SO-CALLED FIBROHISTIOCYTIC TUMOURS: AN OVERVIEW FOCUSSING ON LESIONS IN WHICH BIOLOGIC POTENTIAL MAY BE MISINTERPRETED

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SO-CALLED
FIBROHISTIOCYTIC TUMOURS
COMMONEST MISINTERPRETATIONS
BENIGN LESIONS
DIAGNOSED AS MALIGNANT

Cellular fibrous histiocytoma
Aneurysmal fibrous histiocytoma
Epithelioid fibrous histiocytoma
Atypical fibrous histiocytoma
Deep benign fibrous histiocytoma
(Diffuse-type giant cell tumour)
Atypical fibroxanthoma
SO-CALLED FIBROHISTICYCTIC TUMOURS
MALIGNANT LESIONS DIAGNOSED AS BENIGN
Low-grade myxofibrosarcoma
Much less often a problem
SO-CALLED FIBROHISTICYTIC TUMOURS LESIONS IN WHICH BIOLOGIC POTENTIAL IS DIFFICULT TO PREDICT

Plexiform fibrohistiocytic tumour
Angiomatoid ‘MFH’
Most pursue a benign clinical course but approx. 2% (?) metastasise
CELLULAR BENIGN FIBROUS HISTIOCYTOMA

CLINICAL FEATURES

Wide age range
Peak incidence 15-45 years
Limbs > head & neck > elsewhere
Poorly marginated 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
<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Recurrence Rate</th>
<th>Clinical Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ordinary FH</td>
<td>Approx. 2% recur</td>
<td>Non-destructive</td>
</tr>
<tr>
<td>Cellular FH</td>
<td>15-20% recur</td>
<td>Non-destructive, Very rare metastasis</td>
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<tr>
<td>DFSP</td>
<td>30% or more recur</td>
<td>Locally infiltrative, No metastasis unless FS-DFSP</td>
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</table>
NOTABLE FEATURES OF METASTASISING CUTANEOUS FH

- Frequently preceded by repeated local recurrence
- Predilection to spread to lymph nodes and lung
- Metastases may be delayed for many years; lung lesions may be indolent
- Metastases usually closely resemble the primary lesion
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)
ANEURYSMAL BENIGN FIBROUS HISTIOCYTOMA

CLINICAL FEATURES

Approx. 5% of cutaneous FH
Adults; peak 20-40 years
Females slightly > males
Lower limb ++ > trunk > elsewhere
Red / brown nodule up to 2-3 cm
Occasional rapid growth / pain
15-20% local recurrence
Rare metastasis
ANEURYSMAL BENIGN
FIBROUS HISTIOCYTOMA
DIFFERENTIAL DIAGNOSIS

Angiomatoid “MFH”
Kaposi’s sarcoma
(Spindle cell haemangioma)
(Angiosarcoma)
CELLULAR / ANEURYSMAL VARIANTS
OF BENIGN FIBROUS HISTIOCYTOMA
WORRISOME FEATURES

Frequently large size
Cellularity
Relatively high mitotic rate
Focal necrosis in 10-15%
EPITHELIOID BENIGN FIBROUS HISTIOCYTOMA

Less than 2% of cutaneous FH
Clinically similar to ordinary FH
BUT
Usually polyploid / exophytic
Frequent collarette
At least 50% of cells epithelioid
Polygonal / eosinophilic / binucleate cells
Often prominent vessels
Local recurrence uncommon
EPITHELIOID BENIGN FIBROUS HISTIOCYTOMA
DIFFERENTIAL DIAGNOSIS

Spitz naevus
Juvenile xanthogranuloma
Malignant melanoma
Epithelioid sarcoma
Epithelioid vascular tumour
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 (‘PSEUDOSARCOMATOUS’) FIBROUS HISTIOCYTOMA
MORPHOLOGIC FEATURES

Similar to usual FH
EXCEPT
Scattered large bizarre pleomorphic cells
(often multinucleate / foamy)
30% have atypical mitoses
10% have necrosis
ATYPICAL FIBROUS HISTIOCYTOMA
DIFFERENTIAL DIAGNOSIS

Atypical fibroxanthomama
Pleomorphic sarcoma (“MFH”)
(Sarcomatoid SCC)
(Metastasis)
ATYPICAL FIBROXANTHOMA

‘…histologically bizarre tumor usually found in sun-damaged skin of elderly persons… had been initially misdiagnosed as a variety of sarcomas or carcinomas…benign behavior of these lesions is documented. It is suggested that AFX represents a reactive or reparative process in previously damaged dermis.’

Kempson & McGavran
Cancer 1964; 17:1463-1471
‘...one may speculate that it represents part of a spectrum of reactive processes.... The series of 140 cases....appears to further establish AFX as a mesenchymal proliferation of the dermis characterized by a bizarre and pleomorphic sarcoma-like histologic appearance but but with a disposition to benign biologic behaviour.’

Fretzin & Helwig
Cancer 1973; 31:1541-52
ATYPICAL FIBROXANTHOMA

‘It is histologically indistinguishable from pleomorphic forms of malignant fibrous histiocytoma. From a conceptual point of view, we regard it as a superficial form of that tumor which, by virtue of its superficial location, almost invariably pursues a benign course.’

Enzinger & Weiss, 1st Edn, 1983
‘ATYPICAL FIBROXANTHOMA’ WITH METASTASIS

‘Factors that portend aggressive behavior and metastasis are vascular invasion, recurrence, deep tissue invasion, tumor necrosis…..’

Helwig & May
Cancer 1986; 57:368-376
ATYPICAL FIBROXANTHOMA PROBLEMS

• Diagnostic criteria
• Cases in the pre-immuno era
• Shave biopsies
• Rare keratin-negative cases of spindle cell SCC with ulceration
ATYPICAL FIBROXANTHOMA

CLINICAL FEATURES

Mainly elderly patients
Males > females
Head and neck++ / limbs rare
Rapidly enlarging exophytic
Sometimes multiple / asynchronous

Recurrence infrequent
No metastasis if carefully diagnosed
ATYPICAL FIBROXANTHOMA
MORPHOLOGIC FEATURES

Arise in actinically damaged skin
Usually very cellular / mitotic
Variably pleomorphic / bizarre
Often ulcerated
Frequent collarette
Usually confined to dermis
Smooth deep margin
No epidermal / junctional component

Keratin / S-100 protein / desmin negative
ATYPICAL FIBROXANTHOMA
IMPORTANT CRITERIA

Origin in sun-damaged skin
No epidermal / junctional origin
No subcutaneous (or deeper) invasion
No necrosis (except surface)
No vascular or perineural invasion
Relevant negative immuno
ATYPICAL FIBROXANTHOMA
CONCEPTUAL QUESTIONS

What are they?
What is the role of U-V irradiation?
Do they occur in young patients?
Do they ever metastasise?
Are they related to ‘MFH’?
MYXOFIBROSARCOMA
(FORMERLY MYXOID ‘MFH’)
CLINICAL FEATURES

Adults; peak 50-70 years
Equal sex incidence
Lower limb > upper limb > trunk
Retroperit and head/neck rare
60-70% Subcutaneous / deep dermal
Some tendency to nodal metastasis
Survival depends on grade
MYXOFIBROSARCOMA
METASTASES / TUMOUR-RELATED DEATHS

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<tr>
<th></th>
<th>Superficial</th>
<th>Deep</th>
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<tbody>
<tr>
<td>Low</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Intermed</td>
<td>20%</td>
<td>30%</td>
</tr>
<tr>
<td>High</td>
<td>30%</td>
<td>35%</td>
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Local recurrence(s) may advance in grade
PLEXIFORM FIBROHISTIOCYTIC TUMOUR

CLINICAL FEATURES

Commonest 0-30 years
Wide age range
F > M 3:1
65% upper limb
Slowly growing dermal / subcut mass
20-30% local recurrence
Nodal / systemic metastasis ~ 2% (? more)
PLEXIFORM FIBROHISTIOCYTIC TUMOUR
PATHOLOGIC FEATURES

Most < 3 cm
Poorly demarcated
Centred on dermal / subcut junction
Variable proportions of:
- spindle cell fascicles
- aggregates of histiocytoid cells
Osteoclastic giant cells common
Vascular invasion ~ 30%
PLEXIFORM FIBROHISTIOCYTIC TUMOUR DIFFERENTIAL DIAGNOSIS

Ordinary fibrous histiocytoma
Fibromatosis
Giant cell tumour of soft tissue
(Giant cell tumour of tendon sheath)
(Granulomatous process)
SO-CALLED ANGIOMATOID ‘MFH’

CLINICAL FEATURES

Children / adolescents / young adults
Equal sex incidence
Limbs > trunk
Most often subcutaneous
Slowly growing, usually < 5 cm
Often mistaken for haematoma
Systemic features in < 5%
- fever, weight loss, anaemia, ESR ↑

Local recurrence approx. 10%
Metastasis < 2%
SO-CALLED ANGIOMATOID ‘MFH’
PATHOLOGIC FEATURES

Multinodular, haemorrhagic
Nodules / sheets of
eosinophilic ovoid to spindle cells
Pleomorphism infrequent
Lymphoplasmacytic infiltrate
Dense collagenous stroma
Haemosiderin deposition
Some variability

Desmin / EMA positive in 40-50%
CD68 and CD99 often positive (? significance)
Specific fusion gene(s)
Usually $EWSR1$-$CREB1$; less often $EWSR1$-$ATF1$
SO-CALLED ANGIOMATOID ‘MFH’
DIFFERENTIAL DIAGNOSIS

Aneurysmal benign FH
Diffuse-type giant cell tumour
Organising haematoma
Dendritic cell neoplasm (?)
SO-CALLED ANGIOMATOID ‘MFH’ LINE OF DIFFERENTIATION

Currently unknown
Numerous hypotheses over the years

? Myoid / perivascular differentiation
? Fibroblastic reticulum cell (or similar)
SO-CALLED FIBROHISTIOCYTIC TUMOURS

HOW TO AVOID MISINTERPRETATION?

- Think about clinical context
- Develop understanding of natural history
- Avoid ‘knee-jerk’ response to cytologic atypia or mitoses
- Thoughtful use of immunostains
- Acknowledge uncertainty and, if required, seek consultation