Overview

- Difficult squamous lesions
  - Pseudoepitheliomatous hyperplasia
  - Multiple squamous lesions on severely photodamaged shins
  - Histiocytoid Sweet syndrome
  - Erdheim-Chester disease

"Squamous cell carcinoma" (SCC)

- Clinically
  - A pink nodule, often with obvious scale, may be ulcerated/crusted and tender
  - Fairly rapid growth, sun-exposed area

- Histopathologically
  - Atypical keratinocytes present in the dermis

Disclosures

- No conflicts of interest pertaining to this talk
- Will discuss off-label use of medication
- Royalties from Elsevier and Wiley-Blackwell
Primary cutaneous anaplastic large cell lymphoma (ALCL) with pseudoepitheliomatous hyperplasia

Pink, crusted nodules with atypical keratinocytes in the dermis

Hypertrophic lupus erythematosus

Lesions resolved with IL Kenalog

Helpful clues for DLE > SCC
1. Vacuolar change (+/- necrotic keratinocytes and colloid bodies)
2. Lichenoid/periadnexal inflammation
3. CD123-positive lymphocytic clusters

Mimics of SCC (PEH)

“Pseudoepitheliomatous hyperplasia (PEH)” aka “pseudocarcinomatous hyperplasia” associated with
- Tumors, e.g. anaplastic large cell lymphoma
- Deep fungal infections
- Other, e.g. tattoo

Hypertrophic lupus erythematosus
Hypertrophic lichen planus
Graft-versus-host disease
Overview

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Multiple squamous lesions on severely sun-damaged skin, especially shins

• Generally Caucasian females > age 70
• Multiple nodules or plaques, sometimes crateriform
• Some patients may also have lesions of hypertrophic lichen planus
• Variable histopathologic features
  - Keratoacanthoma (KA)-like or SCC-like
  - Some crateriform, some endophytic, some plaque-like

Photos courtesy David Leffell, MD

Relatively high morbidity from large excisions

3 examples of her “SCC’s”

Diagnosed with 7 “SCCs” on her legs in the span of 2 years

Photos courtesy Peter Heald, MD

My approach: (multiple) squamous lesions on severely sun-damaged skin (leg)

“Multiple KA” of the legs

“Infundibulocystic SCC”

KA=keratoacanthoma
Clinically, lesions were nodular in this series.

- 20/30 cases: TP53 mutations present
- 2/10 in tetramerization domain
- None in DNA-binding domain

SCC hot spots

- 10/30 cases: No TP53 mutation

"Keratoacanthoma-like squamous proliferations" ("KASP")

- Unlike most SCC, lack of common TP53 mutations
- KA-like: clinically nodular to craterform; histopathologic features of KA
- Conservative treatments with follow-up of response/behavior
  - Shave excision +/- cautery at time of presentation
  - Intralesional steroid or methotrexate, intralesional or topical 5-fluorouracil, other
  - Topical steroid under occlusion
  - Oral retinoids

Multiple squamous nodules on the lower extremities

- acitretin 25 mg po daily
- X 12 months

Photos courtesy of Nour Kibbi, MD

"Multiple keratoacanthoma" of the legs

- acitretin x 12 weeks

Photos courtesy of Nour Kibbi, MD

"Infundibulocystic SCC"

- acitretin x 1 year

Photos courtesy of Sean Christensen, MD, PhD
Overview

- Difficult squamous lesions – multiple squamous lesions on severely sun-damaged skin of the lower leg
  - Atypical squamous proliferations (ASP) are the most common - conservative treatment often sufficient
  - Histiocytoid Sweet syndrome
  - Erdheim-Chester disease

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Sweet syndrome criteria

- 2 major criteria needed
  - 1. Typical cutaneous lesions
  - 2. Consistent histopathology
- At least 2 minor criteria needed
  - 1. Particular associations, e.g. malignancy
  - 2. Fever
  - 3. Leukocytosis
  - 4. Steroid-responsive

Diagnostic gray zone

- Histiocytoid Sweet syndrome (HSS)
  - Cells may have identical molecular alterations as systemic disease (e.g. acute myelogenous leukemia, myelodysplastic syndrome [MDS])

“HSS” per authors: patient with MDS with IDH-1 mutation

6 patients with HSS
5/6 with known chromosomal abnormality in bone marrow
4/5 with same abnormality in histiocytoid cells

Histiocytoid Sweet syndrome may indicate leukemia cells: A novel application of fluorescence in situ hybridization


IDH-1 stain

CD68

MPO

Photo courtesy Nour Kibbi, MD
Photomicrographs courtesy of Nathaniel Smith, MD

Cytokines

- IL-1β
- TNF-α
- IL-6

Diagnostic gray zone

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IDH-1 stain
Histiocytoid Sweet syndrome

- Typical clinical lesions

Per Requena et al, clinical course supports HSS even if there are molecular abnormalities in histiocytoid cells

Histiocytoid Sweet syndrome and hematologic disease

- Most studies show an increased rate of hematologic disease compared to mature neutrophlic Sweet syndrome
  - 777 (100%) cases from University of Pennsylvania
  - 1222 (55%) over 9 years in France (1/3 MDS)
  - 2034 (59%) in 3 other series
  - 8/33 (24%) patients over 4 years in Austria

References:
2. Ghoufi L et al, Medicine 2016;95:1
4. Peroni A et al. JAAD 2015;72:131
5. Vignon-Pennamen MD et al, Arch Dermatol 2006;142:1170

Overview

- Difficult squamous lesions
  - Pseudoepitheliomatous hyperplasia
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- Histiocytoid Sweet syndrome
  Most series support a strong association with hematologic disease
  Identical molecular alterations as systemic disease may be found in skin lesions; some consider this leukemia cutis
  Erdheim-Chester disease

Erdheim-Chester disease

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Chavan RN et al, JAAD 2014;80:1021

Review Article

Consensus guidelines for the diagnosis and clinical management of Erdheim-Chester disease

eraldheim-Chester disease

Erdheim-Chester disease 2018 by the Union for International Cancer Control (UICC) and the World Federation of Hematology (WFH) were prepared to ensure uniformity and rational use of the term. As a guide for clinical practice, this document reviews the most important aspects of the disease, including current understanding of pathogenesis, clinical presentation, diagnosis, management, and research. Prepared by a consensus group with expertise in the field, this document was based on a systematic review of the literature and consensus opinion. Although this document is based on the best available evidence, it is not a standard of care and does not represent the opinions of the authors or any US government agency.
Diagnosis of Erdheim-Chester disease

1. Tissue biopsy with foamy histiocytes
   AND
2. Skeletal lesions AND
   1 other organ involved (large vessel, lung, heart, CNS, retroperitoneal)

Patient

Reported CNS involvement (diabetes insipidus) as a young child

Erdheim-Chester disease

Sanchez-Pettito G et al, J Cutan Pathol 2018;45:914.
Munoz J et al, Mayo Clinic Proc 2014;89:985

Langerhans cell histiocytosis
Erdheim-Chester disease
CD1a+
CD68-
CD68+
CD1a-

Bone (osteolytic)
Bone (osteosclerotic)

Blood, 2016, Revised Classification of Histiocytoses

• Patients with ECD – 20% have lesions c/w LCH
• Can be associated with a myeloid neoplasm

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Consider molecular tests (BRAF V600E), imaging to r/o bony involvement, and a paraneoplastic workup

Take-home points

- Common on severely sun-damaged shins
- Histiocytoid Sweet syndrome: MPO+ associated with AML and MDS
- Yellow plaques
- Erdheim-Chester disease: BRAF V600E alteration, consider paraneoplastic w/u