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

Michael Ward

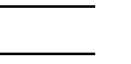
Feb 11th 2020

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

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	 **Malignant Sarcomas**
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	**Use a Descriptive Diagnosis:** "Pleomorphic" (UPS) "Spindled" "Epithelioid" "Round cell" *** Before you use this category make sure: 1- Not melanoma, lymphoma or carcinoma 2- Not a specific linage 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

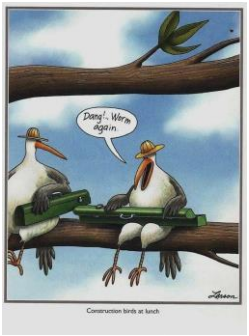
Soft tissue lesions (especially fibrous or vascular lesions) don't release many cells on FNA or touch prep, but seeing rare spindle cells is still helpful:

- 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 that 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)

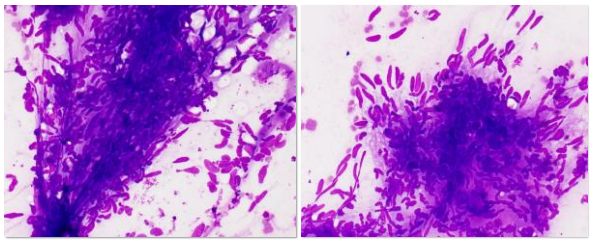


Construction birds at lunch

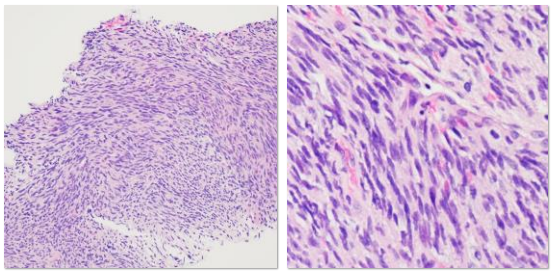
Case # 1

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

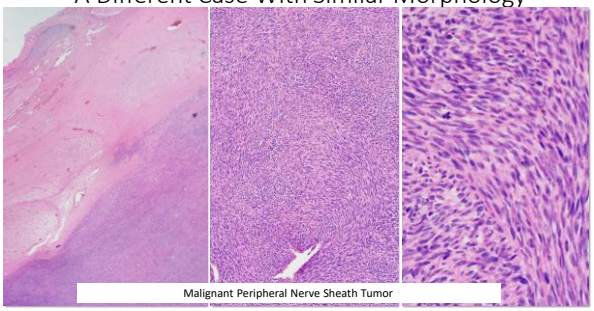
Cytology:
- High cellularity, clusters and dispersed cells, very monomorphic cells, bland nuclear features

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)

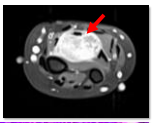
DDx:
- Leiomyosarcoma, MPNST, SFT, Ewing, Metastatic carcinoma, Carcinosarcoma

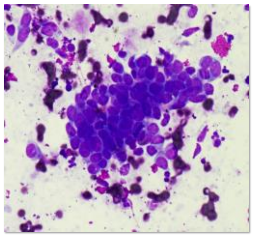
A Different Case With Similar Morphology

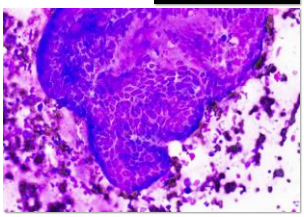


A Case of Biphasic Synovial Sarcoma

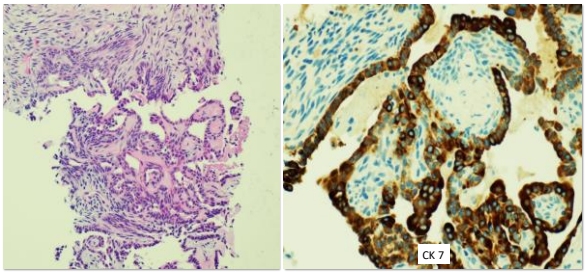
- 33 year old female
- 4 cm mass in deep flexor compartment of forearm







Biphasic Synovial Sarcoma



Sarcomas With True Keratin Expression?

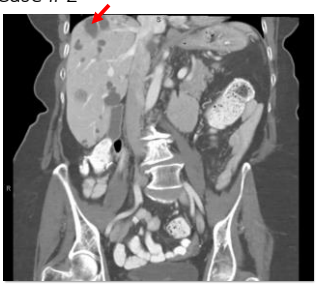
- Synovial Sarcoma
- Epithelioid sarcoma
- Desmoplastic Small Round Cell Tumor

- Remember any sarcoma may show nonspecific keratin expression
- Don't exclude sarcomatoid carcinoma when in/around a solid organ or lymph node

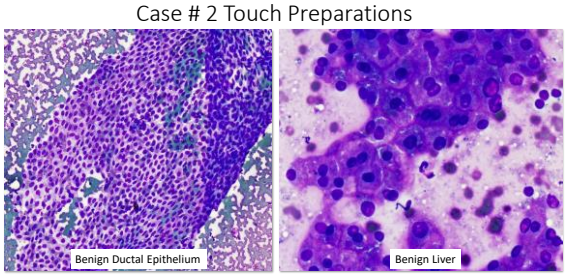
Case # 2

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

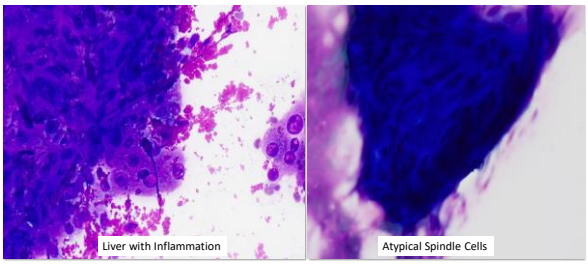
Imaging:
- Multiple liver masses



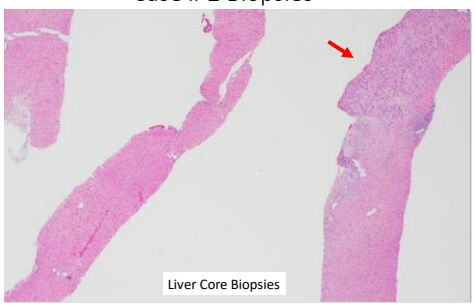
Case # 2 Touch Preparations



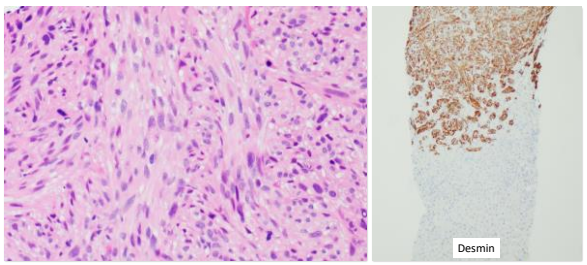
Case # 2 Touch Preparations



Case # 2 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

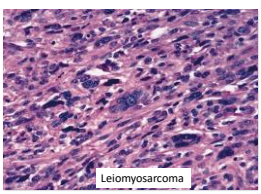
Chart compiled from WHO Bone and Soft Tissue 2013

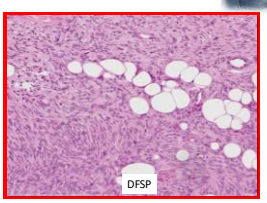
Adipose	Fibroblastic/ Myofibroblastic	Fibro-histiocytic	Smooth Muscle	Skeletal Muscle	Vascular	Neural	Uncertain Differentiation	Undifferentiated/ Unclassified
Lipoma	Nodular Fasciitis	Tenosynovial giant cell tumor: - Local - Diffuse	Leiomyoma	Rhabdomyoma	Hemangioma/ vascular malformation	Neuroma (Traumatic)	Myxoma	 **Malignant Sarcomas**
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 Perineurioma	Atypical Fibroxanthoma (AFX)	
	Solitary fibrous tumor						Myoepithelial tumor	**Use a Descriptive Diagnosis:** "Pleomorphic" (UPS) "Spindled" "Epithelioid" "Round cell"
							Synovial sarcoma	
							Epithelioid Sarcoma	
Well differentiated liposarcoma / Atypical lipomatous tumor	Dermatofibrosarcoma protuberans (DFSP)				endothelioma		Alveolar Soft Part Sarcoma	*** Before you use this category make sure:
Myxoid liposarcoma	Inflammatory myofibroblastic tumor (IMT)			Embryonal RMS			Clear cell sarcoma	1- Not melanoma, lymphoma or carcinoma
	Low grade fibromyxoid sarcoma			Alveolar RMS			Extra-skeletal myxoid chondrosarcoma	2- Not a specific linage 3- Not a de-differentiated sarcoma
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)	

What about a tumor with some muscle differentiation...but not quite leiomyosarcoma?

"High grade sarcoma with myogenic differentiation"

Which Lesion is Translocation associated?



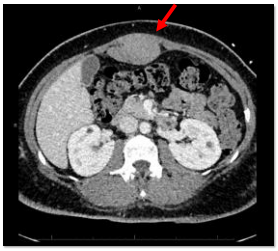


Translocation associated tumors tend to have a very monomorphic appearance

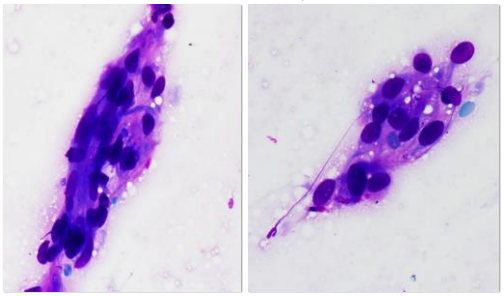
At the worm beach

Case # 3

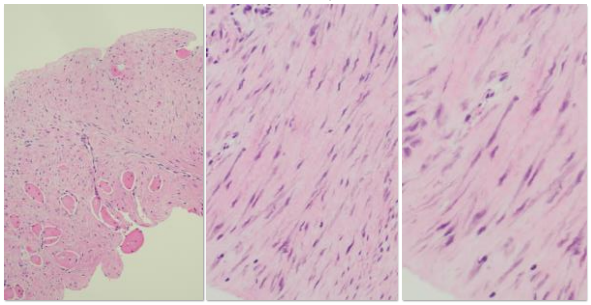
- History: 40 year old woman, recently pregnant mother of 5 children
- Imaging: well circumscribed 4 cm mass in midline anterior rectus abdominis muscle



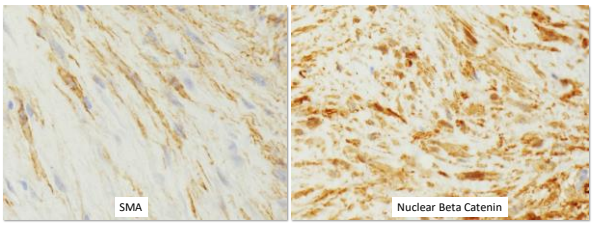
Case # 3 Touch Preparations



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

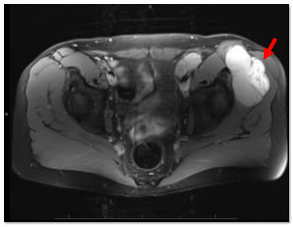
Ancillary:
- Nuclear (abnormal) Beta catenin (>75% of cases)
- Weak SMA positivity

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

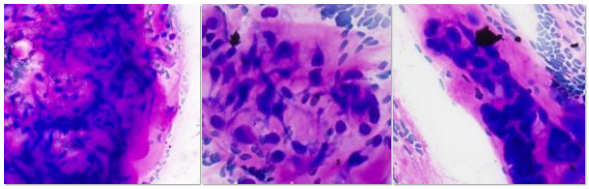
Case # 4

History:
- 53 year old man; slowly growing left hip mass

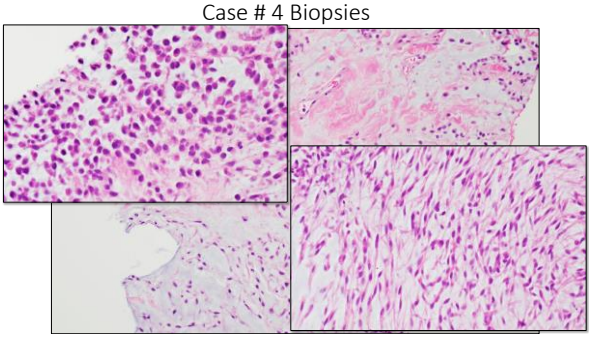
Imaging:
- 9.0 cm L hip mass in the gluteal muscles and abutting the anterior inferior iliac spine; no bone involvement; heterogeneous



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

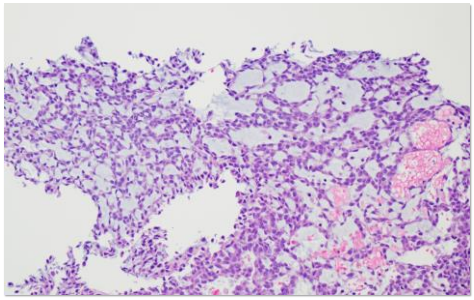
Site:
- Deep soft tissue of proximal extremities

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

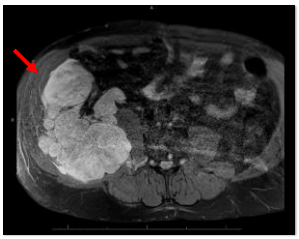
Ancillary:
- NR4A3 rearrangements are diagnostic (present in >90%)
- NR4A3 often rearranged with EWSR1

Another case of Extraskeletal Myxoid Chondrosarcoma

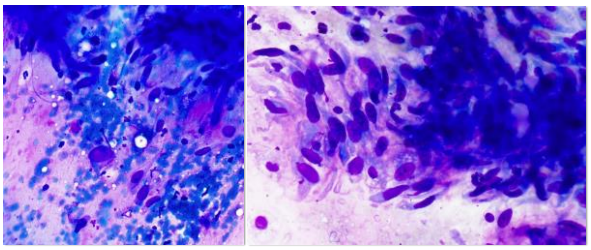


Case # 5

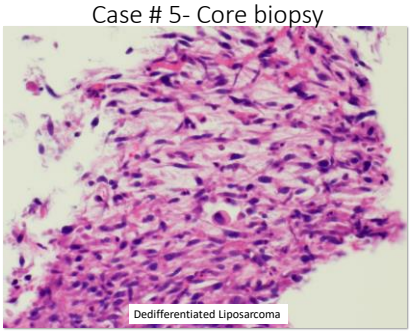
History:
- 58 year old man with a 17 cm right retroperitoneal mass



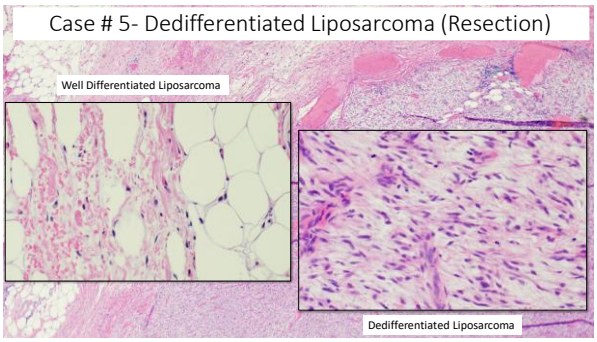
Case # 5- Touch Preparations



Case # 5- Core biopsy



Case # 5- Dedifferentiated Liposarcoma (Resection)



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

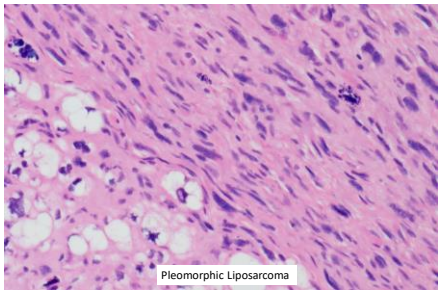
Cytology:
- Increased cellularity, hyperchromasia, atypia

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

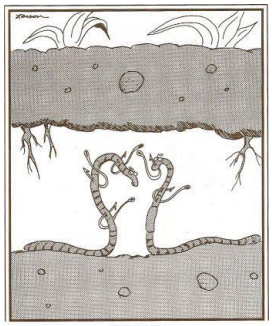
MDM2 Amplification in Problematic Lipomatous Tumors
Analysis of FISH Testing Criteria

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

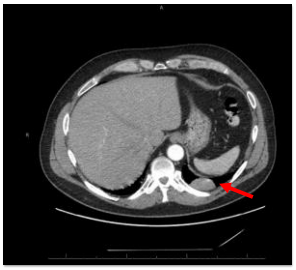


Punk worms

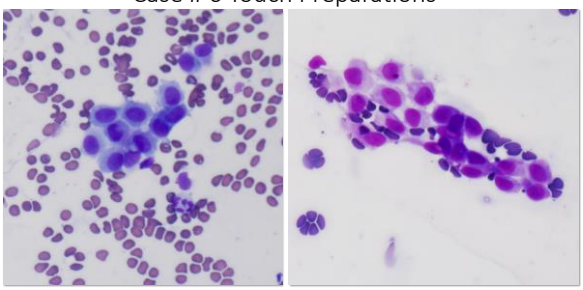
Case # 6

History:

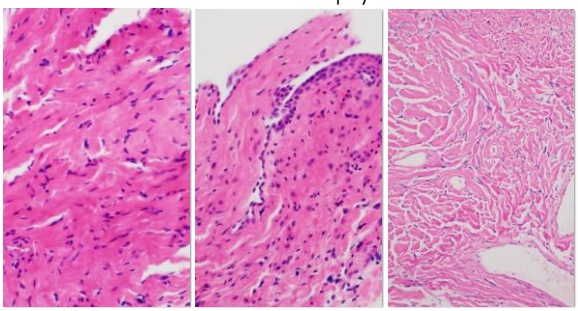
- 64 year old man with an incidentally discovered left lung pleural based lung mass
- Felt very hard upon percutaneous CT-guided needle core biopsy



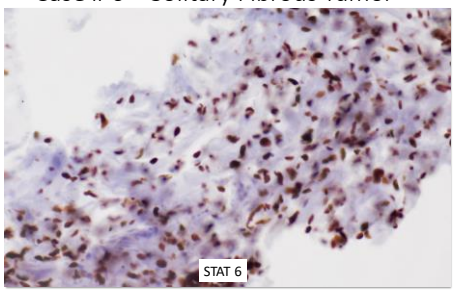
Case # 6 Touch Preparations



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 ropy collagen

Histopathology:
- Monomorphic spindle cells, ropy collagen bundles and staghorn-like (HPC-like) vessels

Ancillary:
- STAT6 and CD34 positive

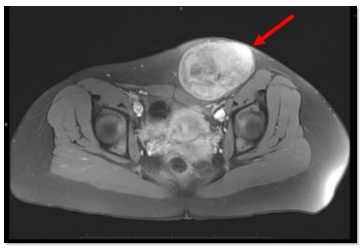
DDX:
- Low Grade Fibromyxoid sarcoma, Low Grade MPNST, Synovial Sarcoma, Desmoid, Desmoplastic Mesothelioma, Thymoma

CD 34 Positive Tumors

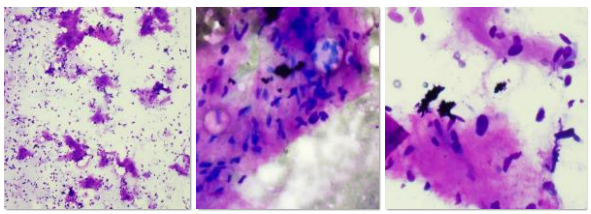
- Solitary Fibrous Tumor
- GIST
- Dermatofibrosarcoma Protuberans
- Angiosarcoma (blood vessels)
- Epithelioid Sarcoma
- Spindle Cell Lipoma

Case # 7

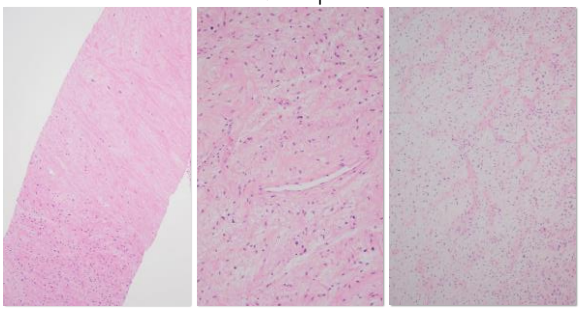
History: 18 year old female with a slowly enlarging left anterior abdominal wall mass



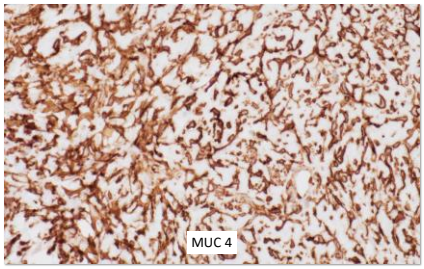
Case # 7 Touch Preparations



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

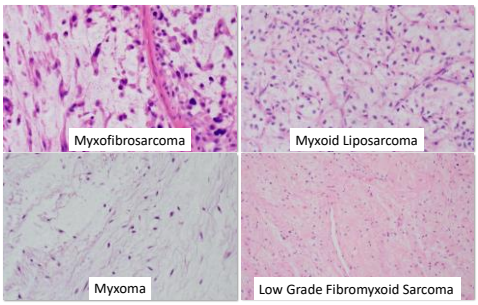
Histopathology:
- Bland whirling spindle cells, alternating collagenous and myxoid areas, curvilinear vessels
- Ancillary:
  - MUC4 positive
  - FUS-CREB translocation

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

Myxoid Lesions: Use the Vessels!

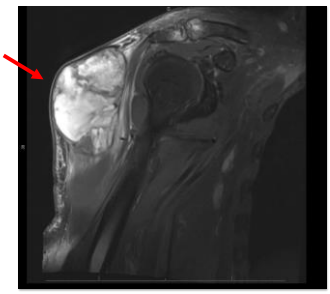
Tumor	Vessels	Other
Myxoid Liposarcoma	Chicken Wire	Bland spindle cells, lipoblasts, pulmonary edema-like areas
Myxoma	Virtually None	Bland stellate cells
Low Grade Fibromyxoid Sarcoma	Curvilinear	Younger people, MUC4+, FUS FISH+, low grade morphology
Myxofibrosarcoma	Curvilinear	Older people, Diagnosis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

Name That Myxoid Mass

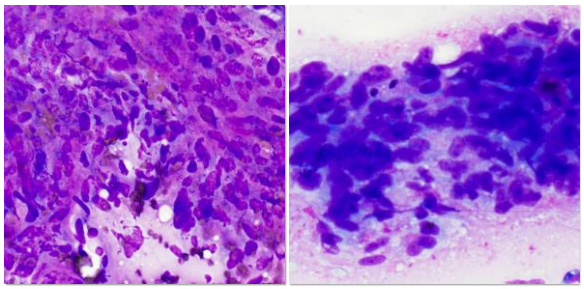


Case 8

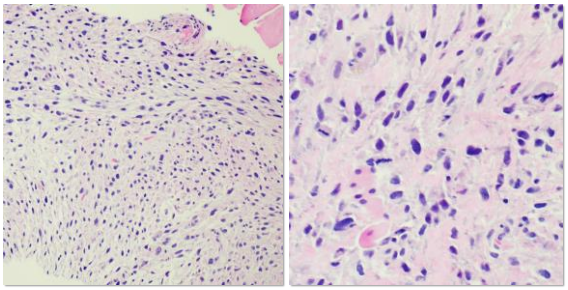
- 54 year old man with a right upper arm mass



Case # 8 Touch Preparations



Case # 8 Biopsies



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

Epidemiology/Clinical features:
- Diagnosis of exclusion
- No identifiably 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

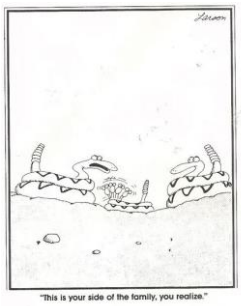
DDX:
- Pleomorphic liposarcoma, pleomorphic rhabdomyosarcoma, dedifferentiated liposarcoma, melanoma, sarcomatoid carcinoma

Sarcoma Metastasis

- Sarcomas most often metastasize to the lungs
- Only a few sarcomas metastasize to lymph nodes:
  - Clear Cell Sarcoma
  - Angiosarcoma
  - Rhabdomyosarcoma
  - Epithelioid Sarcoma
  - Synovial 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