Lymphoma and Pseudolymphoma

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I HAVE NO RELEVANT RELATIONSHIPS WITH INDUSTRY
### Cutaneous T-cell and NK-cell lymphomas

- Mycosis fungoides
- MF variants and subtypes
  - Folliculotropism MF
  - Pagetoid reticulosis
  - Granulomatous slack skin
- Sézary syndrome
- Adult T-cell leukemia/lymphoma
- Primary cutaneous CD30+ lymphoproliferative disorders
  - Primary cutaneous anaplastic large cell lymphoma
  - Lymphomatoid papulosis
- Subcutaneous panniculitis-like T-cell lymphoma
- Extranodal NK/T-cell lymphoma, nasal type
- Primary cutaneous peripheral T-cell lymphoma, unspecified
  - Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma (provisional)
- Cutaneous γ/δ T-cell lymphoma (provisional)
- Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma (provisional)

### Cutaneous B-cell lymphomas

- Primary cutaneous marginal zone B-cell lymphoma
- Primary cutaneous follicle center lymphoma
- Primary cutaneous diffuse large B-cell lymphoma, leg type
- Primary cutaneous diffuse large B-cell lymphoma, other
- Intravascular large B-cell lymphoma

### Precursor hematologic neoplasm

- CD4+/CD56+ hematodermic neoplasm (blastic NK-cell lymphoma)

Outline

• T-cell lymphoma
  – Mycosis fungoides
  – Sézary syndrome
  – CD30-positive lymphoproliferative disorders

• B-cell lymphoma
  – Marginal zone
  – Follicle center
  – Diffuse large B-cell lymphoma, leg type

• B-cell pseudolymphoma
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• B-cell pseudolymphoma
MF: patch stage

- Patchy to band-like lichenoid infiltrate of CD4+ (usually) lymphocytes
- Papillary dermal fibrosis
- Epidermotropism: lymphocytes within the epidermis
Epidermotropism

• Collections of lymphocytes (Pautrier’s collections)
Epidermotropism

- Lymphocytes align along dermal-epidermal junction
Epidermotropism

- Lymphocytes in epidermis with “halo”
Diagnosis of patch-stage MF often challenging
Epidermotropism in early MF

Role for ancillary testing?

- Loss of pan-T-cell antigens (CD2,5,7)
  - Somewhat controversial
  - Can be found in inflammatory conditions

- Detection of a T-cell clone
  - Frequency of clones in early MF ~ 70%
  - PLEVA 100%; Contact dermatitis 14%
  - Identical clone at different sites increases sensitivity and specificity

Best diagnostic maneuver if first biopsy not diagnostic

• More biopsies!!

Bottom line

• At least 2-3 biopsies, broad shaves optimal
• Consider T-cell clonality testing from two biopsies
Histopathology - Plaque

- Extension of infiltrate into reticular dermis
- Band-like lymphocytic infiltrate typically denser than in patch-stage disease
- Both epidermotropism and cytological atypia more evident
Histopathology - Tumor

- Diffuse infiltrate of atypical lymphocytes in diffusely throughout reticular dermis
- Cytologically atypical features often quite marked
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### B-cell Pseudolymphoma
Sézary syndrome

• Triad:
  – Neoplastic lymphocytes in skin → erythroderma
  – Neoplastic lymphocytes in blood
  – Neoplastic lymphocytes in lymph node
Novel and Highly Recurrent Chromosomal Alterations in Sézary Syndrome

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Oncogenomic analysis of mycosis fungoides reveals major differences with Sézary syndrome

Remco van Doorn,1 Marloes S. van Kester,1 Remco Dijkman,1 Maarten H. Vermeer,1 Aat A. Mulder,1 Karoly Szuhai,2 Jeroen Knijnenburg,2 Judith M. Boer,3 Rein Willemze,1 and Cornelis P. Tensen1

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## Results

<table>
<thead>
<tr>
<th>%SS</th>
<th>%MF tumor</th>
<th>Chromosomal alteration</th>
<th>Associated gene</th>
</tr>
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<tbody>
<tr>
<td>75%</td>
<td>23%</td>
<td>Gain 8q24</td>
<td>MYC</td>
</tr>
<tr>
<td>75%</td>
<td>9%</td>
<td>Loss 17p13</td>
<td>p53</td>
</tr>
<tr>
<td>15%</td>
<td>59%</td>
<td>Gain 7q36</td>
<td>FASTK</td>
</tr>
</tbody>
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Skin histopathology

- Dense band-like infiltrate of lymphocytes, some of which exhibit epidermotropism
- Some lymphocytes can be large
Caution

• 40% of patients will not show diagnostic features of Sézary syndrome on skin biopsy

Evaluation of blood in Sézary syndrome

Perspective

Revisions to the staging and classification of mycosis fungoides and Sézary syndrome: a proposal of the International Society for Cutaneous Lymphomas (ISCL) and the cutaneous lymphoma task force of the European Organization of Research and Treatment of Cancer (EORTC)

Elise Olsen,1 Eric Vonderheide,2 Nicola Pimpinelli,3 Rein Willemze,4 Youn Kim,5 Robert Knobler,6 Herschel Zackheim,7 Madeleine Duvic,8 Teresa Estrach,9 Stanford Lamberg,2 Gary Wood,10 Reinhard Dummer,11 Annamari Ranki,12 Gunter Burg,11 Peter Heald,13 Mark Pittelkow,14 Maria-Grazia Bernengo,15 Wolfram Sterry,16 Liliane Laroche,17 Franz Trautinger,6 and Sean Whittaker,18 for the ISCL/EORTC

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Blood diagnostic criteria for Sézary syndrome

Genotypic analysis: T-cell clone detected

AND

Flow cytometry:

• CD4/8 > 10:1

AND/OR

• CD4+/CD7- > 40%

• CD4+/CD26- > 30%

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CD30-positive lymphoproliferative disorders

- Group of primary cutaneous T-cell lymphomas with expression of CD30
- Lymphomatoid papulosis (LyP)
- Primary cutaneous anaplastic large cell lymphoma (ALCL)
Lymphomatoid Papulosis (LyP)

- 5 histopathologic types: A, B, C, D, E
LyP
Lymphomatoid papulosis (LyP) – Type A

- Wedge-shaped infiltrate
- +/- Epidermotropism
- Clusters of or scattered large atypical lymphocytes
- CD4+
- Admixed neutrophils, eosinophils, small lymphocytes
A Variant of Lymphomatoid Papulosis Simulating Primary Cutaneous Aggressive Epidermotropic CD8+ Cytotoxic T-cell Lymphoma. Description of 9 Cases

Andrea Saggini, MD,* † Andrea Gulia, MD,* ‡ Zsolt Argenyi, MD,§ Regina Fink-Puches,* Amelia Lissia, MD,‖ Mario Magaña, MD,¶ Luis Requena, MD,# Ingrid Simonitsch, MD,** and Lorenzo Cerroni, MD*

Abstract: Lymphomatoid papulosis (LyP) is a recurrent, self-healing eruption belonging to the spectrum of cutaneous CD30+ lymphoproliferative disorders. Three main histologic subtypes of LyP are recognized: type A (histiocytic), type B (mycosis fungoides—(MF)-like), and type C (anaplastic large cell lymphoma–like). We reviewed 26 biopsies from 9 patients

Key Words: lymphomatoid papulosis, primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma, mycosis fungoides, cytotoxic lymphoma, cutaneous T-cell lymphoma

(Am J Surg Pathol 2010;34:1168–1175)
Type D LyP

- Histopathology
  - Typical LyP
  - Marked epidermotropism

- Immunophenotype
  - CD8+/CD30+/CD3+

Anaplastic large cell lymphoma (ALCL)
• Histopathology:
  – Diffuse sheets of large and atypical lymphocytes
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Primary cutaneous marginal zone lymphoma
Primary cutaneous marginal zone lymphoma: Histopathology

– Dermal-based infiltrate, epidermal spared
– Reactive lymphoid follicles, often
– Neoplastic cells at periphery
  • Plasma cells and plasmacytoid lymphocytes
Primary cutaneous marginal zone lymphoma

- Normal kappa/lambda ratio 2:1
- Kappa or lambda skewed ratio
  - Kappa:lambda > 10:1
  - Lambda>kappa
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Primary cutaneous follicle center lymphoma – Follicular pattern

- Nodules within the dermis composed of neoplastic lymphoid follicles
- Reduced or absent mantle zones
- Lack of tingible body macrophages
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B-cell pseudolymphoma

• Cutaneous lymphoid hyperplasia, most common type

• Nodules of reactive lymphoid follicles
  – Intact mantles
  – Tingible body macrophages
  – High Ki-67 rate of proliferation
  – Bcl-6 staining only in CD21-positive foci
Cutaneous lymphoid hyperplasia
Cutaneous lymphoid hyperplasia  Follicle center lymphoma

CD21  
Ki67  
Bcl-6

CD21  
Ki67  
Bcl-6
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