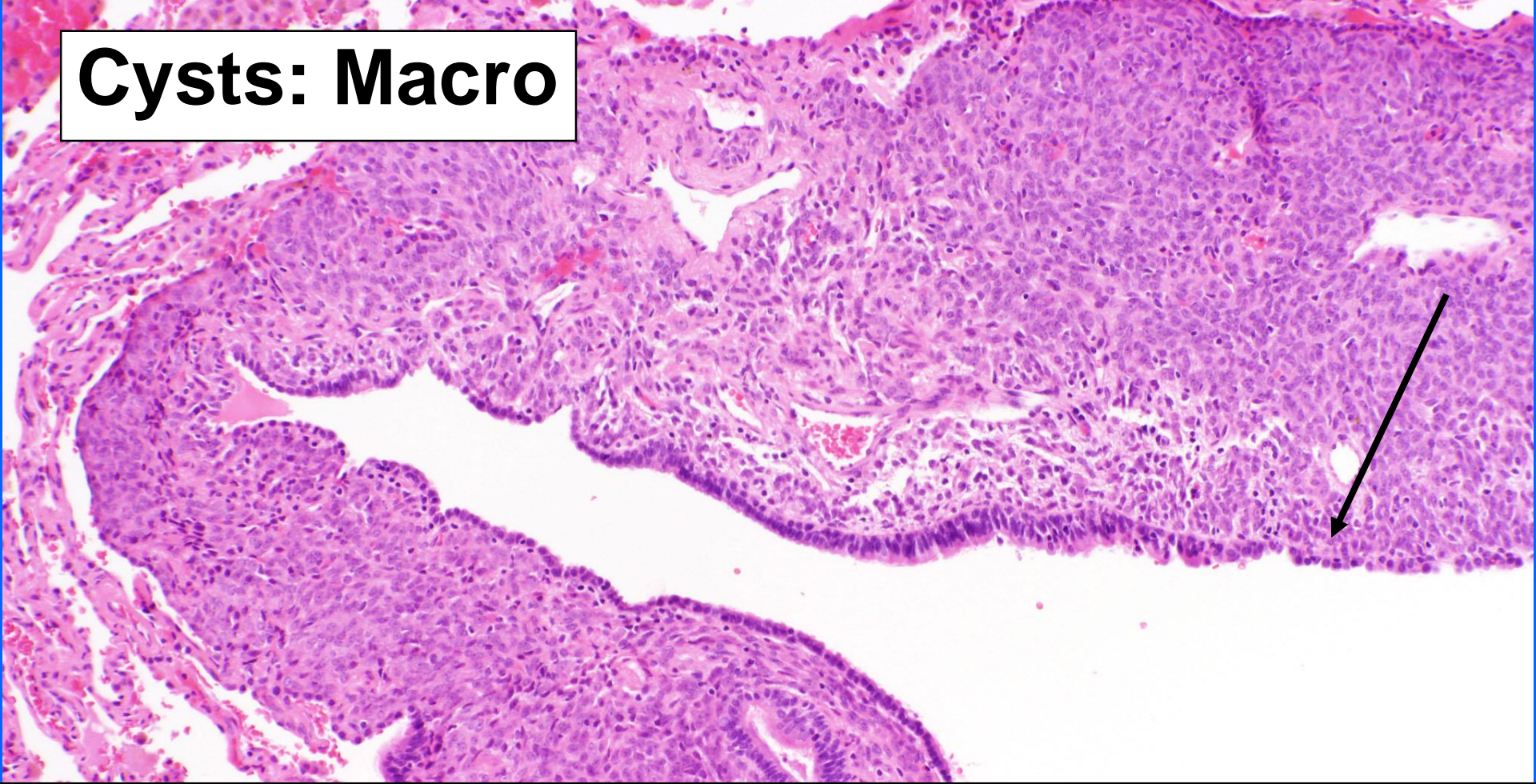


# Biphasic Appearance



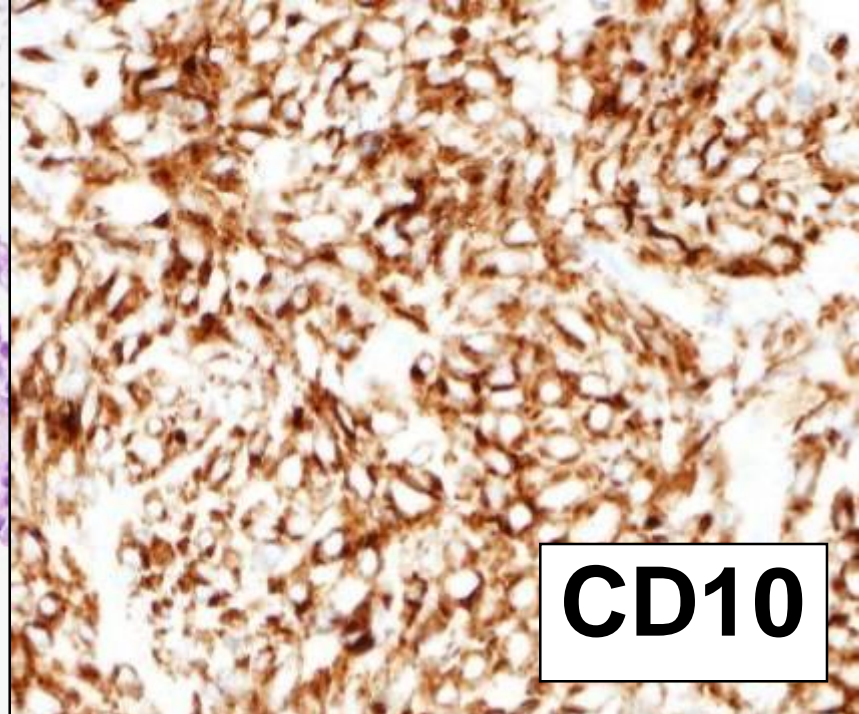
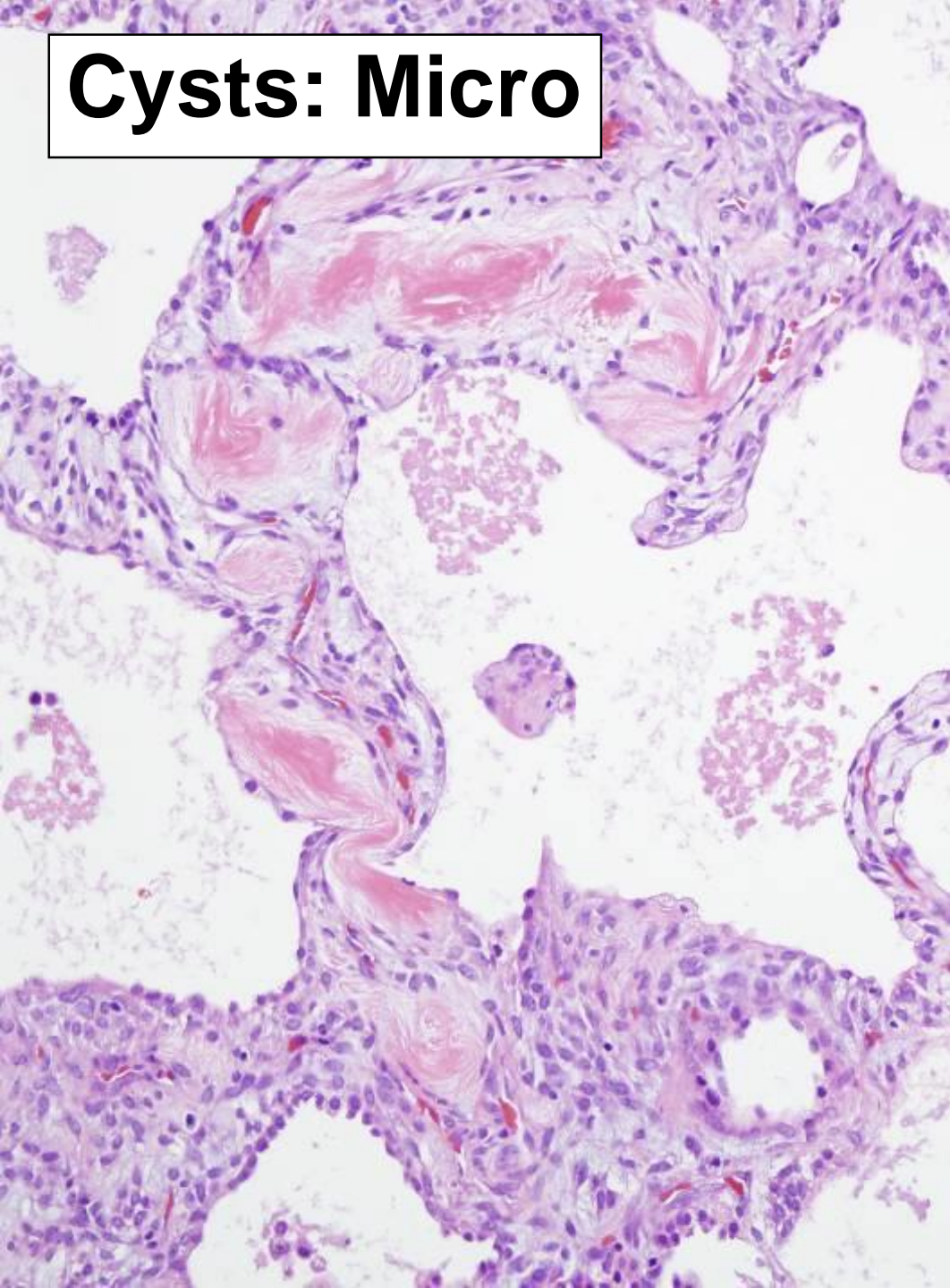


# Cysts: Macro

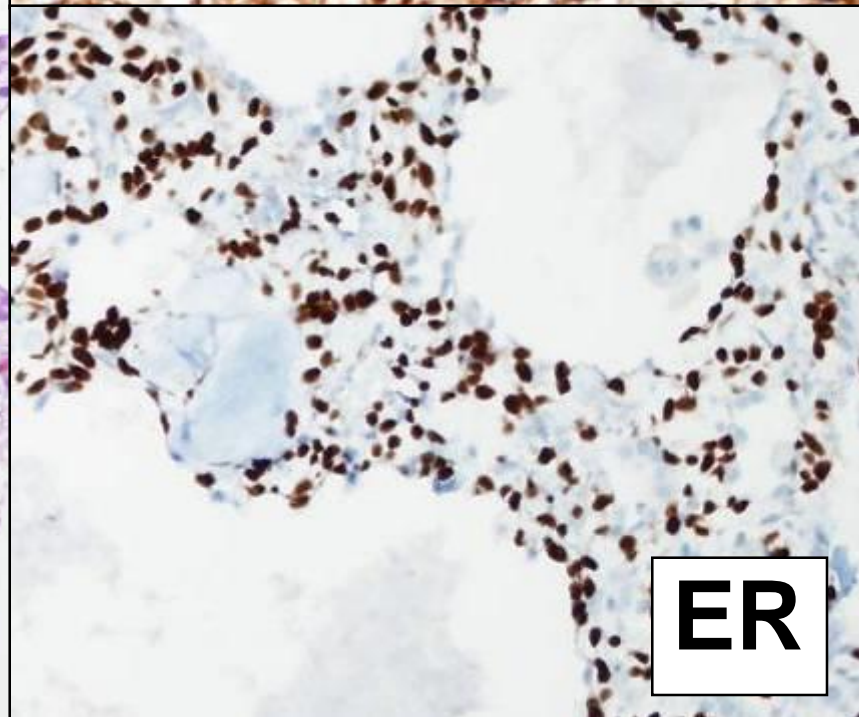




# Cysts: Micro



**CD10**



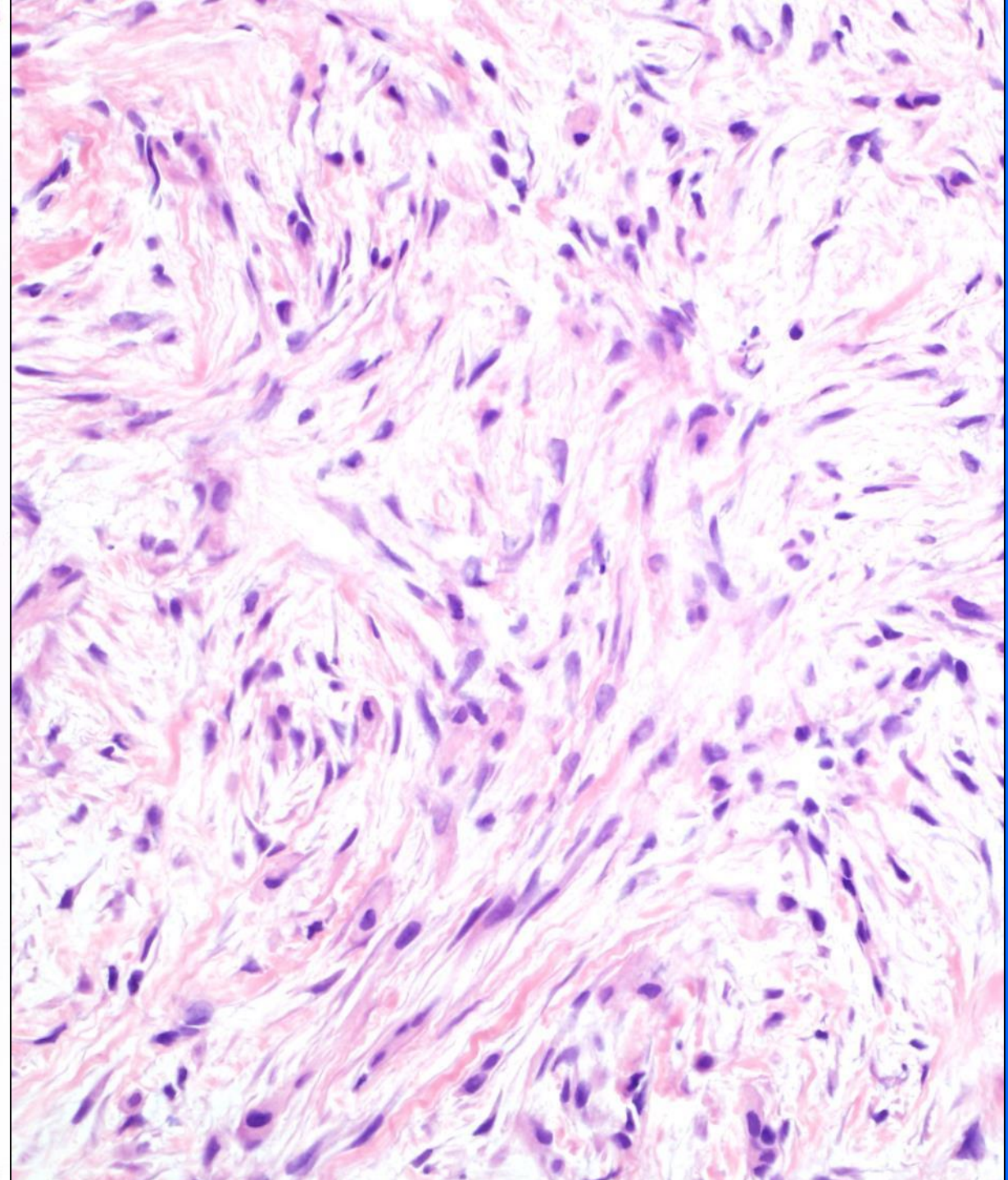
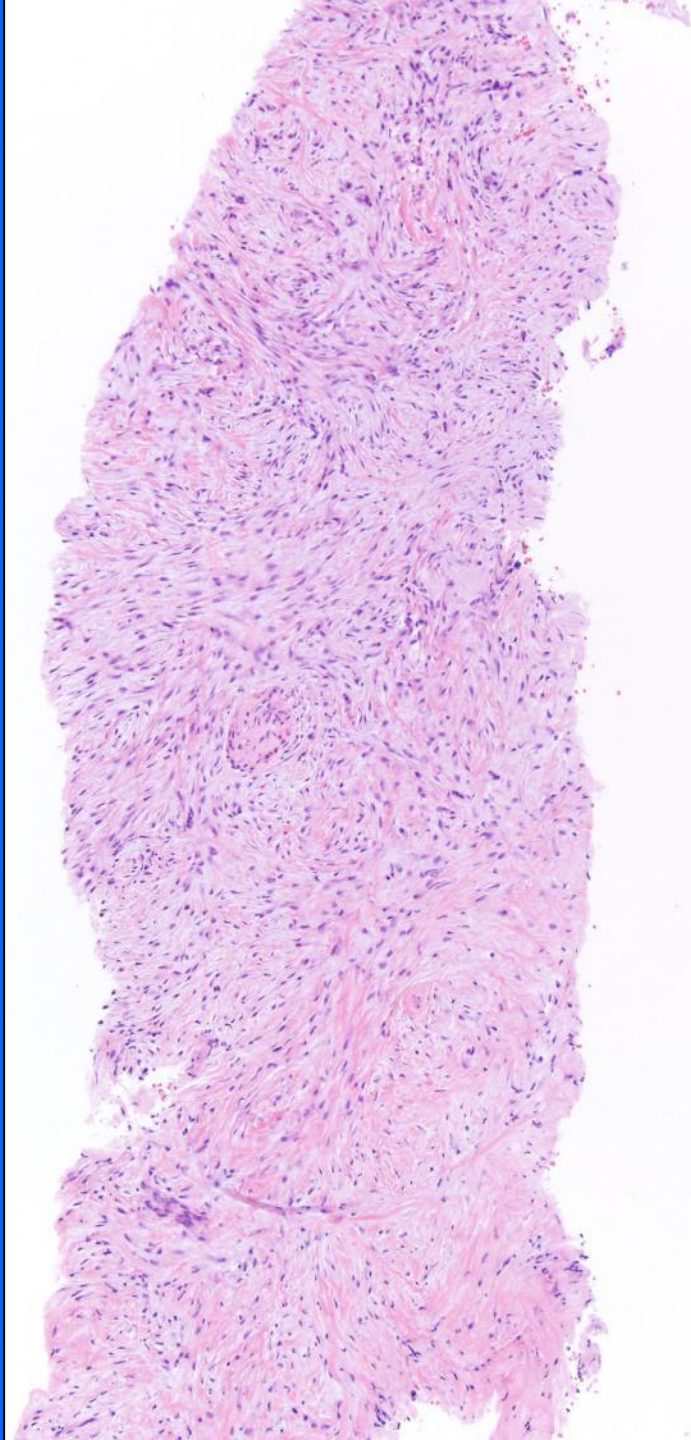
**ER**

# **Metastatic ESS**

## **Differential Diagnosis**

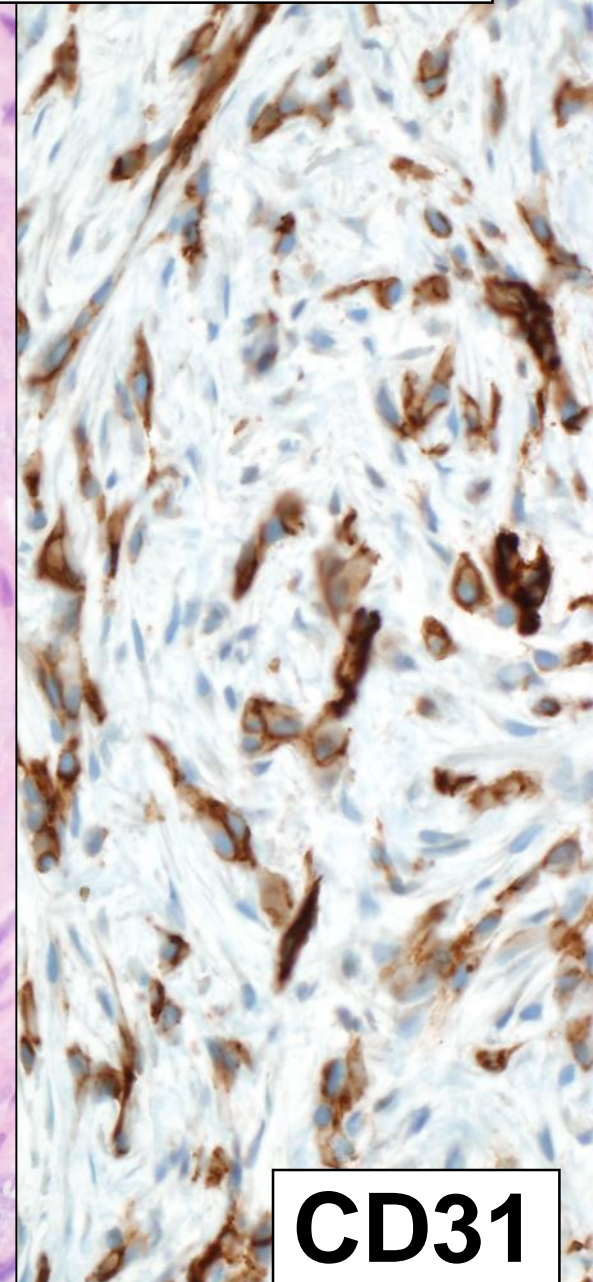
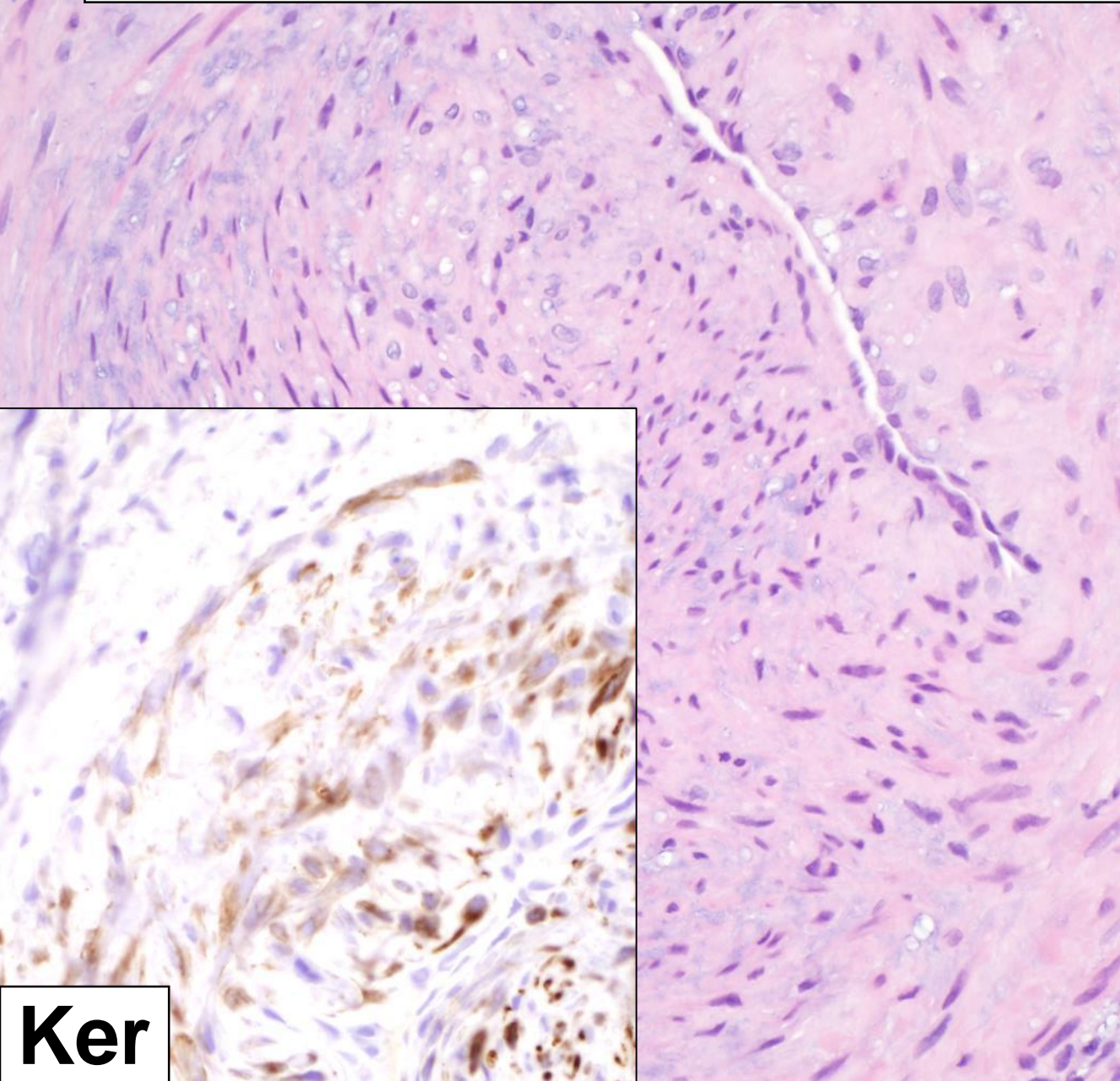
- **Epithelioid hemangioendothelioma**
- **Other metastatic spindle cell tumors (dermatofibroma, DFSP, other sarcomas, PEComa)**
- **Solitary fibrous tumor**
- **Synovial sarcoma**







# Epithelioid Hemangioendothelioma

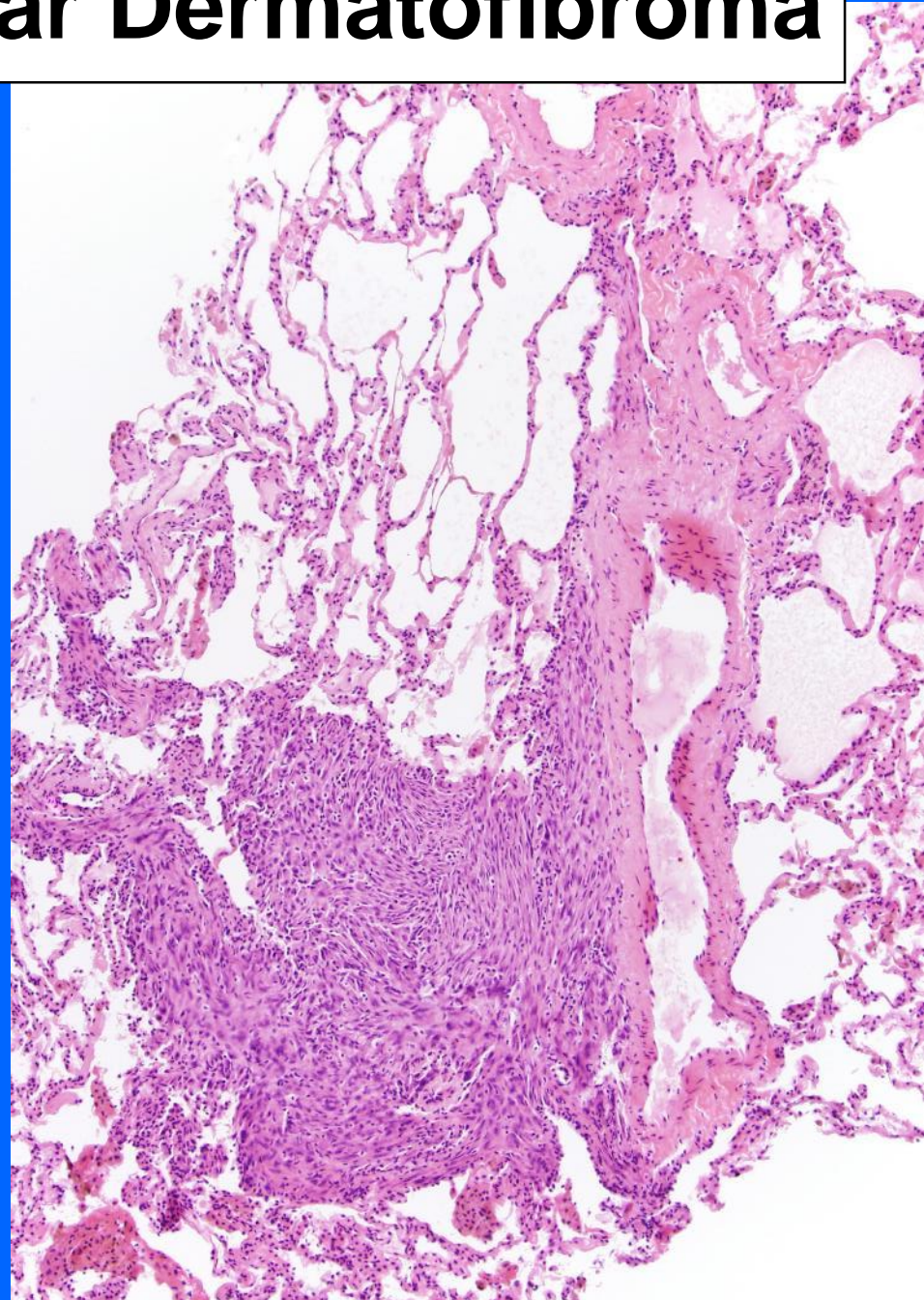
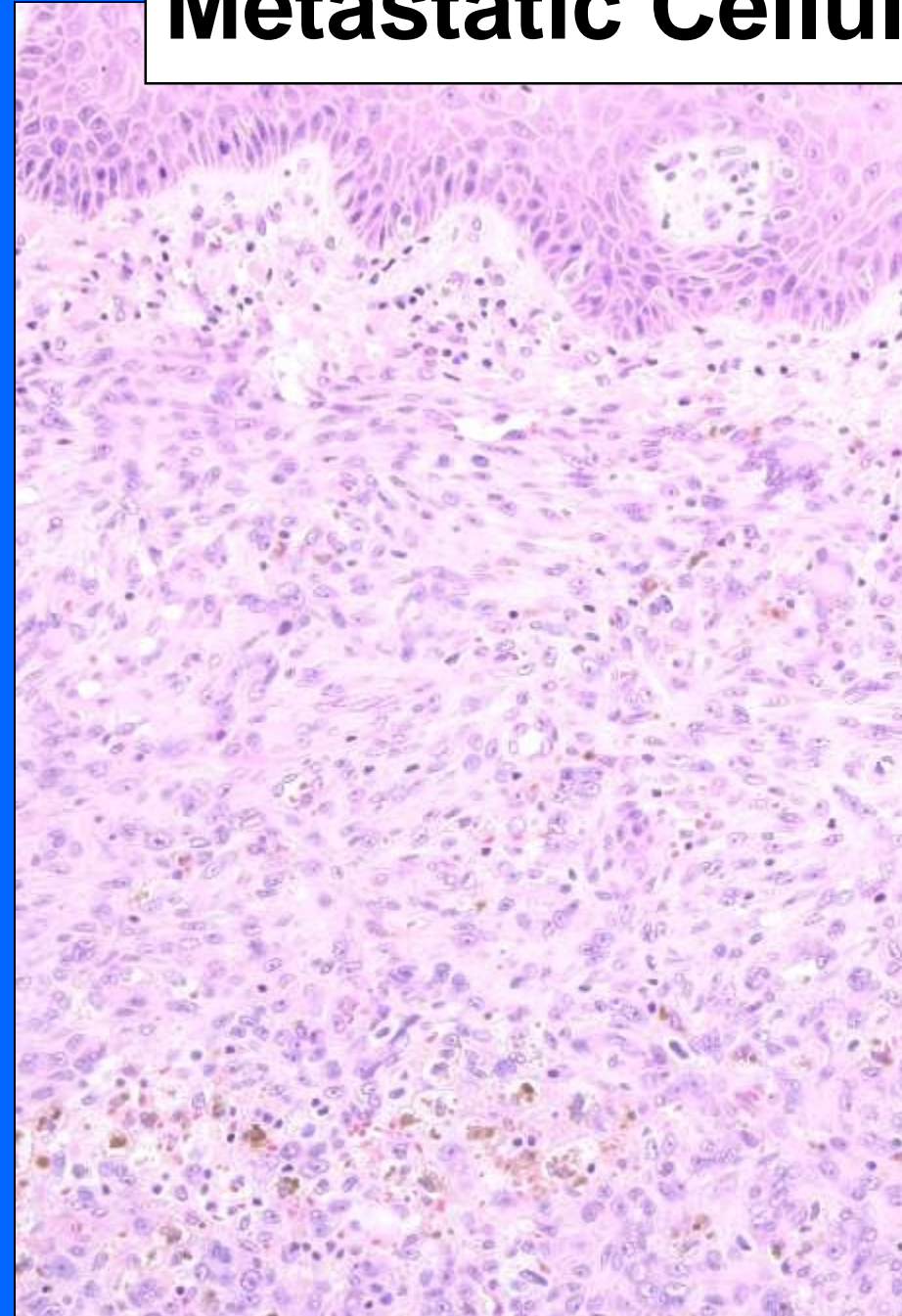


**Ker**

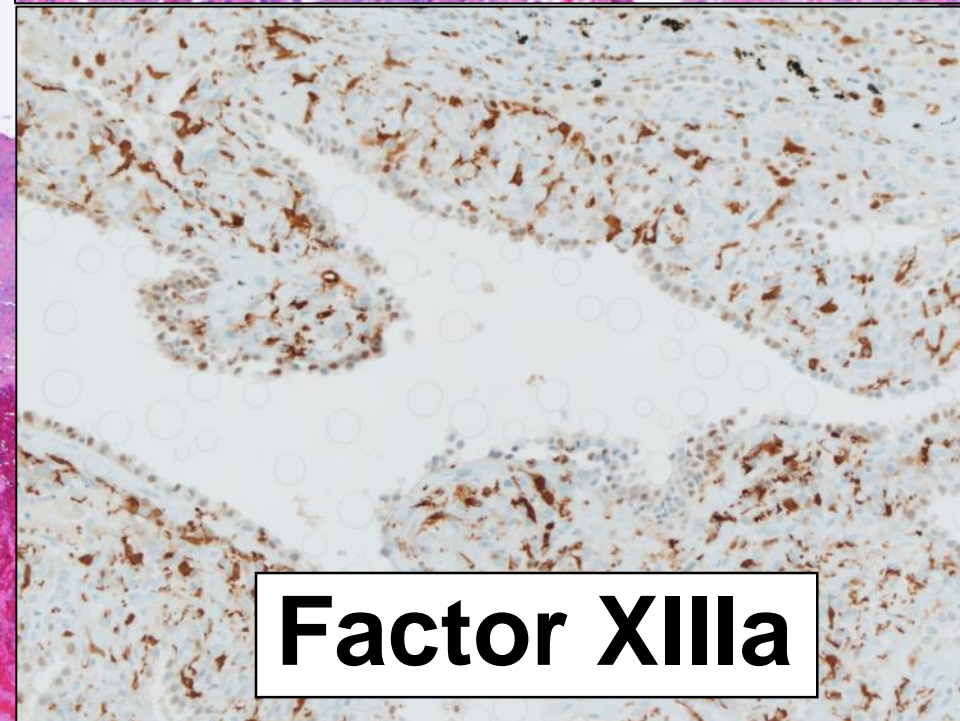
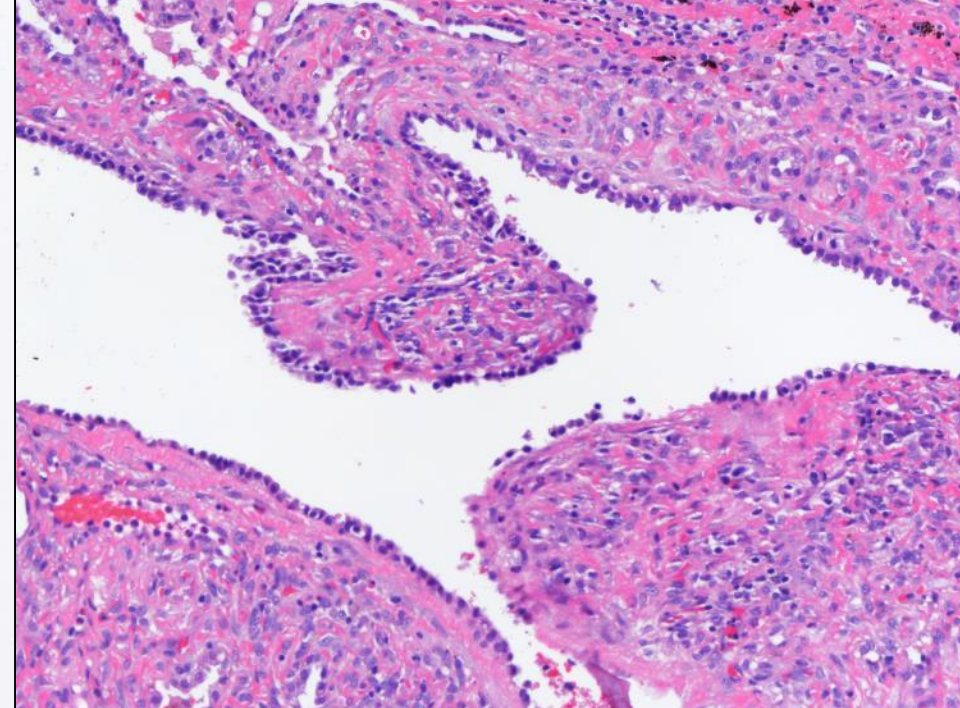
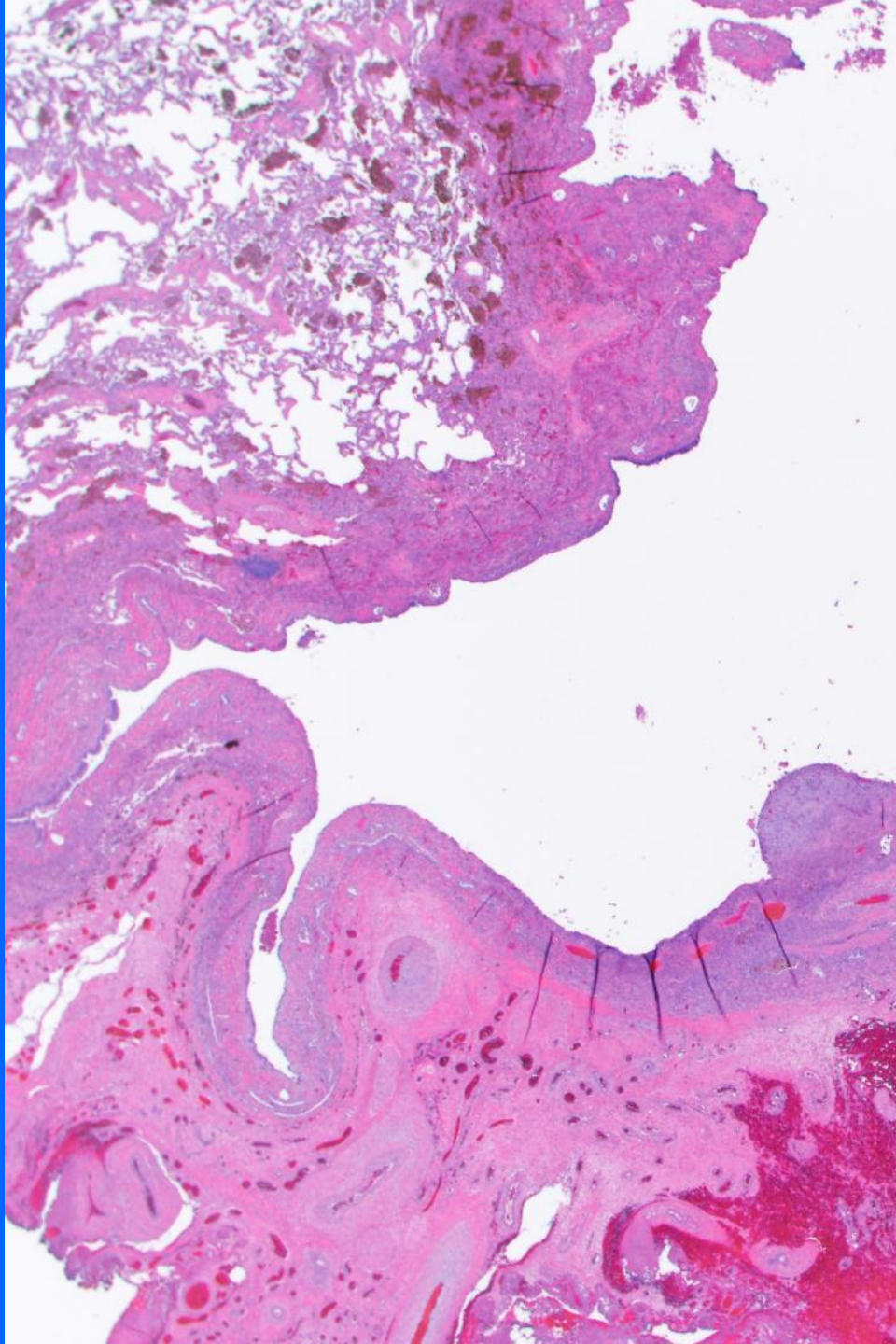
**CD31**



# Metastatic Cellular Dermatofibroma





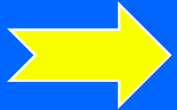


**Factor XIIIa**



# Outline

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

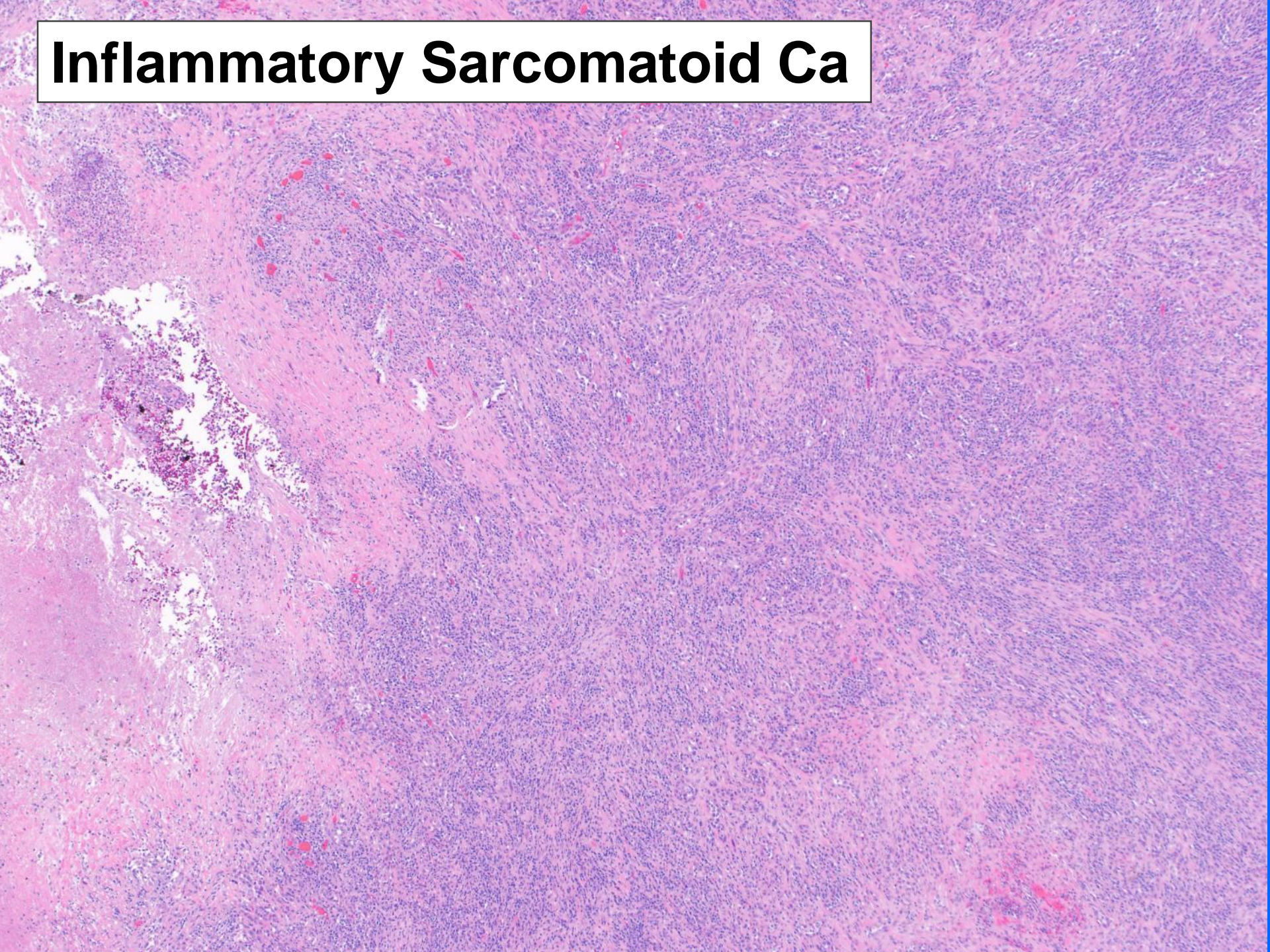


# Inflammatory Sarcomatoid Carcinoma

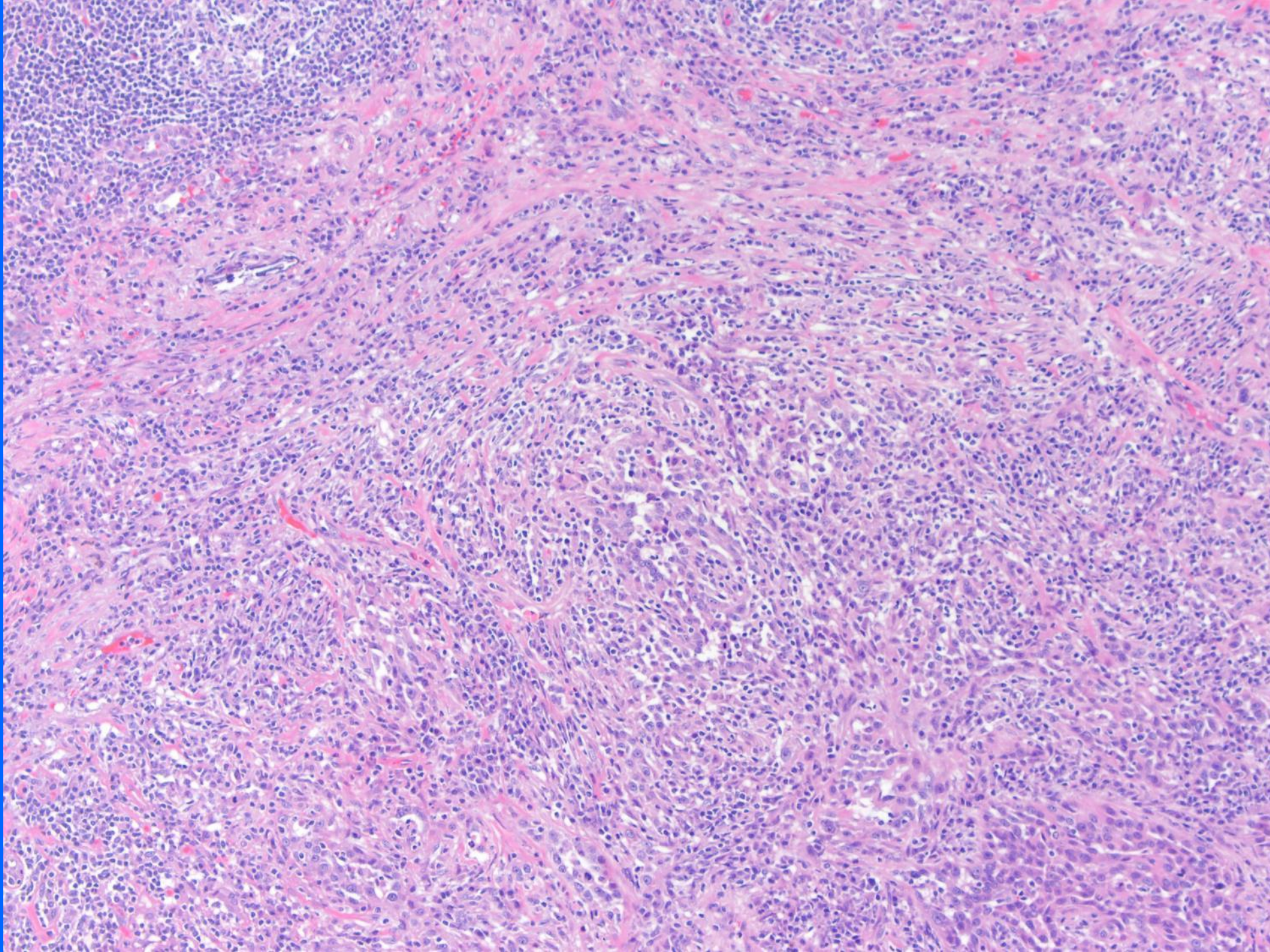
- Variant of Sa Ca with deceptively bland morphology
- Mimics
  - Inflammatory process
  - Lymphoma, incl HD
  - Inflammatory myofibroblastic tumor
  - Fibrous histiocyoma



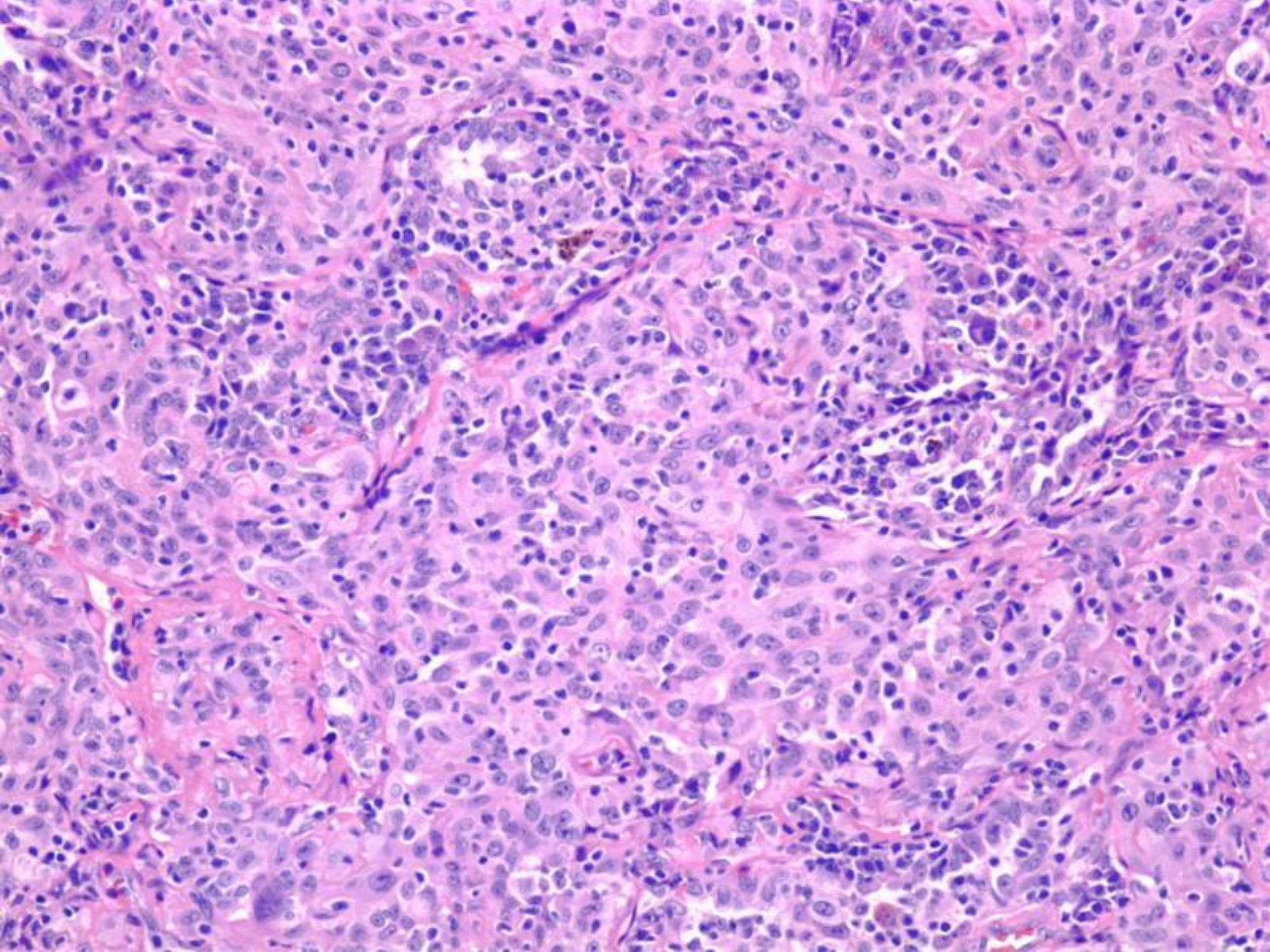
# Inflammatory Sarcomatoid Ca



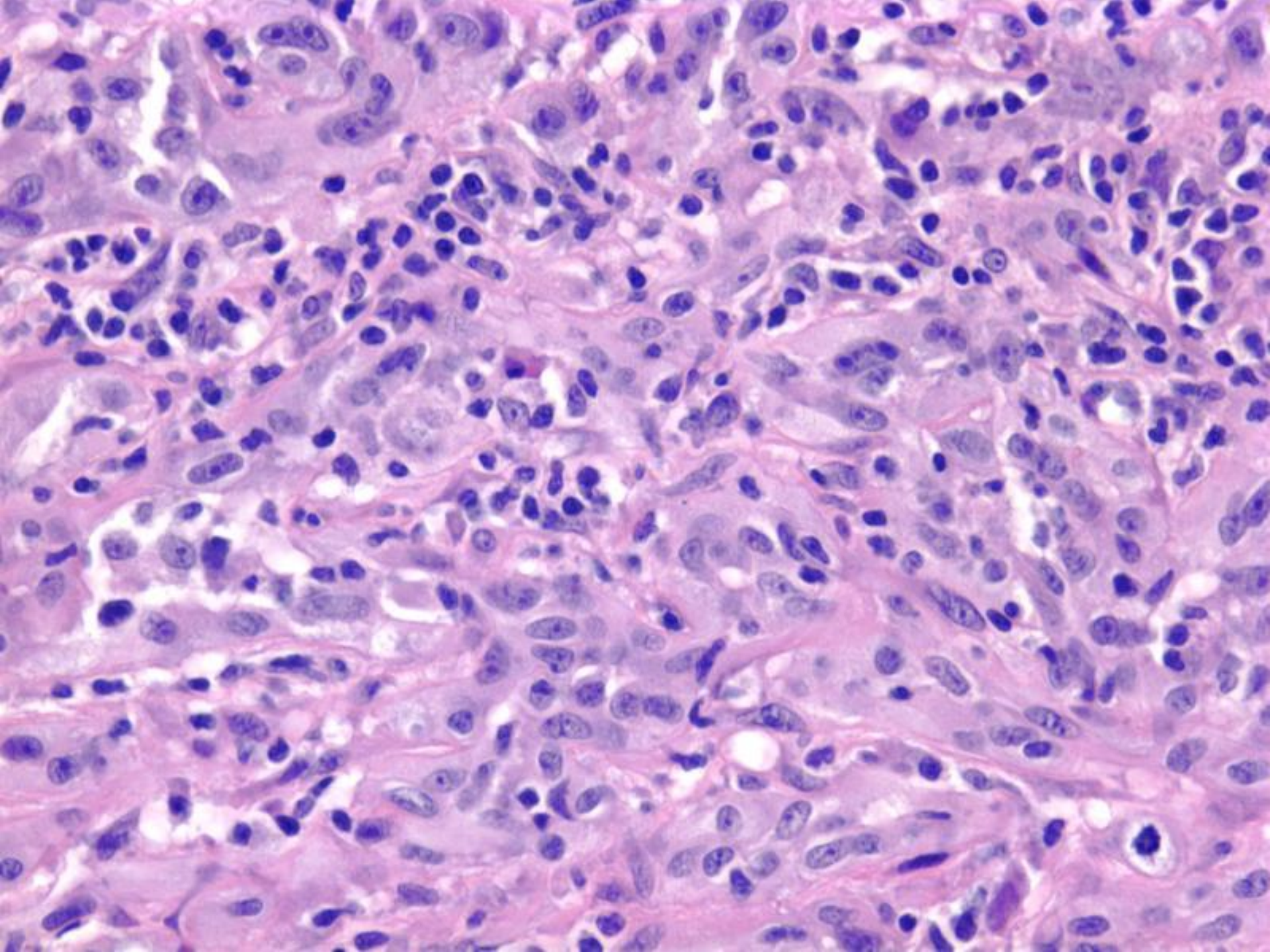




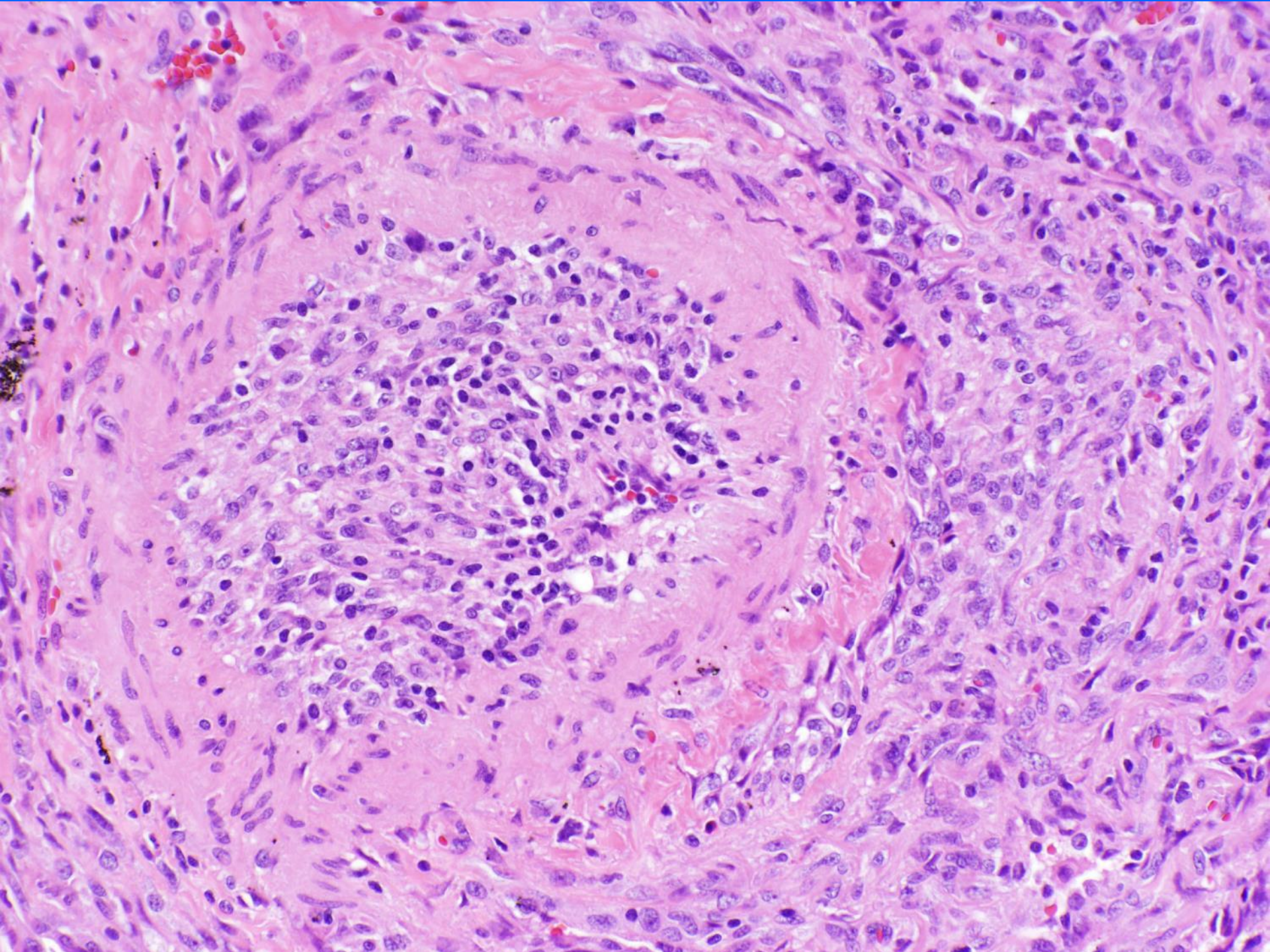








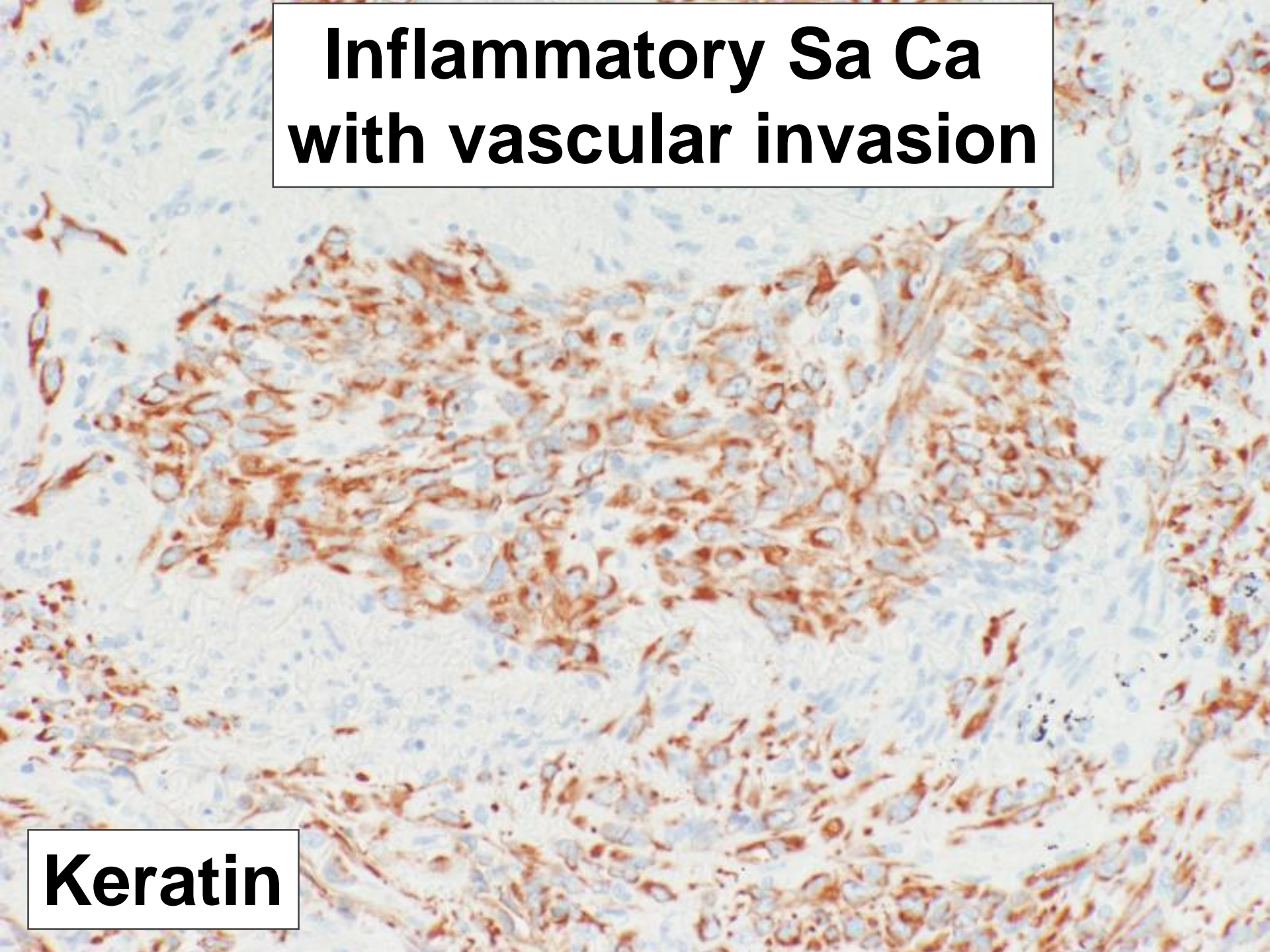






# **Inflammatory Sa Ca with vascular invasion**

**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



# **Sarcomatoid Carcinoma**

## **Differential Diagnosis**

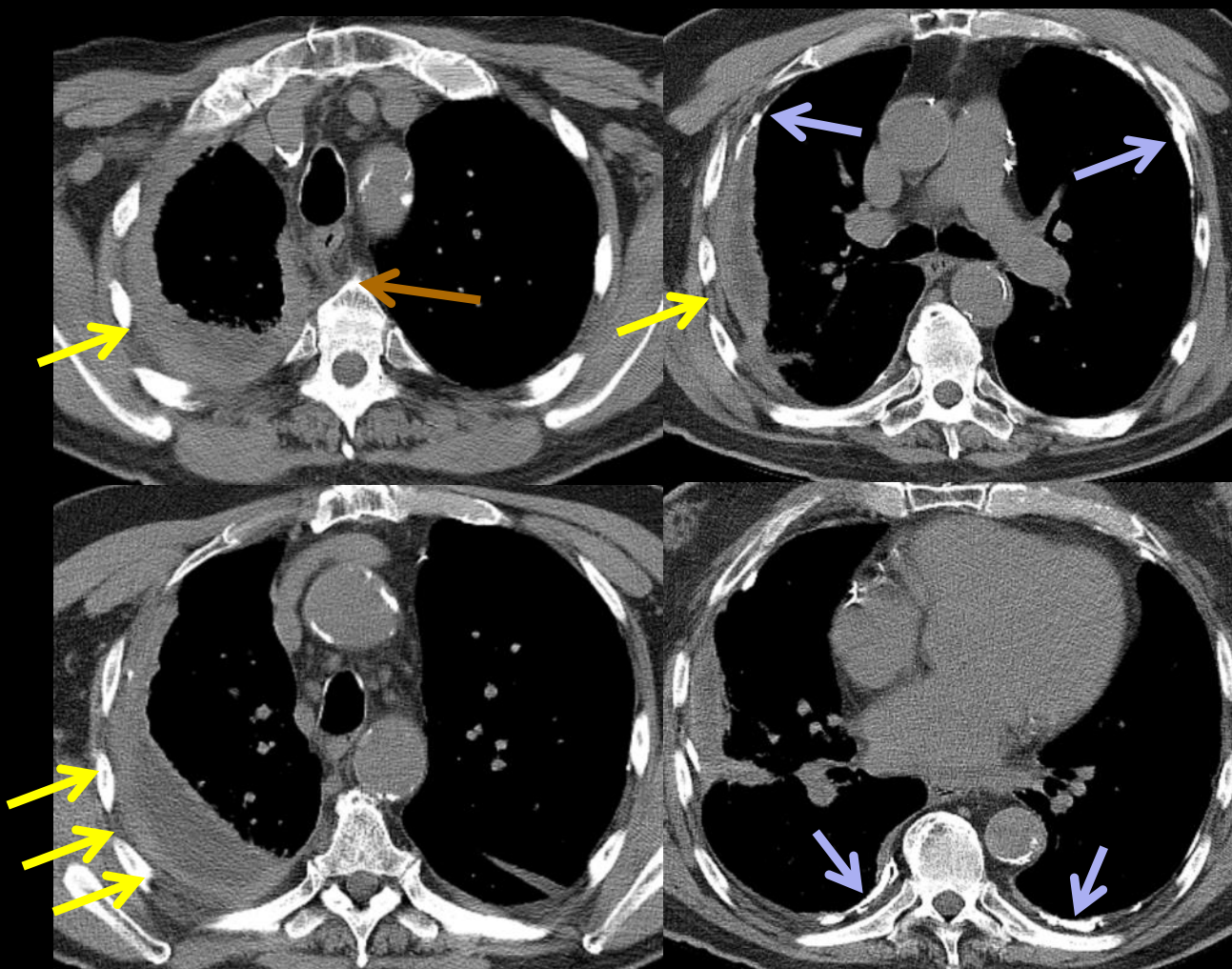
- **Organizing pneumonia**
- **Inflammatory myofibroblastic tumor**
- **IgG 4-related sclerosing disease**
- **Lymphoma, particularly Hodgkin L.**
- **Malignant mesothelioma**



## Case History

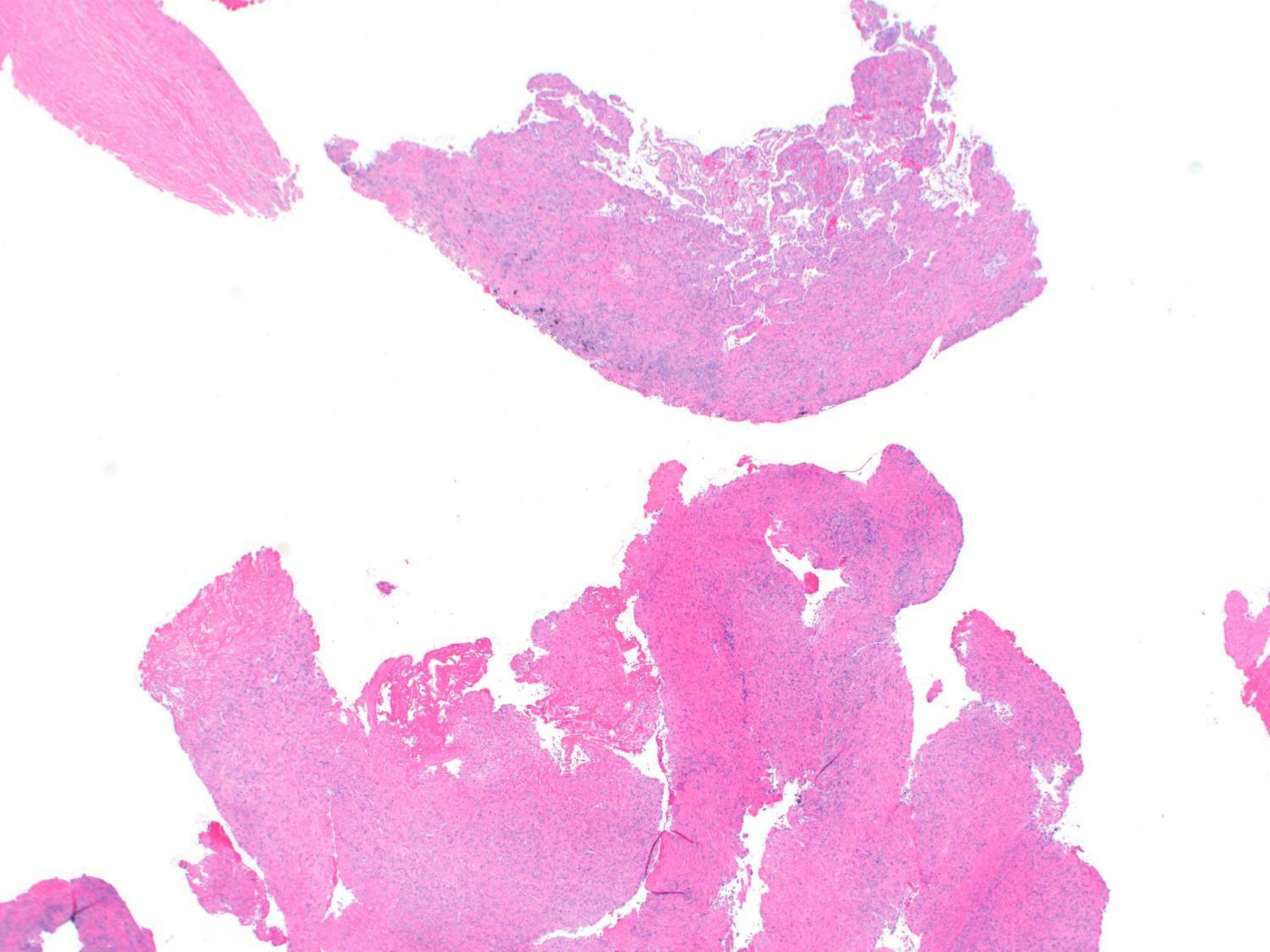
- A 78 yr old man has a recurrent R pleural effusion for which he had talc pleurodesis.
- 1 yr later developed recurrent pleural effusion with nodularity.
- He undergoes VATS biopsy.



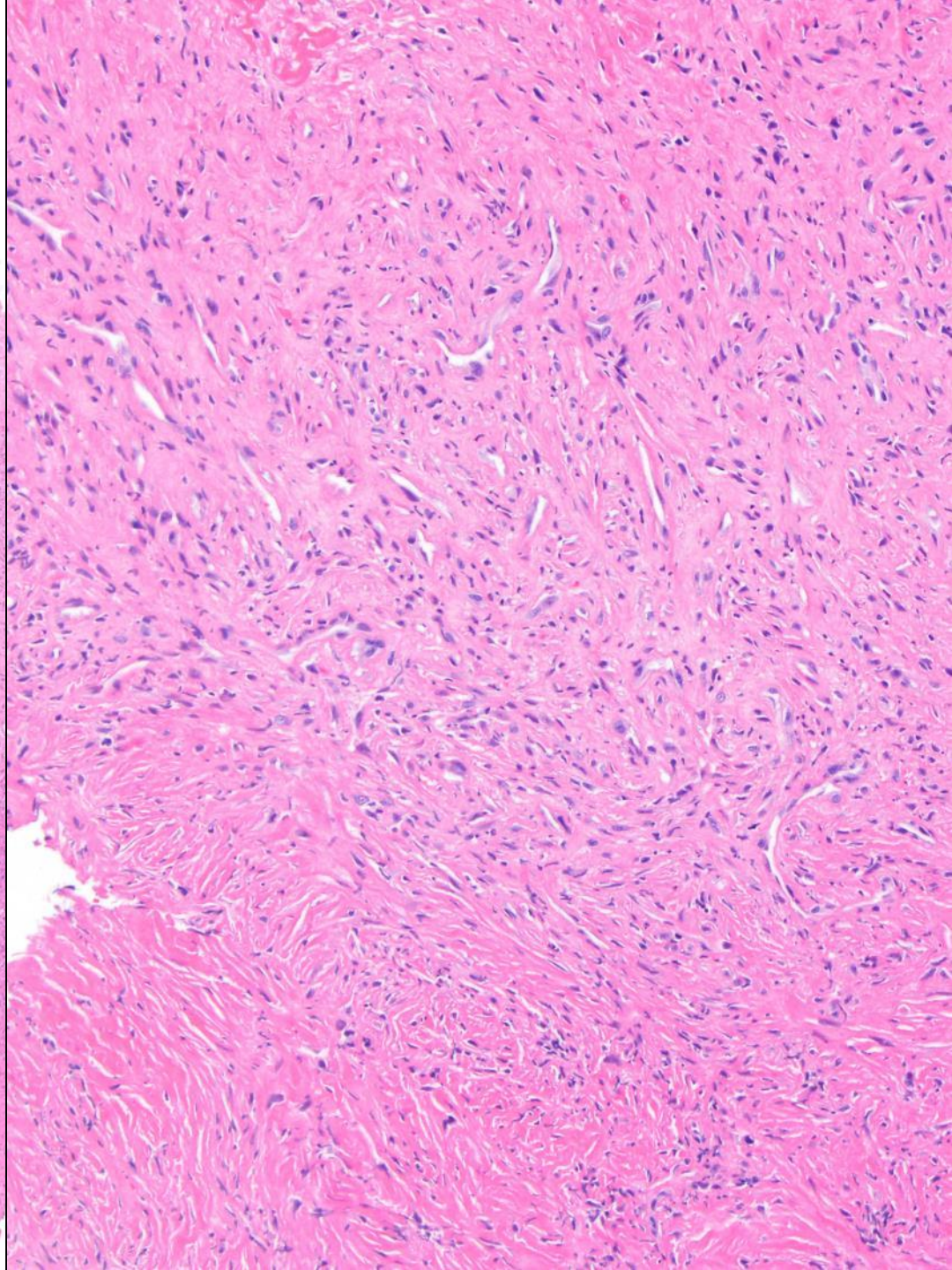
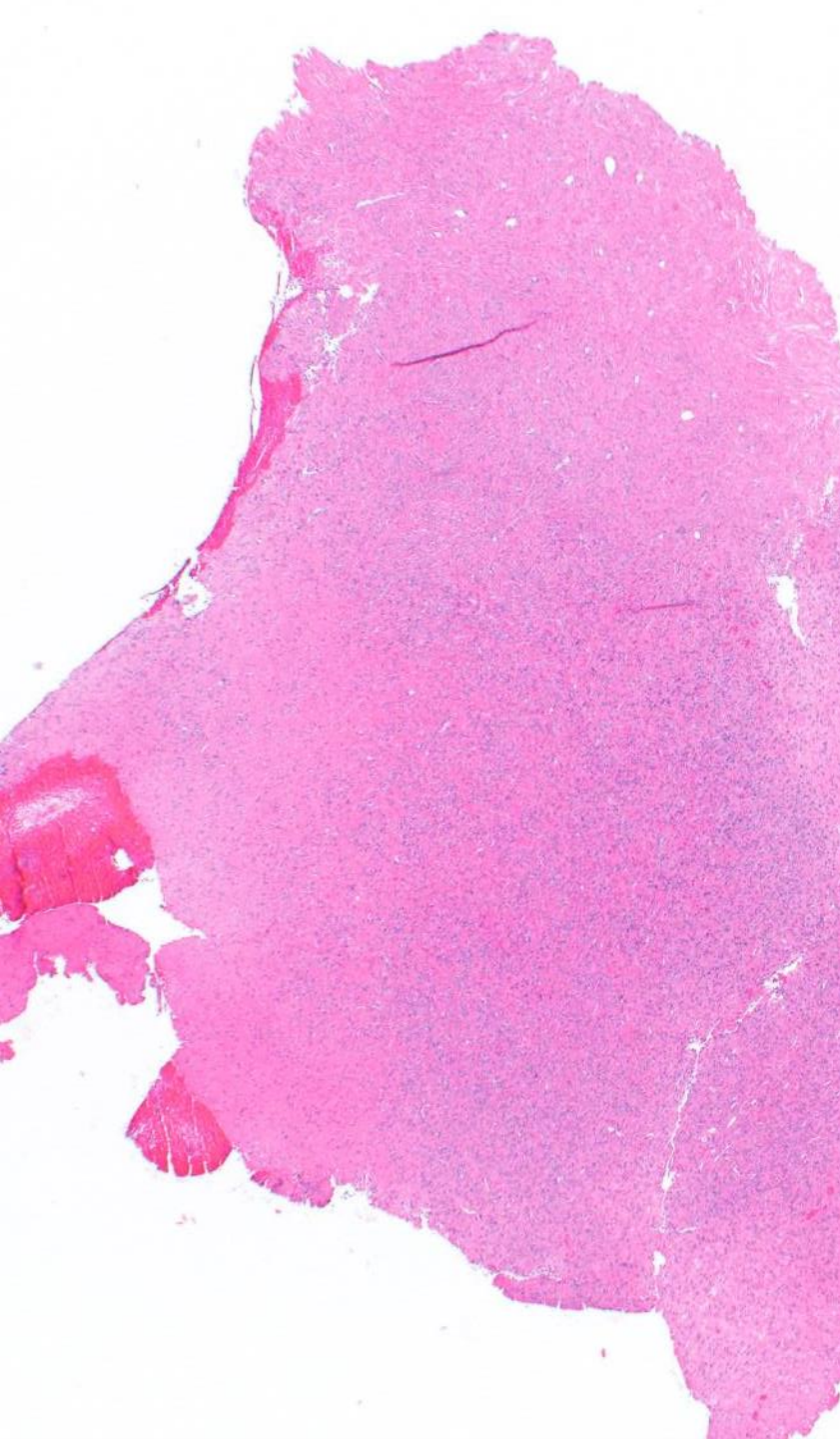


Compliments of Dr. Kristopher Cummings

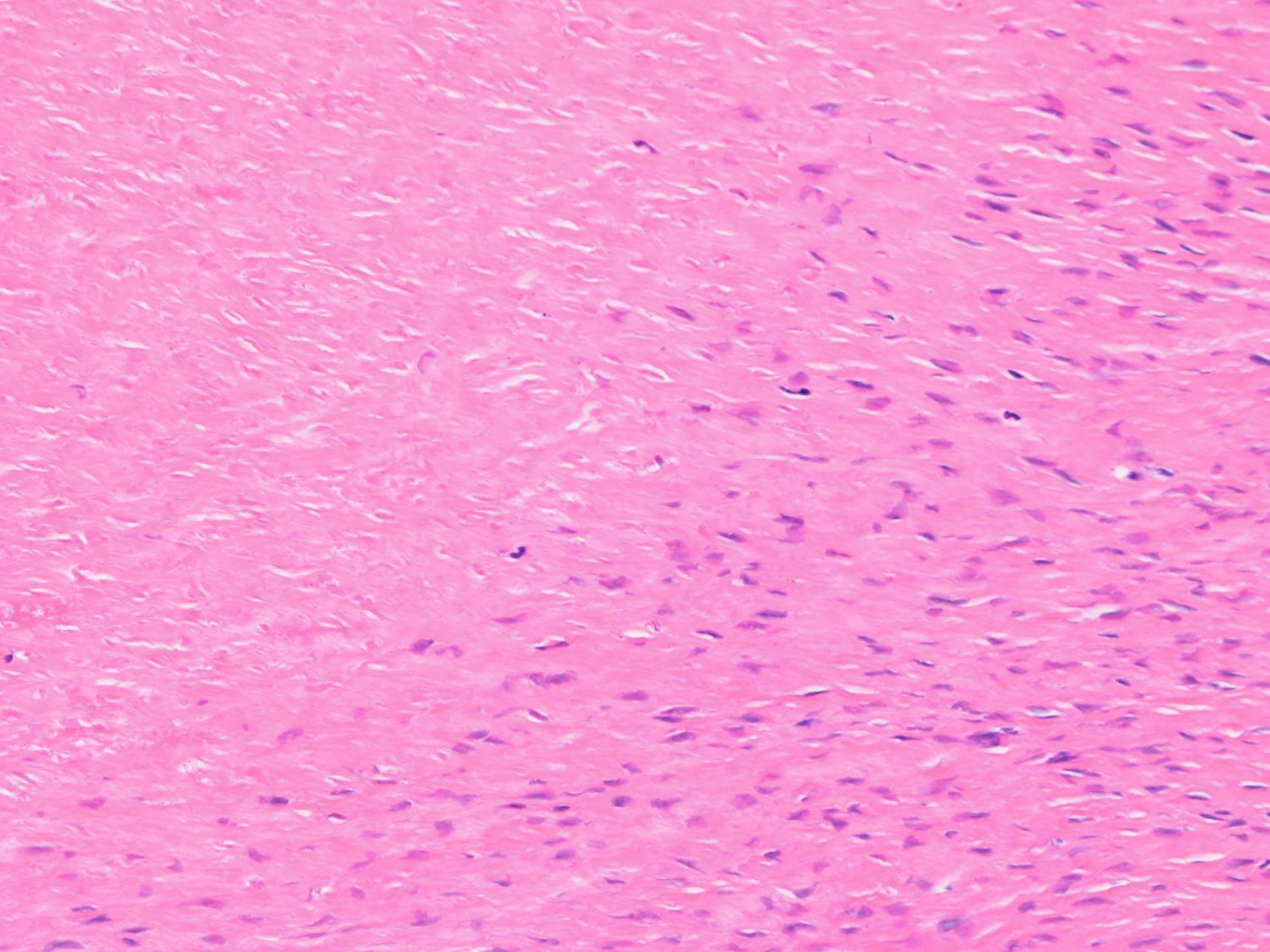




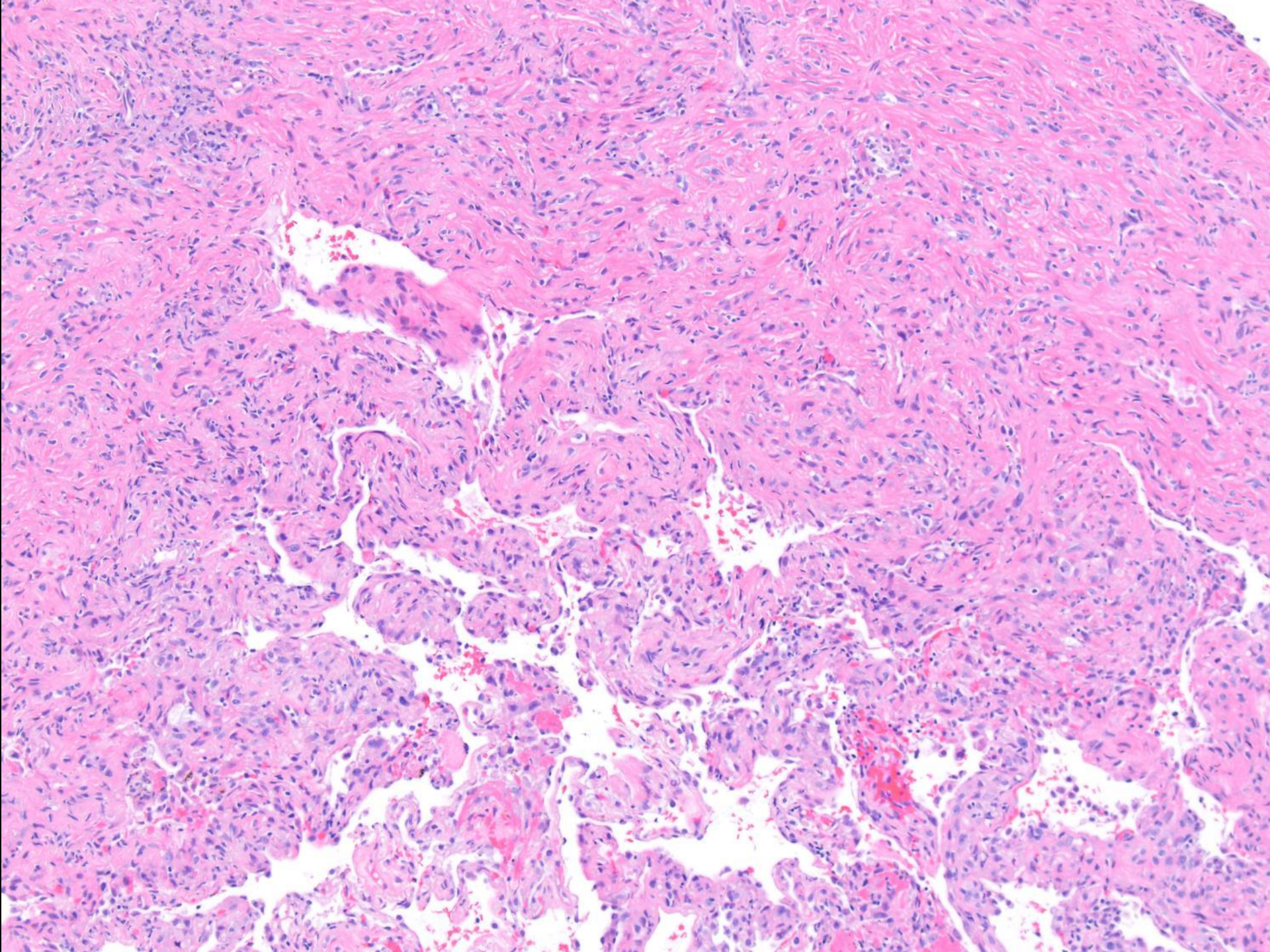




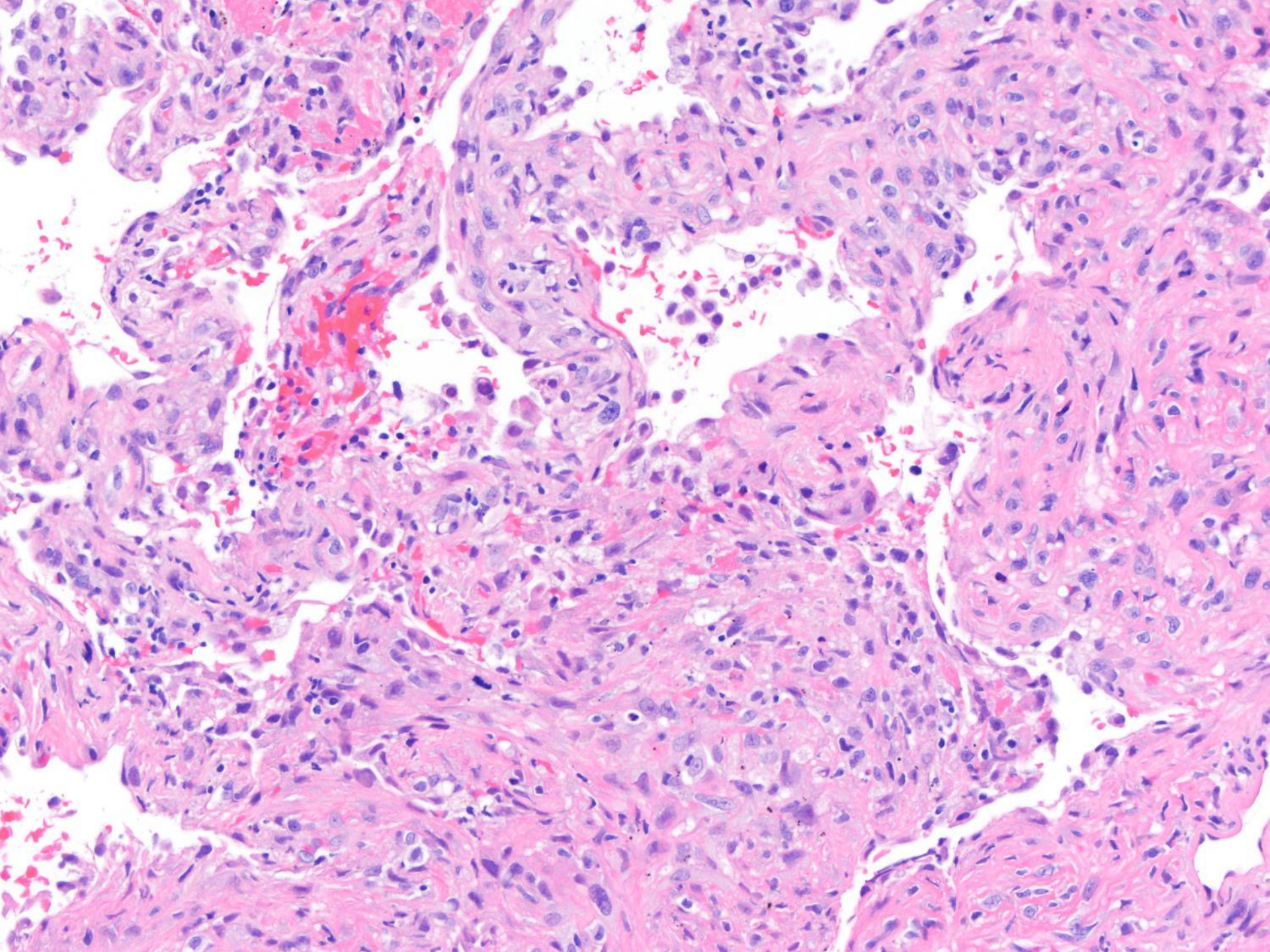




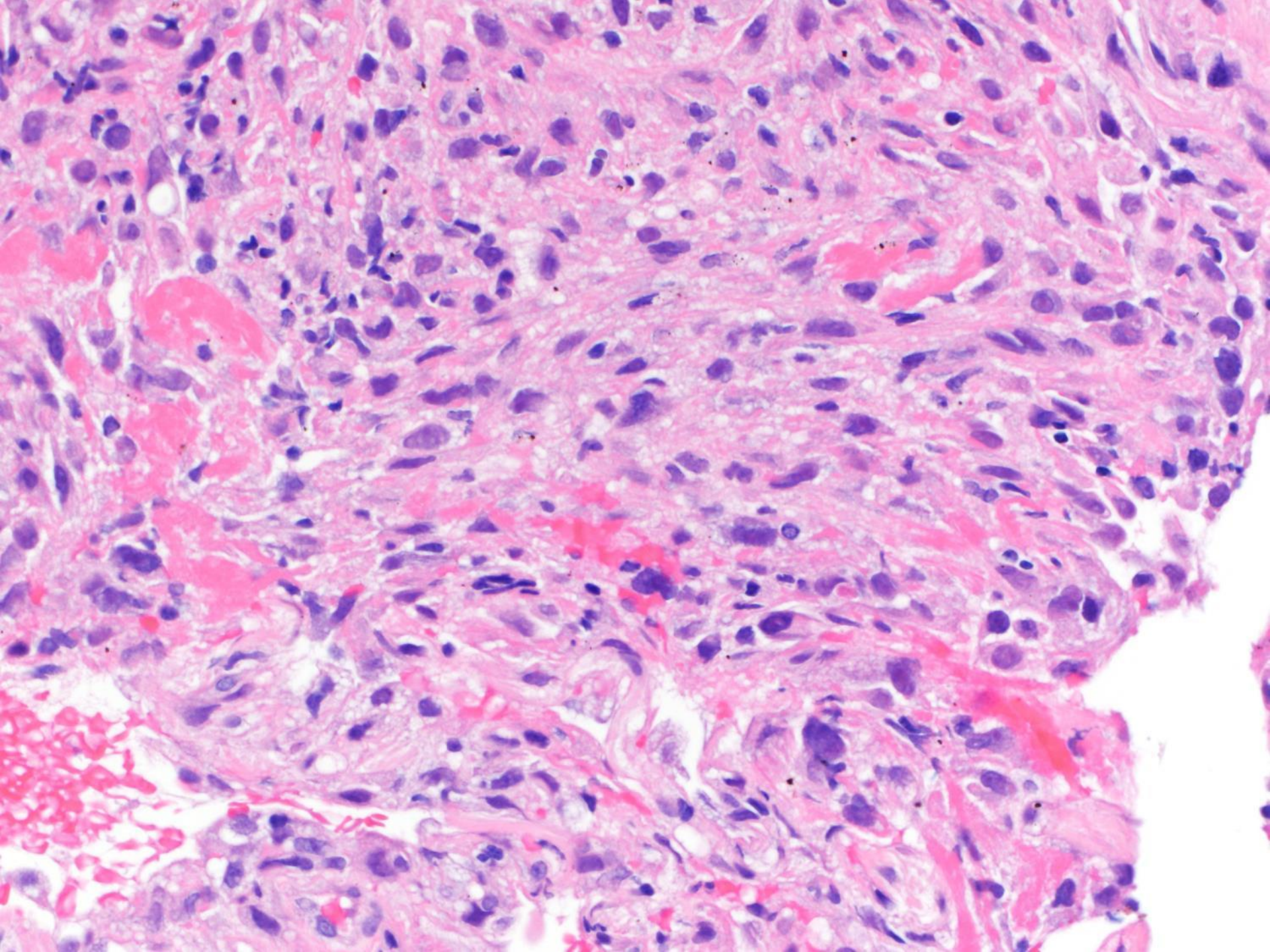










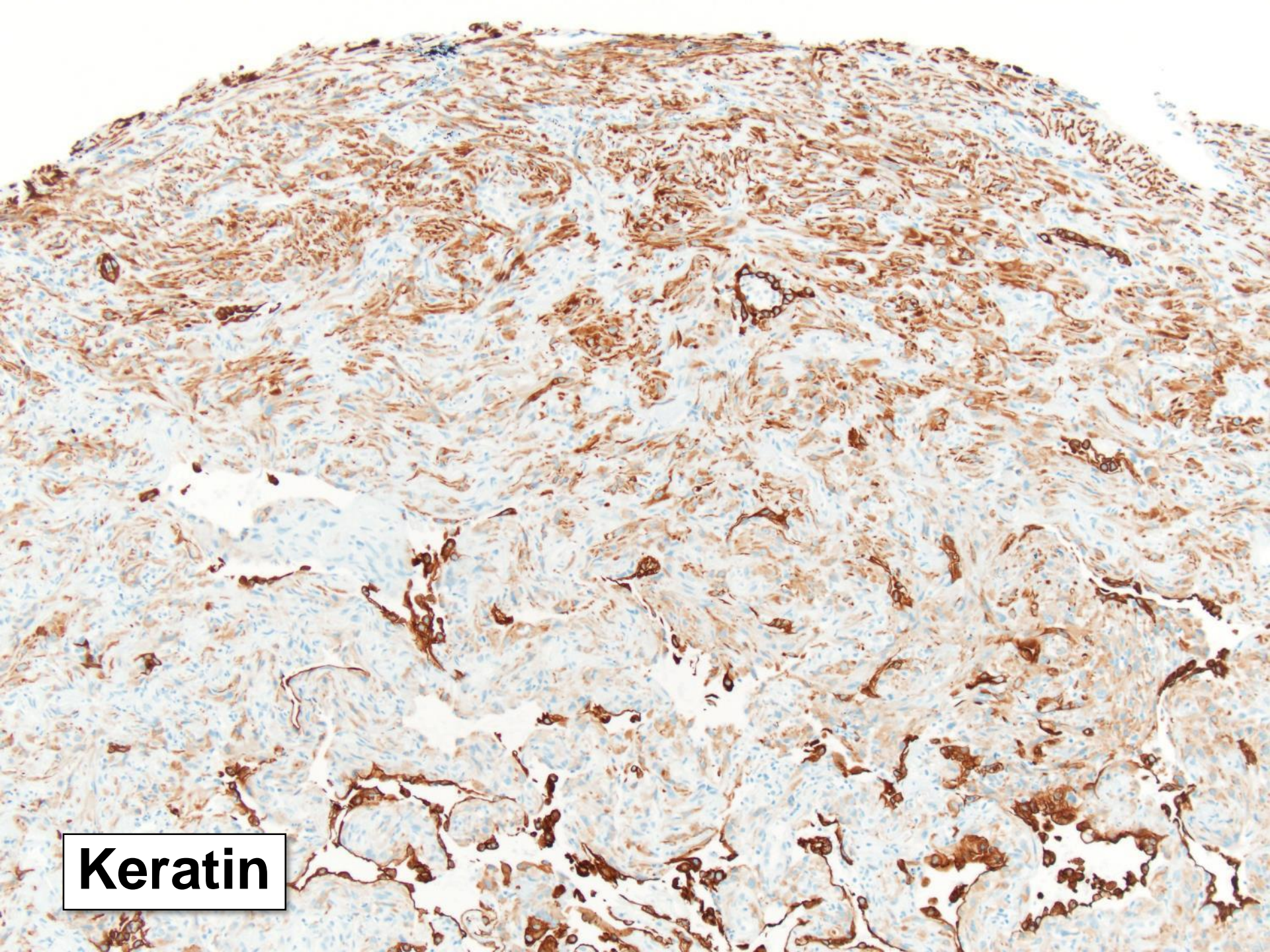




**The single best IHC stain to order on this block is:**

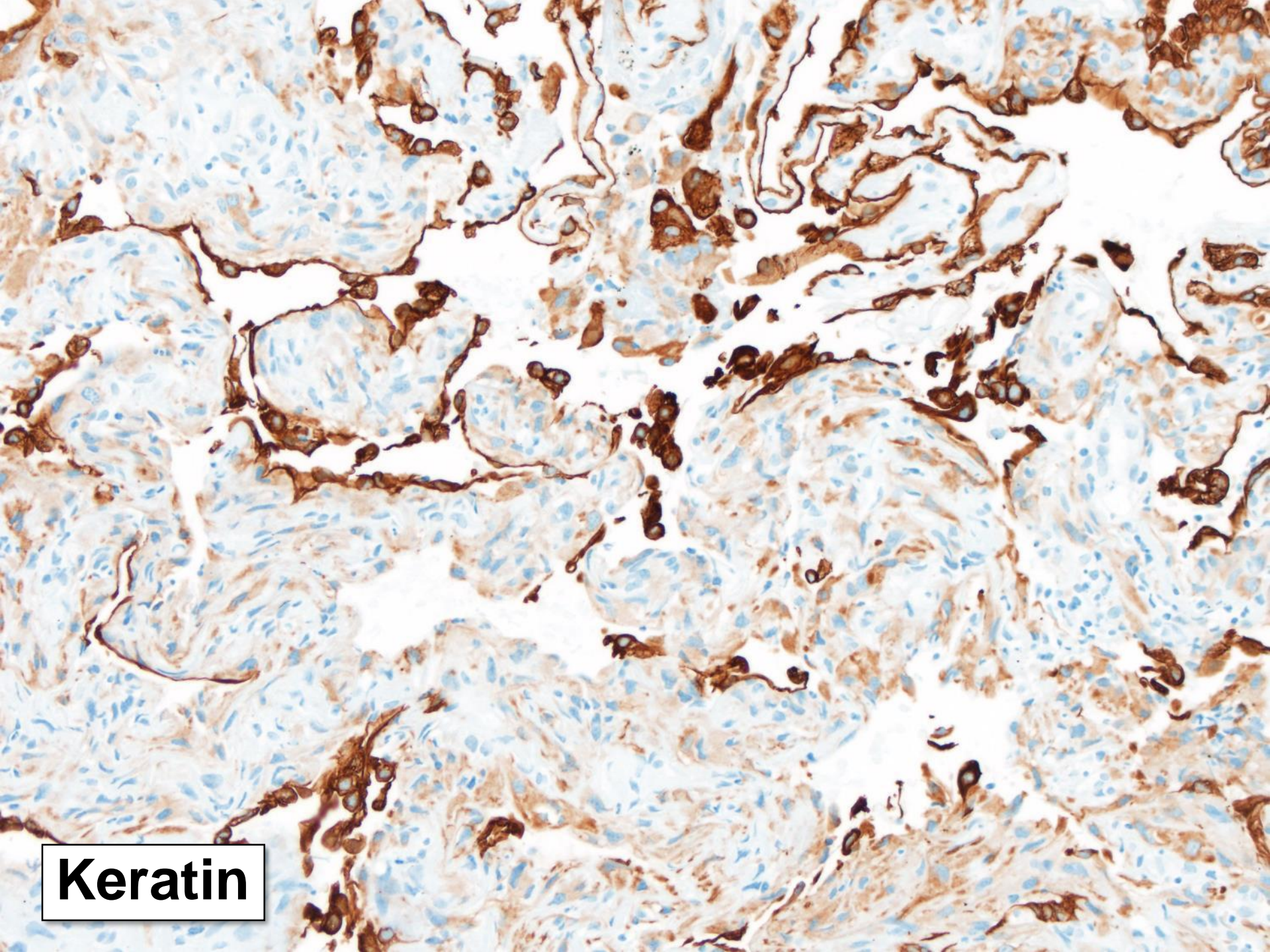
- a. Ber EP4
- b. CEA
- c. CK7
- d. MOC-31
- e. Pan keratin





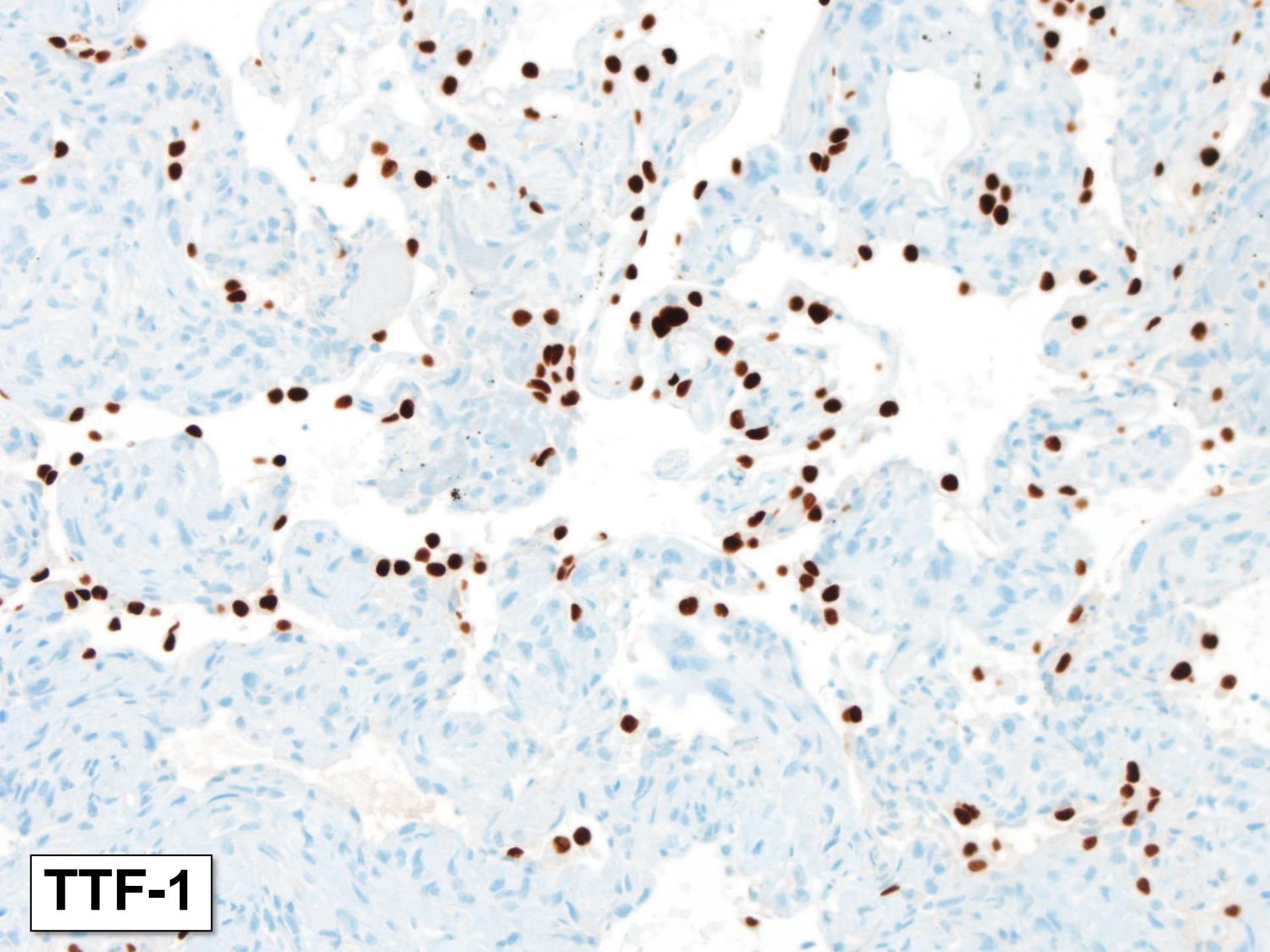
**Keratin**





**Keratin**





**TTF-1**



## The diagnosis is:

**a.** Atypical/suspicious for malignancy

**b.** Desmoplastic mesothelioma

**c.** Fibrous pleurisy

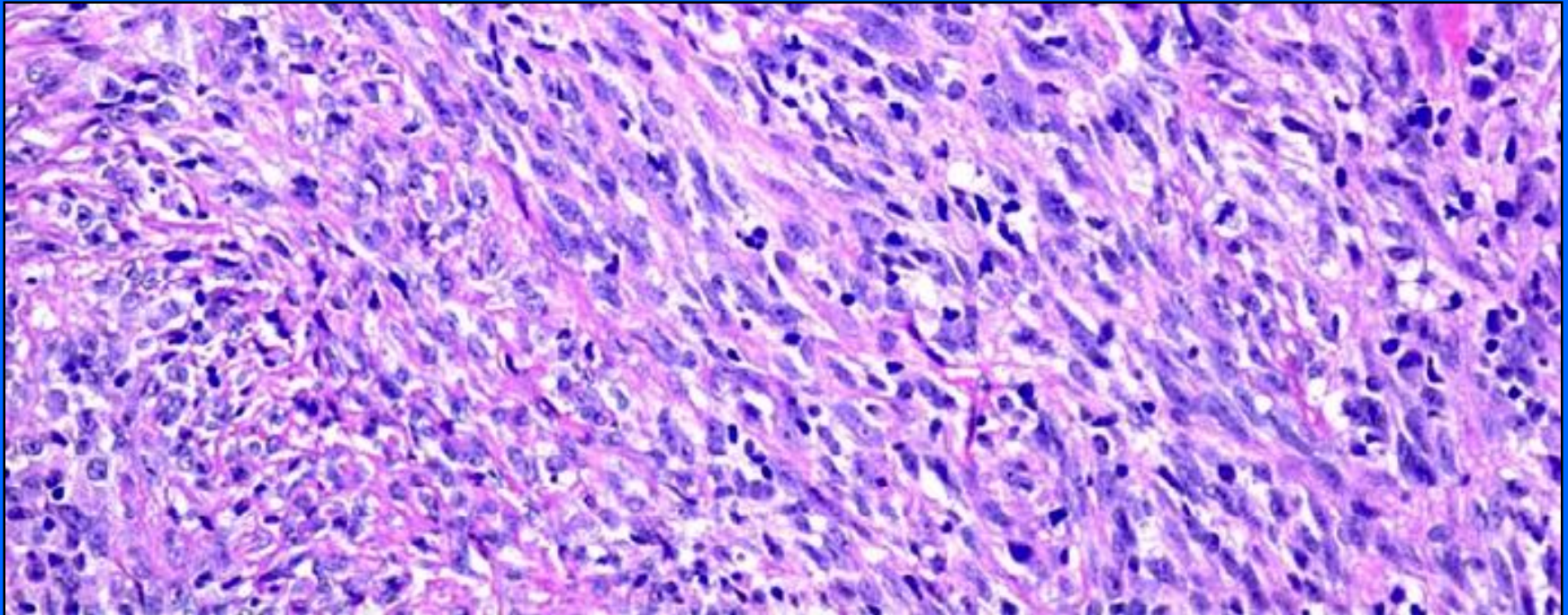
**d.** Pleomorphic lung carcinoma

**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

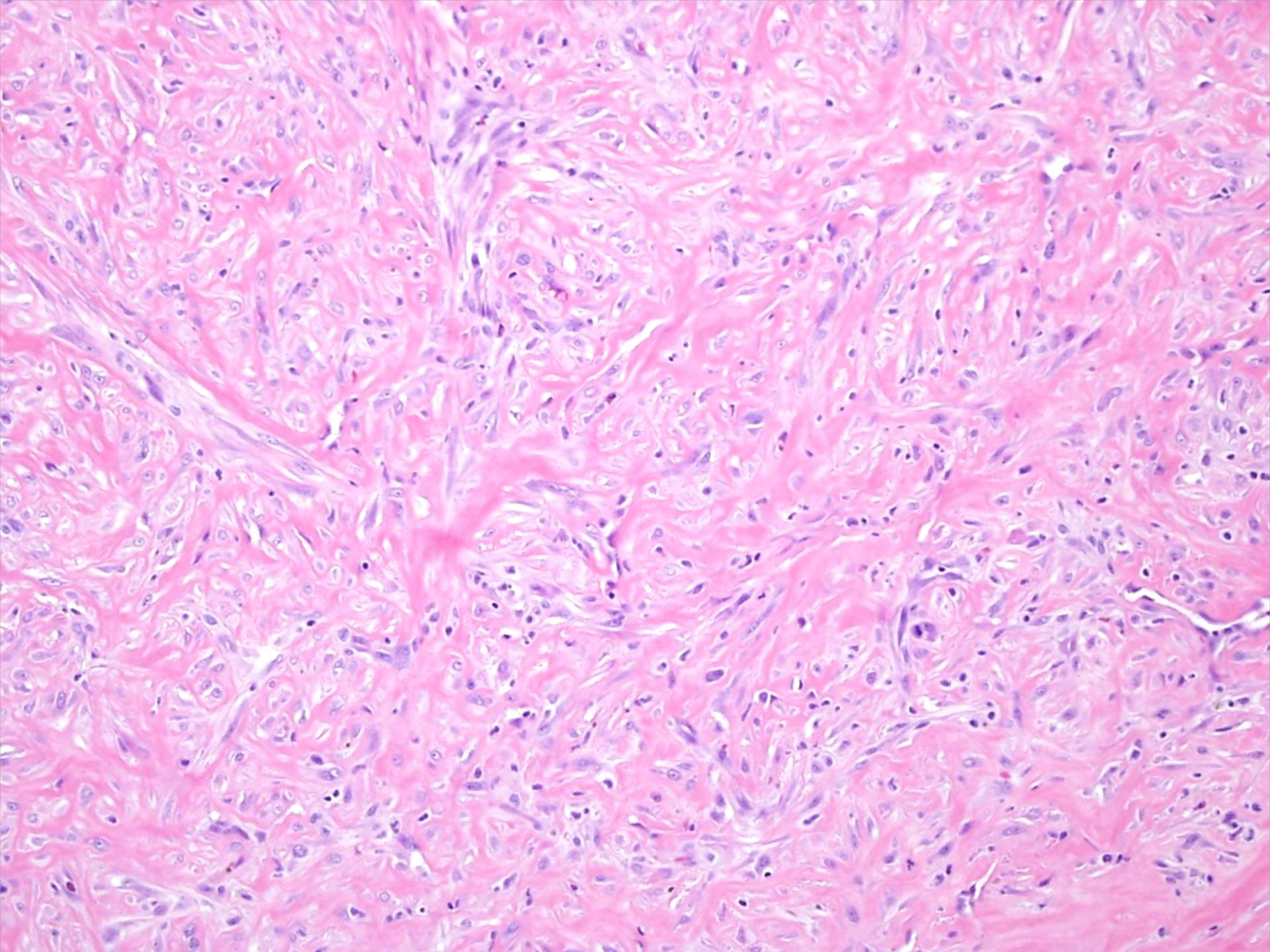


# Desmoplastic Mesothelioma

A histological slide showing a dense population of spindle-shaped cells with elongated, dark purple nuclei and pink cytoplasm/extracellular matrix. The cells are arranged in a disorganized, interlacing pattern, characteristic of a desmoplastic reaction. There are no visible glandular structures or significant cellular atypia.

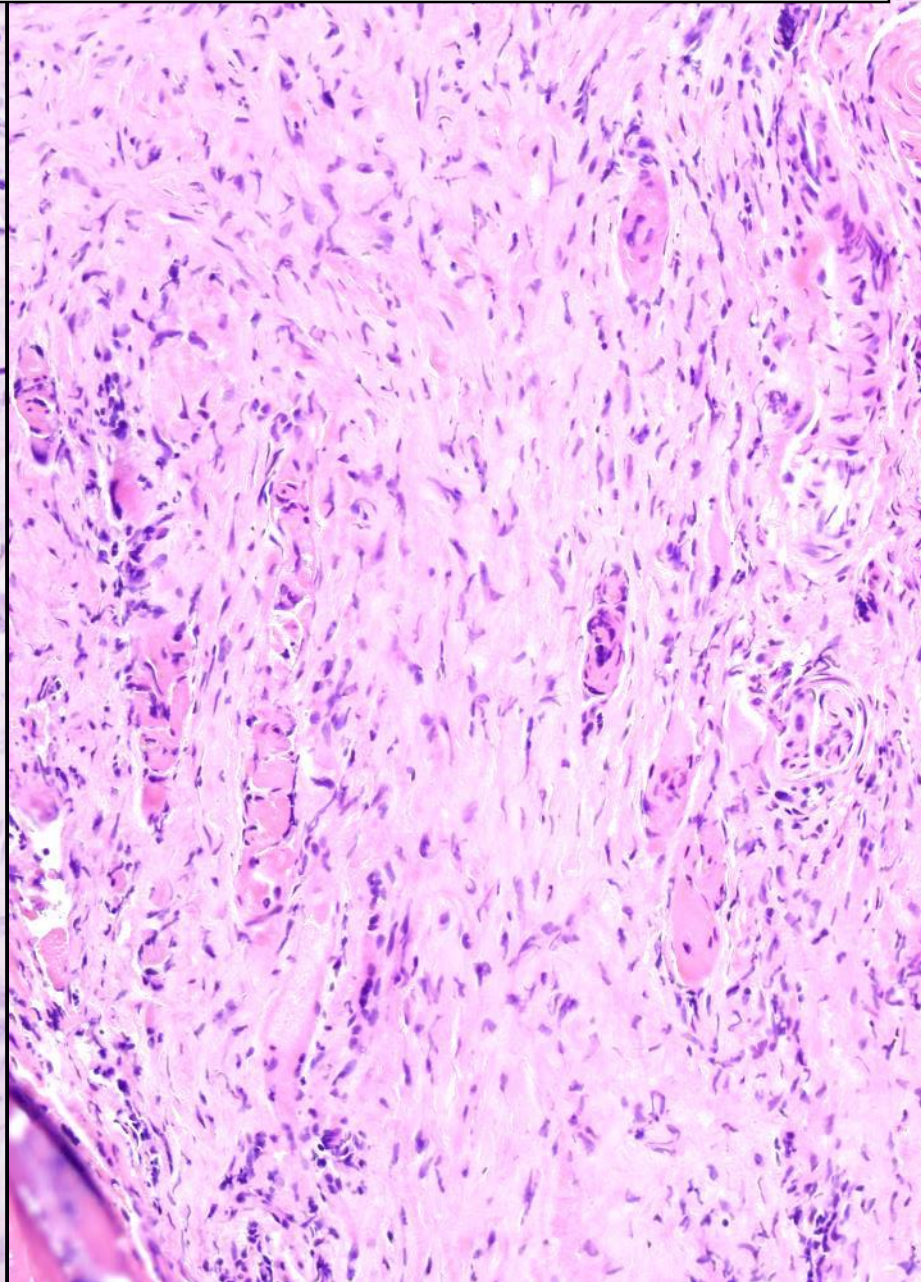
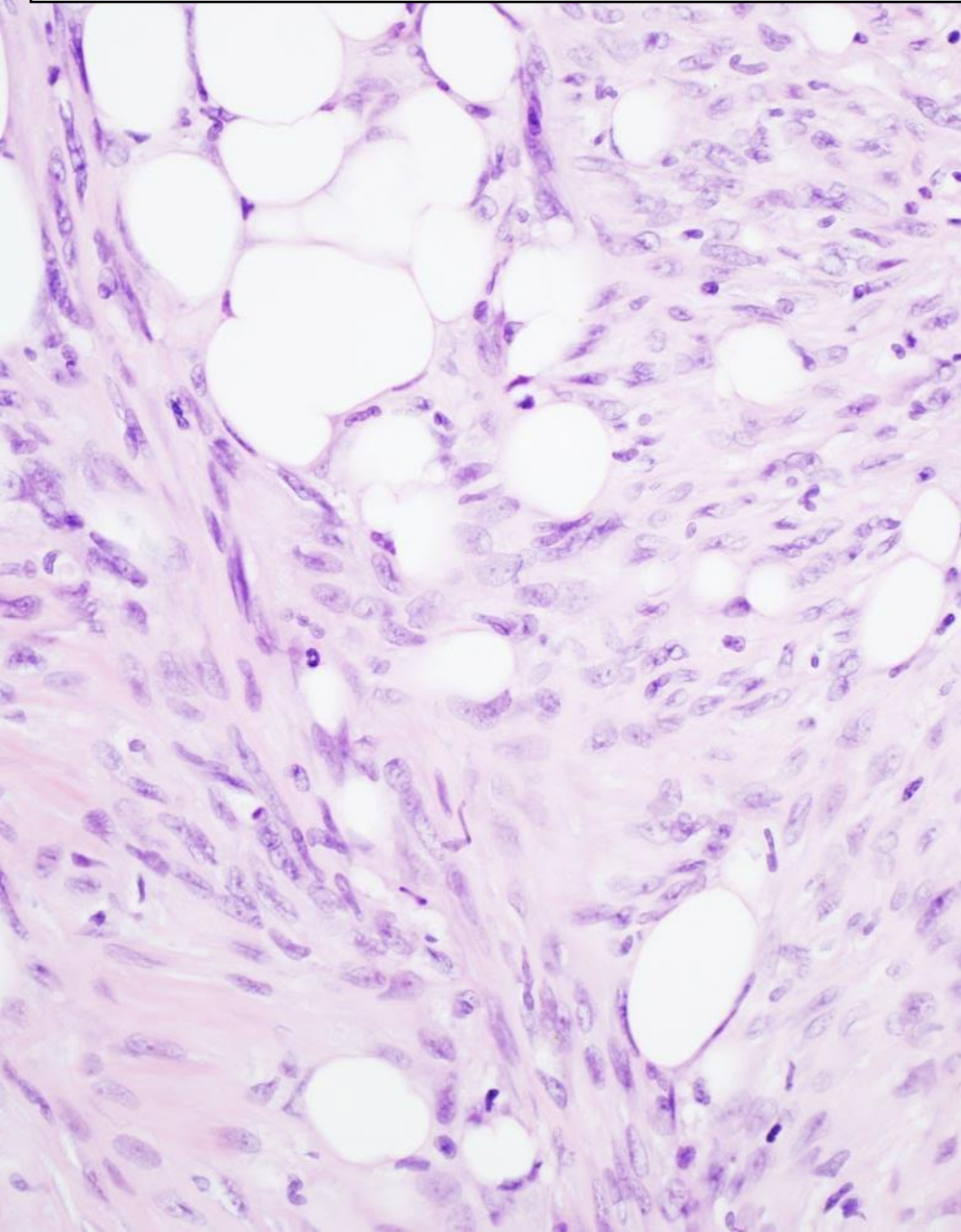
**No atypia**  
**No capillaries**



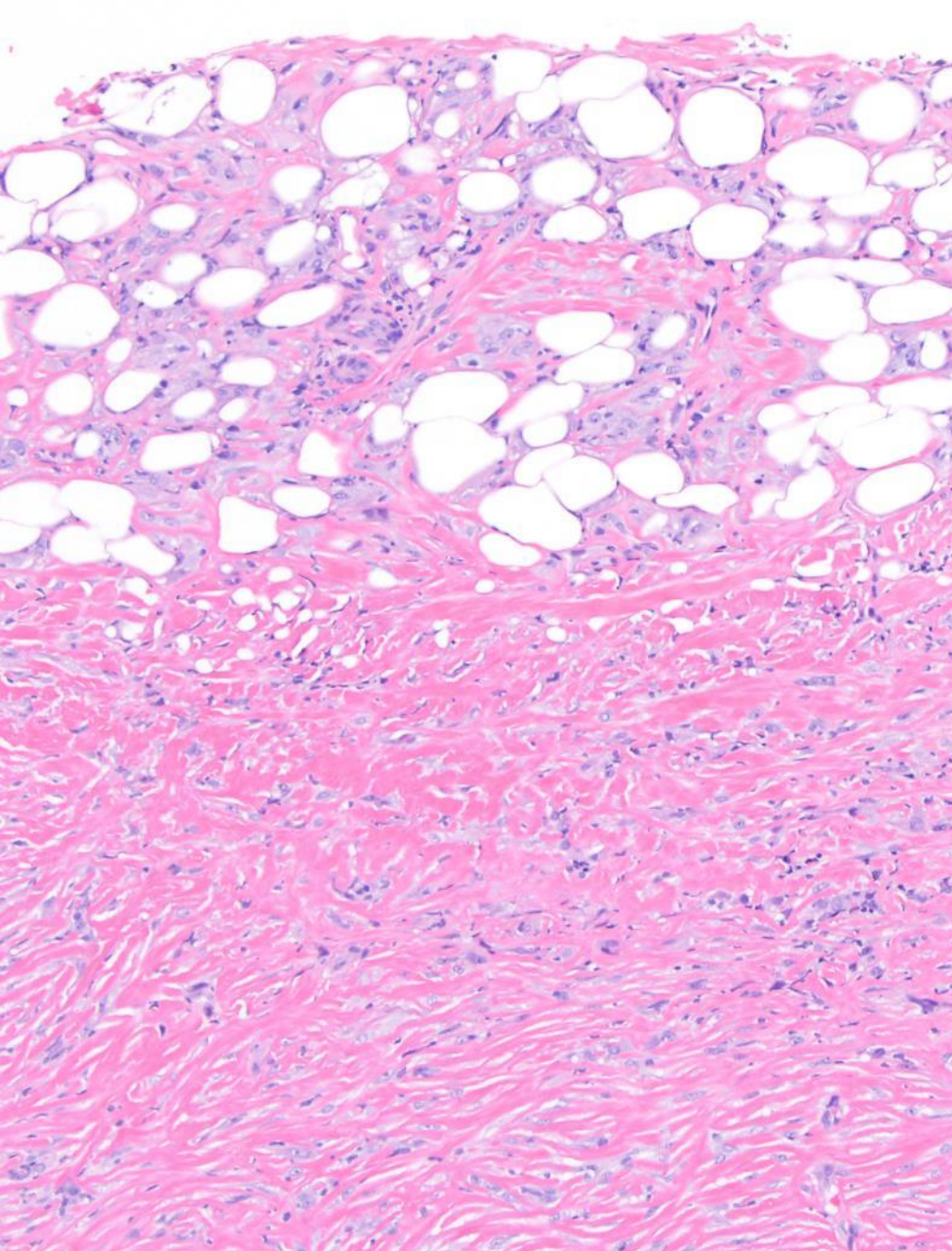




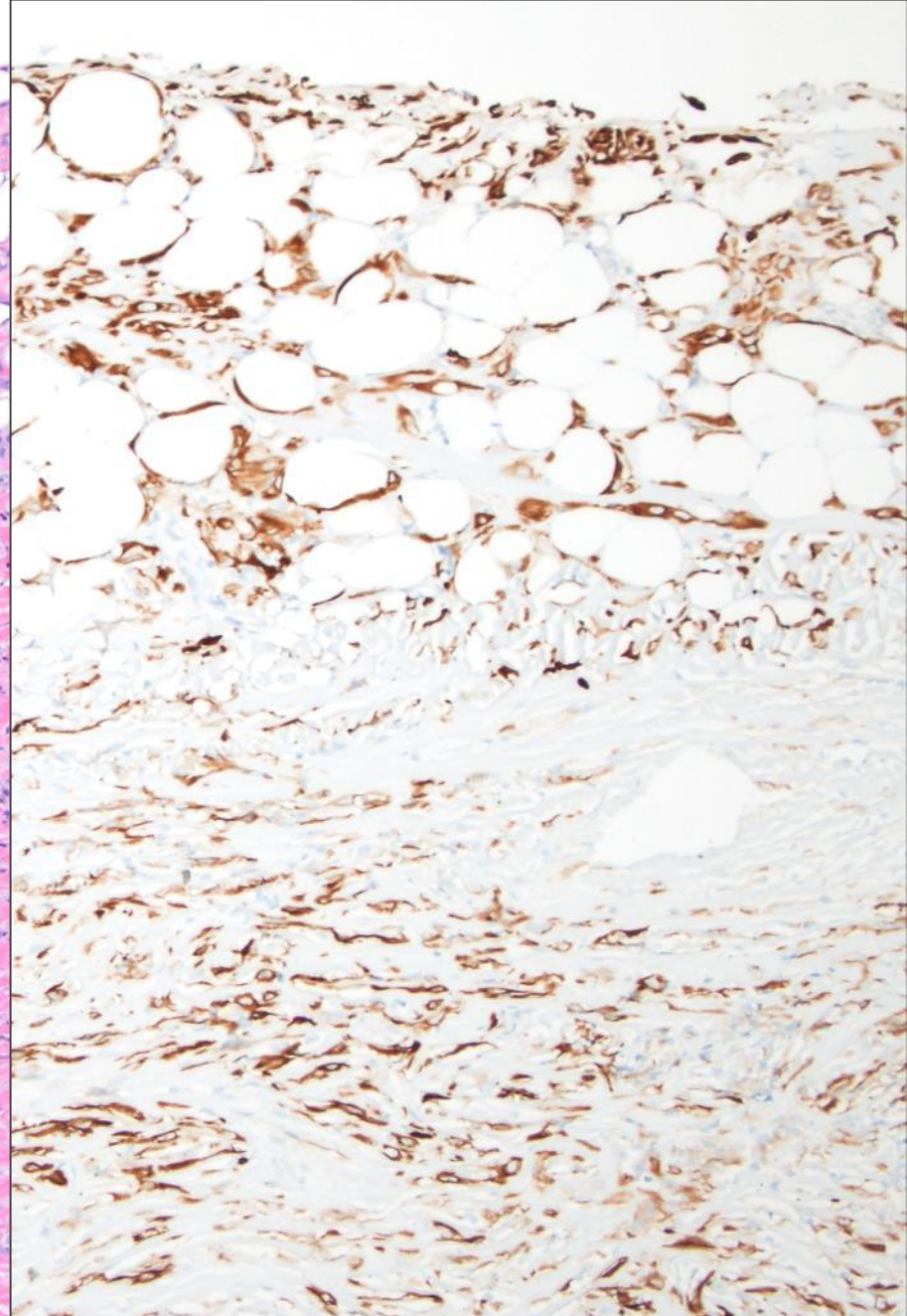
# Desmoplastic Mesothelioma- Invasion







**Desmoplastic Mesothelioma- Invasion**

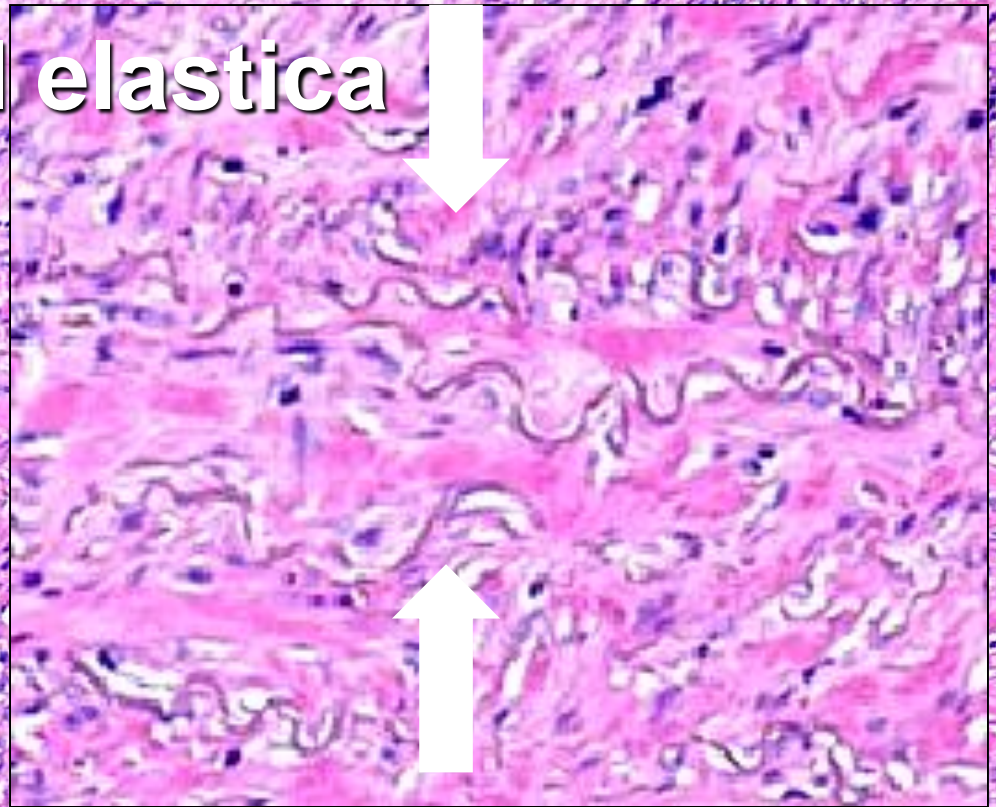


**Keratin**



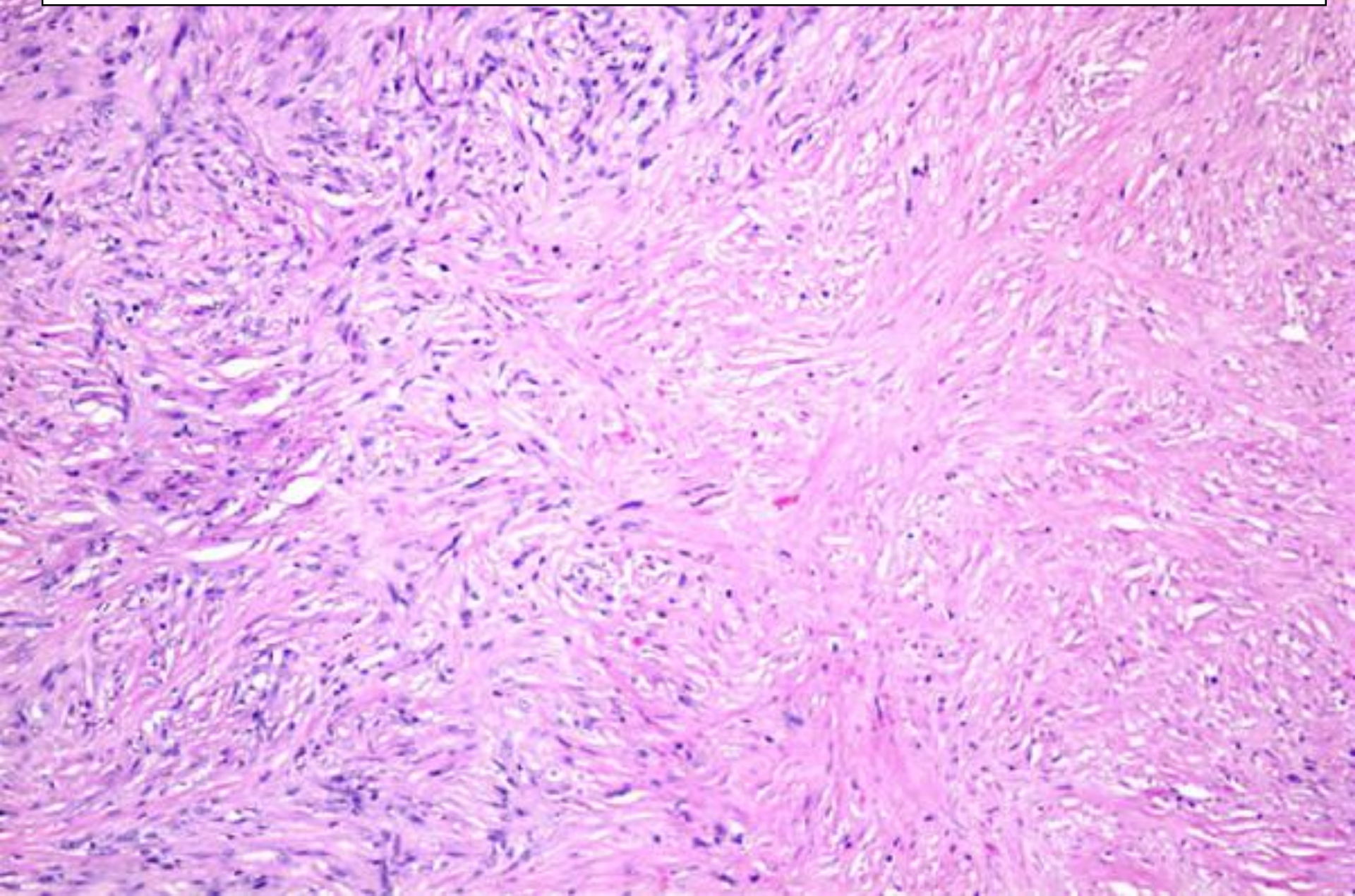
# Desmoplastic Meso - invasion

Pl elastica

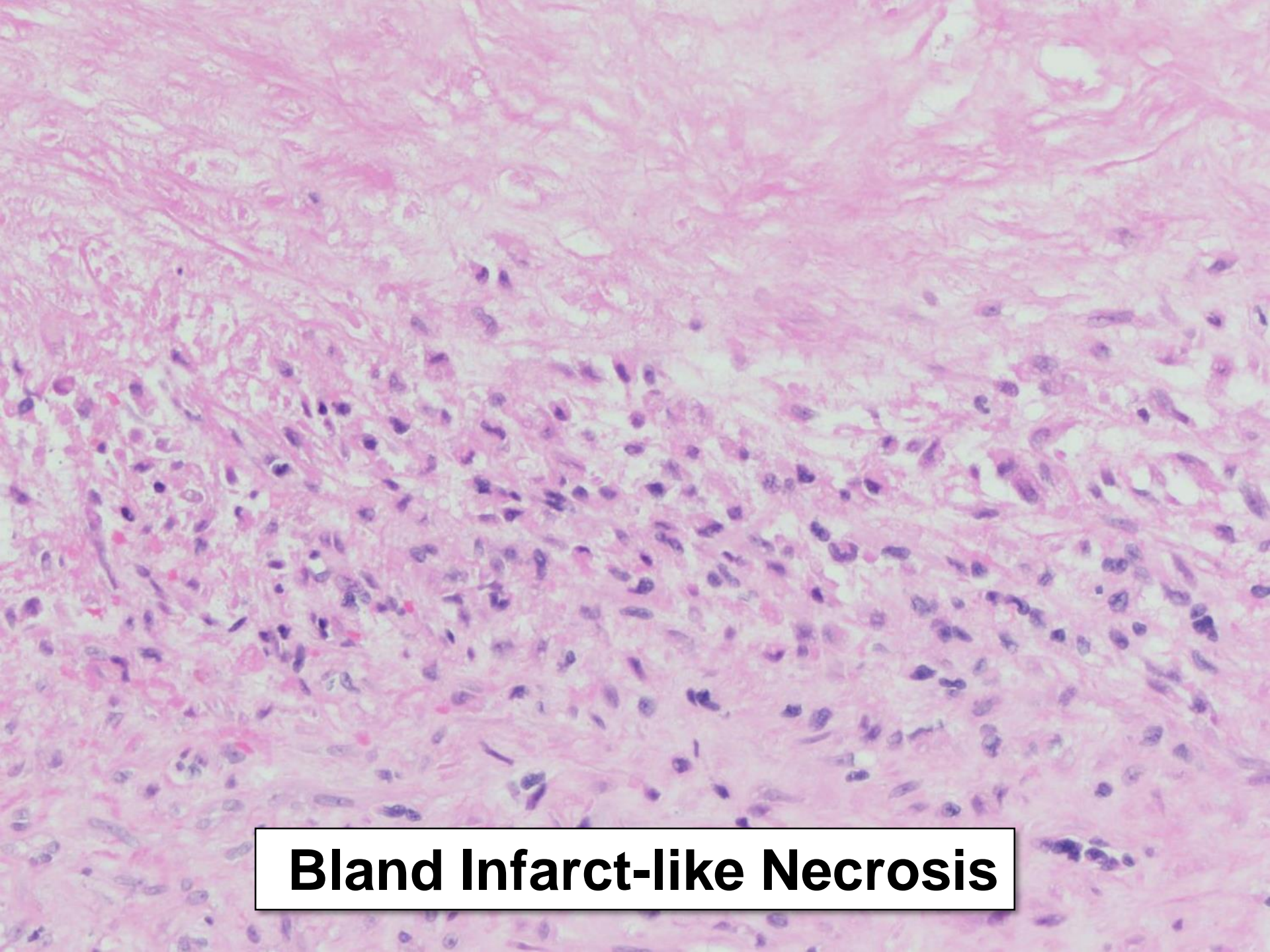




**Desmo'ic Meso- abrupt↑cellularity**



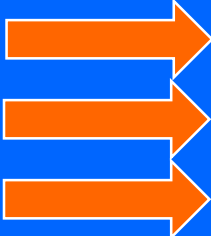





**Bland Infarct-like Necrosis**



# IHC: Sarcomatous Mesothelioma (%)

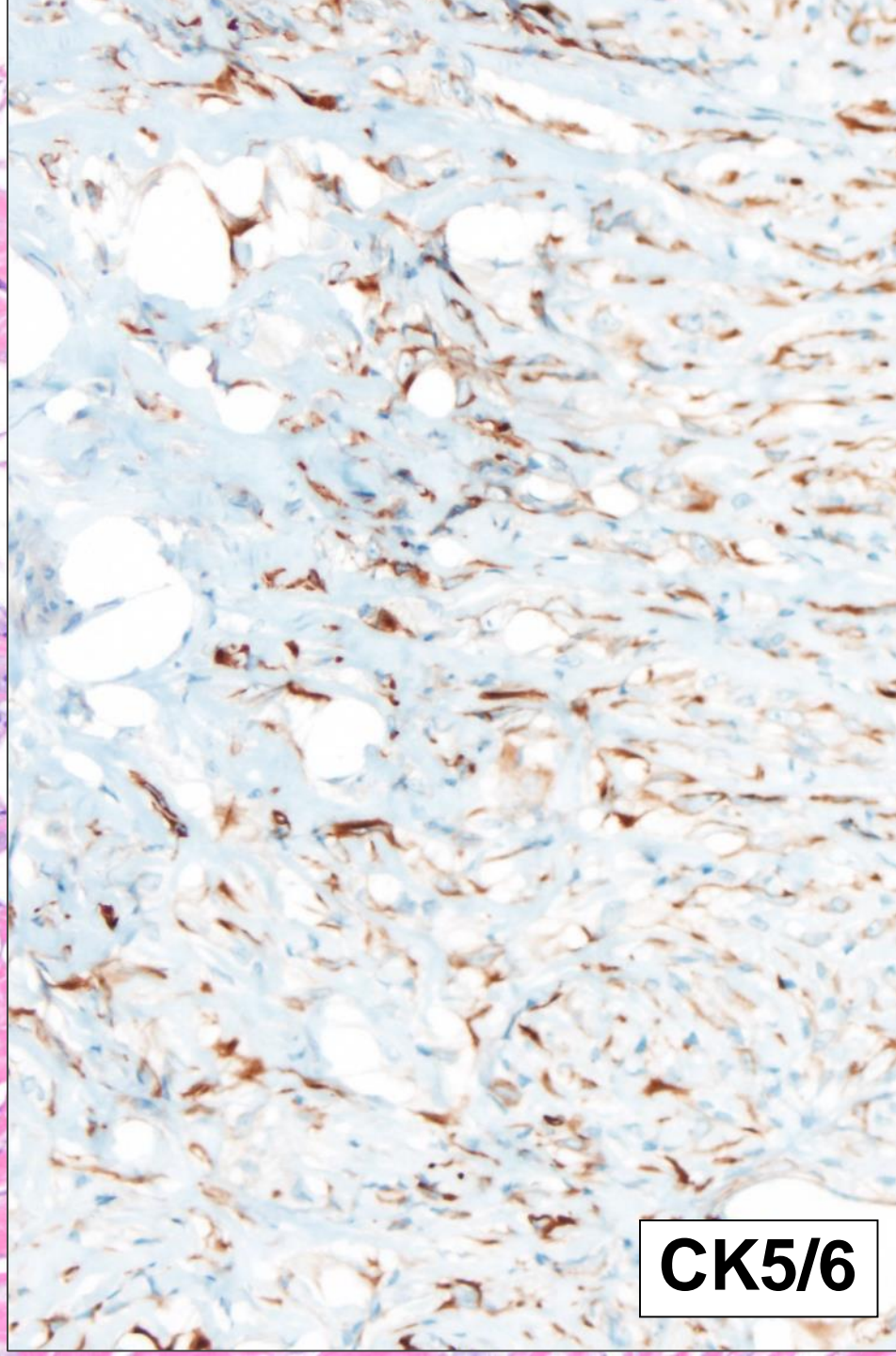
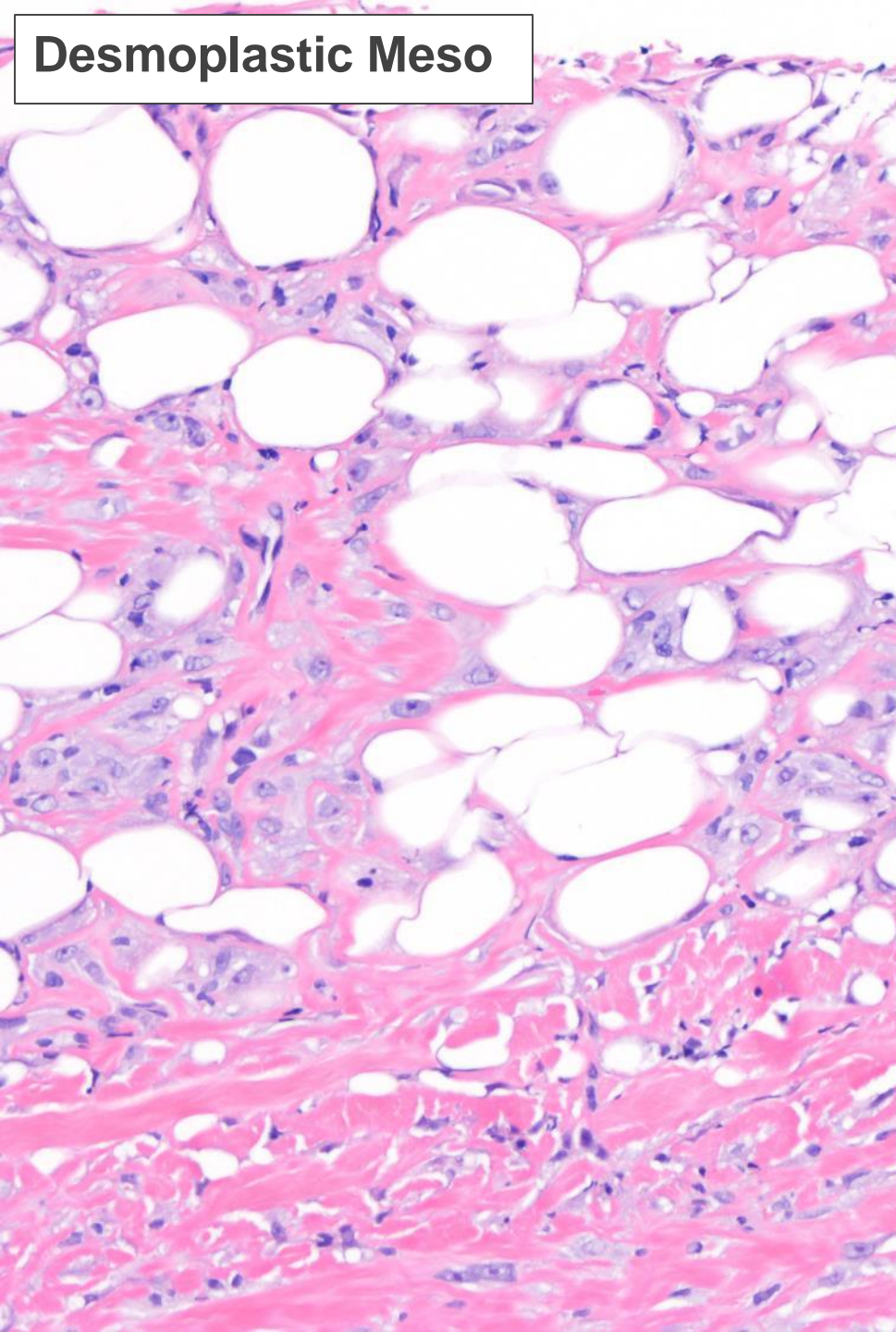


Antibody	Spindle Cell Carcinoma	Sarcomatous Mesothelioma
Keratin (broad sp)	88	89
Calretenin	37	54
D2-40	20	74
WT-1	31	45
CK 5/6	0	26
TTF-1	~17	4.6
GATA-3	15 focal wk	100 strong diffuse

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



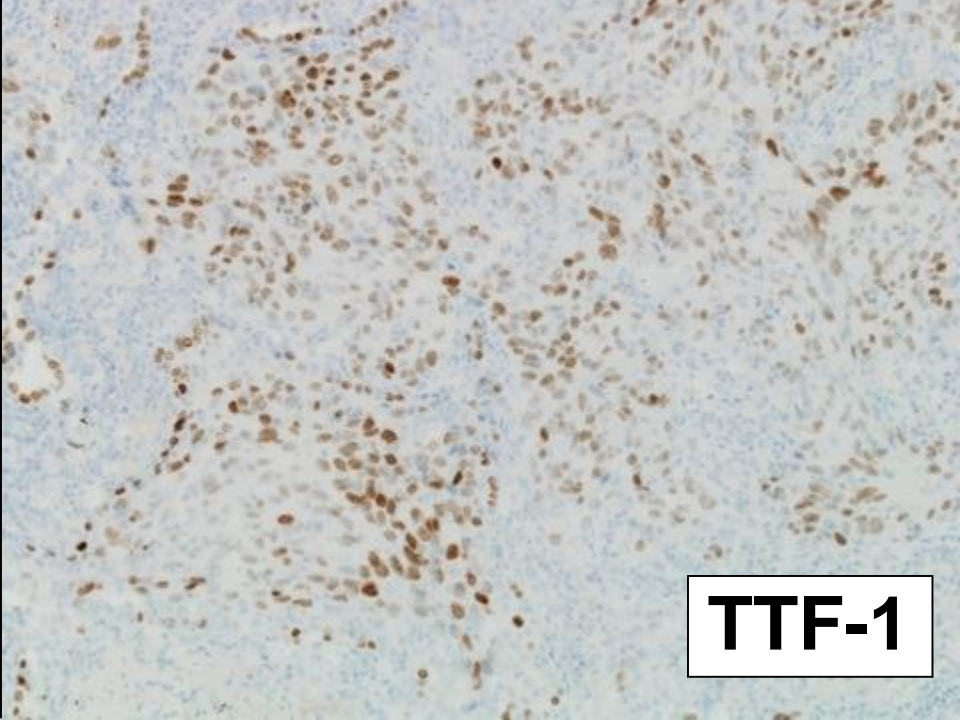
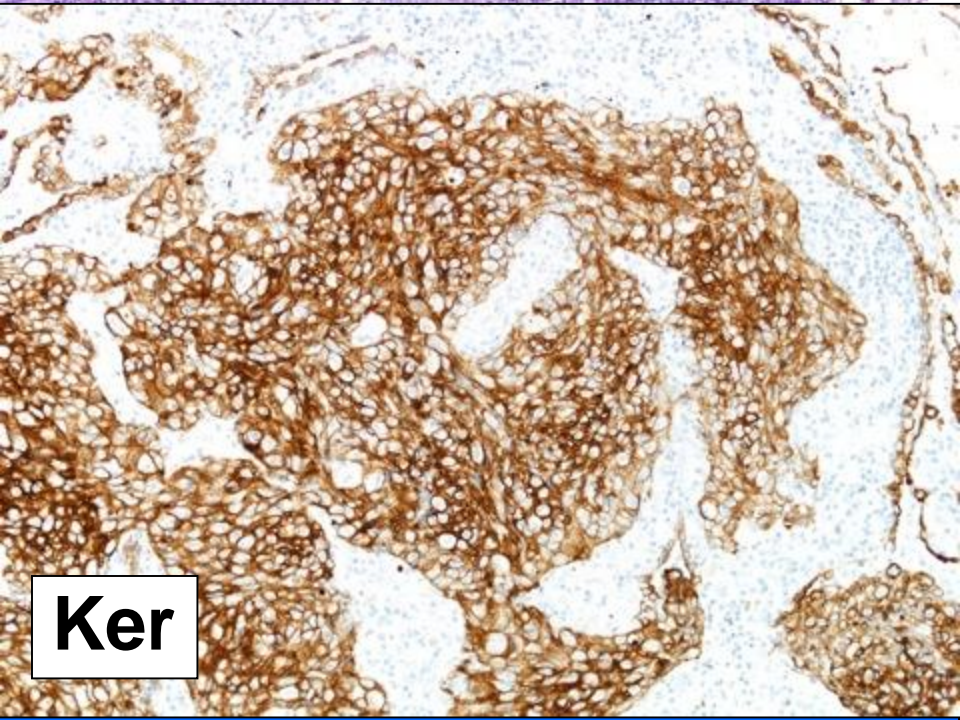
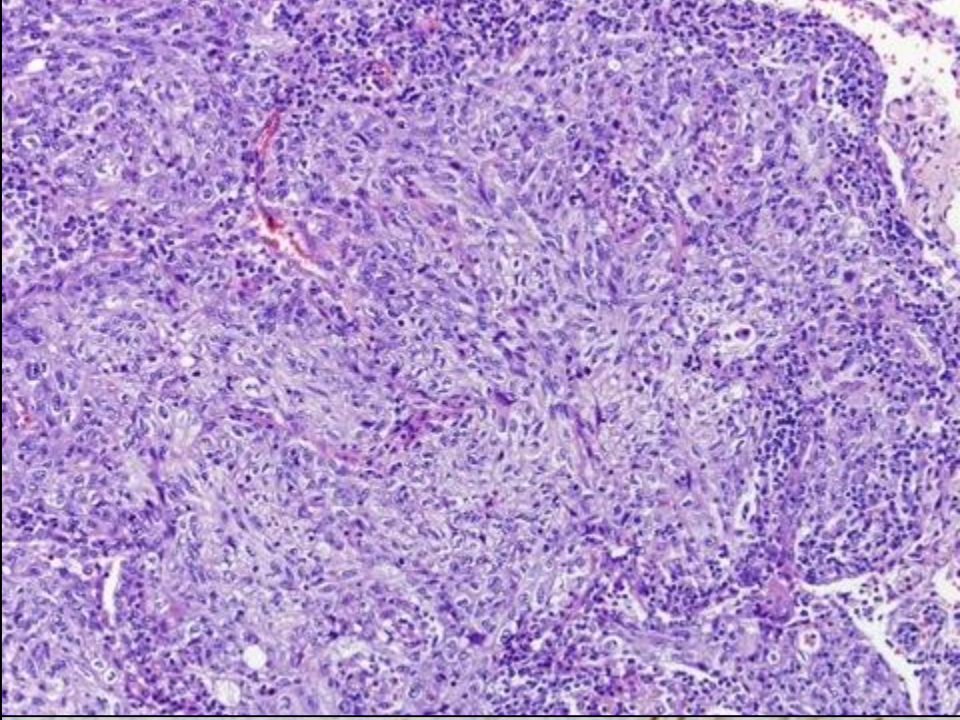
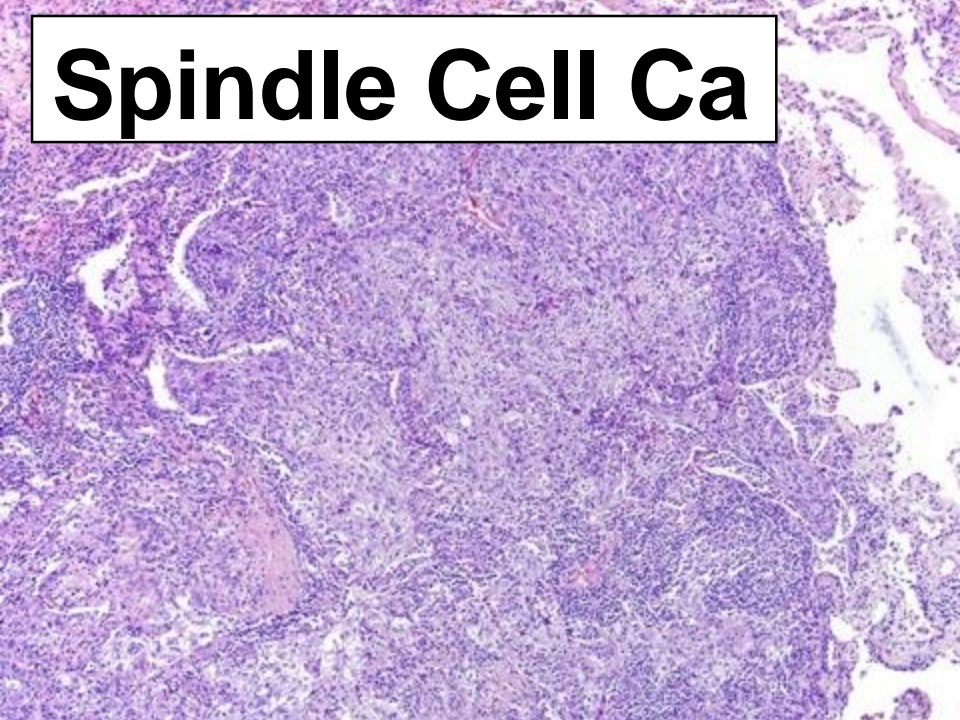
**Desmoplastic Meso**



**CK5/6**



# Spindle Cell Ca

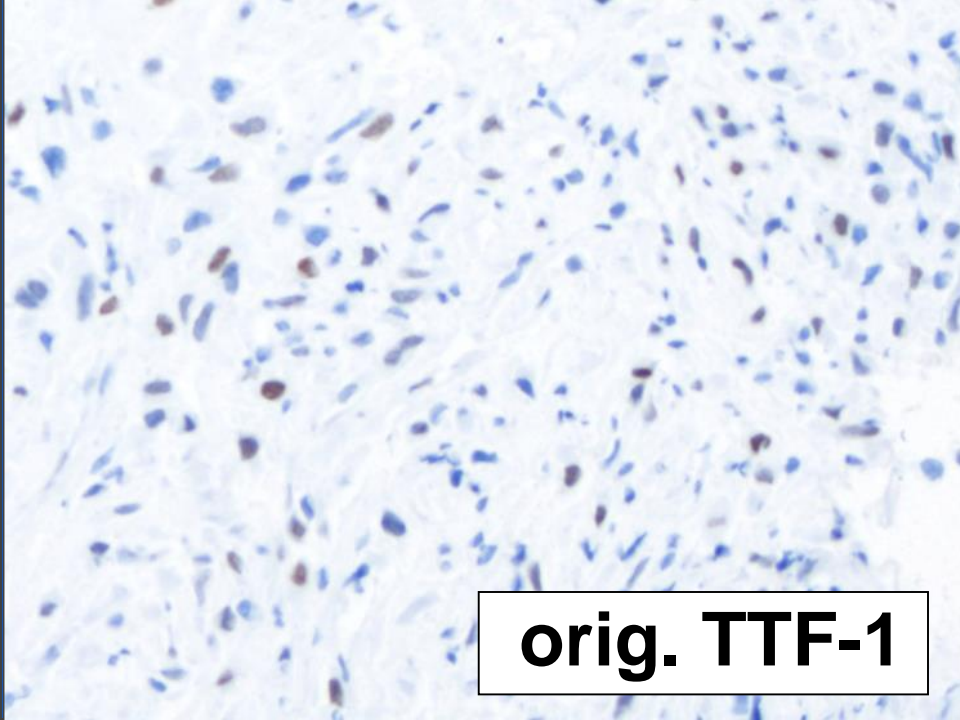
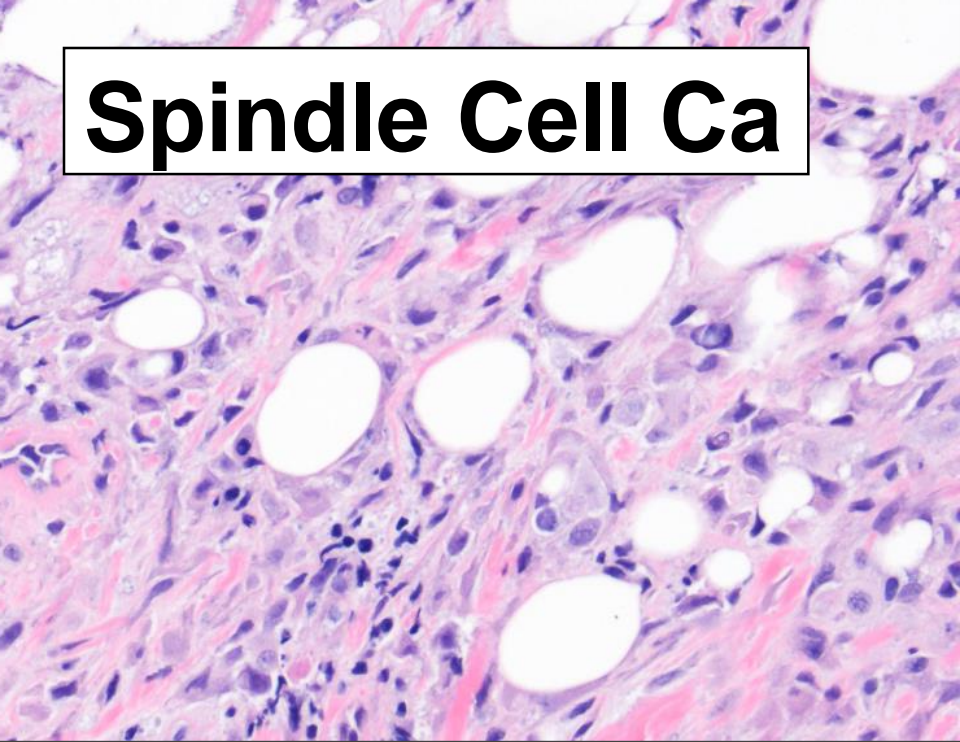


**Ker**

**TTF-1**



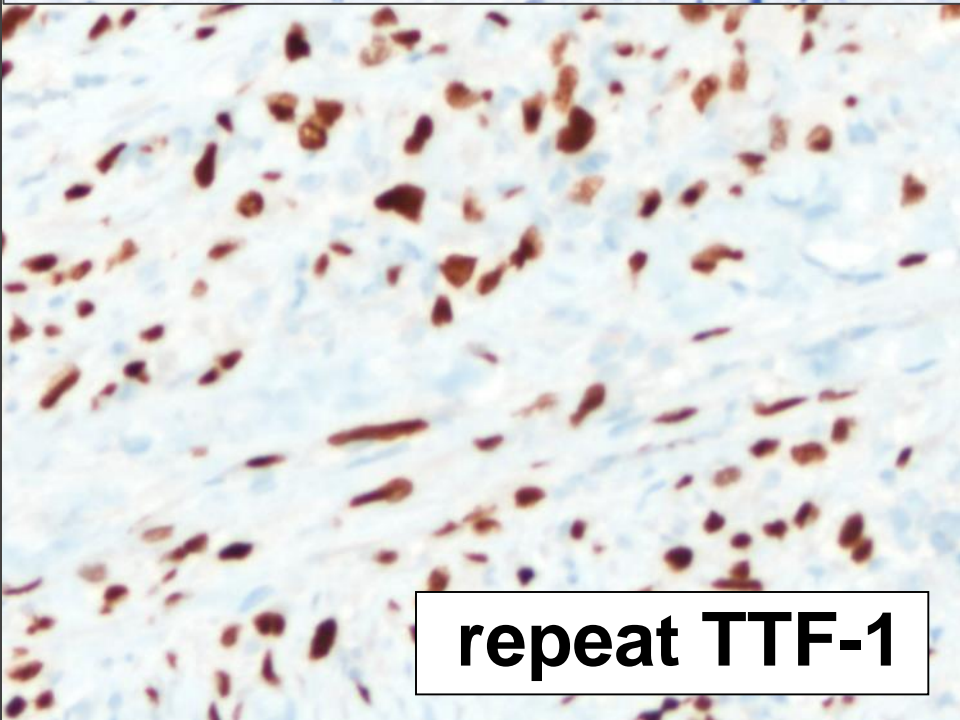
# Spindle Cell Ca



orig. TTF-1



Ker



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”

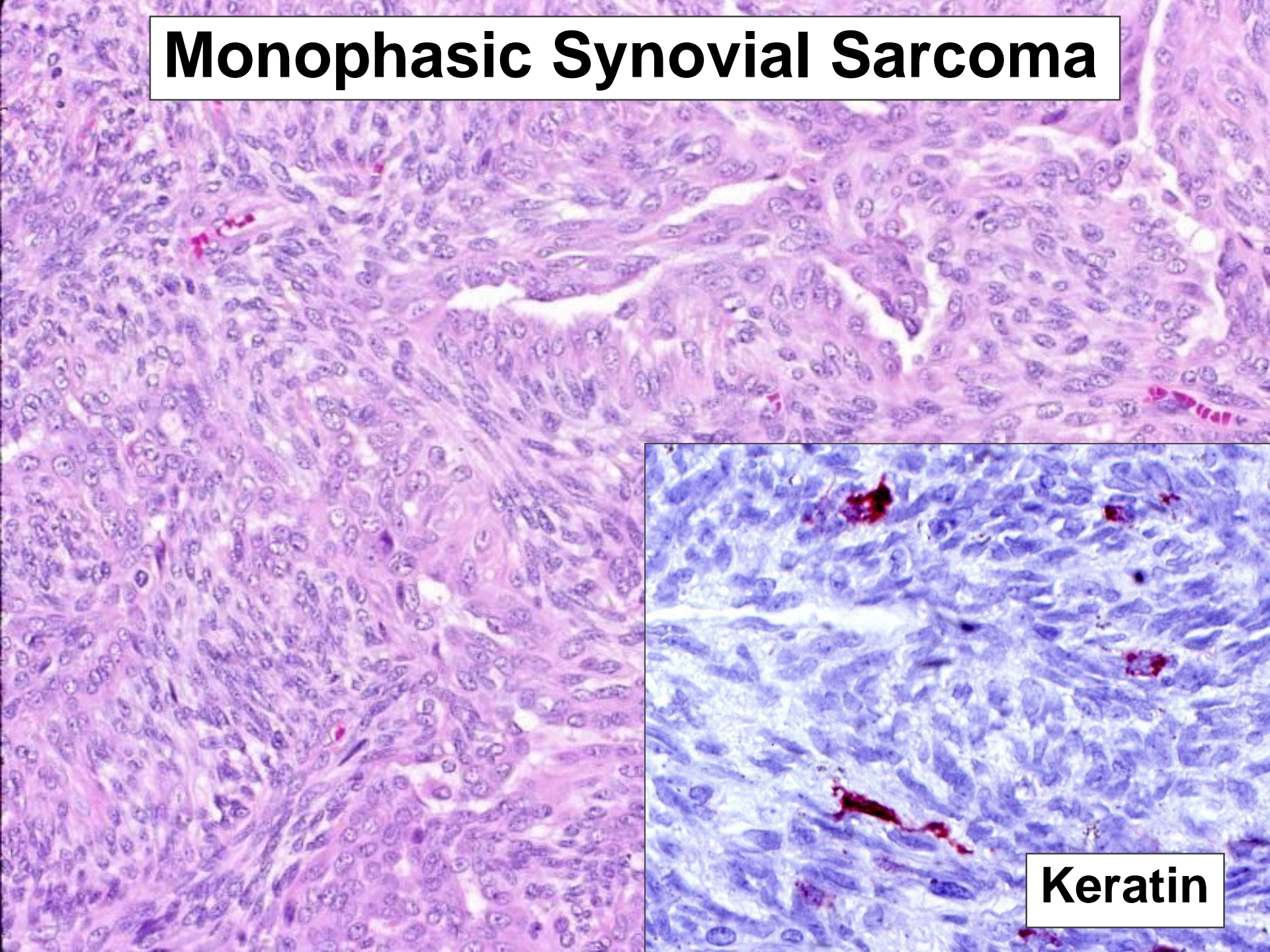


# **Sarcomatous Meso vs. Other Sarcomatous Neoplasms**

- **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





# 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 c

Organizing Pn  
IMT

locally +

Sarcom  
(lung,  
Mesoth  
Carc  
Thyr

oma  
rcoma

Met ESS, DF,

Mesothelioma

coma

Keratin

Synovial Sarcoma

in –

Benign/lo

EHE

grade

Organizing P  
Met ESS, D  
SFT

Angiosarcoma

sarcoma

Desm  
Melan

Infectious

FT  
sarcoma

Pseudoneoplasm

Infect. Pseudoneoplasm





Questions?