Large Neglected Ulcerated Melanoma Mimicking Extramedullary Plasmacytoma

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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

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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 melanomas[2] 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, 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

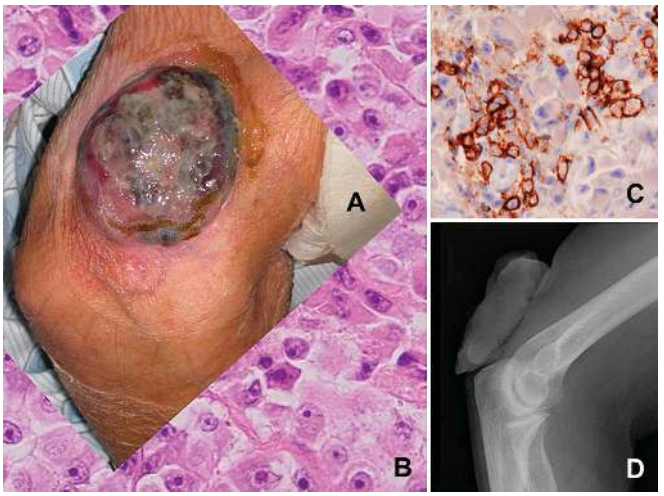

FIGURE 1. A, Clinical photograph of the ulcerated elbow mass. B, Elbow mass biopsy: anaplastic plasmacytoid cellularity. C, Elbow mass biopsy: partial CD138 positivity (×600). D, X-ray indicating the skin lesion's independence from bone.

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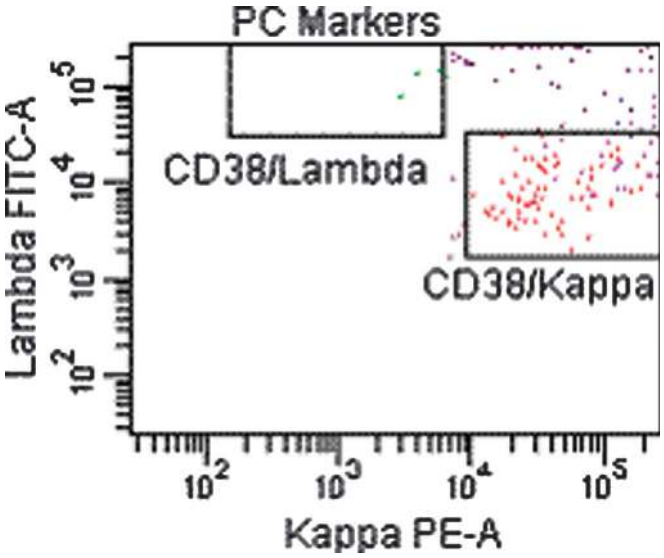

FIGURE 2. Flow cytometry detected a small subset of kappa monoclonal plasma cells. In conjunction with the known history of kappa monoclonal plasma cell myeloma, this resulted in an initial diagnosis of cutaneous plasmacytoma for the elbow mass.

had been hiding from her family until that day. The emergency room physician deemed it "an old injury resulting in granulation tissue."

Diffuse osteopenia and compression fractures in the thoracic spine (eg, T11) of indeterminate age showed on plain films and were confirmed by magnetic resonance imaging. Nonhomogeneous spinal appearance was consistent with myeloma. Bone survey showed multiple small round lucencies in the calvarium consistent with myeloma without lesions in the long bones. A hemoglobin of 7 and hematocrit of 20% indicated anemia likely secondary to the suspected multiple myeloma. A white count of 16,700 cells per microliter comprised segmented neutrophils 53%, bands 2%, lymphs 24%, atypicals 14%, and monocytes 2%. Circulating plasma cells were consistent with multiple myeloma. The eosinophil sedimentation rate was elevated to >150 millimeter per hour, and extensive rouleaux formation was explained by a total protein elevated to 11.8 g/dL with a decrease in albumin to 2.4 g/dL. A monoclonal IgA kappa spike of 6.18 g/dL was detected by electrophoresis.

Aredia 90 mg was given over the course of 2 hours as treatment for hypercalcemia (14.7 mg/dL with corrected calcium of 15.98 mg/dL). Confusion persisted attributed to the hyperviscosity syndrome and minimal improvement with Decadron.

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),[12] 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.[13] 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.[14] It is the second most common hematological malignancy in adults.[15] Plasmacytoma affecting skin without contiguous bony involvement is extremely rare[16] with only 76 cases reported since first described by Bloch in 1910.[17]

Follow-up

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

TABLE 1. Immunohistochemical Stains Used in This Study

Antibody	Clone	Source	Dilution	Specificity	Reactivity		
					Breast	Marrow	Elbow
Lambda	Polyclonal	Dako	Predilute	IgG-λ—heavy chain	−	—	+
Kappa	Polyclonal	Dako	Predilute	IgG-κ—heavy chain	−	+	+
CD3	Polyclonal	Dako	1:100	T lymphocytes	—	+	+
CD20	L26	Dako	1:100	B lymphocytes	—	−	−
CD138	MI15	Dako	1:10	Plasma cells	−	+	+
S-100	4C4.9	Ventana	10 μg/mL	Melanoma	+	—	+
MART-1	A-103	Dako	1:25	Melanoma	+	—	+
Kerratin, CAM 5.2	B22.1, B23.1	Cell Marque	1:100	CK8, 18, 19	+	—	—

TABLE 2. WHO Diagnostic Criteria for Plasma Cell Myeloma

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

*Maroon text indicates the criteria met by the present case.
WHO, World Health Organization.

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

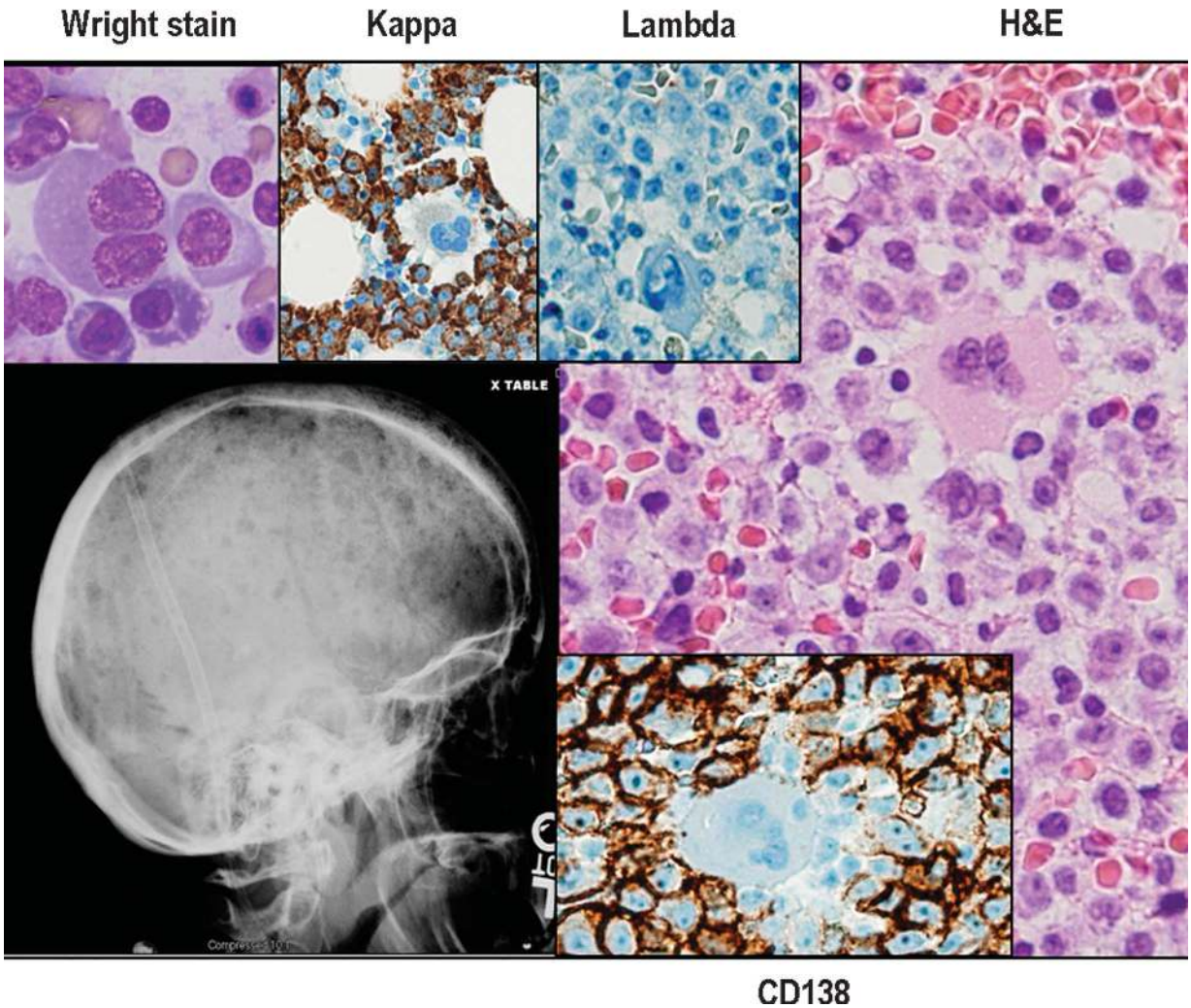

FIGURE 3. Insets from clockwise upper left: atypical and binucleate plasma cells in Wright-stained marrow aspirate; strong kappa positivity of most marrow cells (×250); absent reactivity for lambda (×250); immature cell predominance in the marrow (H&E, ×400); CD138 labels nearly all cells that save a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

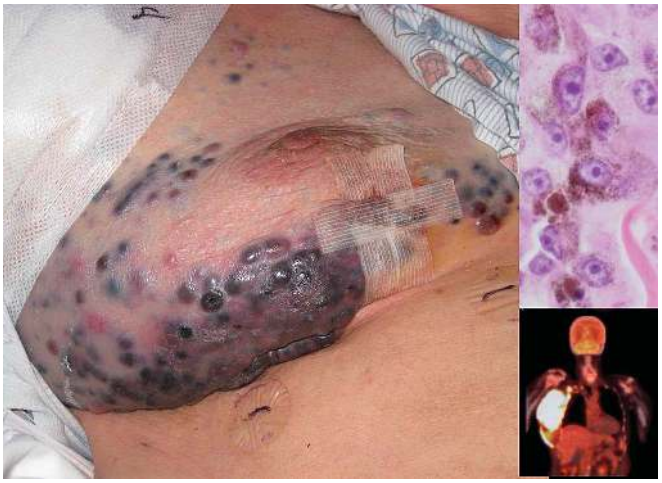

FIGURE 4. ''Explosive'' growth of jet black PET scan–positive tumor on breast, comprising melanized cells. PET, positron emission tomography.

(13.5 × 11.7 cm) lymphadenopathy in the right axilla extending to the supraclavicular 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 CAM 5.2 reaction was also focally positive and is uncommonly reported in malignant melanoma.[18]

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.

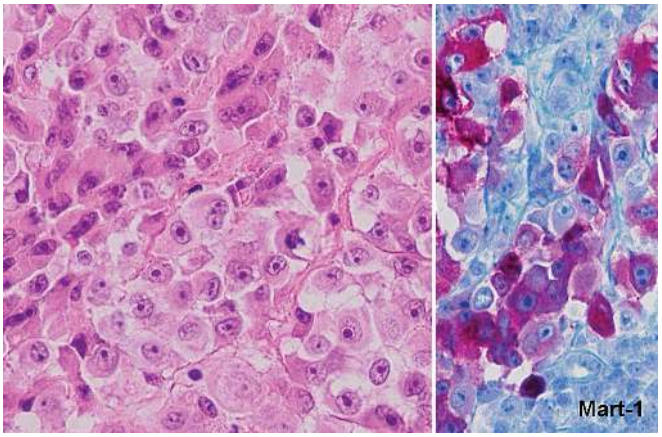

FIGURE 5. Reevaluation of the elbow mass biopsy included an MART-1 reaction, indicating that it predominantly comprised amelanotic melanoma cells with a predominantly reactive plasma cell infiltrate. This admixture, plasma cells and melanoma cells, is not obvious in the H&E view (left). H&E, hematoxylin and eosin.

Plasmacytoid features of the melanoma cells (Fig. 4) including intranuclear inclusions conspired with the clinical setting, radiology, laboratory results, bone marrow examination, and flow cytometry result to eventuate in its initial misdiagnosis as cutaneous plasmacytoma.

The patient's course after breast biopsy was one of rapid deterioration; she went almost immediately to hospice, passing away 15 days after the illuminating breast biopsy. Her death is attributed to metastatic melanoma, the multiple myeloma having been relatively stable.

DISCUSSION

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).[19] 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

1. American Cancer Society.Skin Cancer—Melanoma Detailed Guide. Available at:http://www.cancer.org/Cancer/SkinCancer-Melanoma/DetailedGuide/index. Accessed August 20, 2010.
2. Busam KJ, Hester K, Charles C, et al. Detection of clinically amelanotic malignant melanoma and assessment of its margins by in vivo confocal scanning laser microscopy. *Arch Dermatol*. 2001;137:923–929.

3. Koch SE, Lange JR. Amelanotic melanoma: the great masquerader. *J Am Acad Dermatol*. 2000;42:731–734.
4. Anderson WK, Silvers Dn. Melanoma? It can't be melanoma! A subset of melanomas that defies clinical recognition. *JAMA*. 1991;266:3463–3465.
5. McBurney El, Herron CB. Melanoma mimicking plantar wart. *J Am Acad Dermatol*. 1979;1:144–146.
6. Tschen JA, Fordice DB, Reddick M, et al. Amelanotic presenting as inflammatory plaques. *J Am Acad Dermatol*. 1992;27:464–465.
7. Barnhill RL, Fitzpatrick TB, Fandrey K, et al. Nodular melanoma. In: Barnhill RL, Fitzpatrick TB, Fandrey K, et al, eds. *Color Atlas of Pigmented Lesions*. New York, NY: McGraw-Hill; 1995:177–182.
8. Rahbari H, Nabai H, Mehregan AH, et al. Amelanotic lentigo maligna melanoma: a diagnostic conundrum—presentation of four new cases. *Cancer*. 1996;77:2052–2057.
9. Whitaker DC, Argenyi Z, Smith AC. Desmoplastic malignant melanoma: rare and difficult to diagnose. *J Am Acad Dermatol*. 1992;26:704–709.
10. Holder JE, Colloby PS, Fletcher A, et al. Amelanotic superficial spreading malignant melanoma mimicking Bowen's disease. *Br J Dermatol*. 1966; 134:519–521.
11. Hoiuse NS, Fedok F, Maloney ME, et al. Malignant melanoma with clinical and histologic features of Merkel cell carcinoma. *J Am Acad Dermatol*. 1994;31:839–842.
12. Gocke C. Immunohistology of non-Hodgkin lymphoma. In: David Dabbs, ed. *Diagnostic Immunohistochemistry.* Philadelphia, PA: Churchill Livingstone Elsevier; 2006:146.
13. Swerdlow SH, Campo E, Harris NL, et al. Mature B-cell neoplasms. In: *World Health Organization Classification of Tumors of Haematopoietic and Lymphoid Tissues*. Lyon, France: International Agency for Research on Cancer; 2008:202.
14. Grethlein SJ, Thomas LM. Multiple myeloma. Available at: http://emedicine.medscape.com/article/204369-overview. Accessed August 24, 2010.
15. Micaleff J, Dharsee M, Chen J, et al. Applying mass spectrometry based proteomic technology to advance the understanding of multiple myeloma. *J Hematol Oncol*. 2010;3:13 Available at: http://www.jhoonline.org/content/3/1/13. Accessed September 14, 2010.
16. Requena L, Kutzner H, Palmedo G, et al. Cutaneous involvement in multiple myeloma: a clinicopathologic, immunohistochemical, and cytogenetic study of 8 cases. *Arch Dermatol*. 2003;139:475–486.
17. Bloch B. Uber eine bisher nicht beschriebene, mit eigentumlichen Elastinverand-erungen einhergehende Dermatose bei Bence-Jonesscher Albuminurie: ein Beitrag zur Lehre von den Stoffwechseldermatosen. *Arch Dermatol Syphilol (Berl)*. 1910;99:9–22.
18. Bendic A, Bozic M, Durdov MG, et al. Metaplastic breast carcinoma with melanocytic differentiation. *Pathol Int*. 2009;59:676–680.
19. O'Connell FP, Pinkus JL, Pinkus GS. CD138 (syndecan-1), a plasma cell marker immunohistochemical profile in hematopoietic and nonhematopoietic neoplasms. *Am J Clin Pathol*. 2004;121:254–263.
20. Martorell A, Millan-Parrilla F, Gimeno-Carpio E. Cutaneous involvement in multiple myeloma mimicking acral-lentiginous melanoma. *J Am Acad Dermatol*. 2010;62:1076–1078.
21. Burkhalter A, White WL. Malignant melanoma in situ colonizing basal cell carcinoma. A simulator of invasive melanoma. *Am J Dermatopathol*. 1997;19:303–307.
22. Wilsher MJ. Collision tumour: atypical fibroxanthoma and invasive melanoma. *Pathology.* 2009;41:699–701.
23. Ueyama T, Tsuru T, Tsuneyoshi M, et al. Primary collision neoplasm of malignant melanoma and adenocarcinoma in the lung. A case report. *Pathol Res Pract*. 1993;189:178–183.

