Greatest Clinicopathologic Cases
Summer AAD 27 July, 2019
New York, NY

Jacqueline M Junkins-Hopkins MD
Geisinger Medical Center
Danville, PA
jakki22@gmail.com
DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY

Jacqueline M Junkins-Hopkins MD
Symposium S013: Greatest Clinicopathologic Cases

DISCLOSURES
I do not have any relevant relationships with industry.
CASE 1
Case 1

• 77 year old Caucasian man with several month history of scaly rash
• Not responding to topical steroids
• Meds: DM, HTN
Case 1

- Upper and lower extremities, trunk
- Prior biopsy: psoriasiform spongiotic dermatitis
Which diagnosis do you favor?

1. Lymphomatoid allergic contact dermatitis
2. Spongiotic psoriasis, possibly secondary to medication
3. Crusted scabies
4. Mycosis fungoides
5. ID reaction secondary to impetiginized eczema
Case History

- Developed non-healing ulcer on elbow
- TCR PCR (-) for clone
CD30 (-)
Which diagnosis do you favor?

1. Lymphomatoid allergic contact dermatitis with decubitus ulcer
2. Spongiotic psoriasis, possibly secondary to medication
3. Crusted scabies with decubitus ulcer
4. Mycosis fungoides
5. ID reaction secondary to deep fungal infection
• Circumscribed plaques and patches on buttock, extremities and groin
Which diagnosis do you favor?

1. Lymphomatoid allergic contact dermatitis with decubitus ulcer
2. Spongiotic psoriasis, possibly secondary to medication
3. Crusted scabies with decubitus ulcer
4. Mycosis fungoides
5. ID reaction secondary to deep fungal infection
Spongiotic Mycosis Fungoides

With double negative (CD4- / CD8-) immunophenotype
Mycosis Fungoides

- Patches, plaques, tumors
- Double covered sites
- Erythematous, dyschromic scaly, dry wrinkled, atrophic
- Bizarre shapes, circumscribed
- May simulate psoriasis, eczema (especially folliculotrophic MF)
Case 1
CTCL-MF: Typical Histology

- Epidermotropism of atypical lymphocytes
- Pautrier’s microabscess
- “Beading” of lymphocytes along DEJ
- Peppering of rete
- Absence of epidermal alteration (spongiosis, lichenoid tissue reaction)
- CD4+ CD3+/CD8 (-)
- May be double (-) or CD4+/CD8+
Histopathologic Variants of Mycosis Fungoides

- Lichenoid
- Spongiotic
- Interstitial
- Pigmented purpura*
- Bullous*
- Syringotropic*
- Syringolymphoid hyperplasia
- Granulomatous

*also with distinct clinical features
• Marked spongiosis seen in only 4% of cases
Spongiotic MF

• Rare…. or rarely diagnosed
• Difficult to diagnose without CPC
• Common in folliculotropic MF
• Clues:
  - Peppering of rete
  - Thin rete hyperplasia
  - Papillary dermal fibrosis (not LSC)
  - Prominent atypia---halos
• May require IHC and/or molecular support (may have non-clonal results)
Perinuclear Halos
Perinuclear Halos
Spongiotic MF vs lymphomatoid allergic contact dermatitis

Difficult diagnosis

Hmmm... MF or Contact Derm?
Lymphomatoid contact dermatitis to an exotic wood: a very harmful toilet seat

Contact Dermatitis 2007: 57: 128–130

Khaled Ezzedine, Nadia Rafii and Michel Heenen
FMF may have prominent spongiosis---plus eosinophils
Review of literature:
Many cases with extensive dissemination
Death within weeks in three
• 30 skin biopsies (18 patients) with patch/plaque MF
  • Some with folliculotropic MF
  • One stage III, one developed widespread disease, tumors
MF with epidermal mucinosis

MF with epidermal mucinosis vs Spongiotic dermatitis

<table>
<thead>
<tr>
<th>MF with epidermal mucinosis</th>
<th>Spongiotic dermatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphophilic, granular mucin (HE stain)</td>
<td>Spongiotic eosinophilic serum (HE stain)</td>
</tr>
<tr>
<td>Positive reaction with the colloidal iron stain</td>
<td>Positive reaction with the PAS-D stain</td>
</tr>
<tr>
<td>Epidermal lymphocytes predominate in some foci and a few Pautrier microabscesses</td>
<td>Rarely mucin deposits with the colloidal iron stain</td>
</tr>
<tr>
<td>Lymphocytes with hyperchromatic nuclei and irregular contours</td>
<td>Epidermal scattered lymphocytes</td>
</tr>
<tr>
<td>Rare Langerhans cell granulomas and eosinophils</td>
<td>Frequent Langerhans cell granulomas and eosinophils</td>
</tr>
<tr>
<td>Lack of or minimal serum and scale crust in most cases</td>
<td>Presence of serum and scale crust above areas of spongiosis</td>
</tr>
<tr>
<td>Papillary dermal fibrosis</td>
<td>Papillary dermal edema</td>
</tr>
</tbody>
</table>

Papillary dermal fibrosis, epidermal mucin, absent crusting and Langerhans cell granulomas, rare to absent eosinophils, atypia---favor MF

Male with long history of “rosacea”
Levels sections = Folliculotropic MF
Summary: Spongiotic MF

- Rare
- Often with atypical IHC
- Clues: peppering, skinny rete, papillary dermal fibrosis
- Requires CPC !!!
Case 2

- 48 year old Jamaican man with 3 weeks of severely itchy rash
- Labs notable for hypercalcemia, increased LDH
- Exam: diffuse papular rash, palpable cervical LN
- On numerous medications
What diagnosis do you favor?

1. Lichen myxedematosus
2. Leprosy
3. Disseminated sarcoidosis
4. Disseminated hematologic malignancy
5. Folliculotropic mycosis fungoides
What diagnosis do you favor?

1. Sezary Syndrome with severe pruritus and rubbing-induced papules
2. Papular mycosis fungoides with large cell transformation
3. Disseminated lymphomatoid papulosis
4. Disseminated hematologic malignancy
5. Epidermotropic diffuse large B-cell lymphoma
• (+) CD2, CD4, CD25
• (-) CD30, CD20
• PET/CT: numerous metabolically active LN
• Biopsy cervical LN: Effaced (+) CD2, CD4, CD25 (-) CD7, CD8
• Bone marrow: atypical lymphocytes, same immunophenotype
What diagnosis do you favor?

1. Sezary Syndrome with severe pruritus and rubbing-induced papules
2. Mycosis fungoides with large cell transformation
3. Mycosis fungoides with Lymphomatoid papulosis type C
4. Disseminated hematologic malignancy
5. Epidermotropic B-cell diffuse large B-cell lymphoma
Adult T-cell leukemia/lymphoma

HTVL-1+
Adult T cell Leukemia/Lymphoma (ATLL):

- Leukemia (2/3) or lymphoma a/w human T-cell lymphotropic virus type-1 (HTLV-1) infection

- Endemic regions:
  - Caribbean, Japan
  - Some regions of S. America, Africa, US (SW)

- Skin, organomegaly, hypercalcemia, lymphadenopathy

- Presentation determined by subtype
Shimoyama classification:

- Acute and lymphoma: aggressive (12 month OS, 4 year surv. 5%)
- Chronic and smoldering: indolent (may progress to acute form)

Box 1 Clinical forms of adult T-cell leukaemia/lymphoma (ATLL)

Acute
- Leukaemic picture, organomegaly, high lactate dehydrogenase (LDH) and often hypercalcaemia

Chronic
- Lymphocytosis $>4 \times 10^9/l$ with ATLL cells, skin, lung, liver or node involvement
- Calcium levels normal, LDH normal or less that twice the upper normal limit

Smouldering
- Skin and/or lung infiltrates
- No other organ involvement
- Normal lymphocyte count (1–5% ATLL cells), normal calcium and LDH

Lymphoma
- Organomegaly
- Less than 1% circulating leukaemic cells
- High LDH and possible hypercalcaemia

ATLL Skin involvement

- Skin involvement 39-57%—often chronic and smoldering
- Skin only: rare—may present first in skin
- Heterogeneous clinical and histopathologic features
  - May simulate MF/SS
- Type of eruption related to prognosis
- Patch/plaque—better prognosis
- Erythrodermic/nodulotumor—poor prognosis
Clinical features of ATLL with skin eruptions

A. Poorest prognosis: erythrodermic type, nodulotumoral, multipapular

B. Better prognosis: patch and plaque types

A. Patch type
B. Plaque type
C. Multipapular type
D. Nodulotumoral type
E. Erythrodermic type
F. Purpuric type

Sawada Y Blood. 2011;117(15):3961-3967
Adult T cell leukemia/lymphoma: (HTVL1)

- 5 cases: India (not endemic region)
- Variety of skin lesions:
  - Papules
  - Purpuric macules, hypopigmented and verrucous macules
  - *molluscum*-like lesions
  - Mucosal
- Biopsy +/- epidermotropism

Khader A et al. Indian J Dermatol 2015 Jan-Feb 60:103
ATLL Histopathologic Features

- Dermal infiltrates—often large cells
- Pautrier microabscess helpful
- Angiocentricity = clue
- May have folliculotropism
- Flower cells (smear)
14/17 with skin dx first misdiagnosed on 1st bx (MF 47%)

Bittencourt, AL. Acta Oncologica, 48:4, 598-604
ATLL Immunophenotypic Features

- CD2+/CD4+/CD25+/CD7 (-)/CD8(-)
  - May lose surface CD3
  - May be CD4+/CD8+ or CD8 immunophenotype
- May have prominent CD30+ component
- CD25 not specific to ATLL
- Usually (+) T-cell clone
ATLL: diagnosis

Consider diagnosis of ATLL if:

- From endemic region (Caribbean, Japan, Africa)
- MF/Sezary with rapid progression or initially with papules/nodules
- Prominent dermal large cells with Pautrier microabscesses, and angiocentricity
- Unusual presentation of CTCL
HTLV testing

Demonstration of clonal integration of HTLV-I in tumor:

• Not needed if typical clinical features of ATLL and HTLV-1 (+) by serology

• Helpful if:
  - HTLV-1 (-) serology and suspicious
  - Lymphomatous ATLL to distinguish from other Peripheral TCL
  - Smoldering ATLL to distinguish from healthy carrier of the virus

Clin Pathol 2007;60:1373-1377
Prognosis

- **Acute and lymphoma forms:**
  - median survival <1 year
  - 4-year survival ~5%
- **Chronic and smouldering:**
  - 4-year survival ~26.9% and 62% respectively
- **Main prognostic factors**
  - Clinical form, age 40+, advanced performance status, high LDH, high b2-microglobulin, high serum level of CD25, high serum neuron-specific enolase, hypercalcemia and a high Ki-67, hepatosplenomegaly, lymphadenopathy
- **Skin eruption:** type is independent prognostic factor
- **The presence of skin eruptions may indicate poorer outcome vs no eruptions**

Clin Pathol 2007;60:1373-1377
Blood. 2011;117(15):3961-3967
Adult T-cell leukemia/lymphoma
Case 3

- 10 year old boy
- 6 month history of asymptomatic rash on buttock, arms, lower extremities
- Unresponsive to antibiotics, topical steroids, tacrolimus
Which diagnosis do you favor?

1. Tinea corporis
2. Erythema chronicum migrans
3. Erthema annulare centrifugum
4. Allergic contact dermatitis
5. Nummular eczema
Which diagnosis do you favor?

1. Tinea corporis
2. Erythema chronicum migrans
3. Erthema annulare centrifugum
4. Allergic contact dermatitis
5. Annular pityriasis rosea
Erythema annulare centrifugum (EAC)
...the pattern of spongiosis in pityriasis rosea was similar to that in [superficial] erythema annulare centrifugum, with spongiosis being mostly focal and often associated with isolated vesicles.”
Five children with EAC were treated empirically with oral fluconazole
4 to 14 weeks of oral fluconazole, from 3 to 6 mg/kg/day, with concomitant application of low-
to midpotency topical corticosteroids. (none previously responded to topical steroids)
Pediatric Erythema Annulare Centrifugum Treated with Oral Fluconazole: A Retrospective Series

Lacey L. Kruse, M.D.,*,† Brandi M. Kenner-Bell, M.D.,*,† and Anthony J. Mancini, M.D.,*,†

*Division of Dermatology, Department of Pediatrics, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, †Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, Illinois

Case 3
Erythema annulare centrifugum (EAC)
Thank you!