Two reports of malignant melanoma arising within a new vitiligo-like depigmented patch

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BACKGROUND

There is a known association between variations of vitiligo-like depigmentation and melanoma, with a prevalence of about 2.8% to 7% of malignant melanoma cases.[1-3] It is hypothesized that as transformed melanocyte antigens are detected by the immune system, antimelanoma antibodies are formed, and normal melanocytes may be destroyed.[4,5] This systemic response to a cutaneous process leads to the phenomenon of depigmentation. Halo (Sutton) nevi, halo dermatitis (Meyerson nevus), melanoma regression, depigmentation after immunotherapeutic infusion,[6] and melanoma-associated depigmentation are 5 examples of immune-mediated reactions against melanocyte-specific antigens in the setting of melanoma.[3] Each reaction is characterized by specific clinical, histopathologic, and prognostic features.

Zeff et al[7] describe 2 observations involving the regression reaction mediated by the immune system.[7] The first is that a cytotoxic $CD8^+$ T-lymphocyte and mononuclear cell inflammatory infiltrate is present that surrounds the degenerating nevus cells, contributing to surrounding depigmentation. Second, antibodies directed against nevocellular antigens are present that react with nevus cells in vitro. Melanoma-associated leukoderma or melanoma-associated depigmentation (MAL or MAD) presents with depigmentation in a separate location from the primary or metastasized sites. Teulings et al[8] defined MAL as depigmentation that develops within 1 year before the detection of a primary melanoma or within 3 years before the detection of melanoma metastases with an unknown primary tumor. MAL is associated with a favorable prognosis and response to treatment.[3] Treatment-associated vitiligo-like depigmentation is an independent favorable prognostic factor in stage III and IV metastatic melanoma patients.[9,10] A meta-analysis conducted by Teulings et al[8] found an increased progression-free survival (hazard ratio [HR], 0.51; 95% confidence interval [CI], 0.32 to 0.82; $P < .005$) and overall survival (HR, 0.25; 95% CI, 0.10 to 0.61; $P < .003$) in patients with vitiligo-like depigmentation on immunotherapy.[3]

Abbreviation used:

MAL: Melanoma-associated leukoderma

We report 2 instances of the appearance of a single depigmented patch that underwent change and, when biopsied, proved to contain melanoma in situ and invasive melanoma.

CASE REPORTS

Patient 1

A 47-year-old woman presented with concern regarding an area of discoloration on her arm, stating that the white color emerged 5 months prior with no history of nevus in the area, preceding rash, trauma, or symptoms of itching or scaling. She had no history of skin cancer, melanoma, or vitiligo but a positive family history of nonmelanoma skin cancer. On physical examination, there was a depigmented patch, 20 × 17 mm, on her left upper limb (Fig 1). The etiology was unclear, and no other lesions such as this were present. There was a low suspicion for

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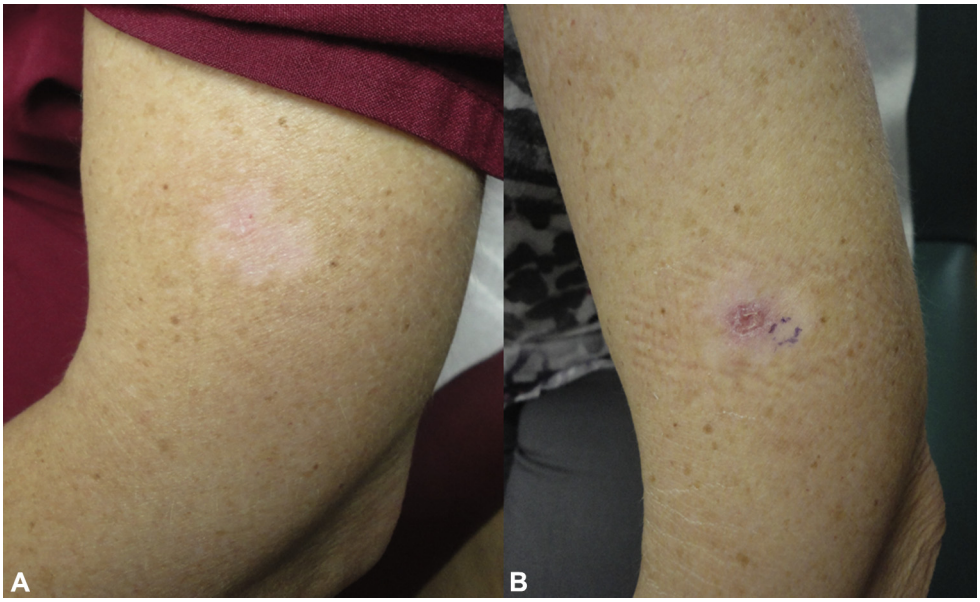

Fig 1. A, Depigmented patch present on the left arm. **B**, Healing former biopsy site of the erythematous macule adjacent to the depigmented area that was marked for biopsy.

vitiligo, as an isolated, unilateral, depigmented patch is not a typical presentation. Clinical monitoring was recommended. The patient returned after 4 months. No interval change was noted in size or color. She then presented 8 months later for evaluation. On physical examination, a new pink macule was noted within the lesion. The patient was scheduled for biopsy to rule out basal cell carcinoma.

A shave biopsy was performed of the erythematous macule in the center of the lesion. Histologic evaluation found malignant melanoma, superficial spreading type, with a Breslow depth of 0.25 mm. The lateral and deep margins were involved. Immunohistochemical staining with Melan-A positively stained confluent atypical cells along the epidermal basal layer as well as foci of pagetoid cells, supporting the histologic diagnosis of in situ melanoma with a small focus of invasive melanoma at 0.25 mm depth. A subsequent punch biopsy was performed on an adjacent area of depigmentation (Fig 1), which showed melanoma in situ, extending to the inked lateral edges of the specimen.

The patient was sent to a surgical oncologist who performed a wide local excision with 1-cm margins. The specimen was read as residual melanoma in situ and scar. Margins were negative. Routine follow-up after 4 years indicates no sign of melanoma recurrence, metastasis, or development of vitiligo.

Patient 2

A 43-year-old woman presented for a routine examination. She had no history of skin cancer, melanoma, or vitiligo. On physical examination, a well-demarcated depigmented patch on her chest, measuring 9 × 5 mm, was noted (Fig 2, *A*). The etiology was unclear, as the patient was asymptomatic, unaware of this spot, and unaware of any prior trauma to the area. Clinical monitoring was recommended with follow-up planned for 4 months later.

The patient returned 1 year and 5 months after her initial visit. She was concerned about a brownish growth that appeared in the depigmented spot on her chest 3 months before this visit. No change in size or color of the growth was noted by the patient after its appearance. On physical examination, a 5- × 3-mm brown papule was present within the depigmented patch (Fig 2, *B*).

A shave biopsy was performed, and histologic evaluation found malignant melanoma, superficial spreading type, with a Breslow depth of invasion of at least 0.6 mm with margins involved by tumor. She was sent to a surgical oncologist who performed a wide local excision with 1-cm margins. In situ and invasive melanoma at a depth of 1.05 mm was noted on final pathology. Margins were negative for melanoma. Follow-up after 1 year, including chest radiograph, was negative for melanoma recurrence, metastasis, or development of vitiligo.

DISCUSSION

We have introduced 2 cases of malignant melanoma developing within a depigmented patch. Melanoma histologic characterization in both cases displayed an absence of ulceration, regression, or

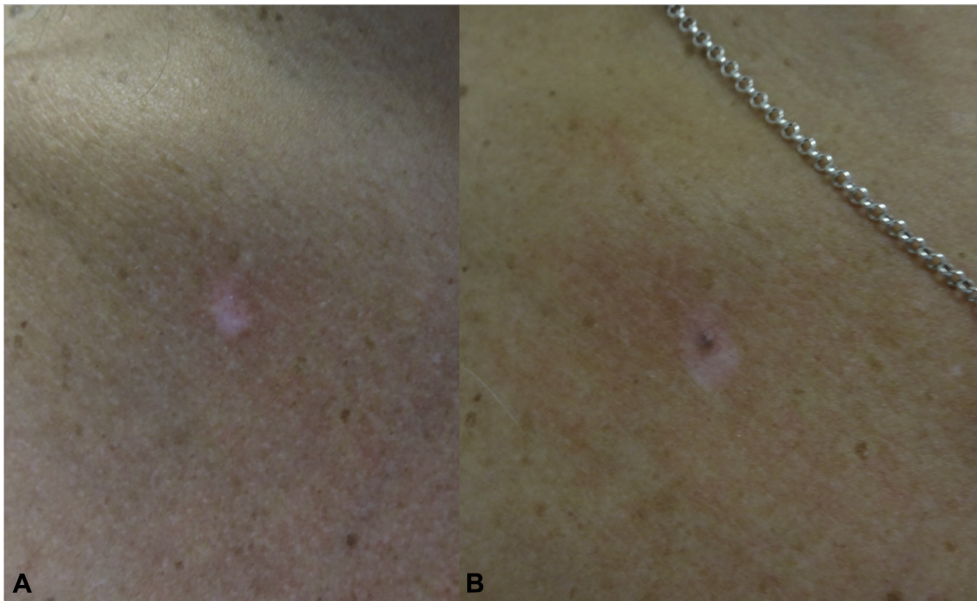

Fig 2. **A**, Depigmented, erythematous macule with irregular borders, 9 × 5 mm in size, present on the right side of the chest. **B**, Brown heterogeneous papule, 5 × 3 mm in size, present within the superior margin of the depigmented patch.

mitotic figures. Tumor-infiltrating lymphocytes were brisk. The etiology of a depigmented patch surrounding melanoma is currently unknown. We hypothesize that an early melanocytic lesion with malignant potential, which was not visible to the naked eye or on dermoscopy, was present within the skin. Melanoma antigens may have been recognized by the immune system, which locally infiltrated, causing the phenomenon of depigmentation. The malignant melanocytes likely escaped the attack and were allowed to proliferate, forming a melanoma. In the setting of a new, solitary, vitiligo-like patch in a patient with no risk factors for vitiligo, clinicians should be aware of the various melanoma-associated depigmentation phenomena, and frequent clinical monitoring should be done.

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