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Keratoacanthoma-appearing melanoma metastases in a patient receiving pembrolizumab therapy



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Key words: keratoacanthoma; melanoma; metastasis; pembrolizumab.

INTRODUCTION

Pembrolizumab is a new monoclonal antibody chemotherapeutic agent that binds to the programmed cell death-1 receptor and decreases the down-regulation of lymphocytes in patients treated for metastatic melanoma.¹ Because this drug is relatively new, little is known about its effect on cutaneous melanoma metastases. We report a case detailing the unexpected keratoacanthomalike appearance of melanoma metastases in a patient receiving pembrolizumab.

REPORT OF A CASE

A 52-year-old man with *BRAF*-negative metastatic melanoma presented to the dermatology clinic for evaluation of rapidly growing lesions on his scalp, chest, mons pubis, and right lateral trunk 1 month after starting pembrolizumab (2 mg/kg). Eighteen months before presentation, he had nodular melanoma (Breslow depth, 4.7 mm) diagnosed on his left buttock. He underwent wide local excision and sentinel lymph node biopsy, which was positive. Magnetic resonance imaging and positron emission tomography scans were negative for metastatic disease. His disease remained quiescent until 14 months after his initial diagnosis when he noted 2 new scalp lesions, which were found to be melanoma metastases. Repeat imaging was negative for systemic disease, and the patient was started on ipilimumab. Unfortunately, his ipilimumab course was complicated by hypophysitis, requiring prednisone therapy and discontinuation of ipilimumab.

Before starting prednisone, the patient had several small red papules that remained stable in size. During his 6 weeks of prednisone therapy, these lesions grew rapidly. Ipilimumab therapy was subsequently discontinued, he transitioned from prednisone to maintenance hydrocortisone, and he started on pembrolizumab. Shortly after starting pembrolizumab, the patient's lesions became painful and developed a dome-like appearance, prompting his presentation in our clinic after completion of his second cycle.

Examination found 4 pink papulonodules with central hyperkeratotic cores on the scalp, chest, midback, and mons pubis ranging in size from 0.9 to 1.3 cm that were consistent with keratoacanthomas (Fig 1).

Histopathology of these lesions found a dome-shaped, dermal melanocytic proliferation with an overall bland architecture at low power. At higher power, the melanocytes showed atypia with numerous mitoses. There was an associated lymphocytic inflammatory infiltrate at the base of the lesions (Fig 2).

The patient completed 2 more cycles of pembrolizumab after the diagnosis of these lesions and new skin lesions continued to develop and were concerning for metastases. Positron emission tomography scan several weeks after he was seen by the dermatology department found widely progressive disease, and he was started on temozolomide with subsequent complete resolution of disease.

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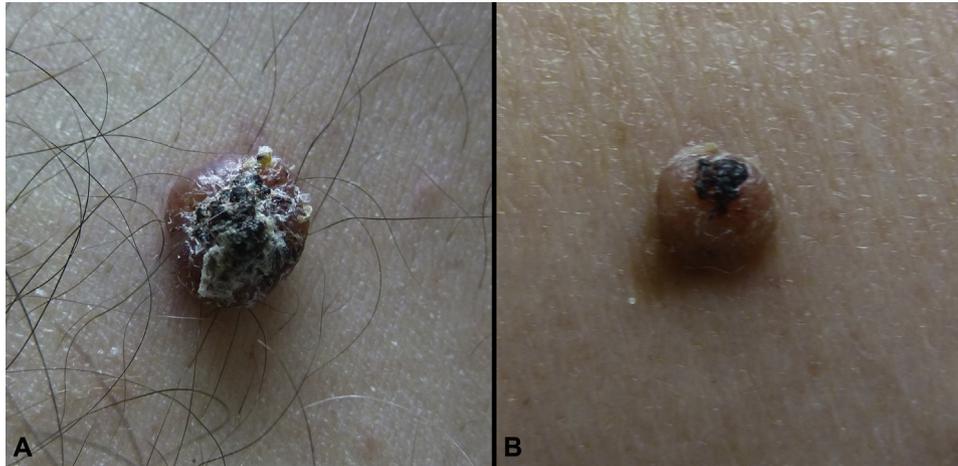


Fig 1. Representative clinical images of keratoacanthomalike melanoma metastases on the left upper chest (1.2 cm) (**A**) and upper back (0.9 cm) (**B**).

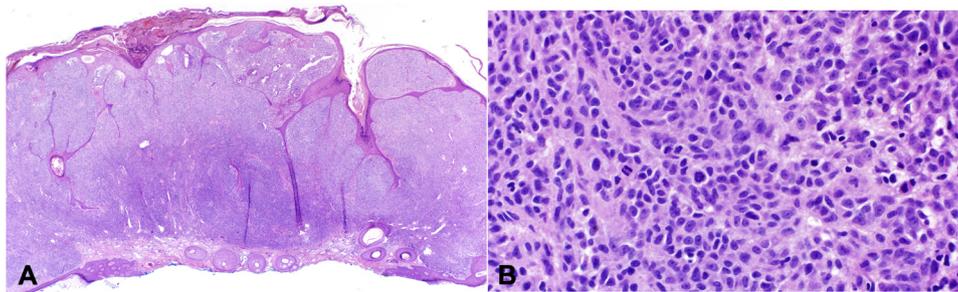


Fig 2. Histopathology of the dermal melanoma metastases. **A**, On low power, there is a well-circumscribed, dome-shaped lesion with lymphocytes at the base. **B**, Higher power showed atypical melanocytes with mitoses (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**, $\times 4$; **B**, $\times 40$.)

DISCUSSION

Pembrolizumab is an antibody that inhibits the programmed cell death-1 receptor, a surface receptor on lymphocytes that down-regulates the activation of T cells.¹ It was approved by the US Food and Drug Administration via the Fast Track Development Program for use in melanoma in September 2014. Early research found pembrolizumab to be effective in prolonging progression-free and overall survival in melanoma patients and be more effective and less toxic than ipilimumab.²

Despite its apparent efficacy, little is known about the adverse effects of pembrolizumab. The few reported adverse effects include autoimmune conditions, such as bullous pemphigoid and autoimmune myocarditis.^{3,4} The development of these autoimmune conditions may be related to pembrolizumab's action of disinhibiting the activation of T cells, which increases the risk of recognition of self-antigens and decreases self-tolerance.

We report a clinically misleading presentation of pembrolizumab's effects on dermal melanoma

metastases. Our patient's most recent metastases developed while he was immunosuppressed with prednisone, and the lesions were painful, a symptom not usually seen with dermal melanoma metastases. We hypothesize that immune activation during pembrolizumab therapy and the resulting tumor-associated lymphocytes confined the tumors to the dermis, aided in tumor shrinkage, and caused the dome-shaped architecture of the lesions. The inflammatory component of the immune response was also likely responsible for the pain the patient reported. This case highlights the potentially unusual clinical appearance of dermal melanoma metastases associated with treatment using pembrolizumab.

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