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Case 1: 48 year old woman. Mass right chest wall. Sarcoma resection post neoadjuvant XRT

Ellipse of skin 130x30x40mm with attached rib and attached parietal pleura
Infiltrative into skeletal muscle. Moderate cellularity, whorls and fascicles
- Moderately cellular, spindled cells
- Fibromyxoid matrix
❖ Occasional giant cells, small vessels,
❖ Little collagen
❖ Mitotic activity, vessels
What Type of Sarcoma is This?

- Low grade fibromyxoid sarcoma: lacks arcuate vessels
- DFSP: no repetitive storiform architecture
- Myxofibrosarcoma: insufficient atypia
- Malignant peripheral nerve sheath tumour: less cellular than most
- Inflammatory myofibroblastic tumour: not many inflammatory cells
- Perineuroma: is not usually myxoid
- Fibromatosis: this lesion is nodular, not arranged as long fascicles
Immunochemistry

- Smooth muscle actin: positive
- EMA: negative
- S-100 protein: negative
- Beta catenin: negative
- CD34: negative
- ALK: negative
❖ Plump nuclei, prominent nucleoli, some nuclear variability
❖ No hyperchromasia, no significant pleomorphism
- Tissue culture fibroblasts and myofibroblasts with mitoses, no atypical division figures, no necrosis
- Fascicles, (C and S shaped), +/- storiform
Cracking and tearing due to myxoid stroma
Extravasated erythrocytes, (lymphocytes, giant cells)
Torn, feathery myxoid stroma, with clefts
Nodular Fasciitis
Prior Core biopsy
Prior Core Biopsy
Nodular Fasciitis

- Arises from fascia, infiltrates into fat, muscle, rarely dermis
- Most <5cm, typically <2cm
- Most above the waist (upper extremity, trunk, head and neck)
- Clonal process:
  - MYH9-USP6 gene fusion is a recurrent aberration in NF
  - Leads to increased expression of the USP6
  - Break apart FISH available and useful in diagnostically challenging cases
  - USP6 fusion also involved in aneurysmal bone cyst
  - Clonal. Idea of “transient neoplasia”
- Self limiting, may regress. Recurrence extremely rare
- To avoid misdiagnosis: have to think of it!
51 year old male. Enlarging subcutaneous nodule

Case 2: Circumscribed, 45x40 mm, homogenous, tan cut surface
❖ Collagenised
❖ Whorling growth pattern, short fascicles
Alternating, collagenised & looser, more myxoid areas
❖ Mild-moderate cellularity. Cytologically bland spindled cells (no hyperchromasia, minimal pleomorphism), rare mitoses

❖ Arcades of vessels
Arcades of curvilinear vessels
❖ Fibroblast like cells
❖ MUC4 positive
Low Grade Fibromyxoid Sarcoma

- Upper extremity, trunk
- Deep to fascia
- Long pre-clinical phase (years)
- Giant collagen rosettes in 30% cases
  - hyalinizing spindle cell tumour with giant rosettes is a former term for a subset
- May transition into sclerosing epithelioid fibrosarcoma like areas
- IHC: MUC4 (highly sen & specific), EMA 80%, SMA occasionally
- Genetics: t(7;16)(q33;p11) in 75%: results in FUS-CREB3L2 fusion
- High rate of recurrence & metastasis with very long follow up (40 years)
  - More recent series indicate a lower rate of metastasis ? greater awareness and complete excision
- Morphology not predictive of outcome (except rare cases with round cell change with osteoblastic dedifferentiation)
Low Grade Fibromyxoid Sarcoma

Source: Enzinger & Weiss
Sclerosing Epithelioid Fibrosarcoma

Source: Enzinger & Weiss
28 year old woman, 11 weeks post partum. 15cm mass anterior bladder, extending into surrounding soft tissue. Transurethral resection

Case 3
Currettings, diffusely involved by a spindle cell proliferation with areas of haemorrhage. Thrombosis. Areas of necrosis

- Monotonous sheets and bundles of a moderately cellular neoplasm. Elongated cells. Somewhat myxoid stroma. Delicate capillary network
Elongated fibroblastic and myofibroblastic cells. Vescicular chromatin. Abundant fibrillar cytoplasm. Inflammatory cells include lymphocytes and plasma cells and neutrophils in the necrotic areas.
Not found: Areas of dense cellularity, pleomorphism, prominent mitotic activity, epithelipid change, or large nucleoli
AE1/3 & SMA

AE 1/3

SMA
Differential Diagnosis & IHC

- Inflammatory myofibroblastic tumour
- Leiomyosarcoma
- Gastrointestinal stroma tumour
- Carcinoma, ? uracheal ca
- Placental site trophoblastic tumour
- Pseudosarcomatous myofibroblastic proliferation of the bladder

IHC
- Positive for SMA, desmin (patchy) Vimentin, AE1/3, beta-catenin (cytoplasmic), ALK
- Negative: S100, CD117
- CD34 highlights vessels
- Serum B HCG negative
- Keratin: positive - is expressed by a third of IMT
Dx: Inflammatory Myofibroblastic Tumour of Classic Subtype

- Young age
- Short history, Clonal appearance
- Classically seen in children, but wide age range described
- No specific association with pregnancy
- Pelvis a favoured site
- IMT is now considered a neoplasm
- 50-60% ALK positive by IHC
- Depending on site, resectability and multifocality may recur locally
- Metastasis in only 1-2% cases. More common with ALK negative cases
- Tx: Surgical excision. Crizotinib for recurrent disease
Inflammatory Myofibroblastic Tumour of Epithelioid Subtype

❖ An aggressive variant
❖ Epithelioid tumour cells with prominent nucleoli
❖ ALK positivity has a nuclear membrane staining pattern
❖ Associated with a RANBP2-ALK rearrangement
❖ Classically seen in children, but wide age range described
❖ Other variants: spindled, myofibroblastic, inflammatory

Source: WHO Blue book
74 yr old woman. New pulmonary nodule, 10mm
Case 4: PMHx of renal cell carcinoma grade IV 5 yrs ago. 1 year ago intramucosal large bowel adenocarcinoma.
Epithelioid cells, abundant granular cytoplasm
Enlarged, atypical nuclei, vacuolated clear cells, CW met RCC
Review of renal cancer: 150mm renal mass, haemorrhage & necrosis, no capsular breach. No involvement of renal pelvis or renal vein

Had epithelioid cells, abundant granular cytoplasm, prominent nucleoli