

# FNA / Needle Core Biopsy of Spindle Cell Lesions: Snakes or Worms?

Michael Ward

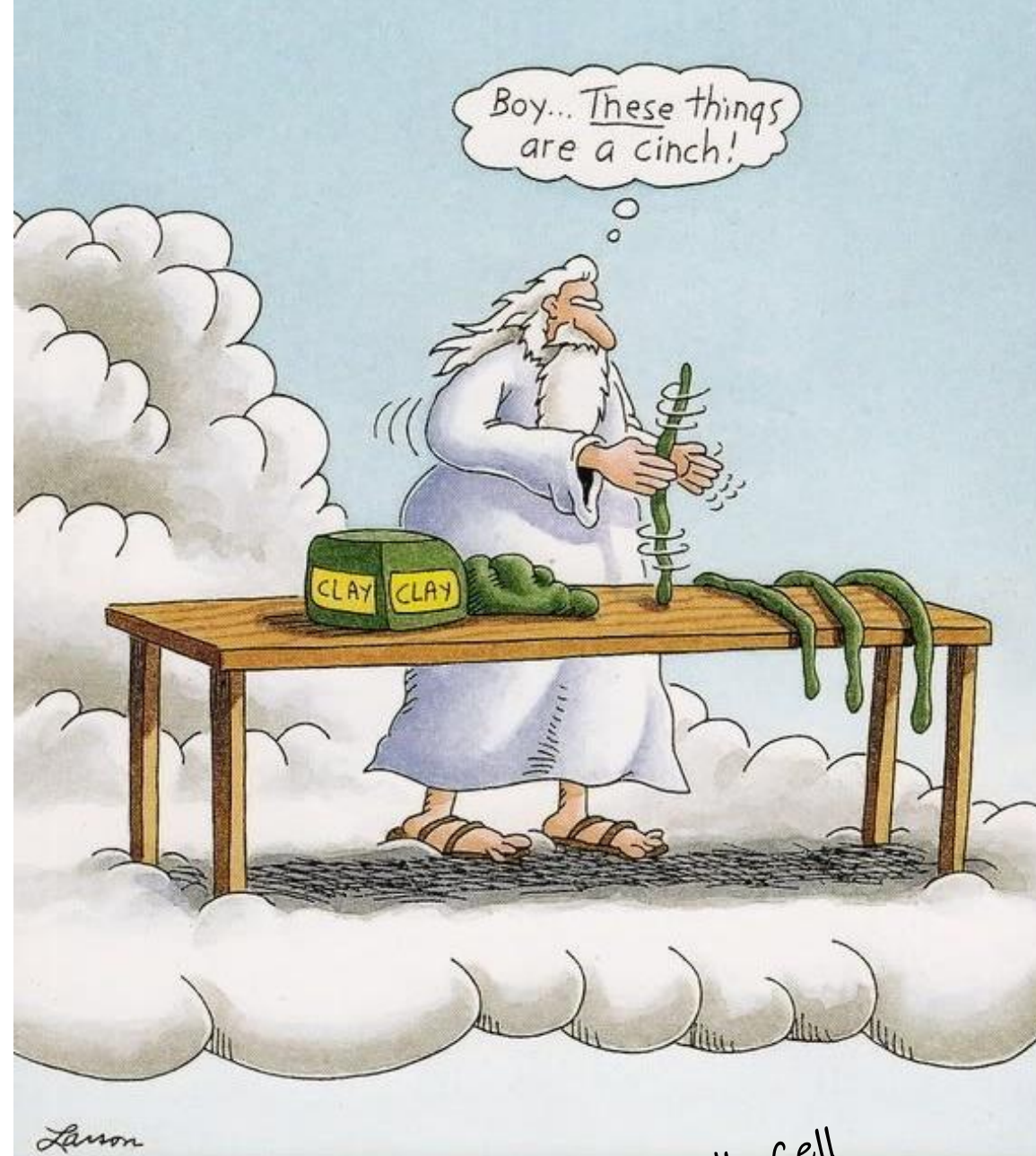
Feb 11<sup>th</sup> 2020



# Objectives


- Appreciate the diversity of spindle cell lesions among all soft tissue tumors (the big picture)
- Understand the role of the FNA/small biopsy in spindle cell lesions and the importance of ancillary techniques
- Examine the cytologic features of high vs low grade spindle cell lesions and the importance of grading
- Discuss the approach to working up spindle cell tumors using practice cases
- Highlight helpful general principles in soft tissue pathology





Larson

Spindle Cell  
God makes the snake.

Tumors of Soft Tissue								Chart compiled from WHO Bone and Soft Tissue 2013
Adipose	Fibroblastic/Myofibroblastic	Fibro-histiocytic	Smooth Muscle	Skeletal Muscle	Vascular	Neural	Uncertain Differentiation	Undifferentiated/Unclassified
Lipoma	Nodular Fasciitis	Tenosynovial giant cell tumor: - Local - Diffuse	Leiomyoma	Rhabdomyoma	Hemangioma/ vascular malformation	Neuroma (Traumatic)	Myxoma	
Spindle cell lipoma Pleomorphic lipoma	Fibromas: Fibroma of T. Sheath Superficial fibromatoses: -Palmar, Plantar, Penile Deep (desmoid) fibromatoses	Benign fibrous histiocytoma				Benign nerve sheath tumors: - Schwannoma - Neurofibroma - Perineuroma	Atypical Fibroxanthoma (AFX)	
	Solitary fibrous tumor				Kaposi Sarcoma	Granular cell tumor	Myoepithelial tumor	<b>Use a Descriptive Diagnosis:</b> “Pleomorphic” (UPS) “Spindled” “Epithelioid” “Round cell”  *** Before you use this category make sure:  1- Not melanoma, lymphoma or carcinoma 2- Not a specific lineage 3- Not a de-differentiated sarcoma
							Synovial sarcoma	
							Epithelioid Sarcoma	
Well differentiated liposarcoma / Atypical lipomatous tumor	Dermatofibrosarcoma protuberans (DFSP)				Epithelioid hemangio-endothelioma		Alveolar Soft Part Sarcoma	
Myxoid liposarcoma	Inflammatory myofibroblastic tumor (IMT)			Embryonal RMS			Clear cell sarcoma	
	Low grade fibromyxoid sarcoma			Alveolar RMS			Extra-skeletal myxoid chondrosarcoma	
De-differentiated liposarcoma	Fibrosarcoma			Spindle Cell/Sclerosing RMS			Perivascular epithelioid cell neoplasms (PEComa)	
Pleomorphic liposarcoma	Myxofibrosarcoma	Malignant Fibrous Histiocytoma	Leiomyosarcoma	Pleomorphic RMS	Angiosarcoma	Malignant Peripheral Nerve Sheath Tumor (MPNST)	Desmoplastic Small Round Cell Tumors (DSRCT)	

# A General Approach to the Spindle Cell Mass

- Overall cellularity
- Dissociated vs cohesive
- Lineage specific clues
  - Fascicles, rhabdomyoblasts, lipoblasts, osteoid, wavy tapered nuclei, blunt-ended nuclei, monomorphic (think translocation associated)
- Ancillary testing:
  - Keratin, S100 or Sox10, Smooth muscle actin, Desmin, Caldesmon, Myogenin/MyoD1, CD31, CD34, MDM2 FISH (depending on the site)
  - Beta Catenin, STAT6, EMA, Myoepithelial markers, INI1 (SMARCB1), MUC4, TFE3, ALK1, CD117, Additional melanoma markers, CD45
  - Other FISH:
    - ESWR1 - Ewing/PNET, DSRCT, Clear cell sarcoma, Myoepithelial tumors, Extraskeletal myxoid chondrosarcoma
    - SYT- Synovial sarcoma
    - FUS - Low grade fibromyxoid sarcoma
    - CHOP/DDIT3 - Myxoid liposarcoma

What is the most important prognostic factor in soft tissue tumors?

- A) Histologic subtype
- B) Grade
- C) Stage/Size
- D) Molecular profile

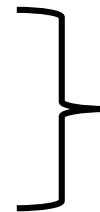
# What is the most important prognostic factor in soft tissue tumors?

- A) Histologic subtype
- B) Grade**
- C) Stage/Size
- D) Molecular profile

- Definitive grading is best done when you know what the specific diagnosis is:

French Federation (FNCLCC) grading system

- Differentiation score
- Mitotic count
- Tumor Necrosis



Histologic Grade: 1 (low) vs 2,3 (High)

- When a specific diagnosis cannot be given, assigning a general category and grade (low vs high) usually leads to the correct clinical management:

“High grade spindle cell sarcoma”

# High grade vs Low Grade Spindle Cell Lesions

Grade often dictates clinical management:

- High grade will get radiation and/or chemotherapy
- Low grade will get resection and surveillance

## *High Grade Cytology:*

High cellularity  
Diffuse hyperchromasia  
Marked nuclear atypia  
Prominent crowding/overlap  
Definite necrosis  
Frequent mitoses  
More dispersed cells



## *Low Grade Cytology:*

Low cellularity  
Minimal crowding/overlap  
Mild nuclear atypia  
Minimal/absent necrosis  
Rare/absent mitoses  
Fewer dispersed cells

# Rapid On Site Evaluation (ROSE) of Spindle Cell Lesions

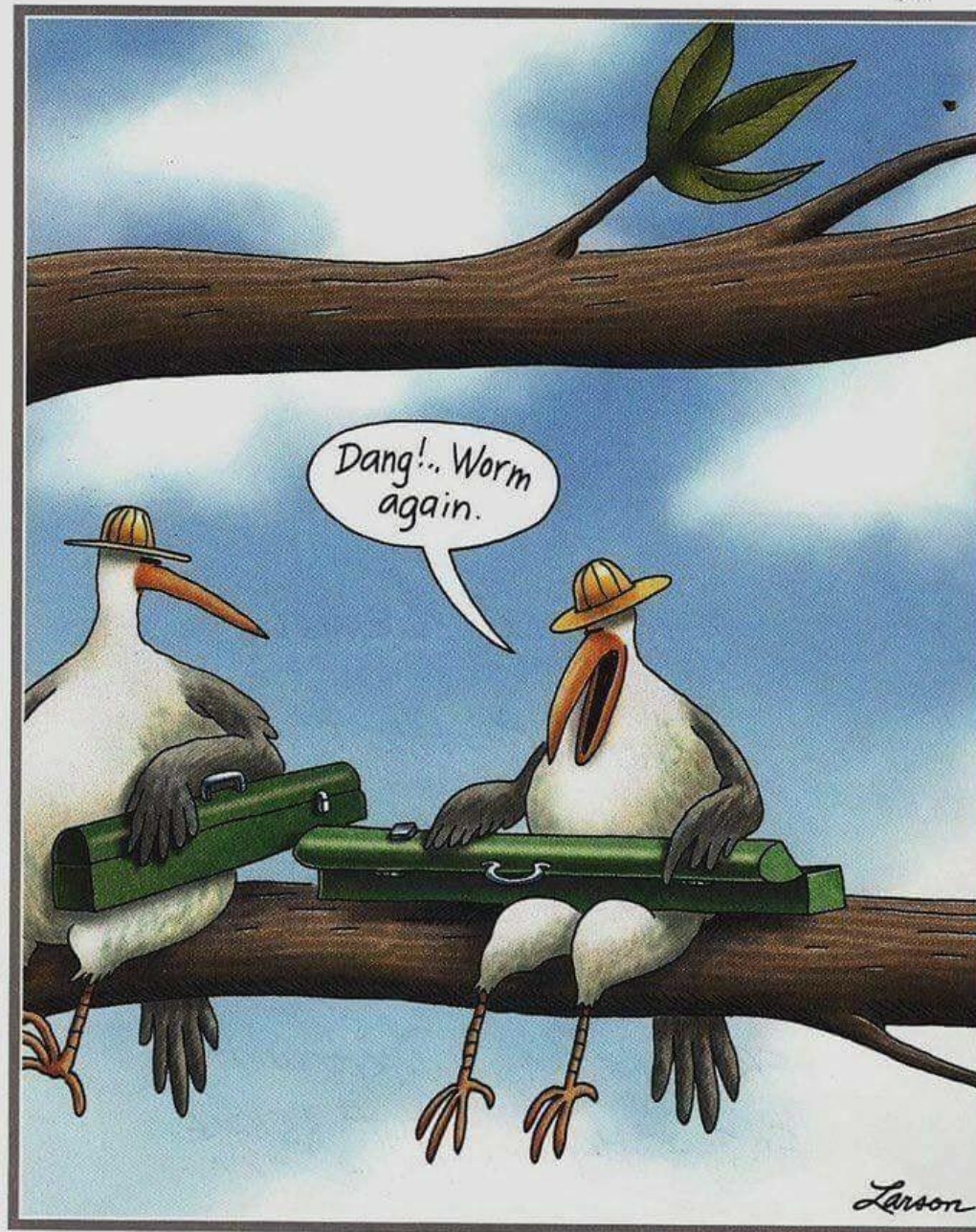
Soft tissue lesions (especially fibrous or vascular lesions) don't release many cells on FNA or touch prep, but seeing rare spindle cells is still helpful:

- Confirm viable material
- Confirm a good site for core biopsy
- May allow preliminary assessment of grade
- While the FNA is very helpful, core biopsies with touch preparations are highly recommended

# Rapid On Site Evaluation (ROSE) of Spindle Cell Lesions

Triage of scarce tissue cores is critical

- Definitive diagnosis on small cores is now feasible; encourage multiple cores
- Remember benign lesions may require as many or more stains than malignant tumors
- Consider placing multiple cores in separate containers
  - Avoid depletion
  - Triage soft fragments to containers that don't need decalcification
    - Decalcification in strong acids will preclude molecular testing (decalcification in EDTA won't)

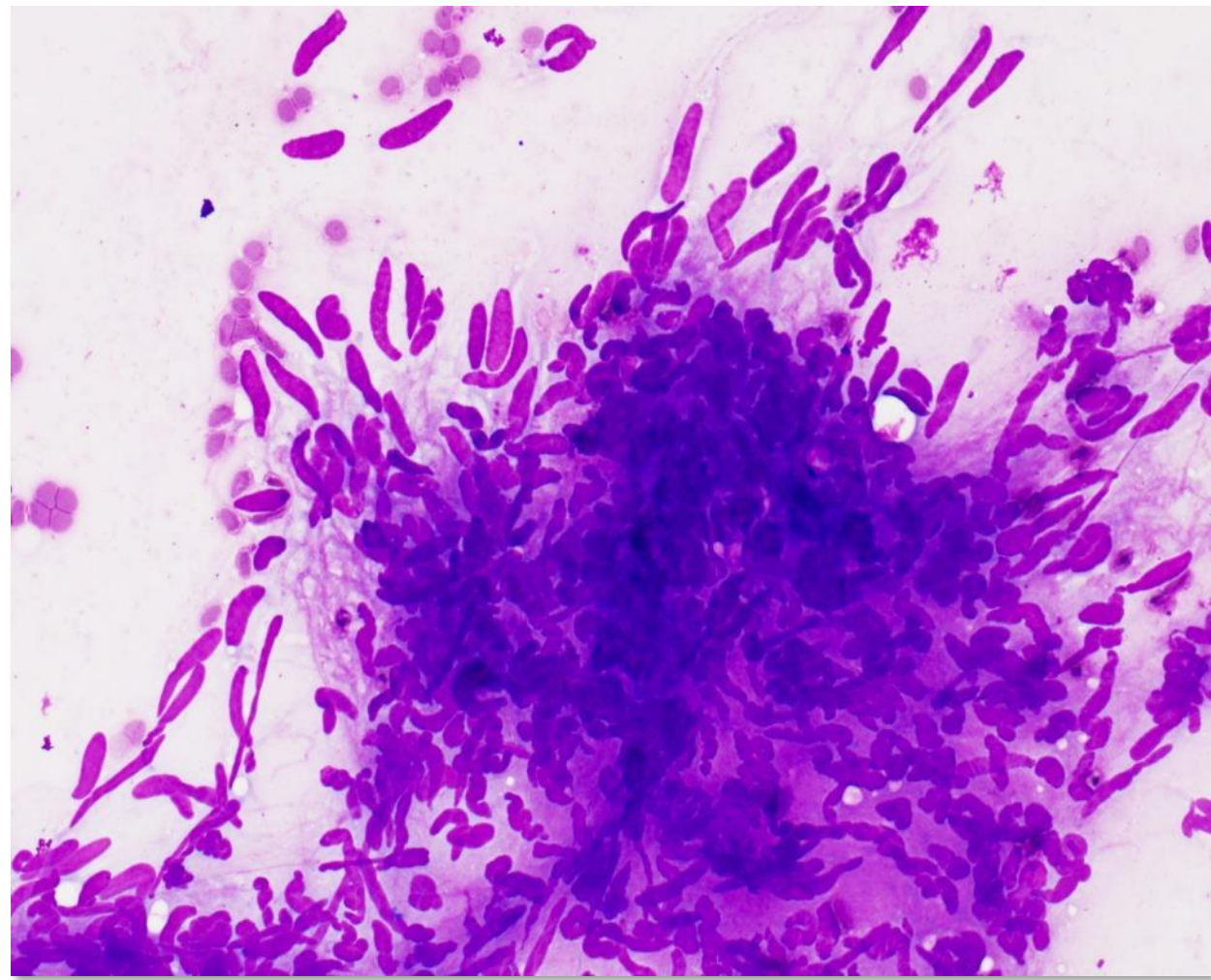
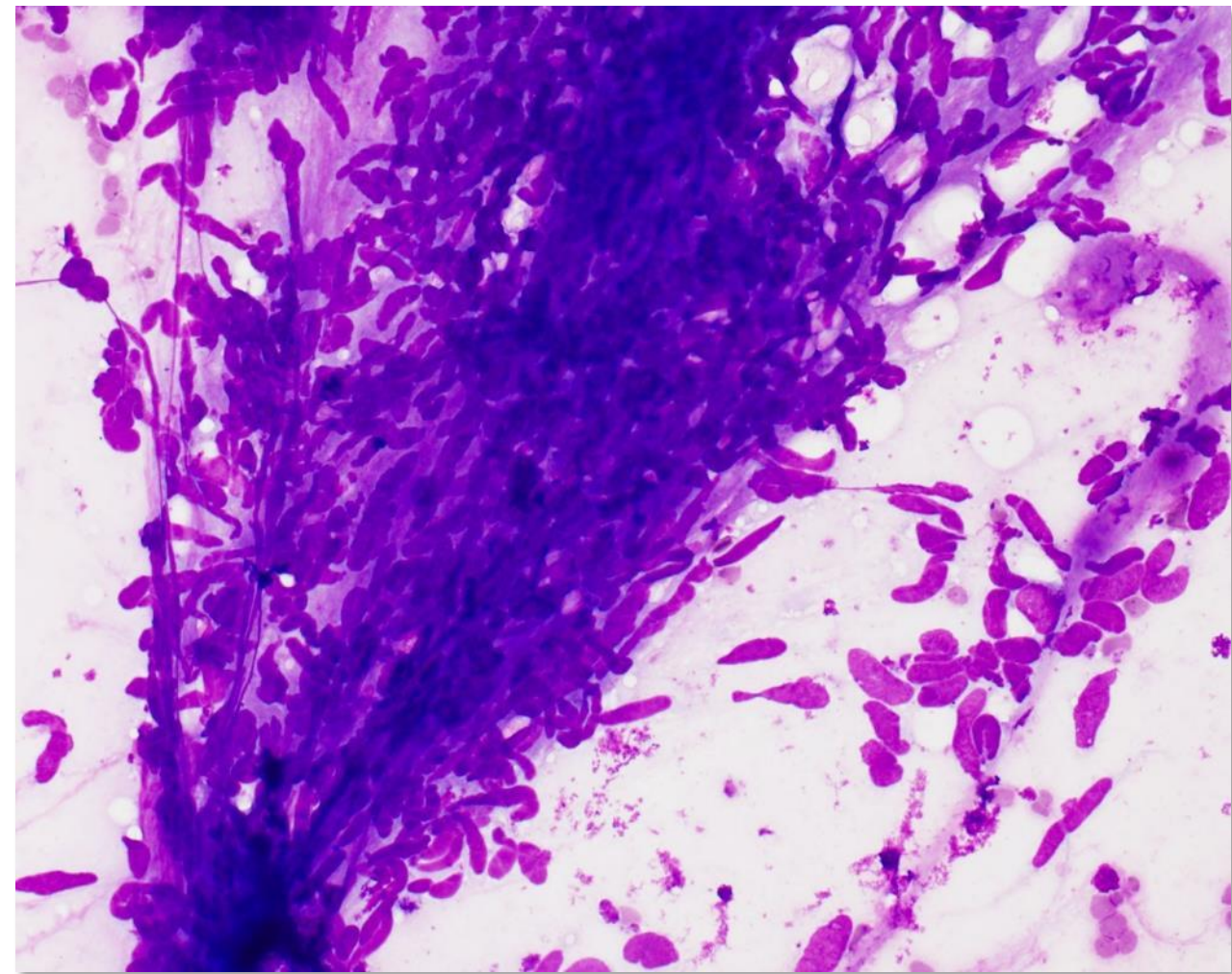


Construction birds at lunch

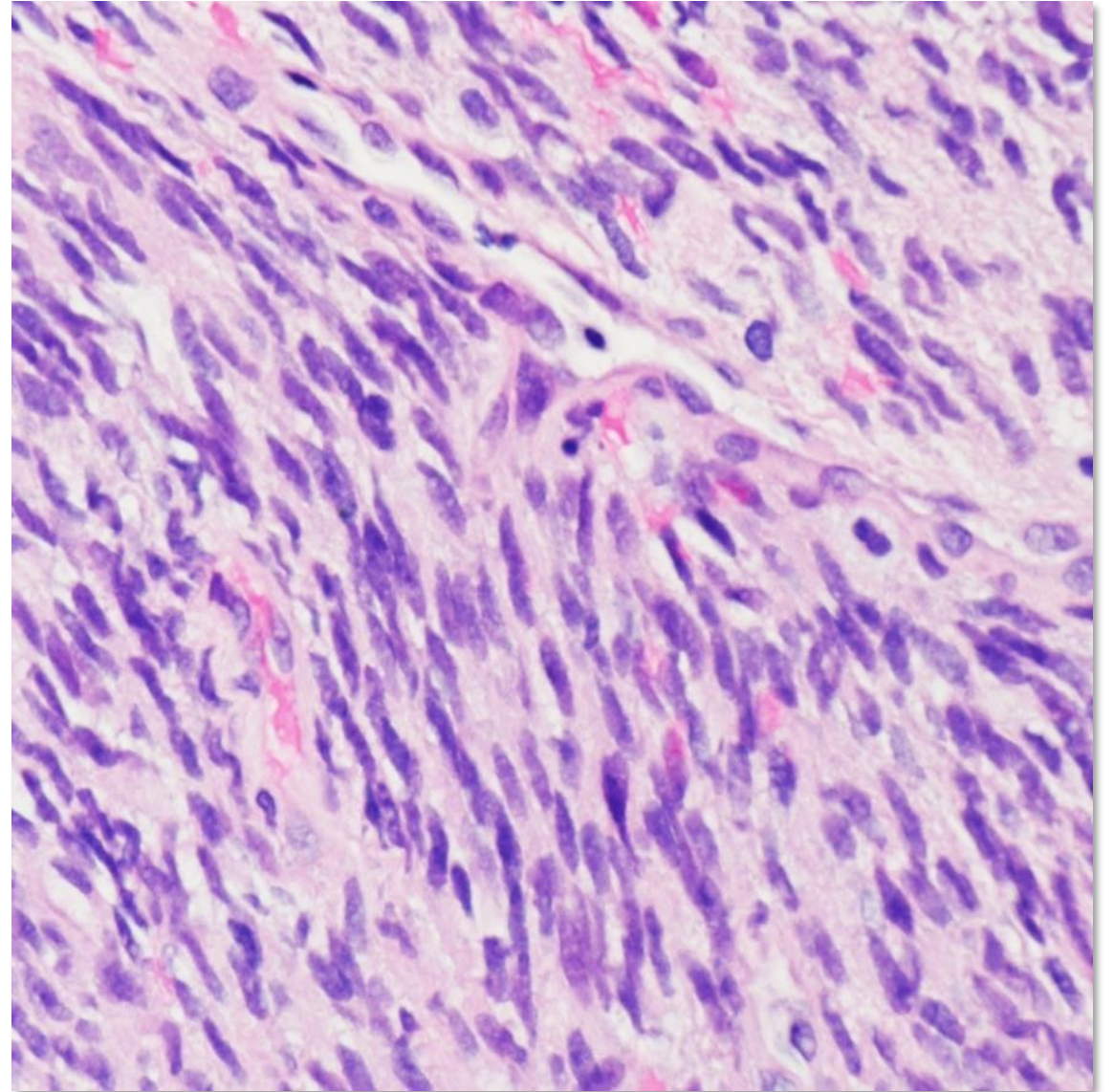
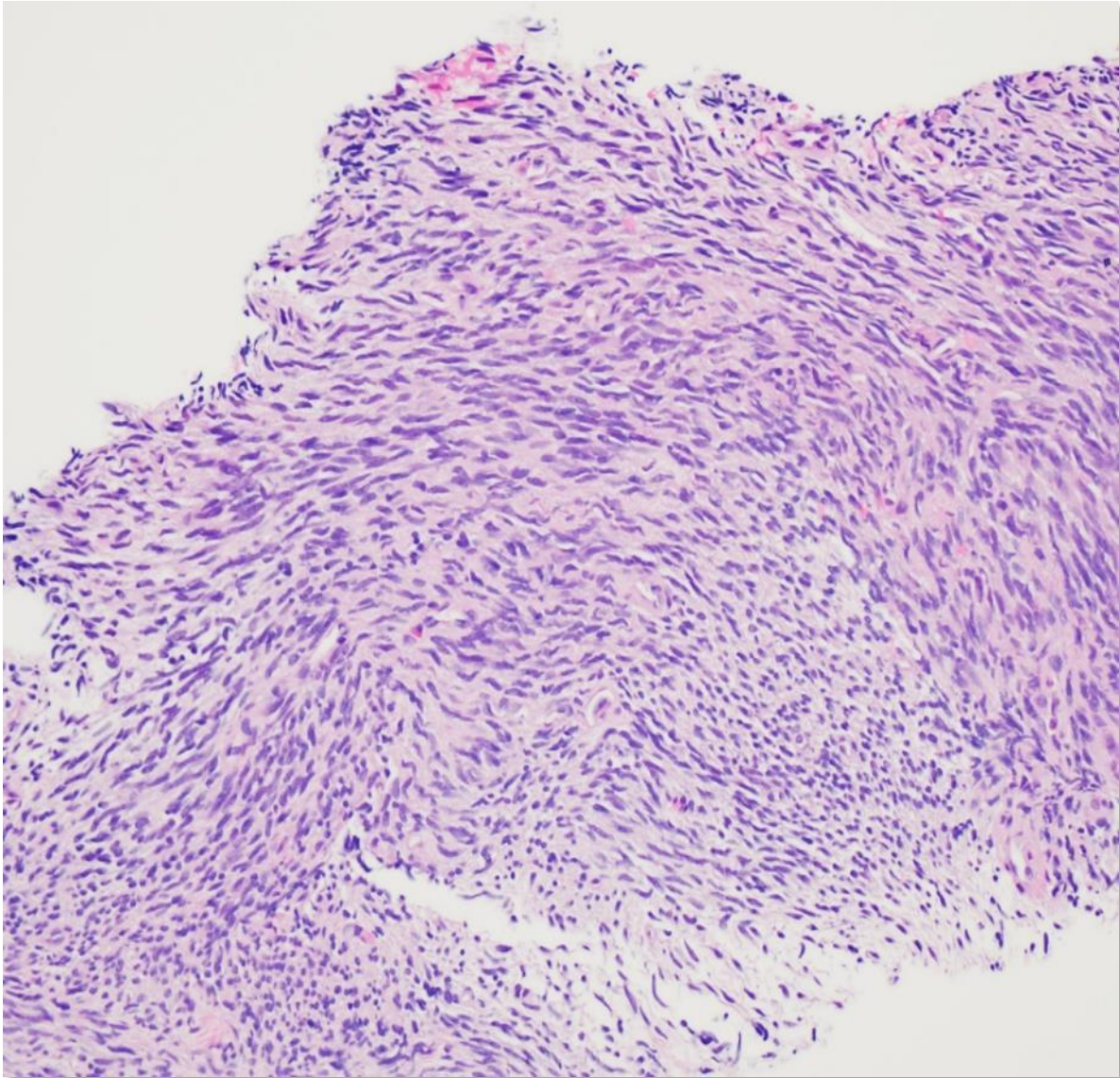
# Case # 1

History: 10 year old boy with a history of papillary thyroid carcinoma with a 1 cm, tender, deep thigh nodule

# Case # 1 Touch Preparations



# Case # 1 Biopsy



# Case # 1 – Synovial Sarcoma

## Epidemiology/Clinical features:

- 10% of sarcomas
- > 50% occur in teenagers and young adults

## Site:

- Wide anatomic distribution, most often in deep soft tissues of extremities, often around joints

## Cytology:

- High cellularity, clusters and dispersed cells, very monomorphic cells, bland nuclear features

## Histopathology:

- Monomorphic population of hyperchromatic spindle cells with high N:C ratios, scattered staghorn-shaped vessels
- Biphasic or monophasic
- Calcifications/and or ossification common

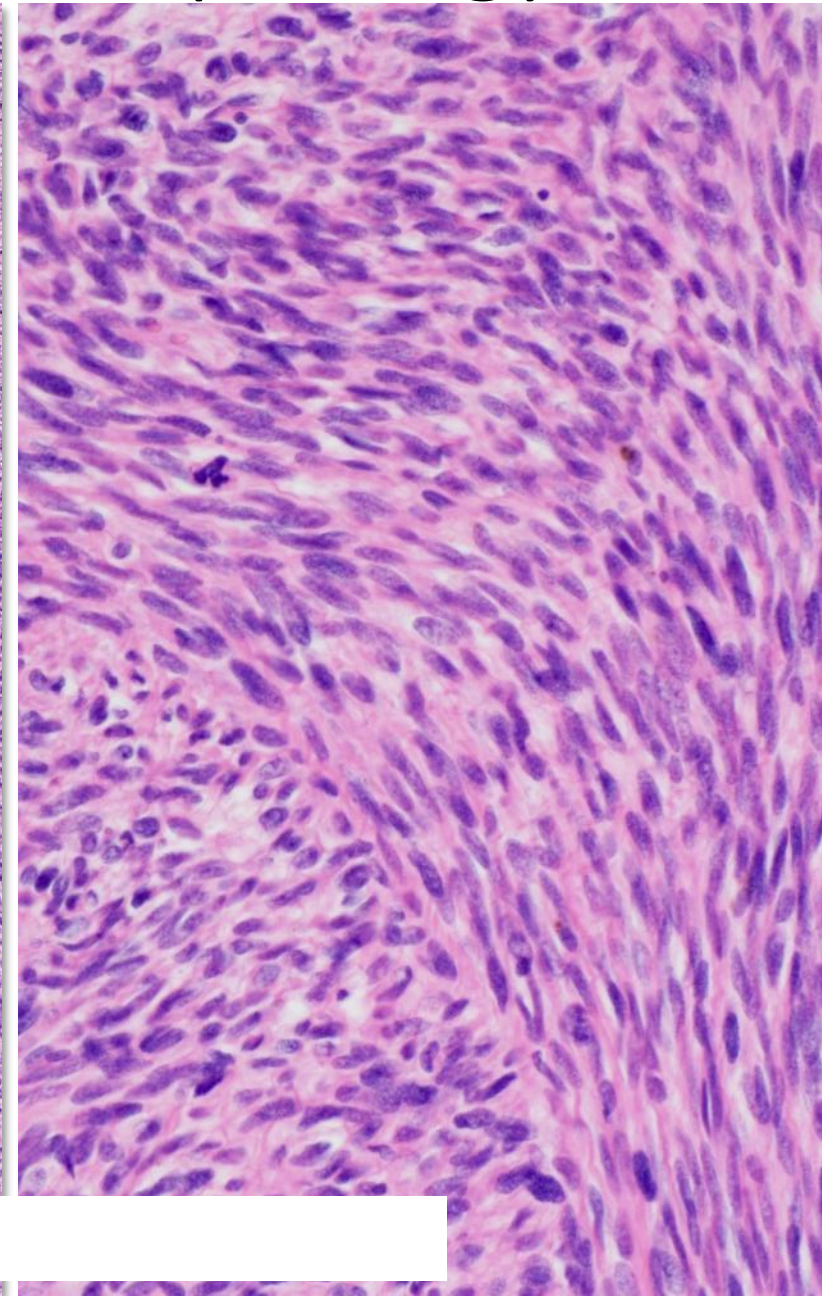
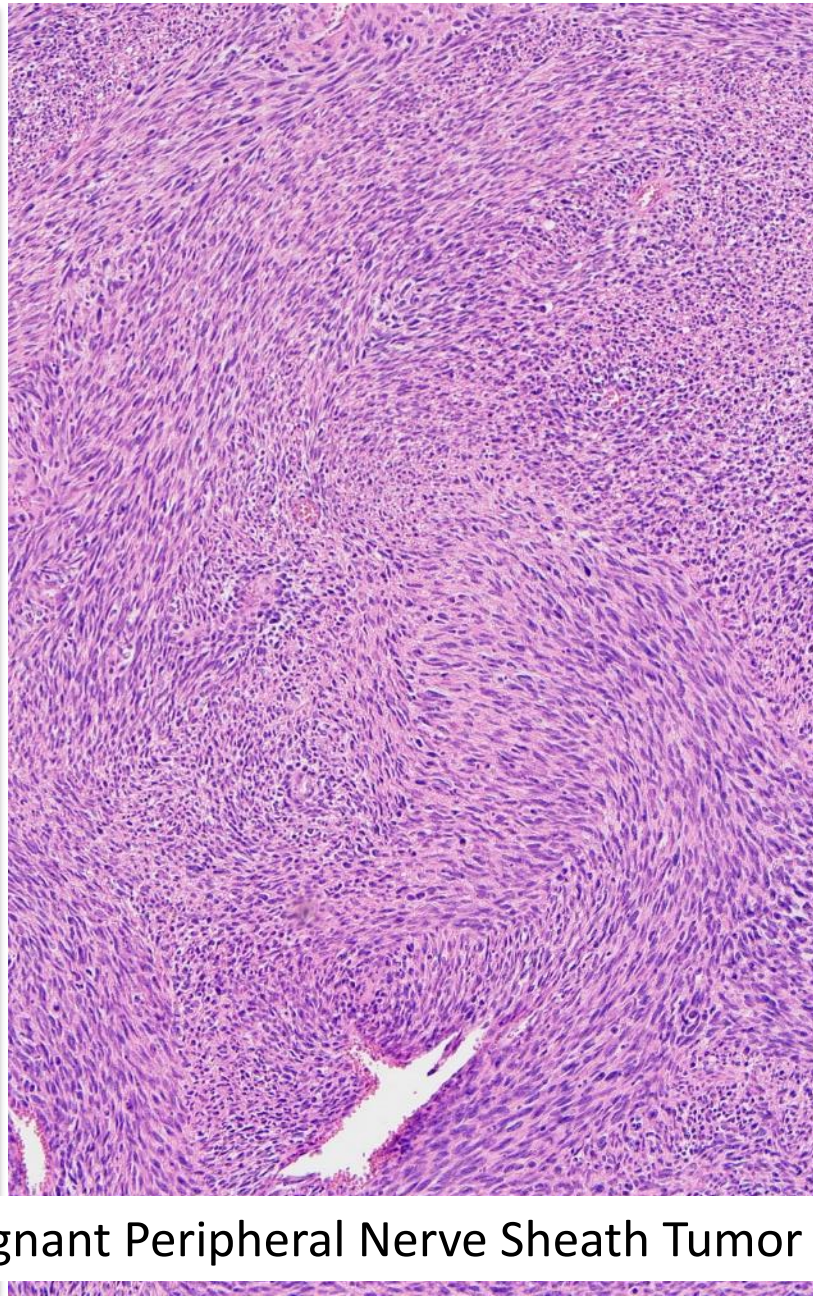
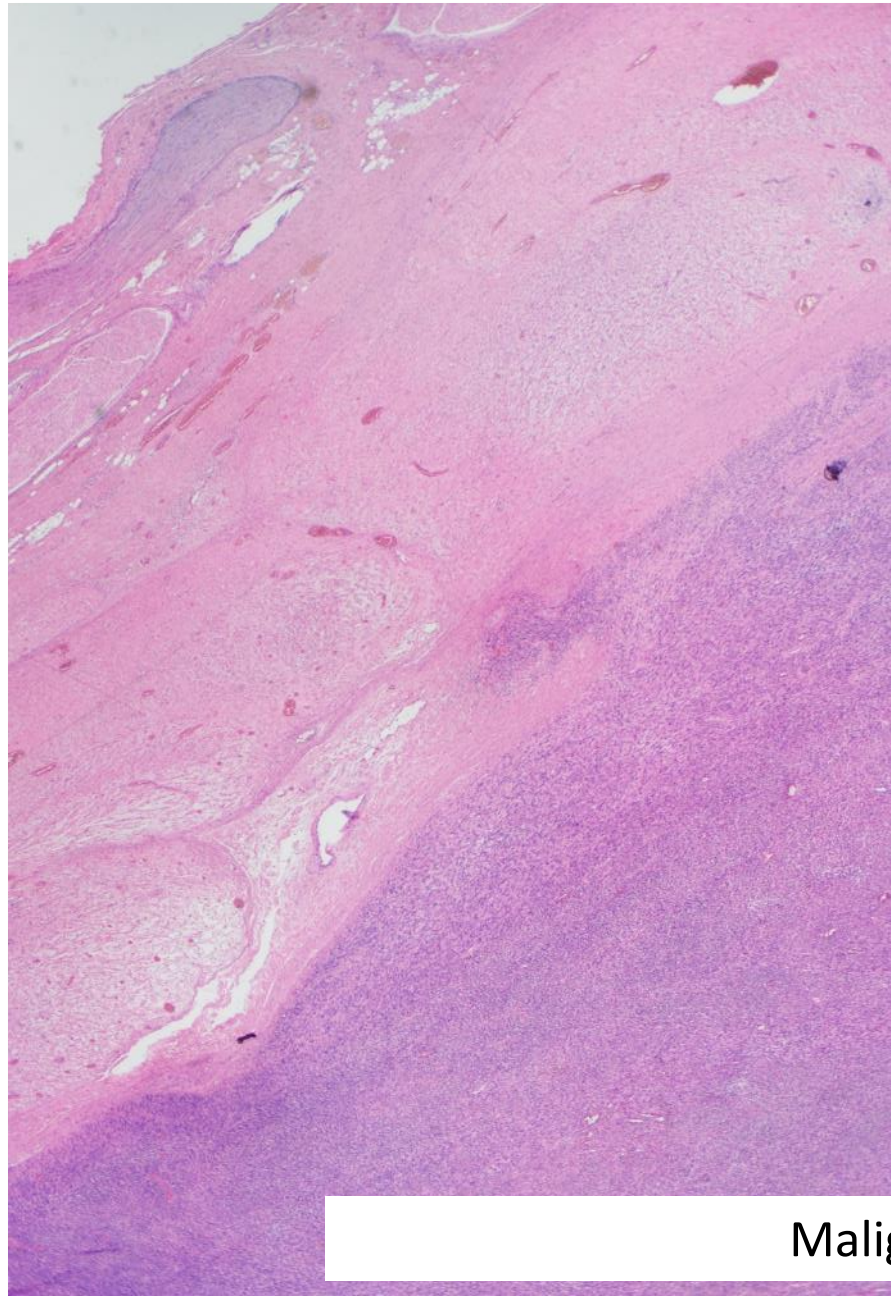
## Ancillary:

- Nearly always show focal keratin expression, especially EMA
- Translocation t(X;18) SSX-SYT fusion is diagnostic (present in >95% of cases)

## DDx:

- Leiomyosarcoma, MPNST, SFT, Ewing, Metastatic carcinoma, Carcinosarcoma

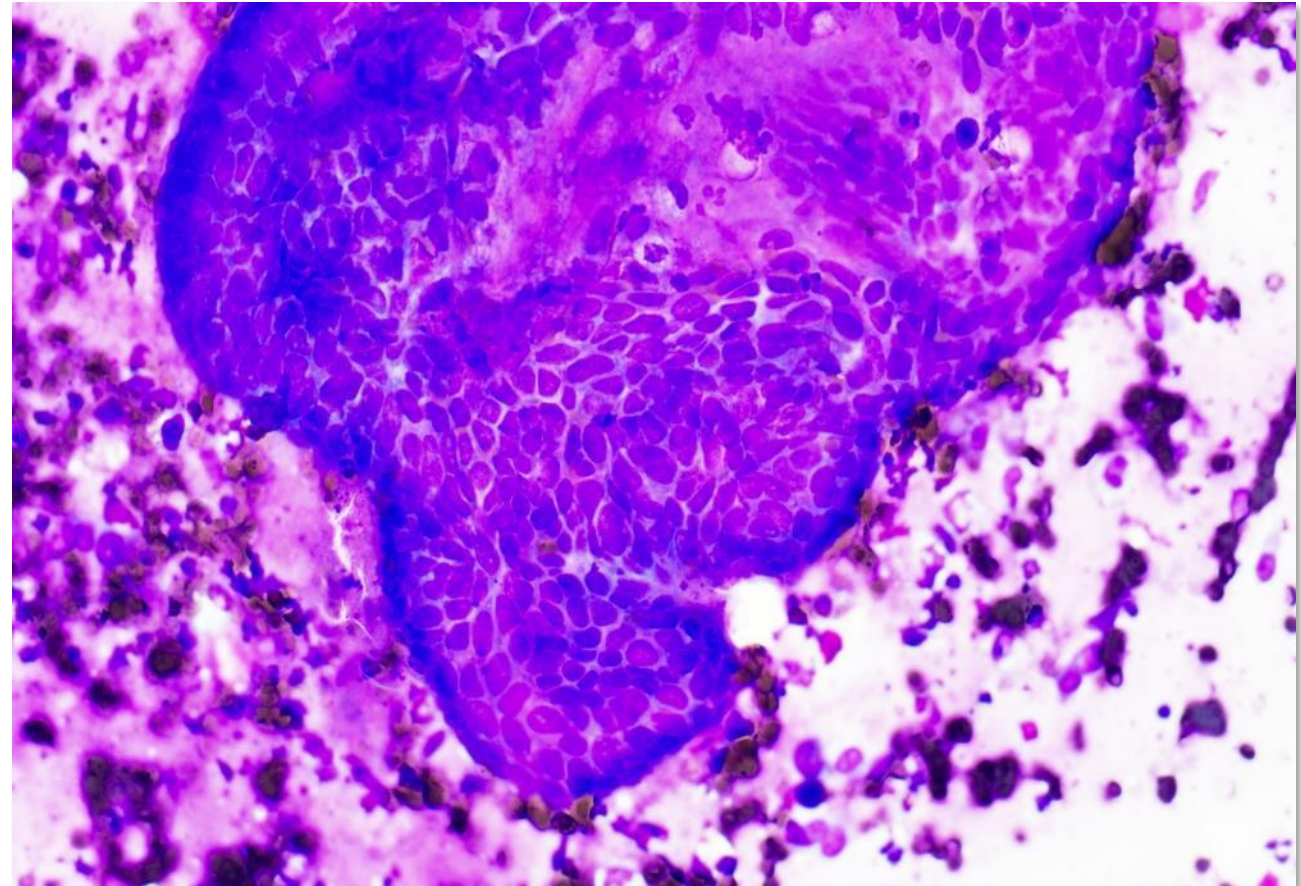
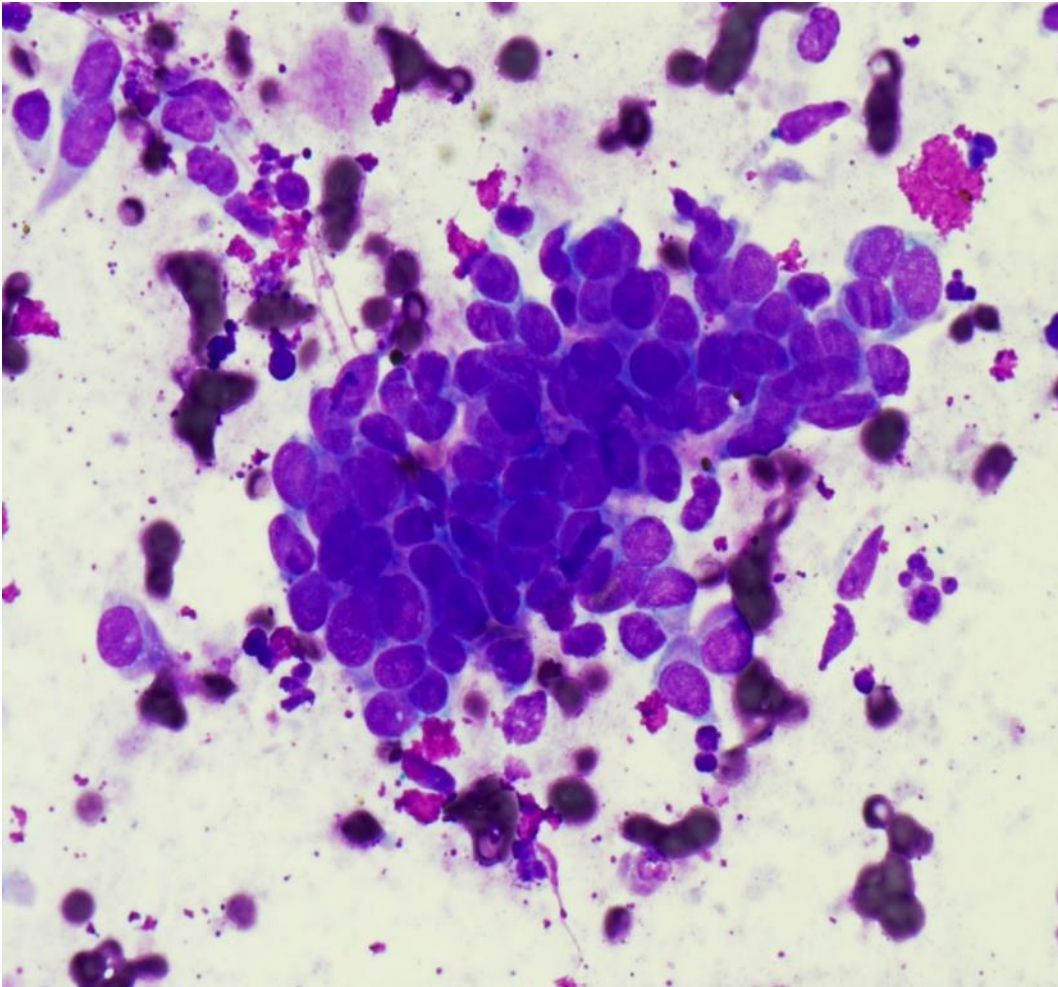
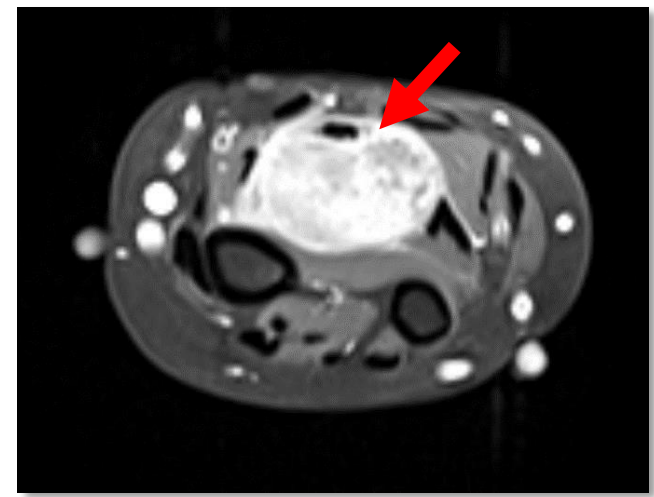
# A Different Case With Similar Morphology



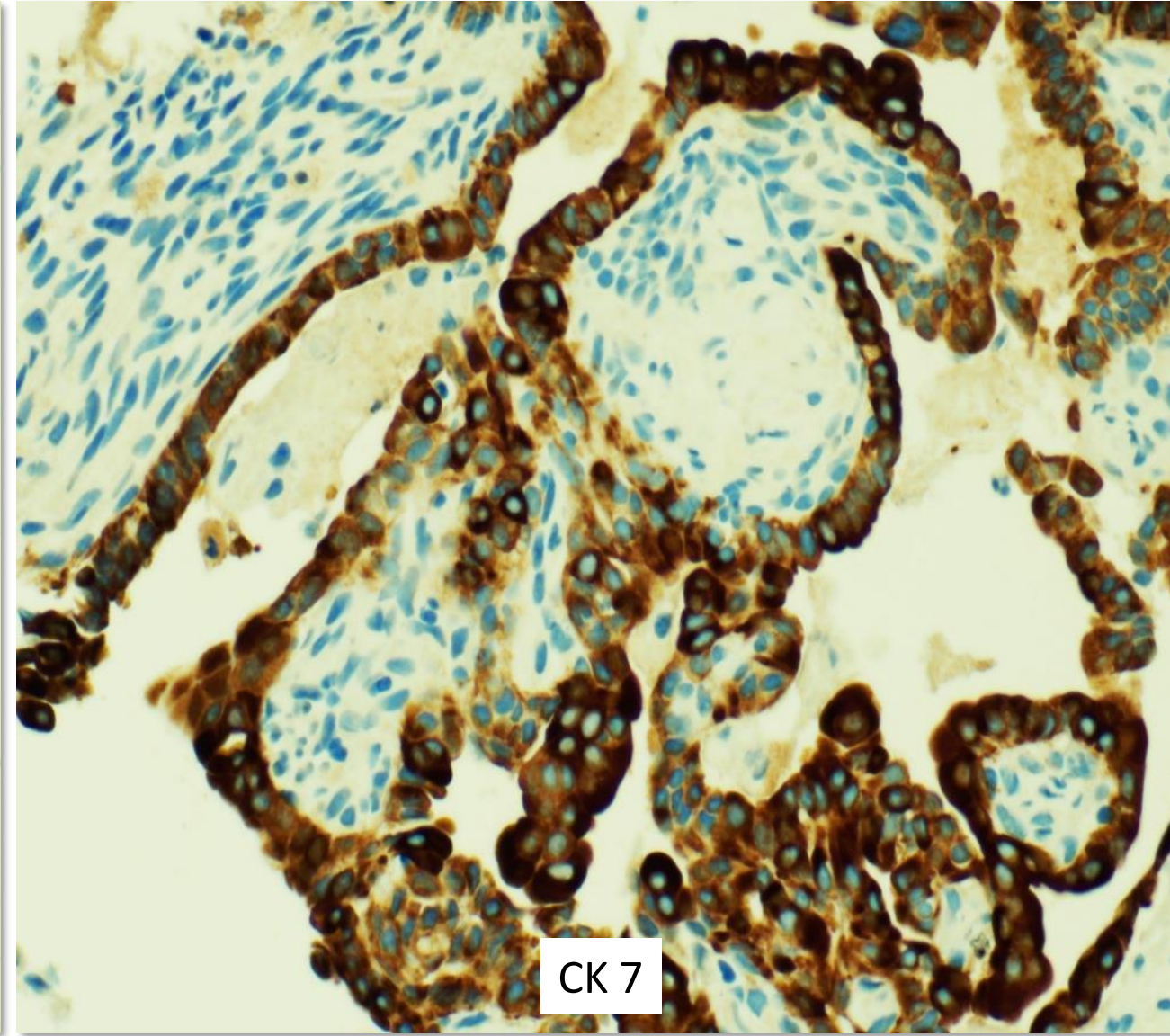
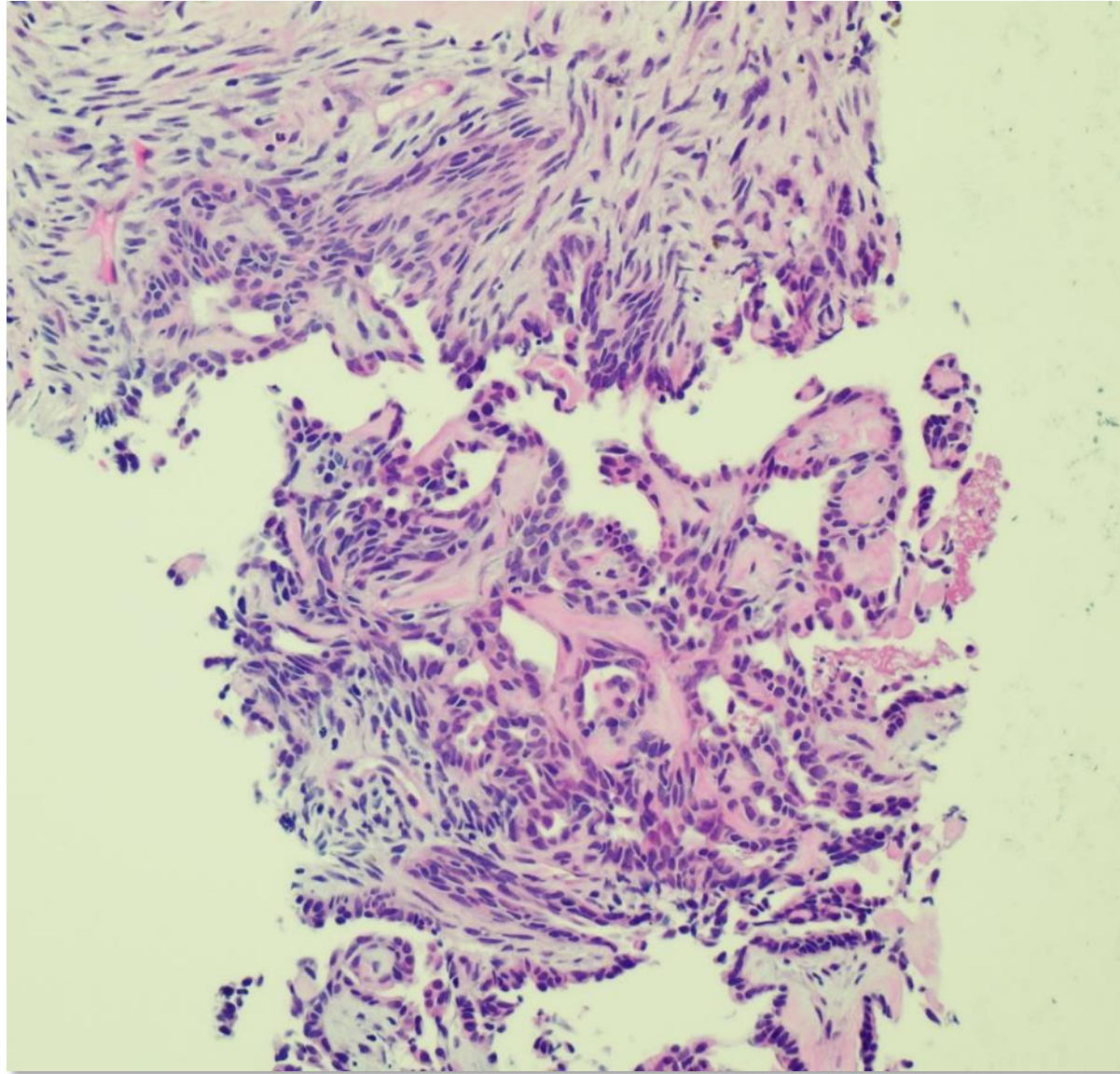
Malignant Peripheral Nerve Sheath Tumor

# A Case of Biphasic Synovial Sarcoma

- 33 year old female
- 4 cm mass in deep flexor compartment of forearm



# Biphasic Synovial Sarcoma





# Sarcomas With True Keratin Expression?

- Synovial Sarcoma
- Epithelioid sarcoma
- Desmoplastic Small Round Cell Tumor
  
- Remember any sarcoma may show nonspecific keratin expression
- Don't exclude sarcomatoid carcinoma when in/around a solid organ or lymph node

## Case # 2

### History:

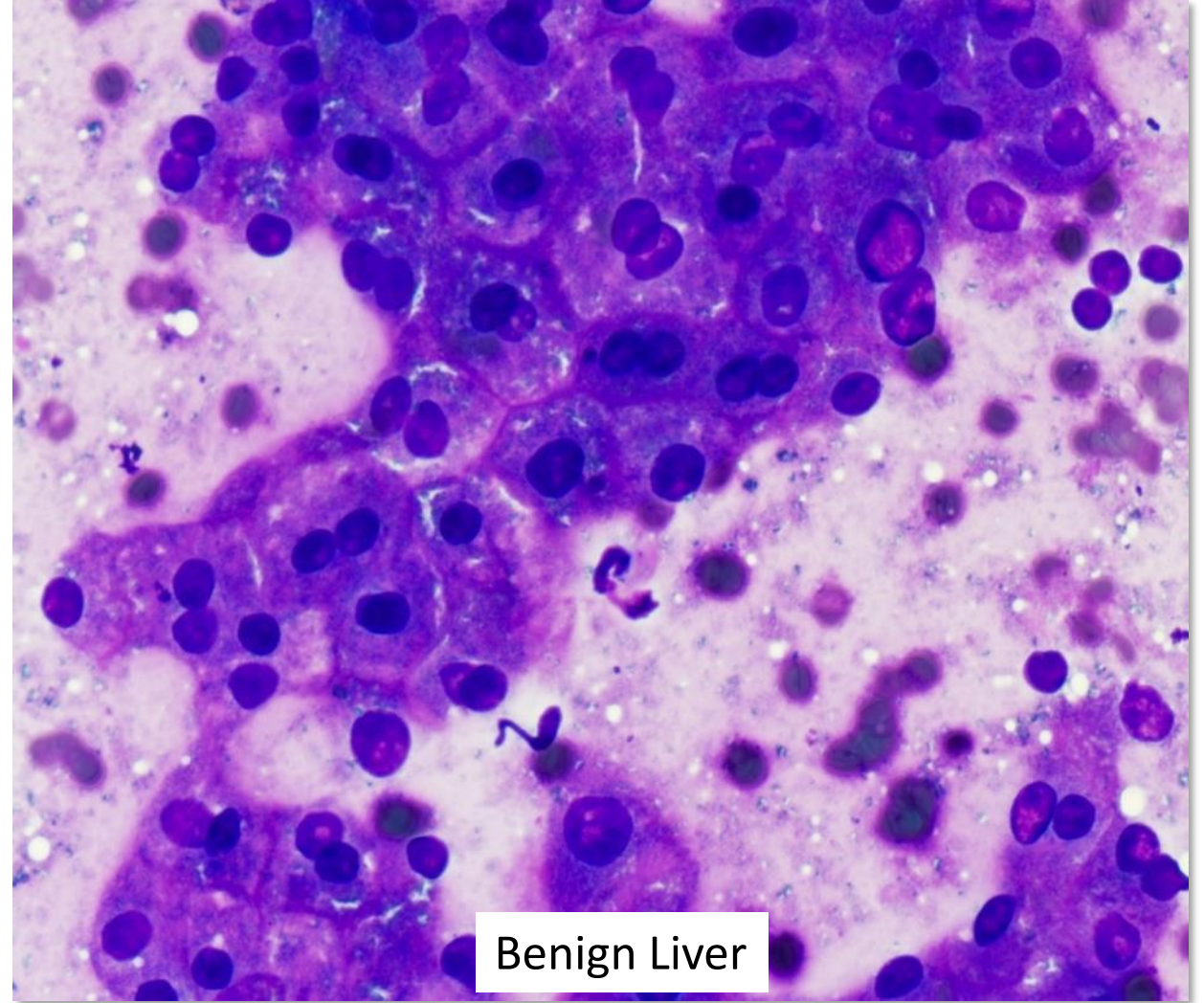
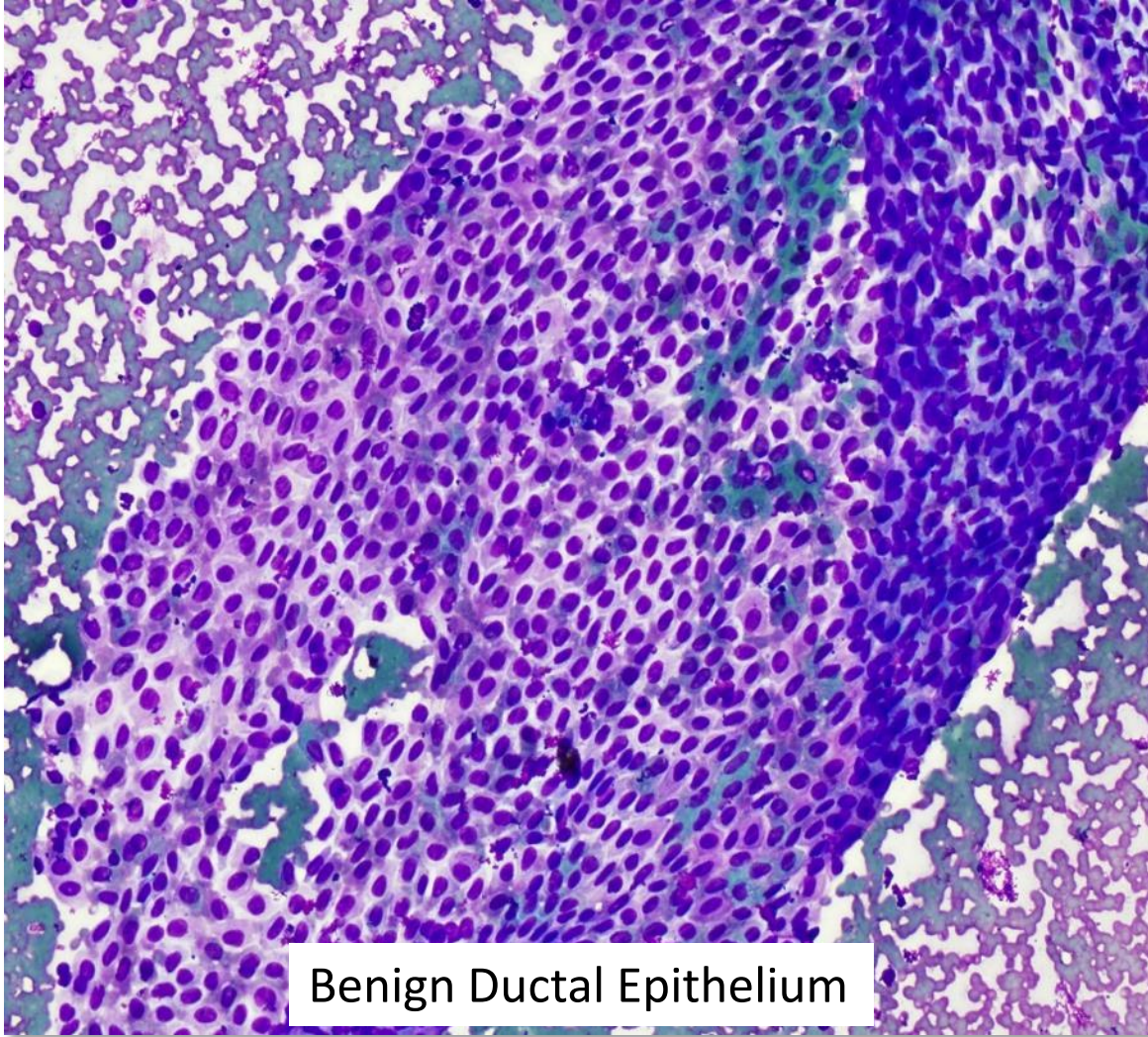
- 72 year old woman with a history of sarcoma several years prior

### Imaging:

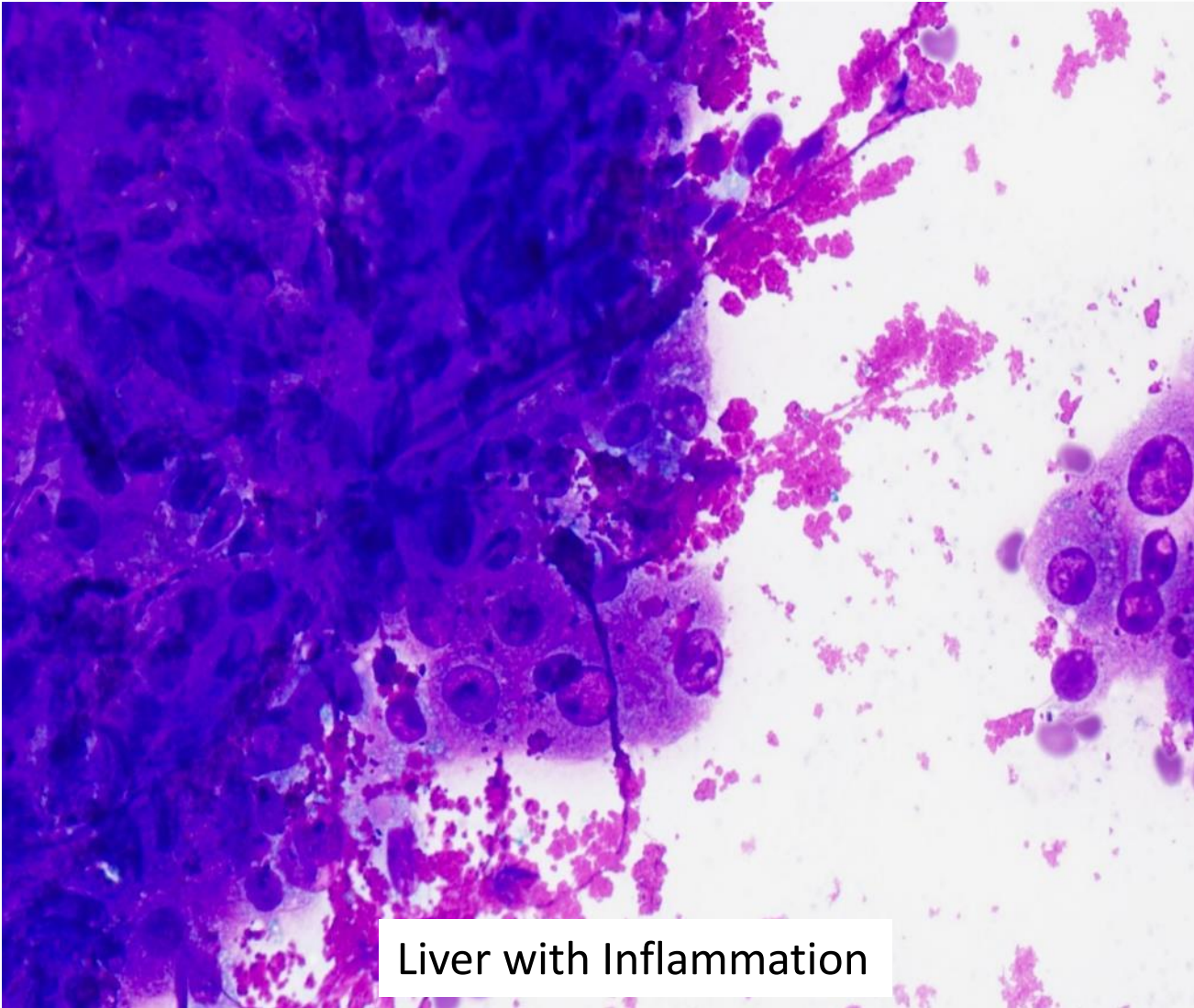
- Multiple liver masses



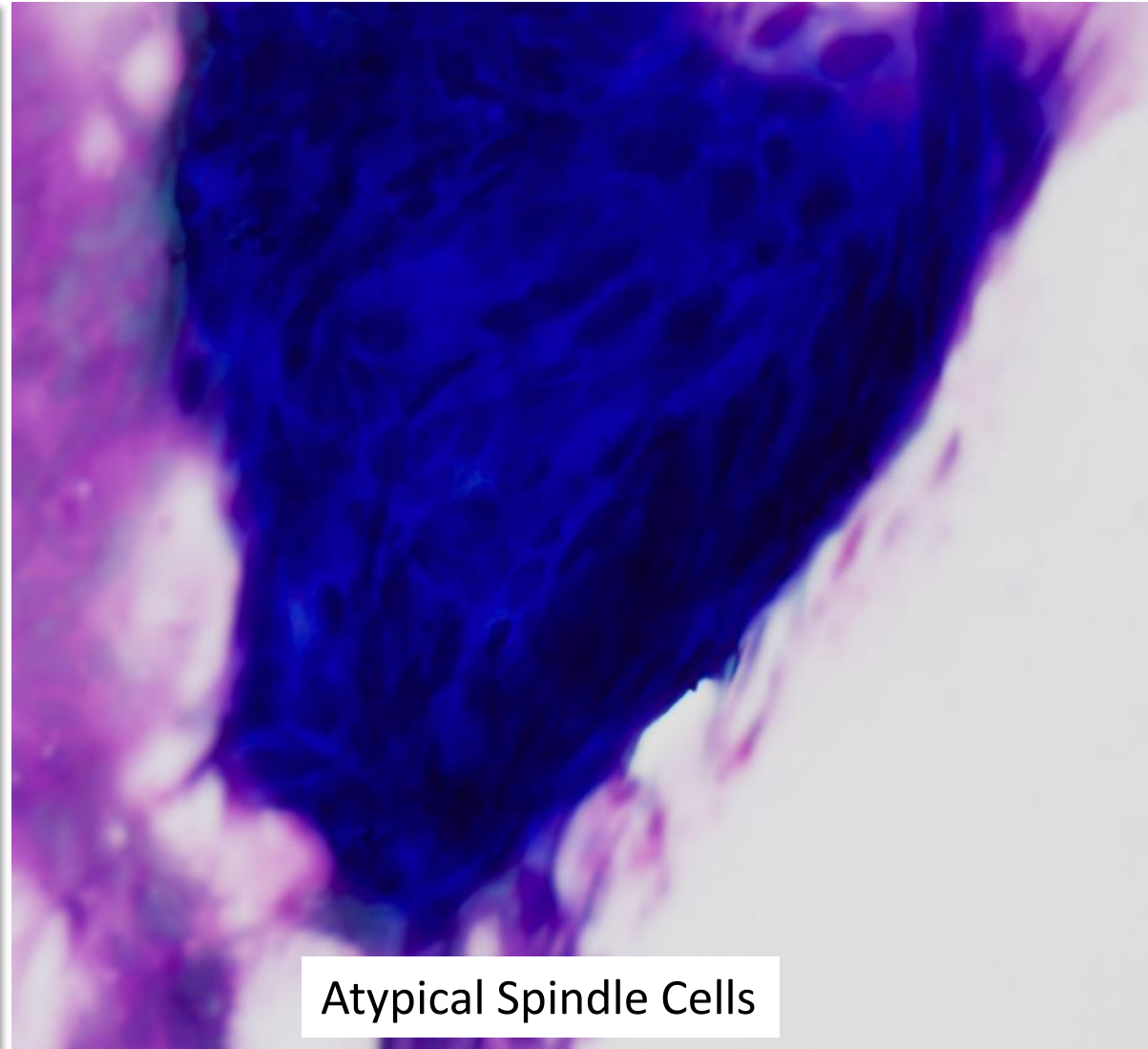
## Case # 2 Touch Preparations



# Case # 2 Touch Preparations

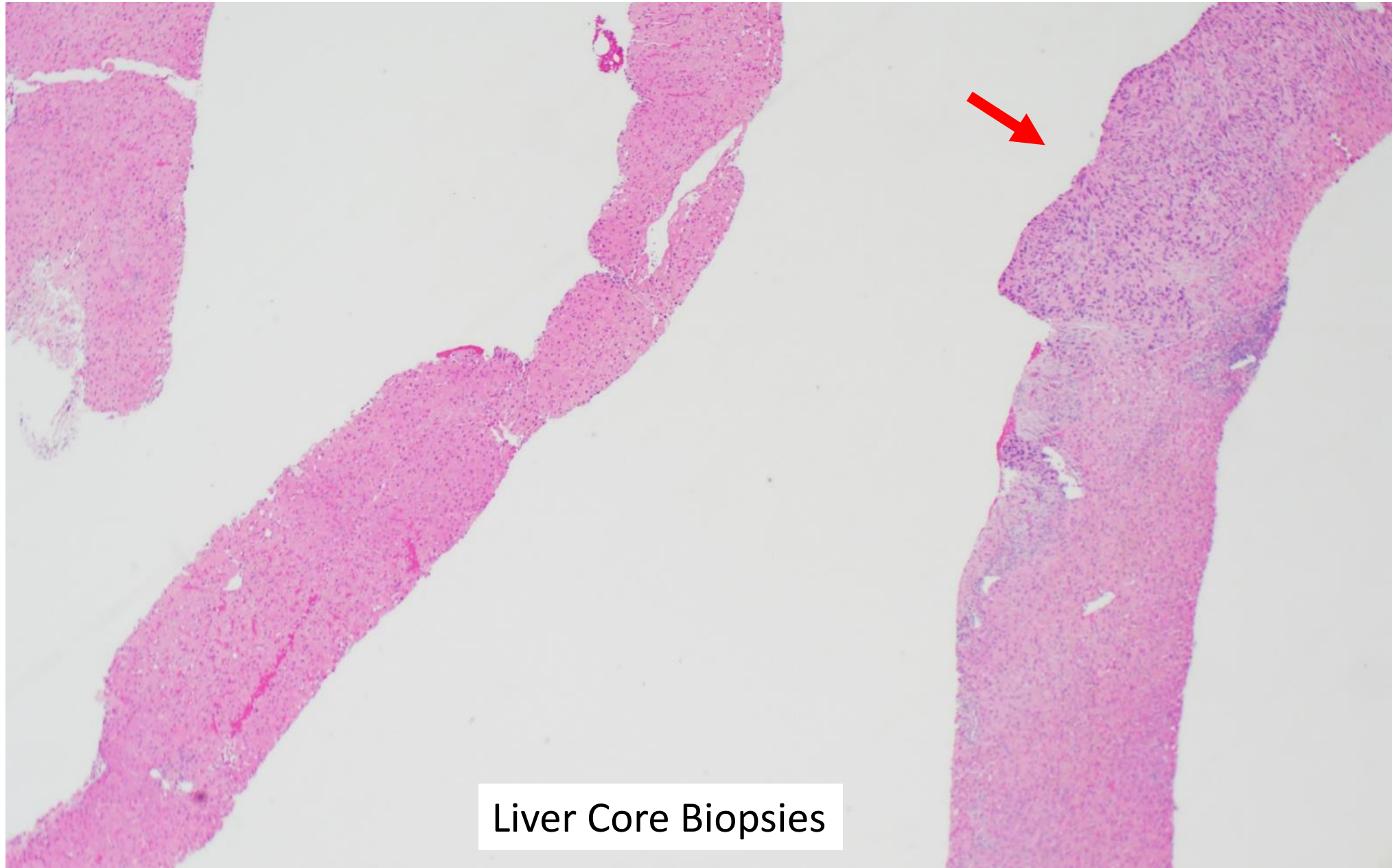


Liver with Inflammation



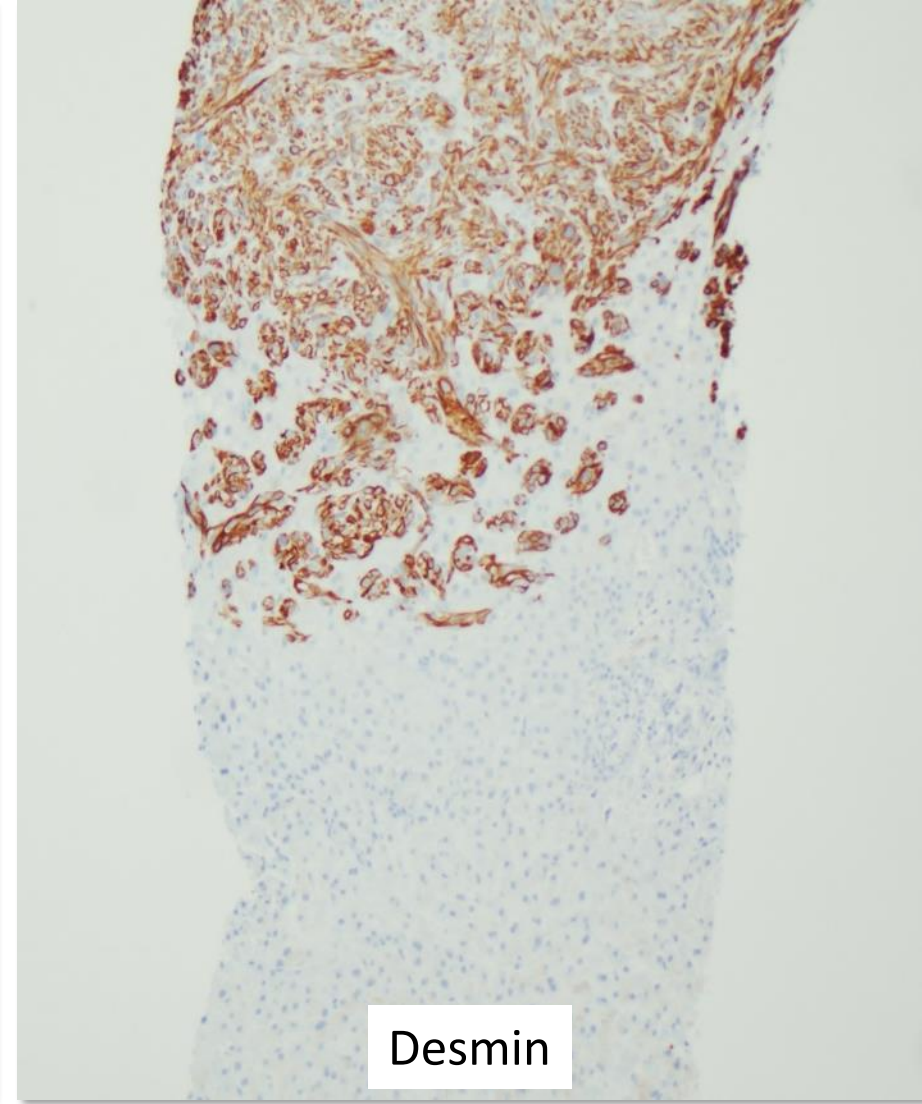
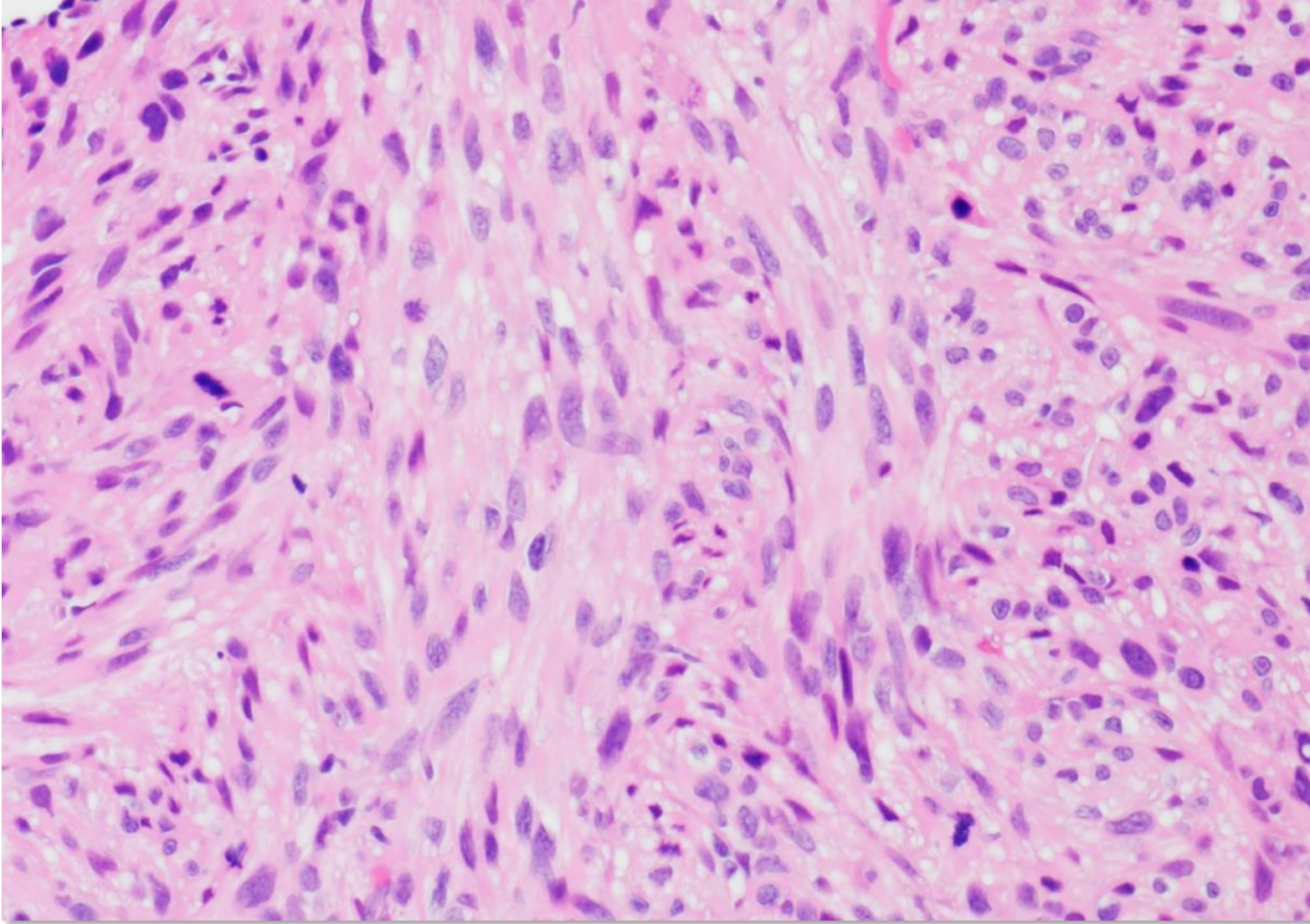
Atypical Spindle Cells

# Case # 2 Biopsies



Liver Core Biopsies

## Case # 2 Biopsies



# Case # 2 – Leiomyosarcoma

## Epidemiology/Clinical features:

- Middle age or older

## Site:

- Retroperitoneum, pelvis, extremities

## Cytology:

- Fascicles of spindle cells with blunt-ended nuclei, moderate amounts of granular cytoplasm, may be low or high grade

## Histopathology:

- Intersecting fascicles, blunt-ended nuclei, hyperchromasia, eosinophilic cytoplasm, variable pleomorphism and mitoses

## Ancillary:


- Positive for SMA, Desmin, Caldesmon
- (muscle markers are not entirely specific, at least 2 positive muscle markers is best)

## DDX:

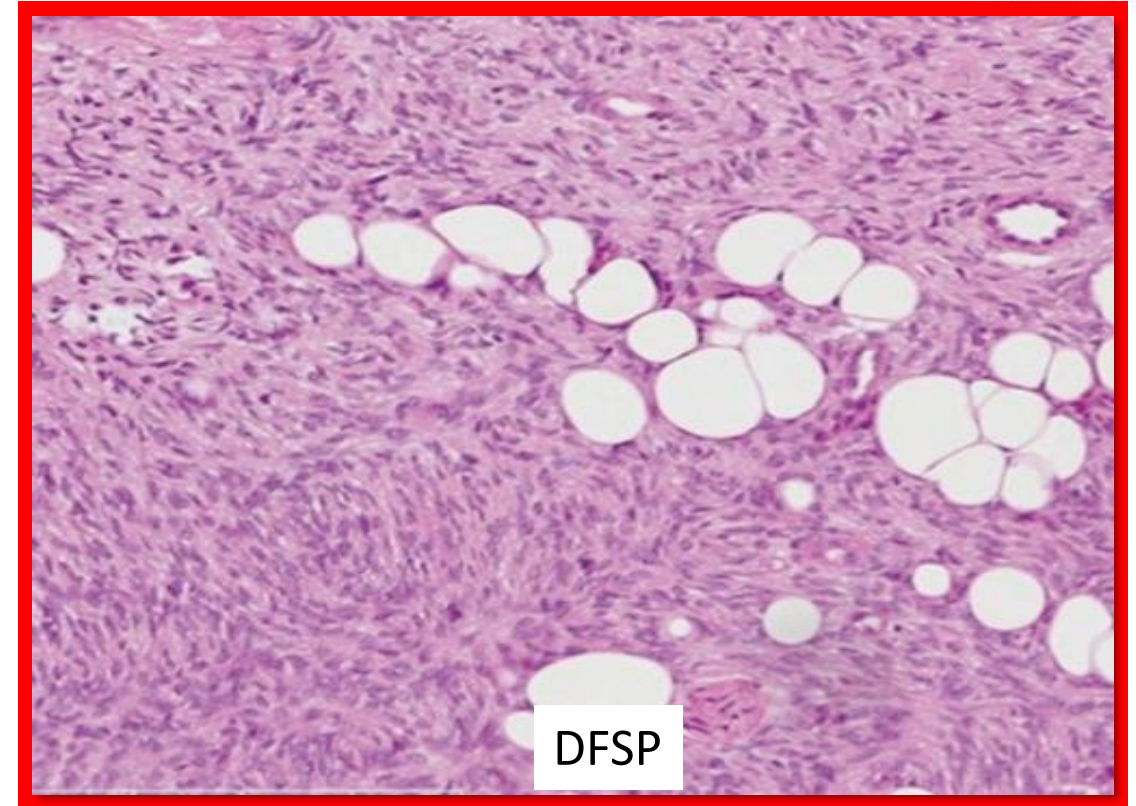
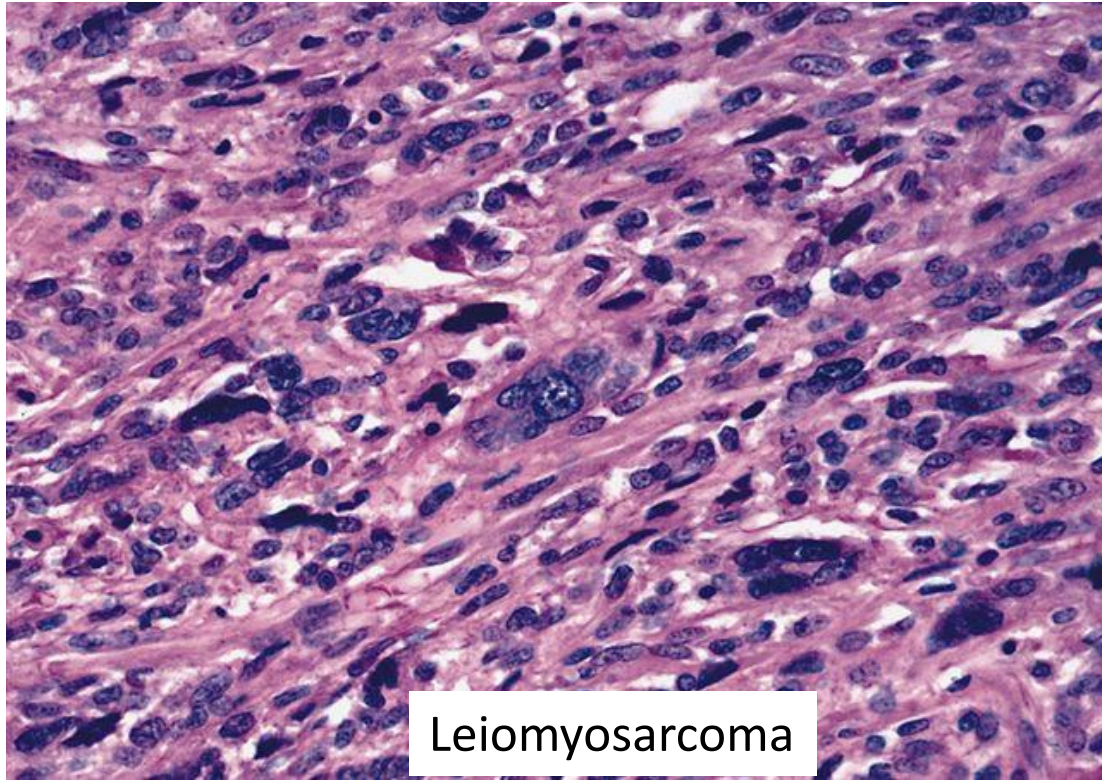
- leiomyoma, Schwannoma, MPNST, GIST, SFT, Desmoid, Unclassified spindle cell sarcoma

# Tumors of Soft Tissue

Chart compiled from WHO Bone and Soft Tissue 2013

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Spindle cell lipoma Pleomorphic lipoma	Fibromas: Fibroma of T. Sheath Superficial fibromatoses: -Palmar, Plantar, Penile Deep (desmoid) fibromatoses	Benign fibrous histiocytoma				Benign nerve sheath tumors: - Schwannoma - Neurofibroma - Perineuroma	Atypical Fibroxanthoma (AFX)	
	Solitary fibrous tumor		<div>What about a tumor with some muscle differentiation...but not quite leiomyosarcoma?</div> <div>“High grade sarcoma with myogenic differentiation”</div>				Myoepithelial tumor	
							Synovial sarcoma	
Well differentiated liposarcoma / Atypical lipomatous tumor	Dermatofibrosarcoma protuberans (DFSP)			Epithelioid Sarcoma		Alveolar Soft Part Sarcoma		
Myxoid liposarcoma	Inflammatory myofibroblastic tumor (IMT)			endothelioma		Clear cell sarcoma		
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Pleomorphic liposarcoma	Myxofibrosarcoma	<i>Malignant Fibrous Histiocytoma</i>	Leiomyosarcoma	Spindle Cell/Sclerosing RMS	Pleomorphic RMS	Angiosarcoma	Malignant Peripheral Nerve Sheath Tumor (MPNST)	Desmoplastic Small Round Cell Tumors (DSRCT)

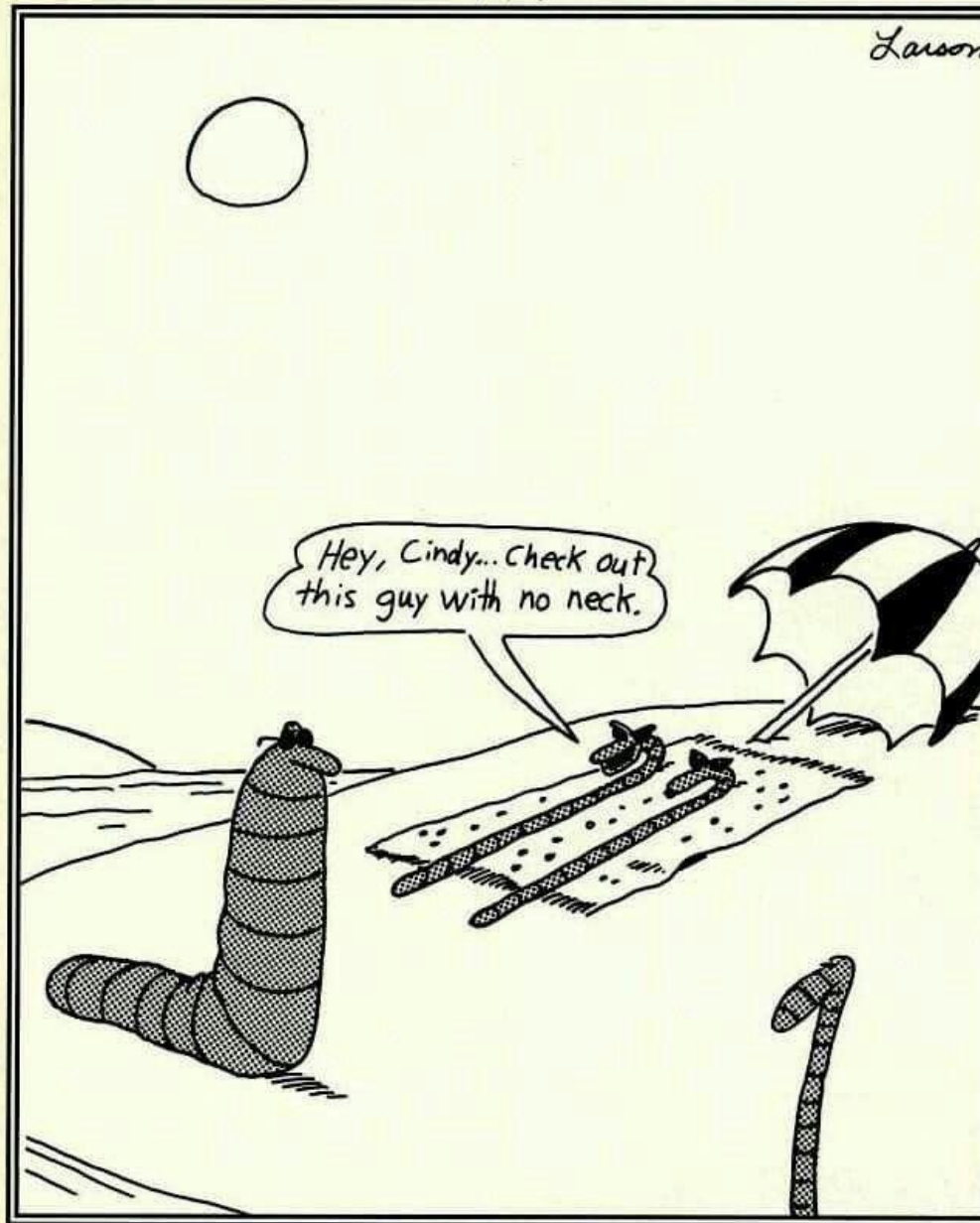
# Which Lesion is Translocation associated?



Translocation associated tumors tend to have a very monomorphic appearance

6/6/87

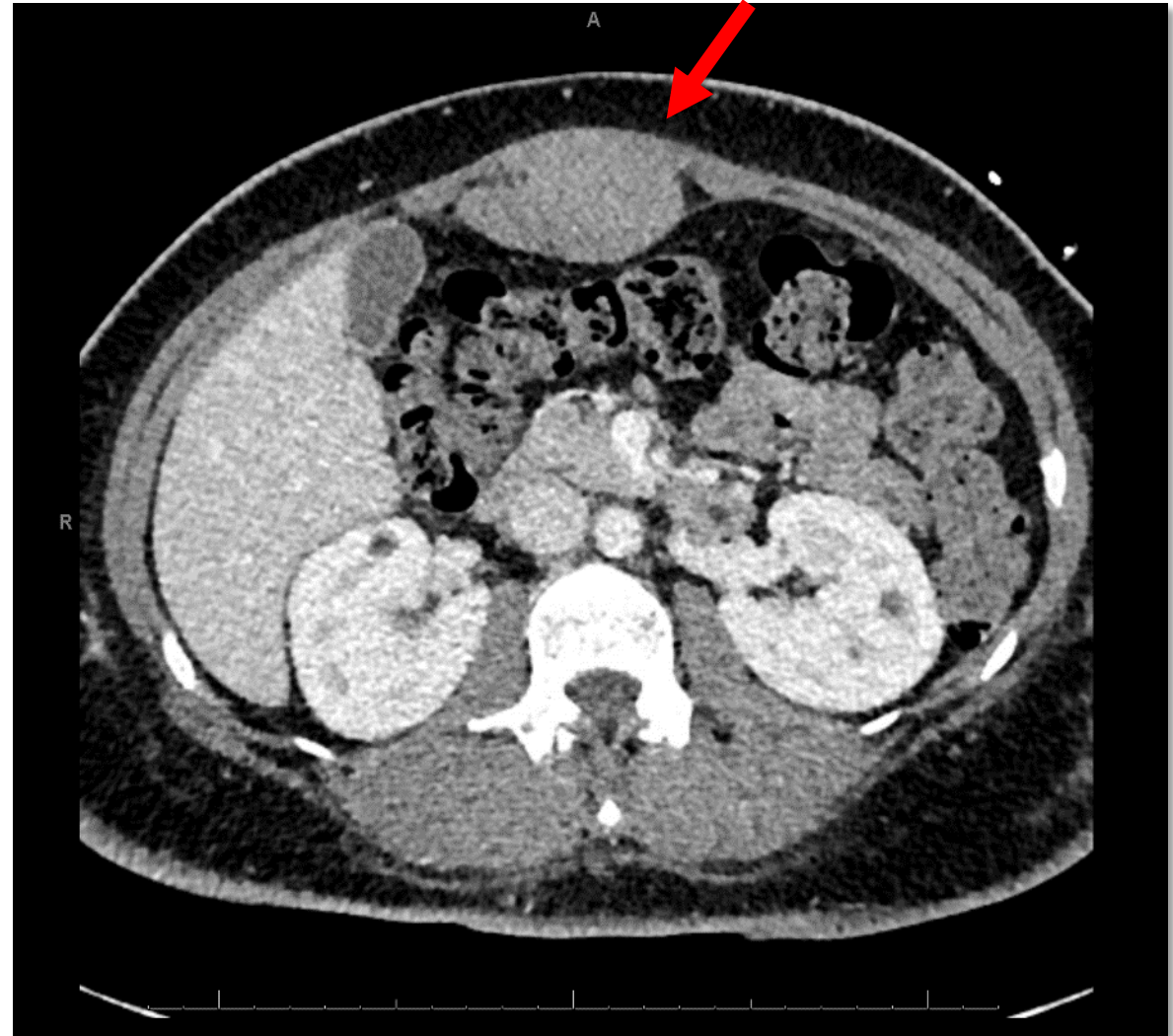
Larson



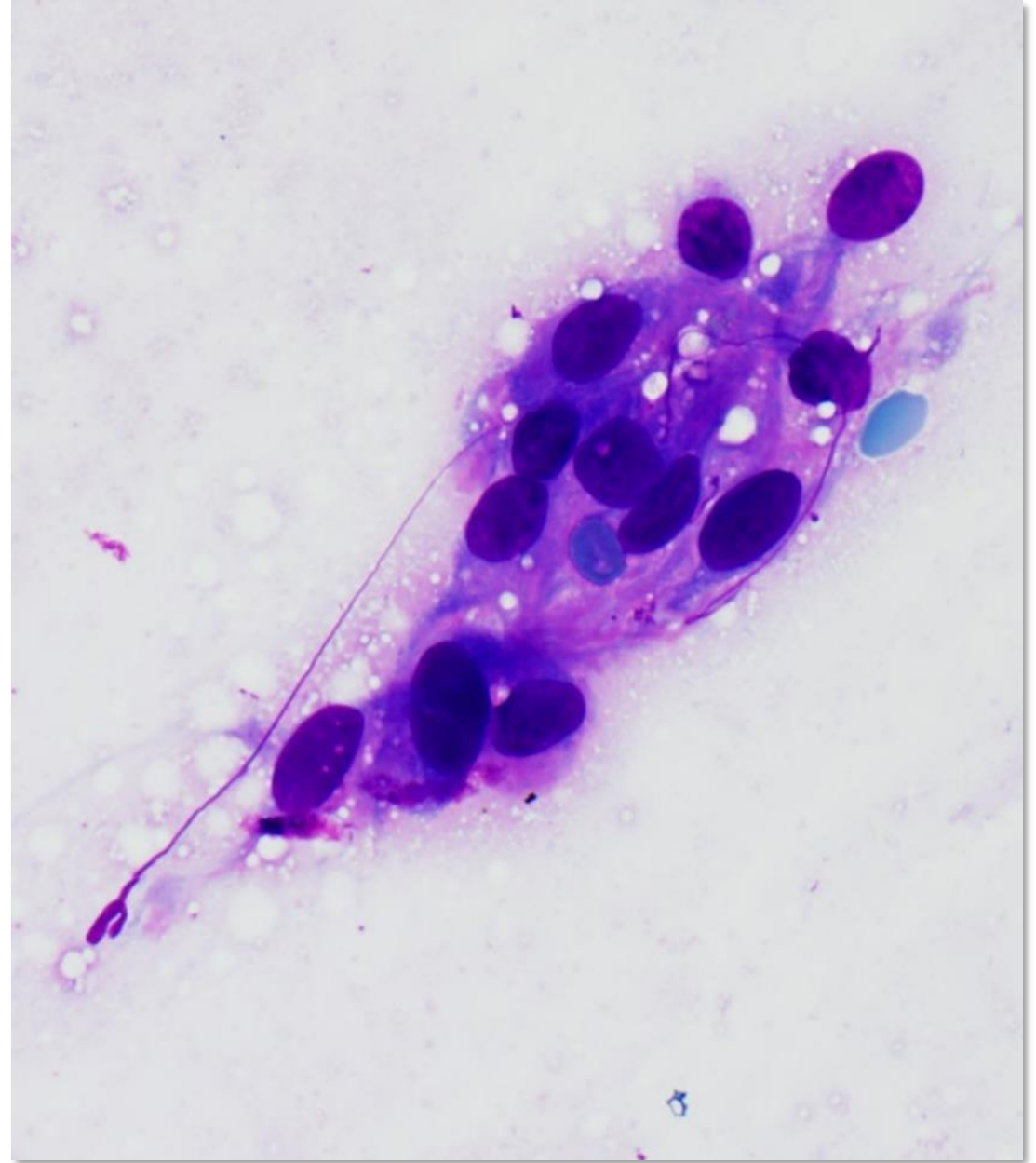
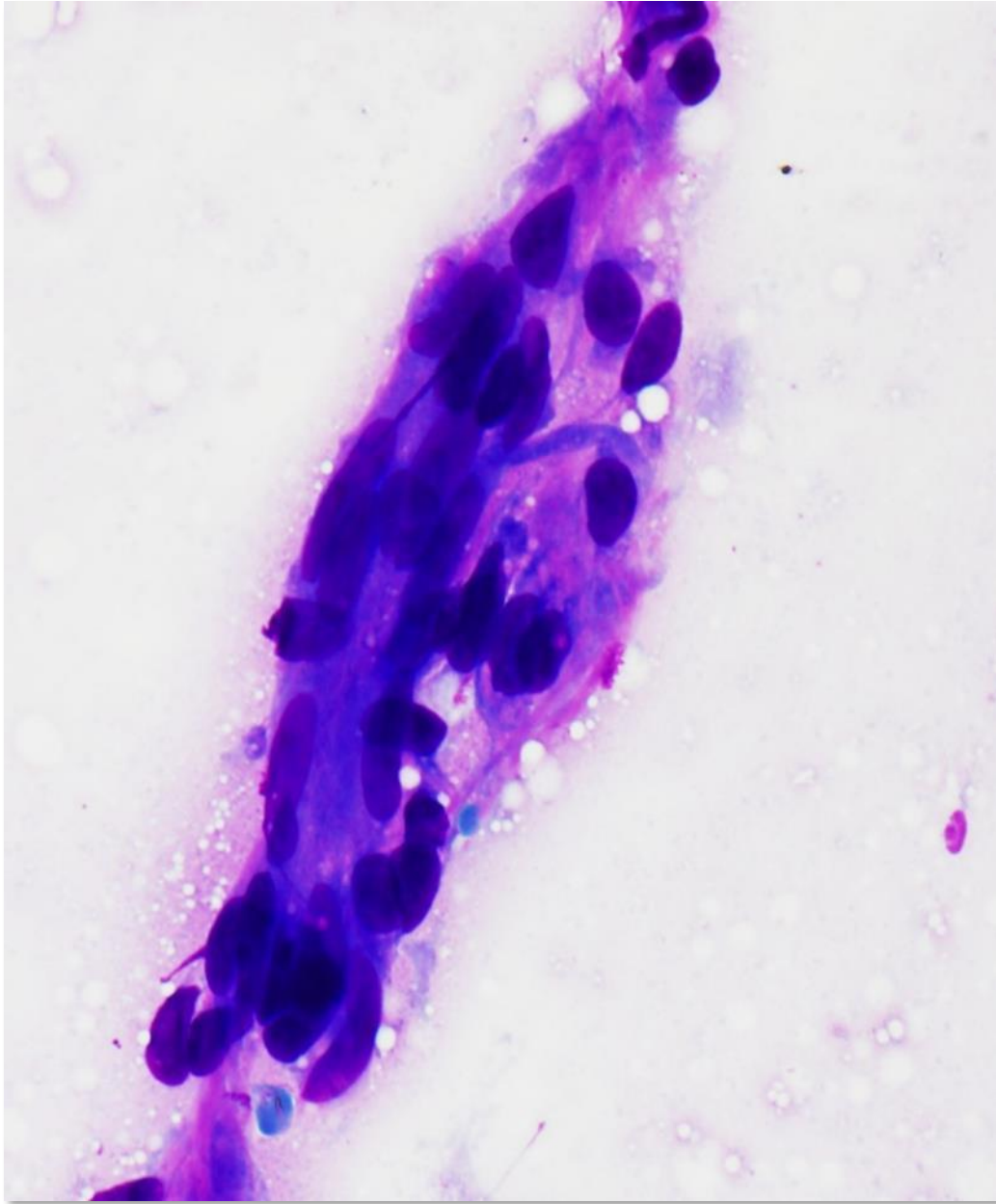
At the worm beach

## Case # 3

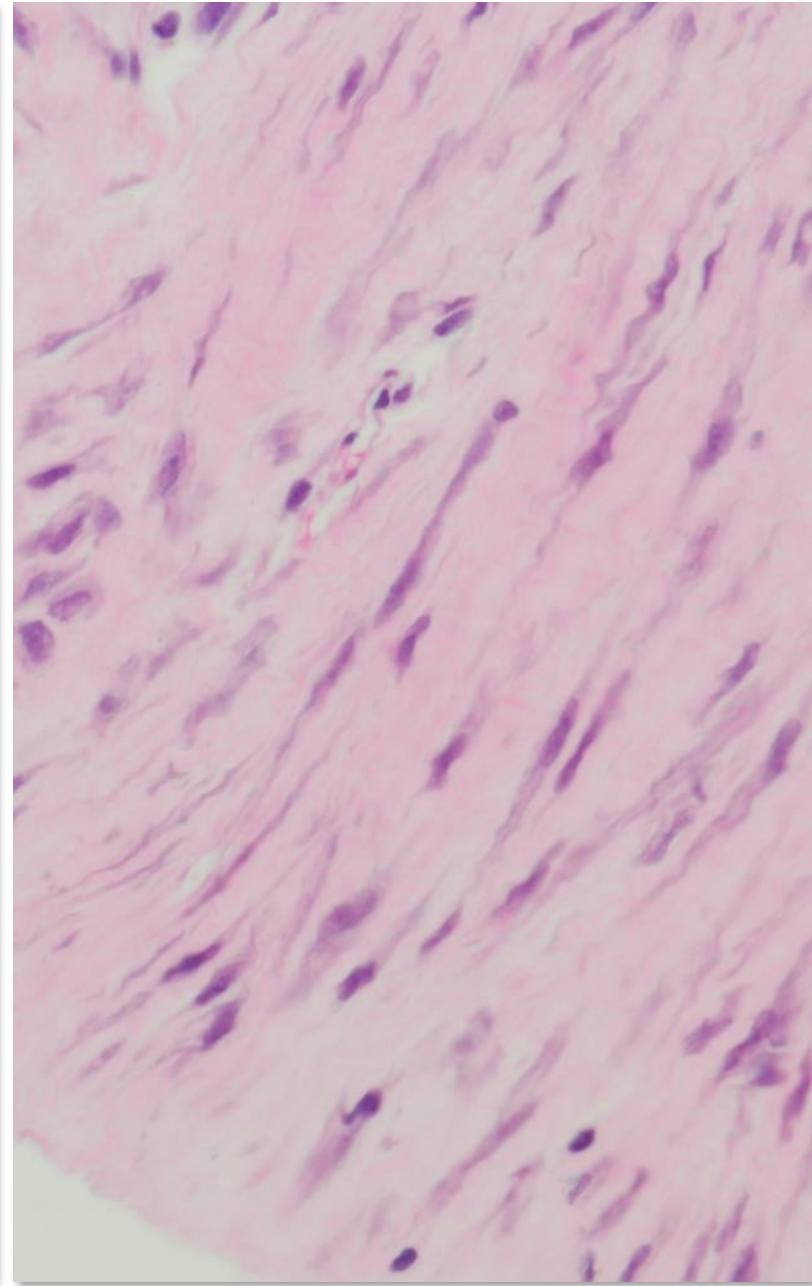
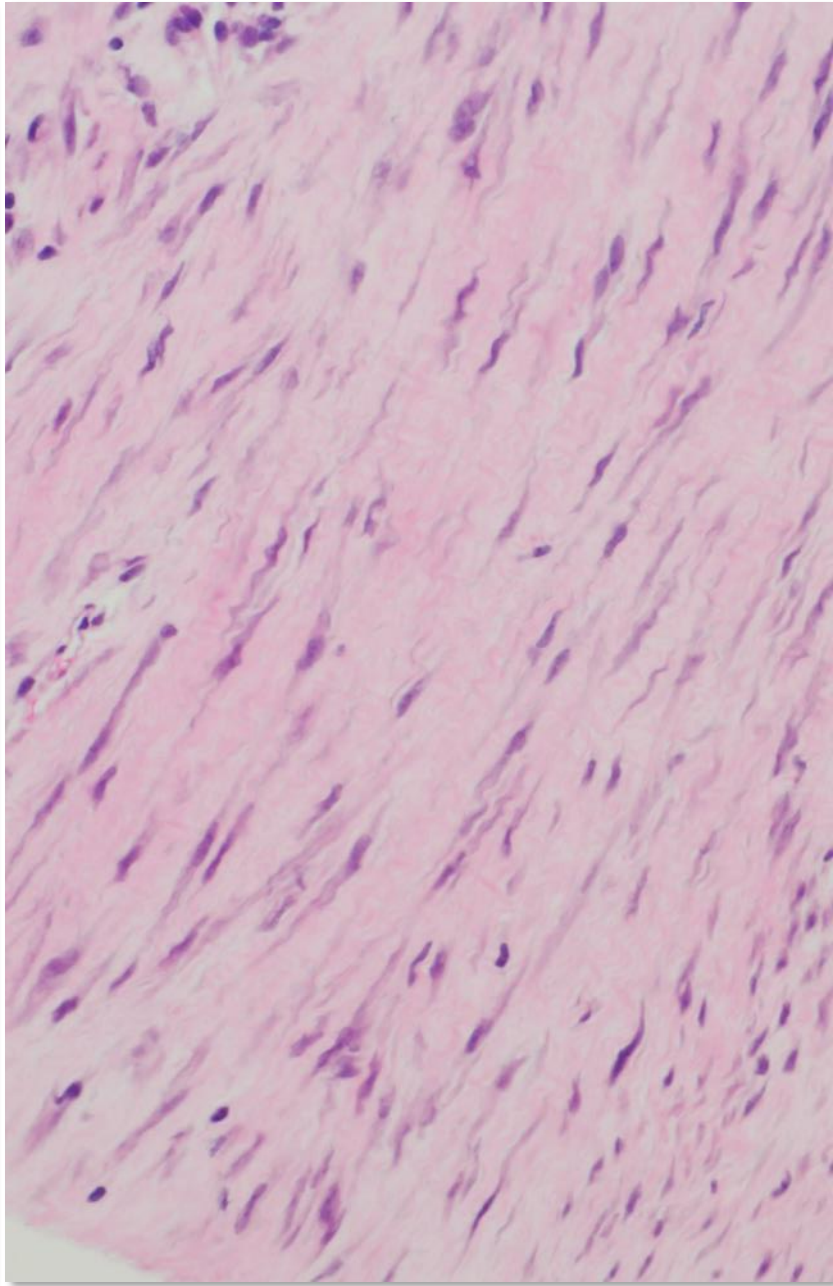
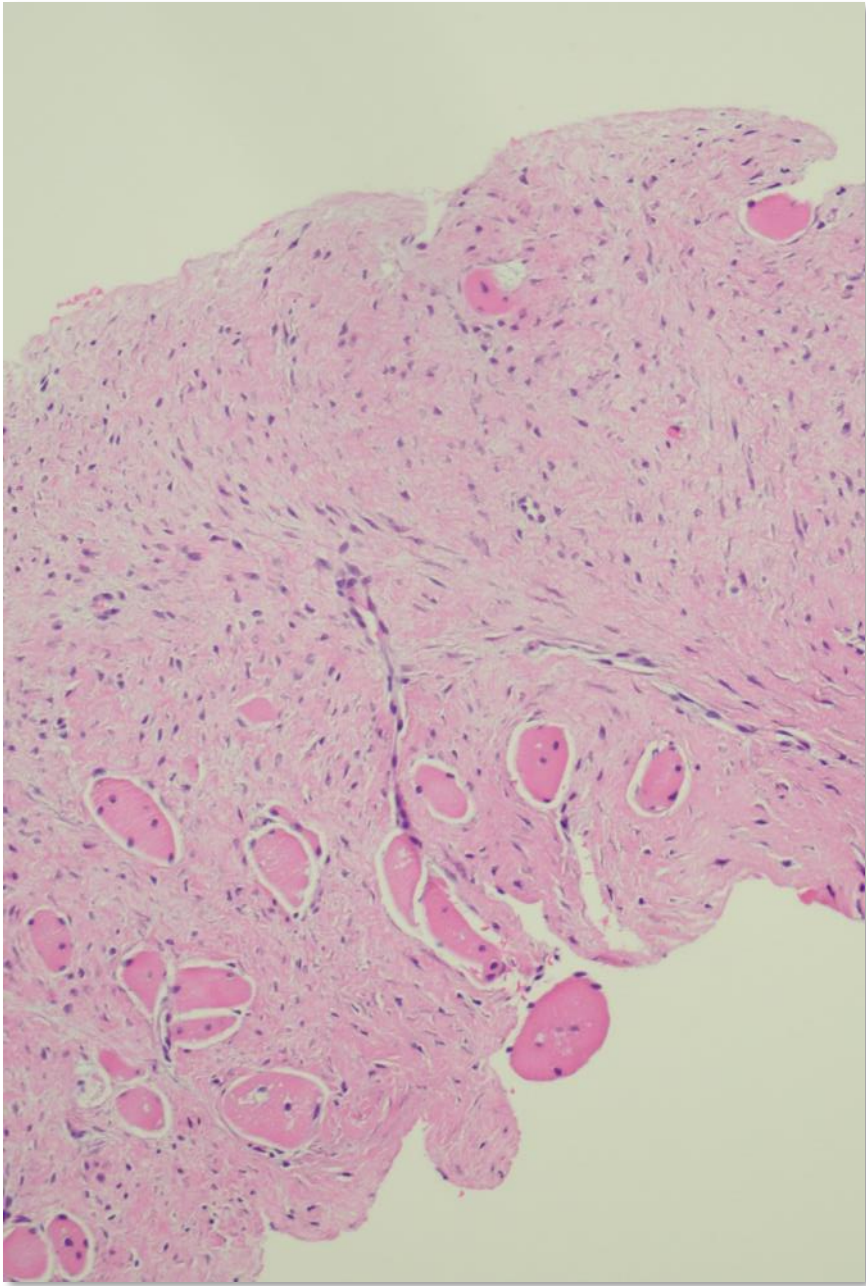
- History: 40 year old woman, recently pregnant mother of 5 children
- Imaging: well circumscribed 4 cm mass in midline anterior rectus abdominis muscle



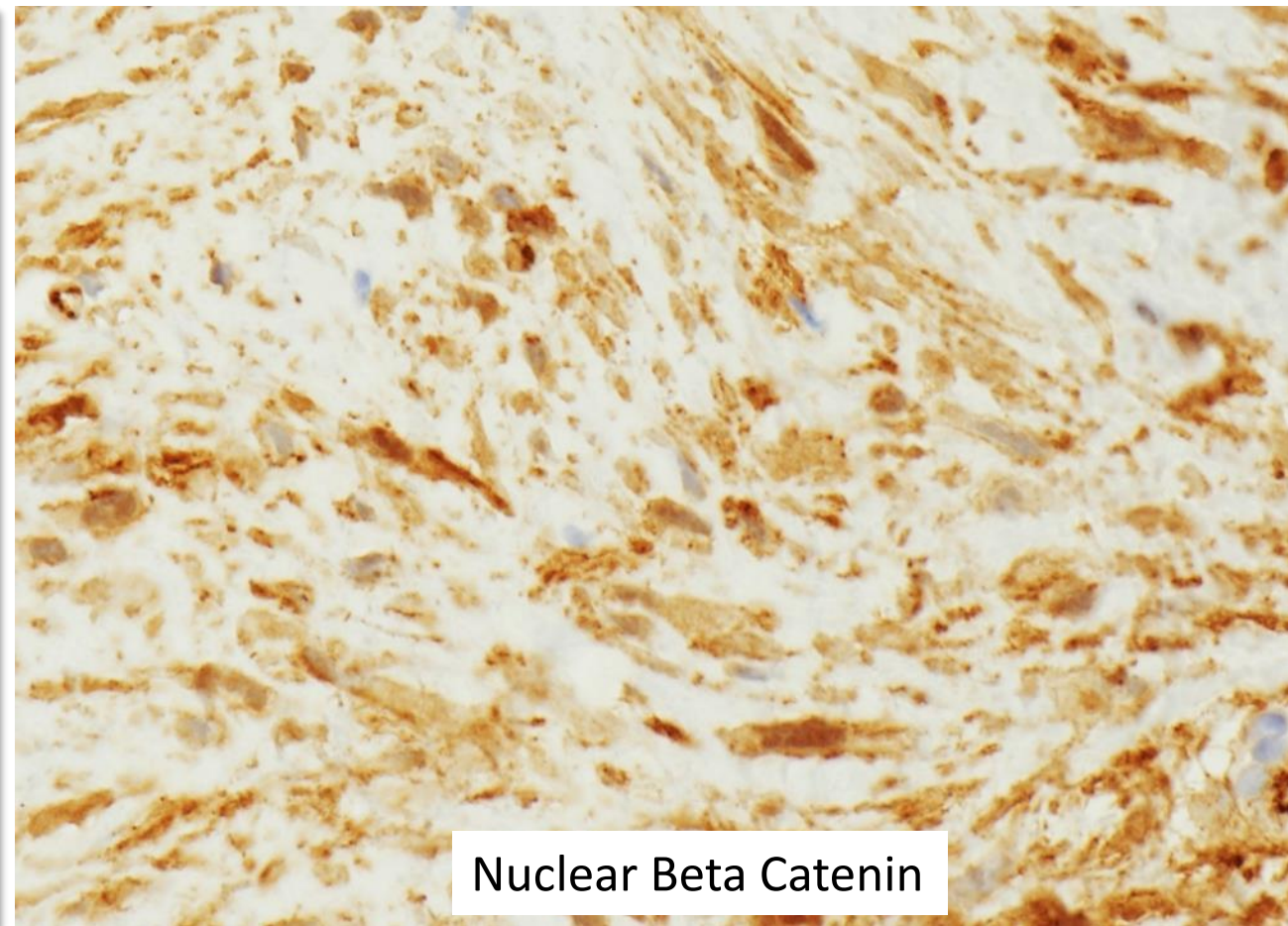
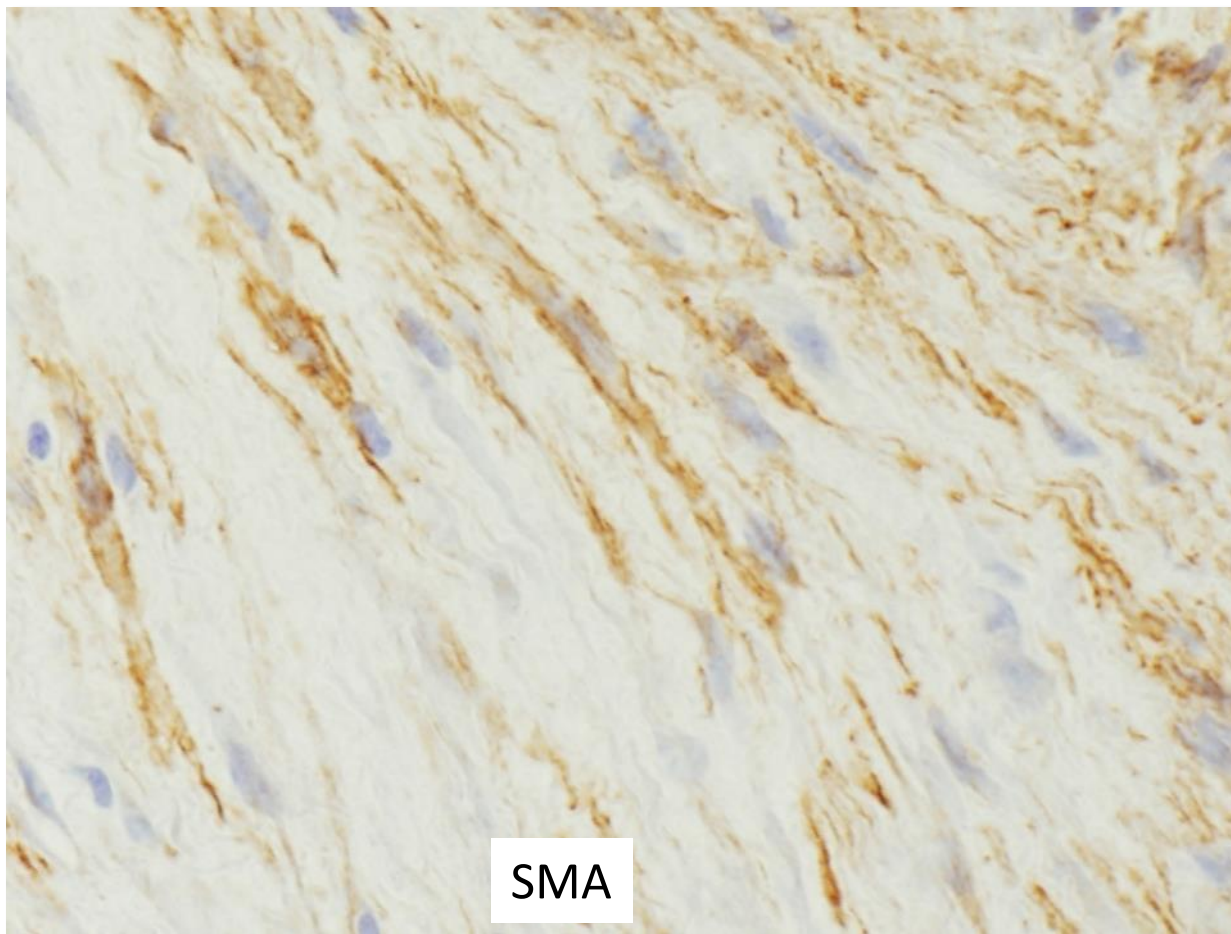
# Case # 3 Touch Preparations



# Case # 3 Biopsies



# Case # 3



# Case # 3 Desmoid-Type Fibromatosis

## Epidemiology/Clinical features:

- Any age; most common in females of child bearing age

## Site:

- Abdominal, extra-abdominal (any site; shoulder, chest wall, H&N, back are common)
- Associated with the fascial coverings of muscles

## Cytology:

- Low cellularity (>50% of the time FNA/touch preps show no cells)
- Long fascicular clusters and isolated bland spindle-shaped fibroblasts, scattered degenerated skeletal muscle

## Histopathology:

- Broad fascicles of bland, evenly spaced, slender spindle cells, with pale nuclei and small micronuclei, collagenous background, infiltrate adjacent skeletal muscle

## Ancillary:

- Nuclear (abnormal) Beta catenin (>75% of cases)
- Weak SMA positivity

## DDX:

- Nodular fasciitis, Low-grade fibromyxoid sarcoma, Scar tissue, Nerve sheath tumor, Smooth muscle tumor, Solitary fibrous tumor, GIST

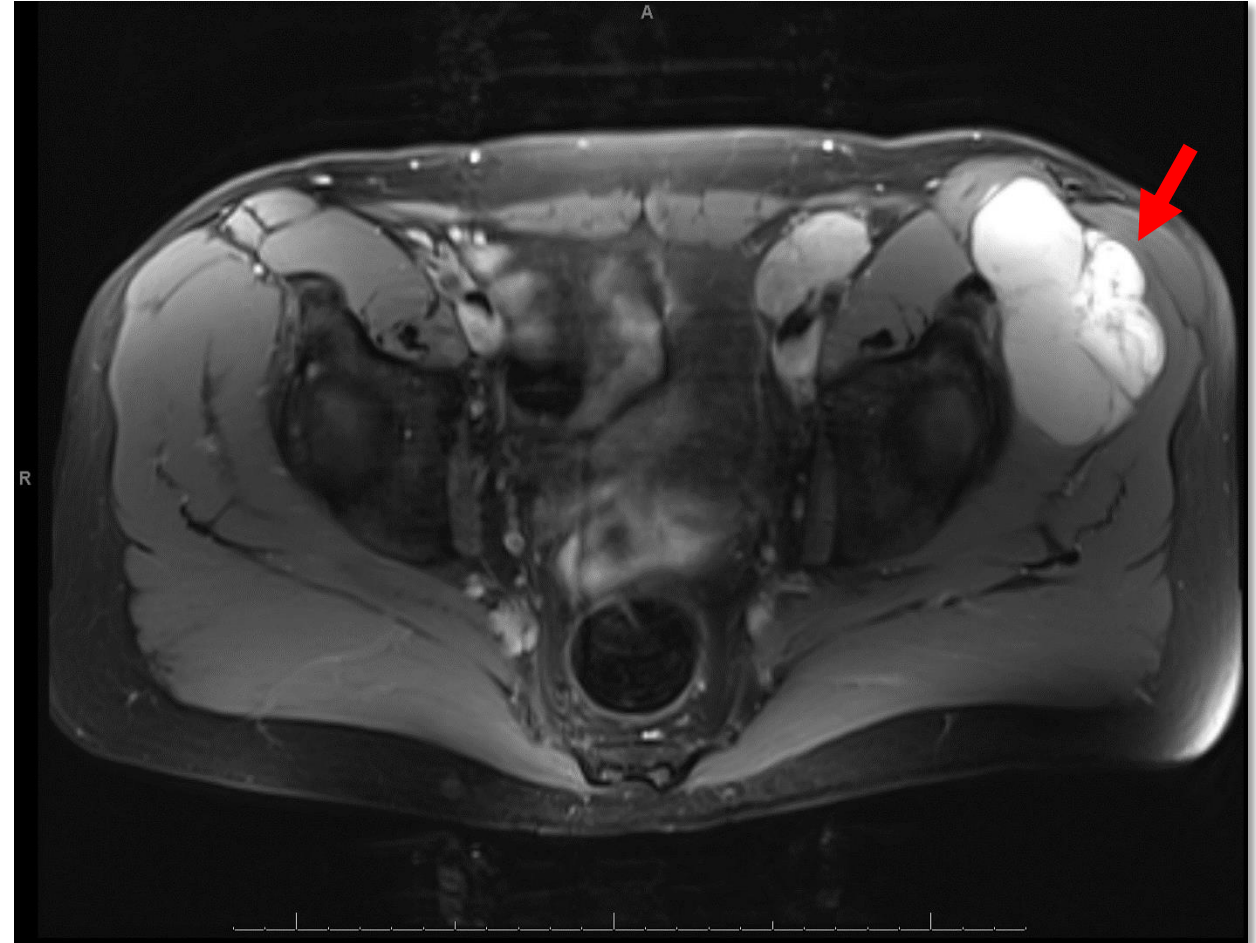
## Case # 4

### History:

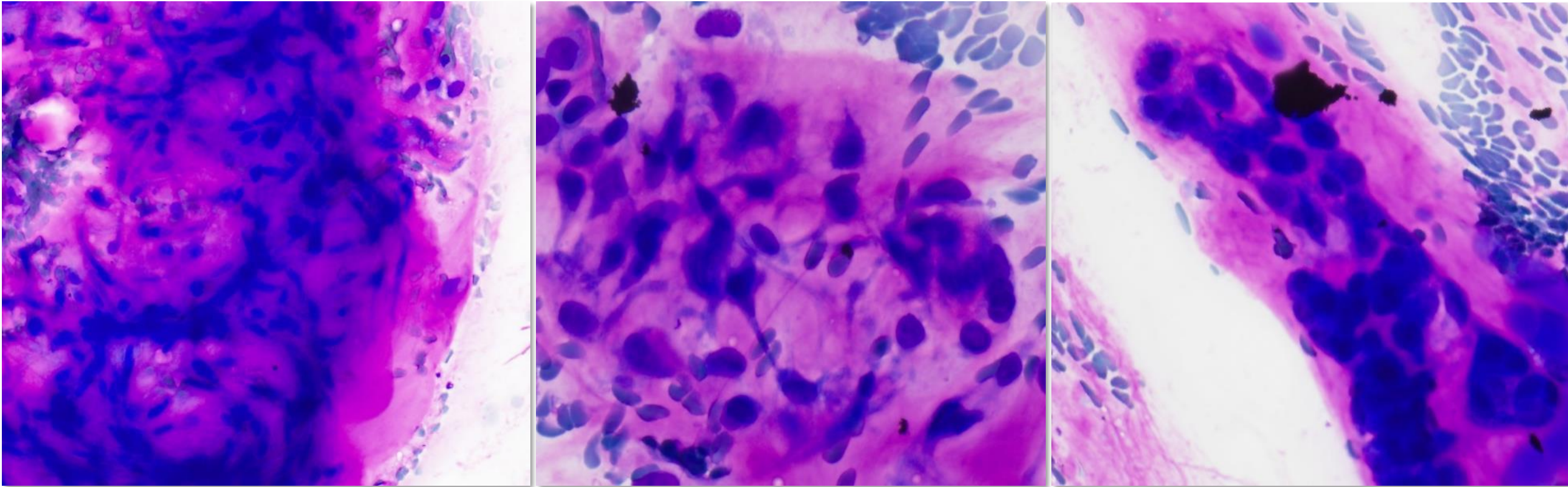
- 53 year old man; slowly growing left hip mass

### Imaging:

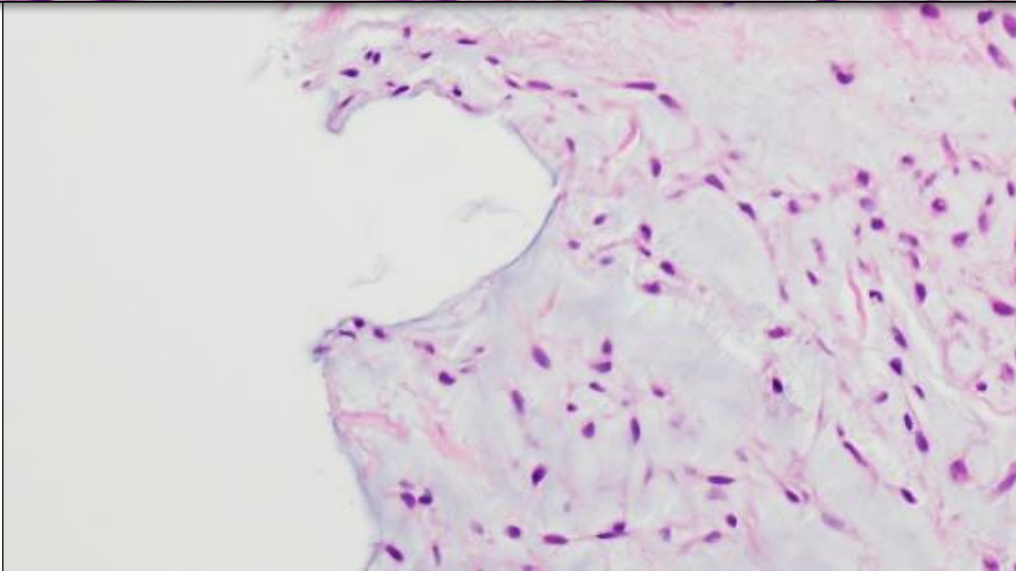
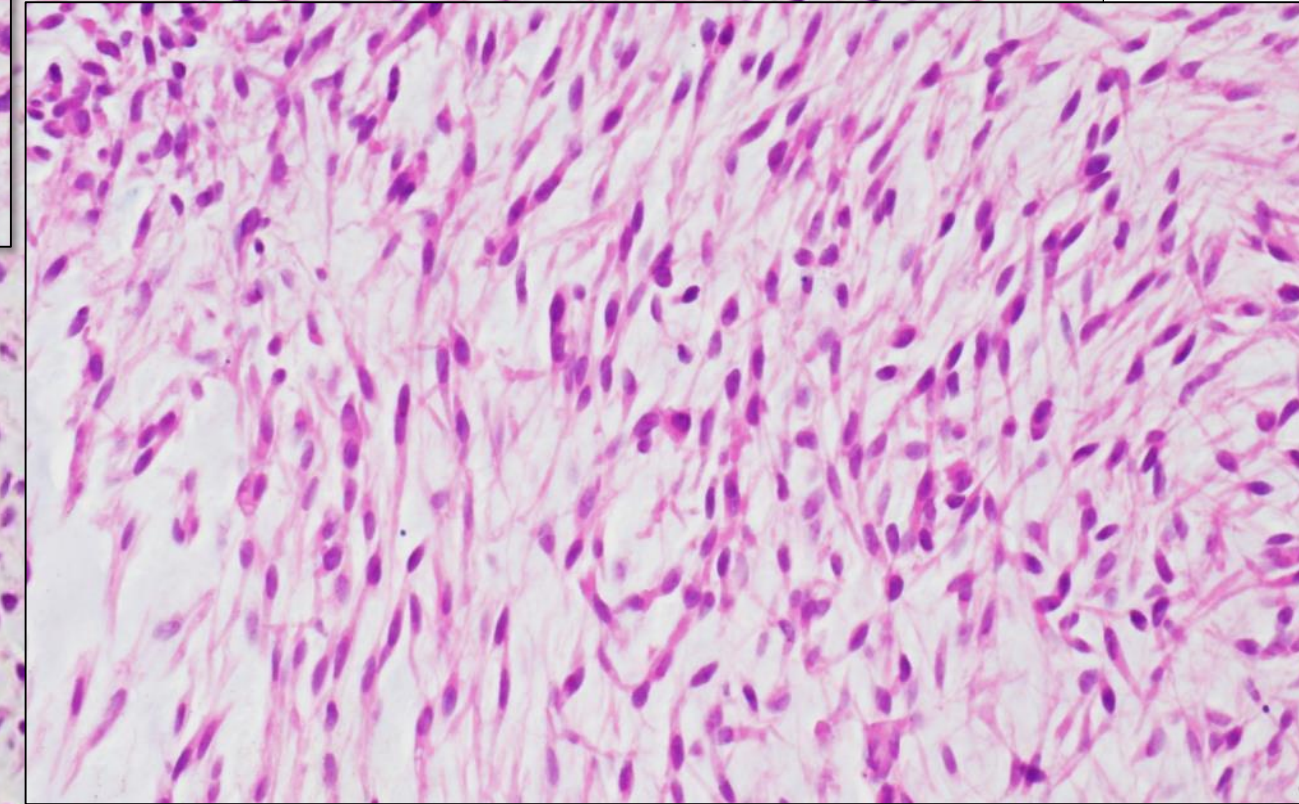
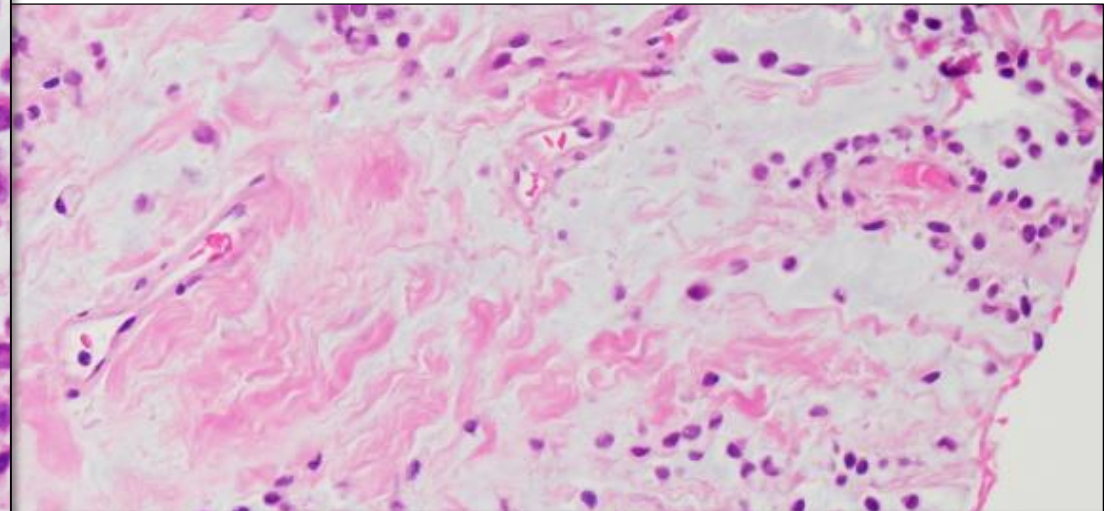
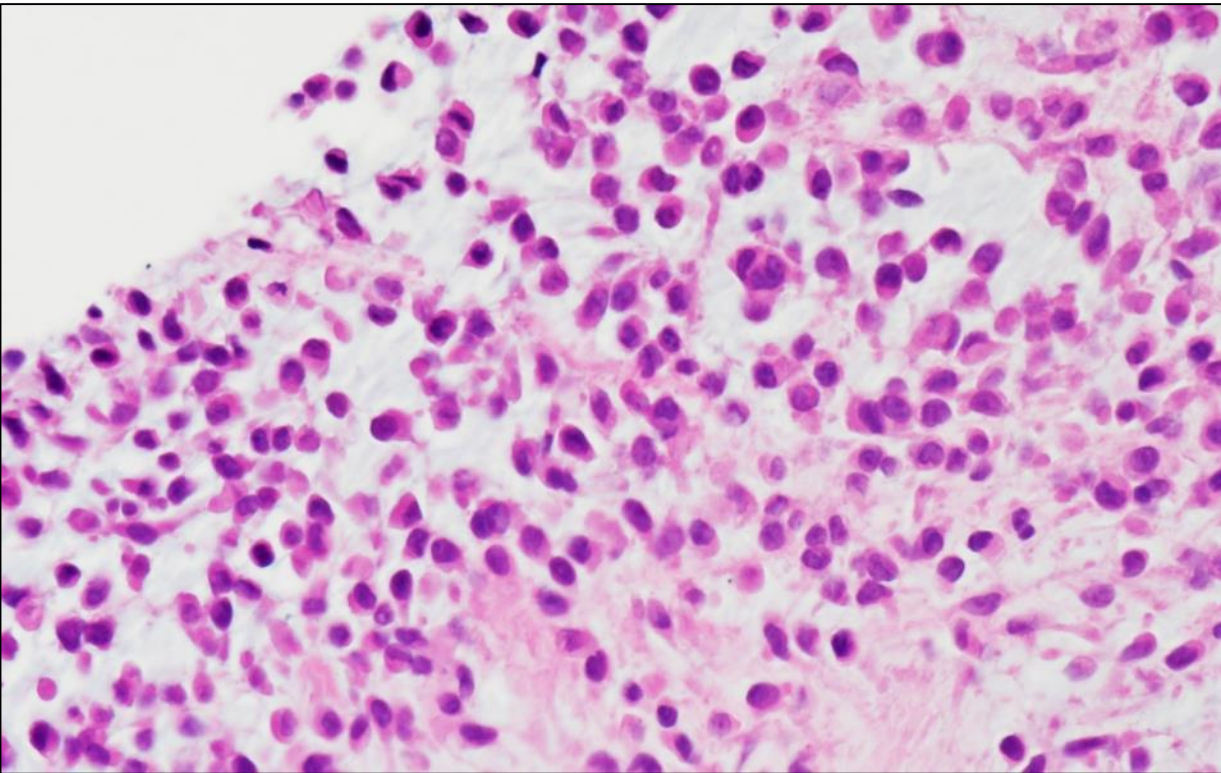
- 9.0 cm L hip mass in the gluteal muscles and abutting the anterior inferior iliac spine; no bone involvement; heterogeneous



# Case # 4 Touch Preparations



# Case # 4 Biopsies



# Case # 4– Extraskeletal Myxoid Chondrosarcoma (EMC)

## Epidemiology/Clinical features:

- Uncommon (<3% of sarcomas)
- Slowly growing, median age 50

## Site:

- Deep soft tissue of proximal extremities

## Cytology:

- Consistently shows bright magenta fibrillary stroma, uniform, bland spindled and or rhabdoid cells in cords or lace-like arrangement

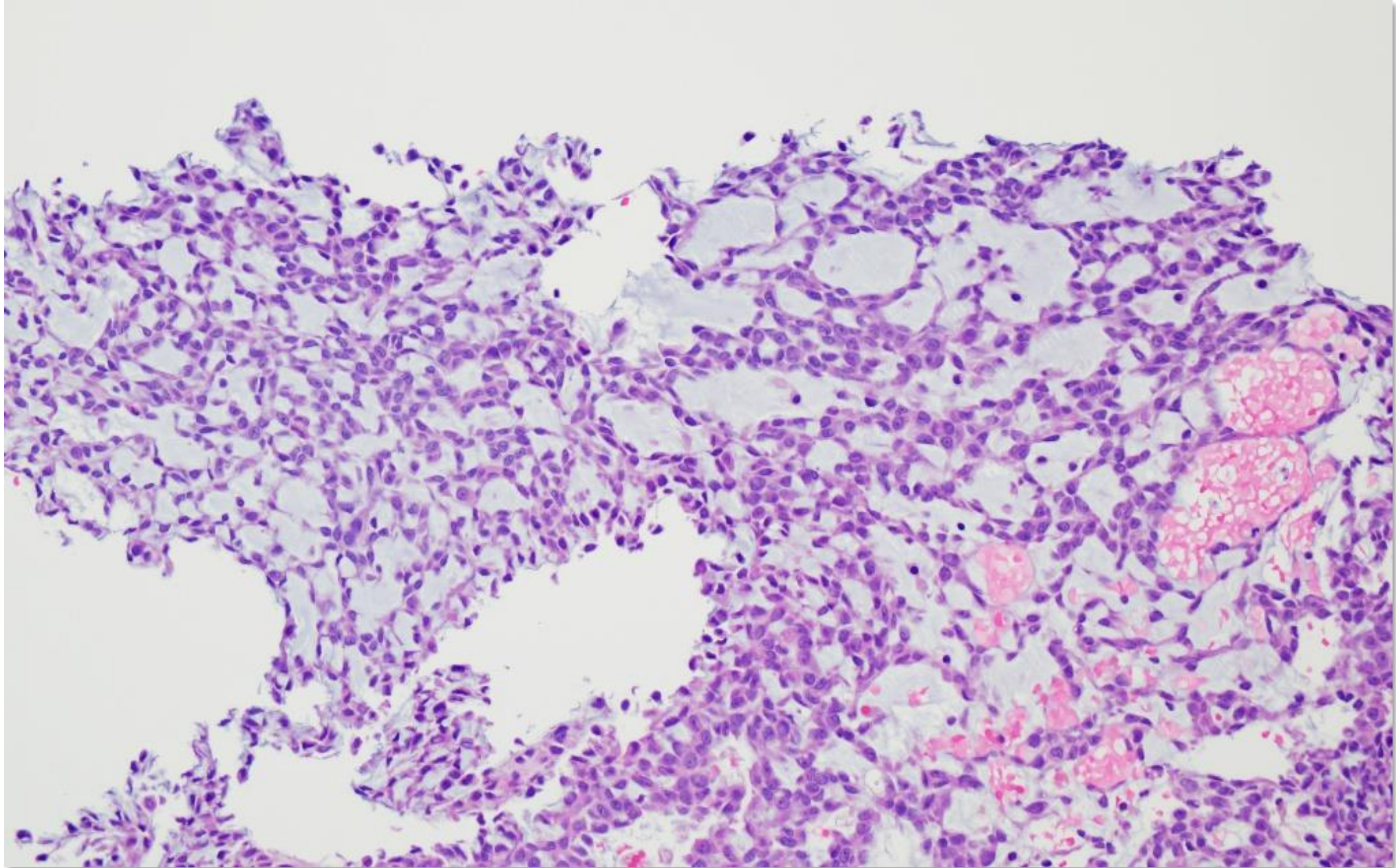
## Histopathology:

- Does NOT have well differentiated cartilage despite the name (unknown differentiation)
- Multinodular, cords, trabeculae, and cribriform arrangements of bland spindle cells
- Rhabdoid cells are variably present

## Ancillary:

- NR4A3 rearrangements are diagnostic (present in >90%)
- NR4A3 often rearranged with EWSR1

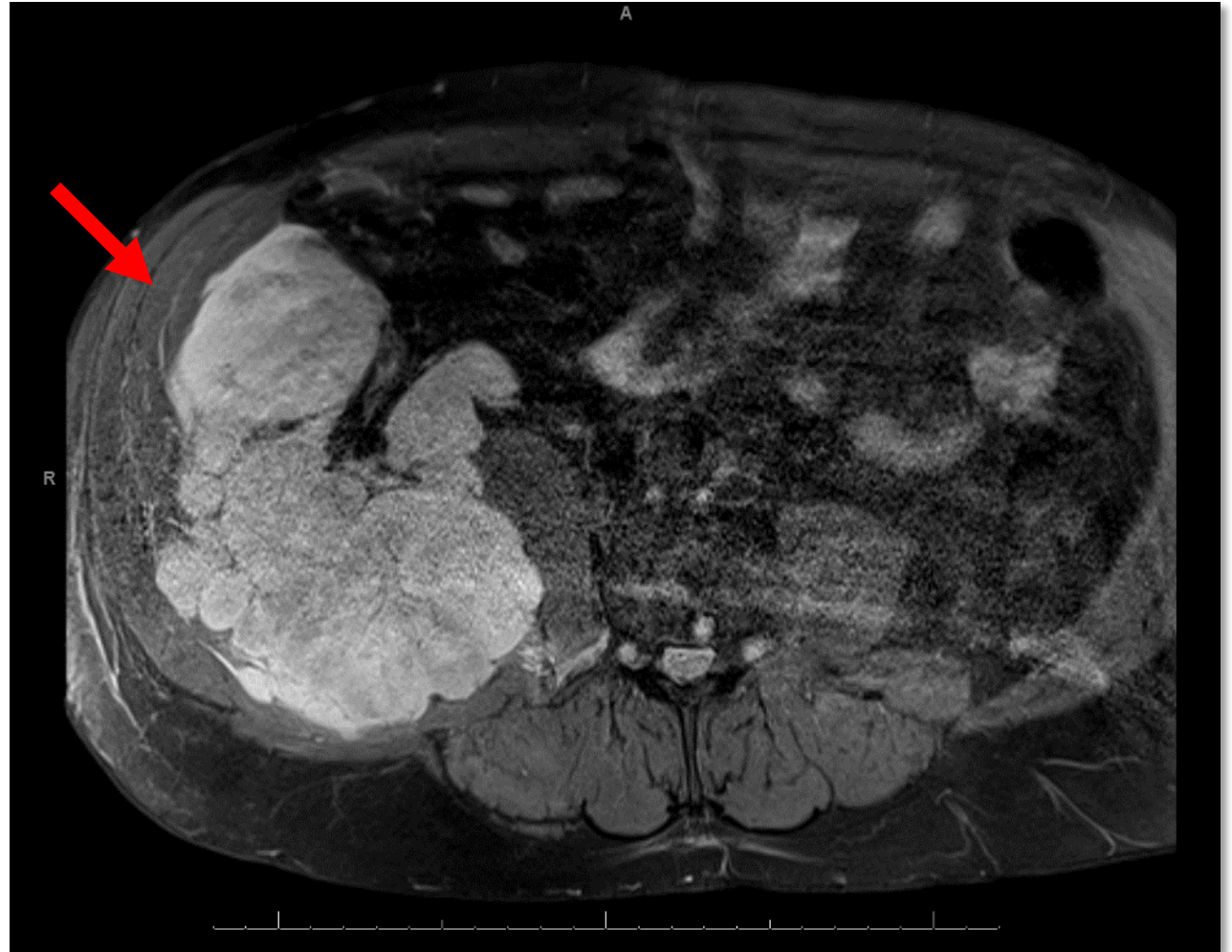
# Another case of Extraskeletal Myxoid Chondrosarcoma



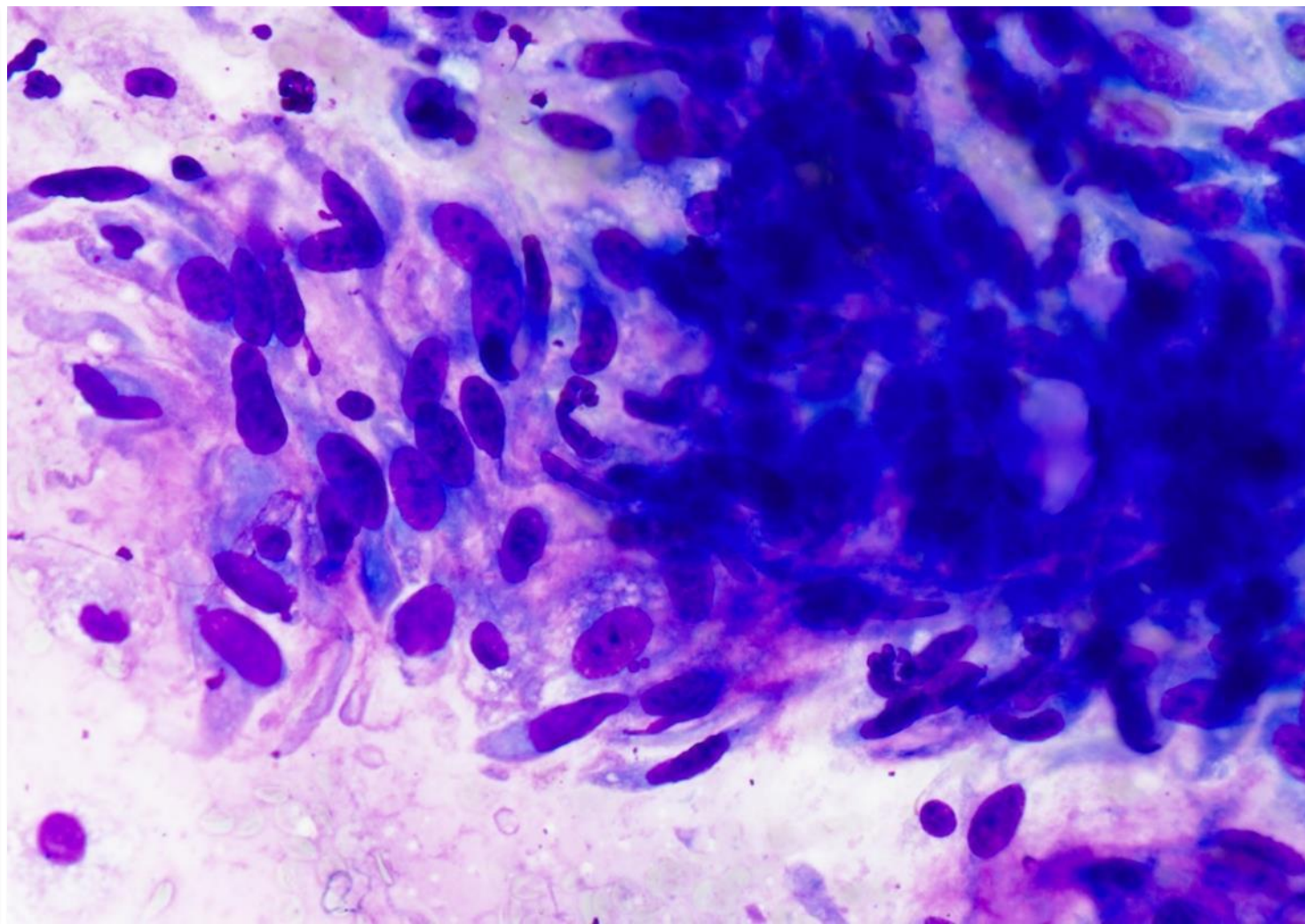
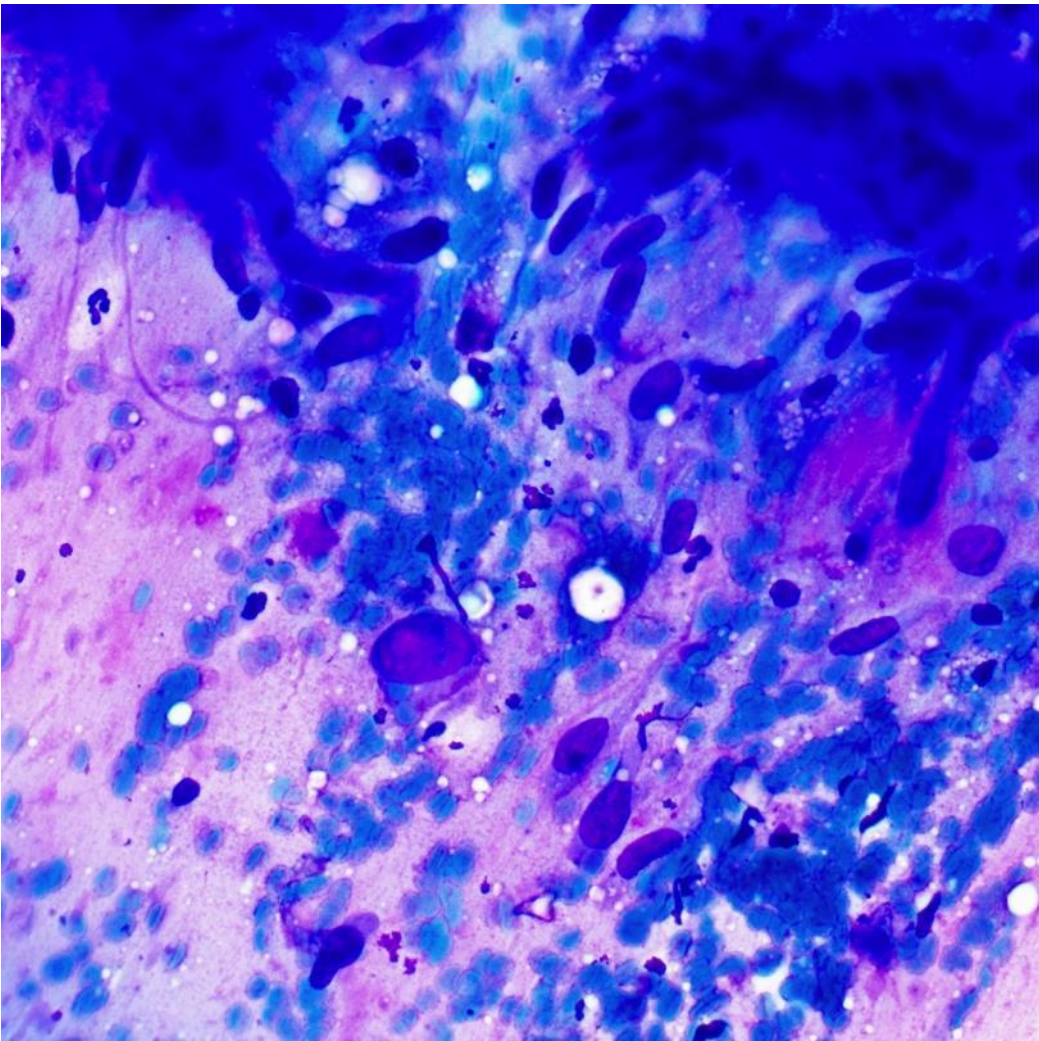
# Case # 5

## History:

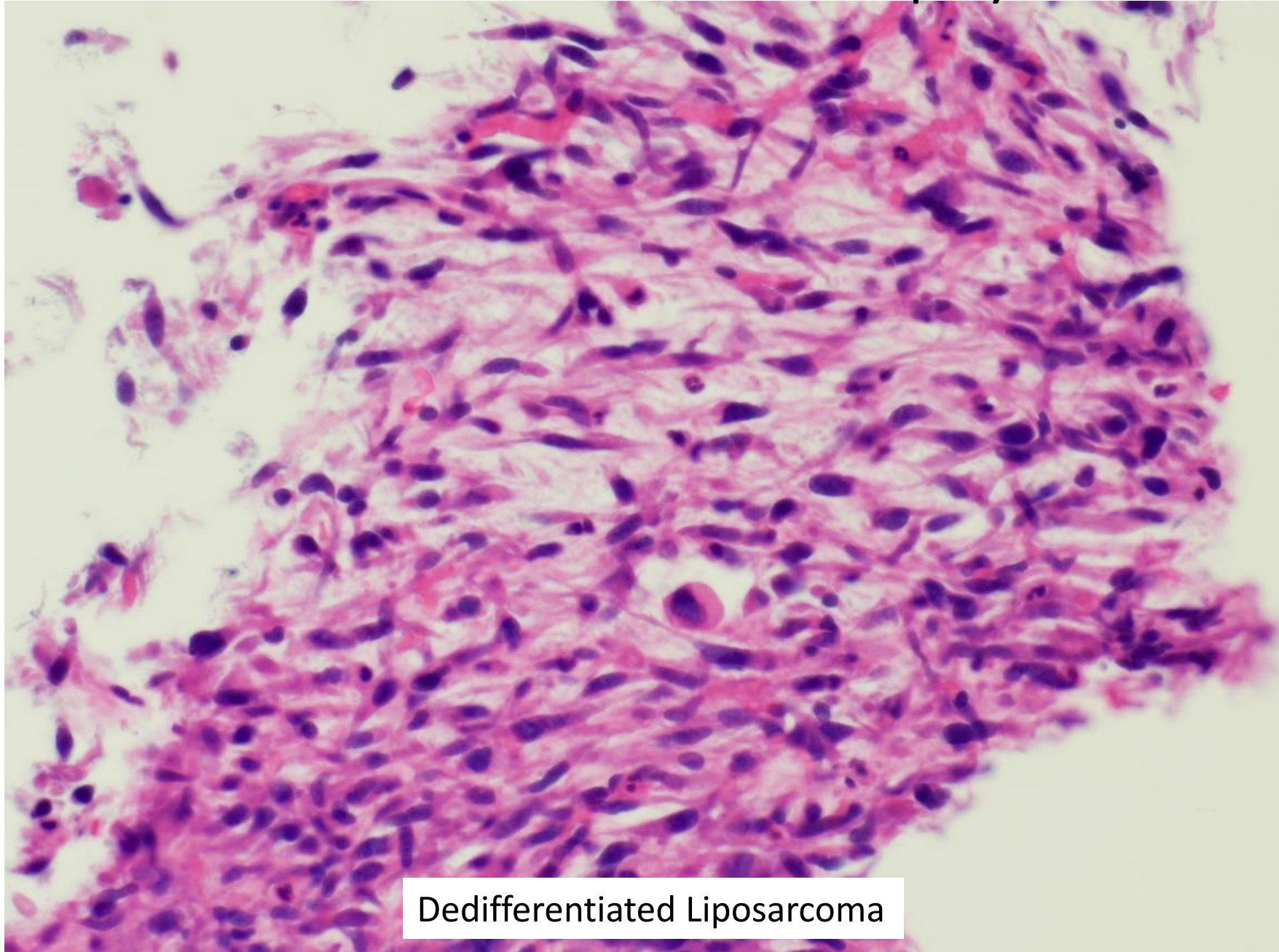
- 58 year old man with a 17 cm right retroperitoneal mass



# Case # 5- Touch Preparations



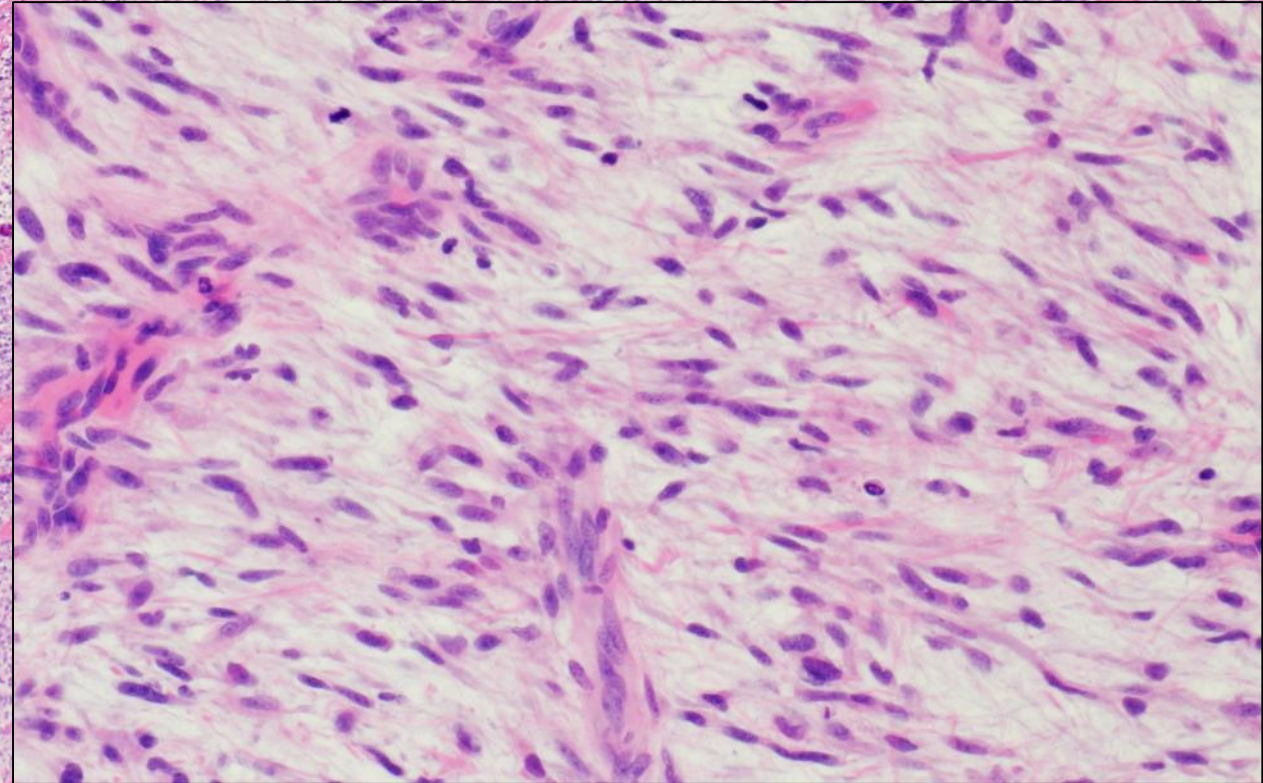
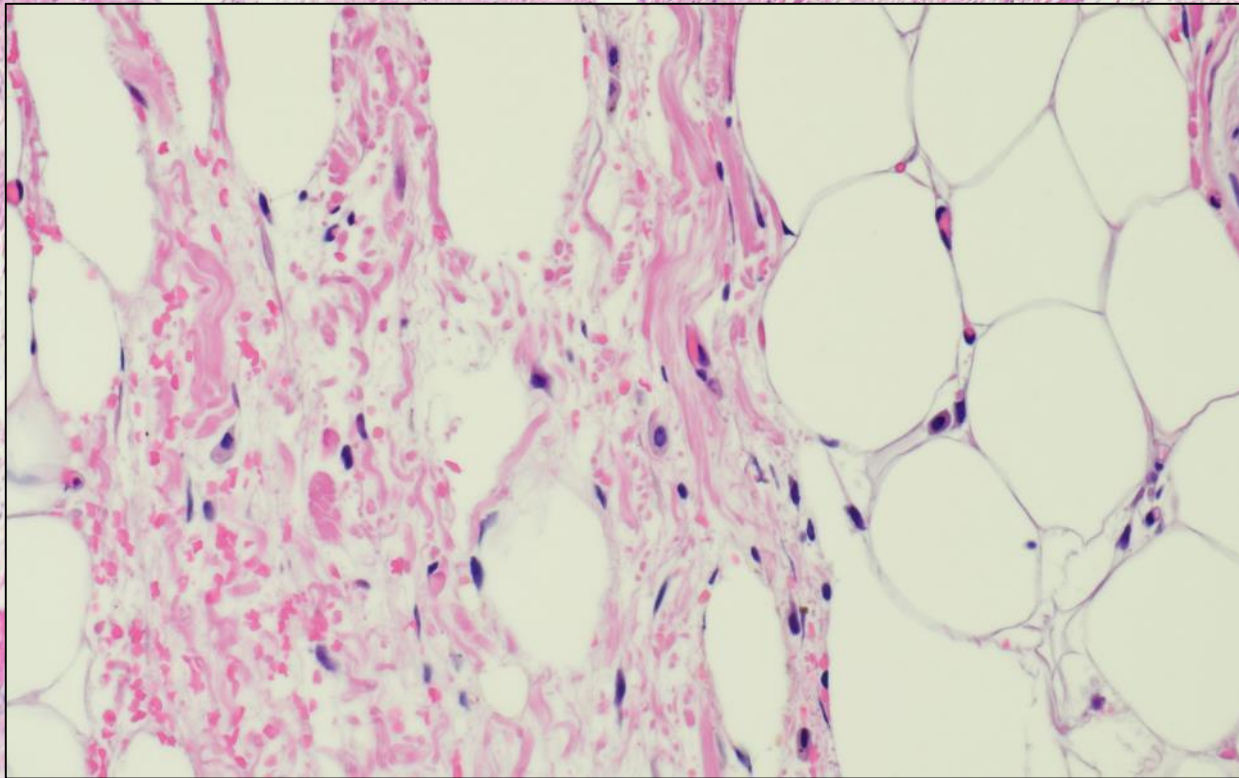
# Case # 5- Core biopsy



Dedifferentiated Liposarcoma

# Case # 5- Dedifferentiated Liposarcoma (Resection)

Well Differentiated Liposarcoma



Dedifferentiated Liposarcoma

# Case # 5- Dedifferentiated Liposarcoma

## Epidemiology/Clinical features:

- ~10% of well differentiated liposarcoma/Atypical lipomatous tumors dedifferentiate

## Site:

- Most common cause of pleomorphic sarcoma in retroperitoneum
- Spermatic cord

## Cytology:

- Increased cellularity, hyperchromasia, atypia

## Histopathology:

- Abrupt transition to cellular, non-lipogenic sarcoma (usually look like high grade pleomorphic or spindle cell sarcoma)
- Don't always see the well differentiated component

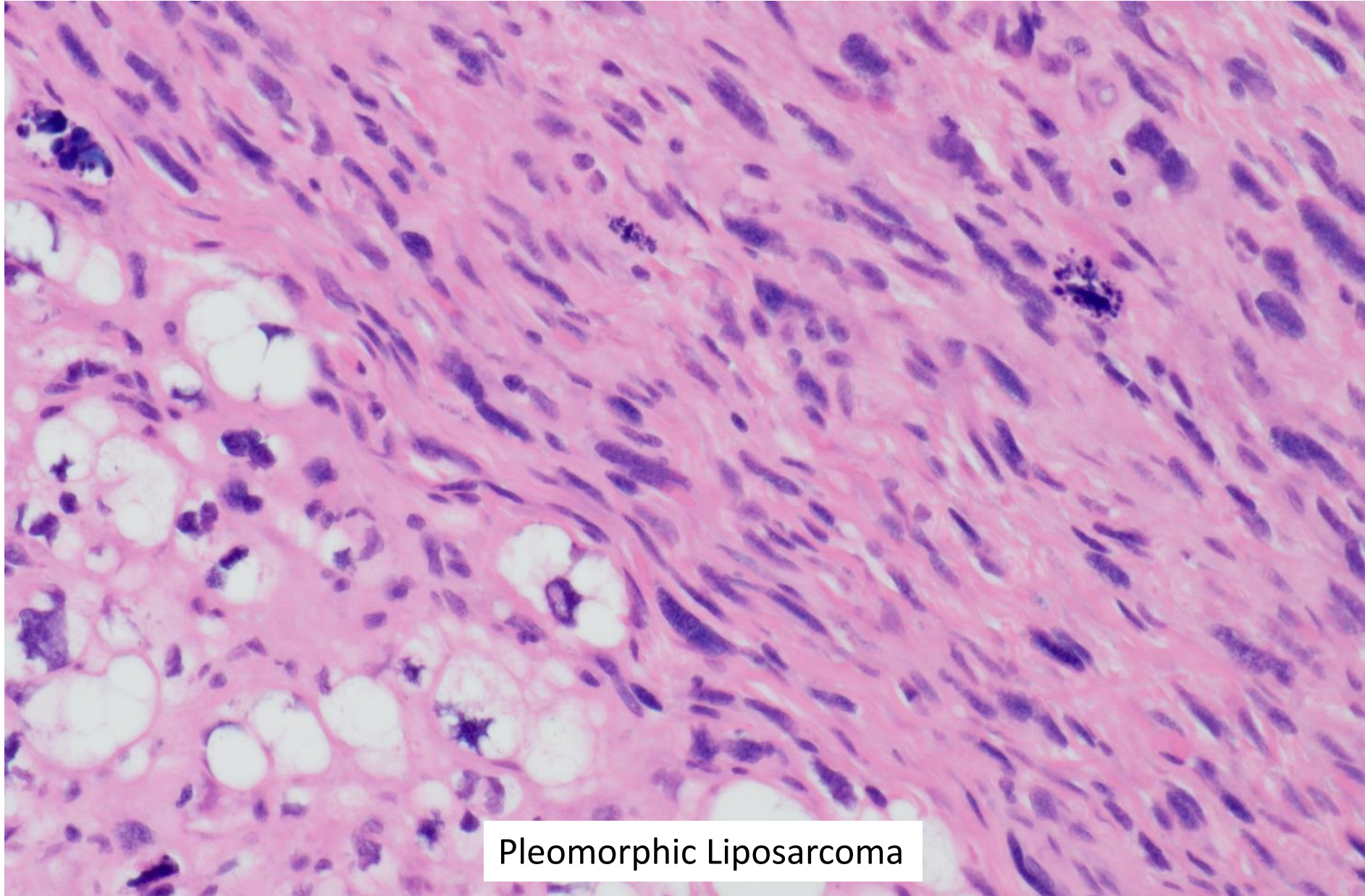
## Ancillary:

- MDM2 amplification

## DDX:

- Unclassified/undifferentiated high grade sarcoma, high grade sarcoma of other lineage, or pleomorphic liposarcoma

# Another Tumor on the Differential



Pleomorphic Liposarcoma

# When to Order MDM2 FISH?

ORIGINAL ARTICLE

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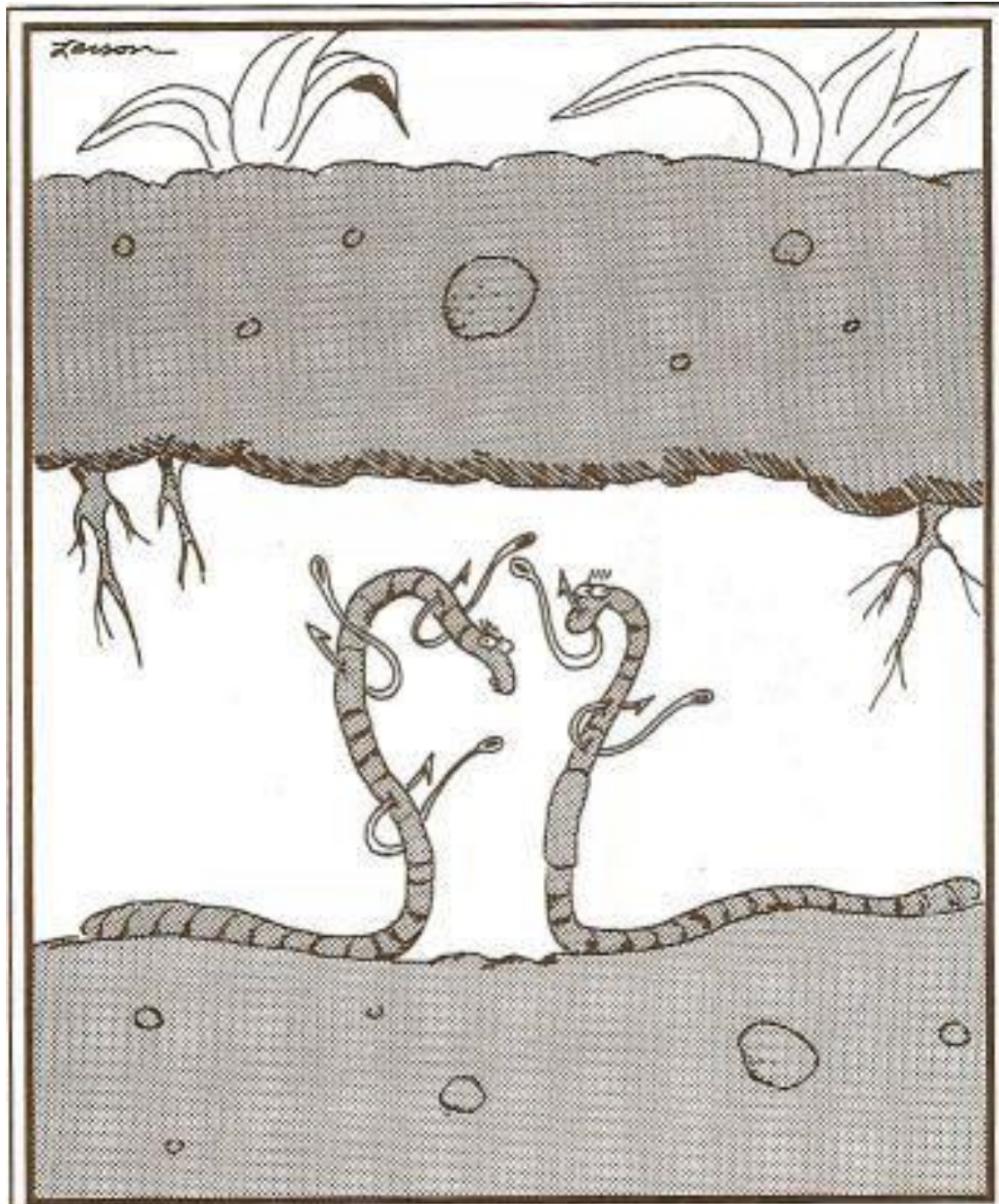
## *MDM2 Amplification in Problematic Lipomatous Tumors Analysis of FISH Testing Criteria*

*Michael R. Clay, MD. Anthony P. Martinez, MD. Sharon W. Weiss, MD. and Mark A. Edgar, MD*

*Am J Surg Pathol • Volume 39, Number 10, October 2015*

MDM2 FISH testing recommended for:

- 1) Recurrent adipocytic lesions
- 2) Deep extremity lesions >10 cm in size in patients over 50 years old
- 3) Adipocytic masses with equivocal atypia
- 4) Lesions in the retroperitoneum, pelvis, and abdomen



Punk worms

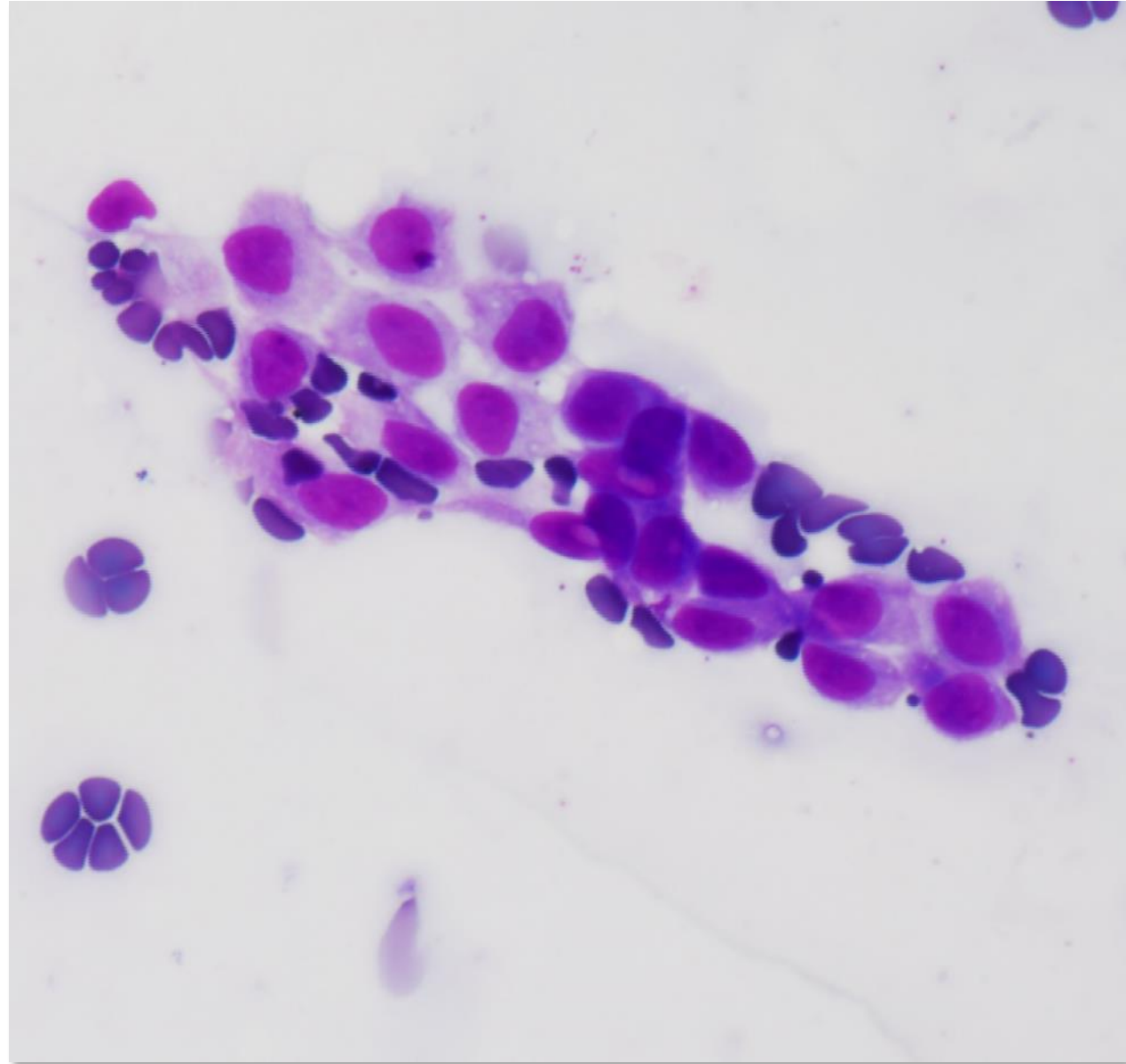
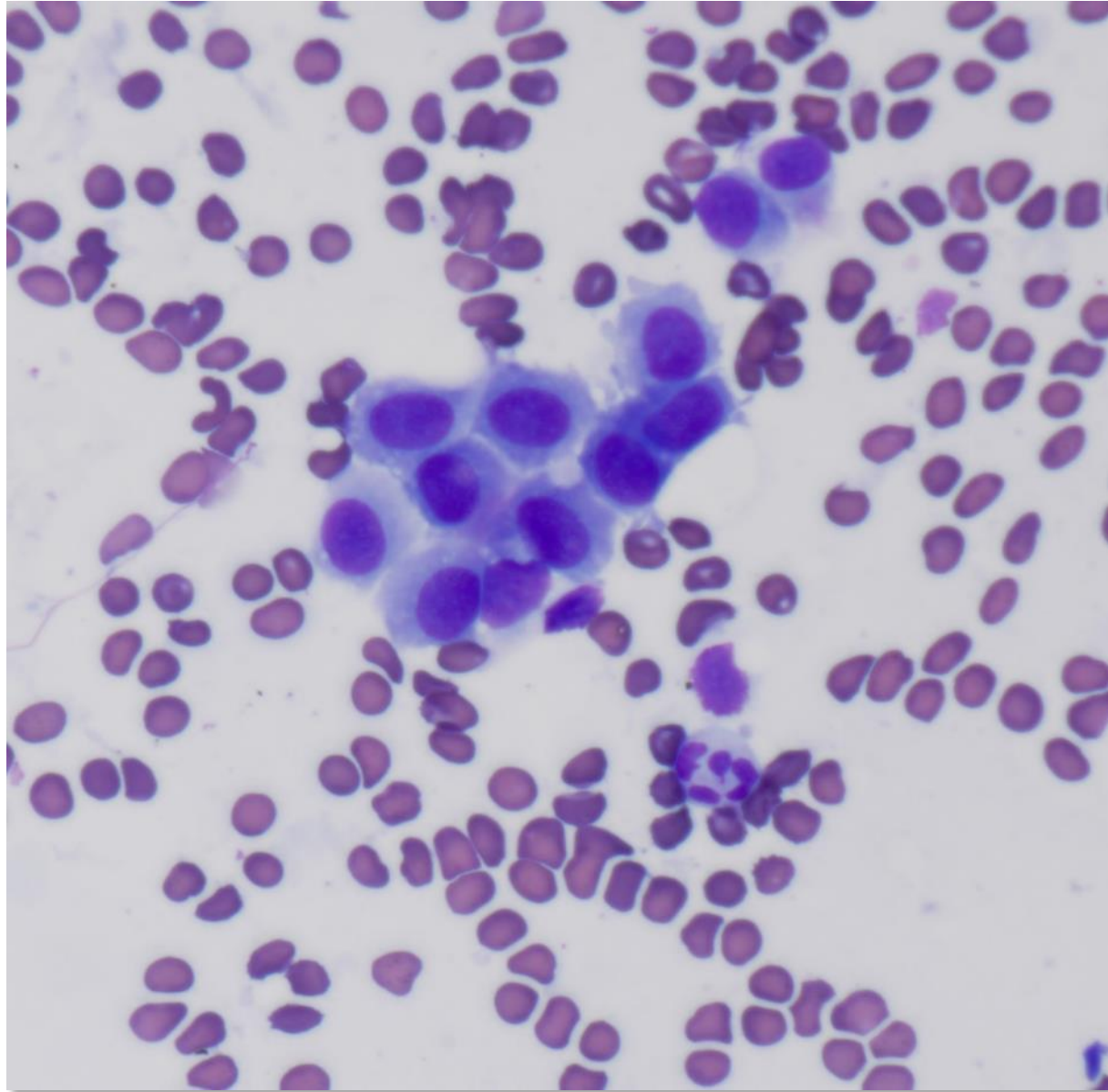
# Case # 6

## History:

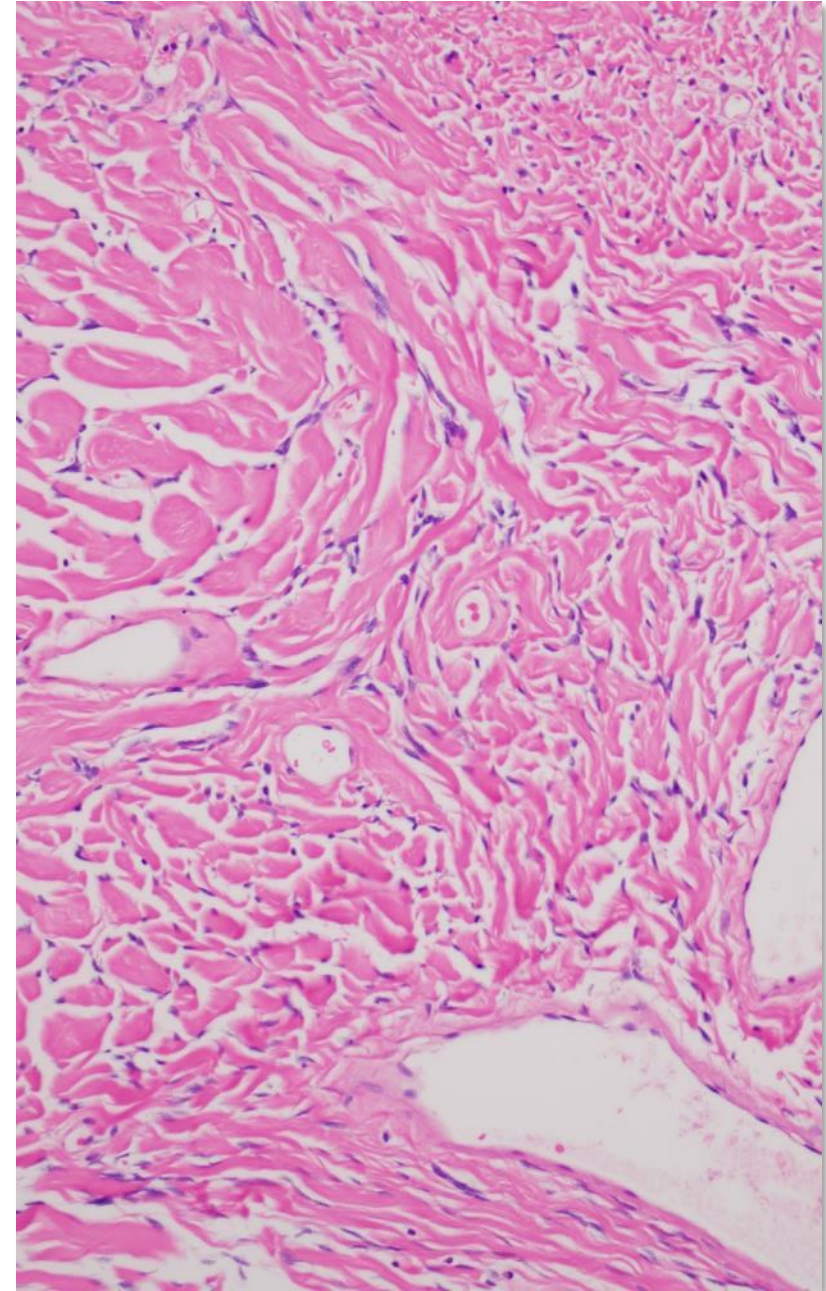
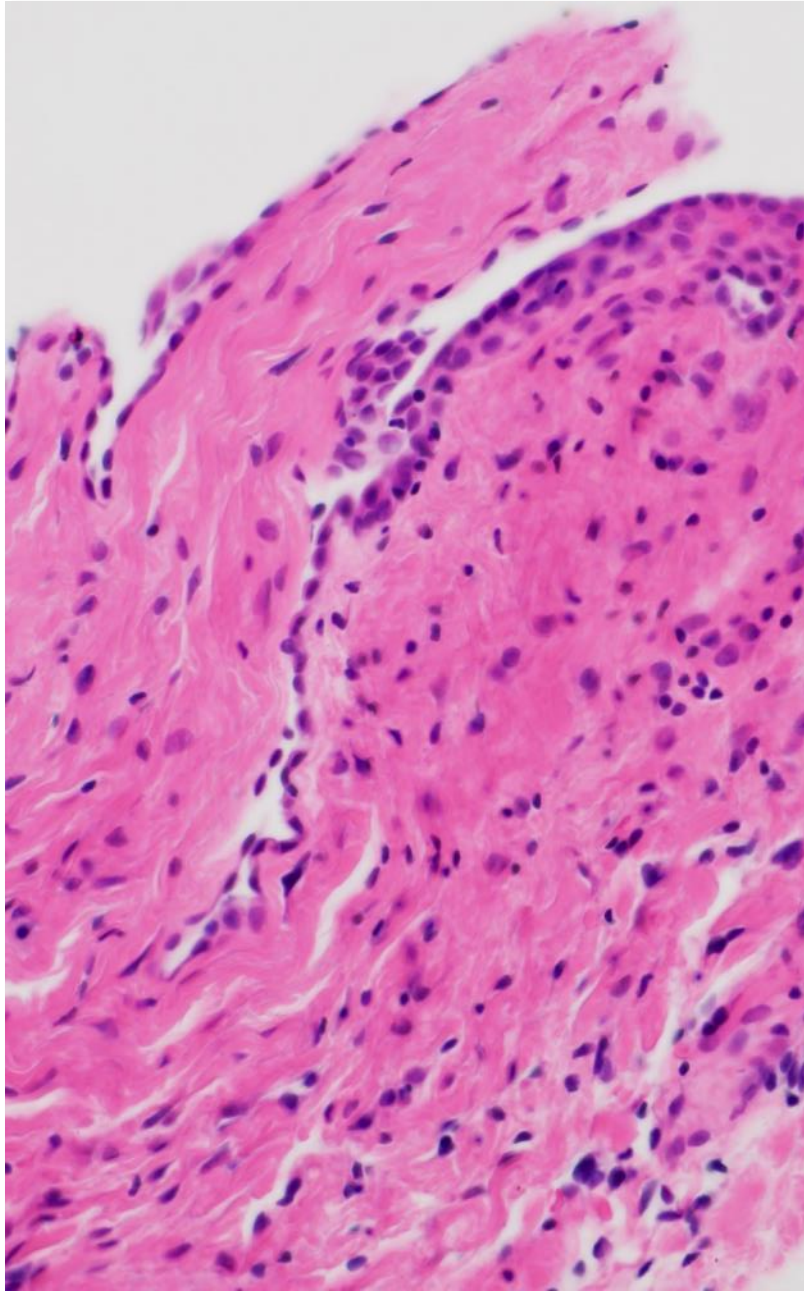
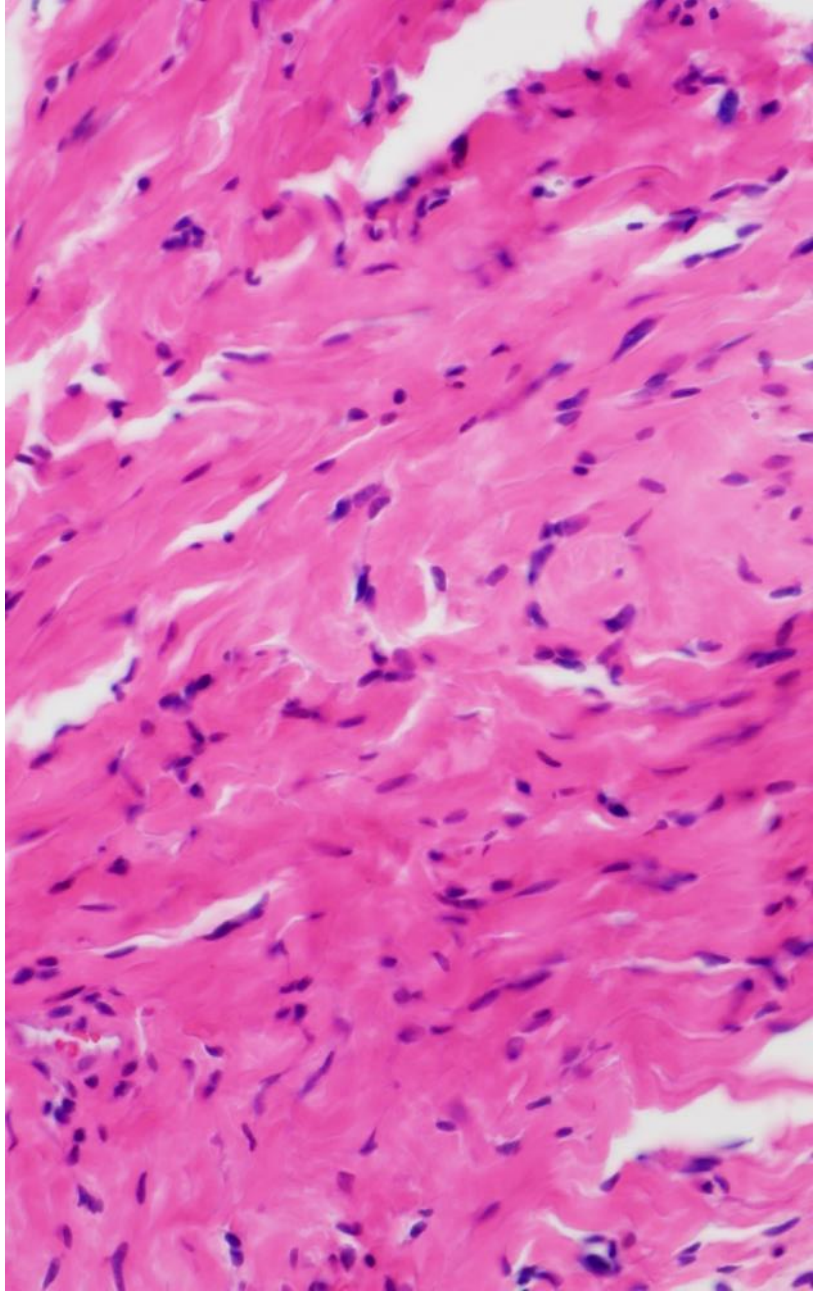
- 64 year old man with an incidentally discovered left lung pleural based lung mass
- Felt very hard upon percutaneous CT-guided needle core biopsy



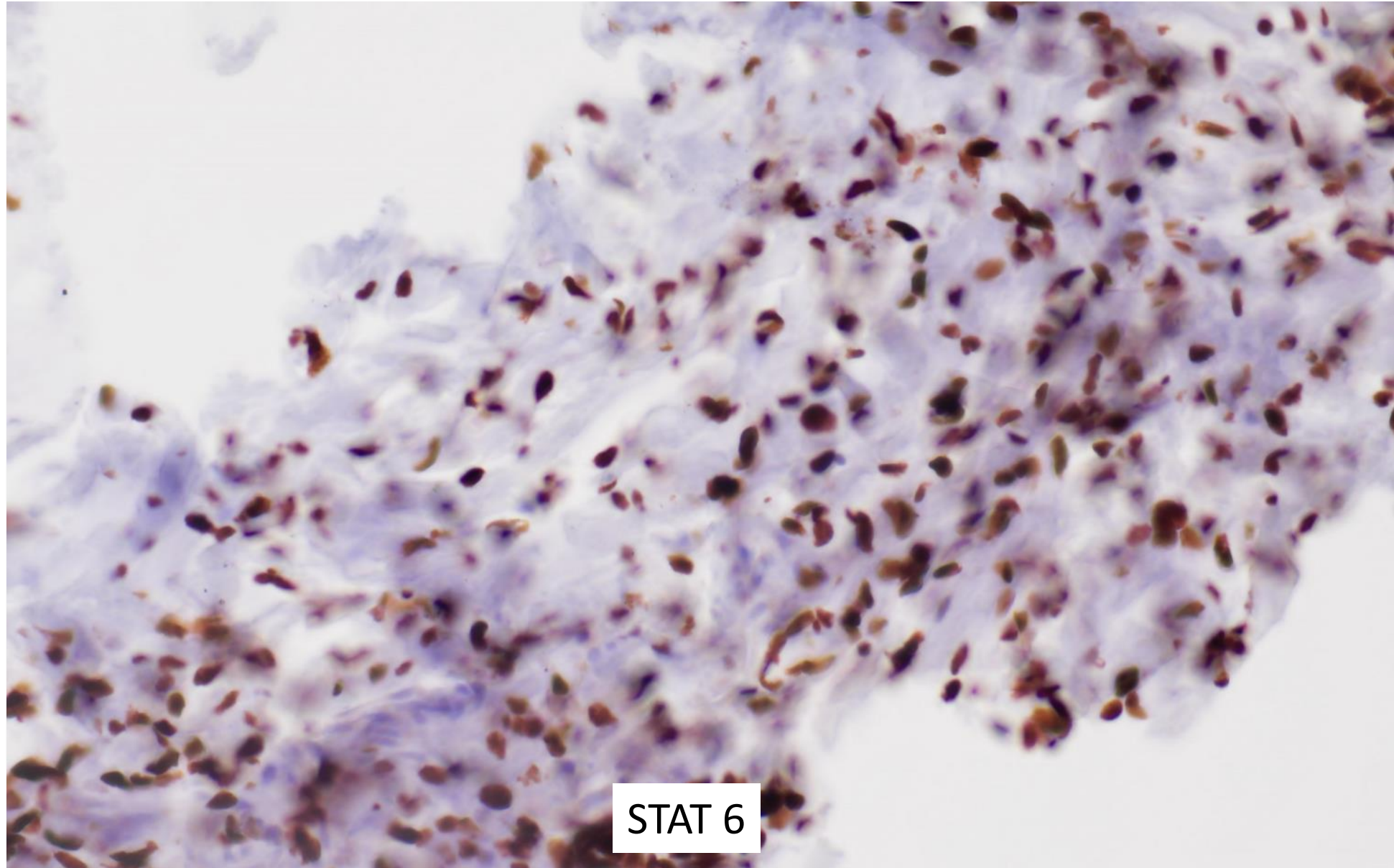
# Case # 6 Touch Preparations



# Case # 6 Biopsy



# Case # 6 – Solitary Fibrous Tumor



# Case # 6- Solitary Fibrous Tumor

## Epidemiology/Clinical features:

- Benign fibroblastic tumor; about 5-10% are malignant

## Site:

- Pleural; wide variety of extra-pleural sites

## Cytology:

- Often low cellularity on cytology preparations, bland spindle cells with rosy collagen

## Histopathology:

- Monomorphic spindle cells, rosy collagen bundles and staghorn-like (HPC-like) vessels

## Ancillary:

- STAT6 and CD34 positive

## DDX:

- Low Grade Fibromyxoid sarcoma, Low Grade MPNST, Synovial Sarcoma, Desmoid, Desmoplastic Mesothelioma, Thymoma

# CD 34 Positive Tumors



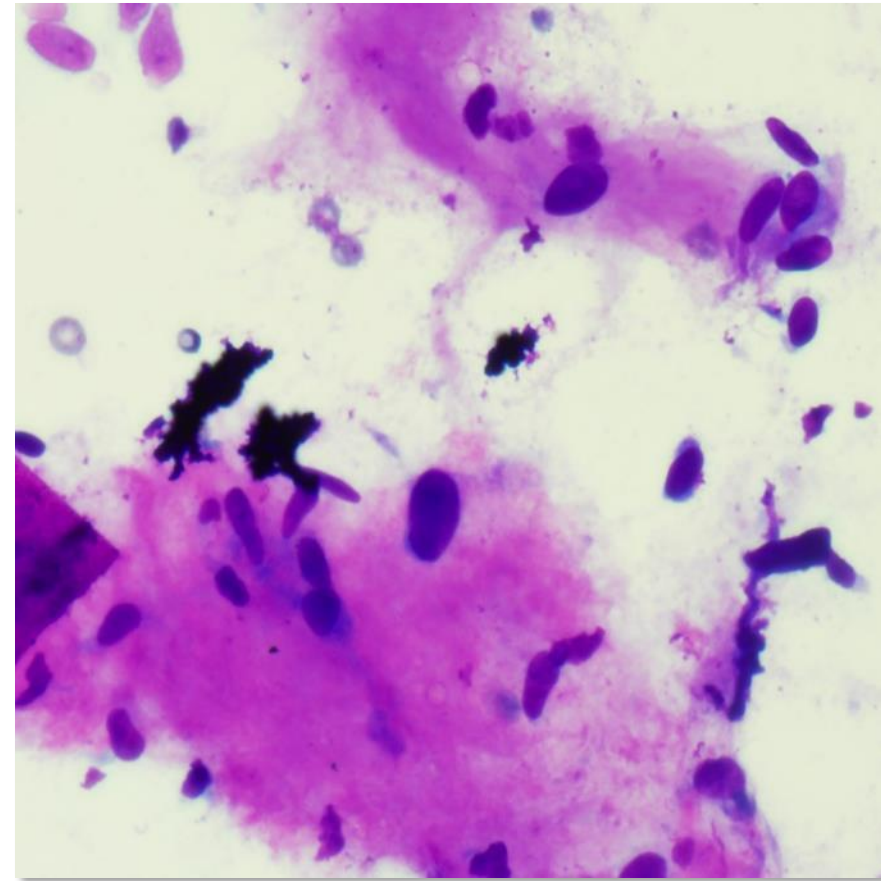
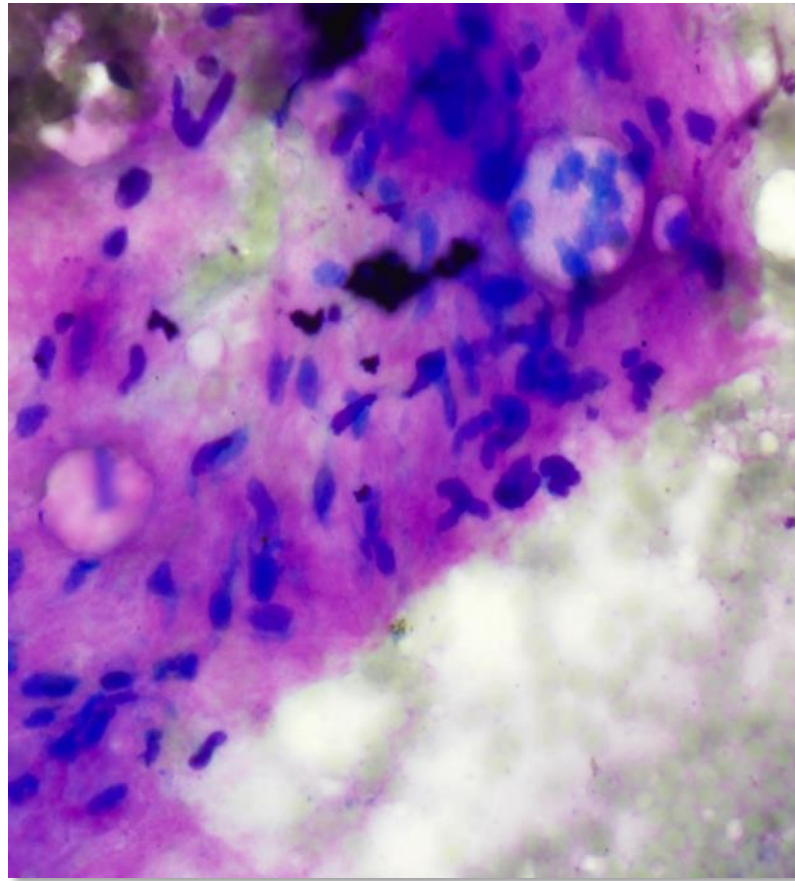
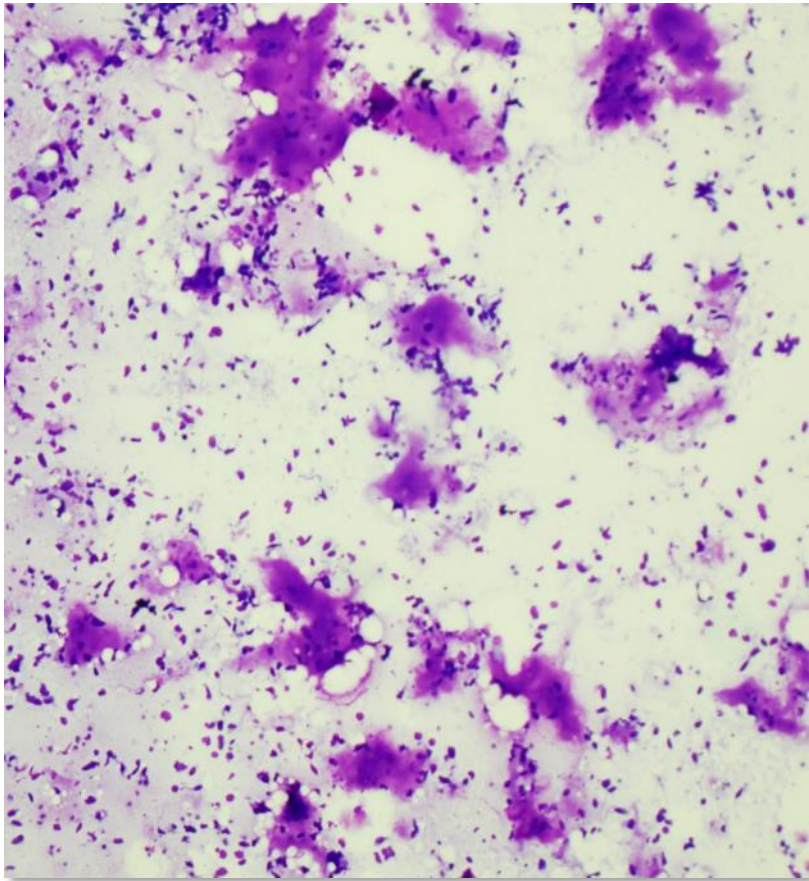
- Solitary Fibrous Tumor
- GIST
- Dermatofibrosarcoma Protuberans
- Angiosarcoma (blood vessels)
- Epithelioid Sarcoma
- Spindle Cell Lipoma

## Case # 7

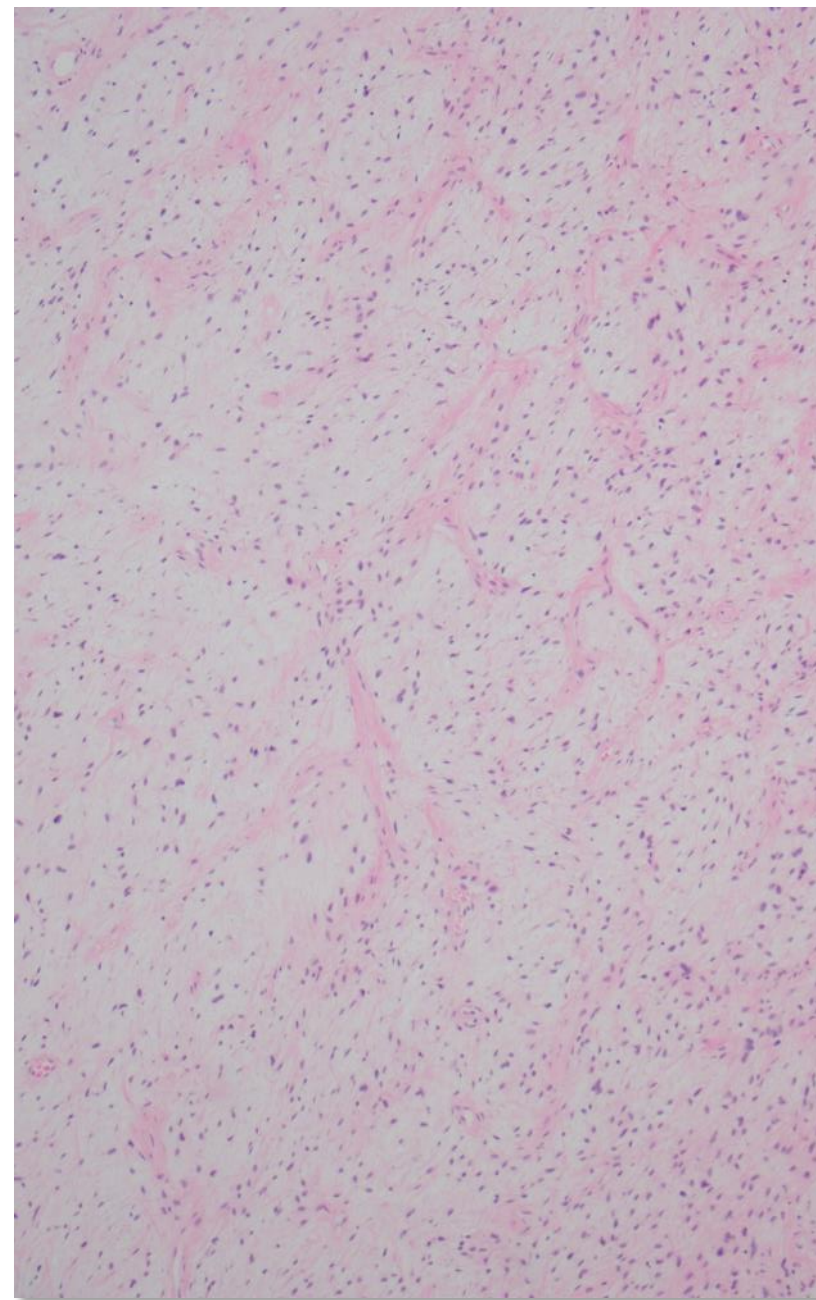
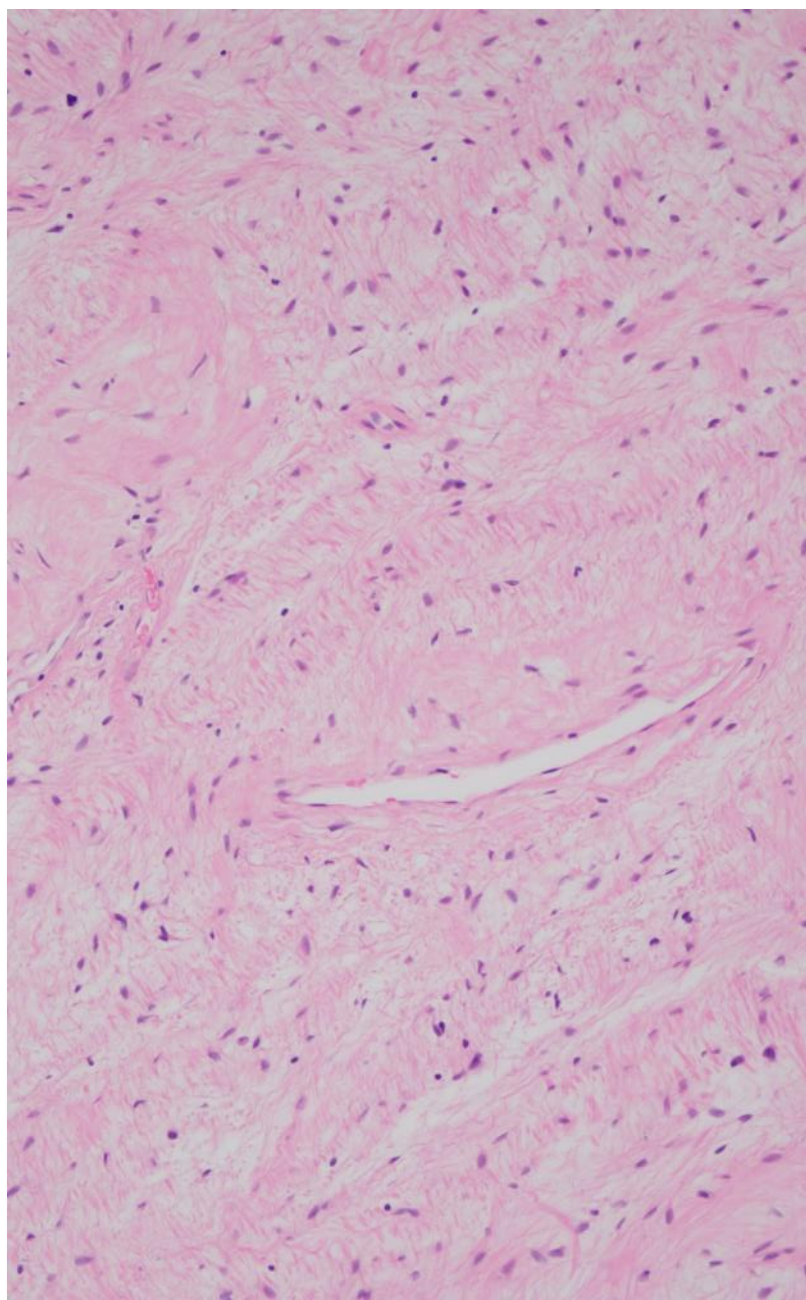
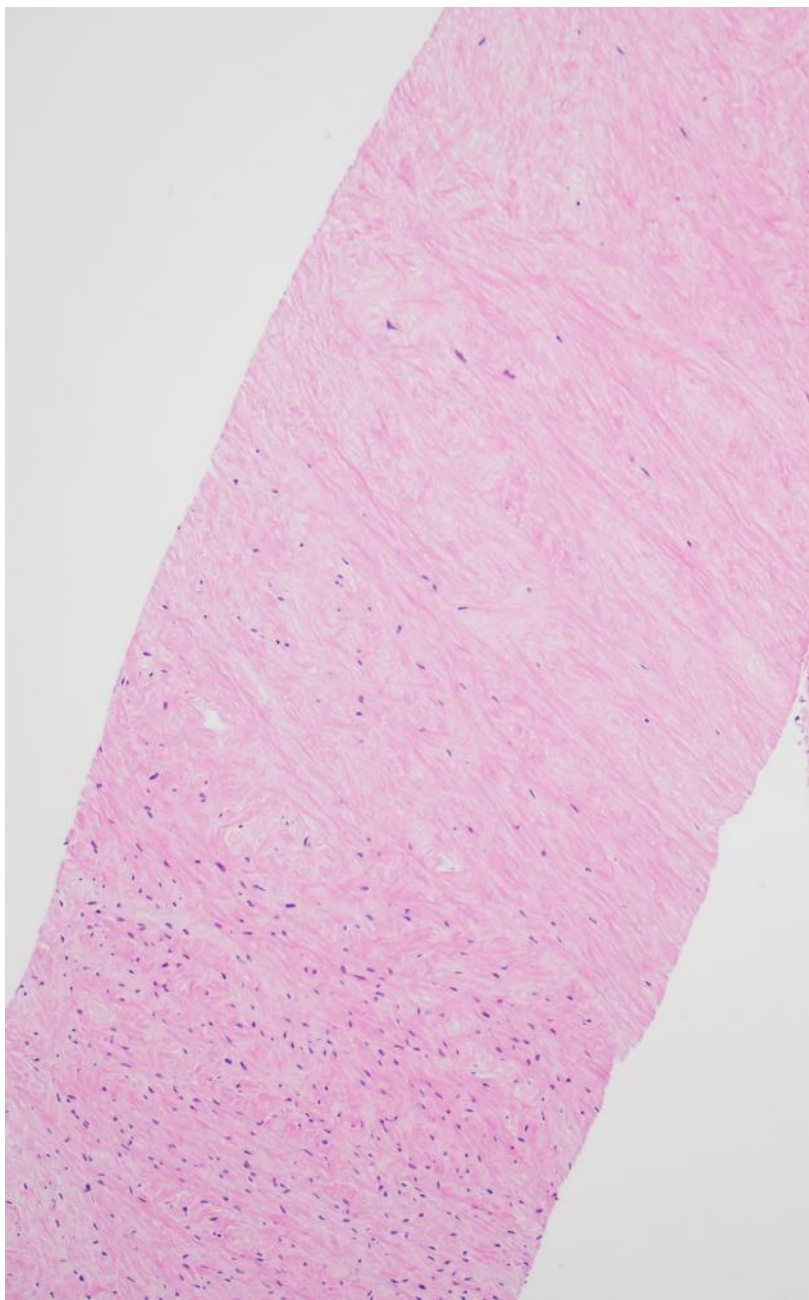
History: 18 year old female  
with a slowly enlarging left  
anterior abdominal wall mass



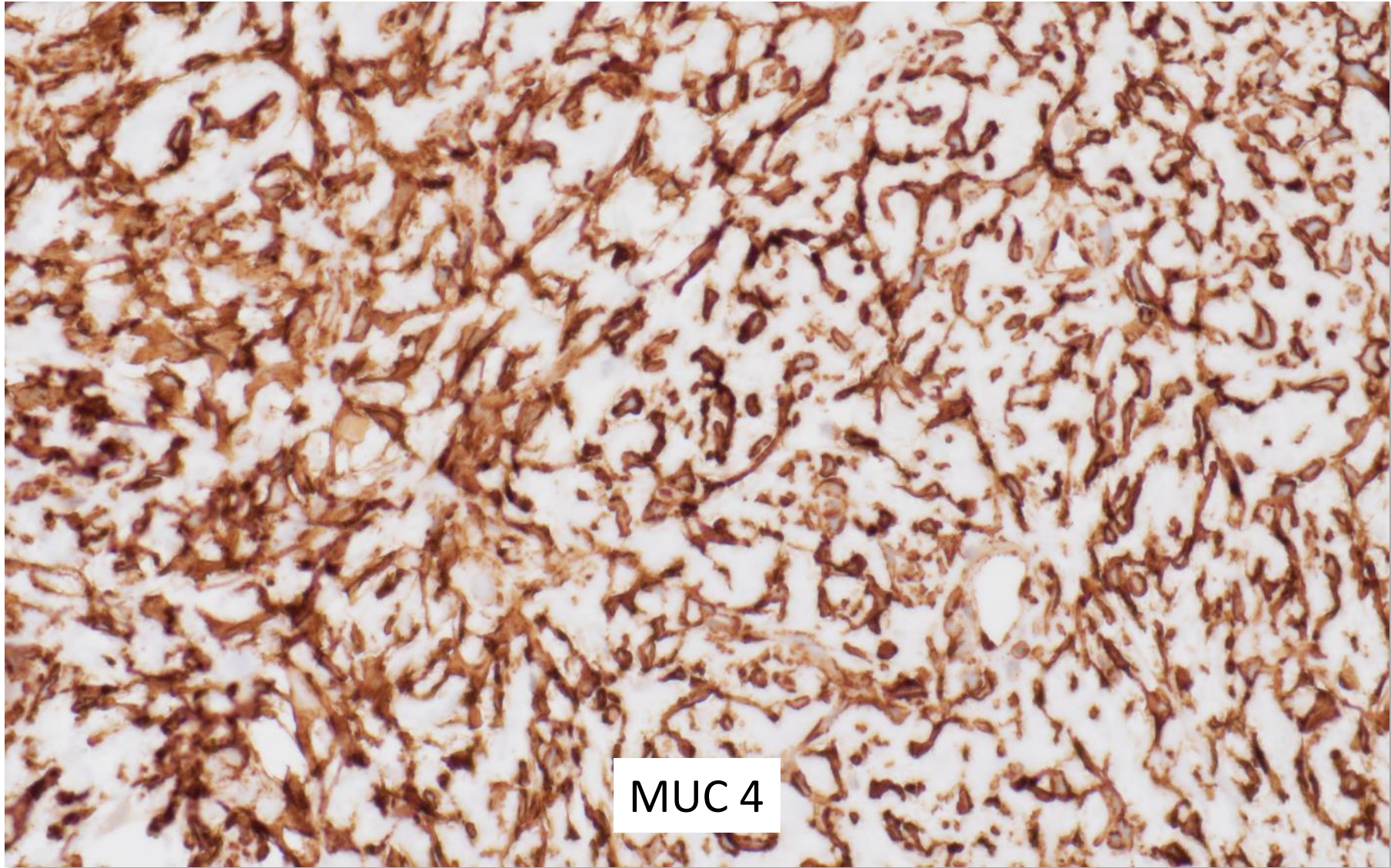
# Case # 7 Touch Preparations



# Case # 7 Biopsies



# Case # 7- Low Grade Fibromyxoid Sarcoma



# Case # 7 Low Grade Fibromyxoid Sarcoma

## Epidemiology/Clinical features:

- Rare tumor of young adults
- Low grade by definition

## Site:

- Proximal extremities or trunk

## Cytology:

- Spindle cells with only mild nuclear atypia; myxoid matrix

## Histopathology:

- Bland whirling spindle cells, alternating collagenous and myxoid areas, curvilinear vessels
- Ancillary:
  - MUC4 positive
  - FUS-CREB translocation

## DDX:

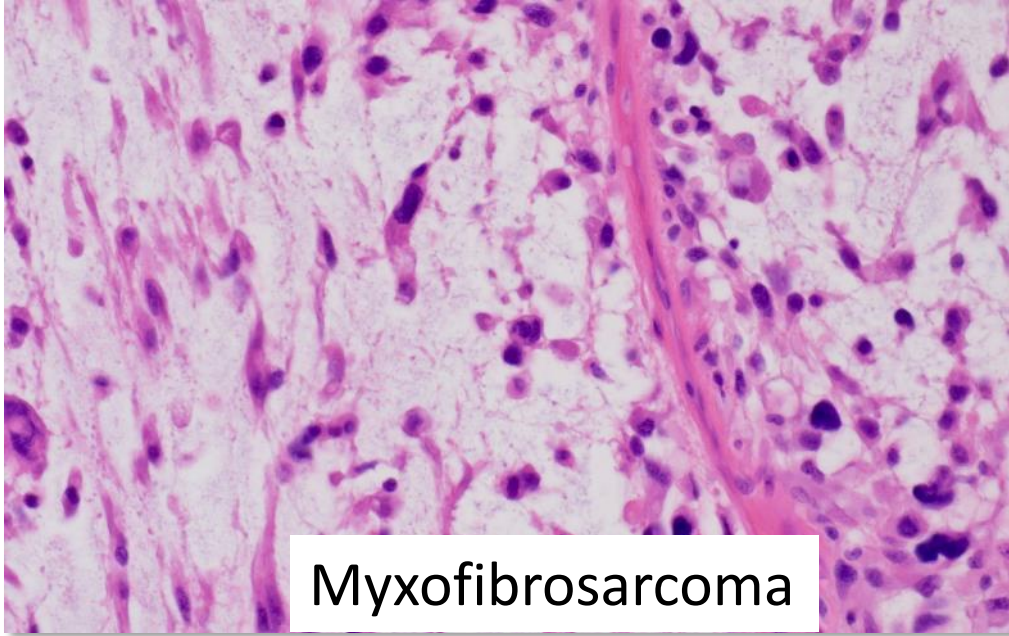
- Myxoma, low grade myxofibrosarcoma, neurofibroma, solitary fibrous tumor, desmoid, perineurioma

# Myxoid Lesions: Use the Vessels!

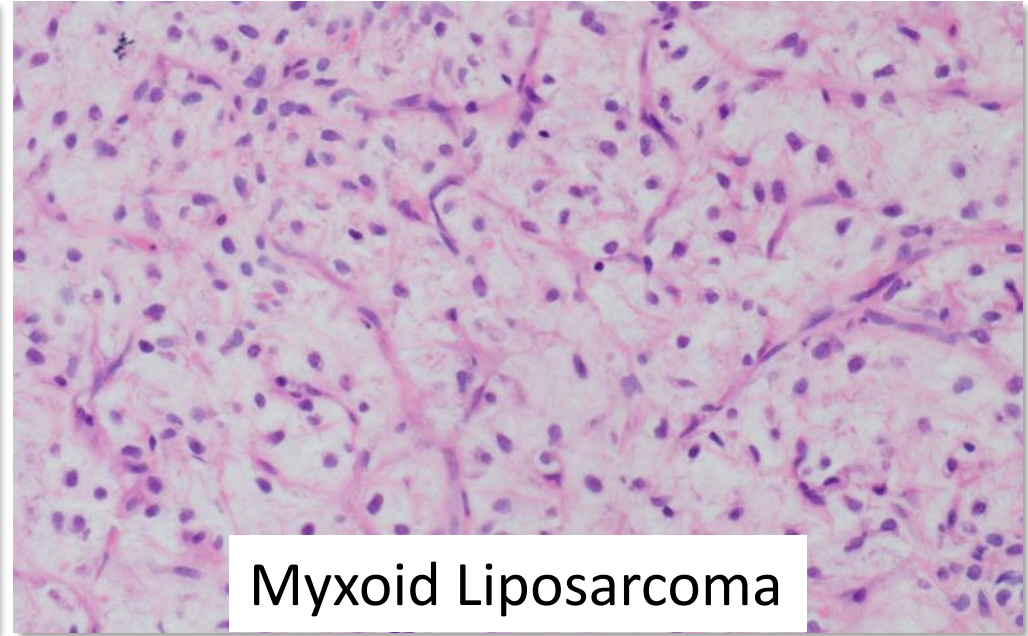


Tumor	Vessels	Other
Myxoid Liposarcoma	Chicken Wire	Bland spindle cells, lipoblasts, pulmonary edema-like areas
Myxoma	Virtually None	Bland stellate cells
Low Grade Fibromyxoid Sarcoma	Curvilinear	Younger people, MUC4+, FUS FISH+, low grade morphology
Myxofibrosarcoma	Curvilinear	Older people, Diagnosis of exclusion, may be low or high grade

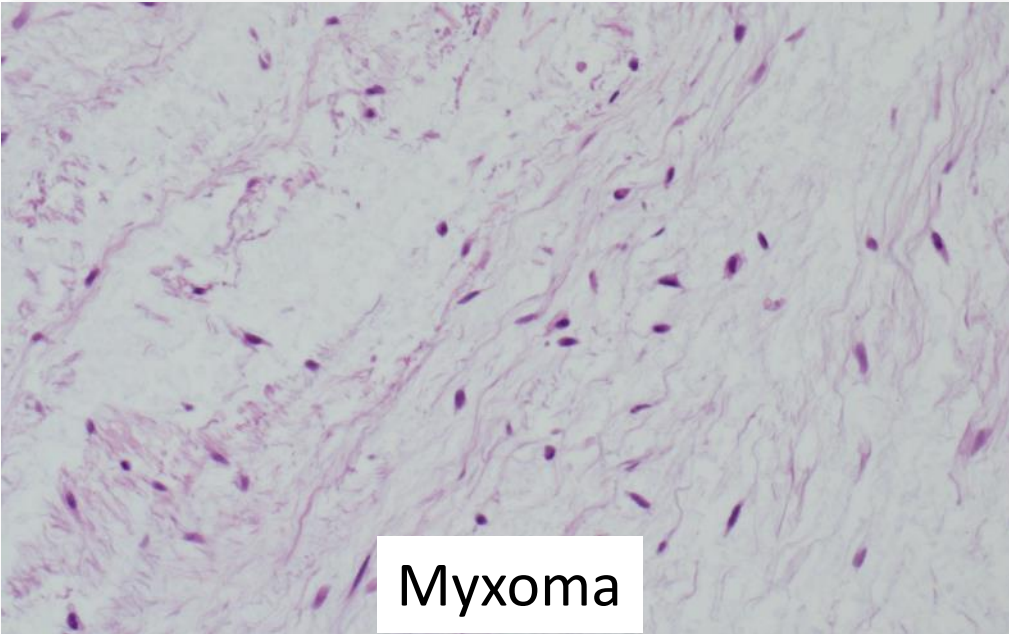
# Name That Myxoid Mass



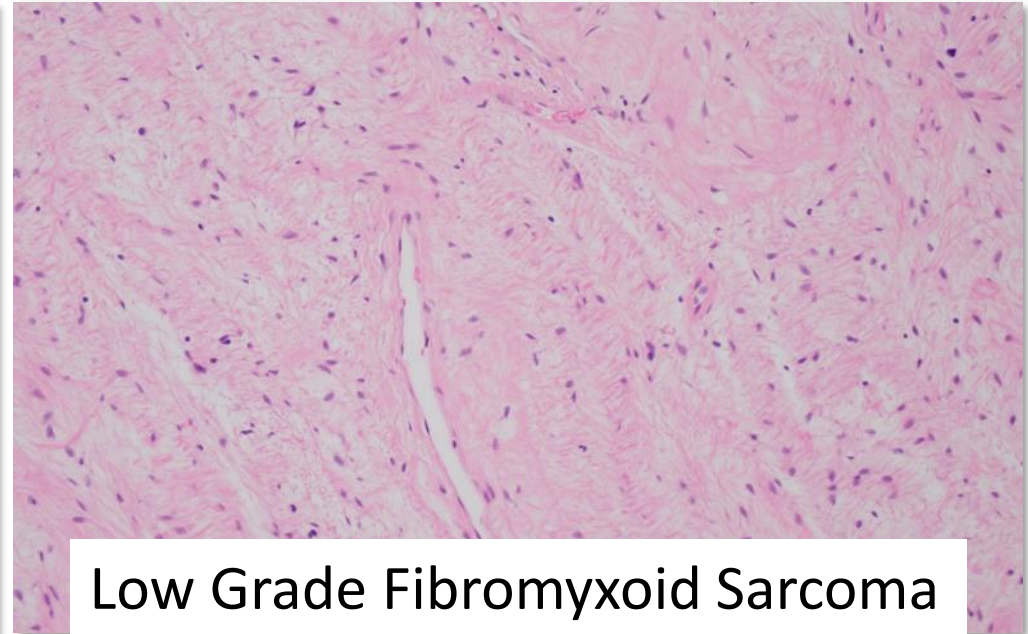
Myxofibrosarcoma



Myxoid Liposarcoma



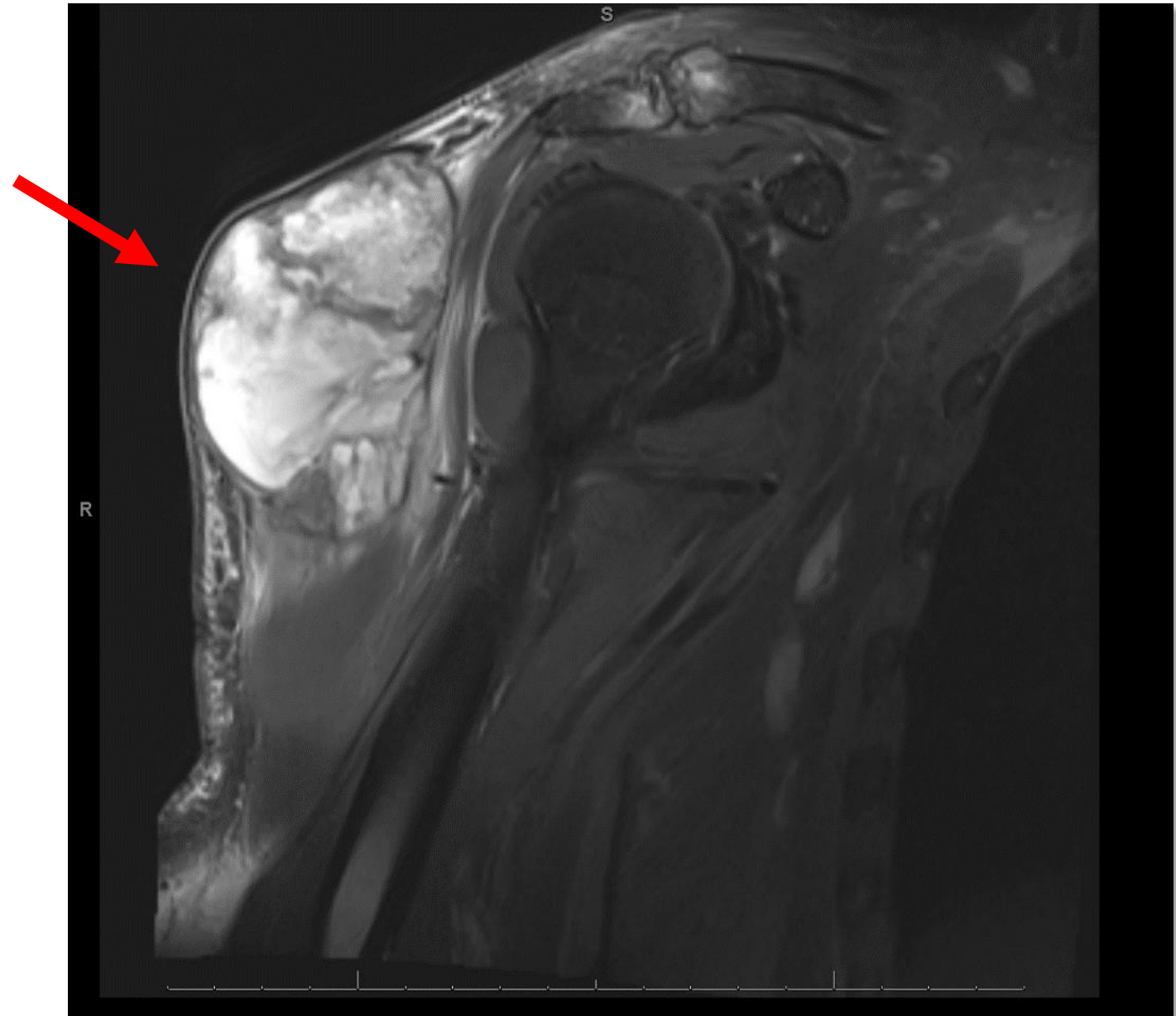
Myxoma



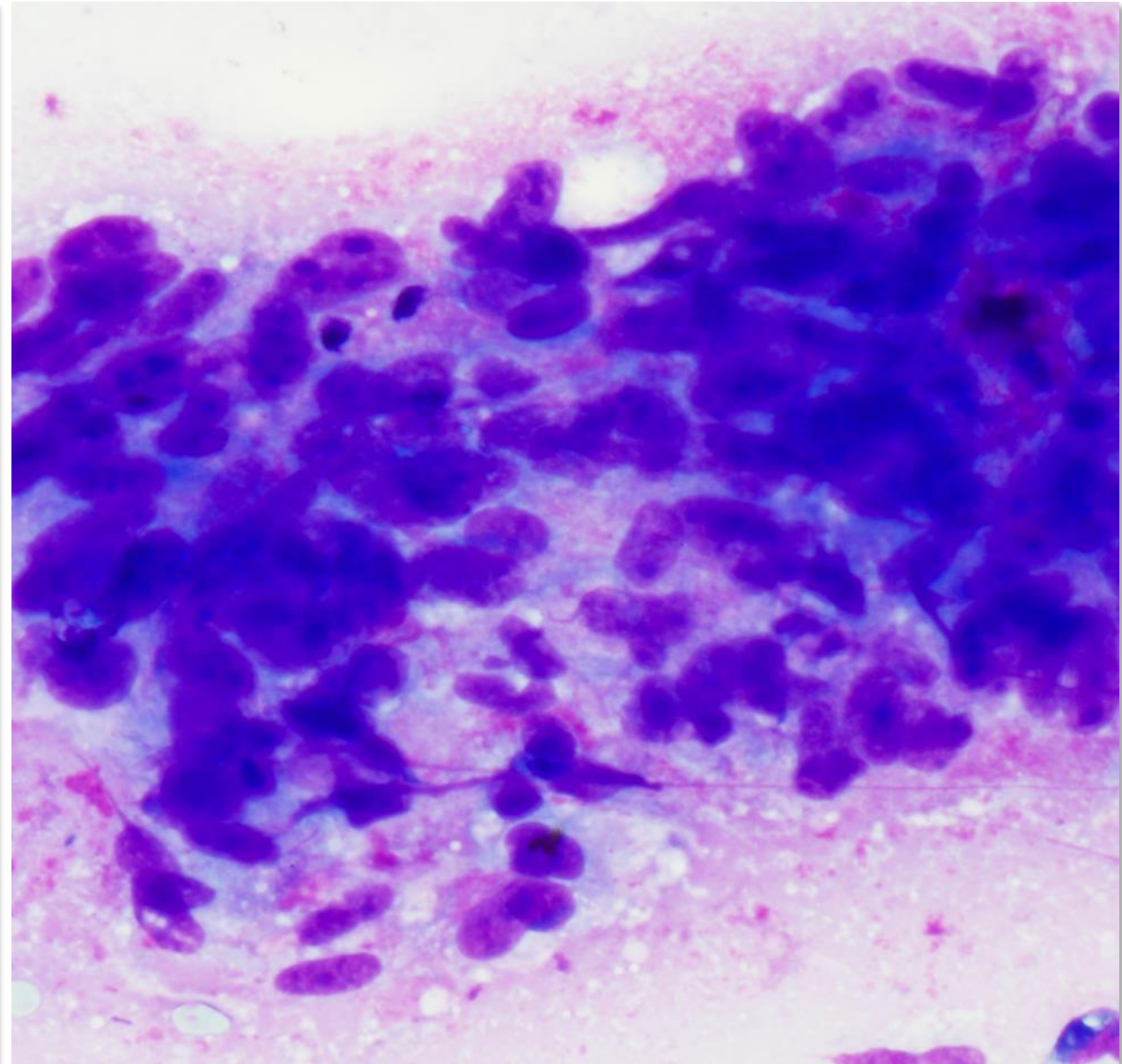
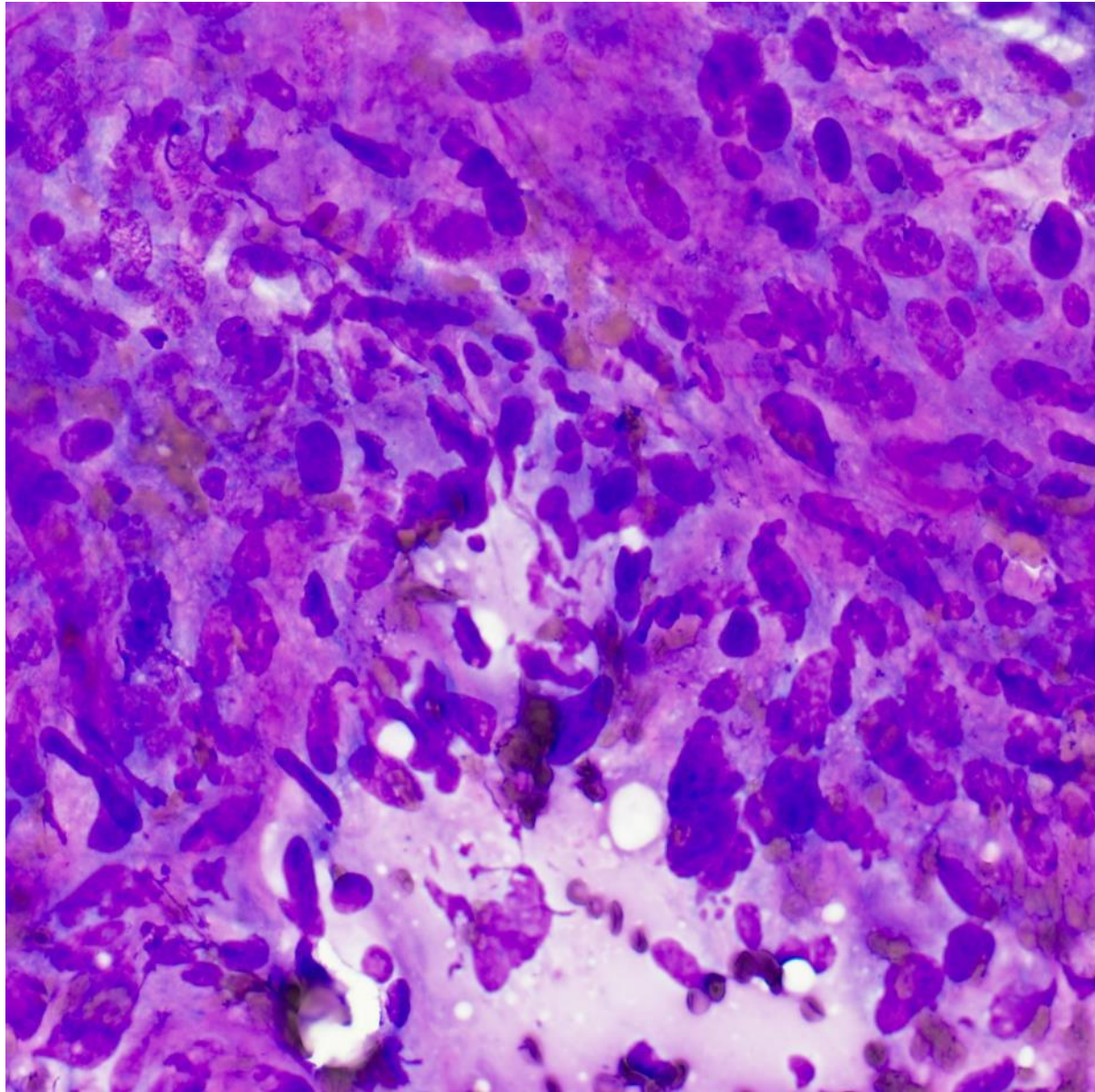
Low Grade Fibromyxoid Sarcoma

## Case 8

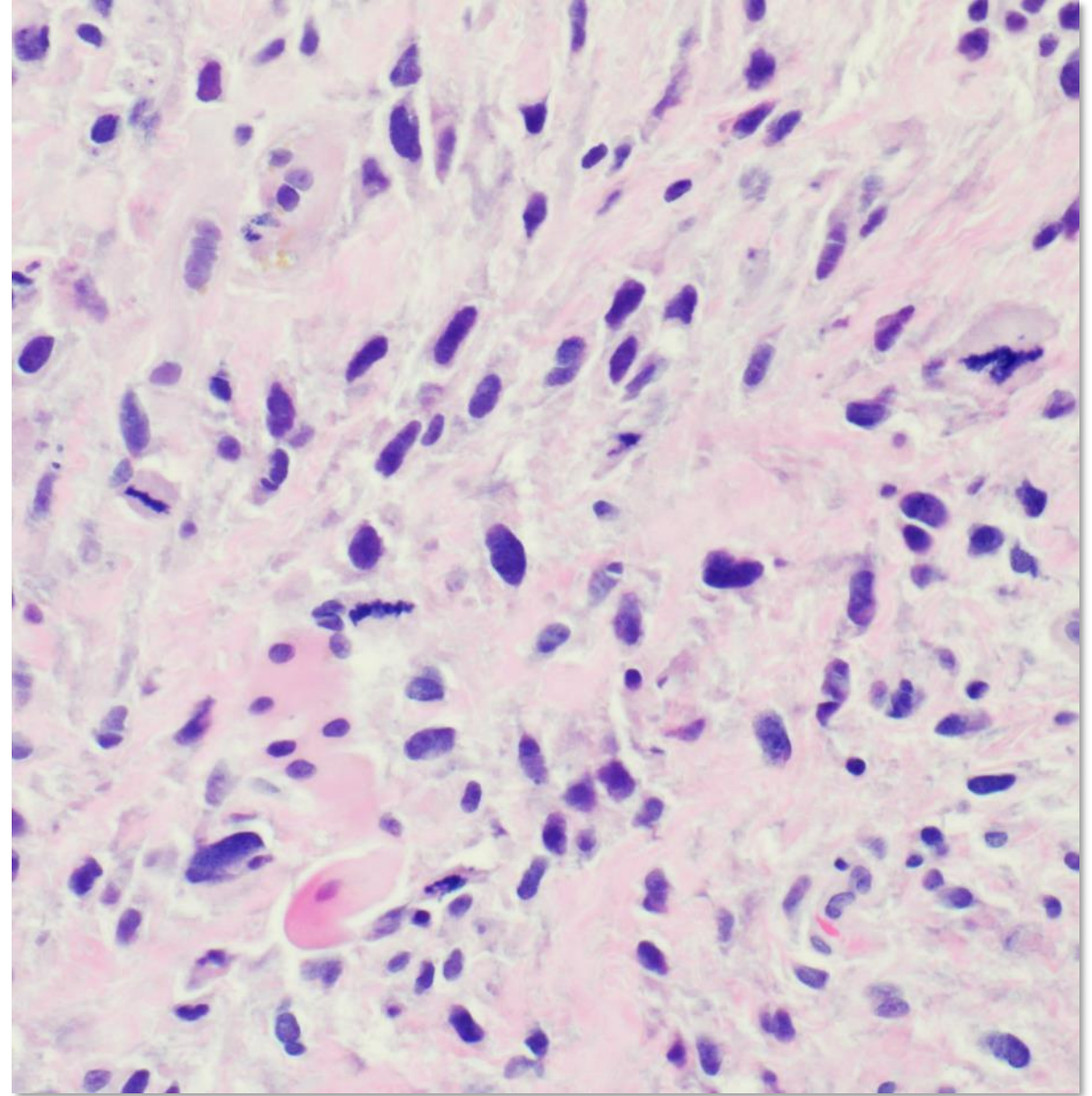
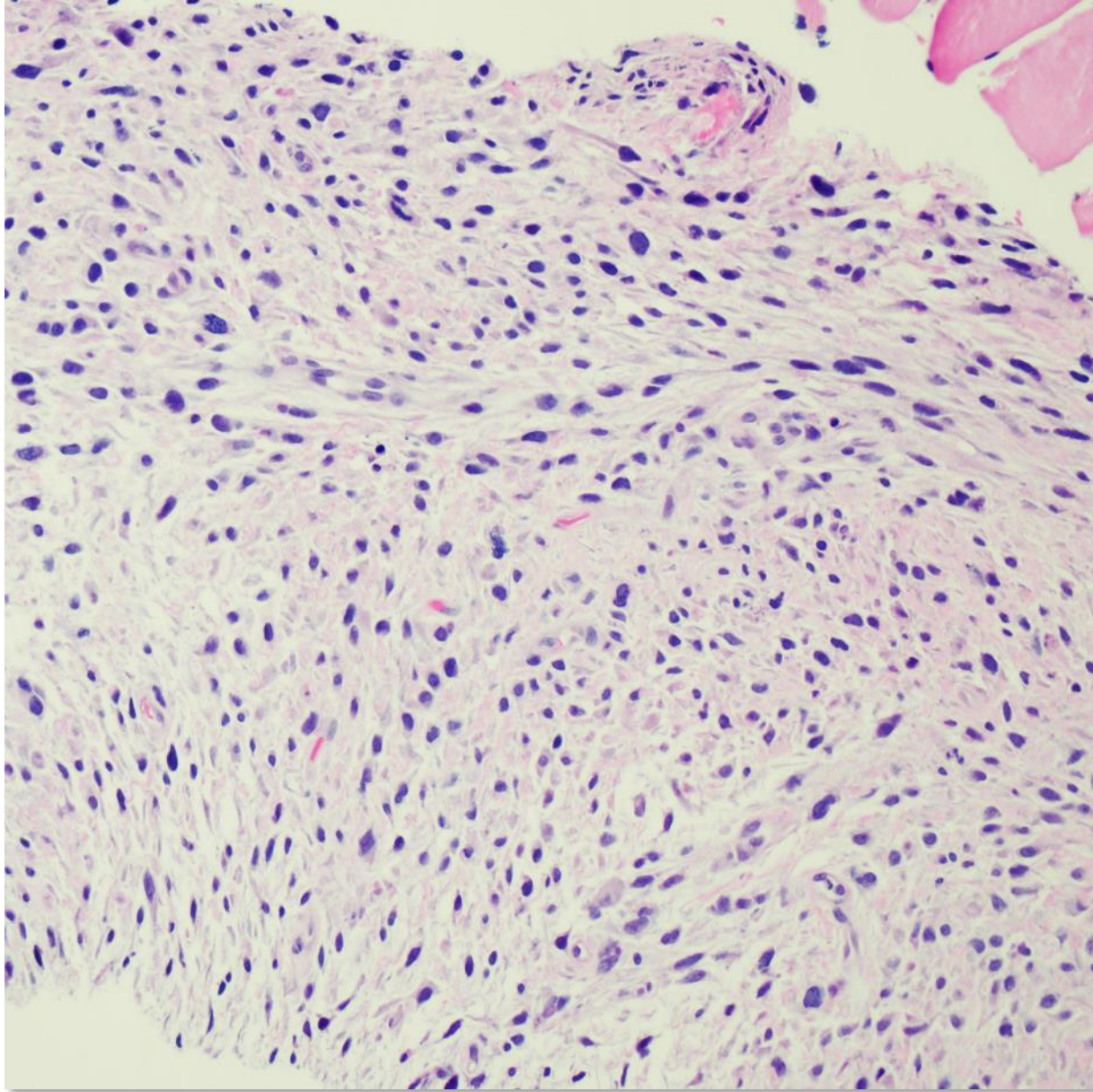
- 54 year old man with a right upper arm mass



# Case # 8 Touch Preparations



# Case # 8 Biopsies



# Case # 8- High Grade Pleomorphic Sarcoma (undifferentiated/unclassified)

## Epidemiology/Clinical features:

- Diagnosis of exclusion
- No identifiable line of differentiation with presently available technology
- May represent up to 25% of malignant sarcomas

## Site:

- Any location; somatic soft tissues

## Cytology:

- High grade features

## Histopathology:

- Descriptive: Pleomorphic (UPS), spindle cell, round, epithelioid

## Ancillary:

- No identifiable differentiation

## DDX:

- Pleomorphic liposarcoma, pleomorphic rhabdomyosarcoma, dedifferentiated liposarcoma, melanoma, sarcomatoid carcinoma

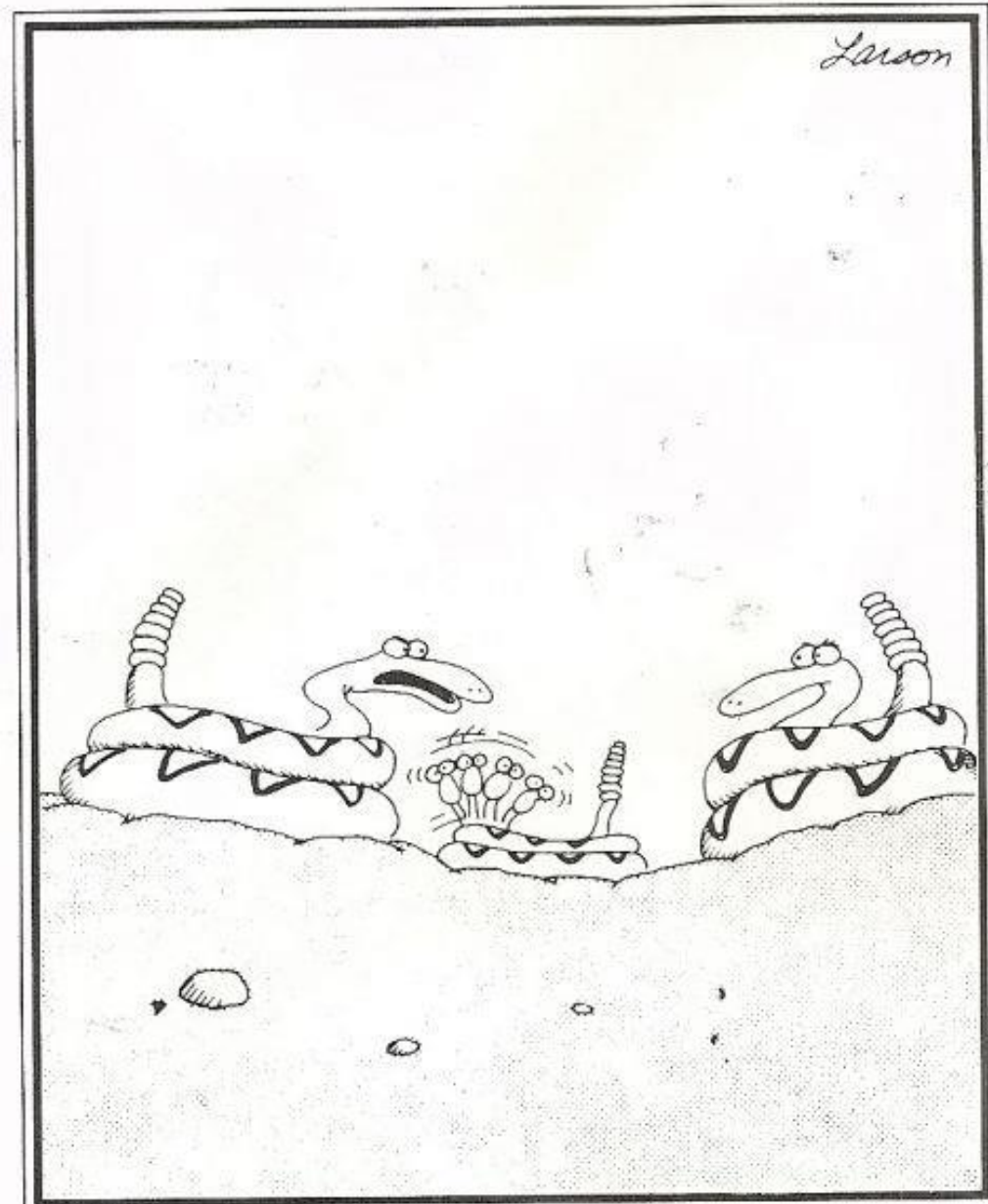


# Sarcoma Metastasis

- Sarcomas most often metastasize to the lungs
- Only a few sarcomas metastasize to lymph nodes:
  - **C**lear Cell Sarcoma
  - **A**ngiosarcoma
  - **R**habdomyosarcoma
  - **E**pithelioid Sarcoma
  - **S**ynovial Sarcoma

Positive Node? Don't forget melanoma and carcinoma!

# Thank You!



"This is your side of the family, you realize."

# References:

- Fletcher C, Bridge JA et al. WHO Classification of Tumors of Soft Tissue and Bone. Lyon (France), 2013.
- Cibas E, Ducatman, B. Cytology. 4th Ed. Philadelphia, PA: Elsevier, 2014
- Brown FM, Fletcher CD. Problems in grading soft tissue sarcomas. Am J Clin Pathol. 2000;114
- Weiss, Sharon W, and John R. Goldblum. Enzinger and Weiss' Soft Tissue Tumors. Philadelphia, PA: Elsevier, 2014