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Mimics of Sarcoma

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Mimics of Sarcoma

**Reactive/’transiently neoplastic’**
- Nodular fasciitis
- Proliferative fasciitis
- Proliferative myositis
- Ischaemic fasciitis
- With heterotopic ossification
  - Ossifying fasciitis
  - Fibro-osseous pseudotumor
  - Myositis ossificans
  - Heterotopic mesenteric ossification
- Massive localised lymphedema of morbid obesity
- Reactive nodular fibrous pseudotumor

**Benign tumors with focal atypia**
- Pleomorphic fibroma
- Leiomyoma with bizarre nuclei
- Atypical cutaneous FH
- Atypical neurofibroma
- Cellular schwannoma
- Spindle and pleomorphic lipoma

**Benign tumors with diffuse atypia**
- Pleomorphic hyalinising angiectatic t.
- Atypical fibroxanthoma
- Atypical intradermal smooth muscle t.

**Non-mesenchymal tumors**
- Sarcomatoid carcinoma
- Melanoma
Benign/Malignant Discordance

2,425 patients

- 341 (14%) had received discordant diagnoses.
  - 124 benign tumors diagnosed as sarcomas
    - 14 (11%) fasciitis
    - 38 (31%) lipomas
  - 77 non-sarcoma malignancies diagnosed as sarcomas
    - 49 (64%) carcinoma
    - 12 (16%) melanoma
Nodular Fasciitis

- Young adults
- Limbs, HN, trunk
- Rapidly growing
- Up to 5 cm
- Dermal
- S/c, fascial
- Intramuscular
- Does not recur
Nodular Fasciitis
SMA

Nodular Fasciitis

calponin

h-caldesmon
Nodular Fasciitis

- $t(17;22)(p13;q12.3-13.1)$
- $USP6-MYH9$ fusion
- $USP6$ rearranged in 74% of NF
- Other partners identified
  - $RRBP1$
  - $CALU$
  - $CTNNB1$
  - $MIR22HG$
  - $SPARC$
  - $TSBH2$
  - $COL6A2$
  - $CDH11$

Erickson-Johnson 2011; Amary 2013; Oliveira 2014; Guo 2016; Patel 2017; Bekers 2018; Erber 2018
Nodular Fasciitis

- t(17;22)(p13;q12.3-13.1)
- USP6-MYH9 fusion
- USP6 rearranged in 74% of NF
- USP6 rearranged in
  - Cellular fibroma tendon sheath
  - Myositis ossificans
  - Aneurysmal bone cyst
  - Giant cell reparative granuloma of hands, feet
  - Fibro-osseous pseudotumor

Sukov 2008; Erickson-Johnson 2011; Amary 2013; Oliveira 2014; Guo 2016; Patel 2017; Bekers 2018; Erber 2018; Flucke 2018
Nodular Fasciitis

- Zonation
- Myxoid $\rightarrow$ cellular $\rightarrow$ fibrous
- Loose storiform, fascicular

- No nuclear pleomorphism
- Mitoses (normal)
- No necrosis

- Red blood cells, lymphocytes
- Small giant cells
Nodular Fasciitis
Differential Diagnosis

- Fibrous histiocytoma
- Fibromatosis
- Fibroma of tendon sheath
- Desmoplastic fibroblastoma
- Low grade myofibrosarcoma
- Leiomyosarcoma
- Myxofibrosarcoma
Cutaneous Fibrous Histiocytoma
Fibromatosis

Beta-catenin
Low-grade Myofibrosarcoma

Various copy number changes
No specific rearrangement
Nodular Fasciitis  Leiomyosarcoma

h-Caldesmon
Fasciitis: Subtypes

- Usual
  - nodular
  - cranial
  - intravascular
- Proliferative
- Ischemic
Proliferative Fasciitis

- Adults 40-70, M = F
- Forearm, thigh
- Rapid growth
- < 5cm
- Trauma in 30%
- Self-limiting
Proliferative Myositis

- Desmin negative
- CK negative
- S100pr negative
- CD34 negative
- CD31 negative
Proliferative Fasciitis/Myositis
Differential Diagnosis

- Carcinoma
- Rhabdomyosarcoma
- Melanoma
- Epithelioid sarcoma
- ES-like (pseudomyogenic) hemangioendothelioma
Ischemic Fasciitis

- F =M, 15-95 years
- Immobilization, trauma
- Shoulder, back, buttock
- Sacrum, greater trochanter
- No ulcer – deep subcutis
- Painless mass 1 – 8 cm
- Rarely recurs

Montgomery 1992; Perosio 1993; Liegl 2008
Ischemic Fasciitis

- Lobular, zonal
- Fibrinoid necrosis
- Myxoid stroma
- Ectatic thin vessels
- Atypical fibroblasts
- SMA, desmin, CD34
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Non-mesenchymal tumors
- Sarcomatoid carcinoma
- Melanoma
Ossifying Fasciitis
Fibro-osseous Pseudotumor of Digits

- Adults, history of trauma
- Fingers (I,M)> toes, prox phalanx
- Rarely other sites e.g. wrist
- Dermis, subcutis
- NF-like background, mitoses
- Bony trabeculae, cartilage
- Can stabilise or regress
- USP6 rearranged

Dupree 1986; De Silva 2003; Moosavi 2008; Chaudhry 2010; Flucke 2018
Myositis Ossificans

- Young adults, M>F
- Rapid growth, trauma history
- Proximal limbs, trunk
- Zoning – peripheral bone
- Metaplastic bone, giant cells, cartilage
- *USP6-COL1A1* fusion – ABC of soft tissue

De Silva 2003; Sukov 2008; Bekres 2018; Flucke 2018
Myositis Ossificans
Heterotopic Mesenteric Ossification

- Males, mean 49 years
- Prior surgery or trauma
- Mesentery, omentum
- Obstruction, sepsis
- Fat necrosis
- Bone, lace-like osteoid
- Cartilage

Wilson 1999; Patel 2006
Extraskeletal Osteosarcoma

- Older adults, extremities
- Some post radiation
- Some in DDL, MPNST, carcinoma
- Subcutaneous or subfascial
- Aggressive
- Histologic subtypes as in bone
Massive Localised Lymphoedema of Morbidly Obese

- Adults, mean 47 years
- Mean body weight 186 kg
- Thigh, leg, genitalia, abdominal wall
- Some had lymphadenectomy
- Ill-defined mass, mean 33cm, 7.4 kg
- Can persist or recur
- Rarely \(\rightarrow\) angiosarcoma

Farshid 1998; Manduch 2009; Shon 2011
Massive Localised Lymphedema of Morbidly Obese

Atypical Lipomatous Tumor/WDL
Massive Localised Lymphedema of Morbidly Obese

- Lobules of mature fat
- Expanded connective tissue septa
  - fine, fibrillary collagen
  - edema fluid
  - uniformly distributed fibroblasts
- Capillaries at interface
- No atypia
Reactive Nodular Fibrous Pseudotumor

- Can be sequel of surgery
- M > F, > 45 years
- Solitary or multiple, 3-10 cm
- Mesentery
- Surface of bowel, pancreas
- Up to 10 cm
- No recurrence

Yantiss 2003; Daum 2004
Reactive Nodular Fibrous Pseudotumor
Reactive Nodular Fibrous Pseudotumor

- Microscopic infiltration
- Bland fibroblasts
- Intersecting fascicles
- Focally keloidal
- Peripheral lymphoid aggregates
- SMA+, desmin+ in some
- CD117 ± (no mutations)
- Beta catenin negative
Atypical Cutaneous Fibrous Histiocytoma

- Extremities
- Polypoid nodule, plaque
- Dermis, superficial subcutis
- Focal pleomorphism
- Atypical mitoses
- Focal SMA, rarely CD34
Atypical Cutaneous Fibrous Histiocytoma
Atypical Fibroxanthoma
Pleomorphic Dermal Sarcoma

- M>F, sun-damaged skin, head.
- NOTCH1/2, FAT1 mutations
- Pleomorphic spindle and polygonal cells
- Atypical mitoses, necrosis
- Invasive into deep s/c, fascia, muscle
- Perineurial, lymphatic invasion
- 28% recurred, 10% metastasised
- Margin status predictive

Miller 2012
Malignancy in Neurofibroma

- Change in morphology
- Widespread atypia
- Cellular crowding
- Mitoses $>1/10$ per 10hpf
- Necrosis
- S100 protein loss
Cellular Schwannoma

- Middle aged females
- Mediastinum, R/P, pelvis
- Visceral locations
- Not associated with NF-1
- Attached to nerve
- Encapsulated, up to 19 cm
- Erodes bone, can recur

Woodruff 1981; White et al, 1990; Casadei et al, 1995
Cellular Schwannoma
Cellular Schwannoma

- Leiomyoma
- Leiomyosarcoma
- Synovial sarcoma
- Pleomorphic hyalinising angiectatic tumor
- MPNST
Pleomorphic Hyalinising Angiectatic Tumour
Pleomorphic Hyalinising Angiectatic Tumour

- Lobulated, infiltrative
- Pleomorphic nuclei, scarce mitoses
- Intranuclear inclusions
- Pseudolipoblasts
- Ectatic vessels, hemosiderin
- Hyalinization, mast cells
- CD34+, S100 pr –
Pleomorphic Hyalinising Angiectatic Tumor

Analysis of 41 Cases Supporting Evolution From a Distinctive Precursor Lesion

Andrew L. Folpe, MD and Sharon W. Weiss, MD

Abstract: The pleomorphic hyalinizing angiectatic tumor (PHAT) is a rare, low-grade neoplasm that features atypical stromal cells containing hemosiderin, partially thrombosed ectatic vessels with circumferential hyalinization, and a variable inflammatory infiltrate. Over the years, we have occasionally observed a monomorphic partially myxoid spindle cell component (provisionally termed “early PHAT”) co-existing with classic PHAT. In some instances, this

Key Words: pleomorphic hyalinizing angiectatic tumor


The pleomorphic hyalinizing angiectatic tumor is a rare tumor of uncertain lineage described by
Hemosiderotic Fibrolipomatous Tumor
Malignant Peripheral Nerve Sheath Tumor
Cellular Schwannoma vs MPNST

- Not associated with NF-1
- Capsule
- Atypia focal
- S100 protein & SOX10 uniformly +
- EMA+ perineurial cells
- H3K27Me3 retained
Malignancy in Schwannoma

- Atypical epithelioid cells
  - abundant cytoplasm
  - vesicular chromatin
  - prominent nucleoli
  - single, cluster, nodule
- Epithelioid MPNST
  - S100 protein +
  - SOX10 +
  - H327Kme3 +
  - INI1 lost 50%
- Angiosarcoma (epithelioid)

Woodruff, 1994; Trassard, 1996; Mentzel, 1999; Ruckert, 2000; McMenamin 2001
Benign Smooth Muscle Tumors

- Cutaneous leiomyoma
  - regular
  - genital-type
- Vascular leiomyoma
- Deep leiomyoma
  - somatic
  - retroperitoneal

- Leiomyomatosis peritonealis
- Intravascular leiomyomatosis
- Benign metastasing leiomyoma
Cutaneous ‘Leiomyosarcoma’
Atypical Intradermal Smooth Muscle Tumor

- M>F
- Trunk, lower limb
- Confined to dermis
- Infiltrative growth pattern
- Mean mitotic index 4.7/10 hpf
- 97% grade 1 (3% necrosis)
- 35% recurred, 0% metastasised
  - margin status predictive
Deep Leiomyoma

- <4% of benign STT
- Slowly growing
- Circumscribed
- Rarely recurrent
- Never metastatic

Myhre-Jensen, 1981
Deep Leiomyoma
Deep Leiomyoma

- Fascicles of spindle cells
- Clear or epithelioid cells
- Myxoid change
- Cyst formation
- Calcification
- Hyalinization
- Fatty component
Deep Leiomyoma

SOMATIC
• Males = Females
• In limbs
• 0.6 - 12.5 cm
• Vessel wall
• No recurrence
• No metastases

RETROPERITONEAL
• Predominantly females
• RPM, pelvis
• Up to 31 cm
• Resembles fibroid
• 2% recur
• No metastases

Kilpatrick 1992; Billings 2001; Paal 2003
Deep Leiomyoma: Retroperitoneal
# Criteria of Malignancy - SMT

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*Billings 2001; Paal 2003*
Sarcomatoid Carcinoma vs Sarcoma

- Organ-based – not sarcoma!
- In situ component
- Epithelial component
- Heterologous elements
- CK positive
Synovial Sarcoma vs Sarcomatoid Ca:

- No in situ component
- Not pleomorphic
- CK more focal
- Bcl-2, CD56 positive
- Mast cells
- SS18 rearrangement
Spindle Cell Melanoma vs MPNST

- Junctional component
- S100pr, SOX10 widespread
- Both lack melanoma Ags
- BRAF, NRAS mutation
Conclusions

• Be aware of the clinical history
  • location
  • duration
  • rate of growth
  • antecedent event
• Be familiar with the diagnostic possibilities
• Seek a further opinion
THE END