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CORRESPONDENCE

Linear lichen planus in the lines of Blaschko suggestive of immune-related adverse event

Dear Editor,

Lichen planus (LP) is a mucocutaneous inflammatory disease with a polygenic background.[1] The cutaneous lesions in LP consist of faint erythematous to violaceous flat-topped papules, preferentially involving the extremities, with a bilaterally symmetrical distribution.[1] Linear LP (LLP), a variant of LP, occurs more often in children and adolescents.[1] Although scattered linear lesions often occur in LP, as in the Koebner phenomenon,[1] LLP lesions generally appear as more extensive unilateral streaks or bands.[2] LLP occasionally follows the lines of Blaschko, which may represent embryological developmental pathways.[2] Programmed cell death-1 (PD-1)/programmed death-ligand 1 (PD-L1) pathway blockade–associated cutaneous immune-related adverse events (irAEs) can manifest as lichenoid reactions[3]; however, the linear variant has rarely been reported. Here, we report a possible case of PD-1 blockade–induced LLP in the lines of Blaschko in a patient with advanced lung cancer.

A 79-year-old Japanese woman was diagnosed with advanced lung adenocarcinoma (Stage IV), and treatment with carboplatin, pemetrexed, and pembrolizumab every four weeks was initiated. She achieved complete remission after six cycles of treatment. However, she developed drug-induced hepatitis, and maintenance therapy with pemetrexed every three weeks was initiated three months later. After the fourth cycle, she developed a skin eruption on the right upper limb (Figure 1A). Physical examination showed linear violaceous macules following the lines of Blaschko on her right upper limb and faint erythematous macules on her right breast (Figure 1B-D). Skin biopsy revealed hyperkeratosis, hypergranulosis, basal liquefaction, Civatte body formation, and a lichenoid inflammatory infiltrate (Figure 1E, F), confirming the histopathological diagnosis of lichenoid reaction. She had no mucocutaneous manifestations suggestive of LP elsewhere. Laboratory tests, including serological tests for hepatitis C, were negative. Although pemetrexed was continued, topical corticosteroids treatment improved the skin lesions after three months.

In our case, the patient developed LLP approximately six months after discontinuing pembrolizumab. Although irAEs usually develop within the first few weeks to months after initiation of the treatment, they can occur even after discontinuation of the treatment.[4] The median interval for developing irAEs after discontinuing immune checkpoint inhibitors is 6 months (range, 3–28 months).[4] Therefore, we reasoned that pembrolizumab could have evoked the lichenoid reaction. However, we should acknowledge the possibility of pemetrexed-induced cutaneous adverse event.[5]

The distribution of the lines of Blaschko represents the mosaicism of keratinocytes[6]; that is, the development of LLP following the lines of Blaschko may be predetermined during embryogenesis with the formation of susceptible keratinocytes and is subsequently caused by potential triggers.[6] In our case, PD-1 blockade may have augmented the $CD8^+$ T cell-mediated autoimmune reaction, a hallmark of lichenoid reactions,[1] in predisposed lesions.

Our case may highlight a new aspect of cutaneous mosaicism, in which skin manifestations would become apparent as a form of an irAE. In accordance with the previous report on lichenoid reactions presenting as irAEs,[3] we demonstrated that LLP as an irAE can be managed with topical corticosteroids. Further molecular-based approaches would be useful to clarify the detailed pathogenesis.

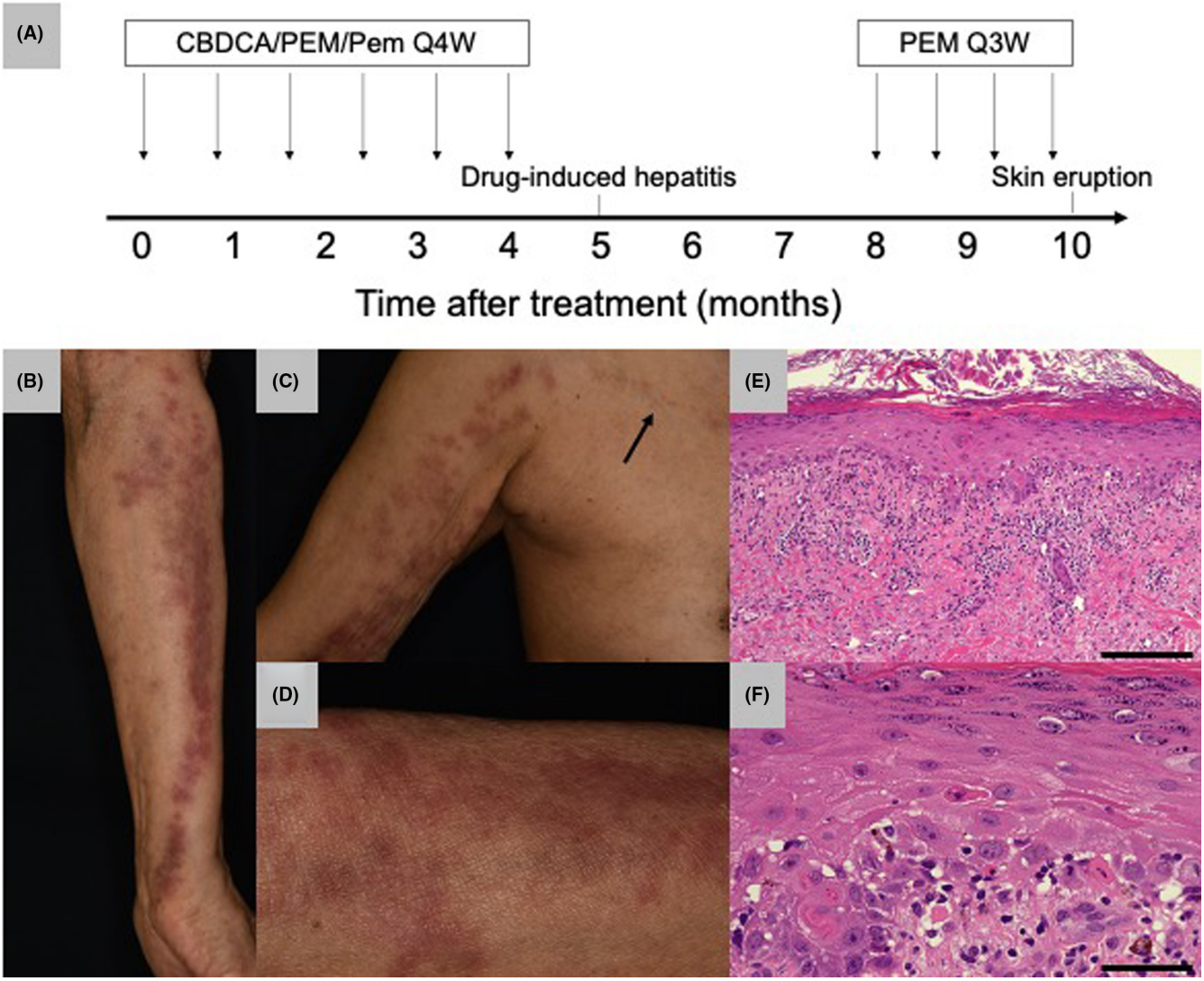

FIGURE 1 Clinical and pathological findings. (A) Graphical representation of the patient's clinical course. (B, C) Unilateral linear violaceous macules along the lines of Blaschko on her right forearm and upper arm, and faint erythematous macules on her right breast (arrow). (D) Close-up of the eruption. (E) Hematoxylin and eosin staining showed hyperkeratosis, hypergranulosis, a band-like infiltrate consisting primarily of lymphocytes in the upper dermis and (F) vacuolar degeneration along the dermoepidermal junction with apoptotic keratinocytes. Bars represent 200 (E) and 50 μm (F). CBDCA, carboplatin; PEM, pemetrexed; Pem, pembrolizumab; Q3W, once every 3 weeks; Q4W, once every 4 weeks

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DECLARATION SECTION

Approval of the research protocol: N/A.

Informed consent: The patient diagnosed at Tsukuba University Hospital was included in this study with written informed consent.

Registry and the registration no: N/A.

Animal studies: N/A.

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