



Lichen planopilaris associated with pembrolizumab in a patient with metastatic melanoma

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Pembrolizumab, a programmed cell death receptor 1 (PD-1) inhibitor, has been used effectively for treatment of metastatic melanoma.¹ Reported cutaneous adverse events ascribed to PD-1 inhibitors include lichenoid reactions such as lichen planus of the skin and oral mucosa, lichen planus pemphigoides, and lichenoid drug eruptions, as well as alopecia areata and vitiligo.²⁻⁵ We present a patient with metastatic melanoma who had lichen planopilaris (LPP) after receiving pembrolizumab. We find no previous report in the literature of LPP in association with PD-1 inhibitors.

CASE REPORT

A 47-year-old man presented with a bleeding nodular growth on the scalp, diagnosed from biopsy results as melanoma. A wide local excision showed no evidence of residual disease, and sentinel lymph node biopsy result was negative for metastases. Several months later, the patient had a new scalp nodule, with pathology findings consistent with those of metastatic melanoma. Positron emission tomography–computed tomography (PET-CT) found 2 fluorodeoxyglucose (FDG)-avid lesions in the left posterior scalp and right suboccipital region concerning for multifocal bilateral metastases. After 3 cycles of pembrolizumab, the patient noted growth and erythema of the nodule and palpable lymphadenopathy. A repeat PET-CT confirmed that the nodule in left posterior scalp had increased in size and FDG uptake, and there were new mildly FDG-avid cervical lymph nodes. He then received 2 cycles of ipilimumab leading to a clinical remission.

Abbreviations used:

FDG:	fluorodeoxyglucose
LPP:	lichen planopilaris
PET-CT:	positron emission tomography– computed tomography
PD-1:	programmed cell death receptor 1

Approximately 2 months after his first pembrolizumab infusion and before starting ipilimumab, oral ulcers developed consistent with oral lichen planus. Several weeks after receiving ipilimumab, he noted gingival swelling and tenderness, hair loss, and scalp pruritus. Physical exam found round incomplete patches of alopecia with perifollicular erythema and scaling on the parietal scalp (Fig 1), diffuse alopecia on the vertex scalp, depigmentation of the hair overlying the metastatic melanoma nodule, and shallow ulcers on the lateral aspects of the tongue. Cutaneous lichenoid papules and oral Wickham striae were not observed. Scalp biopsy found prominent lichenoid inflammation limited to the upper portion of the outer root sheath of the majority of hair follicles, perifollicular fibrosis, and focal follicular scarring (Fig 2, A-D). Based on these findings and clinical presentation, a diagnosis of LPP was made.

Several weeks after completing treatment with ipilimumab and 2 to 3 months after the course of pembrolizumab, the patient received treatment with prednisone, which improved his oral ulcers and resulted in hair regrowth. Additionally, he was given 1 month of systemic minocycline and topical

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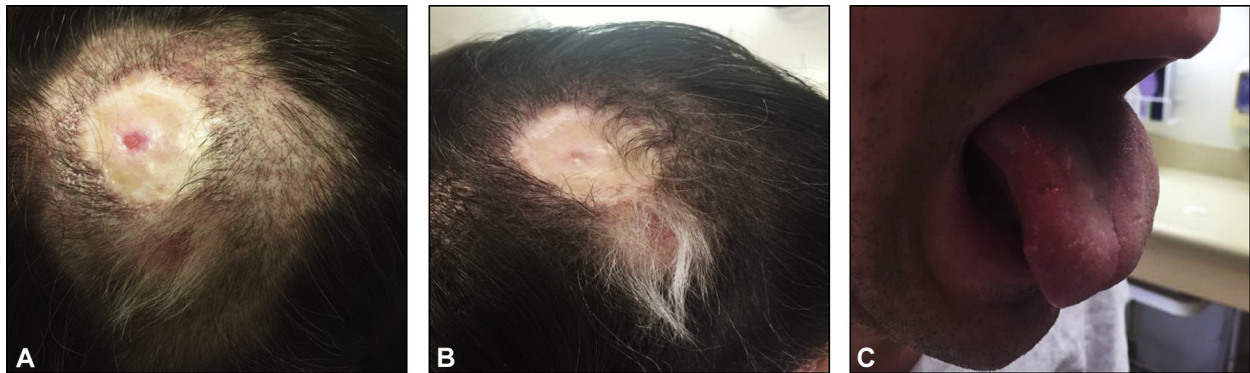


Fig 1. Clinical features of lichen planopilaris and oral ulcers after pembrolizumab. **A**, Perifollicular erythema with hyperkeratosis and alopecia on vertex scalp surrounding central skin graft, with depigmentation of the hair tuft at the site of metastatic melanoma nodule. **B**, Hair regrowth and progressive depigmentation of hair at metastatic melanoma nodule after course of oral prednisone, topical clobetasol, and minocycline. **C**, Shallow ulcer on lateral tongue suggestive of oral lichen planus.

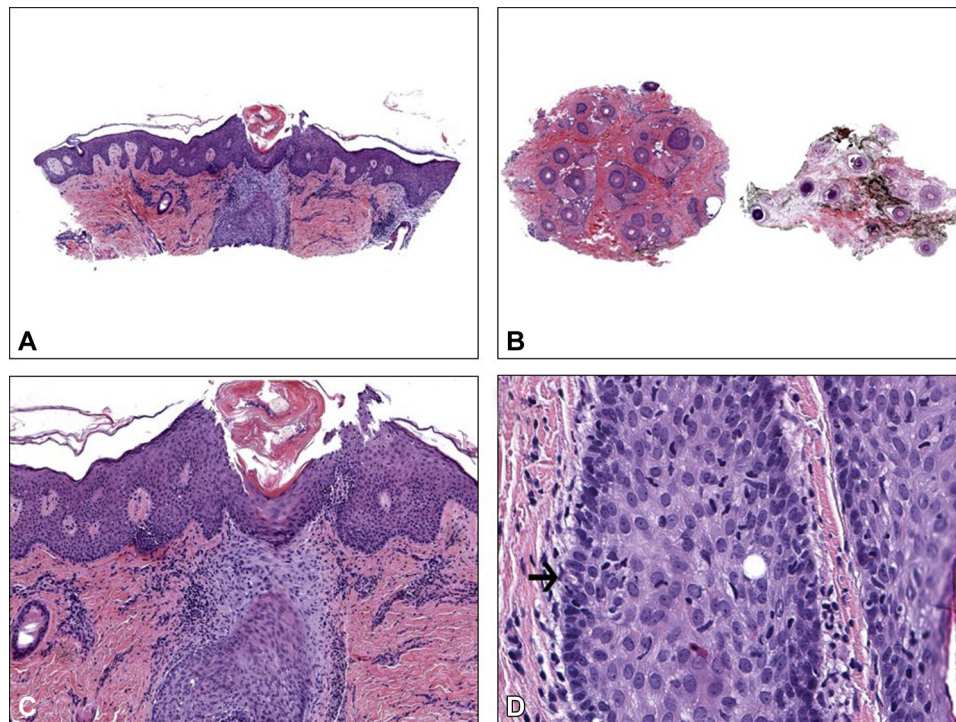


Fig 2. Histopathology of lichen planopilaris in the context of pembrolizumab therapy. Vertical (**A**) and horizontal (**B**) sections of scalp punch biopsy show a lichenoid inflammation limited to the upper portions of the hair follicles. **C**, The absence of lichenoid inflammation in the interfollicular region. **D**, Apoptotic keratinocyte (*arrow*). (Original magnifications: **A**, $\times 40$; **B**, $\times 20$; **C**, $\times 100$; **D**, $\times 200$.)

clobetasol and then discontinued all treatment, as he had near complete hair regrowth.

DISCUSSION

Given that lichenoid reactions (including lichen planus and lichen planus pemphigoides), alopecia

areata, and vitiligo have all been reported previously in association with PD-1 inhibitors, it is not surprising that LPP could also be associated. Checkpoint inhibitors such as pembrolizumab and nivolumab have shown efficacy in melanoma and other malignancies including lung cancer from their immunomodulatory effects. Upon blocking the PD-1

receptor with a checkpoint inhibitor, the negative regulation of the immune system is prevented and subsequently T-cell responses increase.⁴ Thus, it follows that such immune activation that targets tumor cells may more broadly activate inflammatory and autoimmune responses including LPP.

A retrospective analysis by Sanlorenzo et al⁵ found that patients who had cutaneous adverse events in the setting of pembrolizumab had significantly longer progression-free survival. It remains unclear if lichenoid reactions specifically are associated with positive prognostic outcome, thus these merit further study.

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