Soft Tissue Tumors of the Skin

Fibrohistiocytic Tumors: Histopathology 2010, 56:148-165

2020-03-02
Clinically important variants and differential diagnoses

DERMATOFIBROMA VARIANTS
## Variants of Dermatofibroma

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<th>Dermatofibroma Variant</th>
<th>Differential Diagnosis</th>
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<td>Deep penetrating DF</td>
<td>DFSP</td>
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<tr>
<td>Atrophic DF</td>
<td>Atrophic DFSP</td>
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<tr>
<td>Anerysmal DF</td>
<td>Kaposi's Sarcoma</td>
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<tr>
<td>Lipidised (ankle type) DF</td>
<td>Xanthoma</td>
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<td>Palisading cutaneous DF</td>
<td>Schwannoma</td>
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<tr>
<td>Clear cell DF</td>
<td>RCC metastasis</td>
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<tr>
<td>Granular cell DF</td>
<td>Granular cell tumor</td>
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<tr>
<td>Myofibroblastic DF</td>
<td>Myofibroblastoma</td>
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<tr>
<td>Atypical pseudosarcomatous DF</td>
<td>AFX</td>
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<tr>
<td>Myxoid DF</td>
<td>Cutaneous myxoma</td>
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<tr>
<td>Epitheloid cell histiocytoma</td>
<td>Spitz nevus</td>
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<tr>
<td>Cellular DF</td>
<td>Leiomyosarcoma, DFSP</td>
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<tr>
<td>Smooth muscle proliferation in DF</td>
<td>Infantile myofibroma(tosis)</td>
</tr>
<tr>
<td>DF of the face</td>
<td>AFX, DFSP, leiomyosarcoma, low grade</td>
</tr>
<tr>
<td>Metastasizing DF</td>
<td>myofibroblastic sarcoma</td>
</tr>
</tbody>
</table>

### Clinically important variants

*Histopathology* 2000; 36:529-539  
*Histopathology* 2010; 56:148-165
Cellular Dermatofibroma

**Characteristics**
- 5% of dermatofibromas
- Infiltration of superficial subcutis
- Cellular spindle cell fascicles
- Increased proliferative activity
- Central tumor necrosis
- More frequently SMA+
- Peripheral expression of CD34 and Desmin DD: DFSP

Up to 26% local recurrence

→ Complete excision

*Histopathology 2010; 56:148-165*
Aneurysmal Dermatofibroma

Characteristics
<2% of dermatofibromas
Predilection for lower limbs
Rapid recent growth due to hemorrhage
Large and cellular
Infiltration of deep soft tissues
Blood filled spaces without endothelial lining

19% local recurrence
(usually less than 2% in conventional FH)

→ Complete excision

Histopathology 2010; 56:148-165
Atypical Dermatofibroma

**Characteristics**
- Background of common DF
- Spindled fibroblast/myofibroblast-like cells
- Pleomorphic histiocyte-like cells
- Multinucleated giant cells
- 3 mitoses/10 HPF on average
- Occasional atypical mitoses
- Necrosis and deep infiltration possible

14% local recurrence
Rarely distant metastases

→ Complete excision

*Histopathology* 2010; 56:148-165

Dermatofibroma of the Face

Characteristics
Very rare localisation
Rarely suspected by the clinician
Ill-defined
Infiltration of deep structures
More aggressive subtypes
SMA+ spindle cell fascicles

High rate of recurrence (18.5%)
(usually less than 2% elsewhere)

→ Complete/wide excision

Am J Dermatopathol 2001; 23:419-426
49 y ♂

Adnexal tumor on the proximal calf
IHC Results
negative
CK22
S100
HMB-45
CD34
positive
Factor XIIIa
ALK1
Diagnosis:
Epithelioid cell histiocytoma
Epithelioid cell histiocytoma: a new entity

E.WILSON JONES, R.CERIO AND N.P.SMITH
Institute of Dermatology, United Medical and Dental Schools of Guy’s and St. Thomas’s Hospitals, St John’s Hospital for Diseases of the Skin, London, U.K.

Accepted for publication 27 June 1988

- initially described in 1989
  - “epithelioid cell histiocytoma”
- considered a morphologic variant of cutaneous fibrous histiocytoma
- at least 50% epithelioid morphology
some distinct features:
- “grenzzone” generally lacking
- tends to lack lateral entrapment of collagen
- usually lacks a prominent infiltrate of foamy histiocytes and lymphocytes
- EMA + (65%)

such differences have led some authors to suggest that epithelioid fibrous histiocytoma may be a distinct entity
Molecular Evidence

Fusions involving protein kinase C and membrane-associated proteins in benign fibrous histiocytoma


Research letter

Atypical fibrous histiocytoma of the skin with CD30 and p80/ALK1 positivity and ALK gene rearrangement

Epithelioid cell histiocytoma of the skin with clonal ALK gene rearrangement resulting in VCL–ALK and SQSTM1–ALK gene fusions

ALK rearrangement and overexpression in epithelioid fibrous histiocytoma

Leona A Doyle, Adrián Mariño-Enriquez, Christopher DM Fletcher and Jason L Hornick

Department of Pathology, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA

IHC:

• ALK (5A4; Leica Biosystems)
  
• ROS1 (D4D6; Cell Signaling Technology)
  
  – in ALK – cases only

Table 1 Summary of immunohistochemical staining for ALK in epithelioid fibrous histiocytoma and other tumor types

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Total cases</th>
<th>ALK positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelioid fibrous histiocytoma</td>
<td>33</td>
<td>29 (88)</td>
</tr>
<tr>
<td>Aneurysmal fibrous histiocytoma</td>
<td>10</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Atypical fibrous histiocytoma</td>
<td>10</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Atypical fibroxanthoma</td>
<td>5</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Cellular fibrous histiocytoma</td>
<td>10</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Conventional fibrous histiocytoma</td>
<td>11</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Cutaneous syncytial myoepithelioma</td>
<td>10</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

*Mod Pathol. 2015*
Molecular Evidence

- FISH (dual-color break-apart probe; Abbott Molecular) in 14 ALK + and 4 ALK - cases
- Rearrangement in all evaluable ALK + cases
  - 12 cases balanced ALK rearrangement
  - one case unbalanced (with loss of the 5’ signal)
  - percentage of nuclei with rearrangement 20-70%
- No rearrangement in ALK - cases
<table>
<thead>
<tr>
<th>Differential Diagnoses</th>
<th>IHC/ Molecular Findings</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellular neurothekeoma</td>
<td>+NKI/C3, CD10, PGP9.5 -S100, Melan A, GFAP</td>
<td>Am J Surg Pathol. 2007; 31(7):1103-14</td>
</tr>
<tr>
<td></td>
<td><em>EWSR1 rearrangement</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>INi1 loss</em></td>
<td></td>
</tr>
<tr>
<td>Spitz tumors</td>
<td>+ HMB45, MelanA, S100</td>
<td>Nat Commun. 2014;5:3116</td>
</tr>
<tr>
<td></td>
<td><em>ALK, ROS1, NTRK1, BRAF, RET kinase fusions</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>BAP1 loss, BRAF V600E mut.</em></td>
<td></td>
</tr>
</tbody>
</table>
«Wiesner nevus»

Angiomatoid Fibrous Histiocytoma

0.3% of all soft tissue tumors
Subcutaneous tumor
Intermediate malignant potential
All ages (peak first two decades)

50% desmin +, MYOD1-, Myogenin-
EMA, CD99, CD68 +/-

EWSR1-CREB1 fusion in > 90%

WHO blue books skin
Dermatofibrosarcoma Protuberans

**DFSP**
1% of all sarcomas
Low grade, locally aggressive fibroblastic neoplasm
CD34+ S100- Desmin- CK-COL1A1-PDGFB fusion gene

**Important variants**
Myxoid DFSP
Superficial plaque-like
Fibrosarcomatous

*Pathology 2014; 46(2):149-159*
Fibrosarcomatous DFSP

**Characteristics**
- 10-20% of DFSPs
- Metastases ↑
- Abrupt or gradual transformation
- Expansive growth
- Cellular fascicles
- Increased atypia
- Increased proliferation
- Loss of CD34 expression
- Increased p53 expression

Imatinib mesylate as therapeutic option

*J Clin Oncol* 2005;23:866-873

*Pathology* 2014; 46(2):149-159
SPINDLE CELL TUMORS IN SUN-DAMAGED SKIN

AFX, pleomorphic dermal sarcoma and DD
# Atypical Fibroxanthoma (AFX)

<table>
<thead>
<tr>
<th>Gender</th>
<th>59 male, 7 female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55-95y, mean 77y</td>
</tr>
<tr>
<td>Site</td>
<td>64 head, 1 neck, 1 forearm</td>
</tr>
<tr>
<td>Location</td>
<td>dermis 38, subcutis expansile 24, subcutis focally infiltrative 4</td>
</tr>
<tr>
<td>Histology</td>
<td>mixed 40, spindle 22, epitheloid 4</td>
</tr>
<tr>
<td>Additional features</td>
<td>hemorrhagic/ pseudoangiomatous 16, granular cell change 15, keloid-like areas 6, myxoid degeneration 5, osteoclast-like giant cells 4, clear cell change 3</td>
</tr>
</tbody>
</table>

Atypical Fibroxanthoma (AFX)

<table>
<thead>
<tr>
<th>IHC in spindle cell tumors in sun-damaged skin</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>low- and high mw cytokeratins pancytokeratin, p63</td>
<td>sarcomatoid squamous cell carcinoma (SCC: may be negative!), melanoma (rare), epitheloid angiosarcoma (50%)</td>
</tr>
<tr>
<td>EMA</td>
<td>SCC &amp; AFX (24%), angiosarcoma (rare) focally positive</td>
</tr>
<tr>
<td>S100</td>
<td>spindle cell melanoma, dispersed dendritic cells in AFX</td>
</tr>
<tr>
<td>HMB45, Melan A</td>
<td>melanoma (more specific but often negative in spindle cell melanoma), AFX (clear cell variant) epitheloid angiosarcoma (rare)</td>
</tr>
<tr>
<td>SMA</td>
<td>leiomyosarcoma (diffuse), AFX (focal myofibroblastic diff. 45%)</td>
</tr>
<tr>
<td>Desmin</td>
<td>leiomyosarcoma</td>
</tr>
<tr>
<td>CD31, Fli-1, F. VIII, ERG</td>
<td>angiosarcoma, epitheloid AFX (focal cytoplasmic CD31, Fli-1)</td>
</tr>
<tr>
<td>CD10, CD99</td>
<td>AFX (but non-specific and non contributory)</td>
</tr>
</tbody>
</table>

Atypical Fibroxanthomoma (AFX)

**Diagnosis of exclusion**

**No confirmative IHC**
(CD68, CD10, CD99 not helpful!)

**Minimal Panel:**
negative reaction: CK22, CK5/6, ERG, Desmin
S100 (dendritic cells+)

**Additional markers depending on morphology**
AFX or Pleomorphic Dermal Sarcoma?

AFX versus pleomorphic dermal sarcoma?
Superficial biopsy
Atypical Fibroxanthoma (AFX)

AFX versus pleomorphic dermal Sarcoma?

Do not answer this question in a superficial biopsy! Ask for complete excision!

Atypical Fibroxanthoma (AFX):

- Growth into superficial subcutaneous tissue with expansile and well demarcated deepest margin allowed
- Growth around the nerve, but without Infiltration of the perineural space

Diagnosis of exclusion

→ Complete local excision is curative
- Small risk for local recurrence
- No metastases
- No Mortality

J Cutan Pathol 2010; 37(3):301-309. Morphological and immunohistochemical characteristics of atypical fibroxanthoma...
Pleomorphic Dermal Sarcoma:

Invasion of deep subcutis/muscle/fascia > 2cm
Tumor necrosis 53%
L1 26%, Pn1 29%
→
Risk for local recurrence
Metastasis
Rare Mortality