Myxofibrosarcoma, fibromyxoid sarcoma, or myxofibro-something

Refinement or redundancy in soft tissue tumor pathology?

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Outline

- Quiz !
- Mesenchymal lesions with a « myxo-fibro » appearance
- Clinicopathologic features of the most relevant « myxo-fibro» entities
- Differential diagnostic approach
- Conclusions, take home messages
- Quiz (results)…..
QUIZ !
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What is your diagnosis?
QUIZ 2: 7 cm, well-demarcated, slowly-growing, intramuscular mass in the thigh of a 32 year-old male
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What is your diagnosis?
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What is your diagnosis?
Mesenchymal lesions with a « myxofibro » appearance

- Superficial acral fibromyxoma
- Cutaneous myxoma / Superficial angiomyxoma
- Cellular myxoma / Juxtaarticular myxoma
- Ossifying fibromyxoid tumor
- Myxofibrosarcoma (low- & intermediate grade variants)
- Low-grade fibromyxoid sarcoma / hyalinizing spindle cell tumor with giant rosettes
- Inflammatory myxohyaline tumor (myxoinflammatory fibroblastic sarcoma)
Mesenchymal lesions with a « myxofibro » appearance

« Myxofibro » areas observed occasionally

- Soft tissue perineurioma (myxoid variant)
- Desmoplastic fibroblastoma (collagenous fibroma)
- Myxoid neurofibroma
- Myxoid spindle cell lipoma (dendritic fibromyxolipoma)
- Ancient fibrohyalinized nodular fasciitis
- Giant cell fibroblastoma
- Deep « aggressive » angiomyxoma
- Desmoid tumor
- Solitary fibrous tumor (myxoid variant)
- Low-grade malignant peripheral nerve sheath tumor
- Dedifferentiated liposarcoma
- Pleomorphic liposarcoma
- Sclerosing epithelioid fibrosarcoma
Salient clinicopathologic features of the most relevant entities
Superficial Acral Fibromyxoma

**Key features**
- Described in 2001 by Fetsch *et al.* *(Hum Pathol)*
- Middle-aged adults
- Sites:
  - Superficial soft tissues of distal extremities (fingers, palm, toes)
  - Tends to involve the nail region
- Size: 1-2 cm
- Benign lesion. Recurrence rate <5%
Superficial acral fibromyxoma
Superficial acral fibromyxoma
Superficial Acral Fibromyxoma

- **Immunohistochemistry**
  - CD34 positivity (90% of cases)
  - CD99 + (80%)
  - EMA + (70%)
  - Usually negative for smooth muscle actin, desmin, keratins, and S100 protein
Superficial acral fibromyxoma

CD34

CD99
• Differential diagnosis
  – Low-grade sarcomas +++
    • Low to intermediate-grade myxofibrosarcoma
    • Low-grade fibromyxoid sarcoma
    • Low-grade MPNST
    • Acral myxoinflammatory fibroblastic sarcoma
    • Myxoid variant of dermatofibrosarcoma protuberans
  – Benign lesions
    • Sclerosing perineurioma, Periungueal fibrokeratoma, Myxoid fibrous histiocytoma, Cutaneous myxoma, Superficial angiomyxoma
Sclerosing/myxoid perineurioma
• Key features
  – Described in 1987 by Harry Evans
  – Young adults (median 35 yrs); M>F
  – Long-standing, painless mass
  – Deep soft tissue of limbs (thigh +++), limb girdles, trunk
  – Cytogenetics: t(7;16) (q33;p11) FUS/CREB3L2 (90%) or t(11;16) (p11;p11) FUS/CREB3L1 (10%)
  – Local recurrence: 10% (if the lesion is correctly excised \textit{ab initio})
  – Metastatic rate: 5-10% (lungs, pleura, bone) if F-U <5 years, 70% if F-U > 8-10 years
Low-grade fibromyxoid sarcoma
Low-grade fibromyxoid sarcoma
Low-grade fibromyxoid sarcoma
Low-grade fibromyxoid sarcoma
Hyalinizing spindle cell tumor with giant rosettes: a variant of LGFMS
LGFMS, fibroma-like variant

LGFMS, cellular variant
LGFMS resembling a low-grade myxofibrosarcoma
LGFMS with epithelioid features, resembling sclerosing epith. fibrosarcoma
Low-grade fibromyxoid sarcoma

- Immunohistochemistry
  - EMA + : 80%
  - CD99 + : 80%
  - Bcl-2 + : 80%
  - CD34: negative
  - S100: negative
  - SMA: negative
  - Desmin: negative
  - Keratins: negative
Low-grade fibromyxoid sarcoma

[Images showing EMA and CD34 staining for fibromyxoid sarcoma]
Low-grade fibromyxoid sarcoma

- **Differential diagnosis**
  - Perineurioma +++ , fibroma, neurofibroma
  - Desmoid tumor +++
  - Low-grade myxofibrosarcoma +++
  - Low-grade MPNST +++
  - Cellular myxoma (for predominantly myxoid lesions) ++
  - Sclerosing epithelioid fibrosarcoma (for predominantly epithelioid lesions)
  - Leiomyoma & metastatic low-grade endometrial stromal sarcoma (if giant rosettes present)
Soft tissue perineurioma
Cellular myxoma
Low- and intermediate-grade myxofibrosarcoma

• **Key features**
  - Previously called « myxoid MFH »
  - Elderly (median 60 yrs); M>F
  - Superficial : 60%
  - Sites: limbs (lower extrem. +++), limb girdles
  - Size: 5-7 cm
  - Behavior: depends on histologic grade and extent of resection
  - Recurrence rate: 50% (often due to inadequate excisions) – upgrading possible in recurrences
  - Metastases rare in low-grade lesions (lungs, bone): 5-15% , often occurring after multiple recurrences
  - 5-yr disease specific survival rate: >95%
Low-grade myxofibrosarcoma
Low to intermediate-grade myxofibrosarcoma
Low to intermediate-grade myxofibrosarcoma
Low-grade myxofibrosarcoma
Intermediate-grade myxofibrosarcoma
Low- and intermediate-grade myxofibrosarcoma

- Immunohistochemistry

Of no help!
• Differential diagnosis

• Myxoma / Cellular myxoma
• Nodular fasciitis (myxoid variant)
• Low-grade fibromyxoid sarcoma
• Myxoid liposarcoma (if plexiform vessels numerous)
Recognized as a distinct entity in 1998 by two different teams who coined two different terms:


Inflammatory myxohyaline tumor
(Acral myxoinflammatory fibroblastic sarcoma)

• Key features
  – Adults
  – Distal extremities (hand, wrist, foot, ankle). Upper extremities, especially fingers and hands, more frequently affected
  – Often mistaken clinically for a ganglion cyst or tenosynovitis
  – Tumor size: 3-4 cm on average with a gelatinous, multinodular gross appearance
  – Situation: subcutis or deep soft tissues, involving tendon sheaths and the synovium of adjacent joints
Inflammatory myxohyaline tumor (Acral myxoinflammatory fibroblastic sarcoma)

- **Key features** (continued)
  
  - Recurs in about 20% of cases

  The high proportion - 67% - of recurrent cases reported by Meis-Kindblom et al. is probably related to incomplete excisions due to erroneous diagnoses of benignity

  - Metastasizes in less than 5% of cases
Inflammatory myxohyaline tumor
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Inflammatory myxohyaline tumor
(Acral myxoinflammatory fibroblastic sarcoma)

- **Immunohistochemistry**
  - Positivity for vimentin and CD68
  - Occasional reactivity for CD34, smooth muscle actin, and/or cytokeratin
Inflammatory myxohyaline tumor (Acral myxoinflammatory fibroblastic sarcoma)

- **Differential diagnosis**
  - if the inflammation predominates inflammatory processes such as chronic tenosynovitis, inflammatory pseudotumor, mucoid pseudocyst with superimposed inflammatory changes
  - if multinucleated giant cells are numerous giant cell tumor of tendon sheath
  - if cellular atypia predominate malignant tumors such as myxofibrosarcoma (myxoid malignant fibrous histiocytoma), pleomorphic liposarcoma (owing to the presence of pseudolipoblastic cells), and inflammatory fibrosarcoma
Low-grade myxofibrosarcoma (myxoid MFH)
Inflammatory myofibroblastic tumor
Helpful clues in the differential diagnostic approach
Low-grade myxofibrosarcoma (LG-MFS) vs Low-grade fibromyxoid sarcoma (LGFMS)

• **Question**
  – is it clinically relevant to distinguish low-grade myxofibrosarcoma (LG-MFS) from low-grade fibromyxoid sarcoma (LGFMS) ?

• **Yes !**
  – LG-MFS: 50% recurrences; 5-15% mets.
  – LGFMS: 10% recurrences; 10%-70% mets.
LG-Myxofibrosarcoma vs LGFMS

Elderly vs Young adults
LG-Myxofibrosarcoma vs LGFMS

LG-Myxofibrosarcoma:
- Elderly
- Superficial
- Multinodular
- Ill-defined borders

LGFMS:
- Young adults
- Deep
- Uninodular
- Well-demarcated
LG-Myxofibrosarcoma vs LGFMS

Myxoid & cellular areas
No whorls
Cellular atypia
Mitoses/abnormal mitoses
Lipoblast-like cells
No specific chromos abnormalities

Myxoid & collagenous areas
Whorls
No cellular atypia (except cell. forms)
No mitoses (usually)
No vacuolated cells
t(7;16)
Cellular myxoma

vs

Low-grade fibromyxoid sarcoma (LGFMS)

• Question
  – is it clinically relevant to distinguish cellular myxoma from low-grade fibromyxoid sarcoma and myxofibrosarcoma?

• Yes
  – Cellular myxoma = benign. <2% recur.; no mets.
  – LGFMS = sarcoma; 10% recur.; 10%-70% mets.
  – Myxofibrosarc. = sarc.; 50% rec.; 5-15% mets
Cellular myxoma vs LGFMS

Middle-aged adults (F>M) vs Young adults
Ill-defined borders vs Well-demarcated
Gelatinous vs Uninodular

Often solid and fibrous
Cellular myxoma vs LGFMS

No whorls
Well-developed myxoid areas
Curvilinear vessels frequent
Vacuolated cells
CD34 +, SMA ±, EMA ±

Whorls
Myxoid areas usually limited
Curvilinear vessels rare
No vacuolated cells
t(7;16)
EMA +, CD34 -, SMA -
Cellular myxoma vs LG myxofibrosarcoma

Middle-aged adults (F>M) vs Elderly
Cellular myxoma vs LG myxofibrosarcoma

Middle-aged adults (F>M) vs Elderly
Uninodular vs Multinodular
Deep vs Superficial

Images of tissue samples and clinical presentations.
Cellular myxoma vs LG myxofibrosarcoma

- No cellular atypia
- No hyperchromatic nuclei
- No mitoses
- CD34 reactivity frequent

- Cellular atypia
- Hyperchromatic nuclei
- Mitoses, abnormal mitoses
- CD34 reactivity rare
Conclusions - Take home messages

• « Myxo-fibro » mesenchymal lesions are not all the same!
• Myxofibrosarcoma and low-grade fibromyxoid sarcoma are two separate clinicopathologic entities that deserve recognition
• There is some degree of overlap between myxofibrosarcoma and inflammatory myxohyaline tumor
QUIZ: RESULTS
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Low-grade fibromyxoid sarcoma (Evans tumor)
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Inflammatory myxohyaline tumor
Thank you for your attention…. 

.....Louis Guillou