Case 257
Pagetoid Reticulosis

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Clinical History

- 24-year-old woman
- 7-month history of slowly enlarging 1 cm lesion on distal right foot
- Erythematous plaque with central scaling, raised borders
- No other skin or mucosal lesions
Other studies

- Systemic work up for lymphoma including PET scan - negative
Diagnosis

Pagetoid reticulosis
Treatment and Follow-up

• Excision of residual lesion
• No other treatment
• Close follow up for 21 months, no recurrence
Interesting features of this case

• Typical case of Pagetoid reticulosis
• Differentiate from other cutaneous CD8+ T-cell lymphomas with predominant “pagetoid epidermotropic” growth pattern
  – Primary cutaneous CD8 positive aggressive epidermotropic cytotoxic T-cell lymphoma
  – Primary cutaneous gamma-delta T-cell lymphoma
Pagetoid Reticulosis
Woringer-Kolopp disease

• Rare variant of Mycosis Fungoides characterized by
  ▪ Plaques on the distal extremities
  ▪ Cutaneous atypical T lymphocytic infiltrate
  ▪ Marked epidermotropism (pagetoid)
  ▪ Indolent clinical course
History

• 1939: Drs. Woringer and Kolopp reported first case of localized PR
  • 13-year-old boy with a 6 year history of a 6-7 cm solitary lesion on the left forearm...

• 1973: Braun-Falco coined the term PR
  – “Pagetoid”: all discrete nonmalpighian and abnormal malpighian intraepidermal cells occurring singly or as nests in the epidermis.
Epidemiology

• Age:
  o Wide range (2-79 yrs), more frequent in middle aged adults

• Gender:
  o Male predominance (2:1)

• Clinical
  – Solitary
  – Hyperkeratotic
  – Distal extremities
Clinical features

J Cutan Pathol 2007: 34: 644–647

British Journal of Dermatology 2002; 147: 806
Histologic features

- Epidermal changes:
  - Hyperkeratosis
  - Parakeratosis
  - Psoriasiform hyperplasia

- Prominent epidermotropism of atypical lymphoid infiltrate

- Mixed (reactive) dermal infiltrate

- Atypical lymphocytes
Immunophenotypic features

Table 1. Immunophenotype of pagetoid reticulosis of Woringer-Kolopp type

<table>
<thead>
<tr>
<th></th>
<th>CD2</th>
<th>CD3</th>
<th>CD5</th>
<th>CD7</th>
<th>CD4</th>
<th>CD8</th>
<th>CD30</th>
<th>Ki-67 (&gt; 25%)</th>
<th>CD4+/8+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>15</td>
<td>25</td>
<td>13</td>
<td>1</td>
<td>13</td>
<td>19</td>
<td>8</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Negative</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>11</td>
<td>23</td>
<td>17</td>
<td>9</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Total cases</td>
<td>15</td>
<td>25</td>
<td>13</td>
<td>12</td>
<td>36</td>
<td>36</td>
<td>17</td>
<td>10</td>
<td>36</td>
</tr>
<tr>
<td>Percent positivity (%)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>8</td>
<td>36</td>
<td>53</td>
<td>47</td>
<td>60</td>
<td>11</td>
</tr>
</tbody>
</table>

*Cases included from current case report and publications.*

- Clonal TCR gene rearrangement in majority

J Cutan Pathol 2010: 37: 491–496
Differential Diagnoses

1. Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma

2. Primary cutaneous gamma-delta T cell lymphoma

3. Mycosis Fungoides
   1. MF palmaris et plantaris
   2. Unilesional MF
Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma

- Generalized cutaneous and extracutaneous lesions
  - Lung, testis, CNS and oral mucosa
- Ulceration
- Epidermal and dermal neoplastic infiltrate
- Rapid progression
Primary cutaneous gamma-delta T cell lymphoma

- Generalized cutaneous and mucosal lesions
- Epidermal and dermal neoplastic infiltrate
- Hemophagocytosis
- Immunophenotype:
  - CD2+, CD3+, CD5-, CD7+/-
  - CD56+
  - CD4-/CD8- or CD8+
  - TCR-delta positive
  - BF1-
Mycosis Fungoides palmaris et plantaris

- Thin plaques
- Spread to other acral sites
- Epidermal and dermal neoplastic infiltrate
- Eosinophils present
- CD4+ T-helper

Management

• **Complete staging**
  – Rule out other sites of involvement

• **Rx**
  – Topical steroids and nitrogen mustard
  – PUVA and UVB
  – Radiation therapy (for severe disease)

• **Need long-term follow-up**
Summary

• Solitary hyperkeratotic plaque in distal extremities
• Marked epidermotropism
• Dermal non-neoplastic infiltrate without eosinophils
• Differentiate from classical MF and other aggressive cutaneous T-cell lymphomas
• Indolent clinical course
Acknowledgements

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Jeong Hee Cho-Vega, MD, PhD
L. Jeffrey Medeiros, MD
Additional Slides
### CD30 positivity in Pagetoid Reticulosis

#### Spectrum of CD30 positive primary cutaneous lymphoproliferative disorders


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**Table 1. Cases of pagetoid reticulosis of Wöringer-Kolopp type with marked CD30 positivity**

<table>
<thead>
<tr>
<th>Author</th>
<th>Case</th>
<th>Age (years)/sex</th>
<th>Location and size of the lesions</th>
<th>Duration</th>
<th>Phenotype</th>
<th>Percentage of intra-epidermal CD30+ cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mielke et al.⁵</td>
<td>2</td>
<td>31/M</td>
<td>Dorsum of the hand and 2.5 × 1.8 cm</td>
<td>6 years</td>
<td>Double CD4/CD8−</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>26/M</td>
<td>Forearm and 1 × 2 cm</td>
<td>3 months</td>
<td>CD4+, CD8−</td>
<td>20</td>
</tr>
<tr>
<td>Smoller et al.⁶</td>
<td></td>
<td>60/F</td>
<td>Hand and forearm, and &gt; 30 cm</td>
<td>40 years</td>
<td>CD4−, CD8+</td>
<td>&gt; 50</td>
</tr>
<tr>
<td>Haghighi et al.⁸</td>
<td>5</td>
<td>43/F</td>
<td>Tongue and 0.6 cm</td>
<td>3 months</td>
<td>Double CD4/CD8−</td>
<td>&gt; 50</td>
</tr>
<tr>
<td>Current report</td>
<td>6</td>
<td>67/F</td>
<td>Arm and 4 cm</td>
<td>1 year</td>
<td>CD8+, CD4 not done</td>
<td>&gt; 50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>41/M</td>
<td>Almost entire foot</td>
<td>20 years</td>
<td>CD4−, CD8+</td>
<td>&gt; 90</td>
</tr>
</tbody>
</table>

F, female; M, male.

*This patient was also included in the series of Haghighi et al.⁸ (their case 3).
Adhesion molecule	Positivity
tumor cells %	Role	Interaction
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CLA	>90%	Skin homing of lymphocytes	E-selectin on dermal vascular endothelial cells
α4β7	0%	Gut-homing memory T cells	Mucosal addressin MAAdCAM-1
αεβ7	>90%	Intraepidermal lymphocytic localization	E-cadherin on epithelial cells
α3 chain	0%	Crossing of epithelial basement membrane (EBM)	Integrin α3β1 to laminin-5 (EBM )

Expression of adhesion molecules in Pagetoid Reticulosis

Adapted from Drillenburg et al. British Journal of Dermatology 1997; 136: 613-616
First case of localized Pagetoid Reticulosis by Dr. Woringer...

• 1939: Woringer and Kolopp reported the first case of localized PR

• 13-year-old boy with a 6 year history of an asymptomatic, sharply circumscribed 6–7 cm plaque involving the left forearm...


FIGURE 15. First case of Wöringer-Kolopp disease, clinical picture.

FIGURE 16. First case of Wöringer-Kolopp disease, histopathologic image.
Clinical features

- Solitary, erythematous and hyperkeratotic lesion
- Location
  - Distal extremities

British Journal of Dermatology 2002; 147: 806

J Cutan Pathol 2007: 34: 644–647