Lichenoid Tissue Reaction in Malignant Melanoma

A Potential Diagnostic Pitfall

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Abstract

Lichenoid tissue reactions can occur in malignant melanoma and may cause partial regression of the lesion. We studied a series of melanomas to determine how frequently lichenoid tissue reaction obscures the diagnosis of malignant melanoma. We retrospectively reviewed 342 cases of invasive malignant melanoma and melanoma in situ from the head, neck, chest, and back. Of the 342 cases, 23 (6.7%) had a lichenoid tissue reaction obscuring a portion of the lesion. In 6 cases (1.8%), the lichenoid tissue reaction replaced a major portion of the lesion. Knowledge of this phenomenon can prevent misdiagnosis.

Lichenoid tissue reaction can obscure junctional melanocytes, making the diagnosis of malignant melanoma (MM) more difficult. Especially in the setting of clinically amelanotic lesions, this creates a potential for misdiagnosis of invasive or in situ malignant melanoma as benign lichenoid keratosis (BLK). We attempted to determine how frequently lichenoid interface dermatitis obscures the diagnosis of MM or melanoma in situ (MMIS).

Materials and Methods

A total of 342 cases of MM and MMIS were retrieved from the surgical pathology files of Wilford Hall Medical Center and Brooke Army Medical Center, San Antonio, TX, for the period January 1993 to June 2000. We reviewed 200 cases from the head and neck and 142 cases from the chest and back to determine whether a lichenoid tissue reaction obscured portions of the melanoma. The percentage of each lesion obscured by the lichenoid reaction was assessed.

Lichenoid tissue reaction was defined as a band-like infiltrate of lymphocytes in the dermis that obscured the dermal-epidermal junction accompanied by necrotic keratinocytes (Civatte bodies) at the dermal-epidermal junction [Image 1]. The reaction was considered to obscure the melanoma when no melanocytes could be identified in the area of the infiltrate. Standard H&E-stained slides were reviewed, as were all immunohistochemical stains ordered at the time the case was originally signed out. The clinical history of each lesion was reviewed subsequently. Ten BLKs and 10 MMs were selected randomly as control cases and stained with MART-1.
Results

A total of 23 cases (6.7%) were found to have a lichenoid tissue reaction obscuring at least a portion of the lesion \textbf{Table 1}. The Table indicates the percentage of the specimen involved by melanoma and by lichenoid dermatitis. Lichenoid tissue reaction was demonstrated in 11 (5.5%) of 200 cases from the head and neck and 12 (8.5%) of 142 cases from the chest and back. Six cases (1.8%) demonstrated a large percentage of the lesion (30% or more) obscured by a lichenoid tissue reaction.

Three (13%) of the lesions with a lichenoid tissue reaction were clinically amelanotic (cases 1, 2, and 3). All 3 lesions demonstrated areas of in situ melanoma in at least a portion of the specimen with H&E or MART-1 immunostaining. In case 1, the clinical differential diagnosis included basal cell carcinoma, squamous cell carcinoma, and actinic

\textbf{Table 1}  
Cases of Lichenoid Tissue Reaction in Malignant Melanoma and In Situ Lesions

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Clinical Impression</th>
<th>Diagnosis</th>
<th>Size</th>
<th>Percentage Lichenoid</th>
<th>Percentage Melanoma</th>
<th>Percentage Normal</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Nonpigmented</td>
<td>MMIS</td>
<td>5 mm</td>
<td>30</td>
<td>50</td>
<td>20</td>
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<tr>
<td>2</td>
<td>Nonpigmented</td>
<td>MMIS</td>
<td>5 cm</td>
<td>5</td>
<td>95</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>Nonpigmented</td>
<td>MMIS</td>
<td>4 cm</td>
<td>5</td>
<td>95</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
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<td>MM</td>
<td>12 mm</td>
<td>40</td>
<td>60</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>Pigmented</td>
<td>MM</td>
<td>2 cm</td>
<td>2</td>
<td>75</td>
<td>23</td>
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<tr>
<td>6</td>
<td>Pigmented</td>
<td>MM</td>
<td>2 cm</td>
<td>10</td>
<td>50</td>
<td>40</td>
</tr>
<tr>
<td>7</td>
<td>Pigmented</td>
<td>MM</td>
<td>7 mm</td>
<td>2</td>
<td>80</td>
<td>18</td>
</tr>
<tr>
<td>8</td>
<td>Pigmented</td>
<td>MM</td>
<td>8 mm</td>
<td>10</td>
<td>50</td>
<td>40</td>
</tr>
<tr>
<td>9</td>
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<td>MM</td>
<td>6 mm</td>
<td>10</td>
<td>75</td>
<td>15</td>
</tr>
<tr>
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<td>MM</td>
<td>2 cm</td>
<td>30</td>
<td>30</td>
<td>40</td>
</tr>
<tr>
<td>11</td>
<td>Pigmented</td>
<td>MM</td>
<td>2 cm</td>
<td>50</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>12</td>
<td>Pigmented</td>
<td>MM</td>
<td>13 mm</td>
<td>90</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>13</td>
<td>Pigmented</td>
<td>MM</td>
<td>6 mm</td>
<td>2</td>
<td>90</td>
<td>8</td>
</tr>
<tr>
<td>14</td>
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<td>2 cm</td>
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<td>50</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td>Pigmented</td>
<td>MM</td>
<td>&gt;3 cm</td>
<td>5</td>
<td>95</td>
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</tr>
<tr>
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<td>5</td>
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<tr>
<td>17</td>
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<td>10</td>
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<td>0</td>
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<tr>
<td>18</td>
<td>Pigmented</td>
<td>MM</td>
<td>10 mm</td>
<td>5</td>
<td>95</td>
<td>0</td>
</tr>
<tr>
<td>19</td>
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<td>MM</td>
<td>6 cm</td>
<td>2</td>
<td>95</td>
<td>0</td>
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<tr>
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<td>MM</td>
<td>3 cm</td>
<td>2</td>
<td>98</td>
<td>0</td>
</tr>
<tr>
<td>21</td>
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<td>MM</td>
<td>&gt;3 cm</td>
<td>20</td>
<td>80</td>
<td>0</td>
</tr>
<tr>
<td>22</td>
<td>Non history</td>
<td>MMIS</td>
<td>3 cm</td>
<td>10</td>
<td>30</td>
<td>60</td>
</tr>
<tr>
<td>23</td>
<td>No history</td>
<td>MMIS</td>
<td>&gt;3 cm</td>
<td>1</td>
<td>99</td>
<td>0</td>
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</tbody>
</table>

MM, malignant melanoma; MMIS, malignant melanoma in situ.
keratosis. In cases 2 and 3, the clinical differential diagnosis included actinic keratosis and Bowen disease. In cases 1 and 2, the diagnosis was established with the help of MART-1 immunohistochemical staining. In 2 of the 23 lesions (cases 22 and 23), no history was provided. One of the 10 BLK control cases stained with MART-1 demonstrated short runs of confluent melanocytes and several enlarged multinucleated melanocytes adjacent to the lichenoid tissue reaction that were not present on the original H&E-stained section. Deeper sections revealed melanocytic nests confirmed by MART-1 immunostains (see the “Discussion” section).

**Discussion**

In our series, 6.7% (23 of 342 cases) of invasive and in situ melanomas demonstrated a lichenoid tissue reaction obscuring at least a portion of the lesion. A large portion of the lesion was obscured in only 6 cases. Only rarely were melanocytic nests evident within the lichenoid area when immunostains were applied to the sections. This suggests that the phenomenon represents lichenoid regression within the lesion, rather than merely a heavy infiltrate hiding melanocytic nests. There is other evidence to suggest that lichenoid tissue reaction may represent a form of immunologically mediated regression. Turner et al described the treatment of 5 cases of MMIS with interferon alfa in a patient with xeroderma pigmentosum. They found a lichenoid infiltrate with almost complete loss of melanocytes and no evidence of melanoma 50 days after treatment.1 Histologic criteria for regression of MM typically include fibrosis of the papillary dermis and a patchy infiltrate of lymphocytes and melanophages.2-4 Some authors have subdivided regression of MM into different stages.3-4 Blessing and McLaren4 described one of the criteria for active regression as a dense lymphocytic infiltrate surrounding the malignant melanocytes in a lichenoid distribution. The cases in our series demonstrate true lichenoid dermatitis with the presence of necrotic keratinocytes. It may be helpful to conceptualize these lichenoid reactions as a form of regression that may mimic BLK histologically.

Amelanotic lesions present the greatest potential for misdiagnosis. Approximately 2% to 8% of all melanomas are
amelanotic.\textsuperscript{5,6} In this setting, a biopsy demonstrating
lichenoid dermatitis could easily be interpreted as a BLK.

BLKs typically manifest as discrete red or pink macules
or patches on the arms and chest. Clinically, they suggest a
diagnosis of basal cell carcinoma or Bowen disease.\textsuperscript{7} Histologically, BLK is characterized by a lichenoid tissue reaction.\textsuperscript{8} Our study suggests that melanocytic lesions may demonstrate
both the clinical and histologic findings of a BLK. A high
index of suspicion should be maintained, especially when the
biopsy specimen represents only a portion of the clinical
lesion. Lacking clinical history of a pigmented lesion, clues
suggesting lichenoid tissue reaction in a melanocytic lesion,
rather than a BLK, include heavily sun-damaged skin,
absence of a precursor lesion (solar lentigo, seborrheic
keratosis) adjacent to the lichenoid infiltrate, and effacement
of the epidermis \textsuperscript{Image 21}.

Glaun et al\textsuperscript{8} studied deeper sections of 46 cases previ-
ously diagnosed as BLK and found a melanocytic lesion
(melanocytic nevus or melanoma) in 2 cases. In our series,
18 of the 23 lesions with a lichenoid tissue reaction were
clinically pigmented, raising the index of suspicion for
MM. In cases of amelanotic melanoma, the risk of misdi-
agnosis is greatest. In the series of cases included in this
study, only 1 case with a large portion of the lesion
obscured by lichenoid tissue reaction was amelanotic.
However, we have seen 6 additional cases of amelanotic
junctional melanocytic proliferations on sun-damaged skin
with prominent lichenoid tissue reaction since the comple-
tion of the study. In 2 of these cases, lichenoid dermatitis
obscured more than 90\% of the lesion. In 2 cases, the
lichenoid dermatitis completely obscured the junctional
melanocytic proliferation in the initial sections; a single
melanocytic nest was seen in deeper sections. In 1 case, nests
were identified only in sections labeled with a MART-1
immunostain. Our routine is to obtain deeper sections in
cases of lichenoid dermatitis on heavily sun-damaged skin,
as deeper sections may demonstrate melanocytic nests
within or adjacent to the lichenoid infiltrate.

Immunohistochemical stains other than MART-1 have
been used to identify melanocytic nests obscured by inflam-
matory infiltrates. Bhawan\textsuperscript{9} found the antibody Mel-5 useful
for differentiating lentigo maligna with lichenoid inflammation

\textsuperscript{Image 31} A. “Benign lichenoid keratosis” control (H&E,
\times100). B. MART-1 stain of periphery of lesion demonstrating
confluent melanocytes at the dermal-epidermal junction on
sun-damaged skin with an effaced rete ridge pattern (\times100).
C. Multinucleated melanocyte (MART-1, \times400).
from lichen planus–like keratosis (BLK). We found immunostains (MART-1, S-100, HMB-45) helpful in a minority of cases. Melanocytes generally were absent in areas of lichenoid tissue reaction. The correct diagnosis was more likely to be established based on H&E findings in adjacent skin or in deeper H&E-stained sections. One of the 10 control cases of BLK stained with MART-1 showed short runs of confluent melanocytes and enlarged, multinucleated melanocytes Image 3. Deeper H&E-stained sections then were obtained and demonstrated melanocytic nests. The H&E-stained sections demonstrating the nests were destained, and subsequent MART-1 immunohistochemical staining confirmed the nests as melanocytic Image 4. This patient has been contacted to arrange reexcision of the biopsy site with a margin of normal skin. This case highlights the significance of lichenoid regression as a diagnostic pitfall even if the pathologist has a high index of suspicion.

The portion of the lesion replaced by lichenoid tissue reaction in this study ranged from 1% to 90%. In case 12, 90% of the 13-mm lesion demonstrated lichenoid tissue reaction, and only 5% of the dermal-epidermal junction demonstrated melanocytic nests. In general, small biopsies of pigmented lesions should be discouraged. Whenever possible, the entire lesion should be submitted to the pathologist. In cases of amelanotic melanoma, it is more likely that the clinician will sample only a portion of the lesion. Biopsy specimens that demonstrate lichenoid tissue reaction but do not represent the entire lesion should be approached cautiously.

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The opinions expressed are those of the authors and not those of the US Army, Air Force, or the Department of Defense.

References


