Large Neglected Ulcerated Melanoma Mimicking Extramedullary Plasmacytoma

Larisa M. Lehmer, MA,* Bruce D. Ragsdale, MD,* Michael V. Frost, MD,† and Kevin L. Ferguson, MD‡

Abstract: Amelanotic melanoma, a renowned impersonator, has taken on a new persona. A 63-year-old woman was seen in the emergency room with a chief complaint of back pain after a fall and was discovered to have a 15-cm fungating mottled gray mass independent of bone on the right elbow. Initial workup discovered lytic calvarial lesions, anemia (Hb 7; Hct 20%), and circulating plasma cells consistent with plasma cell myeloma. Biopsy of the elbow mass displayed sheets of plasmacytoid cells, some reactive for CD138. Flow cytometry revealed a substantial portion of the plasma cells in the tumor that were kappa restricted consistent with cutaneous plasmacytoma. The elbow mass was initially signed out as extramedullary involvement by her myeloma. Reevaluation of the mass after the patient experienced an explosive growth of multinodular jet black malignant melanoma on ipsilateral breast revealed MART-1 and S-100 reactivity of the majority of the cells. In retrospect, the elbow mass was a neglected primary amelanotic malignant melanoma with neoplastic plasma cells participating in its chronic inflammatory infiltrate.

Key Words: amelanotic melanoma, multiple myeloma, extramedullary plasmacytoma, mimicry

Introduction

Although melanoma accounts for 5% of all cancers according to the American Cancer Society, it is responsible for the majority of skin cancer–related deaths each year.1 Amelanotic melanoma accounts for 7% of cutaneous melanomas2 and produces little to no pigment, allowing it to mimic a variety of benign and malignant lesions.3 Metastatic melanoma often presents with 1 or more amelanotic lesions even when the primary tumor was pigmented. In the present case, the primary melanoma was amelanotic with pigmented metastases. Clinical misdiagnoses of amelanotic melanoma tabulated by Koch and Lange (2000) include intradermal nevus,4 seborrheic keratosis,5 verruca vulgaris,5 dermatitis,6 pyogenic granuloma,7 nevus depigmentosus,8 granuloma annulare, scar, actinic keratosis, lymphocytoma cutis,9 basal cell carcinoma, keratoacanthoma, Bowen disease,10 Merkel cell carcinoma,11 and atypical fibroxanthoma.9 Histologically, amelanotic melanoma has been known to masquerade as breast carcinoma, “histiocytic” tumors, ovarian carcinoma, atypical fibroxanthoma, lymphoma, small cell carcinoma, and signet ring carcinoma. The clinical incidence of additional primary malignancies in patients with confirmed primary malignant melanoma has been reported at 11.6%. Mimicry of another neoplasm is enhanced when amelanotic melanoma presents in a patient with a prior or concurrent malignancy for which it could be mistaken, as exemplified in the present case (this case was first presented as a poster at the International Society of Dermatopathology Annual Meeting on February 3, 2011).

Case History

A 63-year-old woman who had not seen a doctor in over 40 years was admitted to the emergency room. The night before admission, she fell to her knees secondary to weakness. Depressed for some time, she complained of back pain. Physical examination found a 15-cm fungating mass, independent of bone, said to have been present “for a little over a year” on the right elbow (Fig. 1) that she
A bone marrow aspirate showed 70% monoclonal plasma cells (Fig. 2). The oncology consultant proposed if the mass above right elbow was a long-standing plasmacytoma, radiation therapy to it would follow. On the third hospital day, multiple biopsy specimens were taken from the viable edge of the exophytic tumor above the elbow.

**Histopathology**

The biopsy of the ulcerated right arm mass presented a sheet-like proliferation of cells including atypical forms in a background of fibrosis, necrosis, and focal microabscesses (Table 1: immunohistochemistry). A reaction for the plasma cell marker CD138 labeled 10% of the tumor cells, whereas reactions for kappa and lambda found cells reactive for both. Occasional cells had Russell and Dutcher bodies.

**Flow Cytometry**

A portion of the right arm mass was submitted for flow cytometric analysis using CD45 using side light scatter gating parameters. This demonstrated a minor component of plasma cells that were kappa monoclonal. B cells were polyclonal. Although analysis of strong CD138+ events demonstrated plasma cells to account for <1% of the analyzed cells, these elements are typically underrepresented due to their inherent fragility so that they do not survive processing for flow in numbers truly representative. In addition, plasma cells often lack surface immunoglobulin expression. Therefore, both surface and cytoplasmic reactions for light chains were performed for characterization of these elements. Analyzed plasma cells were clearly typed as kappa monotypic (cytoplasmic lambda: cytoplasmic kappa = 10:1), a finding paralleling the immunophenotype of the tissue biopsy. Kappa restriction was demonstrated by 83% of the tumor cells analyzed, consistent with a plasmacytoma; those that did not express kappa were deemed too poorly differentiated.

The World Health Organization asserts the diagnosis of plasma cell myeloma that is based on a combination of pathological, radiological, and clinical features for which the patient easily qualified. The diagnostic criteria are summarized in Table 2. Multiple myeloma is a neoplasm of terminally differentiated B cells, that is, a proliferation of malignant plasma cells, secreting monoclonal paraprotein. It is the second most common hematological malignancy in adults. Plasmacytoma affecting skin without contiguous bony involvement is extremely rare with only 76 cases reported since first described by Bloch in 1910.

**Follow-up**

The multiple myeloma was treated with systemic chemotherapy. Radiation was delivered to the right elbow.

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**TABLE 1. Immunohistochemical Stains Used in This Study**

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Clone</th>
<th>Source</th>
<th>Dilution</th>
<th>Specificity</th>
<th>Reactivity</th>
<th>Breast</th>
<th>Marrow</th>
<th>Elbow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lambda</td>
<td>Polyclonal</td>
<td>Dako</td>
<td>Predilute</td>
<td>IgG-λ— heavy chain</td>
<td>—</td>
<td>—</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Kappa</td>
<td>Polyclonal</td>
<td>Dako</td>
<td>Predilute</td>
<td>IgG-κ— heavy chain</td>
<td>—</td>
<td>—</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>CD3</td>
<td>Polyclonal</td>
<td>Dako</td>
<td>1:100</td>
<td>T lymphocytes</td>
<td>—</td>
<td>+</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>CD20</td>
<td>L26</td>
<td>Dako</td>
<td>1:100</td>
<td>B lymphocytes</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>CD138</td>
<td>M15</td>
<td>Dako</td>
<td>1:10</td>
<td>Plasma cells</td>
<td>—</td>
<td>+</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>S-100</td>
<td>4C4.9</td>
<td>Ventana</td>
<td>10 μg/mL</td>
<td>Melanoma</td>
<td>+</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>MART-1</td>
<td>A-103</td>
<td>Dako</td>
<td>1:25</td>
<td>Melanoma</td>
<td>+</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Keratin, CAM 5.2</td>
<td>B22.1, B23.1</td>
<td>Cell Marque</td>
<td>1:100</td>
<td>CK8, 18, 19</td>
<td>+</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
</tbody>
</table>

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*Images and tables are not visible in this text format.*
A month after discharge, an axillary “abscess” was incised and drained. Three months after that, the right axillary swelling had progressed to 10 cm and had been continuously draining purulent material through a tiny opening. Purulent fluid was surgically evacuated from a loculated 6-cm cavity descending inferiorly. No necrosis was evident, and the adjacent breast had no visible abnormality. No tissue specimen was acquired. The wound was packed with gauze and cultures grew *Escherichia coli*.

About the same time, the patient was found to have an acute right superior ramus fracture explaining recent right hip pain. Further irradiation of this and the multiple pelvic masses that showed on radiologic studies were planned.

Between follow-up visits at approximately 4.5 months after the initial elbow mass biopsy, an explosive growth of a black multinodular lesions appeared on ipsilateral breast, with obvious nodularity in the axilla. A chest PET-CT scan disclosed massive

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**TABLE 2.** WHO Diagnostic Criteria for Plasma Cell Myeloma

<table>
<thead>
<tr>
<th>Symptomatic plasma cell myeloma</th>
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<tbody>
<tr>
<td><strong>M-protein in serum or urine</strong>(^*)</td>
</tr>
<tr>
<td>Bone marrow clonal plasma cells or plasmacytoma</td>
</tr>
<tr>
<td>Related organ or tissue impairment (CRAB: hypercalcemia, renal insufficiency, anemia, bone lesions)</td>
</tr>
<tr>
<td>Asymptomatic (smoldering) myeloma</td>
</tr>
<tr>
<td><strong>M-protein in serum at myeloma levels (&gt;30 g/L)</strong></td>
</tr>
<tr>
<td><strong>AND/OR</strong></td>
</tr>
<tr>
<td>10% or more clonal plasma cells in bone marrow</td>
</tr>
<tr>
<td>No related organ or tissue impairment [end-organ damage or bone lesions (CRAB)] or myeloma-related symptoms</td>
</tr>
</tbody>
</table>

\(^*\)Maroon text indicates the criteria met by the present case.

WHO, World Health Organization.

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**FIGURE 3.** Insets from clockwise upper left: atypical and binucleate plasma cells in Wright-stained marrow aspirate; strong kappa positivity of most marrow cells (×250); absent reactivity for lambda (×250); immature cell predominance in the marrow (H&E, ×400); CD138 labels nearly all cells that save a central megakaryocyte in the marrow aspirate; admission skull film features a multitude of small rounded lytic defects. H&E, hematoxylin and eosin.

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**CD138**
Lymphadenopathy in the right axilla extending to the supravacuicular region contiguous to the breast mass (Fig. 3). Breast biopsy showed obvious dermal melanoma, much of it histologically amelanotic, positive for S-100 protein and MART-1. The pure melanocyte population excluded the rare alternative of metaplastic breast carcinoma composed of both epithelial and melanocytic elements. Additional studies for the plasma cell marker CD138 (syndecan) plus kappa and lambda reactions suggested a scant clonal plasma cell infiltrate in the breast melanoma. A CAM5.2 reaction was also focally positive and is uncommonly reported in malignant melanoma.

The 15-cm elbow mass originally diagnosed as plasmacytoma was reevaluated in light of the breast biopsy findings. Although substantially amelanotic and without pagetoid cells in the epidermis, additional studies for MART-1 and S-100 protein indicated that the elbow mass was an advanced primary melanoma with a chronic inflammatory infiltrate that included some neoplastic plasma cells.

Scattered through the anaplastic cellularity of the elbow mass (Figs. 1A, B) were large malignant cells decorated with the plasma cell marker CD138 (Fig. 1C). Reactions for kappa and lambda suggested excess kappa in slides that were difficult to interpret because of rather diffuse nonspecific background labeling for both immunoglobulins. The flow cytometric detection of a population of kappa monoclonal plasma cells (Fig. 2) taken in the clinical context of lytic bone lesions and obvious kappa monoclonal plasma cell myeloma in the bone marrow resulted in an initial misdiagnosis of the ulcerated elbow mass as a cutaneous plasmacytoma. A clue foreshadowed this pitfall: CD138 labeled all neoplastic cells in the marrow, but only some cells in the elbow tumor; there had to be something else there.

In a 238-specimen series assessing CD138 reactivity, evaluation of 56 nonhematopoietic neoplasms revealed CD138 positivity for melanoma (5 of 10), a variety of epithelial carcinomas (30 of 33), leiomyosarcoma (1 of 2), and synovial sarcoma (2 of 2). All CD138+ melanomas in the cited series exhibited epithelioid morphologic features and showed moderate to strong membranous positivity.

Short stretches of epidermis tapering to ulceration over exposed tumor had inflammatory-related cells and nuclear enlargement that obscured the rare pagetoid cells within it. Later MART-1 slides confirmed pagetoid melanocytosis in this epidermis (Fig. 5).

Cutaneous involvement of multiple myeloma signals a poor prognosis and, like amelanotic melanoma, is frequently misdiagnosed. Martorell et al.20 report a case of cutaneous multiple myeloma mimicking acral lentiginous melanoma in a patient with a decadelong history of multiple myeloma with kappa restriction who died 6 months after biopsy of her right toe. Malignant melanoma has metastasized to other cancer types such as basal cell carcinoma,21 fibroxanthoma,22 and primary adenocarcinomas,23 but the colonization of a primary melanoma by another cancer type is extremely rare. To our knowledge, this is the first report of malignant melanoma colonized by a neoplastic plasma cell component that here was admixed with a diffuse chronic inflammatory infiltrate.

REFERENCES
