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CORRESPONDENCE

Hypertrophic lichenoid dermatitis during pembrolizumab treatment

Dear editor,

A 79-year-old man was referred to our department to evaluate severely pruritic skin eruptions that appeared 40 days earlier. He had received two courses of pembrolizumab at 3-week intervals for unresectable non-small cell lung carcinoma. His skin lesions developed 30 days after the commencement of therapy. Physical examination revealed violaceous papules and plaques, up to 15 mm in diameter, distributed on his trunk and extremities (Figure 1A). Biopsy specimens obtained from a plaque on his right dorsal hand and a papule on his right lower limb showed hyperkeratosis and irregular epidermal acanthosis with elongated and broadened rete ridges (Figure 1B), lichenoid tissue reaction (LTR) and a dense band-like lymphocytic infiltration in the upper dermis (Figure 1C). The diagnosis was hypertrophic lichenoid dermatitis. The appearance of his skin lesions after initiation of pembrolizumab treatment indicated the possibility of an immune-related adverse event (irAE). Application of topical clobetasol propionate ointment in conjunction with oral olopatadine hydrochloride 20 mg daily showed improvements after 4 months. Pembrolizumab therapy was continued with topical treatment until 6 months after his first referral to our department because of the development of severe immune thrombocytopenic purpura. Thereafter, similar skin lesions did not recur.

An irAE is an autoimmune-like or inflammatory side effect seen in patients treated with immune checkpoint inhibitors. Cutaneous irAE is the most common type of irAE, presenting as a maculopapular rash, urticarial dermatitis, vitiligo, Stevens-Johnson syndrome, and so forth.[1] Lichenoid dermatitis and its hypertrophic variant are also reported as cutaneous irAEs.[2–4] Hypertrophic lichenoid dermatitis should be distinguished from well-differentiated squamous cell carcinoma (SCC) because of their clinical and histological similarities.[2,3] In the present case, a differential diagnosis from SCC was needed because the architecture of the acanthosis resembled downward growth of SCC. However, a diagnosis of SCC could be excluded because the cellular atypia of keratinocytes was not obvious and his skin lesions improved with topical corticosteroids.

Until now, a limited number of cases of hypertrophic lichenoid dermatitis as an irAE have been reported in the literature, and the pathogenesis is still unclear. LTR is induced by dermal $CD8^+$ T cells, which are activated by blocking PD-1.[4] In addition, the expression of PD-L1 on keratinocytes of lichenoid lesions has been reported.[5] Immunohistochemistry of the present case showed that $CD8^+$ T cells infiltrated the upper dermis and PD-L1 was expressed on the surface of epidermal keratinocytes (Figure 1D-F). This suggests that the LTR in our case could be attributed to the dermal $CD8^+$ T cells and that anti-PD-1 therapy led to the hypertrophy of the epidermis by blocking the interaction between PD-L1 on keratinocytes and PD-1 on dermal T cells. Further studies are needed to reveal the precise mechanism of the hypertrophic LTR during immune checkpoint therapy.

DECLARATION SECTION

Approval of the research protocol: N/A.
Informed Consent: The written informed consent was obtained from the patient.
Registry and the Registration No.: N/A.
Animal studies: N/A.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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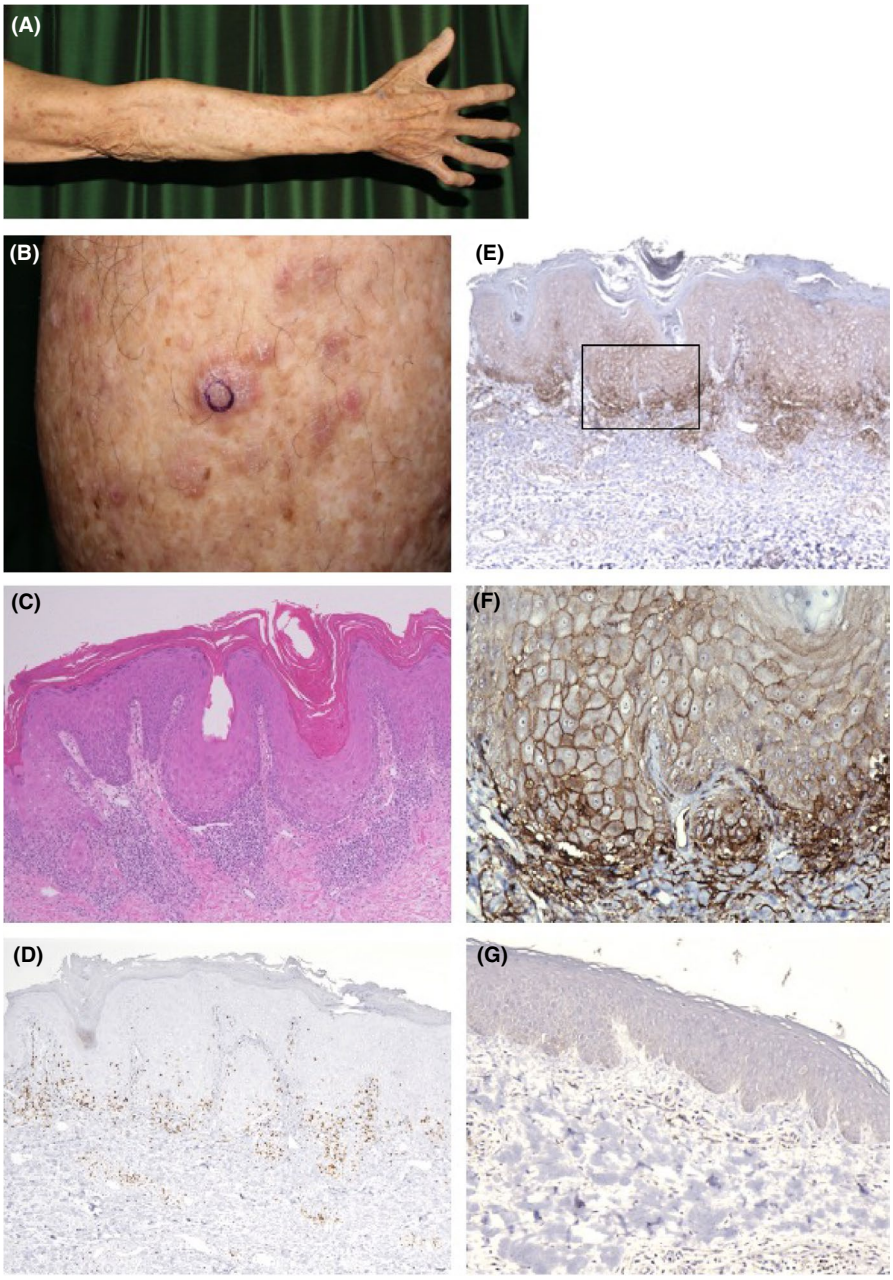

FIGURE 1 Clinical, pathological, and immunohistochemical findings of the patient. Multiple plaques and papules were seen on his right dorsal hand (A) and right lower leg (B). Histopathological findings of biopsy from the red papule of his right lower leg (C) (hematoxylin and eosin stain, original magnification, ×40). Immunohistochemical findings of biopsy (D-F) and normal skin (control) (G); the expression of dermal $CD8^+$ T cells (D) and keratinocytic PD-L1 (E, F) was positive, although the expression of PD-L1 in keratinocyte was not clearly observed in normal skin (G) (brown) (original magnification, D, E, and G, ×40/F, ×200)

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