Amelanotic Malignant Melanoma: Two Collision Tumors Presenting as Basal Cell Carcinoma and Atypical Fibroxanthoma

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Abstract. Collision (contiguous) tumors of the skin can result in misleading clinicopathological presentations, and the choice of appropriate diagnostic techniques may prevent incomplete diagnosis and management. We report 2 cases of collision tumors involving amelanotic malignant melanoma of the back. One patient is a 79-yr-old male with an 8.7 x 5.5 x 4.5 cm polypoid lesion that on shave biopsy was diagnosed as basal cell carcinoma. Subsequent excision showed that the lesion was largely composed of amelanotic melanoma underlying a relatively small and thin basal cell carcinoma, and this probably would have been demonstrated in a punch (rather than shave) biopsy. The other patient is a 71-yr-old male with a 1 cm exophytic lesion on the back, which was determined microscopically to be melanoma, and a 0.6 cm papule on the back. This lesion was composed of 2 distinct contiguous neoplastic infiltrates, the predominant component being an atypical fibroxanthoma and the smaller component an amelanotic melanoma (primary vs metastatic), with diagnostic confirmation requiring multiple immunohistochemical stains.

Keywords: melanoma, collision tumor, basal cell carcinoma, atypical fibroxanthoma

Introduction

Collision (contiguous) tumors are unusual neoplastic events. They have been most frequently reported in the skin, which is not surprising in view of the common etiologic factor of sun exposure, common anatomic locations, and frequency of cutaneous neoplasms. We report 2 cases of cutaneous amelanotic melanoma of the back, with initial clinicopathological presentations as basal cell carcinoma and atypical fibroxanthoma. These cases exemplify the clinicopathological difficulties involved in diagnostic assessment of cutaneous collision tumors, including factors such as biopsy technique, histomorphologic overlap, and immunohistochemical evaluation.

Case Reports

Case #1. A 79-yr-old white male presented with a large tender lobulated polypoid lesion on his upper back/lower posterior neck of unknown duration. Shave biopsy microscopically demonstrated a basal cell carcinoma, nodular type. The entire lesion was excised 6 weeks later. Grossly (Figs. 1a and 1b), the 11.5 x 9.2 cm oval excision of pale tan skin had an 8.7 x 5.5 cm cream-colored, lobulated, pedunculated, polypoid soft lesion extending 4.5 cm above the skin surface. Nearby there were multiple oval to round raised satellite lesions, 0.2 to 0.5 cm in...
dimension, and a contiguous 0.5 x 0.4 cm slightly raised, patchy gray to brown, fairly circumscribed lesion. The cut surface of the bisected specimen demonstrated a generally cream-colored homogeneous appearance. Microscopically (Figs. 2a and 2b), the lesion was composed of a basal cell carcinoma, nodular type, overlying a large amelanotic melanoma (Clark level V, 6.3 cm Breslow thickness from overlying granular layer, 2.3 cm thickness from adjacent granular layer), with a contiguous pigmented seborrheic keratosis (representing the grossly evident gray-brown lesion), and an actinic keratosis. Resection margins were free of involvement. The melanoma was focally in contact with the epidermis but a definite intraepidermal (junctional) component was not identified, and conclusive distinction between primary melanoma with regressed junctional component and metastatic melanoma could not be made. (The patient had no history of prior melanomas.) The diagnosis of melanoma was supported by focally positive immunohistochemical staining for S-100 protein, MART-1, HMB-45, pan-melanoma cocktail (MART-1 and tyrosinase) (Fig. 3), and vimentin, and by negative cytokeratin markers (AE1/AE3 and CAM 5.2). The patient died 9 months following this surgery from respiratory failure due to chronic obstructive pulmonary disease, with no clinical evidence of recurrent malignant melanoma.

Case #2. A 71-yr-old white male presented with 2 skin lesions on his back. The left upper back had a 1 cm exophytic, firm, blue nodule with central hyperkeratosis, and the right upper back had a 0.6 cm pearly papule. Shave biopsy and subsequent excision of the left upper back lesion was microscopically found to be an amelanotic melanoma, nodular type with spindle cell features, Clark level IV, 6.86 mm Breslow thickness. Shave biopsy of the right upper back lesion (the subject of the present report) was microscopically (Figs. 4a and 4b) found to be composed of 2 distinct contiguous and confluent neoplastic dermal infiltrates: a predominant proliferation of highly
atypical and pleomorphic large cells on one side of the lesion, and a smaller component of diffuse and nested atypical ovoid cells with focal epidermal junctional involvement on the other side of the lesion. The pleomorphic large cell proliferation was a dense dermal infiltrate of highly atypical plump spindle and giant cells with histiocytoid features, prominent nucleoli, scattered atypical mitoses, and extension to the dermoepidermal junction bounded by an epidermal collarette. Immunohistochemical staining showed the cells to be positive for CD68, factor XIIIa, and Ki-M1p (undiluted supernatant), focally positive for S-100, and negative for MART-1, HMB45, and pan-melanoma cocktail (MART-1 and tyrosinase) (Fig. 5), and S-100, focally positive for CD68, and negative for factor XIIIa and Ki-M1p (undiluted supernatant). Subsequent excisions revealed residual melanoma, Clark level IV, 6.86 mm Breslow thickness, in the left upper back, and microfocal residual melanoma but no residual atypical fibroxanthoma in the right upper back lesion. Following this surgery the patient was treated with interferon for one mo, and there was no clinical evidence of recurrent lesions until 2 yr following the original surgeries, when palpable right axillary lymphadenopathy developed. Lymph node dissection revealed metastatic melanoma.

Fig. 3: Immunohistochemical staining for pan-melanoma cocktail highlights the malignant melanoma in contrast to the basal cell carcinoma (x100).

Figs. 4a and 4b: Neoplastic infiltrate composed of atypical fibroxanthoma involving the upper and right lower dermis and amelanotic malignant melanoma involving the left lower dermis (H&E, x40 and x100).

Fig. 5: Immunohistochemical staining for pan-melanoma cocktail highlights the malignant melanoma in contrast to the atypical fibroxanthoma (similar microscopic field as shown in Fig. 4a) (x40).
Materials and Methods

Tissues from both cases were fixed in 10% buffered formalin. Immunohistochemical stains were performed using the following antibodies (commercially available, except for Ki-M1p): S-100 protein (Cell Marque; 1:200 dilution, Hot Springs, AR); MART-1 (Signet; 1:100 dilution, Dedham, MA); HMB45 (DAKO; 1:150 dilution, Carpinteria, CA); pan-melanoma cocktail (HMB45, MART-1, and tyrosinase; Biocare Medical; 1:50 dilution, Concord, CA); vimentin (DAKO; 1:80 dilution, Glostrup, Denmark); cytokeratin AE1/AE3 (DAKO; 1:100 dilution, Carpinteria, CA); cytokeratin CAM5.2 (Cell Marque; 1:30 dilution); CD68 (DAKO; 1:100 dilution, Glostrup, Denmark); factor XIIIa (Cell Marque; 1:50 dilution); Ki-M1p (Professor Reza Parwaresch; undiluted supernatant, Kiel, Germany); all used the avidin-biotin complex method with microwave antigen retrieval technique. Appropriate positive and negative controls were used throughout.

Discussion

Collision tumors, contiguous neoplasms of different cell types, are unusual but not infrequently reported findings in various organs. In the skin, so-called basosquamous cell carcinomas are occasionally diagnosed, and those with contiguous distinctly different basal and squamous cell carcinoma may be included among collision tumors.

We report here 2 clinically and pathologically interesting cases of cutaneous collision tumors involving amelanotic malignant melanomas, one associated with basal cell carcinoma and the other with atypical fibroxanthoma. Malignant melanoma has previously been reported as a collision tumor associated with: basal cell carcinoma [1-7], squamous cell carcinoma [8], rectal adenocarcinoma [9], mucoepidermoid carcinoma of maxillary antrum [10], adenocarcinoma of lung [11], and adenocarcinoma of lung metastatic to skin [12].

The present case of malignant melanoma as a collision tumor with basal cell carcinoma is unique for a number of reasons, mainly for its clinical presentation rather than the pathologic diagnostic features. The lesion presented as a large (8.7 x 5.5 x 4.5 cm) protuberant cutaneous mass. Shave biopsy revealed histological features characteristic of basal cell carcinoma, nodular type. Retrospectively, punch rather than shave biopsy might have been a preferable diagnostic procedure, since subsequent excision revealed the major portion of the lesion to be a nodular amelanotic melanoma. This melanoma was focally in contact with the epidermis but was largely underlying the basal cell carcinoma and infiltrated the dermis and subcutaneous tissue to a depth of 6.3 cm (from the overlying granular layer) and 2.3 cm (from the adjacent granular layer). Histologic and immunohistochemical evaluation showed the melanoma and basal cell carcinoma, although focally intermingled, to be morphologically distinct lesions, with no evidence of transition or mutual origin. This morphologically distinct appearance is in contrast to the recently described malignant basomelanocytic tumors [13,14], in which the basal cell and melanocytic components were intimately intermingled both histomorphologically and immunohistochemically.

The other case of malignant melanoma as a collision tumor with atypical fibroxanthoma appears to be the first documented case of such an association. This lesion was initially presumed to represent only an atypical fibroxanthoma, and a major pathologic diagnostic component of this case was determining that 2 distinct neoplasms were involved. Several reports have highlighted the difficulties in distinguishing between atypical fibroxanthoma and spindle cell malignant melanoma [15,16], two tumors with vastly different biologic behaviors. For example, spindle cell features in malignant melanoma (and also squamous cell carcinoma) can mimic atypical fibroxanthoma, and hemosiderin pigment in atypical fibroxanthoma may suggest melanotic melanoma. Resolution of this issue in our case required multiple immunohistochemical stains, including the highly specific macrophage marker Ki-M1p [17].

In addition, the case was referred to the Armed Forces Institute of Pathology (Washington, DC), where multiple immunohistochemical stains were also performed. The immunohistochemical stains were chosen for their sensitivity and/or specificity. The staining results clearly supported 2 distinct neoplasms, with pan-melanoma cocktail positivity only in the melanomatous component. The specific macrophage marker Ki-M2p was diffusely positive only in the atypical fibroxanthoma, although interspersed macrophages in the melanoma were also positive. Similarly, the other histiocytic markers stained reactive histiocytes which had to be histomorphologically distinguished from the
neoplastic malignant melanocytes. Minor spurious staining included focal S-100 positivity in the atypical fibroxanthoma and focal CD68 positivity in the melanoma.

Both of these cases raise the important question of primary vs epidermotropic metastatic malignant melanoma. A number of cases of apparent epidermotropic metastatic melanoma have been reported [18-24]. The difficulty in distinguishing epidermotropic metastatic from primary melanoma [25] and the importance of distinguishing local persistence from local metastasis [26] have been recently reemphasized. Microscopically, the distinction can be difficult. Epidermal involvement suggests local persistence but local metastasis may also show involvement of epidermis and epidermo-dermal junction. Of clinical importance, local persistence of melanoma (resulting from involved margin) indicates no change in prognosis or stage and is treated with reexcision, whereas local metastasis indicates a more grave prognosis, upstaging to M1a, and the possible need for sentinel lymph node biopsy and/or wide local excision. Our case #1 was a large melanoma without history of prior or subsequent melanoma and likely represents a primary, but metastasis cannot be completely excluded since a definite junctional component was not identified. Our case #2 was a right back lesion that was associated with a larger left back melanoma and the possibility of it representing an epidermotropic metastasis would be a consideration.

These cases reemphasize that skin lesions, including amelanotic malignant melanoma, may represent two rather than one neoplastic process, and that various diagnostic procedures may contribute to the determination of the true dual nature of these cutaneous collision tumors.

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References