SURGICAL PATHOLOGIC DIAGNOSIS OF SOFT TISSUE TUMORS: AVOIDING PITFALLS

Christopher D.M. Fletcher M.D. FRCPath
Brigham and Women’s Hospital
and Harvard Medical School
Boston, MA

PITFALL

„An unexpected or unforeseen difficulty or danger’
(A trap)
Not the same as an error!

PITFALLS IN DIAGNOSING SOFT TISSUE TUMORS

Focussing on overinterpretation or underinterpretation of certain morphologic or immunohistochemical features, which in context may be unanticipated or misleading, resulting in a clinically significant misdiagnosis

Examples most often encountered in consult material
PITFALLS IN DIAGNOSING SOFT TISSUE TUMORS

• „Wrong“ tumor in a given location
• Benign lesions with worrisome morphology
• Malignant lesions easily mistaken as benign
• Misleading immunohistochemical stains

„WRONG‘ TUMOR IN A GIVEN LOCATION

• Development of a usually easily recognized lesion at an unexpected site
• Failure to realize / recognize that the proposed morphologic diagnosis doesn’t fit with the clinical / anatomic context

F/66/Breast

F/47/Breast
ANGIOLIPOMA IN BREAST
CLINICOPATHOLOGIC FEATURES

- Middle-aged adults
  - F > M **
- Subcutaneous > parenchymal
  - Usually < 2 cm
- Circumscribed margin
  - Often cellular
- No/minimal endothelial atypia
- Fibrin microthrombi
MYXOID LIPOSARCOMA
EASY WAYS TO MISINTERPRET

- „Wrong” location – likely a metastasis
- Well differentiated liposarcoma/ALT with a myxoid stroma (esp. retroperitoneum)
- Well differentiated liposarcoma with myxoid stroma and branching vessels

Female, 54, axilla
MPNST ARISING IN SKIN

Very rare
Most often arising in neurofibroma

Always remember melanoma!
DESMOPLASTIC/SPINDLE CELL MELANOMA VS MPNST
DIAGNOSTIC CLUES

- Dermal location (MPNST v.v.rare….)
- Lymphocytic infiltrate
- Perineural invasion
- Strong S-100 – often shows ‘bundling’
- Junctional component (often absent)

N.B. 2nd line melanoma markers usually negative
FIBROEPITHELIAL STROMAL POLYPS
OF VULVOVAGINAL REGION

- Polypoid / multilobulated
- Fibrovascular core
- Varying cellularity
- No discrete margin
- Stellate / multinucleate cells
- Occas. very pseudosarcomatous
  - bizarre pleomorphism / atypical mitoses
- Usually desmin positive
BENIGN LESIONS FREQUENTLY HAVING WORRISOME OR MISLEADING MORPHOLOGY

- Pseudomalignant features
  - atypia
  - necrosis
  - lipoblast-like cells
  - cellularity
  - "invasion"
  - mitoses / proliferative activity

CELLULAR BENIGN FIBROUS HISTIOCYTOMA

CLINICAL FEATURES

- Wide age range
- Peak incidence 15-45 years
- Limbs > head & neck > elsewhere
- Poorly margined nodule
  - Most < 3 cm
- May grow rapidly
- Local recurrence in 15-20%
- Exceptionally metastasise
CELLULAR BENIGN FIBROUS HISTIOCYTOMA
DISTINCTIVE HISTOLOGIC FEATURES

- Larger, more cellular
- Often extends into subcutis
- Often fascicular and “myoid”
- Relative paucity of giant or foamy cells
- Frequent mitoses
- Occasional central necrosis
### CELLULAR BENIGN FIBROUS HISTIOCYTOMA

#### CLINICAL RELEVANCE

<table>
<thead>
<tr>
<th>Type</th>
<th>Approx. Recurrence Rate</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ordinary FH</td>
<td>2%</td>
<td>Non-destructive</td>
</tr>
<tr>
<td>Cellular FH</td>
<td>15-20%</td>
<td>Non-destructive, Very rare metastasis</td>
</tr>
<tr>
<td>DFSP</td>
<td>30% or more</td>
<td>Locally infiltrative, No metastasis unless FS-DFSP</td>
</tr>
</tbody>
</table>
CELLULAR BENIGN FIBROUS HISTIOCYTOMA
DIFFERENTIAL DIAGNOSIS
Dermatofibrosarcoma protuberans
- more basophilic
- less polymorphic
- CD34 positive
Cutaneous “leiomyosarcoma”
- cigar-shaped nuclei
- infiltrative dermal growth
- desmin positive (in skin)

ATYPICAL (PSEUDOSARCOMATOUS) FIBROUS HISTIOCYTOMA
CLINICAL FEATURES
Less than 2% of cutaneous FH
Adults; peak 20-40 years
Equal sex incidence
Limbs ++ > Elsewhere
Nodular / polypoid
10-15% local recurrence
Rare metastasis
(a.k.a. “dermatofibroma with monster cells”)
ATYPICAL FIBROUS HISTIOCYTOMA
DIFFERENTIAL DIAGNOSIS

- Atypical fibroxanthoma
- Pleomorphic sarcoma (“MFH”)
  (Sarcomatoid SCC)
  (Metastasis)
BENIGN LESIONS FREQUENTLY HAVING WORRISOME OR MISLEADING MORPHOLOGY

FATTY LESIONS.......
HIBERNOMA MIMICKING ATYPICAL LIPOMATOUS TUMOR

- Usually only a problem in the thigh
- Lipoblast-like cells predominate – too numerous for ALT!
- Lipoblast-like cells lack nuclear atypia
- Granular eosinophilic (brown fat) cells evident at least focally
BENIGN LESIONS FREQUENTLY HAVING WORRISOME OR MISLEADING MORPHOLOGY

LIPOGRANULOMATOUS LESIONS MIMICKING FATTY TUMORS....
MALIGNANT SOFT TISSUE LESIONS EASILY MISTAKEN AS BENIGN

Low-grade fibromyxoid sarcoma
Malignant SFT
Low-grade myxofibrosarcoma
Mammary angiosarcoma
MISLEADING IMMUNOHISTOCHEMICAL STAINS IN SOFT TISSUE TUMOR DIAGNOSIS

- Generalizable problems
  - use of very broad panels
  - excessive antigen retrieval
  - false beliefs regarding specificity
  - over-interpretation of a single result
  - speculative/unvalidated use of an Ab

Must always interpret results in context of the morphology
MISLEADING IMMUNOHISTOCHEMICAL STAINS IN SOFT TISSUE TUMOR DIAGNOSIS

SOME EXAMPLES.......
Neuroendocrine carcinoma, right?

In fact, alveolar rhabdo....
Rhabdomyosarcoma 
Potentially Misleading Immunostains

Alveolar
- 50% Keratin (esp CAM5.2)
- 33% Synaptophysin
- 25% Chromogranin
- < 5% S-100 protein

Embryonal
- 10-15% S-100 protein
- < 5% Keratin
- Neg\text{e} for neuroendocrine markers

CD34
EMA
DES
OTHER POTENTIAL PITFALLS

• Tiny needle biopsies/sampling error
• Grading disconnected from diagnosis
• Mismatch between morphology and behavior
• Location-specific prognostication
• Etc……………

CONCLUSIONS

• Beware preconceptions !
• Know/understand natural history
• Don’t over-react to one feature
• Be willing to say “I don’t know”
• Be willing to say “ Get a better/bigger biopsy”
• Remember there’s no specific nor 100%-sensitive immunostain