Disappearance of All Nevi as Initial Sign of Metastatic Melanoma

Antonio Martinez-Lopez, Gonzalo Blasco-Morente, Israel Perez-Lopez, Salvador Arias-Santiago

From the Dermatology Unit, Complejo Hospitalario Universitario, Granada, Spain.
E-mail: antoniomartinezlopez@aol.com

Indian J Dermatol 2017;62(4):441

Sir,

Vitiligo-like depigmentation, halo nevus, and leukoderma in patients with malignant melanoma are poorly understood phenomena. A clinical case of a female patient referrign that all her nevi had disappeared as the first clinical manifestation of a metastatic melanoma is presented.

A 55-year-old woman without a relevant medical history presented to our hospital referring that all her nevi had disappeared in 2 months and with a subcutaneous lesion that had been previously diagnosed of lipoma. Physical examination revealed that all the nevi, but not lentigines (epidermal hyperplasia with increased keratinocytes), had disappeared leaving a white pigmentation [Figure 1a and b]. She also presented a hard consistency subcutaneous lesion on her right flank that was not clinically compatible with lipoma [Figure 1c]. Fine needle aspiration of the subcutaneous lesion was consistent with metastatic melanoma, and computed tomography scan revealed multiple metastases in lungs (confirmed with biopsy), inguinal and iliac nodes. Skin biopsy of one of the white lesions revealed an inflammatory T CD8+ lymphocytic infiltrate without a melanocytic proliferation but with dermal melanophages. Initial chemotherapy with dacarbazine was prescribed but the patient died 2 months later.

In melanoma, immunogenic factors play a key role in the disease course. Partial regression of primary melanomas was initially associated with bad prognosis; however, some recent series failed to demonstrate a worse prognosis in the melanomas with regression.[1] Complete spontaneous regression of primary cutaneous melanoma is a well-known but uncommon event. Sometimes, it is possible to recognize the presence of a regressed pigmented lesion in the area of lymphatic drainage.[2] Histopathological features of complete cutaneous melanoma are a lymphocytic infiltrate with melanophages, dermal reactive vascular proliferation with perivascular interstitial edema, and dermal fibrosis. Modified criteria for the diagnosis of completely regressed melanoma have been published.[2]

Immunotherapy probably increases the incidence of vitiligo associated with melanoma but the survival in this subgroup of patients is better than expected according to their melanoma stage.[3] There are antibodies that cross-react with antigens on melanocytes and melanoma cells such as tyrosinase, tyrosinase-related protein 1 and 2, melan A, gp100, p16, or CDKN2A.[4] These antigens are expressed through the HLA-I and are recognized by CD8+ T lymphocytes and may lead to disappearance of all nevi and primary tumor regression as in the present case. The loss of expression of the HLA-I has been linked to the progression of the tumor and the presence of distant metastasis (tumor escape mechanism for immune system). Viral vectors are being designed to recover the tumor expression of HLA-I and to improve the response to treatment. This positive correlation between vitiligo and melanoma survival has already been reported in patients treated with classically chemotherapy therapies (carmustine, dacarbazine, and cisplatin) and immunotherapy (interleukin-2 and interferon alfa-2).[6]

Recently, pembrolizumab (a humanized IgG4 monoclonal antibody that increased the CD8+ T lymphocytes antitumor cytolytic functions) has been associated with a 25% developed vitiligo during the treatment. In this group, an objective tumor response has been associated with a higher occurrence of vitiligo.[7]

We believe that in the present case, spontaneous regression of primary cutaneous melanoma and all the nevi occurred through immunologic mechanisms. Although no similar cases have been reported in the literature, we advocate the importance of a careful physical examination, including skin and lymph nodes, for patients with sudden onset of hypochromic changes as in the present case or without known primary melanoma. Finally, the exact mechanism of regression...
remains to be elucidated; hence, more studies are necessary to clarify the role of the immune system in patients with melanoma.

**Financial support and sponsorship**
Nil.

**Conflicts of interest**
There are no conflicts of interest.

**References**
1. Kaur C, Thomas RJ, Desai N, Green MA, Lovell D, Powell BW, et al. The correlation of regression in primary melanoma with sentinel lymph node status. J Clin Pathol 2008;61:297-300.
2. High WA, Stewart D, Wilbers CR, Cockerell CJ, Hoang MP, Fitzpatrick JE. Completely regressed primary cutaneous malignant melanoma with nodal and/or visceral metastases: A report of 5 cases and assessment of the literature and diagnostic criteria. J Am Acad Dermatol 2005;53:89-100.
3. Daneshpazhooh M, Shokoohi A, Dadban A, Raafat J. The course of melanoma-associated vitiligo: Report of a case. Melanoma Res 2006;16:371-3.
4. Ohsie SJ, Sarantopoulos GP, Cochran AJ, Binder SW. Immunohistochemical characteristics of melanoma. J Cutan Pathol 2008;35:433-44.
5. del Campo AB, Aptsiauri N, Méndez R, Zinchenko S, Vales A, Paschen A, et al. Efficient recovery of HLA class I expression in human tumor cells after beta2-microglobulin gene transfer using adenoviral vector: Implications for cancer immunotherapy. Scand J Immunol 2009;70:125-35.
6. Boasberg PD, Hoon DS, Piro LD, Martin MA, Fujimoto A, Kristedjá TS, et al. Enhanced survival associated with vitiligo expression during maintenance biotherapy for metastatic melanoma. J Invest Dermatol 2006;126:2658-63.
7. Hua C, Boussemart L, Mateus C, Routier E, Boutros C, Cazenave H, et al. Association of vitiligo with tumor response in patients with metastatic melanoma treated with pembrolizumab. JAMA Dermatol 2016;152:45-51.