Crusted scabies masquerading as a drug eruption related to nivolumab

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To the Editor:

Anti-programmed death one (PD1) monoclonal antibodies used as checkpoint inhibitors in cancer immunotherapy have been associated with a wide variety of cutaneous eruptions that may appear similar in morphology to other dermatologic diseases [1]. Scabies is a common ectoparasitic dermatosis that is frequently misdiagnosed, leading to institutional outbreaks, administration of inappropriate treatment, and morbidity from untreated disease. We report a case in which the misdiagnosis of crusted scabies as a drug eruption from nivolumab resulted in discontinuation of immunotherapy for metastatic melanoma.

A 64-year-old man presented with an 18-month history of a severely pruritic rash on the trunk and extremities that arose several months after starting nivolumab for metastatic melanoma. Nivolumab was discontinued shortly after rash onset as the favored cause of the suspected drug eruption, but the rash persisted. Therapy was changed to dabrafenib and trametinib, and he was referred to an outside clinic for evaluation.

Punch biopsy performed at the outside clinic revealed psoriasiform spongiotic dermatitis with eosinophils. Although most compatible with an eczematous dermatitis, drug eruption could not be excluded on histopathologic examination. Both dabrafenib and trametinib were held for 30 days owing to continued concerns for drug eruption, but no improvement was noted. The patient had been placed on prednisone for the rash, up to 120mg daily, which alleviated the pruritus but did not clear the skin lesions.

Approximately 6 months after the outside evaluation with punch biopsy, the patient presented to our clinic. At that time, the patient's medications included dabrafenib, trametinib, pantoprazole, metoprolol succinate, lisinopril, furosemide, amlodipine, atorvastatin, rivaroxaban, pioglitazone, insulin aspart, insulin degludec, and homeopathic leg cramp tablets. Physical examination revealed erythematous, crusted papules and pustules involving the finger web spaces, wrists, and dorsal hands along with erythematous, thin, scaly papules diffusely on the trunk, extremities, groin, and buttocks (**Figure 1A, B**). The clinical differential diagnosis included crusted scabies, drug eruption,

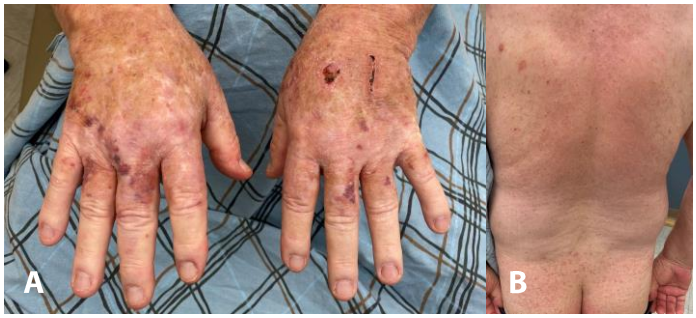

Figure 1. ***A)*** *Erythematous, crusted papules and pustules involving the forearms, wrists, finger web spaces, and dorsal hands.* ***B)*** *Erythematous, thin, scaly papules on the back and buttocks.*

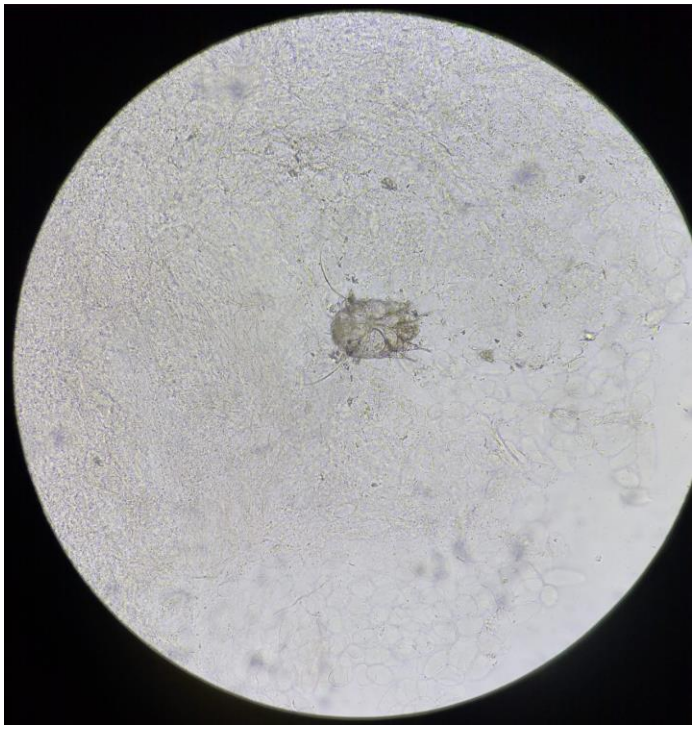

Figure 2: *Scabies mite.*

and contact dermatitis. Microscopic examination of skin scrapings from the hand showed a mite and egg, confirming the diagnosis of crusted scabies (**Figure 2**). Treatment was initiated with oral ivermectin and topical permethrin with resolution of skin lesions and pruritus after several weeks. Subsequently, nivolumab therapy was reinitiated without recurrence of lesions.

Misdiagnosis of scabies is a common occurrence that has been reported to lead to a variety of adverse outcomes including initiation of chemotherapy after scabies was mistaken for Langerhans cell histiocytosis and widespread scabies outbreaks among staff and patients in hospitals and nursing homes after misdiagnosis as a drug eruption [2-4]. Scabies histopathology characteristically shows an egg, mite, or scybala in the stratum corneum along with less specific findings of spongiotic dermatitis with a mixed superficial and deep infiltrate including eosinophils [5]. If the more specific features of scabies are not seen and clinical suspicion for scabies is not high, these non-specific findings may be interpreted as eczematous dermatitis or a drug eruption.

PD1 inhibitors have been associated with a wide variety of cutaneous eruptions including bullous pemphigoid, lichenoid eruptions, and non-specific pruritic rashes [1,6-7]. Treatment varies based on the type of PD1 induced cutaneous eruption, but in general, improvement would be expected with topical corticosteroids, systemic corticosteroids, or immunotherapy cessation in severe cases [1,7].

Although PD1 inhibitors are commonly associated with cutaneous eruptions, alternative diagnoses must be kept in mind. In our case, suspicion for a drug eruption from nivolumab led to discontinuation of first-line immunotherapy for the patient's metastatic melanoma. However, the patient failed to respond to either systemic corticosteroids or discontinuation of immunotherapy, providing evidence against the initial diagnosis. To our knowledge, termination of checkpoint inhibitor immunotherapy related to misdiagnosis of scabies as a drug eruption has not previously been reported. To avoid misdiagnosis leading to significant deviation in the care of medically complex patients, scabies should be included in the differential diagnosis of non-specific, pruritic eruptions, particularly in patient populations at risk for scabies and when the expected clinical response to treatment is not seen.

Potential conflicts of interest

The authors declare no conflicts of interest.

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