How to interpret a descriptive pathology report of a cutaneous lymphoid neoplasm

Laura B. Pincus, MD
Associate Professor of Dermatology and Pathology
Co-Director, Cutaneous Lymphoma Clinic
University of California, San Francisco
I have no disclosures
What is a descriptive pathology report?

- A non-descriptive pathology report
  - Definitive diagnosis is rendered in the line diagnosis

- A descriptive report
  - A definitive diagnosis is not rendered
  - The line diagnosis is a description of the microscopic findings
2 scenarios

• The band-like T-cell infiltrate
• The dermal-based infiltrate
The band-like T-cell infiltrate
SLIDE CONSULTATION REPORT

PATH #: 01112007
PATIENT: [redacted]
SERVICE: 01/11/2017
RECEIVED: 01/11/2017
REPORTED: 01/11/2017
11:20:44PM

CLINICAL DATA: DIGITATE RASH ON UPPER INNER ARMS, THIGHS, PARAPSORIASIS VS. ECZEMATOUS DERM. RESPONDS TO TOPICAL STEROIDS BUT NOT COMPLETELY. WE ARE CONSIDERING ADDITIONAL BIOPSIES ONCE OFF TOPICAL STEROIDS.

DIAGNOSIS: PATCHY LICHENOID, Spongiotic and Psoriasiform Pattern (LEFT BUTTOCK) (D48.5)

NOTE: The differential diagnosis includes a spongiotic dermatitis such as eczematous or allergic contact dermatitis and patch-stage mycosis fungoides. Given the presence of papillary dermal fibrosis and lymphocytes within the epidermis in a few areas without significant concurrent spongiosis, I slightly favor patch-stage mycosis fungoides. However, the findings are not sufficiently developed to render an unequivocal diagnosis of mycosis fungoides at this time. Therefore, I agree with your plan to perform additional biopsies (I suggest at least 2-3) of the eruption. If the pattern in the additional biopsies is also suggestive but not fully diagnostic of mycosis fungoides, then we can send blocks from two separate biopsies for T-cell gene re-arrangement studies. If identical clones are present in both specimens, this will lend additional support to the diagnosis of mycosis fungoides (finding an identical clone in two distinct lesions is more specific than finding a clone in a single lesion). When you do the additional biopsies, please ensure that the patient has not been using topical steroids to the lesions for at least 3 weeks, as it seems you are already ensuring. Of note, review of a submitted PAS-d stain is negative and thus there is no evidence of a tinea infection herein.

SPECIMEN SITE: LEFT BUTTOCK
## Elements of descriptive report

<table>
<thead>
<tr>
<th>Element</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Differential diagnosis</td>
<td>The differential diagnosis includes a spongiotic dermatitis and patch-stage mycosis fungoides (MF).</td>
</tr>
</tbody>
</table>
Elements of descriptive report

<table>
<thead>
<tr>
<th>Element</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Differential diagnosis</td>
<td>The differential diagnosis includes a spongiotic dermatitis and patch-stage mycosis fungoides (MF).</td>
</tr>
<tr>
<td>Favored diagnosis</td>
<td>Given the presence of papillary dermal fibrosis and lymphocytes within the epidermis in a few areas without significant concurrent spongiosis, I slightly favor patch-stage MF.</td>
</tr>
</tbody>
</table>
## Elements of descriptive report

<table>
<thead>
<tr>
<th>Element</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Differential diagnosis</td>
<td>The differential diagnosis includes a spongiotic dermatitis and patch-stage mycosis fungoides (MF).</td>
</tr>
<tr>
<td>Favored diagnosis</td>
<td>Given the presence of papillary dermal fibrosis and lymphocytes within the epidermis in a few areas without significant concurrent spongiosis, I slightly favor patch-stage MF.</td>
</tr>
<tr>
<td>Hedge</td>
<td>However, the findings are not sufficiently developed to render an unequivocal diagnosis at this time and spongiotic dermatitis remains possible.</td>
</tr>
</tbody>
</table>
## Elements of descriptive report

<table>
<thead>
<tr>
<th>Element</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Differential diagnosis</strong></td>
<td>The differential diagnosis includes a spongiotic dermatitis and patch-stage mycosis fungoides (MF).</td>
</tr>
<tr>
<td><strong>Favored diagnosis</strong></td>
<td>Given the presence of papillary dermal fibrosis and lymphocytes within the epidermis in a few areas without significant concurrent spongiosis, I slightly favor patch-stage MF.</td>
</tr>
<tr>
<td><strong>Hedge</strong></td>
<td>However, the findings are not sufficiently developed to render an unequivocal diagnosis at this time.</td>
</tr>
<tr>
<td><strong>Plan</strong></td>
<td>Therefore, I suggest performing additional biopsies (at least 2-3). If the pattern in the those biopsies is also not fully diagnostic of MF, then we can evaluate two separate biopsies for T-cell gene re-arrangements studies. Detection of identical clones in both specimens would lend additional support to the diagnosis of MF.</td>
</tr>
</tbody>
</table>
Rationale

• Additional biopsies are best diagnostic maneuver if first biopsy not diagnostic

• Detection of a T-cell clone
  • Frequency of clones in early MF ~ 70%
  • Identical clone at different sites increases sensitivity (82.6%) and specificity (95.7%)

Thurber et al. JAAD. 2007. 57:782-90
PERFORMED LIMITED IMMUNOPEROXIDASE STAINING ON BIOPSY (C). THE STAINING REVEALED THAT THE INTRAEPIDERMAL CELLS WERE A MIXTURE OF CD3-POSITIVE T-CELLS AND CD1A-POSITIVE LAMBERTIAN CELLS. UNFORTUNATELY, THESE STAINING RESULTS DID NOT ALLOW FOR FURTHER DIFFERENTIATION.

THEY, T-CELL REARRANGEMENT STUDIES WERE PERFORMED ON SPECIMENS (B) AND (C). IN BOTH SPECIMENS (B) AND (C), CLONAL REARRANGEMENTS WERE DETECTED IN THE T-CELL RECEPTOR BETA AND GAMMA CHAIN GENES. FURTHERMORE, BOTH BIOPSIES SHOWED IDENTICAL CLONES. THE PRESENCE OF IDENTICAL CLONES IN TWO DIFFERENT BIOPSIES SUPPORTS THAT THIS ERUPTION REPRESENTS MYCOSIS FUNGOIDES.

I ALSO CONSIDERED THE POSSIBILITY OF A DERMATOPICHY INFECTION, AND THUS I PERFORMED A PAS-D STAIN ON ALL THREE SPECIMENS. THE STAIN DID NOT REVEAL FUNGI IN ANY OF THE SPECIMENS. THEREFORE, THERE IS NO EVIDENCE OF A TINEA INFECTION.

I HAVE ALSO SHARED THIS CASE WITH MY COLLEAGUE, DR. PHILIP LEBOT, WHO AGREES WITH THIS ASSESSMENT.

NOTE: While the dominant microscopic feature in the routinely-stained sections in biopsies (A) and (B) was epidermal spongiosis, in biopsy (C), the features were most suggestive of patch-stage mycosis fungoides. Therefore, my initial impression was that biopsies (A) and (B) represented non-diagnostic biopsies of patch-stage mycosis fungoides. Nevertheless, while the microscopic features in biopsy (C) were suggestive of patch-stage mycosis fungoides, I did not think that they were fully diagnostic and a heavily inflamed spongiod dermatitis was possible as well.

IN ORDER TO FURTHER EVALUATE FOR THE POSSIBILITY OF PATCH-STAGE MYCOSIS FUNGOIDES, I...
Why descriptive?

• Not clear based on the features on the routinely-stained section
• Additional studies required to render the final diagnosis
The dermal-based infiltrate
<table>
<thead>
<tr>
<th>Differential diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-cell lymphoma, marginal zone type</td>
</tr>
<tr>
<td>B-cell lymphoma, follicle-center type</td>
</tr>
<tr>
<td>Primary cutaneous CD4-positive small/medium T-cell lymphoproliferative disorder</td>
</tr>
<tr>
<td>Pseudolymphoma</td>
</tr>
<tr>
<td>Tumor-stage mycosis fungoides</td>
</tr>
</tbody>
</table>
Marginal zone lymphoma

Lambda

Kappa
Follicle center lymphoma

Bcl-6
Primary cutaneous CD4-positive small/medium T-cell lymphoproliferative disorder

PD-1
DENSE LYMPHOID INFILTRATE WITH PD-1 POSITIVITY, COMPATIBLE WITH CD4-POSITIVE SMALL/MEDIUM T-CELL LYMPHOPROLIFERATIVE DISORDER (D48.5)

[LEFT FOREHEAD]

NOTE: I performed immunoperoxidase staining in order to further evaluate this lymphocytic infiltrate since my initial differential diagnosis included a low-grade lymphoma and primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder. The staining reveals that a slight majority of the lymphocytes are CD3-positive T-cells with a sizable minority of CD20-positive B-cells. A CD21 stain does not demonstrate follicular dendritic cell networks and a Bcl-6 stain labels only a few of the lesional lymphocytes, excluding B-cell lymphoma, follicle center pattern. In addition, there is no light chain restriction as assessed by kappa/lambda in situ hybridization, excluding B-cell lymphoma, marginal zone type. A Ki-67 immunoperoxidase stain demonstrates a relatively moderate proliferation among the lesional lymphocytes. A PD-1 stain (which labels follicular helper T cells) shows numerous large clusters and rosette-like aggregations of medium sized cells. Coupling these staining results with the findings on the routinely-stained section, the features in this biopsy are in keeping with primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (see references below).

The phrase “lymphoproliferative disease” is now used instead of “lymphoma” for this condition since the 2016 WHO lymphoma classification was published in order to reflect the indolent behavior of the condition since in a large series of patients, 100% disease specific survival was reported. Most of the cases reported are solitary lesions, frequently on face, neck, or upper trunk, which are usually less than 2.5 cm
<table>
<thead>
<tr>
<th>Element</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Differential diagnosis</td>
<td>The differential diagnosis includes a low-grade lymphoma, primary cutaneous CD4-positive small/medium T-cell lymphoproliferative disorder and pseudolymphoma</td>
</tr>
</tbody>
</table>
## Elements of descriptive report

<table>
<thead>
<tr>
<th>Element</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Differential diagnosis</td>
<td>The differential diagnosis includes a low-grade lymphoma, primary cutaneous CD4-positive small/medium T-cell lymphoproliferative disorder and pseudolymphoma.</td>
</tr>
</tbody>
</table>
| Favored diagnosis        | Immunostaining reveals  
• In situ hybridization for kappa and lambda reveals polytypic plasma, excluding marginal zone lymphoma.  
• A bcl-6 stain labels only a few of the lymphocytes, excluding follicle center lymphoma.  
• A PD-1 stain shows numerous large clusters and rosette-like aggregations of follicular helper T-cells, supporting the diagnosis of CD4-positive small/medium T-cell lymphoproliferative disorder. |
<table>
<thead>
<tr>
<th>Element</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>The hedge</td>
<td>• This condition is characterized by lesions usually on the face, neck or upper trunk which are usually less than 2.5 cm in diameter. If there are multiple lesions or the lesions are large (i.e. greater than 5 centimeters), then the diagnosis will need to be re-considered.</td>
</tr>
</tbody>
</table>
Why make descriptive report?

• Diagnosis in part predicated on clinical presentation, which is often unknown

• Diagnosis still considered provisional in most updated lymphoma classification

DIAGNOSIS: DENSE LYMPHOID INFILTRATE WITH PD-1 POSITIVITY, COMPATIBLE WITH CD4-POSITIVE SMALL/MEDIUM T-CELL LYMPHOPROLIFERATIVE DISORDER (D48.5)

NOTE: I performed immunoperoxidase staining in order to further evaluate this lymphocytic infiltrate since my initial differential diagnosis included a low-grade lymphoma and primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder.

The staining reveals that a slight majority of the lymphocytes are CD3-positive T-cells with a sizable minority of CD20-positive B-cells. A CD21 stain does not demonstrate follicular dendritic cell networks and a Bcl-6 stain labels only a few of the lesional lymphocytes, excluding B-cell lymphoma, follicle center pattern. In addition, there is no light chain restriction as assessed by kappa/lambda in situ hybridization, excluding B-cell lymphoma, marginal zone type. A Ki-67 immunoperoxidase stain demonstrates a relatively moderate proliferation among the lesional lymphocytes. A PD-1 stain (which labels follicular helper T-cells) shows numerous large clusters and rosette-like aggregations of medium sized cells. Coupling these staining results with the findings on the routinely-stained section, the features in this biopsy are in keeping with primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder (see references below).

The phrase "lymphoproliferative disease" is now used instead of "lymphoma" for this condition since the 2016 WHO lymphoma classification was published in order to reflect the indolent behavior of the condition since in a large series of patients, 100% disease specific survival was reported. Most of the cases reported are solitary lesions, frequently on face, neck, or upper trunk, which are usually less than 2.5 cm
Pathology requisition form, “forehead plaque”
SLIDE CONSULTATION REPORT

PATH #:

SERVICE: 01/08/2018
RECEIVED: 01/22/2018
REPORTED: 01/24/2018
12:21:41AM

CLINICAL DATA: NODULES ON CHEEKS, HISTORY OF ATYPICAL LYMPHOID INFILTRATES, ON MTX; R/O LYMPHOMA

DIAGNOSIS: NODULAR TO DIFFUSE DENSE INFILTRATE OF LYMPHOCYTES, EOSINOPHILS AND PLASMA CELLS, CONSISTENT WITH PSEUDOLYMPHOMA (D48.5)

(LEFT CHEEK)

NOTE: My initial differential diagnosis included a low-grade T- or B-cell lymphoma and a pseudolymphoma. Review of select immunoperoxidase stains reveals that the majority of the lymphocytes are CD3-positive T-cells while there is a small minority of admixed CD20-positive B-cells. In situ hybridization for kappa and lambda shows a polyclonal proliferation of plasma cells, thereby excluding B-cell lymphoma marginal zone type. In addition, a bcl-6 stain demonstrates only focal labeling, thereby excluding B-cell lymphoma follicle center lymphoma pattern. A FD-1 stain does not demonstrate large rosettes with positivity, excluding CD4-positive small/medium T-cell lymphoproliferative disorder. Given these staining results along with the findings on routinely stained section, including the fact that most of the lymphocytes are small, I think that the findings in this biopsy are in keeping with pseudolymphoma. My colleague, Dr. Timothy McCalmont, also reviewed these sections and agrees with this assessment.
Elements of descriptive report

<table>
<thead>
<tr>
<th>Element</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Differential diagnosis</td>
<td>The differential diagnosis includes a low-grade B- or T-cell lymphoma and pseudolymphoma.</td>
</tr>
</tbody>
</table>
### Elements of descriptive report

<table>
<thead>
<tr>
<th>Element</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Didx</td>
<td>The ddx includes low-grade B- or T-cell lymphoma and pseudolymphoma.</td>
</tr>
<tr>
<td>Favored diagnosis</td>
<td>• In situ for kappa and lambda show polytypic plasma cells, excluding marginal zone lymphoma.</td>
</tr>
<tr>
<td></td>
<td>• A bcl-6 stain labels a small minority of the lymphocytes, excluding follicle center lymphoma.</td>
</tr>
<tr>
<td></td>
<td>• A PD-1 stain does not show large rosettes of positivity, excluding primary cutaneous CD4-positive small/medium T-cell lymphoproliferative disorder.</td>
</tr>
<tr>
<td></td>
<td>• Given these staining results combined with the findings on the routinely-stained section, including the fact that most lymphocytes are small, I think that the findings in this biopsy are in keeping with pseudolymphoma.</td>
</tr>
</tbody>
</table>
Why descriptive?

- Pseudolymphoma diagnosis of exclusion
- Occasionally non-diagnostic biopsies of marginal zone lymphoma and follicle center lymphoma
Summary

• Descriptive reporting strategy used when an unequivocal diagnosis not possible
• This reporting strategy could reflect
  – The microscopic features show findings of multiple different entities
  – The diagnosis was not straightforward on the routinely-stained section and numerous additional tests were required to make it
  – The diagnosis is predicated in part on the full clinical presentation
  – The diagnosis is a provisional entity
  – The diagnosis is one of exclusion
  – The diagnosis is one of exclusion and the didx includes entities that can sometimes have non-diagnostic biopsies
• Recognize that the diagnosis not as secure as an unequivocal diagnosis and manage the patient accordingly
Acknowledgements

- **UCSF Multidisciplinary Cutaneous Lymphoma Clinic**
  - Weiyun Ai, MD
  - Melissa Kinnebrew, MD, PhD
  - Sue Yom, MD

- **UCSF Dermatopathology**
  - Timothy McCalmont, MD
  - Thaddeus Mully, MD
  - Jeffrey North, MD
  - Philip LeBoit, MD
  - Iwei Yeh, MD, PhD