Pathology Error in the Diagnosis and Staging of Cutaneous Melanoma

Martin J. Trotter MD, PhD, FRCPC
Department of Pathology and Laboratory Medicine
University of Calgary
Calgary Laboratory Services

Uncertainty, Discrepancy, Error

Errors in Diagnosis

Errors in Staging
Trends in Pathology Malpractice Claims

David B. Trevedi, MD  

(% Total Claims)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Miscellaneous surgical pathology</td>
<td>33</td>
<td>15</td>
<td>16</td>
</tr>
<tr>
<td>Gynecologic cytology</td>
<td>20</td>
<td>13</td>
<td>7</td>
</tr>
<tr>
<td>Breast specimens</td>
<td>11</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Melanoma</td>
<td>8</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>System error</td>
<td>1</td>
<td>7</td>
<td>11</td>
</tr>
</tbody>
</table>

95% of errors are false negative; melanoma was missed
How does a pathologist make a diagnosis?

- Clinical information (or lack thereof!)
- H&E-stained glass slides
- Microscope

Melanoma
Pathology Diagnosis

• A pathology report is an interpretation made by a highly-trained medical expert under conditions of high complexity, variability, uncertainty and ambiguity

• All such interpretations have error rates

• A pathology diagnosis cannot consistently and invariably represent the absolute truth

“….morphological diagnosis, whether of birds, fish, plants, or pathological processes in human beings, is 100% subjective. Errors in diagnosis are inevitable; physicians know it and patients should be informed of it….mistakes are not necessarily malpractice and even experts make many of them.”
“I suspect that experts would disagree significantly (benign vs. malignant) on less than 1% of randomly selected melanocytic lesions.

However, as melanocytic lesions are so common, even a small percentage of cases which are difficult result in a large number of problematic cases.”

- Consultants used language suggesting definitive diagnoses in roughly 85% of cases
- But in 25% of cases, two consultants issued the exact opposite diagnosis
- Overall in 36% of cases two consultants disagreed as to whether a tumor was benign or malignant

Scary stuff

Precise and accurate
Precise, not accurate
Not precise, not accurate
Interpretative “Discrepancy”

- Hairstyle
- Upturned face

Correct Diagnosis
No gold standard
Low inter-observer variation

“Rather than acknowledge the diagnostic uncertainty associated with the evaluation of ambiguous evidence, pathologists accept as a gold standard the non-verifiable opinion of individual experts with ‘star status’ based on either personal or institutional reputation.”
- Elliott Foucar

Context Bias

Diagnosis = “B”

Diagnosis = “13”
Errors in Diagnosis

Low-power examination only

Partial Biopsy/Curettings

35F, Right scapula
DN

Communication
- Lesion size
- Complete or partial biopsy

1.8 mm
Inflamed lesions

• Benign lichenoid keratosis
• Halo nevus

Spitz nevus

Cytomorphology and growth pattern can mimic melanoma

Epithelioid
Fusiform
Spindled

Atypical Spitz nevus
Mitotic figure
Regression

Desmoplastic Melanoma

On H&E it looks like a scar!

Desmoplastic Melanoma

Anything in the epidermis?

Why are there lymphoid aggregates?
Desmoplastic Melanoma

Increased cellularity

In situ component

Cytologic atypia

Myxoid stroma

Desmoplastic Melanoma

S100

Desmoplastic Melanoma

Increased cellularity

In situ component

Cytologic atypia

Myxoid stroma
Other spindle cell imitators

- Spindle cell squamous cell carcinoma
- Atypical fibroxanthoma
- Cutaneous leiomyosarcoma
- Other
  - Angiosarcoma
  - Blue nevus
  - DFSP

Spindle cell melanoma

Atypical Fibroxanthoma

Leiomyosarcoma

Spindle cell SCC
Over-diagnosis of melanoma (false-positive)

- Melanocyte activation
  - Irritated nevi
  - Nevi in pregnancy
  - 2° to psoralen or light therapy
- Nevi on special sites
- Spitz nevus and pigmented spindle cell nevus
- Combined nevus
- Deep penetrating nevus
- Cellular blue nevus

Errors in Staging

The Synoptic Report

- Lack of completeness (elements missing)
- Incorrect interpretation of data elements
  1. Breslow thickness
  2. Ulceration
  3. Mitotic count
  4. Vascular invasion
  5. Microsatellites
  6. Margins
Report Completeness

Melanoma Institute Australia vs Community-based Pathologists

Sentinel Lymph Node Biopsy
Sentinel Lymph Node Protocol

Pathologic reporting of lymph nodes

Uncertainties in SLNB interpretation

- Capsular nevus vs. melanoma
- Isolated tumour cells vs macrophages or dendritic cells
- Microstaging
- Extracapsular extension
**S100 immunostaining**

**Melan-A and HMB45 positive macrophages (?)**

**Architectural patterns of SLN metastases (risk of non-SLN involvement)**

<table>
<thead>
<tr>
<th>Subcapsular</th>
<th>Subcapsular and parenchymal</th>
<th>Parenchymal</th>
<th>Extensive (&gt;5 mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5%</td>
<td>10-20%</td>
<td>10-20%</td>
<td>25%</td>
</tr>
</tbody>
</table>
Extracapsular extension

- Most significant risk factor for regional recurrence
- Indication for adjuvant radiation therapy

Pathologic reporting of lymph nodes

Lymph Nodes (required only if lymph nodes are present in the specimen) (select all that apply) (Note H)
Number of sentinel nodes examined: 2
Number of lymph nodes with metastases: 1
*Extracapsular tumor extension:
  - Present
  - Not detected
  - Indeterminate
*Size of largest metastatic focus: 0.4 mm (for sentinel node)
*Location of metastatic tumor (for sentinel node):
  - Subcapsular
  - Paramediullary
  - Subcapsular and intramedullary

Case Presentation

69F, Persistent red plaque on right shin


- Re-excision (Dec 2010) – “Blue nevus with involutional change. The process is noted at the surgical margins”.
• May 2012
• Large 3 x 2.5 cm hard plaque at site of previous excision for spindle cell tumor (right shin)
Diagnosis - “Recurrent / persistent spindle cell tumor”.

Strong labeling for S100. Cytokeratin, MART-1, CD34 – negative. “Complete excision is recommended given the growth pattern and tendency to recurrence”
• Re-excision specimen – sent for consultation

“Desmoplastic melanoma, at least 10 mm thickness, deep margin positive”
(Clark level V)
Wide excision and SLNB December 2012

“Pure” desmoplastic melanoma
1.1 cm thickness
Very close to deep margins on wide-excision specimen

SLNB x2 - Negative
Uncertainty, Discrepancy, Error

Errors in Diagnosis

Errors in Staging

Thank You