“Reactive” myofibroblastic proliferations: Nodular fasciitis and beyond.

Andrew Horvai, MD, PhD
Associate Clinical Professor, Pathology

Disclosures
I have nothing to disclose.

Outline

- Introduction
- Nodular fasciitis
  - Classic
  - Morphologic variants
- Related tumors
  - Ischemic fasciitis
  - Proliferative fasciitis
  - Myositis ossificans
  - Intra-abdominal myofibroblastic proliferations
  - Visceral tumors
    - "Post-operative spindle cell nodule"
    - Inflammatory myofibroblastic tumor (IMT)
- Recent developments

Nodular fasciitis is...

1. A reactive proliferation of myofibroblasts and inflammatory cells
2. A pseudoneoplastic proliferation of myofibroblasts
3. A low-grade mesenchymal neoplasm
4. An inflammatory pseudotumor
5. An infectious process
History

- Rapid growth over <2 weeks, benign course after excision
- Mucoedematous stroma
- Tissue culture growth: cells anastomose by attenuated tips
- Plump myofibroblast like cells, vesicular hyperchromatic nuclei, sizeable nucleoli


Nodular fasciitis

- Clinical
  - Age: Peak 20-40
  - Growth: Rapid (weeks/months)
  - Antecedent trauma: ~50%
  - Spontaneous resolution >98%
  - Recurrence <1% (re-evaluate those!)
- Gross
  - Size: Usually < 5 cm
  - Circumscribed of infiltrative depending on location
- Low power
  - Zonation
  - No characteristic vascular pattern
  - Tissue culture growth
- High power
  - "Reactive myofibroblast" + lymphocytes
  - Brisk mitotic activity
  - Microcysts, extravasated RBC
- Absent
  - Nuclear hyperchromasia, atypical mites, neutrophils, necrosis
Tissue culture growth pattern

Microcysts, extravasated RBC

Nodular fasciitis
Fasciitis. Not always nodular

Giant cells (osteoclast-type)

Nodular fasciitis

Myxoid nodular fasciitis
Intravascular fasciitis

Immunohistochemistry

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Smooth muscle actin

Immunohistochemistry: pitfalls

SMA
Differential diagnosis

- Superficial
  - Dermatofibroma / benign fibrous histiocytoma
  - Myxofibrosarcoma (myxoid “MFH”)
- Deep
  - (Cellular) Myxoma
  - Desmoid fibromatosis
  - Inflammatory myofibroblastic tumor (IMT) and related lesions
  - Leiomyosarcoma
  - Myofibroblastic sarcoma

Dermatofibroma / BFH

Myxofibrosarcoma
Myxoma

Cellular myxoma

Desmoid-type fibromatosis

Desmoid-type fibromatosis
Inflammatory myofibroblastic tumor

Leiomyosarcoma

Leiomyosarcoma

Myofibroblastic sarcoma
Myofibroblastic sarcoma

Immunohistochemistry summary

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Other myofibroblastic proliferations

- Proliferative fasciitis / myositis
- Ischemic fasciitis
- Myositis ossificans
- Visceral tumors
  - Intra-abdominal myofibroblastic proliferations
  - Inflammatory myofibroblastic tumor (IMT)
  - “Post-operative spindle cell nodule”

Proliferative fasciitis/myositis

- Clinical
  - Mean age 50
  - Fasciitis – extremities
  - Myositis – trunk, shoulder girdle
  - Rapid growth
- Gross
  - Infiltrative
  - Scar-like
  - Myositis can be large, 10cm+
  - Low power
    - Ill defined tentacles of tumor into fat, fascia or muscle
    - Myositis: “checkerboard” pattern of entrapped myocytes
  - High power
    - Nodular fasciitis myofibroblasts
    - Ganglion-like cells (amphophilic cytoplasm, macronucleoli)
Ischemic fasciitis

- Clinical
  - Elderly, peak 70-80s
  - Immobilized or disabled
  - Benign
- Gross
  - Large (up to 15 cm), ovoid mass
  - Circumscribed or infiltrative
- Low power
  - Zonation:
    - central fibrinoid degeneration, necrosis
    - Fasciitis layer
    - Reactive periphery: fat necrosis, vascular thrombi
- High power
  - "Reactive myofibroblast" + ganglion-like + lymphocytes
  - Variable mitotic activity, no atypical forms
  - More vascular than nodular fasciitis
Myositis ossificans

- Clinical
  - Young adults, wide age range
  - Rapid onset
  - Trauma <50%
- Gross
  - Small, < 5 cm
  - Calcifications or dense bone depending on chronicity
- Low power
  - Zonation
    - Bone peripheral with osteoblastic activity
    - Nodular fasciitis centrally
- High power
  - Nodular fasciitis myofibroblasts
  - Woven to lamellar bone with benign osteoblasts
  - Hyaline cartilage with endochondral ossification (fracture callus)
- Synonyms: Florid reactive periostitis, Fibro-osseous pseudotumor of the digits

Most mature, calcified, dense bone is at periphery
Myositis ossificans or extraskeletal osteosarcoma?

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<td>Mitotic activity</td>
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Extraskeletal osteosarcoma

- Clinical
  - Mesentery, hollow viscera
  - Recent surgery or instrumentation in <50%
  - Bowel obstruction, mass, hematuria
- Gross
  - Can be large >5 cm
- Low power
  - Infiltrative
  - Entrap muscularis mucosa and propria
- High power
  - Zonation not prominent
  - Microcysts rare
  - Nodular fasciitis-like myofibroblasts
  - Proliferative fasciitis-like ganglion cells
  - Bone or cartilage rarely present

Visceral myofibroblastic proliferations

- Clinical
  - Mesentery, hollow viscera
  - Recent surgery or instrumentation in <50%
  - Bowel obstruction, mass, hematuria
- Gross
  - Can be large >5 cm
- Low power
  - Infiltrative
  - Entrap muscularis mucosa and propria
- High power
  - Zonation not prominent
  - Microcysts rare
  - Nodular fasciitis-like myofibroblasts
  - Proliferative fasciitis-like ganglion cells
  - Bone or cartilage rarely present
Visceral myofibroblastic proliferation

Inflammatory myofibroblastic tumor (IMT)

- Clinical
  - Children, wide range
  - Mesentery and viscera
  - Systemic symptoms: fever, weight loss
  - 30% recur, Metastases <2% (unpredictable)
- Gross
  - Large, average 6 cm
- Low power: 3 patterns
  1) Loose, nodular fasciitis-like
  2) Compact spindle cell, fibromatosis-like
  3) Hypocellular, fibroma-like
- High power
  - Myofibroblasts similar to fasciitis
  - Necrosis, acute inflammation more common than NF
  - Nuclear hyperchromasia and pleomorphism > NF
  - Immuno: Keratin, SMA, desmin, ALK (50%)
  - Genetics: ALK (2p23 rearrangement) especially in children
ALK expression in IMT

IMT: fasciitis-like

IMT: fibromatosis-like

IMT: inflammation

ALK expression in IMT

2p23
TPM3:ALK, RANBP2:ALK & others
Postoperative spindle cell nodule or pseudosarcomatous myofibroblastic proliferation or IMT?

Pseudosarcomatous Myofibroblastic Proliferations of the Bladder: A Clinicopathologic Study of 42 Cases

Inflammatory Myofibroblastic Tumors of the Urinary Tract: A Clinicopathologic Study of 46 Cases, Including a Malignant Example Inflammatory Fibrosarcoma and a Subset Associated With High-grade Urothelial Carcinoma

ALK expression in pseudosarcomatous myofibroblastic proliferations of the genitourinary tract

M S Hiller, P Shah, O & A R Debnath
Department of Pathology, Brigham and Women’s Hospital and Harvard Medical School, Boston, MA, USA
**Pseudosarcomatous myofibroblastic proliferation vs. IMT**

<table>
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<tr>
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**IMT vs. Nod Faciitis**

- **Inflammatory myofibroblastic tumor**
  - Recurrence potential, rare metastasis
  - Sometimes in response to trauma
  - Rapid growth, mitotic activity
  - Reproducible immunophenotype
  - Clonal with genetic abnormality

- **Nodular fasciitis**
  - No recurrence potential, spontaneous regression
  - Sometimes in response to trauma
  - Rapid growth, mitotic activity
  - Reproducible immunophenotype
  - Clonal?

**Nodular fasciitis: Transient neoplasia**

- USP6 overexpressed in 44/48 cases
- MYH9-USP6 fusion in 12/16 cases
- Absent in proliferative fasciitis/myositis
- USP6 de-ubiquitinating enzyme, possibly oncogenic
  - Translocations also in ABC
- MYH9 non-muscle myosin, cell motility
- "Transient neoplasia"


**Take-home messages**

- Nodular fasciitis is a benign, self-limited myofibroblastic proliferation
- It remains to be defined whether nodular fasciitis is a true neoplasm but this distinction is clinically irrelevant
- Clinical history, H&E findings and location are most important to separate nodular fasciitis for mimics
- Inflammatory myofibroblastic tumor is a more aggressive tumor with recurrence and rarely metastatic potential
- The term inflammatory pseudotumor should be avoided since it does not convey a specific diagnosis