Acral Lesions in Dermatopathology

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Overview

• Non-neoplastic
  – Circumscribed palmar hypokeratosis
  – Necrolytic acral erythema
  – TNF-alpha inhibitor reactions
  – Bullous acral erythema
  – APACHE

• Neoplastic
  – Soft tissue lesions
  – Miscellaneous
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Circumscribed palmar/plantar hypokeratosis

- Clinically:
  - Round lesion with very well-defined borders and erythematous central area
  - Tendency for thenar/hypothenar areas, medial side of sole
Histologic Features

- Well-demarcated decrease in thickness of stratum corneum
- Diminished granular layer
- No inflammation
Background
-- Only a few cases have been reported in the literature
-- First described in 2002 (Perez, et al JAAD)
-- Clinical DDx includes porokeratosis or Bowen disease
-- Authors consider it a chronic localized defect in keratinization.

Treatment:
-- Topical corticosteroids or topical retinoids are ineffective
-- possible benefit from photodynamic therapy or calcipotriol treatment
Circumscribed Palmar or Plantar Hypokeratosis: First Report on a Nonacral Site With Unique Histologic Features

Tatyana Groysman, DO,* Jeremy Rothfleisch, MD,† and Marisa F. Baldassano, MD‡
Necrolytic Acral Erythema

• Sharply-demarcated scaly plaques on dorsum of hands and feet
• Appox 50 patients reported since 1996
• Strong association with HCV
Histologic features

• Early lesions may show only psoriasiform hyperplasia with scattered and grouped dyskeratotic cells
• Well-developed lesions include parakeratosis, neutrophils, hypogranulosis
Early lesion
Necrolytic acral erythema is a newly described entity characterized by sharply demarcated scaly plaques on the dorsum of the hands and feet. More than 30 patients have been reported since 1996, all of whom had...
Biologic therapies targeting tumor necrosis factor (TNF)-alpha have become a mainstay in the management of a number of autoimmune diseases. We report a series of adverse skin eruptions in six patients (four females, two males, age: 21–58 years, mean: 39) receiving 4 months to
Palmoplantar pustulosis

Hawryluk et al. *J Cutan Pathol*, 2012
Bullous acral erythema

- Variant of chemotherapy-induced acral erythema
- Acral dysthnesia followed by erythema, blisters, and desquamation
- Approx 30 cases in literature
- Cytarabine and methotrexate most common drugs

Pojjasek and Camilleri, J Cutan Pathol, 2012
Histologic features

Pauci-inflammatory, subepidermal bullae, DIF-negative
Acral pseudolymphomatous angiokeratoma of children (APACHE)
Acral pseudolymphomatous angiokeratoma of children (APACHE)

- APACHE likely represents a spectrum of benign lesions in adults in children
- Multiple, hyperkeratotic erythematous/violaceous papules and nodules that are usually asymptomatic
- Predilection for acral sites
- Etiology unknown
Acral pseudolymphomatous angiokeratoma of children (APACHE)

Subepidermal, dense lymphoid infiltrate. Often proliferation of thick-walled blood vessels.

Predominantly T-cells (mixed CD4 and CD8) with scattered B-cells.
APACHE Proposed alternate name:
T-cell-rich angiomatoid polypoid pseudolymphoma of the skin

J Cutan Pathol, 2011; 38, 6: 475-82
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Soft Tissue Lesions

- Superficial acral fibromyxoma (aka digital fibromyxoma)
- Cellular digital fibroma
- Lipofibromatosis
- DFSP
- Myxoinflammatory fibroblastic sarcoma (aka inflammatory myxohyaline tumor of distal extremities)
- EWSR1-SMAD3-rearranged fibroblastic tumor
- Perineurioma
- Clear cell sarcoma
- Myoepithelioma/myoepithelial carcinoma
• 37 cases from 25 m and 12 f, age 14-72
• toe [20 cases], finger [13], palm [4]
• nail region often affected [16 cases]
• 1-5 cm, usually well-delimited
• dermal
Histologic features

• Moderate cellularity, possible focal cytologic atypia, but low mitotic activity
• Stellate to spindled fibroblasts in myxoid to collagenous stroma
• Minimal inflammation, except mast cells
• EMA, CD34, CD99
• NEGATIVE muscle markers, keratins, S100 protein, HMB45
• Occasional recurrences
DDx:
- Myxoid DFSP
- Myxoid NF
- Digital myxoid pseudocyst
- Myxoinflammatory fibroblastic sarcoma
- Myxoid MFH
intersecting fascicles of relatively bland CD34-positive spindle cells in fibrous or fibromyxoid stroma
Lipofibromatosis

- 45 tumors from 32 boys and 12 girls, 11d-12y
- Hand [18 cases], arm [8], leg [7], foot [6], chest [3], abdomen [2], head [1]
- 8 congenital
- Painless, slow-growing
Lipofibromatosis

- 1-7 cm, poorly marginated, infiltrative
- Abundant fat with accompanying fibroblastic proliferation
- Spindled areas with CD34, CD99, SMA variably bcl-2, S100, MSA
- Recurrences common
Cells reminiscent of lipoblasts in zones where fat and fibroblastic component merge
Dermatofibrosarcoma Protuberans

- Usually young adults
- Recent case series (n=27) on distal extremities and acral sites
- CD34+ by IHC
- COL1A1-PDGFB gene fusion

Myxoinflammatory fibroblastic scarcoma


2002 WHO name: Myxoinflammatory fibroblastic sarcoma
Clinical Features

• All ages: range 4-91 yrs (median 45 years)
• No sex predilection
• Non-tender mass on an extremity (70% upper and 30% lower)
• Recurrence rates vary from 6-67%
• Lymph node metastases have been reported
# Myxoinflammatory fibroblastic sarcoma

## Tumor Depth

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Depth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tendon</td>
<td>35%</td>
</tr>
<tr>
<td>Synovium</td>
<td>20%</td>
</tr>
<tr>
<td>Subcutis</td>
<td>45%</td>
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</tbody>
</table>
Histologic features

- Dense chronic inflammatory infiltrate
- Myxomatous adjacent to hyalinized stroma
- Collections of short spindled and rounded epithelioid cells
• Epithelioid cells may have large, bizarre cells with macronucleoli
• Low mitotic index
• Lesional cells express CD34, EGFR, and CD163
Table 1. Immunohistochemical staining of Acral myxoinflammatory fibroblastic sarcoma (AMFS)

<table>
<thead>
<tr>
<th></th>
<th>No. positive (%)</th>
<th>Average strength of staining when staining present (scale of 1 to 3+, with 3+ strongest)</th>
<th>Average per cent (%) of lesional cells staining when staining present (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD163</td>
<td>16/16 (100)</td>
<td>2.9</td>
<td>50 (5–90)</td>
</tr>
<tr>
<td>CD34</td>
<td>17/18 (94)</td>
<td>2.4</td>
<td>38 (&lt; 10–95)</td>
</tr>
<tr>
<td>EGFR</td>
<td>14/16 (86)</td>
<td>2.3</td>
<td>46 (10–90)</td>
</tr>
<tr>
<td>EMA</td>
<td>13/18 (72)</td>
<td>2.0</td>
<td>15 (&lt; 10–70)</td>
</tr>
<tr>
<td>CD117</td>
<td>7/18 (39)</td>
<td>1.0</td>
<td>25 (&lt; 10–50)</td>
</tr>
</tbody>
</table>

EGFR, epidermal growth factor receptor; EMA, epithelial membrane antigen.
Consistent t(1;10) with Rearrangements of TGFB3 and MGEA5 in Both Myxoinflammatory Fibroblastic Sarcoma and Hemosiderotic Fibrolipomatous Tumor

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1Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY
2Department of Pathology, Massachusetts General Hospital, Boston, MA
3Department of Pathology, Brigham and Women’s Hospital, Boston, MA
EWSR1-SMAD3–rearranged Fibroblastic Tumor
An Emerging Entity in an Increasingly More Complex Group of Fibroblastic/Myofibroblastic Neoplasms

Michael Michal, MD,* †‡ Ryan S. Berry, MD,§ Brian P. Rubin, MD, § Scott E. Kilpatrick, MD, § Abbas Agaimy, MD,|| Dmitry V. Kazakov, MD,* †‡ Petr Steiner, MD,* †‡ Nikola Ptakova, MSc,* †‡ Petr Martinek, PhD,* †‡ Ladislav Hadravsky, PhD,¶ Kvetoslava Michalova, PhD,* †‡ Zoltan Szep, PhD,# and Michal Michal, MD* †‡
Perineurioma
Sclerosing perineurioma

• Children and young adults
• Well-circumscribed dermal or subcutaneous nodules on hands (including palms)
Dense collagenous stroma
Epithelioid and spindle cells with wavy nuclei, elongated cytoplasmic processes
Perineurioma, EMA

EMA (100%) CD34 (65%), Glut 1
Extra-acral cutaneous/soft tissue sclerosing perineurioma: an under-recognized entity in the differential of CD34-positive cutaneous neoplasms

Melanie D. Fox¹, Briana C. Gleason², Antoinette B. Thomas¹, Thomas A. Victor¹ and Thomas L. Cibull¹
Clear Cell Sarcoma

• Young adults, 3rd to 4th decade
• 40% involve foot/ankle
• Slow-growing lesion
• t[12;22] with EWS ATF1 fusion
• 37% - 59% mortality
• Nodal mets in 50%
Myoepithelioma

- Recently described in the skin
- Painless cutaneous nodule
- Involving extremity
- Younger patients (22 yrs median age)
Histologic features

• Epithelioid cells with scant eosinophilic cytoplasm
• Solid, spindled, plasmacytoid, and combinations
• Stroma may vary
• CK+, S100+, and SMA+
Myoepithelial Carcinoma

- No criteria for malignancy in cutaneous lesions
- Presence of cytologic atypia and increased mitotic index are most important factors
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Digital Papillary Adenoma/Adenocarcinoma

Digital papillary adenocarcinoma: a tumour that should be considered in the differential diagnosis of neoplasms involving the digits

RICHARD A. SCOLYER*, ROOSHDIYA Z. KARIM*, JOHN F. THOMPSON†, JONATHAN R. STRETCH†, STANLEY W. McCARthy† and RAJMOHAN MURALI†
• Strong male predominance
• Mean age 43 yrs
• All involved a finger or toe, with most involving the distal part of the digit
• Subcutaneous extension in 50% of cases
• Histologic features (including presence of myoepithelial cells) not predictive of outcome
Extrafacial indolent CD8-positive cutaneous lymphoid proliferation with unusual symmetrical presentation involving both feet

Indolent CD8+ cutaneous lymphoid proliferation represents a recently described entity among cutaneous T-cell lymphomas that typically presents with solitary skin lesions on the face or at acral sites and usually follows an indolent clinical course. Histopathologically, this entity is characterized by a dense dermal infiltrate of non-epidermotropic, small- to medium-sized pleomorphic CD8+ T-cells of the non-activated cytotoxic phenotype showing a clear-cut granzyme and a
Primitive non-neural granular cell tumor (PNGCT)

• 1991 Leboit et al “primitive polypoid granular cell tumor (GCT)”
• Two larger series as “PNGCT” and “dermal non-neural GCT”
• Not neural or Schwannian in origin, but line of differentiation remains unknown
• Solitary painless nodule most typically on extremity of adult
• Typically benign, but one report of a lymph node metastasis has been documented
Histologic features

- Relatively circumscribed
- No well-developed PEH
- Mitotic index from 1-3 per mm² with occasional atypical forms
- S100-, CD68+, NKI-C3+
- EM confirmed lysosomes

Congenital epulis of the newborn

• S100-negative epithelioid granular cells
• Usually involves the alveolar ridge of females
### Suggested reference:

Chalhoub and Al-Rohil, 10 Jan 2019, J Cutan Pathol

Table showing DDx of spindle cell tumors on acral sites

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Clinical Presentation</th>
<th>Histopathologic findings</th>
<th>Immunohistologic findings</th>
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</thead>
</table>
| Plantar/Palmar fibromatosis | Young adults, solitary or multiple nodules affecting aponeurosis. | - Monomorphic bland spindle cells of long fascicles, embedded in a collagenous stroma that blends with the fascia.  
- Can be cellular with plump cells and sometimes display mitotic activity. | Positive for EMA, CD34, Claudin-1 and GLUT-1. |
| Perineurioma             | Young adults, solitary cutaneous or subcutaneous nodule.    | - Well-circumscribed, composed of bland elongated spindle to ovoid cells.  
- Whorled growth pattern.  
- May show myxoid background but lacks curvilinear vessels. | Positive for CD34. |
| Superficial acral fibromyxoma | Usually adults, solitary tumor occurring on subungual/perungual areas of fingers or toes. | - Dome shaped, fibroblastic proliferation in the dermis that is unencapsulated.  
- Usually show alternating fibrous and myxoid stroma. | Positive for CD34. |
| Cellular digital fibroma  | Wide age range, solitary, papule on fingers and toes.      | - Proliferation of uniform slender fibroblasts in short intersecting fascicles in parallel orientation.  
- Associated with variably dense dermal collagen. | Positive for CD34. |
| Inclusion body fibromatosis | Presents in infancy as firm nodule on dorsal or lateral surface of distal phalanges of fingers or toes. | - Bland dermal spindle cells with intracytoplasmic, eosinophilic spherical inclusions in varying amounts of extracellular collagen.  