Challenging cutaneous spindle cell Neoplasms

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low-grade spindle cell sarcoma

spindle cell melanoma

spindle cell thymoma
Diagnosis of cutaneous spindle cell Tumours

Exclusion of nonmesenchymal spindle cell tumours
(spindle cell carcinoma, spindle cell malignant melanoma)

Determination of the dignity

Characterization of the line of differentiation

Grading in cutaneous sarcomas has limited value
(dermal sarcomas have a good prognosis except angiosarcoma, epithelioid sarcoma, malignant dermatofibroma)

Tumour margins

Prognosis, treatment
Diagnosis of spindle cell Tumours

Age of patients

lipofibromatosis: children
kaposiform HE: children

Anatomic distribution

spindle cell lipoma: neck, shoulder, upper back
acral fibromyxoma: finger, toe, periungual

Tumour depth

pilar leiomyoma: common
deep leiomyoma: very, very rare

Evaluation of morphological features

Ancillary techniques

immunohistochemistry, molecular techniques
### Histological Features

#### Architecture of cutaneous spindle cell neoplasms

<table>
<thead>
<tr>
<th>Type</th>
<th>Examples</th>
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<td>storiform:</td>
<td>dermatofibroma, DFSP</td>
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<td>fascicular:</td>
<td>smooth muscle neoplasms</td>
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<td>perivascular:</td>
<td>myopericytoma</td>
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<td>lamellar:</td>
<td>perineurioma</td>
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<tr>
<td>biphasic:</td>
<td>myofibroma</td>
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#### Interphase tumour and adjacent tissues

<table>
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<th>Type</th>
<th>Examples</th>
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<tr>
<td>ill-defined:</td>
<td>dermatofibroma</td>
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<tr>
<td>diffus infiltrative:</td>
<td>DFSP</td>
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<td>well-circumscribed:</td>
<td>perineurioma, low-grade FMS</td>
</tr>
<tr>
<td>encapsulated:</td>
<td>schwannoma, lipoma, spindle cell / pleomorphic lipoma</td>
</tr>
</tbody>
</table>
Tumour stroma
  abundant or scanty stroma
  myxoid stroma
  collagenous stroma
  hyalinised / sclerosing stroma

Vascular pattern
  haemangiopericytoma-like (SFT, MPNST...)
  thin-walled, branching (myx. LS, angiofibroma)
  hyalinised vessel walls (schwannoma)
  abundant vessels (cellular angiofibroma)

Cytomorphology
Proliferative activity, mitoses
  (Cave: neurofibroma, deep seated leiomyoma)
Tumour necrosis
Immunohistochemistry

fibroblastic differentiation:
  😞, procollagen type 1 + ?, CD 34 +/- 
myofibroblastic differentiation
  ASMA +/-, desmin +/-, h-caldesmon -, myf-4 - 
smooth-muscle differentiation
  ASMA +, desmin +/-, h-caldesmon + (2/3 +)
striated muscle differentiation
  ASMA -/+ , desmin +, myf-4 +, MyoD1 +
neural differentiation
  S-100 +, CD 56 +, Sox10 +, p75 + 
perineurial differentiation
  EMA +, Claudin-1 +, Glut-1 +, CD34 +/- 
endothelial differentiation
  ERG +, CD 31 + (histiocytes +), CD 34 +/-
Breakpoint specific Antibodies

A novel SS18-SSX fusion-specific antibody for the diagnosis of synovial sarcoma (E Baranov et al. AJSP 2020; 44: 922-933)
- E9X9V = SS18-SSX fusion antibody
  95% sensitivity, 100% specificity
- E5A2C = SSX-C terminus antibody
  100% sensitivity, 95% specificity

Immunohistochemical detection of PAX-FOXO1 fusion proteins in alveolar rhabdomyosarcoma using breakpoint specific antibodies (DA Azorsa et al. Mod Pathol 2021; 34: 48-57)
- PFM.1 und PFM.2
- 91% sensitivity, 100% specificity
monophasic fibrous synovial sarcoma
The best specificity and sensitivity has an antibody in the first six months after its description.

enthusiastic phase
pessimistic phase
realistic phase
Case 1
M, 33 years, back
follicular cyst was suspected
desmoplastic MM

neurofibroma?
scattered tumour cells with enlarged nuclei atypical neurofibroma?
lymphoid aggregates...
additional piece of tissue...
resection specimen
Diagnosis Case 1: desmoplastic malignant Melanoma

S-100 protein

p75
desmoplastic malignant Melanoma

- variant of spindle cell malignant melanoma, rare variant of malignant melanoma (< 4%)
- mainly elderly patients (BUT...), head / neck > other locations (rarely mucosa, hands, feet)
- indurated, non-pigmented plaques, nodules, often delayed diagnosis
- higher rate of local recurrences than classical MM! lower metastatic rate than classical MM!
Desmoplastic Malignant Melanoma

- Proliferation of atypical spindled cells, slightly enlarged tumour cell nuclei, usually few mitoses only
- Ill-defined, diffuse infiltration, extension into deep dermis / subcutis
- Patchy lymphocytic infiltrate, scar-like desmoplastic stroma
- Associated lentigo maligna (50% of cases), neurotropic, myxoid variants
- S-100 +, p75 +, Sox 10 +, WT1 +, Melan-A -, HMB-45 -
Desmoplastic melanoma: an updated immunohistochemical analysis of 40 cases with a proposal for an additional panel of stains for diagnosis (LA Plaza et al. J Cutan Pathol 2016; 43: 313)
- Sox10, p75, nestin, WT-1 more specific markers

A diagnostic algorithm to distinguish desmoplastic from spindle cell melanoma (SE Weissinger et al. Mod Pathol 2014; 27: 524)
- laminin, HMB-45, Melan-A, p75, c-kit + in SMM
- collagen IV, trichrome, CD68, MDM2 + in DMM
- BRAF mutation in 31% of SMM and 5% of DMM

NF1 mutations are common in desmoplastic melanoma (T Wiesner et al. Am J Surg Pathol 2015; 39: 1357)
Distinction of desmoplastic melanoma from non-desmoplastic melanoma by gene expression profiling (Busam K et al. J Invest Dermatol 2005; 124: 412)

- reduction of the expression of genes for melanocytic differentiation (Melan-A, Mart-1, MiTF, DTC)
- increased expression of genes for neurotropic factors (NGFR) and for extracellular matrix
- high expression of clusterin (involved in cell-stroma interactions)
Distinguishing neurofibroma from desmoplastic melanoma: the value of p53 (Elsensohn A et al. AJSP 2018; 42: 372)

- 20 cases of DM (18 M, 2 F)
  20 cases of NF (12 M, 8 F)
- 19/20 of DM p53 positive
  0/20 NF p53 positive
- detection of p53 by immunohistochemistry is helpful in the differential diagnosis
Malignant Peripheral Nerve Sheath Tumour

rarely superficial
rarely head / neck
S-100 - / focal +
loss of H3K27me3
(Le Guellec S et al.
Mod Pathol 2017; 30: 1677
- may be seen in desmo-
plastic melanoma as well)

F, 60, back
known M.Recklinghausen
F, 13 years, left forearm
cutaneous clear cell Sarcoma

FISH-Analysis for the detection of \textit{EWS} translocation

signals are in different areas of the nucleus = positive (16 out of 65 nuclei)
Clear cell sarcoma versus malignant Melanoma

- t(12;22)(q13;q12) with EWSR1-ATF1 fusion (4 types of EWSR1-ATF1 transcripts)
- t(2;22)(q32;q12) with EWSR1-CREB1 fusion
- additional extra copies of chromosomes 2, 7, 8
- additional abnormalities of chromosome 22
- no BRAF mutations in CCS but common in MM
- MSI is very rare in CCS but common in MM
- no loss of hMLH1, hMSH2 in CCS
- characteristic gene expression profile in CCS
Case 2: Clinical Findings

- F, 30 years
- left lateral thigh
- dermatofibroma was suspected
Differential Diagnosis Case 2

plaque-like, spindle cell, dermal neoplasm
(no atypia, no mitoses, no necrosis)

- flat dermatofibroma
- neurofibroma
- dermatomyofibroma
- plaque-like CD34-positive dermal fibroma
- plaque-like DFSP
flat Dermatofibroma

- hyperplasia of the epidermis
- plump spindled tumour cells
- hyalinised collagenous fibres (entrapment)
- CD34 -, CD64 +, HMGA2 +
diffuse Neurofibroma
- often myxoid stroma
- scattered mast cells
- S-100 +

S-100
Dermatomyofibroma: Clinicopathologic and Immunohistochemical Analysis of 56 Cases and Reappraisal of a Rare and Distinct Cutaneous Neoplasm

Thomas Mentzel, MD and Heinz Kutzner, MD

Abstract: Dermatomyofibroma represents a rare and distinct benign cutaneous mesenchymal neoplasm of fibroblastic/myofibroblastic differentiation. A series of 56 cases of dermatomyofibroma has been analyzed to further characterize the clinicopathologic spectrum of this entity. Forty patients were female and 8 were male (gender was unknown in 8 cases). Patients' age ranged from 3 to 51 years (mean 30.8 years, median 30 years). Interestingly, 6 patients were younger than 16 years, and in this age group, 3 male and 3 female patients, respectively, were noted. The shoulder (13 cases) was the anatomic site most commonly affected, followed by the upper arm (7 cases), the neck (6 cases), the thigh (6 cases), the chest wall (4 cases), the back (3 cases), the axillary fold (2 cases), the abdominal wall (2 cases), and 1 case each was seen on the forearm, the buttock, and the popliteal fossa (exact anatomic location was unknown in 10 cases). One patient presented with 2 lesions arising simultaneously on both shoulders. Histologically, an ill-defined, plaque-like dermal neoplasm of varying solubility was seen in all cases, composed of bland spindle-shapetumor cells often oriented parallel to the overlying epidermis. An orientation of superficial part of the neoplasia was seen in 23 cases, and in 6 cases, deeper parts of the neoplasia were involved by often perpendicularly growing bands of neoplastic cells. Immunohistochemically, tumor cells in 31 of 48 cases tested stained positively for alpha-smooth muscle actin, and a focal expression of this marker was noted in 20 cases. In addition, a focal expression of CD34 was seen in 18 of 40 cases tested. Follow-up information was available in 38 cases (range from 3 to 156 months, median 34 months), and despite marginal or incomplete excision in 17 cases, none of the cases recurred. Dermatomyofibroma represents a benign fibroblastic/myofibroblastic dermal neoplasm.

Key Words: dermatomyofibroma, mesenchymal neoplasms, plaque-like dermal fibromatosis, skin

(Am J Dermatopathol 2009;31:44-49)

INTRODUCTION

The spectrum of fibroblastic/myofibroblastic cutaneous tumors comprises a heterogeneous group of benign, atypical, and malignant neoplasms mainly composed of spindle-shaped tumor cells. Non-neoplastic myofibroblasts resemble fibroblasts; feature immunohistochemically heterogeneous phenotypes with regard to their content of intermediate filaments, muscle actin, and myosin, and are defined ultrastructurally by specialized organelles such as stress fibers and cell to cell attachment sites (so-called fibrocytes). Myofibroblasts are therefore regarded as a functional stage of fibroblasts seen in many physiological and pathological conditions. In addition, with the advent of immunohistochemical markers, an increasing number of benign and more rarely malignant mesenchymal neoplasms showing a myofibroblastic line of differentiation have been reported in the past years. Dermatomyofibroma, first described as a plaque-like dermal fibromatosis, represents a rare but distinct benign dermal proliferation of fibroblasts and myofibroblasts of the skin. We report a series of 56 cases of dermatomyofibroma, discuss histologic and immunohistochemical features, and widen the clinicopathologic spectrum of this entity also in regard to other spindle cell lesions of the dermis and subcutis.

MATERIALS AND METHODS

The tissue in all cases was fixed in 4%-buffered formalin, routinely processed, and embedded in paraffin. 4-μm-thick sections were stained with hematoxylin and eosin, and elastic stain was performed in 43 cases. In addition, representative sections in 48 cases were stained immunohistochemically by the labeled streptavidin-biotin technique using commercially available antibodies; antigen retrieval was used for all antibodies. Staining for alpha-smooth muscle actin (clone; 1:44, dilution: 1:200, source: DAKO), G-actin (Denmark), muscle actin (HRIF3, 1:200; DAKO), b-cadherin (b-cD, 1:200; DAKO), CD34 (1:50; DAKO), desmin (D3, 1:200; DAKO), epithelial membrane antibodies (AE1-3, 1:400; Biogenex, San Ramon, CA), factor VIIIa (AC-1, 1:100; LabVision, Waltham, MA), and S-100 protein (polyclonal, 1:4000; DAKO) were available in a varying number of cases. Appropriate positive and negative controls were used in all cases. Clinical information and follow-up were retrieved from the laboratory request forms and contributing clinicians. Cases 51, 52, and 53 have been reported in detail elsewhere.

RESULTS

The clinical findings are summarized in Table 1. Briefly, the analyzed neoplasms arose in 40 female and 8 male patients (gender was unknown in 8 cases), and patients' age ranged...
F, 31 years, right shoulder
Plaque-like CD34 positive dermal Fibroma ("Medallion-like Dermal Dendrocyte Hamartoma")

**Plaque-like CD34-positive Dermal Fibroma**

("Medallion-like Dermal Dendrocyte Hamartoma")

**Clinicopathologic, Immunohistochemical, and Molecular Analysis of 5 Cases Emphasizing its Distinction From Superficial, Plaque-like Dermatofibrosarcoma Protuberans**

Heinz Kuzner, MD,* Thomas Mentzel, MD,* Gabrielle Palmpeo, PhD,* Markus Hanschke, MD, Arno Rütten, MD,* Bruno E. Paredes, MD,* Leo Schärer, MD,* Carlos Serra Gualda, MD,† and Luis Requena, MD‡

**Abstract:** Medallion-like dermal dendrocyte hamartoma (DH) and superficial (plaque-like) dermatofibrosarcoma protuberans (DFSP) are CD34-positive dermal neoplasms with overlapping clinicopathologic features. We analyzed the clinical, histomorphologic, and molecular criteria of 5 DH and 7 DFSP to delineate diagnostically relevant differences between inoperable DFSP and its benign look-alike: DH. We expand the clinical and histologic spectrum of DH. As medallion-like dermal DH is neither of dermal dendrocyte lineage nor a genuine hamartoma, we propose instead the descriptive term of plaque-like CD34-positive dermal fibroma (PDF). Both PDF/DH and DFSP presented as slightly pigmented and indurated plaques on neck, trunk, and extremities. Histologically, DFSP was characterized by horizontally oriented spindle cell fascicles or by diffusely arranged fibroblasts within a slightly myxoid stroma in the upper two-thirds of the dermis, whereas PDF/DH presented with a cellular band-like fibroblastic proliferation mostly in the papillary and adjacent upper reticular dermis. Only one congenital PDF/DH in a 9-year-old boy extended into the septa of the subcutaneous fat. Formalin-fixed paraffin-embedded archival tissue was used for detection of the COL1A1-PDGFR gene rearrangement by multiplex reverse transcription-polymerase chain reaction (RT-PCR) and by dual color fluorescent in situ hybridization (FISH). Archival blocks older than 4 years did not yield amplifiable RNA because of RNA degradation, whereas FISH analysis was feasible in all investigated cases. FISH analysis revealed COL1A1-PDGFR gene rearrangement in all DFSP cases (6/7), whereas RT-PCR could detect the COL1A1-PDGFR fusion transcript only in 1 DFSP. Two cases were negative. In 4 archival cases with an interval between 4.5 and 12 years, RNA had been degraded in these cases unsuitable for RT-PCR. In PDF/DH, both RT- and FISH analysis did not reveal any evidence of COL1A1-PDGFR gene rearrangement. We show that PDF/DH superficial (plaque-like) DFSP, subtle clinicopathologic cases notwithstanding, are morphologic look-alikes that are kept apart by molecular studies of the COL1A1-PDGFR fusion. For the detection of the COL1A1-PDGFR gene rearrangement in diagnostically difficult cases, RT-PCR and FISH are reliable and helpful diagnostic tools. In arc formalin-fixed paraffin-embedded tissue, however, FISH is more robust and exhibits a higher clinical sensitivity than RT-PCR.

**Key Words:** medallion-like dermal dendrocyte hamartoma, plaque-like CD34+ dermal fibroma, superficial plaque dermatofibrosarcoma protuberans, CD34::COL1A1::PDGFR fusion gene

(Am J Surg Pathol 2010:34:190-201)

The spectrum of CD34-positive (CD34+) tumors of the skin comprises a heterogeneous family of soft tissue neoplasms with multiple lines of differentiation, ranging from the fibroblastic to the hemangiomatous lineage. Among these, those most diagnostic difficulties encountered within the group of dermal fibroplastic soft tissue proliferations, some of which are poorly de and present with a wide clinical and histomorphologic spectrum, showing overlap with congenital dermatofibrosarcoma protuberans (DFSP). We report a series of 5 cases of DH and 7 cases of superficial (plaque-like) DFSP, expand the clinicopathologic spectrum of these neoplasms, and discuss mole methods for differential diagnosis. We will show: multiplex reverse transcription-polymerase chain rea
Plaque-like CD34-positive dermal Fibroma

- children, adults
- bandlike fibroblastic proliferation
- upper half of the dermis
- no involvement of stratum papillare
- adnexal structures are spared
- many vessels
- biphasic growth
no COL1A1 / PDGFB fusion
plaque-like DFSP

- horizontal growth
- also in deeper parts of the dermis
- myxoid stroma
- adnexal structures are not spared
- *COL1A1 / PDGFB* fusion
COL1A1 / PDGFB fusion
Diagnosis Case 2?
- flat dermatofibroma
- neurofibroma
- dermatomyofibroma
- plaque-like CD34-positive dermal fibroma
- plaque-like dermatofibrosarcoma protuberans
Case 2:
separated signals are present in
42 out of 50 nuclei counted
Diagnosis Case 2

plaque-like DFSP
Dermatofibrosarcoma protuberans (DFSP)

**COL1A1::PDGFB** (classic or cryptic)

FISH-probes for t (17;22)
green BAC 93L18 (chromosome 22)
red BAC 506F07 (chromosome 17)
M, 47 years, right shoulder 1982
(history: recurring neurofibroma, neurofibromatosis? multiple lesions between 1962-1981, no histology!)
Fibrosarcomatous DFSP

M, 47 years
multiple lesions
FS-transformation in R liver MTS, DOD
M, 52 years, left groin
Diagnosis: neurofibroma (no IM was done!)
local recurrence at 3 years
Diagnosis: DFSP with giant cell fibroblastoma-like areas
Neurofibromatous changes in dermatofibrosarcoma protuberans: a potential pitfall in the diagnosis of a serious cutaneous soft tissue neoplasm

CL Kovarik et al.
J Cutan Pathol 2004; 31: 492-496

6 cases, 3 M, 3 F, 21-80 years
spindled cells with wavy nuclei in a loose mucinuous stroma suggesting neural differentiation
3 cases: S-100 +, CD 34 +
3 cases: S-100 -, CD 34 +
M, 4 years
COL1A1 dual color break-apart probe, 16 of 50 nuclei positive
Diagnosis:

multicentric, flat DFSP in a young patient with ADA-SCID syndrome (adenosine desaminase-deficient severe combined immunodeficiency)

ADA-SCID:
- rare genetic disorder
- humoral and cellular immunity are affected
- increased risk for life-threatening infections

- 12 patients with ADA-SCID were evaluated
- 8 patients had DFSP
- 7 patients had multiple lesions (4-15 lesions)
- most lesions presented as round, atrophic plaques
- 3 lesions were nodular
- CD34 + in all cases
- t(17;22)(q22;q13) in 6 patients
- FISH: COL1A1-PDGFB fusion in 7 patients
- RT-PCR: COL1A1-PDGFB fusion transcript in 6 patients
Genetics of DFSP

**COL1A1::PDGFB** fusion: majority of cases

**COL6A3::PDGFD** fusion: F, breast
(Dickson BC et al. Genes Chromosomes Cancer 2018; 57: 437)

**EMILIN2::PDGFD** fusion: subcutaneous growth
(Lee PH et al. AJSP 2022; 46: 942)

**PDGFB/D** negative cases with ALK expression/rearrangement
(Agrawal S et al. Mod Pathol 2023; 35: 213A)
Case 3: Clinical Findings

- F, 67 years
- buttock
- DFSP was suspected
Recurrent NTRK1 gene fusions define a novel subset of locally aggressive lipofibromatosis-like neural tumors

8 F, 6 M, 4-38 years, local recurrence in 5/12 cases
upper (6), lower extremity (5), head (2), flank (1)
1.3 - 5.4 cm, subcutaneous lesions
infiltrative spindle cell neoplasms
mild nuclear atypia, no / few mitoses
S-100 +, CD34 + (10/11), ASMA + (3/8), desmin -,
Sox-10 -, HMB-45 -, Melan-A -, STAT6 -, H3K27me3 +
NTRK1 gene rearrangements with NTRK1 staining
Dermal lipofibromatosis-like neural Tumor
(M Llamas-Velasco et al. J Cutan Pathol 2022; 6: 525)

- 5 cases, 3 M, 2 F, 14-68 years
- lower limbs (4), back (1)
- poorly circumscribed dermal neoplasms
- monomorphous spindle-shaped tumour cells
- CD 34 +, S-100 +, NTRK1 +,
  ALK -, EMA -, NKIC3 -, MNF116 -, ASMA -
DD: dermatofibrosarcoma protuberans
  fibrous hamartoma of infancy
  lipofibromatosis
  infantile fibrosarcoma
  low-grade MPNST
Foci of myxoid areas  

NTRK1 +
Superficial ALK-rearranged myxoid spindle cell neoplasm: a cutaneous soft tissue tumor with distinctive morphology and immunophenotype
(JK Dermawan et al. Mod Pathol 2021; 34: 1710)

6 cases (2 F, 4 M), 18-84 years, back (3), leg (3)
concentric whorls and cords of spindled tumor cells +
cellular aggregates of ovoid to epithelioid tumor cells
myxoid to myxohyaline stroma
peripheral lipofibromatosis-like areas in two cases!
ALK +, CD34 +, S100 5/6 +, Sox10 -, CK -, EMA -
ALK-FLNA fusion (3)
ALK-MYH10 fusion (2)
ALK-HMBOX1 fusion (1)
NTRK-rearranged spindle cell Neoplasms

Definition:

Emerging family of rare spindle cell neoplasms with a wide morphological spectrum, from lipofibromatosis-like neural tumour to infantile fibrosarcoma-like lesions; harboring NTRK1/2/3 gene rearrangements or other gene alterations (i.e. RAF1, BRAF, RET) implicated in receptor kinase pathway activation.
**NTRK-fused mesenchymal Neoplasms**

heterogeneous group of mesenchymal tumours with fibroblastic or neural differentiation

lipofibromatosis-like neural tumour

infantile fibrosarcoma (*ETV6::NTRK3*)

MPNST-like tumours (h3K27me3 +)

*LMNA::NTRK1* spindle cell sarcoma

S-100 +, CD 34 +, NTRK +, Sox10 -

treatment with NTRK inhibitors in aggressive neoplasms
Case 4

M, 11 years, retroauricular
Claudin-1 -
Desmin -
Pancytokeratin -
Diagnosis Case 4

Low-grade fibromyxoid Sarcoma


21 out of 33 patients had local recurrence
15 out of 33 patients developed metastases
14 out of 33 patients died of tumour (3-42 years)
Low-grade fibromyxoid Sarcoma

- young adults >> children, soft tissue >> dermis, proximal extremities > trunk > retroperitoneum
- collagenous / myxoid stroma, short fascicles, whorling and swirling, bland, spindled, fibroblastic tumour cells, arcades of blood vessels
- MUC4 +, EMA + (75%), ASMA rarely focal +, CD34 rarely focal +, S-100 -
- translocation associated sarcoma
  \[ t(7;16) \text{ with } FUS-CREB3L2 \text{ (in most cases) } \]
  rarely \[ FUS-CREB3L1 \text{ or } EWS-CREB3L1 \]
F, 36 years, pelvis by courtesy of Prof. Fletcher, USA
FISH-analysis for *FUS* Translocation

WT 689/06

Signals are in different parts of the nucleus = positive

negative control

Signals are close together = negative
Low-grade fibromyxoid Sarcoma with giant rosettes (Lane KL et al. AJSP 1997; 21: 1481)

CD56 +
Histological mimics of low-grade fibromyxoid sarcoma are MUC4 negative.

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<tr>
<th>Tumor Type</th>
<th>Histological Features</th>
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<tr>
<td>Angiofibroma of soft tissue</td>
<td>Variable EMA, CD34 expression, <em>AHRR::NCOA2</em></td>
</tr>
<tr>
<td>Acral fibromyxoma</td>
<td>Fascicular growth, EMA +, CD34 +, nestin +</td>
</tr>
<tr>
<td>Superficial angiomyxoma</td>
<td>Lobular growth, perivascular neutrophils</td>
</tr>
<tr>
<td>Perineurioma</td>
<td>EMA +, claudin-1 +</td>
</tr>
<tr>
<td>Neurofibroma</td>
<td>Tapering nuclei, S-100 +</td>
</tr>
<tr>
<td>Cellular intramuscular myxoma</td>
<td>No arcades of vessels, CD34 +/-</td>
</tr>
<tr>
<td>Myxoid SFT</td>
<td>CD34 +, STAT6 +, HPC-like vessels</td>
</tr>
<tr>
<td>Desmoidfibromatosis</td>
<td>Long fascicles, ASMA +, β-catenin +, LEF 1 +</td>
</tr>
<tr>
<td>Low-grade MPNST</td>
<td>Cytological atypia, S100 / GFAP focal +</td>
</tr>
<tr>
<td>Low-grade myxofibrosarcoma</td>
<td>Cytological atypia, curvilinear vessels</td>
</tr>
</tbody>
</table>
Conclusions Case 4

low-grade fibromyxoid sarcoma may occur in children
low-grade fibromyxoid sarcoma may occur superficially
low-grade fibromyxoid sarcoma is mimicking benign neoplasms
MUC4 represents the most sensitive marker
Case 5

- M, 77 years
- upper back
- subcutaneous lesion
- encapsulated lesion
Diagnosis Case 5

spindle cell Lipoma

BUT
Diagnosis Case 5

encapsulated Neurofibromatosis

BUT
loss of Rb-1 (Sox10 -)
S-100 protein expression of spindle cells in spindle cell lipoma: a diagnostic pitfall
Mentzel T et al. Virchows Archiv 2016; 469: 435

5 cases (1 F, 4 M, 55-89 years, 0.6 - 2.5 cm) nose, chin, neck, forehead, retroauricular dermis (1), subcutis (4) ill-defined (1), encapsulated (4) CD 34 +, S-100 +, Rb -, Sox 10 - DD: Neurofibroma (Sox 10 +, Rb +, unencapsulated) desmoplastic MM (Sox 10 +, cytological atypia, lymphoid aggregates, ass. lentigo maligna) Schwannoma (no fat, hyalinised vessel walls, Rb1 +)
M, 69 years, neck
S-100 positive Spindle cell Lipoma

spindle cells in cases of spindle cell lipoma may show an unusual immunophenotype
(Desmin expression in spindle cell lipomas: a potential diagnostic pitfall
Case 6 (by courtesy of Prof. G. Massi, Rome)
M, 17 years, painful lesions, biopsy
Diagnosis Case 6: spindle cell myogenic neoplasm?
Diagnosis Case 6: pseudomyogenic Haemangioendothelioma („epithelioid sarcoma-like Haemangioendothelioma“)
Pseudomyogenic Hemangioendothelioma: A distinctive, often multicentric tumor with indolent behavior
(Hornick JL, Fletcher CDM AJSP 2011; 35: 190)

- 50 cases, 41 M, 9 F, 14 - 80 years
- lower (54%), upper (24%) extremities, trunk (18%), head / neck region (4%)
- multifocal neoplasms (2-15 neoplasms) (66%)
- fascicles, sheets of plump spindled cells
- few epithelioid cells
- AE1/3 +, Fli-1 +, 22/47 CD 31 +, 7/49 EMA + CD 34 -, INI1 +, S-100 -
- local recurrence (58%), MTS (2 x)
Differential diagnosis: pseudomyogenic Haemangioendothelioma

Cutaneous tumours: dermatofibroma, leiomyoma, myofibroma, epithelioid sarcoma (INI1 -), spindle cell squamous carcinoma

Deep seated tumours: epithelioid sarcoma, epithelioid haemangioendothelioma, angiosarcoma, nodular/proliferative fasciitis

Bone tumours: epithelioid haemangioma, giant cell tumour, osteoblastoma, fibroma
Case 7

- 71-year-old male patient
- indurated dermal lesion
- forehead
- biopsy
- subsequent R0 resection
malignant cutaneous spindle cell tumour in an elderly patient arising on the head
spindle cell malignant Melanoma?
spindle cell sarcomatoid Carcinoma?
myogenic Sarcoma?
Diagnosis Case 7: spindle cell cutaneous Angiosarcoma
Case 8
M, 56 years
biopsy, excision
NSR at 15 months
atypical plump spindled tumour cells
nuclear atypia, numerous mitoses
Diagnosis Case 8:

malignant spindle cell neoplasm of the dermis in a middle-aged male patient ...

? spindle cell melanoma ?
Diagnosis Case 8:

malignant spindle cell neoplasm of the dermis in a middle-aged male patient ...

? spindle cell sarcomatous carcinoma ?
Diagnosis Case 8:

malignant spindle cell neoplasm of the dermis in a middle-aged male patient ...

? high-grade DFSP ?
scattered atypical lymphoid cells
Diagnosis Case 8

cutaneous spindle cell B-cell lymphoma
Cutaneous spindle cell B-cell lymphoma: a morphologic variant of cutaneous large B-cell lymphoma
Cerroni L et al. AJDP 2000; 22: 299
Cutaneous spindle cell B-cell lymphomas: most are neoplasms of follicular center cell origin
Charli-Joseph Y et al. AJSP 2015; 39: 737

- very rare neoplasms (< 30 cases described)
- high-grade cutaneous lymphomas???
- atypical spindled tumour cells
- expression of LCA, B-cell markers
- nuclear expression of bcl-6
- bcl-6 mutations
- no MUM1 expression
- features of germinal center B-cell origin
Case 9: Clinical Findings

- 57-year-old female patient
- multiple lesions on both feet
- exophytic, nodular dermal lesions
- previously blisters have been reported
- fibromatosis has been suspected
- biopsy
abundant collagenous stroma
elongated, bland spindled cells
fibroblastic neoplasm?
neural neoplasm ?
perivascular inflammatory cells
neutrophils, leukocytoclasis
Myeloperoxidase
Diagnosis Case 9

Erythema elevatum et diutinum (tumour stage)
Erythema elevatum et diutinum

• variant of chronic vasculitis
• long duration
• persistent papules, plaques and nodules
• multiple, symmetrical lesions
• distal extremities
• associated systemic diseases
  (MDS, lymphoma, IgA gammopathy...)
• different stages of disease
Erythema elevatum et diutinum

**early lesions:**
- perivascular infiltrate of neutrophils
- leukocytoclasis, fibrin deposition

**established lesions:**
- neutrophilic infiltrate of the entire dermis
- sometimes spongiosis, blister, necrosis

**late lesions:**
- variable fibrosis, capillary proliferation
- tumour-like fibroblastic proliferation
- scattered neutrophils
Conclusions

- intradermal spindle cell proliferations represent a heterogeneous group of neoplasms / lesions
- spindle cell mesenchymal neoplasms of the skin include all lines of differentiation
- be aware of mimics
- immunohistochemical stainings are very helpful in establishing the diagnosis
- be aware of aberrant expression!
- molecular studies are helpful in selected cases
Thank you very much for your attention!