

CD45/CD8 Myeloid Histioid Antigen and Plasma Cell Antibody Immune Response in a Case of Malignant Melanoma

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Abstract

The immune response in metastatic melanoma is not well established and therefore is of particular interest to test for recruitment of immune cells to the tumor. A 46-year-old Caucasian female was evaluated for an asymptomatic right forearm mass. The lesion had been present for at least 4 years and had become painful 4 months ago. Biopsies for hematoxylin and eosin (H and E) staining, as well as immunohistochemical analysis were performed on the primary tumor and on sentinel lymph nodes. The H and E staining was consistent with metastatic melanoma. Positive staining was noted on the tumor cells with S-100, Mart-1/Melan A/CD63, PNL2, HMB45, and tyrosinase. Peritumoral and intratumoral inflammatory cells stained positive for CD8, CD45, PCNA, myeloid histoid antigen, antihuman plasma cell antibody, and focal BRCA1. The staining patterns of CD8/CD45, myeloid histoid antigen and plasma cell antibody on inflammatory cells around the melanoma cells suggest an unusual type of immune response.

Keywords: CD45, CD8, Immune response, Metastatic melanoma, Myeloid histoid antigen, Plasma cell antibody

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Introduction

The immune response in metastatic melanoma is not well known and this makes it difficult to use therapeutic approaches to stimulate the response against the tumor very hard. This case is of importance because it shows a spontaneous immune response *in situ* around the tumor that can give some insights to try to improve the arsenal against metastatic melanoma.

Case Report

A 46-year-old Caucasian female was evaluated for

an asymptomatic right forearm mass. The lesion had been present for at least 4 years, and become painful 4 months before presentation. Physical examination revealed a dermal mass, without pigmentation and mildly tender. A skin excisional biopsy for hematoxylin and eosin (H and E) staining, as well as immunohistochemical analysis was performed. No palpable lymphadenopathy was found. The H and E results indicated possible metastatic melanoma. The patient was then examined using radiological studies, and follow-up surgery was performed on the primary tumor site and on sentinel lymph nodes. Immunohistochemistry (IHC) analysis was performed as previously described.^[1-3] Staining was performed with antibodies to S-100, HMB-45, Mart-1/Melan-A/CD63, PNL2, tyrosinase, CD8, CD45, D2-40, proliferating cell nuclear antigen (PCNA), antihuman plasma cell, antibody myeloid histoid antigen, IMP3, insulin-like growth factor II, mRNA binding protein 3, bromodeoxyurine, topoisomerase II alpha, cyclin D1, BRCA1, p21, p27, p53, epidermal growth factor receptor

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DOI:
10.4103/1947-2714.102006

(EGFR), Cytokeratin AE1/AE3, and von Willebrand factor. Examination of the H and E tissue sections demonstrated an atypical melanocytic proliferation. The epidermal findings were histologically unremarkable. Within the dermis and subcutaneous adipose tissues, a single, well circumscribed, nodular proliferation of atypical melanocytes was present. Within the proliferation, atypical melanocytes were present as nests and sheets. Neoplastic cells displayed poor maturation with progressive descent into the dermis. Individual atypical melanocytes were of small to large size, and displayed epithelioid and spindled/fusiform morphologies; these cells displayed variable cytologic atypia. The atypical melanocytes contained round to oval nuclei with coarse, clumped chromatin and prominent, eosinophilic nucleoli. Focal, infiltrating lymphocytes was noted. No tumoral necrosis was noted. Focal vascular and lymphatic space invasion was noted, but no perineural. No ulceration, or satellitosis was appreciated [Figure 1]. The lesional Breslow thickness measured at approximately 11 mm; frequent tumoral mitoses were quantified at approximately 12 mitoses/mm². A melanoma clinical stage of IIB T4a N0 M0 was established following workup. IHC stain shown diffusely positive, membranous and cytoplasmic staining was noted on the tumor cells on review of the S-100, Mart-1/Melan A/CD63, PNL2, HMB45 and tyrosinase special stains. Focally positive, membranous and cytoplasmic staining was noted on these cells on review of the Cyclin D1 and p53 special stains. Tumoral dermal lymphatic invasion and tumoral lymphatic angiogenesis were appreciated on review of the D2-

40, Von Willebrand, CD31 and CD34 special stain [Figure 1]. Around the central tumor mass, tyrosinase, PNL2, PCNA, and HMB-45 were focally positive as single cells, and nests of cells. Topoisomerase II alpha was well as p53, Cyclin D1 and BRCA1 were also focally positive in areas immediately surrounding the tumor [Figure 1]. Bromodeoxyurine was negative within the tumor but positive in one spot in the "normal" epidermis above the tumor. Staining for CD8, CD45, and myeloid histoid antigen were positive around and between the melanoma cells. p27 and IMP3 were negative within the tumor. Metastatic staging workup included a chest radiograph and positron emission tomography/computed tomography (PET/CT) scan; both failed to demonstrate tumoral masses. Serum lactate dehydrogenase was within the normal range. The patient underwent lymphoscintigraphy using Tc99-m sulfur colloid on the day of surgery, highlighting three sentinel nodes in the right axilla. Axillary sentinel node biopsies were negative for metastatic disease by S-100 and Mart-1/Melan A/CD63 staining, and no residual melanoma disease to be present in the right forearm.

Discussion

Our case was challenging, bringing together a multidisciplinary group of physicians to study and treat the clinical, immunopathological and radiological features of this dermal melanoma mass. The (1) lack of any apparent metastatic tumor primary site, (2) lack of disease within junctional melanocytes of suprajacent

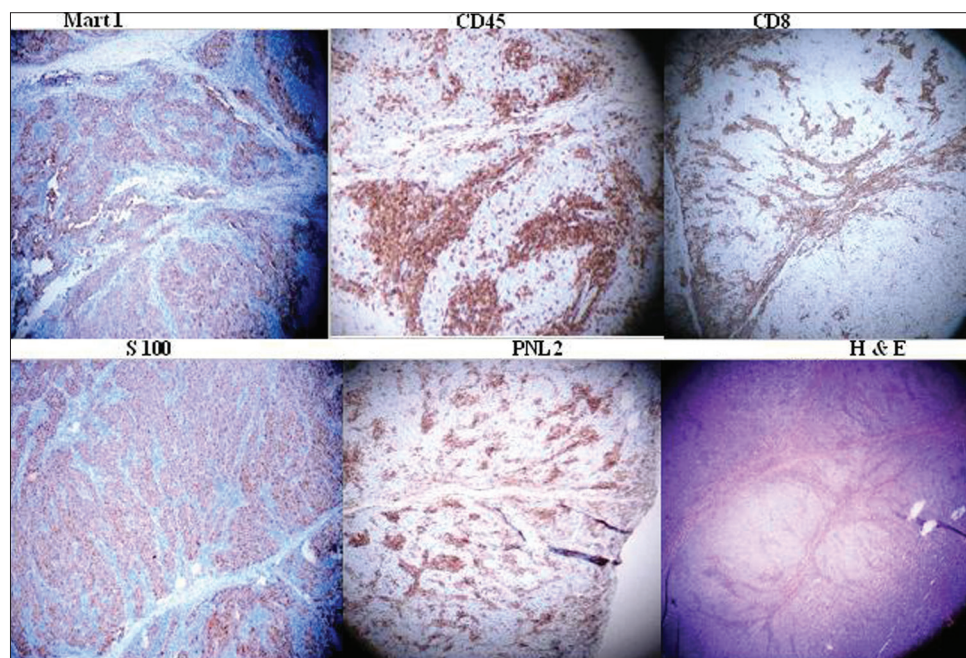


Figure 1: Shows the H and E, as well as some positive IHC staining of the melanoma as well as the cells around the tumor. Upper column left to right: Positive Mart 1, CD45, and CD8 (dark staining). Lower column left to right: Positive S-100, PNL2 and H and E staining

skin above the tumor, and (3) the presence of CD8, CD45 and myeloid histoid antigen positive cells surrounding the tumor cells represented unusual case features. The dermal foci suggestive of tumoral vascular and lymphatic invasion favored a clinical diagnosis of metastatic melanoma over that of primary dermal melanoma.^[4-7] Our findings represent novel discoveries in the immune response *in situ* and may suggest that the spontaneous immune response we detected could already attack and destroy the primary melanoma that we were unable to find. This may explain why no primary distant site melanoma was found despite extensive studies.

As noted, we found positive staining with CD8/CD45 and myeloid histoid antigen antibodies surrounding tumor cells, forming a silhouette-shadow pattern relative to the melanoma cells. We are not sure if this staining pattern could be related to previously reported cannibalism of live lymphocytes by human metastatic (but not primary) melanoma cells.^[8,9] Such cannibalism has been described in other malignant tumors; its biological significance is still largely unknown. Further, possible cannibalism of melanoma cells by CD8, CD45 and myeloid histoid antigen positive cells has never been documented in primary malignant melanoma. These IHC findings created arabesques figures to form a “shadow” and/or “silhouette”. More cases need to be studied to better understand our documented phenomenon.

We conclude that it is possible that in some metastatic melanomas can occur some type of *in vivo* recruitment of immune cells including CD45/CD8 and myeloid histiocytic antigen cells and plasma cell antibody cells that may represent a specific type of immune response against this tumor, and this may lead to the potential of a systemic and or local therapeutic response.

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How to cite this article: Abreu-Velez AM, Howard MS, Pereyo NY, Delman KA, Mihm MC, Rizzo M. CD45/CD8 myeloid histoid antigen and plasma cell antibody immune response in a case of malignant melanoma. *North Am J Med Sci* 2012;4:507-9.

Source of Support: Nil. **Conflict of Interest:** None declared.