CASE REPORT

Vitiligo-like Depigmentation Associated with Metastatic Melanoma of an Unknown Origin

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Although malignant melanoma usually occurs after the diagnosis of vitiligo-like depigmentation, the latter is rarely followed by the former. We herein report on such a case in which recognition of the vitiligo-like depigmentation preceded diagnosing the metastatic melanoma by several months. A 56-year-old woman had first developed vitiligo-like depigmentation on the forehead, eyelids, neck and back 18 months previously and thereafter she detected a hard mass in the left axilla 2 months previously. Based on the histologic findings, the axillary mass was diagnosed as metastatic melanoma. To evaluate the primary tumor focus, thorough examinations that included PET-CT, bone scan and sigmoidoscopy were performed, but we couldn't find any the original primary tumor. Our case suggests that the vitiligo-like depigmentation could be a sign that heralds metastatic melanoma. (*Ann Dermatol* 21(2) 178~181, 2009)

-Keywords-

Metastatic melanoma, Vitiligo-like depigmentation

INTRODUCTION

There have been frequent reports of cutaneous vitiligo-like depigmentation during the course of malignant melanoma¹. The presence of vitiligo-like depigmentation might delay the inevitable outcome, but it does not eradicate the malignancy². In the majority of cases with malignant mela-

noma associated with vitiligo-like depigmentation, the onset of achromic changes was secondary to the diagnosis of malignant melanoma, and the achromic changes usually appeared after the onset of metastatic disease³. In contrast, it has also been recently demonstrated that vitiligo-like depigmentation in patients with a history of melanoma was noted prior to metastatic melanoma⁴. We herein report on another case and discuss the relationship of malignant melanoma and vitiligo-like depigmentation.

CASE REPORT

A 56-year-old woman presented with a 2-month history of a hard mass in her left axilla. The lesion presented as an asymptomatic, deep-seated, movable, firm mass of about 5 cm in diameter. On her past history, she had received excision of a black macule, 5 mm in size on the left axilla 17 years ago, but she didn't know the correct pathological diagnosis that was made at that time. Thereafter, she developed progressive vitiligo-like depigmentation 18 months before her current hospital admission. The skin lesions were asymptomatic, multiple, depigmented macules and patches of various sizes on the forehead, eyelids, neck and back (Fig. 1). Except for these skin lesions, there were no remarkable findings on the physical examination, including the mucosal and ocular areas. There was no family history of vitiligo.

On the CT scan of the chest, there was a lobulated lymph node mass with inhomogeneous enhancement in the left axilla; the mass was 5.4×3.1 cm in dimension and there were no remarkable findings for the lung and breast (Fig. 2). Furthermore, there was no clinical or radiological evidence of any lymph node enlargement elsewhere.

An incision biopsy specimen taken from the mass on her left axilla demonstrated tumor nests surrounded by stroma

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Fig. 1. Vitiligo-like lesions on the forehead, eyelids and back.

Fig. 2. A lobulated lymph node mass 5.4×3.1 cm in dimension with inhomogeneous enhancement in the left axilla.

and inflammatory cells, and a closer view revealed that the tumor was composed of atypical, epithelioid cells with hyperchromatic and pleomorphic nuclei and some mitoses (Fig. 3A). The tumor cells stained positive for vimentin, S-100 protein and HMB-45, whereas they were negative for leukocyte common antigen, CD20 and CD45RO (Fig. 3B). Based on these histologic findings, we diagnosed our case as metastatic melanoma of a left axillary lymph node.

PET-CT, bone scan and sigmoidoscopy were performed to further evaluate the primary tumor focus, but there were no remarkable findings of a primary tumor. We administered adjuvant postoperative radiotherapy to the left axilla (5040 cGy/28fx), and she is now being treated with interferon- α 2b (8.4 MU, intravenous, monthly) and dacarbazine (1,273.6 mg to 1,308 mg, intravenous, monthly) chemotherapy and regular narrow band UVB photo-ther-

apy (DualLight UV 120-2™, 90 mJ to 290 mJ, twice a week) for the vitiligo-like depigmentation for 7 months. Until now, there has been no evidence of any recurrence of the melanoma, and the vitiligo-like depigmentation has slightly improved.

DISCUSSION

The prevalence of vitiligo-like depigmentation in patients with malignant melanoma has been reported to be from 3% to 6% in a few different series, and vitiligo-like depigmentation is estimated to be 7 to 10-fold more frequent in patients with malignant melanoma than in the general population^{5,6}. In another study, vitiligo-like depigmentation was reported in 5~20% of the patients who all had stage III metastatic melanoma prior to detecting the vitiligo-like depigmentation⁷.

The relationship between malignant melanoma and vitiligo-like depigmentation is thought to be the consequence of the dualistic immune-mediated response against antigens shared by normal melanocytes and melanoma cells⁸. It has been shown that malignant melanoma and vitiligo are associated with humoral immune responses to similar antigens⁹. In that process, specific CD8-positive T cells may have an important role as they direct the immune response against melanocytic antigens^{10,11}. In animal models, immunization with malignant melanoma cells can cause vitiligo-like depigmentation¹². The antibodies to the antigens expressed on pigment cells usually preceded or appeared together with tumor regression and the loss of pigmentation¹³.

Fig. 3. (A) The biopsy specimen from the axillary lymph node mass shows the tumor nests (H&E, $\times 100$). Inset: The tumor nests are composed of atypical, epithelioid cells with hyperchromatic, pleomorphic nuclei and some mitoses (H&E, $\times 400$). (B) The tumor cells stained positive for S-100 protein (left: S-100, $\times 200$) and they were positive for HMB-45 (right: HMB, $\times 200$).

Meanwhile, it was observed the tumor cells in our patient's axillary lymph node stained diffusely positive for S-100 protein and it was focally positive for HMB-45. It is known that HMB-45 staining might be patchy, and melanoma cells might be less diffusely positive for HMB-45 than for other markers¹⁴. It has been reported that staining for S-100 in melanoma has a sensitivity of 97~100%, and the sensitivity of HMB-45 for melanoma ranges from 69% to 93%¹⁴. These could explain the different staining patterns of the tumor cells for S-100 protein and HMB-45 in our case.

The occurrence of vitiligo-like depigmentation in malignant melanoma patients is commonly believed to be a positive prognostic factor, suggesting the development of an antitumoral response^{2,3,15}. For patients with metastatic malignant melanoma associated with widespread vitiligo, the 5-year survival rate is 60%, and the survival rate of patients with stage II or III metastatic malignant melanoma is only 30%¹⁶.

Vitiligo-like depigmentation usually appears after metastasis in most cases of melanoma⁸. In contrast, one investigator reported that the prevalence of preexisting vitiligo in a group of patients with malignant melanoma was only about 1.0% (4 of 386 patients)³. In that report, the favorable influence of vitiligo-like depigmentation on the prognosis of metastatic malignant melanoma did not seem to be related to whether or not the depigmentation developed before or after the diagnosis of the malignant melanoma³.

Some conditions such as bruises, generalized melanosis, melanuria, ptosis, Raynaud's phenomenon or systemic vasculitis have been described as early signs that herald metastatic melanoma⁴. Likewise, it has been suggested

that vitiligo-like depigmentation preceding overt distant metastases could be an early warning sign of impending melanoma metastases⁴.

Our case is rather interesting because the recognition of the vitiligo-like depigmentation preceded the axillary lymph node metastasis by several months and a primary focus of melanoma could not be detected despite that we conducted a thorough systemic examination. Together with the previous reports, our case suggests that the development of depigmentation could be a sign that heralds metastatic melanoma and that for such a case, physicians should thoroughly examine the patient to find a primary origin of the metastatic melanoma.

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